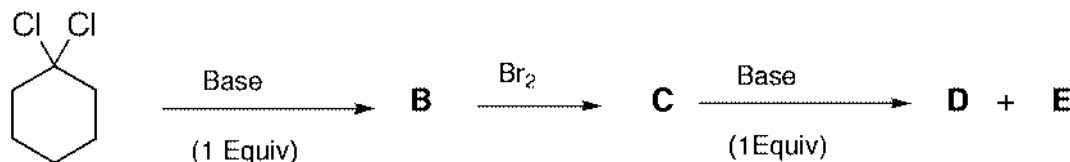


## Problem 25: Cyclohexanes

**B** forms in the reaction of **A** with a strong, non nucleophilic base. **B** reacts with bromine to form racemic **C**. The final products **D** (major) and **E** (minor) form by the reaction of **C** with a strong, non nucleophilic base.



**A**

- 25.1 Draw a 3-D structure of **A** in its most stable conformation. Circle the atoms that are possibly involved in the reaction to **B**.
- 25.2 Draw the structure of **B**.
- 25.3 Draw a 3-D structure of **C** (only one enantiomer needs to be drawn) in its most stable conformation. Circle the atoms that are possibly involved in the reaction of **C** to **D** and **E**.
- 25.4 Draw the structures of **D** and **E**.

## Problem 26: Chiral Compounds

There are a number of compounds with the molecular formula  $\text{C}_4\text{H}_8\text{O}$  but only a few of them are chiral.

- 26.1 What are the compounds having at least one chiral centre (asymmetric carbon atom)? Draw their structural formulae (line-bond structures) with all chiral centres marked by an asterisk.
- 26.2 Some of them show (S)-configuration at all their chiral centres. Draw their configurational formulae.
- 26.3 If there is a meso-compound with this molecular formula draw its configurational formula.

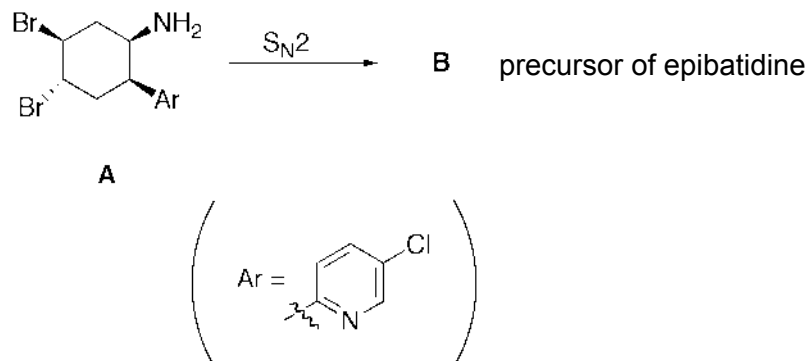
## Problem 27: Monosaccharides

A monosaccharide **A** has a molecular weight of 150 Da. The two stereoisomers **B** and **C**, that are both optically inactive, form when **A** reacts with  $\text{NaBH}_4$ .

- 27.1 Draw the structures of **A**, **B** and **C** according to the Fischer projection.
- 27.2 Determine at all stereocenters in **A** up to **C** the absolute configuration according to the CIP (R/S) nomenclature.
- 27.3 Show all different stereoisomers of **B** and indicate their stereochemical relationship.

## Problem 28: Epibatidine

Epibatidine, isolated from tropical frogs, is about 200 times more effective as a pain reliever than morphine and is not addictive. In the synthesis towards epibatidine, **A** is converted to **B** by an intramolecular  $S_N2$  reaction.



**28.1** Mark all asymmetric stereocenters in **A** by an \*.

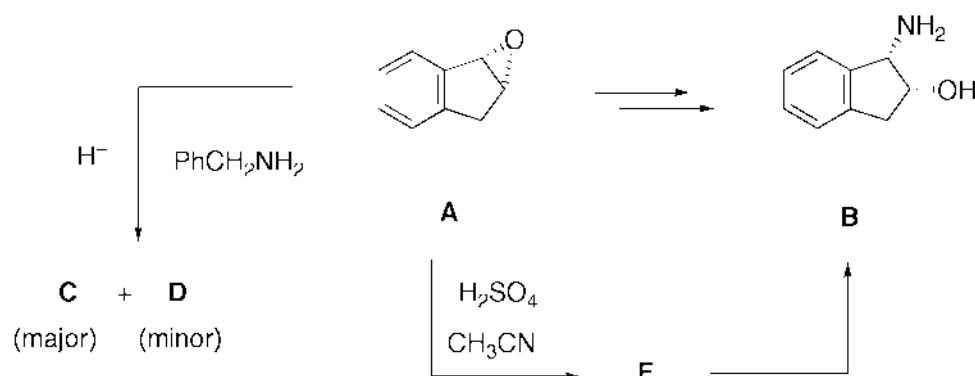
**28.2** Determine the absolute configuration of **A** according to the CIP (R/S) nomenclature at all stereocenters.

**28.3** Draw a 3-D structure of **A** indicating from where the reaction to **B** takes place. Indicate the course of the reaction by an arrow between the reaction centres.

**28.4** Draw a 3-D structure of **B**.

## Problem 29: Crixivan®

Amino alcohol **B** is an important intermediate in the synthesis of Crixivan® that is a potent HIV protease inhibitor. Chemists from Merck wanted to use the epoxide **A** as a starting material of the synthesis process.



**29.1** Upon treatment of **A** with benzyl amine in the presence of a weak acidic catalyst, they obtained mainly the undesired amino alcohol **C** along with some of the desired product **D** that could serve as a precursor of **B**. Draw the structure of **C** and a mechanism leading to this compound. Take into account stereochemical and regiochemical issues.

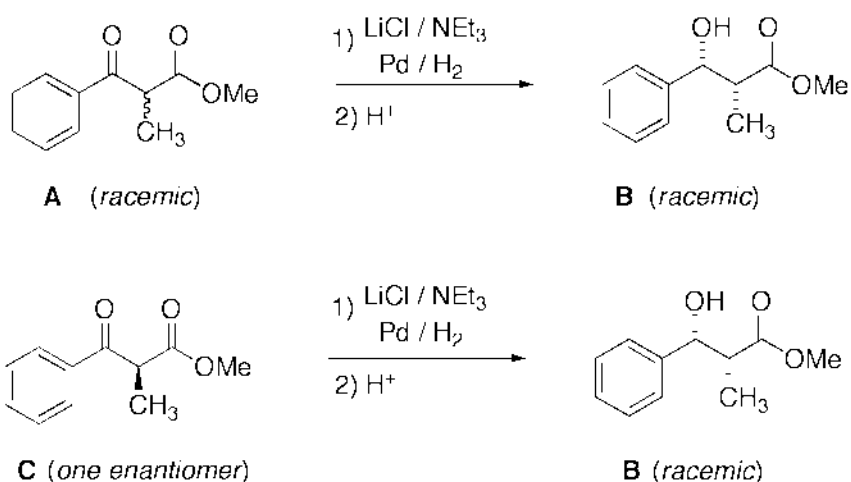
29.2 After the treatment of **A** with concentrated  $H_2SO_4$  and acetonitrile under thermodynamic conditions, only **E** formed that was subsequently hydrolyzed to **B**. Draw the structure of **E** and a mechanism leading to this compound. Take into account stereochemical and regiochemical issues.

### Problem 30: Stereoselective Reduction

In 2001, Prof. R. Noyori received the Nobel prize for his development of stereoselective reductions of C=C and C=O double bonds.

Let us consider a simplified model reaction to understand some of the basic control elements necessary to achieve a stereoselective hydrogenation reaction.

E. g., *racemic*  $\beta$ -ketoester **A** can be reduced by hydrogen to *racemic* **B** with a high *diastereoselectivity* in the presence of a metal catalyst that will chemoselectively hydrogenate C=C double bonds. Enantiomerically pure  $\beta$ -ketoester **C** is *diastereoselectively* reduced to *racemic* **B**. An additive (1 equivalent) such as lithium chloride proved to be highly important for the high diastereocontrol in the reaction.



30.1 Draw the structures of the enantiomers forming *racemic* **B**.

30.2 There are two diastereomers to the compounds of 30.1 that form a *racemic* **B**<sup>\*</sup>. Draw their structures.

30.3 Develop a model showing that in the reaction described above only **B** (but no **B**<sup>\*</sup>) forms.