

## Tautomerism

### Introduction

Isomerism describes different molecules containing the same number of the same kind of atoms where the spatial arrangement of those atoms is different. Such molecules have the same molecular formula and are called isomers. Due to the different arrangements of atoms, isomers will usually have different physical and chemical properties. There are two main groups of isomerism. Constitutional or structural isomers are defined as molecules exhibiting different connectivity and typically include different atom-to-atom bonds. **Table 1** provides examples of constitutional or structural isomerism found in chemistry. Tautomerism is an example of constitutional isomerism, where the isomers differ in the position of hydrogen atoms and electrons.

**Table 1** Constitutional Isomerism

Type	Examples
Chain (Skeletal)	
Positional	
Functional	
Ring-Chain	
Tautomerism	

Stereoisomers describe molecules with the same connectivity, but the atoms are orientated differently in space. **Table 2** describes examples of different examples of stereoisomers.

**Table 2** Stereoisomerism

Type	Examples
E-Z	
cis- & trans-	
Optical	
Conformational	

### Tautomers

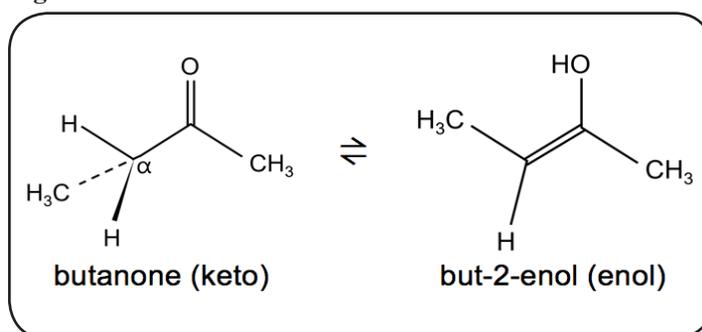
Tautomers are constitutional isomers that exist together in equilibrium. These isomers readily interchange through the migration of an atom or group within the molecule. Tautomerism is usually associated with pairs of polar molecules and ions containing weakly acidic functional groups. The proton is typically located in one of two positions leading to the exchange of a hydrogen atom with a pi-bond. Carbon-carbon double bonds and carbon-oxygen double bonds consist of one sigma-bond and one pi-bond.

#### Key Point:

A pi-bond ( $\pi$ -bond) is a covalent chemical bond formed when two lobes of an electron orbital overlap two lobes of an electron orbital of another atom.

An example is keto-enol tautomerism. A chemical equilibrium is established between an aldehyde or ketone and an enol. An enol is an organic molecule containing a hydroxyl group attached to one end of a carbon-carbon double bond. The enol and keto forms are tautomers. **Figure 1** shows the example of butanone (keto form) and but-2-enol (enol form).

**Figure 1**

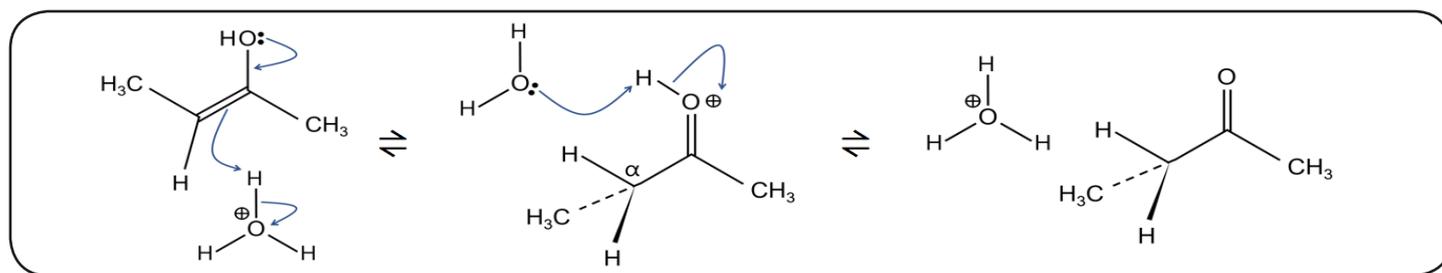


**Note:** E/Z isomerism around the carbon-carbon double bond will occur, but for simplicity only one form is presented here.

### Keto-enol Tautomerism

The keto form is a ketone or an aldehyde. These types of compound contain a carbonyl group that typically forms an equilibrium with the enol tautomer. In most instances the keto form is prominent. **Figure 2** describes the interconversion of the two forms involving the movement of an alpha hydrogen and the shifting of bonding electrons. For the mechanism to proceed, the alpha carbon (i.e. the carbon atom closest to the functional group) must contain at least one hydrogen atom. This is described as the alpha hydrogen.

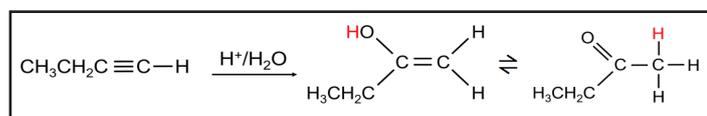
Figure 2



Note that the addition of the proton across the carbon-carbon double bond follows Markovnikov's rule (i.e. the proton is added to the carbon with the most hydrogens). With simple aldehydes and ketones, such as propanone, the keto form is much more stable than the enol form and the equilibrium heavily favours the keto form. That is:

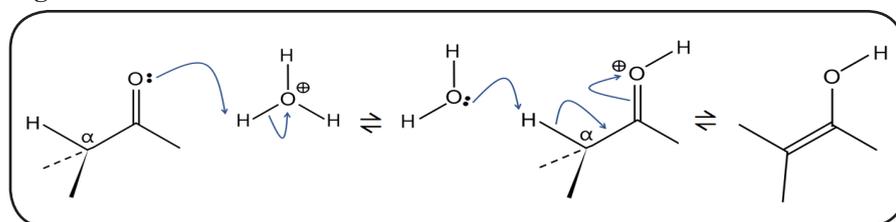
$$K_c = \frac{[\text{keto}]}{[\text{enol}]} \sim 10^5$$

This is because the combination of C=O double bond and C-H single bond has greater stability than the combination of C=C double bond and O-H single bond. In chemical reactions producing enols, for example during the hydration of alkynes, enols formed are spontaneously converted to the keto tautomer. That is, instead of the enol product, an aldehyde or ketone is formed. In the example reaction, the relocated hydrogen atom is shown in red:



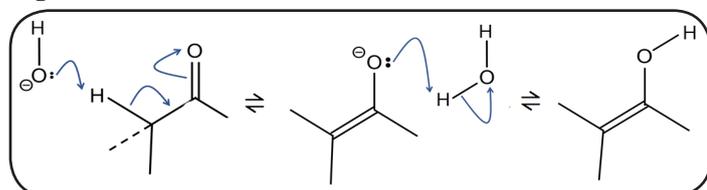
Enolisation is promoted through acid or base catalysis. Figure 3 illustrates the basic mechanism of the acid-catalysed interconversion. Note the related movement of the alpha hydrogen and the shift in bonding electrons. The mechanism involves protonation, leading to the formation of a delocalised cation, which is followed by deprotonation at a different position on the cation.

Figure 3



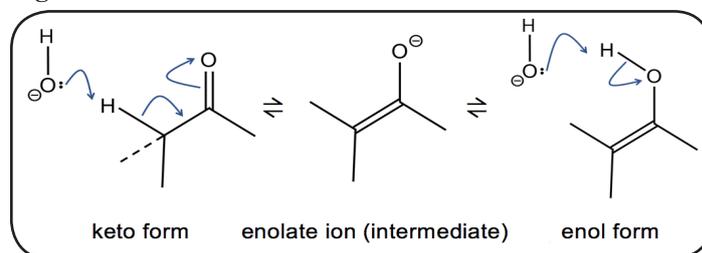
During the base-catalysed reaction, described in Figure 4, the mechanism requires deprotonation, forming a delocalised anion, which is followed by protonation at a different position of the anion.

Figure 4



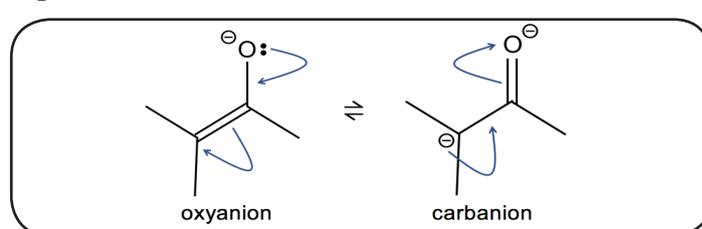
**Note:** The intermediate deprotonated enolate ion formed during the base-catalysed reaction. This is a strong nucleophile and plays an important part in carbonyl chemistry (see Figure 5).

Figure 5



The enolate ion is a delocalised system with negative charge across both carbon and oxygen atoms. The enolate ion can therefore act as an oxyanion reacting through the oxygen, or, as a carbanion reacting through the carbon (see Figure 6).

Figure 6

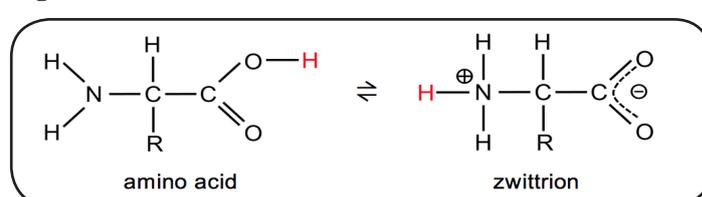


### Prototropic Tautomerism

Amino acids and their zwitterions are an important example of tautomerism, relevant to the behaviour of amino acids. This involves the migration of a proton between the amino- and carboxyl- functional groups to produce a zwitterion (see Figure 7). The relocation of a

proton in a molecule is called prototropic tautomerism. The empirical formula and total charge of each tautomer is the same.

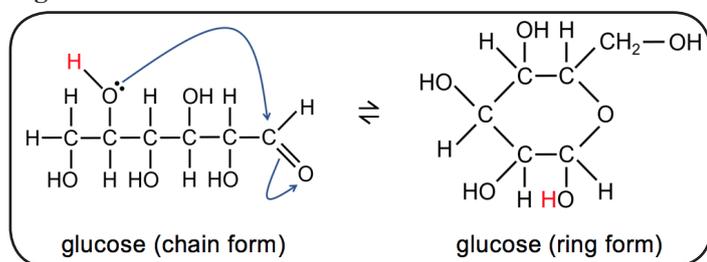
Figure 7



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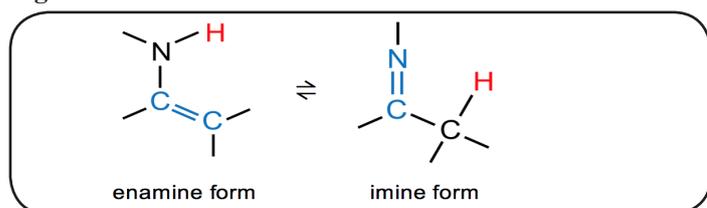
The movement of a proton can also lead to the formation of ring-chain tautomers. These include the open chain and cyclic structures found in some sugars. The ring-chain tautomers of glucose are an example of this type of isomerism (see **Figure 8**). The relocated hydrogen atom is shown in red:

**Figure 8**



Tautomerism also occurs in nitrogen containing organic molecules. These include the enamine-imine tautomeric pairs (see **Figure 9**). In this instant, the proton rearrangement occurs between two nitrogen atoms. The movement of the proton is matched by the switching of bonding electrons and the resulting double-bond. The relocated hydrogen atom is shown in red.

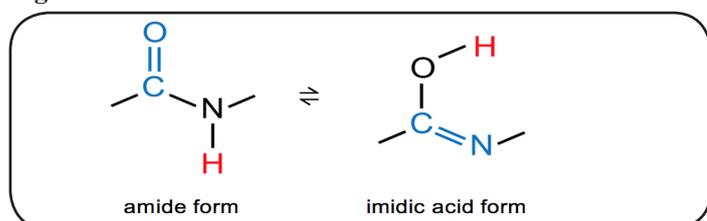
**Figure 9**



Typically, the imine form, which contains a carbon-nitrogen double-bond, is more stable than the enamine form, containing a carbon-carbon double-bond. Therefore, the equilibrium favours the imine form.

Amides undergo similar proton rearrangement to form its tautomeric form, imidic acid. In this case, the movement of the pi-bond is analogous to keto-enol tautomerisation. The proton rearrangement across the amide link is matched by bonding pi-electrons shifting from the C=O double bond in the amide to the C=N double bond in the imidic acid form (see **Figure 10**).

**Figure 10**



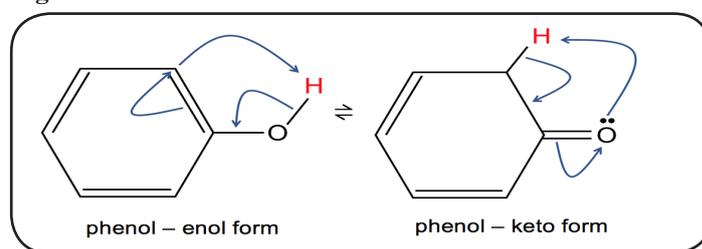
The combination of C=O double-bond and N-H single-bond on the amide is more stable than the C=N double-bond and O-H single bond in the imidic acid form. The equilibrium therefore favours the amide tautomer.

### Phenol

**Figure 11** illustrates the tautomers of phenol with a simplified mechanism illustrating the relative movement of the proton and pi-bond. The aromaticity in the enol means it has greater stability than

the non-aromatic keto form. This results in the equilibrium greatly favouring the enol form, with only a tiny fraction of phenol existing in the keto form. The relocated hydrogen atom is shown in red.

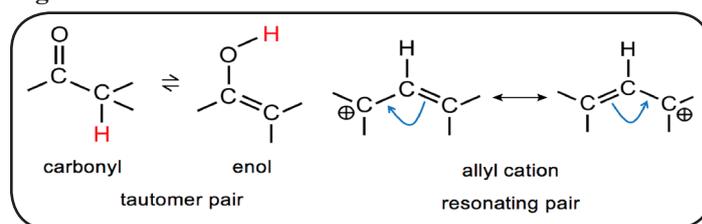
**Figure 11**



### Tautomerisation and Resonance

Tautomerisation differs to resonance in that tautomers are chemically distinct species that may be separated, while resonating forms differ only by the distribution of electrons within the molecules. Resonating forms are imaginary forms and cannot be separated. Tautomers are distinct compounds with different structures in dynamic equilibrium. Resonating structures have the same functional groups and are not in dynamic equilibrium. **Figure 12** contrasts a pair of tautomers with a pair of resonating structures. Note the use of a double arrow,  $\leftrightarrow$ , to represent the resonating pair.

**Figure 12**



### Questions

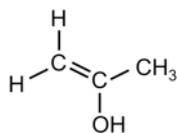
- Describe the key features that distinguish tautomerisation from other types of constitutional or structural isomerisation.
- Which of the following statements best describes tautomerisation?
  - Any two constitutional isomers.
  - The movement of electrons between two atoms within a molecule
  - The rapid equilibrium between two constitutional isomers when a bond moves.
  - The combination of two molecules through the movement of electrons
- Draw the structures for all the possible enol forms from the tautomerism of the following aldehydes/ketones:
  - propanone,  $C_3H_6O$
  - ethanal,  $C_2H_4O$
  - 3-pentanone,  $C_5H_{10}O$
  - cyclohexanone,  $C_6H_{10}O$
- Which of the following does not show tautomerism?
  - 1-phenylethan-1-one,  $C_6H_5COCH_3$
  - propanal,  $CH_3CH_2CHO$
  - 2,2-dimethyl-1-phenylpropan-1-one,  $C_6H_5COC(CH_3)_3$

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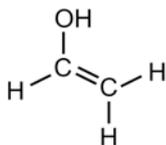
### Answers

- 1) Tautomers readily interconvert forming a dynamic equilibrium. Typically, this involves the relocation of a proton and pi-bond.  
 2) (c) The rapid equilibrium between two constitutional isomers when a bond moves.

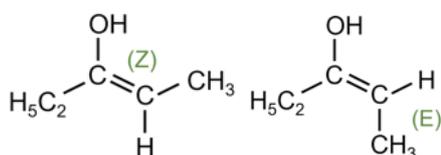
3) a)



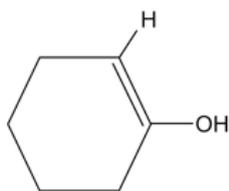
b)



c)



d)



- e) Tautomerisation requires the availability of an  $\alpha$ -hydrogen atom, which is not present in 2,2-dimethyl-1-phenylpropan-1-one,  $C_6H_5COC(CH_3)_3$