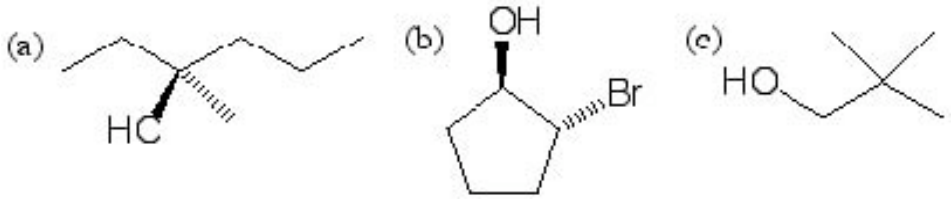
8-1 This exercise combines your knowledge of basic nomenclature rules and concepts of stereochemistry introduced in Chapters 4 and 5.



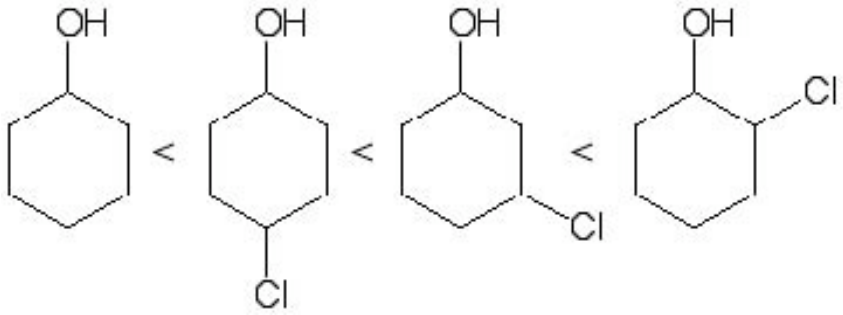
8-2 Keep in mind that faculty at UCSD do *not* require you to be able to derive names from structures.

(a) 4-methyl-2-pentanol
(b) *cis*-4-ethylcyclohexanol
(c) 3-bromo-2-chloro-1-butanol

8-3 This exercise is worked out on page 293 as "Working with Concepts".

8-4 The term "essentially complete deprotonation" is not well defined and up for interpretation. Nonetheless, for the examples given in this exercise, the position of the equilibrium is dramatically to one side. Here, all we need to do is to compare the acidity of methanol (pKa ~16) with that of the conjugate acids of the bases provided. If methanol is the stronger acid, then the base provided will deprotonate methanol in an equilibrium favoring methoxide ion. (a) yes; (b) no; (c) yes; (d) yes; (e) no.

8-5 We expect that the presence of a chlorine atom will withdraw electron density and thus lead to stabilization of an anion. The more stable the anion, the stronger the acid. The effect of the chlorine will be larger the closer it is to the negative charge. For 4-chlorocyclohexanol, the chlorine is sufficiently remote that little effect is expected on stability of the anion and therefore acidity.

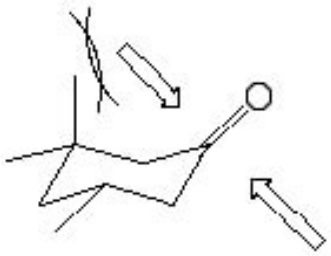


8-6 As in exercise 8-4, we can determine the position of the equilibrium by comparing the acidities of the acids involved. Methanol is a stronger acid than is *t*-butanol so the equilibrium will favor *t*-butanol and methoxide (equilibrium favor the weaker acid).

8-7 Each part of this exercise asks for appropriate reagents for the conversion of an alkyl halide into an alcohol. For the primary chloride in part (a), elimination will not be a major factor and therefore the use of hydroxide ion as a nucleophile will give satisfactory results. For the secondary chloride in part (b), it is best to use the two step sequence involving: 1) substitution with acetate ion followed by hydrolysis of the resulting ester with hydroxide ion. Simple solvolysis of the tertiary chloride in part (c) will suffice.

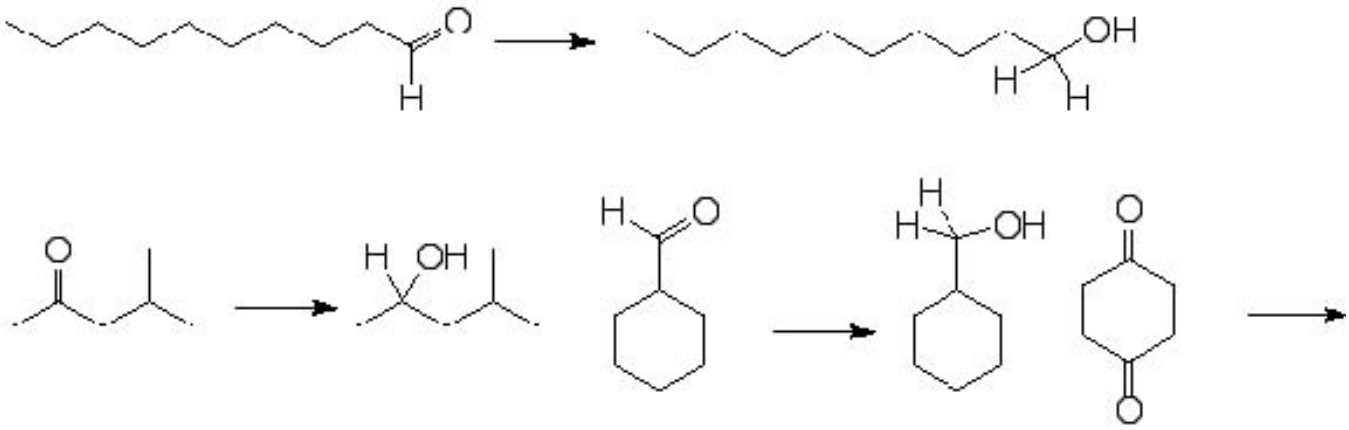
8-8 Reduction of a ketone with sodium borohydride produces a secondary alcohol. This exercise is directed at the possible stereochemical consequences of the conversion of the sp2 carbon of the carbonyl group to the sp3 carbon of the resulting alcohol. For part (a), the product has a new center of chirality and thus there are two enantiomers formed in equal amounts. For part (b), the starting ketone is symmetrical and, as a result, the product alcohol does *not* have a center of chirality. For part (c), a new center of chirality is formed by reduction but because the starting material already has a stereocenter, the two products formed are diastereomers and will be formed in unequal amounts.

8-9 Because there are two methyl groups of one of the carbons 1,3 to the carbonyl carbon, one of them must be axial regardless of which chair conformation is adopted (shown below is the greatly preferred conformation---the other would experience a 1,3 methyl-methyl diaxial interaction. The axial methyl significantly interferes with the approach of reagents from the axial direction.



8-10 The process of reduction of a carbonyl to an alcohol can be simplified to a process that adds an H to the carbonyl carbon, an H to the oxygen, and removes one of the two bonds between the carbonyl carbon and the oxygen. Thus, to obtain the precursor carbonyl compound that would generate and alcohol upon

reduction, it is only necessary to reverse these three operations: remove an H from the carbinol carbon; remove an H from the oxygen; and add a second bond between the carbinol carbon and the oxygen. As a prelude to exercise 9-10, consider the stereochemical consequences of each of the reductions.



8-11 The conversion of an alcohol to a ketone or aldehyde will remove any stereochemical information that might be present at the sp3 hybridized carbon of the alcohol. Reduction of a ketone generates an new sp3 hybrdized carbon that can have stereochemistry. For example, in part (a), oxidation of the alcohol removes the stereochemical information present in the starting material (that the OH and methyl groups are cis) and the subsequent reduction will form a mixture of cis and trans stereoisomers. In part (b), reduction of the two carbonyl groups will form two new stereocenters. Thus, there can be up to 4 possible stereoisomeric products. However, because of symmetry, there are only three, of which one is a meso. In part (c) oxidation of the primary alcohol to an aldehyde (recall that pyridinium chlorochromate is the reagent of choice for this conversion) forms symmetry in the product and thus the stereocenter present in the starting material is lost in the product dialdehyde.

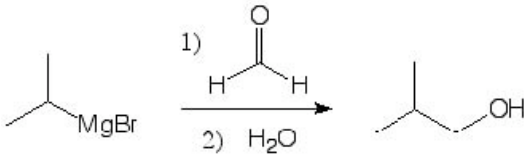
8-12 In this exercise we apply the reverse analysis of that used in exercise 8-9. That is, we are asked to generate a carbonyl compound by oxidation of an alcohol. To obtain the structure of the required alcohol we add an H to the carbonyl carbon, an H to the oxygen, and removes one of the two bonds between the carbonyl carbon and the oxygen.

8-13 This exercise is worked out on page 307 as "Working with Concepts".

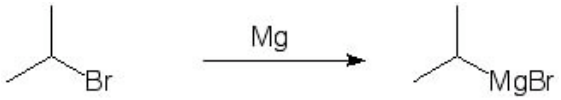
8-14 What we need to do is to completely remove the proton from the oxygen. We know that organometallic compounds do this (recall that we must protect them from water). Thus, we can treat D_3COH with any alkyl lithium or

Grignard reagent and then add a deuterium by adding D_2O.

8-15 To major extent, your success in solving problems such as this one will depend upon the care with which you analyze what must be accomplished in the conversion. The first thing to look for is a change in the number of carbons present in the starting material and product. Here, the starting material has three carbons and the product has four. Thus, without even considering the structures involved, we know that at some point we must use a reaction that forms a C—C bond. Because the ultimate product is an alcohol and we know that the reaction of an organometallic compound with a carbonyl compound forms an alcohol with a new C—C bond, this is a logical choice for the last reaction in the sequence.

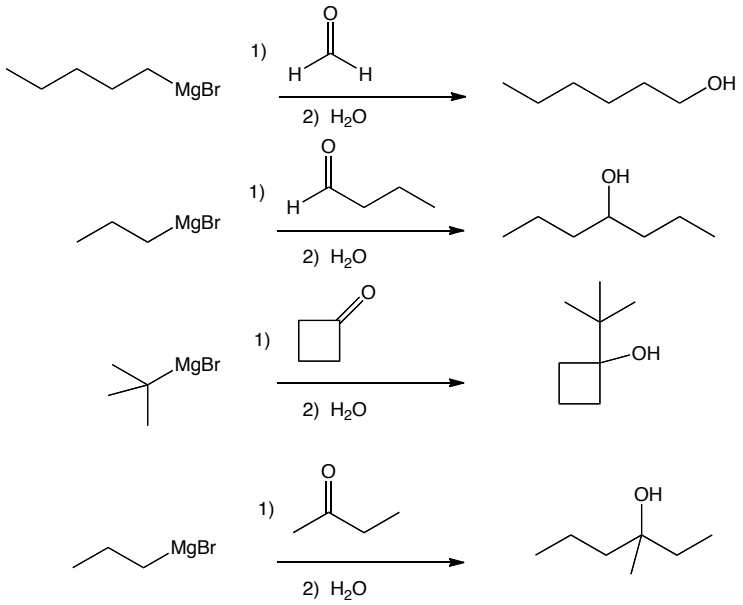


We thus need to prepare the organometallic reagent which we know comes from the reaction of an alkyl halide with the appropriate metal.



Finally, we prepare the alkyl halide from the starting alcohol and the appropriate reagent.

8-16 For each of these product alcohols, we must identify a C–C bond to the carbinol carbon that connects pieces that have no more than four carbon atoms each. For (a), there is only one C–C bond to the carbinol carbon of this primary alcohol so we have no choice. Likewise, for the symmetrical secondary alcohol in (b), the two C–C bonds are identical. For (c) only the non-ring bond of this tertiary alcohol need be considered as the other two do not lead to two separate pieces. All three such bonds for (d) are different but only one leads to two pieces of the size required by the exercise.



8-17 This exercise is worked out on page 312 as "Working with Concepts".

9-18

8-19 For the construction of even relatively simple organic molecules, it is desirable to "connect" smaller pieces together to make a larger product. Thus, it is preferred that we use carbon—carbon bond forming reactions. Starting the retrosynthetic process by disconnecting the carbon—oxygen bond will lead to precursors that have the same carbon skeleton and thus does nothing to build the product from less complex precursors. When possible, we want to disconnect a product at a carbon —carbon bond.

8-20 This exercise is worked out on page 317 as "Working with Concepts".

8-21 It is tempting to start with methane in this exercise as it is given as the starting material. Nonetheless, this is the :"hard" way to work the problem as only the product shows the carbon connectivity that we clearly must construct from a starting material that has no carbon—carbon bonds. Indeed, it is possible to prepare *any* alcohol that contains no rings, no double bonds, and no other functional groups using only the following five reactions: Because each of these reactions produces a different functional group in the product, we can identify which reaction to use by looking at the functional group present in the desired product. In this case, the ultimate product is an alcohol, so we use the first reaction. The starting materials for this reaction are a Grignard reagent and a ketone. We can use the second reaction to prepare the Grignard reagent from an alkyl bromide and the last to prepare the ketone from an alcohol. The

Grignard reagent can be prepared from the alkyl bromide. The alcohol, 2-propanol, can be prepared using the first reaction, and so on and so on. Note that in the particular example of oxidation show above it is not necessary to use PCC which is required only when an aldehyde is the desired product. Nonetheless, PCC can be used for the oxidation of both a primary alcohol to an aldehyde as well as a secondary alcohol to a ketone and thus is a "universal" reagent.