Extra-thermodynamic relationships in chromatography Enthalpy–entropy compensation in gas chromatography

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Abstract

The phenomenon of enthalpy–entropy compensation in gas chromatography is examined. Using 53 probe solutes that span a wide range in size (dispersive interaction), dipolarity, hydrogen-bond-donor and hydrogen-bond-acceptor strength, enthalpy–entropy compensation is not observed, while for probe solutes within a homologous series enthalpy–entropy compensation is observed as predicted by the linear solvation energy relationship methodology.

1. Introduction

The issue of "enthalpy–entropy compensation" is closely related to the effect of temperature on retention in chromatography. Enthalpy–entropy compensation is also called the isokinetic relationship (IKR), the "compensation effect", the "θ" rule, the isoselectivity relationship, etc. It has been found in a wide variety of processes and reaction equilibria including: heterogeneous catalysis; diffusion in metals, ionic crystals, and amorphous polymers; conduction in amorphous semiconductors; and phase equilibria between hydrophobic and hydrophilic phases and between multicomponent fluid phases [1–10]. Despite its utility it has also led to a great deal of misunderstanding and controversy [1–9]. In essence, enthalpy–entropy compensation refers to the experimental observation of a linear

relationship between enthalpy (H) and entropy (S) for a series of related processes as, for example, when a series of similar reactants are subjected to the same reaction:

$$\Delta H = \beta \Delta S + \alpha \qquad (1)$$

Clearly the constant of proportionality (β) in Eq. 1 must have units of absolute temperature. β is called the compensation temperature (see below).

This phenomenon is often called "enthalpy–entropy compensation" because when Eq. 1 is inserted into the fundamental relationship between free energy (G), enthalpy and entropy, the change in ΔG upon change in reactant is always smaller than the change in either ΔH or $T\Delta S$. Thus part of ΔH and ΔS cancel or compensate when ΔH and $T\Delta S$ are combined to give ΔG.

$$\Delta G = \Delta H - T\Delta S$$
$$= \Delta H[1 - (\beta/T)] + \alpha T/\beta = \Delta S(\beta - T) + \alpha \qquad (2)$$

Eq. 2 predicts that when T is equal to β, ΔG

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becomes the same for *all* reactants thus β represents the temperature at which ΔH and ΔS are completely compensated.

It is an axiom of extra-thermodynamic relationships that all sets of reactions (processes) which exhibit enthalpy–entropy compensation are governed by a single mechanism and all related reactions that have the same compensation temperature proceed via the same mechanism [10]. What this means is that only a single characteristic of the solute is needed to describe both ΔH and ΔS and therefore ΔH and ΔS must be linearly correlated. This principle is very important in chromatography. If enthalpy–entropy compensation is observed for a set of solutes then we can conclude that the differences in retention between the solutes are governed by a *single* type of parameter which governs their intermolecular interactions. This conclusion is in accord with the very general model of enthalpy–entropy compensation developed by Boots and de Bokx [11,12]. In their model they describe a suitably defined Gibbs free energy change (similar to our $\Delta G'$, see below) as the product of a temperature-dependent, system-independent factor $y(T)$ and a temperature-independent, system-dependent factor $\sigma(\{f\})$

$$\Delta G = y(T)\sigma(\{f\}) \tag{3}$$

Here the system dependence is described by a collection of parameters $\{f\}$ [similar to our linear solvation energy relationship (LSER) parameters, see below]. They conclude that only when G depends on one parameter, compensation can and must occur. If G depends on more than one parameter, compensation is not guaranteed.

When considered in detail (see below) it becomes clear that the above concepts are at odds with the fundamental basis for the use of LSERs [13] and other models of chromatographic retention such as multicomponent solubility parameter [14] which fundamentally represent solute–solvent interactions as a suite of parameters (dispersive, dipolar, hydrogen bonding). Furthermore it is difficult to imagine how a system governed by a single interaction mecha-

nism could display the very large variations in relative retention and even retention sequences commonly observed in specific forms of chromatography. It is therefore very important to understand the phenomenon of enthalpy–entropy compensation in detail and to assess its limits.

The enthalpies and entropies of solvation processes have been studied by many workers [10,15–20]. Barclay and Butler [16], and Frank and Evans [17,18] extensively studied the enthalpies and entropies of vaporization of pure liquids at 25°C and found that Eq. 4 adequately represented the behavior of most pure liquids. They proposed that it be regarded as a standard relationship representing "normal" behavior.

$$\Delta H_{vap}^0 (\text{J mol}^{-1}) = -43\,012$$

$$+ 3372\Delta S_{vap}^0 (\text{J mol}^{-1}\,\text{K}^{-1}) \tag{4}$$

This is clearly an enthalpy–entropy compensation relationship. The reference or standard states are the pure liquid and pure gas at 1 atm (10^5 Pa) and 25°C. Eq. 4 also applies to the vaporization of a series of dilute solutes from a variety of non-hydroxylic solvents [18]. Although Eq. 4 applies to many series of compounds as a whole [17], better fits are obtained by using separate lines for different types of solutes. The latter procedure is equivalent to assuming that each class of compound has a second interaction mechanism whose magnitude is constant within the class [10]. Appreciable deviations from the standard relationship (Eq. 4) may be taken as evidence for the presence of strong additional interactions [10].

The study of enthalpy–entropy relationships has been of considerable interest in chromatography. For RPLC, Melander *et al.* [21], obtained a linear correlation between the logarithm of the capacity factor, and the corresponding enthalpies for a particular chromatographic process. Since the compensation temperatures were indistinguishable, they concluded that the mechanism of interaction of various solutes with the stationary phase was invariant under the chromatographic conditions examined, even though the nature

and concentration of organic modifier was varied substantially. Subsequently, the same authors developed a simple three-parameter relationship to express retention as a function of mobile phase composition and temperature [22–26].

Following Melander et al.'s work [21], Jinno and co-workers [27,28] investigated the effect of low temperatures (temperature range −50°C to 45°C) in RP-HPLC. Based on their observation that the compensation temperature was within the same range as the other systems, Jinno and co-workers concluded that the retention mechanism at low temperatures is similar to that at higher temperatures. Similar conclusions were drawn by Vigh and Varga-Puchony [29] in a study of retention of members of a homologous series in RPLC.

The influence of intramolecular interactions on the chromatographic behavior of arylaliphatic acids, aryloxoalkanoic acids and arylhydroxylalkanoic acids in RPLC have been explored by means of enthalpy–entropy compensation by Kuchar and co-workers [30,31]. For the three different homologous series of acids, they observed three different slopes for plots of $\log k'$ vs. ΔH^0 (i.e. enthalpy–entropy compensation). It appears that enthalpy–entropy compensation occurs only within a single homologous series. Riley et al. [32] have observed the same phenomenon in ion-pair RPLC.

Although temperature has a much greater effect on retention in GC than in LC, there are only a few reports on the use of temperature to explore retention mechanisms in GLC [33,34]. Kuchar et al. [34] used the enthalpy–entropy compensation concept to explore differences in the mechanism of separation of alkyl and arylalkyl esters of benzoic acids on two capillary columns (SE-30 and OV-351).

It is unfortunately true that it is entirely possible to observe correlations between ΔH and ΔS even though such correlations are adventitious and due only to spurious statistical effects that relate to least squares data fitting. This can happen when ΔH and ΔS are both measured via the temperature dependence of the free energy. That is, when ΔH is taken from the slope of a Van 't Hoff plot [4–7]. This problem cannot

occur when ΔH is obtained by calorimetric methods and ΔS is computed from the measured ΔG. Krug and co-workers [4–7] have shown that due purely to statistical effects apparently high correlations between ΔH and ΔS can be observed when the Van 't Hoff slope is used to obtain ΔH even when in fact no such physical phenomenon is actually taking place. In a recent paper, Reddy et al. [35] also showed that they obtained an excellent correlation between enthalpy and entropy in spite of the lack of good correlations between ΔG and ΔH (i.e., the lack of enthalpy–entropy compensation, see below). Krug [5] has outlined three methods to avoid the observation of false correlations. Unfortunately these methods have been seldom used in chromatographic studies of enthalpy–entropy compensation. All three methods were used in this work.

Krug [5] has pointed out that when ΔH and ΔS compensation is real then plots of ΔG (or an equivalent parameter such as the logarithm of a capacity factor) vs. $1/T$ must intersect at a single temperature for all compounds. Second, when enthalpy–entropy compensation is real then plots of ΔG_{Th} vs. ΔH must form a straight line. ΔG_{Th} is defined as the measured free energy change at the harmonic mean temperature given below:

$$1/T_h = \left(\sum_{i=1}^{n} 1/T_i \right) / n \tag{5}$$

Purely statistical effects cannot cause correlation in such a plot. Furthermore, the slope of such a plot (denoted γ) is related to the compensation temperature (β)

$$\Delta H = \gamma \Delta G + (1 - \gamma) \Delta G_\beta \tag{6}$$

where

$$\Delta G = \Delta G_{Th} = \Delta H - T_h \Delta S$$

$$\Delta G_\beta = \Delta H - \beta \Delta S$$

$$\gamma = 1 / (1 - T_h / \beta) \tag{7}$$

or

$$\beta = T_h / (1 - 1/\gamma) \tag{8}$$

Third, Krug has devised a detailed statistical analysis method based on the analysis of variance method (ANOVA) which allows dissection of the data set, that is the measurements of ΔG for p compounds at q temperatures, into real effects and measurement error. Only when there is a high probability that the variance due to true enthalpy–entropy correlation exceeds random error can one say that enthalpy–entropy compensation is physically real. The reader is referred to refs. 5 and 36 for computational details.

In this work we examined the enthalpy–entropy compensation phenomenon in capillary gas chromatography according to the Krug's procedures and the results were compared with predictions of solvatochromic linear solvation energy relationships.

2. Experimental

The retention data studied here include a set of capacity factors ($\log k'$) for 53 highly variegated compounds that span an extremely wide range in chemical characteristics on eight common capillary columns ranging from a methyl silicone oil to polyethylene glycol. The details of this data base have been published [37].

3. Results and discussion

3.1. Enthalpy–entropy compensation in gas chromatography

To examine whether enthalpy–entropy compensation took place in our data sets, we followed the procedures of Krug [5] for detection of such effects. We examined our retention data on all eight columns but will only present data on one column (DB-1701) as a typical example.

First, we show the result of plotting the values of ΔH^0 and $\Delta S'$ as obtained from a Van 't Hoff plot (Fig. 1). The relationship between ΔH^0 and $\Delta S'$ is shown in Eq. 9. It might be concluded that there is enthalpy–entropy compensation (correlation coefficient > 0.95).
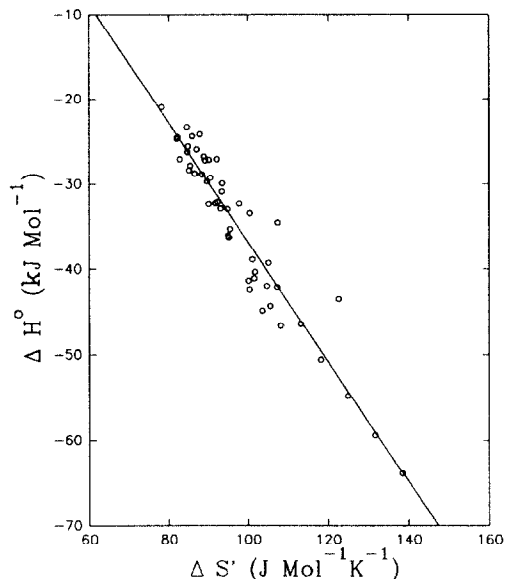

Fig. 1. Plot of ΔH^0 vs. $\Delta S'$ for all compounds on the DB-1701 column.

$$\Delta H^0 (\text{kJ mol}^{-1}) = (33.20 \pm 3.11)$$
$$+ (0.70 \pm 0.03)\Delta S' \qquad (9)$$

S.D. $= 2.9$, $r = 0.95$, $n = 50$

We now test to see if there is a common intersection point in plots of $\log k'$ vs. $1/T$ for all compounds (see Fig. 2). Clearly the lines intersect but they do so over a fairly wide range
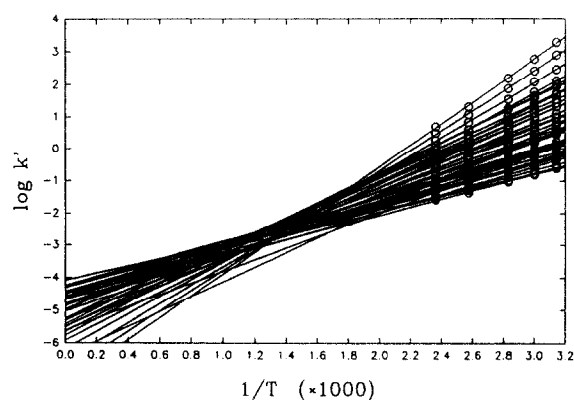

Fig. 2. Plot of $\log k'$ vs. $1/T$ (K) for all compounds on the DB-1701 column.

of temperatures not at a single temperature. A detailed examination suggests the possibility of enthalpy–entropy compensation for some compounds. When we restricted the data set to just the n-alkanes, a single intersection point was observed suggesting real enthalpy–entropy compensation for these solutes (Fig. 3). Similar plots were obtained for other homologous series. From Fig. 3, the compensation temperature for the alkanes determined from the common intersecting point is about 712 K.

Second, $\Delta G'_{Th}$ was calculated ($\Delta G'_{Th} = \Delta H^0 - T_h \Delta S'$, see Table 1). The ΔH^0 vs. $\Delta G'_{Th}$ plot is shown in Fig. 4. We see a similar linear relationship as that observed in Fig. 1 (the solid line represents the least squares line for all solutes). The regression results for all solutes are shown in Eq. 10. We point out that there was no deterioration in the quality of fit compared with Eq. 9. This is not expected since the ΔH^0 vs. $\Delta G'_{Th}$ correlation should remove any statistic effects existing in the ΔH^0 vs. $\Delta S'$ correlation, therefore result in a worse correlation. This might be due to the different coordinates in the two correlations. Again, if we examine only the n-alkanes, a much tighter relationship is obtained (the dashed line in Fig. 4 and Eq. 11).

$$\Delta H^0 = (-34.95 \pm 0.37) + (1.74 \pm 0.07)\Delta G'_{Th}$$
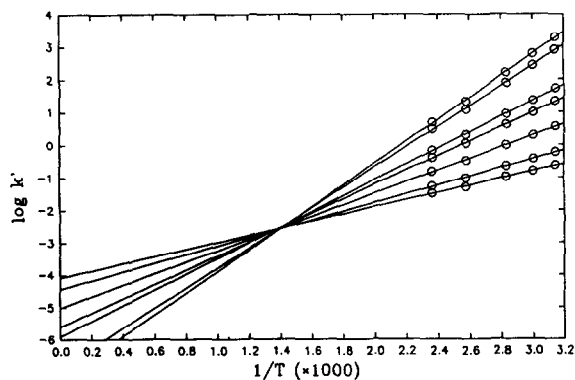
$$(10)$$

S.D. $= 2.58$, $r = 0.96$, $n = 50$

Fig. 3. Plot of log k' vs. $1/T$ (K) for n-alkane solutes on the DB-1701 column.

$$\Delta H^0 = (-35.01 \pm 0.22) + (2.02 \pm 0.03)\Delta G'_{Th}$$

$$(11)$$

S.D. $= 0.54$, $r = 1.00$, $n = 7$

The same compensation temperature (712 K) was obtained for the alkanes by use of Eq. 7. Additional homologous series were examined as shown in Fig. 5. We see that all are straight lines and that they are almost parallel. This strongly suggests that there is more than one interaction mechanism contributing to retention [10].

Similar plots of ΔH^0 vs. $\Delta G'_{Th}$ are obtained for all other phases studied in this work. The compensation temperatures for all solutes and just the n-alkanes are summarized in Table 2. These are based on regression results for ΔH^0 vs. $\Delta G'_{Th}$. Compensation was never observed when all solutes were included. Compensation was observed for the n-alkanes on all columns. Moreover, the compensation temperature for the n-alkanes on all columns are very similar. By and large the compensation temperature for the full solute set does not agree with those for the n-alkanes and vary greatly from phase to phase.

By using Krug's ANOVA method [5], we tested for the existence of enthalpy–entropy compensation for all compounds and for each homologous series. Similar results were obtained (Table 3). That is, there was no compensation for all compounds as a whole, but there was compensation for solutes within a homologous series. Each homologous series has its own compensation temperature. Enthalpy–entropy compensation was not observed for the three aliphatic alcohols. This is not surprising because we only examined retention data for methanol, ethanol and propanol, and usually the first few members of a homologous series behave differently from the higher homologues.

3.2. LSER, the Martin equation and enthalpy–entropy compensation

In a previous study [38], we showed that the following equations describe retention on a wide variety of GC stationary phases.

Table 1
Apparent Gibbs free energy ($\Delta G'$, kJ/mol) at the harmonic temperature

No.	Compound	DB-1 93°C[a]	DB-5 93°C	DB-1301 73°C	DB-1701 86°C	DB-17 93°C	DB-210 73°C	DB-225 93°C	DB-WAX 73°C
1	Cyclohexane	1.78	2.23	b	b	4.00	b	5.28	b
2	1-Hexene	3.39	3.87	3.53	4.79	6.41	5.92	7.47	6.28
3	Pentane	5.34	6.04	5.73	7.11	8.95	7.97	10.14	9.45
4	Hexane	3.27	3.87	3.39	4.93	6.77	6.06	8.11	7.34
5	Octane	-1.02	-0.27	-1.07	0.56	2.57	2.32	4.07	3.43
6	Decane	-5.14	-4.51	-5.52	-3.55	-1.47	-1.23	0.48	-0.35
7	Undecane	-7.20	-6.53	-7.71	-5.71	-3.60	-3.08	-1.48	-2.30
8	Tetradecane	-13.43	-12.71	-14.20	-12.05	-9.85	-8.43	-7.06	-7.99
9	Pentadecane	-15.49	-14.75	-16.36	-14.15	-11.93	-10.20	-8.88	-9.86
10	Ethyl acetate	3.46	3.83	2.43	3.29	4.35	1.72	3.61	1.42
11	Propyl acetate	1.31	1.49	0.12	1.12	2.33	-0.19	1.72	-0.27
12	Ethylether	5.39	5.96	5.24	6.55	7.70	6.71	8.15	6.69
13	Propylether	1.52	2.03	1.14	2.66	3.93	3.57	4.87	3.70
14	Butylether	-2.51	-2.03	-3.16	-1.47	0.02	0.05	1.04	0.14
15	Acetonitrile	b	6.28	4.23	4.22	5.24	1.35	2.49	-0.91
16	Propionitrile	4.45	4.32	2.39	2.37	3.65	-0.28	0.97	-1.36
17	Acetone	5.89	6.15	5.01	5.09	6.56	b	4.49	2.71
18	2-Butanone	3.82	3.90	2.68	2.92	4.32	0.71	2.68	1.05
19	2-Pentanone	1.84	1.99	0.40	1.03	2.44	-0.96	0.98	-0.42
20	Dimethylformamide	0.23	-0.10	-2.56	-2.54	-1.46	-5.87	-4.67	-7.05
21	Dimethylacetamide	-1.68	-1.74	-4.48	-4.36	-3.24	-7.46	-6.25	-8.52
22	Dimethylsulfoxide	-0.84	-1.02	-4.31	-4.61	-3.50	-8.25	-7.66	-11.29
23	Propionaldehyde	6.26	6.03	b	5.39	6.47	3.43	5.00	3.22
24	Tetrahydrofuran	3.11	3.10	b	2.87	3.78	2.13	3.10	1.67
25	Triethylamine	1.77	2.22	1.08	2.67	4.14	2.77	4.79	b
26	Nitromethane	5.08	5.01	2.42	2.51	3.67	0.01	0.64	b
27	Nitroethane	2.96	2.68	0.64	0.73	1.90	-1.66	-0.90	-3.78
28	Nitropropane	1.03	1.00	-1.23	-0.99	0.23	-3.18	-2.34	-4.71
29	Methanol	8.50	9.21	7.34	7.42	b	7.74	6.32	1.25
30	Ethanol	b	7.80	b	6.03	8.03	6.13	5.03	0.49
31	1-Propanol	4.45	5.32	3.08	3.65	5.73	4.05	b	-1.50
32	2-Propanol	5.94	6.55	b	5.23	7.15	5.29	4.71	0.69
33	2-Methyl-2-propanol	5.26	5.61	4.07	4.83	7.01	4.62	4.51	1.30
34	Trifluoroethanol	8.53	7.95	4.02	4.07	9.15	5.63	2.54	-4.16
35	Hexafluoroisopropanol	2.28	6.82	0.47	0.60	b	b	b	b
36	Acetic acid	b	5.14	1.85					b
37	Aniline	-4.03	-4.06	-6.61	-6.32	-5.64	-5.70	-8.44	b
38	N-Methylaniline	-5.80	-5.69	-8.27	-7.75	-7.14	-7.02	-9.18	b
39	Phenol	-3.96	-3.98	-8.15	-8.09	-4.83	-4.38	-10.52	b
40	Benzyl alcohol	-5.09	-5.00	-8.08	b	-6.44	-6.16	-9.88	b
41	m-Cresol	-5.95	b	-10.09	-9.93	-6.77	-6.35	-12.09	b
42	Ethylamine	6.90	7.76	b	7.05	8.45	5.96	7.68	b
43	Propylamine	5.23	5.36	b	5.17	6.29	3.82	5.60	b
44	Butylamine	2.87	2.94	1.46	2.81	4.33	1.62	3.21	b
45	Benzene	1.92	2.21	1.28	2.21	2.67	2.52	2.50	0.16
46	Toluene	-0.24	0.08	-1.01	0.01	0.59	0.55	0.55	-1.69
47	Ethylbenzene	-2.15	-1.81	-3.05	-1.92	-1.37	-1.02	-1.18	-3.28
48	Propylbenzene	-4.01	-3.66	-5.00	-3.77	-3.10	-2.62	-2.75	-4.77
49	p-Xylene	-2.32	-2.01	-3.21	-2.08	-1.38	-1.13	-1.12	-3.42
50	Benzaldehyde	-3.66	-3.82	-5.81	-5.34	-4.94	-6.22	-6.53	-10.26
51	Benzonitrile	-4.13	-4.26	-6.60	-6.26	-5.62	-7.65	-7.77	b
52	NN-Dimethylaniline	-6.52	b	-8.25	-7.57	-7.15	-7.04	-7.78	b
53	Carbontetrachloride	1.94	2.29	1.49	2.68	3.23	b	3.72	1.56

[a] Harmonic mean temperature calculated from Eq. 5.
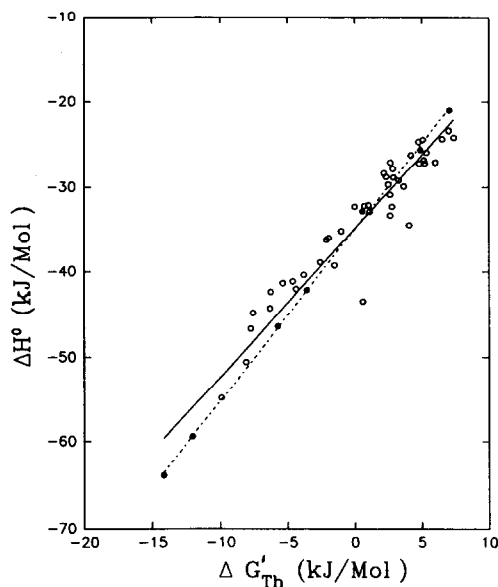[b] No data due to missing ΔH values.

Fig. 4. Plot of ΔH^0 vs. $\Delta G'_{Th}$ for all solutes on the DB-1701 column. The solid line represents the least squares line for all solutes ($\bigcirc$). The dashed line represents the least squares line for the *n*-alkanes ($\bullet$) only.
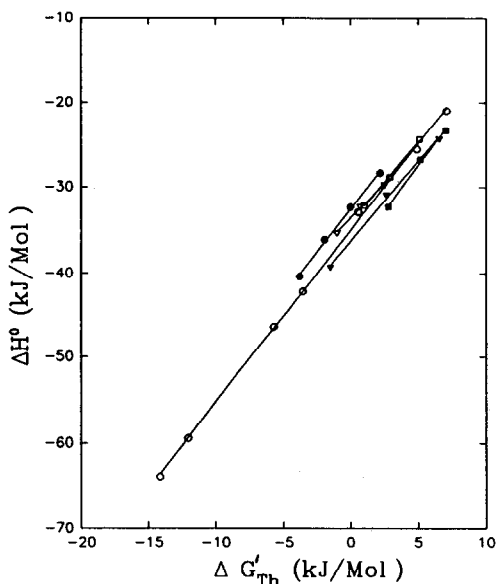

Fig. 5. Plot of ΔH^0 vs. $\Delta G'_{Th}$ for 6 homologous series on the DB-1701 column. $\bigcirc$ = *n*-Alkanes, $\bullet$ = alkylbenzenes, ∇ = nitroalkanes, $\blacktriangledown$ = alkylethers, $\square$ = 2-ketones, $\blacksquare$ = amines.

$$\Delta G'(T) = SP_{o,G} + l_G \log L^{16} + s_G \pi_2^{*,C} + d_G \delta_2$$
$$+ a_G \alpha_2^C + b_G \beta_2^C \tag{12}$$

$$\Delta H^0 = SP_{o,H} + l_H \log L^{16} + s_H \pi_2^{*,C} + d_H \delta_2$$
$$+ a_H \alpha_2^C + b_H \beta_2^C \tag{13}$$

$$\Delta S' = SP_{o,S} + l_S \log L^{16} + s_S \pi^{*,C} + d_S \delta_2$$
$$+ a_S \alpha_2^C + b_S \beta_2^C \tag{14}$$

In Eqs. 12–14, the characteristic constants have the same meaning as before but they now have their respective units. In order for enthalpy–entropy compensation to take place for all compounds, the free energies for all compounds must become equal at $T = \beta$. That is, for all solutes:

$$\Delta G' = \Delta H^0 - \beta \Delta S' = \text{constant}$$

$$= SP_{o,H} - \beta SP_{o,S} + (l_H - \beta l_S) \log L^{16}$$
$$+ (s_H - \beta s_S)\pi_2^{*,C} + (d_H - \beta d_S)\delta_2$$
$$+ (a_H - \beta a_S)\alpha_2^C + (b_H - \beta b_S)\beta_2^C \tag{15}$$

Note that for a given column, $SP_{o,H}$ and $SP_{o,S}$ are independent of solutes, thus evidently:

$$(l_H - \beta l_S) \log L^{16} + (s_H - \beta s_S)\pi_2^{*,C}$$
$$+ (d_H - \beta d_S)\delta_2 + (a_H - \beta a_S)\alpha_2^C$$
$$+ (b_H - \beta b_S)\beta_2^C = \text{constant}' \tag{16}$$

Given that the sets of solutes used in this work were highly variegated it is most unlikely, if not impossible, for Eqs. 15 and 16 to be true for more than a limited set of solutes. If we assume that the solute parameters are essentially uncorrelated that is $\log L^{16}$, $\pi_2^{*,C}$, α_2^C, β_2^C and δ_2 do not covary, which is true, then exact compensation for all solutes can only take place if each coefficient of each parameter in Eq. 16 individually compensates. Thus:

$$l_H = l_S \beta$$

$$s_H = s_S \beta$$

etc.

This is evidently an exceedingly stringent condition for compensation. It is most unreasonable to believe that this can take place *exactly* when

Table 2
Compensation temperatures based on ΔH^0 vs. $\Delta G'_{Th}$ regression for all solutes and for n-alkanes only on all columns[a]

Column	All solutes[b]		n-Alkanes only[c]	
	β^d	Compensation[e]	β	Compensation
DB-1	842	No	712	Yes
	38[f]	28		
DB-5	922	No	719	Yes
	44	11		
DB-1301	808	No	749	Yes
	42	16		
DB-1701	845	No	712	Yes
	34	11		
DB-17	855	No	765	Yes
	20	12		
DB-210	802	No	673	Yes
	27	10		
DB-225	1009	No	729	Yes
	45	18		
DB-WAX	855	No	744	Yes
	31	16		

[a] ΔH^0 and $\Delta G'_{Th}$ are in units of kJ/mol.
[b] All solutes are included in the regression.
[c] Only n-alkane solutes are included in the regression.
[d] Compensation temperature (K) calculated from Eq. 8 as if compensation occurs.
[e] Compensation effect detected by ANOVA (see text).
[f] Standard deviation of the compensation temperature calculated by $S.D.(\beta) = [T_h/(\text{slope} - 1)] \cdot S.D.(\text{slope})$.

Table 3
ANOVA results for detection of the compensation effect

Solutes	Compensation effect[a]	T_C (K)[b]	S.D.[c]
All[d]	No		
Alkanes[e]	Yes	712	10
Ethers[f]	Yes	777	39
2-Ketones[g]	Yes	757	31
Nitroaliphatics[h]	Yes	961	55
Alcohols[i]	No		
Alkylbenzenes[j]	Yes	722	30

[a] Compensation is declared real only when there is a high probability that the variance due to true enthalpy–entropy correlation exceeds the random error.
[b] Compensation temperature calculated using Eq. 8.
[c] Standard deviation of the compensation temperature.
[d] All solutes, n (number of compounds) = 50.
[e] All n-alkane solutes, n = 7.
[f] Ethylether, propylether and butylether.
[g] Acetone, 2-butanone and 2-pentanone.
[h] Nitromethane, nitroethane and nitropropane.
[i] Methanol, ethanol and 1-propanol.
[j] Benzene, toluene, ethylbenzene and propylbenzene.

one considers the very different processes that are involved in each of the individual terms in the LSER. However, we previously showed that approximately linear relationships for the LSER coefficients for $\Delta G'$ and ΔH^0 did exist but the slopes are different for each coefficient. Thus it is impossible to find a single temperature at which each coefficient of each parameter in Eq. 16 will individually compensate.

Compensation can take place *approximately* at least to the extent indicated by the scatter shown in Fig. 4 provided that one term in Eq. 16 dominates and thereby provides most of the variation in the $\Delta G'$ and ΔH^0 (other terms being small or largely compensated). We believe that the dispersive interactions that dominate retention in gas chromatography and are reflected in the $\log L^{16}$ parameter provide the basis for the approximate compensation seen in Fig. 4. A plot of $\Delta G'_{Th}$ vs. $\log L^{16}$ (see Fig. 6) is very similar to Fig. 4.
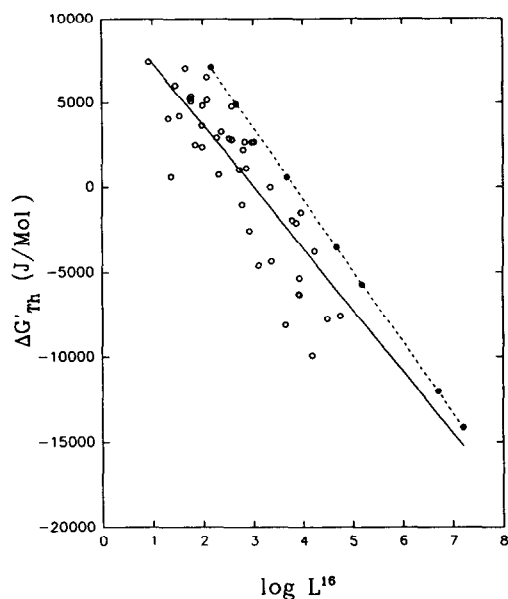
Fig. 6. Plot of $\Delta G'_{Th}$ vs. log L^{16} for all solutes on the DB-1701 column. The solid line represents the least squares line for all solutes (O). The dash line represents the least squares line for the n-alkanes (●) only.

Compensation can take place much more precisely within a homologous series of solutes. Previously we showed [39] that log L^{16} is a linear function of homologue number (HN) (Eq. 17), $\pi_2^{*,C}$ is a constant or an approximately linear function of the homologue number (Eq. 18).

$$\log L^{16} = A_1 + B_1 HN \qquad (17)$$

$$\pi_2^{*,C} = A_2 + B_2 HN \qquad (18)$$

δ_2 is a constant within a homologous series, α_2^C and β_2^C are almost constant within a homologous series [39–41]. Upon substitution of Eqs. 17 and 18 into Eq. 16, we get

$$(l_H - \beta l_S)(A_1 + B_1 HN) + (s_H - \beta s_S)(A_2 + B_2 HN)$$
$$+ (d_H - \beta d_S)\delta_2 + (a_H - \beta a_S)\alpha_2^C$$
$$+ (b_H - \beta b_S)\beta_2^C = \text{constant} \qquad (19)$$

Upon rearranging this equation and setting the coefficients of HN to zero, we can calculate a temperature at which all homologues will have

the same free energy, that temperature should be the compensation temperature.

$$\beta = (B_1 l_H + B_2 s_H)/(B_1 l_S + B_2 s_S)$$
$$= (l_H + \theta s_H)/(l_S + \theta s_S) \qquad (20)$$

$$\theta = B_2/B_1$$

Alternatively, the compensation temperature can be predicted directly from the equations for log $k'(T)$ [38].

$$\log k'(T) = SP_{o,A} + SP_{o,B}/T$$
$$+ (l_A + l_B/T) \log L^{16}$$
$$+ (s_A + s_B/T)\pi_2^{*,C} + (d_A + d_B/T)\delta_2$$
$$+ (a_A + a_B/T)\alpha_2^C + (b_A + b_B/T)\beta_2^C \qquad (21)$$

Upon substituting Eqs. 17 and 18 into Eq. 21, and setting the coefficient of HN to zero, we get

$$\beta = (l_B B_1 + s_B B_2)/(l_A B_1 + s_A B_2)$$
$$= (l_B + \theta s_B)/(l_A + \theta s_A) \qquad (22)$$

$$\theta = B_2/B_1$$

From Eqs. 20 and 22, we can see that within a homologous series, enthalpy–entropy compensation will be observed at the temperature β. However, we must point out that Eqs. 13, 14 and 18 are approximate results, that is to say, the compensation temperature predicted by Eq. 20 or 22 are only qualitative. The most efficient and accurate way to calculate a compensation temperature is by using Eq. 7. For compounds of different homologous series, judging from Eq. 16 or 21, it is not clear at all that there is such a temperature which satisfies either equation.

Previously, we have shown [39] that our LSER equation and parameters are, within any reasonable expectations of the experimental precision, in accord with the Martin equation. That is, our LSER equation and parameters predict that within a homologous series the free energy of retention ($\Delta G'$, Eq. 15) is a linear function of the homologue number. Similarly, from Eq. 16 and 17, one can conclude that within a homologous series the enthalpy and entropy of retention are also approximately linear functions of the homo-

logue number. If the free energy and enthalpy of retention are both linear functions of only the homologue number, then the free energy must be linearly related to the enthalpy of retention, and enthalpy–entropy compensation must then result (see Fig. 5). The above derivation agrees with the much more general model of enthalpy–entropy compensation developed by Boots and de Bokx [11,12].

The fact that a set of LSER parameters ($\log L^{16}$, $\pi^{*,C}$, α_2^C and β_2^C) are needed to describe retention in GC (and in RPLC, octanol–water partitioning, water solubility, etc.) stands in fundamental contradiction to the observation of enthalpy–entropy compensation in view of the Boots–de Bokx rule. We conclude that when such approximate compensation is observed it means nothing more or less than there is only a single dominant variable among the specific set of solutes under study. Thus one can "force" enthalpy–entropy compensation to be observed in chromatography by deliberately or inadvertently choosing a set of solutes in which only dispersive or only dipolar or only hydrogen bond acceptor or acceptor strength are varied.

However, more importantly, when a highly variegated set of solutes is chosen and enthalpy–entropy is still observed then one can usually infer that a single contribution to the retention process is dominant. One must be wary of some special instances as is the case in reversed-phase chromatography where there are very strong correlations between different factors such as the effect of the size of a molecule which simultaneously controls both cavity formation processes and dispersive interactions. In such instance one can observe enthalpy–entropy compensation when there is more than a single major retention process and thus be seriously misled.

3.3. Overview of extra-thermodynamic relationships in chromatography

Elsewhere we considered the phenomena of "$S - \ln k'_w$ compensation" in RPLC [42]. This refers to the observation that the intercepts ($\ln$

k'_w) and slopes (S) of plots of $\ln k'$ versus mobile phase composition in RPLC are often strongly correlated. We showed that such a relationship is actually a specific form of the well known Collander equation [43,44] which specifies that plots of logarithmic capacity factors or logarithmic partition coefficients for a series of solutes in two different stationary phases with a fixed mobile phase are often quite linear. In both these situations and in the case of enthalpy–entropy compensation such must be observed when the variation in retention from solute to solute is governed by a *single* solute-dependent intermolecular parameter. We find it convenient to refer to such a chromatographic system and set of solutes as being "*iso-retentive*". It is evident that a homologous series of solutes represents a trivial case of "iso-retentive" set of solutes.

As shown in Eqs. 15 and 16 it is possible for enthalpy–entropy compensation to take place when the same compensation temperature is observed for each retention controlling process. In this case it will appear as if there is a single solute-dependent retention governing parameter when there is not. We have referred to this situation as being "pseudo iso-retentive".

Whether a chromatographic system behaves "iso-retentively" or not depends both on the nature of the system and the nature of the set of solutes. Consider first a chromatographic system, *e.g.* GC on a totally non-polar phase such as hexadecane. Differences in a solute's ability to donate or accept a hydrogen bond will have no effect on its retention on such a phase. Thus a set of solutes might appear to be iso-retentive in fact they are capable of additional interactions given the right phase system. Conversely suppose we consider the case of RPLC where it has been shown that along with its size the solute's hydrogen bond basicity is very important. If one examines a set of congeners or homologues or molecules that differ only in size but not hydrogen bond basicity one could fallaciously conclude that RPLC is an "iso-retentive" system when in fact it is not. It therefore of utmost importance in all fields of chromatography that one choose a set of probe molecules that truly do explore a wide range in types of molecular interaction

parameters before coming to any general conclusions.

4. Conclusions

Based on several statistically unbiased procedures, we examined the phenomenon of enthalpy–entropy compensation in capillary gas chromatographic retention. For all compounds as a whole, enthalpy–entropy compensation was not observed. For solutes within a homologous series, enthalpy–entropy compensation was observed. Our LSER equation and parameters predict that within a homologous series the free energy, enthalpy and entropy are linear functions of the homologue number and thus enthalpy–entropy compensation will occur within a homologous series but it is most unlikely to occur across a non-homologous sets of solutes of different polarity, hydrogen bond donor and acceptor strength.

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6. References

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