

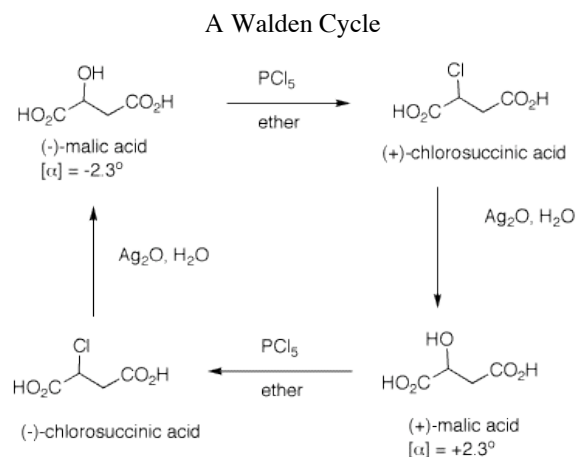
Chem 220 - Organic Chemistry

Problem Set 5

Solution Set

Chapter 6, Alkyl Halides: Substitution and Elimination

Due: Monday, October 11, 2010

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 S_N2 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.

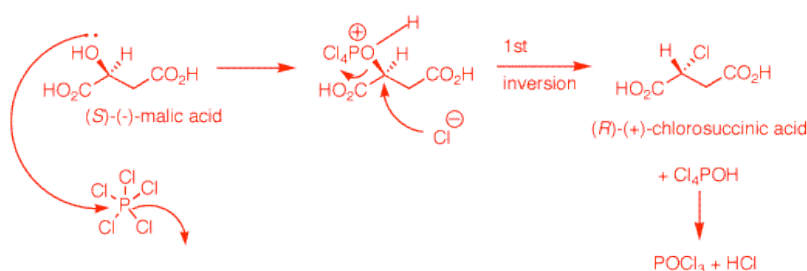
c) Draw these four enantiomers as Fischer projections with the CO_2H closest to the OH or Cl in the topmost position. (-)-Malic acid is of the (*S*)-configuration.

*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.

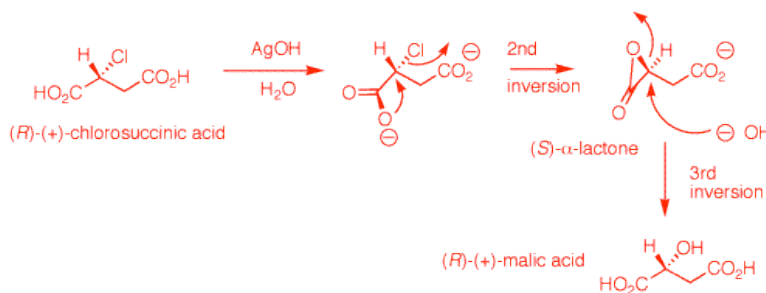
Alternatively, chloride can effect direct S_N2 displacement with inversion of configuration (1st inversion) to form (R)-chlorosuccinic acid, $POCl_3$ and HCl. [Note:

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 S_N2

inversion to form the reactive, transitory (S)- α -lactone. The strain of the α -lactone allows hydroxide to effect a second S_N2 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.



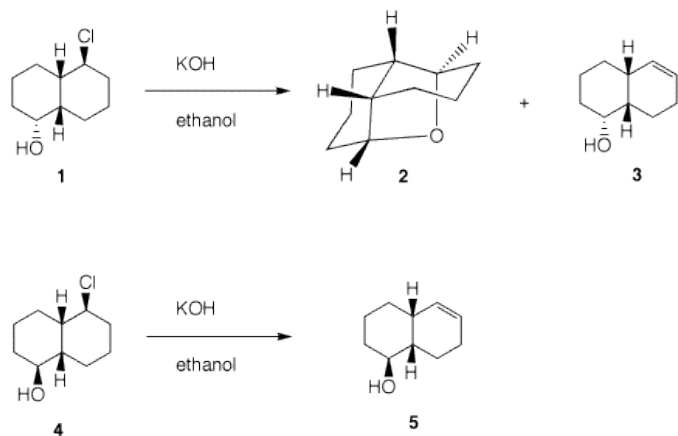
c)



(R)-(+)-malic acid (S)-(-)-malic acid (R)-(+)-chlorosuccinic acid (S)-(-)-chlorosuccinic acid

2. A sample of (-)-2-iodooctane ($[\alpha]_D = -33.3^\circ$) reacts with radioactive iodide (K^{131}I^-) in methanol until 1.5% conversion (i. e.; 1.5% of the isolated 2-iodooctane contains radioactive iodine.) What is the predicted rotation of the isolated sample? *The mechanism is S_N2 . At 1.5% conversion there is 98.5% of (-)-2-iodooctane and 1.5% (+)-2-iodooctane. The optical purity is $(98.5 - 1.5)/100 = 97\%$. Therefore, the expected rotation is $-33.3^\circ \times 0.97 = -32.3^\circ$.*

3. A student familiar with the mechanism of the S_N2 and E2 reactions predicts that the stereoisomer **1** may produce **2** and **3** while stereoisomer **4** will produce only **5** under the conditions shown. Show her reasoning. [*Note: You need to know how to draw cis-decalins. Look [here](#) (.ppt) or [here](#) (.html).*]

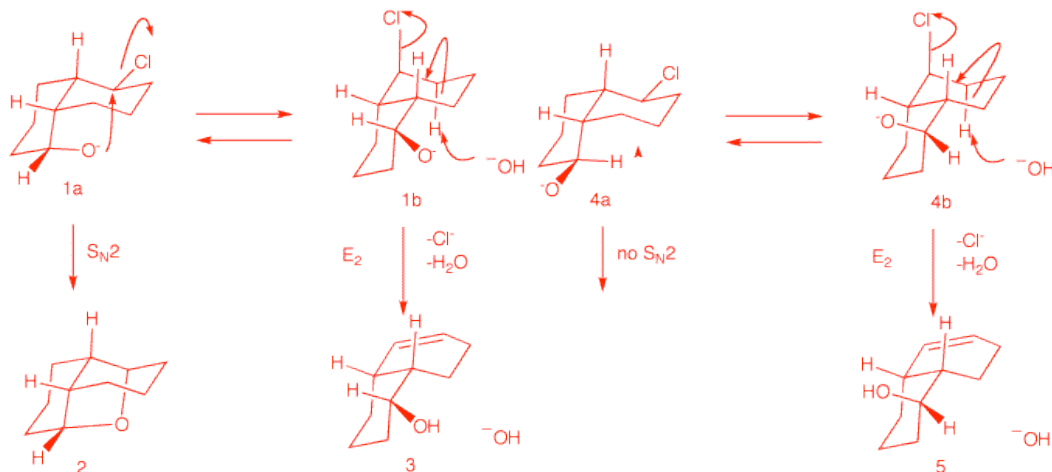


*There are two conformations of cis-decalin **1** --namely, **1a** and **1b**. Conformation **1a** is capable of effecting an S_N2 displacement.*

*Hydroxide reversibly deprotonates the alcohol, which, in turn, does an S_N2 rear side displacement of chloride. Use the Jmol structures of **1a** and **1b** to compare **1a** and **1b**. Rotate the structures to get a good view. [Click here](#). Conformation **1b***

has the alkoxide group remote from the C-Cl bond. The C-Cl bond is axial and may participate in an E2 elimination in only one direction. There is only one axial C-H bond anti to the C-Cl bond.

*Compound **4** is a diastereomer of **1**, differing only at the hydroxyl center. Neither conformation **4a** nor **4b** can effect S_N2 displacement. However, E2 elimination from conformation **4b** is possible. It is likely that during E2 elimination the alkoxides **1b** and **4b** are protonated to form the alcohols.*



4. Provide the unknown product(s) of each reaction. In all cases, provide mechanisms and a rationale.

a) Mercaptans (thiols) are stronger acids than water. See [pKa table](#). Hydroxide converts ethanethiol to its thiolate (mercaptide). The anion is a very good nucleophile. Inversion of configuration occurs. Cl and S are both top priority.

b) Excess methanol as a solvent. Conditions for an S_N1 reaction of the tertiary chloride but **not** the primary bromide. Product is also racemic, even if the chloride had been optically active. Planar carbocation.

c) The dibromide has a two-fold axis of rotation. Both centers are of the same configuration, --- namely, *S*. Sulfide (charge -2) does an intermolecular S_N2 displacement to give an intermediate that has the new site of the opposite, *R*-configuration. now, like **4a**, a second S_N2 displacement occurs intramolecularly to give the tetrahydrothiophene **A**. Both centers have the *R*-configuration. **A** is optically active.

d) Both hydroxyl groups displace bromide from PBr_3 to give a phosphite ($ROPX_2$). The primary group undergoes S_N2 displacement by bromide. Only the secondary site affords information about the inversion of configuration, cis ---> trans.

e) The asymmetric center is stable under the reaction conditions. It remains intact in the products. A small nucleophile and a primary bromide favors S_N2 displacement (Williamson ether synthesis). A minor amount of E2 product is formed.

f) Since **A** and **B** are constitutional (structural) isomers and the halide is secondary, elimination will dominate. **A** is the more substituted isomer, which suffers E2 elimination losing HCl in an anti manner. This elimination leads to the *Z*-isomer shown. Since both asymmetric centers have become sp^2 hybridized, optical activity is lost. The minor E2 product is still optically active.

g) E2 elimination leads to **A** and **A'** having the trisubstituted double bond. **B** and **C** are the minor 1,1-disubstituted double bonds. **B** dominates over **C** because of the isotope effect in E2 eliminations.

h) The D-C-C-Cl dihedral angle is 0° . E2 elimination is syn overriding any isotope effect. DCl is lost.

i) The Chugaev reaction is an infrequently used procedure for forming alkenes from alcohols. The alkoxide of the alcohol adds to CS_2 to give a species, $RO(C=S)S^-$, which, after methyl iodide is added, effects an S_N2 displacement to give a xanthate as shown. Thermolysis gives an intramolecular syn E2 elimination, using the sulfur of the C=S bond as the internal base. In this case, deuterium remains in the alkene.

j) Ionization of the secondary bromide upon heating can occur to capture ethanol in an S_N1 process. The intermediate secondary carbocation can have the vicinal **green hydride** migrate to give a more stable tertiary carbocation, which captures ethanol in an S_N1 process.

