

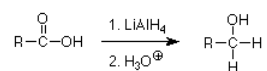
1.13: Alcohols

Making Alcohols

Here's a list of reactions we've already seen which make alcohols. The links will take you back to a previous lecture where the specific reactions are discussed.

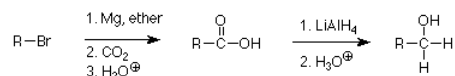
Reaction	Reactants	Product
Grignard Addition	Ketone, Grignard Reagent	Tertiary Alcohol
Grignard Addition	Aldehyde, Grignard Reagent	Secondary Alcohol
Grignard Addition	Formaldehyde, Grignard Reagent	Primary Alcohol
Hydride Reduction	Ketone, NaBH ₄ or LiAlH ₄	Secondary Alcohol
Hydride Reduction	Aldehyde, NaBH ₄ or LiAlH ₄	Primary Alcohol
Hydride Reduction	Ester, LiAlH ₄	Primary Alcohol
Hydride Reduction	Carboxylic Acid, LiAlH ₄	Primary Alcohol

The last reaction needs some further comment. Here's how we would do it:



The mechanism is similar to the mechanism for the reduction of esters by LiAlH₄, so we will not be concerned with the details. We can conclude that LiAlH₄ can be used to make a primary alcohol from either an ester or the corresponding carboxylic acid.

We can extend our understanding of the use of this reaction in synthesis by asking "How could we make the carboxylic acid we need for this reaction?" One particularly important way to do that, important because it makes a carbon-carbon bond, is to make a carboxylic acid by use of the [addition of a Grignard reagent to carbon dioxide](#).

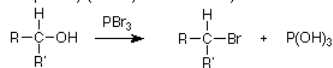


This combination gives us a two step way to convert an alkyl halide (RBr) to a primary alcohol with the addition of one more carbon to the chain.

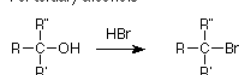
Alcohols to Alkyl Halides and Grignard Reagents

Of course, this raises the question: "Where do we get the RBr?" That takes us into the reactions of alcohols, because the most effective way to make alkyl halides is from alcohols. If we wish to make alkyl bromides, there are two reactions to consider.

For primary (R' = H) and secondary alcohols

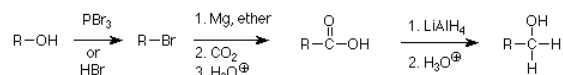


For tertiary alcohols



If the alcohol is primary or secondary, the reagent of choice is phosphorous tribromide (PBr₃). If the alcohol is tertiary, we use hydrogen bromide (HBr) to make the alkyl halide. The situation is similar if we wish to make an alkyl chloride. HCl is used for tertiary alcohols and SOCl₂ is used for primary and secondary alcohols. We'll take up the mechanisms of these reactions later. (If you wish to look ahead, see Chapter 7 in Brown.)

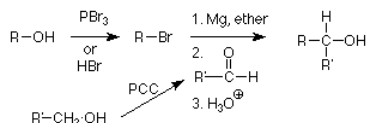
We now have an answer to the question of how to make alkyl bromides, so we can add another reaction to the beginning of the sequence we started with:



The alcohol product of this sequence can be used to make an alkyl halide to start a new sequence, which could be the starting point for a further sequence, etc. This makes alcohols extremely valuable synthetic reagents.

Including Aldehydes or Ketones

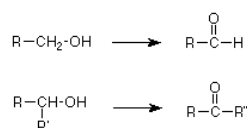
Suppose we used an aldehyde or ketone instead of carbon dioxide in such a sequence:



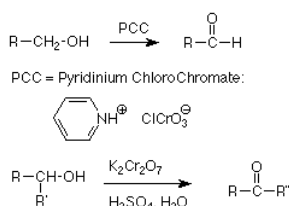
Here the product alcohol is produced directly rather than through a carboxylic acid. Notice that it is a secondary (from an aldehyde) or tertiary (from a ketone) alcohol, as we had seen when we looked at Grignard additions to aldehydes and ketones.

Oxidation of Alcohols to Aldehydes or Ketones

Since this has shown that one of the important components in a Grignard addition can be made from an alcohol, it seems natural to wonder whether the other major component, the aldehyde or ketone can be made from an alcohol. (We won't worry about how to make carbon dioxide -- there's plenty of it around.) The answer is yes, we can make an aldehyde or a ketone from an alcohol. The desired transformation is:



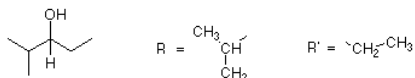
The products of these reactions have fewer hydrogens than the reactants, so these are oxidations. In the case of the ketone, further oxidation would require breaking a carbon-carbon bond to one of the R groups which is quite difficult. We can use chromic acid ($\text{K}_2\text{Cr}_2\text{O}_7 - \text{H}_2\text{SO}_4$). The situation with the aldehyde is more difficult, since we already know that the use of chromic acid will oxidize it to a carboxylic acid. It took considerable research to work out, but the reagent which works here is called pyridinium chlorochromate (PCC for short). Our synthetic reactions for the oxidation of alcohols are then:



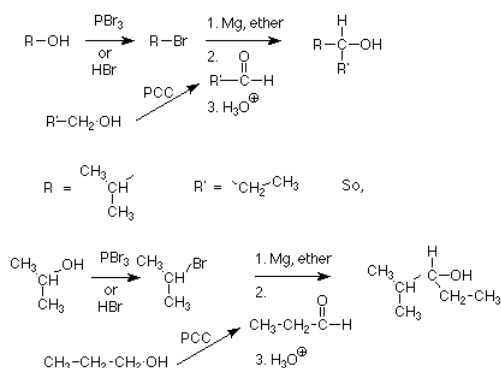
We can add the above reactions to our growing synthetic scheme.

Since the product here is a secondary alcohol, the scheme could be carried onwards through its oxidation to a ketone and/or its conversion to an alkyl bromide, etc.

Let's apply this to a specific example. Suppose we wished to make this compound:



We can compare its structure to the general product of the scheme above and figure out what R and R' are. We then plug the specific identities of R and R' into the scheme to arrive at:



To summarize, since alcohols can be made into alkyl halides and can also be made into aldehydes and ketones, they are important starting points for carrying out a Grignard synthesis. As products of Grignard syntheses, they are also useful materials to begin a new cycle.

The reactions we have looked at today have been those that affected the C-O bond of an alcohol. In making alkyl halides, we broke that bond and made a new bond between the carbon and a halogen. In oxidation, we added a pi bond to the C-O sigma bond of an alcohol.

Alcohols as Nucleophiles

We'll finish today by reminding ourselves of a couple of reactions of alcohols which use their unshared electron pairs, acting as nucleophiles, to make new bonds to carbonyl carbons.

Reaction	Alcohol Reacts With	Product
Hemiacetal Formation	Aldehyde	Hemiacetal
Ester Formation	Acyl Chloride	Ester

One thing to notice about these mechanisms is that the unshared electron pair is used to make the new bond **before** the O-H bond is broken. That's generally true unless there is a strong base present, something we'll take up next time.

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