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:

$$A\text{–}H \ + \ B^- \ \rightleftharpoons \ A^- \ + \ B\text{–}H$$
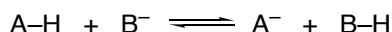
We can estimate the equilibrium constant, K_{eq}, for this process if we know the pKa's of A–H and B–H:

for the above reaction
$$K_{eq} = \frac{[\,A^-\,][\,B\text{–}H\,]}{[\,A\text{–}H\,][\,B^-\,]} \ = \ \frac{[\,A^-\,]}{[\,A\text{–}H\,]} \cdot \frac{[\,B\text{–}H\,]}{[\,B^-\,]}$$

for $\quad A\text{–}H \rightleftharpoons A^- + H^+ \qquad Ka_{AH} = \dfrac{[\,A^-\,][\,H^+\,]}{[\,A\text{–}H\,]} \quad \therefore \quad \dfrac{[\,A^-\,]}{[\,A\text{–}H\,]} = \dfrac{[\,H^+\,]}{Ka_{AH}}$

for $\quad B\text{–}H \rightleftharpoons B^- + H^+ \qquad Ka_{BH} = \dfrac{[\,B^-\,][\,H^+\,]}{[\,B\text{–}H\,]} \quad \therefore \quad \dfrac{[\,B\text{–}H\,]}{[\,B^-\,]} = \dfrac{Ka_{BH}}{[\,H^+\,]}$

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 $\approx$ 25, with NaOEt, pKa $_{EtOH}$ $\approx$ 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:

$\Delta pKa = 25\text{-}18 = 7 = p\{\text{equilibrium constant, } K_{eq}\}$, 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,

$$H\text{-}CH_2\text{-}COOEt\ +\ EtO^{\ominus}\ \rightleftharpoons\ ^{\ominus}CH_2\text{-}COOEt\ +\ EtOH$$
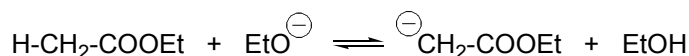
we have:

$$K_{eq} = \frac{[\ ^{\ominus}CH_2\text{-}COOEt\ ]\ [\ EtOH\ ]}{[\ H\text{-}CH_2\text{-}COOEt\ ]\ [EtO^{\ominus}\ ]}$$

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:

$$[\ ^{\ominus}CH_2\text{-}COOEt\ ]^2 \approx K_{eq}\ ;\ [\ ^{\ominus}CH_2\text{-}COOEt\ ] \approx \sqrt{K_{eq}} = 10^{-3.5} \approx 3\times 10^{-4}$$

meaning that approximately 0.03 % ($\approx$ 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:

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

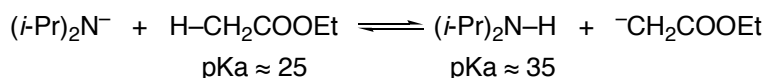where n = number of moles, R = gas constant (=1.98$\cdot$10^{-3} kcal/$^{\circ}$K mol)

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.

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

p K_{eq} = 25 – 35 = – 10 $\therefore$ $K_{eq} \approx 10^{10}$ $>> 1$ $\therefore$ the reaction is favorable

For 1 mole at 25°C (= 298 °K):

$\Delta G = -n\,RT\,\ln K_{eq} = -\,1.98\cdot10^{-3} \cdot 298 \cdot \ln 10^{10} = -\,13.6$ kcal / mol

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