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SOLVENT DEPENDENCE OF GEL SWELLING IN THE SYSTEM OF MERCKOGEL OR-2000 AND VARIOUS ORGANIC SOLVENTS

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SUMMARY

The amount of internal solvent in Merckogel OR-2000 has been determined for ten different solvents using polystyrene (mol. wt., 10,000) as the excluded solute. In this method, dry gel is equilibrated with an organic solution containing a known concentration of a solute which is excluded by the gel. The internal solvent volume of the swollen gel is calculated from the concentration change due to mixing. There are distinct relations between the amount of internal solvent, a solubility parameter and the molar volume of the solvent.

INTRODUCTION

During the course of a study relating to the gel chromatography of metal complexes with β-diketones[1–3], we developed an increasing interest in the influence of the solvent on elution behaviour. In an earlier paper on the elution behaviour of some acetylacetonate complexes of metals(II,III) and n-alkanes in the Merckogel OR-2000–tetrahydrofuran system[2], it was pointed out that the metal complexes and alkanes possess different elution characteristics. It was suggested that these are to some extent due to solute–gel interactions. In an attempt to elucidate these effects, the elution behaviour of n-alkanes was investigated in different organic solvents[3]. It was observed that the distribution coefficients of the n-alkanes were dependent on the solvent, which suggests that differences in solvent–gel interactions are responsible.

The solvent is an essential component in a gel chromatographic system and interacts with both the gel and the solute. Some interesting studies have been reported[4–8] of the solvent effects in gel chromatography with organic solvents, but, in general, little attention has been paid to this problem. Systematic studies of solvent effects are required.

The distribution coefficient of a solute is dependent on both the solvent regain of a gel[9] and on the concentration of the gel matrix in the swollen gel phase[10]. Swelling can be regarded as the result of a solvent–gel interaction, and the degree of swelling or the solvent regain is an important variable in the chromatographic process. Data

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on solvent regain should therefore give information about solvent–gel interactions and the present work was undertaken in order to obtain such data. A common method of determining solvent regain is to measure the amount of solvent in a swollen gel mass after removing interstitial solvent by centrifugation. This method, however, is liable to inaccuracy due to a dependence on the centrifugal force used[11], and also to the retention of solvent on the surface of the gel beads[12]. Further, it is not an easy method to apply to highly volatile solvents.

The volume of the solvent absorbed by the gel can be estimated by means of a column method if two solute molecules are used as the reference species: one solute molecule is sufficiently large as to be completely excluded by the gel network, and the other solute is small enough to penetrate completely all of the pores of the gel. Thus, Sephadex with water as the solvent and Blue Dextran® and labelled water, e.g., tritiated water[13],[14] and [^{18}O]water[15], have been used. However, it is not easy to select a small reference material which is soluble in various organic solvents.

In the present work, solvent regains of Merckogel OR-2000 have been determined in various organic solvents by means of an equilibration method using a reference material which is large enough to be excluded. Gel bed volumes, the convenient and practical measure of the degree of gel swelling, have also been measured for comparison with the solvent-regain data. The organic solvents chloroform, benzene, toluene, p-dioxane, tetrahydrofuran, ethyl acetate, n-butyl acetate, acetone, methyl ethyl ketone and acetylacetone were studied. All of these solvents, except the last which had been used as a solute[2], had been used previously as eluting solvents[3] in our study program.

In order to clarify the solvent–gel interaction, the correlation between the swelling of Merckogel OR-2000 and some physical properties of the solvents is discussed.

The principle of the equilibration method

When W grams of dry gel are equilibrated with V millilitres of solution containing a solute, the relationship between the solute concentration in the initial solution, C_0, and that in the final solution, C_{eq}, is represented by

$$C_0 V = C_{eq} (V - V_t W + K_d V_t W) \qquad (1)$$

where K_d is the distribution coefficient of the solute and V_t is the internal solvent volume of the swollen gel defined as the number of millilitres of solvent taken up by one gram of dry gel. When the solute molecule is large enough to be completely excluded by the gel ($K_d = 0$), eqn. 1 can be modified to give:

$$V_t = V (1 - C_0/C_{eq})/W \qquad (2)$$

Thus, V_t can be calculated from the ratio of the initial and final solute concentrations in the solution equilibrated with the gel beads.

When the density of the gel matrix, d_g, is known, the degree of swelling, Q, defined as the reciprocal of the volume fraction, φ_g, of the gel matrix in the swollen gel, can be estimated as

$$Q = 1/\varphi_g = 1 + V_t/V_g = 1 + V_t d_g \qquad (3)$$

where V_a is the specific volume (ml/g) of the dry gel. The molar solvent regain, S_{rm}, defined as the number of moles of solvent taken up by one gram of dry gel, can be obtained from the following relationship:

$$S_{rm} = V_i \, d_s / M_w = V_i / V_s \qquad (4)$$

where d_s, M_w and V_s are the density, molecular weight and molar volume of the solvent, respectively.

EXPERIMENTAL

Materials

Merckogel OR-2000 (E. Merck, Darmstadt, G.F.R.) was washed with redistilled water, then acetone and methanol, and freed from these solvents *in vacuo*. After drying for 3 days over silica gel at normal pressure, the resulting bulky mass of the gel was finely ground, sieved to obtain 200–300-mesh fractions and then dried over silica gel for 3 days.

Solvents, except for chloroform, were used after purification of the respective commercial materials by appropriate chemical treatments, drying and distillation. Chloroform was of reagent grade and was used without further purification; it contained 1.05% (mole/mole) of ethanol as a stabilizer. Polystyrene (standard grade; mol. wt., 10,000, $M_w / M_n < 1.06$) was obtained from Pressure Chemical Co., Pittsburgh, Pa., U.S.A.

Measurements of internal solvent volume

Sample solutions were prepared by dissolving 35 mg of polystyrene in 50 ml of each solvent. An 8-ml portion of a sample solution was placed in a Pyrex vessel (inner volume, *ca.* 15 ml) containing 1.5 g of dry gel; the vessel was then sealed with a screw-cap. In the case of the system with chloroform, 10.0 ml of a sample solution were used. The contents of the vessel were mixed for 5 h with the aid of a magnetic stirrer in order to attain equilibrium. Preliminary experiments had shown that the system came to equilibrium after stirring for 3 h. After standing for 30 min, 1 ml of the solution phase was removed in a syringe fitted with a filter[*] and subjected to analysis.

The solute concentrations in both the initial and final solutions were determined by a gel chromatographic method using a Merckogel OR-2000 column (30 cm × 8 mm I.D.) and *p*-dioxane as the eluting solvent. A 40-μl portion of each solution was injected on the column, and the concentration of polystyrene in the solution was evaluated from the area or height of its elution peak as recorded by a UV absorptivity detector at 254 nm.

The experiments were carried out at 25°, and each experiment was done in triplicate.

Measurements of the bed volume, V_t

Gel beads which had been allowed to swell in a solvent were placed in a

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[*] The filter was hand-made and consisted of a glass syringe and PTFE filter; the latter was manufactured commercially as a bed support for chromatographic columns.

graduated Pyrex column (15 cm × 8 mm I.D.) and the solvent was pumped through the column at a flow-rate of 0.51 ml/min for 3 h. The volume of the gel bed, V_t', was then measured using the graduations. The gel beads were taken out of the column and weighed after drying under reduced pressure and then further over silica gel at normal pressure for 24 h. The bed volume, V_t, expressed in millilitres of gel bed per gram of dry gel, was obtained by dividing V_t' by the weight of the dry gel.

Each experiment concerning a solvent was carried out in duplicate.

RESULTS AND DISCUSSION

Determinations of the values of both V_i and V_t in various solvent systems were carried out successfully. For the estimation of Q and S_{rm} from V_i, the density of Merckogel OR-2000 was assumed to be equal to that of polyvinyl acetate (1.19 g/ml at 25°)[16], and the values of the solvent densities were taken from ref. 17. The results are summarized in Table I.

The bed volume is the sum of the internal solvent volume, the interstitial solvent volume, and the specific volume of gel matrix, thus:

$$V_t = V_i + V_0 + V_g \tag{5}$$

If the solvent dependence of V_0 is assumed to be negligible, a graph of V_t versus V_i should be linear with a slope of unity, and then V_i may be easily evaluated by measuring the value of V_t. As seen from Table I, it is difficult to correlate the experimental data with respect to a graph of V_t versus V_i. Hence, it would also be difficult to evaluate a value of V_i from V_t. It is suggested that the above assumption is inadequate. However, it has not yet been clarified whether the variation of V_0 or the uncertainties in V_i and V_t values should be taken into account as the most important factor.

On the basis of these findings, it seems reasonable to say that the bed volume

TABLE I

VALUES OF INTERNAL SOLVENT VOLUME, DEGREE OF SWELLING, MOLAR SOLVENT REGAIN AND BED VOLUME FOR MERCKOGEL OR-2000 IN VARIOUS SOLVENTS AT 25°

Solvent			V_i^* (ml per g of dry gel)	Q	S_{rm} (mole per g of dry gel)	V_t (ml per g of dry gel)
No.	Name	δ (cal/ml)$^{\frac{1}{2}}$				
1	Chloroform	9.3[20]	2.60 ± 0.40	4.10	0.032$_1$	5.6
2	Benzene	9.15[20]	1.78 ± 0.32	3.12	0.020$_4$	3.6
3	Toluene	8.9[20]	1.06 ± 0.13	2.26	0.009$_9$	3.0
4	p-Dioxane	10.8[21]	1.95 ± 0.12	3.32	0.023$_0$	3.8
5	Tetrahydrofuran	9.32[**]	1.83 ± 0.09	3.18	0.022$_5$	4.0
6	Ethyl acetate	9.05[21]	1.67 ± 0.04	2.99	0.017$_0$	3.7
7	n-Butyl acetate	8.55[21]	1.20 ± 0.03	2.43	0.009$_9$	2.9
8	Acetone	9.89[22]	1.81 ± 0.08	3.15	0.024$_5$	4.4
9	Methyl ethyl ketone	9.3[22]	1.66 ± 0.05	2.98	0.018$_4$	3.6
10	Acetylacetone	10.6[23]	1.87 ± 0.20	3.23	0.018$_3$	3.1

* 95% confidence limits are given.

** Calculated from the value of the heat of vaporization (7.65 kcal/mole)[17].

is a useful parameter to measure, although it cannot give accurate information on gel swelling. The data of Table I indicate that gel swelling is strongly dependent on the nature of the solvents. In order to elucidate the influence of the solvent on swelling, it is more profitable to discuss it in terms of S_{rm} than in terms of the other variables referring to the volume of solvent, viz., V_t, Q and V_t, although these parameters are useful for practical objectives in chromatography. The S_{rm} data suggest that gel swelling can be related to some physical properties of the solvents.

It is known that the solubility parameter introduced into the theory of regular solutions is convenient for predicting the degree of mutual interaction between the solute and solvent[15]. The solubility parameter is defined as the square root of the cohesive energy density, i.e., of the energy of vaporization, ΔE^v, per unit volume, and is designated by the symbol δ. Thus, $\delta = (\Delta E^v/V)^{\frac{1}{2}}$. By use of this parameter, one can express the heat of dissolution of a solute, ΔH_2, as

$$\Delta H_2 = V_2 \varphi_1^2 (\delta_1 - \delta_2)^2 \tag{6}$$

The subscripts 1 and 2 distinguish the components of the binary mixture, and subscript 2 is customarily reserved for the component which is regarded as the solute. This equation indicates that a decrease either in the value of V_2 or in the difference between δ_1 and δ_2 should lead to a decrease in ΔH_2, that is, to an increase in the solubility of the solute or in the degree of mutual interaction between the solute and solvent. We assume here that the concept of regular solutions can be adopted to explain the effect of the solvent on gel swelling.

In a system of a solvent and a polymer compound, it is reasonable to regard the solvent as the solute species dissolving in the polymer. Therefore, an equation for the solvent–gel system similar to eqn. 6 can be written by the conversion of subscripts 1 and 2 in this equation into g and s, respectively, for the gel matrix and the solvent. Thus:

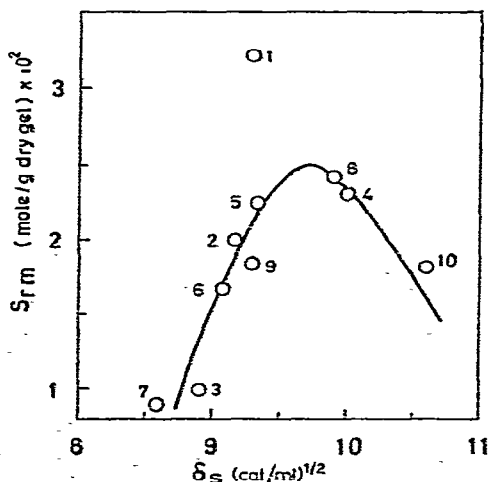$$\Delta H_s = V_s \varphi_g^2 (\delta_g - \delta_s)^2 \tag{7}$$

Fig. 1. Relationship of the molar solvent regain, S_{rm}, and the solubility parameter of the solvent, δ_s. Solvents 1–10 as in Table I. Merckogel OR-2000, 25°.
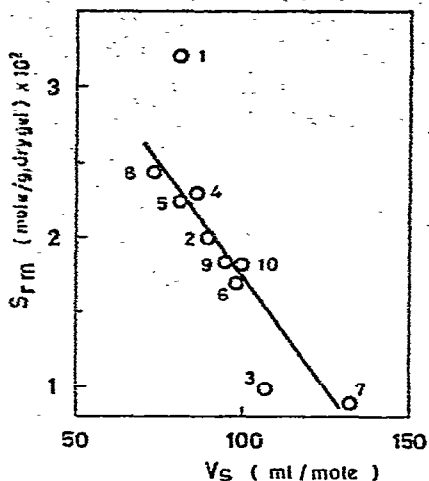
K. SAITOH, T. OZAWA, N. SUZUKI

Fig. 2. Relation of the molar solvent regain, S_{rm}, and the molar volume of the solvent, V_s. Other details as in Fig. 1.

This equation predicts that the mole fraction of the solvent in the swollen gel increases as the value of the solubility parameter of the solvent becomes close to that of the gel matrix and also as the molar volume of the solvent decreases. An increase in the mole fraction of the solvent effects an increase in the value of the solvent regain, S_{rm}. Graphs of S_{rm} against δ_s and V_s shown in Figs. 1 and 2, respectively, lend some support to the above argument. The peak value in Fig. 1 suggests the value for the solubility parameter of Merckogel OR-2000 is *ca.* 9.7. This value is, in fact, near to the solubility parameter of polyvinyl acetate $(9.4)^{19}$. Fig. 2 shows that the smaller the molar volume the more solvent is preferred to the gel, just as occurs when the solvent itself is gel chromatographed.

   It is evident from Table I that the degree of swelling of the gel in chloroform is particularly high, suggesting that hydrogen bonding between chloroform and the basic functional groups in polyvinyl acetate constituting the gel matrix may be responsible.

   In view of the above findings, the most reasonable conclusion to be drawn is that the degree of swelling of Merckogel OR-2000 is strongly dependent on the solvents, and may be expected to be high in a solvent with a δ value of *ca.* 9.7 and with a small V_s value, or in a solvent which can interact specifically with the gel matrix. In order to elucidate solvent effects in gel chromatographic behaviour, solute–solvent and gel–solvent interactions must be studied systematically. The present data relating to the latter interaction will be useful in further studies which are planned for our program dealing with the gel chromatography of metal complexes.

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