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SALTING-IN AND SALTING-OUT OF OXYGEN-CONTAINING COMPOUNDS
IN GAS CHROMATOGRAPHY

ENTROPY AND ENTHALPY ASPECTS*

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SUMMARY

The effect of lithium chloride on the solubility of alcohols, esters and ketones in polyethylene glycol 400 has been studied by gas chromatography. The thermodynamic functions $\Delta G^0_{t,1 \rightarrow 2}$, $\Delta H^0_{t,1 \rightarrow 2}$, and $\Delta S^0_{t,1 \rightarrow 2}$ for the transfer of the solutes from pure polyethylene glycol to the lithium chloride solution have been calculated. The alcohols show entropy and enthalpy effects, while the esters and ketones show mainly entropy effects. These results provide information on the changes induced by lithium chloride in polyethylene glycol.

INTRODUCTION AND SCOPE

There are many examples of the use in gas chromatography (GC) of stationary phases that contain inorganic salts¹⁻¹⁴. The choice of the salt has been suggested by the possibility of the formation of adducts between ions and molecules of the solute, and the selectivity of the stationary phase has been found to depend on the stability constant of the complexes. GC has also been used in the determination of these equilibrium constants¹⁵⁻²⁰. However, the addition of an electrolyte to a partition liquid also involves non-specific interactions (for example, interactions of a predominantly electrostatic nature^{21,22}) and consequently leads to a generic variation of the solubility of a solute in a partition liquid. In this connection, the GC behaviour of solutions of alkali metal chlorides in polyethylene glycol (PEG) as stationary phases has been studied previously. Compared with pure PEG, salting-out effects have been observed for alkanes and aromatic hydrocarbons and salting-in effects for some alcohols²².

In the present work, this type of investigation was continued on PEG with a mean molecular weight of 400, containing lithium chloride, in the gas-liquid chromatographic elution of some classes of aliphatic oxygen-containing compounds (alcohols, esters and ketones). The comparison was made not only by determining the variation in the free energy of solution, but also by determining the relative enthalpy function.

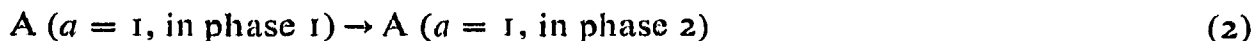
* This investigation was performed with the aid of a contribution from the Consiglio Nazionale delle Ricerche.

The free energy of transfer ($\Delta G_{t,1 \rightarrow 2}^0$) can be determined from GC retention parameters²²:

$$\Delta G_{t,1 \rightarrow 2}^0 = RT_c \ln \left(\frac{V_{gA,1}}{V_{gA,2}} \right) \quad (1)$$

where $V_{gA,1}$ and $V_{gA,2}$ are the specific retention volumes of the solute A in phases 1 (pure PEG) and 2 (PEG + lithium chloride), respectively, T_c is the column temperature ($^{\circ}\text{K}$) and R is the gas constant.

$\Delta G_{t,1 \rightarrow 2}^0$ represents the change in free energy that takes place when 1 mole of solute A is transferred from phase 1 to phase 2 when the activities (approximately equal to the concentrations) of the solute (mole/g) are unity:



A positive value of $\Delta G_{t,1 \rightarrow 2}^0$ indicates a salting-out effect ($V_{gA,1} > V_{gA,2}$), while a negative value indicates a salting-in effect.

The molar transfer enthalpy, $\Delta H_{t,1 \rightarrow 2}^0$, is calculated from the partial molar heats of evaporation ($\Delta H_1^0, \Delta H_2^0$) of the stationary phases 1 and 2:

$$\Delta H_{t,1 \rightarrow 2}^0 = \Delta H_1^0 - \Delta H_2^0 \quad (3)$$

From eqns. 1 and 3, it is possible to calculate the entropy of transfer, $\Delta S_{t,1 \rightarrow 2}^0$, for process 2.

As has been observed previously²², the magnitudes of the thermodynamic parameters relating to process 2 deduced by GC may also include interfacial effects.

EXPERIMENTAL

To determine the free energies of transfer, we used a Fractovap Model GV 200 instrument (Carlo Erba, Milan, Italy), and for the determination of the enthalpies of transfer, a Fractovap Model B instrument thermostatically controlled with a liquid bath ($\pm 0.05^{\circ}\text{C}$). Both instruments were equipped with thermal conductivity detectors. The columns were prepared as described previously²², using PEG-400 (Carlo Erba) sp. gr. at 25°C , 1.122; dielectric constant at 25°C , 13.97), high-purity lithium chloride (Merck, Darmstadt, G.F.R.), and, as the support, silanized Chromosorb P (60–80 mesh) (Carlo Erba) or in some instances Haloport F (30–60 mesh) (Hewlett-Packard) for methanol, ethanol, water, amines, and acids. The solutes were Carlo Erba pure products. To calculate the retention volumes, reference was made to the A.S.T.M. standards²³. Allowing for the error in the specific retention volume, evaluated as described by DONDI *et al.*²⁴, the free energies of transfer (at 78.2°C) were calculated with a precision of about ± 20 cal/mole and an accuracy of about 50 cal/mole, while the differential molar enthalpies of evaporation (between 75 and 85°C) were obtained with both a precision and an accuracy of about ± 50 cal/mole²⁵. For the solutes examined, as found previously²², the values of the free energy of transfer depend on the concentration of the salt and, in the range of concentrations studied (0.7 – 1 *m*), are expressed by an equation that is formally analogous to that of Setschenow. The values for $\Delta G_{t,1 \rightarrow 2}^0$ reported in Tables I and IV relate to the hypothetical 1 molal

concentration of lithium chloride. The values of $\Delta H^0_{t,1 \rightarrow 2}$ also depend on the salt concentration, and the values given in Table III are those obtained for a 1 *m* solution.

RESULTS AND DISCUSSION

Alcohols

The values of the free energy of transfer for alcohols are given in Table I and are shown in Fig. 1 as a function of the number of carbon atoms in the alcohol molecule. Examination of these values confirms the results observed previously²², *i.e.*:

- (1) in general, primary and secondary alcohols have an increased solubility in the phase that contains lithium chloride, while the tertiary alcohols show a decrease;
- (2) for each series of alcohols considered (primary, secondary or tertiary),

TABLE I

FREE ENERGIES OF TRANSFER AT 78.2°C AT A HYPOTHETICAL 1 MOLAL CONCENTRATION OF LITHIUM CHLORIDE

Alcohol	Free energy of transfer (kcal/mole)
Methanol	-0.39
Ethanol	-0.24
Propan-1-ol	-0.17
Butan-1-ol	-0.13
Pentan-1-ol	-0.09
Hexan-1-ol	-0.06
2-Methylpropan-1-ol	-0.09
3-Methylbutan-1-ol	-0.09
2-Methylbutan-1-ol	-0.07
Propan-2-ol	-0.09
Butan-2-ol	-0.03
Pentan-2-ol	+0.02
3-Methylbutan-2-ol	+0.04
2-Methylpropan-2-ol	+0.03
2-Methylbutan-2-ol	+0.09

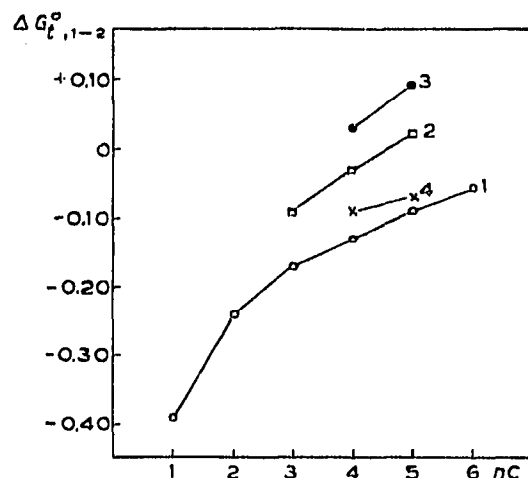


Fig. 1. Free energy of transfer ($\Delta G^0_{t,1 \rightarrow 2}$) for different types of alcohols; 1 = Primary alcohols; 2 = secondary alcohols; 3 = tertiary alcohols; 4 = 2-methylpropan-1-ol and 2-methylbutan-1-ol.

an increase in the number of carbon atoms is reflected in an increase in the free energy of transfer;

(3) isomerization of the carbon chain is reflected in an increase in the free energy of transfer.

The special behaviour of alcohols (salting-in) compared with the behaviour of other classes of solutes has been related to the electrostatic nature of the bond that they can form with pure PEG, and the differences between them have been related to the progressive decrease in the electrostatic contribution to the hydrogen bonding when they behave as proton donors²².

It can be seen in Fig. 1 that no satisfactory linear correlation exists within each series of alcohols between the values of $\Delta G^0_{t,1 \rightarrow 2}$ and the number of carbon atoms in the molecule. On the other hand, good linear correlations and the same parameters for the regression lines are found if the various alcohols are rearranged in terms of successive substitutions of a hydrogen atom by a methyl group on the same carbon atom. For substitution of the carbon atom in position 1, we can consider the following groupings:

a_1 : methanol, ethanol, propan-2-ol and 2-methylpropan-2-ol;

a_2 : propan-1-ol, butan-2-ol and 2-methylbutan-2-ol; "

a_3 : butan-1-ol and pentan-2-ol.

For substitution of the carbon atom in position 2, the following groupings are considered:

b_1 : ethanol, propan-1-ol and 2-methylpropan-1-ol;

b_2 : butan-1-ol and 2-methylbutan-1-ol.

Finally, for the successive substitutions on more remote positions, the following group is considered:

c : propan-1-ol, butan-1-ol, pentan-1-ol and hexan-1-ol.

Table II gives the slope of the linear regression of $\Delta G^0_{t,1 \rightarrow 2}$ versus the number of methyl groups in the molecule and, where available, the correlation coefficients. According to this scheme, the progressive variation in salting-in and salting-out is at a maximum for substitution of the carbon in position 1 (about 140 cal/mole), falling by about 50% for substitution in position 2 and falling further for substitution in more remote positions. This suggests the importance of steric and/or inductive factors in the over-all salting-in and -out effect.

TABLE II

LINEAR REGRESSION BETWEEN VALUES OF $\Delta G^0_{t,1 \rightarrow 2}$ AND THE NUMBER OF METHYL GROUPS SUBSTITUTED ON THE SAME CARBON ATOM

Series		Increment (cal/mole)	Correlation coefficient
a_1	Methanol, ethanol, propan-2-ol, 2-methylpropan-2-ol	141 ± 5^a	0.9986
a_2	Propan-1-ol, butan-2-ol, 2-methylbutan-2-ol	130 ± 6^a	0.9990
a_3	Butan-1-ol, pentan-2-ol	150	—
b_1	Ethanol, propan-1-ol, 2-methylpropan-1-ol	75 ± 3^a	0.9993
b_2	Butan-1-ol, 2-methylbutan-1-ol	60	—
c	Propan-1-ol, butan-1-ol, pentan-1-ol, hexan-1-ol	37 ± 2^a	0.9978

^a Estimated standard deviation.

Other types of correlation were found to be weaker. For example, the correlation of $\Delta G^0_{t,1 \rightarrow 2}$ with the dipole moment is practically zero and that with $1/\epsilon$ (where ϵ is the dielectric constant of the solute) is weak ($\rho = 0.5$). A certain correlation with the values of pK_a was found²².

The negative values of the enthalpy of transfer (Table III) show the existence of stronger interactions in the phase that contains lithium chloride, but it is not possible to determine whether this is due to a reinforcement of the hydrogen bonding or to direct interaction of the alcohol with the electrolyte. More detailed considerations with regard to the various types of alcohols are not possible in view of the errors and of the magnitude of $\Delta H^0_{t,1 \rightarrow 2}$. The entropy of transfer appears to be negative, in general, which is in agreement with the decrease in the degrees of freedom that usually accompany an increase in an interaction. From a comparison between values for $\Delta G^0_{t,1 \rightarrow 2}$, $\Delta H^0_{t,1 \rightarrow 2}$ and $\Delta S^0_{t,1 \rightarrow 2}$, it appears that the salting-in or salting-out effect is determined by the predominance or otherwise of the enthalpy contribution over the entropy contribution. Moreover, for the series of primary alcohols, it appears that the variations in these two contributions are parallel with one another.

TABLE III

ENTHALPIES AND ENTROPIES OF TRANSFER AT A 1 MOLAL CONCENTRATION OF LITHIUM CHLORIDE

<i>Alcohol</i>	$\Delta H^0_{t,1 \rightarrow 2}$ ^a (kcal/mole)	$\Delta S^0_{t,1 \rightarrow 2}$ ^b (e.u.)
Methanol	-0.6	-0.6
Ethanol	-0.3	-0.2
Propan-1-ol	-0.2	-0.1
Butan-1-ol	-0.2	-0.2
Propan-2-ol	-0.2	-0.3
2-Methylpropan-2-ol	-0.2	-0.7

^a Confidence interval (95%) = ± 0.1 kcal/mole.

^b Confidence interval (95%) = ± 0.4 e.u.

Esters and ketones

Esters and ketones have positive values of the free energy of transfer (Table IV), and the linear correlation between $\Delta G^0_{t,1 \rightarrow 2}$ and the number of methylene groups is satisfactory for acetates, formates and ketones (Table V). For the formates and acetates, the addition of a methylene group to the alcohol chain has almost the same effect (equal slopes of the regression lines), while the difference in behaviour is due to the presence of the particular functional group (different intercepts). The series of ketones exhibit values that are characteristic both of the functional group and of the methylene group. In any event, isomerization of the carbon chain does not give rise to appreciable differences in the values of the free energy, contrary to the results observed for the alcohols.

The enthalpy of transfer for all these compounds is approximately zero. The variation in the solubility of the solutes of these classes can therefore be determined mainly by entropy factors. On the basis of this hypothesis, the solute-PEG interactions are not changed by the presence of lithium chloride, but in the electrolyte

TABLE IV

FREE ENERGIES OF TRANSFER AT 78.2°C AT A HYPOTHETICAL 1 MOLAL CONCENTRATION OF LITHIUM CHLORIDE

<i>Compound</i>	<i>Free energy of transfer (kcal/mole)</i>
Acetone	+0.12
Methyl ethyl ketone	+0.17
Methyl propyl ketone	+0.21
Diethyl ketone	+0.21
Methyl isobutyl ketone	+0.24
Methyl formate	+0.16
Ethyl formate	+0.19
Propyl formate	+0.23
Butyl formate	+0.26
Methyl acetate	+0.21
Ethyl acetate	+0.25
Propyl acetate	+0.29
Isopropyl acetate	+0.29
Butyl acetate	+0.32
Isobutyl acetate	+0.31
Amyl acetate	+0.35
Methyl propionate	+0.23

TABLE V

LINEAR REGRESSION BETWEEN THE VALUES OF $\Delta G^0_{t,1 \rightarrow 2}$ AND THE NUMBER OF METHYLENE GROUPS
 $\Delta G^0_{t,1 \rightarrow 2} = A \cdot n_{CH_2} + R$

<i>Class of compound</i>	<i>A (cal/mole)^a</i>	<i>R (cal/mole)^a</i>	<i>Correlation coefficient</i>
Formates	34 ± 1	125 ± 5 (HCOO ⁻)	0.9983
Acetates	35 ± 2	179 ± 7 (CH ₃ COO ⁻)	0.9972
Ketones ^b	45 ± 2	32 ± 7 (=CO)	0.9983

^a The errors are given as estimates of the standard deviations.^b Regression performed with acetone, methyl ethyl ketone and methyl propyl ketone.

solution there is only a decrease in the number of "sites" that are accessible to the solute molecules.

The general salting-out or salting-in behaviour of these classes of compounds falls within the classification of hard and soft acids and bases²⁶: the PEG-400 and solutes are hard bases in competition with respect to the hard acid Li⁺ ion. These predictions have also been confirmed for a wider series of solutes: a decrease in the salting-in for water and acids and an increase in the salting-out for the series *n*-propylamine, tetrahydrofuran, 1,4-dioxan, thiophen, benzene, carbon tetrachloride, di-*n*-propylamine and tri-*n*-propylamine. This order of basicities is the same as that observed by other workers²⁶⁻²⁸: Nevertheless, the observations made here give a more complex illustration of the changes that are induced by the presence of lithium chloride.

What has been shown, above all, is the importance of entropy factors when considering both the degrees of freedom of the solute molecules and the re-structuring of the solvent induced by the salt, even though forces of an electrostatic character between the species present in solution are not negligible.

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