Acidity of alcohols continued ...



What is the influence of substituents? inductive & resonance

As the pK_a values above show, phenol is 10^8 more acidic than cyclohexanol.



Phenol has a pK_a value of 10 (given this information, you should immediately recognize that it is more much acidic (about 6 orders of magnitude) than water (pK_a 15.7) and methanol (pK_a 16) since it has lower pK_a value). As phenol is more acidic, this means that its conjugate anion is more stable. The phenoxide anion is stabilized through resonance (shown above). It has 4 resonance forms, and therefore, more ability to spread the negative charge and be stabilized.

Where does the equilibrium lie for ionization of phenol to phenoxide and a proton (H^+) *?*

Answer: It lies far to the left (not ionized). Even though phenol is 10^6 more acidic than water, its pK_a of 10 tells you that the acidity constant is 10^{-10} or that only one part in 10^{10} is ionized; the rest exists as phenol with H attached to oxygen.

Example: Chlorophenol



Is the anion more or less stabilized compared to phenol?

Answer: More stabilized. The chlorine atom is electron withdrawing, and stabilizes the negative charge at the *para* position through the inductive withdrawing effect. However, it also has a weak resonance donating effect. The inductive effect of chlorine wins over resonance effect in this case (contrast this with electrophilic aromatic substitution where the resonance donating effect wins out against the inductive effect).

Example: para- and meta-nitrophenol



p-nitrophenol has a p K_a value of 7.2, whereas *m*-nitrophenol has a p K_a value of 9.3

Which one is more acidic? Answer: *p*-nitrophenol Why? (Think about conjugate anion stabilization and resonance forms). Resonance forms for *m*-nitrophenoxide anion:



Resonance forms for *p*-nitrophenoxide anion:



The nitro group offers an additional resonance form for *p*-nitrophenol that is not possible for *m*-nitrophenol (we are able to drive electrons all the way in to the nitro group for the *para*- substituted nitrophenol). Since there is an additional reasonable resonance form, the *p*-nitrophenol pK_a 7.2 is about 100 times (10²) more acidic than the *m*-nitrophenol with pK_a 9.3 (pK_a 9.3-7.2 = 2.1 pK_a units)

If there are two nitro groups in the *ortho* and *para* positions of the phenoxide anion, the pK_a of the phenol (2,4-dinitrophenol) drops to 4.5. If three nitro groups are attached, the pK_a of the phenol becomes even lower (2,4,6-trinitrophenol has a pK_a of approximately 0.5). This is because *ortho* and *para* positions are where the negative charge of the resonance form can be located, and addition of a nitro group is able to offer more stabilization. This phenomenon is not observed for the *meta* position.

Extra example: How to make 4-hydroxyacetophenone from benzene?



Ethers

An ether is a substance that has two organic groups bonded to the same oxygen atom, R-O-R', where R and R' can be the same or different, but cannot be carbonyl (C=O), or H directly attached. The organic groups may be alkyl, aryl, or vinylic, and an ether can either be an open chain or a ring. Perhaps the most well known ether is diethyl ether, a familiar substance that has been used medically as an anesthetic, and is used industrially as a solvent.



diethyl ether

Naming Ethers

Two systems for naming ethers are allowed by IUPAC rules. Simple ethers with no functional groups are named by identifying the two organic substituents and adding the word *ether* as in the below examples.

`O´

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₋0

diethyl ether or ethyl ether or ether

anisole methyl phenyl ether

dimethyl ether or methyl ether

ethyl methyl ether

If other functional groups are present, the ether part is considered to be an alkoxy substituent (-OR).

For example, the parent name for the below structure is an alcohol.



1. Intermediate polarity - usually have dipoles & can accept hydrogen bonds

2. Not miscible with water - very slight solubility

3. Good solvents for many organic compounds

4. Less dense than water $\rho < 1.0$ - floats on water

5. Usually chemically unreactive - inert to base or weak acid - can react with very strong acid

Example: THC



You should be able to identify different functional groups in a large molecule like THC, and be able to find stereogenic centers and identify the configurations. If treated with Br₂, which double bond will react? *Answer*: Top one (The non-aromatic alkene).

Stereochemistry Review

Stereochemistry refers to the three dimensional arrangement of atoms in space. Stereoisomers are different compounds that have the same connectivity but a different 3D arrangement of atoms

Conformers are different shapes of the same compound

- Obtained by rotation around single bonds usually rapid at room temp
- 15-20 kcal/mole available at room temp

Resonance forms are different pictures of the same compound

• Obtained by movement of electrons, while keeping atom positions same

A chiral molecule (or object) is one that has a non-superimposable mirror image

An **achiral** molecule has mirror images that are superimposable.

Stereoisomers that are non-superimposable mirror image of each other are **enantiomers**. All other stereoisomers (which are not mirror images) are called **diastereomers**.

Example: Camphor

Molecules are 3 dimensional objects – we usually depict them in 2 dimensions





and

camphor structures - same or different? different: they are enantiomers

Compare:



To compare the relationship of 2 structures:

