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Linear Solvation Energy Relationship (LSER) Analysis of Liquid−Liquid Distribution Constants of 8-Hydroxyquinoline and Its Derivatives

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ABSTRACT: The linear solvation energy relationship (LSER) analysis of liquid−liquid distribution constants of 8-hydroxyquinoline and its derivatives has been performed in terms of hydrophobicity of solutes, property parameters of diluents in the organic phase, and ionic strength of the aqueous phase. The effect of temperature has been also discussed. The obtained correlations permit the evaluation of unknown values of distribution constants of 8-hydroxyquinoline and/or its derivatives in the given extraction system. The set of available systematic experimental data reflects only the effect of temperature on the distribution of 8-hydroxyquinoline and its 2-methyl derivative; however, the distribution constants of the other 8-hydroxyquinolinols were determined sporadically at the different ionic strengths of the aqueous phase and lower or higher temperatures than 298 K. The correlation describing the effect of temperature can be used for the raw estimation of unknown values of distribution constants of 8-hydroxyquinoline and/or its derivatives in the given extraction system within the temperature range from (20 to 50) °C.

1. INTRODUCTION

8-Hydroxyquinoline and its derivatives are known as chelating ligands, forming stable complexes with a great number of metal ions. In chemical analysis, 8-hydroxyquinoline and its alkyl and/or halogen-substituted derivatives of different hydrophobicities are frequently used as chelating extractants suitable for separation and preconcentration of trace elements.[1] The hydrophobic derivative of 8-hydroxyquinoline substituted at position 5 with an octyloxymethyl group has been used for the extractive separation and spectrophotometric determination of copper.[2]

Strongly hydrophobic derivatives of 8-hydroxyquinoline, particularly substituted at position 7 with a long alkyl or alkenyl group, are important industrial chelating extractants. Kelex 100 (Ashland, Sherex) is a well-known trade name for an industrial extractant which has been designed for the extraction of copper and germanium from acidic solutions and gallium from alkaline solutions.[3−6] The active component of Kelex 100 (Ashland) is 7-(5′,5′,7′,7′-tetramethyl-1′-octenyl)-8-hydroxyquinoline. Since 1976, Kelex 100 (Sherex) has contained 7-(4′-ethyl-1′-methyloctyl)-8-hydroxyquinoline. The next extractant of this kind, Kelex 108 (Sherex), contains 7-(2′-ethylhexyl)-8-hydroxyquinoline.[7] LIX 26 (Henkel) is composed of a mixture of 7-alkyl derivatives of 8-hydroxyquinoline.[8] A series of hydrophobic TN extractants substituted at position 7 with a C_{10}−C_{13} hydrocarbon chain has been synthesized especially for the separation and recovery of the platinum group metals. Extractants TN 1911 and TN 2181 contain 7-alkenyl derivatives, whereas TN 2221 and TN 2336 are 7-alkyl derivatives of 8-hydroxyquinolines.[9,10] Further examples of highly hydrophobic derivatives of 8-hydroxyquinoline are 7-(1′-vinyl-1′,5′,9′,13′-tetramethyltetradecanyl)-8-hydroxyquinoline and 7-(1′-ethyl-1′,5′,9′,13′-tetramethyltetradecanyl)-8-hydroxyquinoline, which exhibit the extraction ability of Cu(II) similar to that of Kelex 100.[11] Special attention has been paid to the hydrophobicity of 5-alkoxymethyl-8-hydroxyquinolines, particularly to their 2-methyl-, 2-butyl-, and 2-*t*-butyl derivatives, which are responsible for the effective extraction of Ga(III) from acidic solutions and its separation from Al(III).[12]

It should be noted that different 8-quinolinols and their complexes with Cu(II) are biologically active. They exhibit antifungal action[13−16] and antimalarian activity[17] and inactivate some types of viruses.[18] Recently, a series of compounds with 8-hydroxyquinoline moiety has been synthesized as potential HIV-1 integrase inhibitors.[19]

The distribution of organic solutes in two-phase liquid systems depends on the temperature, pH, and concentration of electrolytes in the aqueous phase and on the composition of the organic phase, respectively.

The distribution of 8-hydroxyquinoline, HQ, in organic solvent−water systems can be written as follows:

$$HQ_{(a)} \leftrightarrow HQ_{(o)} \tag{1}$$

where indices a and o refer to the aqueous and organic phases, respectively.

The distribution constant, K_D, is expressed as the ratio of equilibrium concentrations of 8-hydroxyquinoline in both phases:

$$K_D = \frac{[HQ]_o}{[HQ]_a} \tag{2}$$

The distribution ratio, D, is defined as the ratio of analytical concentrations of 8-hydroxyquinoline in both phases:

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Table 1. Distribution Constants of 8-Hydroxyquinoline and Its Derivatives in the Solvent Extraction Systems[22,25−54]

solute and solvent	t / °C	I	log K_D	ref	solute and solvent	t / °C	I	log K_D	ref
HQ					**HQ**				
hexane	25	0.10	1.33	25	tetrachloromethane	25	0.10	2.05	26
hexane	25	0.10	1.34	26	tetrachloromethane	25	0.10	2.06	25, 31
heptane	25	0.10	1.35	26	1,2-dichloroethane	25	0.10	2.56	25
heptane	30	0.15	1.34	27	1,1,2,2-TCE[a]	20	0.10	2.64	32
octane	25	0.10	1.34	26	trichloroethylene	25	0.10	2.38	25, 31
benzene	25	0.10	2.35	26	chlorobenzene	25	0.10	2.39	26
benzene	25	0.10	2.42	28	1,2-dichlorobenzene	25	0.10	2.48	25
benzene	25	0.10	2.36	28, 29	nitrobenzene	25	0.10	2.59	29, 30
benzene	25	0.10	2.27	28	nitrobenzene	35	0.10	2.58	29
benzene	25	0.10	2.32	28	dibromomethane	25	0.10	2.65	25
benzene	35	0.10	2.30	29	1-bromobutane	25	0.10	2.20	25
benzene	45	0.10	2.28	29	3-pentanone	25	0.10	2.18	31
benzene	25	0.25	2.41	28	4-methyl-2-pentanone	25	0.10	2.13	31
benzene	25	0.25	2.39	28	4-methyl-2-pentanone	25	0.50	2.15	30
benzene	25	0.25	2.26	28	*i*-pentyl acetate	25	0.10	2.24	31
benzene	25	0.25	2.25	28	1-butanol	25	0.10	1.65	31
benzene	25	0.50	2.44	28	1-octanol	25	0	1.94	22, 37
benzene	25	0.50	2.28	28	1-octanol	25	0.01	1.97	38
benzene	25	0.50	2.29	28	1-octanol	20	0.10	1.94	32
benzene	25	0.75	2.46	28	1-octanol	25	0.10	1.96	31
benzene	25	0.75	2.49	28	1-octanol	25	0.10	1.85	39
benzene	25	0.75	2.28	28	**2-M-HQ**				
benzene	25	0.75	2.30	28	heptane	25	0.10	1.93	40
benzene	25	1.00	2.52	28	heptane	45	0.10	2.03	41
benzene	25	1.00	2.51	28	heptane	30	0.15	1.90	27
benzene	25	1.00	2.31	28	toluene	25	0.10	2.75	31
benzene	25	1.00	2.38	28, 30	toluene	30	0.15	2.71	27
benzene	25	1.25	2.55	28	dichloromethane	25	0.10	3.10	31
benzene	25	1.25	2.32	28	chloroform	25	0.10	3.22	31, 34
benzene	25	1.25	2.31	28	chloroform	25	1.00	3.16	36
benzene	25	1.50	2.58	28	tetrachloromethane	25	0.10	2.64	31
benzene	25	1.50	2.32	28	1,1,2,2-tce[a]	20	0.10	3.15	32
toluene	25	0.10	2.21	26, 31	1,2-dichlorobenzene	25	0.10	3.00	31
toluene	25	0.10	2.24	29	3-pentanone	25	0.10	2.52	31
toluene	35	0.10	2.22	29	4-methyl-2-pentanone	25	0.10	2.50	31
toluene	45	0.10	2.20	29	*i*-pentyl acetate	25	0.10	2.61	31
toluene	30	0.15	2.32	27	1-butanol	25	0.10	1.92	31
m-xylene	25	0.10	2.12	26	1-octanol	25	0.10	2.33	31
p-xylene	20	0.10	2.09	32	**4-M-HQ**				
i-propylbenzene	25	0.10	2.03	26	toluene	25	0.10	2.77	31
dichloromethane	25	0.10	2.58	25, 26, 31	dichloromethane	25	0.10	3.17	31
chloroform	18	0.10	2.70	33	chloroform	25	0.10	3.27	31, 34
chloroform	25	0.10	2.58	26	chloroform	20	0.20	2.65	35
chloroform	25	0.10	2.63	29	tetrachloromethane	25	0.10	2.73	31
chloroform	25	0.10	2.64	25, 31, 34	1,2-dichlorobenzene	25	0.10	3.01	31
chloroform	30	0.10	2.60	33	3-pentanone	25	0.10	2.52	31
chloroform	35	0.10	2.60	29	4-methyl-2-pentanone	25	0.10	2.63	31
chloroform	45	0.10	2.53	29	*i*-pentyl acetate	25	0.10	2.69	31
chloroform	50	0.10	2.50	29	1-butanol	25	0.10	1.96	31
chloroform	20	0.20	2.37	35	1-octanol	25	0	2.36	22
chloroform	25	0.50	2.55	30	1-octanol	25	0.10	2.41	31

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Table 1. Continued

solute and solvent	t / °C	I	log K_D	ref
chloroform	25	1.00	2.49	36
5-M-HQ				
chloroform	25	0.10	3.28	42
chloroform	20	0.20	2.83	35
chloroform	25	1.00	3.19	36
1-octanol	25	0	2.37	22
1-octanol	25	0	2.38	37
7-M-HQ				
chloroform	25	1.00	3.38	36
7-E-HQ				
chloroform	25	1.00	4.27	36
5-O-HQ				
chloroform	25	0.10	5.52	43
tetrachloromethane	25	0.10	4.92	43
4,5-DM-HQ				
1-octanol	25	0	2.71	22
5,7-DM-HQ				
chloroform	25	0.10	3.38	44
7-Dodecenyl-HQ				
chloroform	25	0.10	5.52	45
1-octanol	24	1.50	6.70	46
5-OOM-HQ				
heptane	25	0.10	4.60	47
1,2-dichloroethane	25	0.10	5.00	47
2-M-5-MOM-HQ				
heptane	25	0.10	1.63	48
2-M-5-EOM-HQ				
heptane	25	0.10	1.97	40
2-M-5-BOM-HQ				
heptane	25	0.10	3.23	40
heptane	45	0.10	3.35	41
2-M-5-HOM-HQ				
heptane	25	0.10	4.27	40
5-F-HQ				
heptane	30	0.15	1.68	27
toluene	30	0.15	2.41	27
1-octanol	25	0	2.30	49
4-Cl-HQ				
1-octanol	25	0	2.67	22
5-Cl-HQ				
heptane	30	0.15	2.30	27
toluene	30	0.15	3.11	27
chloroform	25	0.10	3.32	34
1-octanol	25	0	2.91	37
1-octanol	25	0.01	2.88	38
1-octanol	25	0.10	2.51	39
5-Br-HQ				
chloroform	25	0.10	3.51	34
5-I-HQ				
chloroform	25	0.10	3.75	34
1-octanol	25	0	3.27	37, 49
5-NO_2-HQ				
benzene	25	0.01	2.53	50
chloroform	25	0.01	2.81	50
chloroform	25	0.10	2.64	34
tetrachloromethane	25	0.01	1.85	50
1,2-dichloroethane	25	0.01	2.70	50
carbon disulfide	25	0.01	1.89	50
1-octanol	25	0.01	1.98	38
4-NH_2-HQ				
1-octanol	25	0	−0.11	22
5,7-DCl-HQ				
toluene	25	0.10	3.25	43
chloroform	25	0.10	3.86	51
tetrachloromethane	25	0.10	3.21	43
chlorobenzene	25	0.10	3.68	43
5-Cl-7-I-HQ				
chloroform	25	0.10	3.88	52
5,7-DBr-HQ				
benzene	25	0	2.29	52
toluene	25	0	2.27	52
chloroform	25	0.10	4.15	51
chloroform	20	3.00	4.35	53
tetrachloromethane	25	0	2.02	52
1,2-dichloroethane	25	0	2.57	52
diethyl ether	25	0	2.12	52
butyl acetate	25	0	2.29	52
1-butanol	25	0	1.54	52
5,7-DI-HQ				
chloroform	25	0.10	4.15	51
2-M-5,7-DCl-HQ				
hexane	25	0.10	3.37	54
hexane	25	0.50	3.33	54
hexane	25	1.00	3.35	54
hexane	25	1.00	3.54	54
hexane	25	1.00	3.39	54
hexane	25	1.00	3.51	54
hexane	25	2.00	3.33	54
hexane	25	3.00	3.67	54
benzene	25	0.10	4.34	54
chloroform	25	0.10	4.55	54
chloroform	25	0.50	4.59	54
chloroform	25	1.00	4.52	54
chloroform	25	1.00	4.87	54
chloroform	25	1.00	4.70	54
chloroform	25	1.00	4.86	54
chloroform	25	2.00	4.51	54
chloroform	25	3.00	4.90	54

[a] 1,1,2,2-TCE: 1,1,2,2-tetrachloroethane.

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Table 2. Test Set of Distribution Constants of 8-Hydroxyquinoline and Its Derivatives in the Solvent Extraction Systems[30,31,54−63]

solute and solvent	t / °C	I	log K_D	ref
HQ				
heptane	45	0.10	1.35	55
octane	25	0.10	1.33	56
toluene	20	0.01	1.94	57
tetrachloromethane	20	1.00	2.10	30
tetrachloromethane	20	1.00	1.97	30
tetrachloromethane	30	0.10	2.30	30
1,2-dichloroethane	20	1.00	2.49	30
1,2-dichloroethane	20	1.00	2.25	30
1,2-dichloroethane	25	0.10	2.26	58
4-methyl-2-pentanone	25	0.10	2.18	30
dioctyl phtalate	25	0.10	1.78	59
Octane/1-Octanol				
x_{ROH} = 0.050	25	0.10	1.41	56
x_{ROH} = 0.163	25	0.10	1.50	56
x_{ROH} = 0.325	25	0.10	1.64	56
x_{ROH} = 0.643	25	0.10	1.82	56
3-methyl-1-butanol	25	0.10	1.79	31
3-methyl-1-butanol	25	0.50	1.79	30
3-methyl-1-butanol	25	1.00	1.80	30
3-methyl-1-butanol	25	1.00	1.85	30
3-methyl-1-butanol	25	2.00	1.97	30
3-methyl-1-butanol	25	2.00	2.09	30
3-methyl-1-butanol	25	2.00	2.00	30
3-methyl-1-butanol	25	2.00	1.95	30
3-methyl-1-butanol	25	2.00	1.85	30
1-octanol	25	0.10	1.94	56
2-M-HQ				
heptane	45	0.10	2.03	55
3-methyl-1-butanol	25	0.10	2.13	31
4-M-HQ				
3-methyl-1-butanol	25	0.10	2.19	31
5-MOM-HQ				
heptane	25	0.10	1.03	60
toluene	25	0.10	2.13	61
chloroform	25	0.10	2.88	60
1,2-dichloroethane	25	0.10	2.56	58
5-EOM-HQ				
heptane	25	0.10	1.48	60
1,2-dichloroethane	25	0.10	2.86	58
5-PrOM-HQ				
heptane	25	0.10	2.22	60
chloroform	25	0.10	3.98	60
1,2-dichloroethane	25	0.10	3.45	58
5-BuOM-HQ				
heptane	25	0.10	2.73	60
5-POM-HQ				
heptane	25	0.10	3.42	60
toluene	25	0.10	4.37	61
chloroform	25	0.10	5.13	60
1,2-dichloroethane	25	0.10	4.52	58
5-HOM-HQ				
heptane	25	0.10	3.94	60
heptane	45	0.10	3.51	55
5-OOM-HQ				
heptane	25	0.10	5.08	60
1,2-dichloroethane	25	0.10	>5	58
dioctyl phtalate	25	0.10	4.38	59
2-M-5-BOM-HQ				
heptane	45	0.10	3.35	55
2-M-5-HOM-HQ				
heptane	45	0.10	4.08	55
5-F3EOM-HQ				
heptane	45	0.10	1.33	55
5-Cl-8-HQ				
heptane	45	0.10	2.27	55
1-octanol	37	0.10	2.57	62
5,7-DCl-HQ				
chloroform	18.5	1.00	3.55	63
chloroform	18.5	1.00	3.93	63
chloroform	25	0.10	4.05	30
pentyl acetate	25	0.10	3.70	30
5,7-DI-HQ				
chloroform	18.5	1.00	4.03	63
2-M-5,7-DCl-HQ				
3-methyl-1-butanol	25	0.10	3.29	54

$$D = \frac{c_{HQ(o)}}{c_{HQ(a)}} \quad (3)$$

In acidic solutions 8-hydroxyquinoline is protonated, and its cationic form, H_2Q^+, behaves as a weak diprotic acid:

$$H_2Q^+_{(a)} \leftrightarrow HQ_{(a)} + H^+_{(a)} \qquad K_{a1} \quad (4)$$

$$K_{a1} = \frac{[H^+]_a[HQ]_a}{[H_2Q^+]_a} \quad (5)$$

$$HQ_{(a)} \leftrightarrow H^+_{(a)} + Q^-_{(a)} \qquad K_{a2} \quad (6)$$

$$K_{a2} = \frac{[H^+]_a[Q^-]_a}{[HQ]_a} \quad (7)$$

The analytical concentration of 8-hydroxyquinoline in the aqueous phase is equal to the sum of equilibrium concentrations of its neutral and ionic species:

$$c_{HQ(a)} = [H_2Q^+]_a + [HQ]_a + [Q^-]_a \quad (8)$$

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From eqs 5, 7, and 8, it follows that:

$$c_{HQ(a)} = \frac{[H^+]_a[HQ]_a}{K_{a1}} + [HQ]_a + K_{a2}\frac{[HQ]_a}{[H^+]_a} = [HQ]_a\left(\frac{[H^+]_a}{K_{a1}} + 1 + \frac{K_{a2}}{[H^+]_a}\right) \quad (9)$$

Assuming that 8-hydroxyquinoline does not associate in the organic phase, one can write:

$$c_{HQ(o)} = [HQ]_o = K_D[HQ]_a \quad (10)$$

The substitution of eqs 9 and 10 into eq 3 leads to the expression:

$$D = \frac{K_D}{\frac{[H^+]_a}{K_{a1}} + 1 + \frac{K_{a2}}{[H^+]_a}} \quad (11)$$

which permits us to evaluate the distribution ratio of 8-hydroxyquinoline within the whole range of pH of the aqueous phase from the corresponding values of distribution constant and both dissociation constants. The above considerations are also valid for other 8-quinolinols because their behavior in the extraction systems is similar to that of 8-hydroxyquinoline.

The diluents applied in metal extractions influence both the physical properties of the organic phase (e.g., density and viscosity) and the interfacial phenomena, as well as extraction equilibria and kinetics.[1,6,20] Solvating and nonsolvating diluents are used in metal extraction systems involving 8-quinolinols.[1,2,11,12] The distribution constants of drugs in cyclohexane−water, chloroform−water, and 1-octanol−water systems are used to characterized their lipophilicity.[21] Also, the biological activity of compounds involving 8-hydroxyquinoline moiety has been correlated with their distribution constants in the 1-octanol−water system.[19,22]

The empirical model of solvent effects developed by Kamlet et al.[23] can be used for interpretation of the effect of diluents upon phenomena and processes governing an extraction system. In the previous paper[24] this model has been applied for the analysis of liquid−liquid distribution constants of 8-hydroxyquinoline, its 2-, 4-, and 5-methyl derivatives, and Kelex 100 (Ashland) in 20 organic solvent−water systems, using three aliphatic and four aromatic hydrocarbons, nine halogenated aliphatic and aromatic hydrocarbons, 4-methyl-2-pentanone, *i*-pentyl acetate, 1-butanol, and 1-octanol. The present work deals with the following subjects: (i) the hydrophobicity and lipophilicity of 8-quinololinols of different structures, which are the factors governing their distribution in a given system of organic solvent/water or aqueous solution; (ii) an analysis of solvent and ionic strength effects on the distribution of 8-hydroxyquinolines at 25 °C; (iii) the effect of temperature on the distribution of different 8-quinolinols.

The structures and names of considered 8-quinolinols are indicated in Appendix A. The distribution constants of 8-hydroxyquinoline and its derivatives determined experimentally in organic solvent/water and/or organic solvent/aqueous solution systems[22,25−63] are collected in Tables 1 and 2.

2. MODELS AND COMPUTING

The model of Kamlet and Taft of solvents effects is a multiparametric linear model:

Table 3. Dimensionless Solvatochromic Parameters[23,64−68] and Cohesive Energy Density of Solvents[69]

solvent	α	β	π^*	δ_H^2 / MJ·m^{-3}
hexane	0.00	0.00	−0.04	225.00
heptane	0.00	0.00	−0.08	231.04
octane	0.00	0.00	0.01	243.36
benzene	0.00	0.10	0.59	353.44
toluene	0.00	0.11	0.54	334.89
i-propylbenzene	0.00	0.12	0.51	327.61
m-xylene	0.00	0.12	0.47	334.89
p-xylene	0.00	0.12	0.43	327.61
dichloromethane	0.13	0.10	0.82	392.04
chloroform	0.20	0.10	0.58	357.21
tetrachloromethane	0.00	0.05	0.28	309.76
1,2-dichloroethane	0.00	0.10	0.81	416.16
1,1,2,2-tetrachloroethane	0.00	0.00	0.95	392.04
trichloroethylene	0.00	0.05	0.53	353.44
chlorobenzene	0.00	0.07	0.71	380.25
1,2-dichlorobenzene	0.00	0.03	0.8	416.16
nitrobenzene	0.00	0.30	1.01	497.29
dibromomethane	0.00	0.00	0.92	441.00
1-bromobutane	0.00	0.13	0.5	316.84
diethyl ether	0.00	0.47	0.27	228.01
3-pentanone	0.00	0.45	0.72	324.00
4-methyl-2-pentanone	0.02	0.48	0.65	313.29
butyl acetate	0.00	0.45	0.46	302.76
pentyl acetate	0.00	0.45	0.46	302.76
i-pentyl acetate	0.00	0.45	0.49	292.41
dioctyl phthalate	0.04	0.39	0.65	331.24
1-butanol[a]	0.85	0.81	0.68	827.00
1-pentanol[a]	0.80	0.78	0.63	625.00
1-octanol[a]	0.81	0.77	0.52	500.00
carbon disulfide	0.00	0.07	0.61	420.25

[a] Alcohols saturated with water.

$$\log P = f(\pi^*, \alpha, \beta, \delta_H^2) \quad (12)$$

where P stands for a solvent-dependent property of solute. Model 12 operates with the dimensionless parameters of dipolarity/polarizability (π^*) and hydrogen-bond donating (α) and accepting (β) abilities of solvents.[23,64−68] The cavity formation term in this model is proportional to the cohesive energy density of solvents expressed as a square of their Hildebrand solubility parameters, δ_H.[69] According to Marcus,[65−67] the organic solvents saturated with water can be considered as "dry" and "wet" solvents, respectively. The "dry" water-saturated solvents exhibit substantially the same properties as neat solvents when the mole fraction of water does not exceed 0.13. The typical "wet" solvents are higher alkanols, for example, 1-butanol and 1-octanol.[65,67]

In the present work, the property P denotes the distribution constants, K_D, of all 8-quinolinols as solutes partitioned between the phases of an extraction system. The property parameters of considered organic solvents are given in Table 3. The unknown property parameters of water-saturated 3-methyl-1-butanol have

Table 4. Molar Intrinsic Volumes, V_x, Hydrophile−Lipophile Balances, HLB^{Go}, of 8-Hydroxyquinoline and Its Derivatives[70,71]

solute	V_x / $cm^3 \cdot mol^{-1}$	HLB^{Go}	solute	V_x / $cm^3 \cdot mol^{-1}$	HLB^{Go}
HQ	110.30	6.28	5-EOM-HQ	158.44	6.16
2-M-HQ	124.39	5.81	5-PrOM-HQ	172.53	5.69
4-M-HQ	124.39	5.81	5-BOM-HQ	186.62	5.22
5-M-HQ	124.39	5.81	5-POM-HQ	200.71	4.74
6-M-HQ	124.39	5.81	5-HOM-HQ	214.80	4.27
7-M-HQ	124.39	5.81	5-OOM-HQ	242.98	3.31
7-E-HQ	138.48	5.33	5-F3EOM-HQ	163.72	5.98
7-Pr-HQ	152.57	4.86	2-M-5-MOM-HQ	158.44	6.16
7-*i*-Pr-HQ	152.57	4.86	2-M-5-EOM-HQ	172.53	5.69
7-Propenyl-HQ	148.27	5.00	2-M-5-BOM-HQ	200.71	4.74
7-Allyl-HQ	148.27	5.00	2-M-5-HOM-HQ	228.89	3.79
2-B-HQ	166.66	4.38	2-M-5-OOM-HQ	257.07	2.84
7-*s*-B-HQ	166.66	4.38	5-F-HQ	112.06	6.22
7-*t*-B-HQ	166.66	4.38	4-Cl-HQ	122.54	5.87
7-*s*-P-HQ	180.75	3.91	5-Cl-HQ	122.54	5.87
5-O-HQ	223.04	2.48	5-Br-HQ	127.80	5.69
7-Dodecenyl-HQ	275.08	0.73	5-I-HQ	142.68	5.19
2,4-DM-HQ	138.48	5.33	5-NO_2-HQ	127.72	5.70
2,7-DM-HQ	138.48	5.33	4-NH_2-HQ	120.28	7.45
3,4-DM-HQ	138.48	5.33	5,7-DCl-HQ	134.78	5.46
4,5-DM-HQ	138.48	5.33	5-Cl-7-I-HQ	148.37	5.00
5,7-DM-HQ	138.48	5.33	5,7-DBr-HQ	145.30	5.10
3-i-Pr-4-M-HQ	166.66	4.38	5,7-DI-HQ	161.96	4.54
5-MOM-HQ	144.35	6.64	2-M-5,7-DCl-HQ	148.87	4.98

been assumed to be the same as those of water-saturated 1-pentanol.

According to McGowan,[70,71] the hydrophile−lipophile balance, HLB, of a given 8-hydroxyquinolinol is defined as follows:

$$HLB = 7 - 0.0337V_x + 1.5n \quad (13)$$

where V_x is its molar intrinsic volume and n denotes the number of oxygen and nitrogen atoms which are able to interact with molecules of water. There are the alkyl-, alkenyl-, and halogen derivatives of 8-hydroxyquinoline, involving only a nitrogen atom in the pyridyl ring and an oxygen atom in the hydroxyl group of the phenyl ring. Therefore, for these solutes the parameter n in eq 13 is equal to 2. Alkyloxymethyl derivatives of 8-hydroxyquinoline, however, involve one nitrogen atom in pyridyl ring and two oxygen atoms of substituents. As a result, the parameter n in eq 13 for alkyloxymethyl-8-hydroxyquinolines is equal to 3. Let us compare now the hydrophobicity of 4-amino-8-hydroxyquinoline and 5-nitro-8-hydroxyquinoline. The molar intrinsic volumes of these compounds are equal to (120.28 and 127.72) $cm^3 \cdot mol^{-1}$, respectively. However, 4-amino-8-hydroxyquinoline is more hydrophilic than 5-nitro-8-hydroxyquinoline since its distribution constant in octanol/water system (I = 0) is 2 orders of magnitude lower than that of 5-nitro-8-hydroxyquinoline in the octanol/aqueous solution (I = 0.01) system. This behavior of 4-amino-8-hydroxyquinoline is justified since its HLB is determined, taking the parameter n equal to 3, in accordance with two nitrogen and one oxygen atoms involved in its molecule, whereas the value of HLB of 5-nitro-8-hydroxyquinoline has been calculated assuming that parameter n in eq 13 is equal to 2, irrespective of nitrogen and oxygen atoms involved in the NO_2 group. The latter assumption seems to be justified since the nitro group is an electron-withdrawing substituent; however, its polar character and ability to form the hydrogen bonds with donors of protons do not promote the solubility of nitro compounds in water and aqueous solutions.[72] The molar intrinsic volumes and HLB of considered 8-hydroxyquinolinols are listed in Table 4.

The distribution constants of different 8-quinolinols can be correlated with the property parameters of solvents and corresponding values of molar intrinsic volumes or HLB:

$$\log K_D = f(\pi^*, \alpha, \beta, \delta_H^2, V_x, V_x^2) \quad (14)$$

$$\log K_D = f(\pi^*, \alpha, \beta, \delta_H^2, HLB, HLB^2) \quad (15)$$

where the squared V_x or HLB are the empirical correction terms for the negative deviations from the straight line dependences log K_D versus V_x or HLB.[73−77]

The effect of solvents on the distribution constants of different 8-quinolinols, which differ in the number of oxygen and nitrogen atoms in their molecules, is adequately described by the model in eq 15.

The ionic strength of the aqueous phase has been calculated from the formula:

$$I = \frac{1}{2}\sum_i c_i z_1^2 \quad (16)$$

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where c_i and z_i stand for the molar concentration and charge of i-th ion. Its effects upon the distribution constants of considered 8-quinolinols in a given system involve only the negligibly small contribution of their dissociation and can be considered in terms of the extension of the Hückel−Debye equation.[78] The extension applied in the present work is based on the linear combination of terms $(I^{1/2})/(1 + \hat{I}^{1/2})$, I, and I^2, respectively. It is known from a few decades of the previous century and was applied for the description of the ionic strength's effect on the equilibria in aqueous solutions.[79−81]

At a constant ionic strength of the aqueous phase, the following dependence of distribution constant, K_D, on temperature:

$$\frac{\partial \log K_D}{\partial(1/T)} = -\frac{\Delta H_D}{2.303R} \quad (17)$$

makes possible the evaluation of thermodynamic functions of distribution of 8-hydroxyquinolinol between the organic and the aqueous phases of a given system. Assuming that the enthalpy change of distribution is constant over the whole range of temperature studied, its value can be found from the plot of $\log K_D$ versus $1/T$. Then, the free enthalpy and entropy changes of distribution can be easily calculated:

$$\Delta G_D = -2.303RT \log K_D \quad (18)$$

$$\Delta S_D = \frac{\Delta H_D - \Delta G_D}{T} \quad (19)$$

At a constant ionic strength (0.1 M $NaClO_4$) of the aqueous phase, the enthalpy and entropy of 8-hydroxyquinoline distribution depend on the properties of organic solvents[29] and differ from those which are characteristic for 2-methyl-8-hydroxyquinoline in the system with 1,1,2,2-tetratrochloroethane.[32,33] Sporadically, the distribution constants of the other 8-hydroxyquinolinols were determined at the different ionic strengths of the aqueous phase and lower or higher temperatures than 298 K.[27,32,35,41,46,53,55,57,62,63] As a result, the effect of temperature upon the distribution constants of different 8-hydroxyquinolinols has been expressed according to the following model:

$$\log K_D = \phi\left[\left(\mathrm{HLB}, \mathrm{HLB}^2, \frac{I^{1/2}}{(1 + I^{1/2})}, I, I^2, \pi^*, \alpha, \beta, {\delta_H}^2\right)/T\right] \quad (20)$$

The liquid−liquid distribution constants of 8-hydroxyquinoline and its derivatives from Tables 1 and 2 have been used as a training and test sets, respectively. All calculations have been performed as previously described[24,73−77] by means of multiple regression analysis and the procedure of the stepwise selection. The selected explanatory variables can be arranged in descending order of their statistical importance, and consequently, some of them can be considered as of primal or secondary statistical significance. The assessment of statistical validity of derived correlations has been made applying the values of the determination coefficient (R^2), standard deviation (SD), and test function, F, of Fisher−Snedecor (F-statistics) calculated for the N experimental point. The predictive power of these correlations has been also evaluated by means of the internal (Q^2) and external (q^2) cross-validation coefficients, respectively. The values of Q^2 coefficients have been calculated applying the training set of data and leave-one-out method.[82,83] The test set of data, not previously considered in the formulation of derived correlations, has been used to calculate the q^2 coefficients.[84]

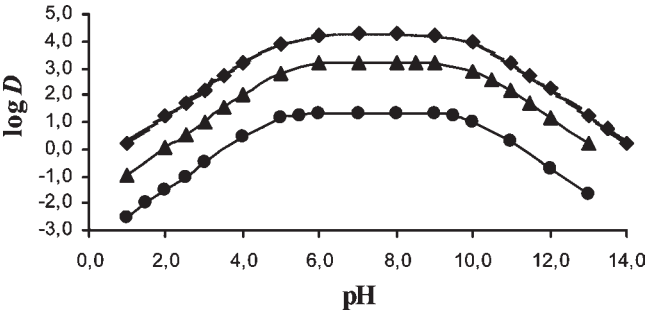

Figure 1. Distribution ratio of different 8-quinolinols: ♦, 2-M-5-HOM-HQ; ▲, 2-M-5-BOM-HQ; ●, 8-HQ; as a function of pH of the aqueous phase.

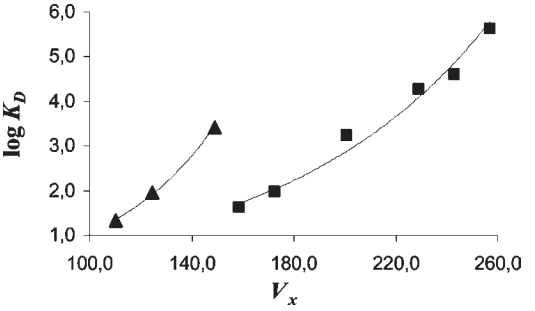

Figure 2. Dependence of distribution constants on the molar intrinsic volumes of 8-hydroxyquinoline, its alkyl and halogenated (▲) as well as alkoxyl and alkoxymethyl (■) derivatives in the systems: alkane/aqueous (I = 0.1) solution.

3. RESULTS AND DISCUSSION

3.1. Distribution of 8-Quinolinols of Different Hydrophobicities in the Given System. At a constant pH of the aqueous phase, the distribution ratio of 8-hydroxyquinolinols depends on their dissociation constants and hydrophobicity. In every case the specific pH region can be indicated in which the distribution of a particular solute is near constant. The effect of pH on the distribution ratio of three different 8-quinolinols in the systems with aliphatic hydrocarbons is presented in Figure 1. As can be seen, the decrease of distribution ratios of 8-hydroxyquinoline, 2-methyl-5-butyloxymethyl-8-hydroxyquinoline, and 2-methyl-5-hexyloxymethyl-8-hydroxyquinoline, observed at pH < 5 as well at pH > 9, is simply related to their increased solubility in acidic and alkaline solutions, respectively. In the whole range of pH the values of distribution ratio depend on the hydrophobicity of compared solutes and increase in the order: 8-HQ < 2-M-5-BOM-8-HQ < 2-M-5-HOM-8-HQ. These results agree well with the findings of Cote and Bauer,[46] Izquierdo and Compano,[54] and Ohashi and co-workers.[60]

Wionczyk and Apostoluk[24] have demonstrated that the molar intrinsic volume, V_x, of 8-hydroxyquinoline and its alkyl homologues is a primal measure of their hydrophobicity. However, this is not the case when one compares 8-hydroxyquinoline and its alkyl and/or halogenated derivatives with the series of analogues involving alkoxyl or alkoxymethyl groups. Figure 2 proves that there is no simple relationship between log D and V_x of

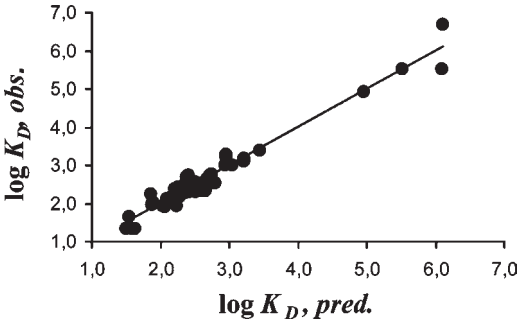

Figure 3. Distribution constants of 8-hydroxyquinoline, its alkyl derivatives, and Kelex 100 in organic solvent/aqueous solution according to eq 22.

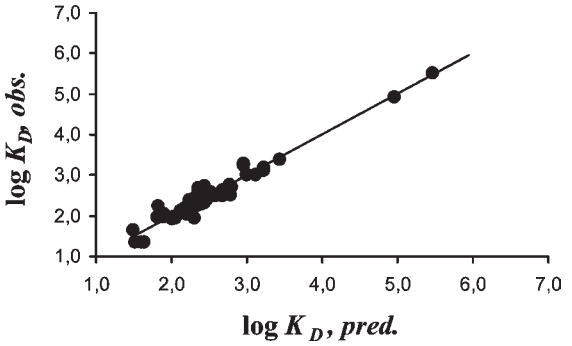

Figure 4. Distribution constants of 8-hydroxyquinoline and its alkyl derivatives in organic solvent/aqueous solution according to eq 24.

8-hydroxyquinoline and its 2-methyl-, 2-methyl-5,7-dichloro-, 5-octyloxymethyl-, and 2-methyl-5-alkyloxymethyl-derivatives distributed at pH 6 in the alkane/aqueous solution (I = 0.1) system. As a result, the single correlation has been derived applying the hydrophile−lipophile balance (HLB) of all compared solutes in the McGowan scale:

$$\log D = (6.22 \pm 0.21) - (0.127 \pm 0.008)\mathrm{HLB}^2$$
$$R^2 = 0.9719, \quad \mathrm{SD} = 0.25, \quad F = 277.3, \quad N = 9 \qquad (21)$$

3.2. Distribution Constants of 8-Hydroxyquinoline, Its Alkyl Derivatives, and Kelex 100 at 25 °C. Strongly hydrophobic alkyl-, alkenyl-, and alkyloxymethyl-derivatives of 8-hydroxyquinoline could be considered as a potential extracting agents in hydrometallurgical technologies of Cu(II), Ga(III), and platinum group metals.[2−12] Therefore, it is convenient to develop a simple method of estimation of the distribution constants of such extractants in the systems involving different organic solvents and the aqueous phase containing significant electrolyte concentrations. On the basis of the data reported in Table 1 the following correlation has been derived:

$$\log K_\mathrm{D} = -(3.58 \pm 0.63) + (0.06015 \pm 0.00728)V_x - (9.864 \pm 1.977)\cdot 10^{-5}V_x^2 + (1.86 \pm 0.66)\frac{I^{1/2}}{1 + I^{1/2}} - (0.93 \pm 0.42)I + (0.50 \pm 0.22)I^2 + (1.699 \pm 0.147)\pi^*(1.018 \pm 0.227)\alpha - (0.804 \pm 0.153)\beta - (2.463 \pm 0.440)\cdot 10^{-3}\delta_\mathrm{H}^2$$
$$R^2 = 0.9460, \quad Q^2 = 0.8840, \quad \mathrm{SD} = 0.19, \quad F = 158.7, \quad N = 82 \qquad (22)$$

Correlation 22, presented in Figure 3, is quite similar to that obtained previously for 8-hydroxyquinoline, its 2-, 4- and 5-methyl derivatives, and Kelex 100 in chloroform/0.10 M (Na,H)ClO_4 (see eq 16 in ref 24). However, the deviations of the distribution constant of Kelex 100 in chloroform/0.10 M (Na,H)ClO_4 and 1-octanol/0.5 M Na_2SO_4 systems are equal to −5.19 and +5.90 SD, respectively. It is also evident that the contributions of I and I^2 terms are of secondary importance. The elimination of both distribution constants for Kelex 100 leads to the correlation in which the latter terms are absent:

$$\log K_\mathrm{D} = -(3.65 \pm 0.76) + (0.06063 \pm 0.00981)V_x - (1.087 \pm 0.299)\cdot 10^{-4}V_x^2 + (0.471 \pm 0.180)\frac{I^{1/2}}{1 + I^{1/2}} + (1.666 \pm 0.120)\pi^* + (0.762 \pm 0.169)\alpha - (0.912 \pm 0.127)\beta - (2.022 \pm 0.342)\cdot 10^{-3}\delta_\mathrm{H}^2$$
$$R^2 = 0.9309, \quad Q^2 = 0.9199, \quad \mathrm{SD} = 0.16, \quad F = 153.0, \quad N = 80 \qquad (23)$$

As can be seen the value of standard deviation in eq 20 is slightly lower that in eq 23; however, the decrease of its statistical quality in terms of determination coefficient and F-statistics is also observed. Therefore, it is justified to exclude only the distribution constant of Kelex 100 in chloroform/0.10 M (Na,H)ClO_4 system and derive the final correlation (Figure 4) of improved quality:

$$\log K_\mathrm{D} = -(2.12 \pm 0.59) + (0.04219 \pm 0.00699)V_x - (4.03 \pm 1.96)\cdot 10^{-5}V_x^2 + (0.488 \pm 0.189)\frac{I^{1/2}}{1 + I^{1/2}} + (1.701 \pm 0.125)\pi^* + (0.843 \pm 0.175)\alpha - (0.854 \pm 0.132)\beta - (2.185 \pm 0.355)\cdot 10^{-3}\delta_\mathrm{H}^2$$
$$R^2 = 0.9529, \quad Q^2 = 0.9176, \quad \mathrm{SD} = 0.16, \quad F = 232.0, \quad N = 81 \qquad (24)$$

The derived correlations 22 to 24 prove that the specific interactions in the organic phase, that is, donor−acceptor interactions between 8-hydroxyquinoline and/or its alkyl derivatives with diluent, play an important role in governing their distribution in the investigated systems. However, it should be emphasized that the contributions of hydrogen bond donation and accepting abilities of diluents partly cancel each other. The contribution of the square of V_x, used as an empirical correction term for the negative deviations from the straight line dependence log K_D versus hydrophobicity, is statistically significant and cannot be omitted. The mentioned correlations prove that the effect of ionic strength of the aqueous on the distribution constants of considered solutes is also important.

3.3. Distribution of 8-Hydroxyquinoline and Its Derivatives in the Extraction Systems at 25 °C. According to the arguments indicated in Section 3.1, the hydrophobicity of compared solutes has been expressed in terms of their hydrophile−lipophile

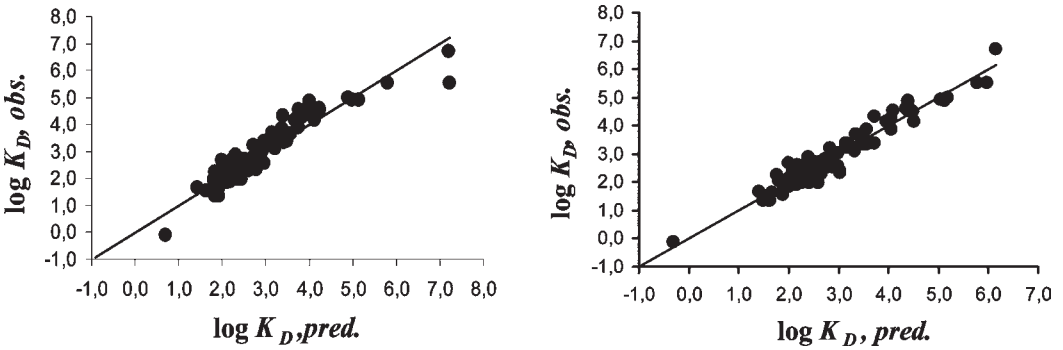

Figure 5. Distribution constants of 8-hydroxyquinoline and its various derivatives in organic solvent/aqueous solution at 25 °C. On the left, according to eq 25; on the right, according to eq 26.

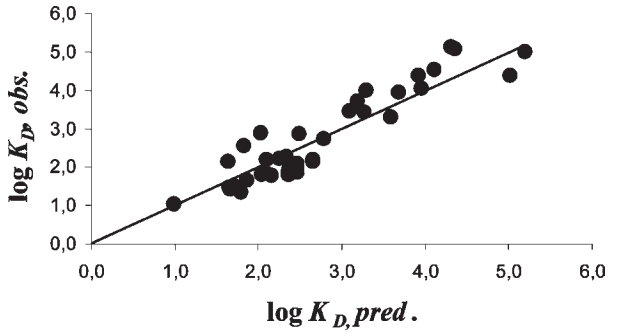

Figure 6. Validation of eq 26 in terms of the test set of experimental data at 25 °C from Table 2.

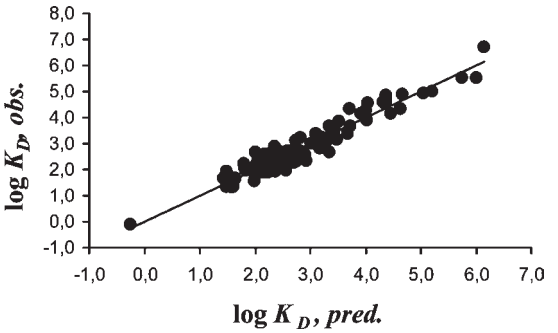

Figure 7. Distribution constants of 8-hydroxyquinoline and its various derivatives in organic solvent/aqueous solution at temperature range from (20 to 50) °C according to eq 27.

balances. The distribution constants of 8-hydroxyquinoline and its derivatives in different extraction systems at 25 °C have been found to fulfill the following correlations:

$$\log K_D = (7.23 \pm 0.25) - (0.814 \pm 0.035)\mathrm{HLB} + (3.53 \pm 0.55)\frac{I^{1/2}}{1 + I^{1/2}} - (1.11 \pm 0.29)I + (0.340 \pm 0.85)I^2 + (1.68 \pm 0.18)\pi^* + (2.00 \pm 0.29)\alpha - (1.30 \pm 0.25)\beta - (3.90 \pm 0.63)\cdot 10^{-3}\delta_H{}^2$$
$$R^2 = 0.8653, \quad \mathrm{SD} = 0.37, \quad F = 103.8, \quad N = 129 \qquad (25)$$

$$\log K_D = (4.96 \pm 0.29) + (0.308 \pm 0.112)\mathrm{HLB} - (0.133 \pm 0.012)\mathrm{HLB}^2 + (4.37 \pm 0.41)\frac{I^{1/2}}{1 + I^{1/2}} - (1.28 \pm 0.21)I + (0.335 \pm 0.062)I^2 + (1.90 \pm 0.13)\pi^* + (1.99 \pm 0.22)\alpha - (1.02 \pm 0.19)\beta - (4.06 \pm 0.46)\cdot 10^{-3}\delta_H{}^2$$
$$R^2 = 0.9282, \quad \mathrm{SD} = 0.27, \quad Q^2 = 0.9120, \quad q^2 = 0.8451, \quad F = 184.8, \quad N = 129 \qquad (26)$$

A comparison of both correlations is presented in Figure 5. It is evident that the square of HLB used as an empirical correction term in correlation 26 improves its statistical quality in comparison with correlation 25. On the other hand, the conclusions concerning the solute−solvent interactions in the organic phase remain the same as those formulated in previous section. The external cross validation coefficient of correlation 26 has been calculated taking from Table 2 the distribution constants of 8-hydroxyquinolinols determined at 25 °C. The results are presented in Figure 6.

3.4. Effect of Temperature on the Distribution of 8-Hydroxyquinoline and Its Derivatives in the Extraction Systems. Application of model 20 to the analysis of all data from Table 1 results in the following equation, which expresses the effect of temperature on distribution constants of 8-hydroxyquinoline and its derivatives in different systems:

$$\log K_D = \frac{1523 \pm 85.0}{T} + \frac{70.9 \pm 33.1}{T}\mathrm{HLB} - \frac{37.11 \pm 3.76}{T}\mathrm{HLB}^2 + \frac{999.8 \pm 105.5}{T}\left(\frac{I^{1/2}}{1 + I^{1/2}}\right) - \frac{1771 \pm 210}{T}I + \frac{113.3 \pm 20.7}{T}I^2 + \frac{564.3 \pm 32.2}{T}\pi^* + \frac{529.0 \pm 58.6}{T}\alpha - \frac{285.9 \pm 52.3}{T}\beta - \frac{1.122 \pm 0.134}{T}\delta_H{}^2$$
$$R^2 = 0.9913, \quad \mathrm{SD} = 0.27, \quad Q^2 = 0.9018, \quad q^2 = 0.8531, \quad F = 1797, \quad N = 159 \qquad (27)$$

It should be pointed out that no deviations exceed the value of ± 3 SD and only the deviation of distribution constant of Kelex 100 (Ashland) in the system of aqueous solution (I = 1.5 M) and octanol[46] is equal exactly to +3.00 SD. Therefore, from the formal point of view, the correlation 27 presented in Figure 7 seems to be of excellent statistical quality. However, the squared cross-validation coefficients, internal Q^2 and external q^2 (Figure 8), respectively, are significantly lower than the determination coeffient

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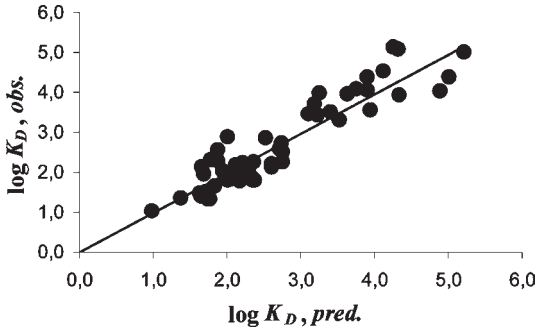


Figure 8. Validation of eq 27 in terms of all experimental data from Table 2.

(R^2). On the other hand, the correlation 27, fairly well reproducing the distribution constants of 8-hydroxyquinoline and its derivatives in different systems at 25 °C, should have squared cross-validation coefficients similar to those in correlation 26. This conclusion is clear since the substitution of temperature 298 K in correlation 27 leads to a equation which is quite similar to correlation 26. The moderate predictive power of correlation 27 indicates that it can be used for the following purposes: (i) the rough estimation of unknown values of distribution constants of considered solutes in the particular system within the range of temperature from (20 to 50) °C; (ii) the verification of distribution constants of 8-hydroxyquinolinols determined experimentally at temperatures ranging from (20 to 50) °C or slightly lower than 20 °C. The latter case can be illustrated by means of following examples:

- In terms of correlation 26, the distribution constant of Kelex 100 (Ashland), log K_D = 6.5 estimated at (24 ± 2) °C in the system of aqueous solution (I = 1.5 M) and kerosene containing 10 % of octanol[46] seems to be overestimated.[46]
- The distribution constants of 5,7-dichloro-, 5,7-dibromo-, and 5,7-diiodo-8-hydroxyquinolines determined experimentally at room temperature [(17 to 20)] °C] in the system 1 M NH_4Cl solution−chloroform[67] can be compared with those calculated from correlation 27 assuming the mean temperature to be equal to 18.5 °C. The obtained results prove that the experimental and calculated distribution constants of both 5,7-dichloro- and 5,7-dibromo-8-hydroxyquinolines are in satisfactory accordance, whereas the experimental distribution constant of 5,7-diiodo-8-hydroxyquinoline is evidently overestimated.

On the other hand, correlation 27 has been derived from model 20 under the assumption that the enthalpy and entropy of distribution depend both on the properties of solutes and diluents, as well as on the ionic strength of the aqueous phase in different extraction systems. However, the available set of systematic experimental data of temperature effect on the distribution of 8-hydroxyquinolinols is limited to 8-hydroxyquinoline and 2-methyl-8-hydroxyquinoline.[29,32,33] Therefore, the further improvement and/or verification of model 20 and correlation 27 is practically impossible as long as the new data on the temperature effect on the distribution constants of 8-hydroxyquinoline and its derivatives will be available. As a result, its application for the estimation of enthalpies and entropies of distribution of 8-hydroxyquinoline and its derivatives should be treated cautiously. Hence, further studies of temperature effects on the distribution of considered solutes in the extraction systems are necessary to validate the importance of the derived correlations.

4. CONCLUSIONS

It has been demonstrated that the hydrophile−lipophile balance in the McGowan scale is a convenient descriptor of 8-hydroxyquinoline and its derivatives distributed in the different extraction systems. For the first time, the distribution constants of 8-hydroxyquinoline and its derivatives have been also correlated with the ionic strength of the aqueous phase. The derived correlations prove that 8-hydroxyquinoline and its derivatives interact with diluents in the organic phase. All derived correlations involve a positive contribution of dipolarity/dipolarizabity term of diluents, which means that polar solvents promote the organic phase in the distribution of these solutes. On the other hand, however, the opposite contributions of hydrogen bond donation and hydrogen bond accepting abilities of diluents correlation indicate that the nature and range of their specific interactions with 8-hydroxyquinoline and its derivatives in the organic phase are rather complicated. Finally, the statistical parameters of quality and predictive power of both correlations 26 and 27 can be compared with the acceptable standards of quantitative structure−activity relationships (QSAR): $R^2 > 0.6$, $q^2 > 0.5$, and $0.85 < k < 1.15$, where k is a slope of the regression line $P_{pred} = kP_{obs}$ passing through the origin.[84] The parameters corresponding to the derived correlations, where log P = log K_D, are as follows:

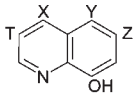
$$R^2 = 0.9282, \quad Q^2 = 0.9120, \quad q^2 = 0.8451, \quad k = 0.9812 \tag{26}$$

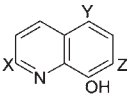
$$R^2 = 0.9913, \quad Q^2 = 0.9018, \quad q^2 = 0.8531, \quad k = 0.9794 \tag{27}$$

According to some authors[85,86] the difference between the values of R^2 and Q^2 should be close to 0. A difference greater than or equal to 0.3 may indicate an overfitted model, the presence of irrelevant explanatory variables, and/or the presence of outliers (i.e., an observation that lies at an abnormal distance from the other experimental points in the analyzed population). For correlations 26 and 27 these differences are to 0.0162 and 0.0895, respectively.

Correlation 27, describing the effect of temperature on the distribution of 8-hydroxyquinoline and its derivatives in considered extraction systems, is of good statistical quality; however, its predictive power is rather moderate. As a result, correlation 27 can be used for the rough estimation of unknown values of distribution constants of 8-hydroxyquinoline and its derivatives in the particular system within the range of temperature from (20 to 50) °C. On the hand, correlation 27 proves that the enthalpy of distribution of 8-hydroxyquinoline and its derivatives depend both on the properties of solutes and diluents, as well as on the ionic strength of the aqueous phase. However, the possible application of correlation 27 for the estimation of thermodynamic functions of distribution of 8-hydroxyquinoline and its derivatives in the two-phase liquid systems should be treated cautiously.

APPENDIX A





T=X=Y=Z = H,	**HQ**	X = CH_3, Y = Z = H,	**2-M-HQ**
X = CH_3, T=Y=Z = H,	**4-M-HQ**	X = C_4H_9, Y = Z = H,	**2-B-HQ**
T=X =Z= H, Y = CH_3,	**5-M-HQ**	X = Y = H, Z = CH_3,	**7-M-HQ**
T=X =Y= H, Z = CH_3,	**6-M-HQ**	X = Y = H, Z = C_2H_5,	**7-E-HQ**
X=Y = CH_3, T=Z=H	**4,5-DM-HQ**	X = Y = H, Z = C_3H_7,	**7-Pr-HQ**
T = *i*-C_3H_7, X = CH_3, Y=Z = H,	**3- *i*-Pr-4-M-HQ**	X = Y = H, Z = *i*-C_3H_7,	**7-*i*-Pr-HQ**
T=X=Z= H, Y = C_8H_{17},	**5-O-HQ**	X = Y = H, Z = CH_3–CH=CH	**7-Propenyl-HQ**
T=X=Z= H, Y = F,	**5-F-HQ**	X = Y = H, Z = CH_2=CH–CH_2	**7-Allyl-HQ**
X = Cl, T=Y=Z = H,	**4-Cl-HQ**	X = Y = H, Z = *s*-C_4H_9,	**7-*s*-B-HQ**
T=X=Z= H, Y = Cl,	**5-Cl-HQ**	X = Y = H, Z = *t*-C_4H_9,	**7-*t*-B-HQ**
T=X=Z= H, Y = Br,	**5-Br-HQ**	X = Y = H, Z = *s*-C_5H_{11},	**7-*s*-P-HQ**
T=X=Z= H, Y = I,	**5-I-HQ**	X = Y = H, Z = Dodecenyl,	**Kelex 100**
X = NH_2, T=Y=Z = H,	**4-NH_2-HQ**	X = H, Y = Z = CH_3,	**5,7-DM-HQ**
T=X=Z= H, Y = NO_2,	**5-NO_2-HQ**	X = H, Y = Z = Cl,	**5,7-DCl-HQ**
T=X=Z= H, Y = CH_3OCH_2	**5-MOM-HQ**	X = H, Y = Z = Br,	**5,7-DBr-HQ**
T=X=Z= H, Y = $C_2H_5OCH_2$	**5-EOM-HQ**	X = H, Y = Z = I,	**5,7-DI-HQ**
T=X=Z= H, Y = $C_3H_7OCH_2$	**5-PrOM-HQ**	X = H, Y = Cl, Z = I,	**5-Cl-7-I-HQ**
T=X=Z= H, Y = $C_4H_9OCH_2$	**5-BOM-HQ**	X = CH_3, Y = Z = Cl,	**2-M-5,7-DCl-HQ**
T=X=Z= H, Y = $C_5H_{11}OCH_2$	**5-POM-HQ**	X = CH_3, Y = CH_3OCH_2, Z = H,	**2-M-5-MOM-HQ**
T=X=Z= H, Y = $C_6H_{13}OCH_2$	**5-HOM-HQ**	X = CH_3, Y = $C_2H_5OCH_2$, Z = H,	**2-M-5-EOM-HQ**
T=X=Z= H, Y = $C_8H_{17}OCH_2$	**5-OOM-HQ**	X = CH_3, Y = $C_4H_9OCH_2$, Z = H,	**2-M-5-BOM-HQ**
T=X=Z= H, Y = $CF_3CH_2OCH_2$	**5-F3EOM-HQ**	X = CH_3, Y = $C_6H_{13}OCH_2$, Z = H,	**2-M-5-HOM-HQ**
		X = CH_3, Y = $C_8H_{17}OCH_2$, Z = H,	**2-M-5-OOM-HQ**
		X = CH_3, Y = Z = Cl,	**2-M-5,7-DCl-HQ**

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REFERENCES

(1) Minczewski, J.; Chwastowska, J.; Dybczyński, R. *Separation and Preconcentration Methods in Inorganic Trace Analysis*; Ellis Horwood Ltd.: Chichester, 1982.

(2) Ohashi, K.; Nakata, S.; Katsume, M.; Nakamura, K.; Yamamoto, K. Effect of Hydrophobic Substituents on Solvent Extraction of Copper-(II) with 5-Alkyloxymethyl-5-quinolinol or 5-Dialkylaminomethyl-8-quinolinol and Separation of copper(II). *Anal. Sci.* **1985**, *1*, 467–471.

(3) Mihaylov, I.; Distin, P. A. Gallium solvent extraction in hydrometallurgy: An overview. *Hydrometallurgy* **1992**, *28*, 13–27.

(4) Marchon, R.; Cote, G.; Bauer, D. Some typical behaviours of β-dodecenyl 8-hydroxyquinoline through its reaction with gernaniun(IV). *J. Inorg. Nucl. Chem.* **1979**, *41*, 1353–1363.

(5) Cote, G.; Bauer, D. Liquid-liquid extraction of germanium with oxine derivatives. *Hydrometallurgy* **1980**, *5*, 149–160.

(6) Szymanowski, J. *Hydroxyoximes and Copper Hydrometallurgy*; CRC Press: Boca Raton, FL, 1993.

(7) Dziwinski, E.; Cote, G.; Bauer, D.; Szymanowski, J. Composition of Kelex100, Kelex100S and Kelex108: a discussion on the role of impurities. *Hydrometallurgy* **1995**, *37*, 243–250.

(8) Citores, M. J.; Alonso, R. M.; Fernandez, L. A. A Study of the Purification and Acid-Base Behavior of the Commercial Extractants KELEX 100 and LIX 26. *Sep. Sci. Technol.* **1994**, *29*, 1441–1459.

(9) Côté, B.; Demopoulos, G. P. New 8-Hydroxyquinoline Derivatives Extractants for Platinum Group Metals Separation Part I: Characterization and HCl Extraction. *Solvent Extr. Ion Exch.* **1993**, *11*, 349–376.

(10) Côté, B.; Demopoulos, G. P. New 8-Hydroxyquinoline Derivatives Extractants for Platinum Group Metals Separation Part 3: Pt(IV) Extraction Equilibria and Stripping. *Solvent Extr. Ion Exch.* **1994**, *12*, 517–540.

(11) Sparfel, D.; Cote, G. Synthesis and Properties of New Highly Hydrophobic 7-Substituted 8-quinolinols. *Solvent Extr. Ion Exch.* **2004**, *22*, 1–12.

(12) Ohashi, K.; Iwata, R.; Mochizuki, S.; Imura, H.; Haratani, K.; Sugihara, H. Effect of alkyl substituents in hydrophobic 8-quinolinol on the extraction of gallium(III) and applications to the separation of gallium(III) from aluminum(III). *Talanta* **1996**, *43*, 1481–1487.

(13) Gershon, H.; McNeil, M. W.; Parmegiani, R.; Godfrey, P. K. Antifungal Activity of 7- and 5,7-Substituted 8-Quinolinols. *J. Med. Chem.* **1972**, *15*, 987–989.

(14) Gershon, H.; Parmegiani, R.; Godfrey, P. K. Antifungal Activity of 5-, 7- and 5,7-Substituted 2-Methyl-8-Quinolinols. *Antimicrob. Agents Chemother.* **1972**, *1*, 373–375.

(15) Gershon, H.; Clark, D.; Gershon, M. Preparation and Fungitoxity of Some Dichloro-8-Quinolinols. *Monatsh. Chem.* **1999**, *130*, 653–659.

(16) Nocolletti, G.; Domalewska, E.; Borland, R. Fungitoxity of oxine and copper oxinate: activity spectrum. *Mycol. Res.* **1999**, *103*, 1073–1084.

(17) Scheibel, L. V.; Adler, A. Antimalarian activity of selected aromatic chelators. III. 8-Hydroxyquinolines (oxines) substituted in positions 5 and 7, and oxines annelated in position 5,6 by an aromatic ring. *Mol. Pharmacol.* **1982**, *22*, 140–144.

(18) W. Rohde, W.; Mikelens, P.; Jackson, J.; Blackman, J.; Whitcher, J.; Levinson, W. Hydroxyquinolines Inhibit Ribonucleic Acid-Dependent Deoxyribonucleic Polymerase and Inactivate Rous Sarcoma Virus and Herpes Simplex Virus. *Antimicrob. Agents Chemother.* **1976**, *10*, 234–240.

(19) Musiol, R.; Jampilek, J.; Buchta, V.; Silva, L.; Niedbala, H.; Podeszwa, B.; Palka, A.; Majerz-Maniecka, K.; Oleksyn, B.; Polanski, J. Antifungal properties of new series of quinoline derivatives. *Bioorg. Med. Chem.* **2006**, *14*, 3592–3598.

(20) Allard, B.; Choppin, G. R.; Musikas, C.; Rydberg, C. Systematics of Solvent Extraction. In *Principles and Practices of Solvent Extraction*; Rydberg, J., Musikas, C., Choppin, G. R., Eds.; Marcel Dekker: New York, 1992; Chapter 6, pp 209−234.

(21) Platts, J. A.; Abraham, M. H.; Butina, D.; Hersey, A. Estimation of molecular linear free energy relationship descriptors by a group contribution approach. 2. Prediction of partition coefficients. *J. Chem. Inf. Comput.* **2000**, *40*, 71–80.

(22) Warner, V. D.; Musto, J. D.; Turesky, S. S.; Soloway, B. Synthesis and In Vitro Evaluation of 8-Hydroxyquinolines as Dental Plaque Inhibitors. *J. Pharm. Sci.* **1975**, *64*, 1563–1566.

(23) Kamlet, M. J.; Abboud, J.-L. M.; Abraham, M. H.; Taft, R. W. Linear solvation energy relationships. 23. A comprehensive collection of the solvatochromic parameters π^*, α and β and some methods for simplifying of the generalized solvatochromic equation. *J. Org. Chem.* **1983**, *48*, 2877–2887.

(24) Wionczyk, B.; Apostoluk, W. Analysis of diluent effects and estimation of distribution constants of 8-hydroxyquinoline and its derivatives in extraction systems. *Hydrometallurgy* **1997**, *45*, 73–81.

(25) Mottola, H. A.; Freiser, H. Some solvent effects on the solvent extraction of quinolinol. *Talanta* **1967**, *14*, 864–869.

(26) Wakabayashi, T. Some applications of regular solution theory to solvent extraction. IV. Oxine − inert solvent system. *Bull. Chem. Soc. Jpn.* **1967**, *40*, 2836–2839.

(27) Kondo, K.; Yano, K.; Matsumoto, M. Synergistic Extraction of Gallium(III) with 2-Ethylhexyl-Phosphonic Acid Mono-2-Ethylhexyl Ester in the Presence of Oxine Derivatives. *J. Chem. Eng. Jpn.* **1996**, *29*, 836–841.

(28) Mason, J. G.; Lipschitz, I. Effect of salts on the partition of 8-quinolinol. *Talanta* **1966**, *13*, 1462–1465.

(29) Mason, J. G.; Lipschitz, I. Thermodynamic of the Partition of 8-Quinolinol Between Several Organic Solvents and Aqueous Buffers. *Talanta* **1971**, *18*, 1111–1115.

(30) Stary, J.; Freiser, H. *IUPAC Chemical Data Series No.18, Equilibrium Constants of Liquid-Liquid Distribution Reactions. Part IV: Chelating Extractants*; Pergamon Press: Elmsford, NY, 1978.

(31) Mottola, H. A.; Freiser, H. Distribution of Certain 8-Quinolinols and Their Copper(II) Chelates in a Series of Organic Solvent Aqueous Pairs. *Talanta* **1966**, *13*, 55–65.

(32) Nakayama, E.; Sohrin, Y.; Issiki, K.; Karatani, H.; Hamada, E. Effect of Temperature on the Solvent Extraction of Zinc and Cadmium

with 8-Quinolinol and 2-Methyl-8-quinolinol into 1,1,2,2-tetrachloroethane, 1-Octanol and p-Xylene. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 2512–2519.

(33) Hellwege, H.; Schweitzer, G. K. Temperature Changes in Solvent Extraction of Cadmium Oxinate. *Anal. Chim. Acta* **1963**, *28*, 236.

(34) Chou, F.-C.; Freiser, H. The Role of Adduct Formation in the Extraction of Zinc with Substituted 8-Quinolinols. *Anal. Chem.* **1968**, *40*, 34–39.

(35) Akaiwa, H.; Kawamoto, H. The Stability of Bis(8-quinolinato)copper(II). *Bull. Chem. Soc. Jpn.* **1979**, *52*, 2435–2446.

(36) Friedrich, A; Bukowsky, H.; Uhlemann, E. Extraktionsverhalten Methylsubstituierter Chinolin-8-ole Gegenüber Kupfer. *Anal. Chim. Acta* **1987**, *193*, 373–379.

(37) Warner, V. D.; Musto, J. D.; Sane, J. N. Quantitative Structure-Activity Relationships for 5-Substituted 8-Hydroxyquinolines as Inhibitors of Dental Plaque. *J. Med. Chem.* **1977**, *20*, 92–96.

(38) Paljk, Š.; Klofutar, C.; Krašovec, F.; Suhač, M. Dissociation of 8-Hydroxyquinoline and its 5-Chloro and 5-Nitro-Derivatives in Aqueous Solutions. *Microchim. Acta* **1975**, 485–492.

(39) Kaiser, S. M.; Escher, B. I. The Evaluation of Liposome-Water Partitioning of 8-Hydroxyquinolines and Their Copper Complexes. *Environ. Sci. Technol.* **2006**, *40*, 1784–1791.

(40) Choi, S.-Y.; Ohashi, K. Large Synergism of 3,5-Dichlorophenol in the Extraction of Gallium(III) with 2-Methyl-8-quinolinol Derivatives. *Anal. Sci.* **2000**, *16*, 169–176.

(41) Choi, S.-Y.; Yoshida, Z.; Ohashi, K. Supercritical carbon dioxide extraction equilibrium of gallium(III) extraction with 2-methyl-8-quinolinol and 2-methyl-5-butyloxymethyl-8-quinolinol. *Talanta* **2002**, *56*, 689–697.

(42) Dyrssen, D. The Influence of the Structure of Chelating Agents on the Complexity and Distribution Constants of Thorium Complexes. *Recl. Trav. Chim. Pays-Bas Belg.* **1956**, *75*, 753–758.

(43) Dietz, M. L.; Freiser, H. Role of the interface in the kinetics and mechanism of nickel extraction with certain halogen- and alkyl-substituted 8-hydroxyquinolinols. *Langmuir* **1991**, *7*, 284–287.

(44) Takayanagi, T.; Kudoh, T.; Yotsuyanagi, T. 5,7-Dimethyl-8-quinolinol as a Specific Non-extracting Reagent for Lanthanide Ions at Usual pH Region. *Chem. Lett.* **1994**, 687–690.

(45) Bag, S. P.; Freiser, H. Liquid Distribution Equilibria in the Copper(II)-7-(1-Vinyl-3,3,6,6-Tetramethylhexyl)-8-quinolinol System. *Anal. Chim. Acta* **1982**, *135*, 319–325.

(46) Cote, G.; Bauer, D. J. Some Typical Behaviours of the β-Dodecenyl 8-Hydroxyquinoline —II. Its Distribution Between Aqueous and Organic Phases. *Inorg. Nucl. Chem.* **1981**, *43*, 1023–1030.

(47) Shioya, T.; Tsukahara, S.; Teramae, N. Adsorption Kinetics of 5-Octyloxymethyl-8-quinolinol at the Liquid-Liquid Interface. *Chem. Lett.* **1997**, 695.

(48) Choi, S.-Y.; Imura, H.; Ohashi, K. Large Extractability of Aluminum(III) with 2-Methyl-8-quinolinol Derivatives in the Presence of 3,5-Dichlorophenol. *Anal. Sci.* **2000**, *16*, 923–928.

(49) Warner, V. D.; Sane, J. N.; Mirth, D. B.; Turesky, S. S.; Soloway, B. Synthesis and in vitro evaluation of 8-hydroxyquinoline analogs as inhibitors of dental plaque. *J. Med. Chem.* **1976**, *19*, 167–169.

(50) Klofutar, C.; Paljk, Š.; Krašovec, F.; Horvat, I. Ionization of 5-Nitro-8-hydroxyquinoline in Aqueous Solutions. *Microchim. Acta* **1973**, 559–568.

(51) Dyrsssen, D.; Dyrssen, M.; Johansson, E. Studies on the Extraction of Metal Complexes. XXXI. Investigation with some 5,7-Dihalogen Derivatives of 8-Quinolinol. *Acta Chem. Scand.* **1956**, *10*, 341–352.

(52) Korenman, Y. I. *Distribution Coefficients of Organic Compounds*; Voronezh University: Voronezh, 1992 (in Russian).

(53) Kniazev, D. A. Issledovanya dissotsyatsyi 5,7-dibro-8-oksikhinolina ekstratsyonnym metodom. *Zh. Anal. Khim.* **1964**, *19*, 273–275.

(54) Izquierdo, A.; Compano, R. Distribution of 5,7-Dichloro-2-methyl-8-hydroxyquinoline in Some Organic Solvent-Aqueous Buffer Systems. *Microchim. Acta* **1983**, 371–380.

(55) Ohashi, A.; Yamato, A.; Imura, K.; Ohashi, H. K. Solvent effects on the distribution equilibrium of 8-quinolinol derivatives between supercritical carbon dioxide and water. *J. Supercrit. Fluids* **2009**, *49*, 315–322.

(56) Yamada, H.; Hayashi, H.; Suzuki, S.; Yasui, T. Solvation Effect on 8-Quinolinol Molecule and Ion-pair Formation of 8-Quinolinium Cation with Some Inorganic Anions in the Partition of 8-Quinolinol between 1-Octanol and Water. *Solvent Extr. Res. Dev. Jpn.* **2004**, *11*, 111–119.

(57) Parthasarathy, N.; Pelletier, M.; Buffle, J. Transport of lipophilic ligands through permeation liquid membranes in relation to natural water analysis. *J. Membr. Sci.* **2008**, *309*, 182–188.

(58) Shioya, T.; Nishizawa, S.; Teramae, N. Complexation Kinetics of 8-Hydroxyquinolinol Derivatives with Ni(II) and Zn(II) at the 1,2-Dichloroethane—Water Interface as Studied by Electrolyte Ascending Electrode Polagraphy. *Langmuir* **1999**, *15*, 2575–2579.

(59) Itoh, Y.; Ueda, Y.; Hirano, A.; Sugawara, M.; Tohda, K.; Akaiwa, H.; Umezawa, Y. Potentiometric Responses of Polymetric Liquid Membranes Based on Hydrophobic Chelating Agents to Metal Ions. *Anal. Sci.* **2001**, *17*, 621–627.

(60) Ohashi, K.; Imura, H.; Mochizuki, S.; Haratani, K. Effect of Alkyl Substituents on the Selective Extraction of Copper(II), Palladium, Pallium(III) and Molybdenum(VI) with Novel 8-Quinolinol Derivatives. *Miner. Process. Extr. Metall. Rev.* **1997**, *17*, 169–194.

(61) Shioya, T.; Nishizawa, S.; Teramae, N. Complexation Kinetics of 8-Hydroxyquinolinols at Liquid — Liquid Interfaces as Studied by Dynamic Interfacial Tensiometry. *Langmuir* **1998**, *14*, 4662–4558.

(62) Angelova, N.; Manolova, N.; Rashkov, I. Partition of Poly(oxyethylene)s with 5-Chloro-8-Quinolinoxyl End-Groups between 1-Octanol and Water. *J. Bioact. Compat. Pol.* **1996**, *11*, 28–42.

(63) Sevastyanov, A. I.; Rudenko, N. P. Konstanty dissotsyatsyi i koefficienty raspredelenya 5,7-dihagalogeno-i 2-metyl-8-khinolinov. *Vest. Mosk. Univ.* **1967**, *22*, 110–113.

(64) Marcus, Y. The Properties of Organic Liquids that are Relevant to their Use as Solvating Solvents. *Chem. Soc. Rev.* **1993**, *22*, 409–416.

(65) Marcus, Y. Correlation of the Distribution of Organic Solutes Between Water and "Wet" Organic Solvents with the Properties of Solutes and Solvents. *Solvent Extr. Ion Exch.* **1992**, *10*, 527–539.

(66) Marcus, Y. Linear solvation energy relationships. Correlation and prediction of the distribution of organic solutes between water and immiscible organic solvents. *J. Phys. Chem.* **1991**, *95*, 8886–8891.

(67) Marcus, Y. The use of chemical probes for the characterization of solvent mixtures. Part 2. Aqueous mixtures. *J. Chem. Soc., Perkins Trans. 2* **1994**, 1751–1758.

(68) Valenta, J. N.; Sun, L.; Ren, Y.; Weber, Sh. G. Solvatochromic Study of Poly(vinyl chloride) Plasticizers and Their Solutions in Chloroform: Applications to Phenobarbital Partitioning and Molecular Recognition of Phenobarbital. *Anal. Chem.* **1997**, *69*, 3490–3495.

(69) Barton, A. F. M. *Handbook of Solubility Parameters and Other Cohesion Parameters*; CRC Press: Boca Raton, FL, 1983.

(70) McGowan, J. A New Approach for the Calculation of HLB Values of Surfactants. *Tenside Surf. Det.* **1990**, *27*, 229–230.

(71) McGowan, J.; Sowada, R. Characteristic Volumes and Properties of Surfactants. *J. Chem. Technol. Biotechnol.* **1993**, *58*, 357–361.

(72) Mastalerz, P. *Organic Chemistry* (in Polish); PWN: Warszawa, 1986; Chapter 12, pp 588—592.

(73) Apostoluk, W.; Szymanowski, J. Application of the Kamlet and Taft Model in Solvent Extraction of Metals. *Anal. Chim. Acta* **1998**, *374*, 137–147.

(74) Apostoluk, W.; Szymanowski, J. Estimation of hydroxyoximes distribution in solvent extraction systems. *Colloids Surf., A* **1998**, *135*, 227–234.

(75) Apostoluk, W.; Gajda, B.; Szymanowski, J.; Mazurkiewicz, M. Estimation of properties of dialkylorganophosphorus acidic extractants in two-phase liquid systems. *Anal. Chim. Acta* **2000**, *405*, 321–333.

(76) Apostoluk, W.; Robak, W. Analysis of liquid-liquid distribution constants of organophosphorus based extractants. *Anal. Chim. Acta* **2005**, *548*, 116–133.

(77) Robak, W.; Apostoluk, W.; Maciejewski, P. Analysis of liquid-liquid distribution constants of nonionizable crown ethers and their derivatives. *Anal. Chim. Acta* **2006**, *569*, 119–131.

(78) Baeza, J. J.; Ramis-Ramos, G. A series of the extended Debye-Hückel equation and application to linear prediction of stability constants. *Talanta* **1996**, *43*, 1579–1587.

(79) Marshall, W. L.; Slusher, S. Thermodynamics of Calcium Sulfate Dihydrate in Aqueous Sodium Chloride Solutions, 0−110°. *J. Phys. Chem.* **1966**, *70*, 4915–4027.

(80) Yeatts, L. B.; Marshall, W. L. Aqueous Systems at High Temperature. XVIII. Activity Coefficient Behavior of Calcium Hydroxide in Aqueous Sodium Nitrate to the Critical Temperature of Water. *J. Phys. Chem.* **1967**, *71*, 2641–2650.

(81) Łętowski, F. *The Basis of Hydrometallurgy* (in Polish); WNT, Warszawa, 1975; Chapter 2, pp 35−43.

(82) Bauman, K. Cross-validation as the objective function for variables selection techniques. *Trends Anal. Chem.* **2003**, *22*, 395–406.

(83) Tropsha, A.; Gramatica, P.; Gombar, V. K. The Importance of Being Earnest: Validation is the Absolute Essential for Successful Application and Interpretation of QSPR Models. *QSAR Comb. Sci.* **2003**, *22*, 69–77.

(84) Nantasenamat, C.; Isarankura-Na-Ayudhya, C.; Naenna, T.; Prachayasittikul, V. A Practical Overview of Quantitative Structure −Activity Relationship. *EXCLI J.* **2009**, *8*, 74–88.

(85) Bolboacă, S. D.; Jäntschi, L. Modelling the property of compounds from the structure: statistical models for their validation. *Environ. Chem. Lett.* **2008**, *6*, 175–181.

(86) Jäntschi, L.; Popescu, V.; Bolboacă, S. D. Toxicity caused by para-substituted phenols on Tetrahymena pyriformis: The structure-activity relationships. *Electron. J. Biotechnol.* **2008**, *11*, 1–12.