Appendix 3: Removal of Functional Groups

A number of functional groups can be removed completely to leave the hydrocarbon skeleton. This can be useful if a functional group has been included in the synthesis to activate a particular position for a reaction, but is not required in the target structure. The following are some common methods for removing functional groups.

App 3.1. Reduction of alkenes, alkynes and aromatic rings

Alkenes are converted to alkanes by treatment with hydrogen over a finely divided metal catalyst such as palladium, nickel or platinum (Fig. 1a).

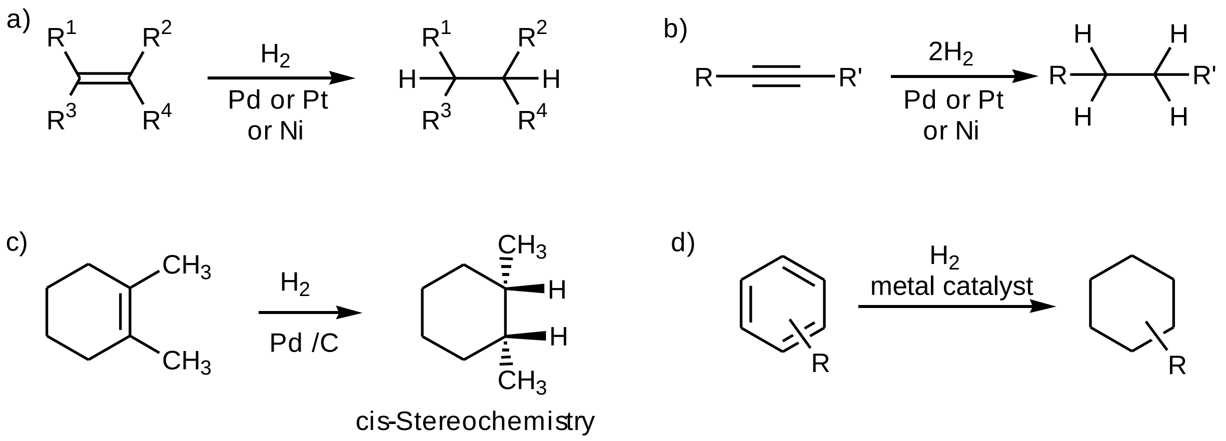

Figure 1 Reduction of a) alkenes and b) alkynes.

This is called a catalytic hydrogenation or reduction reaction and is stereospecific in that both hydrogens are added to the same side of the molecule. With cyclic alkenes, this results in *cis*-stereochemistry (Fig. 1c). In more complex molecules, *cis*-addition takes place to the least hindered face of an alkene, and the reaction occurs more readily for less substituted alkenes. Catalysts such as palladium, nickel or platinum are insoluble under the reaction conditions and act as solid catalytic surfaces for the reaction. Thus, they are known as heterogeneous catalysts. It is also possible to carry out hydrogenations with homogenous catalysts which *are* soluble under the reaction conditions. Wilkinson's catalyst ($(Ph_3P)_3RhCl$) is one such example.

Alkynes can similarly be reduced to alkanes with 2 equivalents of hydrogen gas in the presence of a heterogeneous catalyst (Fig. 1b). Alternatively, a homogeneous catalyst such as Wilkinson's catalyst ($(Ph_3P)_3RhCl$) can be used.
Aromatic rings can be hydrogenated to cycloalkanes with a nickel catalyst, but the reduction has to be carried out under strong conditions using high temperature and high pressure (Fig. 1d). These are much stronger conditions than those required for the reduction of alkenes, because of the inherent stability of aromatic rings. The reduction can also be carried out using hydrogen and a platinum catalyst under high pressure, or with hydrogen and a rhodium/carbon catalyst. The latter is a more powerful catalyst and this reaction can be done at room temperature and at atmospheric pressure.

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App 3.2. Reduction of aldehydes and ketones

Aldehydes and ketones can be reduced to alkanes by three different methods which are complementary to each other. The Wolff-Kishner reduction is carried out under basic conditions, and is suitable for compounds that might be sensitive to acid (Fig. 2a). The reaction involves the nucleophilic addition of hydrazine followed by elimination of water to form a hydrazone, which spontaneously decomposes with the loss of nitrogen gas.

The Clemmenson reduction (Fig. 2b) gives a similar product, but is carried out under acid conditions, and so this is a suitable method for compounds which are unstable to basic conditions.

Compounds which are sensitive to both acid and base can be reduced under neutral conditions by forming a thioacetal or thioketal, then carrying out a reduction with Raney nickel (Fig. 2c). Raney nickel is a catalyst which has hydrogen gas adsorbed onto the nickel surface.

Aromatic aldehydes and ketones can be deoxygenated with hydrogen over a palladium charcoal catalyst (Fig. 2d). The reaction takes place because the aromatic ring activates the carbonyl group towards reduction, but is resistant to reduction itself. This allows the synthesis of alkylbenzenes which cannot be synthesized directly by the Friedel Crafts alkylation reaction. Aliphatic aldehydes and ketones are not reduced in this manner.

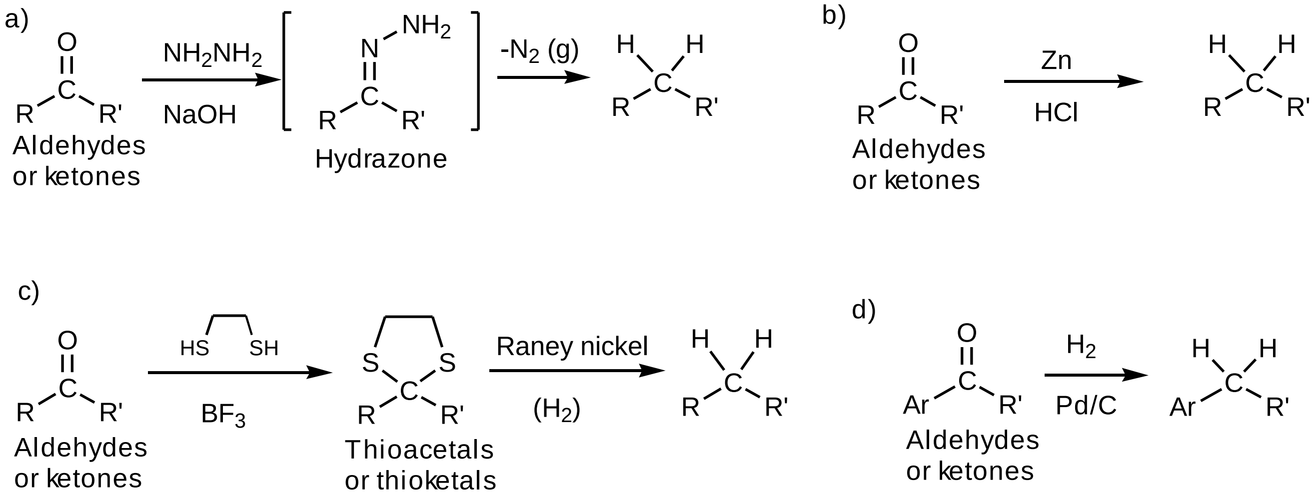

Figure 2 Reduction of aldehydes and ketones. a) Wolff-Kishner b) Clemmenson c) Reduction via thioacetals or thioketals d) Reduction of aromatic aldehydes and ketones.

App 3.3. Removal of aromatic amines or nitro groups

An aromatic amine group can be removed by converting it to a diazonium salt then treating the salt with H_3PO_2 (Fig. 3). Since aromatic nitro groups can be reduced to amines, this is also a means of removing a nitro group from an aromatic ring.

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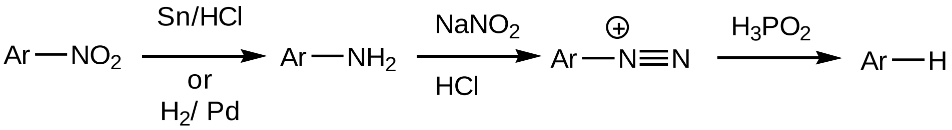

Figure 3 Removal of an aromatic nitro or amine group.

App 3.4. Removal of an alcohol group

An alcohol functional group can be removed in two stages by dehydration to an alkene, followed by reduction with hydrogen gas in the presence of a catalyst (Fig. 4a). An alternative method is to convert the alcohol to a tosylate, then reduce the tosylate with a hydride reducing agent (Fig. 4b). Benzylic alcohols can be removed by reduction with hydrogen gas over palladium charcoal (Fig. 4c).

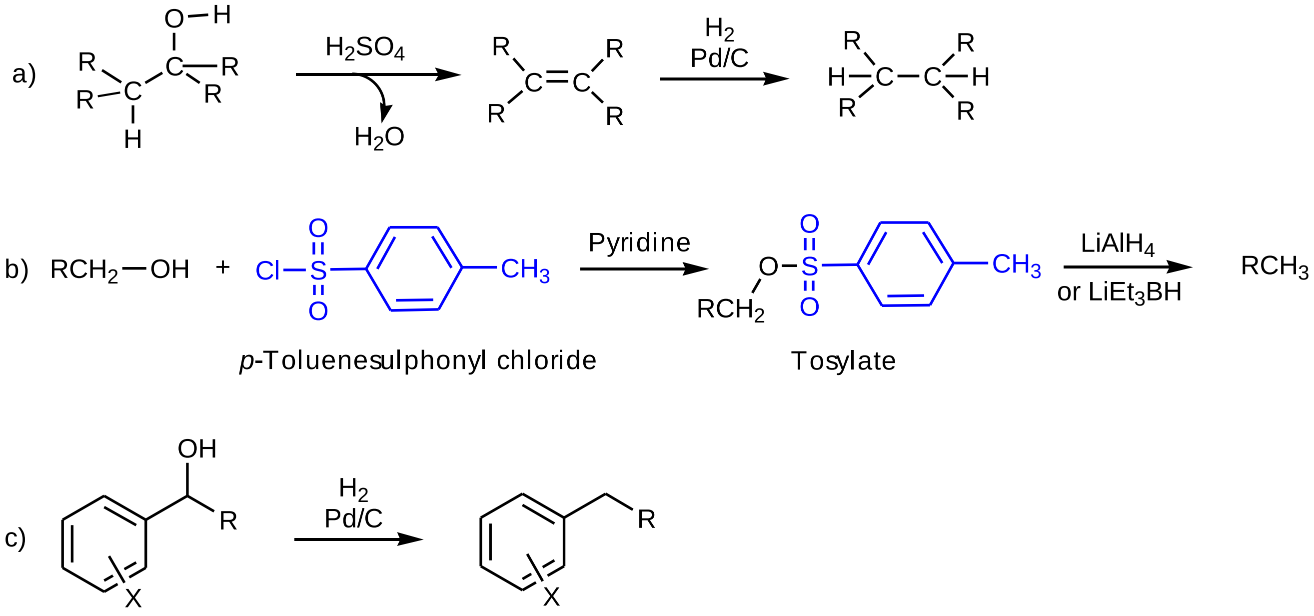

Figure 4 Removal of alcohol groups.

App 3.5. Removal of an alkyl halide - dehalogenation

There are a number of reducing agents available that can remove an alkyl halide. Lithium aluminium hydride or catalytic hydrogenation are frequently used for this purpose (Fig. 5). However, more selective reducing agents may be required if there are other functional groups present which are susceptible to these reagents.

Carrying out the dehalogenation with deuterated $LiAlD_4$ will introduce a deuterium label in place of the halogen and can be useful in isotopic labelling studies (Chapter 11). An alkyl halide can also be converted to an alkane by converting it to a Grignard reagent, then reacting that with water.

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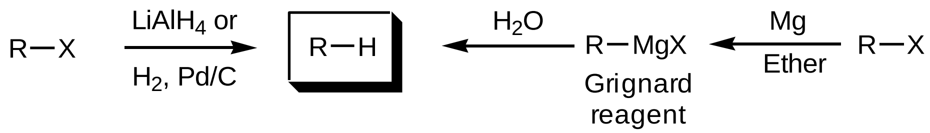

Figure 5 Reduction of an alkyl halide.

App 3.6. Removal of a carboxylic acid or ester

Carboxylic acids and esters can be reduced to alcohols, then treated as described in appendix 3.4. If there is a ketone group at the β-position to a carboxylic acid or ester, then it is possible to remove the carboxylic acid by decarboxylation under hydrolytic conditions.

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