

# Total Synthesis of Propindilactone G and ( $\pm$ )-Schindilactone A

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Checker: Zhang-Pei Chen  
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Yang, z. *et al.* *J. Am. Chem. Soc.* **2015**, *137*, 10120–10123.  
Yang, z. *et al.* *Angew. Chem. Int. Ed.* **2011**, *50*, 7373–7377.

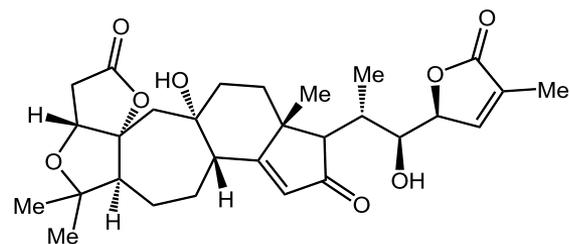
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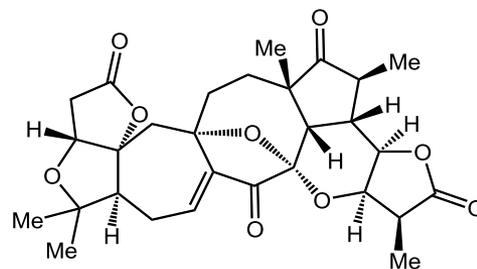
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- ❖ **Total Synthesis of Propindilactone G**
- ❖ **Total Synthesis of Schindilactone A**
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# Introduction

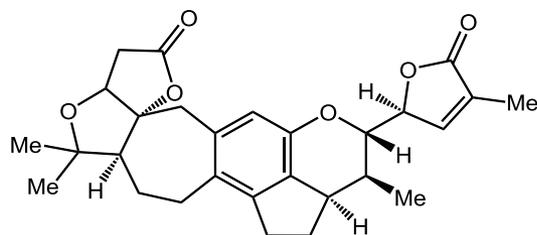
## Schisandracea



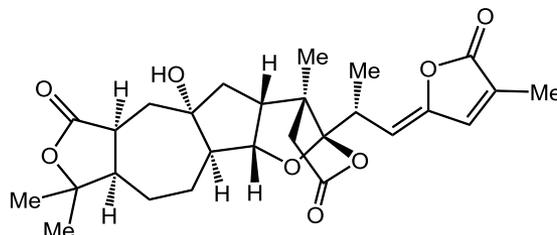
1: propindilactone G



2: schindilactone A



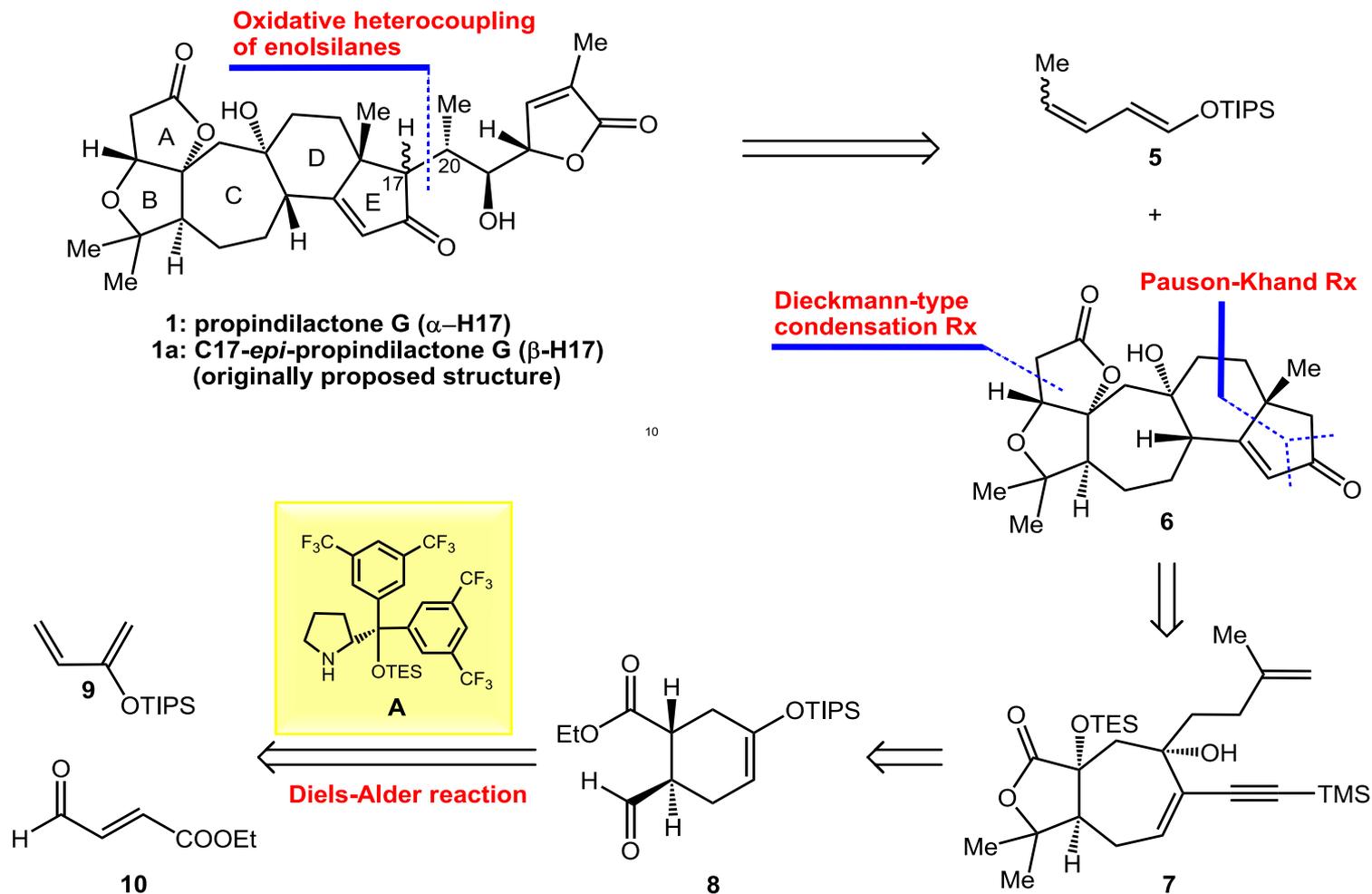
3: rubriflordilactone A



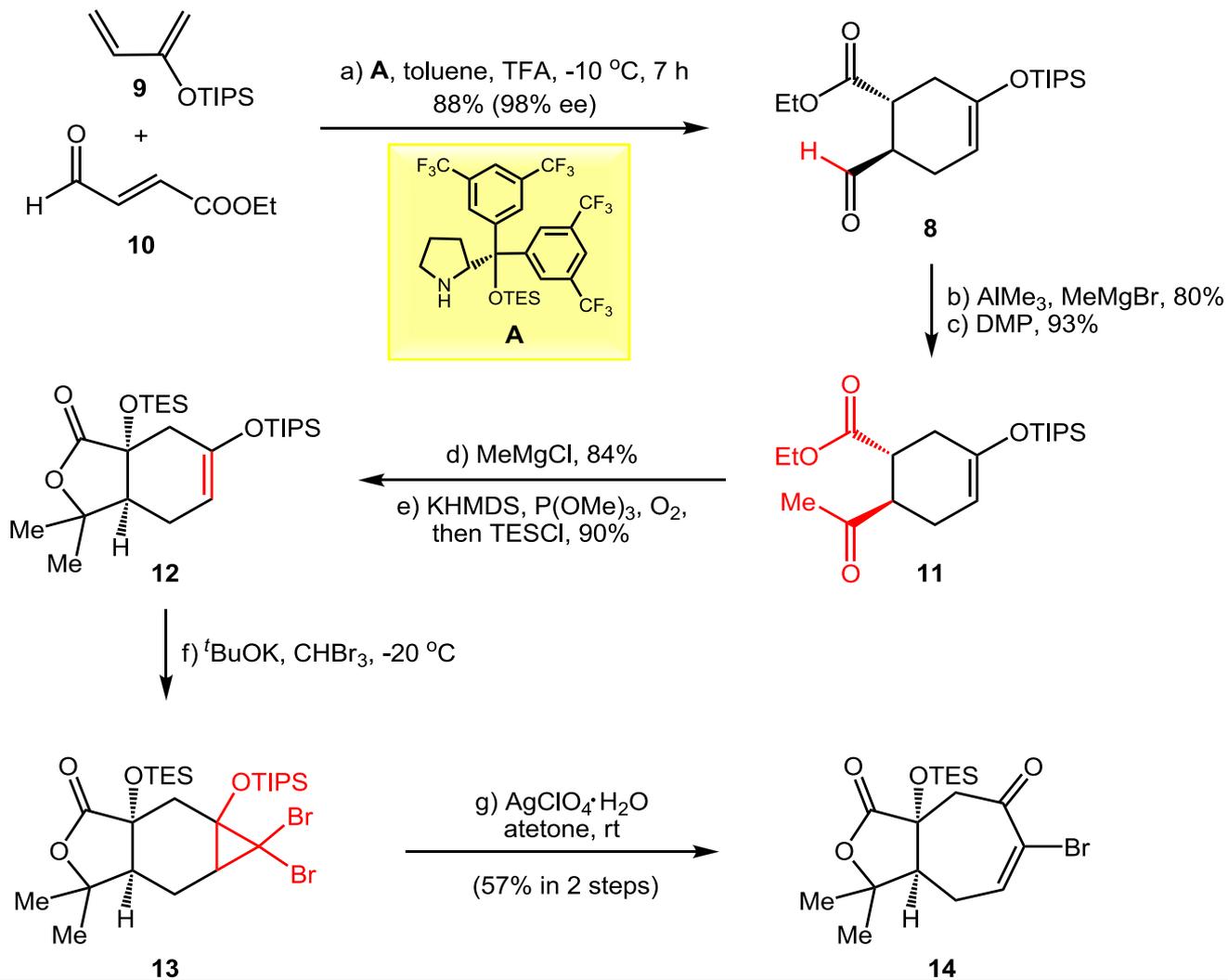
4: schilancitrilactone B



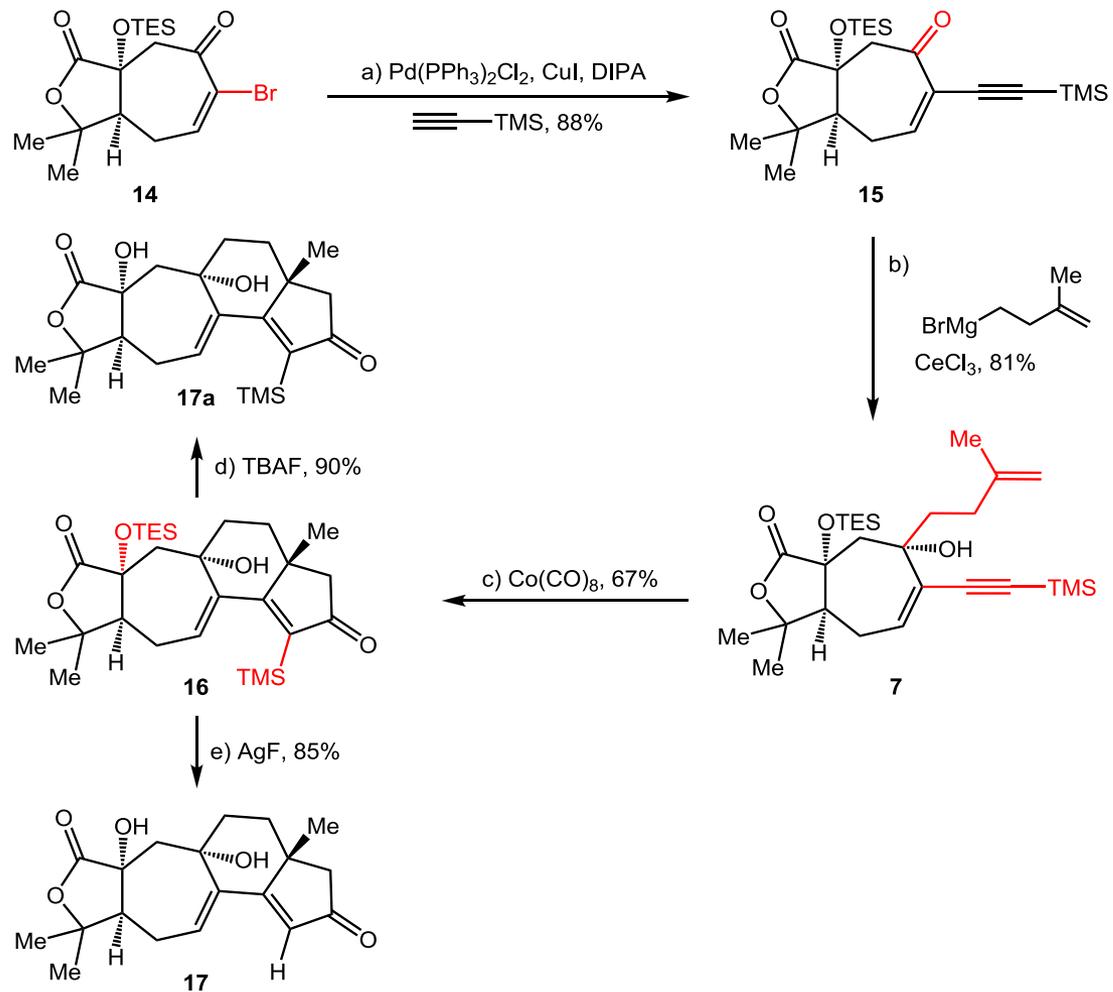
# ➤ Retrosynthetic analysis of propindilactone G



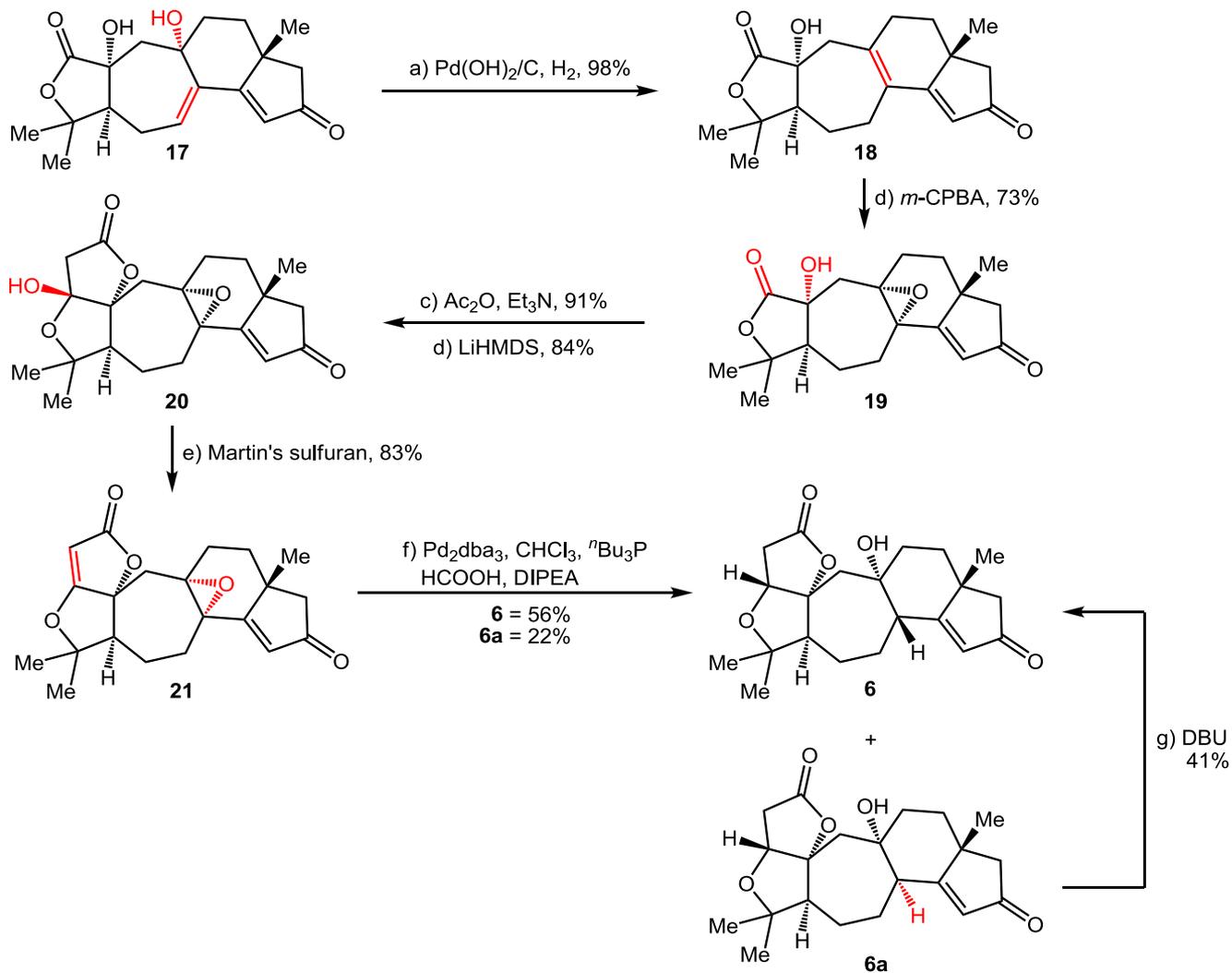
## ► Synthesis of the bromoenone 14



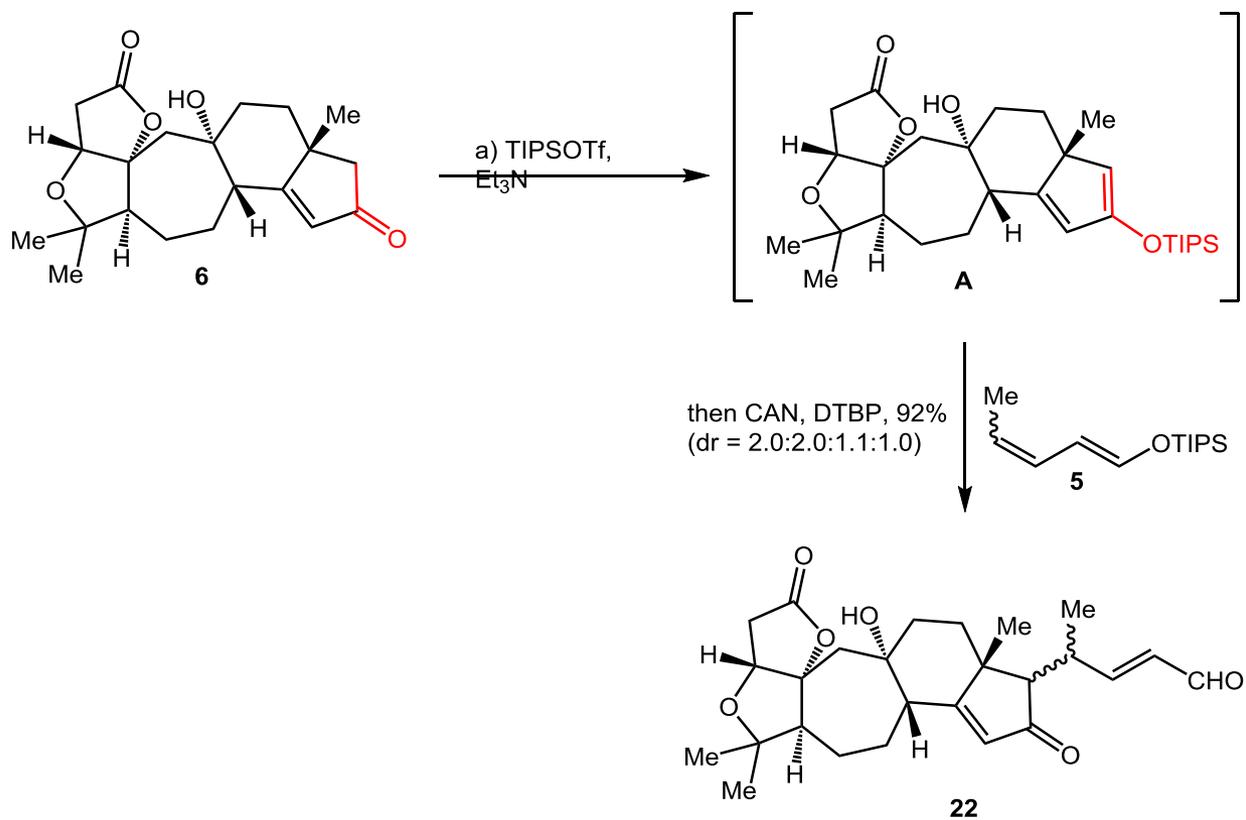
## ► Synthesis of the tetracyclic ring fragment 17



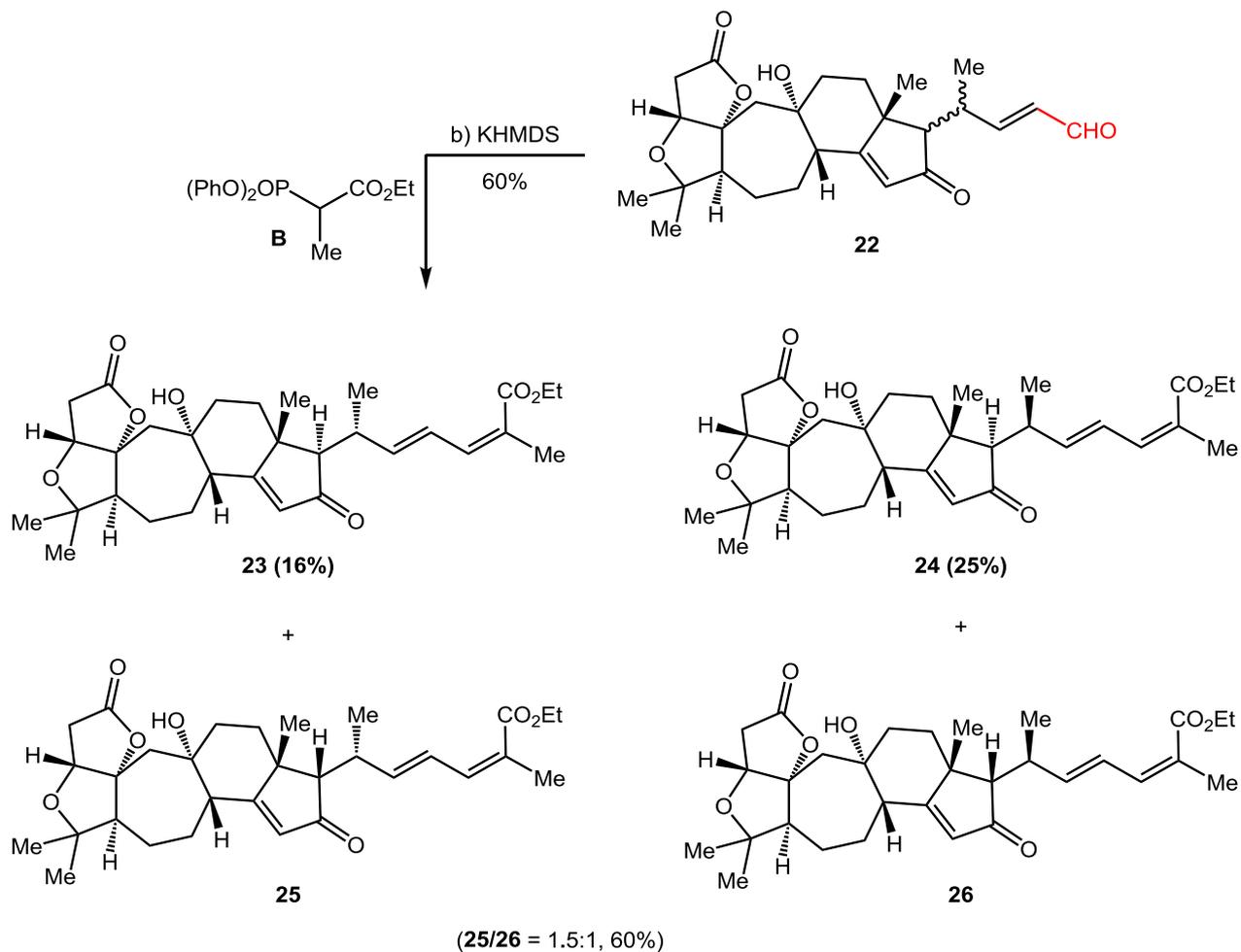
## ► Synthesis of ketolactone 6



## ► Synthesis of compound 22

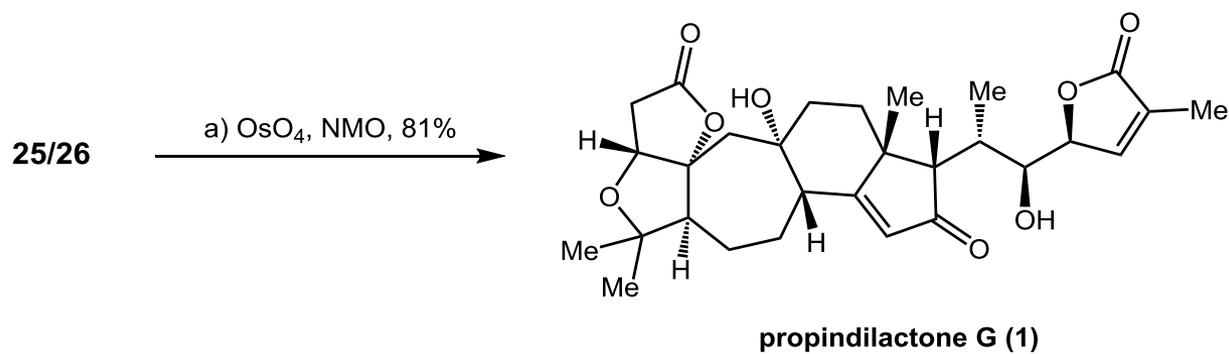


## ► Synthesis of compound 23, 24, and 25/26



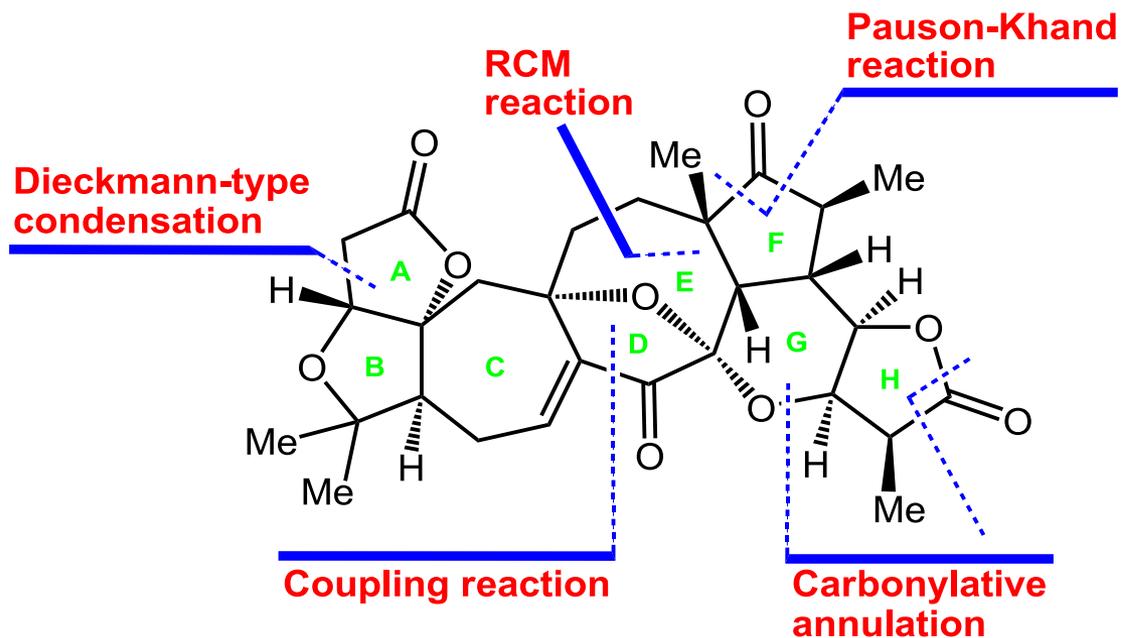
## ➤ Total synthesis of (+)-propindilactone G (1)

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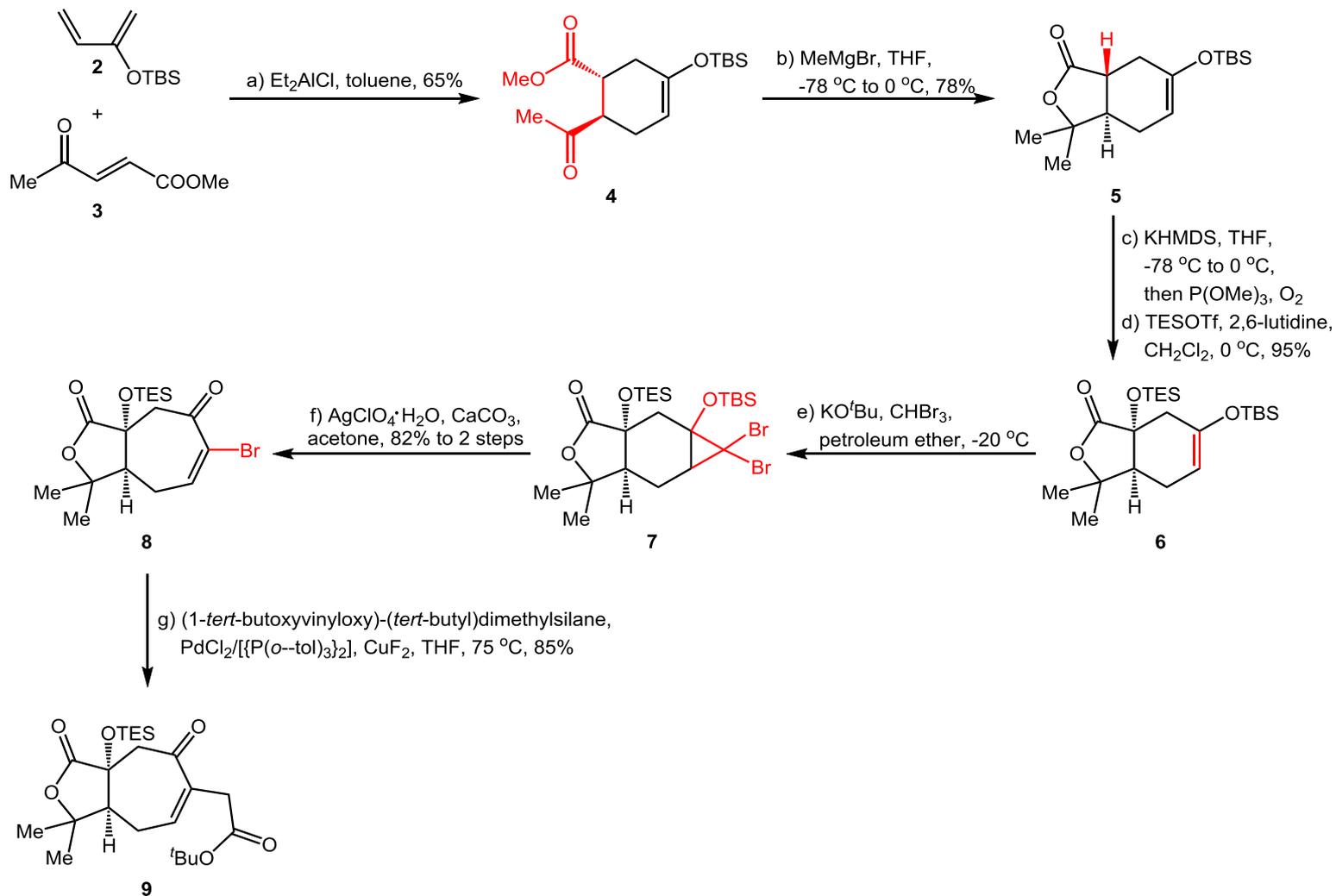
## ➤ Strategic bond disconnections of schindilactone A

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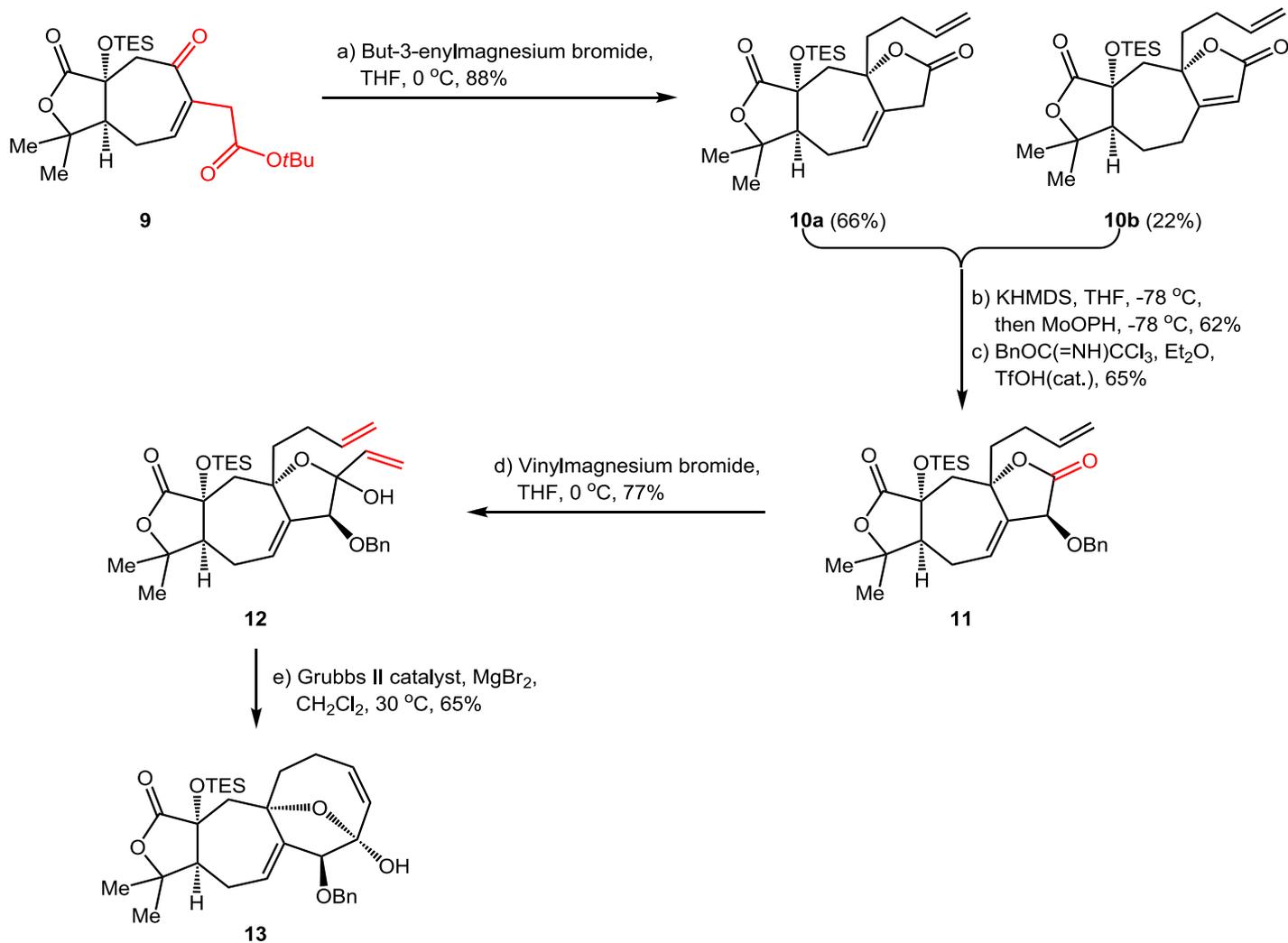


schindilactone A (1)

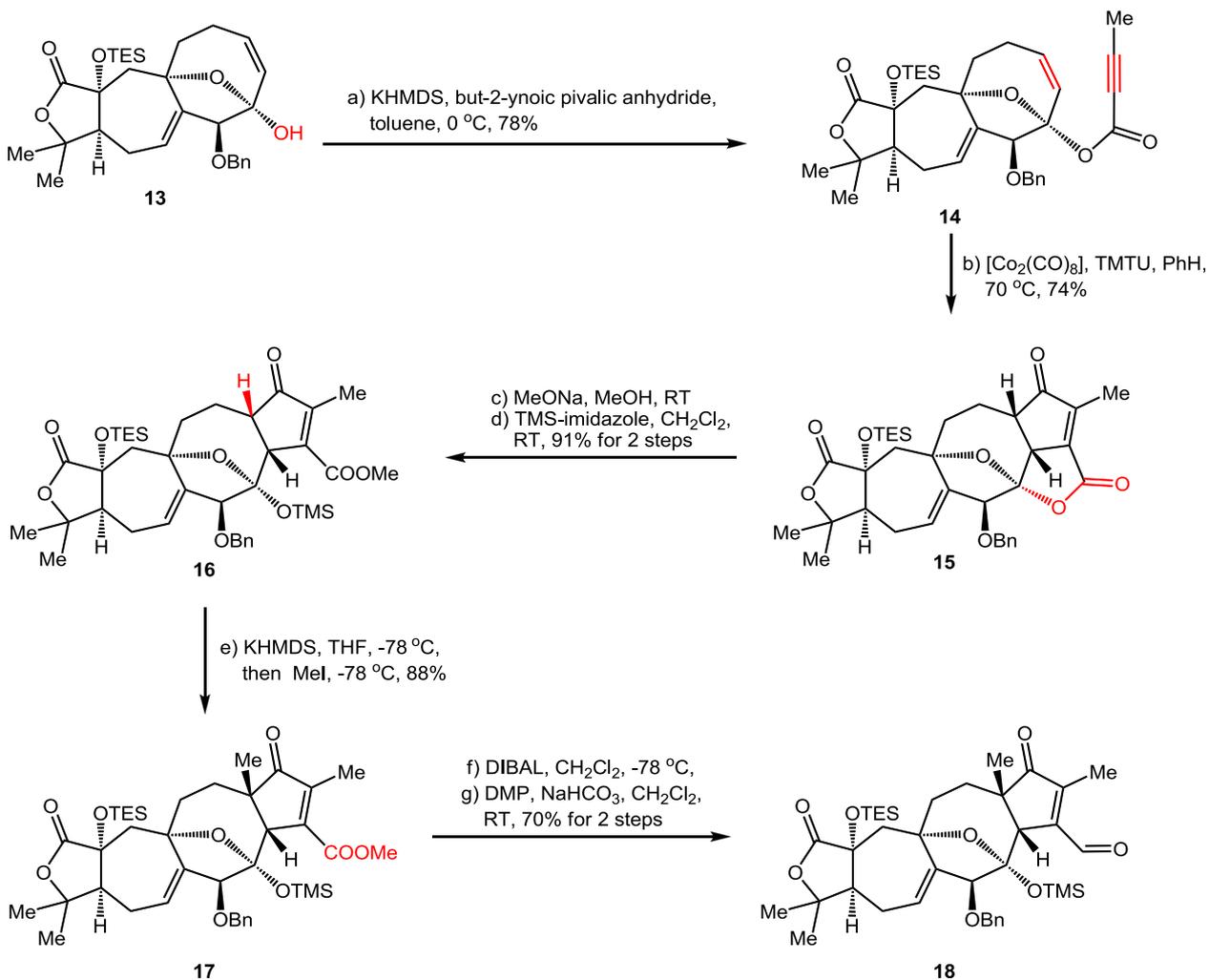
## Synthesis of ketoester 9



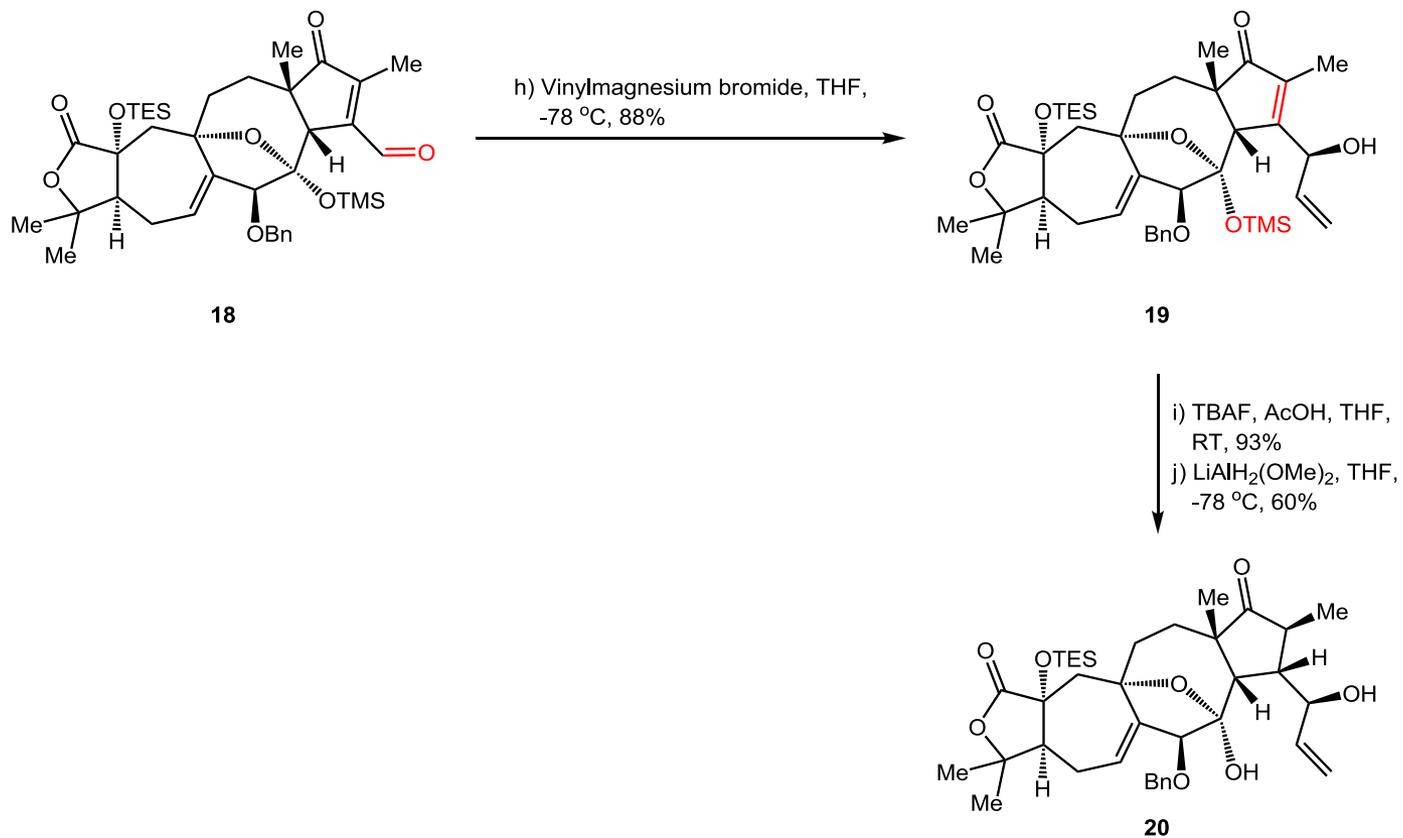
## ► Synthesis of intermediate 13



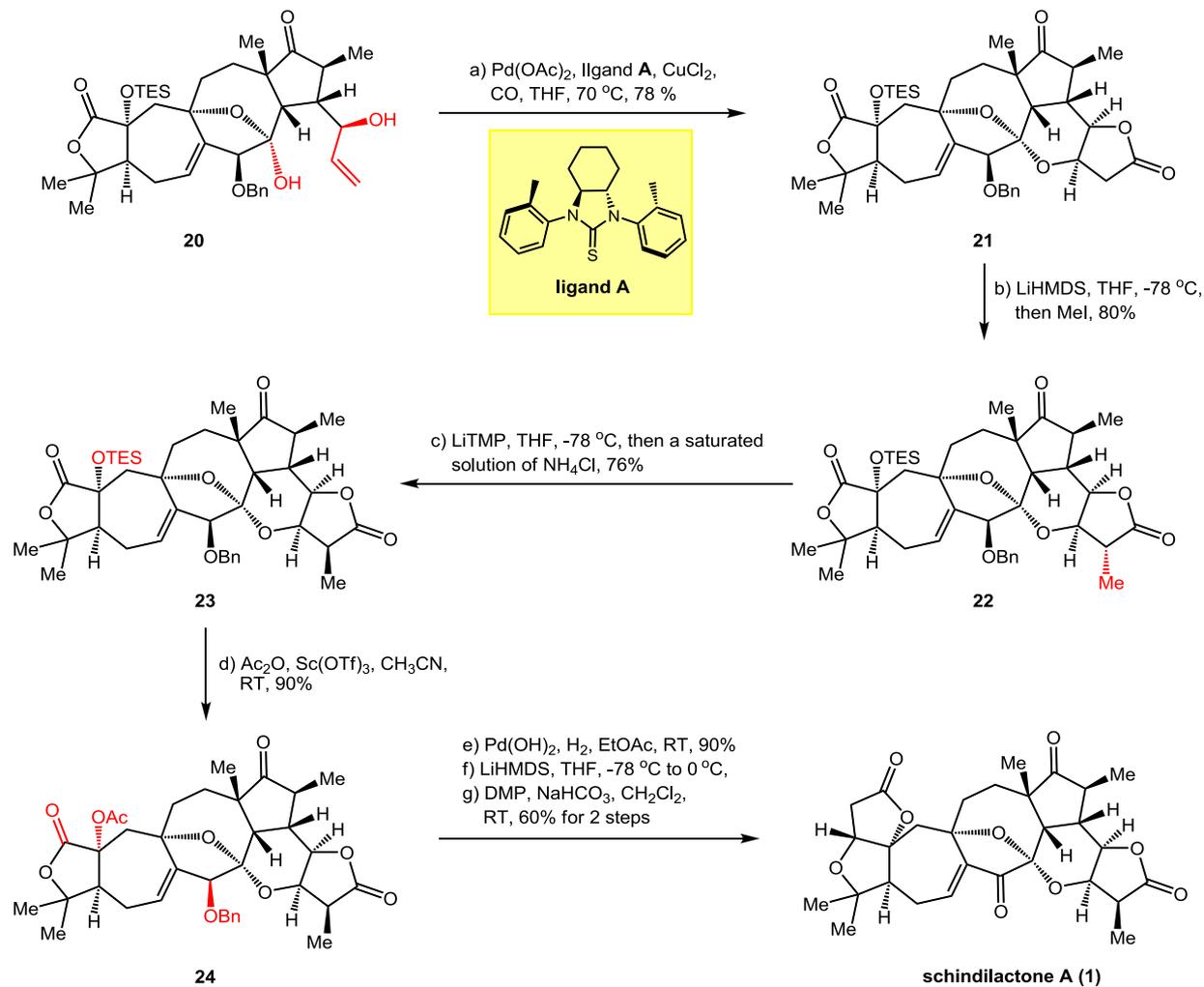
## ► Total synthesis of the intermediate 18



## ► Total synthesis of the intermediate 20

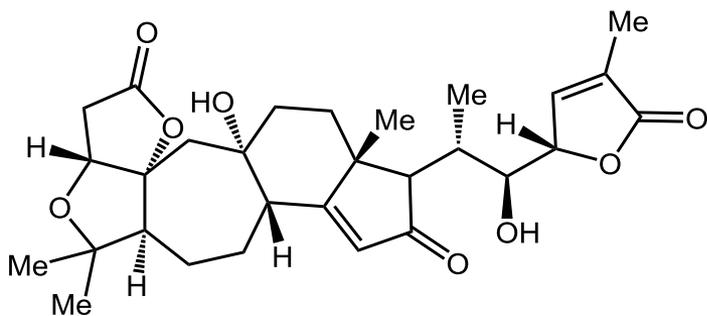


## ➤ Total synthesis of the (±)-schindilactone A (1)



## ► Summary

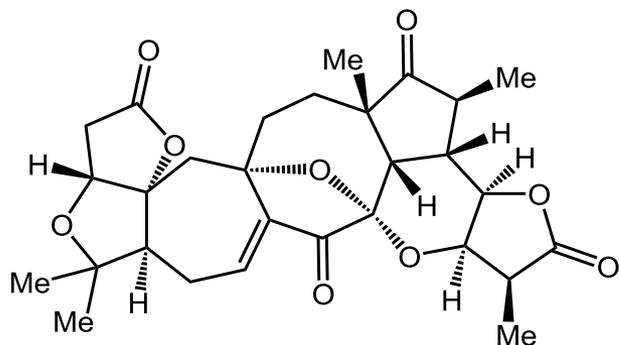
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**Propindilactone G**

### Propindilactone G

- ◆ Asymmetric DA reaction
- ◆ Co-mediated PK reaction
- ◆ Pd-catalyzed reductive hydrogenolysis reaction
- ◆ 20 steps.



**Schindilactone A**

### Schindilactone A

- ◆ Silver-mediated cyclopropane rearrangement
- ◆ RCM reaction
- ◆ Palladium-catalyzed carbonylative annulation
- ◆ Dieckmann-type condensation
- ◆ 29 steps.

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Propindilactone G (**1**) and compounds **2–4** (Chart 1) represent a novel group of nortriterpenoids isolated from various species of *Schisandracea* family by Sun et al. The species are widely distributed throughout Southeast Asia and North America and used as traditional Chinese herb medicines in China for liver protection and immune regulation.

The intriguing chemical structures and potential biological activity of the nortriterpenoids, in combination with their scarcity in nature, which limits their further biological investigation, have spurred considerable interest among the chemistry community, resulting in the total syntheses of schindilactone A (**2**) in 2011 by Yang et al., the total syntheses of rubriflordilactone A (**3**) in 2014 by Li et al., and the total syntheses of schilancitrilactone B (**4**) in 2015 by Tang et al.

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In conclusion, the total synthesis of (+)-propindilactone **1** was accomplished for the first time in 20 steps (longest linear sequence) starting from (buta-1,3-dien-2-yloxy)triisopropylsilane **9** and (*E*)-ethyl 4-oxobut-2-enoate **10**. The key steps in this synthesis were an asymmetric DA reaction, a Co-mediated PK reaction, a Pd-catalyzed reductive hydrogenolysis reaction, an oxidative heterocoupling reaction of enolsilanes, and an OsO<sub>4</sub>-mediated dihydroxylation. This work demonstrates the power of the PK reaction for the stereoselective construction of cyclopentenone bearing an all-carbon quaternary chiral center, and the oxidative heterocoupling reaction of enolsilanes for the concise ligation of cyclopentenone core **6** with its side chain.

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The true structure of **1** was revised in accord with our finding, and the originally proposed structure has been reassigned as C17-*epi*-(+)-propindilactone G (**1a**). The application of the synthetic propindilactone G and its analogues as probes to study their biology is currently underway in our laboratories, and will be reported in due course.

## ➤ The thiourea/palladium catalyzed carbonylative annulation reaction

