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## WATER AND OLEYL ALCOHOL AS STATIONARY LIQUID PHASES IN GAS-LIQUID CHROMATOGRAPHY

### DETERMINATION OF PARTITION COEFFICIENTS OF VOLATILE SUBSTANCES FOR ANALYSIS OF QUANTITATIVE STRUCTURE-ACTIVITY RELATIONSHIPS

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#### SUMMARY

Indirect determination of partition coefficients of volatile substances in the system oleyl alcohol-water for analysis of quantitative structure-activity relationships is discussed. Water and oleyl alcohol were used as stationary liquid phases in gas-liquid chromatography. In order to correct the results for adsorption effects, two new procedures using a standard substance were suggested. The procedures were compared with a procedure used by Conder et al. Comparison of molar hydration enthalpies and entropies derived from experimental results of a series of aliphatic alcohols with calorimetric data proved that all procedures under consideration yielded true partition coefficients.

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Regression analysis of quantitative structure-activity relationships (QSAR) of congeneric compounds is accomplished using the so-called hydrophobic parameters (for example partition coefficients in the *n*-octanol-water or oleyl alcohol-water systems). The determination of partition coefficients of volatile substances is, however, often very difficult and time-consuming. This was the reason for the development of gas-liquid chromatographic (GLC) methods using water and oleyl alcohol as stationary liquid phases (SLP).

The partition coefficient of a compound in the system oleyl alcohol-water is to a fair approximation equal to the ratio of partition coefficients in the systems oleyl alcohol (saturated with water)-N<sub>2</sub> and water-N<sub>2</sub> which may be determined by GLC.

It was Karger and coworkers [1–7] who suggested water as a GLC phase

about ten years ago. However, it was found that interface adsorption of solutes in the column system has a decisive influence upon the retention volumes. Conder and coworkers [8,9] suggested a procedure making it possible to eliminate the influence of adsorption and thus to determine true partition coefficients. From theoretical considerations we proposed two procedures using a structurally related compound as a standard and giving equally reliable results in a shorter time.

We started from the following considerations. Rachinskii [10], Conder et al. [8] and Berezkin and Fateeva [11] formulated several equations describing the dependence of the retention volume  $V_R$  on various parameters. For infinite dilution we may summarize their results in eqn. 1.

$$V_R = K_R d^{-1} \omega + K_R^H A^H + K_R^L A^L + K_R^{HL} A^{HL} \quad (1)$$

where  $K_R^H$ ,  $K_R^L$  and  $K_R^{HL}$  represent adsorption constants of the compound R at the corresponding interfaces of the column (H, support and column material—gas interface, surface saturated with water from the gas phase; L, liquid—gas interface; HL, solid—liquid interface).  $A^H$ ,  $A^L$ ,  $A^{HL}$  represent the corresponding surface areas;  $K_R$  is the partition coefficient in the system bulk liquid phase—gas phase;  $\omega$  is the amount of SLP in the column, and  $d$  the density of SLP. For further considerations parameters  $\alpha$  ("covering ratio"),  $\beta$  and  $V_{R,O}$  may be introduced by means of eqns. 2, 3 and 4.

$$\alpha = \frac{A^{HL}}{A^{Ho}} \quad (2)$$

$$\beta = \frac{A^L}{A^{HL}} \quad (3)$$

$$V_{R,O} = K_R^H A^{Ho} \quad (4)$$

where  $A^{Ho}$  stands for the total surface of the support and column materials (saturated with water from the gas phase).

By means of assumptions 5 and 6

$$K_R^L = k_1 K_R^H \quad (5)$$

$$K_R^{HL} = k_2 K_R^H \quad (6)$$

$$\bar{K}_R = \frac{V_R}{\omega} d \quad (7)$$

where  $k_1$  and  $k_2$  represent substance-independent constants (at least for structurally related substances), eqn. 1 may be rewritten as

$$V_R = K_R d^{-1} \omega + V_{R,O} \epsilon_{\alpha,\beta} \quad (8)$$

$$\epsilon_{\alpha,\beta} = 1 - \alpha (1 - k_1 \beta - k_2) \quad (9)$$

$\epsilon_{\alpha,\beta}$  represents a substance-independent constant which is linearly dependent on  $\alpha$  and  $\beta$  (eqn. 9). This constant characterizes, in fact, the quality of column preparation. The retention volume  $V_{R,O}$  is a measurable quantity.

Eqn. 10, describing in another form the extrapolation procedure according to Conder et al., follows from eqn. 8

$$\bar{K}_R = K_R + V_{R,O} \epsilon_{\alpha,\beta} \cdot \frac{d}{\omega} \quad (10)$$

The apparent partition coefficient  $\bar{K}_R$  is given by eqn. 7.

Extrapolation in the coordinate system  $\bar{K}_R$ ;  $1/\omega$  yields values of true partition coefficients (eqn. 11).

$$\lim_{1/\omega \rightarrow 0} \bar{K}_R = K_R \quad (11)$$

Eqn. 8 is valid also for the standard substance S. Hence

$$\bar{K}_R = K_R + \gamma_{R/S} (\bar{K}_S - K_S) \quad (12)$$

$$\text{where } \gamma_{R/S} = \frac{V_{R,O}}{V_{S,O}} \quad (13)$$

As  $\gamma_{R/S}$  represents a measurable quantity (the ratio of retention volumes of substances R and S in the column, used without a condensed water phase, with water molecules adsorbed on the surface from the gas phase only), it is possible to use eqn. 12 for the determination of  $K_R$  values, knowing the  $K_S$  value. A comparison of the values found by means of this method with values obtained by the method according to Conder et al. is shown in Table I.

As  $K_R$ ,  $K_S$  and  $\gamma_{R/S}$  are constants independent of  $\omega$  and  $\epsilon_{\alpha,\beta}$ , eqn. 12 describes a linear dependence of the corresponding apparent partition coefficients of the substances R and S measured with various columns, i.e. eqn. 14.

$$\bar{K}_R = a \bar{K}_S + b \quad (14)$$

As far as the true partition coefficient of the standard substance ( $K_S$ ) is known, and there is a sufficient number of measurements for determining the constants  $a$  and  $b$ , the  $K_R$  value may be calculated by means of eqn. 15

$$K_R = a K_S + b \quad (15)$$

The validity of the described relationships has been verified with a series of about 50 compounds [12]. Examples of the results obtained are shown in Figs. 1 and 2.

The validity of the assumptions represented by eqns. 5 and 6 was tested by the following experiments. The dependences of the retention volumes of compounds under study on the covering ratio,  $\alpha$ , were investigated in a glass col-

TABLE I

## MOLAR ENTHALPIES AND ENTROPIES OF HYDRATION AND SOLVATION (OLEYL ALCOHOL) OF ALIPHATIC ALCOHOLS

Gas phase standard state: ideal gas at 1 atm. Solution standard state: mole fraction  $x = 1$ ,  $T = 298.15^\circ\text{K}$ . The thermodynamic characteristics were calculated assuming a parabolic temperature dependency of Gibbs energies of hydration or solvation.

Compound	$-\Delta H_h^{\circ}$ (kJ mol <sup>-1</sup> )	$-\Delta H_h^{\circ*}$ (kJ mol <sup>-1</sup> )	$-\Delta H_s^{\circ**}$ (kJ mol <sup>-1</sup> )	$-\Delta S_h^{\circ}$ (J mol <sup>-1</sup> deg <sup>-1</sup> )	$-\Delta S_s^{\circ**}$ (J mol <sup>-1</sup> deg <sup>-1</sup> )
Methanol	45.71	45.22	39.4	143	118
Ethanol	53.18	52.75	47.3	169	138
<i>n</i> -Propanol	57.79	57.74	46.8	186	128
Isopropanol	59.31	58.59	46.2	193	131
<i>n</i> -Butanol	61.53	61.37	52.2	200	136
<i>tert.</i> -Butanol	64.43**	64.10	47.8	213**	134
<i>n</i> -Amyl alcohol	65.72		57.3	217**	145
2-Methyl butanol-2	68.77		50.9	229	136
Cyclopentanol	68.53		56.6	214	141
<i>n</i> -Hexanol	69.60***			232***	
Cyclohexanol	71.33			222	
<i>n</i> -Heptanol	73.70**			248**	
<i>n</i> -Octanol	77.96**			265**	

\*Calorimetric data according to Hill [13] and Krishnan and Friedman [14].

\*\*The partition coefficients were measured using the method suggested by Conder and coworkers [8,9] (see eqn. 10).

\*\*\*The partition coefficients were measured according to the method described by Conder and coworkers [8,9] and one of the suggested procedures (eqn. 12) using *n*-amyl alcohol as the standard substance. Both methods gave the same results. All other values were measured by means of the suggested procedure (eqn. 12) using *n*-amyl alcohol as the standard substance.

umn packed with glass spheres. Corresponding amounts of water were applied to different lengths of the column in such a way that the mean film thickness of water remained constant in the wetted part of the column. According to our experience the covering ratio  $\alpha$  in this part of the column could be assumed as equal to 1. In the uncovered part of the column surface (saturated with vapour from the gas phase only)  $\alpha$  equals zero. The average covering ratio was therefore considered to be equal to the ratio of the wetted length of the column to its total length. In those experiments the covering ratio changed proportionally to the amount of water  $\omega$ . The results obtained with di-(*n*-butyl)-ketone and *n*-hexyl acetate are shown on the left-hand side of Fig. 1.

In further experiments, the total surface of the column was wetted with various amounts of water in a range of  $\omega$  values in which the value of  $\alpha$  amounts to 1. In those cases the average thickness of the liquid phase changed especially with the amount of water. The changes of the  $\beta$  values (eqn. 3) were relatively small in the selected range of the  $\omega$  values. The results are shown on the righthand side of Fig. 1. The dependence degenerates to a single strait line

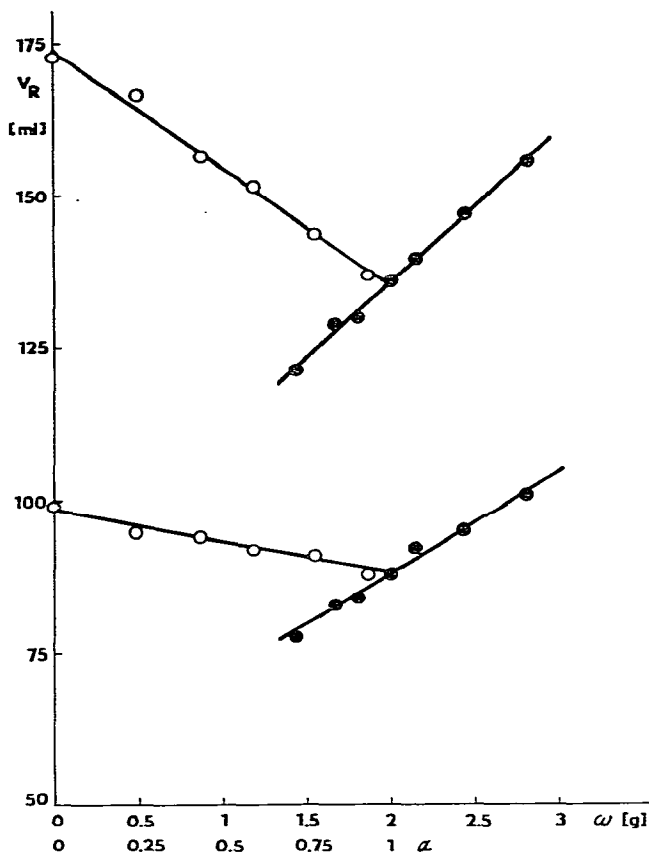


Fig. 1. Dependences of the retention volume  $V_R$  on the amount  $\omega$  of the SLP (water) and the covering ratio  $\alpha$  ( $\circ$ ), and on the amount  $\omega$  of the SLP with  $\alpha = 1$  ( $\bullet$ ).  $T = 310.2^\circ\text{K}$ . Di-(*n*-butyl)ketone (above), *n*-hexyl acetate (below).

with compounds whose interface adsorption in the column was small in comparison with their bulk liquid-gas partitioning. The results obtained with all compounds under study were analogous and the data fulfilled eqn. 8 within the limits of the measuring errors. The linear dependences obtained (according to eqn. 14 and presented in Fig. 2) demonstrate the validity of the assumptions for the system under study (column, support material-glass; liquid phase-water). The results obtained permit the conclusion that eqns. 12 and 14 may be used for determination of true partition coefficients.

Direct proof that results obtained by the suggested methods represent true partition coefficients is not as simple as published data on partition coefficients show considerable discrepancies. We were therefore obliged to find a round-about way. Using the method described by Conder and co-workers [8, 9] and one of the methods suggested, we determined temperature dependences of the partition coefficients and calculated from these data the molar enthalpies and entropies of hydration. As there are exact calorimetric data available for a series of aliphatic alcohols [13,14], a comparison of the results could be achieved (see Table I).

Results of analogous experiments with oleyl alcohol as SLP are shown in

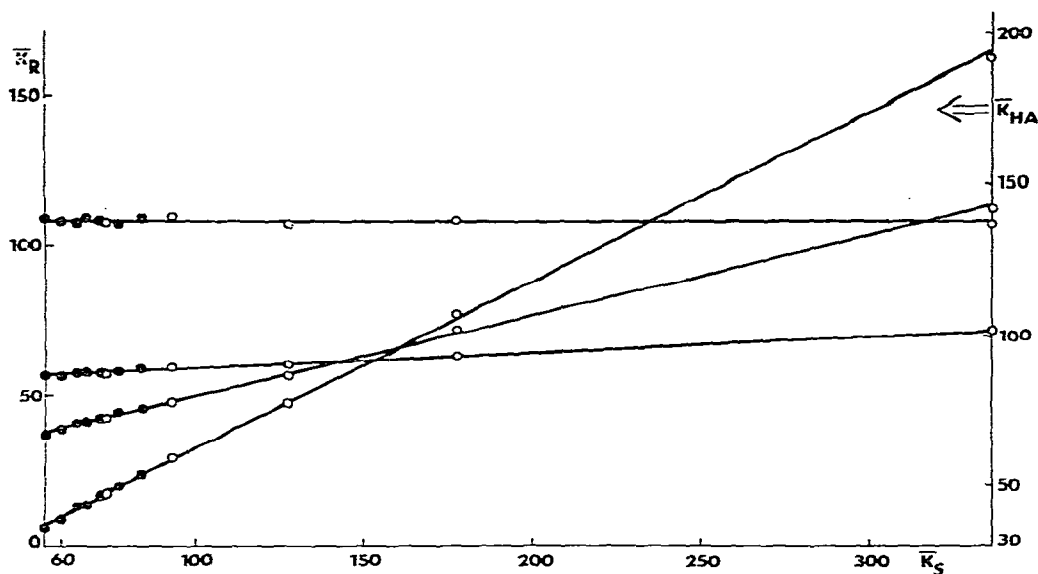


Fig. 2. Linear dependences of apparent partition coefficients  $\bar{K}_R$  of the compounds (from the top) methyl acetate, *n*-propyl acetate, *n*-amyl acetate and *n*-hexyl acetate (HA), on the corresponding apparent partition coefficient  $\bar{K}_S$  of the standard substance (di-*n*-butyl)ketone).  $T = 310.2^\circ\text{K}$ . For the meaning of symbols (●, ○) see Fig. 1.

Table I (molar enthalpies and entropies of solvation).

The comparison shows that the methods under consideration render it possible to measure true partition coefficients in the systems water– $\text{N}_2$  and oleyl alcohol– $\text{N}_2$ . The methods were developed for capillary and packed columns so that partition coefficients in the system water– $\text{N}_2$  in the range 1–50,000, and in the system oleyl alcohol– $\text{N}_2$  in the range 100–50,000, are reproducible and may be measured with errors of about 1–2%.

#### REFERENCES

- 1 B.L. Karger and A. Hartkopf, *Anal. Chem.*, 40 (1968) 215.
- 2 B.L. Karger, A. Hartkopf and H. Posmanter, *J. Chromatogr. Sci.*, 7 (1969) 315.
- 3 B.L. Karger, P.A. Sewell, R.C. Castells and A. Hartkopf, *J. Colloid Interface Sci.*, 35 (1971) 328.
- 4 B.L. Karger, R.C. Castells, P.A. Sewell and A. Hartkopf, *J. Phys. Chem.*, 75 (1971) 3870.
- 5 C. Eon, A.K. Chatterjee and B.L. Karger, *Chromatographia*, 5 (1972) 28.
- 6 A.K. Chatterjee, J.W. King and B.L. Karger, *J. Colloid Interface Sci.*, 41 (1972) 71.
- 7 B.L. Karger and H.S. Liao, *Chromatographia*, 7 (1974) 288.
- 8 J.R. Conder, D.C. Locke and J.H. Purnell, *J. Phys. Chem.*, 73 (1969) 700.
- 9 D.F. Cadogan, J.R. Conder, D.C. Locke and J.H. Purnell, *J. Phys. Chem.*, 73 (1969) 708.
- 10 V. Rachinskii, *Introduction to General Theory of Sorption Dynamics and Chromatography*, Nauka, Moscow, 1964.
- 11 V.G. Berezkin and V.M. Fateeva, *J. Chromatogr.*, 58 (1971) 73.
- 12 K. Boček, in preparation.
- 13 D.J.T. Hill, Ph.D. Thesis, University of Queensland, 1965; in F. Franks (Editor), *Water*, Vol. 2, Plenum Press, New York, London, p. 340.
- 14 C.V. Krishnan and H.L. Friedman, *J. Phys. Chem.*, 73 (1969) 1572.