# Determination of a Partition Coefficient

Theoretical background: P.W. Atkins: *Physical Chemistry*, 26.1–3 (4th Edition), or 25.1–3 (6th Edition) chapters.
Type of practice: Pairwise.
Aim of practice: The partition of a weak carboxylic acid between two immiscible solvents will be studied.

## 1 Introduction

When a substance has affinity to two immiscible solvents, the substance dissolves in both phases when they are in physical contact with each other. The relative amounts of the dissolved substance depend on the relative affinities. The substance is said to be partitioned between the phases. This type of behaviour bears with significant importance for chemical and pharmaceutical industries. Gaining pure materials from mixtures by extraction is based on the partition of the given substance between the solvents. Chromatographic analytical methods, e.g., certain types of gas chromatography also make use of partition between phases.

The efficiency of these processes, the separation of the required substance from the mixture, depends on the difference in the values of equilibrium concentration in the phases. The constant characteristic on this heterogenous equilibrium is the partition coefficient. Its value depends on the nature of substance and the pair of solvents, above the temperature. When the molecular state of the whole amount of solute, in both phases, are the same, the value of the partition coefficient is easy to determine:

$$\mathrm{K_M} = \frac{[\mathrm{HA_W}]}{[\mathrm{HA_O}]} = \frac{\mathrm{c_W}}{\mathrm{c_O}}\,, \tag{1}$$

where HA is the substance partitioned between the phases, and $\mathrm{c_W}$ and $\mathrm{c_O}$ the values of the analytical concentration of the partitioned material in the phases[1]. Mostly one of the solvents is water and the other is an organic solvent immiscible with water. So, the subscripts of W and O will be used accordingly.

When the condition mentioned above was not true for the solute in any or both of the phases, the simple determination of the values of analytical concentration in the phases would be misleeding and produce false result. The partition constant would change when it was determined in samples with various solute content. A weak monocarboxylic acid is the best example of this type of deviation. If HA denotes a carboxylic acid (R-COOH) with a relatively short alkyl-group, the molecule partially dissociates in water:

$$\mathrm{HA_W} \rightleftharpoons \mathrm{H_W^+} + \mathrm{A_W^-}\,. \tag{2}$$

This process is characterized by the dissociation equilibrium constant $\mathrm{K_d}$:

$$\mathrm{K_d} = \frac{[\mathrm{H_W^+}]\cdot[\mathrm{A_W^-}]}{[\mathrm{HA_W}]\cdot \mathrm{c}^{\ominus}}\,, \tag{3}$$

where $\mathrm{c}^{\ominus} = 1\ \mathrm{mol/dm^3}$ is the standard concentration. It can be expressed by the degree of dissociation, $\alpha$:

$$\mathrm{K_d} = \frac{\alpha^2\cdot \mathrm{c_W}}{(1-\alpha)\cdot \mathrm{c}^{\ominus}}\,, \quad \text{where} \quad \alpha = \frac{[\mathrm{H_W^+}]}{\mathrm{c_W}} = \frac{[\mathrm{A_W^-}]}{\mathrm{c_W}}\,. \tag{4}$$

It is a useful form of the equation, since the determination of the analytical concentration of the acid and a search for the dissociation constant of the acid in the chemistry handbooks, make us possible to calculate the degree of dissociation and the equilibrium concentration of the molecular form of the acid. Only a general quadratic equation should be solved.

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[1] The partition coefficient is also used in the characterization of the lipophily of the active ingredient in a pharmaceutic preparation.

On the other hand, the monocarboxylic acids can interact with each other and form associates, in nonpolar environment:

$$\mathrm{n\,HA} \rightleftharpoons \mathrm{(HA)_n}\,. \tag{5}$$

It also leads to equilibrium, and it is characterized by an equilibrium constant, $K_n$:

$$K_n = \frac{[(HA)_{n,O}] \cdot (c^{\ominus})^{(n-1)}}{[HA_O]^n}\,. \tag{6}$$

It is a very difficult case, but a relatively easy way will be shown to achieve a relatively reliable result. First, we apply the following approximations: *(1)* the degree of dissociation is low in water, and *(2)* the degree of association is high in the organic solvent. Both can be achieved by using higher overall solute concentration in the samples. These approximations make it possible to substitute the analytical concentration of the solute by the following expressions:

$$[HA_W] \cong c_W \quad \text{and} \quad n \cdot [(HA)_{n,O}] \cong c_O\,, \tag{7}$$

where the values for $c_W$ and $c_O$ can be determined by any kind of analytical method, e.g., by titration.

Let us substitute $c_W$ into equation (1) and rearrange it to get the $[HA_O] = \frac{c_W}{K_M}$ expression. It can be substituted into the denominator of equation (6), while the other expression $[(HA)_{n,S}] = \frac{c_S}{n}$ goes into the numerator:

$$K_n = \frac{\frac{c_S}{n} \cdot (c^{\ominus})^{n-1}}{\left(\frac{c_V}{K_M}\right)^n} = \frac{c_S \cdot (c^{\ominus})^{n-1}}{n} \cdot \frac{(K_M)^n}{(c_V)^n}\,. \tag{8}$$

After the separation of the constants and experimentally determined values, a new constant, characteristic on the partition equilibrium can be defined:

$$K_h = \frac{n \cdot K_n}{(K_M)^n} = \frac{c_S \cdot (c^{\ominus})^{n-1}}{(c_V)^n} = \frac{\frac{c_S}{c^{\ominus}}}{\left(\frac{c_V}{c^{\ominus}}\right)^n}\,. \tag{9}$$

Taking the logarithm of the new constant:

$$\ln(K_h) = \ln\left(\frac{c_S}{c^{\ominus}}\right) - n \cdot \ln\left(\frac{c_V}{c^{\ominus}}\right) \tag{10}$$

which can be rearranged to obtain a linear function:

$$\ln\left(\frac{c_S}{c^{\ominus}}\right) = n \cdot \ln\left(\frac{c_V}{c^{\ominus}}\right) + \ln(K_h)\,. \tag{11}$$

It can be concluded, that the measurement of the analytical concentration of the solute in both phases, with number of samples, differing in overall concentration, makes us possible to determine the average association number and the new constant. A linear function should be fitted to the data points by the least-square method. The fitted parameters provide the required results.

The partition coefficient will be determined for a short chain monocarboxylic acid between water and an organic solvent using simple acid-base titration.

## 2 Description of the experimental task

An organic solvent will be provided for the experiment, which is unknown to the student, so all manipulations should be performed under the fume cupboard, while the pump should be switched on and the window must be in the properly lowered position. Wearing plastic gloves is also recommended!

The following information will be given by the instructor: *(1)* The name of the carboxylic acid (acetic acid or propionic acid). *(2)* The initial volume of the water and the organic solvent (both should be between 35 – 60 cm$^3$). *(3)* The volume of the first batch of the carboxylic acid to be added to the mixture of the solvents ($V_0$), and the volume of the second, third etc. batches of the carboxylic acid to be added to the system after taking a set of samples ($\Delta V$). If no other instructions are given: *(1)* use propionic acid and *(2)* the initial volume of both phases will be 40 cm$^3$. The first batch of the carboxylic acid shall be 0.50 cm$^3$ propionic acid or 0.80 cm$^3$ acetic acid. After taking a set of samples, further 0.15 cm$^3$ propionic acid or 0.20 cm$^3$ acetic acid shall be added to the system. Upon the first three shaking (or alternatively, upon the first three addition of acid portions, including the very first one), two distinct samples must be withdrawn from both phases. For the rest of the experiment, 6 more sample withdrawal is needed during which only 1–1 sample is taken from both phases. The tasks should be evenly shared by the students performing the experiment to be finished on time!

The solvents should be mixed in a stoppered Erlenmeyer flask with a volume of 250 cm$^3$ by one of the students. The system should be vigorously shaken after the addition of the first batch of carboxylic acid, at least for 10 minutes, to achieve the equilibrium state.

The other student should prepare two NaOH solutions with different concentration in volumetric flasks. If no other instruction is given, the first one should be 0.04 M in concentration and 500 cm$^3$ in volume. Use solid NaOH for the preparation. The second solution should be 0.004 M in concentration and 500 cm$^3$ in volume. Use the solution with higher concentration for dilution. The available burettes should be rinsed and filled up with the NaOH solutions. The one which can be read by higher precision should be used for the more diluted NaOH solution, the other, with less precise scale for the more concentrated NaOH solution.

Allow the phases to separate after finishing the vigorous shaking and take samples from both phases. The volume of the samples must be at least 2 cm$^3$ at the beginning. Use two graded pipettes, the best size is 5 cm$^3$, and do not mix them! Take two samples from both phases after the addition of the first, second and the third batch of carboxylic acid, i.e., twelve samples will be taken. Add at least further six batches of carboxylic acid to the system and take only one sample from both phases, after five minute long, vigorous shaking of the system. So, you will end up with 24 samples. Extraordinary care should be taken, when sampling takes place. The mixing of the phases in the pipette should be avoided. Tilt the Erlenmeyer flask to get thicker phases! Check the bottle of the organic solvent for the density of it, to identify the phases! It is easier to take sample from the upper phase, but the pipette should be bubble while its tip goes through the upper phase to take sample from the bottom phase. Leak a small portion of the liquid while you are withdrawing the pipette through the upper phase. The sample from the organic phase cannot be titrated, when even a tiny bit of the aqueous phase got into it! Always wipe the tip of the pipettes!

The volume of the sample should be changed if the titration results in a very low or very high equivalent volume. The first samples taken from the organic phase might be too low in concentration, and the precision of the equivalent volume is low, so the volume of the next sample can be increased. On the other hand, the concentration of the samples taken from the aqueous phase might strongly increase by the addition of the carboxylic acid batches, and the equivalent volume of the NaOH solution steps over 2/3 of the full volume of the burette. Decrease the volume of the sample, but never go below 0.5 cm$^3$! If it occurs at the titration of the first three batches of carboxylic acid, new NaOH solution should be prepared! Always consult with the instructor about it!

The titration of the samples from the aqueous phase is simpler. Dilute the sample with around 20 cm$^3$ of distilled water, then add a few drops of phenolphthalein indicator and titrate it with the NaOH solution with higher concentration, until a light pink colour occurs and remains until 20–30 seconds after shaking. Make note the volume!

The sample taken from the organic phase should be put into a smaller stoppered Erlenmeyer flask. Add around 20 cm$^3$ of distilled water to it, and shake well, since the titration takes place in water and the acid should be extracted from the organic solvent! Repeat the shaking every time, the light pink colour occurs. Stop the titration when it remains visible for 20–30 seconds. Do not forget the $CO_2$ dissolved from air can affect the result!

The students must work in good coordination! One of them takes the samples and changes the concentration and acid and shakes the system well! The other titrates them continuously, and advices the other about the required changes in the sample volume.

After the titration of the first sample from the aqueous phase, calculate the degree of dissociation by equation (4), using the measured concentration and the dissociation constant of the acid (Propionic acid: $\mathrm{pK_d} = 4.88$; Acetic acid: $\mathrm{pK_d} = 4.756$). If it was more than 10 %, please notify the instructor!

The Erlenmeyer flasks and the pipettes used for the organic phase samples should also be rinsed by acetone to remove the traces of the organic solvent.

# 3 Evaluation of measured data

- The measured and calculated data should be summarized as it follows:

Table 1: Summary of the experimental results.

$\mathrm{V_{water}}$= .... $\mathrm{cm^3}$; $\mathrm{V_{organic\ solvent}}$= .... $\mathrm{cm^3}$; $\mathrm{V_0}$= .... $\mathrm{cm^3}$; $\Delta\mathrm{V}$= .... $\mathrm{cm^3}$; $\mathrm{c_{NaOH}^{concentrated}}$= .... M

$\mathrm{c_{NaOH}^{diluted}}$= .... M; Carboxylic acid: ....; $\mathrm{K_d}$= ....; Degree of dissociation in the first sample, $\alpha$= .... %

| Nr. | Volume of sample / $\mathrm{cm^3}$ | | Equivalent volume / $\mathrm{cm^3}$ | | $\mathrm{c_W/M}$ | $\mathrm{c_O/M}$ | $\ln\left(\frac{\mathrm{c_W}}{\mathrm{M}}\right)$ | $\ln\left(\frac{\mathrm{c_O}}{\mathrm{M}}\right)$ |
|---|---|---|---|---|---|---|---|---|
| | aqueous phase | organic phase | $\mathrm{c_{NaOH}^{concentrated}}$ | $\mathrm{c_{NaOH}^{diluted}}$ | | | | |
| 1. | | | | | | | | |
| 2. | | | | | | | | |
| ⋮ | | | | | | | | |
| 12. | | | | | | | | |

Treat all results as independent measurements, do not average the data gained from samples of the same solution. If you had prepared NaOH solutions with more than two concentrations, add columns in the above table accordingly. The measured volumes should be in the proper columns! Make sure that the steps of the calculation can be followed!

- Prepare a graph according to equation (10). The linear part of the curve can supply the average association number and the constant for the partition equilibrium. Calculate their standard deviations as well. If one or two points in the linear region strongly scatters due to obvious measurement problems, it is allowed to exclude them from the fitted dataset, but those points should still be present in the graph. At least half of the measured points should be used. If there were no linear part of the curve, which might mean that the studied system did not completely fulfill the conditions set up in the deduction of the mathematical model, the following action should be taken. Add further columns to the table, one for the degree of dissociation, $\alpha$, calculated from equation (4), one for the equilibrium concentration of the non-dissociated acid in the aqueous phase, $[\mathrm{HA_W}] = (1-\alpha)\cdot \mathrm{c_W}$, and one for its logarithm, $\ln([\mathrm{HA_W}]/\mathrm{M})$. Add the $\ln(\mathrm{c_0}/\mathrm{M})$ vs. $\ln([\mathrm{HA_W}]/\mathrm{M})$ curve to the graph. Two different y-axes can be used if necessary. This curve is expected to have wider linear range. Fit a linear function like earlier, and calculate n and $\mathrm{K_h}$ and their standard deviations.
- Compare and comment the results gained by both methods in a few sentences. Are the values for n acceptable taking into account the knowledge about the association properties of the carboxylic acids

in non-polar medium? What are the lower and higher limits of its value? How accurate the calculated equilibrium constant is?

Remarks:

- It is important to share and organize your tasks evenly during this practice in order to finish the measurements in time. For example, if the titration of the samples fell behind schedule, both students should take their share from them to finish faster.
- It is not required that the same student should carry out all titrations, while the other does only the sampling and shaking. The tasks can be switched at any time between the students.
- Smaller experimental errors do not lead to completely wrong results, but the titrations must be as accurate as possible. Avoid mixing aqueous phase into the samples of the organic phase!

# Questions

1. What kind of chemical process is the extraction? What is it for?
2. What kind of chemical process the liquid – liquid extraction?
3. Define the partition coefficient for non-dissociating and non-associating substance!
4. What are the conditions to be fulfilled, when the partition equilibrium can be characterized by the ratio of the analytical concentration of the phases?
5. What kind of processes can perturb the partition equilibrium?
6. What kind of chemical equation describes an association process? Define its equilibrium constant?
7. What kind of condition(s) must be fulfilled in the distinct phases to allow to the use the analytical concentrations instead of equilibrium ones, in order to describe the partition equilibrium?
8. What is the definition of $K_h$, why is it important, and how do you determine its value during the practice?
9. Why is it suggested to carry out all manipulations under a fume cupboard?
10. Which way should be prepared 500 $cm^3$ NaOH solution, with 0.04 M concentration, from solid solute? $M_r(NaOH) = 40.00$.
11. Prepare 250 $cm^3$ NaOH solution with 0.01 M concentration, using the solution mentioned in question 10. Which way should it be made?
12. After sample withdrawal, 2.00 $cm^3$ of aqueous sample was titrated with 0.04 M NaOH solution and the equivalent volume was 16.57 $cm^3$, while it was 8.70 $cm^3$ for tirtrating 2.00 $cm^3$ organic phase sample with 0.008 M NaOH solution. Calculate the analytical concentration of the weak acid in the distinct phases!
13. During the titration of the first sample taken from the aqueous phase the acetic acid concentration is found to be 0.39 M ($pK_d = 4.756$). Calculate the degree of dissociation for acetic acid.
14. The concentration of the weak acid was determined in both phases, by titration. $c_W = 0.43$ M and $c_0 = 0.017$ M were found. Calculate the equilibrium constant ($K_h$), if the association was characterized by $n = 2$!