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UTILIZATION OF THE FUNCTIONAL GROUP CONTRIBUTION CONCEPT IN LIQUID CHROMATOGRAPHY ON CHEMICALLY BONDED REVERSED PHASES

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SUMMARY

The possibilities of utilizing the UNIFAC group model of activity coefficients for the prediction of reversed-phase liquid chromatographic retention data are discussed. Provided that the retention of a solute i is due to liquid–liquid partition, the retention constant ($\ln k_i$) is related to the activity coefficient of the solute in the mobile phase ($\ln \gamma_{im}$) by $\ln k_i = \ln \gamma_{im} + \text{constant}$. By comparison of experimentally observed k_i and calculated γ_{im} values, it is shown that for certain solutes the UNIFAC concept can be used for the calculation of changes in solute retention with alterations in mobile phase composition, and for a rough estimation of absolute retention indices. By correlating k_i and γ_{im} values, it is possible to calculate the phase ratio of the chromatographic system and the activity coefficient of a solute in the stationary phase.

INTRODUCTION

One of the main problems in liquid chromatography (LC) is the prediction of solute retention and phase selectivity, and has been gaining increasing attention. As retention in chromatography is controlled by the thermodynamic equilibrium of a solute between the mobile and stationary phases, the prediction of retention is possible in principle from standard Gibbs free molar energies, $\Delta G^\circ = RT \ln K$. Numerical values of ΔG° are too scarce to be of any practical value, so must be made of reliable models for mixtures of liquids utilizing only readily available and simple physical parameters. Such models are the Hildebrand solubility parameter concept[1,2] and the group contribution concept according to Fredenslund *et al.*[3], developed for the prediction of activity coefficients in non-electrolyte liquid mixtures. The shortcoming of the former concept is regarded[4,5] as being its limitation in only qualitatively describing chromatographic behaviour. The later concept combines the solution of functional groups concept with a model of activity coefficients based on an extension of the quasi-chemical theory of liquid mixtures (UNIQUAC)[6]. The resulting UNIFAC model (UNIQUAC functional group activity coefficients) makes it

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possible to calculate activity coefficients in both binary and multi-component liquid mixtures by virtue of structural parameters and binary parameters characterizing the energy of mutual interaction of the functional groups present in the system. The activity coefficient of a component is calculated as the product of a combinatorial and a residual contribution. The combinatorial contribution depends only on the sizes and shapes of the molecules present in the system, whereas the residual contribution depends on the energy of interaction of pairs of functional groups and on the fraction of the surface of these groups available for mutual interaction.

At infinite dilution, the relationship between the capacity ratio of a solute i and the activity coefficients in the mobile (m) and stationary (s) phases is[4,7,8]

$$\ln k_i = \ln K_i + \ln \Phi = \ln \gamma_{im} - \ln \gamma_{is} + \ln \Phi \quad (1)$$

where K_i is the distribution constant of the solute, γ_i is the Raoult law activity coefficient of the solute and Φ is the phase ratio of the chromatographic system. Assuming that γ_{is} and Φ are constants, eqn. 1 represents a linear relationship between $\ln k_i$ and $\ln \gamma_{im}$, with a slope of unity. This offers the possibility of predicting and/or correlating the retention data utilizing the activity coefficients of the solute in a given chromatographic system. Correlations between the retention data and activity coefficients have been studied in liquid–liquid[9], liquid–solid[7] and reversed-phase[10] systems; the activity coefficients have been calculated from the experimental gas–liquid chromatographic data.

The aim of this contribution is to correlate the calculated activity coefficients utilizing the UNIFAC method and the measured retention data by high-performance LC on chemically bonded reversed phases (RP), in order to examine the ability of UNIFAC method to determine quantitatively solute chromatographic behaviour.

EXPERIMENTAL

A Model ALC/GPC 244 liquid chromatograph (Waters Assoc., Milford, MA, U.S.A.) equipped with a Model 440 UV detector and an R401 differential refractometer was employed. The chromatograms were obtained with a Model M 730 data module.

The eluent was methanol (E. Merck, Darmstadt, F.R.G.), pure or mixed with doubly distilled water in various proportions. The flow-rate was 1 ml/min and the column temperature was maintained at 22°C (room temperature). The mobile phase was pre-filtered through a 0.5-μm Millipore filter (Millipore, Bedford, MA, U.S.A.).

A commercial column, 300 × 3.9 mm I.D., packed with μBondapak C_{18}, 10 μm (Waters Assoc.) was used.

The solutes chromatographed and the corresponding capacity ratios (k_i) are given in Table I.

Calculation

A program in BASIC for the calculation of the activity coefficients of solutes at infinite dilution was designed on the basis of the equations and group parameters given by Fredenslund and co-workers[3,11,12].

TABLE I

EXPERIMENTAL CAPACITY FACTORS (k_i) IN THE METHANOL–WATER SYSTEM

Solute	φ							
	0.3	*0.4*	*0.5*	*0.6*	*0.7*	*0.8*	*0.9*	*1.0*
Benzene	17.05	9.23	5.00	2.71	1.47	0.80	0.35	0.23
Toluene		25.03	11.88	5.64	2.68	1.27	0.60	0.29
Ethylbenzene		80.48	32.62	13.22	5.36	2.17	0.88	0.36
n-Propylbenzene			76.32	26.79	9.40	3.30	1.16	0.41
n-Butylbenzene				48.90	15.41	4.85	1.50	0.48
n-Pentylbenzene					28.22	7.85	2.18	0.61
n-Hexylbenzene					46.76	11.36	2.76	0.67
Pentane		31.94	13.46	5.62	2.39	1.03	0.42	0.18
Hexane			27.52	10.23	3.84	1.41	0.54	0.20
Heptane			51.68	17.78	5.88	1.85	0.70	0.23
Octane				29.67	8.85	2.64	0.79	0.24
Nonane				54.27	14.27	3.75	0.99	0.26
Decane					23.01	5.28	1.21	0.28

RESULTS AND DISCUSSION

For the solutes listed in Table II we calculated ln γ_{im} values for ternary systems consisting of a solute and two solvents, water and methanol, using a concentration of solute equal to zero. A linear relationship between the calculated ln γ_{im} values of a solute and the volume fraction of methanol, φ, in the system is obtained over the whole range of methanol concentrations in most instances, and can be presented in the form

$$\ln \gamma_{im} = m\varphi + \ln \gamma_{iw} \tag{2}$$

where γ_{iw} is the activity coefficient of the solute in pure water and m is the constant. Calculated ln γ_{im} values were compared with experimental ln k_i values from the present study and from the literature[8,13–16]. Closer examination reveals that capacity factors, mainly those higher than 1, are also linearly related to φ according to the following equation (see, *e.g.*, refs. 5, 15 and 17–24):

$$\ln k_i = m_i\varphi + \ln k_{iw} \tag{3}$$

where k_{iw} refers to the k_i value for pure water as the mobile phase, and is usually an extrapolated value. The slopes and intercepts of eqn. 1 calculated using linear regression of the experimental ln k_i (Table IV) and corresponding ln γ_{im} (Table II) values for tested solutes at various φ, and also the slopes and intercepts of eqns. 2 and 3, are given in Table III. These data can be classified in two groups, as has been done in Table III. Group I includes solutes having slope coefficients of eqn. 1 close to 1 and identical or similar slope coefficients of eqns. 2 and 3, indicating that the UNIFAC model functional group parameters[3,11,12] used for the calculation of ac-

TABLE II

CALCULATED ln γ_{im} VALUES OF SOLUTES FOR VARIOUS VOLUME FRACTIONS, φ, OF METHANOL IN THE METHANOL–WATER SYSTEM

Temperature (K)	*Solute*	φ										
		0	*0.1*	*0.2*	*0.3*	*0.4*	*0.5*	*0.6*	*0.7*	*0.8*	*0.9*	*1.0*
295	Benzene	7.824	7.240	6.655	6.068	5.474	4.878	4.277	3.668	3.053	2.437	1.825
	Toluene	9.442	8.718	7.995	7.270	6.538	5.806	5.068	4.323	3.572	2.822	2.081
	Ethylbenzene	11.287	10.356	9.445	8.549	7.654	6.767	5.882	4.992	4.102	3.219	2.351
	n-Propylbenzene	12.950	11.842	10.767	9.717	8.673	7.644	6.621	5.596	4.574	3.563	2.574
	n-Butylbenzene	14.604	13.318	12.080	10.875	9.683	8.512	7.350	6.190	5.036	3.897	2.787
	n-Pentylbenzene	16.136	14.718	13.329	11.980	10.648	9.342	8.047	6.756	5.474	4.211	2.982
	n-Hexylbenzene	17.791	16.171	14.620	13.118	11.639	10.191	8.758	7.333	5.920	4.529	3.179
	Benzyl alcohol	6.556	5.720	4.903	4.109	3.332	2.590	1.885	1.232	0.665	0.256	0.227
	2-Phenylethanol	8.028	7.015	6.034	5.086	4.161	3.277	2.434	1.645	0.946	0.410	0.259
	3-Phenylpropanol	9.520	8.329	7.185	6.082	5.009	3.982	3.001	2.077	1.246	0.582	0.310
	Naphthalene	11.889	10.998	10.103	9.201	8.284	7.363	6.428	5.477	4.512	3.541	2.570
	Anthracene	15.880	14.683	13.476	12.260	11.021	9.773	8.505	7.212	5.898	4.571	3.241
	Biphenyl	13.931	12.854	11.773	10.686	9.583	8.475	7.355	6.217	5.065	3.909	2.760
	Phenol	2.323	1.923	1.547	1.193	0.856	0.539	0.241	−0.040	−0.300	−0.533	−0.733
	o-Cresol	3.695	3.156	2.641	2.149	1.674	1.221	0.786	0.369	−0.027	−0.394	−0.723
	2,4-Dimethylphenol	5.081	4.402	3.748	3.119	2.506	1.916	1.344	0.791	0.259	−0.242	−0.700
	Aniline	4.503	4.187	3.861	3.550	3.243	2.946	2.658	2.380	2.121	1.892	1.708
	N-Methylaniline	3.680	2.752	1.871	1.037	0.244	−0.499	−1.194	−1.842	−2.433	−2.954	−3.385
	N,N-Dimethylaniline	5.190	4.422	3.708	3.040	2.409	1.818	1.262	0.740	0.256	−0.183	−0.563
	Chlorobenzene	9.912	9.050	8.233	7.444	6.665	5.900	5.138	4.375	3.611	2.851	2.102

	o-Dichlorobenzene	12.129	10.987	9.939	8.948	7.985	7.049	6.127	5.209	4.296	3.393	2.506
	p-Chlorotoluene	11.518	10.515	9.560	8.633	7.716	6.814	5.916	5.016	4.116	3.222	2.344
	Trichlorotoluene	15.626	14.065	12.646	11.315	10.030	8.787	7.568	6.359	5.162	3.981	2.828
	Methyl benzoate	6.105	5.447	4.801	4.170	3.554	2.968	2.421	1.931	1.543	1.346*	1.601*
	Dimethyl phthalate	4.459	3.727	3.020	2.345	1.707	1.131	0.637	0.267	0.106	0.328*	1.449*
	Diethyl phthalate	9.259	8.023	6.849	5.732	4.662	3.662	2.742	1.933	1.304*	1.004*	1.462*
	Acetophenone	6.953	6.262	5.580	4.910	4.249	3.609	2.994	2.413	1.892	1.473*	1.253*
303	Pentane	11.090	10.066	9.113	8.213	7.344	6.510	5.698	4.903	4.126	3.373	2.654
	Hexane	12.777	11.582	10.470	9.419	8.405	7.430	6.482	5.553	4.645	3.765	2.925
	Heptane	14.444	13.078	11.807	10.605	9.445	8.330	7.245	6.182	5.143	4.137	3.176
	Octane	16.094	14.558	13.127	11.775	10.469	9.214	7.992	6.795	5.625	4.492	3.411
	Nonane	17.732	16.025	14.435	12.932	11.480	10.085	8.727	7.395	6.095	4.835	3.633
	Decane	19.360	17.482	15.733	14.079	12.482	10.946	9.451	7.986	6.554	5.168	3.845
	Cyclohexane	11.675	10.625	9.641	8.706	7.796	6.916	6.054	5.202	4.361	3.537	2.738
	Propanoic acid	2.770	2.303	1.891	1.524	1.189	0.887	0.612	0.363	0.141	−0.047	−0.194
	Butanoic acid	4.261	3.623	3.052	2.534	2.053	1.611	1.200	0.816	0.464	0.149	−0.119
	Pentanoic acid	5.774	4.965	4.234	3.565	2.939	2.357	1.809	1.291	0.808	0.366	−0.023
	Hexanoic acid	7.299	6.319	5.430	4.610	3.838	3.115	2.430	1.779	1.165	0.596	0.087
	Heptanoic acid	8.832	7.681	6.633	5.662	4.745	3.882	3.060	2.275	1.530	0.834	0.204
	Octanoic acid	10.371	9.049	7.841	6.720	5.657	4.653	3.695	2.776	1.900	1.078	0.327
	Nonanoic acid	11.913	10.420	9.054	7.781	6.572	5.429	4.334	3.281	2.274	1.325	0.453
	Decanoic	13.457	11.794	10.268	8.845	7.940	6.206	4.975	3.788	2.650	1.574	0.582
	Dodecanoic acid	16.552	14.547	12.703	10.978	9.332	7.767	6.262	4.807	3.408	2.079	0.844

* Data not used in the linear regression of eqn. 2.

TABLE III

SLOPES AND INTERCEPTS OF EQNS. 1–3 FOR SOLUTES IN TABLE II

Group	*Solute*	*Eqn. 1*			*Eqn. 2*			*Eqn. 3**		
		Slope	*Intercept*	r^{**}	*Slope*	*Intercept*	r^{**}	*Slope*	*Intercept*	r^{**}
I	Benzene	0.98	−2.92	0.9988	−6.00	7.85	0.9999	−5.95	4.82	0.9989
	Toluene	0.95	−2.89	0.9986	−7.37	9.47	1.0000	−7.07	6.16	0.9986
	Ethylbenzene	0.98	−3.05	0.9995	−8.92	11.24	1.0000	−8.68	7.92	0.9995
	n-Propylbenzene	0.99	−3.16	0.9997	−10.35	12.86	0.9999	−10.01	9.37	0.9997
	n-Butylbenzene	0.94	−3.01	0.9996	−11.78	14.47	0.9999	−10.78	10.38	0.9996
	n-Pentylbenzene	0.96	−3.01	1.0000	−13.14	15.99	0.9999	−12.10	11.95	0.9999
	n-Hexylbenzene	1.00	−3.31	1.0000	−14.56	17.58	0.9999	−13.87	13.73	0.9999
	Naphthalene	0.98	−3.90	0.9987	−9.36	12.00	0.9999	−9.35	8.02	0.9990
	Anthracene	0.92	−4.42	1.0000	−12.71	16.07	0.9998	−11.97	10.55	0.9992
	Biphenyl	0.84	−2.90	0.9976	−11.22	14.05	0.9999	−9.64	9.05	0.9978
	Chlorobenzene	1.00	−3.28	0.9985	−7.76	9.82	0.9999	−7.65	6.48	0.9985
	o-Dichlorobenzene	0.96	−3.53	0.9978	−9.52	11.90	0.9999	−8.65	7.50	0.9976
	p-Chlorotoluene	0.96	−3.14	0.9919	−9.13	11.42	0.9999	−8.66	7.75	0.9917
	Trichlorotoluene	0.98	−4.02	0.9976	−12.65	15.27	0.9999	−12.60	10.76	0.9978
	Acetophenone	1.10	−2.70	0.9994	−6.31	6.81	0.9992	−6.35	4.55	0.9969
	Pentane	1.11	−4.63	0.9997	−8.38	10.83	0.9988	−8.68	6.93	0.9999
	Hexane	1.09	−4.79	0.9999	−9.79	12.48	0.9988	−9.88	8.24	0.9999
	Heptane	1.06	−4.82	0.9998	−11.19	14.11	0.9988	−10.94	9.42	0.9998
	Octane	1.06	−5.01	0.9999	−12.60	15.71	0.9988	−12.10	10.64	0.9999
	Nonane	1.05	−5.10	0.9998	−14.01	17.31	0.9988	−13.36	12.01	0.9998

	Decane	1.07	−5.35	0.9999	−15.42	18.90	0.9989	−14.72	13.44	0.9998
	Cyclohexane	1.00	−4.36	0.9999	−8.58	11.20	1.0000	−8.60	6.87	0.9999
	Propanoic acid	0.94	−2.11		−2.94	2.51	0.9987	−3.14	0.27	
	Butanoic acid	0.76	−1.69		−4.35	3.96	0.9993	−4.80	3.97	
	Pentanoic acid	1.00	−2.26	0.9986	−5.76	5.43	0.9995	−5.75	2.98	0.9994
	Hexanoic acid	1.04	−2.44	0.9999	−7.16	6.92	0.9996	−7.10	4.36	0.9997
	Heptanoic acid	1.03	−2.50	0.9999	−8.57	8.41	0.9997	−8.55	5.80	0.9997
	Octanoic acid	1.02	−2.55	0.9999	−9.98	9.90	0.9998	−9.28	6.79	0.9998
	Nonanoic acid	1.01	−2.59	0.9999	−11.39	11.41	0.9998	−10.54	8.12	0.9999
	Decanoic acid	1.00	−2.61	0.9999	−12.79	12.91	0.9997	−11.27	9.06	0.9998
	Dodecanoic acid	0.96	−2.58	0.9999	−15.61	15.92	0.9999	−13.05	11.15	0.9999
II	Benzyl alcohol	0.78	−1.60	0.9981	−6.67	6.20	0.9899	−5.69	3.34	0.9984
	2-Phenylethanol	0.74	−1.54	0.9990	−8.10	7.62	0.9922	−6.36	4.14	0.9997
	3-Phenylpropanol	0.75	−1.41	0.9992	−9.53	9.07	0.9936	−7.64	5.43	0.9995
	Phenol	1.81	−0.76	0.9979	−3.07	2.17	0.9957	−5.39	3.05	0.9986
	o-Cresol	1.48	−0.78	0.9994	−4.43	3.54	0.9978	−6.27	4.25	0.9987
	2,4-Dimethylphenol	1.22	−0.46	0.9888	−5.80	4.92	0.9986	−7.02	5.39	0.9981
	Aniline	1.81	−5.03	0.9980	−2.84	4.42	0.9979	−4.97	2.86	0.9991
	N-Methylaniline	1.03	2.18	0.9979	−7.11	3.31	0.9949	−5.98	4.55	0.9964
	N,N-Dimethylaniline	1.56	0.13	0.9975	−5.75	4.89	0.9954	−7.13	6.31	0.9973
	Methyl benzoate	1.28	−1.86	0.9990	−5.69	5.90	0.9974	−7.63	5.78	0.9985
	Dimethyl phthalate	1.70	−0.77	0.9919	−5.41	4.02	0.9872	−6.95	4.88	0.9910
	Diethyl phthalate	1.09	−1.53	0.9992	−10.20	8.88	0.9982	−9.93	7.46	1.0000

* The mean experimental k_i values from Table IV or experimental data from the literature[8,13,15] were used for calculations of the linear regression coefficients.

** Correlation coefficient of the linear regression.

tivity coefficients of these solutes in the mobile phase are correct. Below we shall first discuss the data of this group, containing mainly solutes of homologous series.

Discussion of data of Group I

The slopes of eqn. 2 can be used directly for the calculation of changes in the retention of a solute with variation in mobile phase composition. However, for the prediction of a solute retention utilizing eqn. 1, it is necessary to know also both γ_{is} and φ. The main problem in the quantitative prediction of the retention of a solute is the fact that constituents of the stationary phase, interacting with the solute in the mobile phase, and their composition are still open to question. The equilibrium isotherms[25–27] measured for the adsorption of organic modifier[25–27] and water[27] from aqueous mixtures on to bonded silica permit a better understanding of such a situation, but it is still insufficient for the creation of any reliable model for the prediction of solute activity coefficients in the stationary phase. On the other hand, as pointed out by Locke[28], for stationary phases of low surface energy, such as *n*-alkyl chains attached to a silica surface, stationary phase interactions will tend to be weak and non-selective. Hence, for the quantitative prediction of the retention of a solute by means of calculated activity coefficients in the mobile phase it is necessary to know the extent to which the stationary phase affects the retention. For example, the intercept of eqn. 1 [$= \ln(\Phi/\gamma_{is})$] equals the retention for $\ln \gamma_{im} = 0$. At this point the mean $\ln(\Phi/\gamma_{is})$ values for alkylbenzenes, alkanes and monocarboxylic acids are -3.05 ± 0.14, -4.95 ± 0.26 and -2.37 ± 0.30, respectively. Differences between these values are significant, indicating that the activity coefficient in the stationary phase depends on the character of the functional group of a homologous series. Also, the decrease in $\ln(\Phi/\gamma_{is})$ values with increase in the number of carbon atoms in *n*-alkyl chain of a homologous compound (Table III) reveals their mutual dependence. Therefore, we calculated $\ln \gamma_{is}$ values for different solutes using eqn. 1, average experimental k_i values from Table IV and $\ln \gamma_{im}$ values from Table II. For these calculations it is necessary to know the value of $\ln \Phi$. Colin *et al.*[29] stated that a typical value of $\ln \Phi$ for LiChrosorb RP-18 and a methanol–water mixture was approximately -2.80. We adopted this value in these calculations, assuming that the phase ratio is constant for a defined column and independent of the concentrations of the mobile phase components. Calculated $\ln \gamma_{is}$ values are presented in Table V. These values should be considered approximate, because the reliability of calculated γ_{is} values depends on the reliability of both the value of the phase ratio in the column and the experimental capacity factors, if, of course, the mobile phase activity coefficients are correct. Hence the interpretation of the values presented in Table V should be general and extremely careful. Calculated $\ln \gamma_{is}$ values of solutes of Group I are independent of the mobile phase composition, indicating the stationary phase composition to be constant over the φ range, as was assumed in eqn. 1. However, $\ln \gamma_{is}$ values of solutes of homologous series are linearly dependent on the number of carbon atoms in the *n*-alkyl chain of a homologue, showing the same behaviour as calculated $\ln \gamma_{im}$ values and/or experimental $\ln k_i$ values (see, *e.g.*, refs. 13, 30 and 31). Hence, when $\ln k_i$ values of homologues have been correlated with corresponding $\ln \gamma_{im}$ values at defined φ, the obtained intercept of the correlation indicates that at $\gamma_{im} = 1$, γ_{is} also tends to be equal to 1, *i.e.*, the mean intercept of such a relationship attained for various homologous series at different φ is equal to -2.72 ± 0.16. This

value is very close to the adopted value of ln Φ. Therefore, correlated values of ln k_i and ln γ_{im} for a homologue at different φ or for different homologues at defined φ do not converge to the common intersection point at ln $\gamma_{im} = 0$ (Fig. 1), because γ_{is} is invariant with φ.

From Table V, it also appears that the polar solutes are more soluble than non-polar solutes in the stationary phase and, of course, the solubility increases with a solute's polarity. For example, alkanes show lower solubility in the stationary phase than acids and alkylbenzenes, while the solubility of each class decreases as the alkyl chain in the solute molecule increases. Hence, monocarboxylic acids show better solubility in both the mobile and stationary phases than, *e.g.*, *n*-alkanes. We consider it unlikely that the solvation layer formed on the surface of bonded silica during the chromatographic process is responsible for such behaviour of solutes in the stationary phase. It seems more probable that free silanol groups on the surface of bonded silica play an active role in the retention process[21].

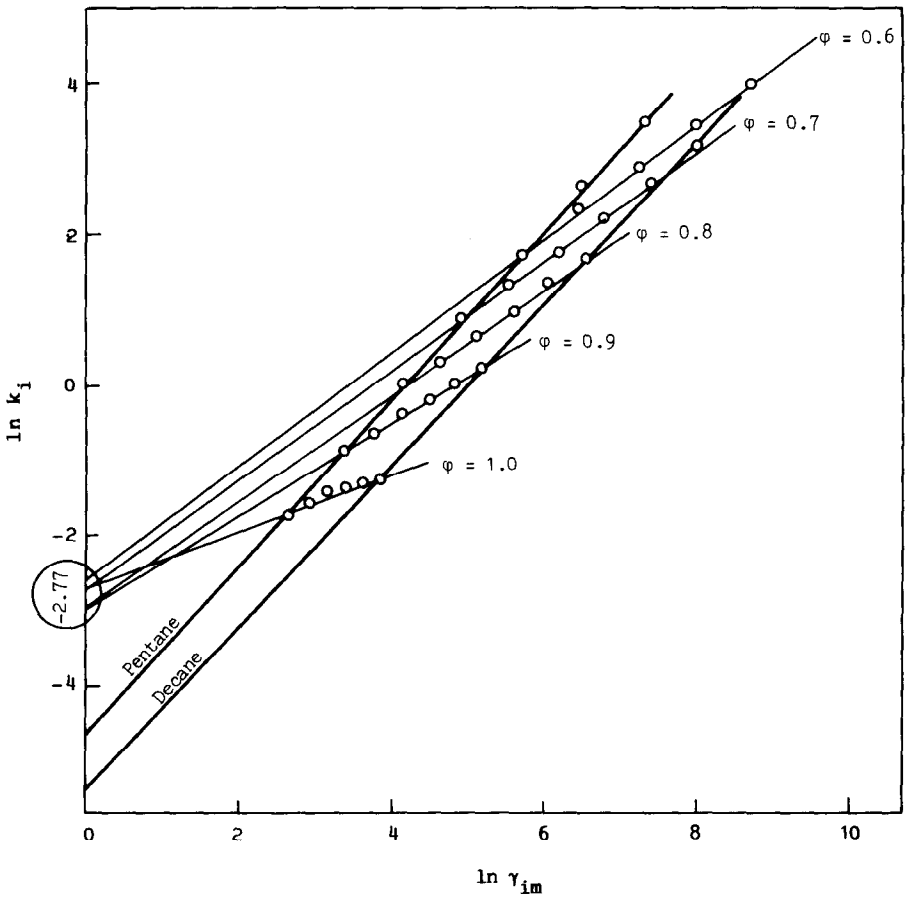

Fig. 1. Plots of the linear relationship between ln γ_{im} and ln k_i values for a defined alkane at different φ (thick lines) and for different alkanes at defined φ (thin lines). The average intercept of the thin lines (in the circle) corresponds to the ln Φ value.

TABLE IV

EXPERIMENTAL AND PREDICTED CAPACITY RATIOS, k_i

Predicted k_i values were calculated using ln γ_{is} values from Table V ($Pred_1$) and ln $\gamma_{is} = 0$ ($Pred_2$). Values designated as $Pred_3$ were calculated using eqns. 6, 7 and 1. Experimental data (Exp.) are the average values of the literature data.

Group	*Solute*	*Parameter*	*φ*									*Ref.*
			0.1	*0.2*	*0.3*	*0.4*	*0.5*	*0.6*	*0.7*	*0.8*	*0.9*	*1.0*	
I	Benzene	Exp.				11.39	6.94	3.34	1.75	1.05	0.60	0.33	8, 13, 14,
		S.d.*				4.73	2.10	1.42	0.79	0.39	0.42	0.14	15, 16**,
		$Pred_1$				12.05	6.64	3.64	1.98	1.07	0.58	0.31	Table I
		$Pred_2$				14.07	7.75	4.25	2.31	1.25	0.68	0.37	
	Toluene	Exp.				26.17	15.89	6.59	3.07	1.67	0.87	0.39	8, 13, 14
		S.d.				16.00	4.98	3.03	1.47	0.58	0.30	0.14	15, Table I
		$Pred_1$				31.56	15.18	7.26	3.45	1.63	0.77	0.37	
		$Pred_2$				40.77	19.61	9.37	4.45	2.10	0.99	0.47	
	Ethylbenzene	Exp.				88.10	36.96	14.42	5.95	2.51	1.22	0.47	8, 14, Table I
		S.d.						2.43	1.09	0.63	0.26	0.12	
		$Pred_1$				92.02	37.90	15.64	6.42	2.64	1.09	0.46	
		$Pred_2$				124.46	51.26	21.16	8.69	3.57	1.48	0.62	
	n-Propylbenzene	Exp.					83.44	28.48	9.97	3.70	1.49	0.54	8, 14, Table I
		S.d.						5.46	3.00	1.21	0.40	0.17	
		$Pred_1$					83.85	30.14	10.82	3.89	1.42	0.53	
		$Pred_2$					123.22	44.30	15.89	5.72	2.08	0.77	
	n-Butylbenzene	Exp.						52.21	16.30	5.54	2.07	0.67	8, 14, Table I
		S.d.						8.71	5.13	1.88	0.59	0.25	
		$Pred_1$						58.85	18.45	5.82	1.86	0.61	
		$Pred_2$						91.83	28.79	9.08	2.91	0.96	
	n-Pentylbenzene	Exp.							32.34	9.60	2.86	0.86	14, Table I
		$Pred_1$							35.81	9.95	2.82	0.82	
		$Pred_2$							50.70	14.07	3.98	1.16	

n-Hexylbenzene	Exp.				55.74	13.90	3.47	0.87	14, Table I
	$Pred_1$				57.51	14.00	3.48	0.90	
	$Pred_2$				90.29	21.98	5.47	1.42	
Pentane	Exp.	31.94	13.46	5.49	2.39	0.98	0.40	0.18	13, Table I
	$Pred_1$	25.89	11.25	4.99	2.25	1.04	0.49	0.24	
	$Pred_2$	91.29	39.65	17.60	7.95	3.65	1.72	0.84	
Hexane	Exp.		27.52	9.97	3.84	1.35	0.52	0.20	13, Table I
	$Pred_1$		22.87	8.86	3.50	1.41	0.59	0.25	
	$Pred_2$		99.48	38.55	15.23	6.14	2.55	1.10	
Heptane	Exp.		51.68	17.75	5.88	1.81	0.66	0.23	13, Table I
	$Pred_1$		46.53	15.72	5.43	1.92	0.70	0.27	
	$Pred_2$		244.69	82.68	28.56	10.10	3.70	1.41	
Octane	Exp.			29.67	8.85	2.56	0.80	0.24	13, Table I
	$Pred_1$			26.90	8.13	2.52	0.81	0.28	
	$Pred_2$			174.51	52.72	16.36	5.27	1.79	
Nonane	Exp.			54.27	14.27	3.75	0.99	0.26	Table I
	$Pred_1$			49.75	13.13	3.58	1.02	0.31	
	$Pred_2$			363.94	96.06	26.18	7.43	2.23	
Decane	Exp.				23.00	5.28	1.21	0.28	Table I
	$Pred_1$				20.61	4.92	1.23	0.33	
	$Pred_2$				173.47	41.43	10.36	2.76	
Hexanoic acid	Exp.	4.75		1.10	0.55				13
	$Pred_1$	4.47		1.09	0.57				
	$Pred_2$	2.74		0.67	0.35				
Heptanoic acid	Exp.	11.26		1.93	0.84				13
	$Pred_1$	10.54		1.95	0.89				
	$Pred_2$	6.79		1.26	0.57				

(Continued on p. 60)

TABLE IV *(continued)*

Group	*Solute*	*Parameter*	*φ*										*Ref.*
			0.1	*0.2*	*0.3*	*0.4*	*0.5*	*0.6*	*0.7*	*0.8*	*0.9*	*1.0*	
	Octanoic acid	Exp.						3.36	1.30	0.54			13
		$Pred_1$						3.27	1.30	0.54			
		$Pred_2$						2.38	0.95	0.39			
	Nonanoic acid	Exp.						5.91	2.05	0.74	0.28		13
		$Pred_1$						5.78	2.02	0.74	0.29		
		$Pred_2$						4.50	1.57	0.57	0.22		
	Decanoic acid	Exp.						10.23	3.17	1.02	0.35		13
		$Pred_1$						10.43	3.18	1.02	0.35		
		$Pred_2$						8.54	2.61	0.84	0.28		
	Dodecanoic acid	Exp.							7.55	2.01	0.56		13
		$Pred_1$							8.06	1.99	0.53		
		$Pred_2$							7.22	1.78	0.47		
	Naphthalene	Exp.					29.23	10.95	4.11	1.80	0.83	0.35	8, 15, 16**
		S.d.						3.02	1.00	0.58	0.35	0.15	
		$Pred_1$					32.88	12.91	4.99	1.90	0.72	0.27	
		$Pred_2$					93.04	36.53	14.11	5.38	2.04	0.77	
	Chlorobenzene	Exp.					14.89	6.75	2.87	1.28	0.74	0.31	8, 15
		S.d.					5.10	2.15	0.93	0.39	0.31	0.11	
		$Pred_1$					14.30	6.67	3.11	1.45	0.68	0.32	
		$Pred_2$					21.54	10.05	4.69	2.18	1.02	0.48	

	Acetophenone	Exp.		32.54	14.00	6.80	3.84	1.84	0.94	0.53	0.38	0.18	8
		$Pred_1$		26.15	13.38	6.90	3.64	1.97	1.10	0.65	0.43	0.35	
		$Pred_2$		15.64	8.00	4.13	2.18	1.18	0.66	0.39	0.26	0.21	
II	Benzyl alcohol	Exp.	16.99	9.47	4.51	2.66	1.83	0.90	0.51	0.31	0.20	0.15	8
		$Pred_1$	33.11	14.63	6.61	3.04	1.44	0.72	0.37	0.21	0.14	0.14	
		$Pred_2$	17.99	7.95	3.59	1.65	0.79	0.39	0.20	0.11	0.08	0.07	
		$Pred_3$	15.97	9.04	5.12	2.90	1.64	0.93	0.53	0.30	0.17	0.10	
	Phenol	Exp.	12.94	7.42	4.20	2.43	1.38	0.83	0.44	0.24	0.18	0.11	8, 15
		S.d.	0.40	0.46	0.44	0.38	0.27	0.21	0.11	0.07	0.08	0.06	
		$Pred_1$	4.75	3.26	2.29	1.64	1.19	0.88	0.67	0.51	0.41	0.33	
		$Pred_2$	0.40	0.28	0.19	0.14	0.10	0.08	0.06	0.04	0.03	0.03	
		$Pred_3$	12.27	7.16	4.17	2.44	1.42	0.83	0.48	0.28	0.16	0.10	
	o-Cresol	Exp.		21.30	11.16	5.61	3.09	1.52	0.77	0.41	0.27	0.15	8, 15
		S.d.			1.54	0.82	0.81	0.31	0.18	0.11	0.11	0.07	
		$Pred_1$		9.71	5.94	3.69	2.35	1.52	1.00	0.67	0.47	0.34	
		$Pred_2$		0.83	0.51	0.31	0.20	0.13	0.09	0.06	0.04	0.03	
		$Pred_3$		20.00	10.69	5.71	3.05	1.63	0.87	0.46	0.25	0.13	
	Aniline	Exp.		6.27	3.90	2.62	1.50	0.87	0.49	0.31	0.20	0.13	8, 16**
		$Pred_1$		2.89	2.12	1.56	1.16	0.87	0.66	0.51	0.40	0.34	
		$Pred_2$		2.80	2.05	1.51	1.12	0.84	0.64	0.49	0.39	0.33	
		$Pred_3$		6.46	3.93	2.39	1.45	0.89	0.54	0.33	0.20	0.12	
	Methyl benzoate	Exp.				15.35	6.83	3.58	1.50	0.82	0.64	0.28	8
		$Pred_1$				9.96	5.55	3.21	1.97	1.33			
		$Pred_2$				2.06	1.15	0.66	0.41	0.28			
		$Pred_3$				15.30	7.13	3.33	1.55	0.72	0.34	0.16	

* Standard deviations were calculated only for three or more experimental data.

** Retention data obtained on hexadecyldimethylsilane–silica packing.

TABLE V

AVERAGE ln γ_{is} VALUES

Calculated using eqn. 1 and experimental data from Table IV. Data in parentheses were calculated using eqn. 6. S.d. = standard deviation; r.s.d. = relative standard deviation.

Group	*Solute*	*ln* γ_{is}	*S.d.*	*R.s.d. (%)*
I	Benzene	0.185	0.07	37
	Toluene	0.286	0.11	38
	Ethylbenzene	0.332	0.07	21
	n-Propylbenzene	0.415	0.05	12
	n-Butylbenzene	0.475	0.11	23
	n-Pentylbenzene	0.376	0.06	16
	n-Hexylbenzene	0.481	0.02	4
	Pentane	1.291	0.19	15
	Hexane	1.502	0.16	11
	Heptane	1.690	0.12	7
	Octane	1.900	0.10	5
	Nonane	2.015	0.10	5
	Decane	2.161	0.12	6
	Hexanoic acid	−0.523	0.06	11
	Heptanoic acid	−0.470	0.07	15
	Octanoic acid	−0.353	0.03	8
	Nonanoic acid	−0.283	0.03	11
	Decanoic acid	−0.225	0.01	4
	Dodecanoic acid	−0.137	0.06	44
	Naphthalene	1.073	0.18	17
	Chlorobenzene	0.436	0.08	19
	Acetophenone	−0.544	0.14	26
II	Benzyl alcohol	−0.640 (−1.127)	0.38	59
	Phenol	−2.496 (−1.800)	0.74	30
	o-Cresol	−2.492 (−1.462)	0.56	22
	Aniline	−0.057 (−0.693)	0.60	1053
	Methyl benzoate	−1.545 (−0.600)	0.37	24

Direct comparison between average experimental k_i values and those calculated using either data from Table V or ln $\gamma_{is} = 0$ ($Pred_1$ and $Pred_2$, respectively, in Table IV) and ln $\Phi = -2.80$ demonstrates that the adsorption or compulsory absorption[32] of a solute in the stationary phase cannot be *a priory* neglected. Consequently, the UNIFAC method can be used merely to give a rough estimation of absolute retention indices of certain compounds in RP chromatographic systems. Also, the agreement between the experimental and calculated ($Pred_1$) capacity factors in Table IV is due to the fact that the same set of data and equation are used both for the calculation of the stationary phase activity coefficients and for back-calculations of capacity factors.

Discussion of data of Group II

For solutes of Group II in Table III, which includes predominantly solutes containing aliphatic or aromatic hydroxy and aromatic amino groups, the UNIFAC parameters produce γ_{im} values that create slopes of eqn. 2 that differ significantly from those obtained using observed k_i values. Consequently, calculated $\ln \gamma_{is}$ values of these solutes in Table V are also unreliable. The reason for this could be sought in the incorrect interaction parameters between hydroxy and amino groups and water, owing to the possible reactions

$$ROH + H_2O \rightleftharpoons RO^- + H_3O^+ \quad (4)$$

$$RNH_2 + H_2O \rightleftharpoons RNH_3^+ + OH^- \quad (5)$$

For phenol and aniline the dissociation constants[33] are $pK_a = 9.89$ at 20°C and $pK_a = 4.63$ at 25°C, respectively. Also, the UNIFAC model is a generalized method[34] preferring no concentration region in selecting the data base of the model. Therefore, the discrepancy between the measured and calculated activity coefficients of a given component in the system is usually greatest at infinite dilution of the component[34].

The imperfection of interaction parameters between some functional groups and water limits the reliability of the calculation of activity coefficients in the mobile phase of several classes of compounds utilizing the UNIFAC method. As water is an irreplaceable component of the mobile phase in RP-LC, the solubility of the solute in water is an important contributor to retention and hence relative retention. Hence an understanding of RP-LC requires an appreciation of solution phenomena in water. Therefore, we checked the validity of the UNIFAC interaction parameters between the functional groups of a solute and water, comparing calculated and experimental[5,15] solubilities of the solutes in water (Table VI). As expected, a good prediction of solubilities in water for hydrocarbons and chlorohydrocarbons is obtained. Also, fairly good agreement is obtained for solutes containing keto, carboxylic, ether and ester groups. However, the experimental and calculated solubilities of aliphatic and aromatic compounds containing hydroxy and amino groups were overestimated by a factor of 1.6–750, confirming that the UNIFAC interaction parameters between these groups and water is incorrect.

It appears that LC can be used advantageously to refine the UNIFAC model by providing for its data base infinite dilution activity coefficients. For example, on the basis of experimentally determined solubilities of a compound in water and the slopes and intercepts of eqn. 3, it is possible to calculate fairly reliable activity coefficients in the mobile and stationary phases using the following equations, based on eqns. 1 and 2:

$$\ln \gamma_{is} = \ln \gamma_{iw,exp} - \ln k_{iw} + \ln \Phi \quad (6)$$

$$\ln \gamma_{im} = m_i \varphi + \ln \gamma_{iw,exp} \quad (7)$$

Calculated $\ln \gamma_{is}$ values for several solutes utilizing eqn. 6 are presented in Table V in parentheses. On the basis of these data and $\ln \gamma_{im}$ values obtained from eqn. 7, we recalculated the capacity factors of these solutes, and the results are given in Table IV as $Pred_3$. Good agreement with experimental data is now obtained.

TABLE VI

EXPERIMENTAL[5,15] AND CALCULATED AQUEOUS SOLUBILITIES (S) FOR SOME ORGANIC COMPOUNDS

Solute	*S (mole/l × 10⁻²)*		*Solute*	*S (mole/l × 10⁻²)*	
	Exp.	*Calc.*		*Exp.*	*Calc.*
Acetophenone	4.95	5.32	Ethyl benzoate	0.50	3.82
Aniline	37.52	61.65	Ethyl propionate	19.33	10.80
Benzene	2.31	2.22	Hexanoic acid	8.60	3.50
Benzyl alcohol	35.83	7.86	1-Hexanol	5.68	0.45
1-Butanol	98.65	9.69	Isobutanol	113.32	5.54
Cyclohexane	0.08	0.05	Isopropylbenzene	0.06	0.01
Chlorobenzene	0.45	0.28	Methyl benzoate	1.84	9.50
1-Chlorobutane	0.76	0.42	2-Methyl-1-butanol	33.44	2.06
Chloroethane	9.22	13.35	3-Methyl-2-butanol	62.27	2.06
1-Chloropropane	3.50	2.37	2-Methylpropanoic acid	201.51	76.83
2-Chloropropane	4.02	1.72	Naphthalene	0.02	0.04
o-Cresol	20.15	138.00	1-Octanol	0.41	0.02
Dibutylamine	3.68	0.07	1-Pentanol	24.79	2.12
o-Dichlorobenzene	0.05	0.03	3-Pentanol	59.47	2.12
1,1-Dichloroethane	5.43	3.07	Phenol	94.25	544.00
1,2-Dichloroethane	9.04	8.02	Propylbenzene	0.05	0.01
Dichloromethane	23.61	21.58	Tetrachloromethane	0.53	0.51
Diethyl ether	80.22	5.59	Toluene	0.58	0.44
2,2-Dimethylbutane	0.02	0.01	1,1,1-Trichloroethane	0.77	4.96
2,3-Dimethylbutane	0.02	0.01	Trichloromethane	5.81	6.24
Dipropylamine	29.10	1.81	Triethylamine	14.90	0.02
Ethyl acetate	92.00	159.00	Vinyl ethyl ether	12.70	18.38
Ethylbenzene	0.16	0.07			

CONCLUSIONS

The UNIFAC method, developed for applications in chemical engineering and correlated here with RP-LC retention data, can merely be used for the calculation of activity coefficients in the mobile phase of certain solutes for which accurate UNIFAC parameters exist. Consequently, it can be used for the calculation of changes in the retention of a solute with variation in mobile phase composition.

By comparing calculated activity coefficients in the mobile phase and the observed capacity factors of solutes of homologous series, it is possible to determine the phase ratio of a chromatographic system and the activity coefficients of solutes in the stationary phase.

The imperfection of the UNIFAC parameters at infinite dilution of the component can advantageously be corrected by means of RP-LC retention data and the experimentally determined aqueous solubility of the component.

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