

## Problem Set 9

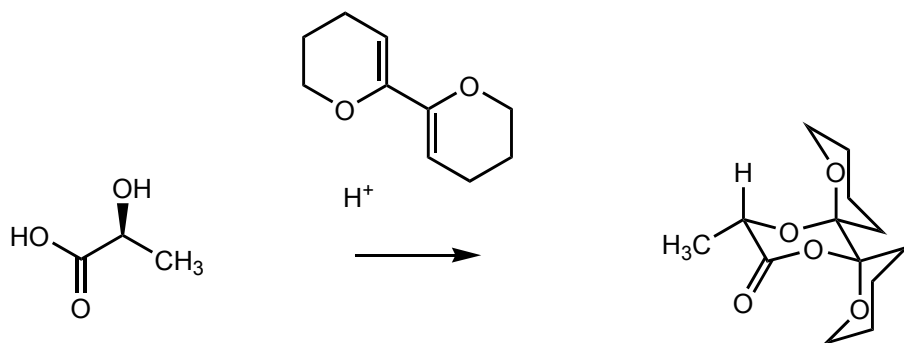
Name: Answer Key TF: \_\_\_\_\_

General Instructions: Neatly, in the space allocated, provide concise answers to the following questions using clear three-dimensional representations for all relevant structures. Address stereochemical and stereoelectronic issues where appropriate.

## Question 1.

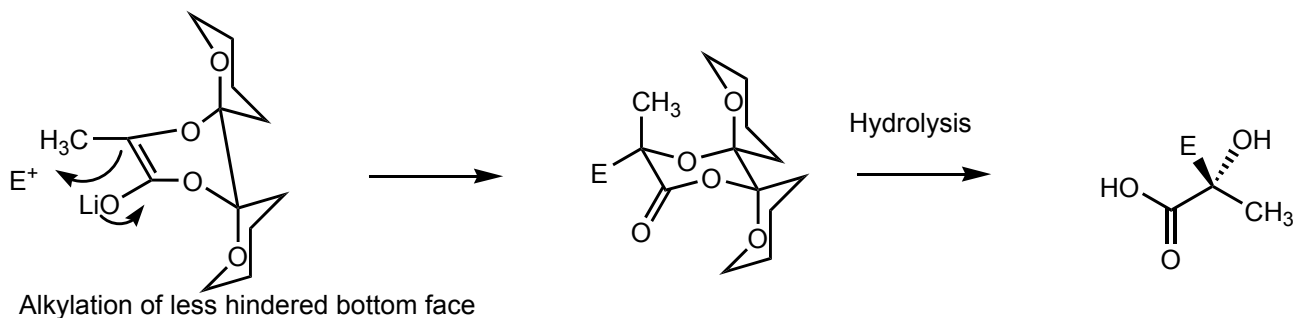
The principal of self-regeneration of stereocentres can be illustrated by the use of the dispoke protecting group in the stereoselective C- alkylation of lactic acid.

a. Draw what you would expect to be the dominant product of the dispoke protection of lactic acid.



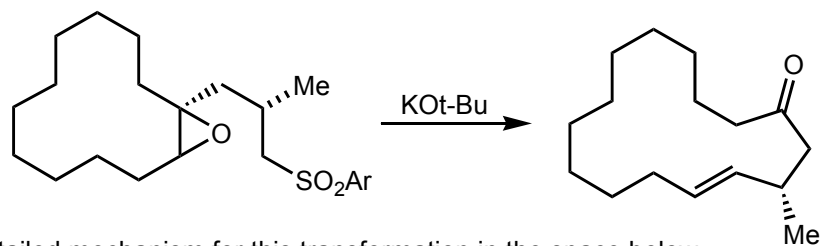
System benefits from maximum of 4  $n_O \rightarrow \sigma^*_{C-O}$  donations

b. The compound drawn above can be deprotonated with LDA, resulting in the destruction of the original stereocentre of lactic acid. The resulting enolate can be alkylated and the dispoke hydrolyzed to give a c-alkylated lactic acid with an e.r. as high as 98:2. Draw a model predicting the absolute sense of induction for this alkylation.

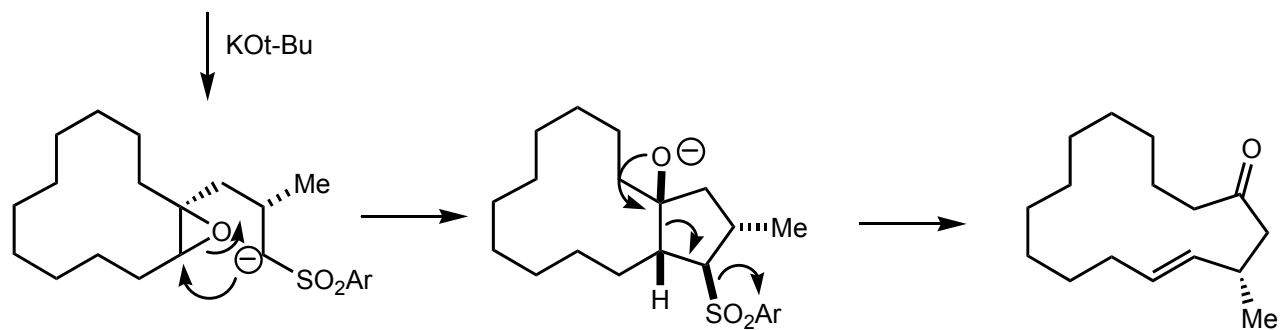


**Question 2.**

Fishli and Branca have reported the annulation reaction sequence shown below.

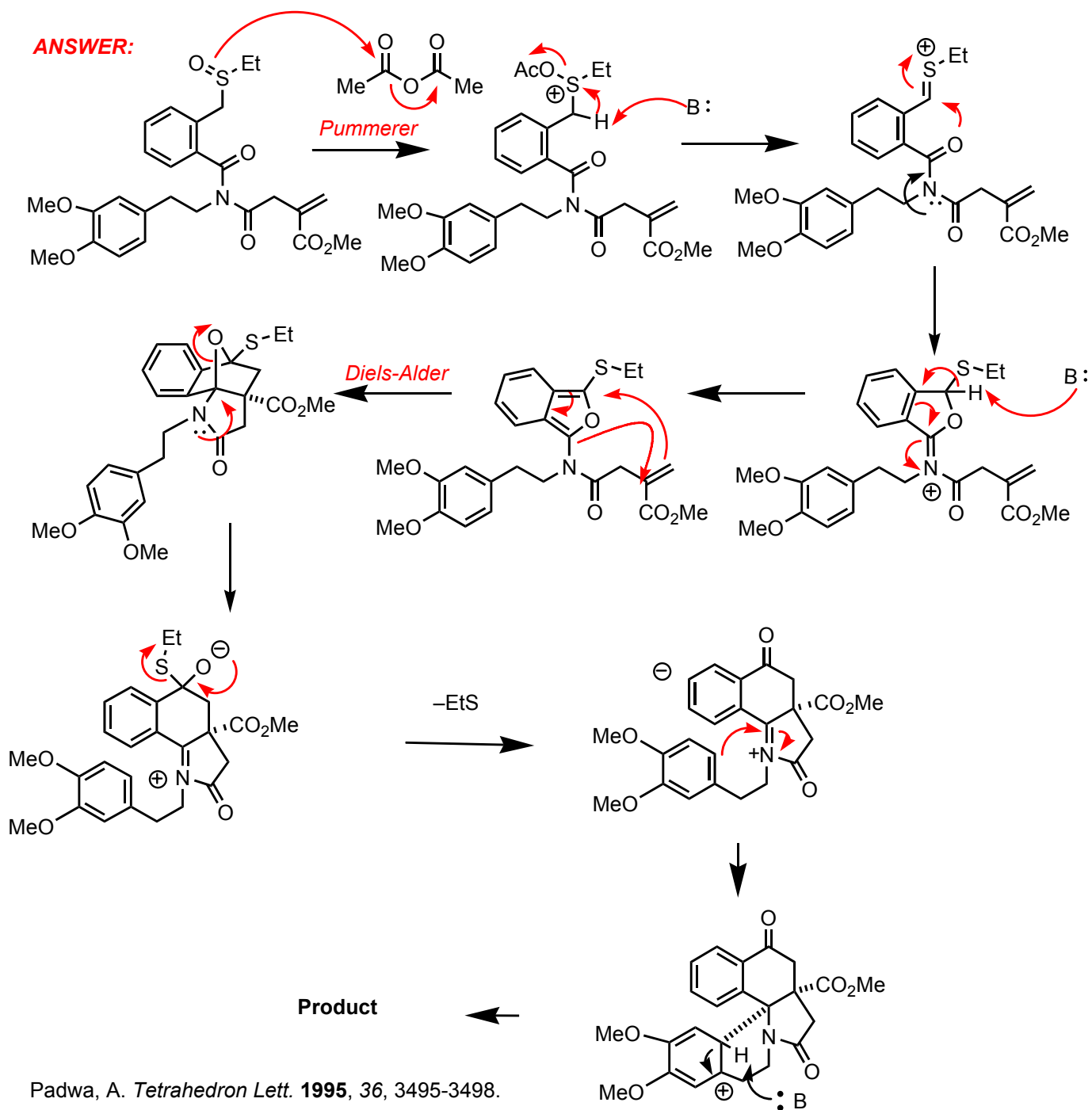
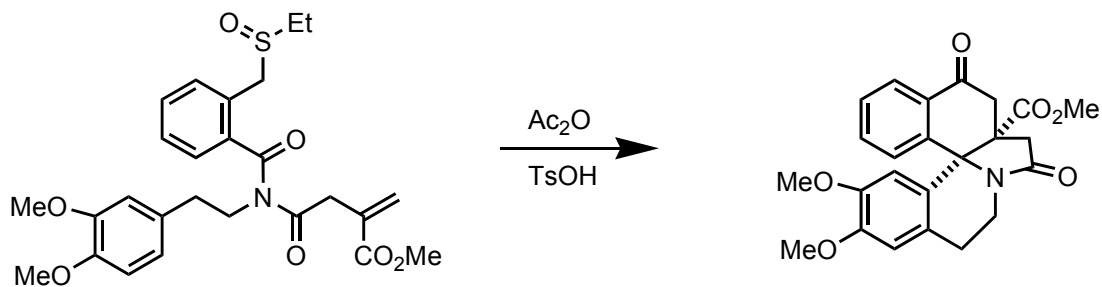


Provide a detailed mechanism for this transformation in the space below.



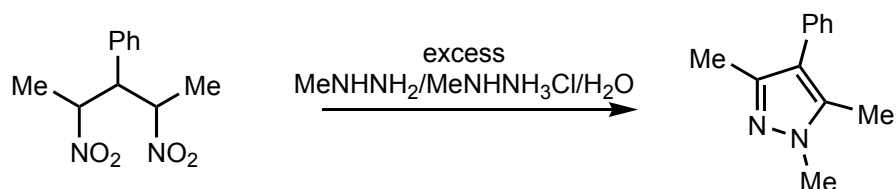
**Question 3.**

Padwa reported the interesting transformation shown below. Provide a detailed mechanism and identify any organic named reactions in this sequence.



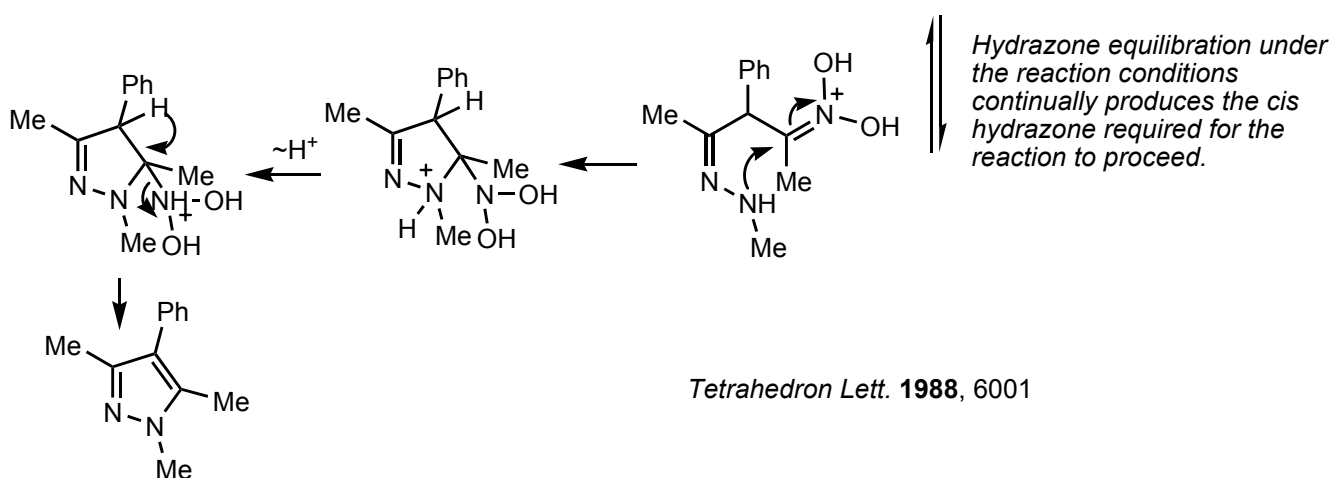
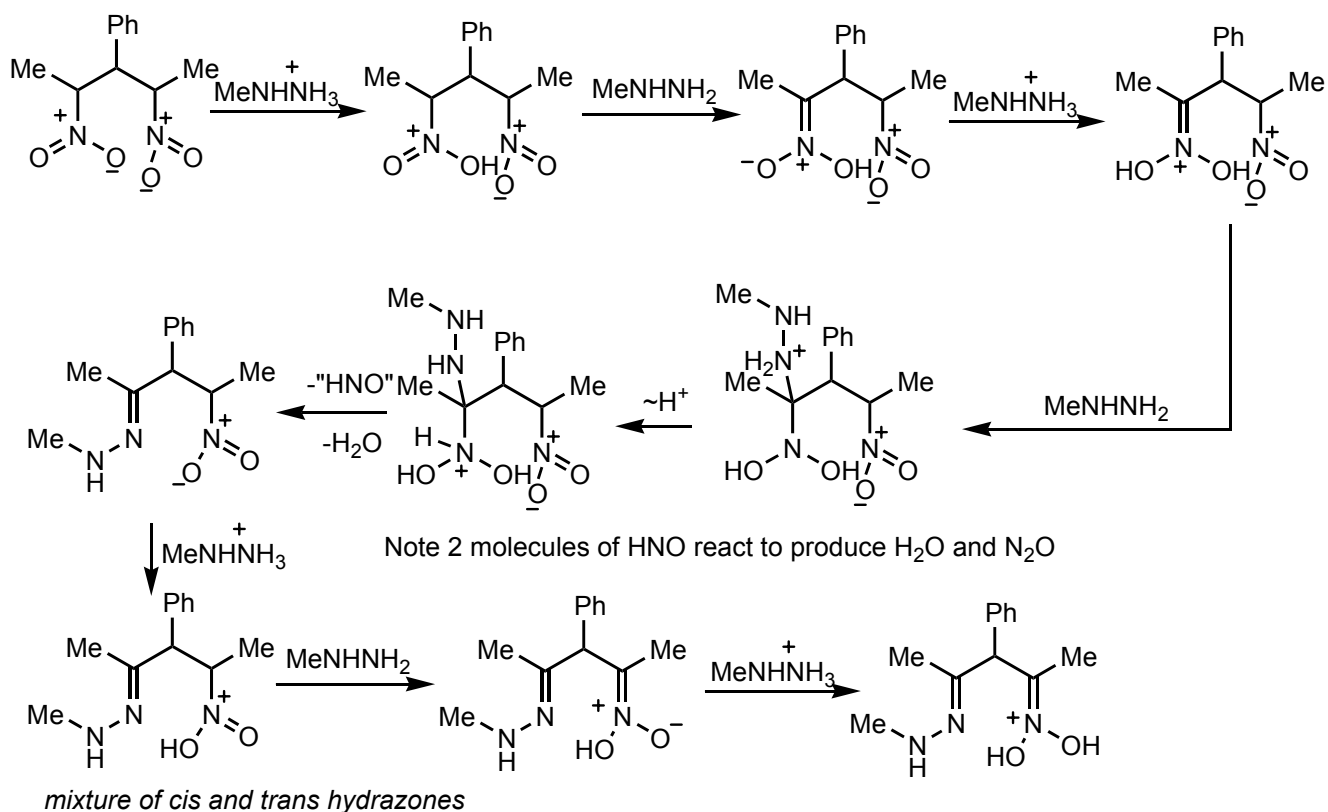
#### Question 4.

Here is a good exercise that deals with the versatility of the nitro group. Provide a detailed mechanism for the following reaction.



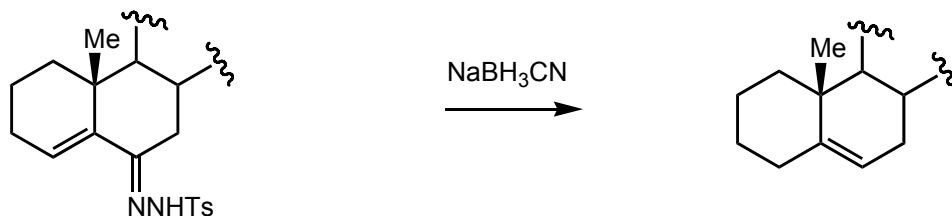
#### Answer

*A double Nef hydrolysis: MeNHNH<sub>2</sub> acts as proton shuttle and bis-nucleophile*

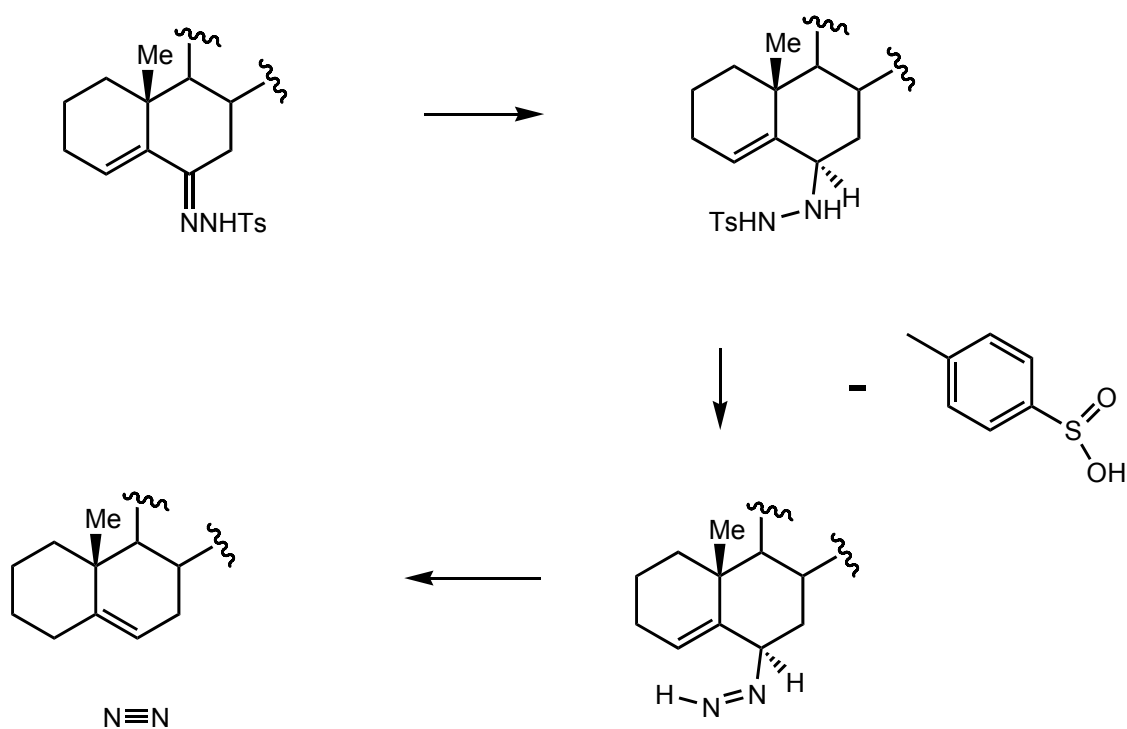


**Question 5.**

Djerassi reports the following alkene walk reaction. Draw a reasonable mechanism for this transformation.

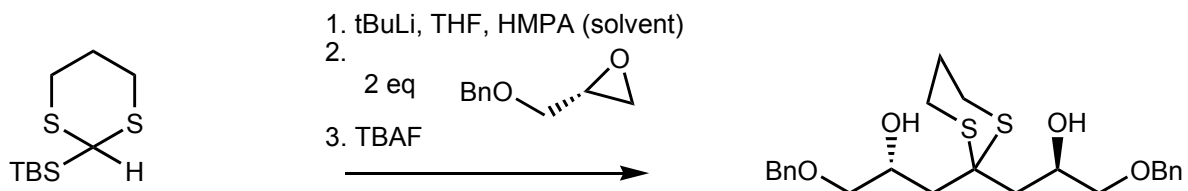


C. Djerassi, et al. *JACS* **1976**, *98*, 2275.



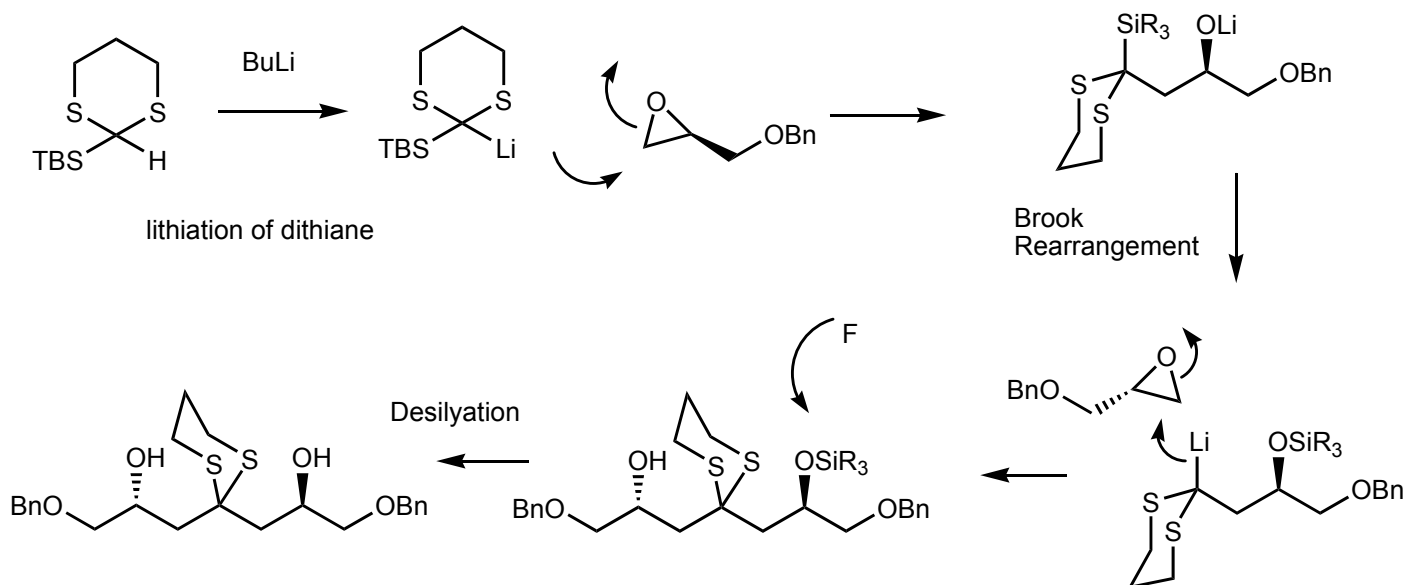
### Question 6.

Smith has developed the so-called "lynchpin" synthesis involving a dithiane. Please provide a reasonable mechanism for this transformation.



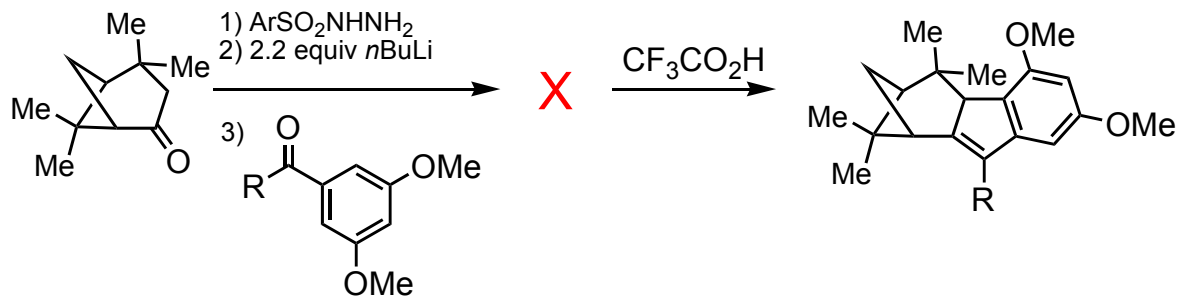
TBS= t-butyl dimethylsilyl

A.B. Smith, *JACS* **2003**, *125*, 14435-14445

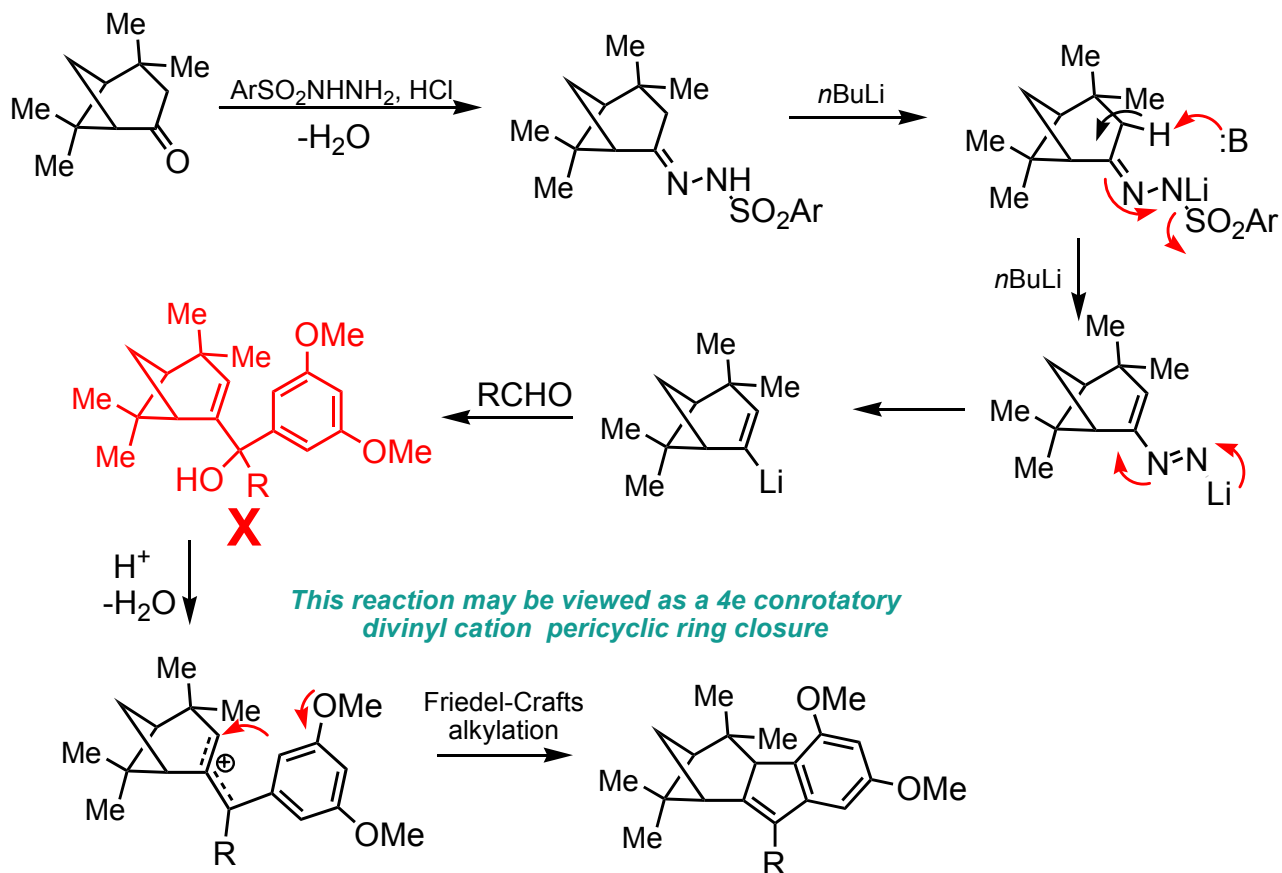


**Question 7.**

Rupert published the following transformation in his effort towards the synthesis of the Verbenindenes (*Organometallics* **2002**, 144).

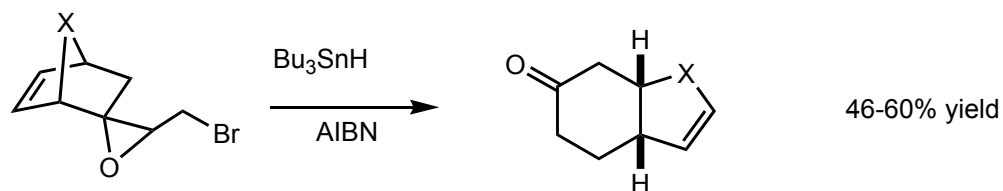


In the space below please provide a reasonable mechanism for the transformations outlined above. Be sure to clearly identify **X**.

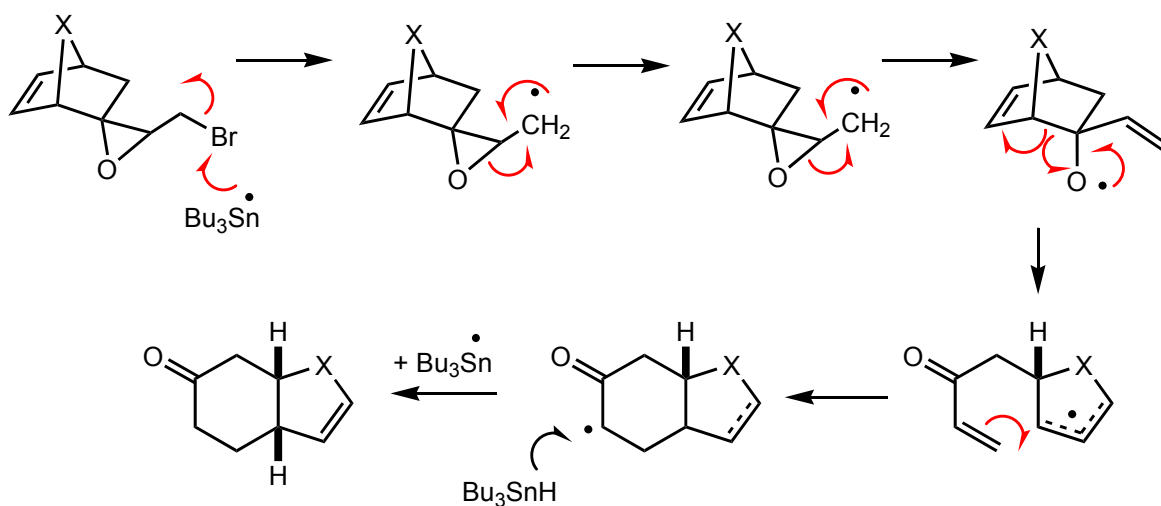


**Question 8.**

Renaud has disclosed an interesting reaction cascade (*Angew. Chem. Int. Ed.* **2002**, *41*, 4321). One of the reported transformations is illustrated below. The paper includes related examples.



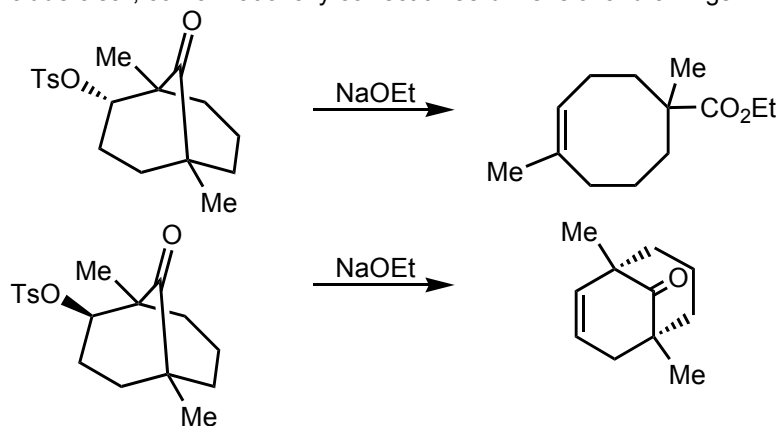
Provide a plausible mechanism for this reaction cascade. Your answer should include three-dimensional structures that accurately depict ground and transition state representations.





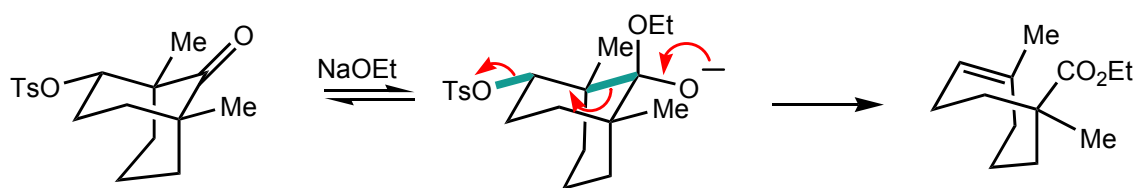
**Question 9.**

Provide mechanisms for the following related reactions, and rationalize the divergent reactivity. (*J. Chem. Soc.* **1964**, 289). Your answer should include clear, conformationally correct three-dimensional drawings.

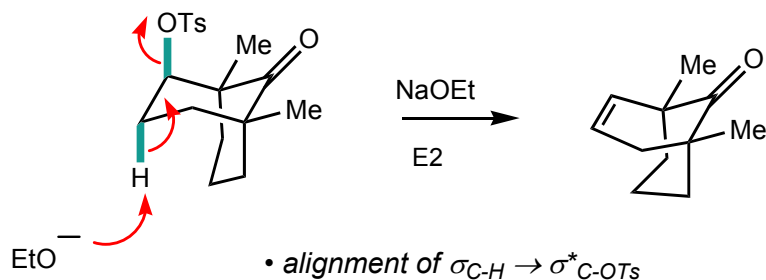


Answer

*Only the bonds antiperiplanar to the leaving OTs group are subject to cleavage.*



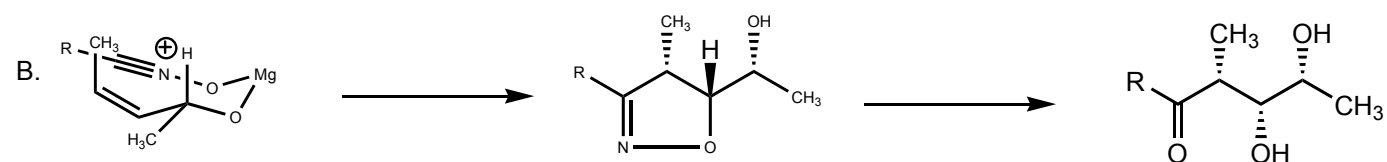
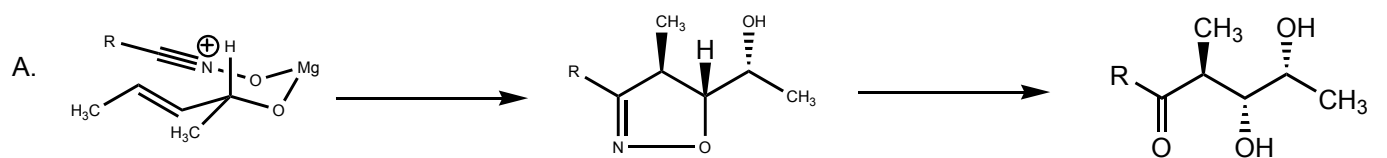
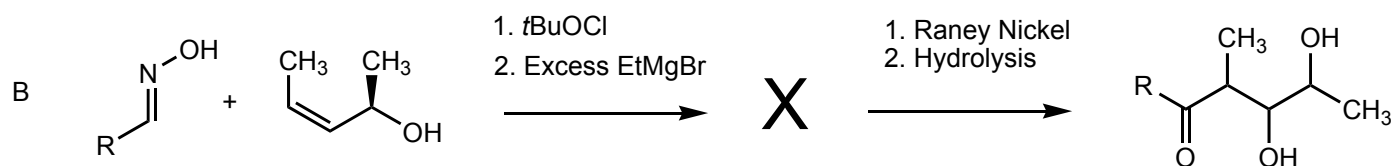
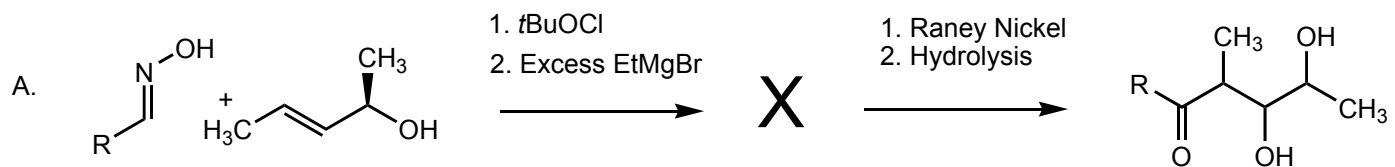
• alignment of  $\sigma_{C-C} \rightarrow \sigma^*_{C-OTs}$



• alignment of  $\sigma_{C-H} \rightarrow \sigma^*_{C-OTs}$

**Question 10.**

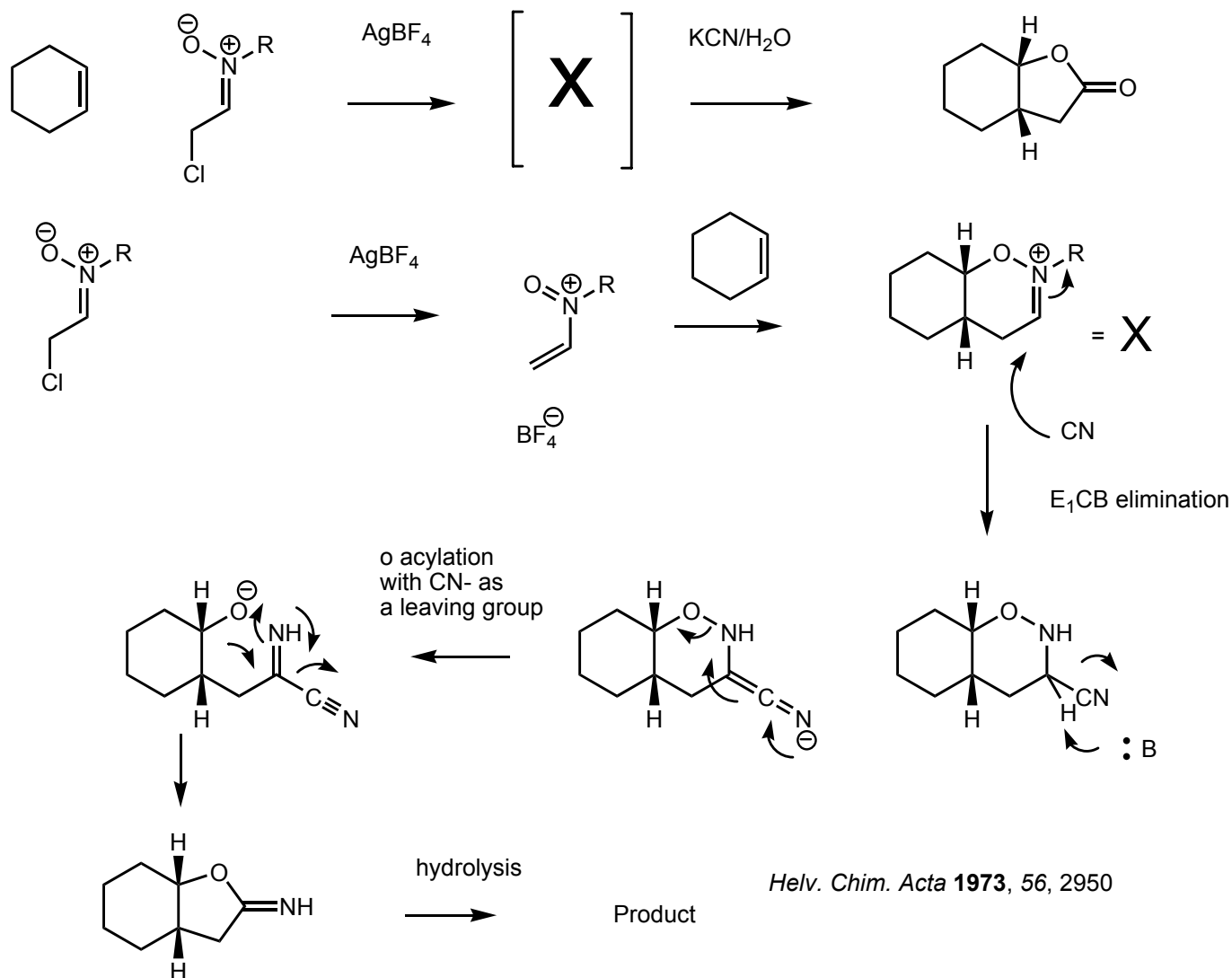
Carreira has developed a magnesium directed cycloaddition of nitrile N-oxides to alkenes into a powerful method of forming aldol products. The N-O bond in the isoxazoline formed from the cycloaddition can be cleaved by Raney nickel, revealing a beta hydroxy ketone. In each of the cases below, draw a transition state model of the cycloaddition to predict the relative and absolute configurations of the final products. (Hint, *t*-Butyl hypochlorite is oxidizes oximes into nitrile N-Oxides.



For an application of this chemistry in total synthesis, see *Angew. Chem. Int. Ed.* **2005**, *44*, 4036-4038

**Question 11.**

Eschenmoser has reported the following transformation which makes use of some concepts in polarity reversal. Please identify intermediate X and suggest a role for the silver in generating the reactive species that adds to cyclohexene to form X. Intermediate X is transformed into the final product by the action of potassium cyanide in water. Suggest a reasonable mechanism for this transformation.



Under treatment with aqueous base, intermediate x produces the dialdehyde shown below. Please draw a mechanism to explain the formation of the dialdehyde.

