

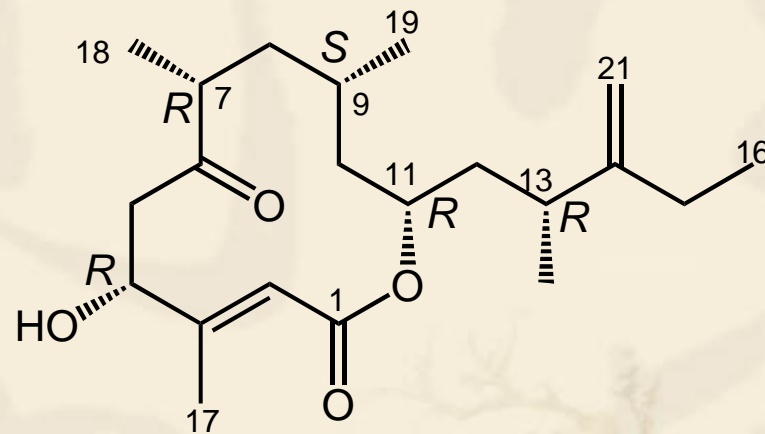
Literature Report 2009-11-3

段英      检查: 陈庆安

## Total Synthesis of Amphidinolide Q

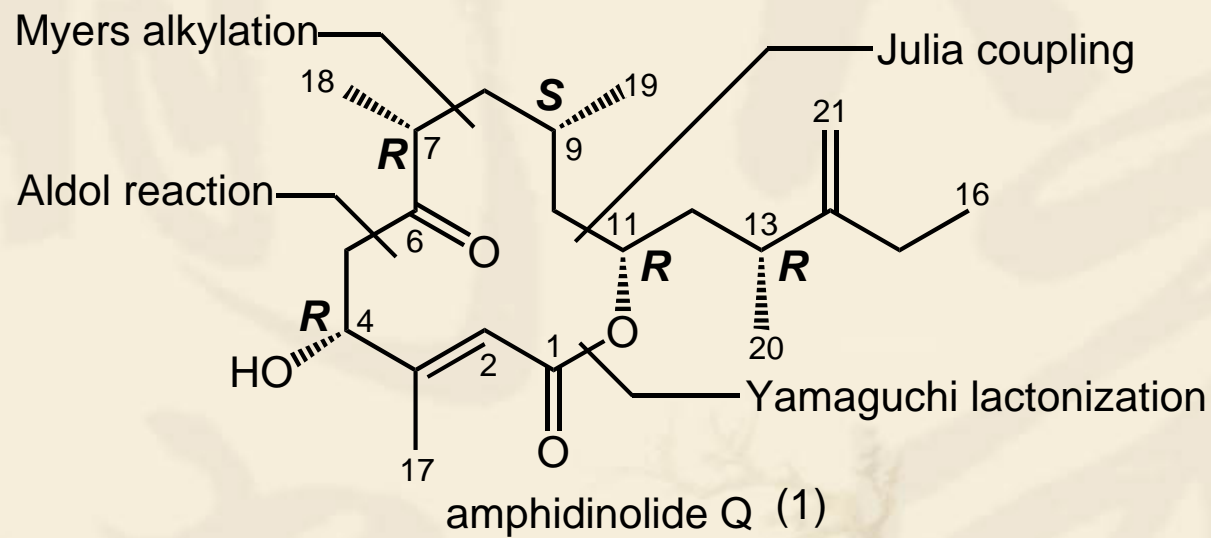
Kobayashi, J.\*, *et al*  
*Org. Lett.* **2009**, 11, 5046-5049

## Structure of Amphidinolide Q

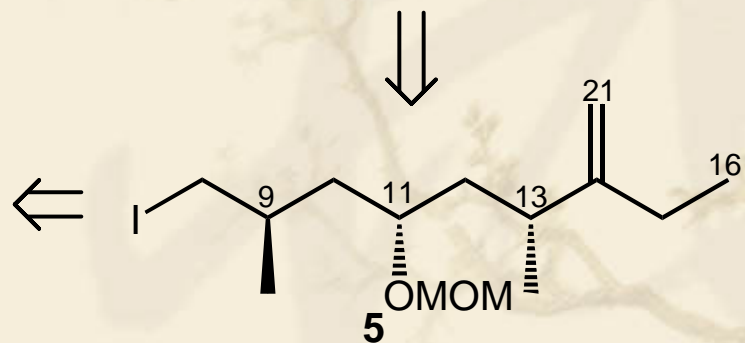
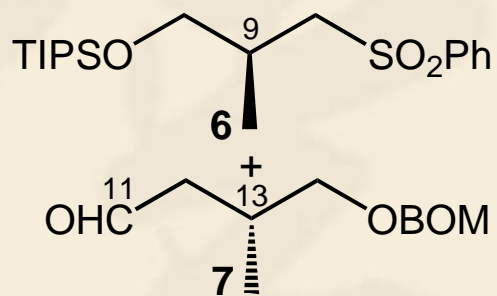
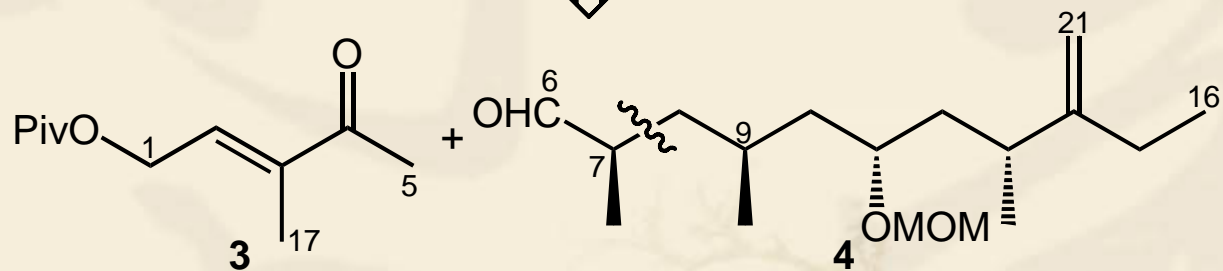
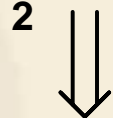
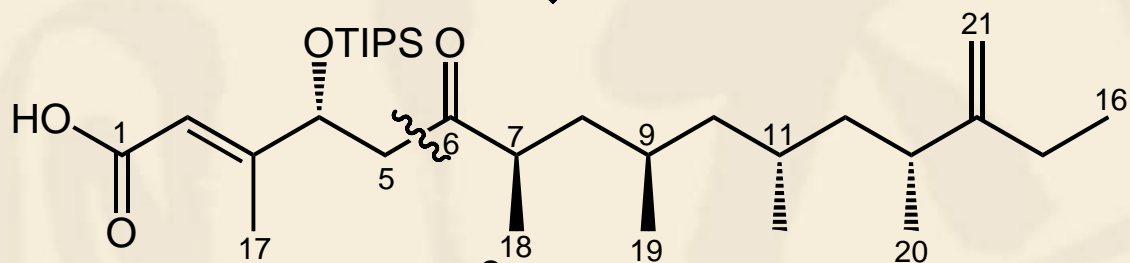


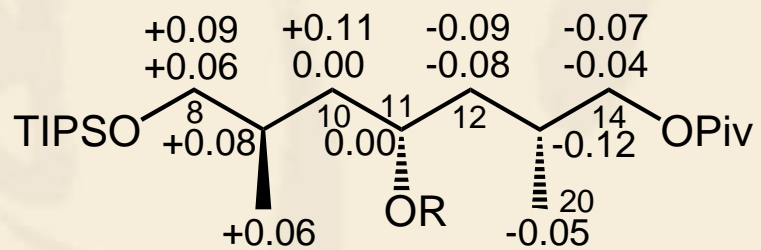
amphidinolide Q (1)

日本化学家Kobayashi从海洋共生体腰鞭毛虫Amphidinium sp中共分离到一类12到29元不等的34个大环内酯化合Amphidinolides A-H、J-T、U-Y以及9个链状的多酮化合物。同时Amphidinolides具有很好的生物活性,对鼠科类的淋巴瘤L1210细胞及人体的表皮癌KB细胞表现出很强的细胞毒素作用。

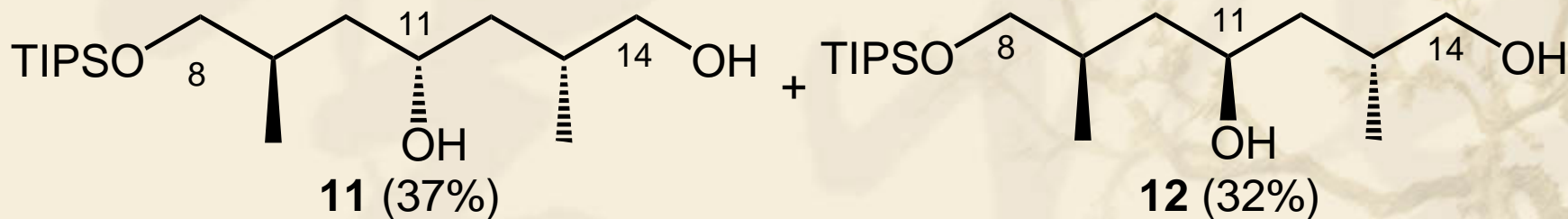
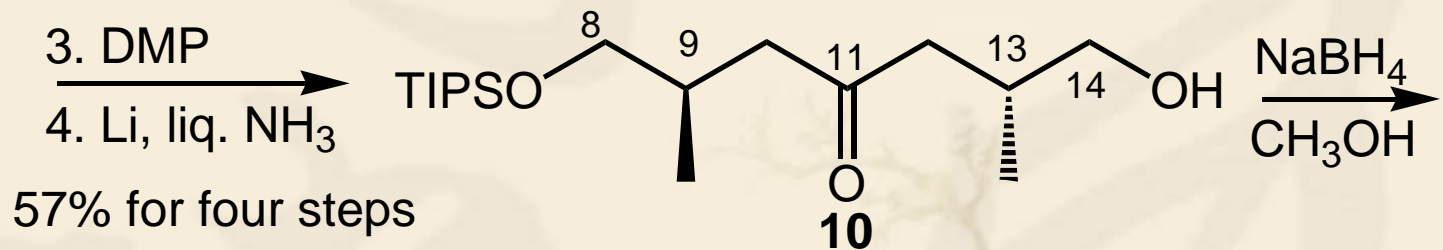
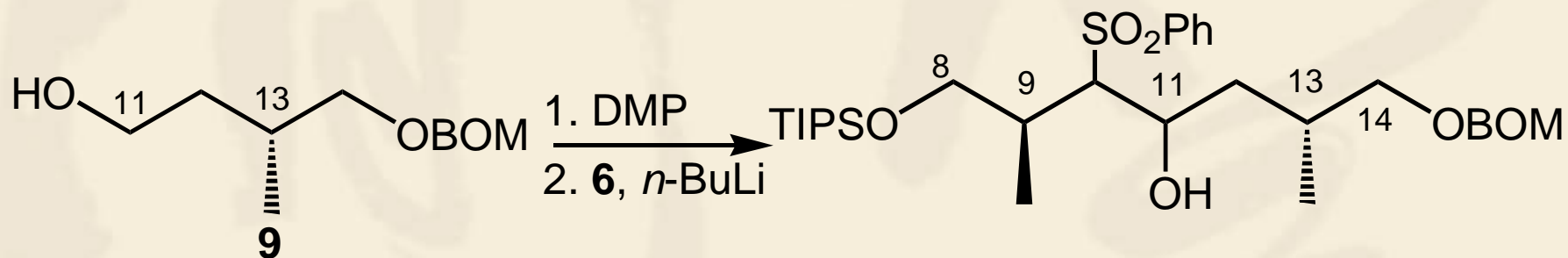
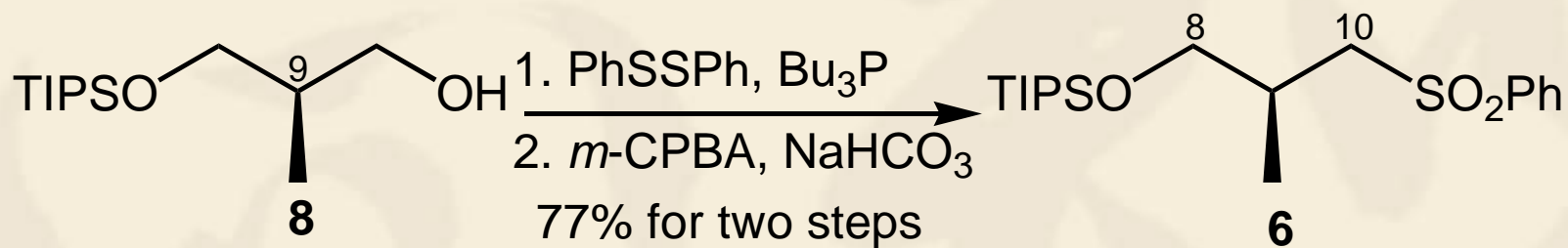


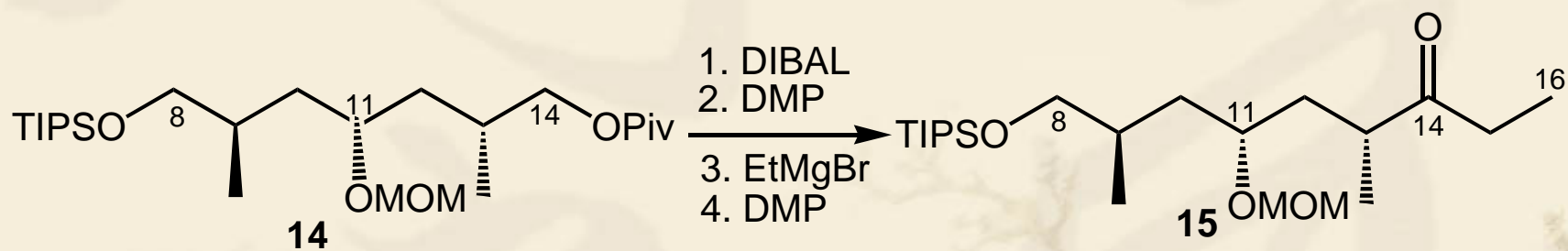
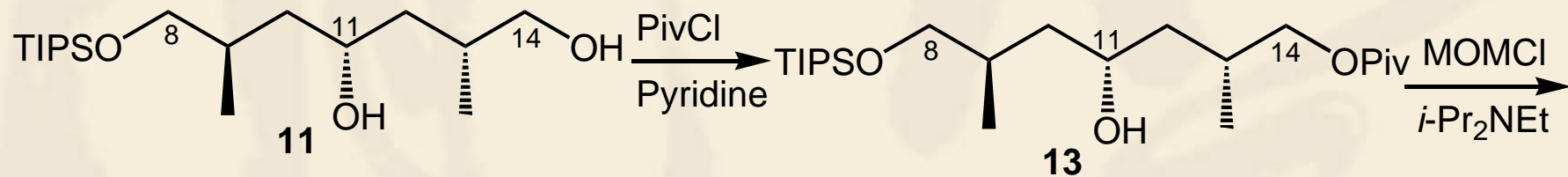
amphidinolide Q (1)



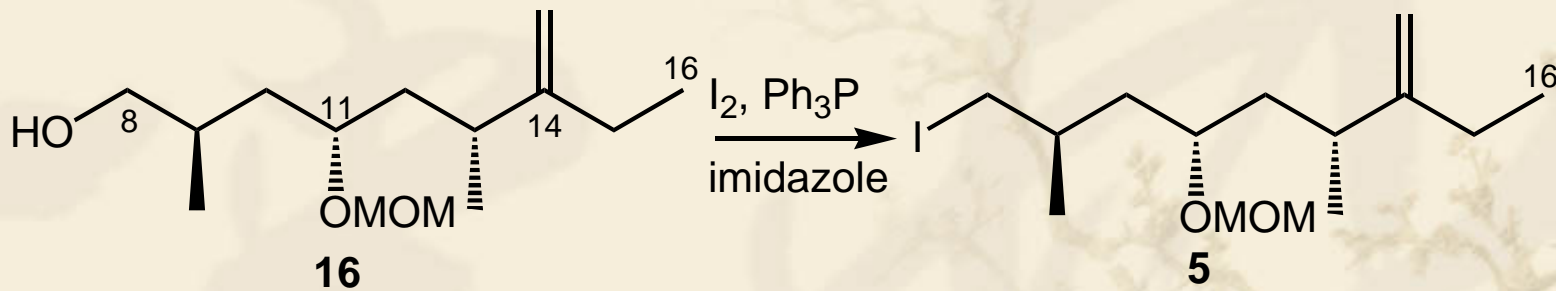
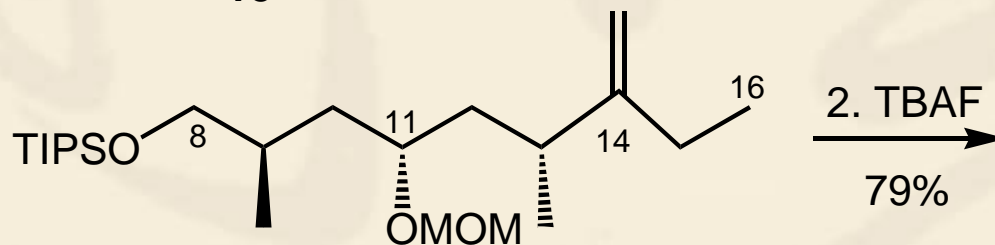
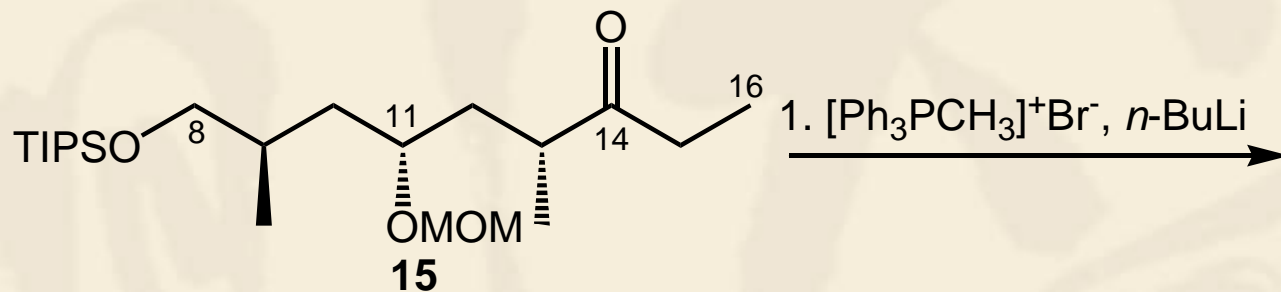


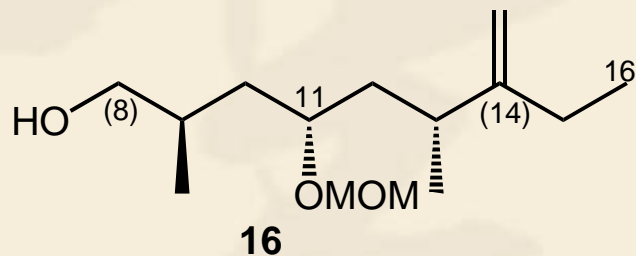
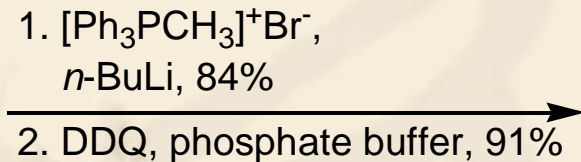
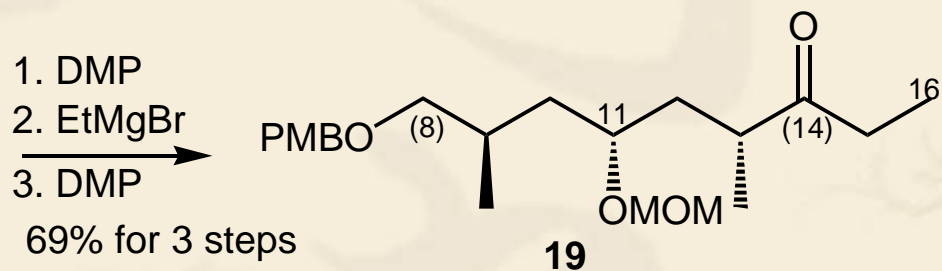
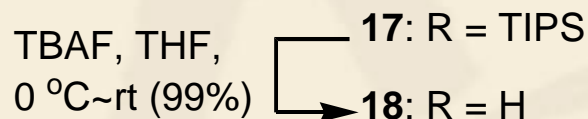
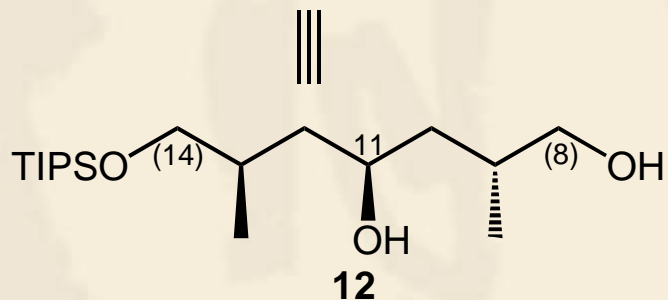
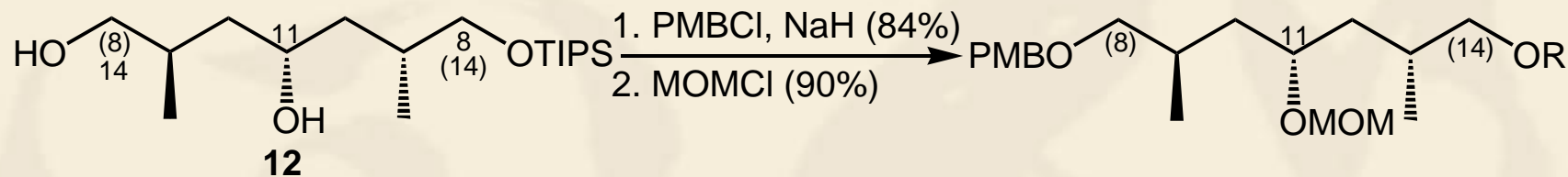
13a: R=(*S*)-MTPA  
13b: R=(*R*)-MTPA

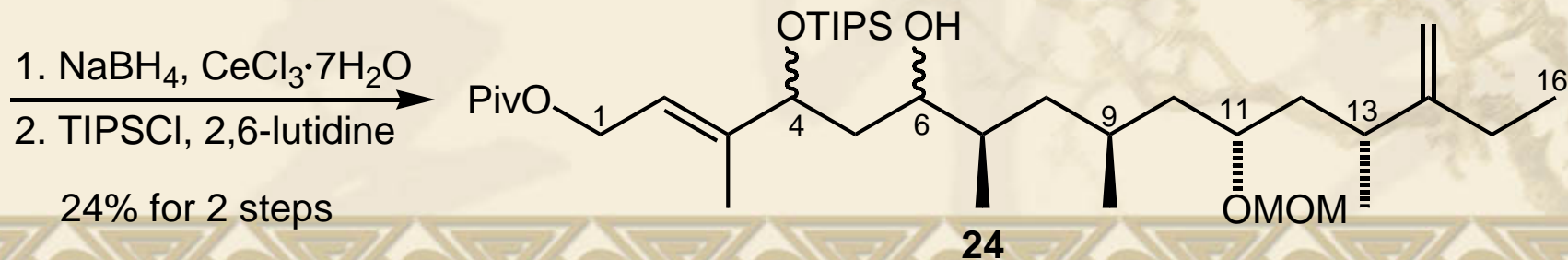
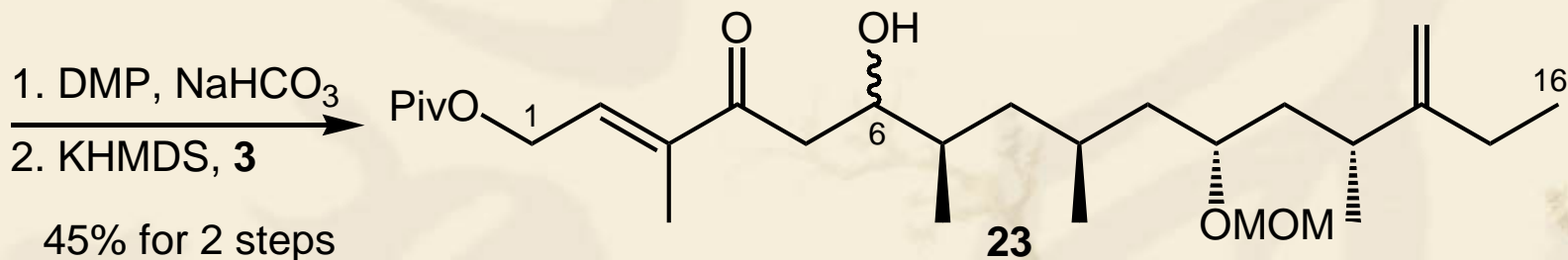
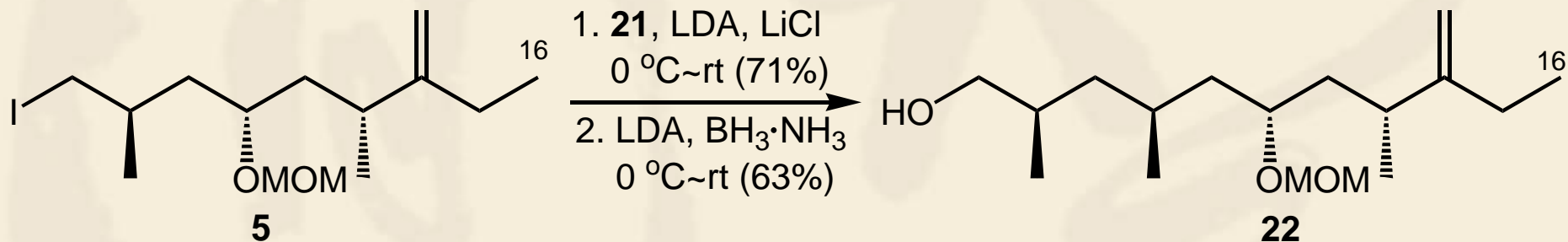
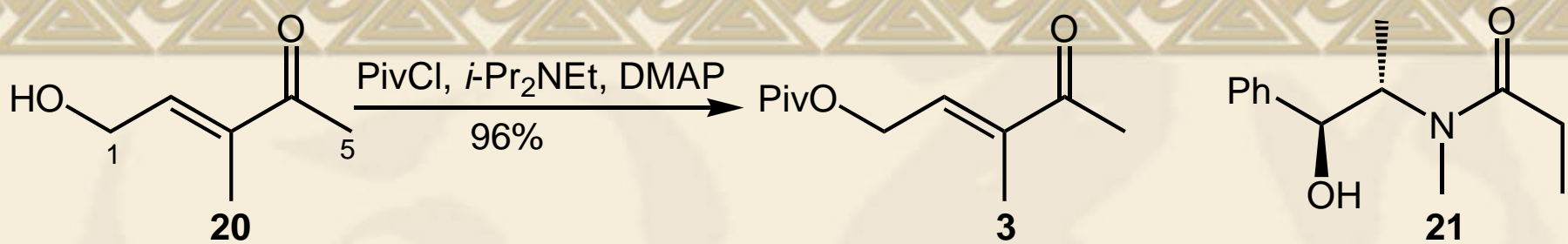


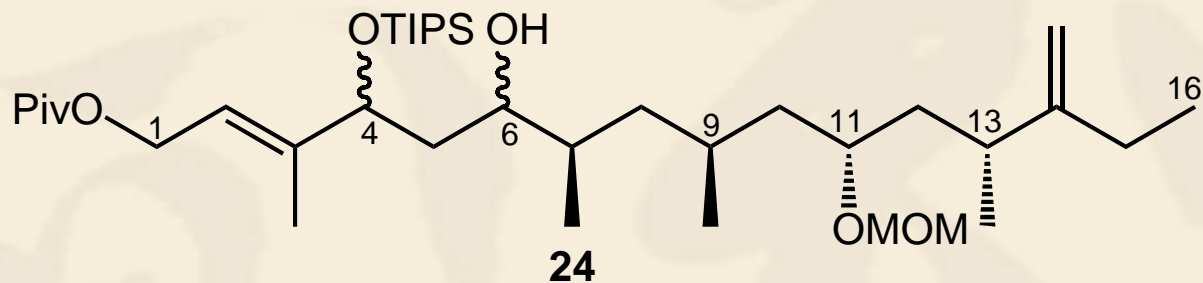




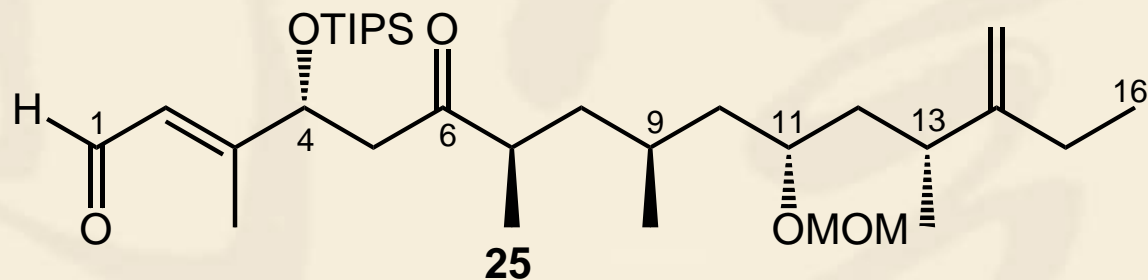






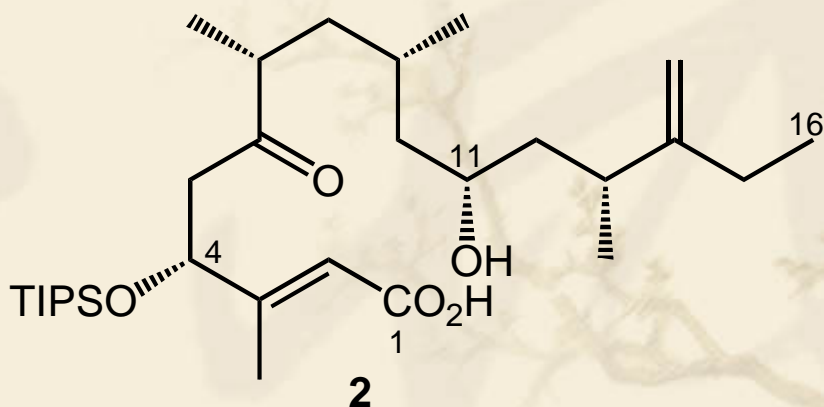


1. DIBAL  
2. DMP, NaHCO<sub>3</sub>

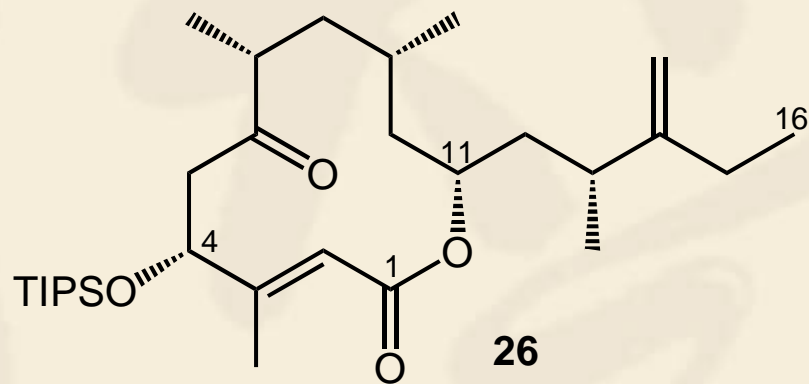


1. NaClO<sub>2</sub>, NaH<sub>2</sub>PO<sub>4</sub>,  
2-methyl-2-butene  
2. PPTS, *t*-BuOH

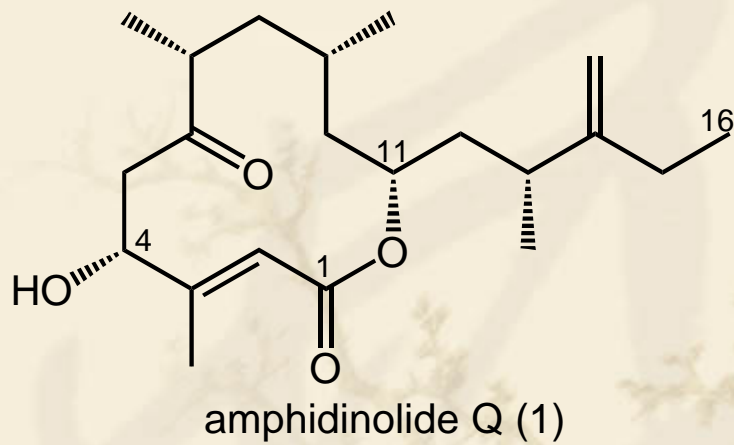
26% for two steps



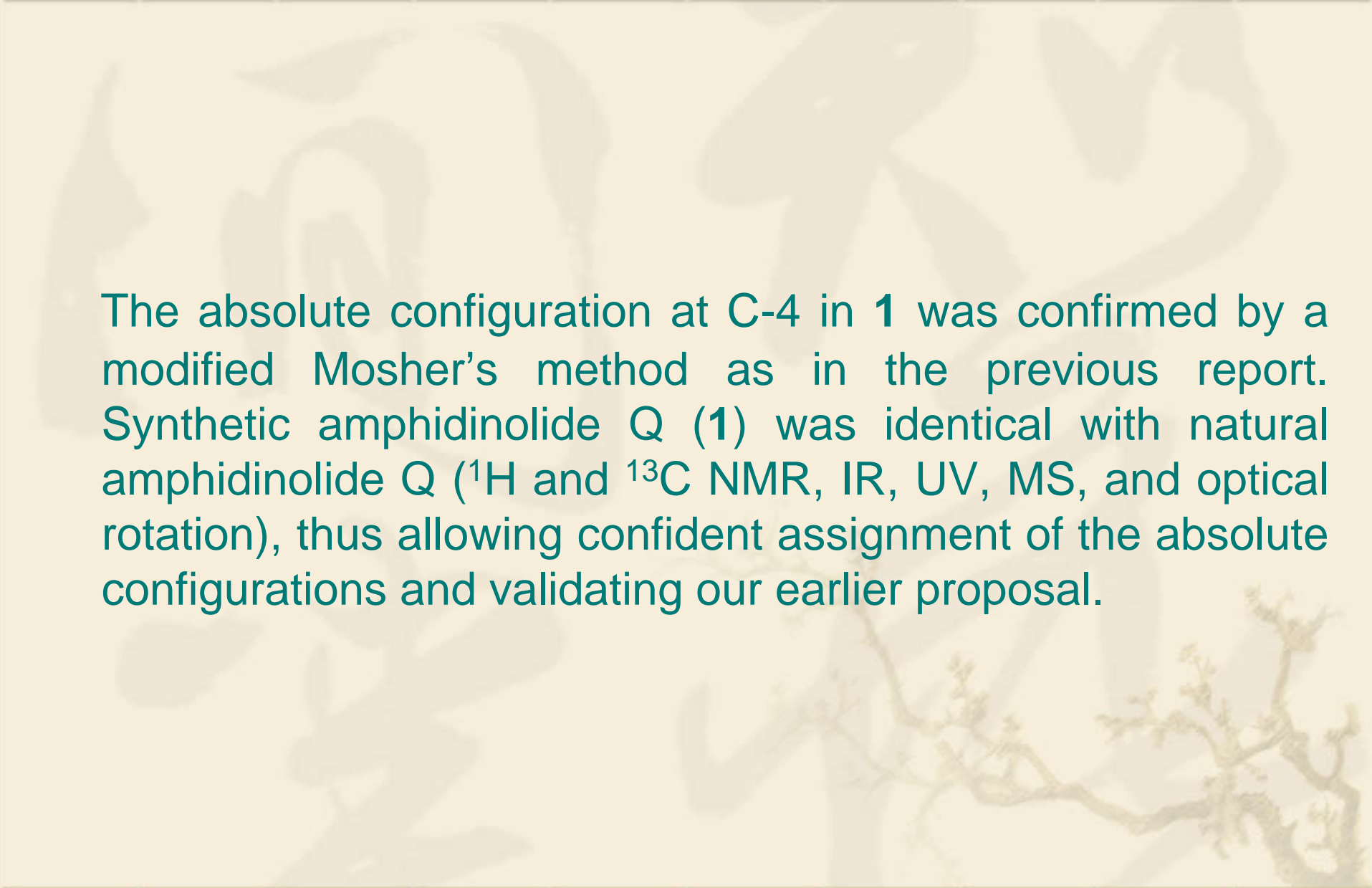

2, 4, 6-trichlorobenzoyl chloride  
Et<sub>3</sub>N, DMAP, 63%



TBAF  
52%



Amphidinolide Q (**1**) is a cytotoxic 12-membered macrolide having C1 branches at vicinal carbons (C-13 and C-14) and an  $\alpha, \beta$ -unsaturated ester moiety, isolated from the cultured dinoflagellate *Amphidinium* sp. (Y-5 strain). Recently, we have proposed the stereoconfiguration of amphidinolide Q as **1** on the basis of extensive NMR experiments, molecular modeling, and chemical derivatization. In this paper, we describe the first total synthesis of amphidinolide Q (**1**) and establish our proposed absolute stereochemistry.



The absolute configuration at C-4 in **1** was confirmed by a modified Mosher's method as in the previous report. Synthetic amphidinolide Q (**1**) was identical with natural amphidinolide Q ( $^1\text{H}$  and  $^{13}\text{C}$  NMR, IR, UV, MS, and optical rotation), thus allowing confident assignment of the absolute configurations and validating our earlier proposal.

