The Partition of Organic Compounds Between Higher Alcohols and Water

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In a recent paper (Collander [1]) the partition of organic compounds between *iso*-butanol and water was examined. Now it has been thought of interest to study the solvent properties of some higher alcohols also, in order to establish the influence of the length of the hydrocarbon chain on these properties. The alcohols chosen for this study were, in the first place, prim. *n*-octyl alcohol and oleyl alcohol. (The last-named substance is of special interest in this connection as it has been recommended by K. H. Meyer and Hemmi [2] as a suitable model for the plasma membrane lipoids.) Some experiments were carried out also with *iso*-amyl alcohol, but they are not reported here in full.

Table 1 contains the partition coefficients referring to the solvent systems octyl alcohol/water and oleyl alcohol/water.

The first column gives the empirical formulae and the names of the solutes studied. The order of the compounds is determined, firstly, by the number of carbon atoms in the molecule, secondly, thirdly, and fourthly by the numbers of nitrogen, oxygen, and hydrogen atoms respectively. Halogen compounds are listed immediately after the corresponding halogen-free compounds.

The second column gives the organic solvent used: Oc = octyl alcohol (B.D.H.), Ol = oleyl alcohol (a commercial product, probably not very pure, from Deutsche Hydrierwerke, Rotleben, Germany).

The third column gives the temperature in degrees centigrade. If not reported, the temperature was between 17 and 22° C.

The fourth and fifth columns give the concentration of the solute in the alcoholic and aqueous phase respectively. All concentrations are expressed as millimols per liter solution.

The last column gives the partition coefficients defined as the ratio of the total concentration of the solute in the alcoholic phase to its total concentration in the aqueous phase. Also the partition coefficients referred to in the text always mean *concentration in the organic phase/concentration in the aqueous phase*, never the inverse value. In the case

of acids and bases with a dissociation constant greater than 10^{-3} the partition of the un-dissociated molecules has been calculated on the assumption that only undissociated molecules are soluble in the organic solvent. The values arrived at in this way are marked with M.

The partition coefficients listed are for the most part thought to be correct within limits of about 20 per cent.

Table 1. Partition of organic compounds between octyl and oleyl alcohols and water.

Solute	Solvent	Temp.	$C_{alcohol}$	C_{water}	Part. coeff.
CH_3I Methyl iodide	Oc	19	2 090	42.4	49
CH_4O Methanol	Oc	19	200	1 300	0.15
CH_2O_2 Formic acid	Oc	20	247	842	0.29
» » »	Ol		103	877	0.12
CH_5N Methylamine	Oc	20	260	970	0.27
CH_3NO_2 Nitromethane	Oc	20	1 500	1 250	1.2
C_2H_6O Ethanol	Oc	20	426	891	0.48
$C_2H_4O_2$ Acetic acid	Oc	20	423	859	0.49
» » »	Ol		180	831	0.22
$C_2H_3BrO_2$ Bromoacetic acid	Oc	20	590	248	2.4 (M 2.6)
$C_2H_4O_3$ Glycolic acid	Oc	19	77.6	1 014	0.077
» » »	Ol	19	19	968	0.020
C_2H_7ON Ethanolamine	Oc	19	94.0	1 926	0.049
C_3H_6O Acetone	Oc	20	506	867	0.58
$C_3H_6O_2$ Methyl acetate	Oc	20	780	526	1.5
»　Propionic acid	Oc	20	880	482	1.8
» » »	Ol		453	558	0.81
$C_3H_5BrO_2$ α-Bromopropionic acid	Oc	20	901	121	7.4 (M 8.3)
$C_3H_8O_2$ Methylal	Oc	19	1 350	1 390	1.0
$C_3H_4O_3$ Pyruvic acid	Ol		102	878	0.12
$C_3H_6O_3$ Lactic acid	Oc	20	177	752	0.24
» » »	Ol		59	957	0.062
$C_3H_4O_4$ Malonic acid	Ol		48	978	0.049 (M 0.052)
C_3H_5N Propionitrile	Oc	18	1 420	1 290	1.1
C_3H_9ON *iso*-Propanolamine	Oc	19	227	2 001	0.11
C_4H_8O Methyl ethyl ketone	Oc	19	631	351	1.8
$C_4H_{10}O$ *iso*-Butanol	Oc	20	2 591	381	6.7
»　Ethyl ether	Oc	20	3 290	486	6.8
$C_4H_8O_2$ Ethyl acetate	Oc	20	645	141	4.6
»　Dioxane	Oc	20	319	840	0.38
»　*n*-Butyric acid	Oc	20	628	102	6.2
» » »	Ol		667	230	2.9
$C_4H_7BrO_2$ α-Br-n-butyric acid	Oc	19	1 028	46.8	22 (M 26)

Solute	Solvent	Temp.	$C_{alcohol}$	C_{water}	Part. coeff.
$C_4H_{10}O_2$ Ethylene glycol monoethyl ether	Oc	19	238	810	0.29
» 2,3-Butylene glycol	Oc	18	150	1 250	0.12
$C_4H_6O_3$ α-Oxy-*iso*-butyric acid	Oc	20	195	447	0.44
» » » » »	Ol		128	890	0.14
$C_4H_4O_4$ Maleic acid	Ol		51	459	0.11 (*M* 0.13)
$C_4H_6O_4$ Succinic acid	Oc	20	132	513	0.26
$C_4H_6O_5$ Malic acid	Oc	20	26.4	483	0.055
» » »	Ol		17.2	976	0.018
$C_4H_{11}N$ *n*-Butylamine	Oc	20	1 294	271	4.8
» Diethylamine	Oc	19	816	299	2.7
$C_4H_{11}O_2N$ Diethanolamine	Oc	19	26.4	704	0.037
$C_4H_4N_2$ Ethylene cyanide	Oc	20	75.0	625	0.12
$C_4H_{10}N_2$ Piperazine	Oc	17	15.1	224	0.067
$C_5H_8O_4$ Glutaric acid	Ol		100	903	0.11
» Dimethylmalonic acid	Ol		254	515	0.49
$C_6H_{12}O_2$ Caproic acid	Ol		984	21.7	45
$C_6H_{10}O_4$ Adipic acid	Oc	20	148	121	1.2
$C_6H_8O_6$ Tricarballylic acid	Ol		30.4	996	0.030
$C_6H_8O_7$ Citric acid	Oc	20	11.5	609	0.019
$C_6H_{15}O_2N$ Di-*iso*-propanol-amine	Oc	19	34.0	222	0.15
$C_8H_{18}O$ prim. *n*-Octanol	Oc	25	6 360	4.51	1 410
$C_9H_{16}O_4$ Azelaic acid	Oc	20	155	4.15	37 (*M* 40)

CONCLUSIONS

According to Frumkin[3] the partition coefficient k equals $e^{W/RT}$, in which W denotes the energy that can be gained by the transport of one mole of the solute from the one phase to the other. Frumkin did not express any views about the nature of this energy, but to-day it seems plausible to assume that it depends principally on the formation and breaking of hydrogen bonds between the solute and the solvent molecules. If this is the case, it is only natural that the greater the difference as to the hydrogen bondedness of the two phases of the solvent systems examined the greater is the difference between two solutes as to their partition coefficients. Tables 2 and 3 give some examples of this.

Table 2 shows that in the butanol/water system the partition coefficient increases by 1.8—2.8 times within each homologous series of solutes from one member to the next. In the octanol/water system the corresponding increase is a little greater and in the oleyl alcohol/water system still somewhat greater.

Table 2. *Increase of the partition coefficient within homologous series of solutes in different alcohol/water systems.*

	Butanol Water	Octanol Water	Oleyl alcohol Water
Acetic acid — Caproic acid	2.8	—	3.8
Br-acetic acid — Br-butyric acid	2.8	3.2	—
Methyl acetate — Ethyl acetate	2.8	3.1	—
Malonic acid — Dimethylmalonic acid	2.6	—	3.1
Methylamine — Butylamine	2.5	2.6	—
Methanol — iso-Butanol	2.4	3.5	—
Succinic acid — Adipic acid	1.9	2.1	—
Glycolic acid — Oxy-iso-butyric acid	1.9	2.4	2.7
Diethanolamine — Di-iso-propanolamine	1.9	2.0	—
Ethanolamine — iso-Propanolamine	1.8	2.2	—

Similarly Table 3 shows that when a hydroxyl group is introduced into a solute molecule the longer the hydrocarbon chain of the alcohol used as a non-aqueous solvent the more reduced will be the partition coefficient of the solute.

As previously stated (Collander [4]) the partition coefficients in different solvent systems composed of monohydric alcohols and water are mutually correlated in such a way that, if k_1 denotes the partition coefficient of a given solute in one solvent system and k_2 that of the same solute in another of the solvent systems here in question, then the following equation is approximately valid:

$$\log k_1 = a \cdot \log k_2 + b \qquad (1)$$

In this equation a and b are two constants characterizing the solvent systems in question.

Table 3. *Influence of a hydroxyl group on the partition coefficient in different alcohol/water systems.*

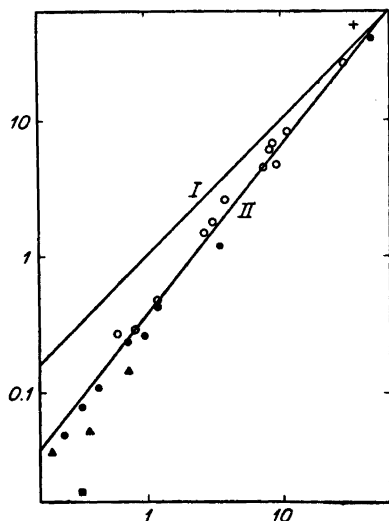|	Butanol Water	Pentanol Water	Octanol Water
Diethylamine — Diethanolamine	4.8	—	8.5
Propionic acid — Lactic acid	4.3	—	7.6
Acetic acid — Glycolic acid	3.6	5.4	6.3
Tricarballylic acid — Citric acid	2.9	4.4	—
Succinic acid — Malic acid	2.6	4.6	4.8
Malic acid — Tartaric acid	2.2	2.3	—

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Fig. 1. Abscissa: partition coefficient in the iso-butanol/water system, ordinate: partition coefficient in the octanol/water system. Line I represents the equation $k_{octanol} = k_{butanol}$, line II the equation (3). + molecule containing no hydrophilic group, o molecule containing one hydrophilic group, ●, ▲, and ▇ molecules containing two, three, or four such groups, respectively.

Thus the organic acids whose partition in the iso-butanol/water and iso-pentanol/water systems has been studied all fit fairly exactly the equation

$$\log \; k_{iso\text{-}pentanol} = 1.17 \; k_{iso\text{-}butanol} - 0.17 \tag{2}$$

On the other hand, a contemplation of Fig. 1 showing the correlation between the partition coefficients in the iso-butanol/water and the prim.-octanol/water systems reveals the fact that although the equation

$$\log \; k_{octanol} = 1.24 \log \; k_{butanol} - 0.42 \tag{3}$$

is approximately valid, there is, never-the-less, a distinct difference between the behaviour of those compounds which contain one hydrophilic group only in their molecule and those which contain two or more such groups. The points representing the former (i. e., the fatty acids, the α-bromo-substituted fatty acids, the monohydric alcohols, the alkyl acetates, the dialkyl ethers, and the alkylamines) are almost all situated more or less above line II representing equation (3) while the points representing the compounds with two or more hydrophilic groups in their molecule are all situated below this line.

The reason for this is not quite clear, but the following hypothesis may perhaps be considered possible: — When an organic compound dissolves in a relatively hydrophilic solvent, like butanol, numerous hydrogen bonds are formed between the solute and the solvent molecules. When, however, the
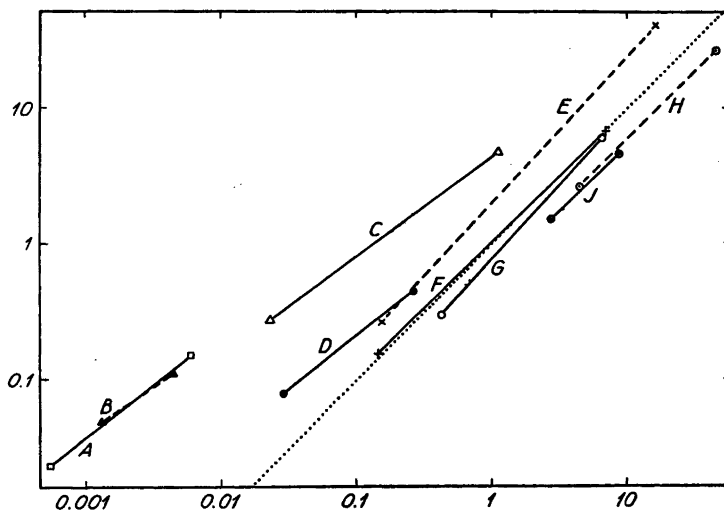
Fig. 2. *Abscissa: partition coefficient in the ethyl ether/water system, ordinate: partition coefficient in the octanol/water system. A dialkanolamines, B monoalkanolamines, C alkylamines, D α-hydroxy-substituted fatty acids, E dicarboxylic acids, F monohydric alcohols, G fatty acids, H α-bromo-substituted fatty acids, I alkyl acetates.*

same substance dissolves in a less hydrophilic solvent, like octanol, hydrogen bonds are to a considerable extent formed between pairs of solute molecules. (In the case of fatty acids this tendency to form double molecules in hydrophobic solvents has been well known for a long time.) The double molecules thus formed are always more hydrophobic than the original single molecules. If, however, the solute molecule contains many hydrophilic groups, in most cases probably only one such group per molecule will be engaged in the formation of molecule pairs. The other hydrophilic groups thus remain unaltered and the increase of the alcohol/water distribution coefficient will therefore be relatively smaller than in the case of molecules containing one hydrophilic group only. (The behaviour of methyl iodide, the only compound studied which is without a single hydrophilic group, seems, however, not to harmonize very well with this hypothesis.)

If the partition coefficients found in the system oleyl alcohol/water are plotted against those in the iso-butanol/water system, we get a graph virtually very like Fig. 1. For the sake of saving space it will not be reproduced here.

A saturated solution of ethyl ether in water at 25° C contains about 5.7 g ether per 100 g solution, while a saturated aqueous solution of prim. octanol at the same temperature contains only about 0.059 g octanol per 100 g solution

(Butler *et al.*[5]). In view of this one would feel tempted to regard octanol as a much less hydrophilic substance than ethyl ether. Such a conclusion would not, however, be consistent with the results visualized by Fig. 2, viz., that strongly hydrophilic solutes are somewhat more soluble in octanol than in ether, while more hydrophobic substances are about as soluble in ether as in octanol. (For the sake of clearness, only a selection of the substances studied in the ether/water and the octanol/water systems has been included in this graph.)

Another thing seen from Fig. 2 is that bases (alkylamines, mono- and dialkanolamines) are relatively more soluble in octanol than in ether. This is probably due to the octanol being (just like *iso*-butanol; *cf.* Collander [1]) of a more acidic nature than ether.

SUMMARY

The partition of some fifty organic compounds (acids, bases, and non-electrolytes) in the solvent systems *iso*-amyl alcohol/water, octyl alcohol/water, and/or oleyl alcohol/water has been determined and compared with their previously studied partition in the *iso*-butanol/water, and ethyl ether/water systems.

The partition in one alcohol/water system can be calculated approximately from that in another such system, using the equation $\log k_1 = a \log k_2 + b$ where k_1 and k_2 denote the partition coefficients in the two solvent systems, while a and b are constants. It should, however, be noted that the "constant" b has not quite the same value in the case of solutes containing one hydrophilic group as in the case of solutes containing two or more such groups. This difference is hypothetically explained as a consequence of the formation of intermolecular hydrogen bonds between the solute molecules in non-aqueous solutions.

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