

Page 1 This page
Page 2 Exam question from Jan 2007
Pages 3-4 Answer. Try the problems before you look at this page!

4. Answer **all** of the following parts.

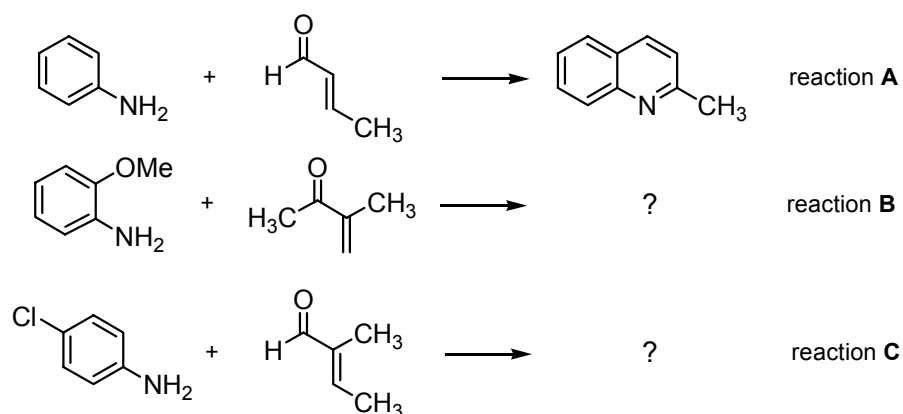
- (a) Using an appropriate example describe the difference between a cyclization reaction and a cycloaddition reaction.

(4 marks)

- (b) Using appropriate examples, describe the two main methods available for the generation of nitrile oxides.

(5 marks)

- (c) Given that in the Doebner-von Miller quinoline synthesis *trans*-but-2-enal and aniline react to give 2-methylquinoline (reaction **A**), formulate the products from reactions **B** and **C**.

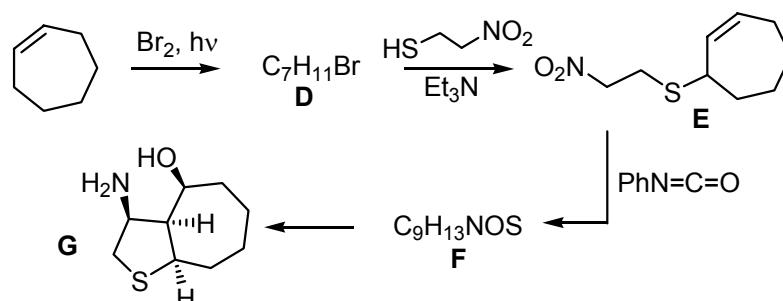


(5 marks)

- (c) Using reaction **A** as an example outline the mechanism of the Doebner-von Miller synthesis. A full mechanism is not required, but key intermediate(s) should be shown.

(5 marks)

- (e) Consider the following scheme and derive structures **D** and **F** in which the transformation **E** to **F** involves a cycloaddition reaction. Suggest reagents for the conversion of **F** to **G** and comment on the stereoselectivity of this conversion.



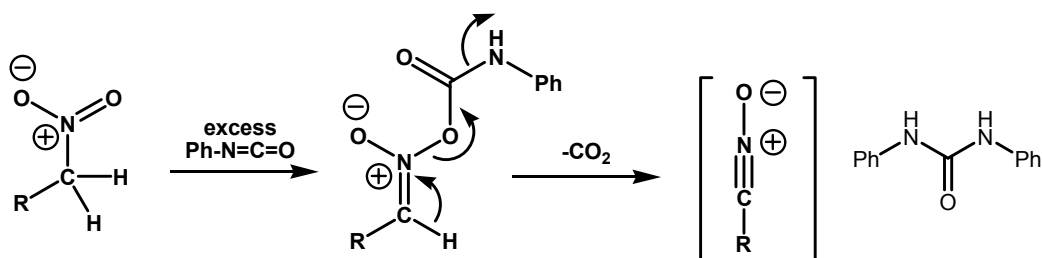
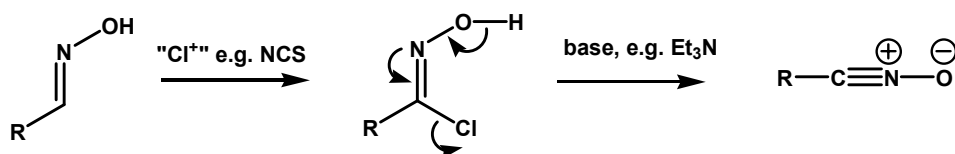
(6 marks)

4

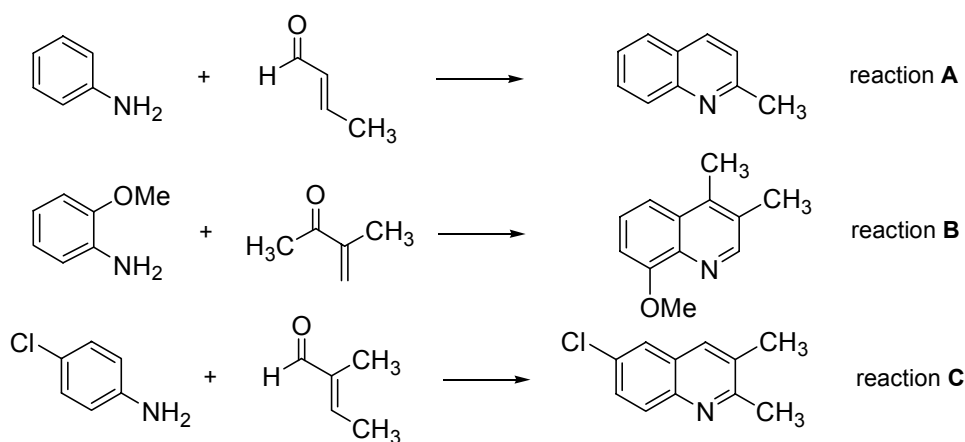
- (a) A cyclization is a step-wise process involving discrete intermediates, and a by-product such as water or an alcohol is produced. An example the Skraup quinoline synthesis.

A cycloaddition is a concerted, one-step process, such as the Diels-Alder reaction or a nitrile oxide [3+2] cycloaddition.

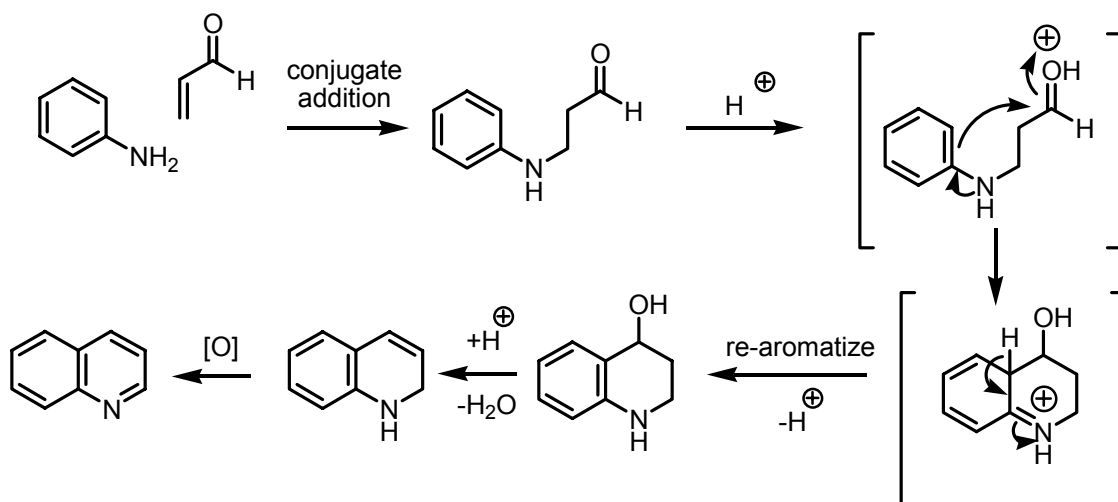
- (b) Nitrile oxides can be formed by dehydrohalogenation of a α -chlorooxime or dehydration of a nitroalkane.



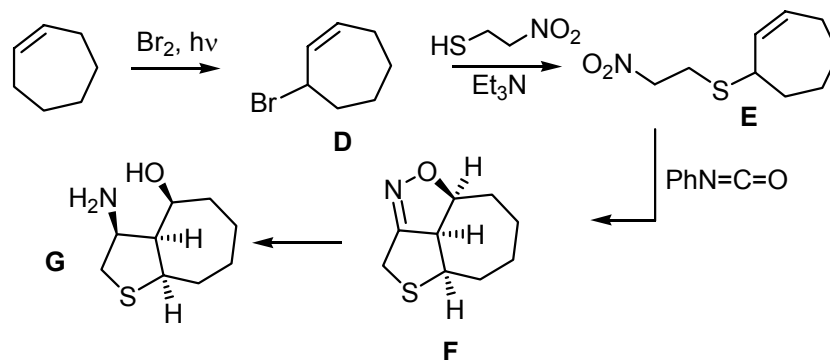
- (c)



(d)



(e)



The conversion of **F** to **G** occurs with addition of hydrogen to the less hindered face of the C=N double bond.

(Notes for information)

step 1 free radical allylic bromination

step 2 nucleophilic substitution

step 3 nitrile oxide cycloaddition (Mukaiyama Hoshino-type process). Alkene (dipolarophile) is *Z* so ring fusion between carbocyclic and isoxazoline ring must also be *cis*. Stereogenic centre next to S must also be “H down” (*NB* relative stereochemistry as could form the enantiomer, i.e. all “H up”) as the 7-5 ring system would be too strained otherwise (make a model!).