Journal of Chromatography, 555 (1991) 33–51
Elsevier Science Publishers B.V., Amsterdam

CHROM. 23 368

Experimental model for predicting solute retention time as a function of mobile phase composition in ternary reversed-phase high-performance liquid chromatography

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(Received February 18th, 1991)

ABSTRACT

It was observed that the variance of the solute retention time with the mobile phase composition in ternary reversed-phase high-performance liquid chromatography (RP-HPLC) approximately obeys a simple exponential model that is involved in the Snyder solvent strength theory. Using Newton or Marquardt algorithms, the values of the unknown non-linear parameters in the model were obtained, and further used to predict the retention time of solute as a function of ternary solvent composition to a good approximation, based upon three isocratic HPLC runs only. No dead time is needed for the prediction here. To test the model further, four sets of experimental data published by other groups were used. Three of the sets of experimental data conformed well with this model, but the other set showed serious deviations. In the latter instance, however, all the mobile phases used contained 5 m*M* heptanesulphonate and 1% acetic acid in addition to methanol, acetonitrile and water. For practical use, some problems in the non-linear least-squares estimation are discussed.

INTRODUCTION

The prediction of solute retention in polynary reversed-phase high-performance liquid chromatography (RP-HPLC) is of significance, because the location of the optimum mobile phase composition for certain separations under polynary conditions is very difficult or even impossible by using trial-and-error methods. Therefore, models describing the relationship between the solute retention and mobile phase composition in binary, ternary and quaternary RP-HPLC with a variety of automated optimization techniques for RP-HPLC separations have been continuously proposed since the 1970s [1–12]. With computers, these approaches have been used more and more widely.

In ternary RP-HPLC, a typical model to describe the relationship between solute retention and mobile phase composition is of the following form [7]:

$$\ln k' = a_1x_1 + a_2x_2 + a_3x_3 + a_{12}x_1x_2 + a_{13}x_1x_3 + a_{23}x_2x_3 + a_{123}x_1x_2x_3 \quad (1)$$

where x_1, x_2 and x_3 are the fraction of each component in the ternary mobile phase and a_1–a_{123} are the coefficients to be calculated. Certainly eqn. 1 has given a fairly complex description of solute–solvent behaviour. However, much experimentation would be needed for acquiring good estimates of the coefficients because there are seven unknown coefficients in the model. Generally, seven HPLC runs would be required. In addition, measurements of the dead times under different mobile phase compositions are essential in order to calculate the capacity factors, which could be difficult to measure accurately and be subject to variations depending on the solvent composition [2,13].

In this paper, we report an experimental model for the prediction of retention times of solutes as a function of mobile phase composition in ternary RP-HPLC. Experiments have shown that most of the relative deviations between the experimental and the predicted retention times for all the solutes tested using this model are within 3%, the maximum being not greater than 6.5%.

We used four other sets of experimental data to examine this model, published out by Bartha *et al.* [14], Issaq *et al.* [15] and Sekulic *et al.* [16]. The results examined are basically in agreement with ours.

We consider that the major merits of this experimental model are that only three RP-HPLC runs are needed for predicting solute retention times to a first approximation as a function of mobile phase composition in ternary RP-HPLC, and dead times are no longer needed for the prediction of solute retention times.

THEORETICAL

In RP-HPLC separations, it is generally observed that there is a linear relationship between log k' and mobile phase composition for certain organic modifiers [1,2]:

$$\log k' = \log k_w + S\varphi \tag{2}$$

where k' is the capacity factor of the solute, k_w is the extrapolated value of k' for pure water as mobile phase, φ is the volume fraction of the organic modifier in the mobile phase and S is a constant for a given solute and organic modifier. According to Snyder *et al.* [17], the coefficient S is related to the strength of the mobile phase; the solvent strength can be an approximate measure of the ability of a solvent to elute a solute from a column [18,19]. Hence, it could be suggested that eqn. 2 be expressed as the following form:

$$\log k' = A + BST \tag{3}$$

where A and B are constants for a given solute, column and solvent system and ST is the total solvent strength of the mobile phase, which can be calculated by using Snyder's appraoch [17–19]:

$$ST = s_1\varphi_1 + s_2\varphi_2 + \dots \tag{4}$$

where s is the solvent strength weighting factor of each component in the mobile phase, being 0 for water, 2.6 for methanol, 3.2 for acetonitrile and 4.5 for tetrahydrofuran [20,21]; φ is the volume fraction of each solvent in the mobile phase. Because the value of s for water is zero, we could rewrite eqn. 2, based on eqn. 4, as

$$\log k' = A + Bs\varphi \tag{5}$$

where s and φ are the solvent strength weighting factor and the volume fraction of the organic modifier only in the binary solvent system of water and the organic component, respectively. The product of s and φ here represents the total solvent strength of the mobile phase. Actually, eqn. 5 is the same as eqn. 2, and both will result in an identical value of the capacity factor in any case in binary RP-HPLC.

Theory predicts that mobile phases of same solvent strength will produce approximately equal ranges of capacity factors [19]. Therefore, the solute capacity factor in ternary RP-HPLC could possibly be expressed as a function of the total solvent strength of the mobile phase. We assume that this function has a similar form to eqn. 3. Substituting eqn. 4 in eqn. 3, we obtain

$$\log k' = A + B(s_1\varphi_1 + s_2\varphi_2) \tag{6}$$

where s and φ refer to the solvent strength weighting factors and the volume fractions of organic modifiers 1 and 2 in the mobile phase consisting of water and two organic solvents, respectively.

On comparing eqn. 6 with eqn. 2, we find that eqn. 6 is not a simple linear combination of two individual binary retention equations, because this kind of linear combination would have the following form:

$$\log k' = A' + S_1\varphi_1 + S_2\varphi_2 \tag{7}$$

or

$$\log k' = A' + B_1s_1\varphi_1 + B_2s_2\varphi_2 \tag{7'}$$

where A', S_1, S_2, B_1 and B_2 are constants.

Using eqn. 6 and the relationship between the retention time and the capacity factor of a solute:

$$t_R = \frac{L}{u}(1 + k') \tag{8}$$

we can obtain the following equation:

$$t_R = a \exp [b(s_1\varphi_1 + s_2\varphi_2)] + c \tag{9}$$

where the linear velocity of the mobile phase is assumed to be constant. In eqns. 8 and 9, t_R is the retention time of the solute, L is the column length and u is the linear velocity of the mobile phase; a, b and c are constants for a given solute, column and ternary solvent system. From eqn. 9, it could be seen that there are only three unknown parameters, and therefore it is possible to use three RP-HPLC runs to predict the retention time of a solute as a function of mobile phase composition.

EXPERIMENTAL

A Model LC-4A liquid chromatographic system (Shimadzu, Kyoto, Japan) with an SPD-2AS UV spectrophotometric detector (Shimadzu) set at 254 nm was used in

TABLE I

COEFFICIENTS OF EXPONENTIAL CURVE FITTING OF RETENTION TIMES *VS.* MOBILE PHASE COMPOSITIONS FOR THE SOLUTES IN GROUP 1 WITH TERNARY SOLVENT MIXTURES CONSISTING OF METHANOL, ACETONITRILE AND WATER, USING THE SOLVENT STRENGTH WEIGHTING FACTORS IN RP-HPLC

Solute	*a*	*b*	*c*
p-Chloronitrobenzene	290.7344	−2.4904	0.5296
8-Hydroxyquinoline	85 127.6833	−5.5284	1.3039
Benzophenone	335.1216	−2.3112	−0.2481
Naphthalene	572.9292	−2.5280	0.0062
Phenergan	738.7899	−2.6006	−0.5138
Diazepam	−4.1073	0.6115	17.0027
Dibutyl phthalate	9249.3730	−3.3599	−4.2784
Phenanthrene	557.1322	−1.8788	−6.5645
Acetanilide	3.9642	−0.8168	0.8501

the ternary RP-HPLC experiments. A Model C-R2AX data processing system (Shimadzu) was employed to record the experimental data. The non-linear least-squares fitting programs of the Newton [22] and Marquardt [23] algorithms were written in Pascal and BASIC, which were run on an AST computer (AST Research, Irvine, CA, USA) and an Apple II plus, respectively.

A stainless-steel column (150 × 4 mm I.D.) was packed with 10-μm YWG-$C_{18}H_{37}$ material (Second Chemical Reagent Factory, Tianjing, China). Methanol (CH_3OH), acetonitrile (ACN), tetrahydrofuran (THF) and water were used for two ternary mobile phase systems; nineteen solutes were eluted by one or another ternary solvent mixture. The flow-rate of the mobile phase was fixed at 1.0 ml/min.

Three mobile phase compositions were taken as the raw experimental data sampling points, where the values of the retention times of the solutes of interest were recorded by the C-R2AX data system. Therefore, we can obtain three sets of raw

TABLE II

COEFFICIENTS OF EXPONENTIAL CURVE FITTING OF RETENTION TIMES *VS.* MOBILE PHASE COMPOSITIONS FOR THE SOLUTES IN GROUP 2 WITH TERNARY SOLVENT MIXTURES OF METHANOL, TETRAHYDROFURAN AND WATER IN RP-HPLC, USING THE SOLVENT STRENGTH WEIGHTING FACTORS IN RP-HPLC

Solute	*a*	*b*	*c*
Toluene	−57.3852	0.0227	63.9574
Ethylbenzene	62.8576	−0.0468	−52.0560
Biphenyl	34.4027	−0.5650	−4.3960
Nitrobenzene	−0.00046	2.4683	2.4528
Chlorobenzol	−2.3026	0.2984	7.9513
p-Dichlorobenzene	−3.6346	0.3402	12.4137
o-Dichlorobenzene	−55.2138	0.0459	65.2931
m-Dichlorobenzene	−22.2652	0.1184	33.9193
Methyl salicylate	9.3597	−0.8188	1.3190
Benzyl acetate	103.2134	−2.8445	2.1003

experimental data about the retention times and the corresponding mobile phase compositions for each solute. The choice of the raw experimental data points will be discussed below.

The three sets of raw experimental data for each solute mentioned above were used to fit eqn. 9. This is the so-called non-linear least-squares fitting. Hence Newton [22] or Marquardt [23] algorithms can be used to find the values of a, b and c. Generally, the problem here is the choice of the initial values of a, b and c before the iteration. This is discussed below.

TABLE III

COMPARISON BETWEEN EXPERIMENTAL AND CALCULATED RETENTION TIMES OF THE SOLUTES IN GROUP 1 WITH TERNARY MOBILE PHASES CONSISTING OF METHANOL, ACETONITRILE AND WATER USING THE SOLVENT STRENGTH WEIGHTING FACTORS IN RP-HPLC

Solute	Parameter[a]	Retention time (min)						
		1	2	3	4	5	6	7
p-Chloronitrobenzene	Exp.	2.167	2.337	2.850	3.506	4.315	4.693	5.940
	Calc.	2.167	2.375	2.873	3.506	4.310	4.790	5.940
	r.d. (%)	0	−1.62	−0.81	0	0.12	−2.06	0
8-Hydroxyquinoline	Exp.	2.167	2.352	3.433	4.557	7.025	8.833	13.565
	Calc.	2.167	2.429	3.217	4.557	6.835	8.516	13.565
	r.d. (%)	0	−3.29	6.28	0	2.71	3.59	0
Benzophenone	Exp.	2.490	2.750	3.567	4.520	5.910	6.465	8.055
	Calc.	2.490	2.811	3.571	4.520	5.704	6.403	8.055
	r.d. (%)	0	−2.23	−0.12	0	3.48	0.96	0
Naphthalene	Exp.	2.988	3.350	4.322	5.476	7.012	7.958	10.040
	Calc.	2.988	3.373	4.297	5.476	6.978	7.878	10.040
	r.d. (%)	0	−0.68	0.57	0	0.48	1.01	0
Phenergan	Exp.	2.792	3.183	4.198	5.657	7.400	8.600	11.005
	Calc.	2.792	3.232	4.294	5.657	7.407	8.460	11.005
	r.d. (%)	0	−1.52	−2.28	0	−0.09	1.63	0
Diazepam	Exp.	2.350	2.633	3.485	4.350	5.385	5.402	6.077
	Calc.	2.350	2.774	3.585	4.350	5.071	5.416	6.077
	r.d. (%)	0	−5.35	−2.87	0	5.82	−0.27	0
Dibutyl phthalate	Exp.	4.253	5.475	9.378	14.830	23.218	26.493	38.520
	Calc.	4.253	5.746	9.562	14.830	22.103	26.721	38.520
	r.d. (%)	0	−4.95	−1.96	0	4.80	−0.86	0
Phenanthrene	Exp.	4.625	5.522	7.715	11.000	15.307	17.100	21.007
	Calc.	4.625	5.681	8.101	11.000	14.472	16.457	21.007
	r.d. (%)	0	−2.88	−5.01	0	5.46	3.76	0
Acetanilide	Exp.	1.575	1.590	1.683	1.732	1.850	1.875	1.923
	Calc.	1.575	1.604	1.665	1.732	1.804	1.842	1.923
	r.d. (%)	0	−0.88	1.04	0	2.49	1.76	0
Mobile phase composition (%)								
CH_3OH		80.0	72.0	56.0	40.0	24.0	16.0	0
ACN		0	5.0	15.0	25.0	35.0	40.0	50.0
Water		20.0	23.0	29.0	35.0	41.0	44.0	50.0

[a] r.d. (%) = 100 (exp. − calc.)/exp.

RESULTS AND DISCUSSION

In Tables I and II, the values of the non-linear parameters in eqn. 9 are listed for the solutes in two groups eluted by two different ternary solvent systems. The

TABLE IV

COMPARISON BETWEEN EXPERIMENTAL AND CALCULATED RETENTION TIMES OF THE SOLUTES IN GROUP 2 WITH TERNARY MOBILE PHASES CONSISTING OF METHANOL, TETRAHYDROFURAN AND WATER, USING THE SOLVENT STRENGTH WEIGHTING FACTORS IN RP-HPLC

Solute	Parameter[a]	Retention time (min)						
		1	2	3	4	5	6	7
Toluene	Exp.	4.157	3.890	3.690	3.558	3.458	3.173	2.953
	Calc.	4.157	3.918	3.678	3.558	3.437	3.196	2.953
	r.d. (%)	0	−0.72	0.32	0	0.59	−0.72	0
Ethylbenzene	Exp.	5.667	5.158	4.773	4.490	4.247	3.792	3.337
	Calc.	5.667	5.193	4.723	4.490	4.257	3.795	3.337
	r.d. (%)	0	−0.68	1.04	0	−0.25	−0.09	0
Biphenyl	Exp.	7.908	6.595	5.421	5.200	4.458	3.703	3.088
	Calc.	7.908	6.743	5.689	5.200	4.735	3.870	3.088
	r.d. (%)	0	−2.25	−4.95	0	−6.20	−4.52	0
Nitrobenzene	Exp.	2.412	2.398	2.400	2.332	2.328	2.195	2.095
	Calc.	2.412	2.390	2.356	2.332	2.303	2.221	2.095
	r.d. (%)	0	0.34	1.85	0	1.09	−1.19	0
Chlorobenzol	Exp.	3.988	3.758	3.583	3.432	3.290	2.992	2.798
	Calc.	3.988	3.774	3.549	3.432	3.312	3.062	2.798
	r.d. (%)	0	−0.43	0.95	0	−0.66	−2.33	0
p-Dichlorobenzene	Exp.	5.663	5.100	4.800	4.573	4.492	3.822	3.307
	Calc.	5.663	5.246	4.804	4.573	4.335	3.836	3.307
	r.d. (%)	0	−2.87	−0.88	0	3.50	−0.37	0
o-Dichlorobenzene	Exp.	5.267	4.865	4.300	4.042	3.757	3.248	2.792
	Calc.	5.267	4.780	4.289	4.042	3.794	3.295	2.792
	r.d. (%)	0	1.75	0.26	0	−0.99	−1.45	0
m-Dichlorobenzene	Exp.	6.300	5.605	5.238	4.823	4.525	3.833	3.267
	Calc.	6.300	5.718	5.125	4.823	4.518	3.899	3.267
	r.d. (%)	0	−2.02	2.16	0	0.15	−1.73	0
Methyl salicylate	Exp.	3.428	3.175	2.908	2.790	2.680	2.495	2.345
	Calc.	3.428	3.145	2.900	2.790	2.688	2.504	2.345
	r.d. (%)	0	0.95	0.28	0	−0.29	−0.36	0
Benzyl acetate	Exp.	2.683	2.408	2.295	2.267	2.223	2.150	2.148
	Calc.	2.683	2.454	2.314	2.267	2.230	2.179	2.148
	r.d. (%)	0	−1.89	−0.85	0	−0.32	−1.35	0
Mobile phase composition (%)								
CH_3OH		70.0	56.0	42.0	35.0	28.0	14.0	0
THF		0	12.0	24.0	30.0	36.0	48.0	60.0
Water		30.0	32.0	34.0	35.0	36.0	38.0	40.0

[a] r.d. (%) = 100 (exp. − calc.)/exp.

experimental and the calculated solute retention times with seven ternary mobile phase compositions are compared in Tables III and IV. In these cases, points 1, 4 and 7 are the raw experimental data sampling points, at which the calculated retention times of the solutes are the fitted values; points 2, 3, 5 and 6 are the random points which were used to examine this experimental model.

TABLE V

USING THE EXPERIMENTAL DATA OF BARTHA *ET AL.* [14]: RESULTS OF EXPONENTIAL CURVE FITTING OF SOLUTE RETENTION TIMES *VS.* MOBILE PHASE COMPOSITIONS AND COMPARISON BETWEEN EXPERIMENTAL AND CALCULATED SOLUTE RETENTION TIMES USING THE SOLVENT STRENGTH WEIGHTING FACTORS IN RP-HPLC

Solute	Parameter[a]	Retention time (min)					Fitted coefficients
		1	2	3	4	5	
Benzyl alcohol	Exp.	4.02	3.34	3.51	3.40	3.45	$a = 4.50 \cdot 10^{-7}$
	Calc.	4.02	3.341	3.49	3.399	3.431	$b = 8.3573$
	r.d. (%)	0	−0.022	0.63	0.03	0.55	$c = 3.2390$
Dimethyl phthalate	Exp.	4.79	5.49	4.75	5.03	4.94	$a = 2.71 \cdot 10^{10}$
	Calc.	4.77	5.48	4.88	5.06	4.97	$b = -16.5096$
	r.d. (%)	0.32	0.19	−2.84	−0.50	−0.55	$c = 4.7621$
Phenol	Exp.	6.20	3.72	4.39	4.05	4.18	$a = 8.73 \cdot 10^{-4}$
	Calc.	6.20	3.72	4.47	4.05	4.21	$b = 4.8394$
	r.d. (%)	0	0	−1.74	0	−0.68	$c = 2.6197$
Benzonitrile	Exp.	6.29	5.49	5.33	5.36	5.33	$a = 4.92 \cdot 10^{-17}$
	Calc.	6.288	5.42	5.46	5.43	5.44	$b = 21.7654$
	r.d. (%)	0.03	1.27	−2.45	−1.31	−2.04	$c = 5.4162$
p-Cresol	Exp.	7.71	4.51	5.40	5.00	5.33	$a = 0.0110$
	Calc.	7.71	4.51	5.58	5.00	5.22	$b = 3.6112$
	r.d. (%)	0	0	−3.32	0	1.98	$c = 2.2435$
Diethyl phthalate	Exp.	8.19	9.76	8.16	8.87	8.73	$a = 4.85 \cdot 10^{9}$
	Calc.	8.19	9.76	8.48	8.87	8.67	$b = -14.7940$
	r.d. (%)	0	0	−3.89	0	0.67	$c = 8.1462$
3,4-Dimethylphenol	Exp.	9.37	5.49	6.67	6.13	6.33	$a = 0.0489$
	Calc.	9.37	5.49	6.86	6.13	6.42	$b = 2.9352$
	r.d. (%)	0	0	−2.84	0	−1.36	$c = 1.7787$
Benzene	Exp.	11.91	8.42	9.07	8.80	8.73	$a = 6.14 \cdot 10^{-5}$
	Calc.	11.91	8.42	9.32	8.80	8.99	$b = 6.5021$
	r.d. (%)	0	0	−2.80	0	−3.02	$c = 7.5206$
2,4-Dimethylphenol	Exp.	11.48	6.21	7.87	7.09	7.39	$a = 0.0829$
	Calc.	11.48	6.21	8.09	7.09	7.48	$b = 2.8220$
	r.d. (%)	0	0	−2.76	0	−1.24	$c = 0.8854$
Mobile phase composition (%)							
ACN		0	46.1	26.1	35.7	32.3	
THF		38.2	0	16.6	8.6	11.5	
Water		61.8	53.9	57.3	55.7	56.2	

[a] r.d. (%) = 100 (exp. − calc.)/exp.

Tables III and IV indicate that each ternary solvent system actually consisted of two binary solvent systems of an organic modifier and water. The mobile phase compositions at the three raw experimental data sampling points 1, 4 and 7 were 100:0, 50:50 and 0:100, representing the ratios of the volume fractions of two binary solvent mixtures in the ternary solvent systems. From the tables, it can be seen that the maximum relative deviation between the experimental and the calculated solute

TABLE VI

USING THE EXPERIMENTAL DATA OF BARTHA *ET AL.* [14]: RESULTS OF EXPONENTIAL CURVE FITTING OF SOLUTE RETENTION TIME *VS.* MOBILE PHASE COMPOSITIONS AND COMPARISON BETWEEN EXPERIMENTAL AND CALCULATED VALUES OF SOLUTE RETENTION TIMES USING THE SOLVENT STRENGTH WEIGHTING FACTORS IN TERNARY RP-HPLC

Solute	Parameter[a]	Retention time (min)					Fitted coefficients
		1	2	3	4	5	
Benzyl alcohol	Exp.	4.33	3.77	4.17	3.95	4.02	$a = -628.257$
	Calc.	4.33	3.77	4.08	3.95	3.98	$b = -5.0666$
	r.d. (%)	0	0	2.06	0	1.06	$c = 5.2077$
Dimethyl phthalate	Exp.	6.95	7.23	7.75	7.53	7.81	$a = -2.3 \cdot 10^{-19}$
	Calc.	6.96	7.39	7.31	7.36	7.35	$b = 32.4709$
	r.d. (%)	−0.15	−2.18	5.62	2.23	5.84	$c = 7.4068$
Phenol	Exp.	4.33	4.35	4.49	4.30	4.49	$a = 400.212$
	Calc.	4.320	4.332	4.325	4.328	4.327	$b = -8.2249$
	r.d. (%)	0.23	0.42	3.680	−0.64	3.63	$c = 4.3109$
Benzonitrile	Exp.	5.95	7.23	6.63	6.85	7.04	$a = 133.610$
	Calc.	5.95	7.23	6.55	6.85	6.78	$b = -2.6355$
	r.d. (%)	0	0	1.21	0	3.72	$c = 1.5763$
p-Cresol	Exp.	6.33	5.70	6.35	6.00	6.25	$a = -1.5 \cdot 10^{10}$
	Calc.	6.33	5.70	6.16	6.00	6.04	$b = -19.7860$
	r.d. (%)	0	0	3.06	0	3.42	$c = 6.4373$
Diethyl phthalate	Exp.	17.15	15.55	18.92	17.51	18.48	$a = -2.8 \cdot 10^{19}$
	Calc.	17.54	15.77	17.29	16.90	17.02	$b = -36.8231$
	(r.d. (%)	−2.28	−1.40	8.62	3.47	7.89	$c = 17.5922$
3,4-Dimethylphenol	Exp.	9.23	7.23	8.87	8.11	8.54	$a = -8.26 \cdot 10^{8}$
	Calc.	9.23	7.23	8.61	8.11	8.24	$b = -16.3428$
	r.d. (%)	0	0	2.96	0	3.48	$c = 9.7412$
Benzene	Exp.	11.43	11.80	11.42	11.52	11.91	$a = 4.5 \cdot 10^{18}$
	Calc.	11.41	11.79	11.47	11.55	11.52	$b = -36.5770$
	r.d. (%)	0.16	0.09	−0.40	−0.25	3.25	$c = 11.4005$
2,4-Dimethylphenol	Exp.	10.80	8.58	10.41	9.50	10.07	$a = -5.43 \cdot 10^{7}$
	Calc.	10.80	8.58	10.05	9.50	9.64	$b = -13.9296$
	r.d. (%)	0	0	3.41	0	4.22	$c = 11.5699$
Mobile phase composition (%)							
CH_3OH		49.9	0	24.4	13.2	15.0	
ACN		0	37.5	19.2	27.6	26.3	
Water		50.1	62.5	56.4	59.2	58.7	

[a] r.d. (%) = 100 (exp. − calc.)/exp.

TABLE VII

USING THE EXPERIMENTAL DATA OF ISSAQ *ET AL.* [15]: RESULTS OF EXPONENTIAL CURVE FITTING OF SOLUTE RETENTION TIMES *VS.* TERNARY MOBILE PHASE COMPOSITIONS AND COMPARISON BETWEEN EXPERIMENTAL AND CALCULATED RETENTION TIMES OF THE SOLUTES USING THE SOLVENT STRENGTH WEIGHTING FACTORS IN RP-HPLC

Solute	Parameter[a]	Retention time (min)					Fitted coefficients
		1	2	3	4	5	
Anthraquinone	Exp.	7.23	8.26	9.57	11.65	16.44	$a = 1.12 \cdot 10^{15}$
	Calc.	7.23	8.09	9.57	12.10	16.44	$b = -17.9503$
	r.d. (%)	0	2.03	0	3.88	0	$c = 6.0213$
2-Methylanthraquinone	Exp.	8.98	10.30	11.98	14.75	21.20	$a = 5.81 \cdot 10^{15}$
	Calc.	8.98	10.07	11.98	15.33	21.20	$b = -18.7129$
	r.d. (%)	0	2.23	0	−3.93	0	$c = 7.5331$
Naphthalene	Exp.	7.23	9.16	11.30	14.67	22.41	$a = 2.13 \cdot 10^{14}$
	Calc.	7.23	8.76	11.30	15.49	22.41	$b = -16.7368$
	r.d. (%)	0	4.32	0	−5.58	0	$c = 4.8771$
2-Ethylanthraquinone	Exp.	10.94	13.27	15.82	19.98	30.19	$a = 2.56 \cdot 10^{15}$
	Calc.	10.94	12.74	15.82	21.11	30.19	$b = -18.0000$
	r.d. (%)	0	4.02	0	−5.66	0	$c = 8.4306$
Biphenyl	Exp.	8.98	11.77	15.13	20.38	34.03	$a = 1.19 \cdot 10^{16}$
	Calc.	8.98	11.21	15.13	22.00	34.03	$b = -18.7119$
	r.d. (%)	0	4.72	0	−7.93	0	$c = 6.0135$
Mobile phase composition (%)							
ACN		60.0	45.0	30.0	15.0	0	
THF		0	10.0	20.0	30.0	40.0	
Water		40.0	45.0	50.0	55.0	60.0	

[a] r.d. (%) = 100 (exp. − calc.)/exp.

TABLE VIII

COEFFICIENTS OF EXPONENTIAL CURVE FITTING OF RETENTION TIMES *VS.* MOBILE PHASE COMPOSITIONS FOR THE SOLUTES IN GROUP 1 WITH TERNARY SOLVENT MIXTURES OF METHANOL, ACETONITRILE AND WATER, USING THE SOLVENT POLARITY PARAMETERS IN RP-HPLC

Solute	*a*	*b*	*c*
p-Chloronitrobenzene	102.0783	−1.0129	0.5296
8-Hydroxquinoline	8333.9404	−2.2488	1.3039
Benzophenone	126.8513	−0.9401	−0.2482
Naphthalene	197.9749	−1.0283	0.0062
Phenergan	247.6103	−1.0579	−0.5138
Diazepam	−5.3106	0.2487	17.0021
Dibutyl phthalate	2253.0161	−1.3667	−4.2784
Phenanthrene	252.9215	−0.7642	−6.5646
Acetanilide	2.8122	−0.3323	0.8500

TABLE IX

COMPARISON BETWEEN EXPERIMENTAL AND CALCULATED RETENTION TIMES OF THE SOLUTES IN GROUP 1 WITH TERNARY MOBILE PHASES CONSISTING OF METHANOL, ACETONITRILE AND WATER, USING THE SOLVENT POLARITY PARAMETERS IN RP-HPLC

Solute	Parameter[a]	Retention time (min)						
		1	2	3	4	5	6	7
p-Chloronitrobenzene	Exp.	2.167	2.337	2.850	3.506	4.315	4.693	5.940
	Calc.	2.167	2.375	2.873	3.506	4.310	4.790	5.940
	r.d. (%)	0	−1.62	−0.81	0	0.12	−2.06	0
8-Hydroxyquinoline	Exp.	2.167	2.352	3.433	4.557	7.025	8.833	13.565
	Calc.	2.167	2.429	3.217	4.557	6.835	8.516	13.565
	r.d. (%)	0	−3.29	6.28	0	2.71	3.59	0
Benzophenone	Exp.	2.490	2.750	3.567	4.520	5.910	6.465	8.055
	Calc.	2.490	2.811	3.571	4.520	5.704	6.403	8.055
	r.d. (%)	0	−2.23	−0.12	0	3.48	0.96	0
Naphthalene	Exp.	2.988	3.350	4.322	5.476	7.012	7.958	10.040
	Calc.	2.988	3.373	4.297	5.476	6.978	7.878	10.040
	r.d. (%)	0	−0.68	0.57	0	0.48	1.01	0
Phenergan	Exp.	2.792	3.183	4.198	5.657	7.400	8.600	11.005
	Calc.	2.792	3.232	4.294	5.657	7.407	8.460	11.005
	r.d. (%)	0	−1.52	−2.28	0	−0.09	1.63	0
Diazepam	Exp.	2.350	2.633	3.485	4.350	5.385	5.402	6.077
	Calc.	2.350	2.774	3.585	4.350	5.071	5.416	6.077
	r.d. (%)	0	−5.35	−2.87	0	5.82	−0.27	0
Dibutyl phthalate	Exp.	4.253	5.475	9.378	14.830	23.218	26.493	38.520
	Calc.	4.253	5.746	9.562	14.830	22.103	26.720	38.520
	r.d. (%)	0	−4.95	−1.96	0	4.80	−0.86	0
Phenanthrene	Exp.	4.625	5.522	7.715	11.000	15.307	17.100	21.007
	Calc.	4.625	5.681	8.101	11.000	14.472	16.457	21.007
	r.d. (%)	0	−2.88	−5.01	0	5.46	3.76	0
Acetanilide	Exp.	1.575	1.590	1.683	1.732	1.850	1.875	1.923
	Calc.	1.575	1.604	1.665	1.732	1.804	1.842	1.923
	r.d. (%)	0	−0.88	1.04	0	2.49	1.76	0
Mobile phase composition (%)								
CH_3OH		80.0	72.0	56.0	40.0	24.0	16.0	0
ACN		0	5.0	15.0	25.0	35.0	40.0	50.0
Water		20.0	23.0	29.0	35.0	41.0	44.0	50.0

[a] r.d. (%) = 100 (exp. − calc.)/exp.

retention time [the r.d. (%) values in the tables] is not greater than 6.5%, and most are within 3%.

The results in Tables V–VII are based on experimental data published by Bartha *et al.* [14] and Issaq *et al.* [15]. In Tables V and VI, points 1, 2 and 4 were the raw experimental data sampling points and points 3 and 5 were used as the test points. In

Table VII, points 1, 3 and 5 were the raw experimental data points and points 2 and 4 were used as the test points. The tables show that the prediction model for the solute retention time described in this paper really does work. In some instances, *e.g.*, in Table V, the r.d. (%) values are even better than our experimental results.

An interesting fact is that a similar model to eqn. 9 will also be effective for predicting solute retention times, which could have the following form:

$$t_R = a' \exp\left[b'(P'_1\varphi_1 + P'_2\varphi_2)\right] + c' \tag{10}$$

where P' refers to the Snyder solvent polarity parameter of the organic modifier in mobile phases, being 5.1 for CH_3OH, 5.8 for ACN, 4.0 for THF (and 10.2 for water) [18,19]. In Tables VIII–XI are given the non-linear least-squares fitted coefficients and a comparison of the experimental and calculated retention times of the solutes by using Snyder polarity parameters based on our experimental data. Tables XII–XIV give the fitted coefficients and a comparison between the predicted and experimental retention times of the solutes by using the experimental data reported by Bartha *et al.* [14] and Issaq *et al.* [15], based on Snyder solvent polarity parameters. From the tables, it can be seen that the solute retention times predicted by using the solvent strength weighting factors are mostly close to those obtained by using the solvent polarity parameters with the same compositions of the mobile phase, although the fitted coefficients are different from each other.

However, no ternary solvent system conforms with eqn. 9. For instance, some systems containing supplementary chemicals in a ternary mobile phase of water, CH_3OH, ACN or THF show serious deviations from eqn. 9. Table XV gives typical results based on the experimental data reported by Sekulic *et al.* [16] by using Snyder solvent polarity parameters. In their experiment, all the mobile phases contained 5 m*M* heptanesulphonate and 1% acetic acid in addition to water, CH_3OH and ACN. Nevertheless, the situation would be even more serious if the solvent polarity parameters were replaced with the solvent strength weighting factors. Because of the

TABLE X

COEFFICIENTS OF EXPONENTIAL CURVE FITTING OF RETENTION TIMES *VS.* MOBILE PHASE COMPOSITIONS FOR THE SOLUTES IN GROUP 2 WITH TERNARY SOLVENT MIXTURES OF METHANOL, ACETONITRILE AND WATER, USING THE SOLVENT POLARITY PARAMETERS IN RP-HPLC

Solute	*a*	*b*	*c*
Toluene	−63.5506	−0.1704	63.9574
Ethyl benzene	50.9036	0.0352	−52.0560
Biphenyl	2.6993	9.4249	−4.3961
Nitrobenzene	−30.8040	−1.8565	2.4528
Chlorobenzol	−8.8305	−0.2244	7.9512
p-Dichlorobenzene	−16.8285	−0.2559	12.4131
o-Dichlorobenzene	−67.9021	−0.3453	65.2930
m-Dichlorobenzene	−37.8762	−0.0893	33.8358
Methyl salicylate	0.2340	0.6158	1.3190
Benzyl acetate	0.0003	2.1394	2.1003

TABLE XI

COMPARISON BETWEEN EXPERIMENTAL AND CALCULATED RETENTION TIMES OF THE SOLUTES IN GROUP 2 WITH TERNARY MOBILE PHASES CONSISTING OF METHANOL, TETRAHYDROFURAN AND WATER, USING THE SOLVENT POLARITY PARAMETERS IN RP-HPLC

Solute	Parameter[a]	Retention time (min)						
		1	2	3	4	5	6	7
Toluene	Exp.	4.157	3.890	3.690	3.558	3.458	3.173	2.953
	Calc.	4.157	3.918	3.678	3.558	3.437	3.196	2.953
	r.d. (%)	0	−0.72	0.32	0	0.59	−0.72	0
Ethylbenzene	Exp.	5.667	5.158	4.773	4.490	4.247	3.792	3.337
	Calc.	5.667	5.193	4.723	4.490	4.257	3.795	3.337
	r.d. (%)	0	−0.68	1.04	0	−0.25	−0.09	0
Biphenyl	Exp.	7.908	6.595	5.421	5.200	4.458	3.703	3.088
	Calc.	7.908	6.743	5.689	5.200	4.735	3.870	3.088
	r.d. (%)	0	−2.25	−4.95	0	−6.20	−4.52	0
Nitrobenzene	Exp.	2.412	2.398	2.400	2.332	2.328	2.195	2.095
	Calc.	2.412	2.390	2.356	2.332	2.303	2.221	2.095
	r.d. (%)	0	0.34	1.85	0	1.09	−1.19	0
Chlorobenzol	Exp.	3.988	3.758	3.583	3.432	3.290	2.992	2.798
	Calc.	3.988	3.774	3.549	3.432	3.312	3.062	2.798
	r.d. (%)	0	−0.43	0.95	0	−0.66	−2.33	0
p-Dichlorobenzene	Exp.	5.663	5.100	4.800	4.573	4.492	3.822	3.307
	Calc.	5.663	5.246	4.804	4.573	4.335	3.836	3.307
	r.d. (%)	0	−2.87	−0.88	0	3.50	−0.37	0
o-Dichlorobenzene	Exp.	5.267	4.865	4.300	4.042	3.757	3.248	2.792
	Calc.	5.267	4.780	4.289	4.042	3.794	3.295	2.792
	r.d. (%)	0	1.75	0.26	0	−0.99	−1.45	0
m-Dichlorobenzene	Exp.	6.300	5.605	5.238	4.823	4.525	3.833	3.267
	Calc.	6.300	5.718	5.125	4.823	4.518	3.899	3.267
	r.d. (%)	0	−2.02	2.16	0	0.15	−1.73	0
Methyl salicylate	Exp.	3.428	3.175	2.908	2.790	2.680	2.495	2.345
	Calc.	3.428	3.145	2.900	2.790	2.688	2.504	2.345
	r.d. (%)	0	0.95	0.28	0	−0.29	−0.36	0
Benzyl acetate	Exp.	2.683	2.408	2.295	2.267	2.223	2.150	2.148
	Calc.	2.683	2.454	2.314	2.267	2.230	2.179	2.148
	r.d. (%)	0	−1.89	−0.85	0	−0.32	−1.35	0
Mobile phase composition (%)								
CH_3OH		70.0	56.0	42.0	35.0	28.0	14.0	0
THF		0	12.0	24.0	30.0	36.0	48.0	60.0
Water		30.0	32.0	34.0	35.0	36.0	38.0	40.0

r.d. (%) = 100 (exp. − calc.)/exp.

interaction between the solvents and the supplementary chemicals, the calculation of the total solvent strength of the mobile phase may become more complex. Therefore, some modification to eqn. 9 might be needed if this kind of ternary mobile phase is used.

TABLE XII

USING THE EXPERIMENTAL DATA OF BARTHA *ET AL.* [14]: RESULTS OF EXPONENTIAL CURVE FITTING OF SOLUTE RETENTION TIMES *VS.* TERNARY MOBILE PHASE COMPOSITIONS AND COMPARISON BETWEEN EXPERIMENTAL AND CALCULATED VALUES OF SOLUTE RETENTION TIMES, USING SNYDER'S SOLVENT POLARITY PARAMETERS IN RP-HPLC

Solute	Parameter[a]	Retention time (min)					Fitted coefficients
		1	2	3	4	5	
Benzyl alcohol	Exp.	4.02	3.34	3.51	3.40	3.45	$a =$ 33.9121
	Calc.	4.02	3.34	3.48	3.40	3.43	$b =$ −2.4664
	r.d. (%)	0	0	0.72	0	0.73	$c =$ 3.2372
Dimethyl phthalate	Exp.	4.79	5.49	4.75	5.03	4.94	$a =$ $1.22 \cdot 10^{-6}$
	Calc.	4.79	5.49	4.88	5.03	4.96	$b =$ 5.6449
	r.d. (%)	0	0	−2.69	0	−0.44	$c =$ 4.7833
Phenol	Exp.	6.20	3.72	4.39	4.05	4.18	$a =$ 34.0663
	Calc.	6.20	3.72	4.44	4.05	4.17	$b =$ −1.4867
	r.d. (%)	0	0	−1.16	0	0.20	$c =$ 2.6866
Benzonitrile	Exp.	6.29	5.49	5.33	5.36	5.33	$a =$ 3138.2
	Calc.	6.289	5.42	5.45	5.43	5.43	$b =$ −5.3613
	r.d. (%)	0.01	1.23	−2.20	−1.27	−1.92	$c =$ 5.4206
p-Cresol	Exp.	7.71	4.51	5.40	5.00	5.33	$a =$ 29.5279
	Calc.	7.71	4.51	5.54	5.00	5.17	$b =$ −1.1238
	r.d. (%)	0	0	−2.67	0	2.95	$c =$ 2.4072
Diethyl phthalate	Exp.	8.19	9.76	8.16	8.87	8.73	$a =$ $6.79 \cdot 10^{-5}$
	Calc.	8.19	9.76	8.49	8.87	8.71	$b =$ 4.2867
	r.d. (%)	0	0	−4.09	0	0.21	$c =$ 8.1427
3,4-Dimethylphenol	Exp.	9.37	5.49	6.67	6.13	6.33	$a =$ 29.8979
	Calc.	9.37	5.49	6.82	6.13	6.35	$b =$ −0.9241
	r.d. (%)	0	0	−2.19	0	−0.32	$c =$ 2.0853
Benzene	Exp.	11.91	8.42	9.07	8.80	8.73	$a =$ 89.2399
	Calc.	11.91	8.42	9.29	8.80	8.95	$b =$ −1.9784
	r.d. (%)	0	0	−2.44	0	−2.50	$c =$ 7.5679
2,4-Dimethylphenol	Exp.	11.48	6.21	7.87	7.09	7.39	$a =$ 39.5542
	Calc.	11.48	6.21	8.03	7.09	7.392	$b =$ −0.8906
	r.d. (%)	0	0	−2.01	0	−0.02	$c =$ 1.3124
Mobile phase composition (%)							
ACN		0	46.1	26.1	35.7	32.3	
THF		38.2	0	16.6	8.6	11.5	
Water		61.8	53.9	57.3	55.7	56.2	

[a] r.d. (%) = 100 (exp. − calc.)/exp.

Although eqn. 9 is based on eqn. 6, the precision of the prediction of capacity factors using eqn. 6 is not as good as that for retention times in some instances. This could be due to the fact that the dead time is not easy to measure exactly and is subject to variations with the mobile phase composition [2,13]. Tables XVI–XIX show that the relative deviations between the experimental and calculated capacity factors are

TABLE XIII

USING THE EXPERIMENTAL DATA OF BARTHA *ET AL.* [14]: RESULTS OF EXPONENTIAL CURVE FITTING OF SOLUTE RETENTION TIMES *VS.* MOBILE PHASE COMPOSITIONS AND COMPARISON BETWEEN EXPERIMENTAL AND CALCULATED VALUES OF SOLUTE RETENTION TIMES USING THE SOLVENT POLARITY PARAMETERS IN TERNARY RP-HPLC

Solute	Parameter[a]	Retention time (min)					Fitted coefficients
		1	2	3	4	5	
Benzyl alcohol	Exp.	4.33	3.77	4.17	3.95	4.02	$a = -30.6719$
	Calc.	4.33	3.77	4.08	3.95	3.98	$b = -1.4320$
	r.d. (%)	0	0	2.06	0	1.06	$c = 5.1318$
Dimethyl phthalate	Exp.	6.95	7.23	7.75	7.53	7.81	$a = -1.8 \cdot 10^{-14}$
	Calc.	6.954	7.38	7.34	7.37	7.37	$b = 12.1074$
	r.d. (%)	−0.06	−2.13	5.25	2.09	5.65	$c = -3.4654$
Phenol	Exp.	4.33	4.35	4.49	4.30	4.49	$a = 1.7983$
	Calc.	4.323	4.330	4.326	4.328	4.327	$b = -0.0110$
	r.d. (%)	0.17	0.47	3.65	−0.65	3.62	$c = 2.5739$
Benzonitrile	Exp.	5.95	7.23	6.63	6.85	7.04	$a = 28.1515$
	Calc.	5.95	7.23	6.55	6.85	6.79	$b = -0.7897$
	r.d. (%)	0	0	1.21	0	3.55	$c = 2.1771$
p-Cresol	Exp.	6.33	5.70	6.35	6.00	6.25	$a = -78\,604.9$
	Calc.	6.33	5.70	6.16	6.00	6.04	$b = -5.3260$
	r.d. (%)	0	0	3.06	0	3.42	$c = 6.4321$
Diethyl phthalate	Exp.	17.15	15.55	18.92	17.51	18.48	$a = -5.6 \cdot 10^{19}$
	Calc.	17.44	15.60	17.39	17.17	17.25	$b = -19.5712$
	r.d. (%)	1.67	−0.32	8.10	1.92	6.68	$c = 17.4385$
3,4-Dimethylphenol	Exp.	9.23	7.23	8.87	8.11	8.54	$a = -36\,734.4$
	Calc.	9.23	7.23	8.61	8.11	8.22	$b = -4.4142$
	r.d. (%)	0	0	2.96	0	3.72	$c = 9.7156$
Benzene	Exp.	11.43	11.80	11.42	11.52	11.91	$a = 4.27 \cdot 10^{10}$
	Calc.	11.42	11.795	11.46	11.53	11.51	$b = -11.6984$
	r.d. (%)	0.09	0.04	−0.35	−0.13	3.33	$c = 11.4150$
2,4-Dimethylphenol	Exp.	10.80	8.58	10.41	9.50	10.07	$a = -10\,867.7$
	Calc.	10.80	8.58	10.05	9.50	9.62	$b = -3.7755$
	r.d. (%)	0	0	3.44	0	4.45	$c = 11.5299$
Mobile phase composition (%)							
CH_3OH		49.0	0	24.4	13.2	15.0	
ACN		0	37.5	19.2	27.6	26.3	
Water		50.1	62.5	56.4	59.2	58.7	

[a] r.d. (%) = 100 (exp. − calc.)/exp.

usually greater than those for the retention times, although the correlation coefficient (R) and remainder standard deviation (S.D.) are statistically acceptable. Hence we suggest that eqn. 9 be used instead of eqn. 6 in practice.

From the fitted and the regression coefficients of the same solutes in Tables I and XVI using the solvent strength weighting factors, and in Tables VIII and XVIII using

TABLE XIV

USING THE EXPERIMENTAL DATA OF ISSAQ *ET AL.* [15]: FITTING RESULTS OF SOLUTE RETENTION TIME *VS.* MOBILE PHASE COMPOSITION AND COMPARISON BETWEEN EXPERIMENTAL AND CALCULATED RETENTION TIMES OF THE SOLUTES BY USING THE SOLVENT POLARITY PARAMETERS IN TERNARY RP-HPLC

Solute	Parameter[a]	Retention time (min)					Fitted coefficients
		1	2	3	4	5	
Anthraquinone	Exp.	7.23	8.26	9.57	11.65	16.44	a = 65.1583
	Calc.	7.23	8.09	9.57	12.10	16.44	b = −1.1458
	r.d. (%)	0	2.03	0	3.88	0	c = 6.0213
2-Methylanthraquinone	Exp.	8.98	10.30	11.98	14.75	21.20	a = 92.3943
	Calc.	8.98	10.07	11.98	15.33	21.20	b = −1.1944
	r.d. (%)	0	2.23	0	−3.93	0	c = 7.5331
Naphthalene	Exp.	7.23	9.16	11.30	14.67	22.41	a = 96.8694
	Calc.	7.23	8.76	11.30	15.49	22.41	b = −1.0683
	r.d. (%)	0	4.32	0	−5.58	0	c = 4.8770
2-Ethylanthraquinone	Exp.	10.94	13.27	15.82	19.98	30.19	a = 136.7754
	Calc.	10.94	12.74	15.82	21.11	30.19	b = −1.1489
	r.d. (%)	0	4.02	0	−5.66	0	c = 8.4306
Biphenyl	Exp.	8.98	11.77	15.13	20.38	34.03	a = 189.3861
	Calc.	8.98	11.21	15.13	22.00	34.03	b = −1.1944
	r.d. (%)	0	4.72	0	−7.93	0	c = 6.0135
Mobile phase composition (%)							
ACN		60.0	45.0	30.0	15.0	0	
THF		0	10.0	20.0	30.0	40.0	
Water		40.0	45.0	50.0	55.0	60.0	

[a] r.d. (%) = 100 (exp. − calc.)/exp.

the solvent polarity parameters, it is found that there is no potential correlation between the values of b in eqn. 9 and B in eqn. 6. In theory, they could be expected to be identical. The values of c could represent the dead time, so all the values of c for the solutes eluted using same column and solvent system must be identical. In fact, however, these values are different from each other. This might be due to the fact that the approximative solution of eqn. 9 is not unique for the Newton or Marquardt algorithm [24]. Often, the iteration results are relevant to the initial values of a, b and c in eqn. 9 [24], even though the Marquardt algorithm is not as restricted as the Newton iteration in assuming the initial values for the iteration. In our experience, the initial values of a, b and c could be assumed by taking advantage of the Taylor expansion of eqn. 9 with the Lagrange remainder item at the three raw experimental data sampling points, no matter what algorithm is used, which could be:

$$b' = \frac{2\ln\left|\dfrac{[t_R(3) - t_R(2)][x(2) - x(1)]}{[x(3) - x(2)][t_R(2) - t_R(1)]}\right|}{x(3) - x(1)} \tag{11}$$

TABLE XV

USING THE EXPERIMENTAL DATA OF SEKULIC *ET AL.* [16]: FITTED PARAMETERS AND COMPARISON BETWEEN EXPERIMENTAL AND CALCULATED RETENTION TIMES OF THE SOLUTES USING THE SOLVENT POLARITY PARAMETERS IN RP-HPLC[a]

Solute[b]	Parameter[c]	Retention time (min)						Fitted coefficients
		1	2	3	4	5	6	
PPA	Exp.	2.13	1.03	2.18	1.67	1.78	1.67	$a = -1.06 \cdot 10^{19}$
	Calc.	2.16	1.06	1.95	1.61	1.73	1.61	$b = -20.6478$
	r.d. (%)	−1.31	−2.66	10.63	3.31	2.83	3.31	$c = 2.1579$
PEA	Exp.	2.23	1.10	2.30	1.81	1.94	1.81	$a = -1.62 \cdot 10^{12}$
	Calc.	2.30	1.23	1.93	1.62	1.71	1.62	$b = -13.2459$
	r.d. (%)	−3.12	−11.44	16.04	10.59	11.60	10.59	$c = 2.3030$
MePEA	Exp.	2.20	1.16	2.42	1.89	2.04	1.89	$a = -1.98 \cdot 10^{13}$
	Calc.	2.28	1.29	1.97	1.68	1.77	1.68	$b = -14.4677$
	r.d. (%)	−3.71	−11.47	18.44	11.13	13.12	11.13	$c = 2.2836$
AMPH	Exp.	2.70	1.14	2.86	2.06	2.26	2.06	$a = -1.46 \cdot 10^{19}$
	Calc.	2.74	1.18	2.45	1.97	2.14	1.97	$b = -20.6342$
	r.d. (%)	−1.62	−3.78	14.47	4.21	5.49	4.21	$c = 2.7439$
DiMePEA	Exp.	2.10	1.23	2.46	1.98	2.08	1.98	$a = -7.77 \cdot 10^{15}$
	Calc.	2.21	1.37	2.00	1.74	1.83	1.74	$b = -17.3663$
	r.d. (%)	−5.04	−11.15	18.77	11.97	12.17	11.97	$c = 2.2063$
BuPEA	Exp.	4.10	1.86	5.35	4.08	4.52	4.08	$a = -5.62 \cdot 10^{17}$
	Calc.	4.46	2.28	3.99	3.32	3.54	3.32	$b = -18.9375$
	r.d. (%)	−8.82	−22.58	25.51	18.62	21.60	18.62	$c = 4.4624$
DiPEA	Exp.	7.25	1.84	8.96	5.33	6.20	5.33	$a = -5.62 \cdot 10^{17}$
	Calc.	7.50	2.09	6.47	4.83	5.40	4.83	$b = -20.7051$
	r.d. (%)	−3.45	−13.36	27.74	9.31	12.92	9.31	$c = 7.5011$
Mobile phase composition (%)								
CH_3OH		50.0	0	22.5	15.0	17.5	15.0	
ACN		0	36.5	18.1	23.9	21.9	23.9	
Water		50.0	63.5	59.4	60.1	60.6	60.1	

[a] All mobile phases contained 5 m*M* heptanesulphonate and 1% acetic acid.

[b] PPA = phenylpropanolamine; PEA = phenethylamine; MePEA = N-methyl-2-phenethylamine; AMPH = amphetamine; DiMePEA = N,N-dimethyl-2-phenethylamine; BuPEA = N-*n*-butyl-2-phenethylamine; DiPEA = 2,2′-diphenylethylamine.

[c] r.d. (%) = 100 (exp. − calc.)/exp.

TABLE XVI

REGRESSION COEFFICIENTS FOR CAPACITY FACTORS OF THE SOLUTES IN GROUP 1 *VS.* MOBILE PHASE COMPOSITION IN TERNARY SOLVENT SYSTEM OF METHANOL, ACETONITRILE AND WATER, USING SNYDER'S SOLVENT STRENGTH WEIGHTING FACTORS IN RP-HPLC

Solute	*A*	*B*	*R*[a]	S.D.[a]
p-Chloronitrobenzene	7.6131	−3.7986	−0.9988	0.0626
8-Hydroxyquinoline	11.6661	−5.7629	−0.9999	0.1753
Benzophenone	8.1797	−3.9201	−0.9978	0.1344
Naphthalene	8.1232	−3.7378	−0.9991	0.1445
Phenergan	8.9823	−4.2004	−0.9978	0.1724
Diazepam	7.1939	−3.4766	−0.9815	0.2306
Dibutyl phthalate	12.5494	−5.5757	−0.9950	0.3404
Phenanthrene	9.4033	−4.0186	−0.9954	0.1311
Acetanilide	3.4977	−2.3284	−0.9996	0.3704

[a] *R* = Correlation coefficient; S.D. = remainder standard deviation.

TABLE XVII

COMPARISON BETWEEN EXPERIMENTAL AND CALCULATED CAPACITY FACTORS OF THE SOLUTES IN GROUP 1 WITH TERNARY MOBILE PHASES CONSISTING OF METHANOL, ACETO NITRILE AND WATER, USING SNYDER'S SOLVENT STRENGTH WEIGHTING FACTORS IN RP-HPLC

Solute	Parameter[a]	Capacity factor						
		1	2	3	4	5	6	7
p-Chloronitrobenzene	Exp.	0.731	0.992	1.375	1.964	2.474	3.298	4.526
	Calc.	0.750	0.900	1.296	1.866	2.687	3.224	4.643
	r.d. (%)	−2.59	9.33	5.77	4.99	−8.59	2.23	−2.59
8-Hydroxyquinoline	Exp.	0.731	1.005	1.861	2.852	4.656	7.089	11.619
	Calc.	0.726	0.957	1.664	2.893	5.031	6.634	11.536
	r.d. (%)	0.71	4.80	10.59	−1.44	−8.05	6.42	0.71
Benzophenone	Exp.	0.989	1.344	1.973	2.821	3.758	4.920	6.493
	Calc.	1.025	1.237	1.802	2.626	3.826	4.619	6.729
	r.d. (%)	−3.64	7.99	8.62	6.90	−1.80	6.13	−3.64
Naphthalene	Exp.	1.387	1.856	2.602	3.629	4.646	6.288	8.340
	Calc.	1.417	1.695	2.427	3.475	4.975	5.953	8.522
	r.d. (%)	−2.19	8.65	6.70	4.24	−7.09	5.32	−2.19
Phenergan	Exp.	1.230	1.714	2.498	3.782	4.958	6.875	9.237
	Calc.	1.278	1.564	2.340	3.503	5.242	6.413	9.598
	r.d. (%)	−3.96	8.75	6.33	7.39	−5.72	6.72	−3.91
Diazepam	Exp.	0.877	1.245	1.904	2.677	3.336	3.947	4.653
	Calc.	0.963	1.138	1.589	2.219	3.098	3.661	5.111
	r.d. (%)	−9.84	8.55	16.54	17.12	7.13	7.25	−9.84
Dibutyl phthalate	Exp.	2.397	3.668	6.815	11.536	17.694	23.261	34.833
	Calc.	2.591	3.386	5.782	9.876	16.867	22.043	37.647
	r.d. (%)	−8.08	7.69	15.15	14.39	4.68	5.24	−8.08
Phenanthrene	Exp.	2.694	3.708	5.429	8.298	11.324	14.659	18.541
	Calc.	2.842	3.447	5.070	7.456	10.966	13.299	19.561
	r.d. (%)	−5.50	7.03	6.62	10.15	3.16	9.28	−5.50
Acetanilide	Exp.	0.258	0.355	0.403	0.464	0.490	0.717	0.789
	Calc.	0.260	0.291	0.364	0.455	0.569	0.637	0.796
	r.d. (%)	−0.95	18.08	9.52	1.87	16.33	11.19	−0.95
Mobile phase composition (%)								
CH_3OH		80.0	72.0	56.0	40.0	24.0	16.0	0
ACN		0	5.0	15.0	25.0	35.0	40.0	50.0
Water		20.0	23.0	29.0	35.0	41.0	44.0	50.0

[a] r.d. (%) = 100 (exp. − calc.)/exp.

$$a' = \frac{\dfrac{t_R(3) - t_R(2)}{x(3) - x(2)}}{b' \exp\{b'[x(3) + x(2)]/2\}} \tag{12}$$

$$c' = t_R(2) - a' \exp\{b'[x(1) + x(3)]/2\} \tag{13}$$

where a', b' and c' represent the initial values of a, b and c in eqn. 9 when the iteration process started; $x(i) = s_1\varphi_1(i) + s_2\varphi_2(i)$ $(i = 1, 2, 3)$, where $\varphi_1(i)$ and $\varphi_2(i)$ are the

TABLE XVIII

RESULTS OF REGRESSION ANALYSIS OF EQN. 2 FOR THE SOLUTES IN GROUP 1 WITH TERNARY SOLVENT MIXTURES CONSISTING OF METHANOL, ACETONITRILE AND WATER, USING SNYDER'S SOLVENT POLARITY PARAMETERS IN RP-HPLC

Solute	A	B	R[a]	S.D.[a]
p-Chloronitrobenzene	6.0164	−1.5452	−0.9988	0.0626
8-Hydroxyquinoline	9.2437	−2.3442	−0.9999	0.1033
Benzophenone	6.5317	−1.5949	−0.9978	0.1355
Naphthalene	6.5521	−1.5205	−0.9991	0.1455
Phenergan	7.2167	−1.7086	−0.9978	0.1732
Diazepam	5.7326	−1.4142	−0.9815	0.2879
Dibutyl phthalate	10.2057	−2.2681	−0.9950	0.3451
Phenanthrene	7.7141	−1.6347	−0.9954	0.3691
Acetanilide	2.5190	−0.9472	−0.9996	0.3699

[a] R = Correlation coefficient; S.D. = remainder standard deviation.

TABLE XIX

COMPARISON BETWEEN EXPERIMENTAL AND CALCULATED CAPACITY FACTORS OF THE SOLUTES IN GROUP 1 WITH TERNARY MOBILE PHASES CONSISTING OF METHANOL, ACETONITRILE AND WATER, USING THE SOLVENT POLARITY PARAMETERS IN RP-HPLC

Solute	Parameter[a]	Capacity factor						
		1	2	3	4	5	6	7
p-Chloronitrobenzene	Exp.	0.731	0.992	1.375	1.964	2.474	3.298	4.526
	Calc.	0.750	0.900	1.296	1.866	2.687	3.224	4.643
	r.d. (%)	−2.59	9.33	5.77	4.99	−8.59	2.23	−2.59
8-Hydroxyquinoline	Exp.	0.731	1.005	1.861	2.852	4.656	7.089	11.619
	Calc.	0.726	0.957	1.664	2.893	5.031	6.634	11.536
	r.d. (%)	0.71	4.80	10.59	−1.44	−8.05	6.42	0.71
Benzophenone	Exp.	0.989	1.344	1.973	2.821	3.758	4.920	6.493
	Calc.	1.025	1.237	1.802	2.626	3.826	4.619	6.729
	r.d. (%)	−3.64	7.99	8.62	6.90	−1.80	6.13	−3.64
Naphthalene	Exp.	1.387	1.856	2.602	3.629	4.646	6.288	8.340
	Calc.	1.417	1.695	2.427	3.475	4.975	5.953	8.522
	r.d. (%)	−2.19	8.65	6.70	4.24	−7.09	5.32	−2.19
Phenergan	Exp.	1.230	1.714	2.498	3.782	4.958	6.875	9.237
	Calc.	1.278	1.564	2.340	3.503	5.242	6.413	9.598
	r.d. (%)	−3.96	8.75	6.33	7.39	−5.72	6.72	−3.91
Diazepam	Exp.	0.877	1.245	1.904	2.677	3.336	3.947	4.653
	Calc.	0.963	1.138	1.589	2.219	3.098	3.661	5.111
	r.d. (%)	−9.84	8.55	16.54	17.12	7.13	7.25	−9.84
Dibutyl phthalate	Exp.	2.397	3.668	6.815	11.536	17.694	23.261	34.833
	Calc.	2.591	3.386	5.782	9.876	16.867	22.043	37.647
	r.d. (%)	−8.08	7.69	15.15	14.39	4.68	5.24	−8.08
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	Calc.	2.842	3.447	5.070	7.456	10.966	13.299	19.561
	r.d. (%)	−5.50	7.03	6.62	10.15	3.16	9.28	−5.50
Acetanilide	Exp.	0.258	0.355	0.403	0.464	0.490	0.717	0.789
	Calc.	0.260	0.291	0.364	0.455	0.569	0.637	0.796
	r.d. (%)	−0.95	18.08	9.52	1.87	16.33	11.19	−0.95
Mobile phase composition (%)								
CH_3OH		80.0	72.0	56.0	40.0	24.0	16.0	0
ACN		0	5.0	15.0	25.0	35.0	40.0	50.0
Water		20.0	23.0	29.0	35.0	41.0	44.0	50.0

volume percentages of organic modifiers 1 and 2 in the mobile phase at raw experimental data point i; and $t_R(i)$ ($i = 1, 2, 3$) is the retention time of a solute at the ith raw experimental data sampling point. If the above choice of a', b' and c' cannot make the iteration continue or the obtained a, b and c values result in unacceptable r.d. (%) values, possibly another choice for the initial values of a, b and c is needed [24]. Generally, the Marquardt method is likely to be more powerful than the Newton algorithm in our experience. However, the former would take much more computer time than the latter.

In order to improve further the prediction of retention times, we tried to modify eqn. 9. For example, we added a solvent interaction term:

$$t_R = a \exp [b(s_1\varphi_1 + s_2\varphi_2 + G\, s_1\varphi_1 s_2\varphi_2)] + c \qquad (14)$$

where G is a weighting factor. We tried many different values of G, including the positive and negative values, but the r.d. (%) values using eqn. 14 were always poorer than those using eqn. 9. From eqn. 9, we can see that the b is likely to connect $s_1\varphi_1$ and $s_2\varphi_2$. In other words, it belongs to two organic modifiers simultaneously. Hence it can be questioned whether b in eqn. 9 is involved in the interaction between the solvents. Certainly this aspect needs to be investigated further.

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