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## MEANINGFUL ERROR ANALYSIS OF THERMODYNAMIC MEASUREMENTS BY GAS-LIQUID CHROMATOGRAPHY

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### SUMMARY

The usefulness of a simplified error analysis procedure for infinite-dilution partition coefficients ( $K_R$ ) as measured by gas-liquid chromatography is established by comparison of calculated with experimental relative standard deviations. It is shown that the determination of the column liquid-phase volume,  $V_L$ , is the largest source of random error, other error sources, such as that for retention times, being trivial by comparison. As a result, simple apparatus is found to be adequate for the described measurements. An inter-laboratory comparison of partition coefficients shows, further, that the reproducibility of these data can be as good as  $\pm 1\%$ , these findings, in addition, excellent agreement with those determined by a static technique.

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### INTRODUCTION

The advantages of gas-liquid chromatography (GLC) for the measurement of thermodynamic properties of solutions, wherein one component is at infinite dilution, have long been recognized<sup>1,2</sup>. The GLC technique requires that the solute partition coefficient,  $K_R$ , or the specific retention volume,  $V_g^0$ , be determined. These are found, in practice, from the relation,

$$K_R = \frac{t'_{Rj} F_c}{V_L} = \frac{V_g^0 \rho_L T}{273.15} \quad (1)$$

where  $t'_{Rj}$  is the solute retention time corrected for dead space,  $j$  is the James-Martin<sup>3</sup> gas compressibility correction factor,  $F_c$  is the volume flow-rate at the column outlet re-calculated from ambient temperature to the column temperature,  $T$ , after correction for the presence of water vapour pressure if a soap-bubble flow meter is employed, and  $V_L$  is the volume of liquid (stationary) phase of density,  $\rho_L$ , in the column.

Activity coefficients may be derived from  $K_R$  data and fugacity corrections then applied<sup>4</sup> to provide values of  $\gamma_i^\infty$ .

The essential simplicity of the GLC approach is so attractive that it is somewhat surprising that it has not been more widely used for thermodynamic studies. It seems to us possible that this reluctance springs from a lack of certainty with regard to the quality of reported data. Indeed, a recently published<sup>5</sup> comprehensive list of GLC-determined activity coefficients indicates that inter-laboratory agreement of  $\gamma_f^\infty$  data is poor, amounting to, at best,  $\pm 5\%$ , agreement of GLC with static (non-chromatographic) data being no better. Some of the apparent irreproducibility of GLC data from laboratory to laboratory is to be attributed to the use of initial (rather than peak-maximum) retention times in several early studies. Nevertheless, even allowing for this, it is clear that other factors may, in addition, be operative. For example, failure to recognize and to correct for gas-liquid interfacial adsorption is not uncommon while, in converting  $\gamma_p^\infty$  to  $\gamma_f^\infty$  values, inappropriate correction can be identified even in recent work.

At the practical level, since GLC studies often involve the use of high-molecular-weight solvents, it is likely that attainment of consistent levels of liquid-phase purity may also present difficulties. But, in the main, workers in the field have generally attributed discrepancies in  $K_R$  and  $V_g^0$  data to instrumental sources and as a result, considerable effort has been expended in developing more reliable apparatus and concomitant error analysis procedures (*e.g.*, refs. 6-9). Our own experience, on the other hand, has led us to question the importance of instrumental factors in comparison with the problems associated with measurement of  $V_L$ , as noted by, for example, Wicarova *et al.*<sup>6</sup>. The current study is therefore aimed at defining the various sources of random error and the limits of accuracy of GLC data. To this end, two studies have been concurrently duplicated in laboratories which, where it will be useful, will be herein identified as A and B.

## EXPERIMENTAL

The solutes employed were reagent-grade *n*-alkanes ( $C_5$ - $C_8$ ), cyclohexane, methylcyclohexane, benzene and toluene, the solvents used being dinonyl phthalate (di-3,5,5-trimethylhexyl phthalate, DNP) and squalane (2,6,10,15,19,23-hexamethyl-tetracosane, SQ). The former was obtained in two lots from BDH (Poole, Great Britain), the latter separately from BDH and Applied Science Labs. (State College, Pa., U.S.A.) and both were used as received. These particular solvents were chosen for this study in order to allow comparison of the chromatographic data with data obtained by extrapolation from finite-concentration of conventionally derived vapour-liquid measurements<sup>10</sup>.

The solid support used throughout was Chromosorb G (60-80 mesh, AW DMCS) which was dried overnight, prior to use, in an air oven at 100°C and subsequently stored in a vacuum desiccator over magnesium perchlorate. The material was obtained separately from Applied Science Labs. and Jones Chromatography (Cardiff, Great Britain).

The required amount of liquid phase was dissolved in a volatile solvent (A: methylene chloride; B: acetone + benzene), the support added, and the solvent removed by aspiration. The packing was then finally dried by rotary evaporation.

Coiled stainless-steel columns (0.25 in. O.D.) were packed by applying suction to one end, which had been plugged with silanized glass wool, pouring the packing

into the other end, and gently tapping until no more could be added. Glass wool was then inserted into the filling end. The columns were used as packed, *i.e.*, the filling end was connected to the injector and the suction end to the detector. Liquid loadings of 7–10% (w/w) were used.

Thermo-regulated water-baths were used as column thermostats in both studies. These comprised a Neslab PBC-2 immersion cooling unit and a Vycor 250-W immersion heater coupled to a mercury thermometer-switch (A) and an integrated system based on a Grant, Ltd., 50-l water-bath unit (B). Temperatures were measured with an NBS-calibrated 29.5–30.5°C thermometer (A) or a Hewlett-Packard Model 2802A platinum resistance system (B). The temperature in each system was maintained at  $30.00 \pm 0.03^\circ\text{C}$ .

Solutes were injected either as individual or as mixed vapours from a 10- $\mu\text{l}$  syringe into a heated Hamilton flash-vaporization unit (A) or a heated injection port constructed from a tube Tee-junction (B), the temperature in either case being maintained at *ca.* 200°C, *i.e.*, above the boiling point of the least volatile solute used.

Both experimental systems employed thermal conductivity detection, the devices used being a Gow-Mac Model 10-952 (A) and a Pye Model 12143 (B). The units and connecting lines were heated to *ca.* 200–250°C with heating tape or Nichrome wire.

The flow of the helium carrier gas was controlled by a conventional cylinder regulator followed in series by one non-lagged (A) or two lagged (B) Negretti-Zambra R-182 NC precision pressure regulators. The column inlet pressure ( $p_i$ ) was measured with a calibrated U.S. Gauge pressure gauge (A) and a mercury manometer (B), the outlet pressure ( $p_o$ ) in each case being atmospheric. Column pressure drops ranged from 0.1 to 8 p.s.i. Flow-rates were measured with a water-jacketted 0- to 50-ml soap-bubble flow meter and stopwatch, rates of 20 to 150 ml/min being employed.

### *Measurement of $V_L$*

The column packing weight was determined by removing the injection-end glass wool plug and displacing the column contents by suction into a single-hole, stoppered, tared vacuum flask, the side-arm of which was fitted with a coarse glass frit. The weight percent of liquid on the support was measured by replicate ashings at red heat (700–1000°C) of tared amounts of packings in porcelain crucibles with a Bunsen burner (A) or a muffle furnace (B). Heating was applied for at least 4 h. Bare support weight losses, due to decomposition of the silanised surface, were determined by the same method and were corrected for when the liquid-phase weight percent was calculated.  $V_L$  was calculated from the column packing weight, the weight percent, and the 30°C density of the phases, 0.9638 g/ml (DNP) and 0.8028 g/ml (SQ).

## RESULTS

Replicate analysis of the weight loss (mg) per gram of heated support gave, on average, 2.1<sub>2</sub> (A) and 2.7<sub>7</sub> (B) mg/g. These showed some variation when different batches were tested, but the differences were on the order of the errors in weighing milligram amounts. Table I presents the ashing data for all coated packings. Retention data, measured from the air peak, were determined in duplicate with flow-rates being measured before and after all solutes were run, a period of approximately

TABLE I  
STATIONARY-PHASE LIQUID LOADINGS (% w/w) DETERMINED BY ASHING

Run No.	Series A				Series B			
	SQ		DNP		SQ		DNP	
	Col. 1	Col. 2	Col. 3	Col. 4	Col. 1	Col. 2	Col. 3	Col. 4
1	8.45 <sub>7</sub>	9.73 <sub>3</sub>	7.93 <sub>6</sub>	9.85 <sub>3</sub>	9.79 <sub>6</sub>	9.95 <sub>2</sub>	9.80 <sub>6</sub>	9.86 <sub>6</sub>
2	8.39 <sub>7</sub>	9.78 <sub>5</sub>	7.83 <sub>1</sub>	9.76 <sub>5</sub>	9.82 <sub>3</sub>	10.00 <sub>9</sub>	10.00 <sub>1</sub>	9.93 <sub>3</sub>
3	8.37 <sub>6</sub>	9.74 <sub>7</sub>	7.78 <sub>8</sub>	9.66 <sub>6</sub>	9.71 <sub>0</sub>	10.01 <sub>2</sub>	9.98 <sub>4</sub>	9.91 <sub>3</sub>
4	—	—	—	—	9.85 <sub>4</sub>	9.92 <sub>2</sub>	9.95 <sub>2</sub>	9.86 <sub>4</sub>
5	—	—	—	—	—	10.05 <sub>0</sub>	9.92 <sub>4</sub>	9.85 <sub>9</sub>
Average ( $\bar{X}$ )	8.41 <sub>0</sub>	9.75 <sub>5</sub>	7.85 <sub>2</sub>	9.75 <sub>9</sub>	9.79 <sub>4</sub>	9.98 <sub>9</sub>	9.93 <sub>5</sub>	9.88 <sub>7</sub>
( $\sigma_{\bar{X}}/\bar{X}$ ) · 100	0.50	0.28	0.97	0.99	0.63	0.51	0.78	0.34

TABLE II  
COLUMN AND RETENTION DATA FOR LISTED SOLUTES WITH SQUALANE AT 30°C

Solute	$t'_R$ (min)							
	Series A				Series B			
	Column 1		Column 2		Column 1		Column 2	
<i>n</i> -Pentane	1.85	± 0.00	1.95	± 0.01	1.86	± 0.00	1.79	± 0.01
<i>n</i> -Hexane	5.72	± 0.00	6.01	± 0.01	5.79	± 0.01	5.62	± 0.00
Cyclohexane	10.84	± 0.01	11.44	± 0.00	—	—	—	—
<i>n</i> -Heptane	17.36	± 0.02	18.30	± 0.01	17.61	± 0.00	17.09	± 0.02
Methylcyclohexane	21.79	± 0.07	23.01	± 0.01	—	—	—	—
<i>n</i> -Octane	52.37	± 0.09	55.09	± 0.09	—	—	—	—
Benzene	8.09	± 0.02	8.59	± 0.01	8.24	± 0.01	7.99	± 0.00
Toluene	26.49	± 0.02	28.33	± 0.04	27.11	± 0.02	26.15	± 0.01
$jF_c$ (ml/min)	69.70	± 0.05	78.26	± 0.07	132.33	± 0.49	144.45	± 0.08
$V_L$ (ml)	1.3061	± 0.0065	1.5449	± 0.0043	2.4945	± 0.0157	2.6438	± 0.0135

TABLE III  
COLUMN AND RETENTION DATA FOR LISTED SOLUTES WITH DINONYL PHTHALATE AT 30°C

Solute	$t'_R$ (min)							
	Series A				Series B			
	Column 3		Column 4		Column 3		Column 4	
<i>n</i> -Pentane	0.89	± 0.02	1.07	± 0.00	1.23	± 0.01	1.25	± 0.00
<i>n</i> -Hexane	2.65	± 0.01	3.20	± 0.01	3.68	± 0.00	3.73	± 0.00
Cyclohexane	5.23	± 0.02	6.28	± 0.04	—	—	—	—
<i>n</i> -Heptane	7.79	± 0.01	9.39	± 0.04	10.80	± 0.00	10.94	± 0.02
Methylcyclohexane	10.04	± 0.01	12.07	± 0.04	—	—	—	—
<i>n</i> -Octane	22.61	± 0.02	27.40	± 0.02	—	—	—	—
Benzene	8.96	± 0.00	10.83	± 0.01	12.40	± 0.02	12.59	± 0.02
Toluene	27.77	± 0.00	33.65	± 0.01	38.18	± 0.06	39.16	± 0.02
$jF_c$ (ml/min)	75.36	± 0.18	78.54	± 0.11	114.49	± 0.60	111.36	± 0.07
$V_L$ (ml)	1.0138	± 0.0698	1.2740	± 0.0126	2.1253	± 0.0166	2.1180	± 0.0072

2-4 h. The averaged  $t'_R$  and  $jF_c$  data are shown in Tables II and III. Reduction of these data according to eqn. 1 yielded the solute partition coefficients shown in Tables IV and V where the data extrapolated from the results of Ashworth<sup>10</sup> using a static system are also presented.

TABLE IV

PARTITION COEFFICIENTS ( $K_R$ ) OF LISTED SOLUTES WITH SQUALANE SOLVENT AT 30.0°C

Solute	Series A			Series B			Static*
	Col. 1	Col. 2	Ave.	Col. 1	Col. 2	Ave.	
<i>n</i> -Pentane	98.73	98.78	98.76	98.66	97.80	98.23	98.08
<i>n</i> -Hexane	305.3	304.5	304.9	307.1	307.1	307.1	305.5
Cyclohexane	578.5	579.5	579.0	—	—	—	584.4
<i>n</i> -Heptane	926.4	927.0	926.7	934.0	933.8	933.9	927.0
Methylcyclohexane	1163	1166	1164	—	—	—	—
<i>n</i> -Octane	2795	2791	2793	—	—	—	2790
Benzene	431.7	435.1	433.4	437.1	436.6	436.9	434.8
Toluene	1414	1435	1425	1439	1429	1434	—

\* Calculated from eqn. 1 and data of ref. 10.

TABLE V

PARTITION COEFFICIENTS ( $K_R$ ) OF LISTED SOLUTES WITH DINONYL PHTHALATE SOLVENT AT 30°C

Solute	Series A			Series B			Static*
	Col. 1	Col. 2	Ave.	Col. 1	Col. 2	Ave.	
<i>n</i> -Pentane	66.46	65.96	66.21	66.26	65.72	65.99	66.14
<i>n</i> -Hexane	197.0	197.3	197.2	198.2	196.1	197.2	197.4
Cyclohexane	388.8	387.2	388.0	—	—	—	388.2
<i>n</i> -Heptane	579.1	578.9	579.0	581.8	575.2	578.5	572.7
Methylcyclohexane	746.3	744.1	745.2	—	—	—	—
<i>n</i> -Octane	1681	1689	1685	—	—	—	1672
Benzene	666.0	667.7	666.9	668.0	662.0	665.0	670.5
Toluene	2064	2075	2070	2057	2059	2058	—

\* Calculated from eqn. 1 and data of ref. 10.

## DISCUSSION

For a generalized function,  $Q$ , such that

$$Q = a^m b^n c^p \dots \quad (2)$$

the fractional standard deviation,  $(\sigma_Q/Q)$ , is given by<sup>11</sup>:

$$\frac{\sigma_Q}{Q} = \left[ m^2 \left( \frac{\sigma_a}{a} \right)^2 + n^2 \left( \frac{\sigma_b}{b} \right)^2 + p^2 \left( \frac{\sigma_c}{c} \right)^2 + \dots \right]^{\frac{1}{2}} \quad (3)$$

In terms of  $K_R$ , eqn. 3 becomes:

$$\frac{\sigma_{K_R}}{K_R} = \left[ \left( \frac{\sigma_{t'_R}}{t'_R} \right)^2 + \left( \frac{\sigma_{jF_c}}{jF_c} \right)^2 + \left( \frac{\sigma_{V_L}}{V_L} \right)^2 \right]^{\frac{1}{2}} \quad (4)$$

The relative standard deviation to be expected for any set of  $K_R$  measurements may therefore be calculated provided reasonable estimates for  $\sigma_{t'_R}$ ,  $\sigma_{jF_c}$ , and  $\sigma_{V_L}$  are available. This treatment differs slightly from that of, for example, Wicarova *et al.*<sup>6</sup>, in that sources of random error affecting the parameters,  $t'_R$ ,  $jF_c$ , and  $V_L$ , are taken to be reflected adequately by the mean of the parameters themselves, rather than the terms comprising the parameters. For example, calculation of  $jF_c$  requires measurement of  $p_1$ ,  $p_o$ ,  $F$ ,  $T$ ,  $T_a$ ,  $p_a$ , and  $p_w$ , for which an expression of the form of eqn. 3 could be written. The relative standard deviation obtained from such a formulation must, however, be very nearly identical to the  $\sigma_{jF_c}/jF_c$  value calculated from the average of measurements of  $jF_c$ . Thus, eqn. 4 will provide a reasonable estimate of experimental error in  $K_R$ .

Table VI lists the calculated and experimental standard deviations for the  $K_R$  data. The legitimacy of eqn. 4 is clearly borne out by this comparison even though

TABLE VI

COMPARISON OF PREDICTED WITH EXPERIMENTAL RELATIVE STANDARD DEVIATIONS FOR  $K_R$  DATA

<i>Solute</i>	<i>Series A</i>			
	$(\sigma_{K_R}/K_R) \cdot 100$			
	<i>SQ</i>		<i>DNP</i>	
	<i>Predicted</i>	<i>Experimental</i>	<i>Predicted</i>	<i>Experimental</i>
<i>n</i> -Pentane	0.45	0.04	1.86	0.53
<i>n</i> -Hexane	0.41	0.19	1.13	0.11
Cyclohexane	0.41	0.12	1.21	0.29
<i>n</i> -Heptane	0.43	0.05	1.08	0.02
Methylcyclohexane	0.47	0.18	1.05	0.21
<i>n</i> -Octane	0.47	0.10	1.02	0.34
Benzene	0.48	0.55	1.02	0.18
Toluene	0.43	1.04	1.02	0.38
Average	0.44	0.28	1.17	0.26
	<i>Series B</i>			
	$(\sigma_{K_R}/K_R) \cdot 100$			
	<i>SQ</i>		<i>DNP</i>	
	<i>Predicted</i>	<i>Experimental</i>	<i>Predicted</i>	<i>Experimental</i>
<i>n</i> -Pentane	0.76	0.62	0.91	0.58
<i>n</i> -Hexane	0.65	0.00	0.70	0.75
<i>n</i> -Heptane	0.65	0.02	0.71	0.81
Benzene	0.65	0.08	0.73	0.64
Toluene	0.65	0.49	0.71	0.07
Average	0.67	0.24	0.75	0.57

only two values for each partition coefficient were determined in each study. We note parenthetically that Wicarova *et al.*<sup>6</sup> reported a  $V_g^0$  value for *n*-hexane which, when converted to  $K_R$ , gave 291.9 which is in error by 5% from the mean of all  $K_R$  data for *n*-hexane with squalane given in Table IV.

The largest contribution to  $\sigma_{K_R}/K_R$  is that from  $V_L$  as shown previously by, for example, the comparison of ashing with high-temperature evaporation techniques reported by Petsev *et al.*<sup>12,13</sup>. The former was there found to be more accurate than Soxhlet extraction owing, it was suggested, to the presence of extractable inorganic materials in common supports.

Since squares of relative standard deviations are additive, error sources other than  $V_L$  become important only when they approach approximately 10% of the error in this parameter, as shown in Table VII which lists  $\sigma_{K_R}/K_R$  as a function of  $\sigma_{t'_R}/t'_R$ ,  $\sigma_{jF_c}/jF_c$ , and  $\sigma_{V_L}/V_L$ . An increase of from 0.1% to 0.5% in both  $\sigma_{t'_R}/t'_R$  and  $\sigma_{jF_c}/jF_c$  increases  $\sigma_{K_R}/K_R$  only from 1.100% to 1.225%. Thus, there is little point in improving control of the pressures and/or flow-rate, or indeed, using automated data acquisition systems if thermodynamic information reliable to  $\pm 1\%$  is to be determined by GLC since, in any event, current practice in the measurement of  $V_L$  precludes a higher accuracy than this. Relatively simple apparatus is therefore adequate for measurements of this kind, until such time as more reliable techniques for determination of  $V_L$  are available.

TABLE VII

EFFECTS OF VARIATION OF  $\sigma_i/i$  ON  $\sigma_{K_R}/K_R$  CALCULATED FROM EQN. 4

Relative standard deviation $\times 100$			
$\sigma_{V_L}/V_L$	$\sigma_{t'_R}/t'_R$	$\sigma_{jF_c}/jF_c$	$\sigma_{K_R}/K_R$
1.0	0.1	0.1	1.1000
1.0	0.5	0.1	1.1225
1.0	0.5	0.5	1.2248
1.0	1.0	0.1	1.4178
1.0	1.0	0.5	1.5000
1.0	1.0	1.0	1.7321

We regard the results given in Tables IV and V as the most accurate data yet reported for the systems listed, and suggest their use for the evaluation of accuracy and reproducibility of other studies.

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