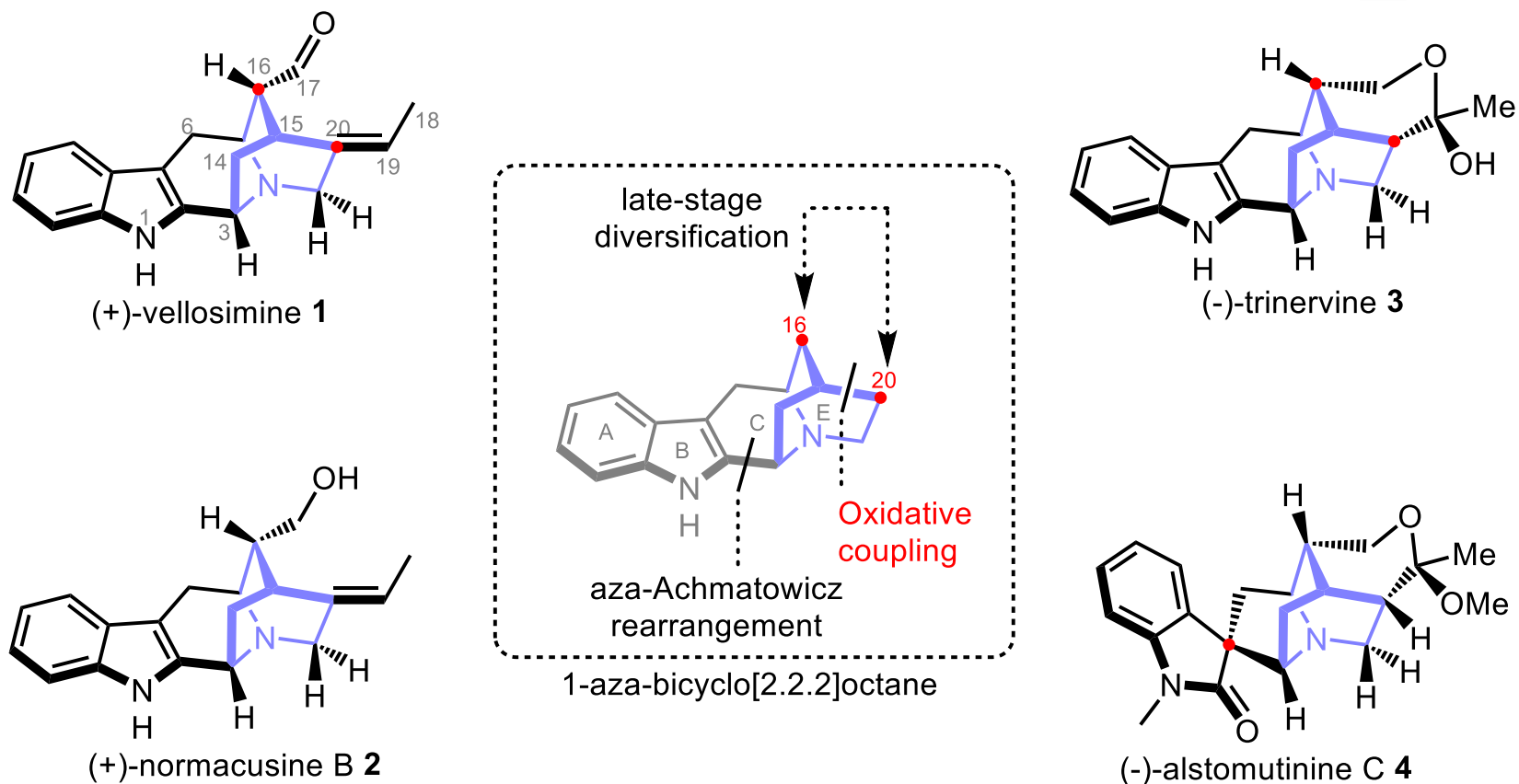
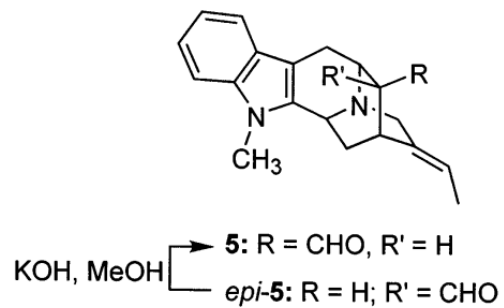
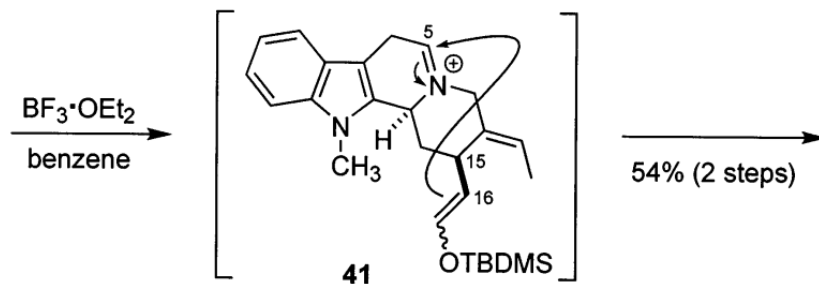
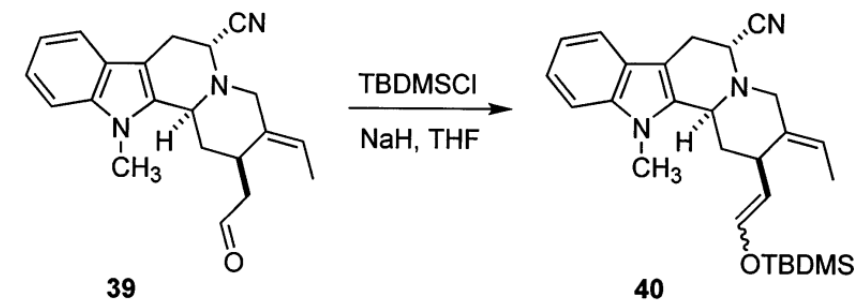


Oxidative Coupling Approach to Sarpagine Alkaloids: Total Synthesis of (-)-Trinervine, Vellosimine, (+)-Normacusine B, and (-)-Alstomutinine C

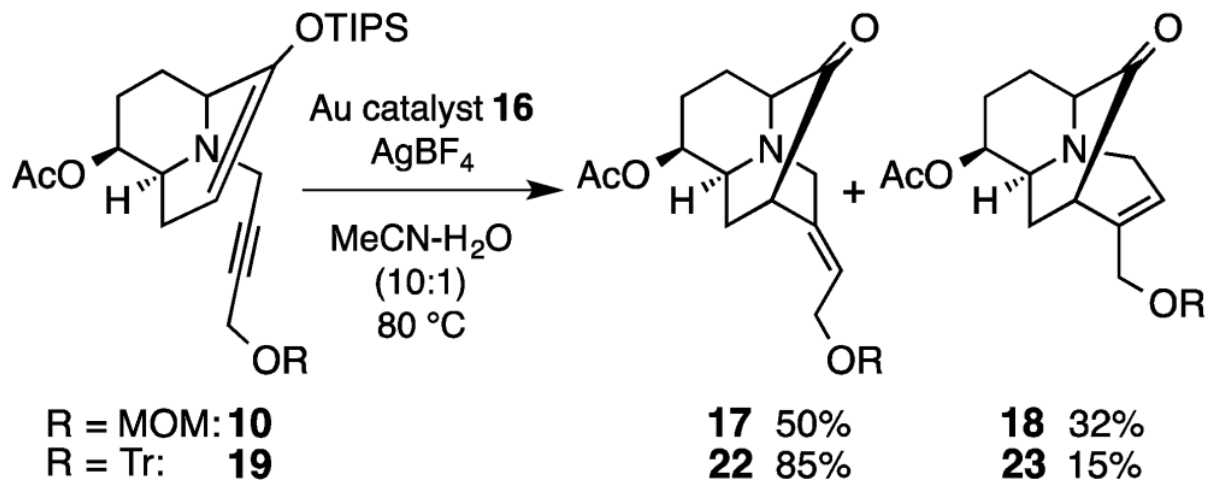
Ye Zhang,^{[a], [b]} Lei Zhang,^[b] and Xiangbing Qi^{*[b], [c]}



[2.2.2] 桥环C5-C16键的构建——形成亚胺中间体

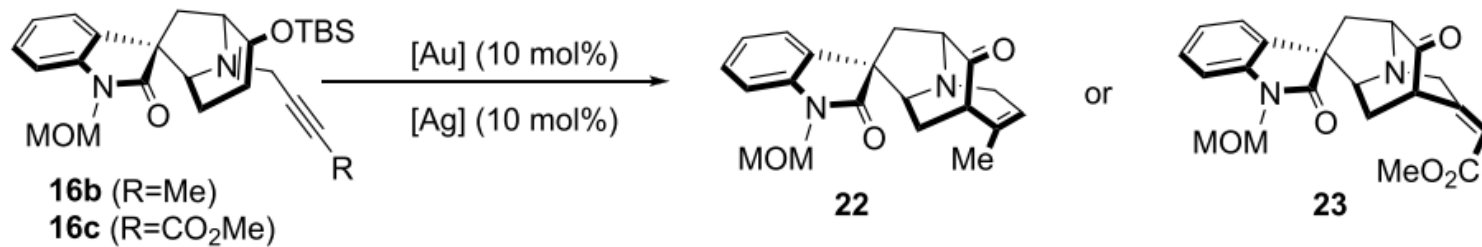


[2.2.2] 桥环C5-C16键的构建——金催化炔烃活化



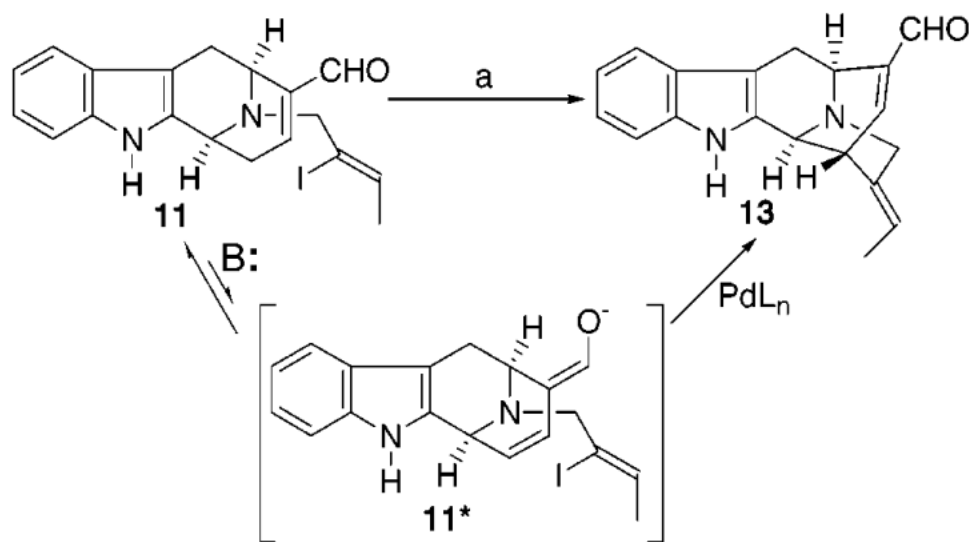
Au catalyst **16**

Org. Lett., **2016**, 18, 1912.



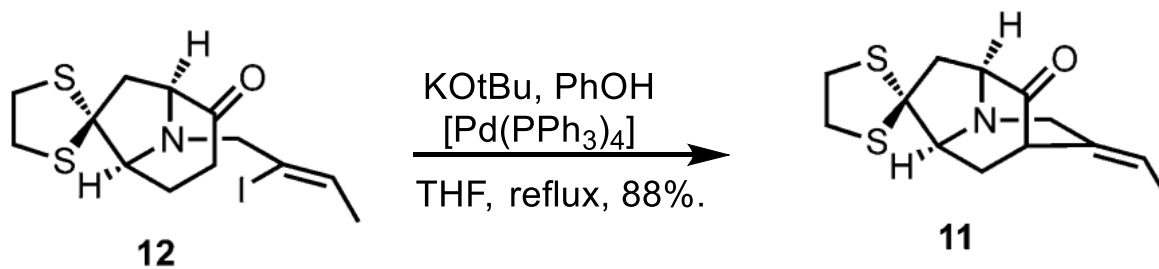
Org. Lett., **2020**, 22, 2022.

[2.2.2] 桥环——过渡金属催化

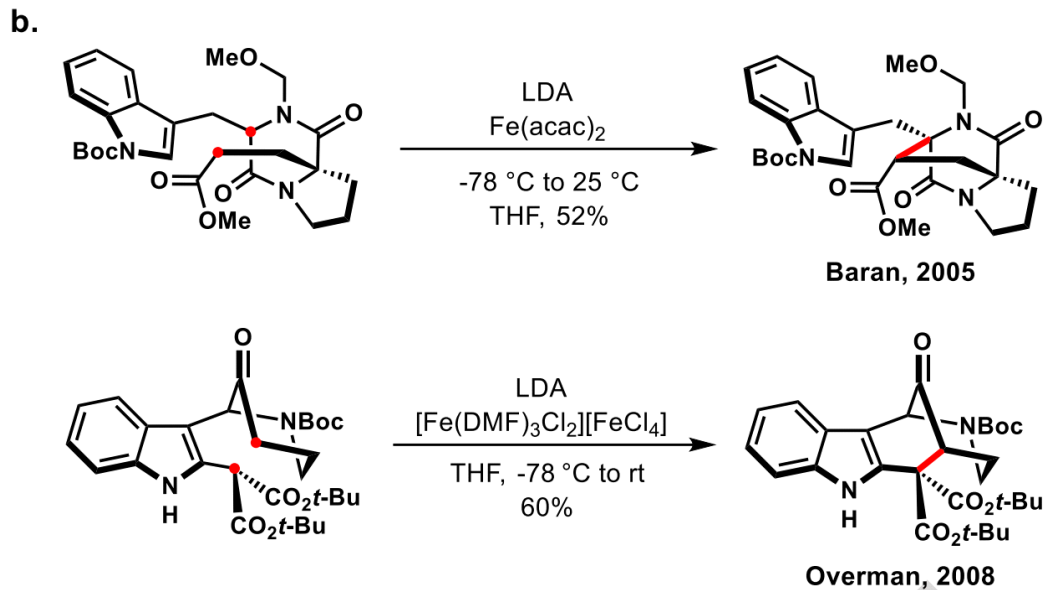
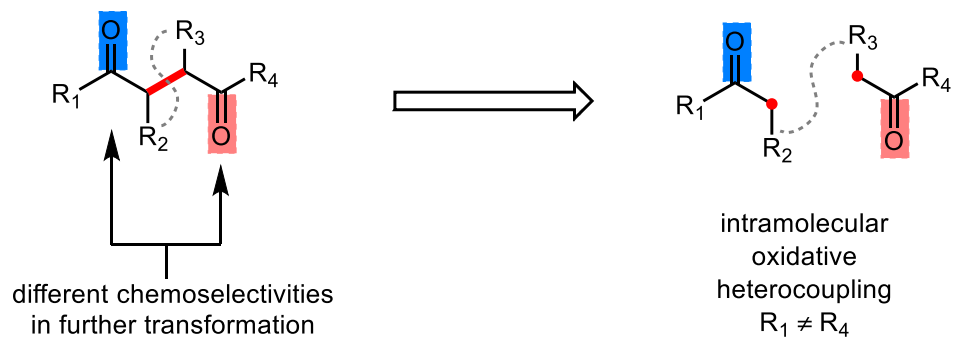
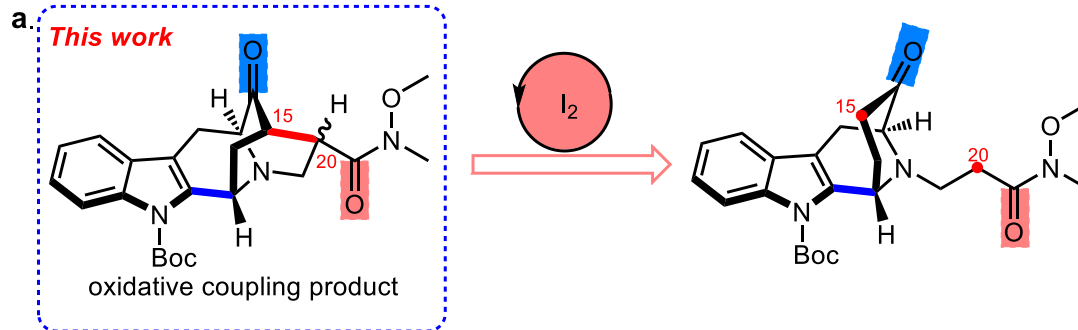


(a) Pd(OAc)₂, PPh₃, Bu₄NBr, K₂CO₃, DMF-H₂O (9:1), 70 °C.

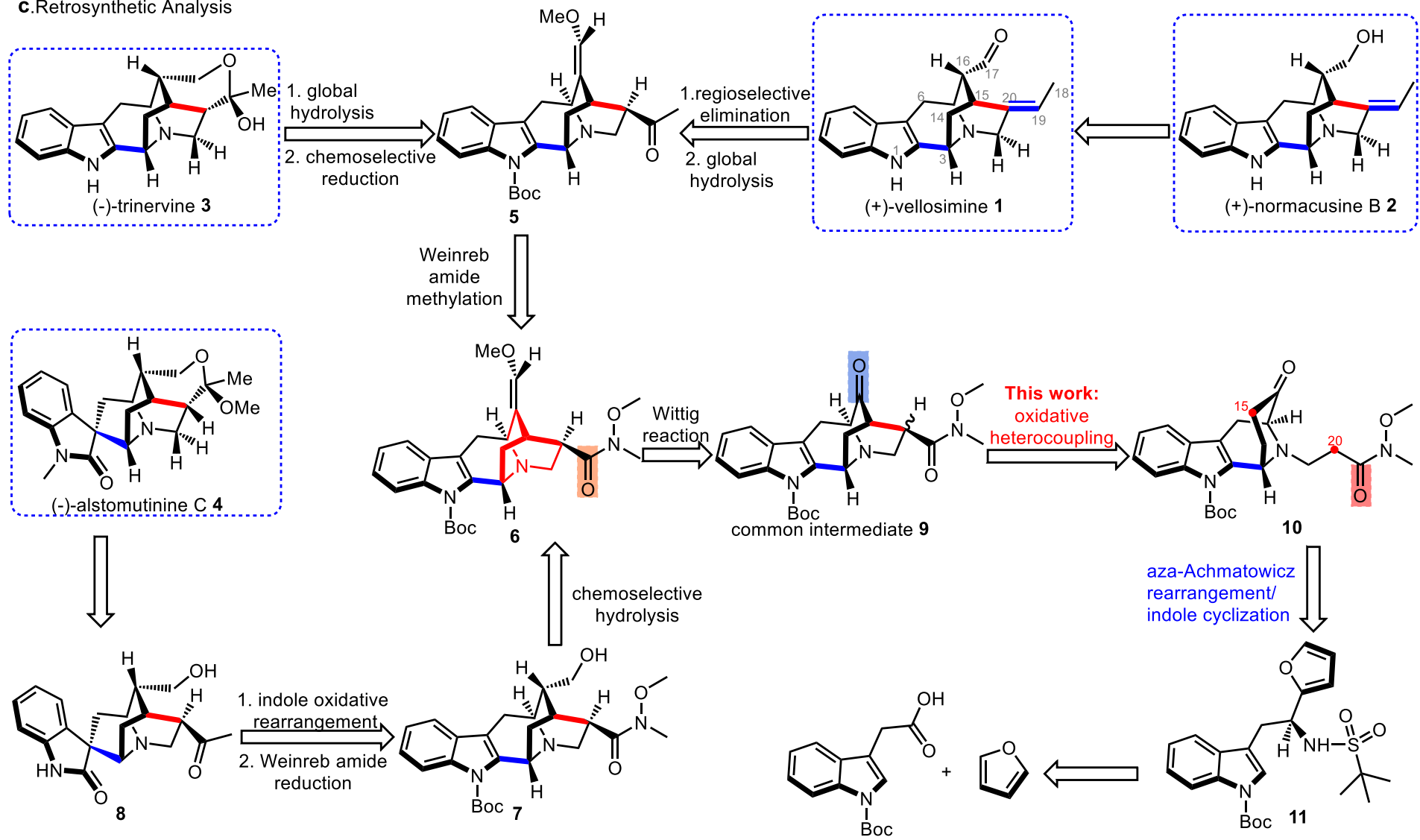
Org. Lett., **2000**, 2, 2057.

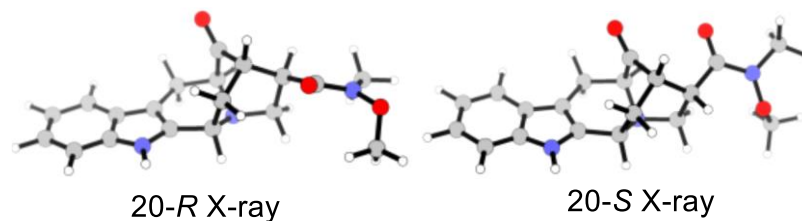
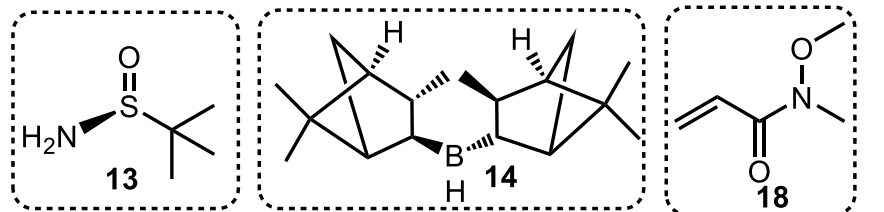
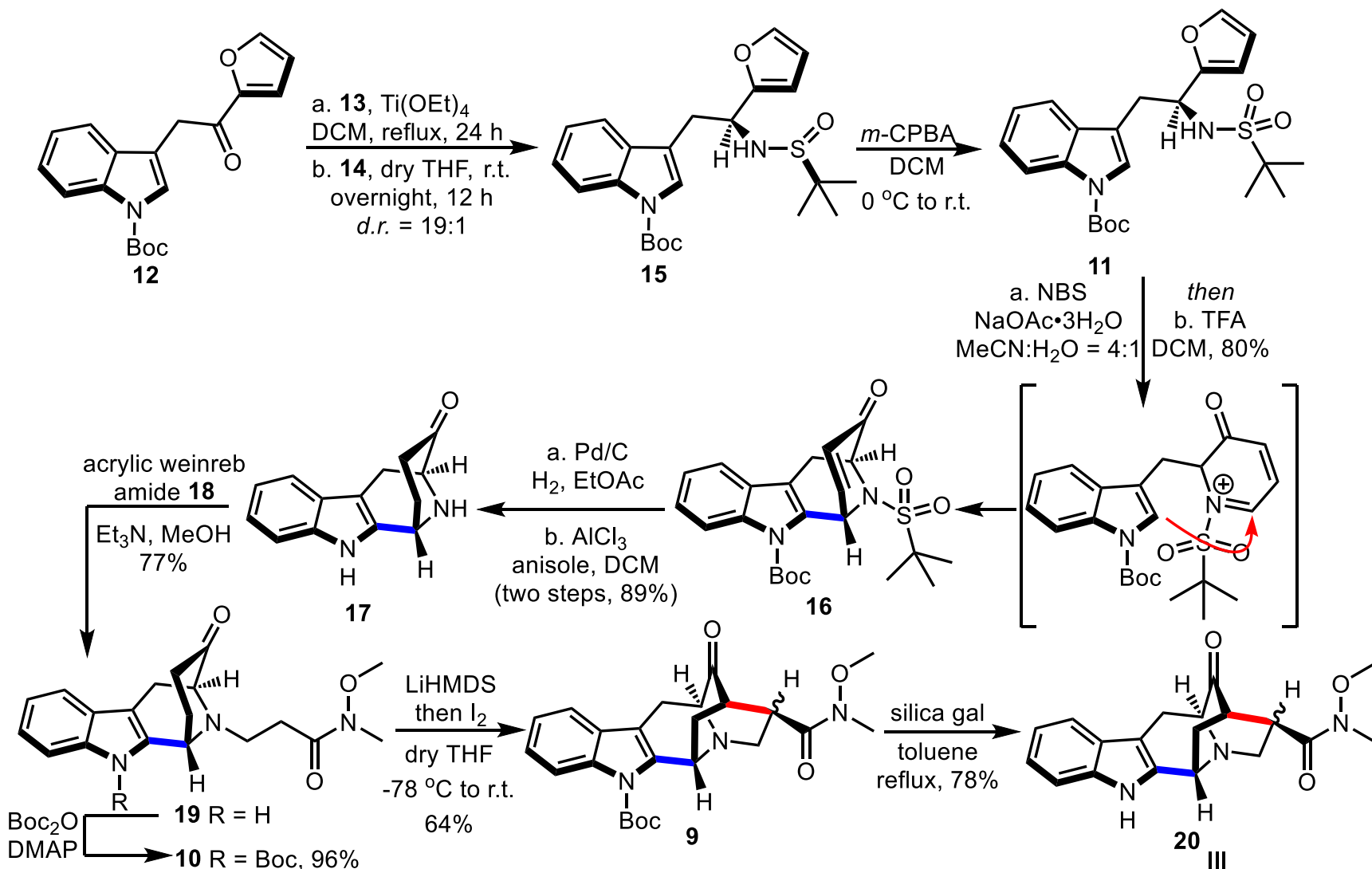


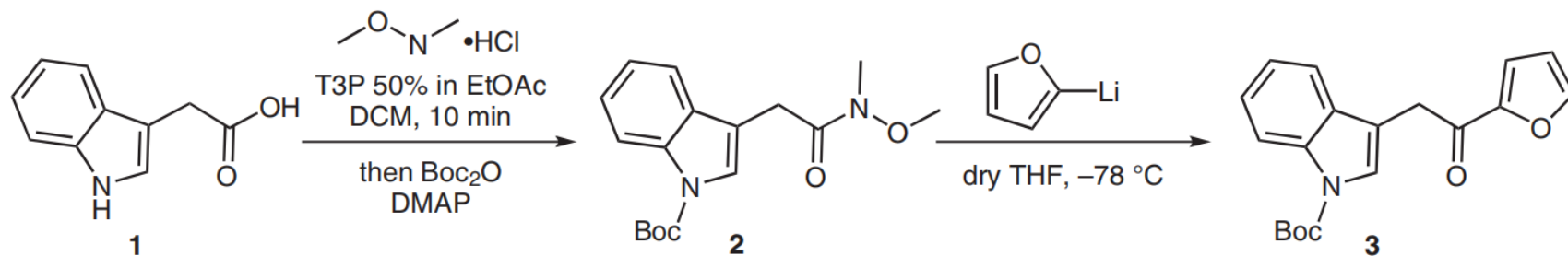
Angew. Chem. Int. Ed., **2015**, 54, 315.



C. Retrosynthetic Analysis

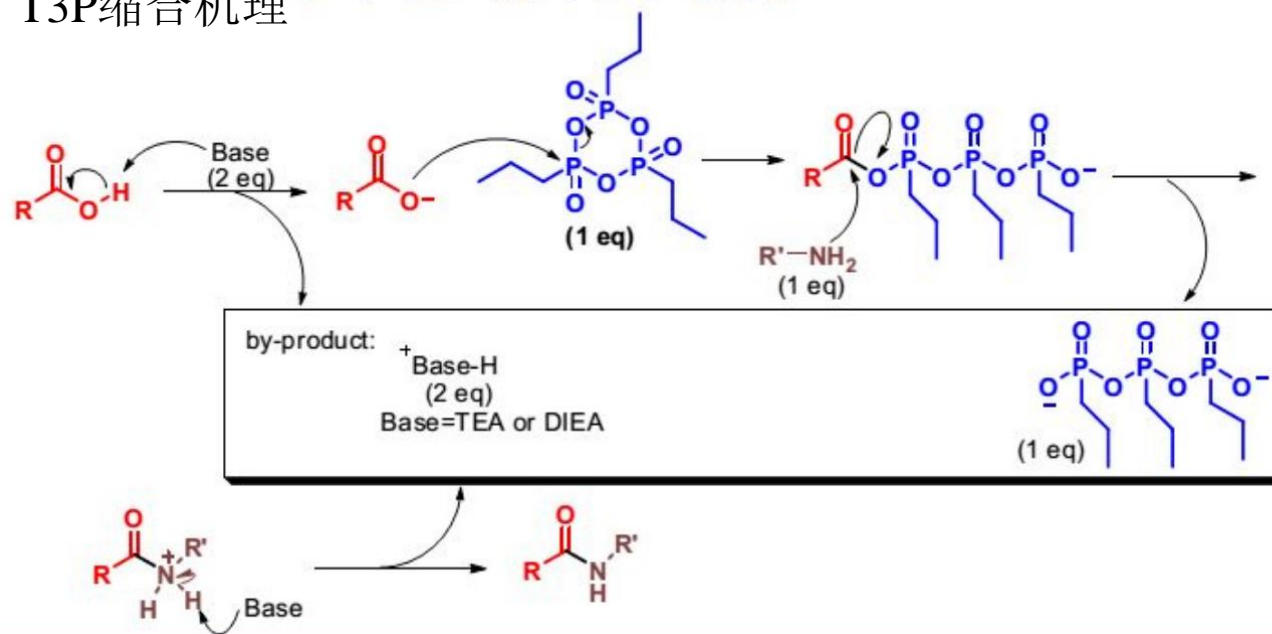




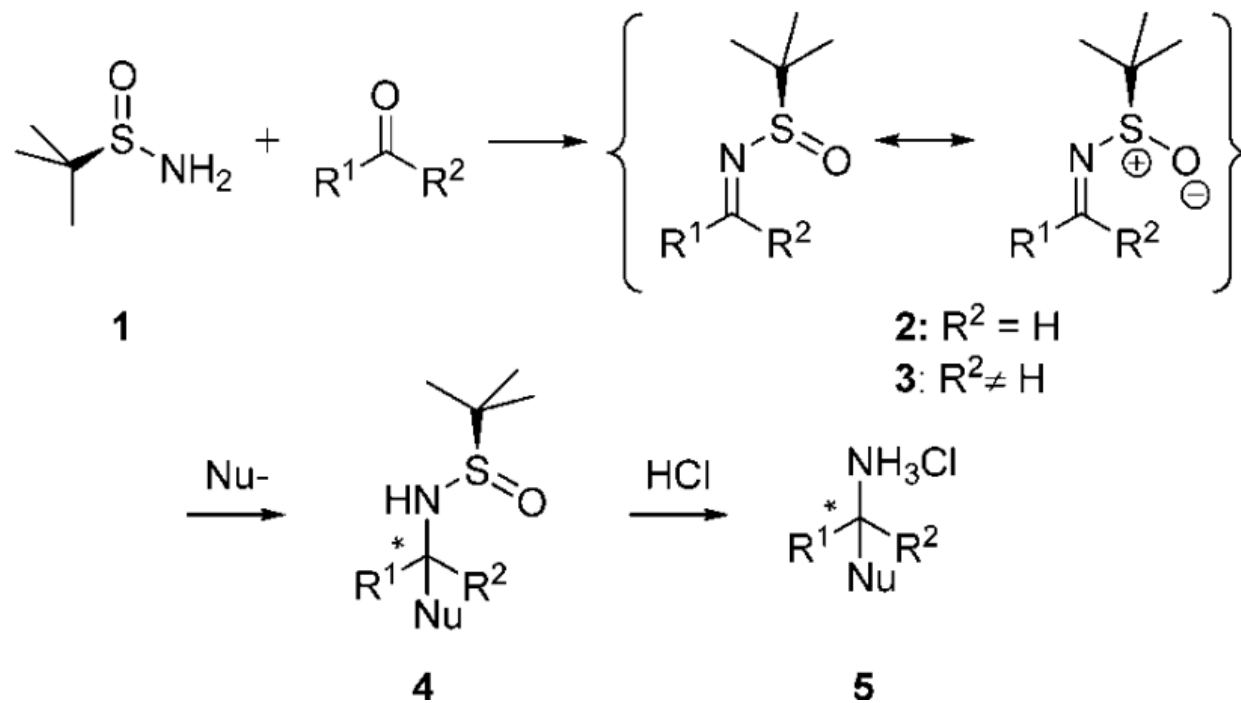


Synlett., 2020, 31, 7.

T3P缩合机理

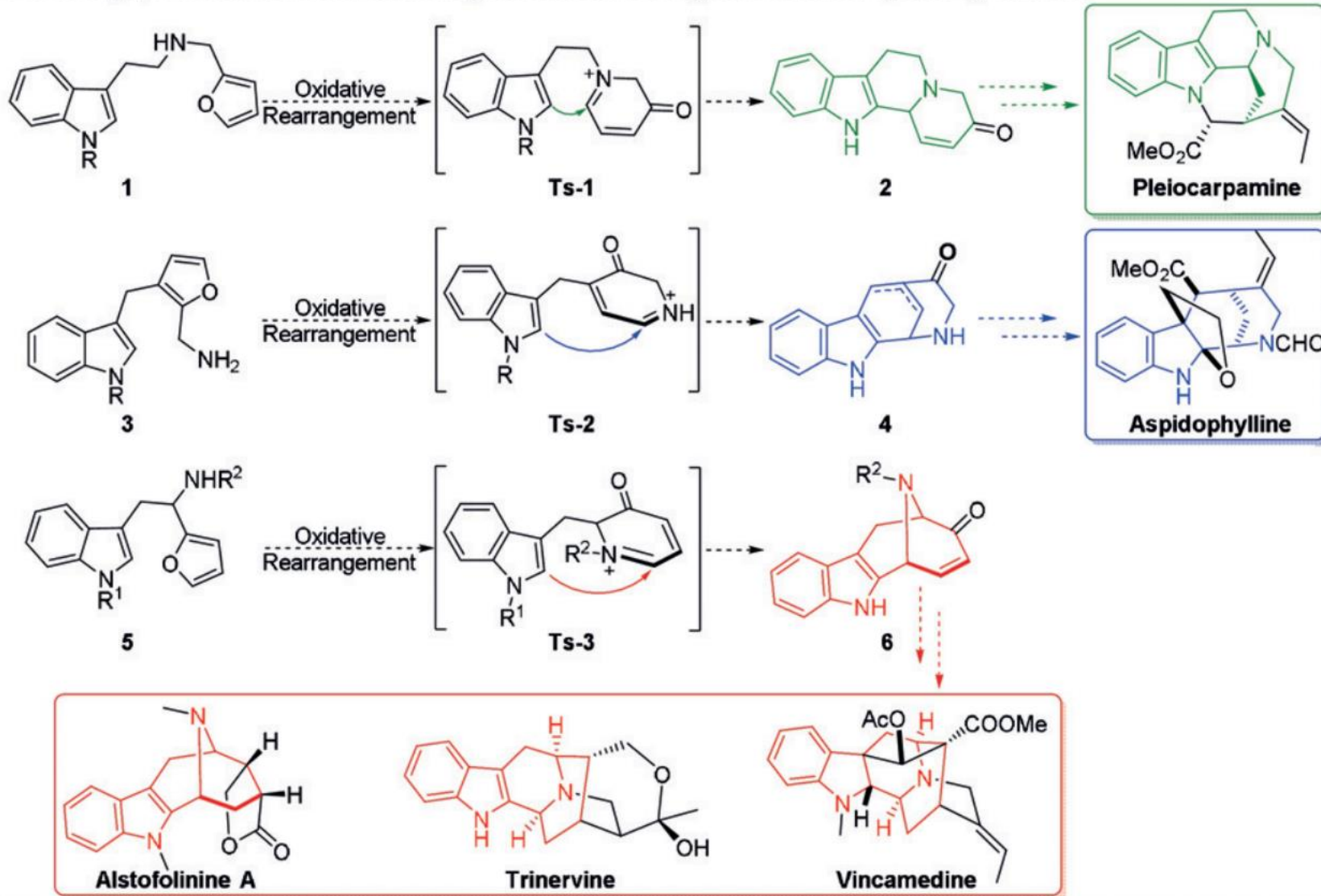


Ellman's sulfinamide

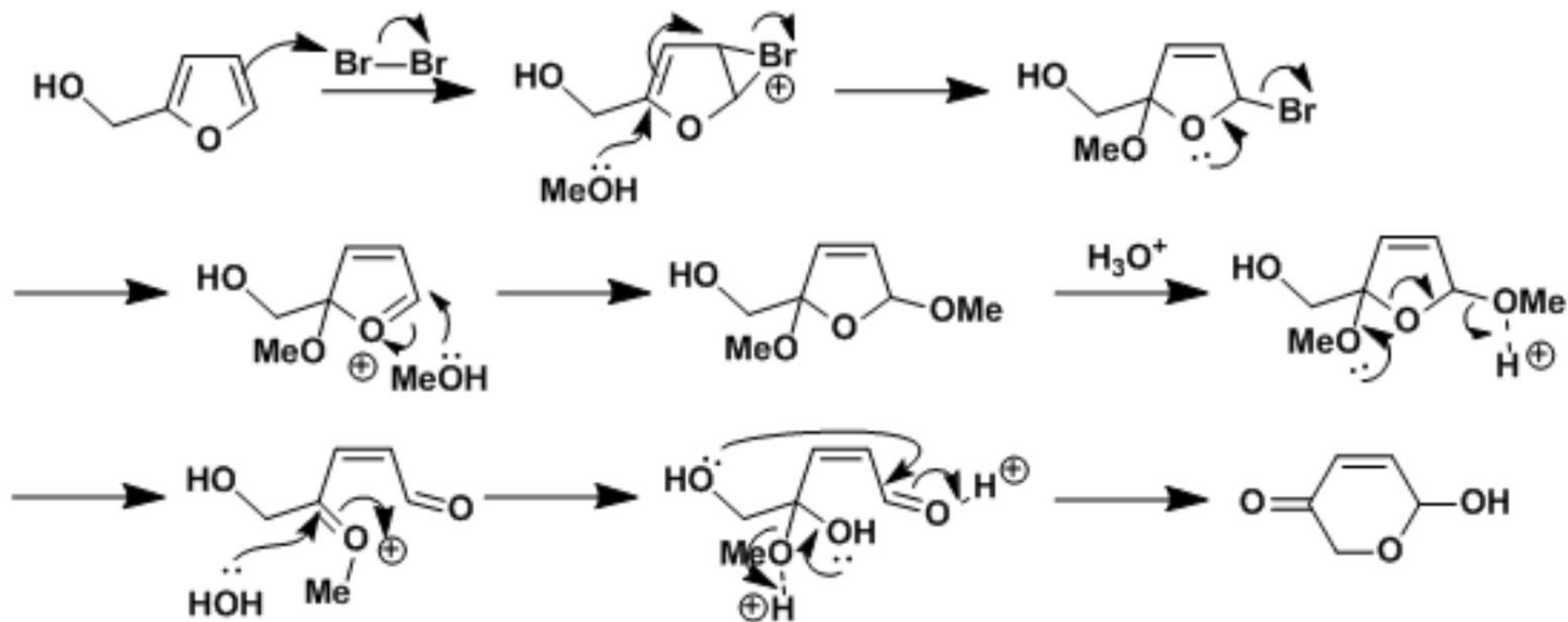


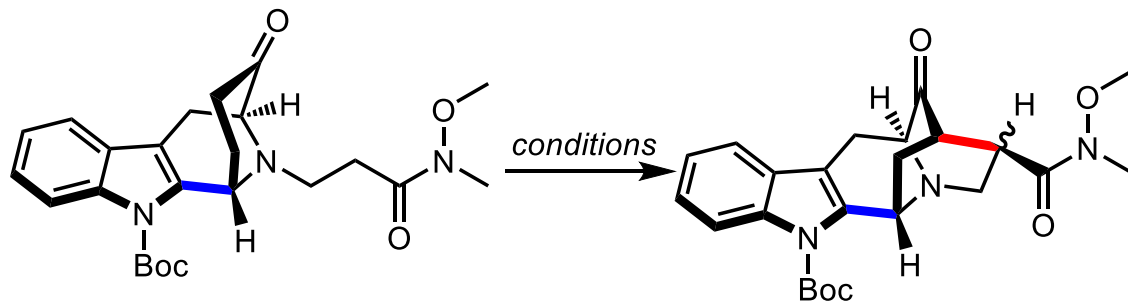
Chem. Rev., **2010**, *110*, 3600.

Our design, aza-Achmatowicz rearrangement followed by indole nucleophilic cyclization



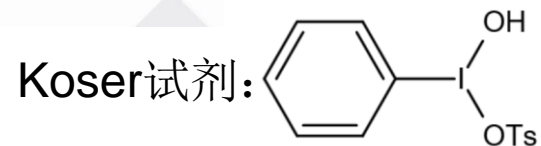
Achmatowicz rearrangement 反应

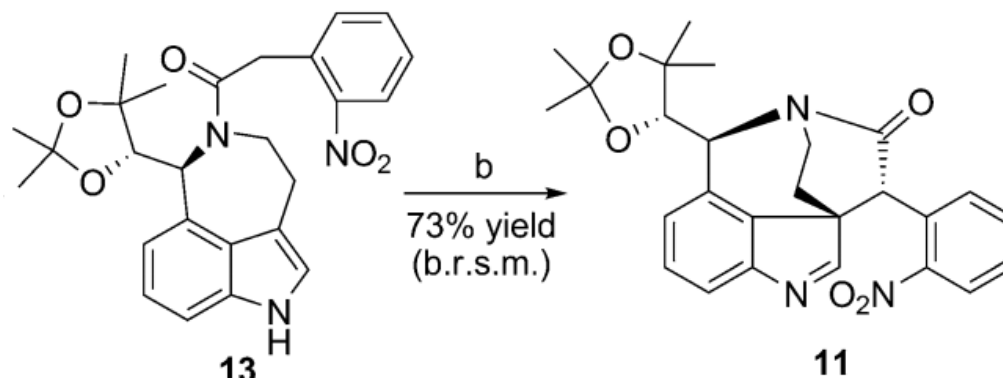




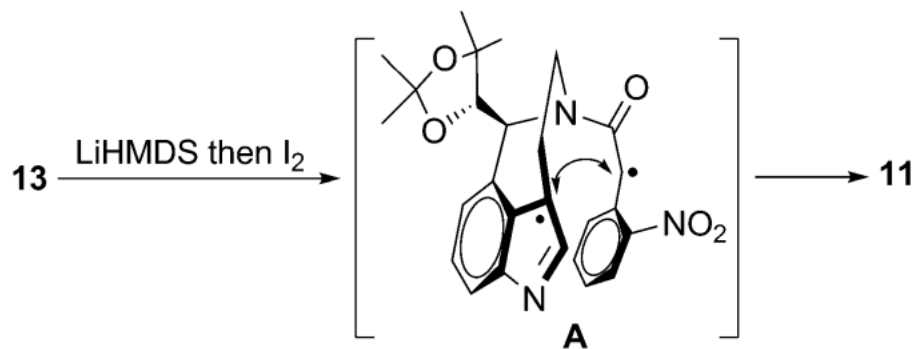
Entry	Base (2.2 equiv)	Oxidant (1.2 equiv)	Yield [%]	dr ^[c]
1	LiHMDS	Cu(OTf) ₂	n/d	
2	LiHMDS	[Fe(DMF) ₃ Cl ₂][FeCl ₄]	n/d	
3	LiHMDS	Koser's reagent	n/d	
4	LiHMDS	PIFA	n/d	
5	LiHMDS	I ₂	61% ^[a] (60% ^[b])	1.6:1
6	LiHMDS	ICl	60% ^[a] (63% ^[b])	1:1.3
7	LiHMDS	IBr	59% ^[a] (59% ^[b])	1:1
8	LiHMDS ^[e]	I ₂	64% ^[a] (61% ^[b] , 52% ^{[a], [d]})	1.4:1
9	NaHMDS	I ₂	21% ^[a] (23% ^[b])	1:6.2
10	KHMDS	I ₂	n/d	
11	LiHMDS	I ₂ ^[f]	56% ^[a] (57% ^[b])	2.0:1

These reactions were performed on a 0.05 mmol scale, -78°C, THF. [a] Isolated yield. [b] ¹H NMR yield, 1,3,5-trimethoxybenzene as the internal standard. [c] dr was determined by ¹H NMR analysis of the crude material. [d] This reaction was performed on a 1.0 mmol scale. [e] LiHMDS (2.5 equiv). [f] This reaction was performed in the presence of TEMPO (1.0 equiv). n/d=not detected, NaHMDS=sodium bis(trimethylsilyl)amide, KHMDS=potassium bis(trimethylsilyl)amide, PIFA=(bis(trifluoroacetoxy)iodo)benzene, TEMPO=2,2,6,6-tetramethyl-1-piperinedinyloxy.



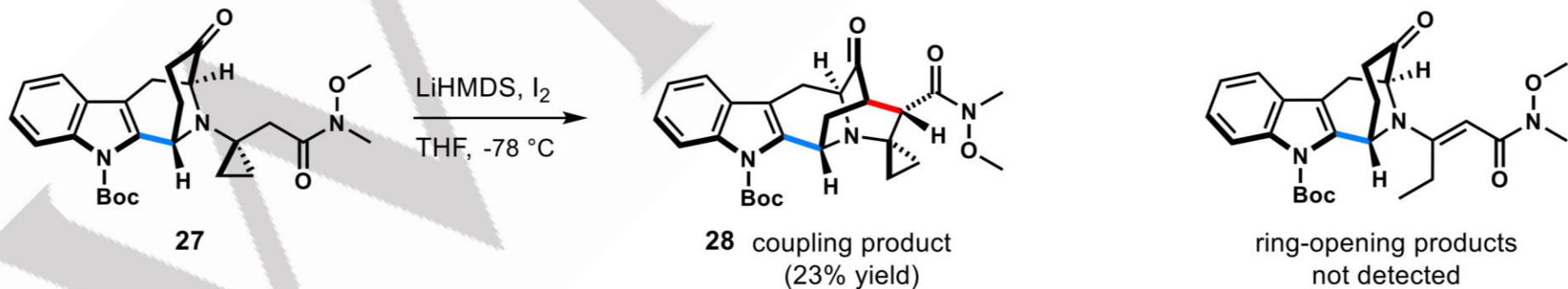


b) LiHMDS, then iodine, THF, -78 °C;



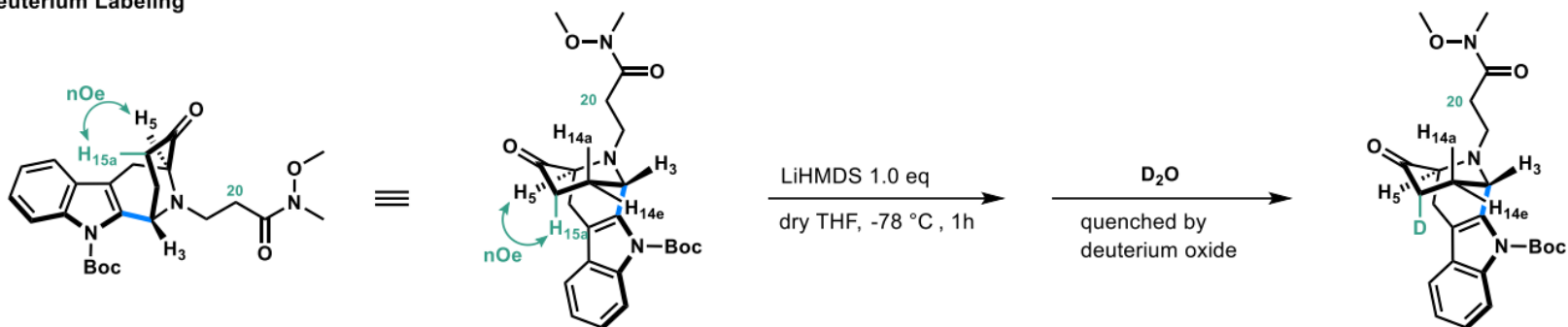
Angew. Chem. Int. Ed., **2011**, *50*, 12008.

b. Radical Clock Experiment

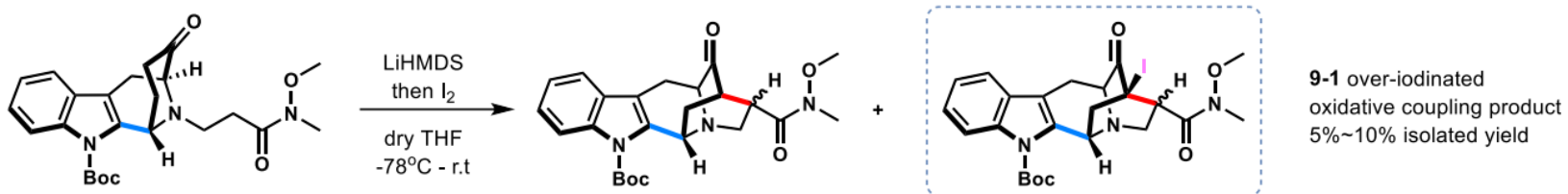


Scheme S-4.

a. Deuterium Labeling

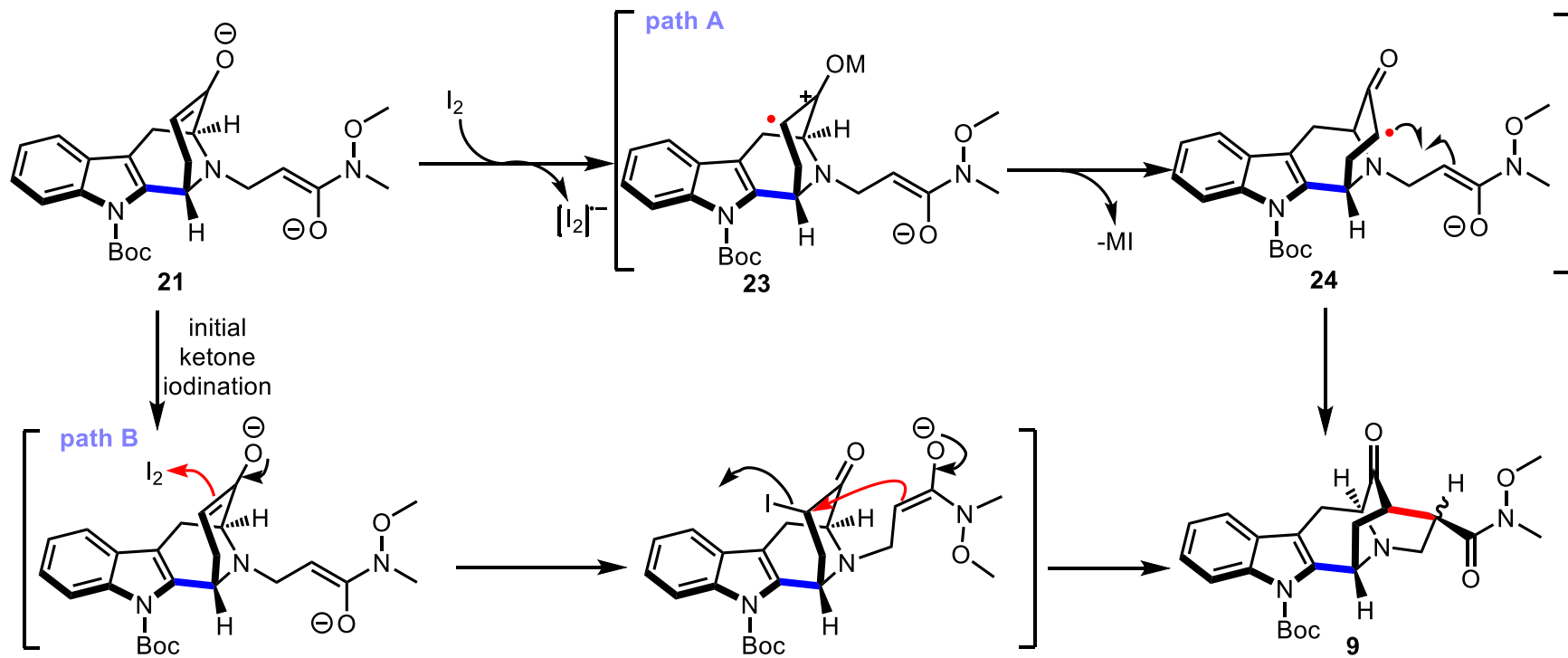


b. Over-iodinated Coupling Product



自由基钟实验（常用环丙基甲基自由基）：很多情况下，研究者利用环丙基甲基自由基可以重排形成烯丁基自由基的特点，来证明反应是否是自由基过程。比如说鉴定结构发现产物是环丙基破坏以后形成的产物，则证明反应中一定经历了环丙基甲基自由基的过程。如反应是离子型反应则不会出现破坏的产物。

J. Am. Chem. Soc., **2016**, *138*, 12692.



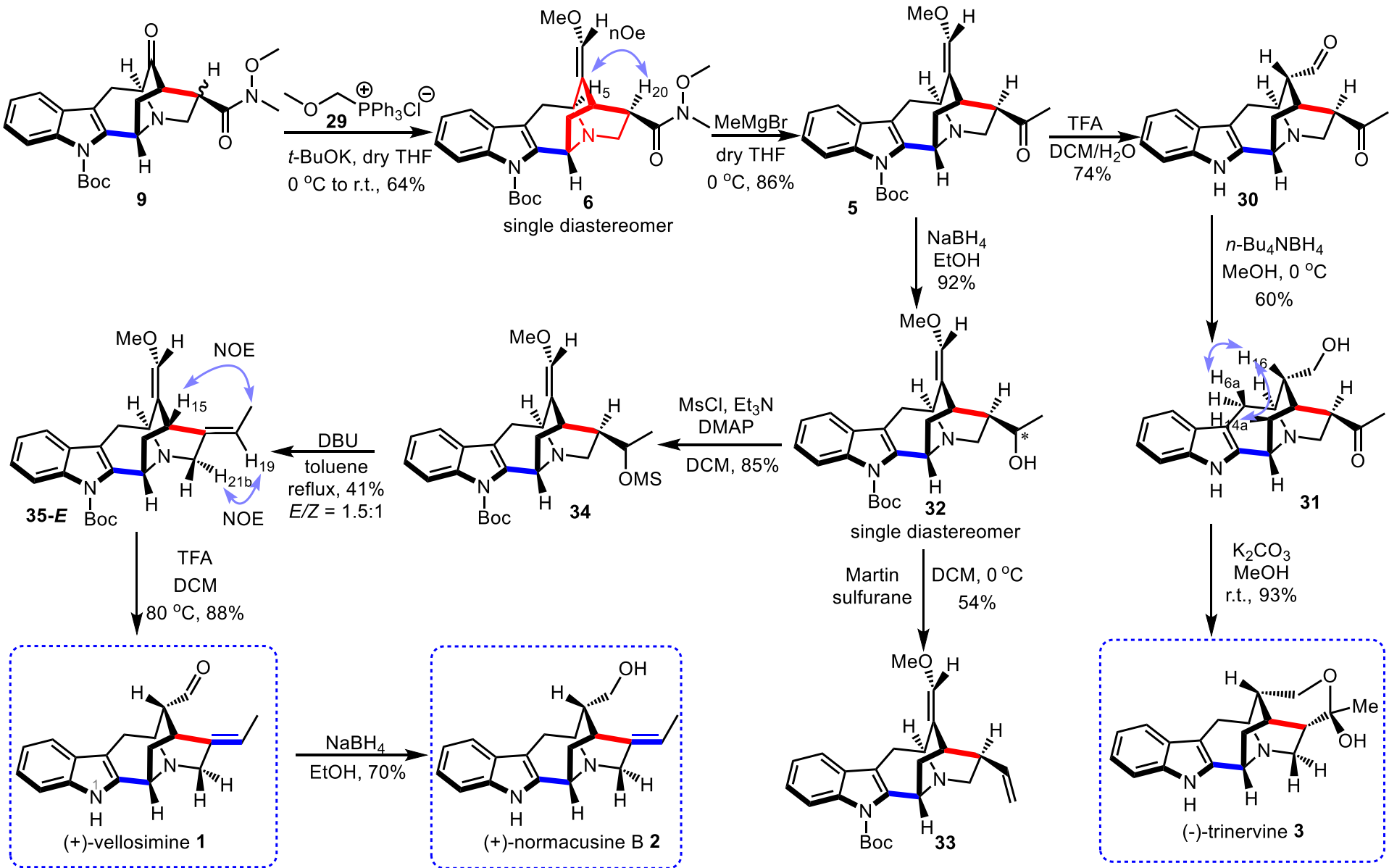
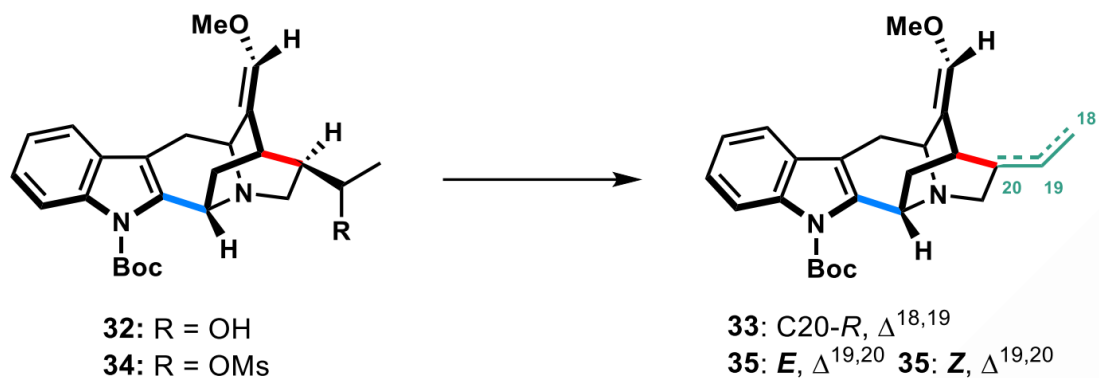


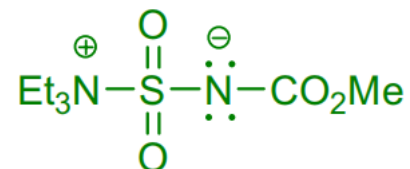
Table 2. Dehydration/elimination conditions.

Entry	R	Reagent	Solvent	Temp.	Yield [%] ^[a]
1	OH	POCl ₃	pyridine	0 °C-rt	n/d
2	OH	SOCl ₂	pyridine	0 °C-rt	trace
3	OH	Burgess' reagent	toluene	120 °C	complex mixture
4	OH	Martin's sulfurane	DCM	0 °C-rt	33: 54% 35-E: n/d, 35-Z: n/d
5	OMs	DBU	toluene	120 °C	33: n/d 35-E: 24%, 35-Z: 16%

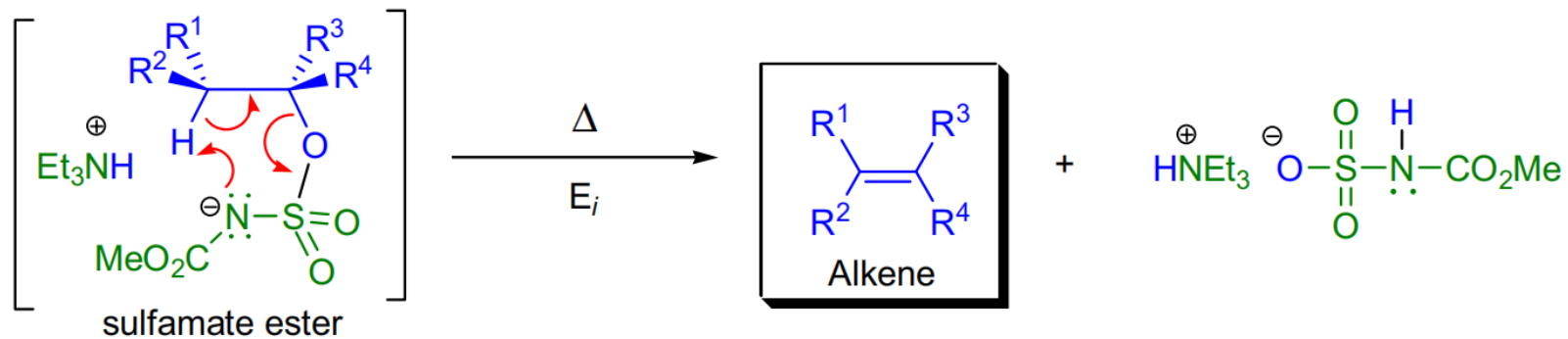
[a] Yield of the isolated product.

BURGESS DEHYDRATION REACTION

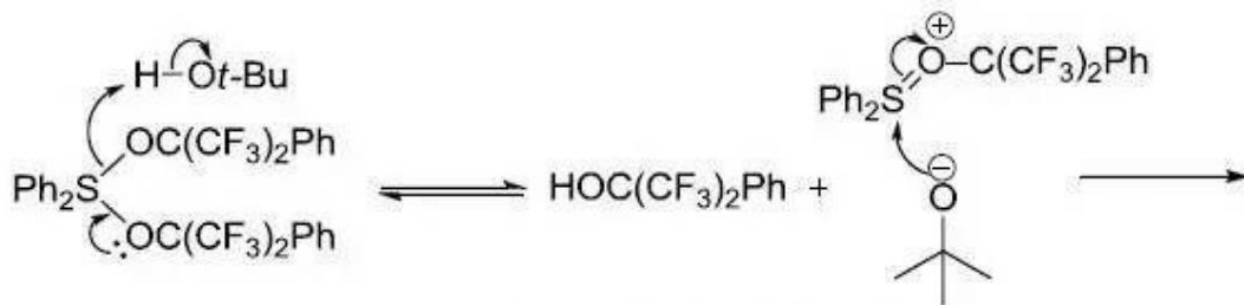
(References are on page 556)



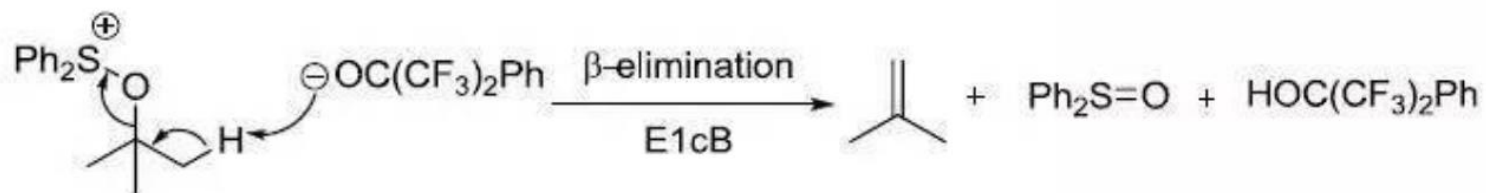
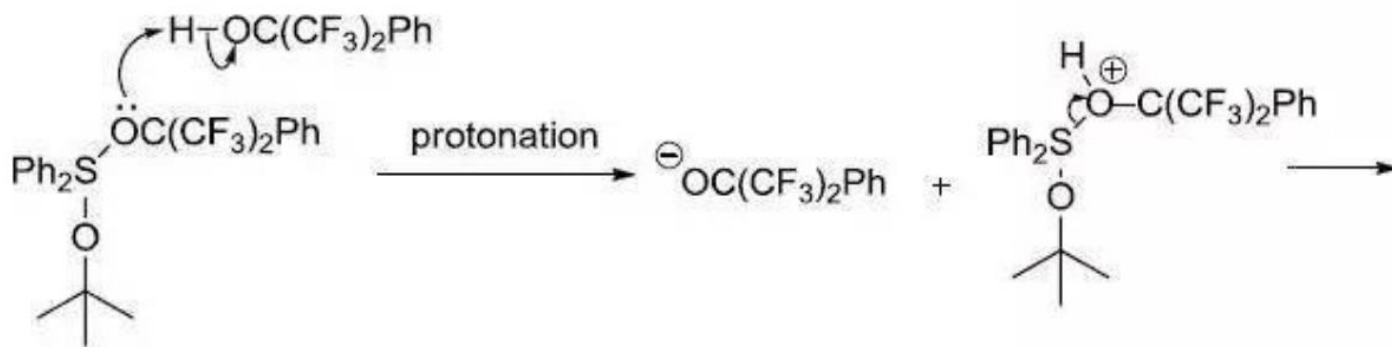
(Burgess reagent = BR)



Martin 硫化物脱水试剂



The alcohol is acidic



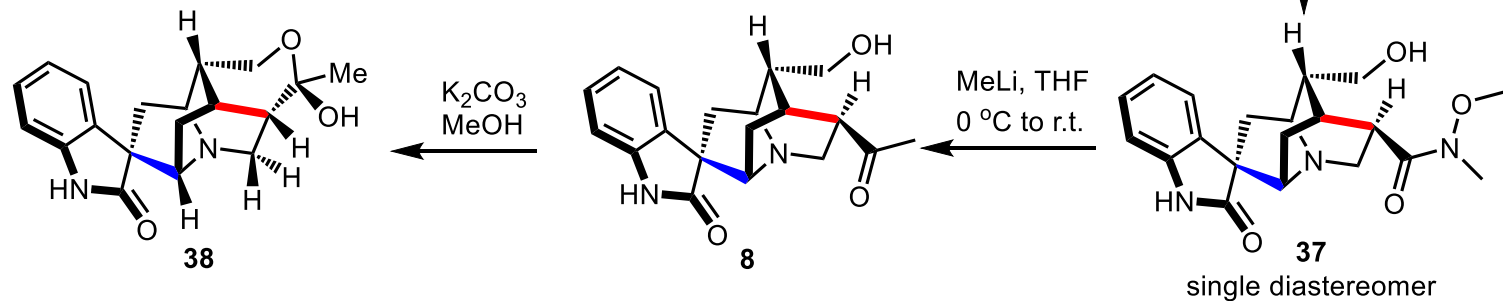
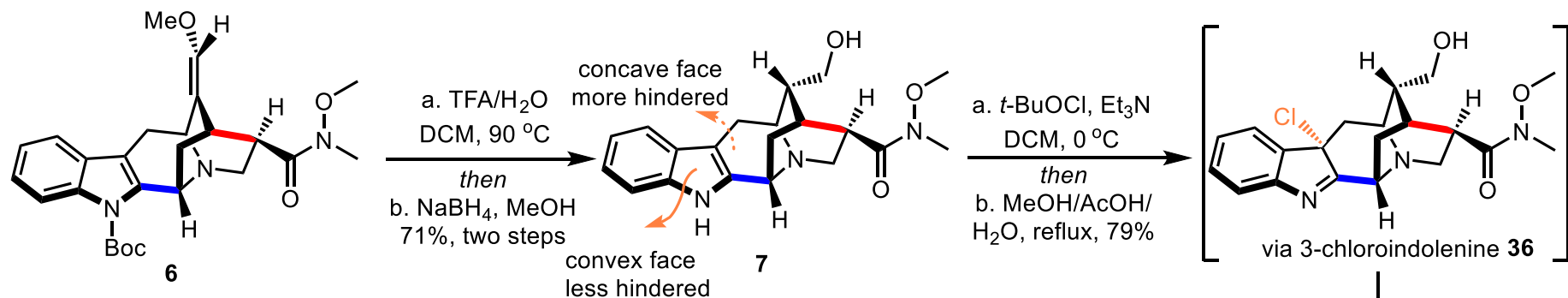
1.8 TETRABUTYLAMMONIUM BOROHYDRIDE: $n\text{-Bu}_4\text{NBH}_4$

This reagent is soluble in alcohols, ethers, CH_2Cl_2 , and toluene [PS1, RG1]. In hot CH_2Cl_2 , it decomposes slowly to borane. It is usable on solid supports [BI1].

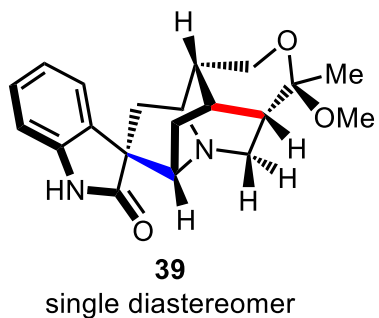
1.11 SODIUM AND TETRABUTYLAMMONIUM CYANOBOROHYDRIDES 7

$n\text{-Bu}_4\text{NBH}_4$ is a very mild reducing agent. The reactivity order in CH_2Cl_2 is as follows: $\text{RCOCl} > \text{RCHO} > \text{RCOR}' \gg \text{RCOOR}'$, esters being reduced only under reflux. This reagent reduces aldehydes selectively in the presence of ketones (Section 3.2.1). In organic acid media, tetrabutylammonium acyloxyborohydrides are formed. Under reflux in C_6H_6 , these reagents also reduce aldehydes selectively without affecting the ketones (Section 3.2.1) [GN1]. Borohydrides supported on exchange resin [GB5, GW3, YK5, YP3] exhibit a similar, although weaker, reducing power to the standard reagents.

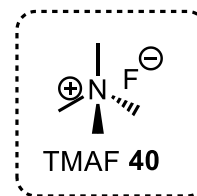
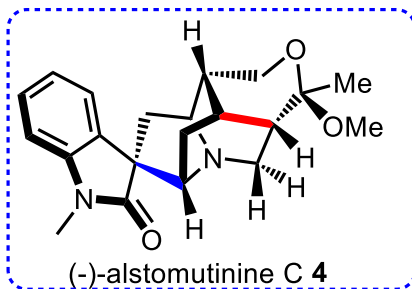
—Reductions by the Alumino and Borohydride in Organic Synthesis

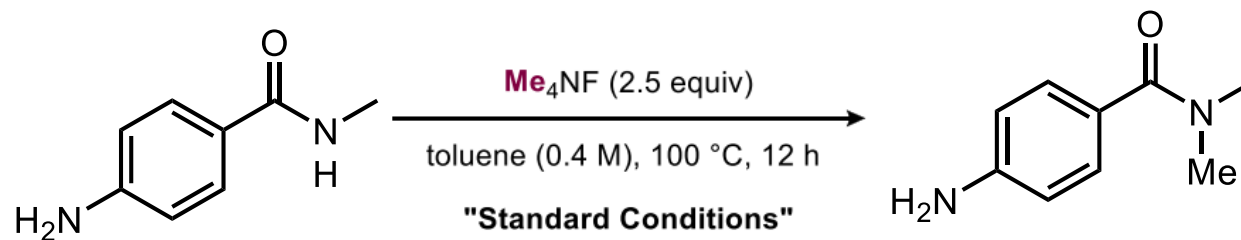


PTSA
 MeOH
 56%, 3 steps



TMAF **40**
 toluene
 100 $^\circ\text{C}$, 81%





b *Computational Study*

