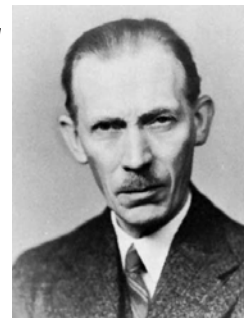


Exercise 6

Fig. X6-1



Johannes N. Brønsted (1879 - 1947)

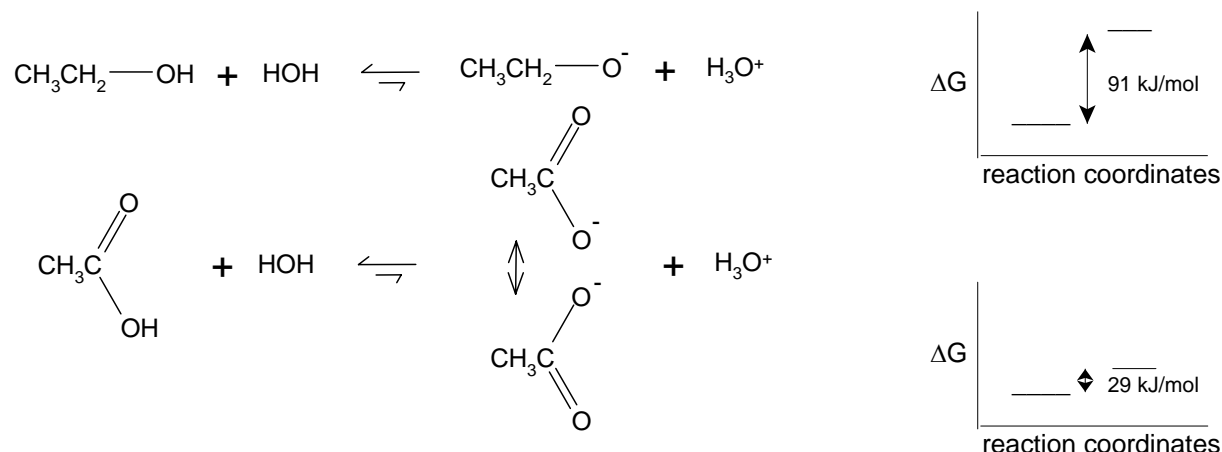
<http://www.jergym.hiedu.cz/~canovm/objevite/objev2/broa.htm>

Structure - Activity Relationships: Acidity and pK_a Values

An understanding of the concepts and mechanisms in organic chemistry gives you the valuable ability to predict how structural and solvent changes can influence the properties of organic compounds. Organic chemists use inductive, resonance, steric, hybridization and hyperconjugation effects to explain and predict changes in properties and reactivity. Complicating the situation, structural changes usually result in changes to more than one of the variable effects. Since the magnitudes of the effects are difficult to quantify and the effects often lead to opposite predictions, considerable experience is needed to be able to confidently predict how a structural change will affect properties. This exercise has been designed to give you some experience with the influence of inductive and resonance effects on the acidity of organic compounds. Acidity plays an extremely important role in the grand scheme of things in organic chemistry. For example, synthetic organic chemists take advantage of the acidity of hydrogens that are α to a carbonyl or on acetylenic carbons to run many reactions that form carbon - carbon bonds.

Whenever you are attempting to develop an argument for the direction of change of a property as a result of a structural change, you are really asking how the free energy of activation is affected if rates of reactions are at issue or how the free energy is affected if an equilibrium is involved. Since pK_a values are an equilibrium issue, we need to consider how the free energy of the reaction is affected by the structural change. It is imperative that we remember that the free energy of the reaction is the difference between the free energy of the reactants and the products. We must consider how structural changes affect the free energy of both the reactants and products. That being said, the least stable state is usually but not always more sensitive to structural changes (aromatic amines are a prominent exception). Since the pK_a values for almost all organic compounds are 5 or greater (the percent of ionization is 1% or less), the right side of the reaction (conjugate base side) is less stable than the left side (unionized acid). Consistent with this argument, the free energy of the conjugate base of organic compounds is generally much more sensitive to structural changes than the original organic compound. This enables us to focus our attention on how structural changes affect the conjugate base.

The first step in any structure - activity consideration is to understand the process. For pK_a predictions, be sure to write equations for the reactions that are being compared. As an example, the acidities of ethanol and acetic acid will be compared. First, assume the solvent is water and write the reactions for the protonation of water by ethanol and acetic acid.



As you can see from the structures above, the conjugate base of acetic acid is resonance stabilized. As a result, the free energy difference for the second reaction is about 29 kJ/mol compared to 91 kJ/mol for the ethanol reaction. The pK_a values are about 5 and 16 for acetic acid and ethanol.

For each pair of compounds, write the pertinent reaction and predict which compound of the pair should be the strongest acid. Explain your answer.

- acetic acid or chloroacetic acid
- 2-chloropropanoic acid or 3-chloropropanoic acid
- chloroacetic acid or fluoroacetic acid
- propane or ethanol
- propane or acetone
- ethane or acetylene

Although most tables of electronegativities list a value of 2.5 for the electronegativity of carbon, a closer examination reveals not surprisingly that electronegativity depends on hybridization. For carbon, the Mulliken-Jaffe electronegativity scale gives the values 2.99, 2.66, 2.48 for sp , sp^2 and sp^3 hybridized carbon respectively. For more information on electronegativity, see:

http://www.meta-synthesis.com/webbook/36_eneq/electroneg.html

- Comment on whether these values are consistent with hybridization models and electronegativity concepts.
 - Are these electronegativity values consistent with the acidity rankings of ethane, ethylene and acetylene? Explain your answer.
- methylcyclohexane or toluene
 - benzoic acid or 4-nitrobenzoic acid
 - benzoic acid or 4-chlorobenzoic acid
 - ethanol or ethanethiol
 - ethanol or 2,2,2-trifluoroethanol
 - cyclopentane or cyclopentadiene
 - acetone or acetic acid
 - acetone or 2,4-pentanedione
 - cyclohexanol or phenol
 - phenol or 4-nitrophenol
 - 3-nitrophenol or 4-nitrophenol
 - phenol or 4-methylphenol
 - ethane or nitromethane
 - ethane or acetonitrile