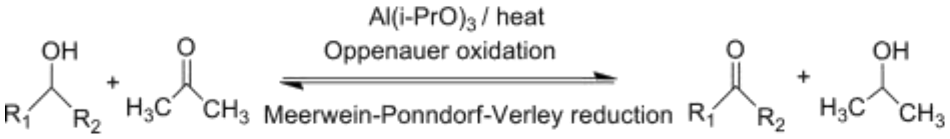
Meerwein–Ponndorf–Verley reduction

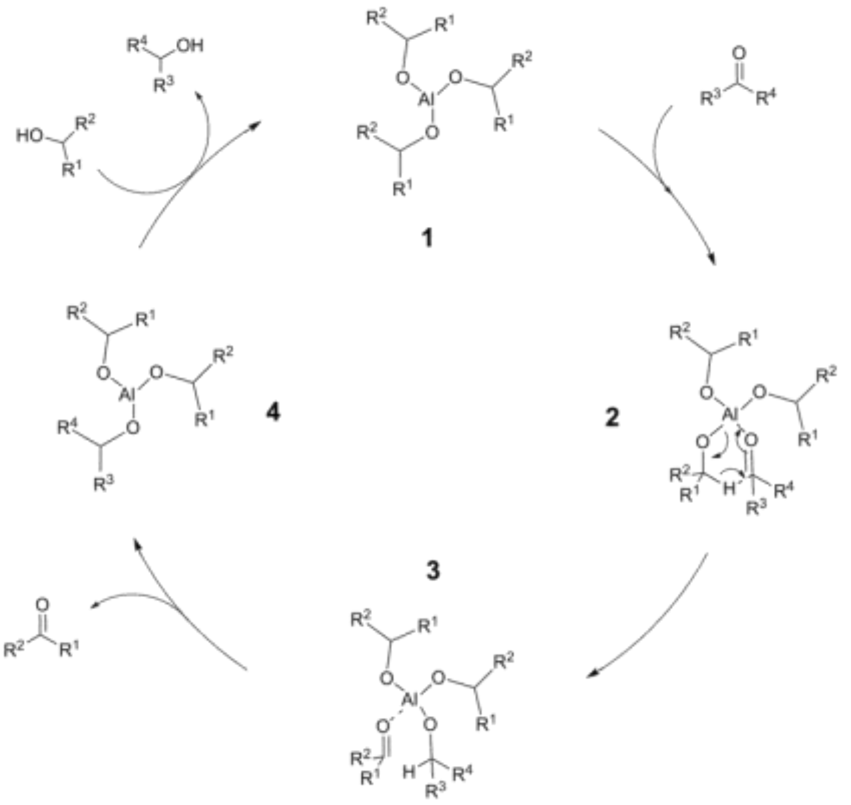
The Meerwein–Ponndorf–Verley (MPV) reduction in organic chemistry is the reduction of ketones and aldehydes to their corresponding alcohols utilizing aluminium alkoxide catalysis in the presence of a sacrificial alcohol. The advantages of the MPV reduction lie in its high chemoselectivity, and its use of a cheap environmentally friendly metal catalyst.



It has found that a mixture of aluminium ethoxide and ethanol could reduce aldehydes to their alcohols. Ponndorf applied the reaction to ketones and upgraded the catalyst to aluminium isopropoxide in isopropanol

Mechanism[edit]

The MPV reduction is believed to go through a catalytic cycle involving a six-member ring transition state as shown in Figure 2. Starting with the aluminium alkoxide 1, a carbonyl oxygen is coordinated to achieve the tetra coordinated aluminium intermediate 2. Between intermediates 2 and 3 the hydride is transferred to the carbonyl from the alkoxy ligand via a pericyclic mechanism. At this point the new carbonyl dissociates and gives the tricoordinated aluminium species 4. Finally, an alcohol from solution displaces the newly reduced carbonyl to regenerate the catalyst 1.



Each step in the cycle is reversible and the reaction is driven by the thermodynamic properties of the intermediates and the products. This means that given time the more thermodynamically stable product will be favored.

Chemoselectivity

One of the great draws of the Meerwein–Ponndorf–Verley reduction is its chemoselectivity. Aldehydes are reduced before ketones allowing for a measure of control over the reaction. If it is necessary to reduce one carbonyl in the presence of another, the common carbonyl protecting groups may be employed. Groups, such as alkenes and alkynes, that normally pose a problem for reduction by other means have no reactivity under these conditions.

Stereoselectivity

The aluminium based Meerwein–Ponndorf–Verley reduction can be performed on prochiral ketones leading to chiral alcohols. The three main ways to achieve the asymmetric reduction is by use of a chiral alcohol hydride source, use of an intramolecular MPV reduction, or use of a chiral ligand on the aluminium alkoxide.

One method of achieving the asymmetric MPV reduction is with the use of chiral hydride donating alcohols. The use of chiral alcohol (R)-(+)-sec-o-bromophen-ethyl alcohol gave 82%ee (percent enantiomeric excess) in the reduction of 2-chloroacetophenone.[7] This enantioselection is due to the sterics of the two phenol groups in the six membered transition state as shown in Figure 3. In Figure 3, 1 is favored over 2 due to the large steric effect in 2 from the two phenyl groups.

Relative Configuration

Relative configuration refers to the configuration of a molecule in relation to other atoms on the same molecule, in relation to other molecules, or in relation to another form of the same molecule.

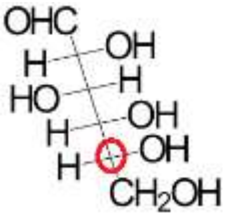
There are several different types of relative configurations possible, these include:

1- Alpha and beta

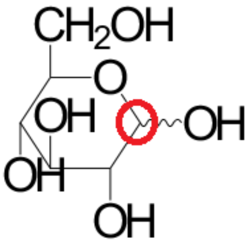
2-Cis and trans

1-Alpha and Beta Configuration

Alpha and beta are used specifically for describing the relative configuration of carbohydrate molecules.

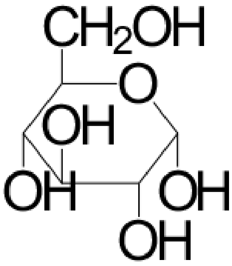


They are used to describe the relationship between the orientation of one of the OH molecules on the cyclic compound. When carbohydrates go from the linear form (shown in the Fischer projection) to the cyclic form,

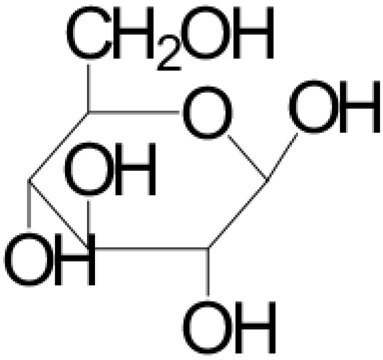


In the linear form, there is only one way that D-glucose can present itself. Now, notice carbon 5, circled in red. In this carbon, the OH group is on the right, which is the same as though it is pointing up or out of the page. Now, let's turn this glucose molecule into the cyclic form. Notice that what was carbon 5 in now carbon 1, circled again in red:

The OH group on C-1 doesn't actually show if it is up or down, it is simply shown with a squiggly line. This is because when this molecule is formed it allows for either the OH to end up pointing up or pointing down:



alpha



Beta

one of the carbon atoms (C-5 in the linear form and C-1 in the cyclic form) can change the orientation of the OH group during the transition. If the orientation stays on the same side in the cyclic form as in the linear form, this is an **alpha** relationship. If the orientation switches sides in the cyclic form from the linear form, this is a **beta** relationship.