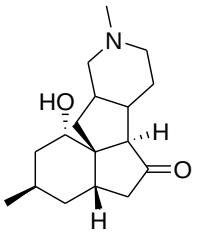
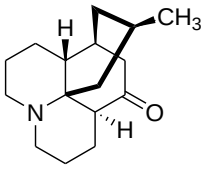
Total synthesis of (+)-paniculatine[1]



1
(+)-paniculatine



2
lycopodin

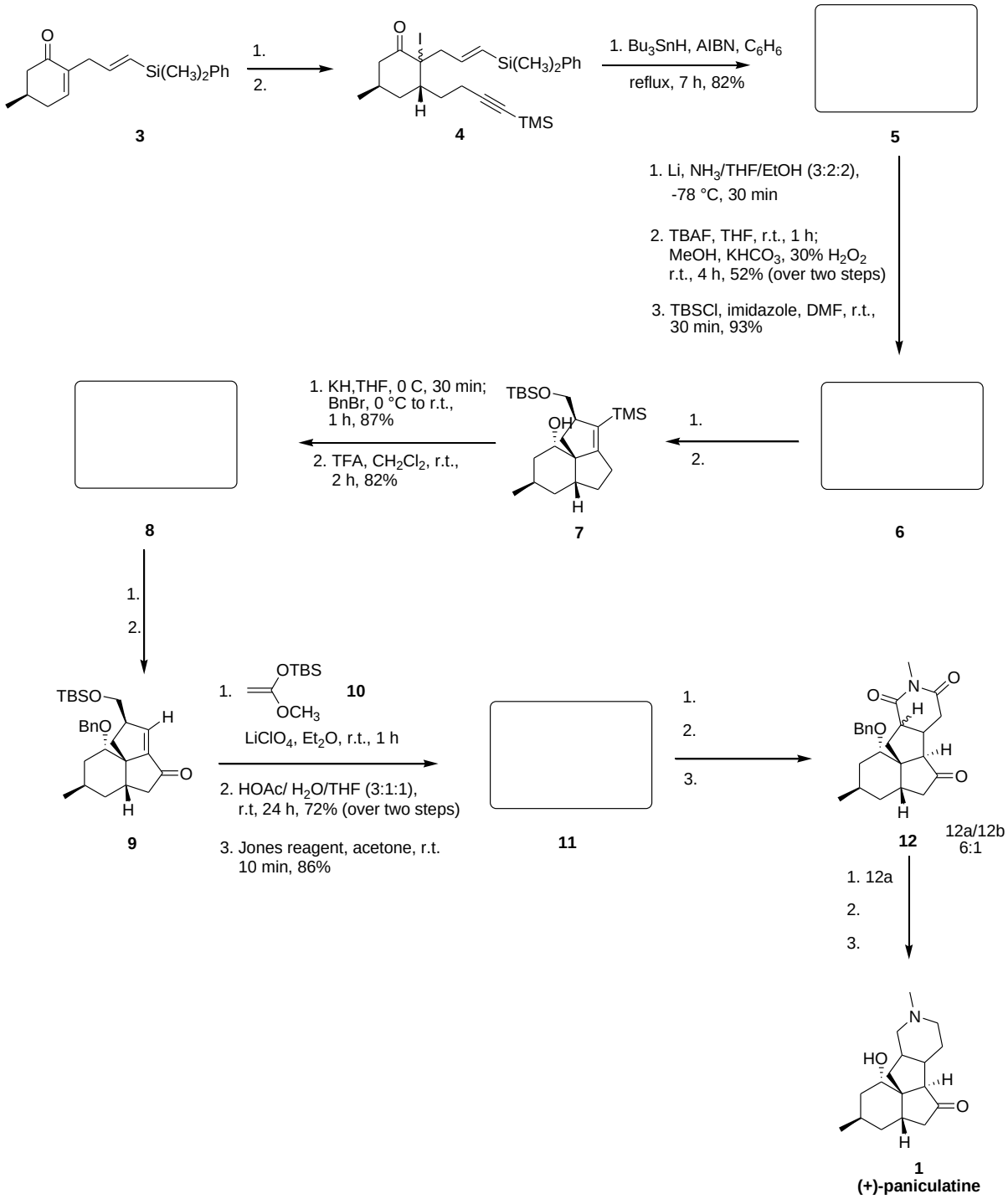
Paniculatine (**1**) was isolated from club moss paniculatum by Castillo *et. al*. in the mid of the 1970s and belongs to a subclass of *Lycopodium* alkaloids.[2] The main alkaloid of the $C_{16}N$-type of the *Lycopodium* alkaloids is lycopodin (**2**), which is toxic and shows paralyzing effect. In China different alkaloids of this type are traditionally used to medicate skin diseases.

This problem deals with the first total synthesis of **1** finished by Sha and co-workers via a α-carbonyl radical cyclisation as the main step in 1999. [1] Although no biological activity and pharmacological potential have so far been published, other *Lycopodium* alkaloids are reported to be potent acetylcholinesterase inhibitors or show promising results in the treatment of Alzheimer's disease.[3]

Questions:

Please complete the synthesis shown in scheme 1, giving reagents and mechanisms where appropriate.

Scheme 1: Synthesis of (+)-paniculatine (**1**)



Reference

1. Sha, C.-K.; Lee, F.-K.; Chang, C.-J., *J. Am. Chem. soc.* **1999,** 121, 9875-9876.
2. Castillo, M.; Morales, G.; Loyola, L. A.; Singh, I.; Calvo, C.; Holland, H. L.; McLean, D. B., *Can. J. Chem.* **1975,** 53, 2513-2514.
3. Ayer, W. A., *J. Nat. Prod. Rep.* **1991,** 8, 455-463.