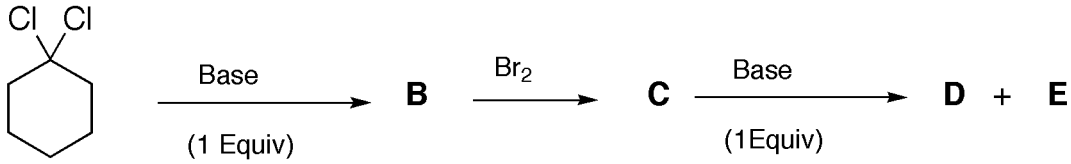
Problem 25: Cyclohexanes

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 C_4H_8O 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 $NaBH_4$.

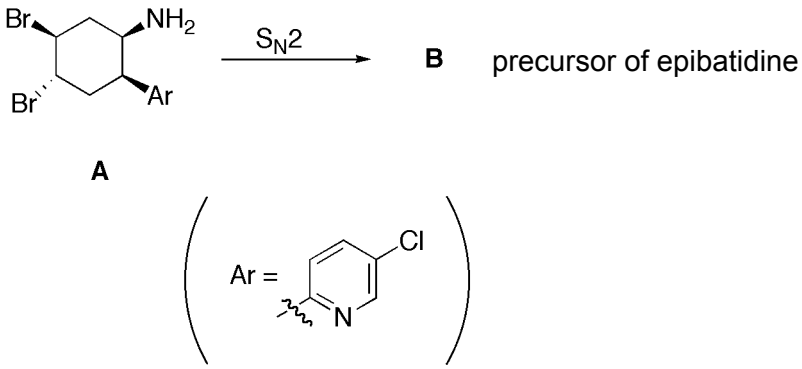
27.1 Draw the structures of A, B and C according to the Fischer projection.

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 reliefer 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 *.

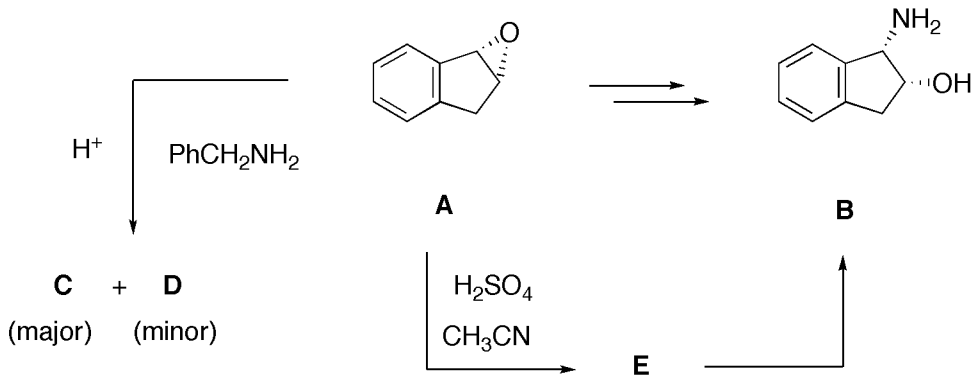
28.2 Determine the absolute configuration of A according to the CIP (R/S) nomenclature at all stereocenters.

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.



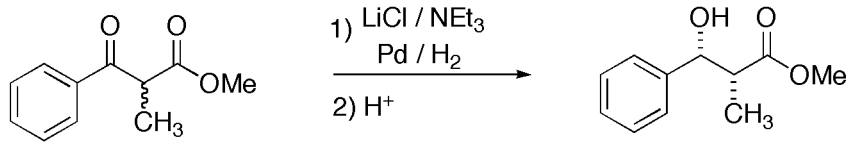
29.1 Upon treatment of A with benzyl amine in the presence of a weak acidic catalyst, they obtained mainly the undesired amino alcohol C along with some of the desired product D that could serve as a precursor of B. Draw the structure of C and a mechanism leading to this compound. Take into account stereochemical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

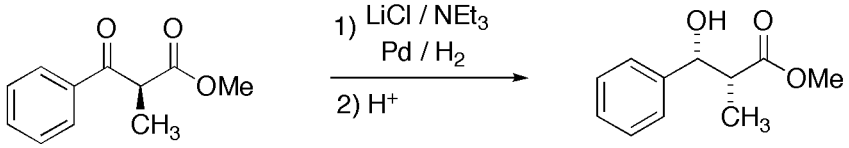
Problem 30: Stereoselective Reduction

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* β-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 β-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.



A (*racemic*) **B** (*racemic*)



C (*one enantiomer*) **B** (*racemic*)

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*. Draw their structures.

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