

Reducing Agents

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Reduction is defined in chemistry as loss of oxygen, gain of hydrogen or gain of electrons; the gain of electrons enables you to calculate an [oxidation state](#).

Hydride Reagents and Dihydrogen

Lithium aluminum hydride

LiAlH_4 is a strong, unselective reducing agent for polar double bonds, most easily thought of as a source of H^- . It will reduce aldehydes, ketones, esters, carboxylic acid chlorides, carboxylic acids and even carboxylate salts to alcohols. Amides and nitriles are reduced to amines. In each case the partially negative hydrogen reacts with the partially positive carbon of the substrate. It can also be used to reduce nitro groups and even as a nucleophile to displace halide from an sp^3 carbon or open an epoxide.

Why does it work? Remember that aluminum is a metal with a low electronegativity; thus, the Al-H bond is strongly polarized with Al positive and H negative. The abnormal polarization (and oxidation state of -1) for hydrogen, which is normally positive, results in a high reactivity, especially with atoms that can accept electrons (be reduced), allowing the hydrogen to become positive again (normal oxidation state of +1).

Precautions: It reacts with other positive centers as well, especially any slightly acidic hydrogens, like those of alcohols, water, carboxylic acids or alkynes to produce hydrogen gas, which is highly flammable and can readily explode (e.g. the Hindenberg). LiAlH_4 requires anhydrous conditions for the reaction and usually an excess of the reagent (to soak up any water that was missed in the glassware or reagents); the most common solvent for the reactions is diethyl ether. "Workup" at the end of the reaction is usually done by careful addition of aqueous acid (remember the flammable hydrogen gas and ether), followed by extraction of the organic products from the water-soluble salts.

To make LiAlH_4 less reactive and more selective, the hydride is made more hindered, e.g., in the compound $\text{LiAl}(\text{O}t\text{Bu})_3\text{H}$. It can reduce acid chlorides (and some esters) quickly, but is slow to react with aldehydes; therefore $\text{LiAl}(\text{O}t\text{Bu})_3\text{H}$ provides a convenient way to synthesize aldehydes by reduction of acid chlorides, something that can't be done with LiAlH_4 or NaBH_4 .

Boron Hydrides

Sodium borohydride

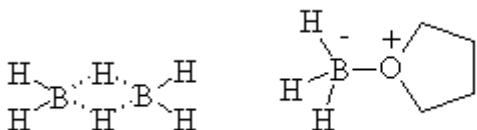
NaBH_4 is less reactive than LiAlH_4 but is otherwise similar. It is only powerful enough to reduce aldehydes, ketones and acid chlorides to alcohols: esters, amides, acids and nitriles are largely untouched. It can also behave as a nucleophile toward halides and epoxides. It is also convenient that, although LiAlH_4 is strong enough to reduce the $\text{C}=\text{C}$

of a conjugated carbonyl compound, NaBH_4 is not; thus the carbonyl group can be reduced without the alkene.

Precautions: NaBH_4 is unreactive enough that the reductions can be done in alcohol solution, or even water (as long as they don't take too long); this can be advantageous for polar compounds which can be pretty insoluble in ether. Hydrolysis with acid and water followed by extraction is used to isolate the product (hydrogen gas is produced).

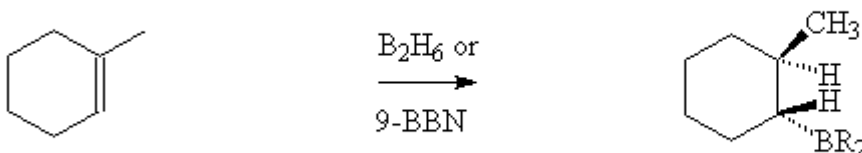
Diborane and 9-BBN

B_2H_6 is the actual molecular formula for a reagent whose simplest formula is BH_3 . The boron would have only 6 electrons in BH_3 ; its attempt to get 8 electrons results in its sharing hydrogens and their electrons in a bridged structure shown below.



You will often find this reagent referred to as just BH_3 , since it is commonly sold in solution as a complex with a base such as methylamine or in solution of a moderately high boiling ether such as THF (tetrahydrofuran) with which it also forms a complex, shown above.

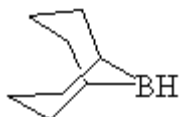
B_2H_6 does not behave as a source of hydride; instead it adds to carbon-carbon double bonds in a concerted manner to place the boron (somewhat positive) on the less substituted carbon and the hydrogen (somewhat negative) on the more substituted carbon (better able to support a slight positive charge as the electrons are being reshuffled in the transition state). This addition results in an addition to (a reduction of) the double bond which puts the heteroatom on the *less substituted* carbon.



Since boron is less electronegative than carbon, the B is somewhat positive, and can only be replaced by other slightly positive things. Useful things like halides and hydroxides are negative and won't work; instead sources are needed which can produce positive halogen or oxygen - oxidizing agents! Reaction with bromine or chlorine (Br_2 , Cl_2) produces the less substituted halide from the alkene, reaction with hydrogen peroxide (H_2O_2) the alcohol and chloramine (NH_2Cl) the amine. See the essays on [halogens](#) and [peroxides](#) as oxidizing agents.

Because the reaction of the B-H bond with the C=C bond is concerted, it is also stereospecific. Moreover, the subsequent reaction of the oxidizing agent retains that stereochemistry. Thus, B_2H_6 provides a method for producing not only the less substituted alcohol, etc., but only one diastereomer thereof. This control of both the *regiochemistry* and *stereochemistry* is important in the synthesis of natural products such as pheromones and antibiotics.

To improve the selectivity of the boron for the less substituted carbon, a bulky group can be added; the most common reagent of this type is 9-borabicyclo[3.3.1]nonane, 9-BBN, below. B_2H_6 can also be used to reduce carbonyl groups, but it is less convenient to use than $NaBH_4$.



Precautions for B_2H_6 : Similar to $NaBH_4$ and $LiAlH_4$, with extra care since B_2H_6 is a gas. The ether solutions are of course flammable.

Dihydrogen

Since reduction is defined as addition of hydrogen, dihydrogen (H_2) would seem to be the ideal reducing agent. However, the strength of the H-H bond and the lack of polarizability of the molecule makes it extremely unreactive. Fortunately some precious metals - platinum, palladium, nickel - "react" with dihydrogen in a rather unusual way. The metals dissolve dihydrogen and partially bond to it, effectively breaking the H-H bond; platinum will dissolve more than a mole of hydrogen and swells visibly in the process - it is like a sponge. Thus these metals serve as catalysts for reactions of dihydrogen. Typically dihydrogen adds to multiple bonds - alkenes, alkynes, carbonyl compounds - in the presence of these catalysts. Since the hydrogenation reaction takes place on the surface, it is stereospecific *syn*.

By careful control of the reaction conditions and the exact nature of the catalyst, it is possible to reduce one kind of multiple bond without some others that are present reacting. An alkyne can be reduced to a *Z* (*cis*) alkene by "poisoning" the Pt catalyst so that the addition stops at the alkene; reagents that have been used are sulfur compounds such as barium sulfate, organic amines such as quinoline. A weakened palladium catalyst called Lindlar's catalyst (Pd with $CaCO_3$ and $Pb(OAc)_2$) is very popular too. With a weaker catalyst or much milder conditions, it is possible to reduce an alkene without reducing a carbonyl in the same molecule, even if they are conjugated.

Metals and Organometallic Reagents

The Grignard Reagent

Reaction of an alkyl halide with magnesium metal in diethyl ether results in the formation of an organometallic compound with the magnesium replacing the halide; the second valence of the magnesium (II) is satisfied by the halide removed from the carbon.

the corresponding Grignard reagent at higher temperatures, e.g. using THF as a solvent. Alkyl Grignards are most easily prepared from primary halides, followed by secondary; tertiary are difficult; the negative carbon is responsible for these differences (compare the order of stability of positive carbon in carbocations). Halide reactivity toward magnesium is in the order $I > Br > Cl$.

Dialkylcopper Lithium (Lithium Dialkylcuprate) Reagents

The dialkyl copper lithium reagents are often made from Grignard reagents. R_2CuLi reagents are less reactive and more selective than Grignard reagents. They react with aldehydes and ketones only slowly but with carboxylic acid chlorides very quickly. As a result they can be used to reduce carboxylic acid chlorides to ketones without further reduction to the tertiary alcohol. Since they are often made from the Grignard reagent, the same precautions and restrictions on structure apply. Note that their selectivity is like that of [LiAl\(OtBu\)₃H](#), discussed above, but of course the variable R group gives them more versatility.

Sodium, Alkyl Sodium and Alkyl Lithium

Treatment of alkyl halides with sodium results in a rapid oxidation of the metal, but the negative carbon of the corresponding RNa reacts with the positive carbon of the remaining RX to give RR (like a Grignard does without the ether); this is called coupling, or sometimes the Wurtz reaction. RLi 's are more manageable and is used as nucleophilic reagents for addition to carbonyl groups. More often, they are just used as strong bases, e.g. to convert an alkyne to its conjugate base.

Treatment of compounds with even slightly acidic protons with sodium metal will result in the same reaction as occurs with the acidic hydrogen of water, namely reduction of that somewhat positive hydrogen to H_2 and oxidation of the sodium to Na^+ . Useful examples include: alcohol to alkoxide (base and nucleophile), and alkyne to alkynide (nucleophile).

Acidic Reducing Agents

If you look at the reducing agents above, you will note that they are all basic. But there is a family of reducing agents that are acidic - a moderately reactive metal with hydrochloric acid. The Clemmensen reduction uses a liquid amalgam (metal solution) of zinc and mercury with HCl to reduce ketones to hydrocarbons. Tin (Sn) or iron (Fe) with HCl can be used to reduce nitro groups to amino groups; this reduction is especially useful for making anilines since the nitrobenzenes are easy to make.