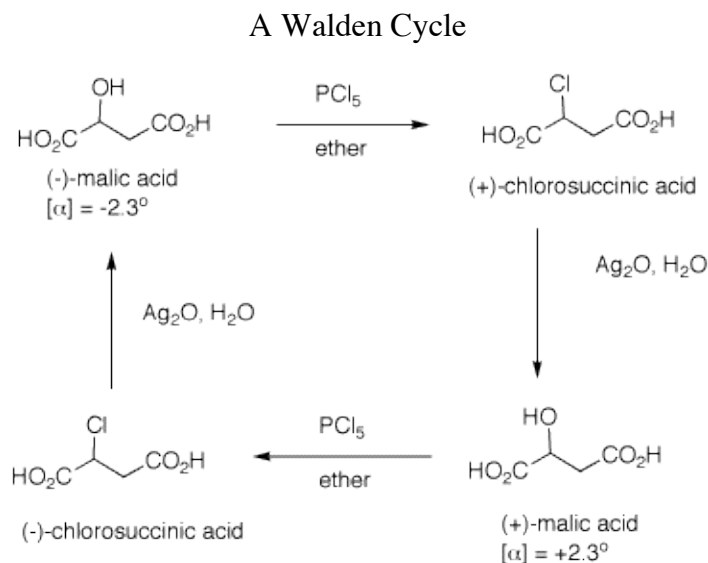


Chem 220 - Organic Chemistry

Problem Set 5, Solution Set

Chapter 6, Alkyl Halides: Substitution and Elimination

Due: Monday, October 12, 2009

Study #2 and #3 in the Alkyl Halide module and #1 in the Ether module in [ORGO](#).

[Paul Walden \(1863-1957\)](#)

[here also](#)

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1. The inversion of configuration in an $\text{S}_{\text{N}}2$ reaction is often called a Walden inversion, named after its discoverer, Paul Walden. In the cycle shown above, the overall conversion of one enantiomer of malic acid to the other one must require an inversion of configuration. Similarly, the same is true of the chloro acids. More generally, each interconversion of enantiomers must require an odd number of inversions. The PCl_5 reaction requires a single inversion which means that the Ag_2O reaction involves an even number of inversions of configuration, namely two in this instance. (-)-Malic acid is of the (*S*)-configuration.

a) Show how malic acid, like any alcohol, might react with PCl_5 and then undergo inversion to form a chloride. Remember that phosphoric acid is a strong acid and its conjugate base and analogs thereof are also good leaving groups.

b) Silver oxide is an anhydrous form of AgOH . The carboxylic acid group closest to the hydroxyl group plays a role in the process. The reaction medium is mildly alkaline. Using these data, show how there is net retention of configuration.

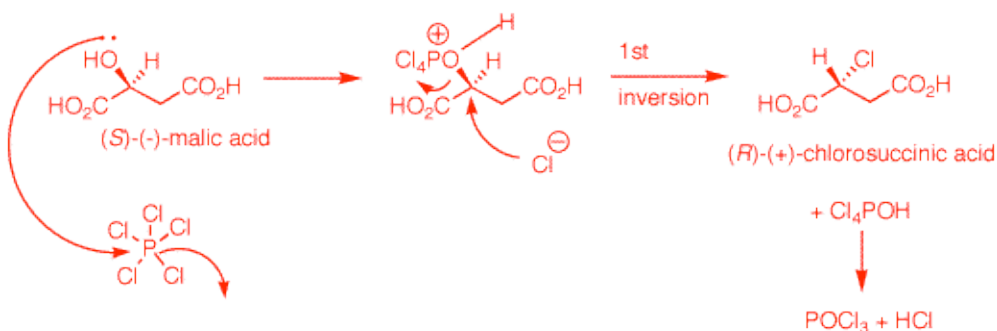
c) Draw these four enantiomers as Fischer projections with the CO_2H closest to the OH or Cl in the topmost position. (-)-Malic acid is of the (*S*)-configuration.

a) An electron pair on the hydroxyl group of (S)-malic acid does the equivalent of an S_N2 displacement of chloride on the phosphorus atom of PCl_5 . The proton at the positive site may be removed by chloride at this point and then chloride from dissociated HCl can effect an S_N2 displacement.

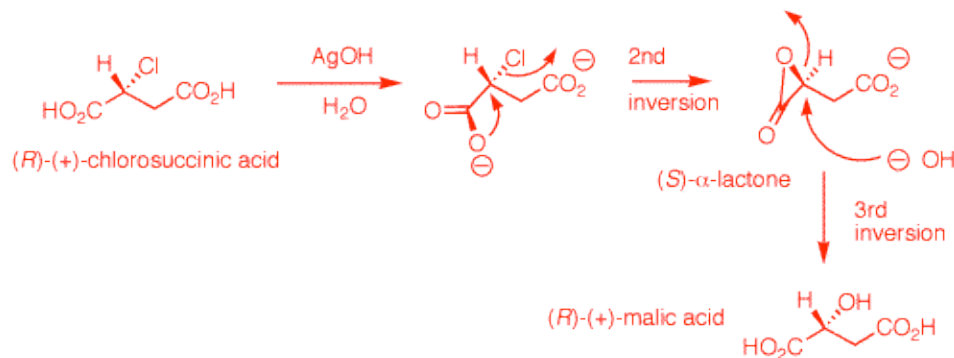
Alternatively, chloride can effect direct S_N2 displacement with inversion of configuration (1st inversion) to form (R)-chlorosuccinic acid, $POCl_3$ and HCl . [Note:

It is also likely that the carboxyl groups are converted to acyl chlorides during the reaction. Aqueous workup would rapidly reform carboxyl groups].

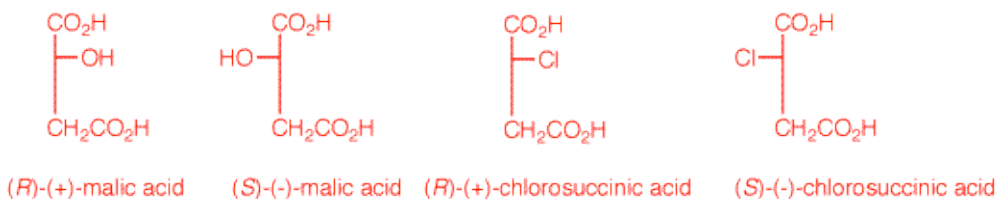
b) (R)-Chlorosuccinic acid under alkaline conditions is converted to its dicarboxylate salt. Ag^+ may or may not complex with the chlorine atom at this point to enhance chloride as a leaving group. $AgOH$ is not critical. The



reaction works using NaHCO_3 as a base. The proximate carboxylate acts as a nucleophile with $\text{S}_{\text{N}}2$ inversion to form the reactive, transitory (R)- α -lactone. The strain of the α -lactone allows hydroxide to effect a second $\text{S}_{\text{N}}2$ displacement to form (R)-malic acid upon acidification. This step has an even number of inversions -- net retention. The overall process of (R)- to (S)-malic acid has an odd number of inversions -- net inversion.



c)

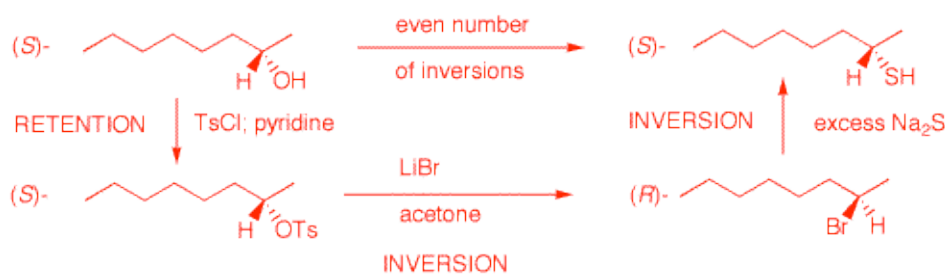


a) This is a primary bromide that is chiral by virtue of the H, D, Br and n-butyl group attached to carbon 1. RSH : $\text{pK}_a = 10$; H_2O : $\text{pK}_a = 15.7$. Go here for [pKa's](#).

2.

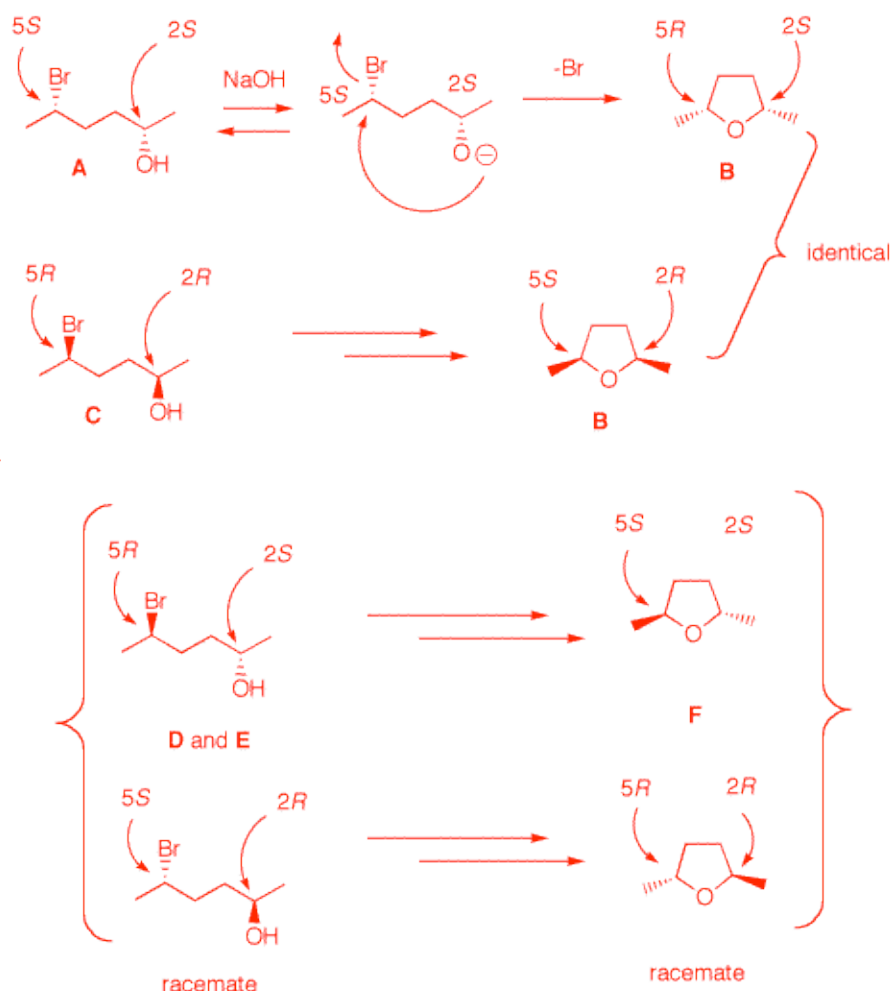
RSH is a weaker acid than water, so the equilibrium

(S)-2-octanol. [Hint: how do you make a secondary hydroxyl group a good leaving group for an S_N2 reaction?] For net retention you need an even number of inversions of configuration. First, make a leaving group with retention: the tosylate. Now do two inversions.



4. (2S,5S)-5-Bromo-2-hexanol (**A**) is expected to form optically inactive **B** (C₆H₁₂O) upon exposure to aqueous NaOH. An optically active stereoisomer of **A**, namely, **C** also forms optically inactive **B** under the same conditions. Two other optically active stereoisomers of **A**, namely **D** and **E** as a racemic mixture, form optically inactive **F**, a diastereoisomer of **B**. What are the structures of **A-F**? The structures **D** and **E** are not distinguishable. Explain and illustrate with mechanisms. Why are **B** and **F** both optically inactive?

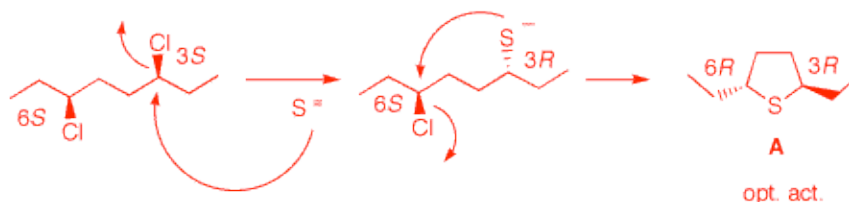
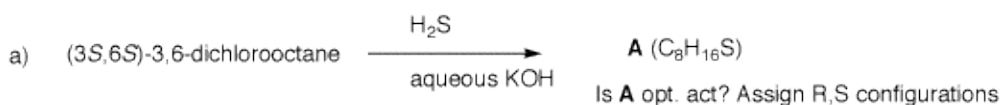
A and **B** differ in formula by HBr. The base reversibly forms the alkoxide of **A** which does an intramolecular S_N2 displacement (Williamson ether synthesis) on the C-Br bond, inverting the C₅ configuration. **B** has a plane of symmetry. It is achiral and necessarily optically inactive. **2S** mirrors **5R**. **C** is the enantiomer of **A**. It also gives **B** by the same mechanism. The diastereomers of **A** and **B** are **D** and **E**. Both are optically active but they are present as a racemate. They afford the racemate **F**, a diastereomer of **B**. **D** or **E** as a single enantiomer would give the respective enantiomers of **F**. **D** and **E** are not distinguishable in this problem. **F** is optically inactive because it is a racemate.



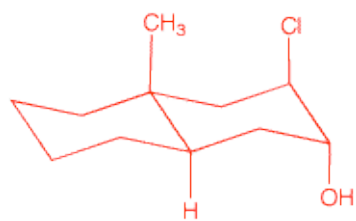
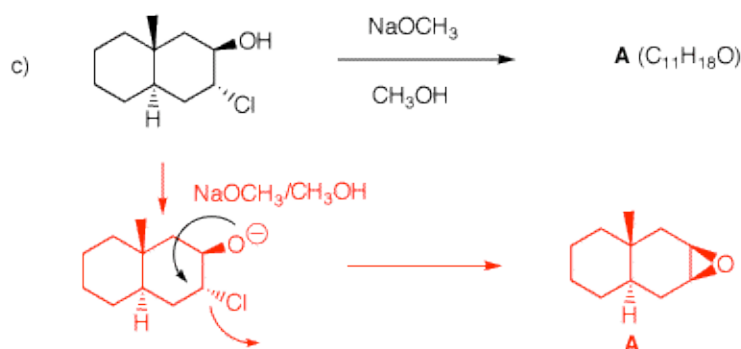
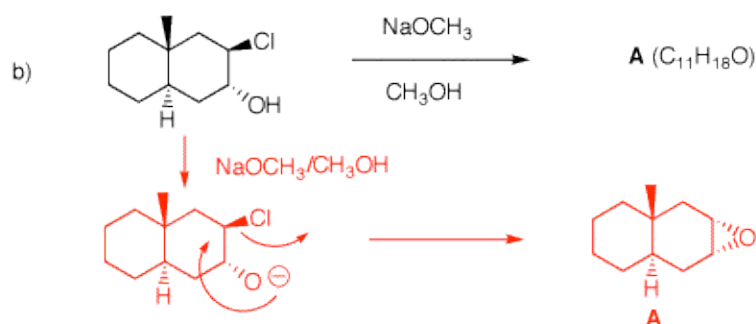
5. Provide the unknown product of each reaction. In all cases, provide

mechanisms and a rationale.

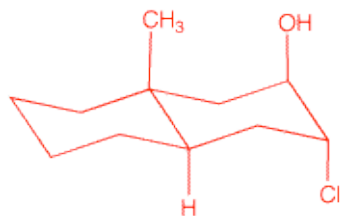
a) Similar to #4. This time there is a double displacement. Both centers are inverted. A is tetrahydrothiophene.



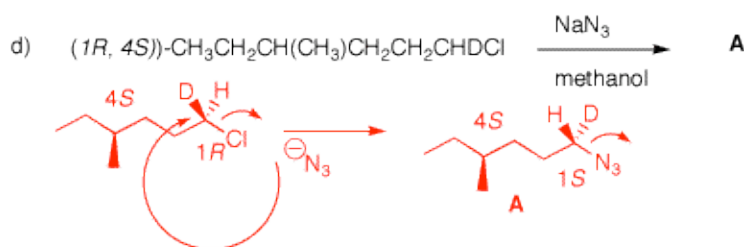
b) The chlorohydrin is a trans-decalin. Both rings are in chair conformations. The methyl and hydrogen are necessarily axial. The chlorine is 1,3 to the methyl. It is also axial. The same is true of the relationship between the hydrogen and the hydroxyl group. This means that the chlorine and hydroxyl group are both well disposed for epoxide formation with the epoxide on the same side of the rings as the hydrogen.



c) The same as b) except that the epoxide is now on the same side of the rings as the methyl group.



d) The same as 2a. The 4S



site is not affected.