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## INVESTIGATIONS OF THE RELATIONSHIP BETWEEN MOLECULAR STRUCTURE AND CHROMATOGRAPHIC PARAMETERS

### X. EXTRACTION OF ORGANIC SOLUTES WITH MIXTURES OF CHLOROFORM AND ELECTRON-DONOR SOLVENTS

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#### SUMMARY

A mathematical model of the partition of organic solutes in solvent systems of the type proton-donor solvent + electron-donor solvent-water is described. Chromatographic results obtained for phenols, anilines and quinolines as solutes and mobile phases composed of chloroform and four electron-donor solvents (diisopropyl ether, methyl *n*-propyl ketone, diisobutyl ketone and tri-*n*-butyl phosphate) are interpreted in terms of the model.

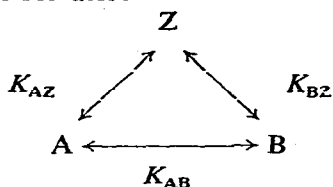
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#### INTRODUCTION

Solvent composition effects have so far been investigated (ref. 1 and earlier papers cited therein) for mixtures composed of a polar solvent and a non-polar diluent, cyclohexane. Frequently, mixtures of two polar solvents are used as the stationary or mobile phase and the relationships between partition parameters and solvent composition are then much more complex. Among the types of binary mixtures classified according to the ability of the components to form hydrogen bonds<sup>2</sup> the A + B binary mixtures (that is, composed of a proton-donor solvent and an electron-donor solvent) are relatively simple. In this paper, an attempt is made to formulate a mathematical description of liquid-liquid partition systems of such type, that is solvent A + solvent B-water (or formamide, etc.), in which the two solvents, A and B, are miscible with each other but virtually immiscible with the polar phase at all compositions. The approach is based on the application of the law of mass action to the formation equilibria of various molecular complexes in the mixed phase and one of its main aims is to find correlations between the partition behaviour of various organic solutes and their molecular structure, especially their ability to form hydrogen bonds with the component solvents A and B. Analogous considerations for systems of the type carrier gas-binary stationary phase have recently been published by Mathiasson<sup>3</sup>.

## THEORETICAL

The interactions in the mixed phase are represented by the following scheme and stability constants of the solvates:



$K_{AZ} = c_{AZ}/c_A c_Z$ ,  $K_{BZ} = c_{BZ}/c_B c_Z$  and  $K_{AB} = c_{AB}/c_A c_B$ , where  $c$  denotes molar concentrations of the molecular species indicated by the subscripts. The solute  $Z$  therefore belongs to the AB class<sup>2</sup> and is capable of forming hydrogen bonds with solvents of both class A and class B. Another system of this type would be formed by an organic ampholyte  $Z$  (e.g., an aminocarboxylic acid) and two ion-pairing reagents (cation exchanger A and anion exchanger B) in a suitable diluent. The discussion is limited to the formation of simple 1:1 solvation complexes or ion pairs. It is assumed that the activity coefficients are constant and that the solute does not associate ( $K_{ZZ} = 0$ ) owing to its relatively low concentrations and the polar medium in the whole composition range. It is also assumed that water (or another associated solvent forming the other liquid phase) dissolved in the mixed phase does not influence the partition equilibrium.

At equilibrium, the concentrations of the free molecules and molecular complexes should be in agreement with all three stability constants and with the partition coefficient of the uncomplexed solute,  $k_d$ . In view of the low concentration of solute that is typical of chromatographic systems, it can be assumed that solute molecules interact only with free molecules of solvents A and B. The actual concentrations of A and B,  $c_A$  and  $c_B$ , are lower than their nominal concentrations  $c_A^0$ ,  $c_B^0$  owing to the formation of molecular complexes, AB.

One of the ways of describing the competitive equilibria is to calculate the actual concentrations of A and B and then to substitute these values into the equation of the distribution ratio ( $D = c_{\text{org}}/c_{\text{aq}}$ ):

$$\begin{aligned}
 D &= \frac{c_Z + c_{AZ} + c_{BZ}}{c_{Z(\text{aq})}} = \frac{c_Z (1 + K_{AZ} c_A + K_{BZ} c_B)}{c_{Z(\text{aq})}} \\
 &= k_{d(z)} (1 + K_{AZ} c_A + K_{BZ} c_B) \quad (1)
 \end{aligned}$$

$$\left( R_F = \frac{Dr}{Dr + 1} \text{ and } R_M = -\log Dr, \text{ where } r = V_{\text{org}}/V_{\text{aq}} \right).$$

The calculations of the  $R_M$  versus (nominal) composition relationships would thus require a knowledge of several constants that should be determined independently if a strict comparison between experimental data and the theoretical model is to be made. However, interesting conclusions can also be drawn by means of theoretical considerations of hypothetical cases with various values of the constants. Let us con-

sider a simple case when the molar volumes of the component solvents A and B are  $100 \text{ cm}^3/\text{mole}$ , so that for pure solvents  $c_A = c_B = 10 \text{ M}$ . Neglecting any changes in volume on mixing the solvents, their nominal concentrations  $c^0$  change with the solvent compositions as shown in Fig. 1 (continuous lines). The actual concentrations,  $c_A$  and  $c_B$ , lowered owing to A-B interactions, can be calculated from the condition

$$K_{AB} = \frac{c_{AB}}{c_A c_B} = \frac{c_{AB}}{(c_A^0 - c_{AB})(c_B^0 - c_{AB})} \quad (2)$$

(neglecting relatively small concentrations  $c_{AZ}$  and  $c_{BZ}$ ). For a known value of  $K_{AB}$ , the equation can be solved for  $c_{AB}$ , the actual concentrations of A and B (Fig. 1, dashed lines) and then values of  $D$  calculated (eqn. 1), if the values of the solvation constants and  $k_{d(z)}$  are known<sup>3</sup>:

$$c_{AB} = 1/2 \left[ c_A^0 + c_B^0 + K_{AB}^{-1} - \sqrt{(c_A^0 + c_B^0 + K_{AB}^{-1})^2 - 4 c_A^0 c_B^0} \right] \quad (3)$$

Table I illustrates such calculations for  $K_{AB} = 1$ ,  $k_{d(z)} = 1$ ,  $K_{AZ} = 5$  and  $K_{BZ} = 20$ . Needless to say, in addition to hydrogen bonding in the binary phase, there are other interactions involved: non-specific interactions in the mixed phase as well as hydration and hydrophobic interactions in the aqueous phase. These interactions, which determine the value of the partition coefficient,  $k_d$ , form a background to hydrogen bonding. In a strict approach, the activity coefficients should be taken into account. Fig. 2 represents theoretical  $\log D$  versus (nominal) composition curves calculated in the manner described above for various values of the constants  $K_{AB}$ ,  $K_{AZ}$  and  $K_{BZ}$  ( $\log D = -R_M$  when  $r = 1$ ). The curves have different shapes; one of the interesting features is that minima can sometimes be obtained due to mutual "cancellation" of the polarity of the complex. It can be seen from the theoretical curves that the appearance of minima, and their depth, are favoured by (a) strong A-B interactions (higher values of  $K_{AB}$ ) and (b) strong interactions of the solute with both solvents (high values of both  $K_{AZ}$  and  $K_{BZ}$ ). These parameters are in turn deter-

TABLE I

CALCULATION OF A THEORETICAL  $\log D$  versus  $c_B^0$  CURVE $K_{AB} = 1$ ;  $K_{AZ} = 5$ ;  $K_{BZ} = 20$ ;  $k_z = 1$  (upper curve in Fig. 2b).

$c_A^0$	$c_B^0$	$c_{AB}$	$c_A$	$c_B$	$c_A K_{AZ}$	$c_B K_{BZ}$	$D$
10	0	0.00	10.0	0.00	50.0	0.0	51.0
9	1	0.89	8.11	0.11	40.55	2.2	43.75
8	2	1.725	6.275	0.275	31.375	5.5	37.88
7	3	2.46	4.54	0.54	22.70	10.8	34.50
6	4	3.00	3.00	1.00	15.00	20.0	36.0
5	5	3.21	1.79	1.79	8.95	35.8	45.75
4	6	3.00	1.00	3.00	5.00	60.0	66.0
3	7	2.46	0.54	4.54	2.70	90.8	94.5
2	8	1.725	0.275	6.275	1.375	125.5	127.9
1	9	0.89	0.11	8.11	0.55	162.2	163.75
0	10	0.00	0.00	10.00	0.00	200.0	201.0

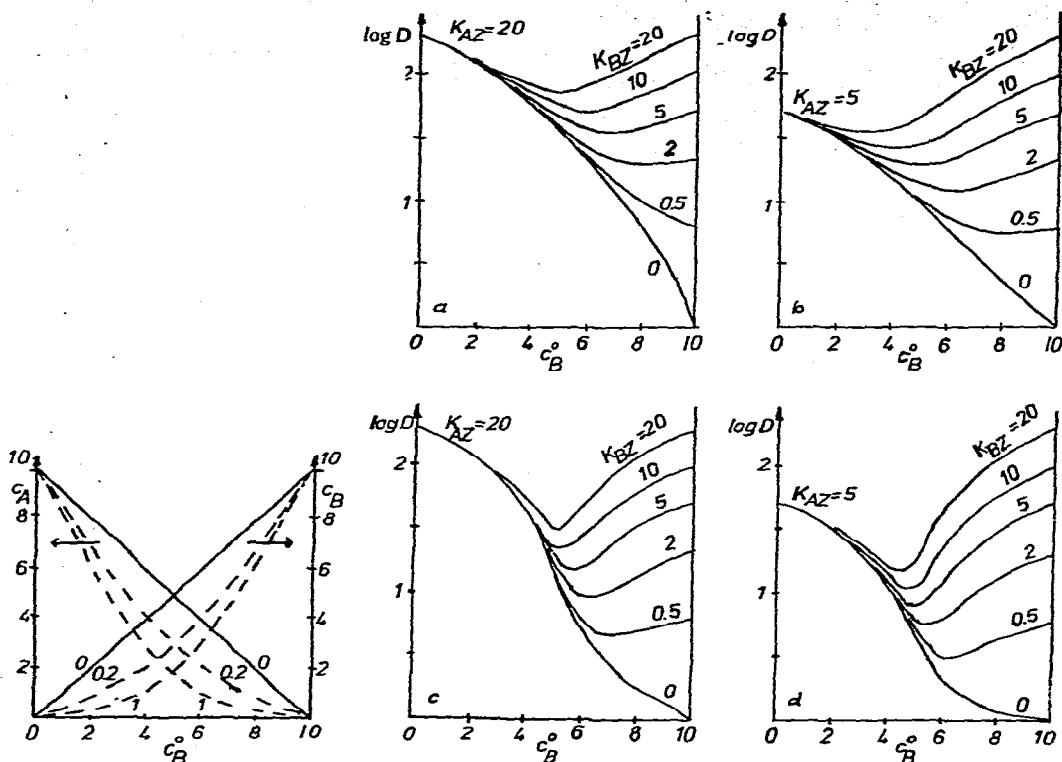


Fig. 1. Variation of nominal (solid lines) and actual concentrations (broken lines) in mixtures of two solvents of class A and B for various values of  $K_{AB}$ . (For  $K_{AB} = 1$ , compare Table I.)

Fig. 2. Variation of  $\log D$  with nominal concentration of electron-donor solvent for various values of  $K_{AB}$ ,  $K_{AZ}$  and  $K_{BZ}$ . Molar volumes of component solvents,  $100 \text{ cm}^3/\text{mole}$ ;  $K_{AB} = 1.0$  (a and b) or 10 (c and d).

mined by the molecular structures of the solvents and solute, mainly by the type of hydrogen bonding groups.

The aim of the experimental section is to test these conclusions with real solute-solvent systems. The solutes chromatographed in solvent systems of the type chloroform (A) + electron-donor solvent (B)-water had the following hydrogen bonding groupings:  $-\text{OH}$  (strong interactions with A and especially with B),  $-\text{NH}_2$ ,  $=\text{NH}$  (strong interactions with A, weaker with B) and heterocyclic nitrogen (strong interactions with A, very weak interactions with B).

## EXPERIMENTAL

Whatman No. 4 paper strips were impregnated with McIlvaine's buffer solution (pH 2.6), blotted between two sheets of filter-paper and dried in air until the content of buffer solution decreased to 0.5 g per gram of dry paper. The strips were then transferred immediately into all-glass chromatographic tanks for descending development<sup>4</sup>. Under these conditions, the ratio of the volumes of the two liquid phases,  $V_{\text{org}}/V_{\text{aq}}$ , is ca. 2.0.

The spots of phenols and anilines were detected with bisdiazotized benzidine reagent after spraying with a saturated solution of sodium hydrogen carbonate, and those of quinolines with Dragendorff's reagent.

Nuclear magnetic resonance (NMR) spectra were obtained using a BS 487-C NMR spectrometer (Czechoslovakia); the magnetic field employed was *ca.* 2 T, corresponding to a precession frequency for the protons of 80 MHz. The chemical shift of the chloroform proton was measured at 24° with an accuracy of 0.2 Hz using tetramethylsilane as an internal standard.

## RESULTS AND DISCUSSION

The experimental data are presented in Figs. 3–6 as  $R_M$  versus volume composition plots and in Table II. The solutes investigated form three groups of curves: extraction of phenols, more strongly solvated with electron-donor solvents, increases with  $c_B^0$ ; nitrogen bases are generally more strongly solvated by chloroform and their curves usually have negative slopes. However, the curves of the derivatives of aniline (class AB) are less steep and for more polar solvents of class B (especially for tri-*n*-butyl phosphate) pass through a distinct minimum, while those of quinoline bases, which cannot form hydrogen bonds with solvents of class B, decrease more steeply, especially for systems with diisopropyl ether. The extraction of phenols by electron-donor solvents is so much stronger that for these solutes chloroform can be considered as an almost inert diluent; in fact, the  $R_M$  values are linearly dependent on the logarithm of the concentration of class B solvents (Figs. 7 and 8).

NMR data (maximal value of  $\Delta\nu$  and shift of the peak of chloroform with increasing concentration of the electron-donor solvent, Fig. 9) indicate that interactions of chloroform with the electron-donor solvents, and thus  $K_{AB}$  values, increase in the following order: diisopropyl ether < diisobutyl ketone < methyl *n*-propyl ketone < tri-*n*-butyl phosphate. For instance, Wiley and Miller<sup>5</sup> reported the following values of  $K_{AB}$  for interactions of some electron-donor solvents with chloroform

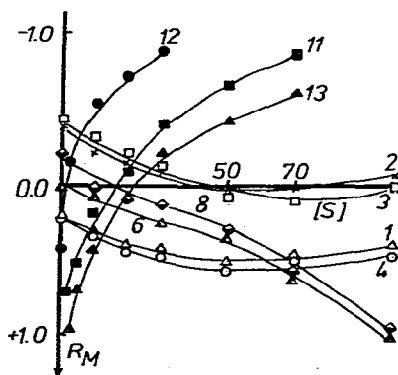
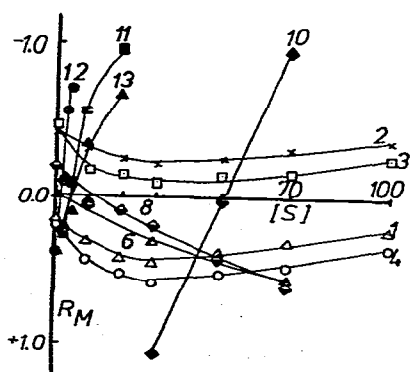


Fig. 3.  $R_M$  of solutes plotted against concentration (% v/v) of electron-donor solvent (tri-*n*-butyl phosphate). Proton donor component of mobile phase: chloroform. For notation of solutes, see Table II.

Fig. 4.  $R_M$  of solutes plotted against concentration (% v/v) of electron-donor solvent (diisopropyl ether). Proton donor component of mobile phase: chloroform. For notation of solutes, see Table II.

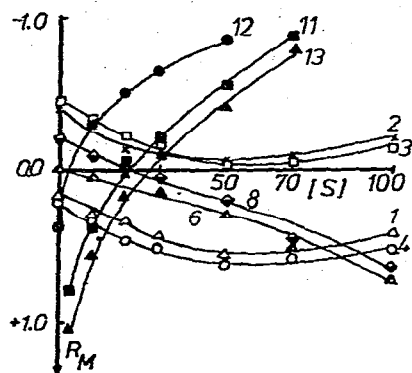
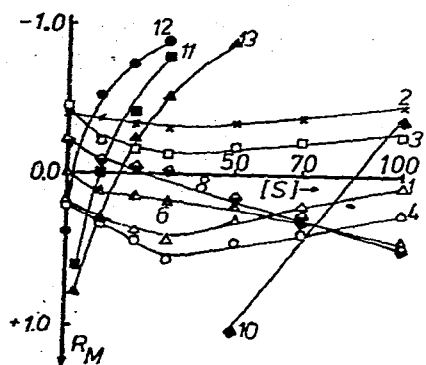


Fig. 5.  $R_M$  of solutes plotted against concentration (% v/v) of electron-donor solvent (methyl *n*-propyl ketone). Proton donor component of mobile phase: chloroform. For notation of solutes, see Table II.

Fig. 6.  $R_M$  of solutes plotted against concentration (% v/v) of electron-donor solvent (diisobutyl ketone). Proton donor component of mobile phase: chloroform. For notation of solutes, see Table II.

(cyclohexane medium, at 28°, NMR): acetone, 0.751; cyclohexane, 1.023; di-*n*-butyl ether, 0.243; triethyl phosphate, 4.637. For tri-*n*-butyl phosphate, Nishimura *et al.*<sup>6</sup> reported a value of 5.2 (21°), and for diisopropyl ether Wong and Ng<sup>7</sup> reported  $K_{AB} = 0.30$  (34°). Hence the chromatographic results can be qualitatively interpreted as follows.

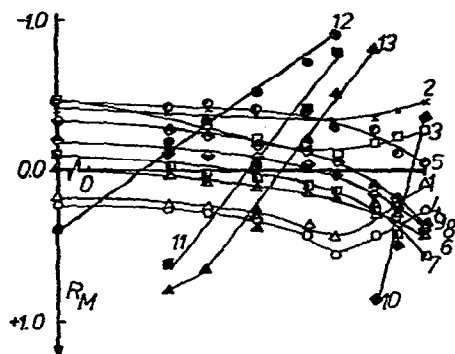
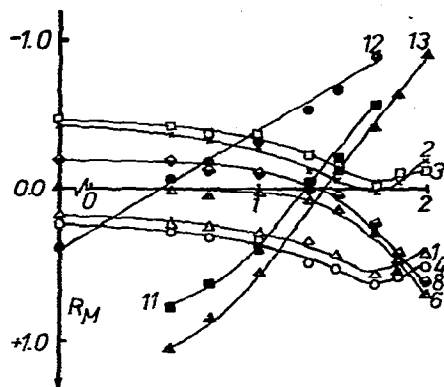
For quinolines (class B),  $K_{AZ}$  is markedly higher than  $K_{BZ}$  (strong interaction with chloroform, weak interaction with electron-donor solvents). The  $\log D$  versus  $c_B^0$  lines have negative slopes over the whole composition range, irrespective of the value of  $K_{AB}$ . Phenols have opposite properties (interaction with a solvent of class B is much stronger than with chloroform, *i.e.*,  $K_{AZ} \ll K_{BZ}$ ), so that their curves have positive slopes in all three solvent systems investigated.

TABLE II

$R_F \times 100$  VALUES OF SOLUTES FOR VARIOUS CONCENTRATIONS OF ELECTRON-DONOR COMPONENT IN THE DEVELOPING SOLVENT

Proton-donor component: chloroform.

No.	Solute	Tri- <i>n</i> -butyl phosphate (% v/v)								Diisopropyl ether (% v/v)						
		0	3	5	10	20	30	50	70	100	3	5	10	20	30	50
1	Aniline	40	38	35	33	29	27	30	33	37	36	36	32	30	28	24
2	2-Methylaniline	72	71	69	66	64	62	64	66	68	68	64	62	60	58	44
3	3-Methylaniline	74	64	62	60	58	56	58	60	64	72	70	68	62	58	44
4	4-Methylaniline	38	34	30	28	24	20	24	26	32	36	32	32	28	26	22
5	Quinoline	74	72	70	68	66	62	44	25	—	72	70	68	62	60	52
6	Isoquinoline	50	49	48	46	44	34	28	23	—	49	48	46	44	36	32
7	3-Methylisoquinoline	56	46	42	46	32	24	22	—	—	54	52	50	46	38	28
8	4-Methylquinoline	62	56	54	48	46	40	28	22	—	56	52	48	46	44	34
9	2,6-Dimethylquinoline	68	62	58	46	42	38	32	25	—	66	64	62	58	52	38
10	Phloroglucinol	0	0	0	0	2	8	50	90	—	0	0	0	0	0	0
11	1,5-Dihydroxynaphthalene	6	36	54	78	90	—	—	—	—	16	23	40	58	72	82
12	2,3-Dihydroxynaphthalene	30	78	84	—	—	—	—	—	—	58	64	78	84	88	—
13	2,7-Dihydroxynaphthalene	3	30	44	68	82	90	—	—	—	10	16	28	46	62	73

Fig. 7. Data of Fig. 5 presented as an  $R_M$  versus  $\log \%B$  plot.Fig. 8. Data of Fig. 6 presented as an  $R_M$  versus  $\log \%B$  plot.

For anilines the curves are more differentiated, depending on the proton-acceptor ability of the electron-donor component solvent. Thus, for the system with the weakly polar diisopropyl ether,  $K_{AZ}$  is distinctly higher than  $K_{BZ}$  and  $K_{AB}$  is low (see above), so that the curves have small negative slopes. More polar electron-donor solvents, such as methyl *n*-propyl ketone and tri-*n*-butyl phosphate, have extraction abilities comparable to that of chloroform ( $K_{AZ} \approx K_{BZ}$ ) and the  $K_{AB}$  values are greater than in the former system so that minima appear in the  $\log D$  versus  $c_B^0$  relationships.

The relationships are thus in qualitative agreement with theoretical predictions, although a quantitative comparison would require the independent determination of all formation constants of the solvation complexes, which will constitute the subject of future investigations.

The experimental data indicate that mixtures of interacting solvents, *e.g.*, of

Methyl <i>n</i> -propyl ketone (% <sub>v</sub> , v/v)										Diisobutyl ketone (% <sub>v</sub> , v/v)							
70	100	3	5	10	20	30	50	70	100	3	5	10	20	30	50	70	100
26	37	36	35	33	31	28	34	38	46	38	36	34	32	28	22	26	28
50	54	72	71	70	68	66	68	70	73	70	68	66	56	54	50	54	60
46	50	70	66	62	58	56	60	62	64	72	70	68	62	58	50	52	58
24	26	35	34	32	28	22	28	30	35	34	33	32	26	24	20	22	24
36	24	72	72	70	68	66	64	56	52	73	72	70	68	66	56	44	38
20	9	48	46	44	42	40	38	34	28	50	49	48	46	42	34	22	16
16	7	50	48	46	44	40	34	28	21	54	52	48	44	40	26	20	16
22	10	58	56	54	52	48	40	36	28	62	58	56	50	48	38	26	20
24	12	65	63	61	58	54	44	39	30	68	66	64	62	56	44	30	22
3	8	0	0	0	0	2	12	36	70	0	0	0	0	0	0	2	15
88	92	20	28	50	72	86	92	—	—	14	20	30	52	62	78	88	—
—	—	60	66	76	84	88	92	—	—	54	58	68	76	82	88	92	—
80	92	14	18	32	62	76	88	92	—	8	12	22	40	54	72	86	90

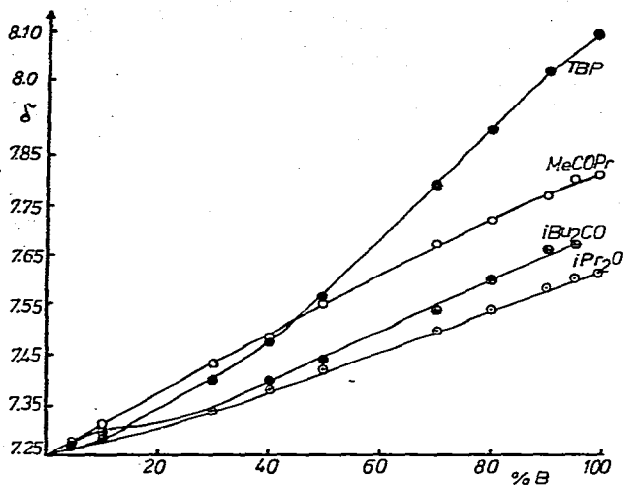


Fig. 9. NMR frequencies of chloroform in mixtures with four electron-donor solvents (diluted with chloroform in a 1:1 volume ratio).

the A + B type, cannot be regarded as solutions whose donor and acceptor properties can be expressed as proportional to the concentrations of the two component solvents on the additivity principle (Fig. 1). The partial cancellation of opposing properties can also play a role in other phenomena, such as adsorption from solutions. The relationships become even more complex for bifunctional and polyfunctional solutes, especially those with functional groups with opposite properties.

From the viewpoint of chromatographic analysis, it should be noted that more complex solvent systems provide more diverse relationships, sensitive to differences in the molecular structure of the solute and have a greater capacity, and are thus more versatile than solvent systems composed of a polar solvent and a non-polar diluent; complications in gradient chromatography are apparent.

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