Alcohols are very weak Brønsted acids with pKₐ values generally in the range of 15 - 20. Because the hydroxyl proton is the most electrophilic site, proton transfer is the most important reaction to consider with nucleophiles. There are small differences in the acidities of aliphatic alcohols in aqueous solution, which are due to differences in structure and, more importantly, solvation.

### General Assessment of Acidities

When considering alcohols as organic reagents, pKₐs are often used because they reflect reactivity in aqueous solution. In general, alcohols in aqueous solution are slightly less acidic than water. However, the differences among the pKₐs of the alcohols are not large. This is not surprising because all alcohols are oxy-acids (OH), and the differences in acidities are due to the effect of substituents in the 1-position removed from the acidic site. Moreover, the more highly substituted alcohols vary only in the structure two positions removed from the acidic site. The marginal effects of additional substituents at the carbon two positions removed from the acidic site are even evident in the gas-phase enthalpies of reaction for the reaction

\[ROH \rightarrow RO^- + H^+ \tag{1}\]

The pKₐs and gas-phase enthalpies of reaction for various alcohols, ROH, with various substituents (R) are shown in Table 1 below.

<table>
<thead>
<tr>
<th>R</th>
<th>Name</th>
<th>(pK_a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>water</td>
<td>14.0</td>
</tr>
<tr>
<td>CH₃</td>
<td>methanol</td>
<td>15.5</td>
</tr>
<tr>
<td>CH₂CH₂</td>
<td>ethanol</td>
<td>15.9</td>
</tr>
<tr>
<td>(CH₃)₂CH</td>
<td>propan-2-ol (isopropyl alcohol)</td>
<td>16.5</td>
</tr>
<tr>
<td>(CH₃)₃C</td>
<td>2-methylpropan-2-ol (t-butanol)</td>
<td>17.0</td>
</tr>
<tr>
<td>C₆H₅ (phenyl)</td>
<td>phenol</td>
<td>9.95</td>
</tr>
</tbody>
</table>

### Interpretation of the Relative Acidities of Alcohols

There are many sites on the internet with explanations of the relative ordering of alcohol acidities in aqueous solution. The general explanation is that the larger substituents are better electron donors, which destabilize the resulting alkoxide anions. Because hydrogen is least donating of the substituents, water is the strongest acid. Unfortunately, although this belief persists, it is incomplete because it does not account for the gas-phase results. The problem with the electron donation explanation is that it suggests that the order of acidity is due solely to the intrinsic electronic effects of the...
substituents. However, if that were the case, the electron donating effect should also be evident in the gas-phase data. However, the relative acidities in the gas phase are opposite to those in aqueous solution. Consequently, any interpretation of the acidities of alcohols must take the gas phase data into account.

The inversion of the acidities of alcohols between the gas phase and aqueous solution was pointed out by Brauman and Blair in 1968. They proposed that the ordering of acidities of alcohols in solution is predominantly due to the combination of a) polarizibility and b) solvation, and that the electron donating ability of the substituent does not play a significant role.

Polarizibility almost completely accounts for the trend in gas-phase acidities. As the size of the substituent increases, the acid becomes stronger due to the ability for the charge to be distributed over a larger volume, thereby reducing the charge density and, consequently, the Coulombic repulsion. Therefore, in the gas-phase, t-butanol is the most acidic alcohol, more acidic than isopropanol, followed by ethanol and methanol. In the gas phase, water is much less acidic than methanol, which is consistent with the difference in polarizibility between a proton and a methyl group. As before, the fact that water is less acidic than methanol in the gas phase is not consistent with the expected electronic donating capabilities of the two substituents. Given the absence of a solvent, the gas-phase properties reflect the intrinsic effects on the acidities.

In solution, however, the ions can be stabilized by solvation, and this is what leads to the inversion of acidity ordering. Brauman and Blair showed that smaller ions are better stabilized by solvation, which is consistent with the Born equation. Therefore, methanol is more acidic than t-butanol because the smaller methoxide ion has a shorter radius of solvation, leading to a larger solvation energy, which overcomes the stabilization that results from polarization of the charge. Because the solvation energy of hydroxide is even larger than that of methoxide, water is more acidic than methanol.

Note: Phenol

Discussions of acidities of alcohols usually include phenol in which the enhanced acidity is generally attributed to stabilization of the phenoxide ion by resonance delocalization. In this case, the gas-phase results agree with the solution trend that phenol is a much stronger acid than the aliphatic alcohols, and the difference is certainly due to electronic effects. However, this commonly encountered explanation is incomplete because it ignores the role that inductive effects have on acidities of oxy-acids. However, it is true that the acidity of phenol is much more a result of resonance stabilization than, for example, the acidities of carboxylic acids.

Practical Considerations

With $pK_a$ values in the 15.5 - 20.0 range, useful concentrations of alkoxides cannot be formed by proton transfer with hydroxide:

$$[\text{ROH} + \text{OH}^- \rightarrow \text{RO}^- + \text{H}_2\text{O}]$$

The equilibrium constant for the proton transfer reaction is on the order of $10^{-2}$-$10^{-6}$. Phenoxide can be formed almost completely by reaction with aqueous alkaline base because the value of the equilibrium constant is roughly $10^4$. The acidity of alcohols also indicates that it will react by proton transfer with any base more basic than hydroxide, which includes most organic bases, such as acetylide ions, cyanide, and vinyl/phenyl/alkyl anions. Therefore, alcohols
will protonate most organic nucleophiles and effectively destroy most organometallic reagents, including *Grignard* or *organolithium* reagents.

**Formation of alkoxide ions**

Alkoxide ions can be formed by deprotonating alcohols with an extremely strong base such as an amide ion, NH$_2^-$.

However, this method is rarely used. Alkoxides are more often formed by reaction of an alkali metal such as sodium with the pure alcohol:

\[
2\text{ROH} + 2\text{Na} \rightarrow 2\text{RO}^- + 2\text{Na}^+ + \text{H}_2
\tag{3}\]

**Conclusions**

Relative acidities of all acids depend on many factors, including intrinsic electronic factors such as electronegativity, inductive and resonance effects, and polarizibility, as well as extrinsic factors such as solvation. For aliphatic alcohols, the most important effects are polarizibility and solvation, not electronic donation, as is generally assumed. In systems where the intrinsic factors are large, their effects are manifested in the overall properties, regardless of the medium.

**References**

1. [http://research.chem.psu.edu/brpgrou...ompilation.pdf](http://research.chem.psu.edu/brpgrou...ompilation.pdf) with correction for pK$_a$ of water