

B.Sc Semester – IV MJC – 6(T) Organic Chemistry: Compounds with Oxygen Containing Functional Groups(T)

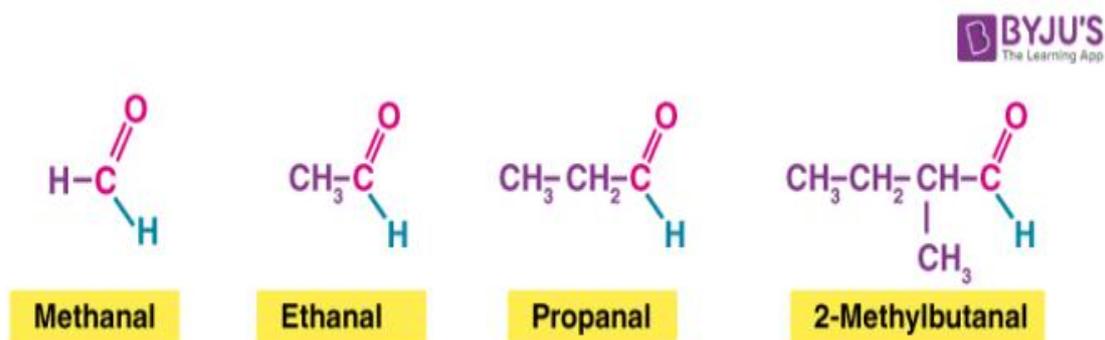
Unit – 2 Aldehydes and ketones

What are Aldehydes and ketones?

Aldehydes and ketones incorporate a carbonyl functional group, $C=O$. These are organic compounds with structures $-CHO$ and $RC(=O)R'$, where R and R' represent carbon-containing substituents respectively.

In aldehydes, the carbonyl group has one hydrogen atom attached to it together with either a 2nd hydrogen atom or a hydrogen group which may be an alkyl group or one containing a [benzene ring](#).

Example:

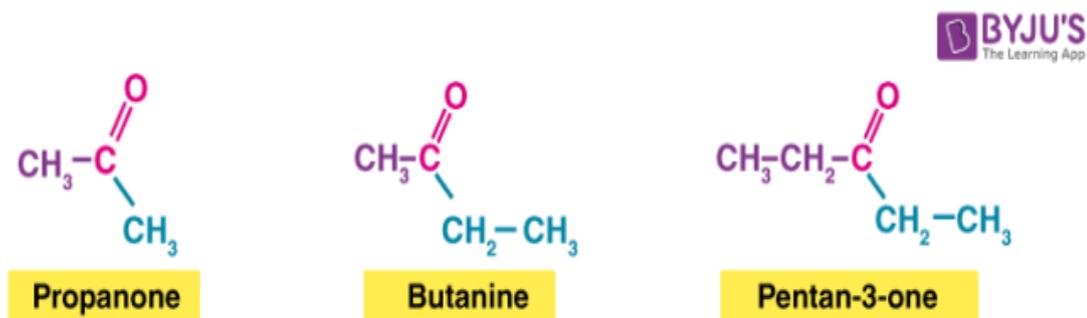


One can notice that all these have the exact same end to the molecule. The only difference is the complexity of the other attached group.

What are Ketones?

In ketones, the carbonyl group has 2 hydrocarbon groups attached to it. These can be either the ones containing benzene rings or alkyl groups. Ketone does not have a [hydrogen](#) atom attached to the carbonyl group.

Example:



Propane is generally written as CH₃COCH₃. In pentanone, the carbonyl group could be in the middle of the chain or next to the end – giving either pentan-3-one or pentan-2-one.

The Simple Two-Step Pattern For Seven Key Reactions Of Aldehydes And Ketones

“There are just so many reactions! I can’t remember all the mechanisms!!” – *distressed organic chemistry student*

Yes, yes there are a lot of reactions, particularly in second semester organic chemistry. But there is good news on this front: there is a tremendous amount of repetition in these reactions.

For instance, what if I told you that there was a simple, two-step pattern behind **seven different reactions** that each work for aldehydes and ketones? By learning this key pattern, you’d therefore know the mechanism for $7 \times 2 = 14$ **different reactions**.

1. The “Two-Step” Pattern For Addition Reactions To Aldehydes and Ketones

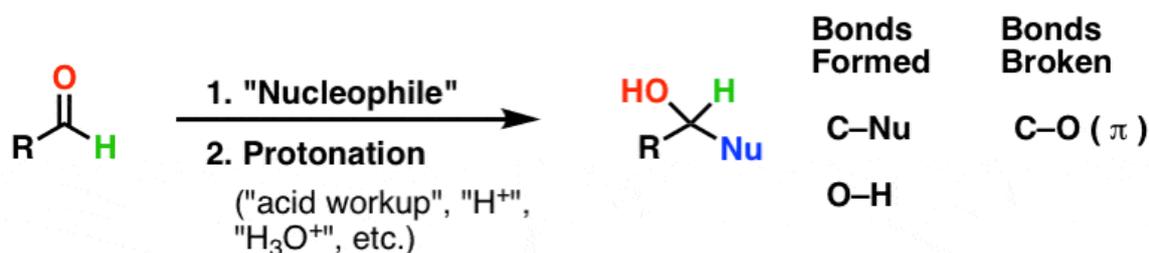
The two steps are the following:

1. Addition of a nucleophile to an aldehyde or ketone
2. Protonation of the negatively charged oxygen with acid (often called “acidic workup”)

That’s it.

Here’s the general case for the reaction. I’ve drawn an aldehyde here, but everything I will say here also applies to ketones.

Pay attention. What bonds form, and what bonds break?



*Aldehyde shown here,
but also applies to ketones*

Hopefully you can see that a C–O (π) bond is being broken, a C–Nu bond is being formed, and an O–H bond is formed also.

Any mechanism we draw has to account for these bond-forming and bond-breaking events.

- Step 1 is addition of a nucleophile to the electrophilic carbonyl carbon. This forms C–Nu and breaks C–O (π), resulting in a negatively charged oxygen.

- Step 2 is addition of an acid (“protonation”), which results in formation of the O–H bond. This is generally done after the reaction with the nucleophile is complete – otherwise the acid would destroy the nucleophile, sometimes in violent fashion (e.g. LiAlH_4 is **not** something you’d want to bring in close proximity to acid).

2. The Generic Mechanism Behind This “Two Step” Pattern For Addition Reactions Of Aldehydes And Ketones

Here’s the general mechanism. First comes addition of the nucleophile, and second comes protonation of the resulting alkoxide.

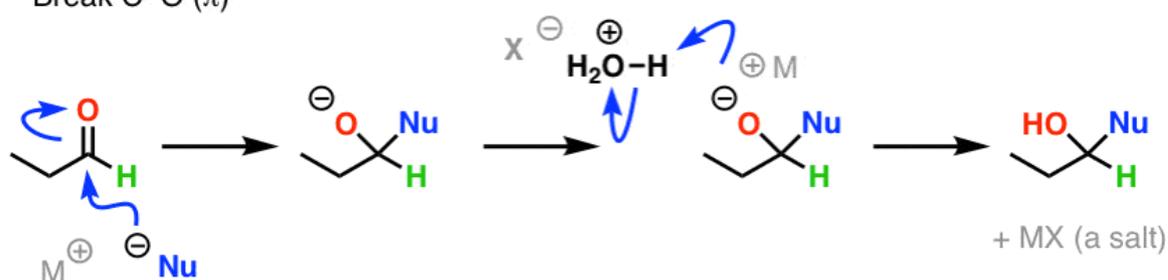
The General Two-Step Mechanism

Step 1: Addition

- Form C–Nu
- Break C–O (π)

Step 2: Protonation (Acid Workup)

- Form O–H

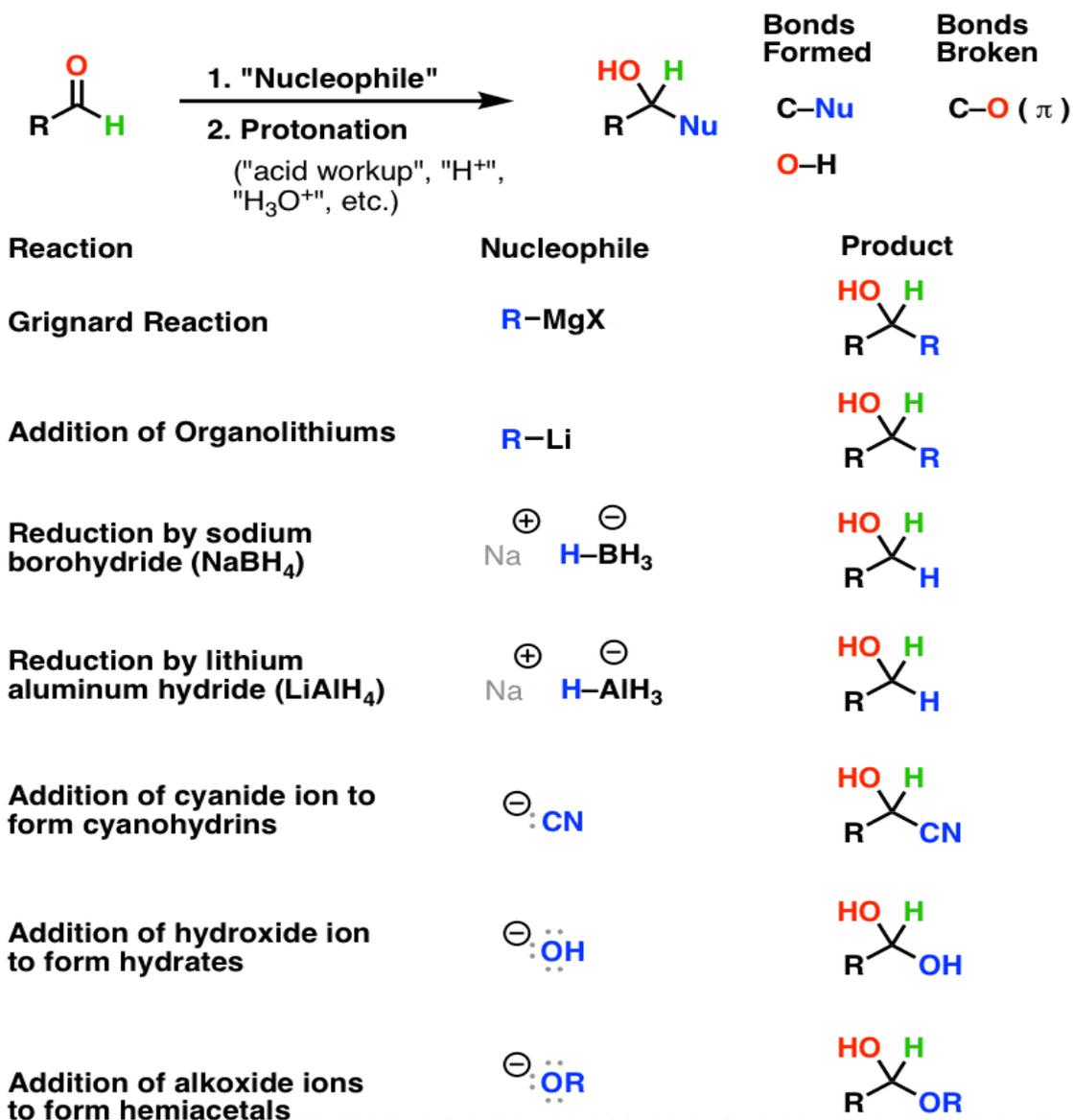


That’s it for the general example. Now let’s get to specifics.

3. A Table Showing How The “Two Step” Mechanism Is Applied In Reactions Of Aldehydes With Grignards, Organolithiums, NaBH_4 , LiAlH_4 , Cyanide Ion, Hydroxide Ion, And Alkoxide Ions

This two-step pattern is behind the following seven reactions:

The simple "Formula" for Seven Key Reactions of Aldehydes & Ketones



Again, although aldehydes are pictured here, the reaction applies equally well to ketones. So this represents fourteen reactions that proceed through this two step mechanism.

These types of mechanistic patterns are a little bit like Hollywood movies: there's only so many different kinds of plot elements, and they repeat. If you're familiar with the Hero's Journey, you'll recognize a lot of similarities between *Star Wars: A New Hope* and *Happy Gilmore*, even though the latter film is ostensibly about a hockey goon turned professional golfer. Likewise, the number of discrete mechanistic steps you will learn in organic chemistry could be counted on your fingers and toes.

Hope you find this useful.

4. So You Want The Mechanisms Of These Seven Reactions Drawn Out In Detail? OK

Wait. You want *specifics*? Like, each reaction written out individually, with a general example, a specific example, and then a mechanism?

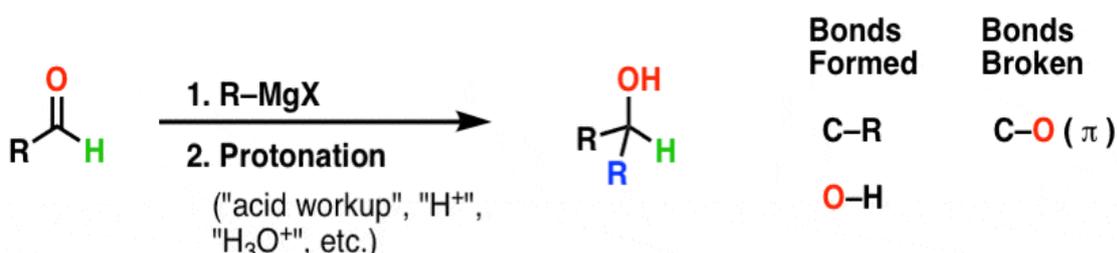
That sounds like overkill. But this is MOC. Overkill is what we do here.

Here's each of those seven reactions treated individually.

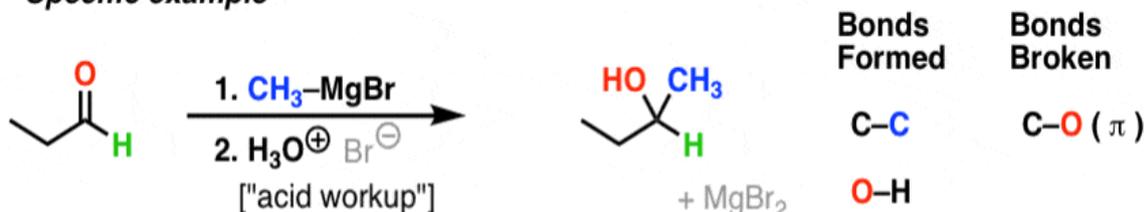
5. The Grignard Reaction With Aldehydes And Ketones: Mechanism

The Grignard reaction is the addition of an organomagnesium compound to a carbonyl species. Recall that carbon is significantly more electronegative (2.5) than magnesium, so the partial negative charge is on carbon. In this example I used R-MgBr, although other halides (Cl, I) also work. Also, in the acid workup step I showed the spectator anion for H₃O⁺ which is generally not necessary, but I like to balance the charges so you can see all the byproducts.

1. Grignard Reaction: Addition of Grignard Reagents To Aldehydes

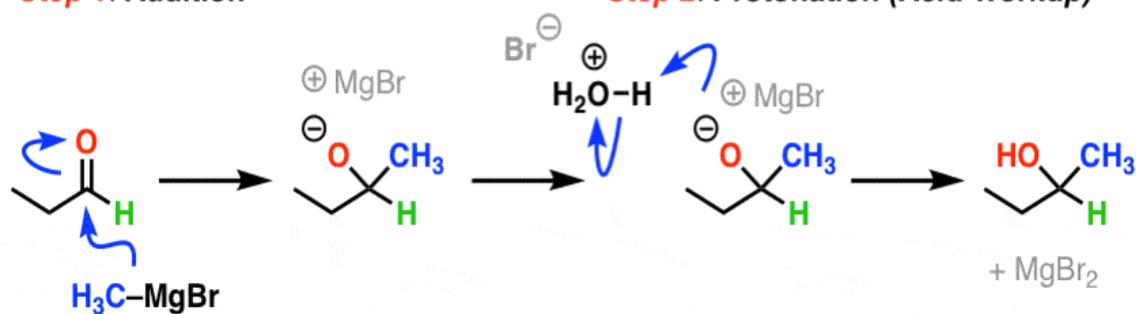


Specific example



Mechanism

Step 1: Addition

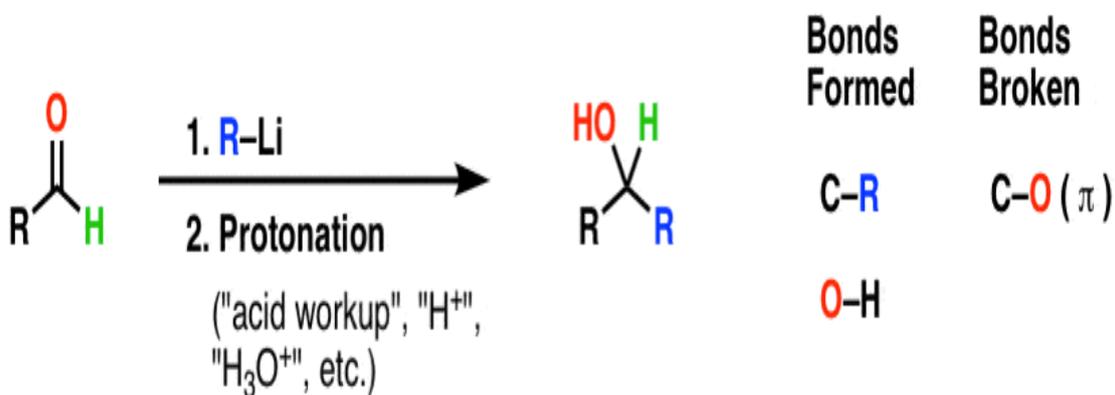


Note: using Br as a specific example, but could use other halides too (Cl, I)

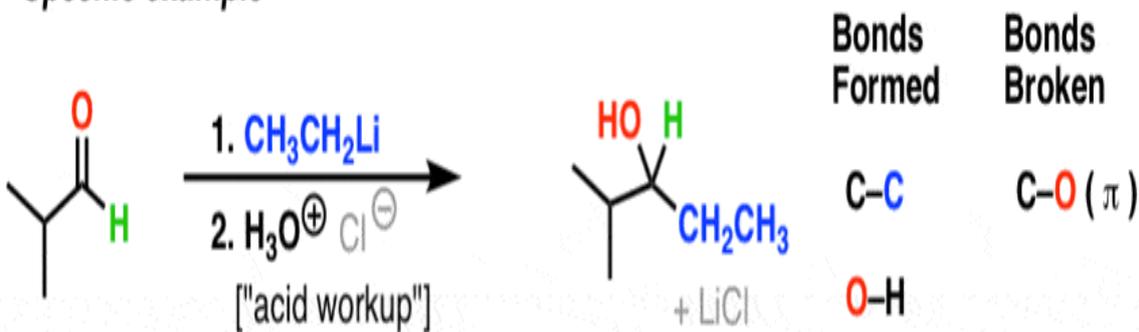
6. Addition of Organolithium Reagents To Aldehydes: Mechanism

For our purposes, essentially the same as the Grignard reaction for aldehydes and ketones.

2. Addition of Organolithium Reagents to Aldehydes



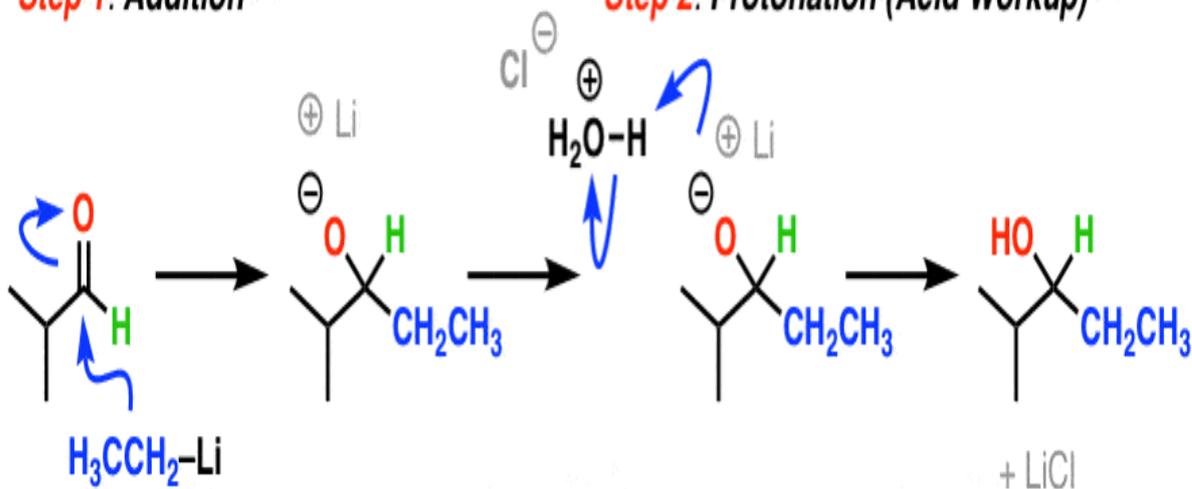
Specific example



Mechanism

Step 1: Addition

Step 2: Protonation (Acid Workup)

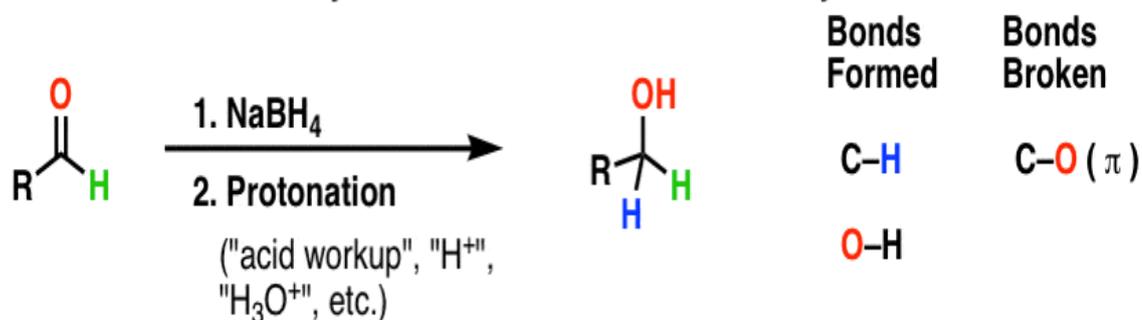


7. Reduction of Aldehydes and Ketones with Sodium Borohydride: Mechanism

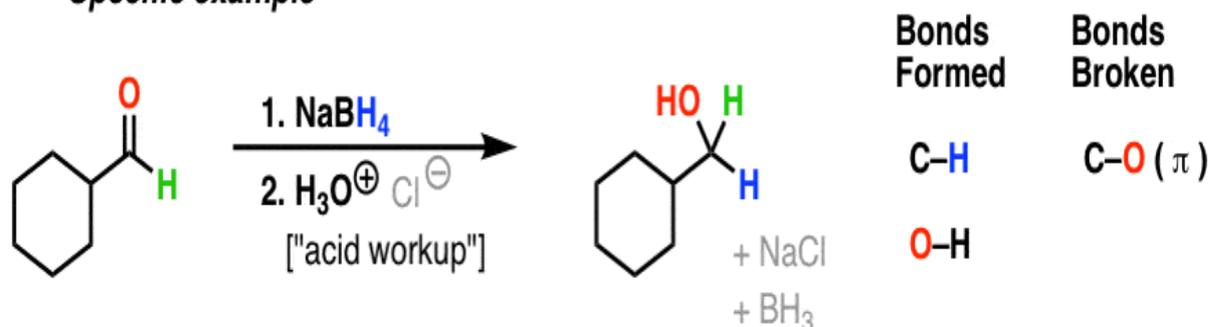
In the borohydride anion (BH_4^-) it's important to remember that hydrogen has a higher electronegativity (2.2) than boron (2.0). This means that although boron has the negative "formal" charge, the *partial charges* are on hydrogen. Hence, it's the **hydrogen** that acts as a nucleophile [technically, "hydride" (H^-)].

The mechanistic pattern is the same – addition to carbonyl carbon, followed by protonation of oxygen.

3. Reduction Of Aldehydes/Ketones With Sodium Borohydride

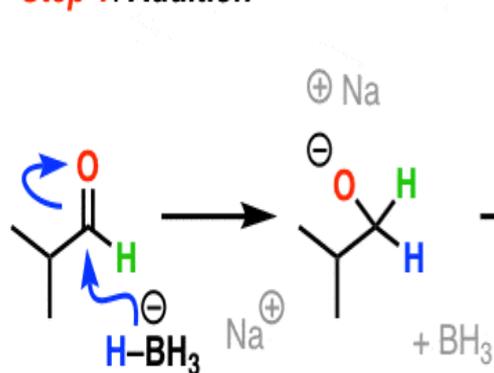


Specific example

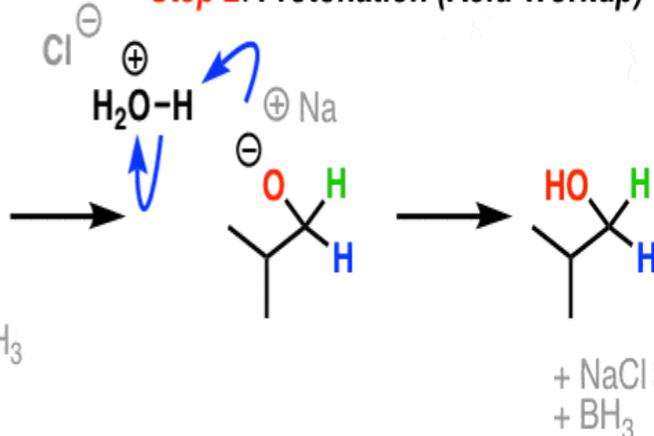


Mechanism

Step 1: Addition



Step 2: Protonation (Acid Workup)

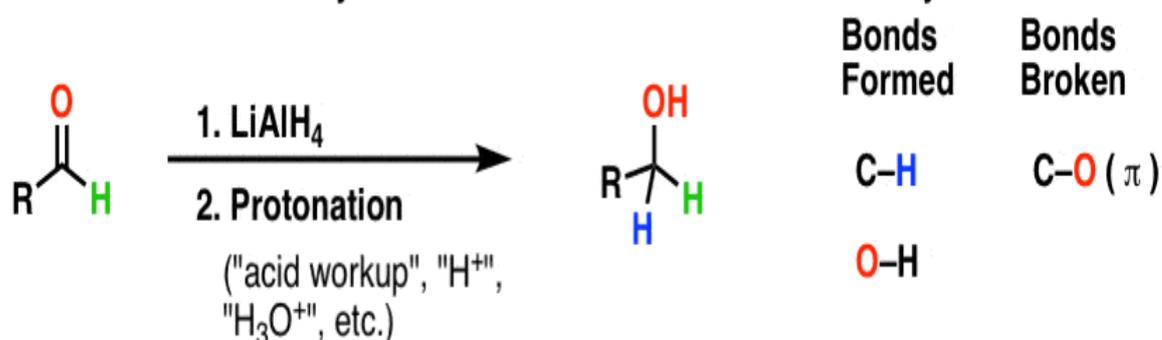


In practice, reduction with NaBH_4 is often run at low temperature with methanol as a solvent, with the subsequent workup step being addition of a mild acid such as NH_4Cl to ensure full protonation of the alkoxide.

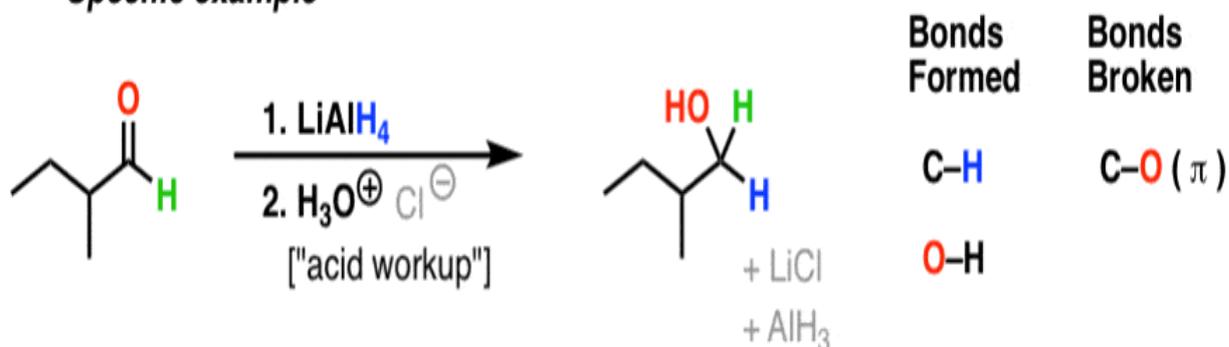
8. Reduction of Aldehydes and Ketones With LiAlH_4 : Mechanism

Everything I said above with respect to NaBH_4 applies to LiAlH_4 which is also a source of nucleophilic hydride. On paper, NaBH_4 and LiAlH_4 are equally effective in performing the reduction of an aldehyde or ketone to an alcohol. In practice, LiAlH_4 is a much stronger reductant that will also reduce esters and carboxylic acids to alcohols. NaBH_4 will not. Using LiAlH_4 to reduce an aldehyde or ketone is like using a sledgehammer to kill a fly.

4. Reduction Of Aldehydes/Ketones With Lithium Aluminum Hydride

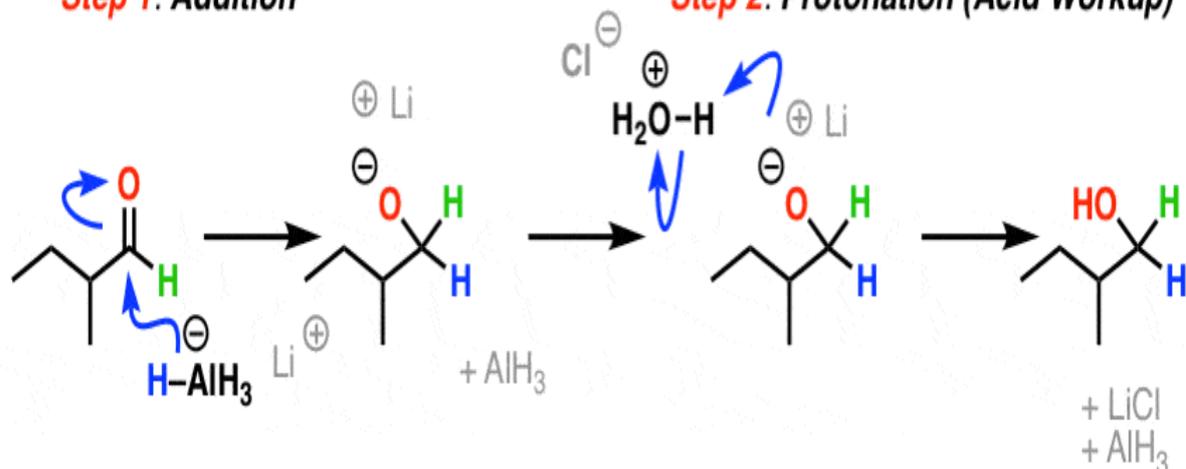


Specific example



Mechanism

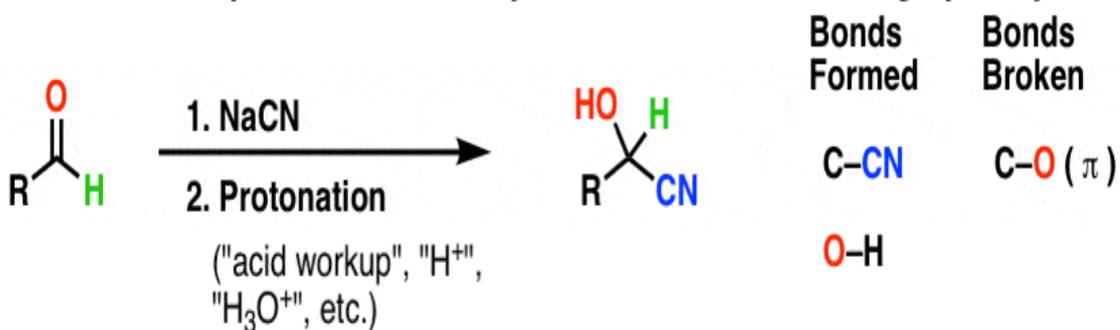
Step 1: Addition



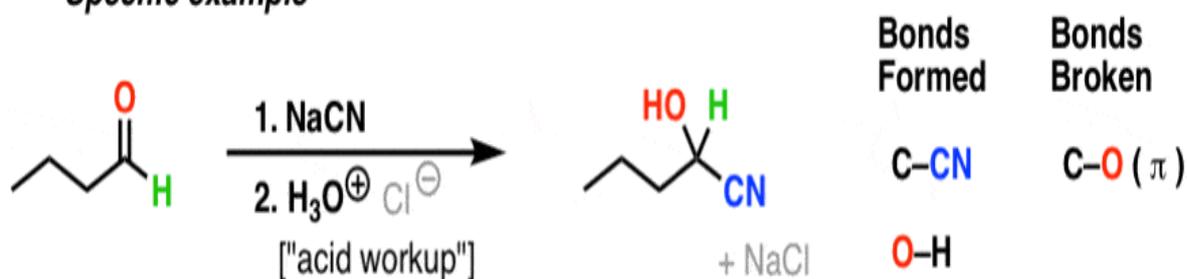
9. Addition of Cyanide Ion To Aldehydes And Ketones: Mechanism

Addition of cyanide ion (CN^-) to aldehydes and ketones will result in a cyanohydrin. On paper, this also follows the two-step sequence of addition-protonation, although in practice the reaction can be run in the presence of a proton source such as H_2O ; unlike Grignards and some hydrides, cyanide ion is only weakly basic and will not be irreversibly destroyed by protonation. *[In practice, however, care must be taken not to lower the pH too much; that may result in the formation of deadly HCN gas.]*

5. Addition of Cyanide Ion To Aldehydes And Ketones, Forming Cyanohydrins

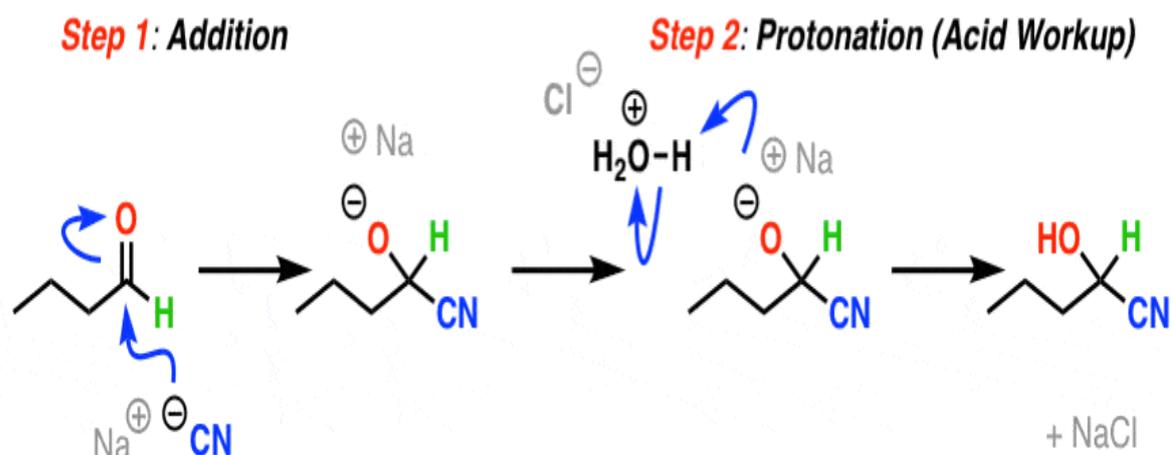


Specific example



Mechanism

Step 1: Addition

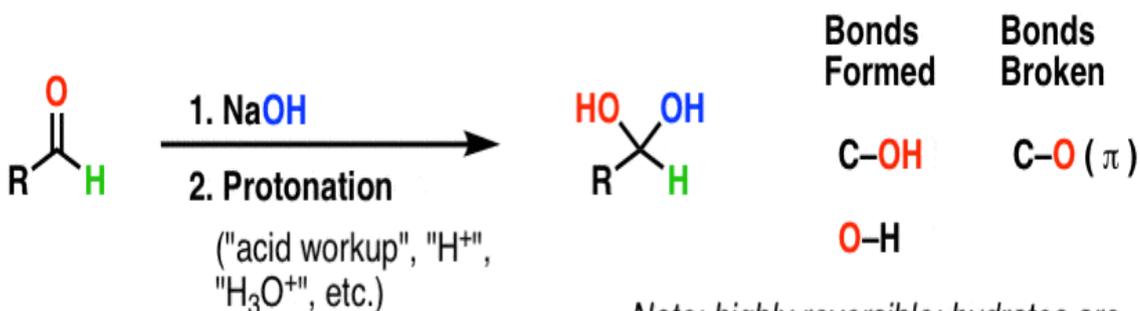


A related process, the [Strecker synthesis](#) of amino acids, begins with the addition of cyanide ion to an imine.

10. Addition Of Hydroxide Ion To Aldehydes To Form Hydrates (“geminal diols”): Mechanism

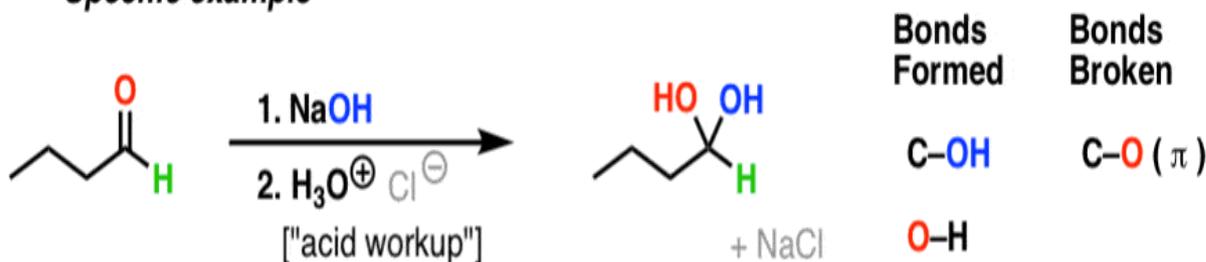
Hydroxide ion will add to aldehydes or ketones to form hydrates, the mechanism of which also follows the two-step pattern. In practice, this doesn't involve a separate workup step; hydroxide ion would be administered with at least some water as a co-solvent.

6. Addition of Hydroxide Ions To Aldehydes and Ketones, Forming Hydrates



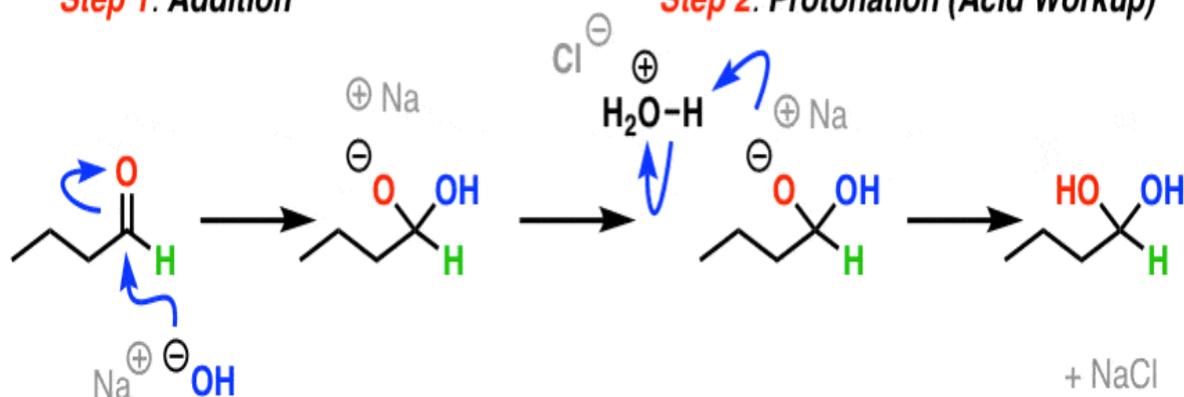
Note: highly reversible; hydrates are not easily isolated

Specific example



Mechanism

Step 1: Addition

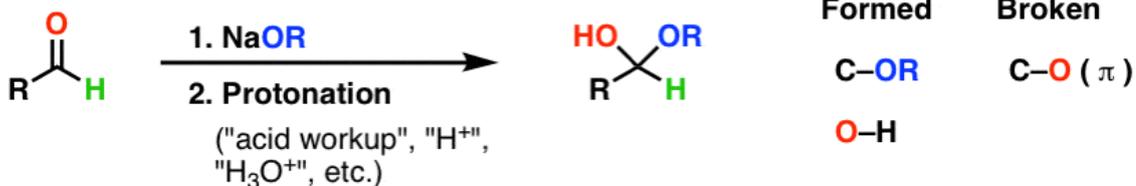


One thing to know about hydrates, however; they aren't easily isolated, except for cases where the carbonyl is adjacent to an electron withdrawing group, such as in the case of [chloral hydrate](#) (a solid)

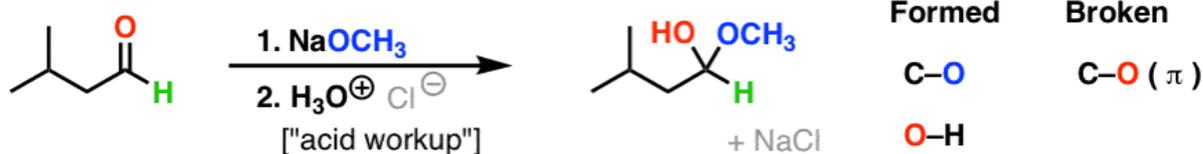
11. Addition of Alkoxides To Aldehydes And Ketones To Form Hemiacetals: Mechanism

Last example. Addition of alkoxides to aldehydes and ketones will result in the formation of a hemiacetal.

7. Addition of Alkoxide Ions To Aldehydes and Ketones, Forming Hemiacetals

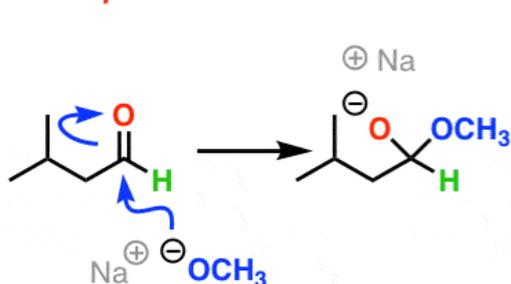


Specific example



Mechanism

Step 1: Addition



Step 2: Protonation (Acid Workup)

