

Acid-Base Chemistry of Sugars

Lewis acids are electron pair acceptors while Lewis bases are electron pair donors. Last time we saw that sugar molecules have a carbonyl carbon that acts as a Lewis acid site and many hydroxy groups that can function as Lewis bases.

Bronsted acids are proton donors and Bronsted bases are proton acceptors. The hydroxy groups on sugars can both accept and donate protons.

Acid-base chemistry plays an important role in reactions of sugars in aqueous solution, including in biological media. Acid-base reactions of sugars are examples of chemical equilibria.

Outline

- [Acids and Bases in Water](#)
- [Acid-Base Properties of Sugars](#)
- [Reactions with Strong Acids and Bases](#)
- [Homework](#)



Acids and Bases in Water

Self-ionization of Water

Liquid water is in equilibrium with solvated hydroxide and solvated protons. We typically use a value related to the equilibrium constant to define the concentration of these solvated ions in water. The **water dissociation constant**, K_w , is 1×10^{-14} .



$$K_w = K_{\text{eq}} [\text{H}_2\text{O}] = [\text{HO}^-][\text{H}^+] = 1 \times 10^{-14}$$

pH and **pOH** are important values for acidic and basic solutions. These are the log base 10 of the hydrogen ion concentration or of the hydroxide ion concentration, respectively.

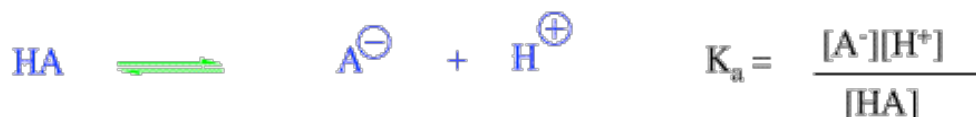
$$\text{pH} = -\log[\text{H}^+]$$

$$\text{pOH} = -\log[\text{HO}^-]$$

$$14 = \text{pH} + \text{pOH}$$

LeChateliers principle tells us that the addition of one of the products to a system at equilibrium will shift the equilibrium towards reactants. Acids and bases dissolve in water and, because they increase the concentration of one of the products of water self-ionization, either protons or hydroxide ions, they suppress water dissociation.

For any acid, K_a is the equilibrium constant for the acid dissociation reaction in water. See the [tables page](#) for a list of K_a values at room temperature. Note that both A^- and H^+ are surrounded and stabilized by water molecules. We could also write these as $[A(H_2O)_x]^-$, $[H(H_2O)_x]^+$ or $A_{(aq)}^-$, $H_{(aq)}^+$.

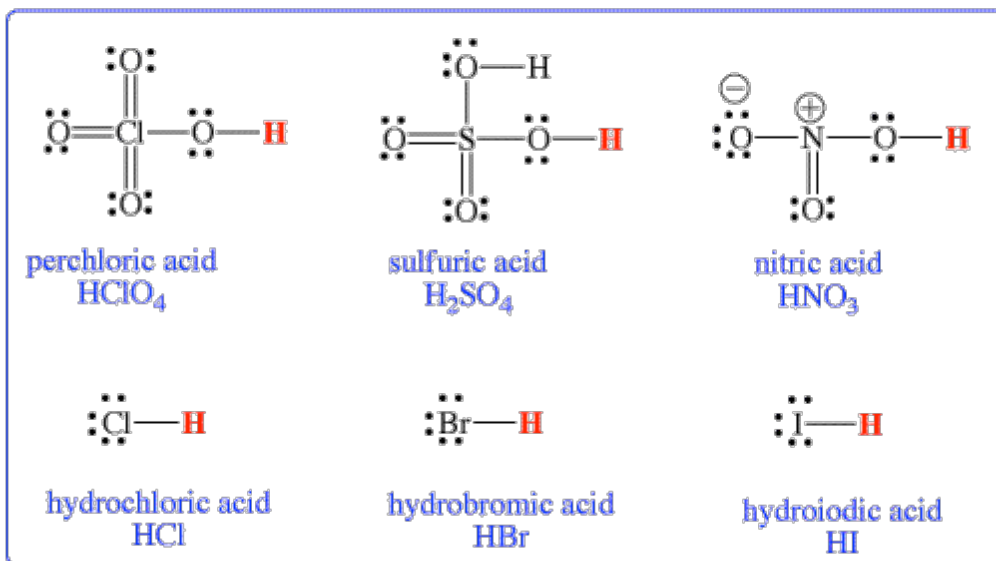


pH and pOH are frequently used to describe solutions of acids and bases in water. In pure water, the concentration of solvated protons equals the concentration of solvated hydroxide anions and the pH is 7. Acidic solutions have a lower pH while basic solutions have a higher one.

$$\begin{aligned} \text{pH} &= -\log[H^+] & \text{pOH} &= -\log[OH^-] \\ [H^+][OH^-] &= 10^{-14} & \text{pH} + \text{pOH} &= 14 \end{aligned}$$

Strong Acids

Strong acids dissociate completely in aqueous solution and have negative values for K_a . We can assume that the $[H^+]$ in a solution of a strong acid is equal to the initial concentration of the acid. Strong acids are listed below.



Weak Acids

Weak acids are only partially dissociated in aqueous solution. The K_a values describe the equilibrium and the $\text{p}K_a = -\log(K_a)$. Some of the weak acids are in the table below.

Acid	Reaction	pK _a
hydrofluoric acid	$\text{HF} \rightleftharpoons \text{H}^+ + \text{F}^-$	3.17
carbonic acid	$\text{H}_2\text{CO}_3 \rightleftharpoons \text{H}^+ + \text{HCO}_3^-$	6.37
bicarbonate	$\text{HCO}_3^- \rightleftharpoons \text{H}^+ + \text{CO}_3^{2-}$	10.25
bisulfate	$\text{HSO}_4^- \rightleftharpoons \text{H}^+ + \text{SO}_4^{2-}$	1.99
ammonium	$\text{NH}_4^+ \rightleftharpoons \text{H}^+ + \text{NH}_3$	9.24
hydrogen sulfide	$\text{H}_2\text{S} \rightleftharpoons \text{H}^+ + \text{HS}^-$	7.0
water	$\text{H}_2\text{O} \rightleftharpoons \text{H}^+ + \text{HO}^-$	15.74
ammonia	$\text{NH}_3 \rightleftharpoons \text{H}^+ + \text{NH}_2^-$	38

Strong Bases

Strong hydroxide bases are completely dissociated in aqueous solution. Other strong bases react completely with water. Strong bases include NaOH, LiOH, Ca(OH)₂, NaNH₂.



$$K_{\text{eq}} = \frac{[\text{NH}_3][\text{HO}^-]}{[\text{NH}_2^-][\text{H}_2\text{O}]} \quad K_{\text{b}} = \frac{[\text{NH}_3][\text{HO}^-]}{[\text{NH}_2^-]}$$

$$\left. \begin{array}{l} K_{\text{a}} = \frac{[\text{NH}_2^-][\text{H}^+]}{[\text{NH}_3]} \\ K_{\text{w}} = [\text{H}^+][\text{HO}^-] \end{array} \right\} \longrightarrow K_{\text{b}} = K_{\text{w}}/K_{\text{a}}$$

Weak Bases

Weak bases are in equilibrium with water. The K_b values describe the equilibrium and the pK_b = -log(K_b).



$$K_b = K_w/K_a = \frac{[BH^+][HO^-]}{[B]}$$

$$pK_b = pK_w - pK_a$$

Some weak bases are in the table below.

Base	Reaction	pK _b
NH ₃	NH ₃ + H ₂ O ⇌ NH ₄ ⁺ + HO ⁻	4.76
HS ⁻	HS ⁻ + H ₂ O ⇌ H ₂ S + HO ⁻	7
CO ₃ ⁻²	CO ₃ ⁻² + H ₂ O ⇌ HCO ₃ ⁻ + HO ⁻	3.75
SO ₄ ⁻²	SO ₄ ⁻² + H ₂ O ⇌ HSO ₃ ⁻² + HO ⁻	12.01

Buffers

A solution containing a weak acid and its conjugate base resists changes in pH if small amounts of acid or base are added. A solution that contains equal concentrations of both the weak acid and the conjugate base has a pH equal to the pK_a of the acid. For example, the pH of a solution that is 0.1 M in HSO₄⁻² and 0.1 M in SO₄⁻² will be about 2.

$$K_a = 10^{-2} = \frac{[H^+][SO_4^{-4}]}{[HSO_4^-]} = \frac{(x)(0.1)}{(0.1)} = x$$

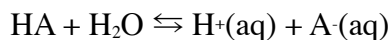
$$pH = -\log(10^{-2}) = 2$$

Acid-Base Properties of Sugars

Water as an Acid

Water, of course, is both an acid and a base. It is in equilibrium with solvated protons (acid) and solvated hydroxide (base). Water is deprotonated by strong bases and protonated by strong acids.

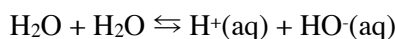
The water dissociation equilibrium is different from the acid dissociation equilibrium of water and they have different constants. In general, for the dissociation of an acid HA:



$$K_{\text{eq}} = [\text{H}^+(\text{aq})][\text{A}^-(\text{aq})]/[\text{HA}][\text{H}_2\text{O}]$$

$$K_{\text{a}} = K_{\text{eq}} \times [\text{H}_2\text{O}] = [\text{H}^+(\text{aq})][\text{A}^-(\text{aq})]/[\text{HA}]$$

For the acid dissociation of water as an acid:



$$K_{\text{eq}} = [\text{H}^+(\text{aq})][\text{HO}^-(\text{aq})]/[\text{H}_2\text{O}][\text{H}_2\text{O}]$$

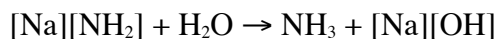
$$K_{\text{w}} = 10^{-14} = [\text{H}^+(\text{aq})][\text{HO}^-(\text{aq})]$$

$$K_{\text{a}} = K_{\text{w}}/[\text{H}_2\text{O}]$$

Water density = 1 g/mL = 1000 g/L or 55.56 mol/L

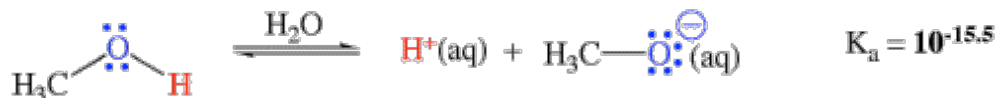
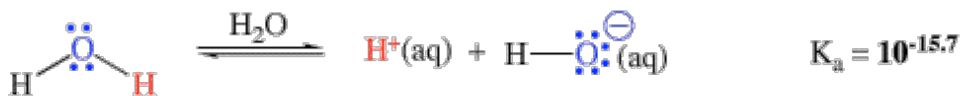
$$K_{\text{a}} = 10^{-14} / 101.74 = 10^{-15.74}$$

Very strong bases (stronger than HO⁻) react completely with the weak acid water.



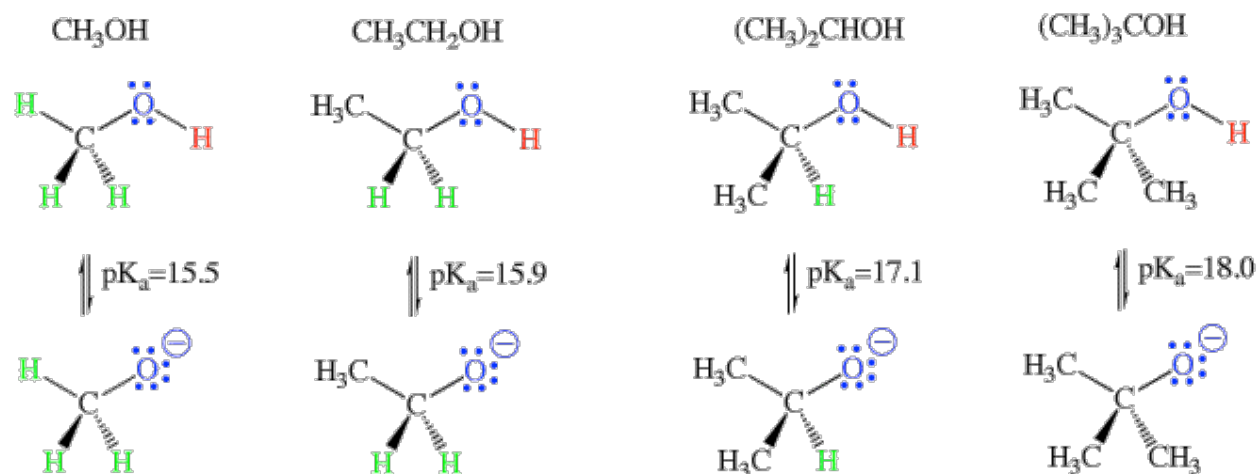
Alcohols as Acids

Water and alcohols are similar as Bronsted acids and they also have similar acid dissociation constants.



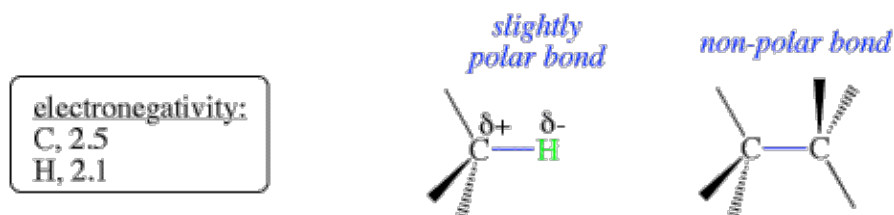
The conjugate base of an alcohol is called an alkoxide. Above we see the dissociation of methanol to a solvated proton and the conjugate base methoxide.

The K_a of an alcohol varies with the nature of the alcohol. You can see below that the extent of acid dissociation decreases (pK_a increases) as methyl groups replace hydrogen atoms on methanol. *Why is this?*



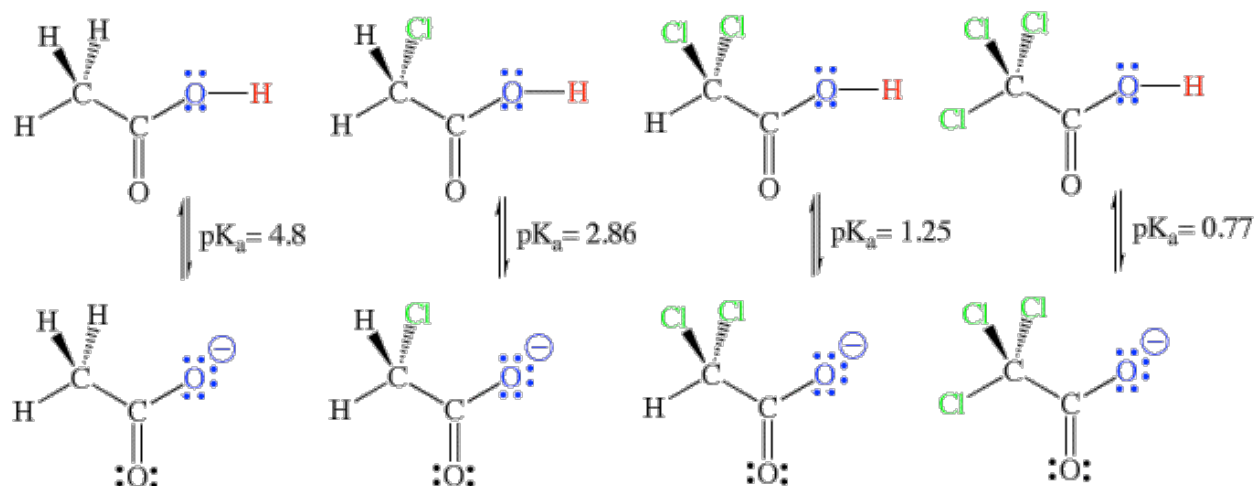
What makes an acid stronger?

The hydrogen is a little less electronegative than the carbon so a C-H bond is slightly polarized with more electron density on carbon. Excess electron density on a carbon adjacent to a negatively charged oxygen atom (in the alkoxide) destabilizes the conjugate base and makes the acid a little weaker.

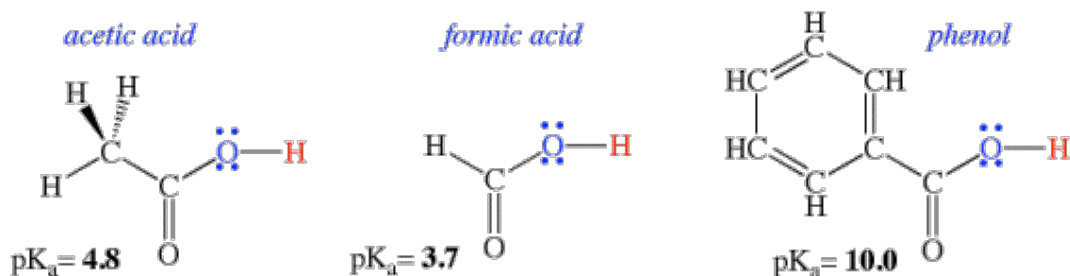


Any factor that stabilizes the conjugate base of an acid makes the acid stronger. Anything that destabilizes the conjugate base makes an acid weaker.

We can see a much bigger effect with substituted carboxylic acids. Electron-withdrawing groups stabilize the conjugate base while electron-donating groups destabilize the conjugate base.

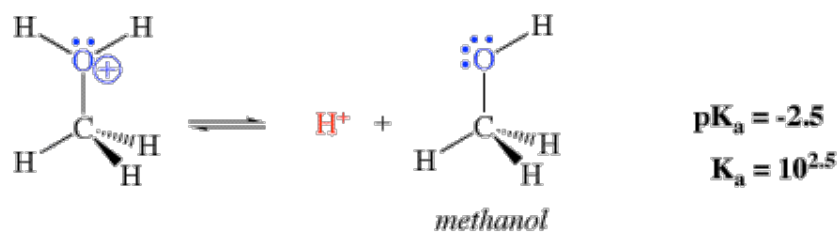
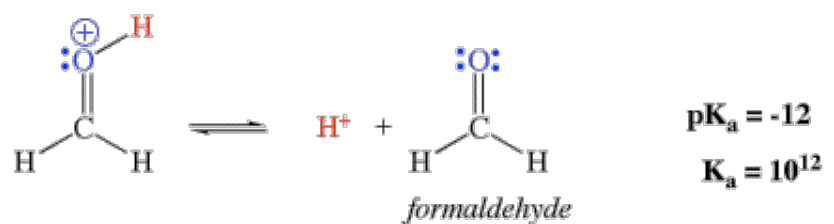


Can you explain the differences in the acidity of formic acid, acetic acid and phenol?



Protonated Aldehyde

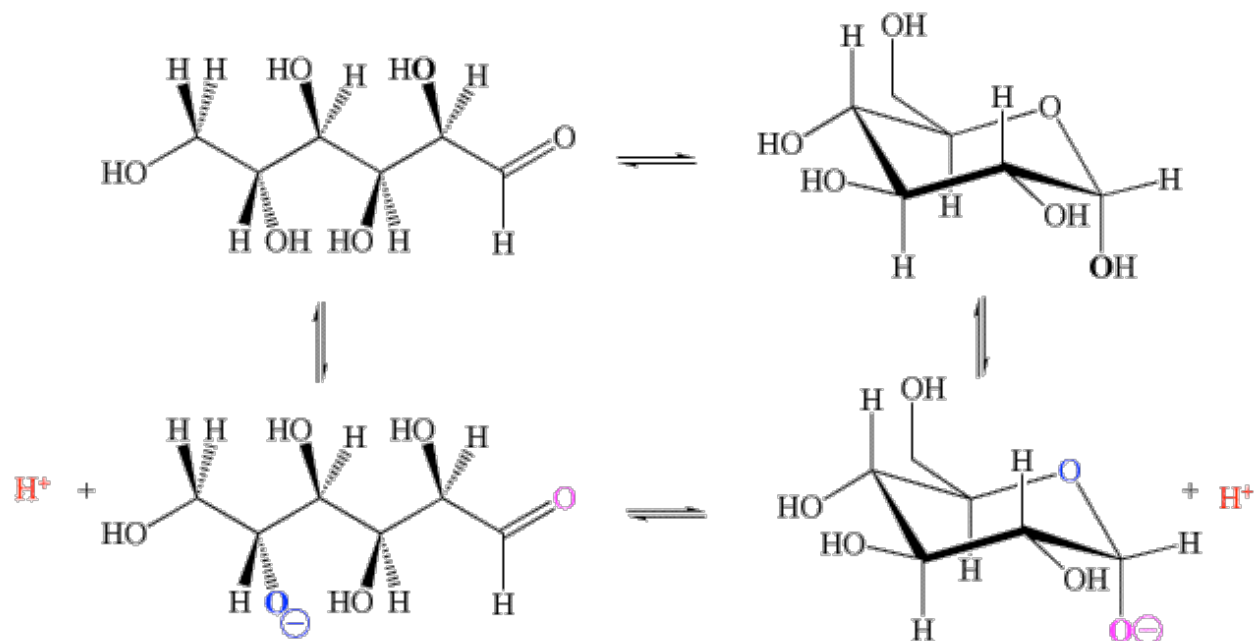
Water, alcohols, and aldehydes have oxygen atoms with non-bonding electron pairs. These are Bronsted bases in that they can accept a proton. Protonated water, protonated alcohols, and protonated aldehydes are all very strong acids though.



Acidity of Glucose

Glucose is more acidic than simple alcohols with a pK_a of about 12 ($K_a = 10^{-12}$). Compare this to methanol with a pK_a of 15.5 ($K_a = 10^{-15.5}$). The electronegative oxygen atoms in the molecule pull electron density away from the carbon atom bearing the negatively charged oxygen in the conjugate base, stabilizing it.

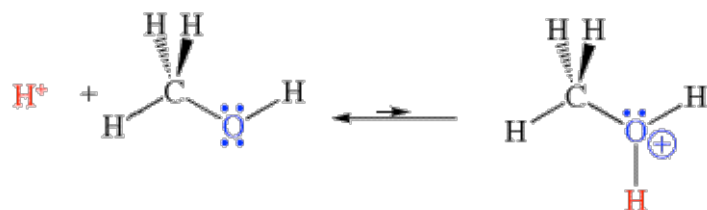
Glucose is a polyprotic acid with 5 OH groups. One of the protonation/deprotonation equilibria for linear glucose and one of the 6-membered ring isomers is shown here.



Deprotonation of an alcohol group in glucose can facilitate the cyclization reaction because the conjugate base (alkoxide) is a much stronger nucleophile. It more rapidly adds to the electrophilic aldehyde carbon.

Reaction of Glucose with Acids

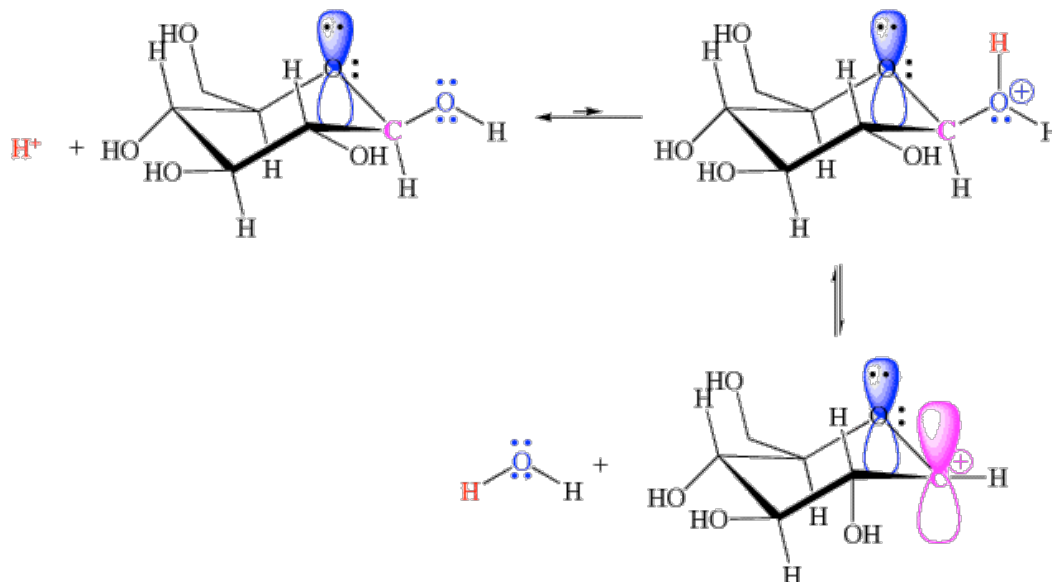
Alcohols are very weak bases so their conjugate acids are strong.



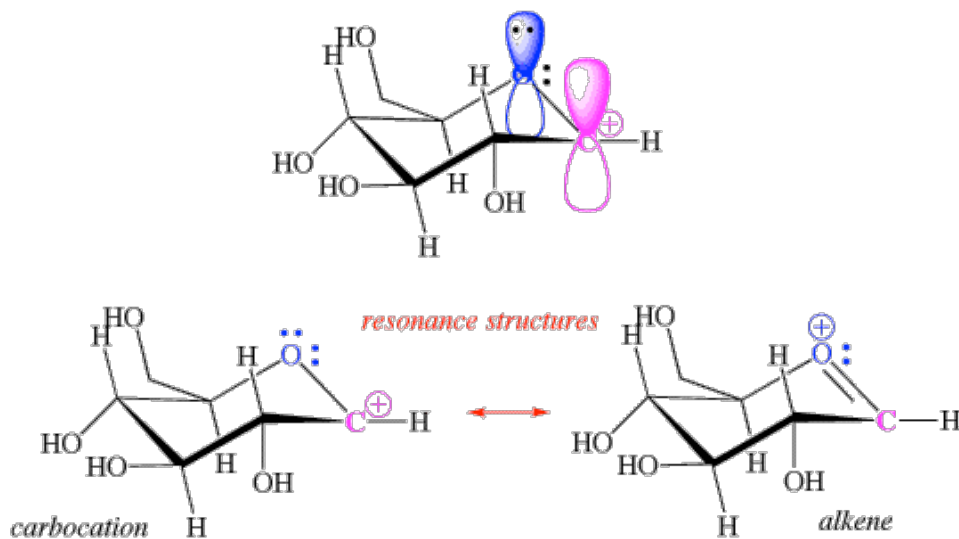
Each of the OH groups on glucose could be reversibly protonated by strong acids just like the OH group in the methanol molecule above.

For the cyclic isomers of glucose, one hydroxy group is unique. This is the one derived from nucleophilic attack on the aldehyde functional group. The carbon bearing that OH group is also bonded to another oxygen atom.

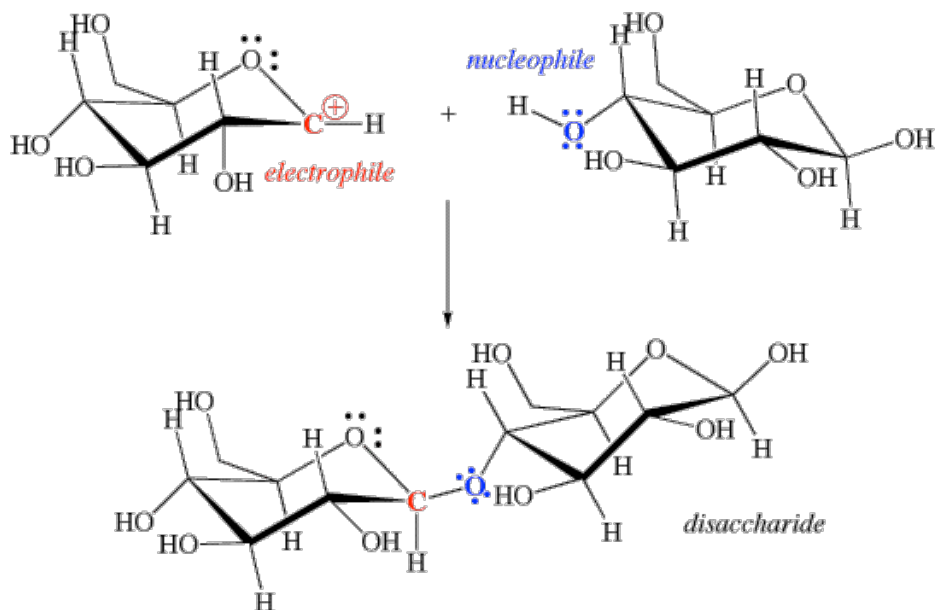
When that OH group is protonated, the bond between that oxygen and the ring carbon can break to form water. The ring carbon then has only three bonds and a positive charge. VSEPR tells us that the carbon will have a trigonal planar geometry with an empty p orbital perpendicular to the plane. The adjacent ring oxygen atom has two non-bonding electron pairs. One of these is in an orbital that lines up with carbon's empty p orbital.



The filled ring oxygen orbital and the empty carbon p orbital overlap to form a partial pi bond. This stabilized the carbocation (positively charged carbon atom).



The positively charged carbon is a very electrophilic. Nucleophiles, such as water or an alcohol can add to carbon. When one of the oxygen atoms of another sugar molecule adds to the carbocation and a proton is lost, a disaccharide is formed.



Because the carbocation is planar, two structural isomers could be formed when a particular nucleophile adds. The nucleophile could add above the plane (as shown above) or below the plane.