More about pKa's and acid-base equilibria

CHEM 330 handout

In CHEM 330, we often deal with acid-base equilibria, e.g., in the context of deprotonation reactions (formation of enolates, etc.). The following questions may surface during such discussions:

> Suppose that we treat a weak carbon acid, A–H (e.g., an enolizable carbonyl compound), with a base, B^- :
>
> (i) how can we estimate the equilibrium constant of the ensuing deprotonation reaction?
>
> (ii) how can we estimate the equilibrium concentrations of the various species present in solution?
>
> (iii) how can we estimate the ΔG for the deprotonation reaction?

This handout provides answers to the above.

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Consider the equilibrium:

$$\text{A–H} + \text{B}^- \rightleftharpoons \text{A}^- + \text{B–H}$$

We can estimate the equilibrium constant, K_{eq}, for this process if we know the pKa's of A–H and B–H:

for the above reaction

$$Keq = \frac{[\,\text{A}^-\,][\,\text{B–H}\,]}{[\,\text{A–H}\,][\,\text{B}^-\,]} = \frac{[\,\text{A}^-\,]}{[\,\text{A–H}\,]} \cdot \frac{[\,\text{B–H}\,]}{[\,\text{B}^-\,]}$$

for $\text{A–H} \rightleftharpoons \text{A}^- + \text{H}^+$

$$Ka_{AH} = \frac{[\,\text{A}^-\,][\,\text{H}^+\,]}{[\,\text{A–H}\,]} \quad \therefore \quad \frac{[\,\text{A}^-\,]}{[\,\text{A–H}\,]} = \frac{[\,\text{H}^+\,]}{Ka_{AH}}$$

for $\text{B–H} \rightleftharpoons \text{B}^- + \text{H}^+$

$$Ka_{BH} = \frac{[\,\text{B}^-\,][\,\text{H}^+\,]}{[\,\text{B–H}\,]} \quad \therefore \quad \frac{[\,\text{B–H}\,]}{[\,\text{B}^-\,]} = \frac{Ka_{BH}}{[\,\text{H}^+\,]}$$

Substitution gives:

$$Keq = \frac{Ka_{AH}}{[H^+]} \cdot \frac{[H^+]}{Ka_{BH}} = \frac{Ka_{AH}}{Ka_{BH}}$$

$$\therefore\ pKeq = p\left\{\frac{Ka_{AH}}{Ka_{BH}}\right\} = pKa_{AH} - pKa_{BH}$$

Example:

Suppose that one treats ethyl acetate ("EtOAc"), pKa ≈ 25, with NaOEt, pKa $_{EtOH}$ ≈ 18. Deprotonation will be incomplete because EtO^{-} is a weaker base than the enolate of EtOAc. For simplicity, suppose also that the initial concentrations of the two reactants are identical and equal to 1 M. The equilibrium constant for the process is roughly equal to:

ΔpKa = 25-18 = 7 = p{equilibrium constant, K_{eq}}, so, $K_{eq} \approx 10^{-7}$

We can estimate the extent of deprotonation of EtOAc under these conditions from the expression of K_{eq}. For the process,

$$\text{H-CH}_2\text{-COOEt} + \text{EtO}^{\ominus} \rightleftharpoons {}^{\ominus}\text{CH}_2\text{-COOEt} + \text{EtOH}$$

we have:

$$K_{eq} = \frac{[\,{}^{\ominus}\text{CH}_2\text{-COOEt}\,]\ [\,\text{EtOH}\,]}{[\,\text{H-CH}_2\text{-COOEt}\,]\ [\text{EtO}^{\ominus}\,]}$$

Because for each molecule of enolate that forms one also creates one molecule of EtOH, the solution concentrations of enolate and of EtOH will be essentially identical; furthermore, because the extent of deprotonation is small, the concentrations of EtOAc and of EtO^{-} will not change much: they will be nearly equal to the initial value of 1M. The above expression may then be simplified (oversimplified?) as follows:

$$[\,{}^{\ominus}\text{CH}_2\text{-COOEt}\,]^2 \approx K_{eq}\ ;\ [\,{}^{\ominus}\text{CH}_2\text{-COOEt}\,] \approx \sqrt{K_{eq}} = 10^{-3.5} \approx 3 \times 10^{-4}$$

meaning that approximately 0.03 % (≈ 1 part in 3,000) of the starting EtOAc will be present as the enolate under these conditions.

In general, the square root of K_{eq} provides an estimate of the extent of deprotonation. As a guideline, meaningful reaction rates are achieved when this value is $> 10^{-6}$

The Gibbs equation relates equilibrium constants to ΔG's:

$$\Delta G = -n \, RT \ln K_{eq}$$

where n = number of moles, R = gas constant ($= 1.98 \cdot 10^{-3}$ kcal/°K mol)

Because changes in pKa are associated with ΔG's, one may use ΔpKa's to estimate whether a reaction step involving basic agents will be thermodynamically favorable or unfavorable:

A step that produces a weaker base at the expenses of a stronger base is thermodynamically favorable (because $\Delta G < 0$)

A step that produces a stronger base at the expenses of a weaker base is thermodynamically unfavorable (because $\Delta G > 0$)

Example:

Determine whether the deprotonation of ethyl acetate with the anion of diisopropylamine at 25°C is thermodynamically favorable or unfavorable and estimate the ΔG associated with the reaction.

$$(i\text{-Pr})_2N^- + \underset{pKa \approx 25}{H{-}CH_2COOEt} \rightleftharpoons \underset{pKa \approx 35}{(i\text{-Pr})_2N{-}H} + {}^-CH_2COOEt$$

$$p\,Keq = 25 - 35 = -10 \quad \therefore \quad Keq \approx 10^{10} \quad >> 1 \ \therefore$$ the reaction is favorable

For 1 mole at 25°C (= 298 °K):

$$\Delta G = -n \, RT \ln K_{eq} = -\,1.98 \cdot 10^{-3} \cdot 298 \cdot \ln 10^{10} = -\,13.6 \text{ kcal / mol}$$

$\Delta G < 0 \ \therefore$ the reaction is favorable