ELSEVIER

Evaluation of a structure-driven retention model for temperature-programmed gas chromatography

Mohamed I. Nawas, Colin F. Poole*

Department of Chemistry, Wayne State University, Rm. 180, Detroit, MI 48202, USA

Abstract

The solvation parameter model is suitable for describing the retention properties of compounds of varied structure in temperature-programmed gas chromatography. An empirical second-order model provides a good account of the change in system constants as a function of program rate. These relationships codify the reduction in retention time at higher program rates and changes in elution order (selectivity) with program rate. The prediction of retention times from structure, while quite good, is probably adversely affected by descriptor quality and the possibility of a mixed retention mechanism on polar stationary phases. Plots of experimental against predicted temperature-programmed retention times for varied compounds are linear but generally contain a small bias from an ideal model (slope of one and an intercept of zero). The average absolute deviation in temperature-programmed retention times on three columns (DB-210, DB-1701 and EC-Wax) varied from 0.15 to 0.89 min with the best results obtained at higher program rates on the columns of lower polarity.
© 2003 Elsevier B.V. All rights reserved.

1. Introduction

A rigorous theoretical treatment of retention in temperature-programmed gas chromatography is far from straightforward [1–3]. The fundamental equation for linear temperature programs is in integral form with no analytical solution. Consequently, either numerical methods or simplifying assumptions employing computer simulations is required for even the simplest case. Computer simulations can be conveniently divided into two approaches. Those employing isothermal retention data or retention indices to predict temperature-programmed retention times and those using a small number of temperature-programmed separations to predict retention times for other programmed conditions.

In the first case, two or three isothermal separations at different temperatures are used to estimate appropriate values for the phase ratio and the standard enthalpy and entropy for solute transfer from the gas phase to the stationary phase [4–10]. The column hold-up time and its variation with operating conditions is obtained from either direct measurements on the column selected for the separation, or by calculation considering all temperature-dependent parameters and their changes during the program segments. The temperature-programmed retention times are then obtained by summation of the retention factors for each solute calculated from the thermodynamic data for all segments in the program and the effective column hold-up time. Alternatively, the temperature-programmed retention times can be determined by dividing the chromatographic process into a series of short segments corresponding to very small time intervals within which both the retention factor and carrier gas velocity are assumed to be constant. Using experimental column hold-up times to calculate the carrier gas velocity and taking into account the change in viscosity and gas compressibility with temperature, allows calculation of the total distance traveled by a solute by summation of the distance traveled in each time segment. The solute retention time in the specified program is equivalent to the sum of the individual time segments corresponding to a migration distance equal to the column length. These methods are flexible enough to allow simulation of retention for temperature programs containing different program rates and isothermal periods.

* Corresponding author. Tel.: +1-313-577-2881;
fax: +1-313-577-1377.
E-mail address: cfp@chem.wayne.edu (C.F. Poole).

A significant advance in the simulation of temperature-programmed separations was the demonstration that the linear elution strength model (analogous to the linear solvent strength model for gradient elution in liquid chromatography) affords accurate predictions of temperature-programmed retention times [11–14]. The experimental data required for computer simulation is the measurement of solute retention times in two linear temperature-programmed separations over the same temperature range at different program rates. The initial program conditions are used to calculate the program-steepness parameter, b, and the initial value of the retention factor for the temperature program, k_0 for each solute by numerical solution of the retention time equation:

$$b = \frac{t_M(T_f - T_0)S}{t_p} \tag{1}$$

$$t_R = \left(\frac{t_M}{2.3b}\right) \ln[e^{2.3b}(k_0 + 1) - k_0] \tag{2}$$

where t_M is the column hold-up time, T_f the final program temperature, T_0 the initial program temperature, and t_p is the program time for the linear temperature program. The retention factor and the program-steepness parameter for the initial experimental conditions allow the constants A' and S_l (related to the thermodynamic parameters of the system) to be estimated from:

$$\log k = A' - S_l T \tag{3}$$

from which separations at other conditions can be simulated. Typical errors in simulated temperature-programmed chromatograms are about ±1–5% for retention time [12,13,15].

Computer simulations are fast and practical for optimization of specified mixtures but provide no insights into the underlying retention mechanism.

For isothermal separations by gas chromatography, the solvation parameter model has been widely used to establish the contribution of stationary phase intermolecular interactions to retention [16–18]. The solvation parameter model in a form suitable for describing retention in gas chromatography is set out below:

$$\log k = c + lL + eE + sS + aA + bB \tag{4}$$

where k is the retention factor and c the model constant (which is dominated by the phase ratio). The lower case letters (l, e, s, a, b) are the system constants representing the stationary phase contributions to defined intermolecular interactions. The capital letters (L, E, S, A, B) are the solute descriptors for the complementary interactions with the system constants of the stationary phase. The solute descriptors are: L the gas–liquid distribution constant on hexadecane at 298 K; E the excess molar refraction; S the ability of the solute to stabilize a neighboring dipole by virtue of its capacity for orientation and induction interactions; A the solute's effective hydrogen-bond acidity; and B the solute's effective hydrogen-bond basicity. The complementary stationary phase system constants are identified as the contribution from cavity formation and dispersion interactions, l the contribution from interactions with solute n- or π-electrons, e the contribution from dipole-type interactions, s the contribution from hydrogen-bond basicity (because a basic phase will interact with an acidic solute), a and b the contribution from hydrogen-bond acidity. Our laboratory has compiled a database of system constants for 32 open-tubular columns representing 25 stationary phase types determined at 20 °C intervals over the temperature range 60–140 °C using a standard protocol. These studies are reviewed elsewhere [17–19], with additional data for poly(dimethylsiloxane) and poly(ethylene glycol) stationary phase mixtures in [20], sol–gel stationary phases in [21] and dissolved cyclodextrin derivatives in a poly(cyanopropylphenyldimethylsiloxane) solvent in [22].

Application of the solvation parameter model to isothermal retention times is consistent with the thermodynamic theory of solute transfer from gas to liquid. The success of the linear elution strength model for temperature-programmed gas chromatography suggests that retention in temperature-programmed gas chromatography is correlated with isothermal retention conditions. That being the case, it should be possible to use the solvation parameter model to characterize the retention properties of stationary phases under temperature program conditions and to estimate temperature-programmed retention times from structure. The solvation parameter model was shown to provide useful models of gradient retention times for reversed-phase liquid chromatography [23,24]. Although in this case, linear solvent strength theory indicates that the agreement is fortuitous and requires that the solute-specific S_l parameter takes a narrow range of values [25,26].

2. Experimental

2.1. Materials

The DB-1701 (15 m × 0.32 mm, film thickness 0.25 μm) and DB-210 (15 m × 0.32 mm, film thickness 0.50 μm) open-tubular columns were obtained from Agilent Technologies (Folsom, CA, USA). The EC-Wax (15 m × 0.32 mm, film thickness 0.25 μm) open-tubular column was obtained from Alltech (Deerfield, IL, USA). Solutes for column evaluation were obtained from Sigma–Aldrich (Milwaukee, WI, USA) and dissolved in ethyl acetate to a final concentration of about 0.5–2.0 mg/ml.

2.2. Instrumentation

Gas chromatographic measurements were made with an Agilent Technologies HP 6890 gas chromatograph (Wilmington, DE, USA) employing chemstation software (Rev. A.04.02) for data acquisition. Nitrogen was used as the carrier gas with a constant mass flow rate corresponding to a

velocity of 35 cm/s, except as noted in the text. For the constant pressure experiments, the column inlet pressure was 8.2 psi Methane was used to determine the column hold-up time. Sample volumes of about 0.1 μl were introduced by split injection (split ratio 10:1). The injection and detector temperature were 220 °C. Retention times were measured in a linear temperature program starting at 60 °C and terminated at 160 °C with different program rates as indicated in the text.

2.3. Calculations

Multiple linear regression analysis and statistical calculations were performed on a Gateway E-4200 computer (North Sioux City, SD, USA) using the program SPSS v10.0 (SPSS, Chicago, IL, USA). The solute descriptors used to determine system constants at different program rates were taken from an in-house database and are summarized in Table 1. Temperature-programmed retention times from two programmed separations with different program rates were calculated using DryLab 2000 (rel. 01/2002a) from LC Resources (Walnut Creek, CA, USA).

3. Results and discussion

Screening experiments were used to identify an appropriate dependent variable for use in the solvation parameter model for temperature-programmed separations with different program rates. The retention time, t_g and $\log t_g$, and the retention factor, $\log k$, were considered. In general, the relationship between each retention variable and program rate is non-linear, as indicated in Fig. 1 for $\log t_g$. Therefore, the descriptive statistics for the fit of each retention variable to the solvation parameter model was used to select the preferred variable for modeling retention related properties. In each case, a reasonable model was obtained, with the best fit provided by $\log t_g$. Since in the constant flow mode the column hold-up time is constant, both $\log t_g$ and $\log k$ can be used with equal facility. The use of $\log t_g$ allows a discussion in terms of retention time errors and was selected for this study. Reasonable, if different models, were obtained
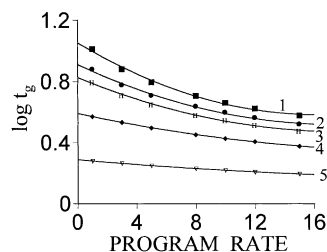

Fig. 1. Plot of the temperature-programmed retention times ($\log t_g$) as a function of the program rate (°C/min) for the DB-210 column. Identification: 1, 2-octanone; 2, acetamide; 3, pentafluorophenol; 4, bromobenzene; and 5, nitromethane.

Table 1
Compounds used to establish the solvation parameter models for temperature-programmed conditions

Solute	Solute descriptors				
	E	S	A	B	L
Acetamide	0.460	1.30	0.54	0.68	2.825
Acetonitrile	0.237	0.90	0.07	0.32	1.739
Acetophenone	0.818	1.01	0	0.49	4.501
Aniline	0.955	0.96	0.26	0.53	3.993
Benzyl alcohol	0.832	0.95	0.37	0.56	4.245
Bromobenzene	0.882	0.72	0	0.09	4.041
n-Butyl ether	0	0.25	0	0.45	3.924
Carbon tetrachloride	0.458	0.38	0	0	2.823
Chlorobenzene	0.718	0.65	0	0.07	3.657
Cyclohexanone	0.403	0.86	0	0.56	3.792
Cyclohexene	0.395	0.20	0	0.10	3.021
Cyclopentanone	0.373	0.86	0	0.52	3.221
n-Decane	0	0	0	0	4.686
n-Dodecane	0	0	0	0	5.696
2,4-Dichlorophenol	0.960	0.84	0.53	0.19	4.953
2,6-Dimethylphenol	0.860	0.79	0.39	0.39	4.680
3,5-Dimethylphenol	0.820	0.84	0.57	0.36	4.856
Dioxane	0.321	0.75	0	0.64	2.892
n-Heptanal	0.140	0.65	0	0.45	3.885
3-Heptanone	0.106	0.66	0	0.51	3.776
4-Heptanone	0.113	0.66	0	0.51	3.705
Heptan-1-ol	0.211	0.42	0.37	0.48	4.115
n-Hexadecane	0	0	0	0	7.714
2-Methoxyethanol	0.269	0.50	0.30	0.84	2.490
Methyl benzoate	0.733	0.85	0	0.46	4.704
3-Methyl-2-butanone	0.134	0.65	0	0.51	2.692
Methyl isobutyl ketone	0.111	0.65	0	0.51	3.089
Methyl nonanoate	0.056	0.60	0	0.45	5.321
Methyl octanoate	0.065	0.60	0	0.45	4.383
3-Methylphenol	0.822	0.88	0.57	0.34	4.310
4-Methylphenol	0.820	0.87	0.57	0.31	4.312
Nitrobenzene	0.871	1.11	0	0.28	4.511
Nitroethane	0.270	0.95	0.02	0.33	2.414
2-Nitrophenol	1.015	1.05	0.05	0.37	4.760
1-Nitropropane	0.242	0.95	0	0.31	2.894
Nonan-1-ol	0.193	0.42	0.37	0.46	5.223
2-Nonanone	0.119	0.68	0	0.51	4.735
n-Octane	0	0	0	0	3.677
n-Octanal	0.160	0.65	0	0.45	4.360
2-Octanone	0.108	0.68	0	0.51	4.257
Pentafluorophenol	0.360	0.83	0.79	0.09	3.568
Pentan-1-ol	0.219	0.42	0.37	0.48	3.108
2-Pentanone	0.143	0.68	0	0.51	2.755
Phenol	0.805	0.89	0.60	0.31	3.766
Pyridine	0.794	0.87	0	0.62	3.003
Tetrahydrofuran	0.289	0.52	0	0.48	2.636
Toluene	0.601	0.52	0	0.14	3.325
1,2,4-Trichlorobenzene	0.997	0.725	0	0	5.229
1,2,4,5-Tetrachlorobenzene	1.160	0.711	0	0	5.926
o-Xylene	0.663	0.56	0	0.16	3.939
m-Xylene	0.623	0.52	0	0.16	3.839
p-Xylene	0.613	0.52	0	0.16	3.839

for temperature-programmed separations in both the constant mass flow and constant inlet pressure modes. The more popular constant flow mode was selected for the comprehensive evaluation.

Table 2
System constants and model constant determined for different program rates with $\log t_g$ as the dependent variable

Program rate (°C/min)	System constants					Statistics[a]			
	e	s	a	l	c	ρ	S.E.	F	n
DB-1701									
1	−0.113 (0.047)	0.663 (0.056)	0.819 (0.057)	0.432 (0.014)	−1.535 (0.068)	0.988	0.073	356	43
3	−0.100 (0.035)	0.556 (0.042)	0.664 (0.042)	0.374 (0.011)	−1.301 (0.050)	0.991	0.054	468	43
5	−0.089 (0.029)	0.499 (0.035)	0.573 (0.035)	0.337 (0.009)	−1.169 (0.042)	0.992	0.046	531	43
8	−0.073 (0.024)	0.438 (0.029)	0.497 (0.030)	0.299 (0.008)	−1.035 (0.035)	0.993	0.038	601	43
15	−0.054 (0.018)	0.357 (0.021)	0.400 (0.021)	0.246 (0.005)	−0.856 (0.026)	0.994	0.027	772	43
DB-210									
1	−0.364 (0.032)	1.067 (0.041)	0.085 (0.036)	0.403 (0.010)	−1.429 (0.052)	0.990	0.052	472	44
3	−0.327 (0.018)	0.939 (0.025)	0.073 (0.021)	0.339 (0.006)	−1.194 (0.031)	0.995	0.029	972	44
5	−0.277 (0.019)	0.789 (0.024)	0.064 (0.021)	0.294 (0.006)	−0.991 (0.031)	0.993	0.030	733	44
8	−0.247 (0.015)	0.695 (0.020)	0.052 (0.017)	0.259 (0.005)	−0.859 (0.025)	0.994	0.025	826	44
15	−0.192 (0.012)	0.558 (0.016)	0.039 (0.014)	0.206 (0.004)	−0.679 (0.021)	0.994	0.020	806	44
EC-Wax									
1	0.148 (0.057)	1.001 (0.069)	1.293 (0.079)	0.399 (0.016)	−1.699 (0.081)	0.989	0.100	430	45
3	0.135 (0.040)	0.838 (0.049)	0.989 (0.056)	0.319 (0.011)	−1.356 (0.057)	0.991	0.071	566	46
5	0.118 (0.033)	0.779 (0.039)	0.847 (0.047)	0.283 (0.009)	−1.221 (0.048)	0.992	0.060	632	46
8	0.110 (0.039)	0.719 (0.033)	0.686 (0.039)	0.249 (0.008)	−1.101 (0.041)	0.993	0.048	741	46
15	0.097 (0.023)	0.562 (0.028)	0.614 (0.032)	0.205 (0.006)	−0.904 (0.033)	0.993	0.040	736	46

$b = 0$ in all cases.

[a] ρ is the multiple correlation coefficient, S.E. the standard error in the estimate, F the Fischer statistic and n is the number of solutes included in the model.

3.1. Affect of program rate on the system constants

The system constants for the solvation parameter models at program rates of 1, 3, 5, 8, 15 °C/min for the three stationary phases DB-1701, DB-210 and EC-Wax are summarized in Table 2. The descriptive statistics for the models are good and only just slightly worse than the fit for isothermal models for the same stationary phases [19,20,27]. The system constants make chemical sense and display similar general characteristics to the isothermal system constants. For example, the b system constant is zero for all phases. The magnitude and sign of the system constants show rough agreement (the only negative system constants are the e system constant), and the a/s system constant ratio shows the same trends for each column as the isothermal system constants. There is, however, no simple relationship between the temperature-programmed and isothermal system constants on which to base a persuasive argument that the chemical sense of the temperature-programmed system constants has been placed on firm ground. All that can be said is that they appear to convey believable chemical information in line with reasonable expectations without predicting properties that would be unlikely or impossible given what is known of the chemistry of the stationary phases. Further work is in hand to test and/or establish whether a direct relationship exists between the isothermal and temperature-programmed system constants.

The change in system constants with program rate is important as an indication of selectivity changes associated with program rate. The change in system constants with program rate are adequately fit by a second-order model,

Table 3, of the form:

$$\text{system constant} = a_0 + a_1 x + a_2 x^2 \qquad (5)$$

where x is the program rate (°C/min). The effect of the program rate on selectivity is best conveyed graphically, as shown in Fig. 2, for the DB-210 column. The variation of the system constants with program rate is larger for slow

Table 3
Models for the fit of the system constants and model constant to the program rate (Eq. (5))

| System constant	Coefficients			
	a_2	a_1	a_0	r^2
DB-1701				
e	-2.024×10^{-4}	7.480×10^{-3}	-0.1206	0.999
s	1.614×10^{-3}	-4.675×10^{-2}	0.697	0.990
a	2.579×10^{-3}	-6.978×10^{-2}	0.870	0.988
l	8.917×10^{-4}	-2.715×10^{-2}	0.454	0.995
c	-3.610×10^{-3}	0.1004	-1.613	0.992
DB-210				
e	-7.382×10^{-4}	2.408×10^{-2}	-0.388	0.993
s	2.705×10^{-3}	-7.943×10^{-2}	1.143	0.994
a	2.014×10^{-4}	-6.493×10^{-3}	0.092	1.000
l	1.057×10^{-3}	-3.048×10^{-2}	0.427	0.992
c	-4.516×10^{-3}	1.244×10^{-1}	-1.531	0.993
EC-Wax				
e	2.989×10^{-4}	-8.398×10^{-3}	0.156	0.971
s	1.647×10^{-3}	-5.537×10^{-2}	1.027	0.969
a	5.730×10^{-3}	-0.1378	1.396	0.988
l	1.223×10^{-3}	-3.254×10^{-2}	0.420	0.979
c	-4.801×10^{-3}	0.1144	-1.739	0.960
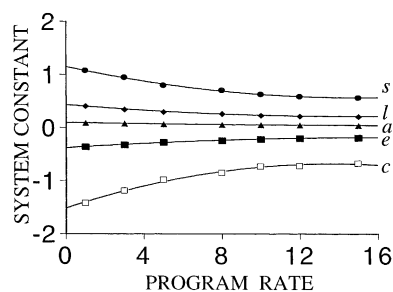
Fig. 2. Plot of the system constants and model constant c as a function of program rate (°C/min) for the DB-210 column.

program rates becoming shallow at high program rates. The system constants are also smaller at higher program rates. In addition, for each stationary phase the change in individual system constant with program rate is not identical, demonstrating the possibility of selectivity changes. These features provide a chemical basis for the observations that high program rates reduce retention time the most and the elution order at different program rates are not always identical.

3.2. Validation of program rate models

The temperature-program-rate models developed above were validated in two ways. Firstly, by their ability to predict the system constants for program rates not used to establish the original models. Secondly, by their ability to predict retention times for two sets of varied compounds at program rates not used for the original models. The compounds selected were the original compounds used to establish the models (Table 1) and an independent group of compounds not included in the original models.

The system constants determined with the program rates 1, 3, 5, 8 and 15 °C/min were used to predict the system constants at 10 and 12 °C/min using Eq. (5) and the coefficients in Table 3. These values are compared with the experimentally determined system constants at 10 and 12 °C/min in Table 4. There is good agreement between the predicted and experimental system constants for the three columns at program rates of 10 and 12 °C/min with only a few instances where the differences are significant at the 95% confidence level. In all cases, these differences are small and the agreement is reasonable for estimating retention properties. The fit of a second-order model, Eq. (5) to all the experimental data (i.e. 1, 3, 5, 8, 10, 12 and 15 °C/min) causes little change in the model coefficients or the coefficient of determination for the models in Table 3. This confirms the acceptance of a second-order model to describe the change in the system constants as a function of the program rate.

For DB-210 as an example, the temperature-programmed retention times estimated at 10 °C/min using the equations in Table 3 are compared with the experimental values in Fig. 3. The equation for a linear model is:

$$t_g(\text{ex}) = -0.116(\pm 0.069) + 1.058(\pm 0.019)t_g(\text{pr})$$
$$(r^2 = 0.987, \text{S.E.} = 0.190, F = 3173, n = 44) \qquad (6)$$

The fit is acceptable with a standard error in the estimate of 0.19 min. The slope and intercept, while close to their target values of one for the slope and zero for the intercept, are slightly different and a small bias exists compared with an ideal model. The average absolute deviation between the experimental and predicted temperature-programmed retention times is 0.16 min (S.D. = 0.156, $n = 44$).

Table 4
System constants and model constant predicted from the data in Table 3 and determined experimentally at program rates of 10 and 12 °C/min

| Predicted		Experimental		Statistics	
10 °C/min	12 °C/min	10 °C/min	12 °C/min	10 °C/min	12 °C/min
DB-1701					
$c = -0.970$	$c = -0.928$	$c = -0.952$ (0.024)	$c = -0.905$ (0.023)	$\rho = 0.996$	$\rho = 0.996$
$e = -0.066$	$e = -0.060$	$e = -0.083$ (0.016)	$e = -0.072$ (0.016)	S.E. = 0.022	S.E. = 0.027
$s = 0.391$	$s = 0.369$	$s = 0.389$ (0.021)	$s = 0.367$ (0.020)	$F = 1077$	$F = 1049$
$a = 0.430$	$a = 0.404$	$a = 0.474$ (0.021)	$a = 0.435$ (0.020)	$n = 43$	$n = 43$
$l = 0.271$	$l = 0.256$	$l = 0.278$ (0.005)	$l = 0.262$ (0.005)		
DB-210					
$c = -0.739$	$c = -0.730$	$c = -0.804$ (0.022)	$c = -0.746$ (0.021)	$\rho = 0.996$	$\rho = 0.995$
$e = -0.221$	$e = -0.205$	$e = -0.226$ (0.018)	$e = -0.207$ (0.012)	S.E. = 0.020	S.E. = 0.019
$s = 0.619$	$s = 0.579$	$s = 0.646$ (0.018)	$s = 0.603$ (0.017)	$F = 988$	$F = 956$
$a = 0.049$	$a = 0.043$	$a = 0.045$ (0.014)	$a = 0.039$ (0.013)	$n = 44$	$n = 44$
$l = 0.228$	$l = 0.213$	$l = 0.241$ (0.004)	$l = 0.225$ (0.004)		
EC-Wax					
$c = -1.003$	$c = -0.954$	$c = -1.043$ (0.037)	$c = -0.990$ (0.034)	$i = 0.992$	$\rho = 0.992$
$e = 0.102$	$e = 0.098$	$e = 0.109$ (0.025)	$e = 0.102$ (0.023)	S.E. = 0.044	S.E. = 0.041
$s = 0.638$	$s = 0.600$	$s = 0.678$ (0.031)	$s = 0.641$ (0.028)	$F = 560$	$F = 591$
$a = 0.592$	$a = 0.568$	$a = 0.609$ (0.048)	$a = 0.573$ (0.044)	$n = 45$	$n = 45$
$l = 0.230$	$l = 0.206$	$l = 0.234$ (0.007)	$l = 0.222$ (0.007)		
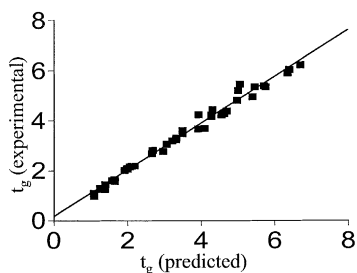
Fig. 3. Plot of the experimental temperature-programmed retention times against the model predicted retention times at a program rate of 10 °C/min for the DB-210 column.

For the other two columns, the equations for a linear model for the predicted temperature-programmed retention times at 10 °C/min and the experimentally determined values are:

$$t_g(\text{ex}) = 0.012(\pm0.065) + 1.10(\pm0.020)t_g(\text{pr})$$
$$(r^2 = 0.988, \text{S.E.} = 0.196, F = 2947, n = 43) \quad (7)$$

for DB-1701 and

$$t_g(\text{ex}) = -0.193(\pm0.138) + 1.140(\pm0.035)t_g(\text{pr})$$
$$(r^2 = 0.965, \text{S.E.} = 0.511, F = 1084, n = 45) \quad (8)$$

for EC-Wax. For DB-1701, the fit is acceptable with a standard error in the estimate of about 0.20 min, similar to DB-210. For EC-Wax, five compounds with residuals greater than two standard deviations adversely affect the standard error in the estimate (0.51 min) and the quality of the fit. If these compounds are removed the new model has an intercept of −0.24 (±0.05), slope = 1.14 (±0.02), and r^2 = 0.993, S.E. = 0.18, F = 4446 and n = 40. The average absolute deviation between the experimental and predicted temperature-programmed retention times is 0.40 min (S.D. = 0.52, n = 45) and with removal of compounds with extreme values 0.23 min (S.D. = 0.20, n = 40). The intercept and slope are slightly different to their target values for the DB-1701 and EC-Wax columns indicating a small bias in the models compared with an ideal model.

The bias in the prediction of temperature-programmed retention times compared with an ideal model is small enough not to be of general concern. It likely arises from two sources. The uncertainty that exists in the experimental system constants and the added uncertainty induced by the choice of a second-order model to represent the relationship between the system constants and the program rate.

To estimate the predictive ability of the temperature-programmed models (Table 3), a second data set of 20

Table 5
Estimation of temperature-programmed retention times on DB-210 for compounds not included in the construction of the solvation parameter models (Table 3)

Compound	Retention time (min)					
	3 °C/min		10 °C/min		12 °C/min	
	Experimental	Predicted	Experimental	Predicted	Experimental	Predicted
Benzaldehyde	7.00	6.85	4.44	4.07	4.09	3.82
Benzonitrile	9.35	9.44	5.37	5.12	4.90	4.68
1-Bromohexane	3.07	2.94	2.48	2.36	2.37	2.25
2-Bromophenol	6.46	7.44	4.16	4.31	3.86	3.92
n-Butylbenzene	4.75	4.92	3.39	3.32	3.15	3.10
Butyl acetate	2.81	2.81	2.31	2.39	2.20	2.28
Cyclopentanol	2.02	1.97	1.78	1.79	1.74	1.74
1,2-Dichlorobenzene	5.53	6.09	3.83	3.79	3.52	3.52
1,2-Dichloroethane	1.37	1.42	1.29	1.40	1.26	1.41
Ethylbenzene	2.27	2.32	1.95	2.00	1.89	1.93
Heptan-2-one	5.23	4.77	3.53	3.24	3.28	3.04
Iodobenzene	4.99	5.17	3.50	3.43	3.27	3.18
Naphthalene	11.13	9.58	5.99	5.25	5.40	4.79
1-Naphthol	23.32	26.19	10.01	9.95	8.82	8.69
2-Nitrophenol	12.17	12.34	6.43	6.05	5.78	5.48
3-Nitrotoluene	16.63	19.10	7.97	8.07	7.08	7.15
n-Nonane	1.67	1.67	1.54	1.62	1.51	1.58
Octan-2-ol	4.67	4.81	3.26	3.28	3.04	3.05
Pentan-1-al	2.16	2.14	1.81	1.89	1.76	1.82
4-Picoline	4.26	4.02	3.10	2.87	2.92	2.72
Pyrrole	2.08	1.96	1.85	1.77	1.79	1.72
Model statistics						
Slope	0.882 (±0.023)		1.025 (±0.022)		1.030 (±0.02)	
Intercept	0.496 (±0.020)		0.0004 (±0.094)		−0.030 (±0.08)	
r^2	0.988		0.991		0.998	
S.E.	0.63		0.22		0.17	
F	1449		2198		2639	
d	0.51 (±0.83)		0.16 (±0.17)		0.14 (±0.17)	

Table 6
Estimation of temperature-programmed retention times on DB-1701 for compounds not included in the construction of the solvation parameter models (Table 3)

Compound	Retention time (min)					
	3 °C/min		10 °C/min		12 °C/min	
	Experimental	Predicted	Experimental	Predicted	Experimental	Predicted
Benzaldehyde	4.54	4.70	3.14	3.09	2.93	2.89
Benzonitrile	5.67	5.61	3.70	3.49	3.42	3.25
1-Bromohexane	2.85	2.74	2.24	2.11	2.13	2.02
2-Bromophenol	8.39	10.98	4.74	5.39	4.29	4.89
n-Butylbenzene	5.13	5.05	3.40	3.26	3.14	3.05
Butyl acetate	1.72	1.87	1.52	1.60	1.48	1.55
Cyclopentanol	1.88	2.46	1.63	1.87	1.58	1.79
1,2-Dichlorobenzene	5.22	5.56	3.48	3.48	3.22	3.24
1,2-Dichloroethane	1.05	0.92	1.00	0.95	1.00	0.95
Ethylbenzene	1.99	2.20	1.71	1.80	1.65	1.74
Heptan-2-one	2.83	2.92	2.23	2.20	2.13	2.09
Iodobenzene	5.24	5.43	3.50	3.43	3.33	3.20
Naphthalene	10.10	10.60	5.45	5.52	4.91	5.02
2-Nitrophenol	9.47	10.07	5.23	5.28	4.73	4.80
3-Nitrotoluene	12.43	13.62	6.26	6.58	5.58	5.92
n-Nonane	1.87	1.88	1.61	1.62	1.55	1.57
Octan-2-ol	5.02	7.02	3.32	3.95	3.08	3.63
Pentan-1-al	1.19	1.21	1.12	1.21	1.10	1.19
4-Picoline	2.50	2.84	2.04	2.15	1.95	2.06
Pyrrole	2.03	2.49	1.71	1.86	1.65	1.78
Model statistics						
Slope	1.109 (±0.042)		1.041 (±0.032)		1.050 (±0.033)	
Intercept	−0.040 (±0.239)		−0.0253 (±0.108)		−0.042 (±0.103)	
r^2	0.973		0.982		0.981	
S.E.	0.61		0.22		0.20	
F	687		1050		988	
d	0.47 (±0.69)		0.16 (±0.18)		0.15 (±0.16)	

varied compounds, none of which were used to establish the original solvation parameter models was created. The experimental and predicted temperature-programmed retention times for program rates of 3, 10 and 12 °C/min are summarized in Table 5 for the DB-210 column, in Table 6 for the DB-1701 column, and in Table 7 for the EC-Wax column. The results for DB-210 and DB-1701 are quite similar and EC-Wax not quite as good. The predictive properties of the models improve at higher program rates where the system constants are smaller and change less rapidly with temperature. At the 10 and 12 °C/min program rates for DB-210 and DB-1701 the average absolute deviation in retention time is about 0.16 min. At 3 °C/min it is closer to 0.50 min. The statistics for the model fit are good for the three columns and three program rates with a coefficient of determination that varies from 0.998 to 0.965.

Certain factors are likely to affect the performance of the solvation parameter model for predicting temperature-programmed retention times. The most important is probably descriptor quality. Solute descriptors are average values derived from experimental measurements in a wide range of partition systems, including many non-chromatographic methods [17,28]. For individual compounds, they possess different levels of uncertainty reflecting their origins.

These same uncertainties affect the performance of computer programs designed to calculate descriptors from structure by summation of fragments since these programs are trained to reproduce the experimental values [17,29].

The retention mechanism in gas–liquid chromatography is dominated by gas–liquid partitioning, but in some cases may include contributions from interfacial adsorption, particularly adsorption at the gas–liquid interface [3,30]. Interfacial adsorption generally grows in importance when the polarity of the solute and stationary phase are different, for example, the retention of hydrocarbons on polar stationary phases, such as poly(ethylene glycols) [27]. Since the sorption characteristics of the interface and bulk solvent are not identical [31], for different compounds some dispersion of predicted retention times is expected when retention occurs by a mixed mechanism. In addition, the relative importance of adsorption and absorption as a retention mechanism is temperature dependent [30] and is expected to vary during temperature-programmed separations. Of the three stationary phases studied here, interfacial adsorption is expected to affect retention on the EC-Wax column the most. This may explain in part, why the agreement between the predicted and experimental temperature-programmed retention times

Table 7
Estimation of temperature-programmed retention times on EC-Wax for compounds not included in the construction of the solvation parameter models (Table 3)

Compound	Retention time (min)					
	3 °C/min		10 °C/min		12 °C/min	
	Experimental	Predicted	Experimental	Predicted	Experimental	Predicted
Benzaldehyde	9.21	7.64	5.06	4.37	4.59	3.56
Benzonitrile	11.38	9.54	5.93	5.13	5.32	4.14
1-Bromohexane	2.06	2.16	1.77	1.73	1.70	1.48
2-Bromophenol	21.43	22.86	8.26	8.42	7.35	6.59
n-Butylbenzene	4.17	4.62	2.97	2.96	2.78	2.43
Butyl acetate	1.53	1.64	1.38	1.44	1.34	1.27
Cyclopentanol	4.02	3.18	2.86	2.09	2.68	1.82
1,2-Dichlorobenzene	7.99	7.37	4.67	4.19	4.25	3.39
1,2-Dichloroethane	1.52	1.04	1.48	1.03	1.34	0.95
Ethylbenzene	1.89	2.24	1.65	1.79	1.59	1.55
Heptan-2-one	2.39	2.67	1.96	2.03	1.88	1.74
Iodobenzene	8.66	8.70	4.95	4.75	4.50	3.82
Naphthalene	15.20	18.49	7.27	8.08	6.46	6.20
2-Nitrophenol	16.36	18.01	7.41	7.85	6.55	6.09
3-Nitrotoluene	18.18	21.93	8.25	9.13	7.27	6.94
n-Nonane	0.94	0.90	0.91	0.91	0.90	0.81
Octan-2-ol	6.61	6.01	3.97	3.16	3.63	2.61
Pentan-1-al	1.15	1.27	1.08	1.21	1.07	1.09
4-Picoline	3.87	3.78	2.84	2.64	2.68	2.24
Pyrrole	4.74	4.59	2.88	2.67	2.76	2.33
Model statistics						
Slope	0.919 (±0.041)		0.904 (±0.043)		1.059 (±0.048)	
Intercept	0.524 (±0.421)		0.465 (±0.187)		0.295 (±0.164)	
r^2	0.968		0.965		0.969	
S.E.	1.26		0.45		0.37	
F	515		448		494	
d	0.89 (±1.07)		0.36 (±0.32)		0.48 (±0.36)	

is not as good for the EC-Wax column as for DB-1701 and DB-210.

3.3. Comparison with DryLab predictions

The approach for estimating temperature-programmed retention times using DryLab and the solvation parameter model are different. DryLab is an optimization program and uses experimental retention times from two temperature-programmed separations with different program rates to estimate retention times at other program rates. Additional compounds cannot be added without measurement of their retention times in the two foundation temperature-programmed separations. The solvation parameter model is not an optimization method alone. It provides chemical information about system properties and allows an

Table 8
Examples of the prediction of temperature-programmed retention times using DryLab

DB-210

Foundation program rates 3 and 15 °C/min to predict retention times at 8 °C/min for 42 compounds from Table 2
    For a linear model
        Slope = 0.983 (±0.028) r^2 = 0.9998   S.E. = 0.028   F = 251139
        Intercept = 0.021 (±0.008)   Average absolute deviation = 0.044 (s = 0.043)

Foundation program rates 3 and 12 °C/min to predict retention times at 10 °C/min for 21 compounds from Table 5
    For a linear model
        Slope = 0.995 (±0.002) r^2 = 0.999   S.E. = 0.015   F = 431849
    Intercept = 0.014 (±0.007)   Average absolute deviation = 0.012 (s = 0.014)

EC-Wax

Foundation program rates 5 and 12 °C/min to predict retention times at 10 °C/min for 40 compounds from Table 2
    Slope = 0.989 (±0.004) r^2 = 0.999   S.E. = 0.056   F = 76401
    Intercept = 0.027 (±0.015)   Average absolute deviation = 0.036 (s = 0.053)

estimate of temperature-programmed retention time for any compound with solute descriptors. Estimates do not require any further experiments once a general model for the system constants as a function of program rate is established. It is useful, however, to assess how well the solvation parameter model performs in estimating temperature-programmed retention times by comparison with the results from DryLab for the same experimental conditions. Some typical DryLab simulations are summarized in Table 8. DryLab is able to estimate temperature-programmed retention times to better than 0.05 min on average. This is at least a factor of three better than the solvation parameter model for the DB-1701 and DB-210 columns and better still for the EC-Wax column. The solvation parameter model is not as effective as DryLab for optimization of temperature-programmed separations where all the compounds of interest are available to run trial separations to gather the initial experimental data to build a model. On the other hand, the solvation parameter model affords a wider range of possibilities for stationary phase selection and initial conditions selection. For optimization of separations of difficult mixtures improvements in descriptor quality and probably a method to modify partition models to allow for interfacial adsorption are required.

4. Conclusions

The solvation parameter model is suitable for modeling retention in temperature-programmed gas chromatography using temperature-programmed retention times ($\log t_g$) as the dependent variable. The system constants of the solvation parameter model change smoothly with program rate and can be described by an empirical second-order model. In a qualitative sense, the system constants make chemical sense and are probably more than mere fitting constants. The solvation parameter model provides a useful tool for estimating temperature-programmed retention times from structure, that is for compounds with known solute descriptors and possibly for compounds with computer generated solute descriptors. Two problems that affect the practical utility of computer simulations for method development are descriptor quality and probably mixed retention mechanisms. In its present form the solvation parameter model is most likely to prove useful for initial conditions selection (e.g. stationary phase, program rate, separation time, etc.) For the present, the prediction of temperature-programmed retention times is not sufficiently accurate for selectivity optimization of difficult mixtures.

References

[1] W.E. Harris, H.W. Habgood, Programmed Temperature Gas Chromatography, Wiley, New York, 1967.
[2] F.R. Gonzalez, A.M. Nardillo, J. Chromatogr. A 842 (1999) 29.
[3] C.F. Poole, The Essence of Chromatography, Elsevier, Amsterdam, 2003.
[4] E.E. Akporhonor, S. Le Vent, D.R. Taylor, J. Chromatogr. 405 (1987) 67.
[5] T.I. Al-Bajjari, S. Levent, D.R. Taylor, J. Chromatogr. A 683 (1994) 367, 377.
[6] E.V. Dose, Anal. Chem. 59 (1987) 2414, 2420.
[7] G. Castello, P. Moretti, S. Vezzani, J. Chromatogr. 635 (1993) 103.
[8] S. Vezzani, P. Moretti, G. Costello, J. Chromatogr. A 767 (1997) 115.
[9] H. Snijders, H.-G. Janssen, C. Cramers, J. Chromatogr. A 718 (1995) 339.
[10] J.P. Chen, L.F. Zhang, Y.Z. Tian, L.X. Wang, J. Chromatogr. A 795 (1998) 305.
[11] D.E. Bautz, J.W. Dolan, W.D. Raddatz, L.R. Snyder, Anal. Chem. 62 (1990) 1560.
[12] D.E. Bautz, J.W. Dolan, L.R. Snyder, J. Chromatogr. 541 (1991) 1.
[13] M.C. Roman, R.W. Siergiej, J. Chromatogr. 589 (1992) 215.
[14] J.P. Chen, X.M. Liang, Q. Zhang, L.F. Zhang, Chromatographia 53 (2001) 539.
[15] A. Jayatilaka, C.F. Poole, J. Chromatogr. 617 (1993) 19.
[16] C.F. Poole, T.O. Kollie, S.K. Poole, Chromatographia 34 (1992) 281.
[17] M.H. Abraham, C.F. Poole, S.K. Poole, J. Chromatogr. A 842 (1999) 79.
[18] C.F. Poole, S.K. Poole, J. Chromatogr. A 965 (2002) 263.
[19] C.F. Poole, Q. Li, W. Kiridena, W.W. Koziol, J. Chromatogr. A 912 (2001) 107.
[20] C.F. Poole, W. Kiridena, M.I. Nawas, W.W. Koziol, J. Sep. Sci. 25 (2002) 749.
[21] W. Kiridena, C.F. Poole, W.W. Koziol, Analyst 127 (2002) 1608.
[22] W. Kiridena, C.F. Poole, M.I. Nawas, W.W. Koziol, J. Sep. Sci. 26 (2003) 1111.
[23] J. Li, B. Cai, J. Chromatogr. A 905 (2001) 35.
[24] C.M. Du, K. Valko, C. Bevan, D. Reynolds, M.H. Abraham, Anal. Chem. 70 (1998) 4228.
[25] N.C. Dias, M.I. Nawas, C.F. Poole, Analyst 128 (2003) 427.
[26] Y. Chu, C.F. Poole, Chromatographia, 2004, in press.
[27] C.F. Poole, Q. Li, W. Kiridena, W.W. Koziol, J. Chromatogr. A 898 (2000) 211.
[28] A.M. Zissimos, M.H. Abraham, M.C. Barker, K.J. Box, K.V. Tam, J. Chem. Soc. Perkin Trans. 2 (2002) 470.
[29] J.A. Platts, D. Butina, M.H. Abraham, A. Hersey, J. Chem. Inf. Comput. Sci. 39 (1999) 835.
[30] S.K. Poole, T.O. Kollie, C.F. Poole, J. Chromatogr. A 664 (1994) 229.
[31] Q. Li, C.F. Poole, Chromatographia 52 (2000) 639.