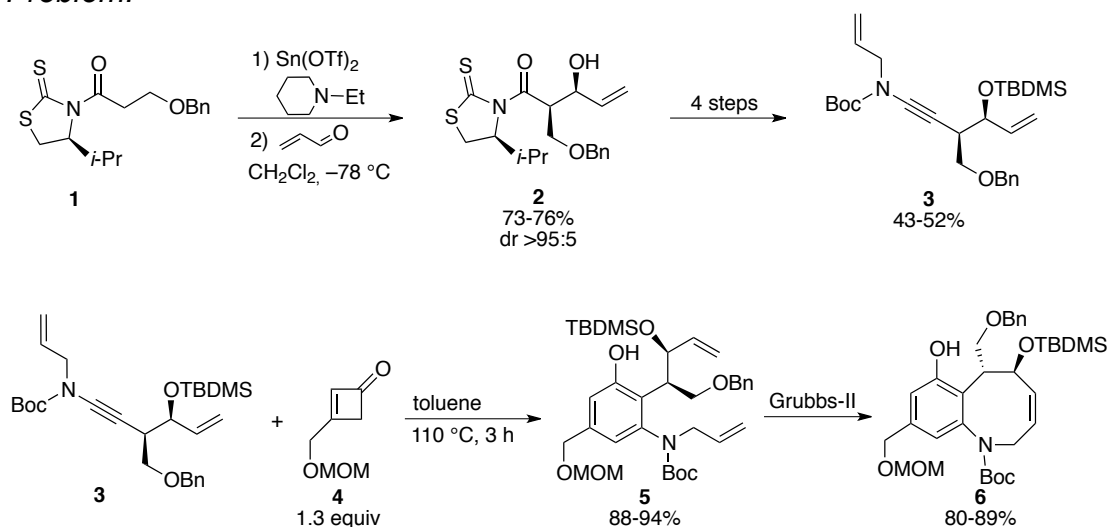


Synthesis of the Benzazocine Core of (+)-FR900482

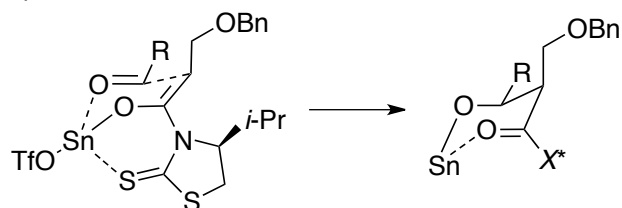
Problem:



- Propose a transition state that rationalizes the diastereoselectivity observed for the formation of **2**. Disregarding any diastereoselectivity issues, which problem may be encountered when using other metal enolates (Li, Ti...)?
- Proposed a mechanism for the formation of **5**.
- Envisage a sequence for the transformation of **2** into **3**.

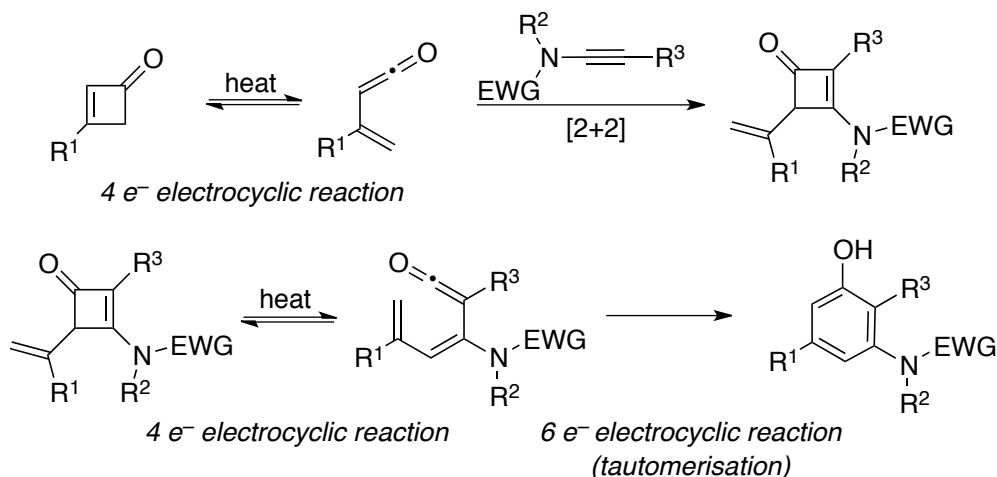
Solution:

1)

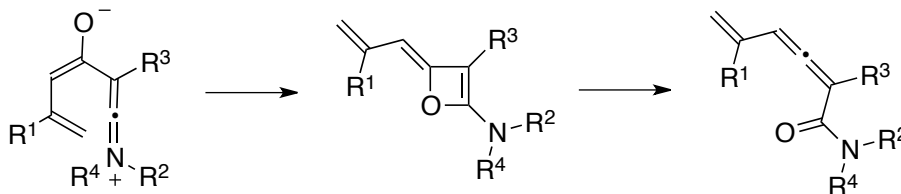


Tin enolates are less prone to undergo β -elimination of the alkoxy group.

2)



N.B: When a more nucleophilic ynamine is used, formation of a zwitterionic intermediate leads to an allenic amide as a byproduct.



3)

a) TBDMSOTf, 2,6-lutidine, CH_2Cl_2 , $0\text{ }^\circ\text{C}$.

b) DIBAL-H, CH_2Cl_2 , $-78\text{ }^\circ\text{C}$.

c) $\text{Ph}_3\text{P}=\text{CBr}_2$, THF, $0\text{ }^\circ\text{C}$; then KOt-Bu (4 equiv), $-78\text{ }^\circ\text{C}$, 20 min.

d) AllylNHBOc, CuSO_4 cat., 1,10-phenanthroline, K_3PO_4 , toluene, $85\text{ }^\circ\text{C}$, 46 h.

References:

Original paper: X.Y. Mak, A. L. Crombie, R. L. Danheiser, *J. Org. Chem.* **2011**, *76*, 1852–1873.

Thiourea as chiral auxiliaries in aldol reactions: Y. Nagao, Y. Hagiwara, T. Kumagai, M. Ochiai, T. Inoue, K. Hashimoto, E. Fujita, *J. Org. Chem.* **1986**, *51*, 2391–2393.

Keywords: tin enolate, cyclobutenone, pericyclic reactions