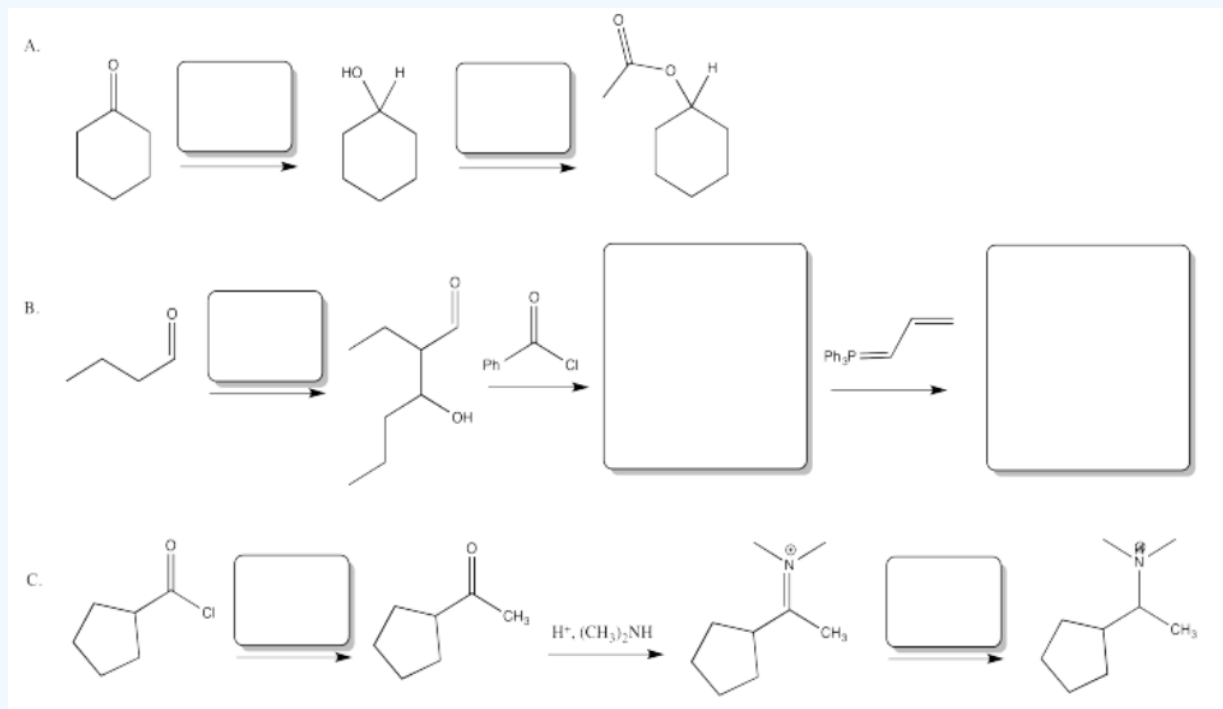


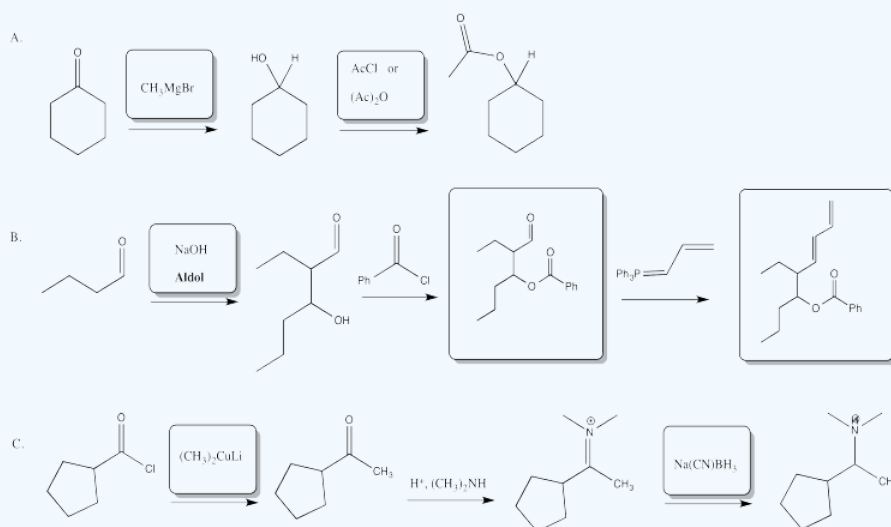
## 5.3: Additional Problems

### Exercise 5.3.1

Fill in the blanks in the following syntheses.



### Answer

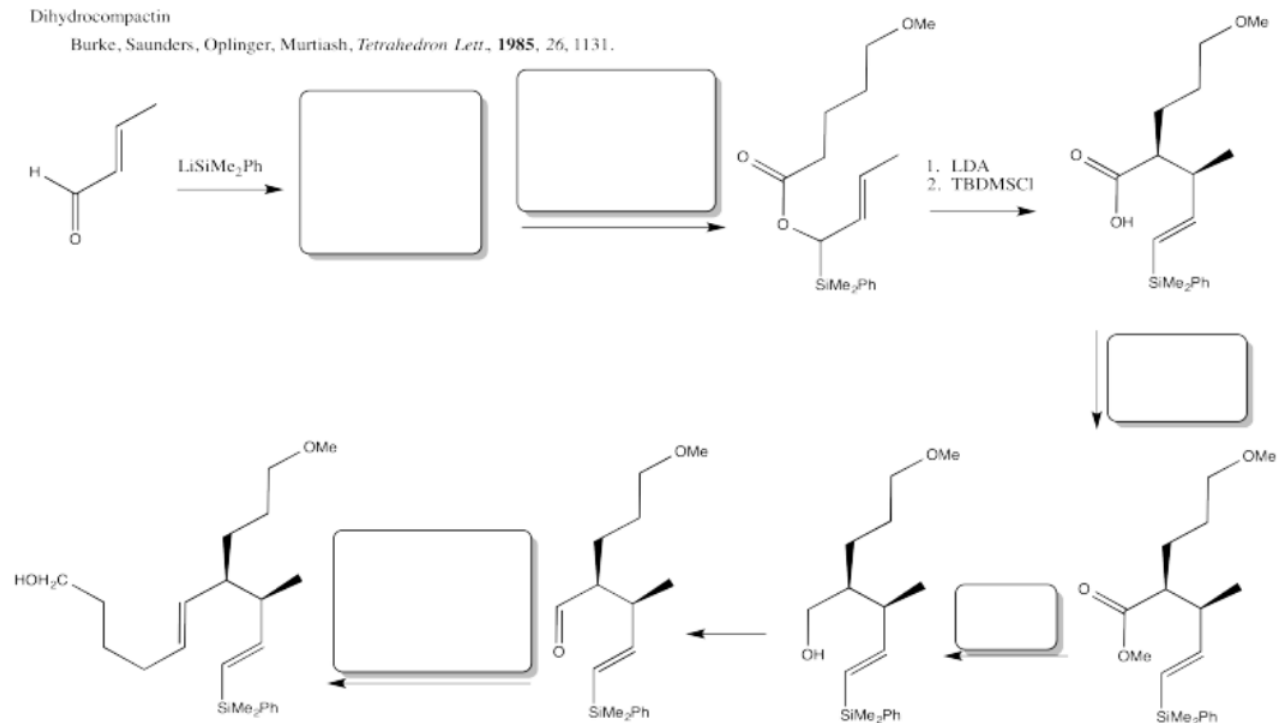


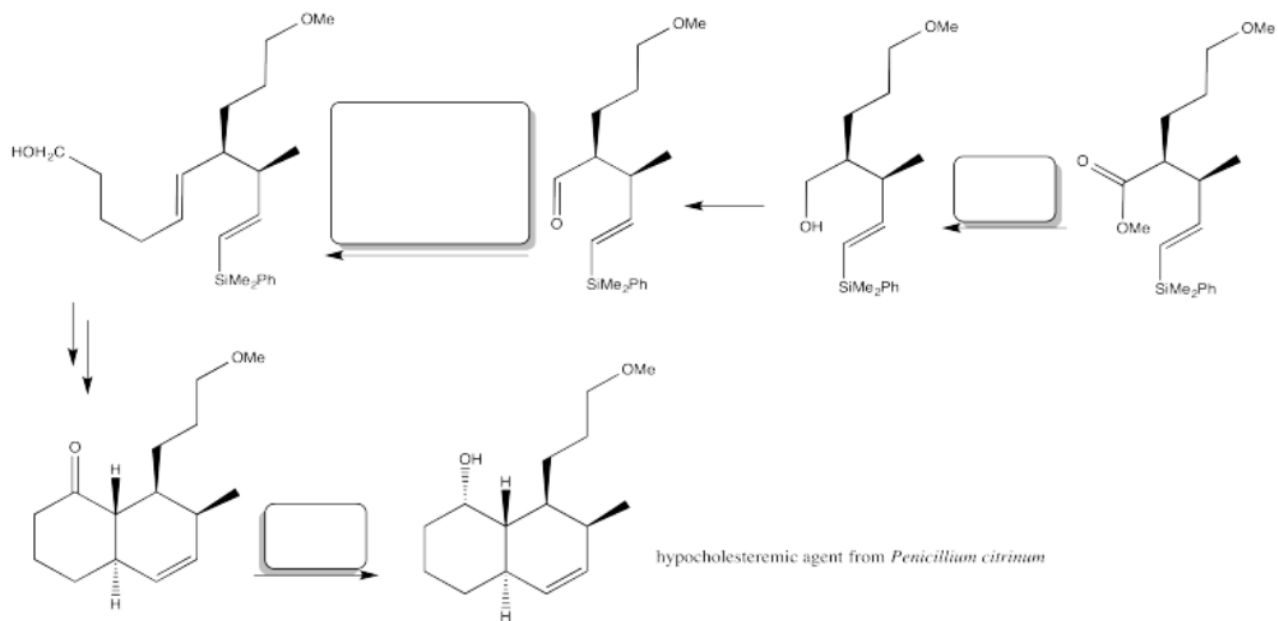
### Exercise 5.3.2

Fill in the blanks in the following synthesis involving *anionic nucleophilic addition to carbonyl* and *nucleophilic substitution at carboxyl*.

Dihydrocompactin

Burke, Saunders, Oplinger, Murtiash, *Tetrahedron Lett.*, **1985**, 26, 1131.

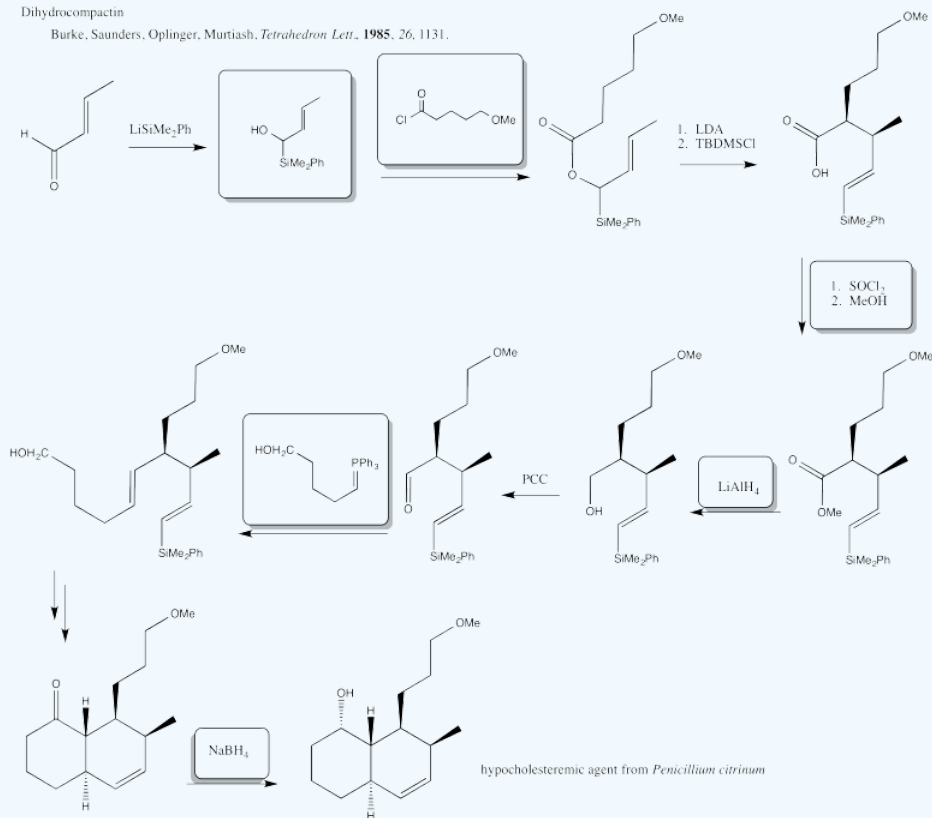




### Answer

Dihydrocompactin

Burke, Saunders, Oplinger, Murtiash, *Tetrahedron Lett.*, **1985**, 26, 1131.

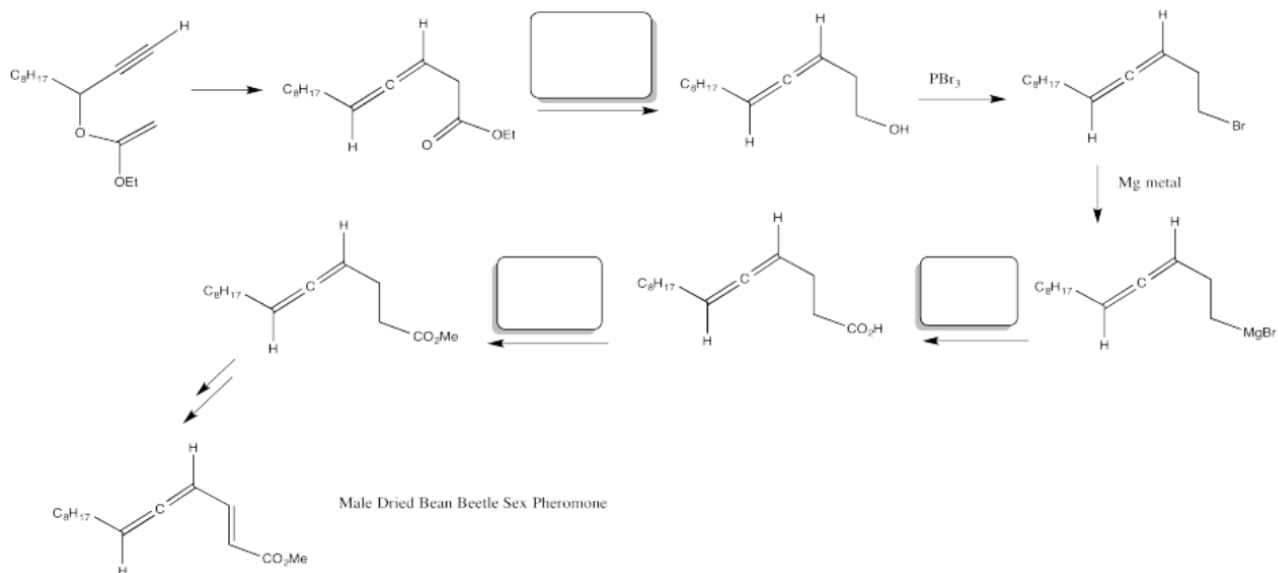


### Exercise 5.3.3

Fill in the blanks in the following synthesis involving *anionic nucleophilic addition to carbonyl* and *nucleophilic substitution at carboxyl*.

Male Dried Bean Beetle Sex Pheromone

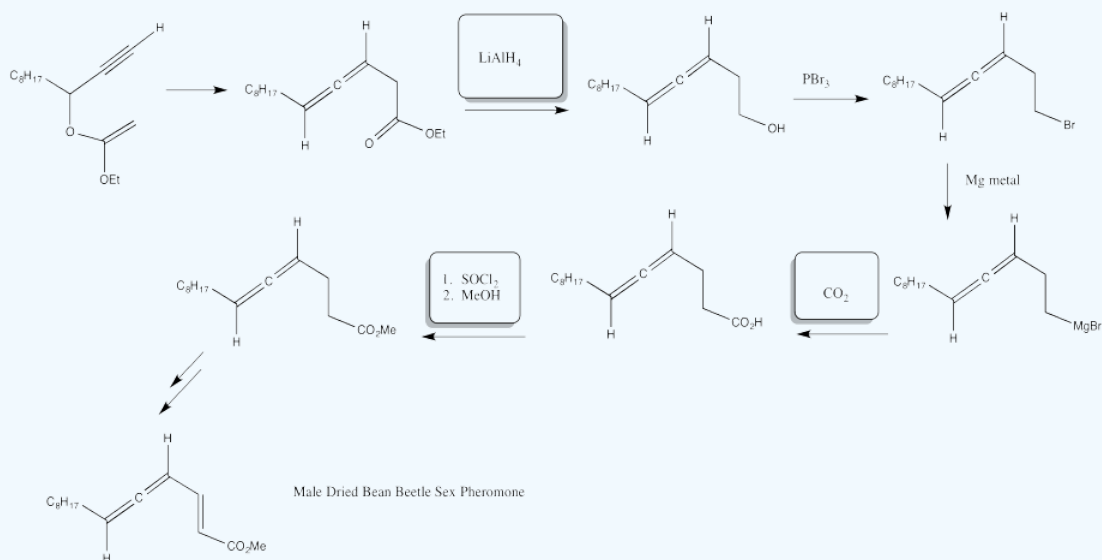
Kocienski, Cernogliaro Feldstein, *J. Org. Chem.*, **1977**, 2, 353.



## Answer

Male Dried Bean Beetle Sex Pheromone

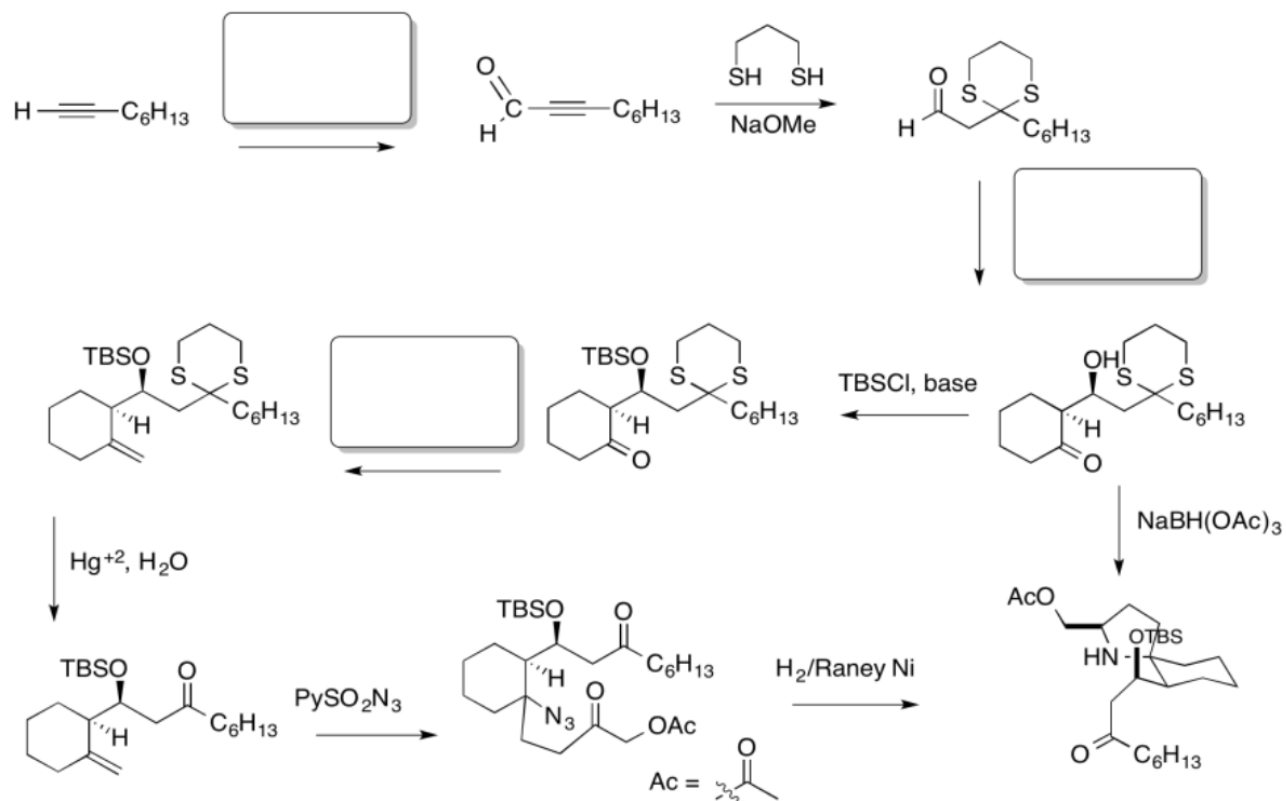
Kocienski, Cernogliaro Feldstein, *J. Org. Chem.*, **1977**, 2, 353.

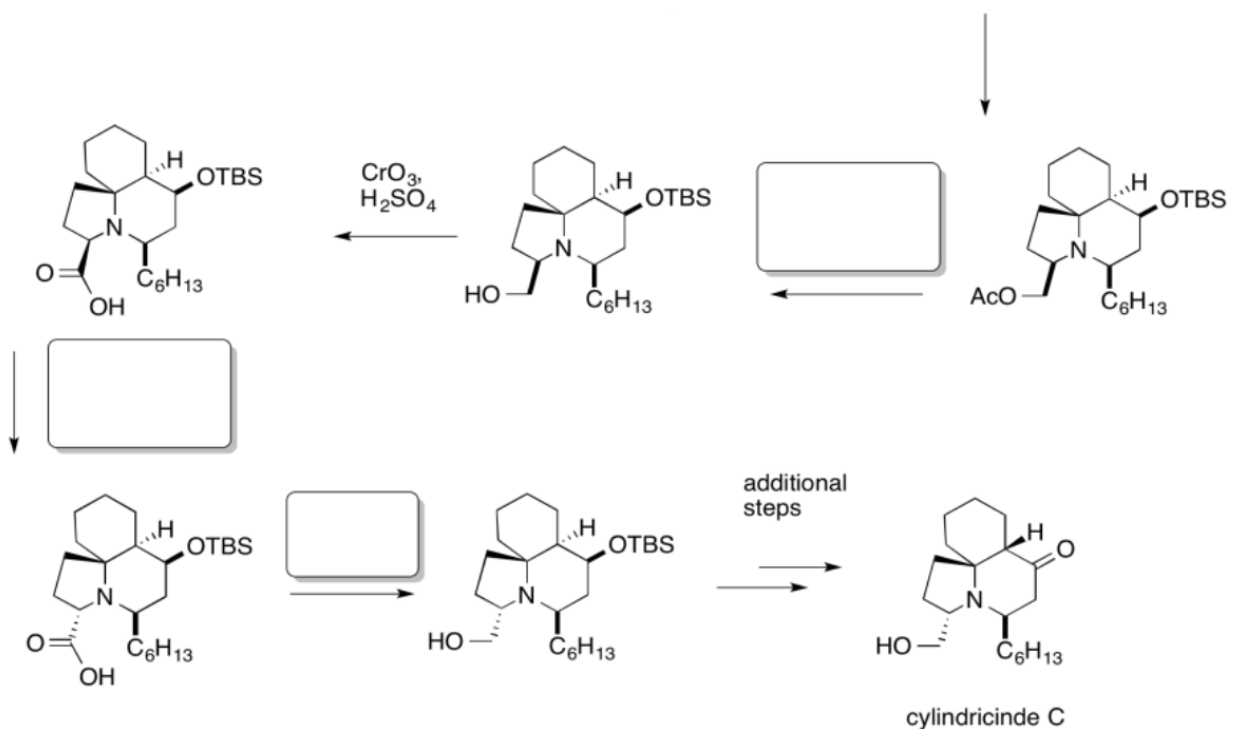


## Exercise 5.3.4

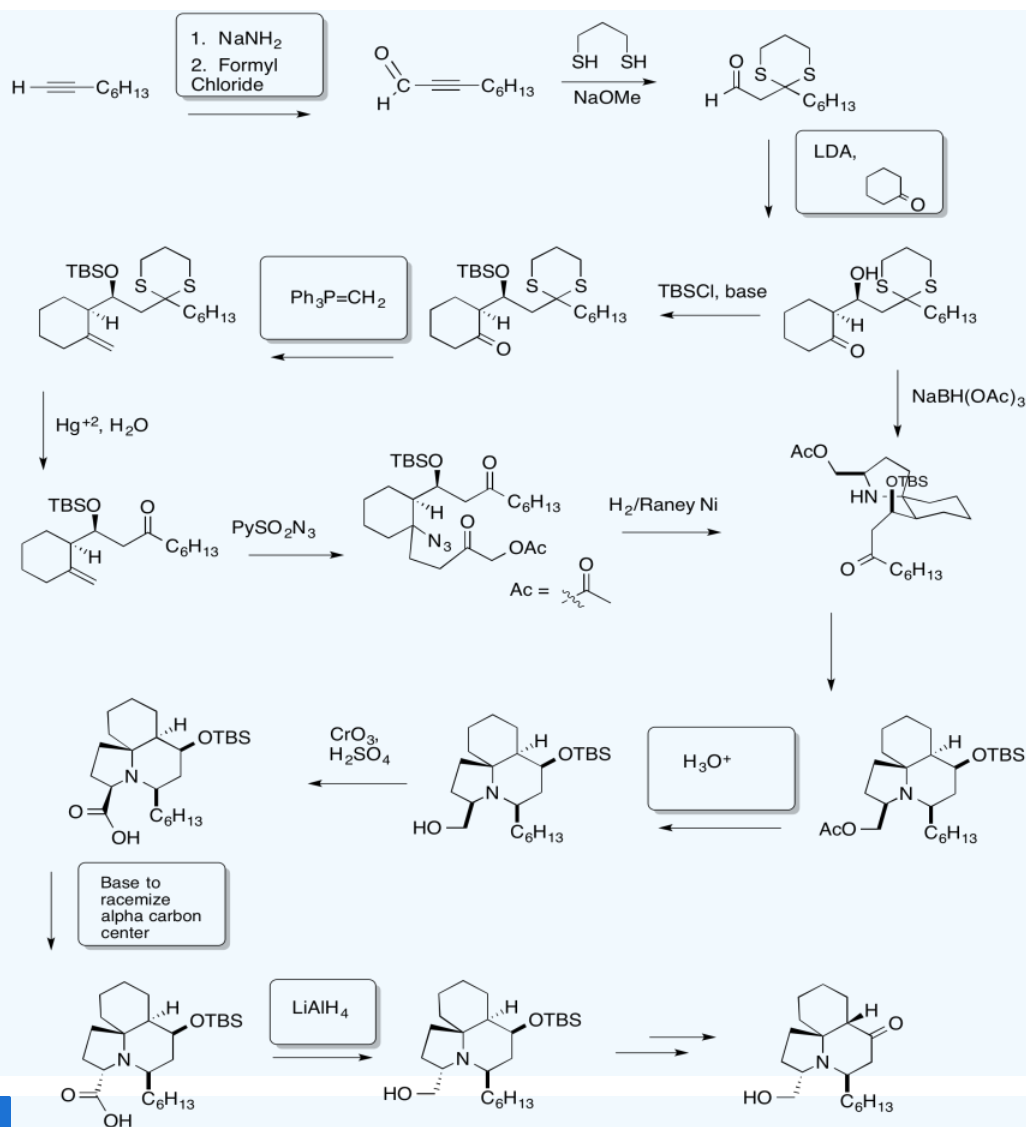
Fill in the blanks in the following synthesis involving *anionic nucleophilic addition to carbonyl* and *nucleophilic substitution at carboxyl* (including Wittig and aldol reactions).

Total Synthesis of Cylindricine C, Lapointe, Schenk, and Renaud, *Org Lett*, **2011**, 13(18), 4774-4777.



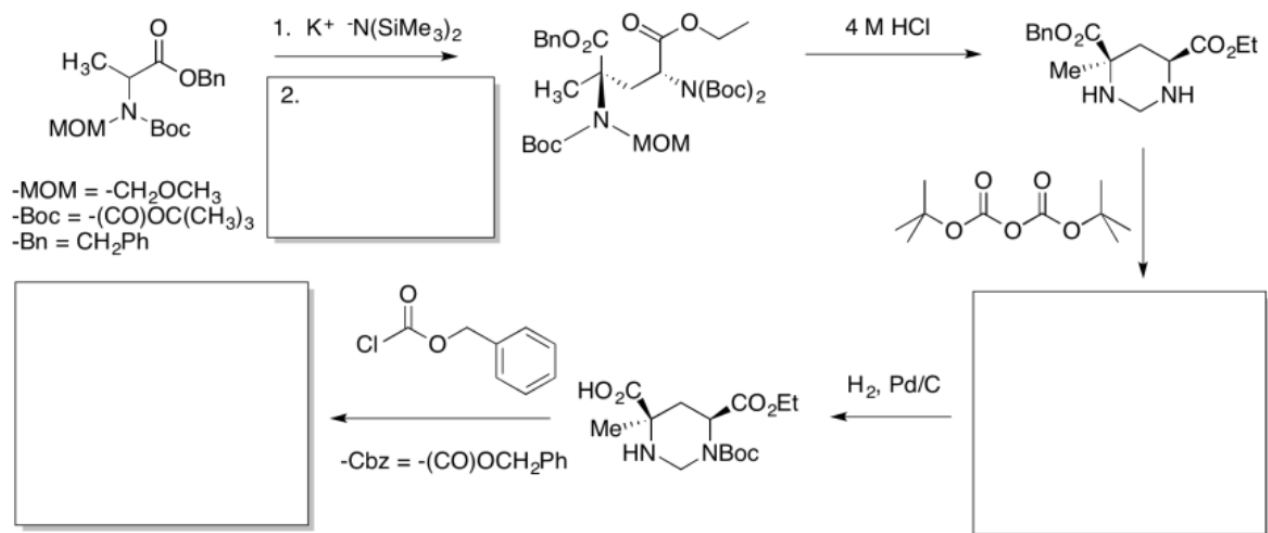


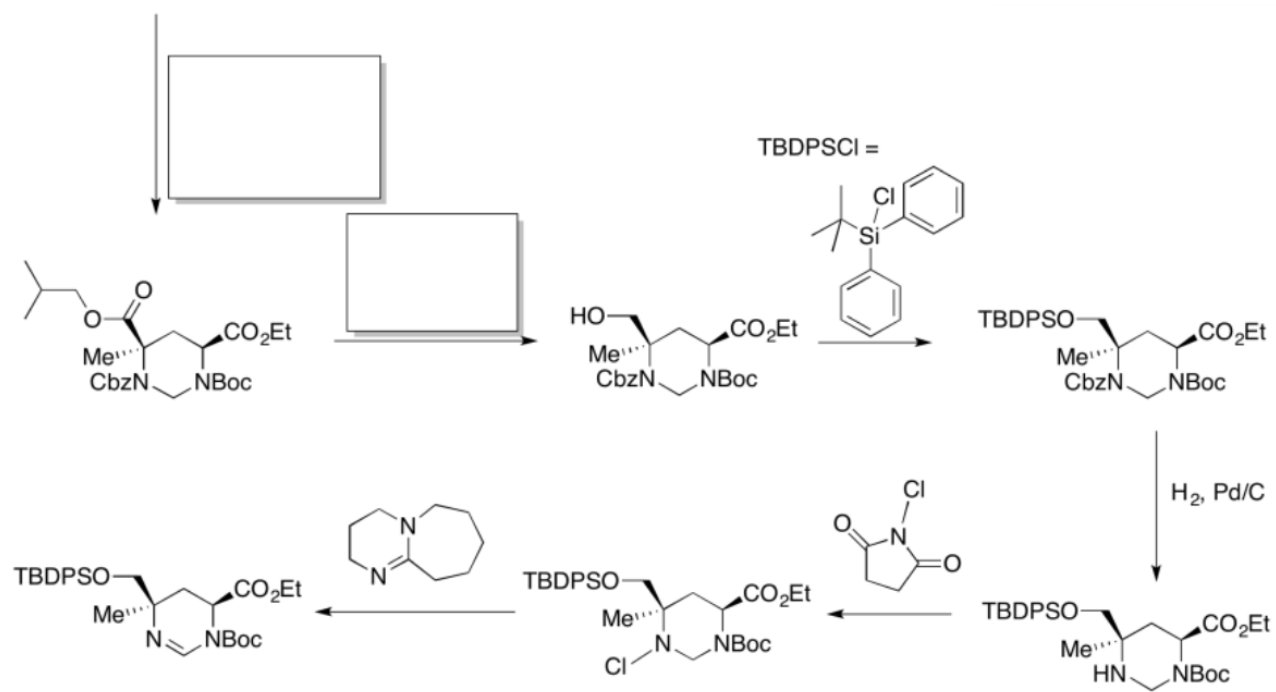
**Answer**



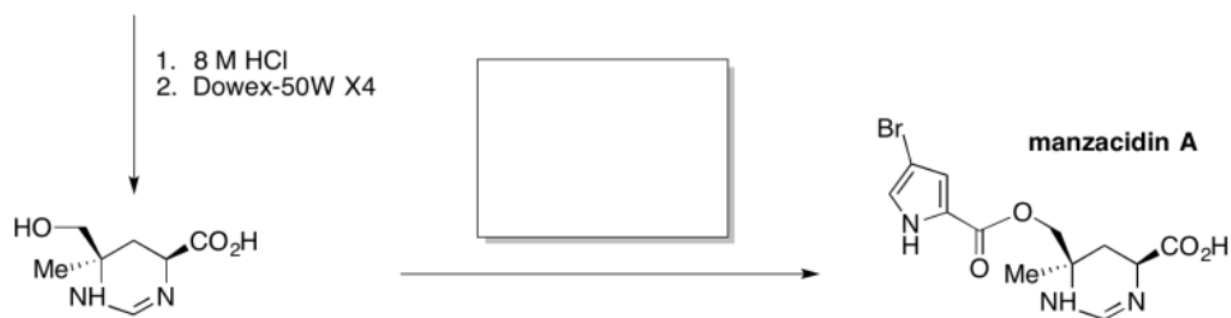
### Exercise 5.3.5

Fill in the blanks in the following synthesis involving *nucleophilic substitution at carboxyl*.

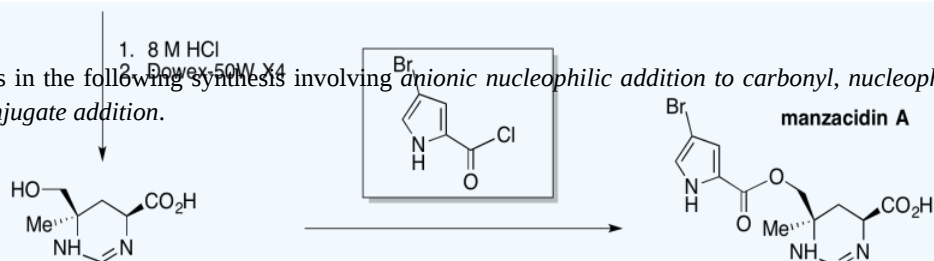
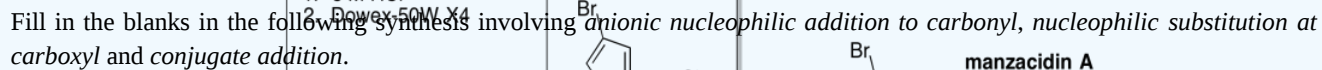


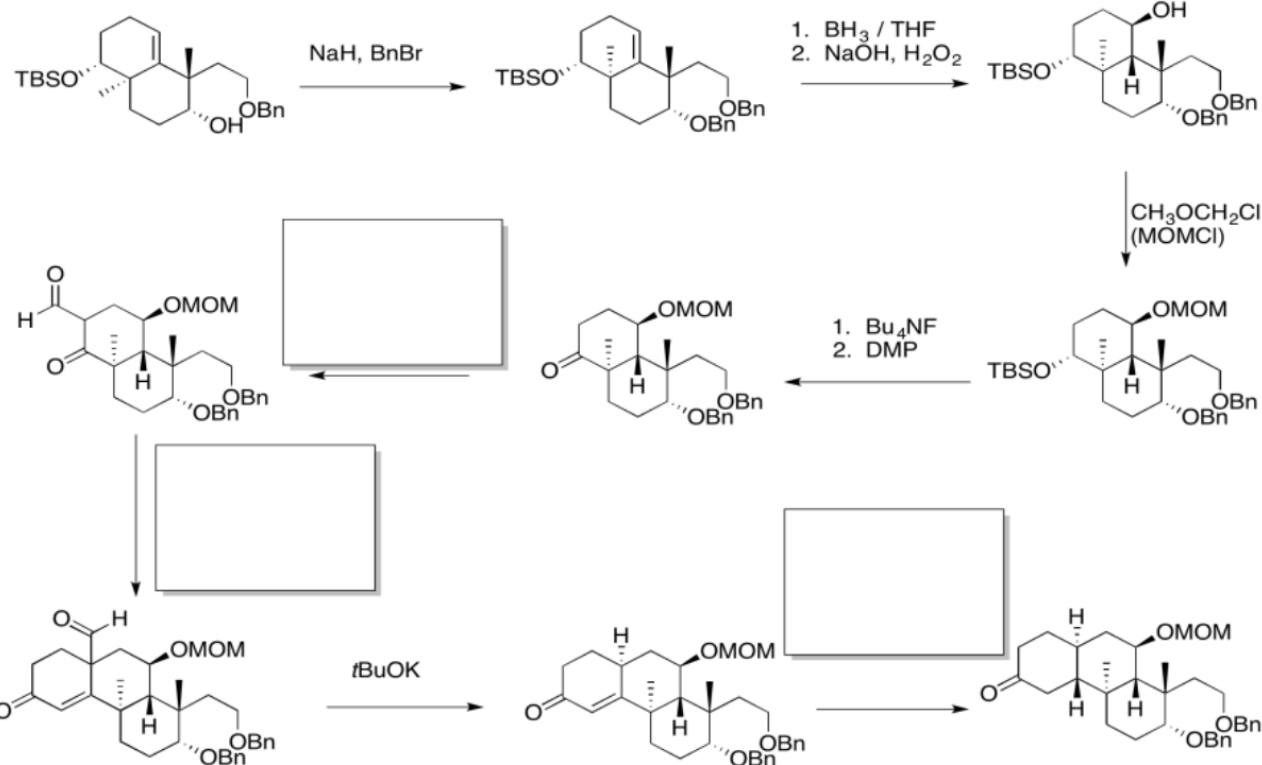


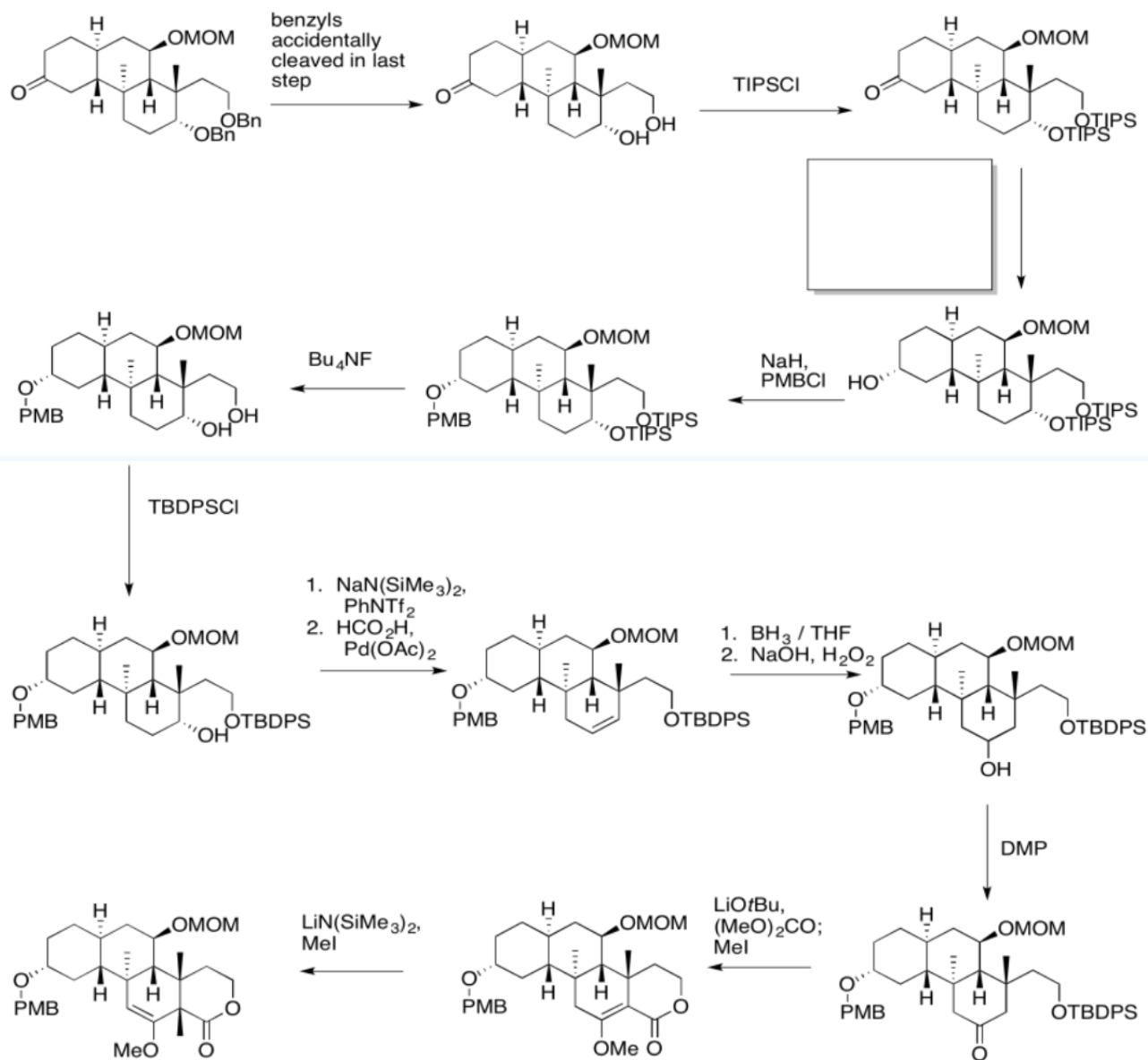


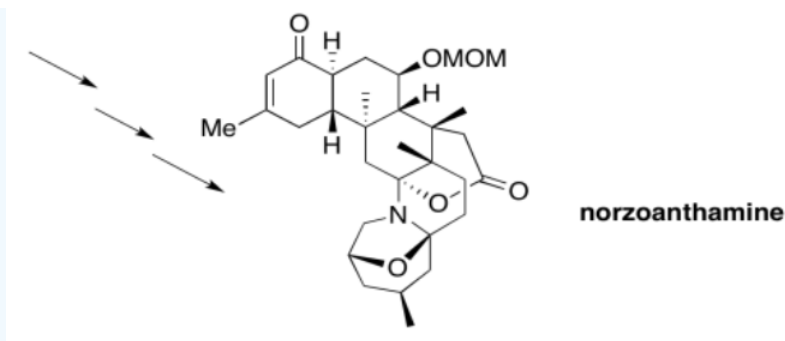


Answer



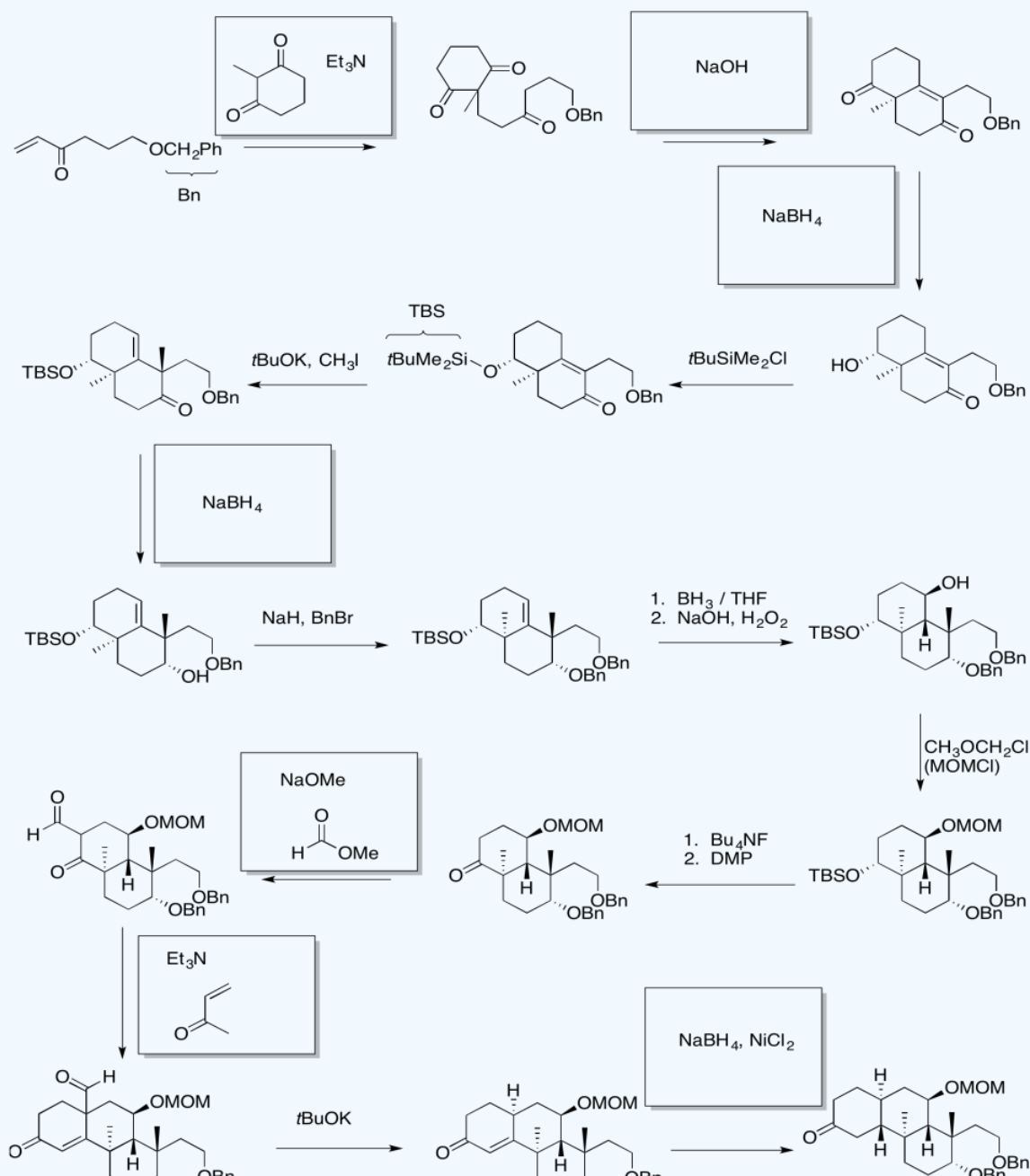


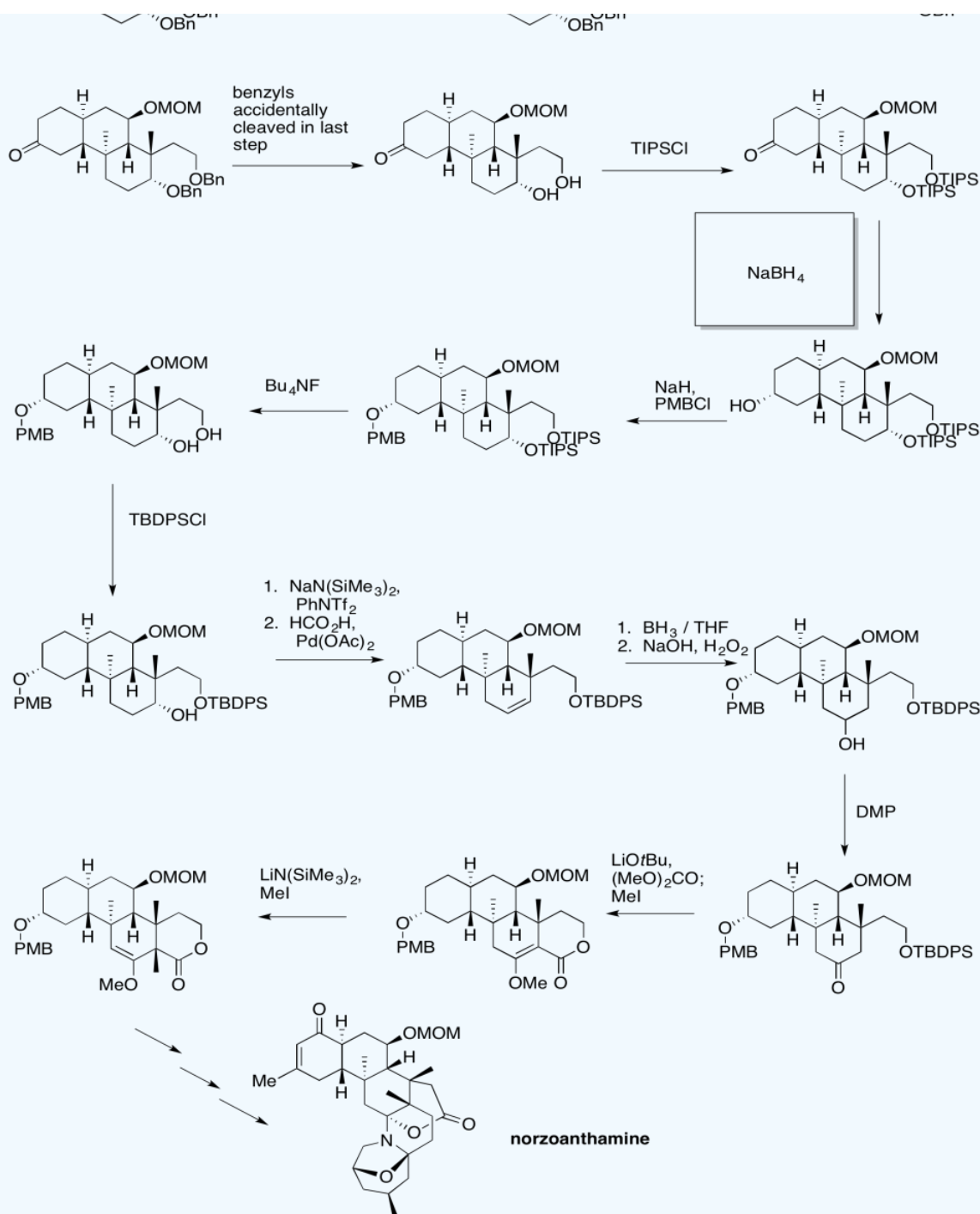




## Answer

Partial Syntheses of Norzoanthamine (Thoedorakis, UCSD, 2011)  
Marine natural product of *Zoanthus sp.* Demonstrated anti-osteoporotic effects in mice.



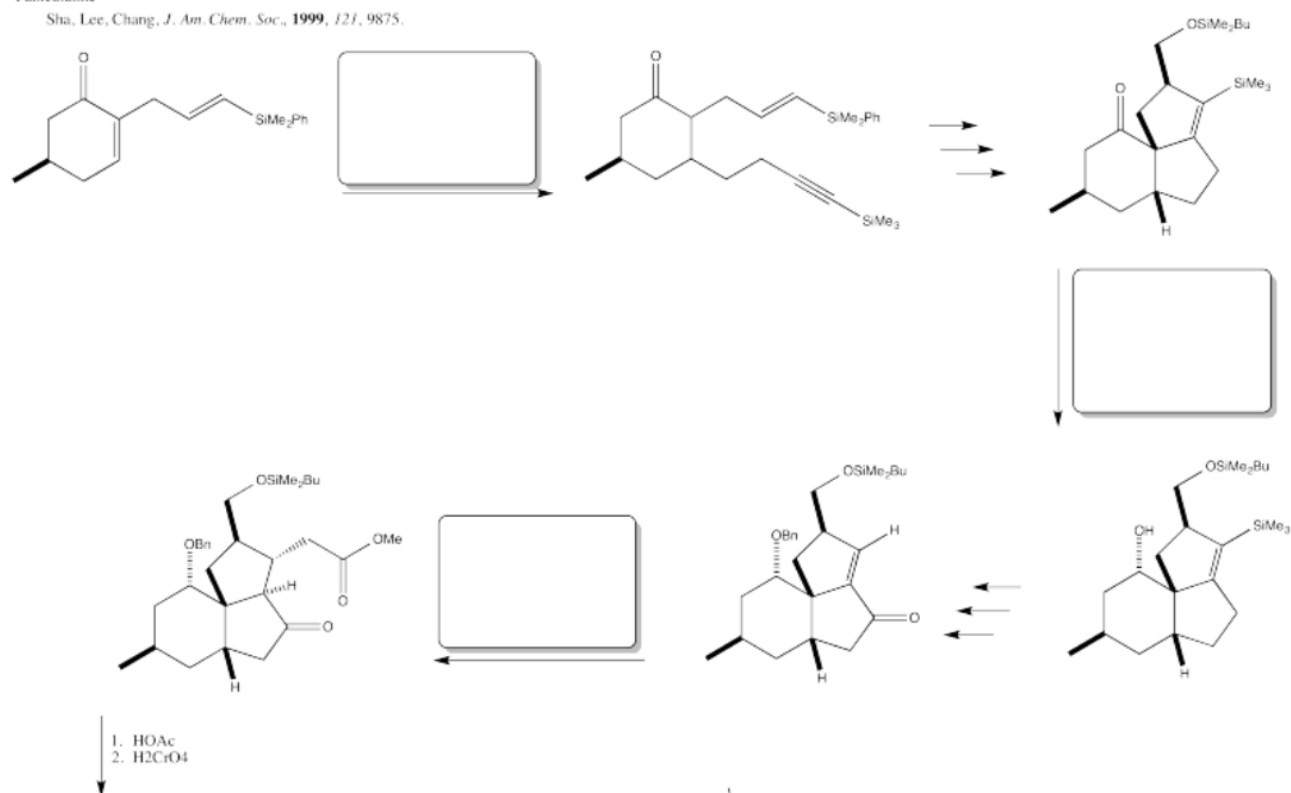


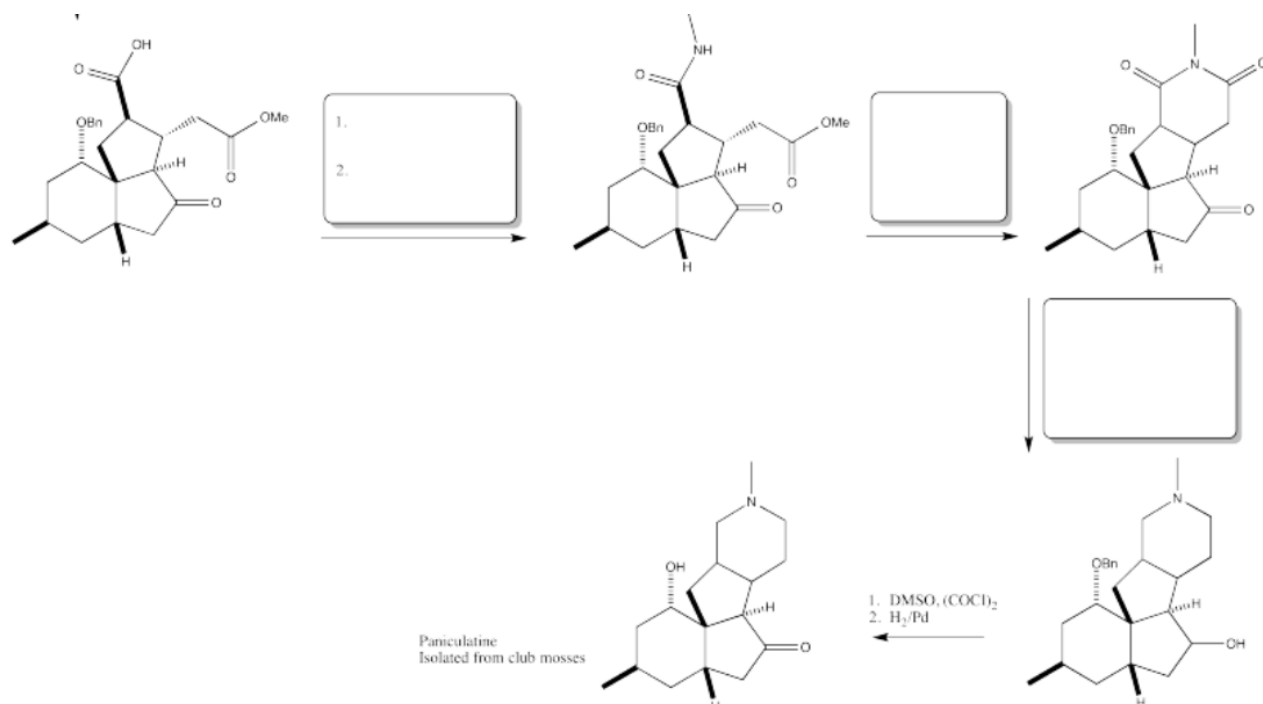
### Exercise 5.3.7

Fill in the blanks in the following synthesis involving *anionic nucleophilic addition to carbonyl*, *conjugate addition* and *nucleophilic substitution at carboxyl*.

Paniculatin

Sha, Lee, Chang, *J. Am. Chem. Soc.*, **1999**, *121*, 9875.



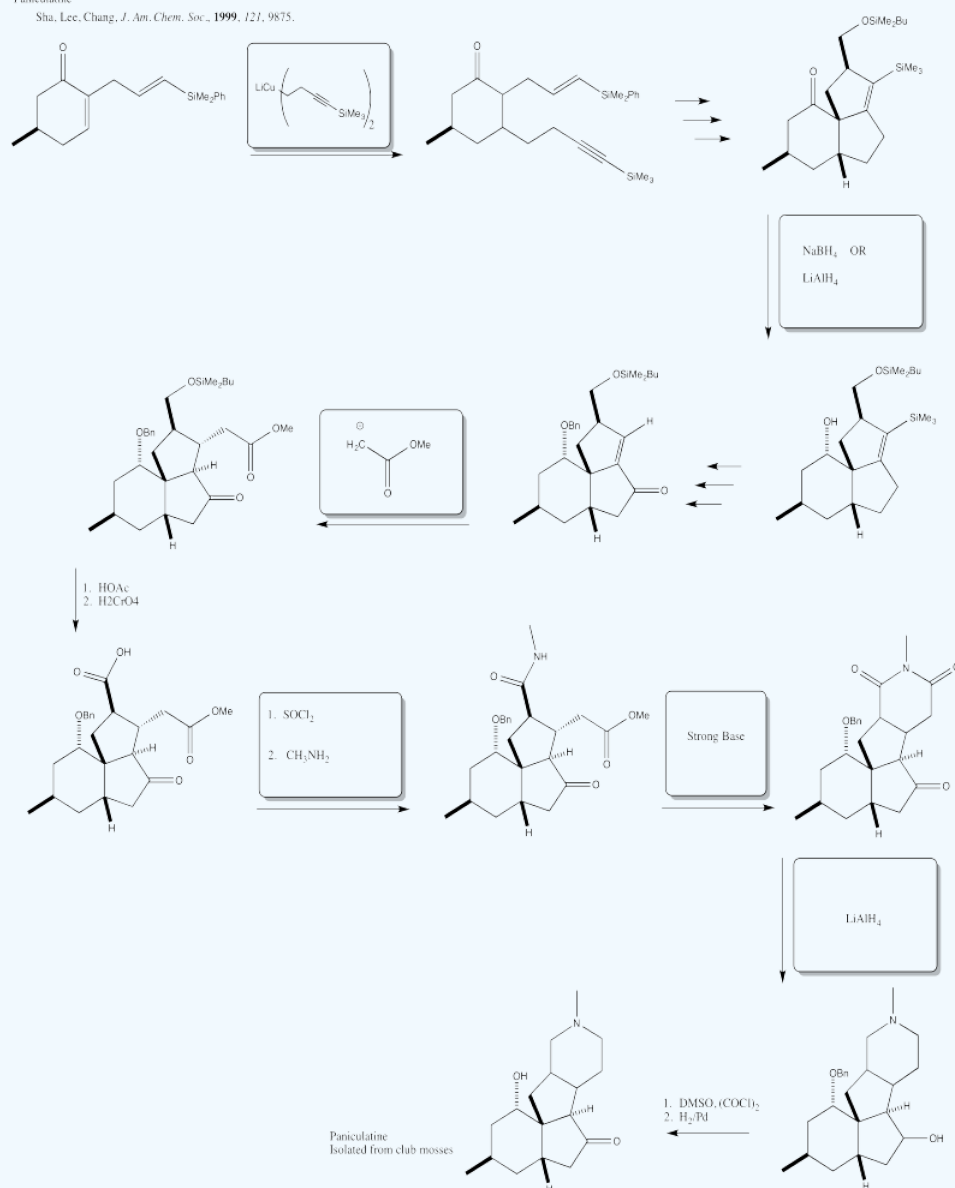


Answer



Paniculatin

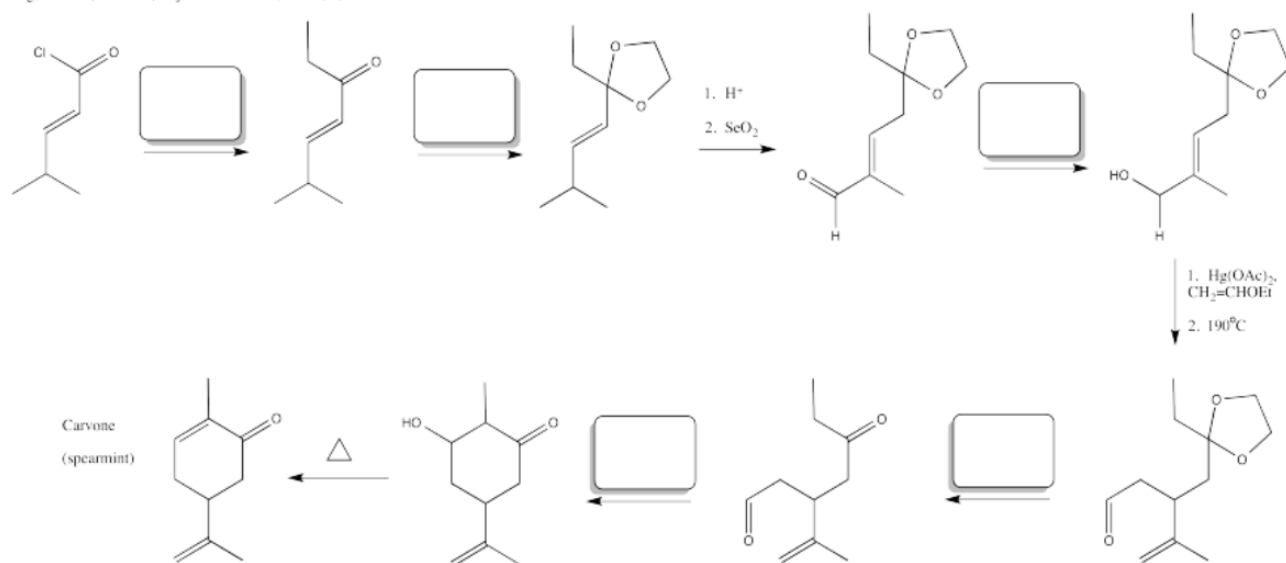
Sha, Lee, Chang, *J. Am. Chem. Soc.*, **1999**, *121*, 9875.



### Exercise 5.3.8

Fill in the blanks in the following synthesis involving *anionic nucleophilic addition to carbonyl*, *nucleophilic substitution at carboxyl* and *neutral nucleophilic addition to carbonyl*.

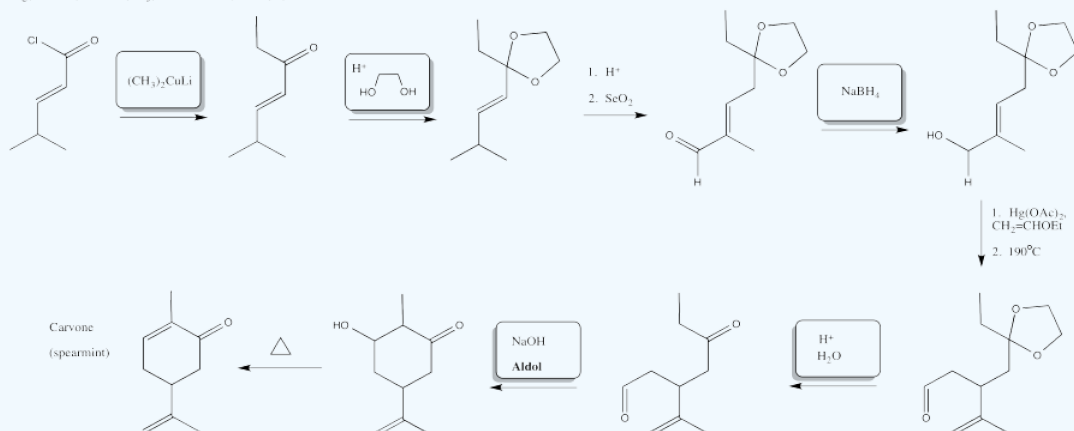
Vig, Sharma, Chander, Raj, *Ind. J. Chem.*, **1966**, *4*, 275.



**Answer**

Carvone

Vig, Sharma, Chander, Raj, *Ind. J. Chem.*, **1966**, *4*, 275.

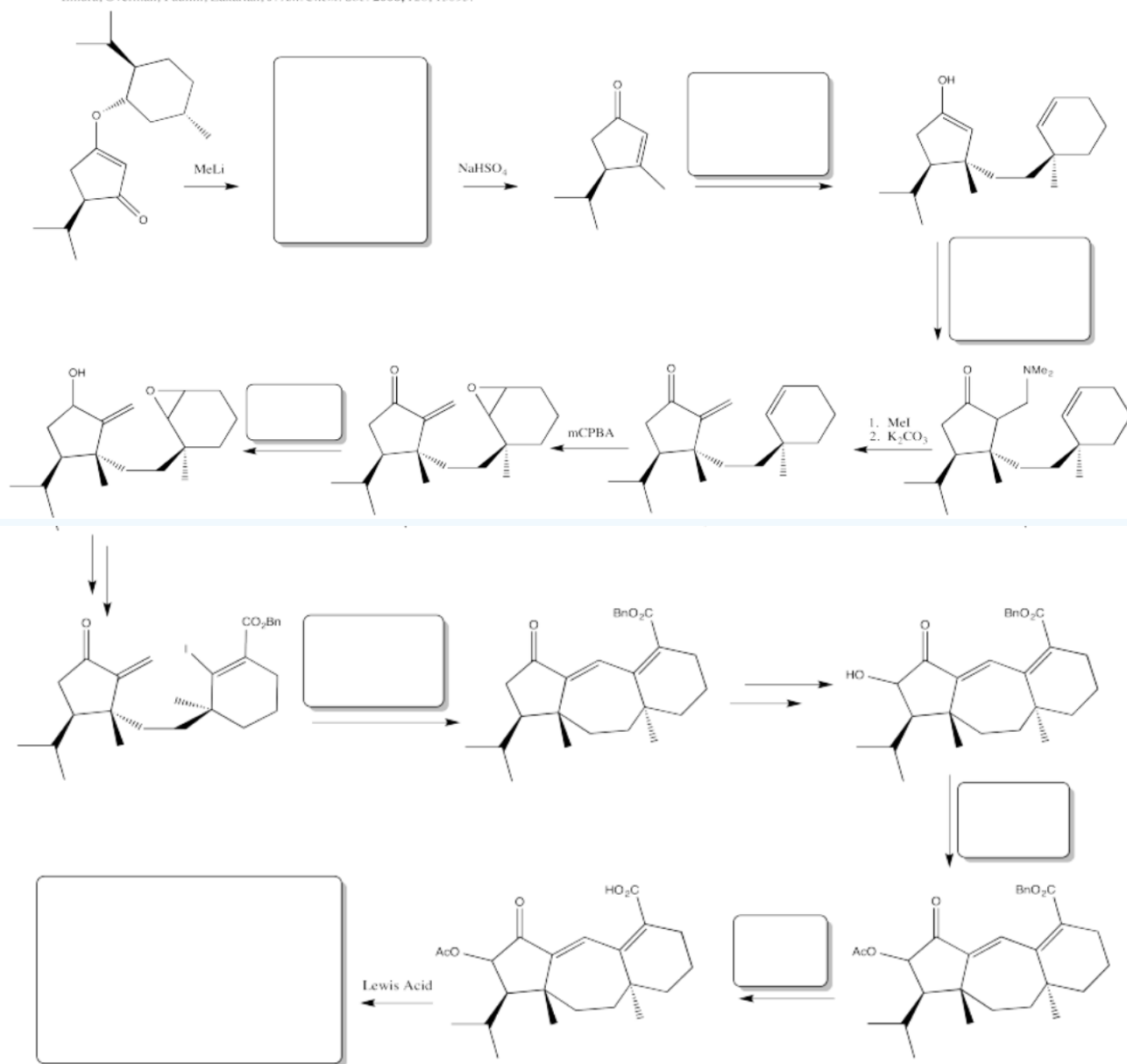


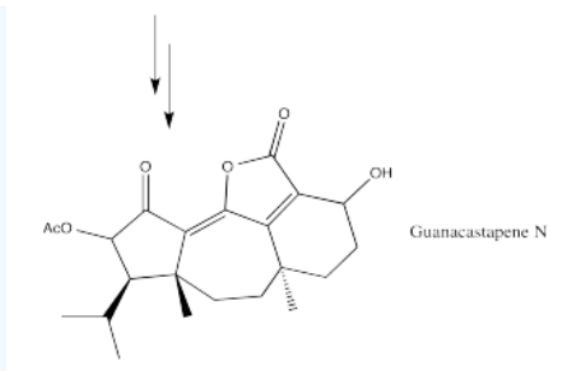
### Exercise 5.3.9

Fill in the blanks in the following synthesis involving anionic nucleophilic addition to carbonyl/em>, conjugate addition, nucleophilic substitution at carboxyl and transition metal-catalysed coupling.

Guanacastepene N

Imura, Overman, Paulini, Zakarian, *J. Am. Chem. Soc.* **2006**, *128*, 13095.

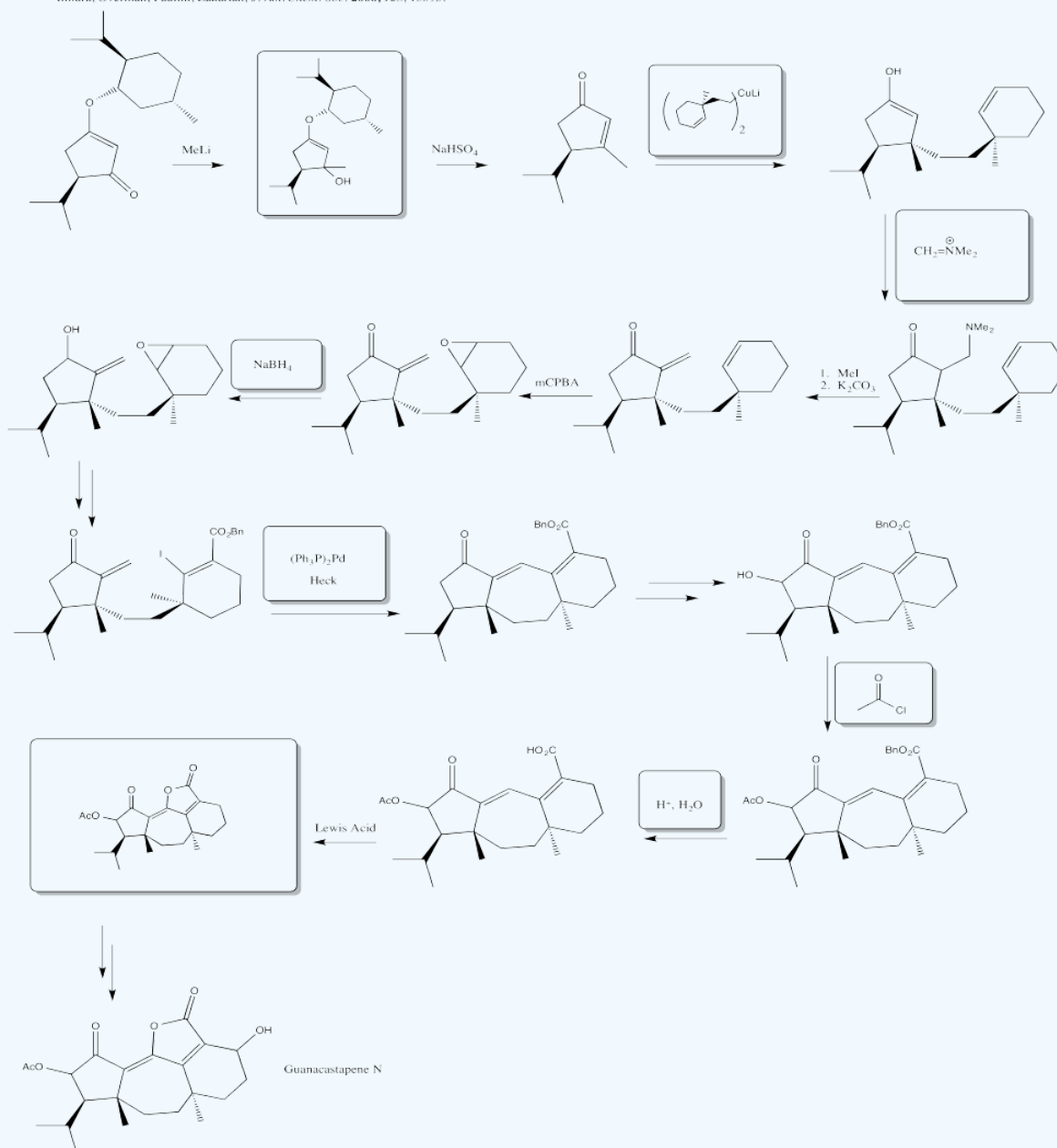




## Answer

Guanacastapene N

Imura, Overman, Paulini, Zakarian, *J. Am. Chem. Soc.* **2006**, 128, 13095.

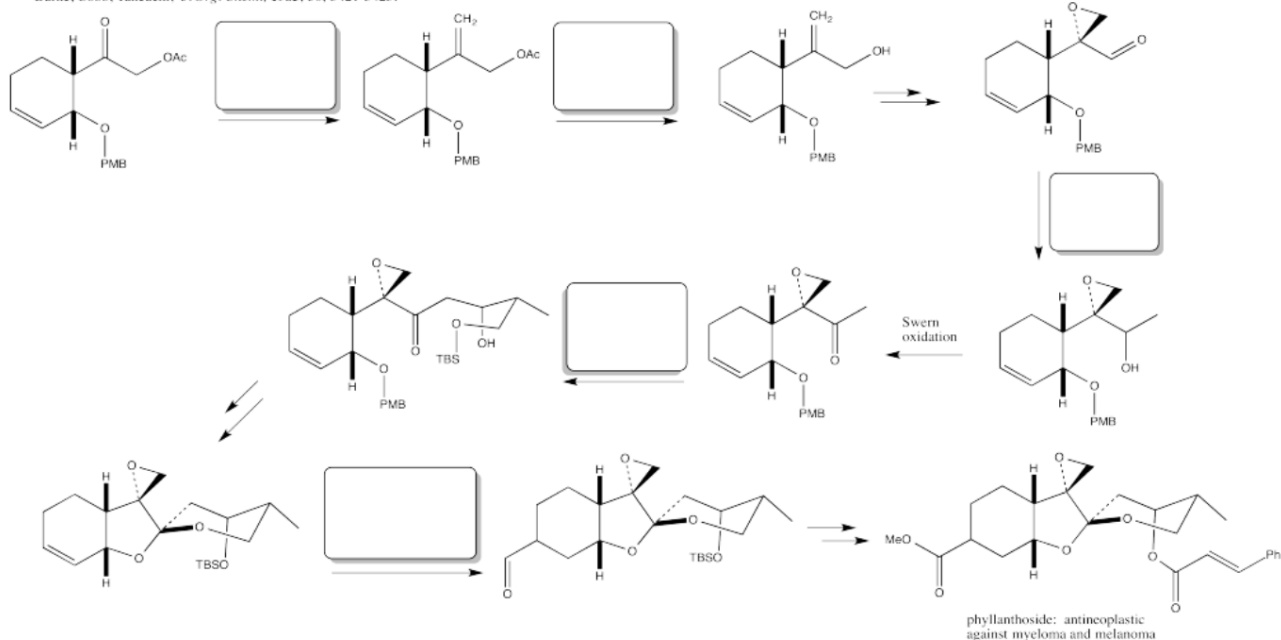


### Exercise 5.3.10

Fill in the blanks in the following synthesis involving *anionic nucleophilic addition to carbonyl*, *conjugate addition*, *nucleophilic substitution at carboxyl* and *transition metal-catalysed coupling*.

Phyllanthocin

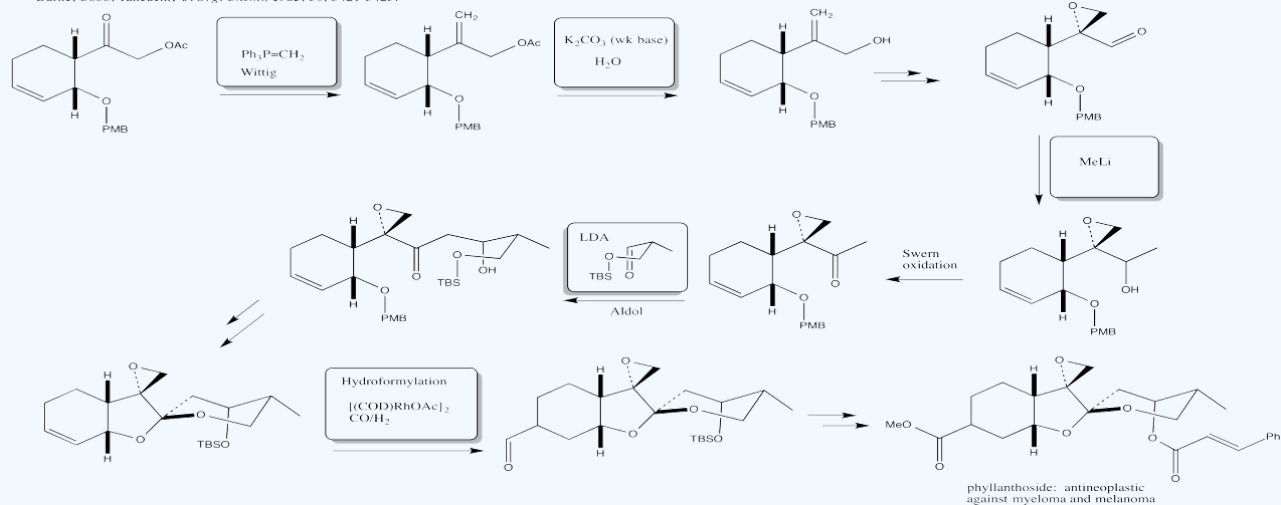
Burke, Cobb, Takeuchi, *J. Org. Chem.*, **1985**, *50*, 3421-3423.



Answer

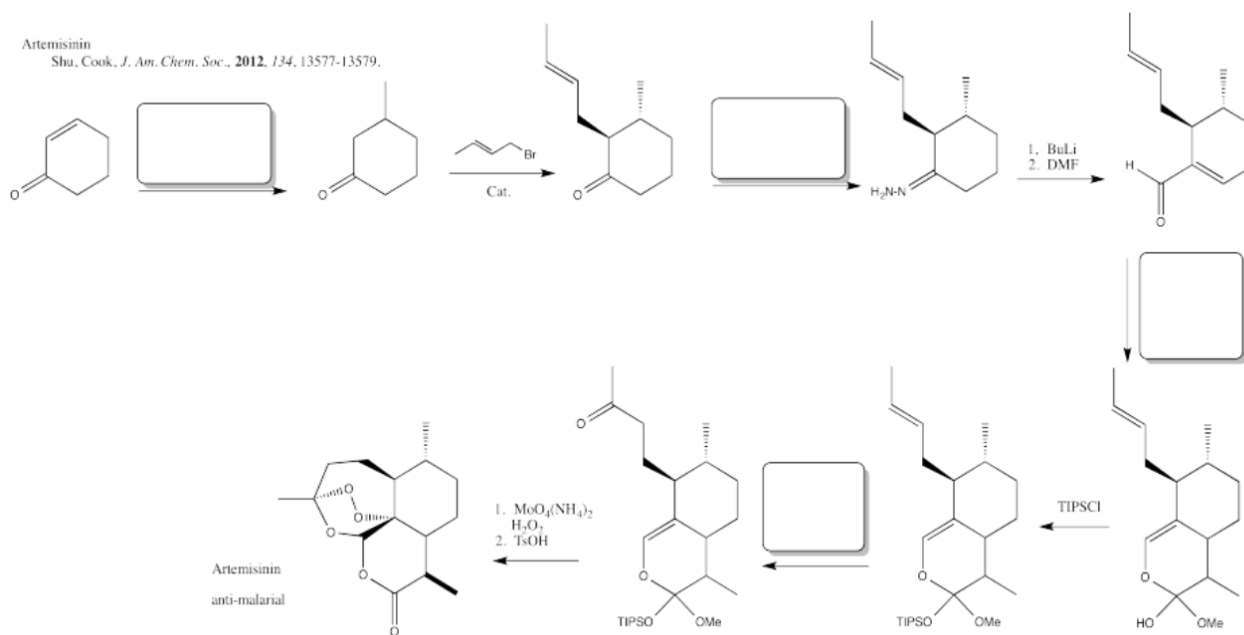
Phyllanthocin

Burke, Cobb, Takeuchi, *J. Org. Chem.*, **1985**, *50*, 3421-3423.

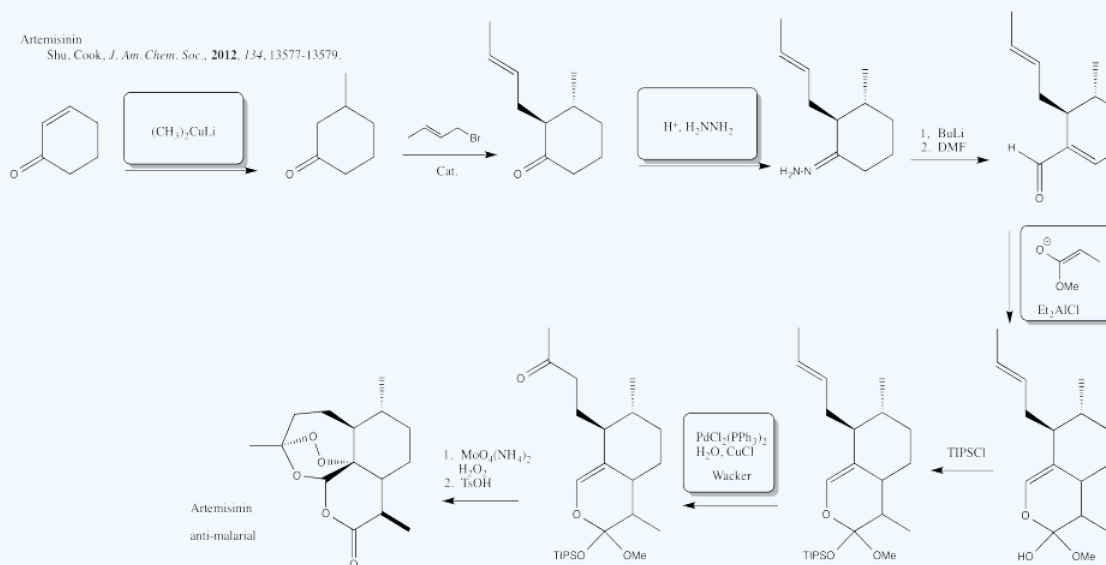


Exercise 5.3.11

Fill in the blanks in the following synthesis involving anionic nucleophilic addition to carbonyl, conjugate addition, nucleophilic substitution at carboxyl, transition metal-catalysed coupling and neutral nucleophilic addition to carbonyl.



### Answer

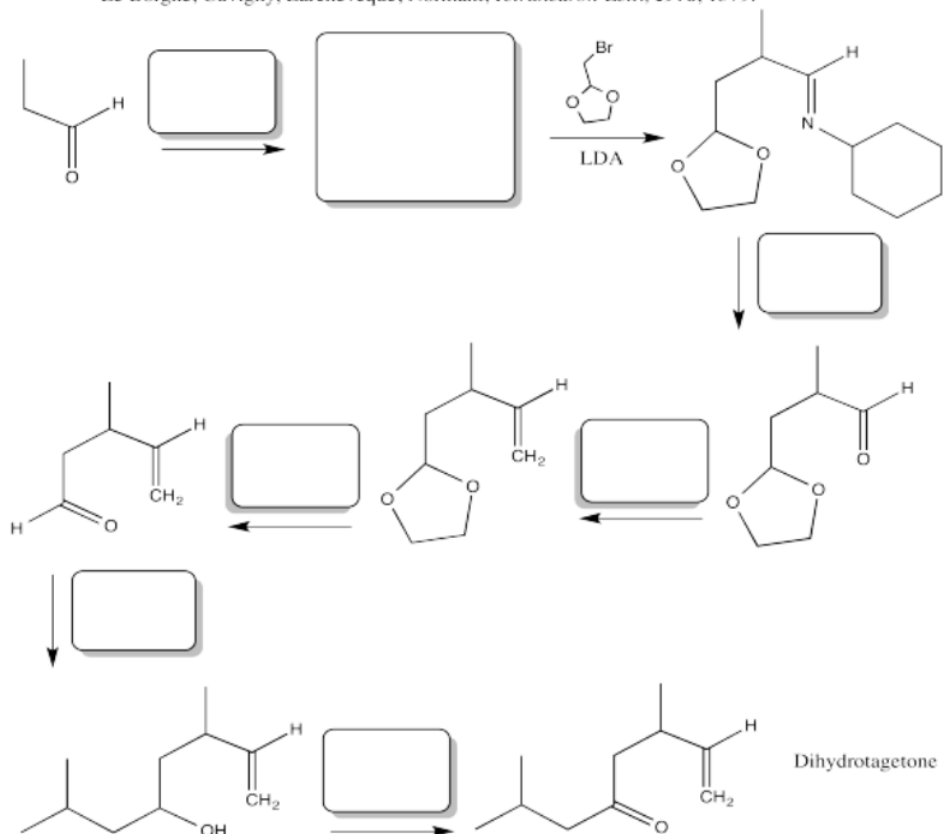


### Exercise 5.3.12

Fill in the blanks in the following synthesis involving anionic nucleophilic addition to carbonyl, conjugate addition, nucleophilic substitution at carboxyl, transition metal-catalysed coupling and neutral nucleophilic addition to carbonyl.

# Dihydrotagetone

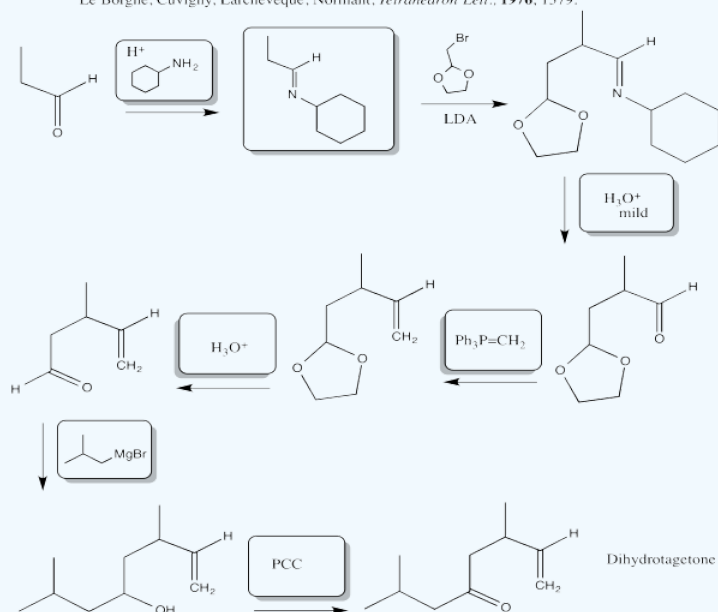
Le Borgne, Cuvigny, Larcheveque, Normant, *Tetrahedron Lett.*, **1976**, 1379.



## Answer

### Dihydrotagetone

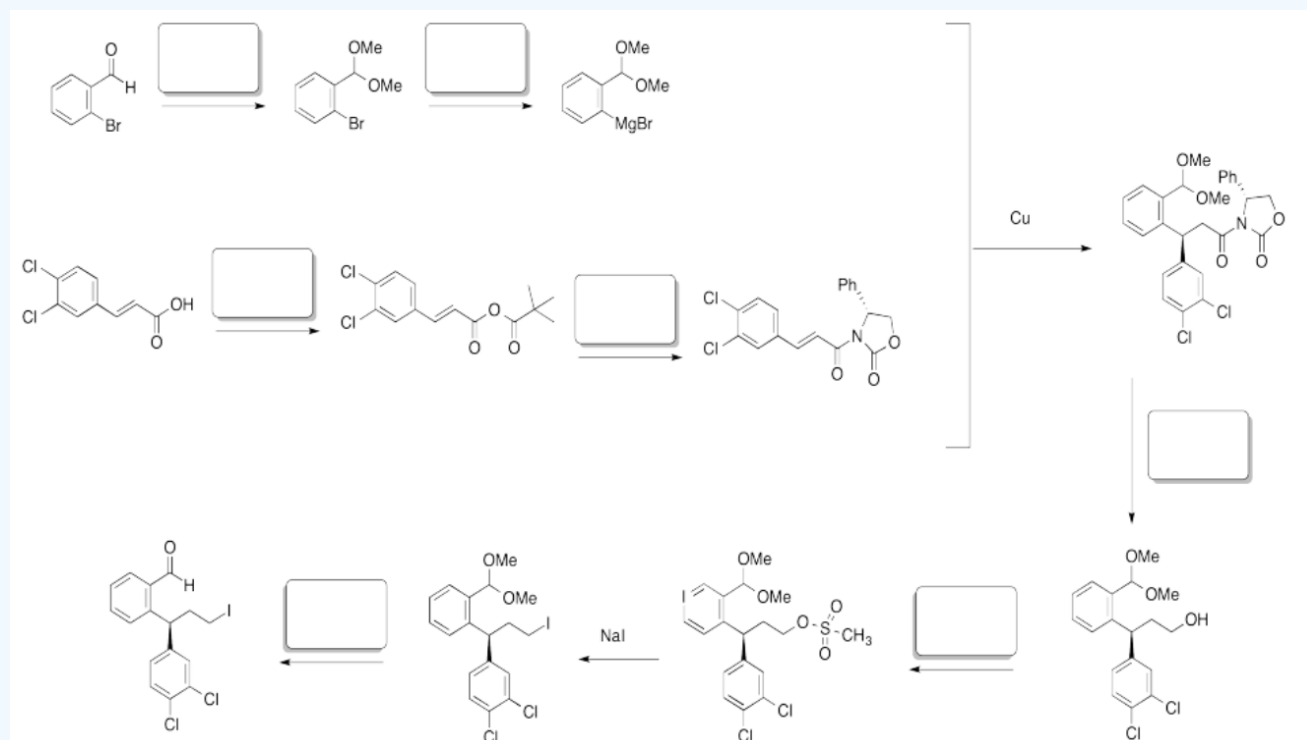
Le Borgne, Cuvigny, Larcheveque, Normant, *Tetrahedron Lett.*, **1976**, 1379.

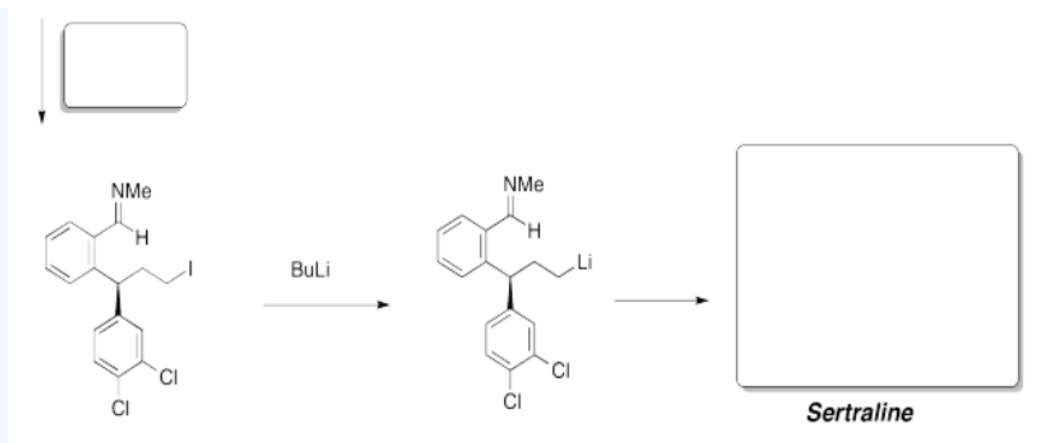




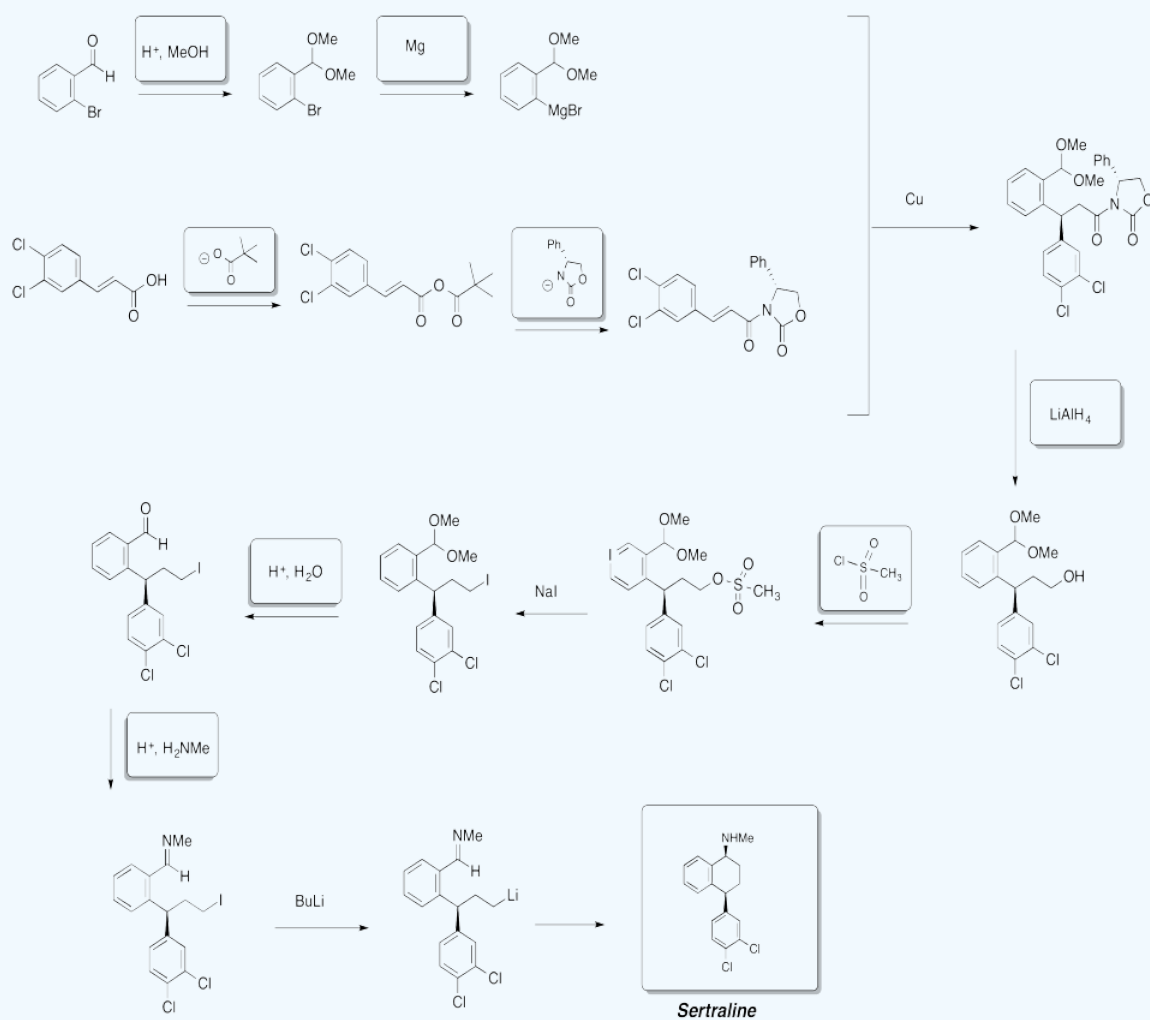
### Exercise 5.3.13

Fill in the blanks in the following synthesis involving anionic nucleophilic addition to carbonyl, conjugate addition, nucleophilic substitution at carboxyl, transition metal-catalysed coupling and neutral nucleophilic addition to carbonyl.



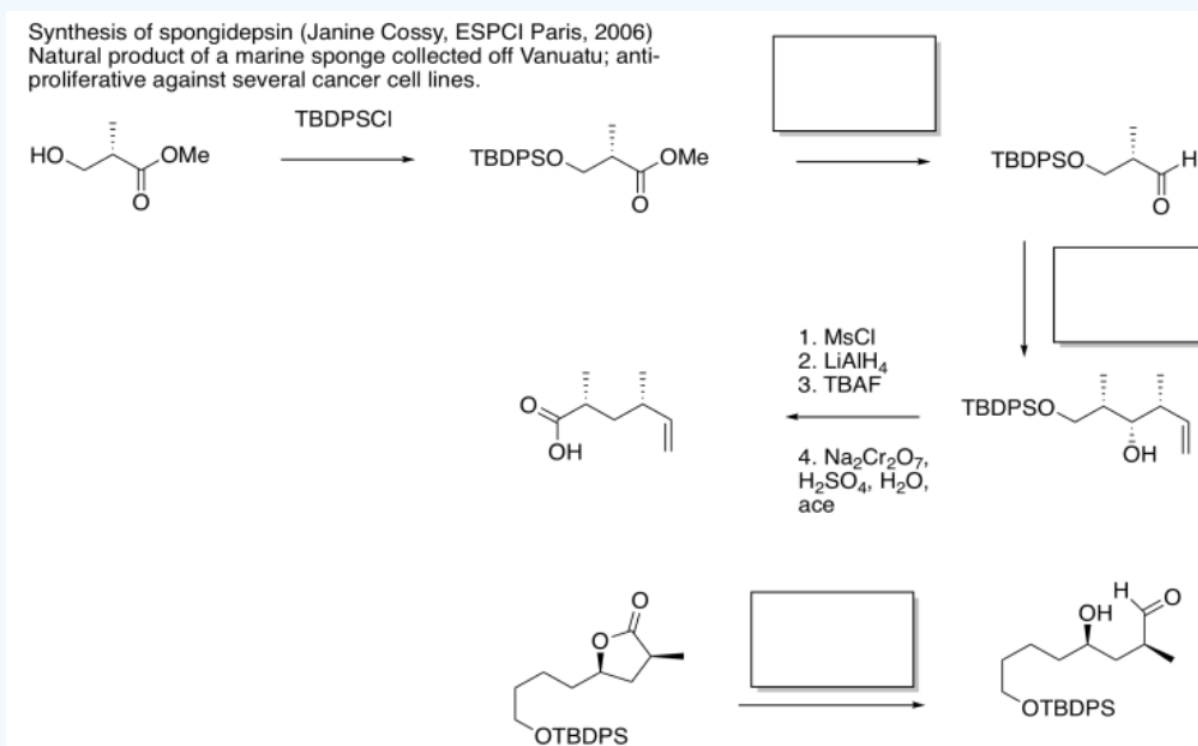


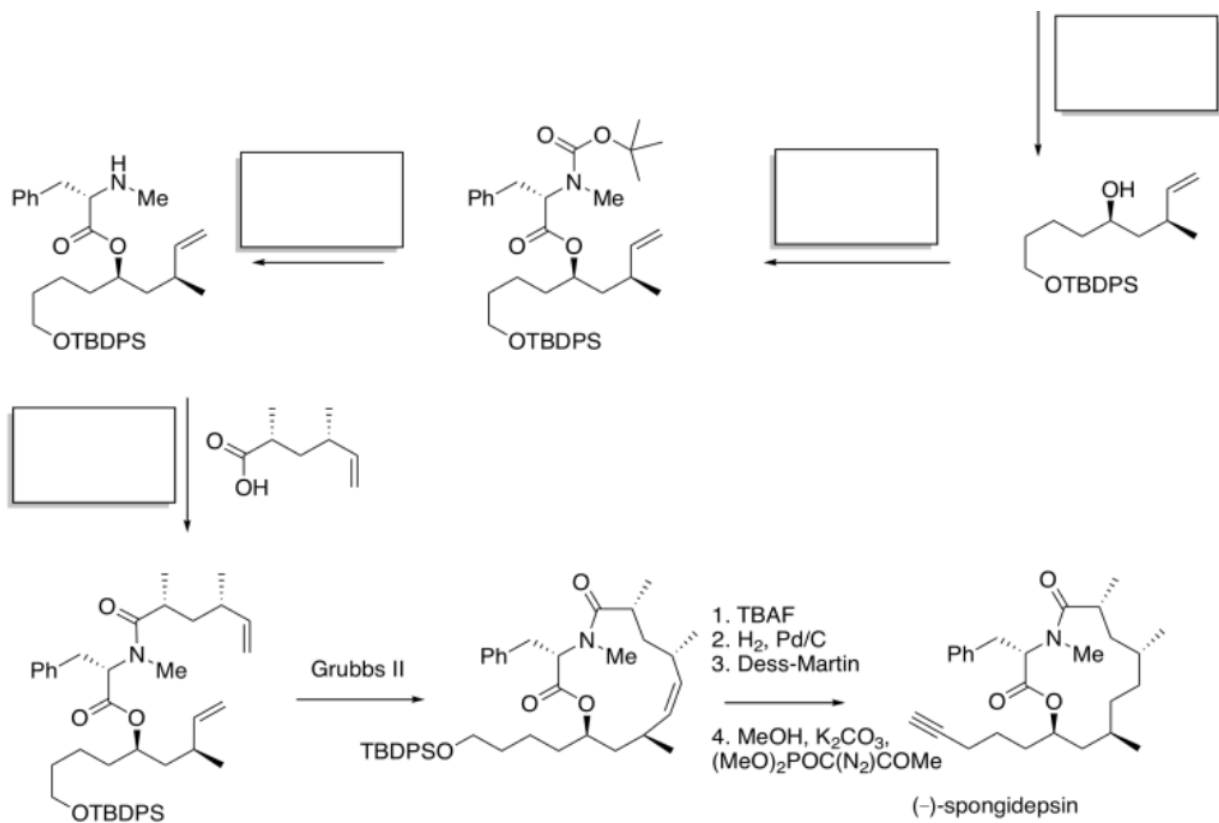
### Answer



### Exercise 5.3.14

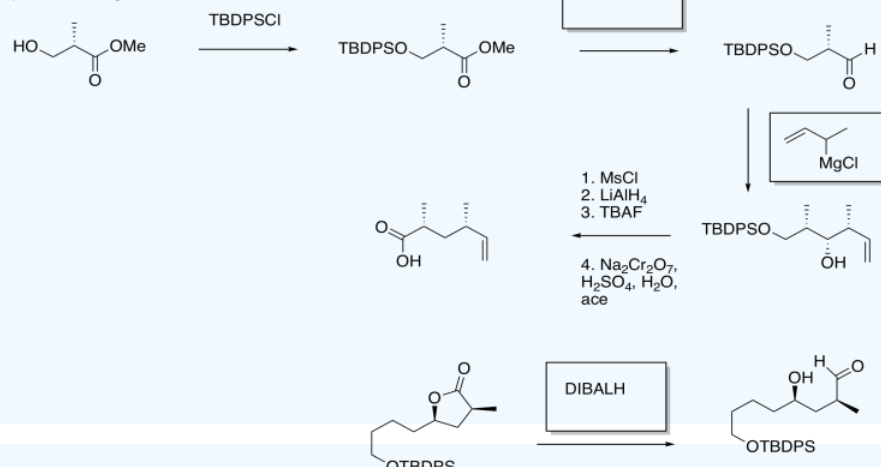
Fill in the blanks. Requires knowledge of formation of esters and amides as well as Wittig or Horner-Wadworth-Emmons reactions.





**Answer**

Synthesis of spongidepsin (Janine Cossy, ESPCI Paris)  
Natural product of a marine sponge collected off Vanuatu; anti-proliferative against several cancer cell lines.

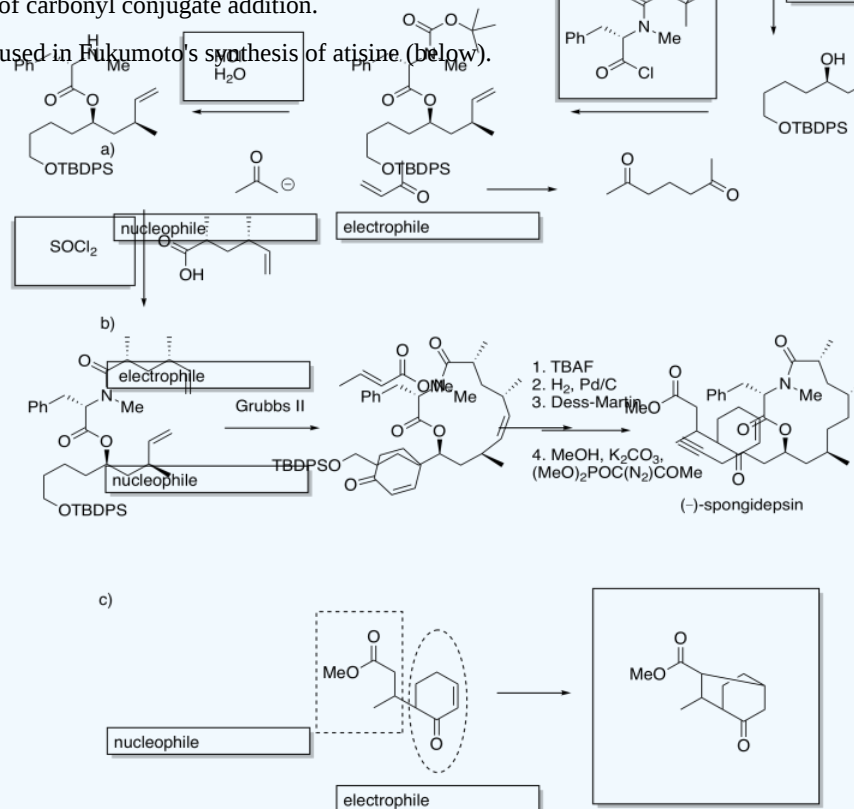


### Exercise 5.3.15

In each case, analyse whether the starting material is a nucleophile or electrophile. Fill in the product in part (c). This question requires knowledge of carbonyl conjugate addition.

These strategies are used in Fukumoto's synthesis of atisine (below).

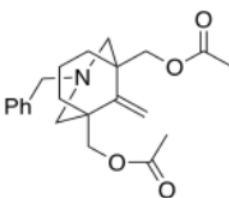
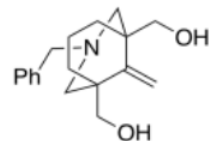
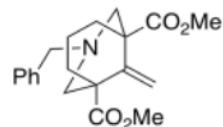
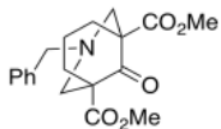
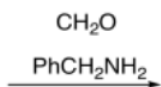
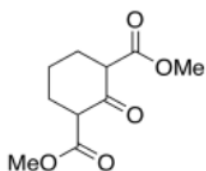
Answer



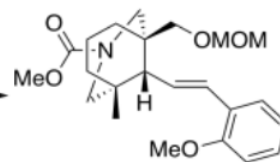
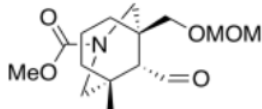
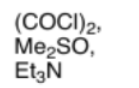
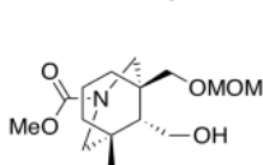
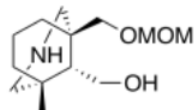
### Exercise 5.3.16

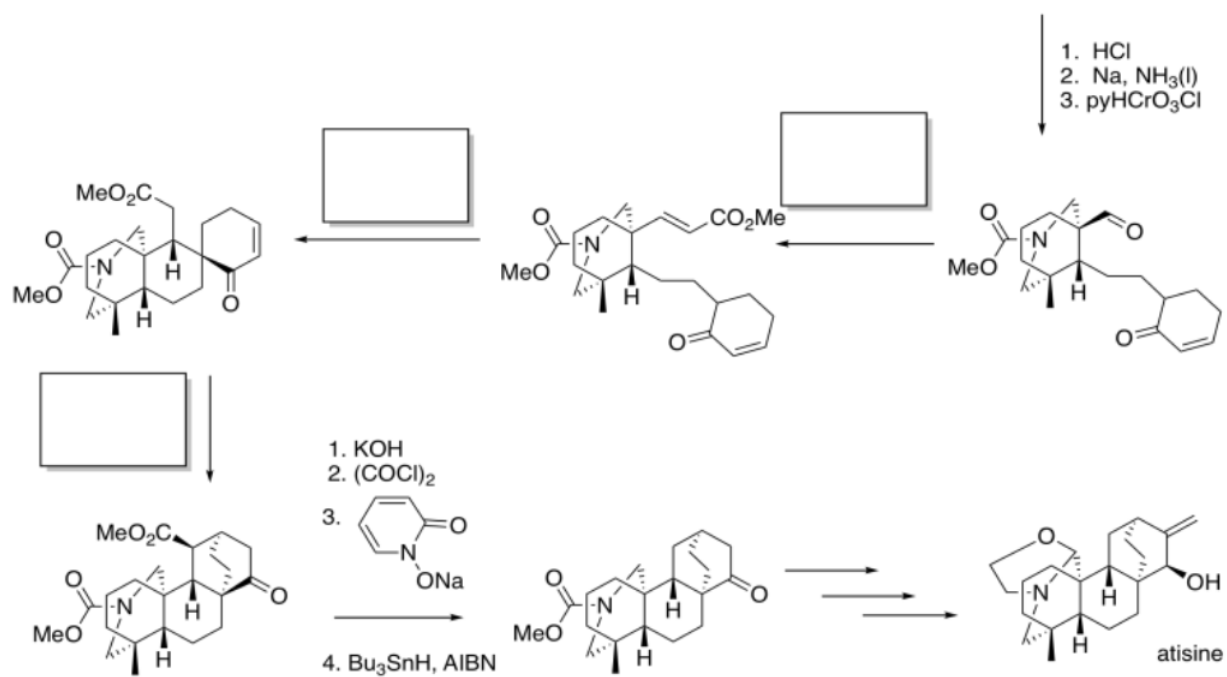
Fill in the blanks in the following synthesis of atisine (Keiichiro Fukumoto, Tohoku University). Atisine is a natural product of *Aconitum sp.*, the family of poisonous plants that includes wolfsbane.

Requires knowledge of conjugate addition / Michael reaction, ester reductions, formation of esters and amides, and Wittig or Horner-Wadworth-Emmons reactions.

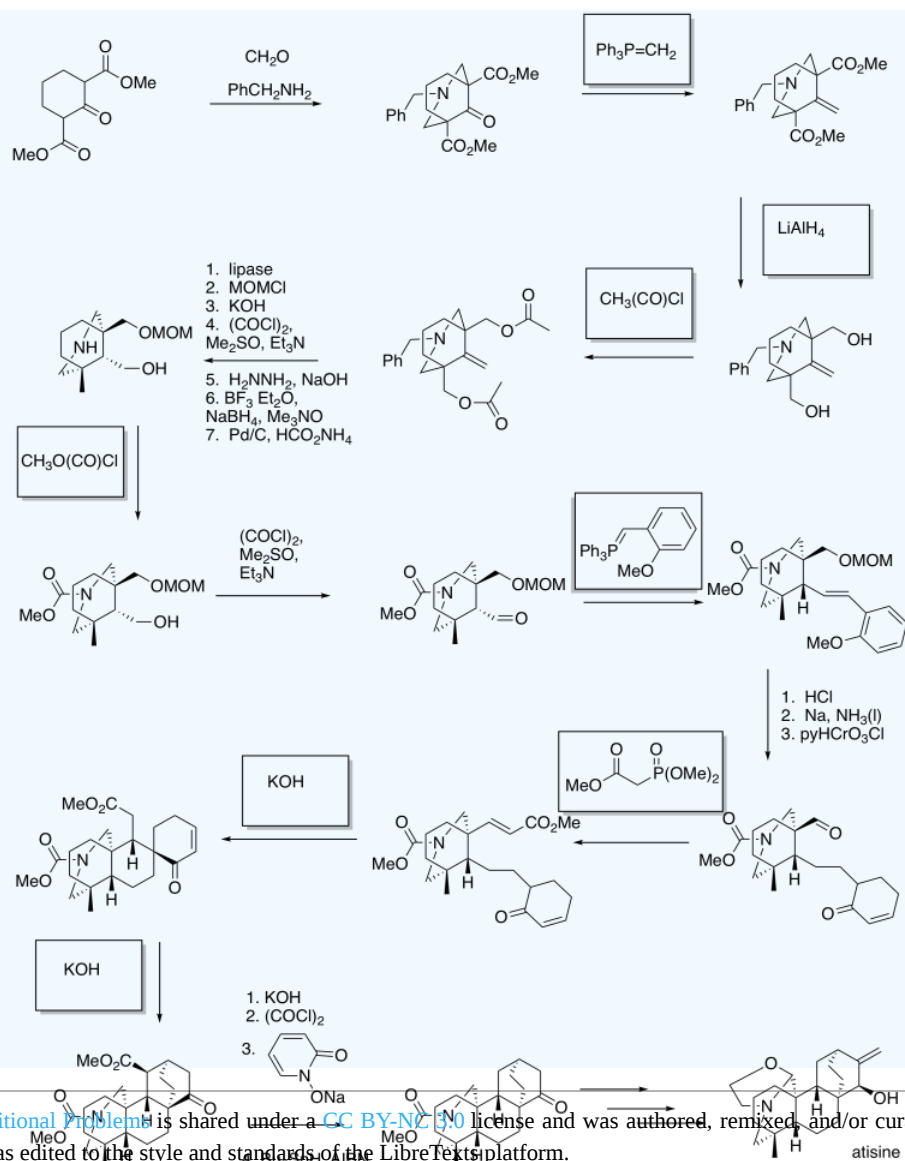


1. lipase
2. MOMCl
3. KOH
4.  $(\text{COCl})_2$ ,  $\text{Me}_2\text{SO}$ ,  $\text{Et}_3\text{N}$
5.  $\text{H}_2\text{NNH}_2$ ,  $\text{NaOH}$
6.  $\text{BF}_3 \cdot \text{Et}_2\text{O}$ ,  $\text{NaBH}_4$ ,  $\text{Me}_3\text{NO}$
7.  $\text{Pd/C}$ ,  $\text{HCO}_2\text{NH}_4$





Answer



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