Correlation of Solubility Data: IV. Prediction of Solubilities of Homologous and Analogous Long Chain Compounds in Related Solvents

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Abstract

A new method of correlation and prediction of solubility data for long chain compounds is described. It is based on the linear relationship between $1/T_a$ and $1/T_r$ derived from the freezing point depression equation. T_a and T_r represent temperatures in degrees Kelvin at which the mole % solubility of a compound, a, in a given solvent is the same as that of an analogous reference compound, r, in a related solvent. The validity of the method has been confirmed by applying it to the extensive literature data on the solubilities of saturated and unsaturated fatty acids. Four families of related solvents were examined: (a) benzene, hexane, cyclohexane, chlorobenzene, *o*-xylene and toluene; (b) acetone, butanone, ethyl acetate and butyl acetate; (c) isopropanol, 95% ethanol, butanol, *p*-dioxane and diethyl ether; and (d) carbon tetrachloride and 1,2-chloroethane. Complete solubility data for a compound can be predicted from the linear $1/T_a$ vs. $1/T_r$ plot based on the melting point and one experimental solubility determination.

Introduction

Previous papers in this series have described graphical methods of correlation and prediction of solubility data for homologous (1–4) and analogous (4) compounds in a given solvent. A similar method has now been developed for correlating the solubility of a long chain compound in one solvent with its solubility or the solubility of a homologous or analogous compound of about the same molecular weight in another solvent.

Theoretical Basis

Single Solvent. Complete solubility data for a long chain compound, a, can be predicted from scant experimental data by the isopleth reference method (4) if complete data are known for a homologous or analogous reference compound, r, in the same solvent. The method was based on the following relationship, derived from ideal binary freezing point behavior:

$$1/T_a = (\Delta H_r/\Delta H_a)(1/T_r) + C \qquad [1]$$

T and ΔH are the respective freezing points (°K) and differential heats of solution of the two compounds at the same mole % concentrations in the given solvent and C is a constant. The isopleth reference plots, $1/T_a$ at specific concentrations vs. $1/T_r$ at the same concentrations, were straight or slightly curved lines. This proved that the basic requirement for the validity of this method of correlation was satisfied; namely, that the relative levels of departure from ideality of the two compounds in the given solvent, as indicated by the ratio $\Delta H_r/\Delta H_a$, remain substantially constant over a wide range of concentrations.

Related Solvents. It has now been found that this requirement is also satisfied when two related solvents are involved. Thus Equation 1 with a slight change in the designation of symbols becomes the basis of another type of isopleth reference plot. Here T_r represents the solubility temperatures for a reference system, i.e., for a reference compound in a given solvent. T_a represents the corresponding solubility temperatures for the same compound or for a homologous or analogous compound of about the same molecular weight at the same specific concentrations in a related solvent.

Two solutes are considered analogous if the solubility data for one in a given solvent can be used as a reference system to give a satisfactory linear isopleth plot for the other in the same (or a related) solvent.

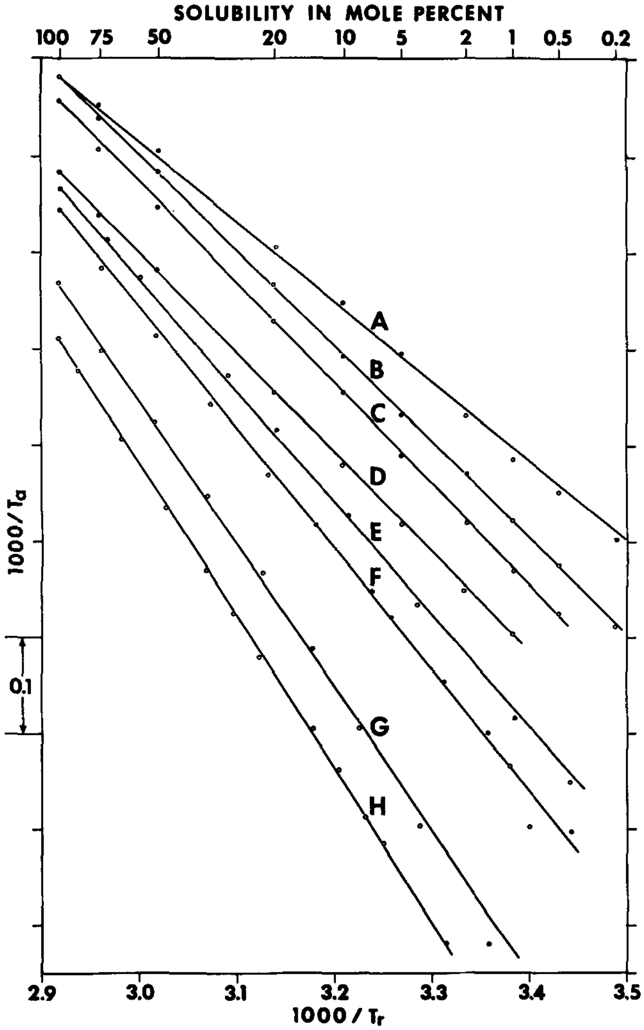

FIG. 1. Isopleth reference plots for A, stearic acid in hexane; B, stearic acid in *o*-xylene; C, heptadecanoic acid in cyclohexane; *D*, stearic acid in chlorobenzene; *E*, elaidic acid in toluene; *F*, oleic acid in hexane; *G*, linoleic acid in hexane; and *H*, oleic acid in *o*-xylene. Reference system, stearic acid in benzene.

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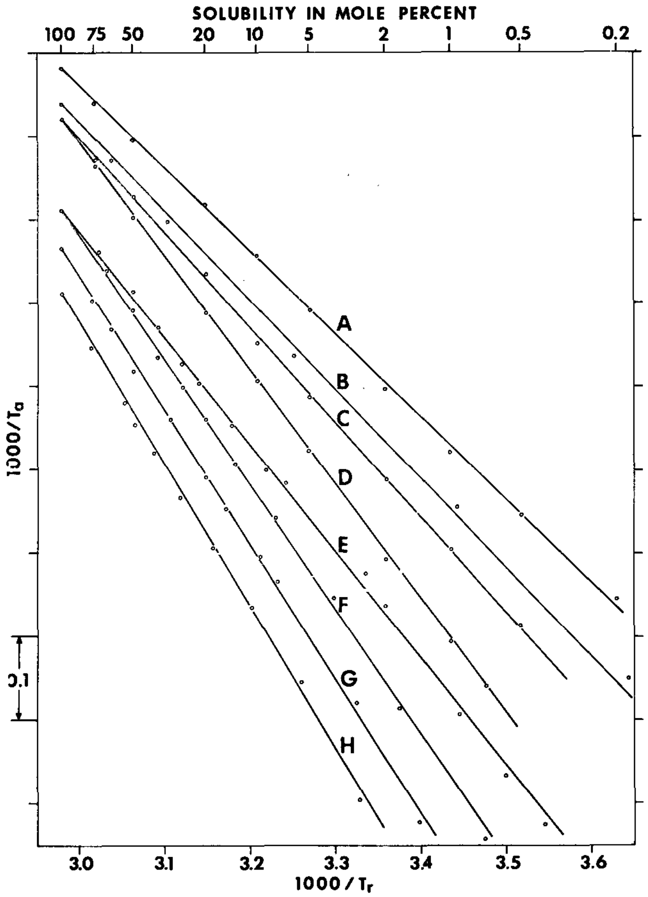

FIG. 2. Isopleth reference plots for A, stearic acid in butanone; B, stearamide in butyl acetate; C, palmitic acid in ethyl acetate; D, palmitic acid in butyl acetate; E, oleic acid in butanone; F, oleic acid in ethyl acetate; G, linoleic acid in butanone; and H, oleic acid in butyl acetate. Reference system, palmitic acid in acetone.

Two solvents are considered related if the solubility data for a compound in one solvent can be used as a reference system to give a satisfactory linear isopleth plot for the same (or an analogous) compound in the other solvent.

Application to Fatty Acid Solubilities

The publications of Ralston, et al., on the solubilities of the long chain saturated (5–8) and unsaturated (9) fatty acids in a large number of solvents afforded the necessary data for investigating the validity and scope of this new version of the isopleth reference method. Most of these solubilities were reported only at 10-degree intervals. More complete experimental data for specific solvents were available for oleic and linoleic acids (9,10) and for behenic, elaidic, petroselinic and petroselaidic acids (4). When necessary, the solubility temperatures for specific mole % concentrations were obtained by interpolation from log N vs. 1000/T plots.

Four series of related solvents were examined: (a) Those based on the benzene-stearic acid system as reference included hexane, cyclohexane, chlorobenzene, *o*-xylene and toluene. (b) Those based on the acetone-palmitic acid system as reference included butanone, ethyl acetate and butyl acetate. (c) Those based on the isopropanol-stearic acid system included butanol, 95% ethanol, *p*-dioxane and diethyl ether. (d) 1,2-Dichloroethane was the only related solvent found based on the carbon tetrachloride-stearic acid system as reference.

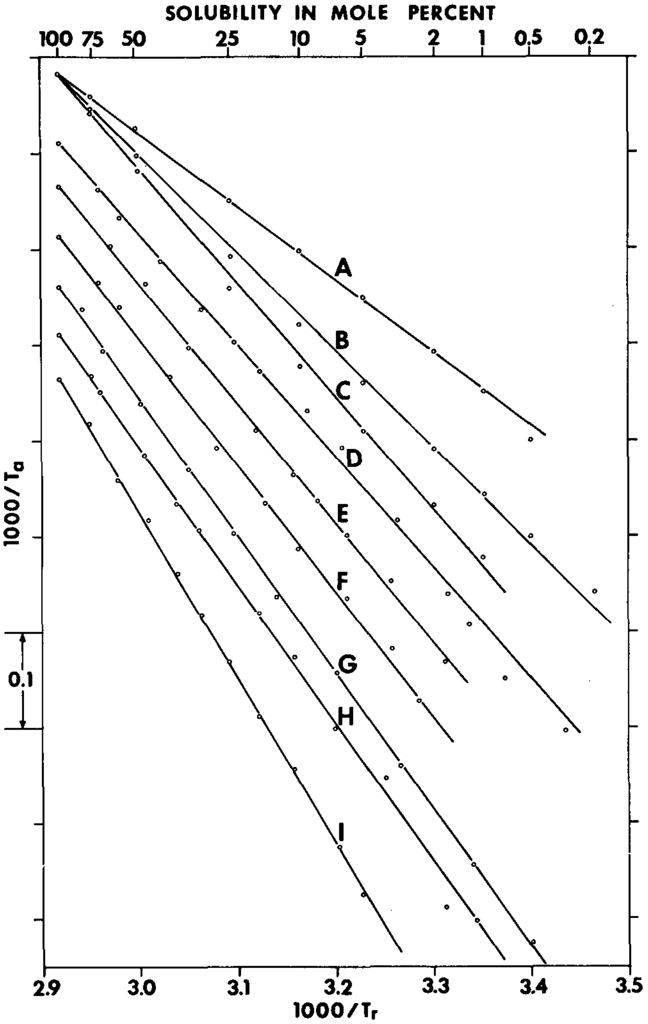

FIG. 3. Isopleth reference plots for A, stearic acid in 95% ethanol; B, stearic acid in butanol; C, stearic acid in *p*-dioxane; D, oleic acid in 95% ethanol; E, linoleic acid in methanol; F, linoleic acid in 95% ethanol; G, oleic acid in diethyl ether; H, oleic acid in butanol; and I, linoleic acid in butanol. Reference system, stearic acid in isopropanol.

Using the solubility data for stearic acid in benzene as the reference system, isopleth plots were constructed for behenic, stearic, heptadecanoic, palmitic, oleic, petroselinic, elaidic, petroselaidic and linoleic acids in various solvents including hexane, cyclohexane, chlorobenzene, *o*-xylene and toluene. Straight lines were obtained extending down to 1 mole %, or, when data for lower concentrations were available, usually down to 0.5 or 0.2 mole %.

Typical plots are shown in Figure 1. Most of the individual points fell within a few tenths of a degrees C of the straight lines. The largest deviation of a few scattered points was rarely more than one degree. For some systems, e.g., stearic acid in hexane, the points seem to fall on a slightly curved line. However, a straight line which passes within one degrees C or less of all the points can still be drawn. The same is true of the systems for which the individual points suggest double curvature.

The deviation of the points from linearity can be estimated by inspection of this and the following figures. In converting these deviations to degrees C however, it is important to note that the temperature interval in degrees C equivalent to a difference of 0.10 in the value of 1000/T decreases with decreasing temperature. Thus, for the saturated acids, oleic acid and linoleic acid, respectively, it ranges from about 10 to 7, from 8 to 5.7, and from 6.8 to 5 as the concentration decreases from 100 to 1 mole %.

Figure 2 shows typical isopleth plots for the various fatty acids and amides in several solvents with the palmitic acid-acetone system as the reference system. Butanone, ethyl acetate and butyl acetate were found to behave as related solvents. The data for palmitic and stearic acids in the ester solvents gave satisfactory isopleths down to about 3% only, as compared to 0.2% in butanone.

Butanol, 95% ethanol, *p*-dioxane and diethyl ether proved to be related solvents when the stearic acid-isopropanol system was used as the reference (Fig. 3). Although the data for linoleic acid in methanol gave a satisfactory isopleth down to 2%, the corresponding plots for the other acids in this solvent showed marked double curvature.

Using the stearic acid-carbon tetrachloride system as a reference system, 1,2-dichlorethane, but not chloroform, proved to be a related solvent.

All the isopleth plots for oleic acid except that for the hexane system intercepted the vertical axis at a point corresponding to the freezing point of the metastable form of the acid. It can be concluded that this was the solid phase at equilibrium in all these solubility determinations. For the oleic acid-hexane system, however, the data are for the stable form.

The range of concentrations for which satisfactory isopleth plots are obtained usually tends to decrease as the difference in the chain lengths of the two compounds involved increases. This seems to be more critical in some instances than in others.

Slopes

The slopes of the various isopleth reference plots, including those systems not shown in the Figures, are listed in Table I. The values given for the slopes represent the difference between the values of 1000/T at 100 and 1.0 mole % for each solute. The slopes for the various systems follow a consistent pattern. In the hydrocarbon series, for example, the palmitic acid (C_{16}) slopes are about 0.01 higher than the heptadecanoic (C_{17}) slopes and about 0.05 higher than the stearic (C_{18}) slopes. The values for oleic acid, with the exception of the butanol and 1,2-dichloroethane systems, are very much higher and those for linoleic acid are still higher.

It seems logical to assume from Table I that the C_{17} slopes for chlorobenzene, *o*-xylene and *p*-dioxane are about 0.515, 0.510 and 0.535, respectively. The slope for arachidic acid (C_{20}) in toluene, estimated with reasonable accuracy from the C_{16}, C_{18} and C_{22} values by graphical interpolation, is very close to 0.440. The isopleth plots corresponding to these slopes can be constructed and used to predict the C_{17} and C_{20} acid solubilities in these solvents by graphical interpolation. The solubility data for C_{17} in chlorobenzene and toluene will be identical when expressed in mole fraction.

New solutes and solvents cannot be definitely classified a priori among analogous compounds or related solvents without some experimental evidence. However, as a general rule it seems that compounds which behave as analogous compounds in one solvent, and therefore in a family of related solvents, can be expected to be analogous in another family. It was found, for example, that satisfactory isopleth plots were obtained for the solubilities of palmitamide and stearamide in butanol with the stearic acid-isopropanol system as reference. The published solubility data for these amides (11) are rather incomplete because their melting points are so far above the boiling points of most of the solvents used. Adequate data were available, however, to show that the solubilities of these amides in butyl acetate give fairly satisfactory isopleths with the palmitic acid-acetone system as a reference system (Fig. 2).

Prediction of Solubilities

This correlation method can be used for the prediction of complete solubility data from scant experimental data. It is apparent from Figures 1, 2 and 3 that a reasonably accurate isopleth reference plot can be constructed from the melting point of a compound and the temperature at which its solubility in a given solvent is about 5 mole %. Thus, with a single accurate experimental determination one can draw an isopleth plot using as a reference system the complete accurate solubility data for an analogous compound in a related solvent. Solubility data from 100% down to at least 1% can then be determined by graphical interpolation. This procedure should make it possible to predict complete solubility data for the C_{16}, C_{17}, C_{18}, C_{19} and C_{20} saturated, monounsaturated (*cis,trans,* and position isomers), and diunsaturated fatty acids in any of the 19 solvents mentioned above from one solubility determination.

TABLE I

Slopes[a] of Isopleths for Fatty Acid Solubilities

Solvent	C_{18}	C_{17}	C_{16}	Oleic	Linoleic	Other
Reference system: stearic acid in benzene						
Hexane	0.385	0.425	0.430	0.590	0.700	
Cyclohexane	0.460	0.490	0.500			
Chlorobenzene	0.480		0.525	0.720		
o-Xylene	0.470		0.520	0.740		
Toluene	0.480	0.515	0.525			0.410[b], 0 540[c] 0.525[d], 0.590[e]
Reference system: palmitic acid in acetone						
Butanone	0.455	0.500	0.525	0.580	0.740	
Ethyl acetate	0.445	0.480	0.515	0.680		
Butyl acetate	0.540	0.595	0.620	0.775		0.505[f], 0.550[g]
Reference system: stearic acid in isopropanol						
95% Ethanol	0.340	0.365	0.390	0.500	0.580	
Butanol	0.450	0.480	0.510	0.630	0.735	0.535[f], 0.600[g]
Dioxane	0.520		0 550			
Diethyl ether				0.630		
Methanol				0.520		
Reference system: stearic acid in carbon tetrachloride						
1,2-Dichloroethane	0.335		0.360	0.425		

[a] 1000/T at 1 mole % —1000/T at 100 mole %.
[b] Behenic acid, C_{22} (4).
[c] Elaidic acid (4).
[d] Petroselaidic acid (4).
[e] Petroselinic acid (4).
[f] Stearamide (11).
[g] Palmitamide (11).

There is no reason to suppose that this method of correlation and prediction is limited to the fatty acids. It would be expected to be applicable also to homologs or analogs of other long chain derivatives or even aromatic or cyclic compounds.

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