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The Distribution of Organic Compounds Between *iso*-Butanol and Water

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In the course of an investigation into the distribution of solutes between organic solvents and water (*cf.* Collander [1, 2]) it was thought of interest to study the solvent system *iso*-butanol/water, partly in order to have a monohydric alcohol included amongst the solvents studied, but also because the *iso*-butanol is a fairly good solvent even for decidedly hydrophilic substances, such as sugars and amino-acids.

Hitherto, the distribution of solutes between *iso*-butanol and water seems to have been studied scarcely at all. The distribution in the solvent system *n*-butanol/water, too, has been studied with regard to a few substances only, *viz.*, amino-acids by England and Cohn [3], some fatty acids by Archibald [4], and some organic dyes by Reinders [5].

METHODS AND EXPERIMENTAL RESULTS

Table 1 contains the distribution coefficients of some solutes in the *iso*-butanol/water system as found by the author. These distribution coefficients have been determined in about the same manner as those in the previously studied ether/water system (*cf.* Collander [2]). The *iso*-butanol used in almost all determinations was from Dr. Theodor Schuchardt, Görlitz, Germany (quality: "purum"). Most of the solutes were ordinary reagent grade. A suitable amount of the solute was shaken vigorously for about 5 minutes with butanol and water in a glass-stoppered separatory-funnel. After complete separation of the layers the concentration of the solute in each of them was determined using some of the following analytical methods: — 1. Acidimetric or alkalimetric titration in the case of almost all the acids and bases. — 2. Kjeldahl determination in the case of many compounds containing nitrogen.

— 3. Evaporation of the solvent and weighing of the non-volatile residue. — 4. If the methods 1—3 were not applicable, more specific methods were used.

The determinations do not pretend a very high degree of accuracy. Errors of about 10—20 per cent might frequently occur. The most uncertain results are given in brackets.

The first column of Table 1 gives the brutto formulae and the names of the solutes studied. The order of the compounds is determined, in the first place, by the number of carbon atoms in the molecule, in the second place, by that of nitrogen atoms, in the third and fourth place by the numbers of oxygen and hydrogen atoms. Sulphur compounds are listed immediately after the corresponding oxygen compounds, halogen compounds after the corresponding halogen-free compounds.

The second column gives the temperature in degrees centigrade.

The third column gives the concentration of the solute in the aqueous phase. The concentrations are expressed as millimols per liter solution.

The fourth column gives the distribution coefficients k_{butanol} defined as the ratio of the total concentration of the solute in the *iso*-butanol phase to its total concentration in the aqueous phase. Also the distribution coefficients referred to in the text always mean *concentration in the organic phase/concentration in the aqueous phase*, never the inverse value. In general only gross distribution ratios are given. However, in the case of acids and bases with a dissociation constant greater than 10^{-3} the distribution of the undissociated molecules has been calculated assuming that only undissociated molecules are soluble in the butanol phase. The values arrived at in this way are marked with *M*. In the case of the very strongest electrolytes, *viz.*, tetraethylammonium hydroxide, trichloroacetic acid, the sulfonic acids, and the aliphatic amino-acids, it was not, however, possible to calculate the distribution of the molecules alone.

In order to get an idea of the dependence of the distribution coefficient on the concentration, the distribution of 26 acids was studied at two different concentrations, one being roughly 10 times greater than the other. The results of these experiments are included in Table 1. (The first figure in the fourth column of this table always refers to the more dilute solution while the second refers to the more concentrated one.) It is seen that in 23 cases out of 26 the two distribution coefficients found did not differ by more than about 20 percent. Moreover, the three acids — trichloroacetic acid, oxalic acid, and salicylic acid — showing a greater difference are all very strong acids and their aberrant behaviour is thus easily explicable as a consequence of their varying degree of dissociation.

Table 1. Distribution coefficients iso-butanol/water as compared with the distribution coefficients ether/water.

Solute	°C	c_{water}	k_{butanol}	k_{ether}
CH_3I Methyl iodide	20	20.8	35	84
CH_4O Methanol	20	(2 600)	(0.6)	0.14
CH_2O_2 Formic acid	20	54.6—583	0.85—0.84	0.42
CH_5N Methylamine	20	670	0.62	0.023
CH_3ON Formamide	19	1 738	0.22	0.0014
CH_4ON_2 Urea	19	3 090	0.13	0.0_347
C_2H_5I Ethyl iodide	20	6.17	74	280
C_2H_4O Acetaldehyde	19	818	1.8	0.41 *
C_2H_6O Ethanol	20	(2 000)	(1.0)	0.26
$C_2H_4O_2$ Acetic acid	19	30.3—296	1.2—1.2	0.52
$C_2H_3ClO_2$ Chloroacetic acid	20	50.8—420	2.5—2.5 (M 2.6)	M 2.9
$C_2HCl_3O_2$ Trichloroacetic acid	18	22.0—126	2.5—5.7 (M ?)	4.2—10 (M ?)
$C_2H_3BrO_2$ Bromoacetic acid	20	81.3—263	3.7—3.5 (M 3.8)	M 4.4
$C_2H_3JO_2$ Iodoacetic acid	21	150	5.9	7.2
$C_2H_4O_3$ Glycolic acid	21	78.3—748	0.35—0.33	0.028
$C_2H_2O_4$ Oxalic acid	23	71.4—581	0.39—0.61(M 0.75)	M 0.12
C_2H_7N Ethylamine	18	44.0	1.2	0.060
» Dimethylamine	21	47.9	1.2	0.055
C_2H_7ON Ethanolamine	20	165	0.24	0.0013
$C_2H_5O_2N$ Acetamide	19	1 750	0.33	0.0025
$C_2H_4N_2$ Dicyandiamide	19	170	0.43	0.0029
$C_2H_8N_2$ Ethylenediamine	22	85.6	0.23	0.0_333
$C_2H_6ON_2$ Methyl-urea	19	982	0.24	0.0012
C_3H_6O Propionaldehyde	18	290	6.7	2.0
$C_3H_4O_2$ Acrylic acid	19	12.2—240	3.9—3.3	2.3
$C_3H_6O_2$ Methyl acetate	20	239	2.6	2.7
» Propionic acid	20	23.9—239	3.3—3.1	1.8
$C_3H_5ClO_2$ α-Chloropropionic acid	19	114	7.6 (M 8.4)	M 11*
$C_3H_5BrO_2$ α-Bromopropionic acid	20	77.7	10 (M 11)	M 15*
$C_3H_6O_3$ Lactic acid	21	60.5—612	0.66—0.72	0.091
» β-Hydroxypropionic acid	20	57.3	0.74	0.084
» Methoxyacetic acid	19	314	0.81	0.18*
$C_3H_8O_3$ Glycerol	19	2 170	0.10	0.0_366
$C_3H_4O_4$ Malonic acid	21	60.6—613	0.69—0.70(M 0.73)	M 0.10
$C_3H_6O_4$ Glycerinic acid	20	87.0—697	0.18—0.22	0.0090
C_3H_9N Propylamine	19	84.6	3.7	0.29
» Trimethylamine	21	25.5	3.1	0.46
C_3H_7ON Propionamide	19	1 020	0.69	0.013
C_3H_9ON *iso*-Propanolamine	21	385	0.43	0.0043
$C_3H_7O_2N$ α-Alanine	19	2 080	0.0069	0.0_514
$C_3H_{10}N_2$ 1,2-Propylenediamine	20	590	0.34	0.0011
» Trimethylenediamine	22	76.1	0.36	(0.0_37)

Solute	°C	c_{water}	k_{butanol}	k_{ether}
$C_3H_6O_2N_2$ Malonamide	19	911	0.086	$0.0_{3}30$
$C_3H_{10}O_2N_2$ 1,3-Diaminopropanol-2	21	820	0.12	$0.0_{3}20$
C_4H_8O Butyraldehyde	20	113	16	
$C_4H_{10}O$ *iso*-Butanol-1	20	1 124	8.5	6.9
$C_4H_8O_2$ Ethyl acetate	20	166	7.2	8.5
» *n*-Butyric acid	—	10.3—97.6	9.4—8.1	6.5
$C_4H_7BrO_2$ *a*-Bromo-*n*-butyric acid	19	30.3	25 (*M* 29)	*M* 45
$C_4H_6O_3$ *a*-Hydroxy-*iso*-butyric acid	20	46.0—452	1.2—1.2	0.26
$C_4H_4O_4$ Fumaric acid	20	18.4	4.6 (*M* 5.8)	*M* 1.5
» Maleic acid	19	54.7—247	0.88—0.98 (*M* 1.3)	*M* 0.15
$C_4H_6O_4$ Succinic acid	23	50.8	0.96	0.15
$C_4H_5BrO_4$ Bromosuccinic acid	20	39.2	4.4 (*M* 5.6)	*M* 2.9
$C_4H_{10}O_4$ Erythritol	20	(2 300)	0.037	$0.0_{3}11$
$C_4H_6O_5$ Diglycolic acid	20	345	0.49	0.030
» Malic acid	22	75.4—746	0.35—0.37	0.015
$C_4H_6O_6$ Tartaric acid	21	79.7—792	0.15—0.17	0.0034
$C_4H_{11}N$ *n*-Butylamine	19	72.8	9.2	1.1 *
» Diethylamine	21	19.1	4.4	0.53
C_4H_9ON *n*-Butyramide	18	690	1.5	0.058
$C_4H_9O_2N$ *a*-Amino-*n*-butyric acid	20	1 286	0.016	$0.0_{5}26$
$C_4H_{11}O_2N$ Diethanolamine	18	173	0.19	$0.0_{3}54$
$C_4H_7O_4N$ Aspartic acid	20	36.6	(0.010)	—
$C_4H_{10}N_2$ Piperazine	18	77.8	0.24	$0.0_{3}52$
$C_4H_{12}N_2$ Tetramethylenediamine	22	62.8	0.69	0.0013
$C_5H_{10}O_2$ *iso*-Valeric acid	20	4.6—51	21—19	20
» Trimethylacetic acid	21	15.6	32	32
$C_5H_8O_3$ Levulinic acid	20	287	1.2	0.26
$C_5H_6O_4$ Itaconic acid	22	34.4	1.8 (*M* 1.9)	*M* 0.35
$C_5H_8O_4$ Glutaric acid	19	34.4	2.0	0.27
» Dimethylmalonic acid	19	16.3	4.9	1.6
$C_5H_{12}O_4$ Pentaerythritol	19	411	0.14	$0.0_{3}30$
$C_5H_{10}O_5$ Arabinose	20	(2 000)	0.019	$(0.0_{4}38)$
C_5H_5N Pyridine	19	22.5	7.3	1.2
$C_5H_{11}N$ Piperidine	19	19	4.6	0.57
$C_5H_6N_2$ 2-Aminopyridine	—	93.2	4.5	0.77
$C_5H_{14}N_2$ Pentamethylenediamine	22	42.1	1.5	0.0025
$C_6H_{12}O_2$ Caproic acid	19	11.9	75	93
$C_6H_6O_2S$ Benzenesulfonic acid	19	73.0	0.40 (*M* ?)	0.0013
$C_6H_{10}O_4$ Adipic acid	22	22.9	3.5	0.54
$C_6H_{10}O_4$ Ethylene diacetate	20	117	2.7	2.0
$C_6H_{14}O_4$ Triethylene glycol	19	939	0.26	0.0031
$C_6H_{12}O_5$ Rhamnose	20	(1 000)	0.057	$0.0_{3}19$
$C_6H_6O_6$ Aconitic acid	20	15.6—162	2.2—1.9 (*M* 2.1)	*M* 0.50
$C_6H_8O_6$ Tricarballylic acid	20	38.9—232	0.95—0.94	0.060

Solute	°C	c_{water}	k_{butanol}	k_{ether}
$C_6H_{12}O_6$ Glucose	18	1 911	0.011	0.0_545
» Fructose	19	1 960	0.017	—
$C_6H_{14}O_6$ Mannitol	19	962	0.014	—
$C_6H_8O_7$ Citric acid	21	79.6—788	0.28—0.32	0.0086
$C_6H_{12}O_7$ Gluconic acid (+ lactone)	20	950	0.034	(0.0_32)
$C_6H_{15}N$ Hexylamine	19	8.2	83	16 *
» Dipropylamine	20	18.6	33 (*M* 41)	*M* 8.9
» Triethylamine	20	27	21	5.9
$C_6H_{15}ON$ Diethylethanolamine	23	23.3	3.1	0.35
$C_6H_{13}O_2N$ Leucine	18		0.062	0.0_412
$C_6H_{15}O_2N$ Di-*iso*-propanolamine	21	515	0.70	0.0059
$C_6H_5O_3N$ *o*-Nitrophenol	18	—	40	150
» *m*-Nitrophenol	18	—	62	160
» *p*-Nitrophenol	18	—	58	110
$C_6H_{15}O_3N$ Triethanolamine	23	167	0.26	0.0011
$C_6H_{12}N_4$ Hexamethylenetetramine	18	252	0.067	0.0_326
$C_6H_{18}N_4$ Triethylenetetramine	20	735	0.15	0.0_468
$C_7H_6O_2$ Benzoic acid	21	19.4—171	49—54	78
$C_7H_6O_3$ *o*-Hydroxybenzoic acid	22	1.6—11.1	61—85 (*M* 117)	*M* 236
» *m*- » »	20	13.1	25	21
» *p*- » »	20	11.6	27	26
$C_7H_{12}O_4$ Pimelic acid	20	40.7	7.3	1.5
» Diethylmalonic acid	19	8.4—60.1	11—12 (*M* 15)	*M* 11
$C_7H_{12}O_6$ Quinic acid	21	89.9—378	0.081—0.084	0.0_331
$C_7H_{14}O_6$ α-Methylglucoside	20	1 603	0.039	0.0_45
C_7H_9N Benzylamine	21	9.7	(9.5)	1.9
$C_7H_7O_2N$ *o*-Aminobenzoic acid	20	23.7	15	27
» *m*- » »	20	33.0	2.9	1.5
» *p*- » »	20	17.9	7.7	7.6
$C_8H_8O_2$ Phenylacetic acid	18	3.7—33.3	27—28	37
$C_8H_8O_3$ Mandelic acid	20	15.9—138	5.3—5.1	3.2
$C_8H_6O_4$ *o*-Phthalic acid	23	15.5	5.5 (*M* 7.2)	*M* 1.6
$C_8H_{18}O_5$ Tetraethylene glycol	19	732	0.24	0.0024
$C_8H_{17}N$ Coniine	18	1.75	51	—
$C_8H_{19}N$ Octylamine	19	(2.5)	(176)	—
» Di-*iso*-butylamine	21	5.05	179	151
$C_8H_{15}ON$ Tropin	19	19.2	3.1	0.053
$C_8H_{21}ON$ Tetraethylammonium hydroxide	19	129	0.015	0.0_52
$C_8H_{10}O_2N_4$ Caffeine	—	17.8	1.2	0.060
$C_9H_{16}O_4$ Azelaic acid	20	4.35	43 (*M* 46)	*M* 16
$C_9H_6O_6$ Trimesic acid	21	3.70	30	11
$C_9H_{22}N_2$ 2-Amino-5-diethylaminopentane	20	25.8	11	0.58

Solute	°C	c_{water}	k_{butanol}	k_{ether}
$C_{10}H_3O_3S$ α-Naphthalenesulfonic acid	23	42.6	1.4 (*M* ?)	0.0051
$C_{10}H_{10}O_4$ Benzylmalonic acid	—	11.0	22	15
$C_{10}H_{15}ON$ Ephedrine	18	1.96	15	2.0
$C_{11}H_{12}ON_2$ Antipyrine	20	127	3.2	0.073
$C_{12}H_{16}O_7$ Arbutine	22	201	0.28	0.0_374
$C_{12}H_{22}O_{11}$ Sucrose	18	1 300	0.0056	(0.0_511)
» Maltose	19	853	0.0040	—
$C_{13}H_{18}O_7$ Salicine	22	94.9	0.40	0.0_349
$C_{13}H_{20}O_8$ Pentaerythritol tetra-acetate	20	23.1	9.4	9.3
$C_{13}H_{20}O_2N_2$ Novocaine	19	1.69	63	64
$C_{15}H_{26}N_2$ Sparteine	—	1.2	(110) (*M* ?)	65
$C_{15}H_{16}N_4$ Neutral red (base)	20	(0.03)	110	5.0
$C_{17}H_{23}O_2N$ Atropine	17	(0.69)	(67)	(4.1)
$C_{17}H_{19}O_3N$ Morphine	19	(2.1)	(7.4)	(0.21)
$C_{17}H_{21}O_4N$ Cocaine	20	(0.40)	(107)	(138)
$C_{18}H_{21}O_3N$ Codeine	19	(2.0)	(16)	(0.80)
$C_{19}H_{21}O_3N$ Thebaine	—	(0.41)	(104)	(16)
$C_{20}H_{19}O_5N$ Berberine	18	(10)	(0.071)	< 0.005
$C_{32}H_{26}O_4N_2$ Brucine	18	(0.57)	(21)	(0.18)
$C_{32}H_{49}O_9N$ Cevadine	19	(0.37)	(146)	(280)

The distribution coefficients used in the following chapters are always those referring to the highest concentration studied or those referring to the undissociated molecules.

In the last column of Table 1 the distribution coefficients ethyl ether/water are given for the sake of comparison. These values are taken from Collander [2]. Only those values marked with an asterisk are based on later determinations not yet published.

THE DISTRIBUTION AS INFLUENCED BY THE CHEMICAL CONSTITUTION OF THE SOLUTE

On the whole the distribution of organic compounds in the solvent system *iso*-butanol/water depends on the constitution of the solutes in much the same way as their distribution in the previously studied solvent system ethyl ether/water (cf.[2]) except that the differences in the distribution coefficients are smaller in the butanol/water than in the ether/water system.

Table 2. Increase of the distribution coefficient within homologous series.

Solutes	q_{butanol}		q_{ether}
Erythritol — Pentaerythritol	$0.14 : 0.037$	= 3.8	2.7
α-Chloroacetic acid — α-Chloropropionic acid	$8.4 : 2.6$	= 3.2	3.8
Acetaldehyde — Butyraldehyde	$\sqrt{16 : 1.8}$	= 3.0	
Arabinose — Rhamnose	$0.057 : 0.019$	= 3.0	(5.0)
Acetic acid — Caproic acid	$\sqrt[4]{75 : 1.2}$	= 2.8	3.7
Methyl acetate — Ethyl acetate	$7.2 : 2.6$	= 2.8	3.1
α-Bromoacetic acid — α-Bromo-n-butyric acid	$\sqrt{29 : 3.8}$	= 2.8	3.2
Methanol — *iso*-Butanol	$\sqrt[3]{8.5 : (0.6)}$	= (2.4)	3.7
Methylamine — Di-*iso*-butylamine	$\sqrt[7]{179 : 0.62}$	= 2.2	3.5
α-Alanine — Leucine	$\sqrt[3]{0.062 : 0.0069}$	= 2.1	(2.0)
Methyl iodide — Ethyl iodide	$74 : 35$	= 2.1	3.3
Malonic acid — Diethylmalonic acid	$\sqrt[4]{15 : 0.73}$	= 2.1	3.2
Acetamide — *n*-Butyramide	$\sqrt{1.5 : 0.33}$	= 2.1	4.8
Malonic acid — Azelaic acid	$\sqrt[6]{46 : 0.73}$	= 2.0	2.3
Glycolic acid — α-Hydroxy-*iso*-butyric acid	$\sqrt{1.2 : 0.33}$	= 1.9	3.0
Ethylenediamine — Pentamethylenediamine	$\sqrt[3]{1.5 : 0.23}$	= 1.9	2.0
Diethanolamine — Di-*iso*-propanolamine	$\sqrt{0.70 : 0.19}$	= 1.9	3.3
Ethanolamine — *iso*-Propanolamine	$0.43 : 0.24$	= 1.8	3.3
Urea — Methylurea	$0.24 : 0.13$	= 1.8	2.6
Formamide — Acetamide	$0.33 : 0.22$	= 1.5	1.8
Formic acid — Acetic acid	$1.2 : 0.84$	= 1.4	1.2
Oxalic acid — Malonic acid	$0.73 : 0.75$	= 1.0	0.8

This being so it may suffice here to point out, very briefly, only some of the most conspicuous relations existing between the chemical constitution of different solutes and their distribution in the butanol/water system.

In studying the ether/water system it was found that the distribution coefficients of the members of each homologous series increase, with but a few exceptions, by a factor (q_{ether}) of about 2—4 for every new CH_2 group incorporated in the solute molecule. As seen from Table 2 the corresponding factor in the butanol/water system mostly varies between 1.8 and 3.0. Both from Table 2 and Fig. 1 it is seen that the first members of a given homologous series often differ less from each other in this respect than the following. This is especially obvious in the case of the fatty acids, the fatty acid amides, and the dicarboxylic acids. In the ether/water system the same phenomenon was observed.

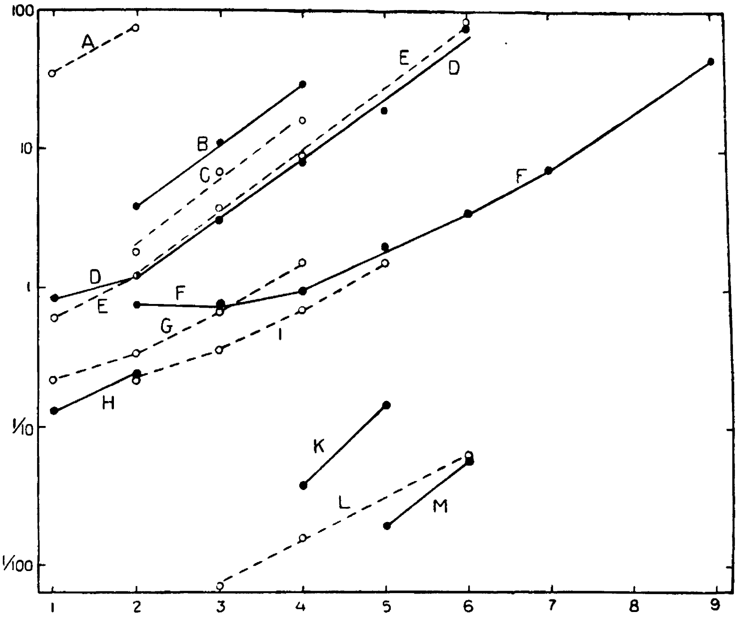

Fig. 1. Ordinate: distribution coefficient iso-butanol/water, abscissa: number of carbon atoms of the solute molecule. A alkyl iodides, B a-bromo-substituted fatty acids, C alkyl aldehydes, D fatty acids, E alkyl amines, F dicarboxylic acids, G fatty acid amides, H alkyl-ureas, I polymethylenediamines, K tetrahydric alcohols, L a-amino-acids, M pentoses.

An alcoholic hydroxyl group was found to reduce the distribution coefficient by about 5—50, sometimes even by about 190 times in the ether/water system. Correspondingly this group is now found to reduce the distribution coefficient by about 2—6 times in the butanol/water system (Table 3). More-

Table 3. Influence of an alcoholic hydroxyl group on the distribution coefficient.

Solutes	Butanol	Ether
iso-Butanol : Erythritol	$\sqrt[3]{8.5 : 0.037} = 6.1$	40
Phenylacetic acid : Mandelic acid	28 : 5.1 = 5.5	12
Ethylamine : Ethanolamine	1.2 : 0.24 = 5.0	46
Diethylamine : Diethanolamine	$\sqrt{4.4 : 0.19} = 4.5$	31
Propionic acid : α-Hydroxypropionic acid	3.1 : 0.72 = 4.3	20
» » β- » »	3.1 : 0.74 = 4.2	21
Triethylamine : Triethanolamine	$\sqrt[3]{18 : 0.26} = 4.1$	17
Acetic acid : Glycolic acid	1.2 : 0.33 = 3.6	17
Lactic acid : Glyceric acid	0.72 : 0.22 = 3.3	9.3
Tricarballylic acid : Citric acid	0.94 : 0.32 = 2.9	7.0
Succinic acid : Malic acid	0.96 : 0.37 = 2.6	10
Malic acid : Tartaric acid	0.37 : 0.17 = 2.2	4.4

Table 4. Influence of an amino-group on the distribution coefficient.

Solutes	Butanol	Ether
Caproic acid : Leucine	75 : 0.062 = 1 210	7.8×10^6
n-Butyric acid : α-Amino-*n*-butyric acid	8.1 : 0.016 = 506	2.5×10^6
Propionic acid : α-Alanine	3.1 : 0.0069 = 449	1.3×10^6
Benzoic acid : *m*-Aminobenzoic acid	54 : 2.9 = 19	52
Propylamine : 1,2-Propylenediamine	3.7 : 0.34 = 11	264
» Trimethylenediamine	3.7 : 0.36 = 10	(410)
Benzoic acid : *p*-Aminobenzoic acid	54 : 7.7 = 7.0	10
Ethylamine : Ethylenediamine	1.2 : 0.23 = 5.2	182
Ethanol : Ethanolamine	(1.0) : 0.24 = 4.2	200
Benzoic acid : *o*-Aminobenzoic acid	54 : 15 = 3.6	2.9
Propanolamine : Diaminopropanol	0.43 : 0.12 = 3.6	22
Pyridine : 2-Aminopyridine	7.3 : 4.5 = 1.6	1.6

Table 5. Influence of the substitution of a CH_3 group by a COOH group on the distribution coefficient.

Solutes	Butanol	Ether
Butylamine : α-Aminobutyric acid	9.2 : 0.016 = 575	4×10^5
Propylamine : α-Alanine	3.7 : 0.0069 = 536	2×10^5
Caproic acid : Adipic acid	75 : 3.5 = 21	172
Ethyl iodide : Iodoacetic acid	74 : 5.9 = 13	47
n-Butyric acid : Succinic acid	8.1 : 0.96 = 8.4	45
Propionic acid : Malonic acid	3.1 : 0.73 = 4.2	18
Ethanol : Glycolic acid	(1.0) : 0.33 = (3.0)	9.3
Acetic acid : Oxalic acid	1.2 : 0.75 = 1.6	4.4

Table 6. Influence of the substitution of a COOH group by a $CONH_2$ group on the distribution coefficient.

Solutes	Butanol	Ether
n-Butyric acid : *n*-Butyramide	8.1 : 1.5 = 5.4	110
Propionic acid : Propionamide	3.1 : 0.69 = 4.5	140
Formic acid : Formamide	0.84 : 0.22 = 3.8	300
Acetic acid : Acetamide	1.2 : 0.33 = 3.6	210
Malonic acid : Malonamide	$\sqrt{0.73 : 0.086} = 2.9$	18

Table 7. Influence of a halogen atom on the distribution.

Solutes	Butanol	Ether
α-Chloropropionic acid : Propionic acid	8.4 : 3.1 = 2.7	6.1
Chloroacetic acid : Acetic acid	2.6 : 1.2 = 2.2	5.6
Bromosuccinic acid : Succinic acid	5.6 : 0.96 = 5.8	19
α-Bromobutyric acid : Butyric acid	29 : 8.1 = 3.6	6.9
α-Bromopropionic acid : Propionic acid	11 : 3.1 = 3.5	8.3
Bromoacetic acid : Acetic acid	3.8 : 1.2 = 3.1	8.5
Iodoacetic acid : Acetic acid	5.9 : 1.2 = 4.9	14

over, the more numerous and the more effective the hydrophilic groups that the molecule initially contains, the smaller is in general the effect of the incorporation of a new hydroxyl group. This is readily understandable, for if such a group is introduced into a molecule containing hydrophilic groups already in advance, this generally results in the formation of an intramolecular hydrogen bond between the new hydroxyl group and an initially existing hydrophilic group. Hereby the capacity of these groups to form hydrogen bonds with the solvent molecules is, of course, reduced.

The influence of an amino-group on the distribution is very similar to that of a hydroxyl group, only somewhat stronger (Table 4). If, however, the amino-group is introduced into the molecule of an aliphatic acid so that a strongly dissociated amino-acid results, the change in distribution is, of course, much greater.

If a CH_3 group is substituted by a COOH group, the distribution coefficient ether/water gets about 4—170 times smaller, while the distribution coefficient butanol/water gets 1.6—21 times smaller (Table 5). In this case, also, the formation of strongly dissociated amino-acids causes a much stronger diminution of the distribution coefficients.

When a COOH group is substituted by a $CONH_2$ group the distribution coefficient ether/water becomes 18—300 times smaller while the distribution coefficient butanol/water becomes 2.9—5.4 times smaller (Table 6).

A halogen atom, quite in contrast so the substituents hitherto mentioned, makes the distribution coefficient greater: by about 5.6—19 times in the ether/water system and by about 2.2—5.8 times in the butanol/water system (Table 7). This effect increases in the series $Cl < Br < I$.

On the whole, the distribution of organic compounds between *iso*-butanol and water, just like that between ether and water, is largely understandable if we assume that it is principally due to the formation of hydrogen bonds between solute and solvent molecules.

THE DISTRIBUTION IN THE SOLVENT SYSTEM ISO-BUTANOL/WATER AS COMPARED WITH THAT IN THE ETHER/WATER SYSTEM

A comparison of the distribution in the butanol/water system with that in the ether/water system may profitably be based on Fig. 2. In this graph all 138 solutes whose distribution in both these solvent systems has been studied are represented by points, with the only exception of those 10 solutes whose ether/water distribution coefficient is smaller than 1/10 000. If the distribution coefficients in the butanol/water system were identical with those in the ether/water system, all the points would evidently lie on the straight line

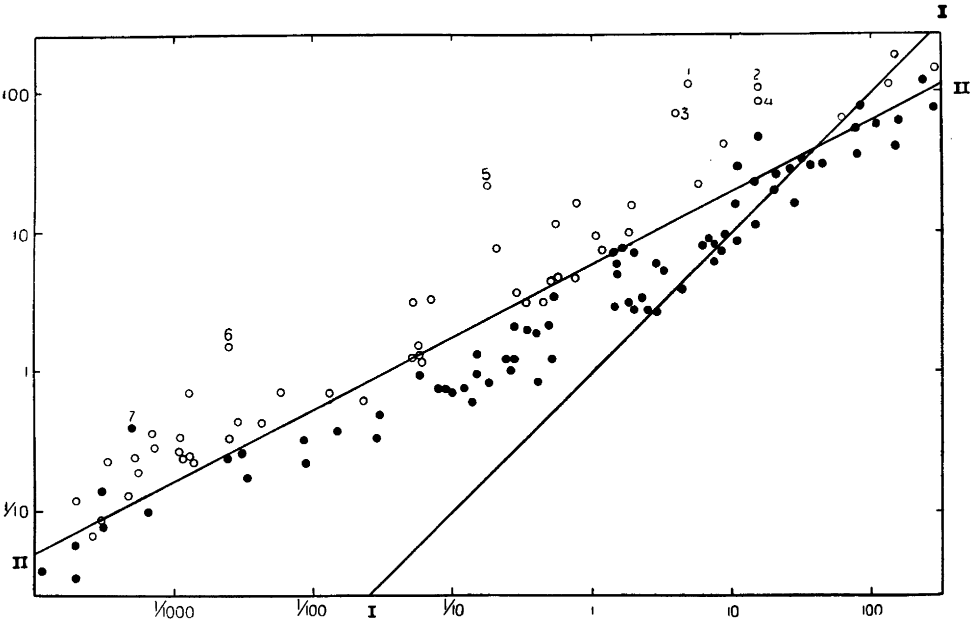

Fig. 2. Abscissa: distribution coefficient in the ether/water system, ordinate: distribution coefficient in the iso-butanol/water system. ● *N-free compounds, nitro-compounds, and amino-acids,* ○ *amines, imines, and amides. The most aberrant points are: 1 neutral red, 2 thebaine, 3 atropine, 4 di-iso-butylamine, 5 brucine, 6 pentamethylenediamine, 7 salicine.*

I whose slope is 45°. In reality, however, the points are scattered along the straight line II whose slope is much less steep. This is an expression of the already stated fact that the distribution coefficients of different solutes in the butanol/water system differ much less from each other than the corresponding distribution coefficients in the ether/water system. Thus, if the distribution coefficients of two solutes in the ether/water system are as, say, 1 : 1 000 000, then their distribution coefficients in the butanol/water system will be as about 1 : 1 000.

Mathematically the correlation existing between the distribution coefficients in these two solvent systems may be expressed by the equation

$$\log k_{\text{butanol}} = a \cdot \log k_{\text{ether}} + b.$$

In this equation a, which is an expression for the slope of the line II, has a value of about 0.5, while b, which is an expression for the height of the same line, has a value of about + 0.8. (*Cf.* Collander[1, p. 368].)

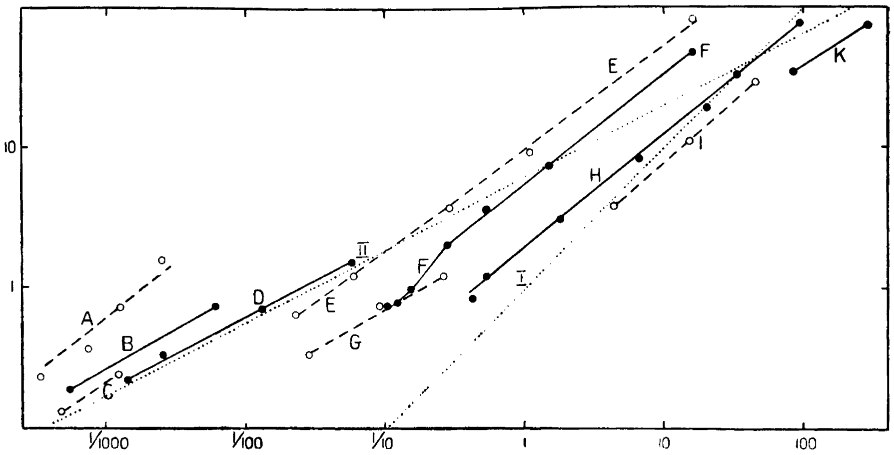

Fig. 3. Relations between ether/water distribution coefficients (abscissa) and iso-butanol/water distribution coefficients (ordinate) in some homologous series. A polymethylenediamines, B aminodiols, C alkyl-ureas, D fatty acid amides, E alkylamines, F dicarboxylic acids, G a-hydroxy-substituted fatty acids, H fatty acids, I a-bromo-substituted fatty acids, K alkyl iodides.

The relative smallness of the differences between the distribution coefficients of different solutes in the butanol/water system is a consequence of the fact that butanol is a considerably more hydrophilic, *i. e.*, a more hydrogen bonded solvent than, *e. g.*, ethyl ether. For, owing to the relative similarity of butanol and water as solvents, the work necessary to transport one mole of a solute from the aqueous phase to the butanolic phase, or vice versa, is evidently much smaller than the work necessary to transport the same amount of the same solute from the aqueous phase to the ether phase, or vice versa.

From Fig. 2 it is, however, also seen that the points representing the different solutes are not irregularly scattered on both sides of line II, but that the overwhelming majority of the points representing more or less basic compounds (amines, imines, amides) lie above this line while the points representing neutral or acidic compounds lie, for the most part, below it. Butanol is thus, *ceteris paribus*, a better solvet for basic compounds than is ether. This is almost certainly due to the fact that butanol, like other alcohols, is a more acidic compound than ether.

Fig. 3 shows more in detail how the distribution of some homologous series in the butanol/water system is correlated with their distribution in the ether/water system. For the sake of clearness solutes belonging to 10 series only are included in this graph. The lines I and II are the same as in Fig. 2. It is seen that the lines representing different homologous series are, as was to be expected, scattered along line II, the series comprising basic compounds being situated a little above it, the series of neutral or acidic compounds a little below it. It is, however, also seen that the lines representing homologous series do not run exactly parallelly with line II but have a somewhat steeper slope so that many of them begin below line II but end above it. This means that, although all differences in the distribution coefficients of different solutes are smaller in the butanol/water than in the ether/water system, this diminution of the differences in the first-named system is less marked if we compare solutes which differ as to the length of their carbon chains than if we compare solutes differing as to their more or less hydrophilic substituents. The reason for this is not quite clear.

Finally it may be pointed out that the most aberrant points in Fig. 2 nearly all represent very large molecules, *e. g.*, alkaloids. This is probably no mere chance but a circumstance connected with the just-mentioned fact that the points representing higher homologues are situated higher in Fig. 2 than the points representing lower homologues.

SUMMARY

The distribution of 145 organic compounds between *iso*-butanol and water has been determined experimentally. The distribution coefficients thus found are given in Table 1.

An inspection of them shows that the distribution in this solvent system is influenced by the chemical constitution of the solute in much the same way as the previously studied distribution of the same solutes in the solvent system ether/water.

The distribution coefficients of the different solutes differ, however, considerably less in the butanol/water system than in the ether/water system. Thus, if the distribution coefficients of two solutes in the latter system are as 1 : 1 000 000 they will be, in the first-named system, as about 1 : 1 000. (*Cf.* Fig. 2.) This is a consequence of the fact that butanol is a much more hydrogen bonded solvent than is ether.

Basic compounds (amines, imines, amides) have *ceteris paribus* a relatively greater solubility in butanol than have neutral or acidic compounds. This is very probably due to the more acidic nature of butanol as compared with ether.

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