In 1915, Paul Sabatier, a pioneer in hydrogenation chemistry who had shared the 1912 Nobel Prize with Victor Grignard, observed that single C-O bond benzyl ethers (ROCH$_2$Ph) in molecules were selectively cleaved, under standard hydrogenation conditions, into the alcohol (ROH) and toluene (CH$_3$Ph). The observation was quite general, and the reaction, called hydrogenolysis (to cleave with hydrogen), could be used reliably to reverse the formation of a benzyl ether and restore the hydroxyl group. As illustrated in Figure 1620, the two hydroxyl groups in glyceraldehyde can be transformed into their benzyl ethers. The aldehyde, as before, can be reduced, and the substitution to make a methyl ether can be performed. Because the hydrogenolysis reaction is selective for benzyl ethers, the hydrogenolysis reaction only releases the original two hydroxyl groups and leaves the methyl ether alone.

The mechanism for the hydrogenolysis reaction probably involves single-electron oxidation-reduction of the C-O sigma bond, and we are not concerned, here, with those details.

Unlike the esters, the benzyl ethers will not react with strong nucleophiles such as organometallic reagents. So, in place of the sodium borohydride reaction in Figure 1620, any nucleophilic carbonyl addition reaction of aldehydes could be carried out without worrying about competition from the hydroxyl groups, including the use of organometallic reagents (Figure 1621).

Figure 1621

A strategy to carry out organometallic reactions on glyceraldehyde using the reversible formation of benzyl ethers.
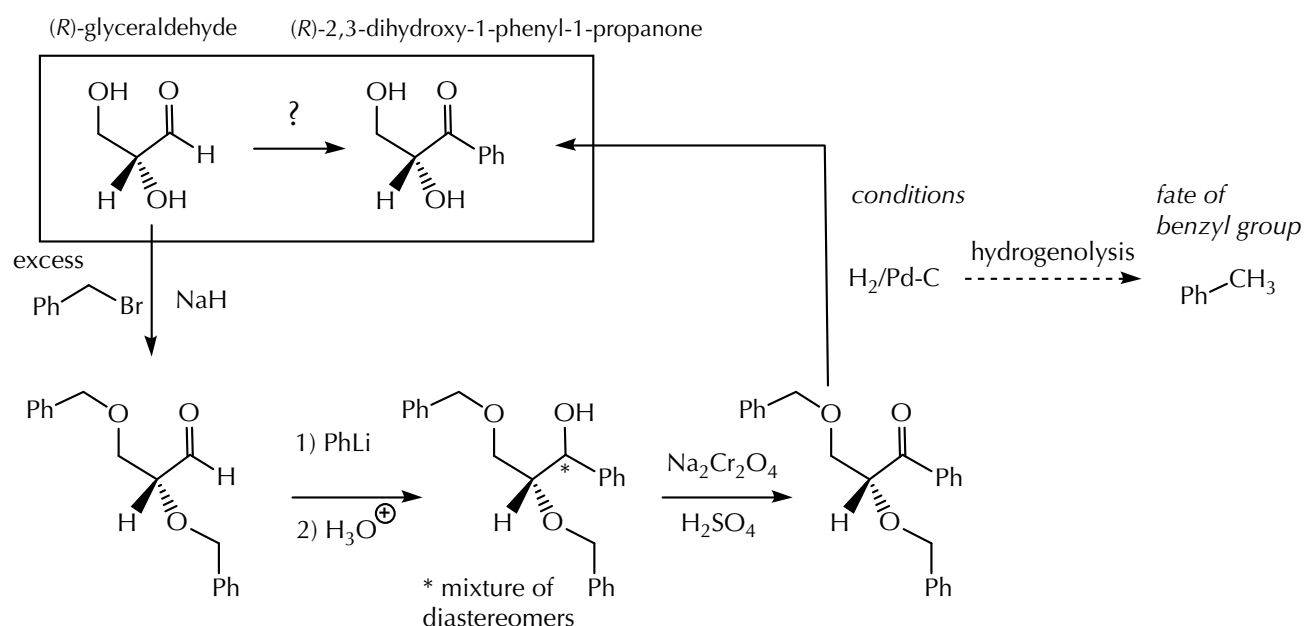
In this reaction sequence, a mixture of diastereomers forms in the carbonyl addition reaction with phenyl-lithium because of the existing stereocenter, but that mixture is inconsequential because the subsequent oxidation reaction returns the carbon to its original form of a carbonyl group.

Another nucleophilic reaction of hydroxyl groups is their use in forming acetals and ketals from aldehydes and ketones, respectively. The two hydroxyl groups in glyceraldehyde are perfectly positioned with respect to one another to react with carbonyl compounds and form five-membered ring acetals or ketals under catalytic acid conditions (Figure 1622). Acetone is a common choice for making these ketals as it is inexpensive, does not create a new stereocenter, and it's easy to remove from the reaction. Aldehydes (e.g., benzaldehyde) create new stereocenters and can result in mixtures of diastereomers.