Reduction of Aldehydes and Ketones using NaBH₄ or LiAlH₄

Aldehydes are converted to primary alcohols, and ketones to secondary alcohols, by treatment with either NaBH₄ (sodium borohydride) or LiAlH₄ (lithium aluminum hydride).

Notice that although these reactions achieve the same overall result, the conditions for the reactions are rather different. How do these two reagents function, and why are the reaction conditions particular to each case?

These reactions are generally presented in textbooks (including Klein’s book, Sections 13.4 and 20.9) in a highly simplified form. From the point of view of just understanding what the organic product of these reactions will be, this simplified mechanism is just fine. But many students look at the simplified presentation and immediately notice big gaps. Then they get worried about what they might be missing, and wonder if there are secrets concealed in the apparently trivial reaction mechanisms.

The answer is Yes! But mostly it doesn’t matter so don’t worry!

Let’s take a look at what is going on in these reactions and decide what parts matter and what parts don’t. Some of these things may have relevance for the laboratory portion of the course, because they explain some observations and why some steps in the procedures are required.

The simplified mechanism

Klein shows separate mechanisms (Mechanism 13.1 and 13.2) for reactions of carbonyls with NaBH₄ and LiAlH₄, but fundamentally both mechanisms are the same. The generic scheme below depicts these two reactions, where “M” is either boron or aluminum. There are essentially only two steps: nucleophilic attack of a hydride ion on the electrophilic carbonyl carbon; and protonation of the resulting alkoxide by water or some other acid. This latter step may occur in the same medium as the first step, or the proton source may be added later.
Both BH₄⁻ and AlH₄⁻ deliver hydride as a nucleophile to the carbonyl carbon. We have to be very clear about this: hydride ions are negatively charged and behave as bases or nucleophiles, unlike protons which are positively charged and are Lewis acidic. Do not confuse hydrogen atoms, hydride ions or protons with one another!

But what happens to the reagent?
After donating a hydride to the carbonyl carbon, BH₄⁻ (borohydride) is converted to BH₃ (borane), and AlH₄⁻ (aluminohydride) is converted to AlH₃ (alane). BH₃ and AlH₃ are Lewis acidic since they are formally electron-deficient six-valence-electron compounds. They will therefore form complexes with any Lewis bases they encounter. The alkoxide formed by attack of hydride on the carbonyl is certainly one Lewis base present during the reaction.

This suggests that perhaps a complex like the one shown might be present rather than the simple alkoxide during the reduction reaction.

The proton transfer step (workup).
Klein shows the workup step, addition of water to the reaction, simply as proton transfer to the alkoxide formed by reduction. But what about any unreacted hydride reagent? What would happen to this in the presence of water or any other protic material? Because hydride is also basic, BH₄⁻ and AlH₄⁻ both react with Brønsted acidic substances to form dihydrogen. BH₃ or AlH₃ are also produced, and these can react with the conjugate base of the Brønsted acid (A⁻) to form complexes.

All of the hydrides will react in this way when exposed to sufficient amounts of a protic substance.

This is what occurs during the workup after the reduction is complete. Water and possibly some acid is added carefully to the reaction mixture. This protonates any alkoxide, and converts any remaining M-H species to M-OH species. If the alkoxide has formed a complex with borane or alane, the water/acid will hydrolyze the metal-oxygen bond, liberating the alcohol product we want to isolate. The boron or
aluminum will ultimately be converted into an unreactive oxide, which may be water-soluble (in the case of borate) or hopefully form an easily filtered solid (in the case of alinate). We will discuss what is present in the reaction mixtures when the workup begins for each specific reagent, since the situation is quite different for each.

The differences between NaBH₄ and LiAlH₄
We have seen that these reagents follow essentially the same mechanism when they react with carbonyl groups. Why then do we talk about two different reagents? Even though they follow the same mechanism, NaBH₄ and LiAlH₄ are very different in terms of reactivity. Sodium borohydride is much less reactive as a base or nucleophile than is lithium aluminum hydride.

This can be understood by considering the electronegativities of boron, aluminum and hydrogen and what they tell us about the metal-hydrogen bonds. The difference between B and H is much smaller than the difference between Al and H, so B-H bonds are much more covalent and stronger than are Al-H bonds. The lower polarity of the B-H bond versus the Al-H bond means that the hydrogens in BH₄⁻ are less "hydridic" than are those in AlH₄⁻.

The difference between Na⁺ and Li⁺ counter ions also plays a role in making LiAlH₄ a “stronger” (more reactive) hydride donor.

The greater reactivity of LiAlH₄ means that it is capable of reducing less-reactive functional groups which will not be reduced by NaBH₄. On the other hand, NaBH₄ may be more selective than LiAlH₄ when multiple functional groups are present. The difference in reactivity also dictates that different reaction conditions must be used for the two reagents.

Protic and aprotic solvents
Because of the very high reactivity of LiAlH₄, it reacts rapidly and exoergically with protic solvents. If LiAlH₄ is added to water or an alcohol solvent, the formation of H₂ (g) is violently rapid and likely to cause a fire. In contrast, NaBH₄ reacts with these solvents slowly enough that the consumption of hydride and the evolution of hydrogen gas can be neglected.

In order for a reaction to occur at a reasonable rate, the reagent and the reactant should both be soluble in the reaction solvent, at least to a fair extent. Both LiAlH₄ and NaBH₄ are ionic materials, which means that they will only dissolve in relatively polar solvents. But this is where the differences in reactivity become important, since many polar solvents will react with hydride reagents. Obviously, carbonyl-containing solvents like acetone cannot be used either since they will be reduced too. The solvent has to be chosen to fit the particular reagent we are using.

Lithium aluminum hydride reactions: ether-type solvents
The violent reaction of LiAlH₄ with even weakly acidic substances like water or alcohols means that these are incompatible with this reagent. As a result, chemists use solvents like tetrahydrofuran (THF) or diethyl ether (Et₂O) that have been carefully treated to remove traces of water when carrying out reactions with LiAlH₄. These solvents are used because the oxygen atoms are Lewis bases that can coordinate to Li⁺ ions, helping to dissolve LiAlH₄. Only when the desired reduction reaction is complete
will small amounts of water be cautiously added as a workup, to quench the remaining reagent and protonate the product.

The fact that the solvent is aprotic means that the only thing available for the Al-H bonds to react with is the carbonyl reactant. All of the Al-H groups can react in principle, so theoretically we only need 0.25 moles of LiAlH$_4$ per mole of carbonyl.

However, you can see that the result is likely to be very sterically crowded, which means that each successive step will likely be slower than the one before it. As a result, we don’t usually do these reactions with the minimum theoretical amount of LiAlH$_4$. Most often we will use close to 1 mole of LiAlH$_4$ per mole of carbonyl, which is a 4-fold excess of hydride. This means that on average each LiAlH$_4$ only reacts once, and when all the carbonyl compound has been consumed we have really only one species in our mixture.

This is the situation then when we proceed to the workup. Because there will always be a fair bit of Al-H left, it is essential to proceed cautiously when working up LiAlH$_4$ reactions.

There is one practical issue that deserves mention, but which you don’t need to worry about on test questions. It is easier said than done to get the aluminum into a form that can be separated from the organic product. Various special workup processes have been devised to address this problem, and any students who go on to do laboratory research and actually use LiAlH$_4$ are advised to look into these methods. For the purposes of our course, we will simply write “H$_2$O workup”.

**Sodium borohydride reactions: alcohol or water solvents**

Because it is much less reactive than LiAlH$_4$, NaBH$_4$ reactions may be performed using water, methanol, ethanol, or isopropanol solvents. NaBH$_4$ is in fact not soluble enough in THF or Et$_2$O for reactions to be performed in these solvents. Reactions conducted in alcohol solvents will be accompanied by slow
formation of dihydrogen as the reagent reacts with the OH groups of the solvent, but this is usually not a problem since there is usually an excess of hydride present.

Most organic reactions are performed in fairly dilute solutions, between 0.1 and 1.0 molar. In the reduction of a carbonyl compound by NaBH₄ in an alcohol solvent, the high concentration of the solvent (ethanol is about 36 molar) relative to the product alcohol will shift the equilibrium away from making a product/borane complex towards a solvent/borane complex.

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\text{R-CO-R + NaBH}_4 \xrightarrow{\text{EtOH (solvent)}} \text{R-OH} + \text{EtO-BH}_3 \text{Na}
\]

The reaction mixture actually becomes extremely complex as the reduction proceeds because all the B-H bonds can react, either with the carbonyl compound or with the solvent alcohol, and every species containing a B-O group can exchange with other alcohol groups in the mixture. Here is a hint of how complicated the situation can be in these “simple” reactions.

Obviously there are several paths that can be followed through this scheme, and since what we care about is converting all of the carbonyl compound into the corresponding alcohol, it doesn’t really matter to us which exact path is followed. This means that several balanced equations can be written, depending on what we choose to focus on. A few possible overall balanced equations before workup could be:
No matter what the actual composition of the reaction mixture, once TLC tells us all the carbonyl has been consumed we will perform a water/acid workup as previously described. This will convert all the boron into water-soluble borate oligomers such as $\text{[B}_4\text{O}_5\text{(OH)}_4\text{]}^{2-}$.

The product alcohol is released so that it can be extracted into a neutral organic solvent for purification.

**Summary**

It is convenient to use a simplified mechanism to describe the hydride reduction of carbonyl compounds mainly because the details are extremely complex but do not generally affect the organic product. We can just note the key features without getting too concerned about all the details. Understanding how reagents like LiAlH$_4$ and NaBH$_4$ react allows us to make wise choices when going into the laboratory, to avoid mixing them with inappropriate solvents and to choose workup conditions that lead to easy isolation of the compound we are trying to make.