Monatshefte für Chemie 118, 879—882 (1987)

Monatshefte für Chemie
Chemical Monthly

Chromatographic Determination of the Solubility of Low Soluble Substances—A Practical Possibility

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(Received 28 March 1986. Accepted 24 April 1986)

Using selected examples we demonstrate the determination of solubility of low soluble substances with the help of planar chromatography, which is a new, simple and rapid approach to the problem, to a certain extent challenging the established methods. Our approach is a practical consequence of the thermodynamic view of the chromatographic processes, involving either the adsorption or partition mechanism of separation.

(Keywords: Chromatography; Solubility determination; Thermodynamics)

Chromatographische Bestimmung der Löslichkeit von schwerlöslichen Substanzen — eine praktische Möglichkeit

An den gewählten Beispielen wird die Bestimmung der Löslichkeit schwerlöslicher Substanzen mit Hilfe der planaren Dünnschichtchromatographie demonstriert. Dieses Verfahren stellt eine neue, einfache und schnelle Methode dar, die in einem gewissen Maß in Konkurrenz zu den älteren und anerkannten Methoden tritt. Die Methode ist die praktische Konsequenz der thermodynamischen Betrachtung des chromatographischen Prozesses in der Adsorptions- und Verteilungsdünnschichtchromatographie.

In paper [1] we pointed out the possibility of using planar chromatography for the determination of solubility of organic substances, due to certain physico-chemical dependences ruling chromatographic processes in partition and adsorption chromatography. Coupling three thermodynamic models of planar chromatography (by *Martin* and *Synge*, *Snyder* and *Kowalska*) we managed to derive relationships enabling the calculation of the molar fraction of a given substance (d_i) in the mobile phase, employing a limited number of easily measurable chromatographic parameters.

Combining Eqs. (7 b) and (11 b) from paper [1] with Eq. (9) from paper [2] we obtain the ultimate relationships, given below:

$$d_i \simeq \frac{c_i (R'_f V_s)^{1-R'_f}}{c_{ch} [(1-R'_f) V_m]^{1-R'_f}} \tag{1}$$

$$d_i \simeq \frac{c_i (R'_f V_a W_a)^{1-R'_f}}{c_{ch} [(1-R'_f)(V_m - V_a W_a)]^{1-R'_f}} \tag{2}$$

applicable to partition and adsorption chromatography, respectively. $R'_f = \xi \cdot R_f$ (in this paper $\xi = 1.1$); V_m: volume of the mobile phase; V_s: volume of the stationary phase in partition chromatography; V_a: volume of the adsorbed mobile phase in adsorption chromatography [Eqs. (58′) and (58 a) in [3]]; W_a: the weight of sorbent; c_i and c_{ch}: molar concentrations of solute and solvent, respectively, in the chromatographic "binary solutions" model [1, 2].

It is the aim of this paper to verify Eqs. (1) and (2) upon practical examples. However, first one should carefully discuss the experimental conditions allowing the application of these two relationships.

If we wish to utilize planar chromatography as a tool for determination of solubility of the chromatographed substance, the working conditions have to be chosen in such a way that the applied solvent might simultaneously act as a mobile phase. Further one ought to remember that in the course of the chromatographic process the concentration of solute in the mobile phase gradually decreases, mainly due to diffusion. For this reason we would like to suggest that the chromatographic spot of an examined substance should be developed at the utmost height of 2 cm, or even less, as we intend to check the saturated solution of this substance in the mobile phase (or a solution only infinitesimally differing). From our studies it comes out that 2 cm is a maximal height, providing satisfactory evaluation of solubility and simultaneously enabling a correct measurement of the experimental R_f value. Last but not least, quite special requirements should be fulfilled in the visualization of the chromatogram. Visualization ought to be carried out in such a way that the sharp contour of the spot is perfectly distinct upon the contrast background. Moreover, no negative effects, such as, e.g., tailing should occur in the chromatographic process, and the applied visualizing agent should not contribute to the diffusion of the analyzed substance upon the chromatographic layer.

Our demonstration of the new approach comprises paper chromatography (PC), commonly regarded as partition chromatography, and adsorption thin-layer chromatography (TLC), carried out on silica.

Paper Chromatography

Measuring temperature: 20 ± 0.5 °C. Solutes: cetyl alcohol, stearyl alcohol, palmitic acid, stearic acid (0.05 *M* solutions in CCl_4, spotted in the aliquots of 20 μl). Solvent (= mobile phase): decalin. Stationary phase: water impregnating the cellulose support (Whatman No. 2 paper, Whatman, Maidstone, U.K.). Height of development: 2 cm for each chromatographic spot. Visualization: alcohols with a 5% $K_2Cr_2O_7$ solution in 50% sulphuric acid; acids by means of bromocresol green [4]. Determination of the chromatographic parameters: c_i as described in paper [5]; $c_{ch} = 0.637\,M$; $V_s = 0.023\,\text{cm}^3/\text{g}$; $V_m = 0.756\,\text{cm}^3/\text{g}$ (determined by means of the weight measurement [3]). Reference determination of solubility: saturation of 400 cm^3 decalin with a solute; filtration; collection of three samples 100 cm^3 each; evaporation of solvent; weighing of the dry residue.

The remaining chromatographic parameters [see Eq. (1)] and molar fractions of the examined substances (d_i) in decalin, determined chromatographically and by means of the reference method are collected in Table 1.

Table 1. *Numerical values of d_i (two methods of determination) and of the respective chromatographic parameters for cetyl alcohol, stearyl alcohol, palmitic acid and stearic acid at 20 °C; solvent: decalin*

Substance	R_f'	c_i [*M*]	d_i		error of chromatogr. determination [%]
			weight	chromat.	
Cetyl alcohol	0.905	0.01849	0.0299	0.0258	13.7
Stearyl alcohol	0.874	0.00728	0.0121	0.0094	22.3
Palmitic acid	0.947	0.01447	0.0233	0.0220	5.6
Stearic acid	0.826	0.00370	0.0054	0.0042	22.2

As it comes out from the data given in Table 1, determination of solubility by means of the two methods results in virtually coinciding numerical values. The observed good correlation of the both d_i series seems satisfactory.

Adsorption Thin-Layer Chromatography

Measuring temperature: 20 ± 0.5 °C. Solutes: 1,2-, 1,3- and 1,4-bis(bromomethyl)benzene (0.1 *M* solutions in acetone, spotted in the aliquots of 10 μl). Solvent (= mobile phase): carbon tetrachloride. Stationary phase: Kieselgel GF_{254} (the ready-made plates, E. Merck, Darmstadt, Federal Republic of Germany; specific surface of silica: 375 m^2/g). Height of development: 1.5 cm for each chromatographic spot. Visualization: UV light. Determination of the chromatographic parameters: c_i as described in paper [5]; $c_{ch} = 8.24\,M$; $V_a = 0.098\,\mathrm{cm}^3/\mathrm{g}$; $V_m = 1.600\,\mathrm{cm}^3/\mathrm{g}$; $W_a = 1\,\mathrm{g}$. Reference determination of solubility: saturation of $100\,\mathrm{cm}^3$ carbon tetrachloride with a solute; filtration; collection of three samples $30\,\mathrm{cm}^3$ each; evaporation of solvent; weighing of the dry residue.

The other chromatographic parameters [see Eq. (2)] and molar fractions of the examined substances (d_i) in CCl_4 determined on the two independent ways are shown in Table 2.

Table 2. *Numerical values of d_i (two methods of determination) and of the respective chromatographic parameters for 1,2-, 1,3- and 1,4-bis(bromomethyl)benzene at 20 °C; solvent: carbon tetrachloride*

Substance	R'_f	c_i [M]	d_i		error of chromat. determin. [%]
			weight	chromat.	
1,2-bis(bromomethyl)benzene	0.805	0.1389	0.0186	0.0129	30.6
1,3-bis(bromomethyl)benzene	0.749	0.1389	0.0074	0.0112	51.4
1,4-bis(bromomethyl)benzene	0.505	0.0516	0.0048	0.0017	64.6

The two series of the d_i values from Table 2 show less of mutual agreement compared to the previous case. Still the two approaches result in the same magnitude of orders, which is far from being a general rule, when comparing the results of solubility determination achieved by a number of different ways.

Thus we believe to have practically proved the usefulness of planar chromatography for the determination or at least for the rough estimation of solubility of organic substances.

References

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