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Edward Soczewiński[a]; Jerzy Kuczyński[a]
[a] Department of Inorganic and Analytical Chemistry, Medical Academy, Lublin, Poland

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Solubility and R_M Values in Certain Partition Chromatographic Solvent Systems

EDWARD SOCZEWIŃSKI and JERZY KUCZYŃSKI
DEPARTMENT OF INORGANIC AND ANALYTICAL CHEMISTRY
MEDICAL ACADEMY
LUBLIN, POLAND

Summary

Parallelism of R_M vs. composition and log C_s vs. composition relationships has been found (C_s = solubility, moles per liter), in spite of the strong molecular interactions involved, for three alkaloids chromatographed in solvent systems of the type (*m*-xylene + *n*-pentanol)/buffer solution and (tetralin + cyclohexanone)/buffer solution. Some correlation has also been found between the solubility of two naphthols in nonpolar and weakly polar solvents (hydrocarbons, chlorinated hydrocarbons) and the R_M values in the corresponding solvent systems of the type organic solvent-formamide. The differences of R_M coefficients and log C_s values were found to be individual for a given solute and solvent system, even for closely related solutes (e.g., 1-naphthol and 2-naphthol) for which the ΔR_M values and Δ log C_s values tend to be constant for various systems (in other words, $\Delta R_M \neq \Delta \log C_s$).

It has been shown in our previous papers on the parallelity of solubility and partition chromatographic parameters (*1*,*2*) that it is possible in certain cases to relate the R_M value of a solute to its solubility (expressed as log molar concentration of saturated solution) in one of the phases. If the distribution coefficient of a solute is equal to the ratio of its solubilities in the two liquid phases, then we have, for varying solubility (C_s) of the solute in one of the phases (e.g., due to changes in the composition of the phase) and a constant solubility in the other phase,

$$R_M = \text{const.} \pm \log C_s \qquad (1)$$

The constant depends on the ratio of the volumes of the two phases and on the solubility of the solute in the phase of fixed composition. An idealized model of the chromatographic process is assumed, as in the hypothesis of additivity of R_M values (*3*).

Although Eq. (1) is a rather crude approximation, some quantitative parallelism of R_M coefficients and log C_s values is to be expected since the same intermolecular forces determine both the partition of a solute between two phases and its solubility; the forces can be classified as those causing solvation of the solute S–Z and the competitive interactions causing the association of the solute Z–Z and of the solvent S–S. The interactions (e.g., in the organic phase) may be represented by the following scheme:

S–S–Z–Z

The S–Z interactions tend to increase the solubility and shift the partition in favor of the phase which is being considered, and the S–S and Z–Z interactions act in the opposite direction. In the case of partition the situation is more complicated since the solution is saturated with the other liquid phase (e.g., the chloroform phase is saturated with water).

When one of the phases is a mixed solvent, two limiting types of R_M vs. composition and corresponding log C_s vs. composition relationships can be discerned (for detailed discussion, cf. Ref. *4*).

1. If the molecular interactions in the mixed phase (solvent 1 + solvent 2 + solute) are weak and spherically symmetrical, then the R_M coefficients and log C_s values vary linearly with the composition of the mixed phase, both relationships being theoretically parallel in accordance with Eq. (1). Experimental illustrations of such relationships were given in the preceding papers from this series (*1*,*2*).

2. In the case of strong, oriented interactions (especially H bonding) leading to the formation of relatively stable solvation and association complexes, the equilibria being governed by the law of mass action, strong deviations from linearity of R_M vs. X_s and log C_s vs. X_s relationships are often observed, unless some compensation of solvation and association effects occurs. Relatively simple relationships are obtained when one of the component solvents, having a very weak tendency to association (S–S), forms stable

solvation complexes with the solute (S–Z) [for instance, quinoline in the system (chloroform + heptane)/water, in view of the strong H bonding between chloroform and quinoline]. As Bush (Ref. 3, p. 395) pointed out, in these cases the R_M vs. $\log X_{CHCl_3}$ relationships should be analogous to the R_M vs. pH relationship of organic electrolytes; the slope of the line approaches unity in the composition range in which the chloroform–quinoline complexes predominate and decreases gradually to zero as chloroform becomes diluted with the inert solvent, heptane.

There were numerous attempts to find quantitative relationships between the solubility and composition of mixed solvents; a review on this subject is given in a paper of Milicevic and Ivekovic (5), who proposed a general equation and demonstrated that the equations derived in earlier papers (cf., e.g., Ref. 6) are special cases of the general formula which describes both types (1 and 2) of log solubility vs. composition relationships.

The purpose of the present work is to investigate whether the parallelism of R_M vs. composition and log C_s vs. composition relationships also occurs in the case of strong interactions between the component solvents and the solute. R_M vs. composition and log C_s vs. composition relationships of several alkaloids in two systems were determined:

(*m*-xylene + *n*-pentanol)/water (strong positive deviations)
(tetralin + cyclohexanone)/water (negative deviations)

Furthermore, parallelism of R_M and log C_s values of two naphthols was investigated in weakly polar solvent–formamide systems, using a number of pure weakly polar and nonpolar solvents of class A and N (7).

EXPERIMENTAL

The alkaloids and naphthols were chromatographed by the descending technique in tanks 6 × 12 × 21 cm using Whatman No. 4 paper strips, 5 × 23 cm, cut at right angles to the machine direction. The distance of development was 16 cm; the temperature was 21 ± 1°C.

In the case of alkaloids (brucine, cynchonine, and codeine), the strips were impregnated with McIlvaine's buffer solution of pH 6.2

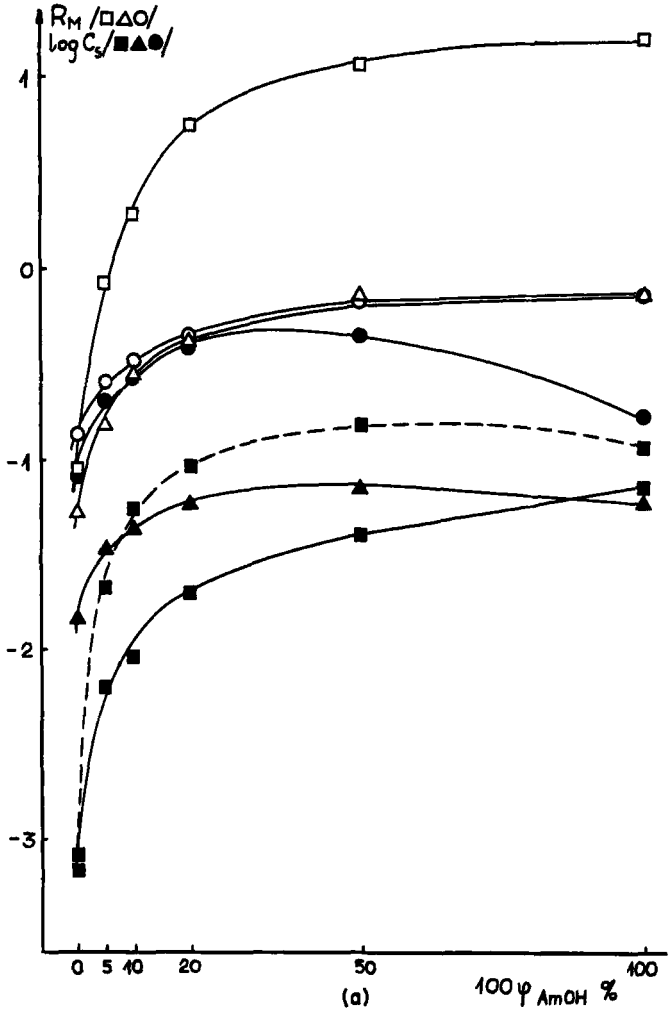
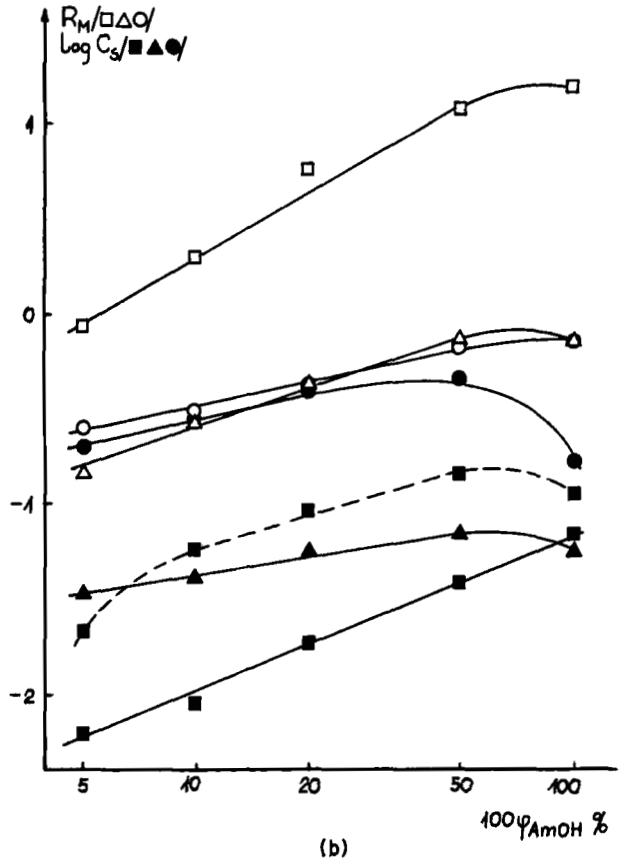


FIG. 1. (a) R_M coefficients (open symbols) and log C_s values (concentrations in moles per liter, solid symbols) plotted against the volume composition of a mixed organic phase composed of *m*-xylene and *n*-pentanol. □ ■, cynchonine; ○ ●, codeine; △ ▲, brucine. Dashed line, solubility in "dry" mixed solvents. (b) Same data plotted against volume composition in logarithmic scale. φ, volume fraction.



(mixed mobile phase composed of *m*-xylene and *n*-pentanol) or pH 6.3 (mixed phase composed of tetralin and cyclohexanone). The strips were immersed in the buffer solution and blotted between two sheets of filter paper; the solutions of alkaloids (1 w/v%, in chloroform) were spotted on the start line. The strips were then dried in horizontal position until the weight of the buffer solution dropped to 0.5 ml/1 g of dry paper; the strips were then immediately transferred to the tank and developed. The spots were detected by spraying with Dragendorff's reagent.

The solubilities of the alkaloids were determined by preparing their saturated solutions in the solvents which were also saturated

with water to secure conditions analogous to partition between two liquid phases (i.e., solubility was determined for saturated three-phase systems: solid solute–water–solvent). A 2-ml sample of the solvent phase was evaporated and the amount of the alkaloid determined by weighing; for the system tetralin + cyclohexanone, the solubility was determined by potentiometric titration with 0.1 M $HClO_4$ in anhydrous acetic acid. The solubility of cynchonine was also determined for "dry" mixtures of m-xylene and n-pentanol.

The experimental results are presented in Figs. 1(a), 1(b), and 2. The R_M values were calculated using Reichl's definition (8), $R_M = \log[R_F/(1 - R_F)]$, so that R_M values increase in a parallel manner with $\log C_s$.

In view of the parabolic shape of the R_M and $\log C_s$ values plotted against volume composition of the mixed phase composed of m-xylene and n-pentanol [Fig. 1(a)], the same results have been

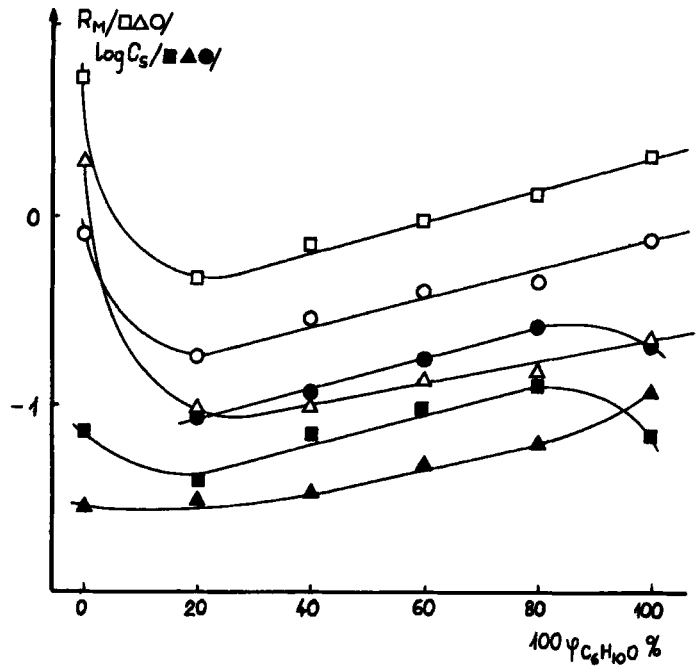


FIG. 2. Results analogous to those in Fig. 1 for the system (tetralin + cyclohexanone)/buffer solution pH 6.3.

replotted in Fig. 1(b) against log v/v% pentanol; it can be seen that this resulted in some straightening of the relationships, especially in the range of moderate concentrations of pentanol.

The two naphthols were chromatographed using Whatman No. 4 paper strips impregnated with 1:4 solution of formamide in acetone (0.5 g of formamide per 1 g of dry paper). The chromatograms were developed with volatile solvents of class N and A; solvents of class B and AB eluted the formamide from the strip or gave R_F values of the naphthols that were too high. The spots were detected by spraying with saturated solution of $NaHCO_3$ and immersing in a freshly prepared 1:1 mixture of 10% $NaNO_2$ and 0.5% benzidine hydrochloride (9).

The solubilities of the naphthols were determined by preparing saturated solutions of the naphthols and evaporating 2-ml samples of the solutions to constant weight. "Dry" solvents were used in this series of experiments (i.e., not saturated with formamide).

DISCUSSION OF RESULTS

Figures 1 and 2 indicate that parallelism of variations of R_M and log C_s values with the composition of the mixed phase is also observed (1) in the case of strong deviations from linearity due to strong interactions of the solute with one of the component solvents (Fig. 1, positive deviations) and (2) in the case of negative deviations (Fig. 2).

In systems of the type (*m*-xylene + *n*-pentanol)/buffer solution, the R_M values are approximately linearly dependent on the log concentration of pentanol in the organic phase; this indicates strong solvation of the active centers of the alkaloids (electron donor groups; first of all, nitrogen) by alcohol molecules (*4*). The slope of the R_M vs. log φ lines is near unity in the case of cynchonine and somewhat lower for brucine and codeine. The effect of composition of the mixed phase on R_M and log C_s values involves several contributions in addition to increasing concentrations of the active solvent. It should be kept in mind that the solubility of water in the organic phase varies with concentration of pentanol so that the organic phase is essentially a three-component system. Undoubtedly, the association of pentanol, tending to decrease the effective concentration of free hydroxyl groups, also plays an important role; as Littlewood and Willmott (*10*) have pointed out, in mixed solvents of the type inert liquid + alcohol, the class B groups (nitrogen

atoms, carbonyl, ether oxygen) can interact only with the end group of the linear polymer. Therefore, a formal increase of the total concentration of alcohol may be compensated by the increased degree of polymerization tending to decrease the actual concentration of free hydroxyl groups.

The corresponding R_M vs. composition and log C_s vs. composition lines are distinctly parallel, especially evident in Fig. 1(b); the parallelism is also observed for solubility in "dry" mixtures of xylene and pentanol (Fig. 1, dashed line). Marked deviations are observed only for pure pentanol, probably due to increased solubility of water. On the other hand, the distances between the corresponding pairs of lines (i.e., R_M–log C_s) are quite different for the three solutes: very large for cynchonine (somewhat smaller for "dry" mixed solvents), moderate for brucine, and quite small for codeine. The interpretation of this differentiated behavior is difficult in view of the complex molecular structure of the solutes and the complicated molecular interactions involved.

The peculiar shape of R_M vs. composition and log C_s vs. composition relationships was obtained for systems of the type (tetralin + cyclohexanone)/buffer solution. Tetralin is a quite good extractant for alkaloids; small amounts of cyclohexanone decrease the R_M values sharply and then the R_M values increase linearly with the concentration of cyclohexanone in the mixed phase. The corresponding log C_s vs. composition lines are almost parallel, with deviations observed for the pure component solvents (the solubility of codeine in pure tetralin saturated with water could not be determined due to technical difficulties, but was relatively high). The distances of the corresponding lines (R_M–log C_s) are also different in this case, although the differences are much less pronounced than in the former system.

The results of the third series of experiments (using paper impregnated with formamide) are presented in Fig. 3 as R_M vs. solvent and log C_s vs. solvent "spectra" subordinated to an arbitrary linear R_M vs. solvent relationship of 2-naphthol which determined the position of the solvents on the abscissa (cf. Refs. *11* and *12*). It can be seen that the difference in R_M values of the two naphthols is small in all cases ($\Delta R_M = 0.1$ to 0.3). The log C_s values are lower than the corresponding R_M coefficients, the Δ log C_s values being similar in most cases (ca. 0.6 units), although much higher than ΔR_M values (i.e., R_M–log C_s are different for the two solutes, as in previous instances). This discrepancy is probably due to the fact that the partition coefficient is determined by the solvation energies of

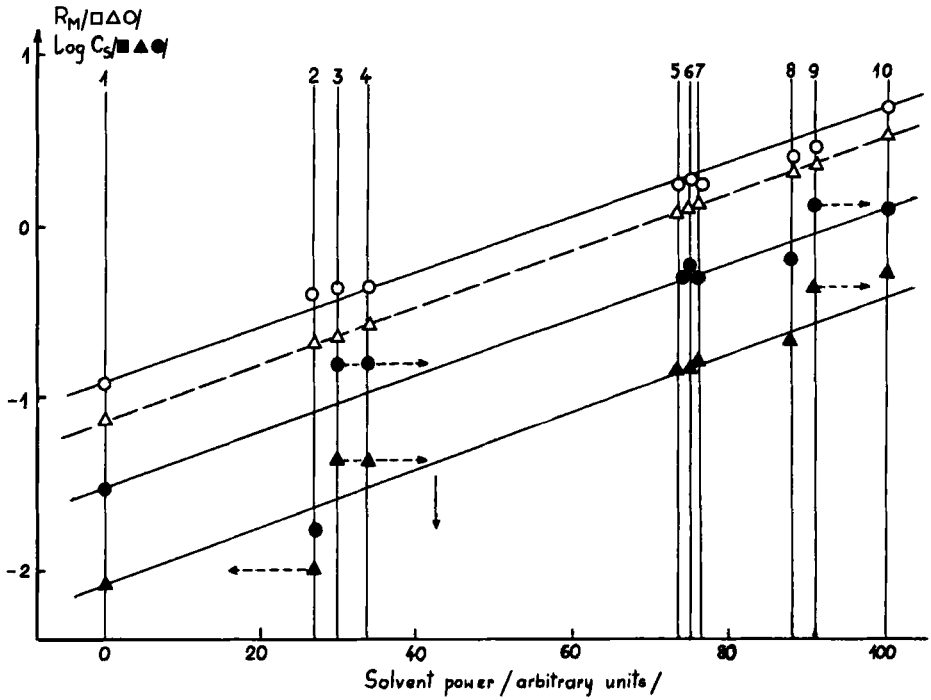


FIG. 3. R_M–solvent spectra of 1-naphthol (○) and 2-naphthol (△). The solvents are arranged on the abscissa so that a straight (dashed) line is obtained for 2-naphthol: 1, cyclohexane; 2, decalin; 3, tetrachloroethylene; 4, carbon tetrachloride; 5, *m*-xylene; 6, ethylbenzene; 7, chlorobenzene; 8, 1,1'-dichloroethane; 9, chloroform; 10, 1,2-dichloroethane. The black circles and triangles correspond to log C_s values.

the solute in the two phases and by the displacement effect in the polar (associated) phase, while the solubility depends also on the energy of the crystal network which may differ even for closely related solutes.

Although the solubility of naphthols has been determined for dry solvents (i.e., not saturated with formamide), it is seen that in some cases the log C_s values of the naphthols fall on straight lines parallel to the reference (dashed) R_M vs. solvent line of 2-naphthol. However, some log C_s values show more or less marked deviations from the points expected from the chromatographic spectra. The deviations are probably due to saturation of the nonpolar solvent in the chromatographic systems with formamide.

The position of the solvent on the abscissa characterizes its extraction power in relation to dilute solutions of naphthols in formamide. Since the naphthols belong to class AB (proton donor properties predominating), the sequence of solvents is somewhat different from that observed for the case of extraction of quinoline bases [class B (*13*)]. It can be seen that the lowest solvent power is observed in the case of class N solvents: aliphatic hydrocarbons (*1*,*2*) and chlorinated hydrocarbons (*3*,*4*). Aromatic hydrocarbons (*5*–*7*) have much higher extraction power due to the formation of π complexes with hydroxyl groups (*14*); partly chlorinated hydrocarbons [class A (*8*–*10*)] are still better extractants. Solvents of class B, which in relation to quinolines have low extraction power, comparable to inert solvents of class N, are the best extractants in the case of naphthols (strong interactions —O—H · · · O); in the arbitrary scale in Fig. 3 they have values above 100, since the naphthols migrate close to the solvent front when formamide-impregnated paper is developed with weakly polar solvents of class B (e.g., isoamyl ether). This discrepancy of sequences of solvents arranged by their extraction power demonstrates the limited applicability of empirical solvent series; it seems, however, that such series of solvents can be arranged for solutes of analogous molecular structures (and this denotes, first of all, the number and type of H-bonding groups). As Hermanek et al. (*15*) pointed out, the task is easier for adsorption where the elution power is determined mainly by interactions between the solvent and the active groups of the adsorbent surface (e.g., hydroxyl groups in the case of silica gel).

Since some of the log C_s values deviate from the straight lines parallel to the reference line (R_M values of 2-naphthol), the characteristics of the solvents in question with respect to their solution power are somewhat different from the values on the extraction power scale, as indicated by arrows in Fig. 3. Thus decalin would possess a solvent power of approximately zero (similar to cyclohexane); on the other hand, tetrachloroethylene and carbon tetrachloride have solvent power ca. 40, i.e., higher than that expected from the chromatographic data. Similarly, chloroform would have solvent power similar to 1,2-dichloroethane, i.e., ca. 100.

To sum up the results of the experiments described in the three papers in this series, in most cases striking parallelism of solubility

(log C_s) and partition chromatographic behavior (R_M) has been observed; only in sporadic cases have some deviations appeared. It is remarkable that the values of (R_M − log C_s) of individual solutes, tending to be constant for various solvents or their mixtures, differed markedly for various solutes, even those having analogous molecular structure (e.g., for the two naphthols, cf. Fig. 3). Formally, the discrepancies are due to nonparallel variations of the activity coefficients with the concentration of the solutes.

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