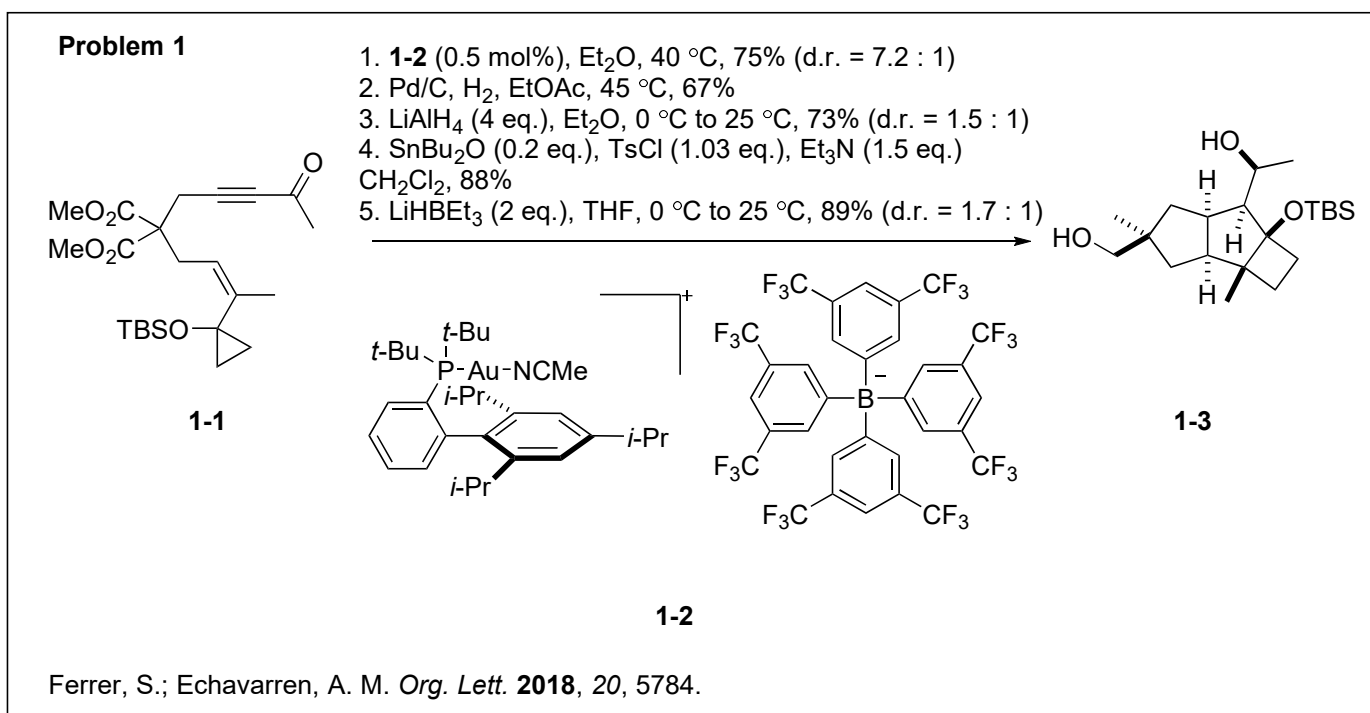
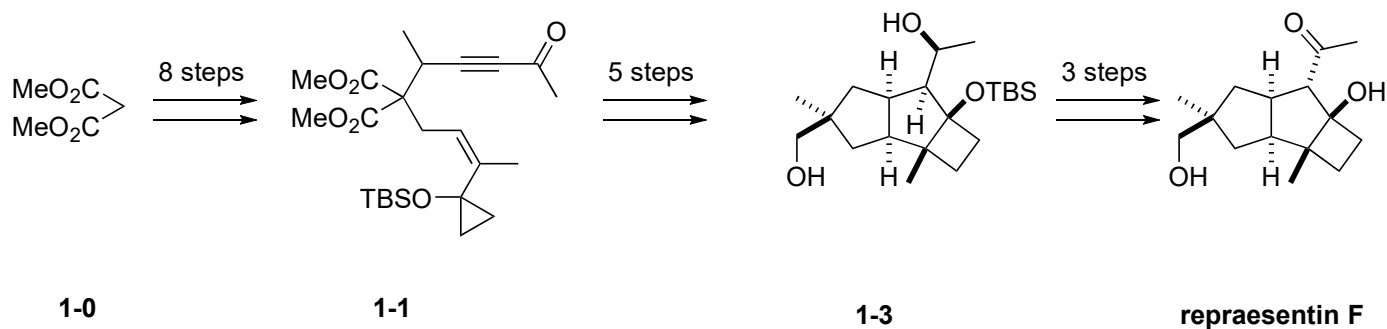


Problem Session (1) -Answer-

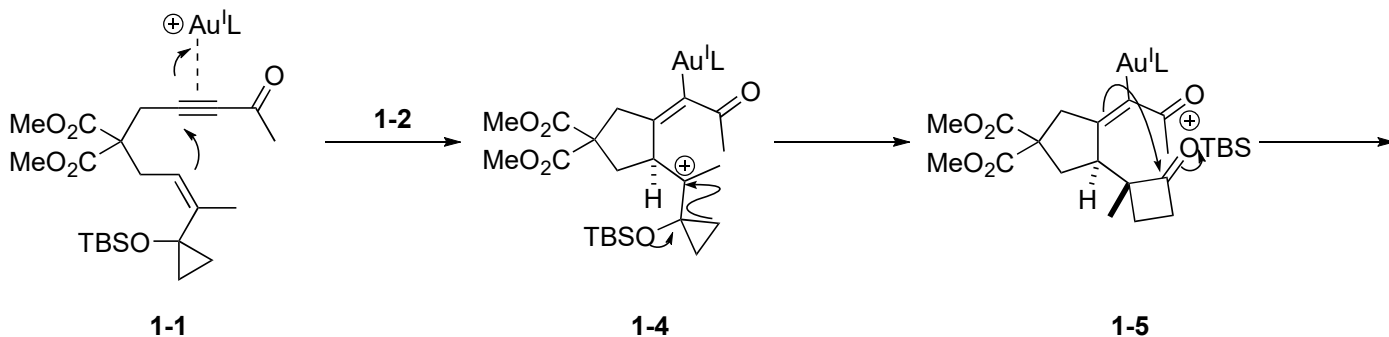
2019/12/21 Yuma Komori

Topic: Total synthesis of protoilludane sesquiterpenes

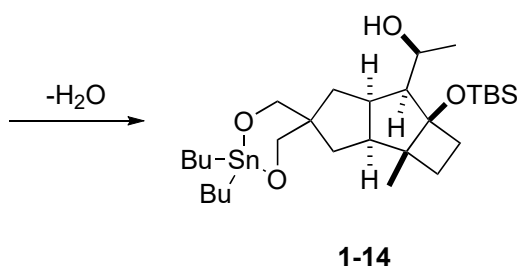
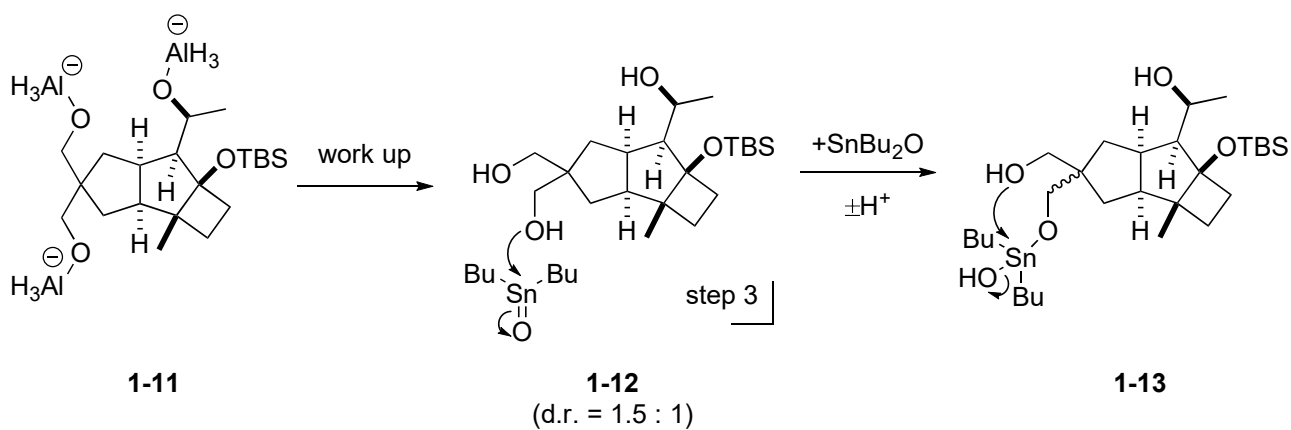
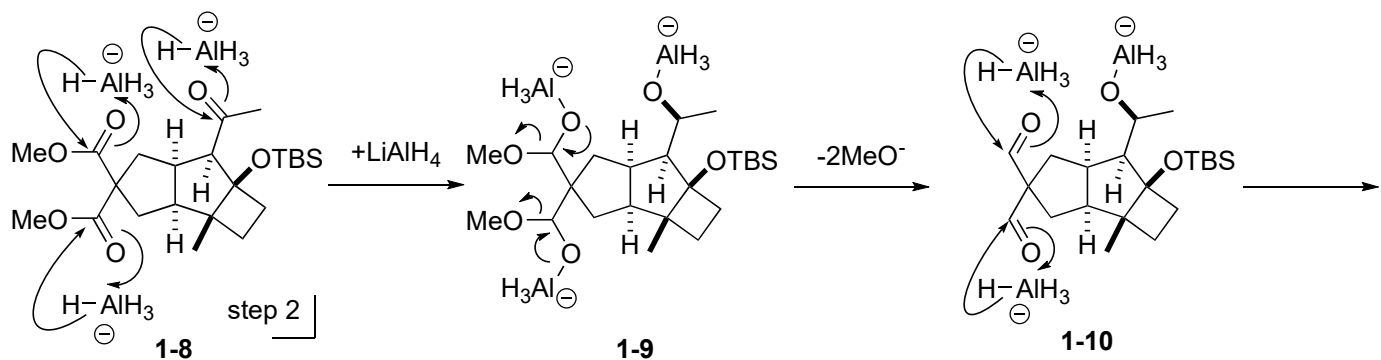
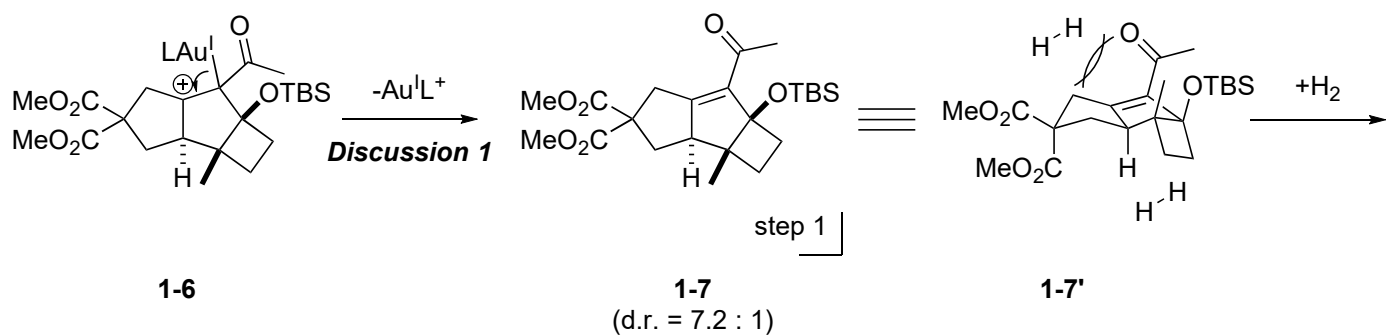
Introduction of problem 1: Total synthesis of repressentin F



Answer

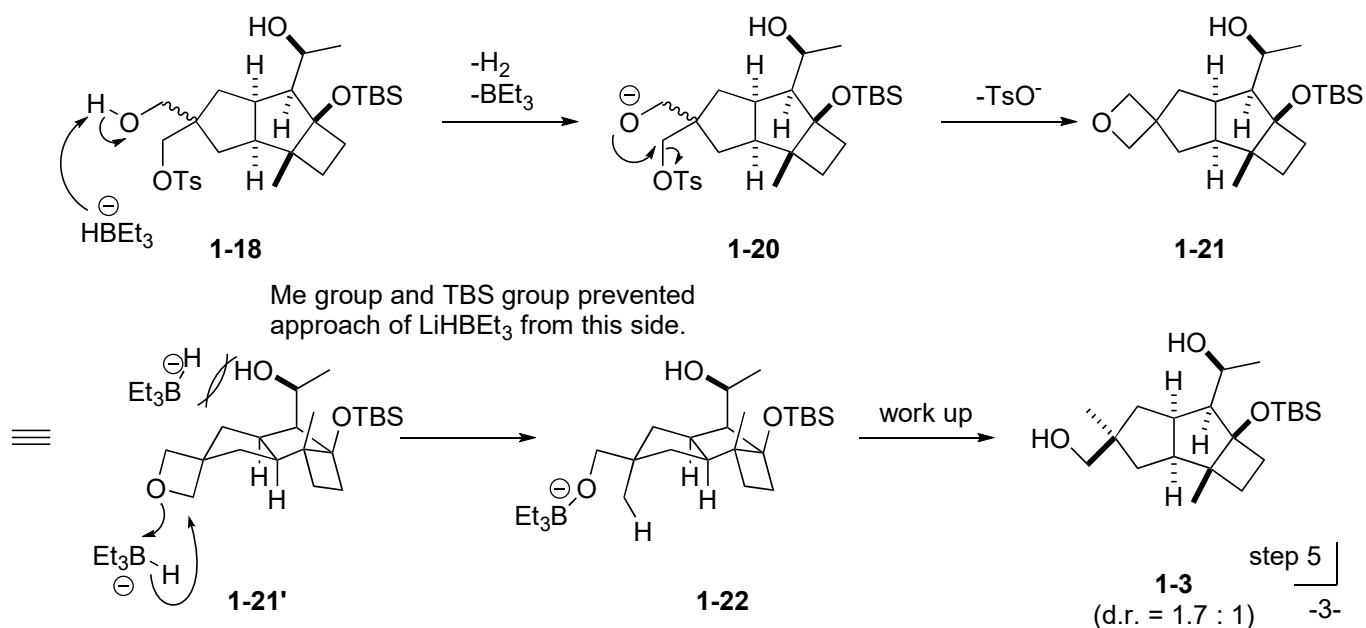
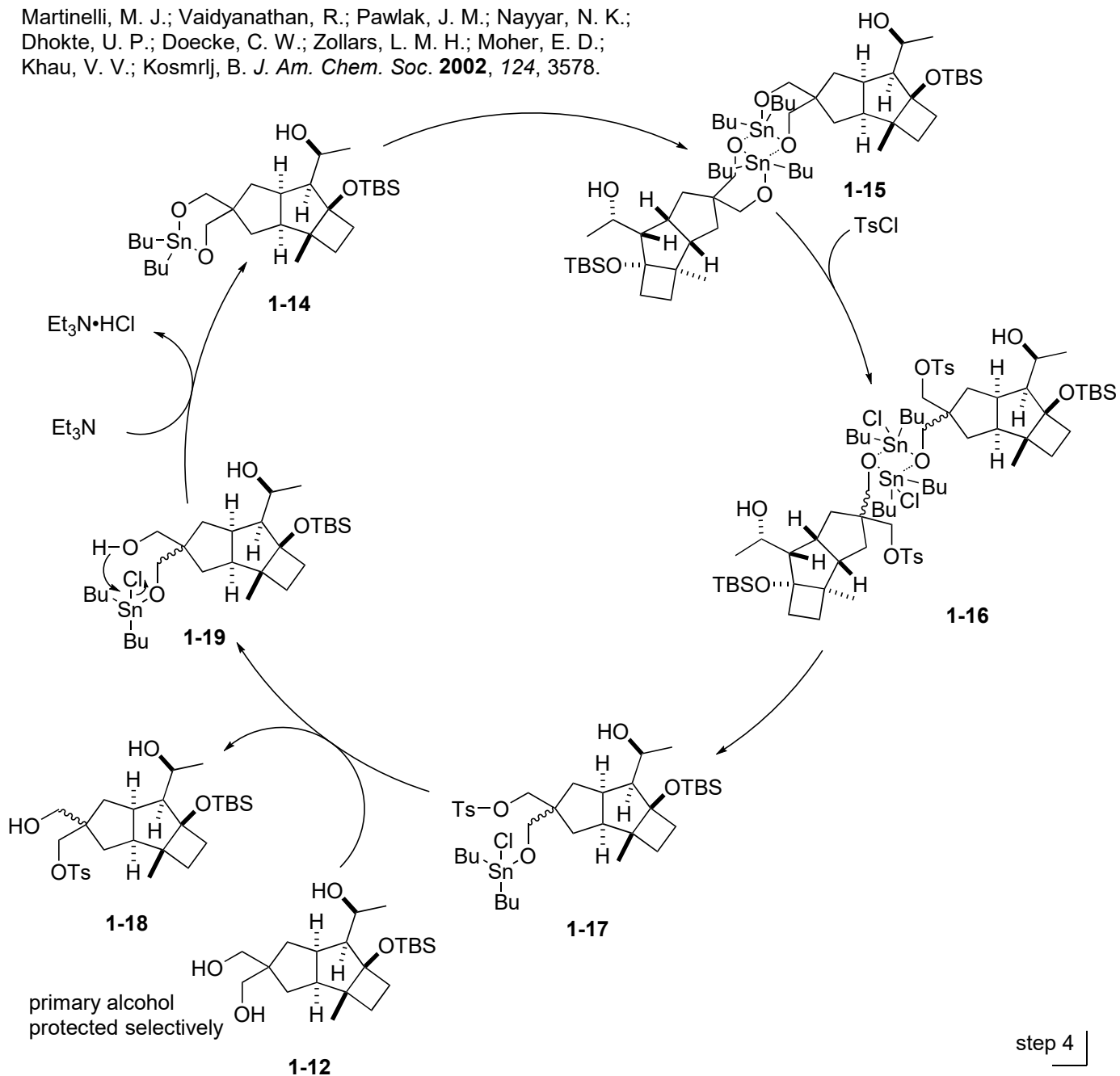


Me group and TBS group prevented approach of H₂ from this side.



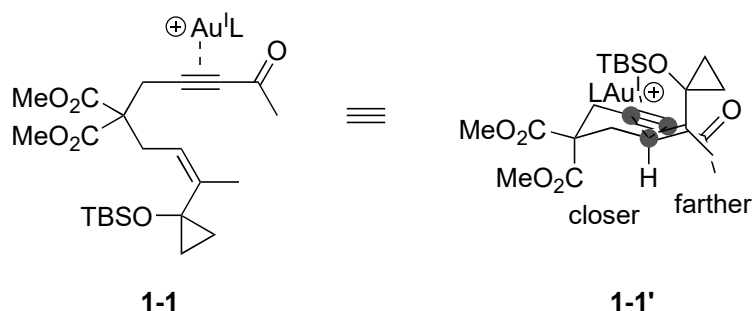
catalyst cycle

Martinelli, M. J.; Vaidyanathan, R.; Pawlak, J. M.; Nayyar, N. K.; Dhokte, U. P.; Doecke, C. W.; Zollars, L. M. H.; Moher, E. D.; Khau, V. V.; Kosmrlj, B. *J. Am. Chem. Soc.* **2002**, *124*, 3578.



Discussion 1: Gold (I) catalyzed cyclization

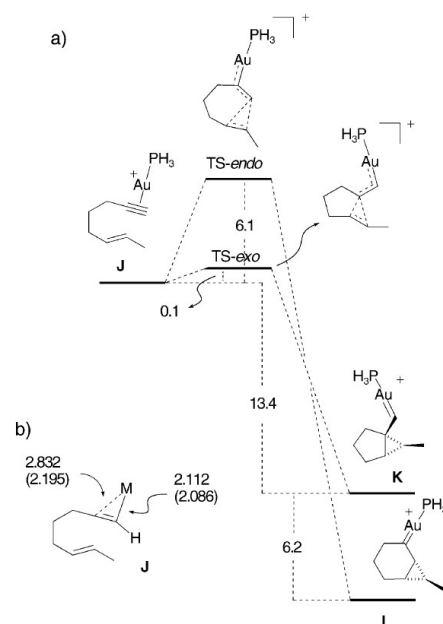
1.1. 5-exo-dig vs 6-endo-dig



DFT calculation

Nieto-Oberhuber, C.; Munoz, M. P.; Bunuel, E.; Nevado, C.; Cardenas, D. J.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2004**, *43*, 2402.

Activation energy to transition state is lower in 5-exo cyclization than in 6-endo cyclization. It is because reactive sites of 6-endo cyclization is farther than those of 5-exo cyclization. It shows that 5-exo cyclization is favored to 6-endo cyclization.



1.2. Stereoselectivity

Jimenez-Nunez, E.; Claverie, C. K.; Nieto-Oberhuber, C.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2006**, *45*, 5452.

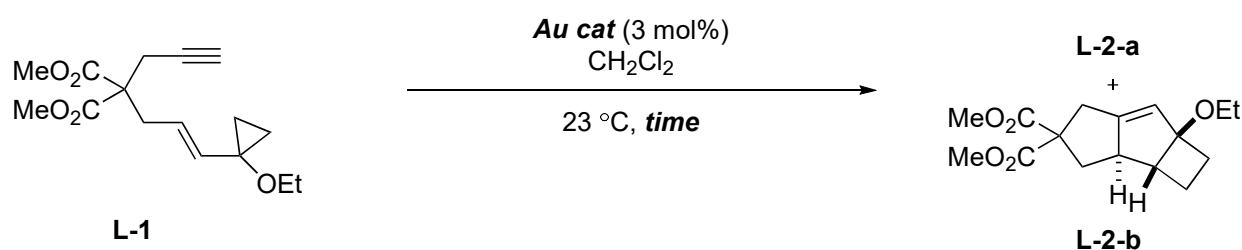
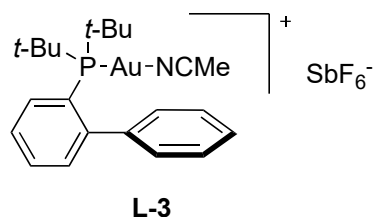


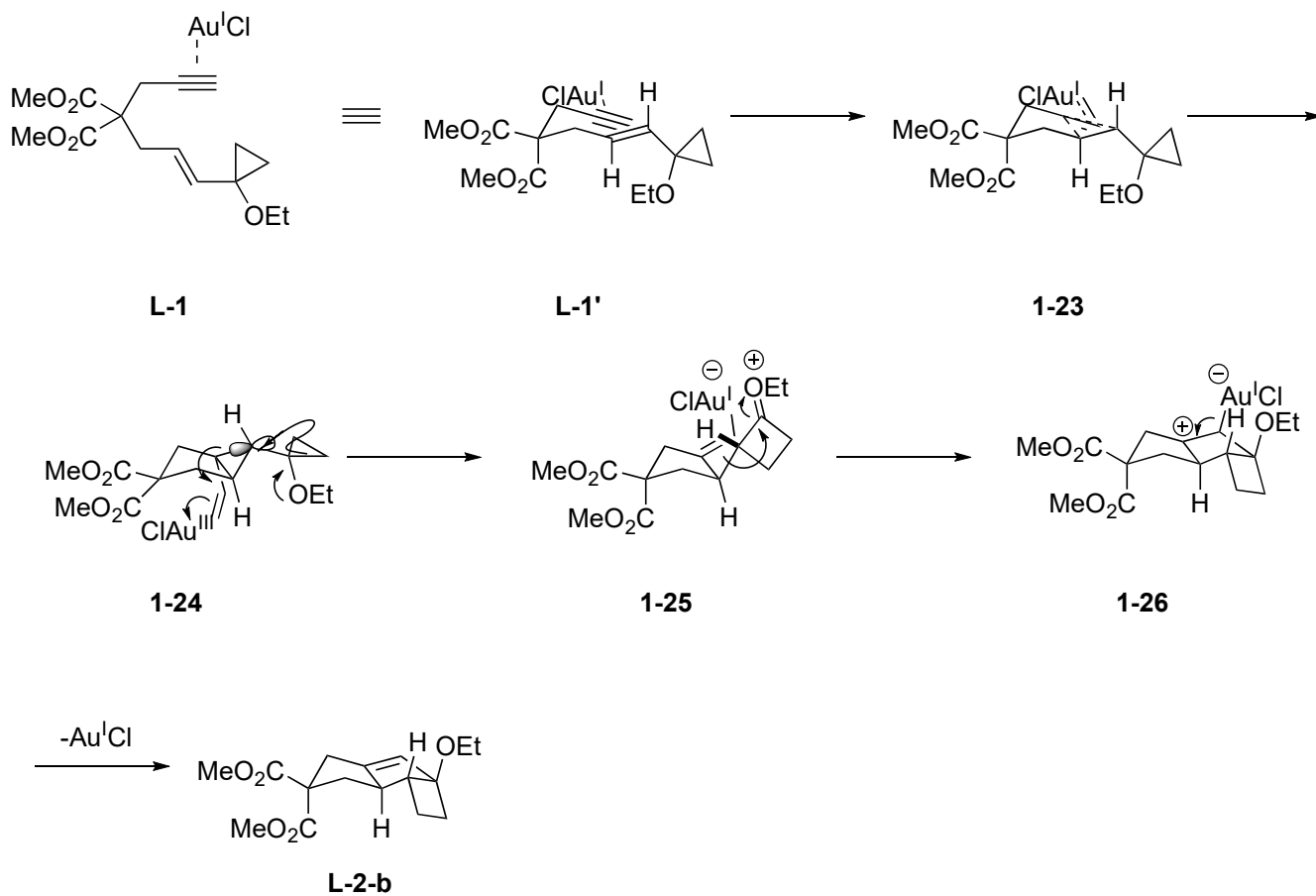
Table 1

Entry	Au cat	time	product	yield
1	AuCl	24 h	L-2-a/L-2-b (1:30)	80%
2	L-3	5 min	L-2-a/L-2-b (1:1)	88%

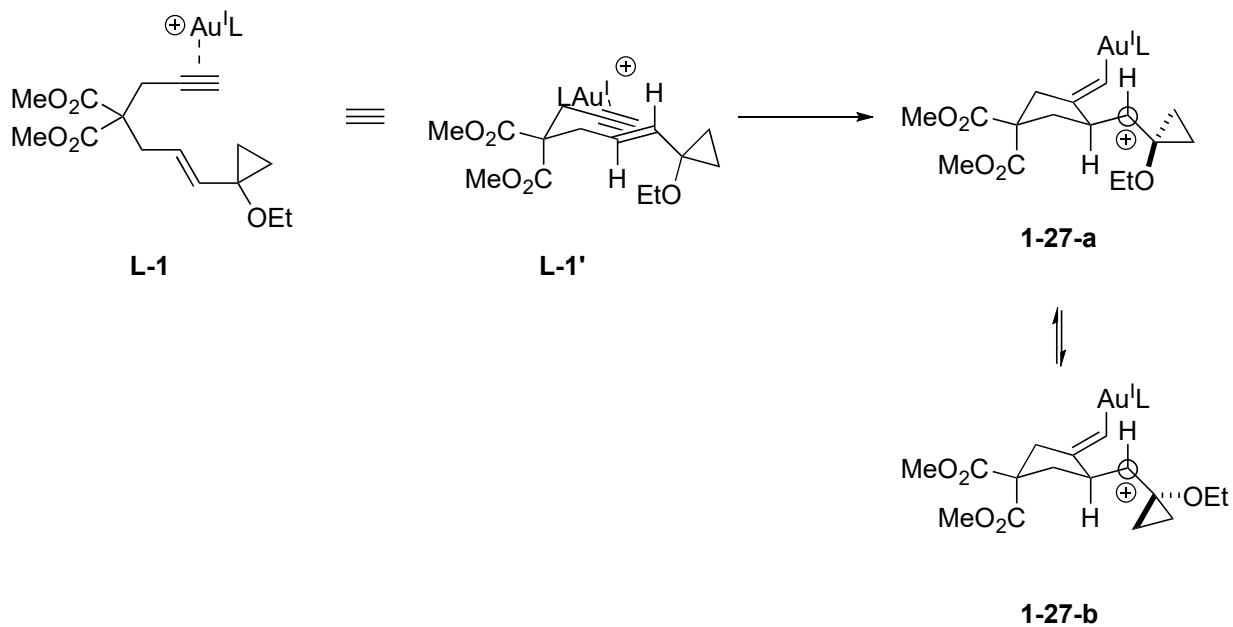


Entry 1, reaction proceeded stereoselectively. Authors insist that when AuCl is used, reaction mechanism is concerted. On the other hand, there was no stereoselectivity in entry 2. It shows that when cationic Au^I catalyst is used, reaction mechanism is cationic. Cationic Au^I catalyst attracts electron more than AuCl. It causes cationic path.

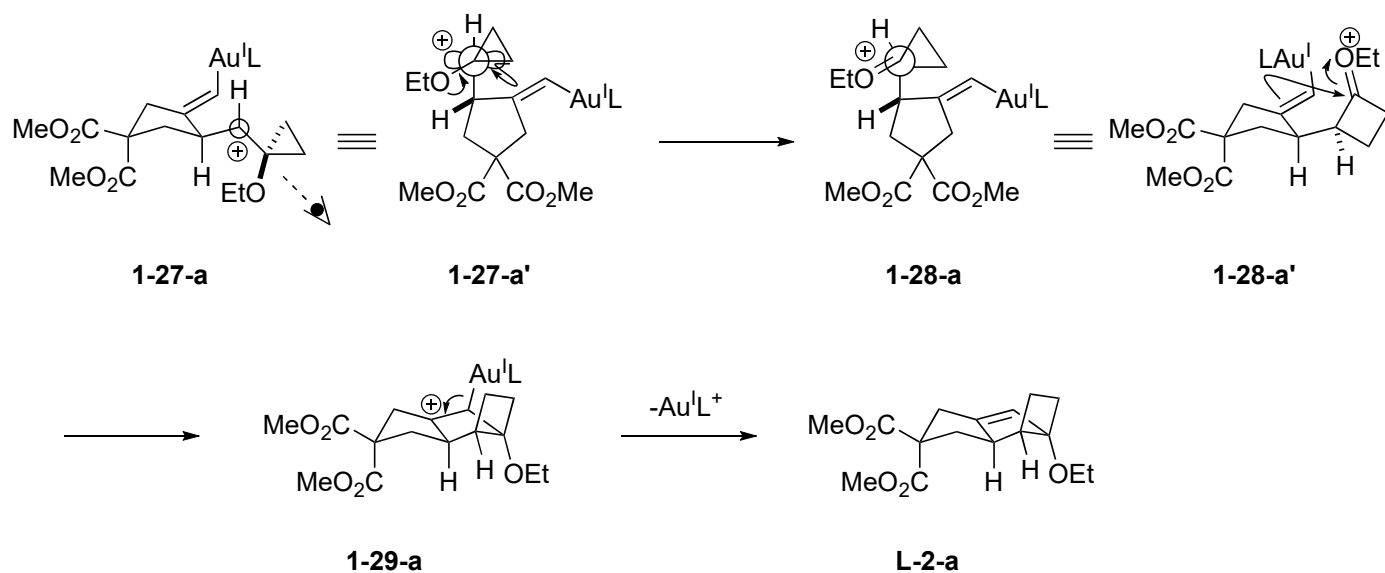
Entry 1



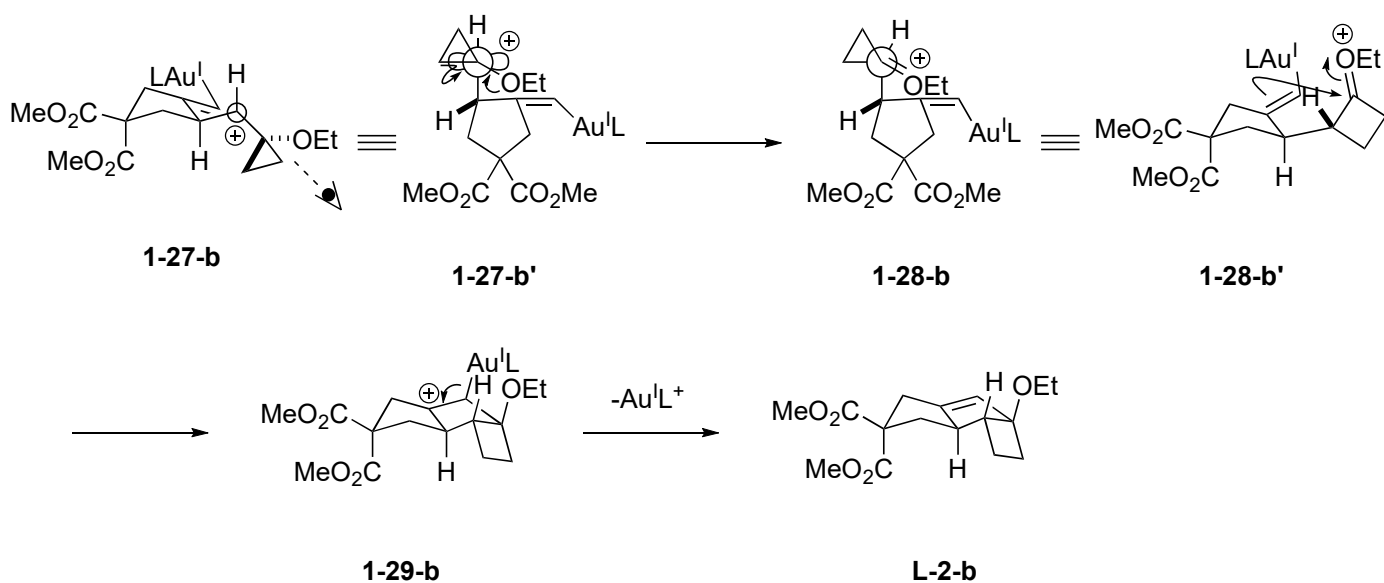
Entry 2



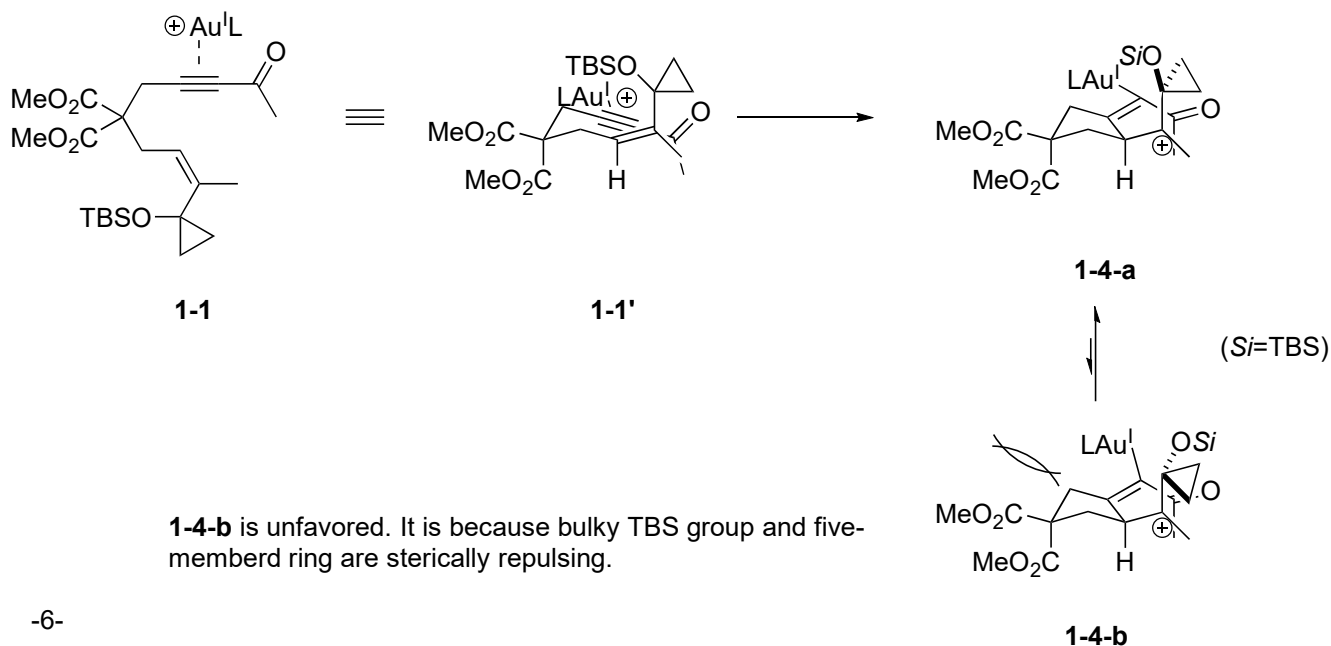
From **1-27-a**



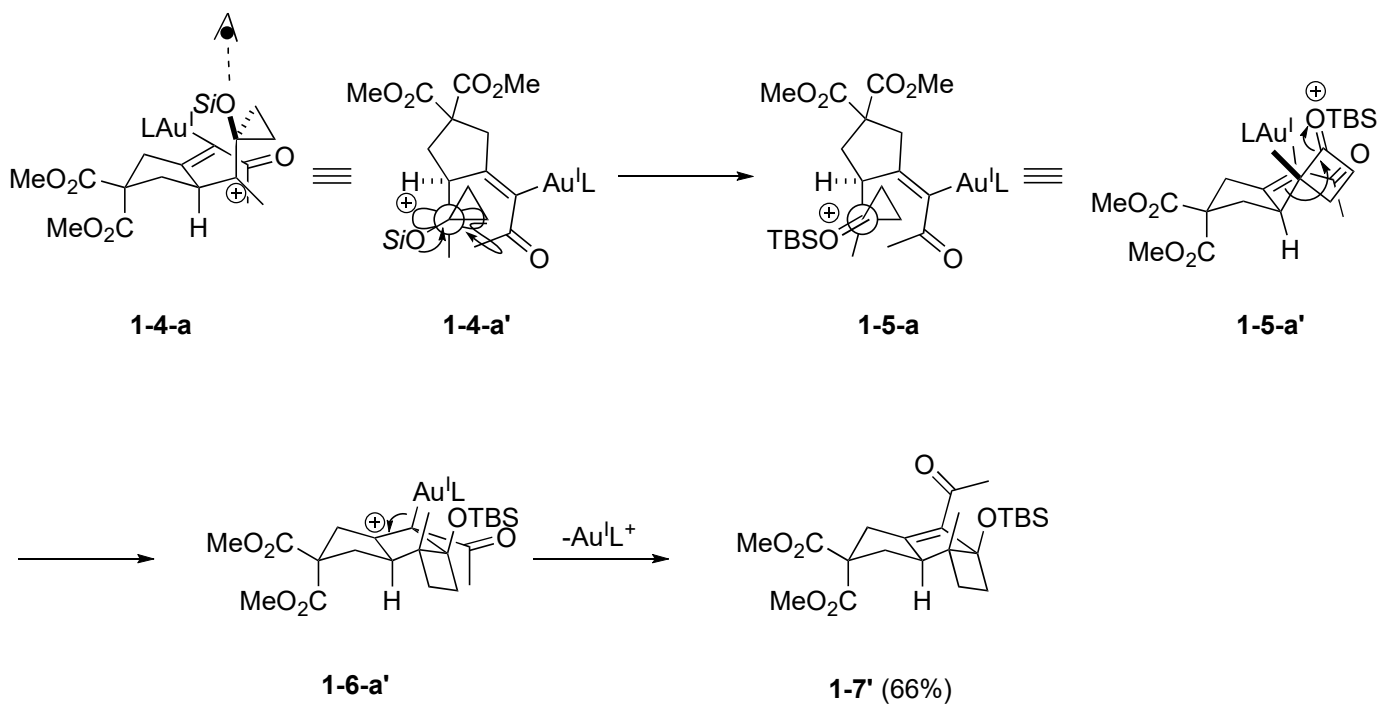
From **1-27-b**



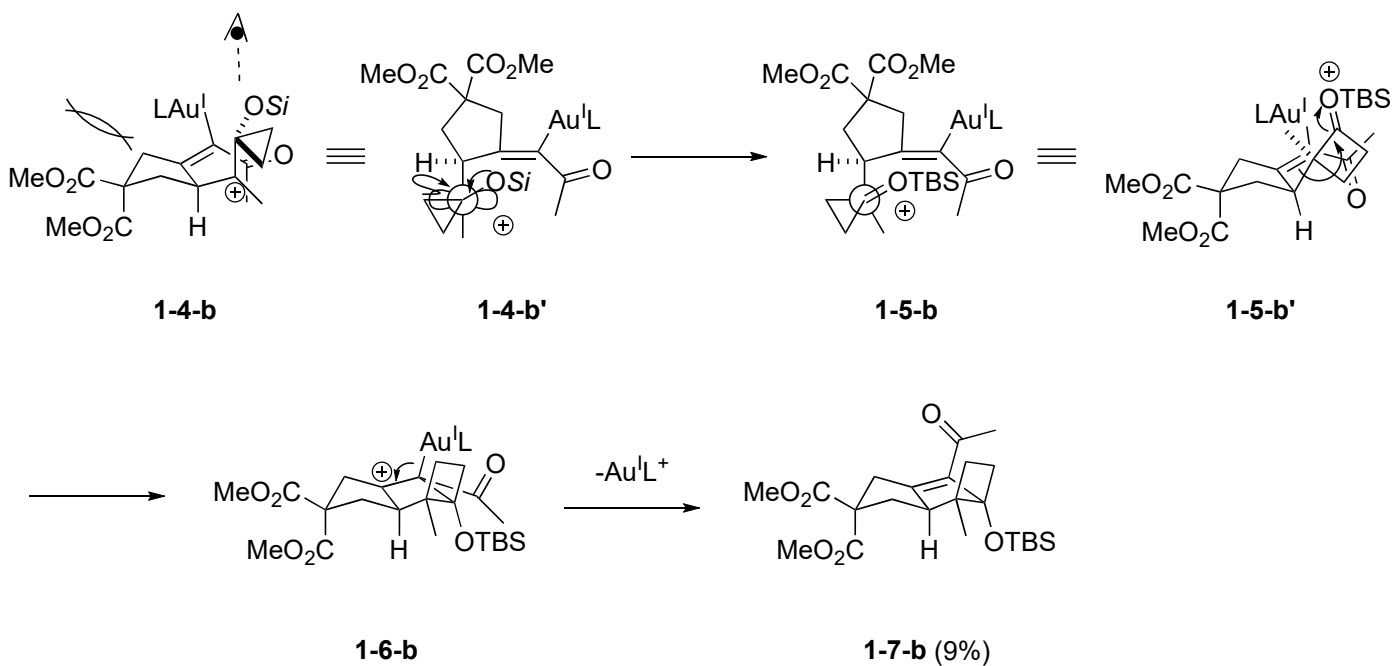
In the reaction of **1-1**, cationic path proceeded.



From **1-4-a** (major path)

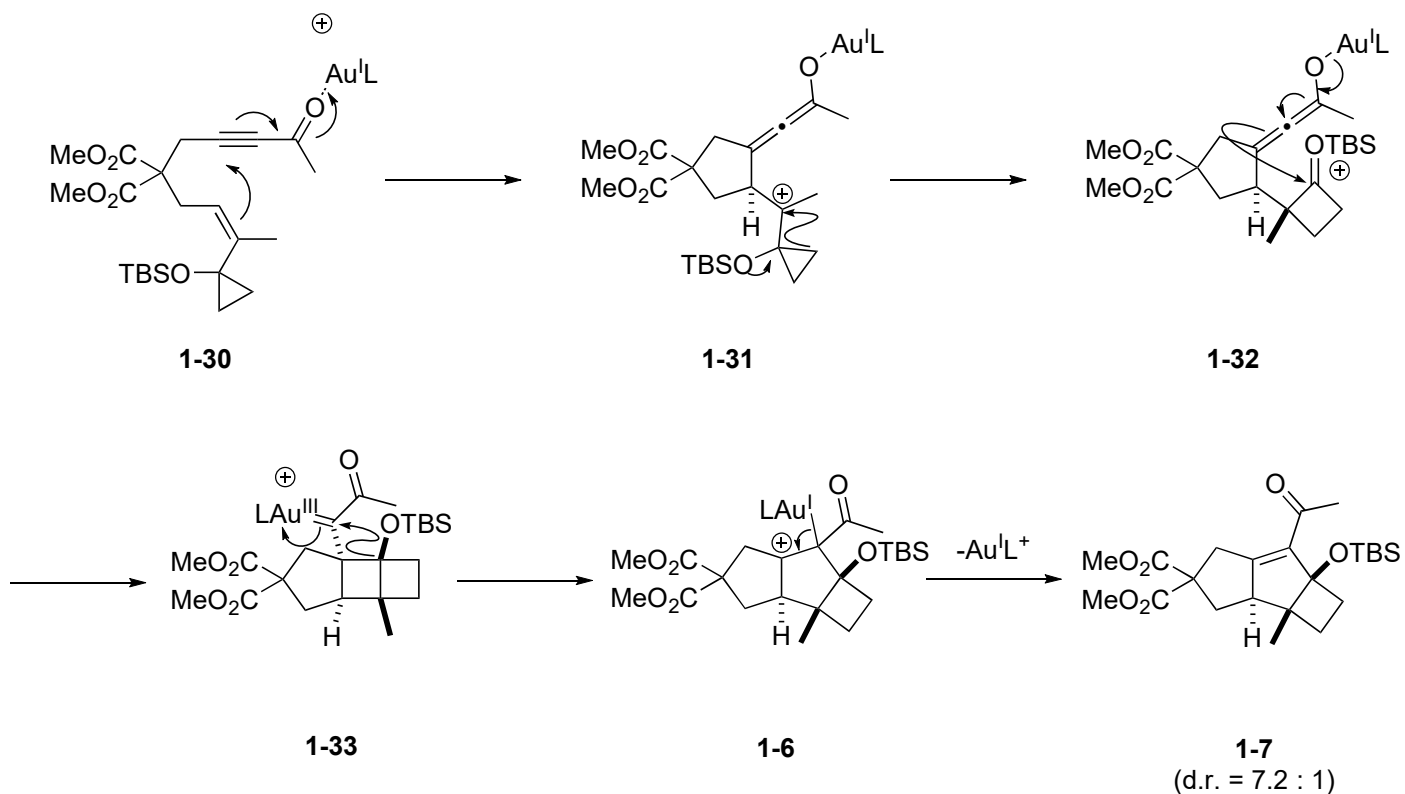


From **1-4-b** (minor path)

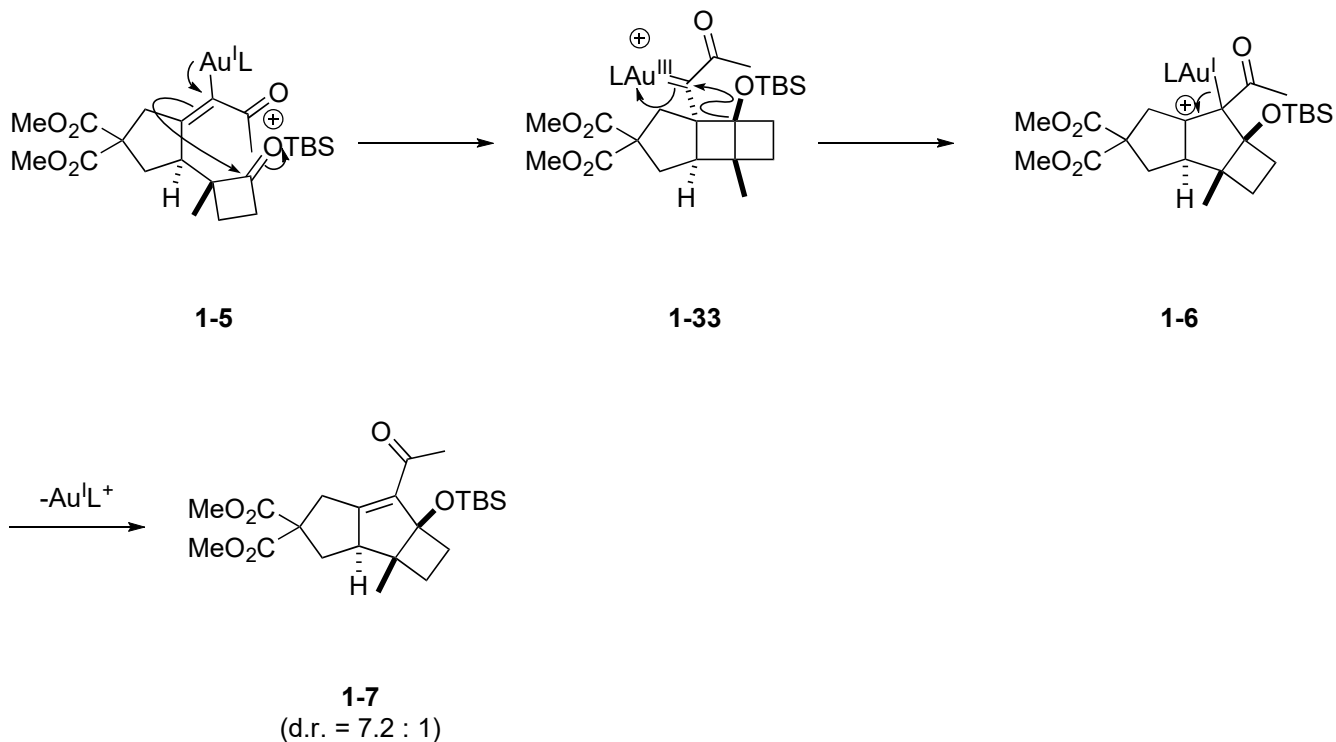


Another possible path to make 5-5-4 ring system

1. Au^I catalyst activated ketone

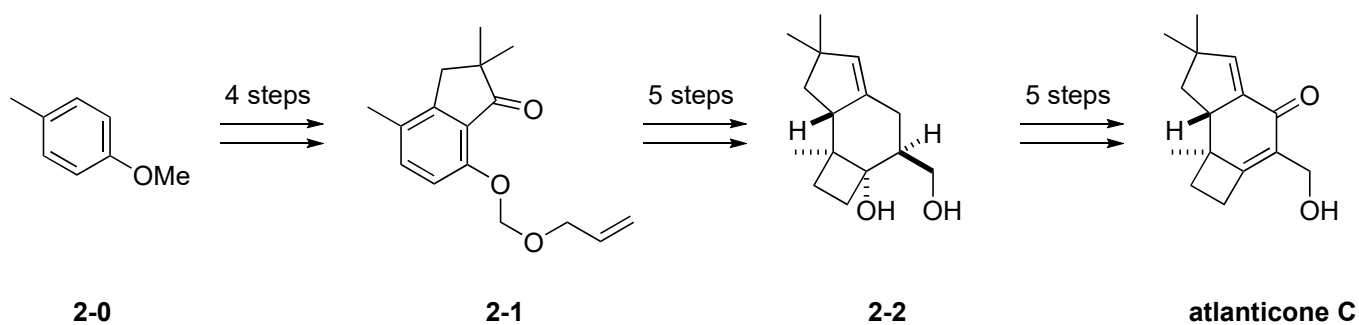


2. Gold carbene before producing carbocation



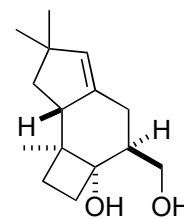
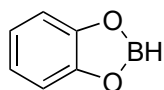
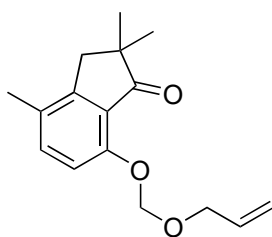
Before producing tertiary cation, gold(III) carbene was produced. When using gold(I) catalyst with electron-rich ligand, these paths are reasonable.

Introduction of problem 2: Total synthesis of atlanticone C



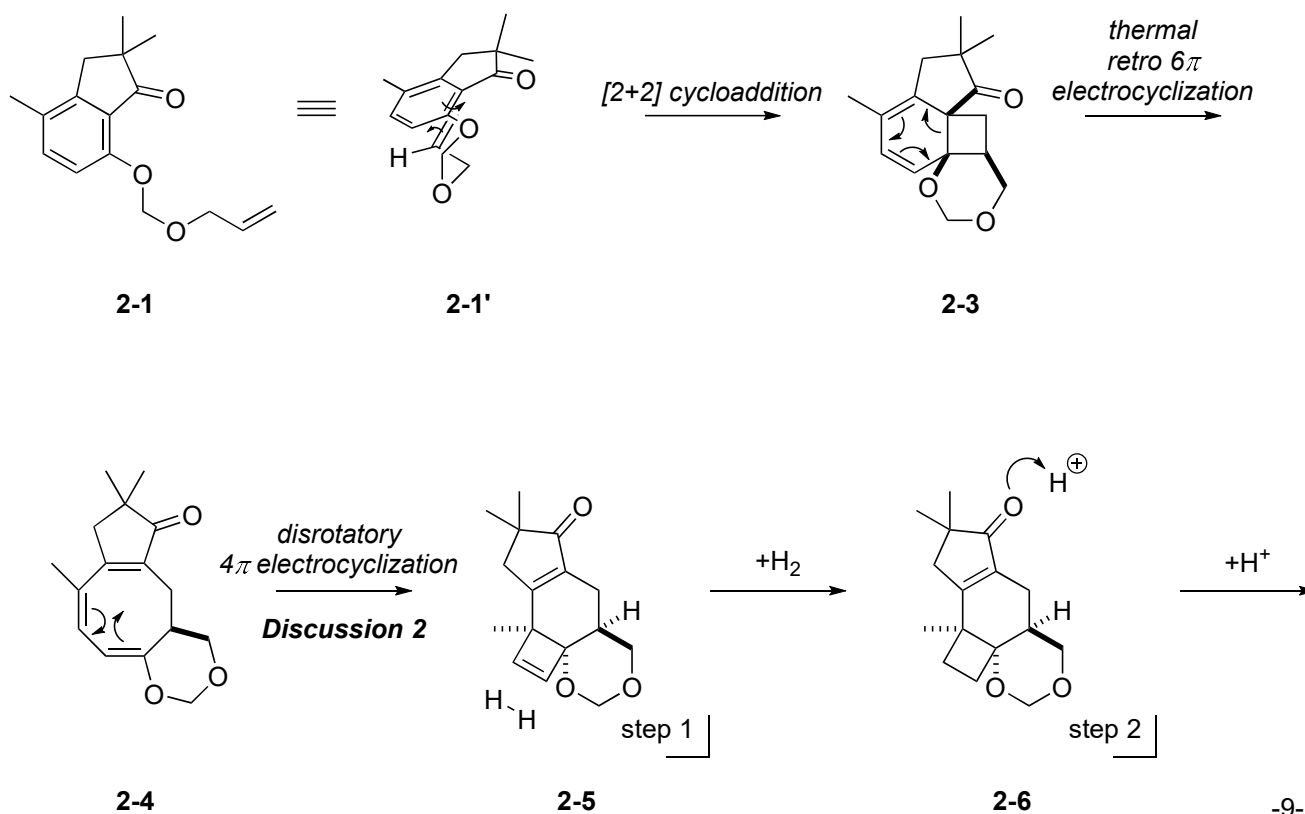
Problem 2

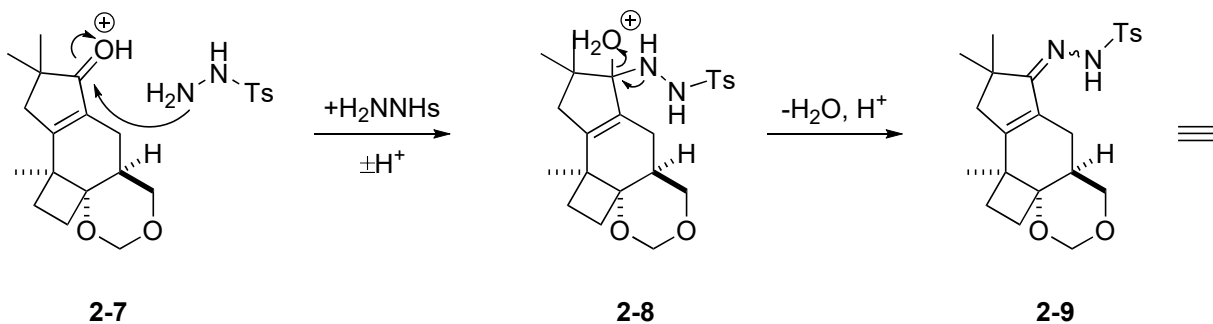
1. $h\nu$ (350 nm), MeOH, 60%
2. Pd/C, H_2 , EtOAc, 99%
3. H_2NNHTs (1.5 eq.), H_2SO_4 (0.1 eq.), MeOH, 65 °C, 58%
4. catecholborane (4.0 eq.), AcOH (8.0 eq.), $CHCl_3$, -40 °C; NaOAc \cdot 3 H_2O (16 eq.), 52 °C, 92%
5. KO t -Bu (10 eq.), n -BuLi (10 eq.), $BF(OMe)_2\cdot OEt_2$ (14 eq.); NaOH (50 eq.), H_2O_2 (50 eq.), 87%



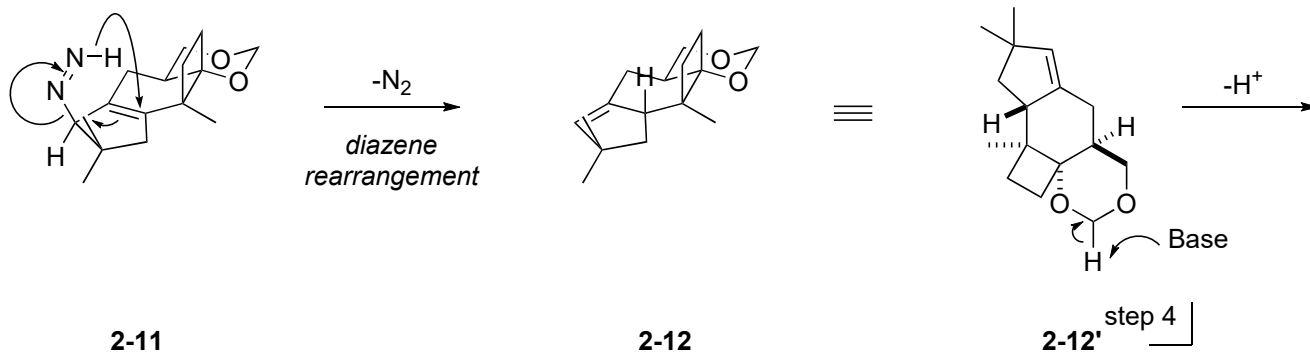
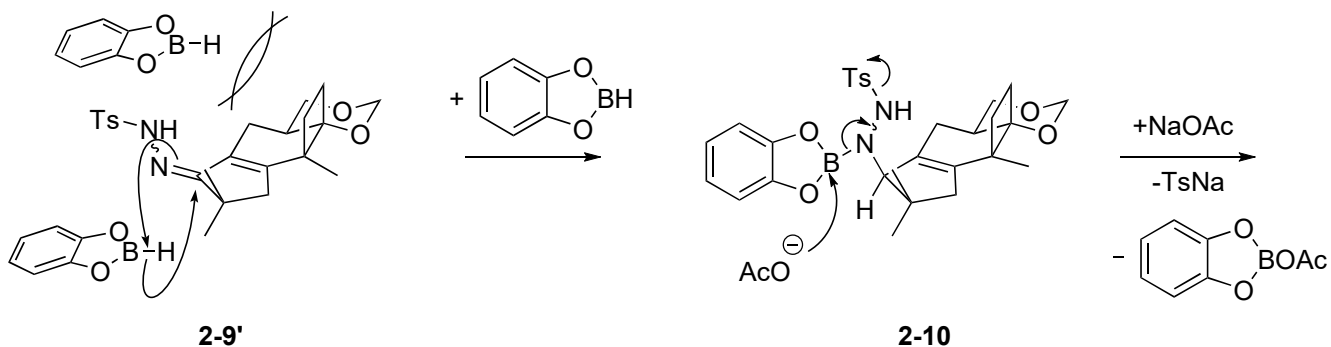
Zech, A.; Jandl, C.; Bach, T. *Angew. Chem. Int. Ed.* **2019**, *58*, 14629.

Answer

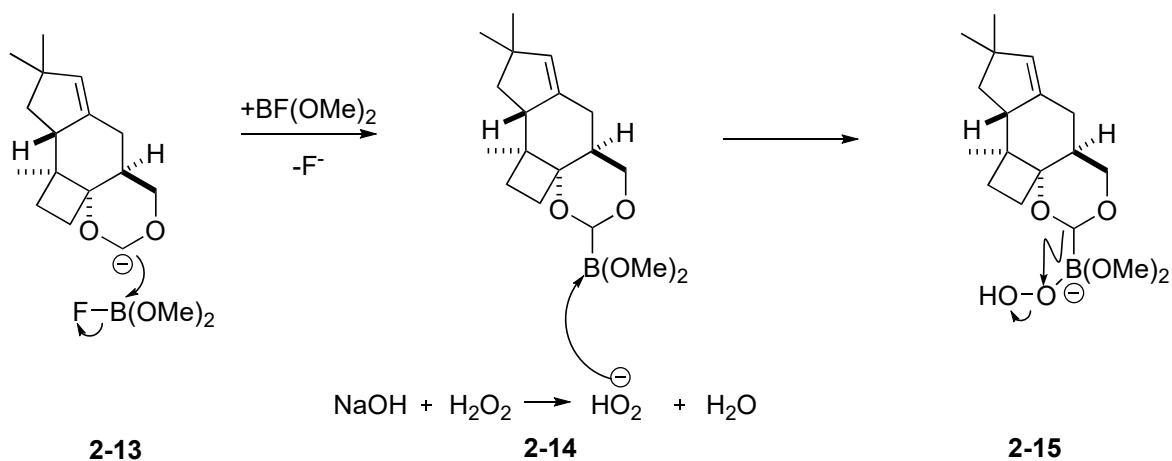


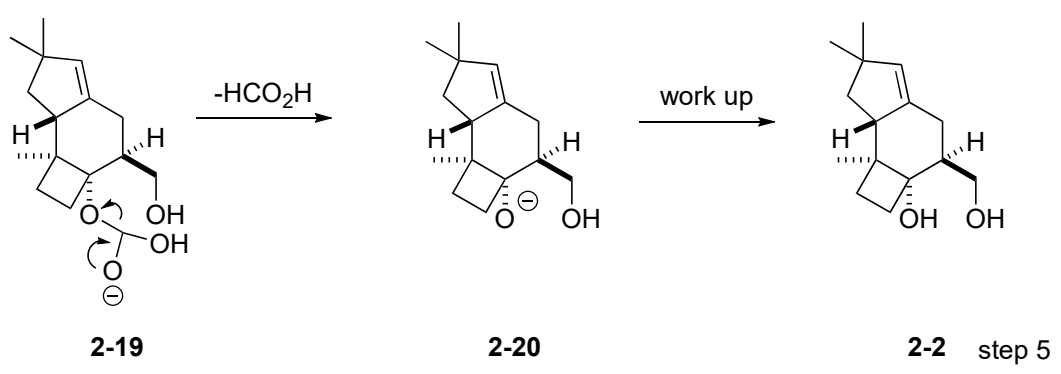
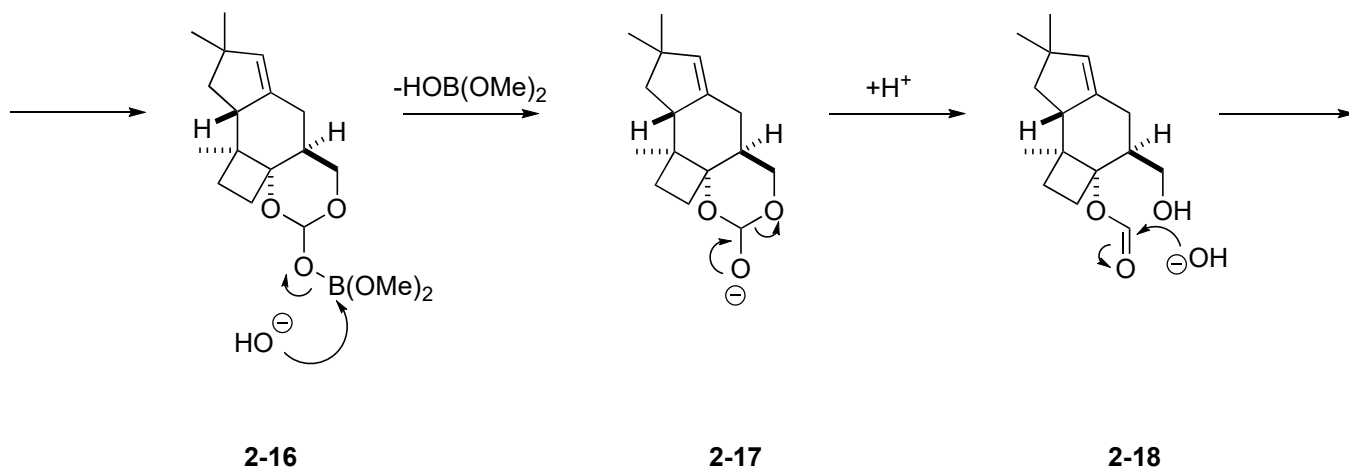


step 3



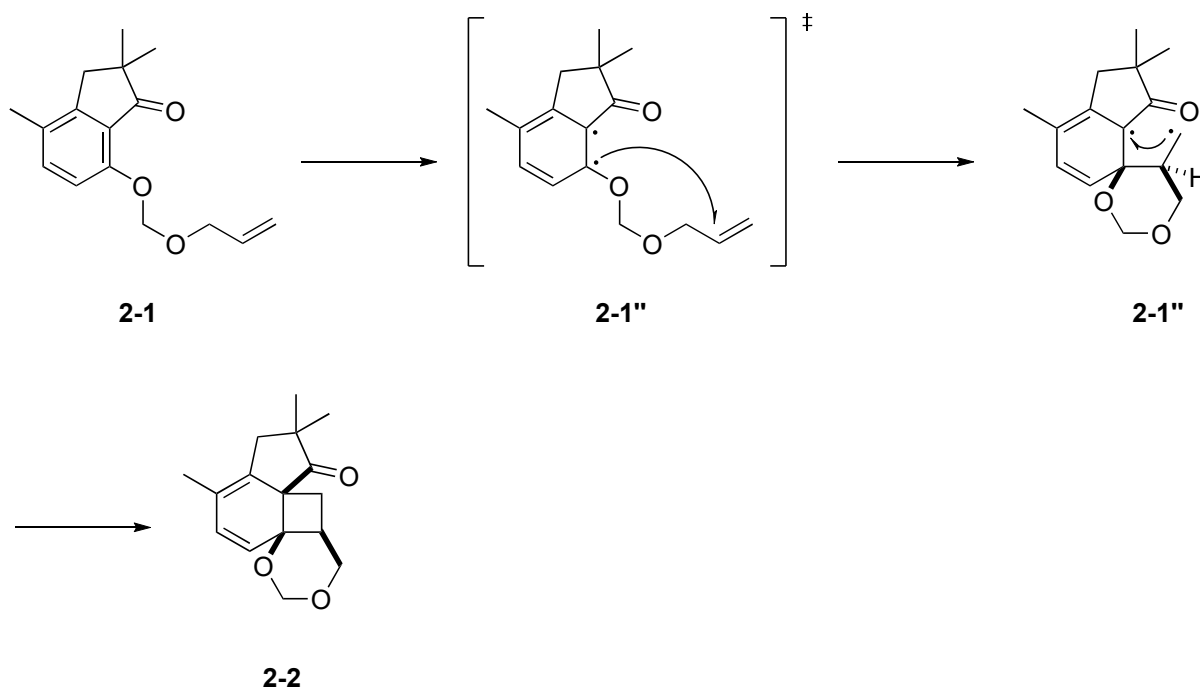
Comment: KO^t-Bu and *n*-BuLi are used as base. This mixture is called Lochmann-Schlosser superbase. This base has several structural motifs, so it is unclear which structure abstracted proton.





Discussion 2: Photocycloaddition and electrocyclization

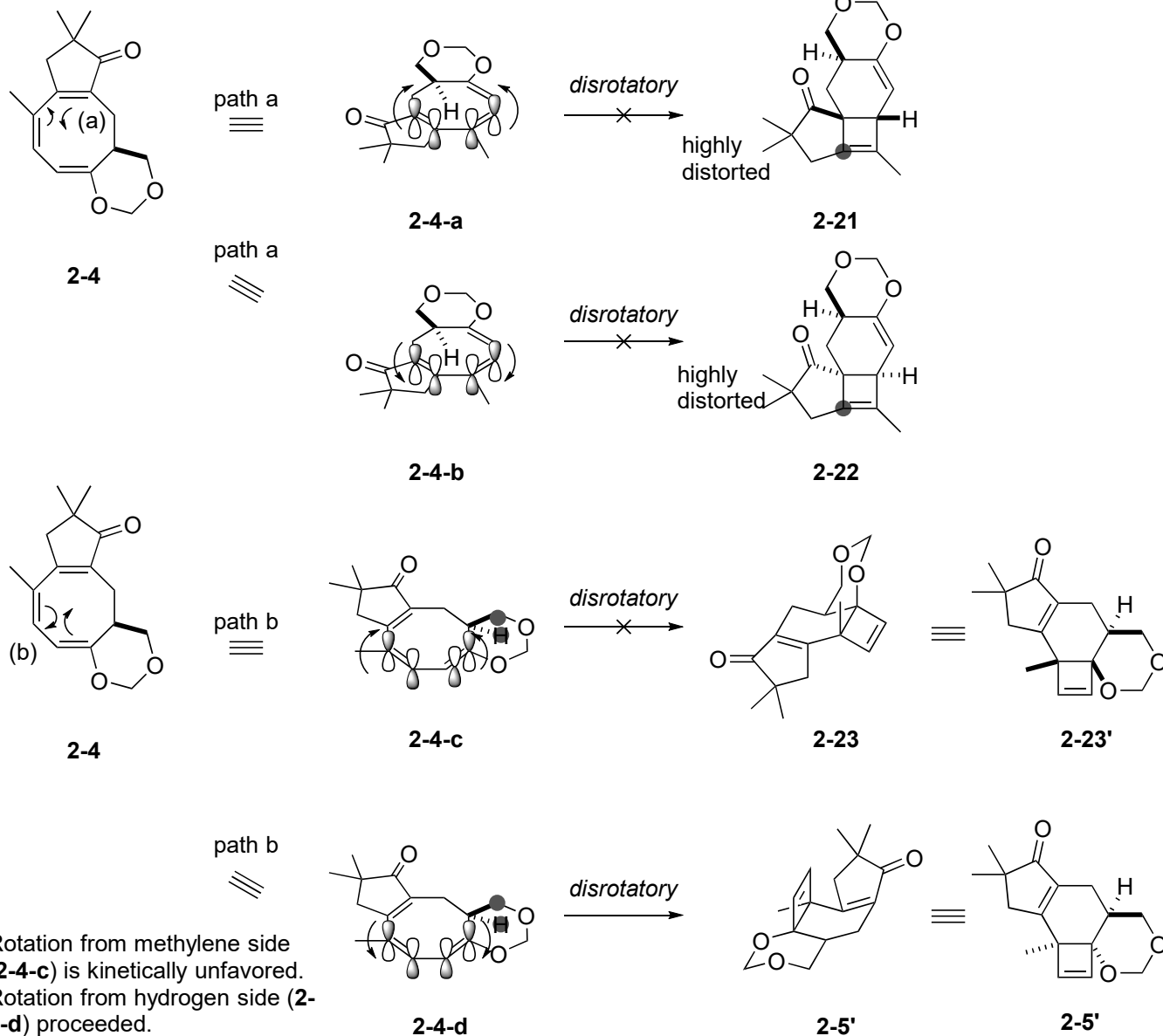
2.1. Regioselectivity in photocycloaddition



By the effect of ketone, biradical **2-1''** was produced. This transition state led to 1,2-*ortho* photocycloaddition.

2.2. Regioselectivity and stereoselectivity in electrocyclicization

4 π electrocyclicization



6 π electrocyclicization

