Organic Chemistry-2

Semester-2, CBCS

Course: CEMA CC-2-3-TH

Course taught by: Kaushik Basu, Department of Chemistry, SPCMC, Kolkata

email: chiralkaushik@gmail.com

Recommended texts:

Tautomerism in Organic Chemistry

Keto-enol tautomerism: Exclusive keto forms:

In our discussions regarding the keto-enol tautomerism we have seen so far that the keto form is in general much more stable than its enol counterpart, and consequently dominates the tautomeric equilibrium.

Barring a few special cases, where certain features (such as H-bonding, extended conjugation, steric crowding etc.) stabilise the enol forms, most carbonyl compounds exist almost exclusively in the keto form, with very small percentages of enol content.

Some keto compounds, such as the ones cited below, in fact exist entirely in the keto form:

Why? In both cases the respective enol forms are unstable for different reasons:

- C=C at bridgehead - extremely unstable.

v. strained - three sp2 carbons in a four-membered ring

antiaromatic

The other end of the spectrum: Almost exclusive enol forms: Phenols

There are also examples of compounds where the enol is vastly more stable and there is almost no keto form to be found for those. The aromatic enols, more commonly known as phenols, represent such a class of compounds.

The name phenol itself is evocative of high enol content for the compound. Outlined above is the tautomeric equilibrium for the simplest representative of that class, phenol which exists almost entirely in the enol form.
Tautomerism in Organic Chemistry

Phenol-keto tautomerism:

The aromatic enols, more commonly known as phenols, represent such a class of compounds. The name phenol itself is evocative of high enol content for the compound. Here is the tautomeric equilibrium for the simplest representative of that class, along with the pKa values of the enol and the two keto tautomers:

Recall that,

$$K_E = \frac{K_a^{\text{enol}}}{K_a^{\text{keto}}}$$

i.e. $$pK_E = pK_a^{\text{keto}} - pK_a^{\text{enol}}$$

These enolisation constant and acid ionization constants indicate that:

i) the enolic form totally dominates the tautomeric equilibrium,
ii) there are two possible keto forms, keto-1 by shifting the proton from oxygen to one of the ortho-carbons, and keto-2, by shifting the proton to the para-carbon, the former is less stable than the latter,
iii) both the keto forms are extremely strong carbon acids.

Let us now try to explain why the enolic form is so dominant here. The energy factors that favour the keto and enols forms are listed below:

i) the keto forms enjoy almost 15 kcal/mol stabilisation in terms of bond energies,
ii) for keto-1, there is extended conjugation providing additional 5 kcal/mol stability, while for keto-2 there is conjugation between C=O and C=C, but it is a cross-conjugated system as well.
iii) the enol form is aromatic and enjoys large stabilisation energy of 36 kcal/mol. This energy gain more than offsets the energy penalty incurred by converting the enol to either of the two keto forms, both of which are, non-aromatic. By our simple (and inexact) calculations, the phenol form is more stable than either of the the keto forms by at least 16 kcal/mol.

This is also why the two keto forms are so acidic; their conjugate base, the phenoxide ion, is aromatic. So proton departure is associated with a large decrease in the free energy.
Tautomerism in Organic Chemistry

Phenol-keto tautomerism:

Phenols exist in (almost) completely enolic form:

Keto-1 has extended conjugation while keto-2 is a cross-conjugated system, yet, contrary to your expectation based upon this argument, keto-2 is more stable.

At this stage it would be difficult for you to fully understand why this is so. But note the following points:

- i) the \(s\)-trans form of the 1,3-butadiene (this is a system that you know) is more stable than the \(s\)-cis form, for obvious reasons:

\[
\begin{align*}
\text{s-cis} & \quad \leftrightarrow \quad \text{s-trans}
\end{align*}
\]

- ii) \(o\)-benzoquinone (this is a system you don’t know, yet) is less stable than \(p\)-benzoquinone:

\[
\begin{align*}
\text{o-benzoquinone} & \quad \leftrightarrow \quad \text{p-benzoquinone}
\end{align*}
\]

Because of the greater dipolar repulsion present in the former structure.

Phenols exist in (almost) completely enolic form: Reason for the dominance of the enolic form is aromatic stabilization that overcompensates the keto forms favourable bond energy.

Form the discussion so far we understand that to increase the population of the keto form in phenol-keto tautomerism of phenols there has to be present additional factors which in one way or another would reduce the difference between enolization and aromatic \(\pi\)-conjugation energies.

These factors are:

(i) an increase in the number of hydroxy groups leads to equalization of the aromatic conjugation energy to the total enolization energy of several carbonyl groups; in other words, as we go on piling more hydroxyl groups onto the aromatic ring, and at appropriate positions so that all those may simultaneously move over to the keto forms, the bond energy advantage of the keto form may compete with the aromatic stability of the enol,

(ii) one or more aryl rings annulated with the phenolic cycle decrease the total aromatic conjugation energy; because as we go on fusing aromatic rings together, there is a diminishing return in terms of the gain in aromatic stabilization for each ring that is fused into its precursor; this will encourage the keto form because its difference of stability with the enol form has decreased in the fused system,

(iii) bulky groups in the ortho-positions of phenol create a steric hindrance which stabilizes a quinonoid structure;

(iv) electron-withdrawing substituents in the ortho- and para-positions of phenol give rise to a redistribution of the electron density in the system and result in lowering the aromatization energy; besides, the nature of the keto-enol tautomerism in this situation can change since the proton migrates to the electronegative substituent but not to the aromatic ring.
Tautomerism in Organic Chemistry

Phenol-keto tautomerism:

Factors that contribute to increase the keto content in the phenol-keto tautomerism:

(i) Polyhydroxy monocyclic phenols: The introduction of additional hydroxy groups into the phenolic ring assists the development of a ketonic character because the energy released by formation of multiple keto groups compensates for the loss of resonance stabilization. There are many examples. We will consider a few.

Case of resorcinol: the two hydroxyls are meta to each other, and both can go over to the keto structure without interfering one another,

\[
\begin{align*}
\text{OH} & \quad \leftrightarrow \quad \text{OH} \\
\text{O} & \quad \text{H} \\
\text{H} & \quad \text{O} \\
\text{H} & \quad \text{O} \\
\text{H} & \quad \text{O}
\end{align*}
\]

Two keto groups are, surely, better than one? Yes, indeed; resorcinol shows characteristics of both enol (aromatic) and keto forms, as evident from the following scheme:

\[
\begin{align*}
\text{OH} & \quad \leftrightarrow \quad \text{OH} \\
\text{O} & \quad \text{H} \\
\text{H} & \quad \text{O} \\
\text{H} & \quad \text{O} \\
\text{H} & \quad \text{O}
\end{align*}
\]

aromatic electrophilic substitution 
\[
\begin{align*}
\text{HNO}_3, \text{H}_2\text{SO}_4 & \quad \rightarrow \quad \text{H}_2, \text{Ni}, \text{NaOH} & \quad \text{under pressure, then acid work-up} \\
& \quad \text{chemoselective reduction} \\
\text{O}_2\text{N} & \quad \text{OH} \\
\text{OH} & \quad \text{NO}_2
\end{align*}
\]

A simple (but inexact) bond energy calculation predicts that the triketone form would be more abundant for phloroglucinol but experimental data tells us otherwise, highlighting the limitations of our calculation methods. More refined computations indicate that the enolic form is by far more stable than the keto form, but, as expected, the latter is more abundant in the phloroglucinol system than is the keto form of phenol (i.e. keto form-1 or 2) in the phenol system.
Tautomerism in Organic Chemistry

Phenol-keto tautomerism:

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(i) Polyhydroxy monocyclic phenols: The introduction of additional hydroxy groups into the phenolic ring assists the development of a ketonic character because the energy released by formation of multiple keto groups compensates for the loss of resonance stabilization. There are many examples. We will consider a few.

Just dumping a lot of hydroxyl groups on the benzene ring does not guarantee emergence of ketonic behaviour. Consider the cases of 1,2,3- and 1,2,4-trihydroxybenzenes.

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1,2,3,4-Tetrahydroxybenzene can exist in the two tautomeric forms. An addition of acid to an alkaline solution of the phenol results in the formation of the solid diketo tautomer that is stable at room temperature owing to intramolecular hydrogen bonds. The aromatization occurs only by heating of 2,3-dihydroxycyclohex-2-en-1,4-dione (I) in acidic solution.

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Phenol-keto tautomerism:

Factors that contribute to increase the keto content in the phenol-keto tautomerism:

ii) Polycyclic phenols:

The tautomeric properties of hydroxynaphthalenes demonstrate in the most unambiguous manner that the naphthalene system is less aromatic than that of benzene.

Naphthalene has a resonance energy of 61 kcal/mol which is less than twice that of benzene, 36 kcal/mol.

\[
\text{1-naphthol enol form} \quad \text{1-naphthol keto form} \quad \text{p-naphthol enol form} \quad \text{p-naphthol keto form}
\]

\[ \text{loss of RE on going over to the keto form} = 61 - 36 = 25 \text{ kcal/mol} \]

As the aromatic stabilisation does not increase as much as it should by the fusing of additional benzene rings, in polycyclic systems, the resonance energy advantages associated with the aromatic tautomers is noticeably compromised.

Consequently, even the monohydroxy naphthalenes display in their chemical reactions properties typical for the tautomeric keto form. A case in point is the Bucherer reaction of 2-naphthol:

\[
\beta\text{-naphthol} \quad \text{NH}_3, (\text{NH}_4)_2\text{SO}_3 \quad \text{heat, pressure} \quad \text{2-naphthylamine}
\]

The reaction is believed to proceed through the keto tautomer of 2-naphthol:

This retains the benzene ring. So, in terms of RE, a penalty of (61-36) = 25 kcal/mol is paid on moving from the phenol to the keto form. However, the keto has 15 kcal/mol bond energy advantage. Although these calculations are not exactly accurate, these definitely indicate that the keto content should be higher for naphthols than it is for phenols.
Tautomerism in Organic Chemistry

Phenol-keto tautomerism:

Factors that contribute to increase the keto content in the phenol-keto tautomerism:

ii) Polycyclic phenols:

Ketonic forms gather more prominence as we go on increasing the number of fused rings.

Thus, 9-hydroxyanthracene (anthrol) undergoes a reversible conversion into ketone (anthrone) in which two separate aromatic rings are conjugated with a carbonyl group. This conjugation stabilizes very much the keto form.

Anthrone is a stable solid and dissolves in warm alkali. On acidification the anthrol form gets precipitated, through the selective protonation of the oxygen atom that bears most of the negative charge in the conjugate base.

The keto tautomer becomes even more stable in the higher polycyclic phenols.

iii) The influence of bulky ortho-substituents on the tautomerism of phenols:

When present, these substituents sterically protect the keto form from going over to the phenol.

A case in point is the isolation of a long-lived quinonoid intermediate in the bromination reaction of 2,6-di-tert-butylphenol:

Study Guide to Organic Chemistry
- Saha et al. Volume 2 (ISBN 978812669588)