

# Problem Session (4) -Answer

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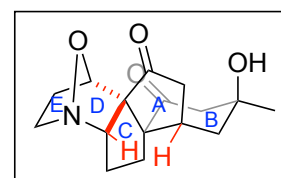
**Topic:** Total Synthesis of Fawcettimine-Type Alkaloid, Lycojaponicum A

## 0. Introduction

### 0-1. Isolation:

*Lycopodium japonicum* THUNB

(Li, Y. et al. *Org. Lett.* **2012**, *14*, 2614.)



**(0-1)**

Lycojaponicum A

### 0-2. Bioactivity:

inhibition toward lipopolysaccharide (LPS)-induced pro-inflammatory factors

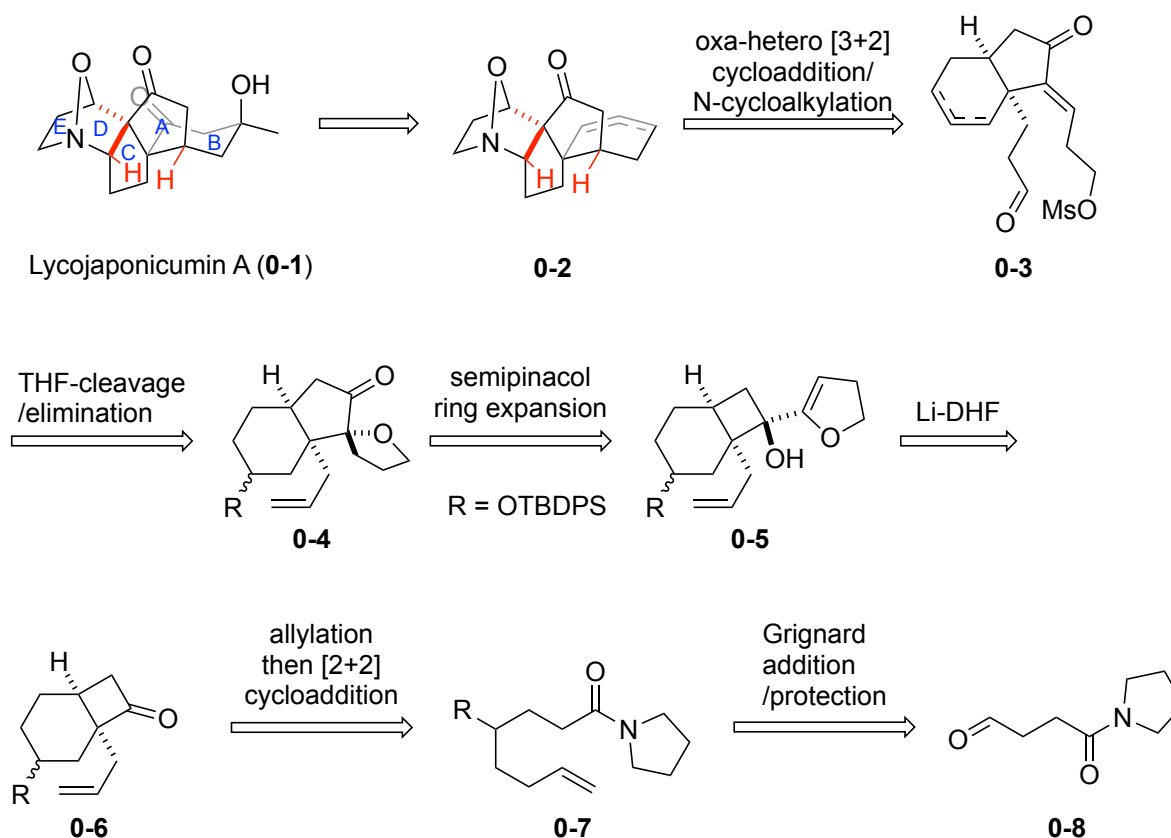
(Li, Y. et al. *Org. Lett.* **2012**, *14*, 2614.)

### 0-3. Structural features

[6,5]-bicyclic moiety (A and B rings)

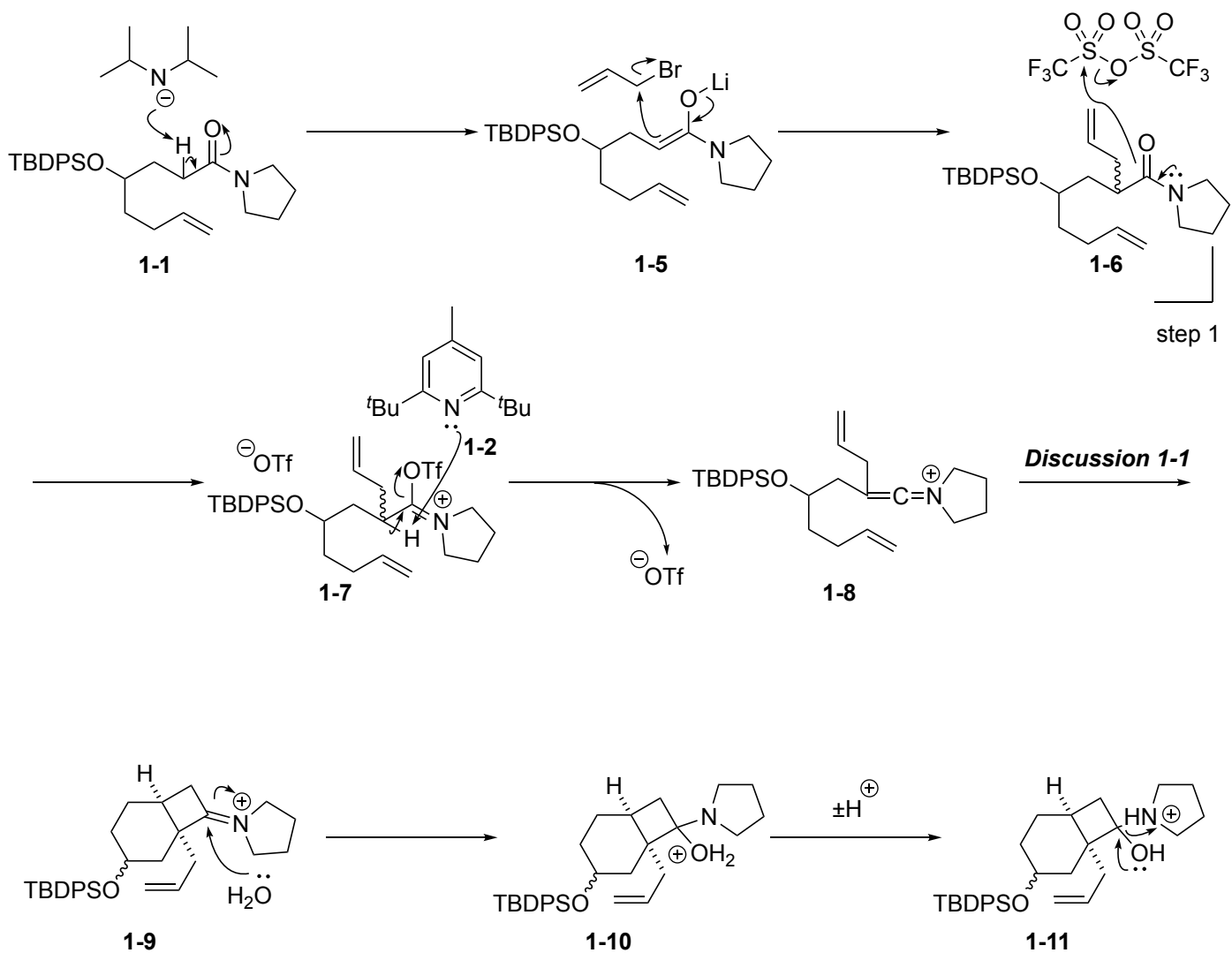
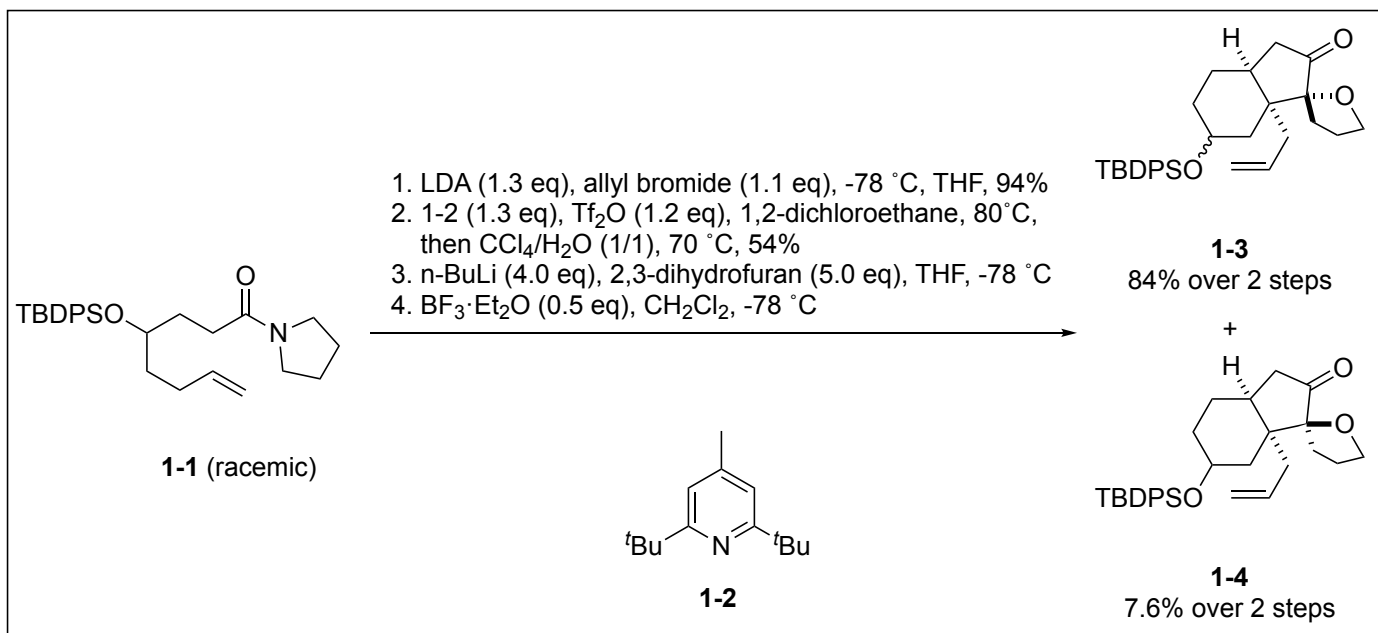
a highly strained tetrahydroisoxazole-contained system (rings C–E).

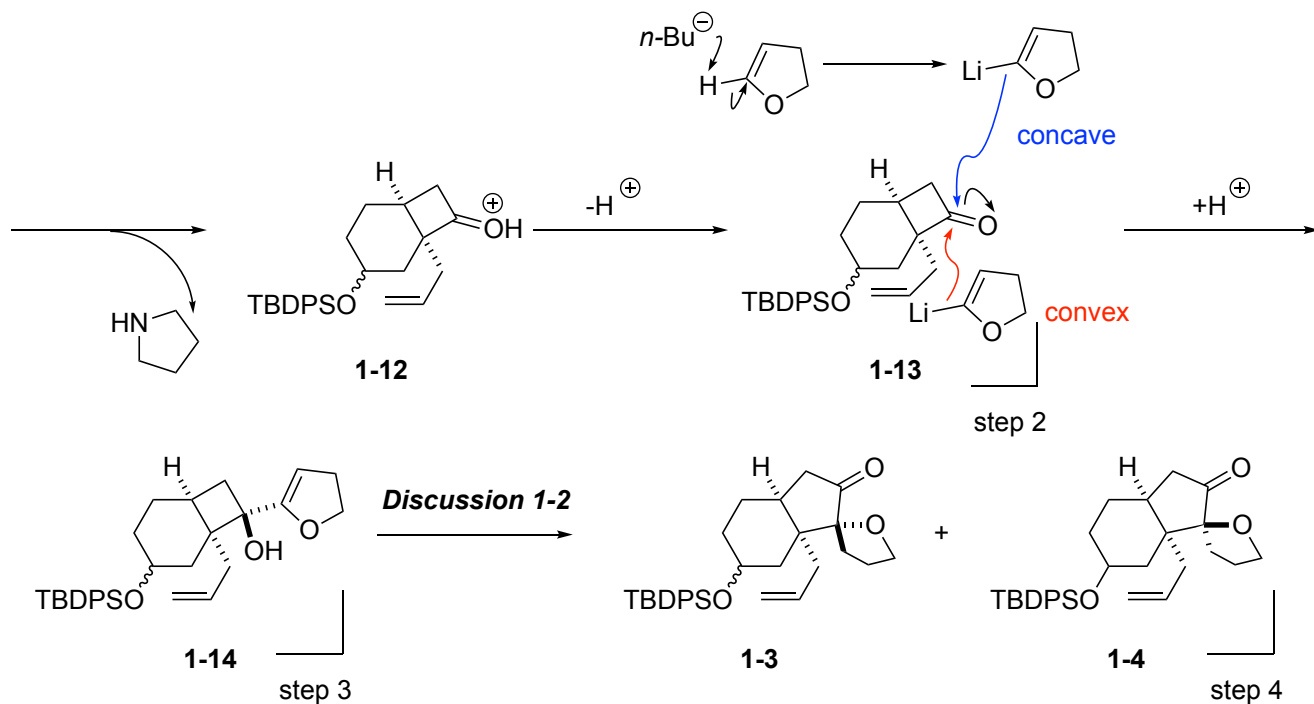
### 0-4. Retro-synthesis



Shao, H. et al. *Org. Lett.* **2020**, *22*, 3775.

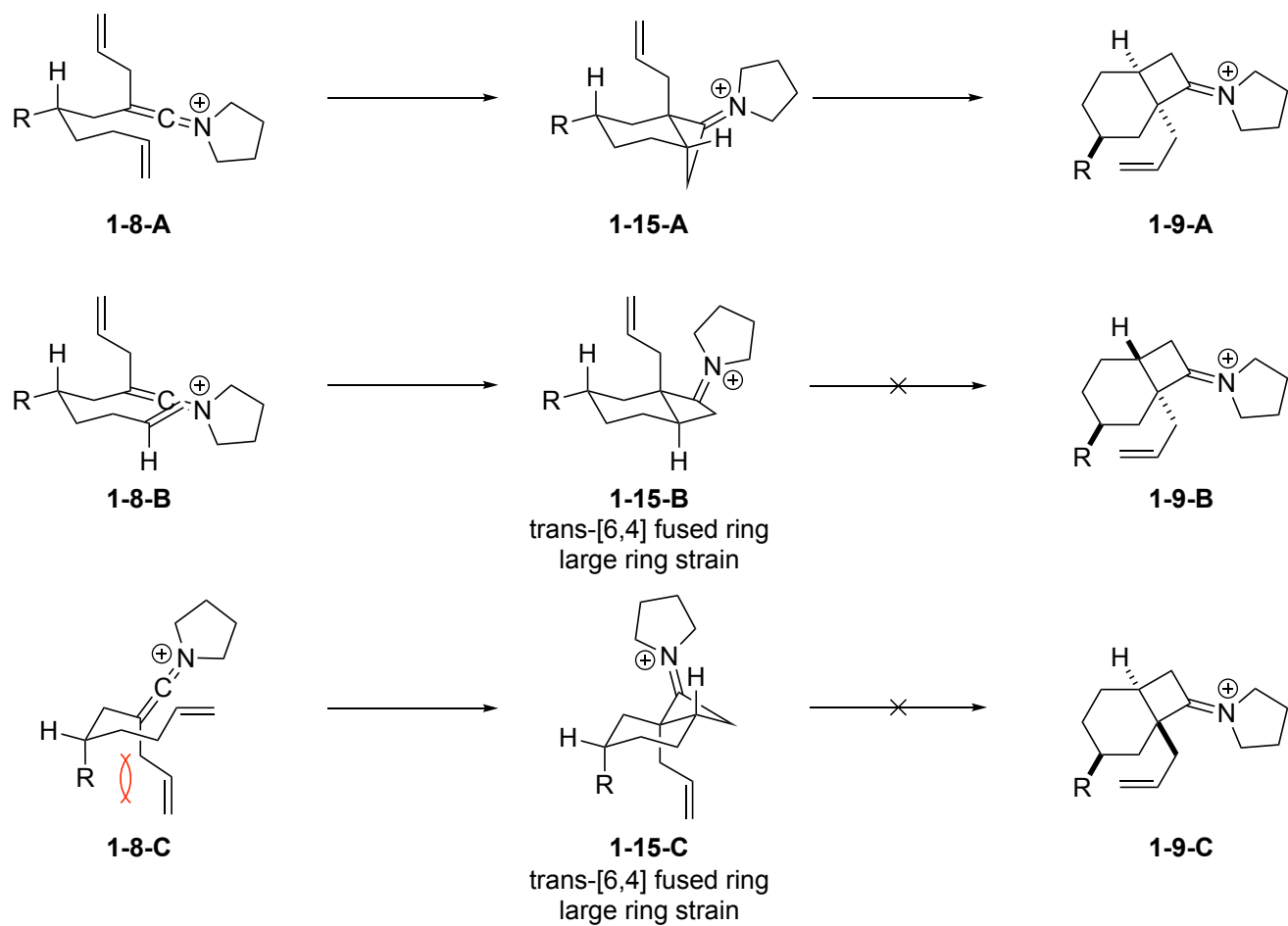
**Problem 1**

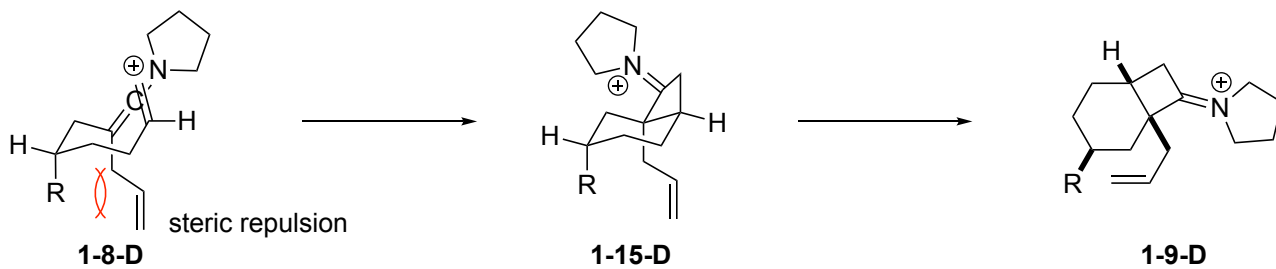




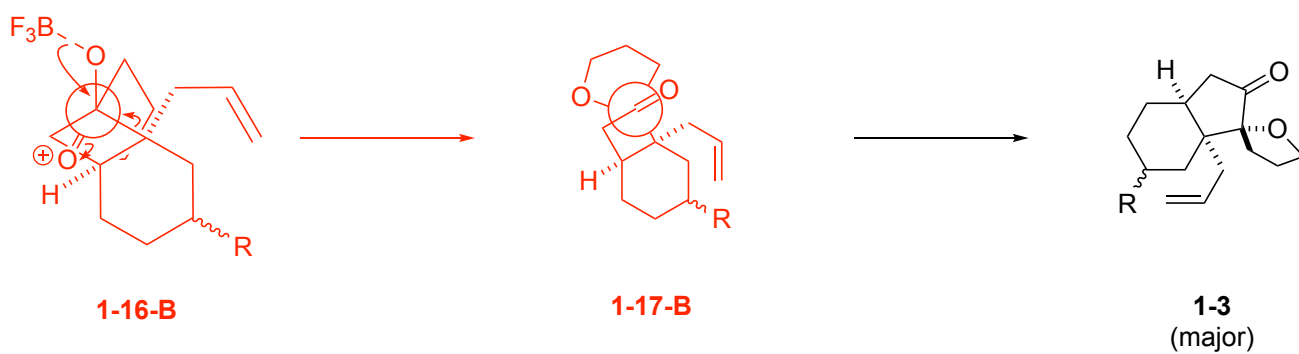
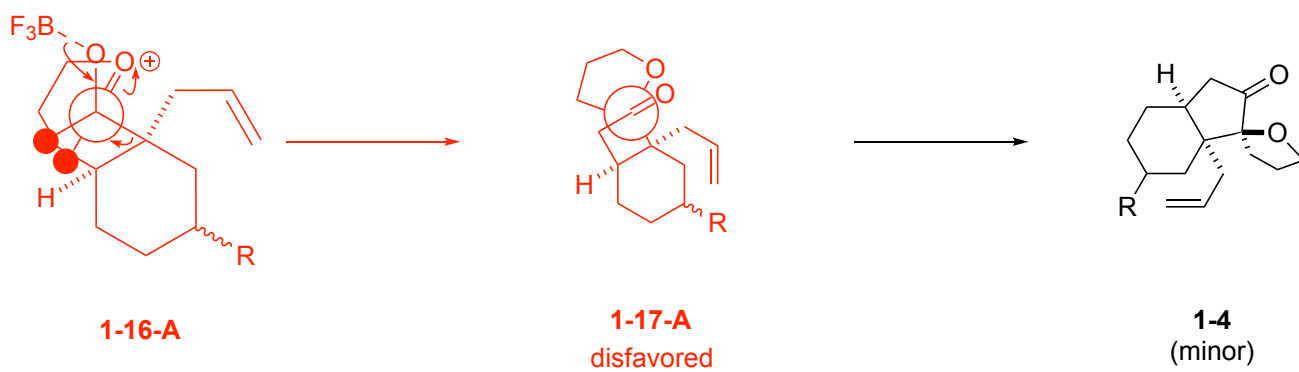
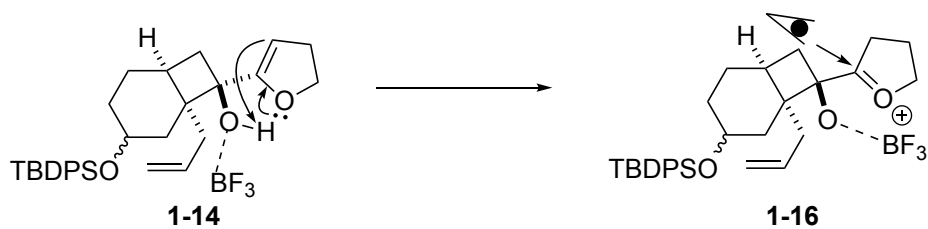
### Discussion 1-1

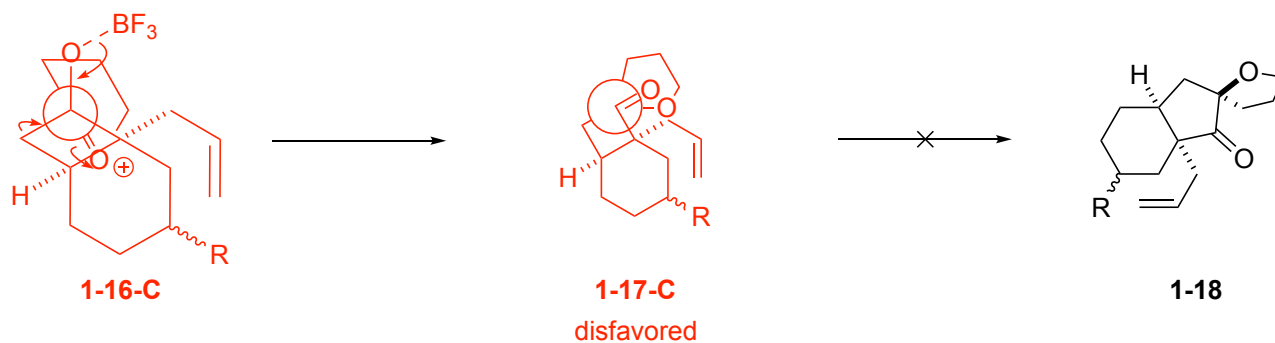
R = OTBDPS



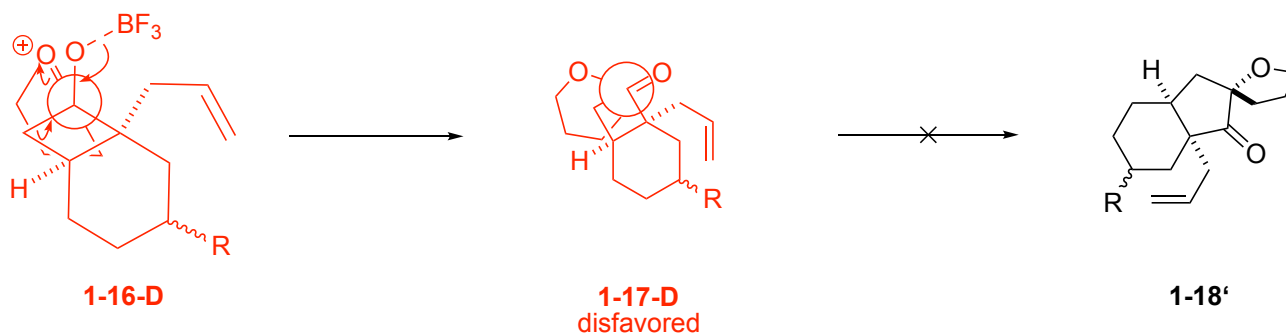


**Discussion 1-2**



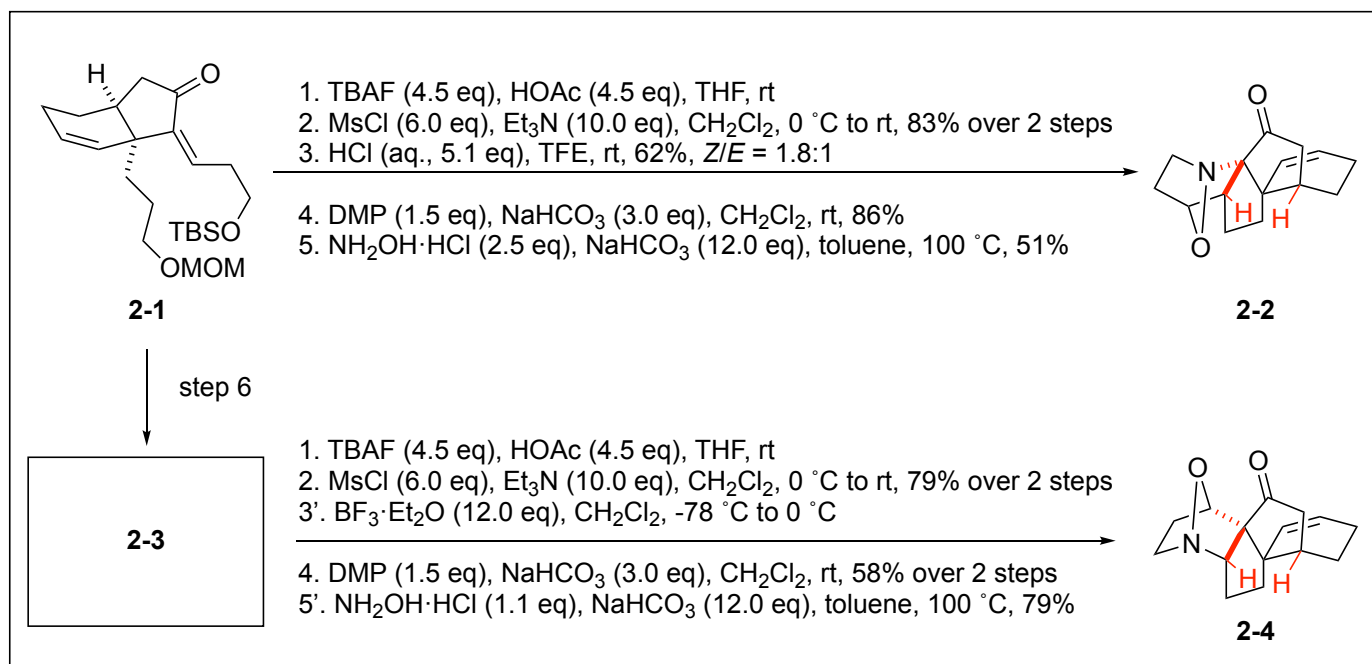


The electron-rich quaternary carbon is more favorable to afford rearrangement.

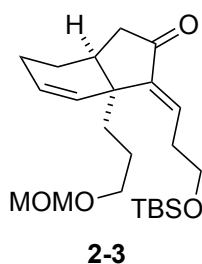


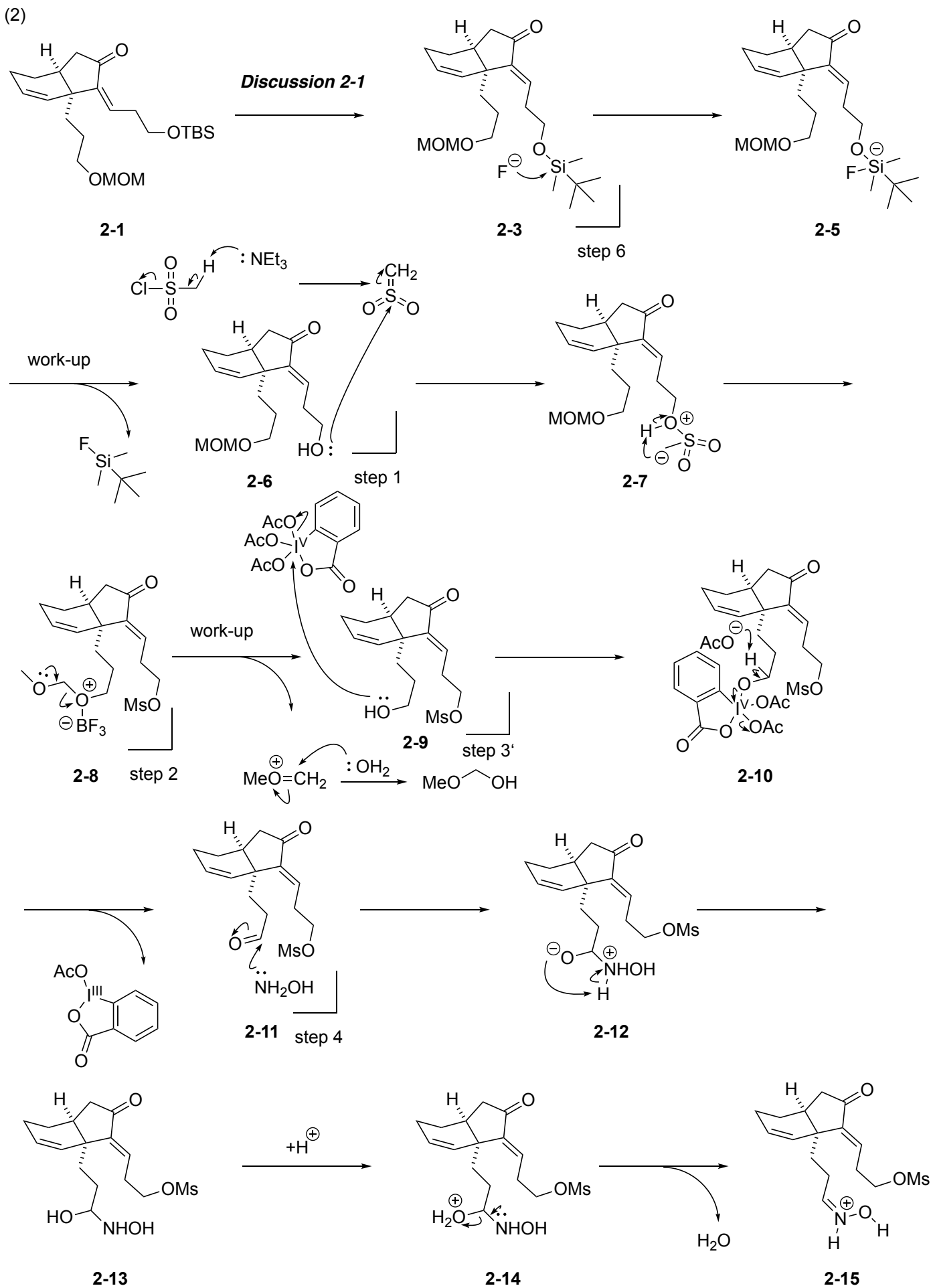
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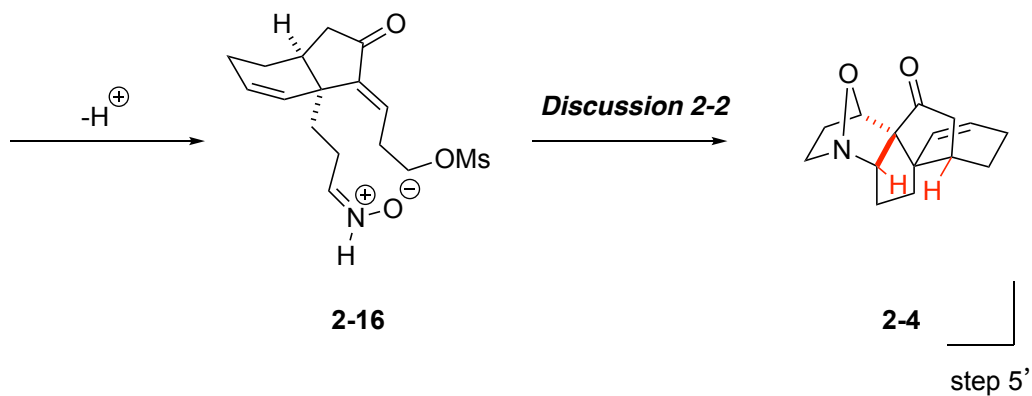
## Problem 2



(1) step 6: hv (395 nm, 50W), MeCN, rt





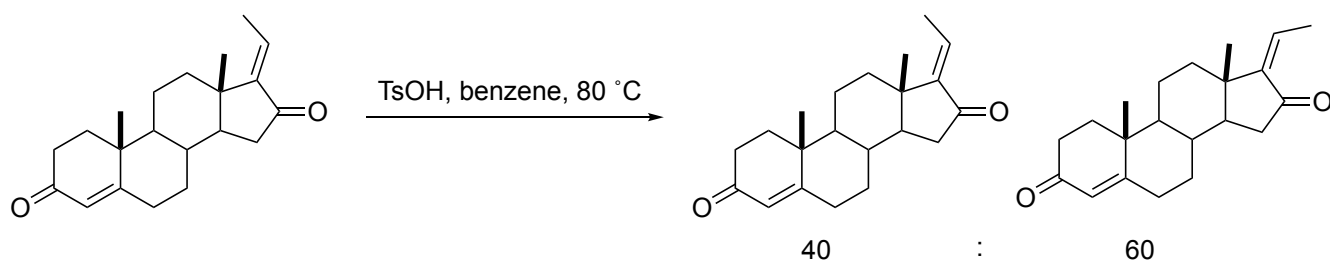


The mechanism of **2-1** to **2-2** was similar to **2-3** to **2-4**, so it is neglected here.

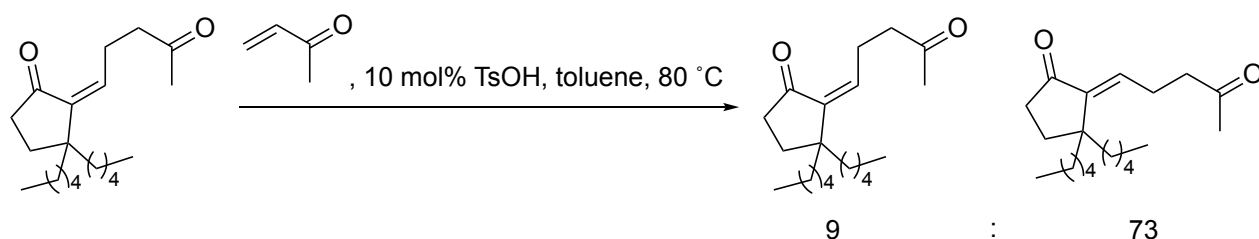
### Discussion 2-1

According to the author, although a wide variety of acidic and thermodynamic conditions were screened, isomerization of **2-1** to **2-3** could not be realized.

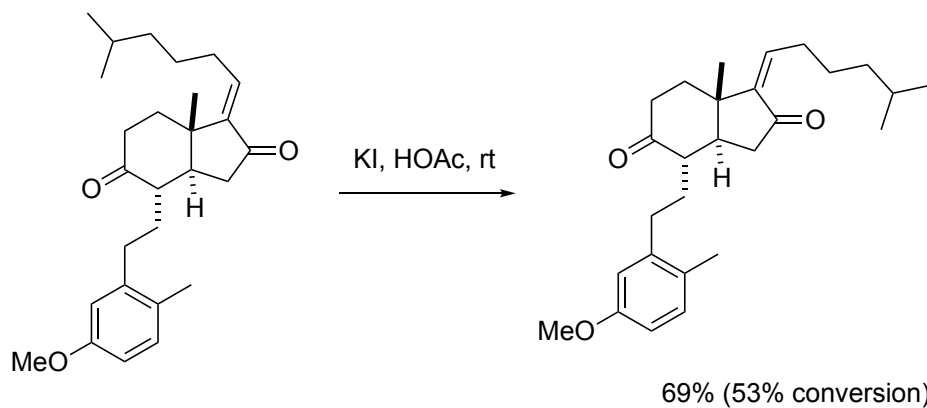
examples:



Ham, J.; Chin, J.; Kang, H. *Molecules* **2011**, *16*, 4165.

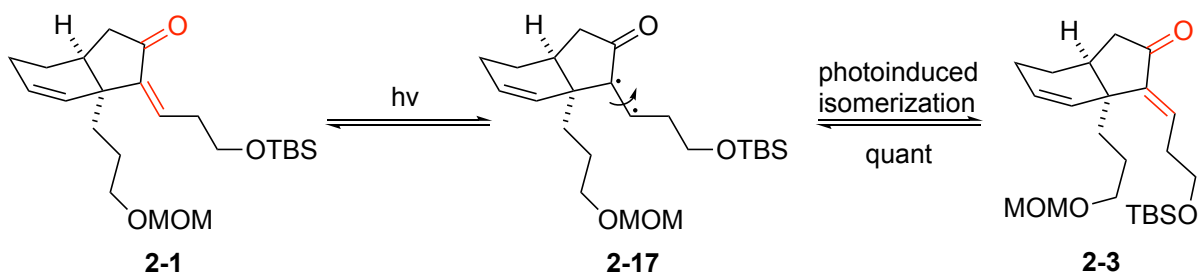


Sugimoto, K.; Yoshida, M.; Ihara, M. *Synlett* **2006**, *2006*, 1923.



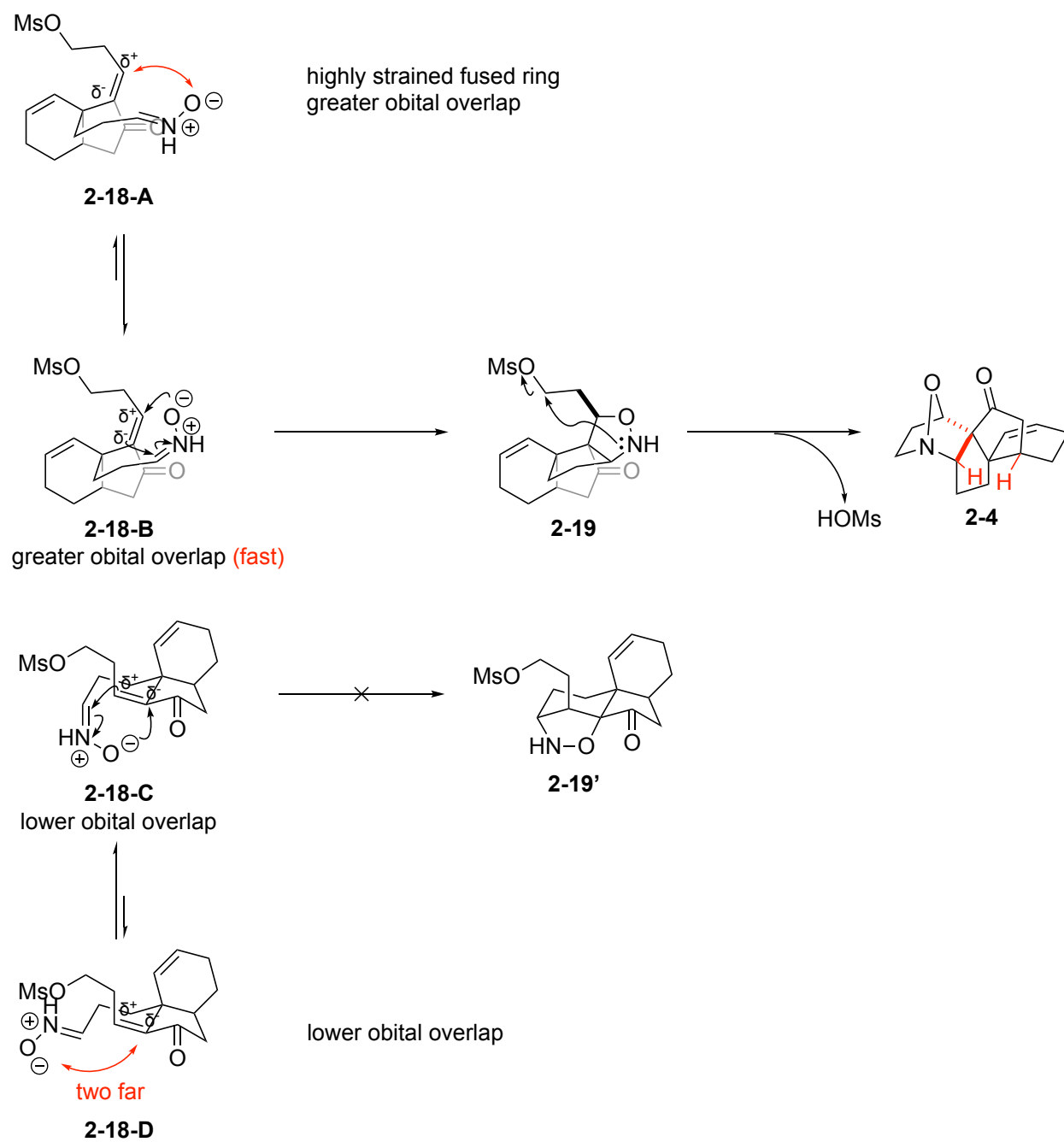
Taber, D. F.; Jiang, Q.; Chen, B.; Zhang, W.; Campbell, C. L. *J. Org. Chem.* **2002**, *67*, 4821.

photoinduced isomerization:



The ketone and the olefin (marked as red) were easier to stay in one plane in **2-1** than **2-3**, thus **2-1** is easier to absorb UV energy.

### Discussion 2-2



### Reference:

1. Shim, P. J.; Kim, H. D. *Tetrahedron Lett*, **1998**, 39, 9517.