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DESCRIPTION OF SUBSTITUENT EFFECTS IN GAS-LIQUID CHROMATOGRAPHY

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SUMMARY

Substituent effects in gas-liquid chromatography are defined as the deviations, $\Delta\Delta\log V_N$, of the additivity of group contributions to $\log V_N$. To determine $\Delta\Delta\log V_N$ values, corrected net retention volumes, V_N , were measured for *o*-, *m*- and *p*-substituted anilines, phenols and pyridines, and for monosubstituted benzenes, cyclohexanes and hexanes on polyethylene glycol 20,000 (at several temperatures) and on Apiezon M (at 206°), the substituents being H, CH₃, C₂H₅, F, Cl, Br, I, OCH₃, CN and NO₂. The $\Delta\Delta\log V_N$ values were correlated with Hammett-type substituent constants using a three-parameter regression equation. The precision of the regressions was generally comparable to the experimental precision. The correlations provide information on the mechanism of the interaction between solutes and stationary phases. An interpretation of the effect of sample size on V_N is given.

INTRODUCTION

Many investigators have studied the partition coefficients of solutes in two-phase systems, with the aim of discovering factors that influence partition behaviour. Leo *et al.*¹ showed that interest in liquid-liquid partition coefficients can be found in many fields of science, in particular the field of structure-activity relationships in biological processes. They did not stress the importance of a knowledge of partition behaviour for separation science. However, with the realization that partition coefficients are directly related to retention behaviour in partition chromatography, the scope of the application of an insight into partition behaviour becomes even wider.

Ever since the introduction of gas chromatography by James and Martin in 1952², scientists have searched for factors that influence the distribution of a solute between the gas phase and a liquid phase (solvent, stationary phase). The ultimate aim of their efforts was the prediction of retention volumes, which on the one hand would facilitate the identification of compounds on the basis of their experimental retention volume, and on the other would help in choosing optimal conditions for separation problems.

In gas chromatography, partition coefficients are mostly expressed in terms

of $\Delta\mu^0$, the standard chemical potential difference for vaporization of a solute from the liquid phase, or in well known quantities that are linearly related to $\Delta\mu^0$ such as $\log V_N$ (where V_N is the net retention volume), or the Kováts retention index, I (refs. 3-6). An underlying common feature of many studies on partition equilibria is the concept that the solute is thought to consist of several groups, each of which gives an additive contribution (or group increment) to $\Delta\mu^0$ or I values^{7,8}. An early test of the validity of this concept was the observation that a plot of $\Delta\mu^0$ values for a homologous series of solutes against the number of carbon atoms is linear^{3,4}. These $\Delta\mu^0$ values are said to be composed of methylene group increments. In general, however, this system of additive group contributions does not give precise predictions of $\Delta\mu^0$ values^{7,8}, because the effect on partition behaviour of one group in the solute is influenced by other groups (or substituents). In this work, attention is focused upon such substituent interactions in the solute.

THEORETICAL

Quantitative measures that represent the effect of substituent interactions in the solute on partition equilibria can be derived from partition coefficients in the following way^{9,10}. Consider the phase equilibrium XNY (phase 1) \rightleftharpoons XNY (phase 2), where X is a variable substituent, Y is a fixed substituent, and N is a common carbon skeleton (aliphatic or aromatic). For the partition coefficient, P_X , it holds that

$$2.3 RT \log P_X = \mu_{XNY}^0 \text{ (phase 1)} - \mu_{XNY}^0 \text{ (phase 2)} = \Delta\mu_{XNY}^0 \quad (1)$$

where μ^0 is the standard chemical potential. Subtraction of the corresponding equation for the case when $X = H$ (hydrogen) gives

$$\log P_X - \log P_H = \frac{1}{2.3 RT} \cdot (\Delta\mu_{XNY}^0 - \Delta\mu_{HNY}^0) \quad (2)$$

For the partition coefficient of XNZ for the same phases, where Z is another fixed substituent (and may even be hydrogen), a similar equation holds, and subtraction of this equation from eqn. 2 gives

$$\log \left[\frac{P_{X(Y)}}{P_{X(Z)}} \right] - \log \left[\frac{P_{H(Y)}}{P_{H(Z)}} \right] = \frac{1}{2.3 RT} \cdot (\Delta\mu_{XNY}^0 - \Delta\mu_{HNY}^0 - \Delta\mu_{XNZ}^0 + \Delta\mu_{HNZ}^0) \quad (3)$$

Now, consider $\Delta\mu^0$ to be composed of additive group contributions and an interaction contribution, *e.g.*, for $\Delta\mu_{XNY}^0$ we have $\Delta\mu_X^0$, $\Delta\mu_N^0$, $\Delta\mu_Y^0$ and $\Delta\mu_{X \leftrightarrow Y}^0$, and let hydrogen be the reference atom for all interaction contributions: $\Delta\mu_{X \leftrightarrow H}^0 = 0$. If these assumptions are applied to eqn. 3, the result is

$$\log \left[\frac{P_{X(Y)}}{P_{X(Z)}} \right] - \log \left[\frac{P_{H(Y)}}{P_{H(Z)}} \right] = \frac{1}{2.3 RT} \cdot (\Delta\mu_{X \leftrightarrow Y}^0 - \Delta\mu_{X \leftrightarrow Z}^0) \quad (4)$$

If $Z = H$, eqn. 4 reduces to

$$\log \left[\frac{P_{X(Y)}}{P_{X(H)}} \right] - \log \left[\frac{P_{H(Y)}}{P_{H(H)}} \right] = \frac{1}{2.3 RT} \cdot \Delta\mu_{X \leftrightarrow Y}^0 \quad (5)$$

Any interaction contributions of the substituents X, Y or Z and the skeleton N cancel out in eqn. 3, if the skeleton of the molecules XNY and of the reference molecules XNZ is the same. The left-hand side of eqn. 5 is therefore a quantitative measure of the effect of the interaction of the substituents X and Y on the partition of a compound XNY between two phases. In a recent paper by De Ligny *et al.*¹⁰, it is shown that a Hammett-type relationship should be applicable in the description of partition coefficients. It is demonstrated that a quantity can be derived from chemical equilibrium constants that is formally identical with the right-hand side of eqn. 3. Therefore, descriptions of substituent effects in chemical equilibria, *i.e.*, descriptions with Hammett-type σ constants, should also be applicable to the left-hand side of eqn. 3, which is derived from partition coefficients.

About 10 years ago, Karger and co-workers^{11,12} presented an approach to the interpretation of substituent effects in gas-liquid partition equilibria that differs from the approach represented by eqns. 3-5. They transformed $\Delta\mu^0$ values into activity coefficients, γ , with the equation^{3,5,6}

$$\Delta\mu_0^0 = RT\ln\gamma = \Delta\mu^0 + RT\ln P^0 \quad (6)$$

In this equation $\Delta\mu^0$ is the standard chemical potential difference for vaporization of the solute from the solvent and P^0 represents the saturation vapour pressure of the solute at the temperature T at which the $\Delta\mu^0$ value is obtained; R is the gas constant and the quantity $-\Delta\mu_0^0$ is the standard chemical potential difference for mixing of the pure solute with the solvent.

One cannot hope that addition of $\Delta\mu^0$ and $RT\ln P^0$, resulting in $\Delta\mu_0^0$, will give information about the interactions between the solute and the solvent *only*. The $\Delta\mu_0^0$ values contain contributions originating from interactions in the pure liquid solutes. For different solutes the latter contributions can be very variable, especially if the solutes differ greatly in dipole moments and hydrogen bonding capabilities. Therefore, it is to be expected that $\Delta\mu_0^0$ values for polar systems are very complex quantities which are not easily interpretable*. Karger and co-workers^{11,12} calculated $\Delta\mu_0^0$ values for a number of substituted anilines and phenols, and a variety of liquid phases, from gas chromatographic retention data. Their results show that $\Delta\mu_0^0$ values in general do not correlate well with Hammett substituent constants**.

In the approach given by eqns. 3-5, all $\Delta\mu^0$ values are referred to two fixed standard states, *viz.*, ideal solutions in a fixed liquid phase (phase 1) and in the gas phase (phase 2). In this paper, it will be shown that the left-hand sides of eqns. 3-5 for gas-liquid partition coefficients can be interpreted well with Hammett-type substituent constants. The failure of Karger and co-workers and their followers¹³ to achieve a similar aim with the $\Delta\mu_0^0$ values must be the result of the use of a varying standard state (the various pure liquid solutes).

* In 1965, James *et al.*⁹ warned of the "thermodynamic pitfalls" in approaches that combine data derived from two different standard states, *viz.*, ideal solutions of the solute in a solvent and the pure liquid solute.

** In ref. 12, Karger *et al.* were reasonably satisfied with the results of the regression calculations. However, the relatively large intercepts in the Hammett plots indicate a poor description for the unsubstituted compound. (Karger *et al.* did not give standard deviations of the regressions.) Fig. 1 in ref. 11 is also a good illustration of the failure to describe $\Delta\mu_0^0$ values with Hammett σ values.

In this work, we have tested the validity of the equation

$$\log (V_N^{\text{XNY}}/V_N^{\text{HNY}}) - \log (V_N^{\text{XNZ}}/V_N^{\text{HNZ}}) = \rho_I \sigma_I + \rho_R \sigma_R + \rho_E \sigma_E \quad (7)$$

In this equation, the gas chromatographic corrected net retention volumes, V_N , in millilitres per gram of stationary phase, are related to the liquid-gas partition coefficients, P , on the molar scale, by

$$V_N = P/d \quad (8)$$

where d is the density of the stationary phase. Therefore, the left-hand side of eqn. 7 is equal to the left-hand side of eqn. 3.

The right-hand side of eqn. 7 is an extension of Hammett's $\rho\sigma$ relationship (see the Appendix and refs. 14 and 15). Values of ρ can be found by linear regression of the experimental data (*i.e.*, the left-hand side of eqn. 7) on the σ_I , σ_R and σ_E values, tabulated in Table XII and refs. 14 and 15.

For liquid-liquid partition coefficients, a description analogous to eqn. 7 was shown to be successful by Fujita *et al.*¹⁶. For the gas-liquid partition equilibrium no similar approach could be found, except for the work of Keiko *et al.*¹⁷. Moreover, suitable sets of precise experimental data to test eqn. 7 are not available. [Eqn. 7 is applied to the data of West and Hall¹⁸ for substituted chlorobenzenes in the last part of this paper, but the number of data (or substituents X) is rather small. Also, in principle the data in ref. 10 can be used, but the model system shows unexpected effects, *viz.*, apparent mesomeric resonance effects in an aliphatic system.]

In this investigation, V_N values were determined for six series of volatile compounds (solutes): *ortho*-, *meta*- and *para*-substituted anilines, phenols and pyridines, and 1-monosubstituted *n*-hexanes, cyclohexanes and benzenes. The latter three series are intended as reference series, *viz.*, as the compounds XNZ in eqn. 7, while the former three series correspond to the compounds XNY of eqn. 7 (Y is NH₂, OH and the pyridine nitrogen atom, respectively, and Z = H). The set of substituents (X) not only included mesomeric electron donors such as CH₃, C₂H₅, F, Cl, Br, I and OCH₃, but also the mesomeric acceptors CN and NO₂. The inclusion of the last two substituents caused some practical difficulties, which will be discussed later. Polyethylene glycol (PEG) 20,000 and Apiezon M were chosen as examples of polar and apolar stationary phases (solvents), respectively. On PEG, retention volumes were determined at several temperatures, partly with the aim of investigating the effect of temperature on substituent interactions, but mainly for the following practical reason: the extreme difference in the polarities of, *e.g.*, *n*-hexane and *p*-nitrophenol has the consequence that at the highest temperature (103°C) at which the retention time of *n*-hexane (5 sec) can be determined with acceptable precision, the elution of *p*-nitrophenol would require at least 48 h. Therefore, not all solutes could be chromatographed at the same standard temperature (206°C). For a number of solutes the retention volume at 206°C had to be estimated from data at other temperatures.

On Apiezon M, data for all solutes could be determined at 206°C. No measurements at other temperatures were made, partly because it was expected that no fundamentally new information could be extracted from such data, and partly because of the practical difficulties in the measuring procedure.

EXPERIMENTAL

Chemicals

Apiezon M was supplied by Apiezon Products (London, Great Britain) and PEG 20,000 by Fluka (Buchs, Switzerland). Gas-Chrom Z, 60–80 mesh (Applied Science Labs., State College, Pa., U.S.A.), was used as the support to minimize adsorption. The solutes that were supplied commercially (Fluka), were of the highest purity available. Most of them were stored in black-painted bottles but nevertheless some (especially the anilines) turned brown after a few weeks, probably owing to the formation of small amounts of oxidized products. Some solutes were of unknown origin and purity. We did not purify these compounds because gas chromatographic measurements showed the amounts of the impurities to be less than 5%, and because the peaks of the impurities did not interfere with the peak of the major component. However, the presumably oxidizing nature of the brown impurities (see ref. 19, p. 564) may have affected the stationary phase, as will be discussed below.

Cyclohexyl methyl ether and *n*-hexyl methyl ether were synthesized by standard procedures¹⁹. 4-Nitropyridine was obtained by reducing 4-nitropyridine N-oxide according to the method of Ochiai²⁰. Solutions of 4-chloropyridine in benzene were prepared by extraction of a neutralized solution of 4-chloropyridinium chloride, shortly before the gas chromatographic measurement. The same procedure was tried for 4-bromopyridine, but this compound proved to be very unstable; no peak for this solute could be found in the chromatograms.

Apparatus and procedure

The apparatus employed was manufactured by Becker (Delft, The Netherlands). The temperature at the position of the column in the air thermostat was measured with Anschütz thermometers and was estimated to be accurate to within $\pm 0.3^\circ\text{C}$. Helium was used as the carrier gas. The pressure drop across the column was measured with a calibrated manometer to 1 mmHg. The outlet pressure was equal to the barometric pressure. The carrier gas velocity was measured with a calibrated soap-film flow meter. The eluted substances were detected by a katharometer placed in the thermostat (bridge current 150 mA) and registered with a Servogor recorder, the chart speed of which was calibrated.

Stainless-steel columns (length 200 or 100 cm, I.D. 4 mm) were used. The Gas-Chrom Z support was coated with 10% PEG 20,000 or Apiezon M*. The columns were conditioned at 250°C for 16 h. The samples were injected directly on to the column with a Hamilton syringe. For the PEG column, and with toluene and propanol-1 as solutes, the minimal HETPs were 1.5 and 1.8 mm, respectively, at the start of the measurements (at 100°C). For the Apiezon columns, with both phenol and *n*-decane as solutes, the minimal HETP was mostly 2.0 mm (at 206°C). The corresponding carrier gas velocities were $30\text{ ml}\cdot\text{min}^{-1}$ for PEG and $16\text{--}20\text{ ml}\cdot\text{min}^{-1}$ for Apiezon.

All liquid compounds were injected as such; solid compounds were mostly

* The coating percentage was determined by weighing a dried sample of the column filling before and after extraction with ethanol (PEG) or *n*-hexane (Apiezon). A correction for loss of stationary phase during conditioning was made by weighing the column before and after conditioning.

dissolved in methylene chloride to near saturation. Compounds that were insoluble in that solvent (*e.g.*, nitrophenols and nitroanilines) were dissolved in ethanol. However, the concentration in these solutions was sometimes still so low that the sample size had to be as large as 10 μl . The V_N values (corrected net retention volumes, in millilitres of carrier gas under column conditions per gram of stationary phase) were calculated from the gas chromatograms and the experimental data mentioned above.

The position of the peak maximum in the chromatograms depended greatly on the injection volume. Therefore, the following procedure was maintained. For each solute, a number of five to ten chromatograms with varying sample sizes was obtained. Then the V_N values were plotted against the corresponding sample sizes, which resulted in straight lines. From extrapolation to zero sample size by the method of least squares, the correct V_N value was calculated. The points for small sample sizes often showed positive deviations from the straight lines, probably originating from adsorption of the solute to the support, and were therefore omitted from the calculation. On PEG, linear plots were obtained for the liquid compounds *o*-toluidine and *m*-fluorophenol at 206°C for sample sizes varying from 0.3 to 5 μl .

The PEG column showed a serious loss of stationary phase (bleeding) at 165.5°C and higher temperatures (the advised maximal temperature is 225°C). Therefore, from the start of the measurements and at regular intervals thereafter, the retention volume of a reference solute was measured. The resulting plot of retention volume against effective measuring time (in days) was used to correct all other retention volumes for the effect of bleeding. It is well known that PEG is very sensitive to oxidation²¹. Therefore, the bleeding may be caused partly by the oxidizing impurities in some solutes. Also, the use of air as the dead-volume marker may have contributed to oxidation and bleeding. No change in the polarity of PEG could be detected. This was checked by measuring at various times replicate V_N values for a number of randomly chosen solutes of both polar and apolar character (at 206°C, 17 were chosen). The agreement between such replicate V_N values (relative to that of the reference solute) was generally within 1%, even after the column had been used for 18 months.

The bleeding of the column had some effect on the choice of sample sizes. At the start of the measurements no adsorption of the solutes at the support could be detected for samples larger than 0.2 μl . The range of sample sizes was then mostly 0.2–1.4 μl for a liquid solute and about 0.5–2.5 μl for solid solutes dissolved in methylene chloride. However, with increasing loss of stationary phase, adsorption became evident with larger sample sizes. Therefore, in the end, samples had to be used in the range 0.8–2.0 μl for liquid solutes and 2–5 μl for solid solutes in methylene chloride.

No bleeding of the Apiezon column could be detected, but it did show a change in polarity. After the column had been used for some time, apolar solutes (*e.g.*, octane, benzene and ethylbenzene) showed decreases in the V_N values of about 10%, while polar solutes (*e.g.*, *o*-bromophenol, *m*-fluoroaniline and *p*-methoxyphenol) showed increases varying from 5 to 12%. Apparently, the Apiezon had become more polar, either because the brown impurities of some solutes had accumulated in the column, or because these impurities (or some solutes) had oxidized part of the Apiezon. To avoid errors due to a change in the polarity of the column, the following procedure was adopted. During the measurements, V_N values of the reference solutes

octane and phenol were measured very frequently. As soon as these values tended to decrease (octane) or increase (phenol) by more than about 1.5%, measurements on that column were stopped and a new Apiezon column was prepared. The V_N values of most of the colourless solutes were determined first. The 2-m Apiezon column employed showed no significant alteration during these measurements. Thereafter, for the sake of convenience, measurements were performed on 1-m columns, using the reference solutes *m*-fluorophenol, iodocyclohexane and octane (in total, six columns were used and V_N for octane was determined about 70 times). The sample sizes were of the same magnitude as for the PEG column.

RESULTS AND DISCUSSION

The results of the measurements are presented as $\log V_N$ values in Tables I–III.

The precision of the V_N values (relative standard deviation) for the PEG column for most solutes is about $\pm 1.5\%$, as estimated from replicate measurements and from the standard deviation of the regression of V_N on sample size. For *m*- and *p*-nitro- and -cyano-phenols and -anilines, the precision is less (about $\pm 3\%$), as these compounds showed extremely long retention times, during which experimental conditions such as pressure drop or carrier gas velocity may change slightly (at 206°C, *p*-nitrophenol had a retention time of about 4 h). An indication of the accuracy of the relative retention data for the PEG column is given by a plot of $\Delta \log V_N$ values for some phenols at 165.5°C ($\Delta \log V_N = \log V_N^{\text{XNY}} - \log V_N^{\text{HNY}}$) versus the corresponding values of Elmehrik²², measured at 168°C*. The result, for 10 phenols, is

$$\Delta \log V_N (\text{Elmehrik}) = (0.955 \pm 0.014) \Delta \log V_N (\text{this work}) + (0.009 \pm 0.006) \quad (9)$$

The standard deviation of the regression is ± 0.011 . This corresponds to an error of $\pm 1.8\%$ in the V_N values, which is in good agreement with our earlier estimate.

For Apiezon, the precision of the V_N values ($\pm 2\%$) could be estimated in the same way as for PEG, and from the fluctuations in the V_N values for the reference solutes. For the substituted benzenes, there is an excellent correlation between the retention indices, given by Cook and Raushel⁷ for Apiezon L at 160°C, and the $\log V_N$ values obtained in this work.

An aspect of the measuring procedure that remains to be discussed is the dependence of the position of the peak maximum on the injection volume. This effect is frequently encountered in gas chromatography and can often be recognized by the shape of the peaks. An asymmetric peak with its steep side directed towards the injection point marker in the chromatogram (tailing) indicates that with increasing sample size the distance between the peak maximum and the injection point marker will decrease, resulting in a negative correlation between V_N and the sample size, and *vice versa*. In this study, both negative and positive correlations were found,

* Elmehrik²² used Carbowax 2000; however, no significant difference in the $\Delta \log V_N$ values measured on Carbowax 2000 and on PEG 20,000 is expected.

TABLE I
VALUES OF LOG V_N (V_N IN $\text{ml} \cdot \text{g}^{-1}$) FOR ANILINES, PHENOLS AND PYRIDINES ON PEG 20,000 AT DIFFERENT COLUMN TEMPERATURES

The values in parentheses were calculated as described in the text (eqn. 13).

Substituents	No.	Anilines			Phenols			Pyridines		
		165.5 °C	206 °C	231 °C	165.5 °C	206 °C	231 °C	130 °C	165.5 °C	206 °C
Ortho:										
H		2.490	2.017	1.770	2.870	2.314	2.030	1.940	1.623	1.297
CH ₃	1	2.573	2.089	1.830	2.862	2.302			1.656	1.310
C ₂ H ₅	2	2.662	2.162		2.973	2.388			1.746	1.399
F	3	2.987	1.922		2.492	2.005		2.008	1.656	1.328
Cl	4	2.798	2.277		2.628	2.115			2.128	1.738
Br	5	3.003	2.472		2.825	2.285			2.385	1.956
I	6	3.289	2.707		3.242	2.624				
OCH ₃	7	2.830	2.292		2.650	2.164		2.116	1.745	((1.407))
CN	8	((3.515))	2.865	2.536	((3.781))	3.087	2.739		2.764	2.282
NO ₂	9	((3.795))	3.116	2.787	((2.654))	2.175	1.940			
Meta:										
CH ₃		2.640	2.140		3.005	2.420			1.807	1.448
C ₂ H ₅		2.778	2.256		3.146	2.549			1.953	1.568
F		2.699	2.181		3.074	2.473				
Cl		3.176	2.586		3.551	2.887			1.890	1.534
Br		3.426	2.801		3.796	3.106			2.138	1.746
I		3.709	3.041		4.089	3.350			2.460	2.020
OCH ₃		3.204	2.605		3.562	2.879				
CN		((3.928))	3.208	2.848	((4.341))	3.550	3.157		2.480	2.050
NO ₂		((4.190))	3.439	3.074	((4.604))	3.770	3.359			
Para:										
CH ₃		2.596	2.112		2.997	2.418		2.177	1.792	1.457
C ₂ H ₅		2.742	2.228		3.140	2.542			1.942	1.584
F		2.611	2.097		3.026	2.439				
Cl		3.174	2.574		3.555	2.884				
Br		3.422	2.789		3.798	3.097			1.879	1.539
I		3.719	3.046		4.111	3.349	2.981			
OCH ₃		3.078	2.504		3.498	2.830				
CN		((4.239))	3.488	3.128	((4.524))	3.717	3.327		2.365	1.964
NO ₂		((4.668))	3.862	3.490	((4.836))	3.984	3.577		2.511	2.082

TABLE II

VALUES OF LOG V_N FOR BENZENES, CYCLOHEXANES AND HEXANES ON PEG 20,000 AT DIFFERENT COLUMN TEMPERATURES

The values in parentheses were calculated as described in the text (eqn. 13).

Class of compound	Substituent	Column temperature (°C)					231
		75	103	130	165.5	206	
Benzenes	H	1.979	1.643	1.385	1.143	(0.913)	
	CH ₃		1.893	1.603	1.331	1.064	
	C ₂ H ₅		2.107	1.787	1.460	1.182	
	F		1.740	1.449	1.209	0.942	
	Cl		2.314	1.984	1.638	1.336	
	Br		2.629	2.265	1.879	1.539	
	I				2.166	1.791	
	OCH ₃		2.614	2.223	1.832	1.485	
	CN				2.309	1.891	
	NO ₂				2.522	2.070	1.847
Cyclohexanes	H	1.350	1.099	0.904		(0.562)	
	CH ₃	1.479	1.214	1.029		(0.667)	
	C ₂ H ₅	1.841	1.523	1.259		(0.807)	
	Cl		2.153	1.839	1.524	1.248	
	Br		2.447	2.111	1.753	1.456	
	I			((2.366))	1.973	1.635	
	OCH ₃		1.921	1.621	1.334	1.089	
	CN			((2.515))	2.097	1.738	
	NO ₂			((2.782))	2.307	1.893	
1-X- <i>n</i> -Hexanes	H	0.960	0.713	((0.500))			
	CH ₃	1.231	0.969	((0.818))			
	C ₂ H ₅	1.526	1.214	0.963			
	F	1.635	1.336	1.091			
	Cl		1.885	1.570	1.280		
	Br		2.172	1.831	1.493	1.200	
	I			((2.074))	1.713	1.386	
	OCH ₃		1.613	1.338	1.074	0.836	
	CN			((2.317))	1.916	1.556	
	NO ₂			((2.514))	2.069	1.660	

and on PEG the correlation even changed sign for one particular solute as the column temperature increased.

In the following discussion, the quantity $dV_N/V_N dV_S$ is defined as the relative change in net retention volume per microlitre of sample size (V_N in the denominator of this quantity is the value found from extrapolation to zero sample size). A correlation was found between $dV_N/V_N dV_S$ (measured at a fixed temperature) and the boiling points (T_b)* of the solutes¹⁰. The parameters a and b of the equation

$$T_b = adV_N/V_N dV_S + b \quad (10)$$

are given in Table IV.

* The boiling points (°C) at atmospheric pressure were obtained from refs. 23 and 24.

TABLE III
VALUES OF LOG V_N ON APIEZON M AT 206 °C

Substituent	Substituted anilines				Substituted phenols				Substituted pyridines				Substituted benzenes	Substituted cyclohexanes	1-X-n-Hexanes	
	2-	3-	4-	4-	2-	3-	4-	4-	2-	3-	4-	4-				
H																
CH ₃	1.783	1.776	1.766	1.644	1.684	1.437							1.004	1.027	0.798	
C ₂ H ₅	1.928	1.937	1.935	1.805	1.844	1.684	1.654	1.368	1.366	1.265	1.368	1.368	1.221	1.166	0.995	
F	1.488	1.571	1.557	1.292	1.460	1.458	1.833	1.562	1.551	1.433	1.562	1.562	1.402	1.381	1.187	
Cl	1.902	2.007	2.002	1.644	1.906	1.883	1.458	1.441	1.454	1.078	1.441	1.441	0.971	1.496	0.916	
Br	2.097	2.206	2.210	1.845	2.091	2.082	1.883	1.667	1.667	1.523	1.667	1.667	1.607	1.694	1.318	
I	2.348	2.460	2.483	2.112	2.357	2.344	1.737	1.934	1.934	1.737	1.934	1.934	1.862	1.930	1.747	
OCH ₃	1.926	2.039	2.006	1.761	1.926	1.918	1.670	1.512	1.571	1.670	1.512	1.512	1.470	1.379	1.198	
CN	2.064	2.222	2.336	1.819	2.101	2.206	1.670	1.724	1.571	1.670	1.512	1.512	1.560	1.610	1.445	
NO ₂	2.364	2.467	2.671	1.930	2.341	2.469	1.670	1.724	1.571	1.670	1.512	1.512	1.804	1.802	1.592	

TABLE IV

RESULTS OF THE ANALYSES OF THE REGRESSIONS OF BOILING POINTS ON $dV_N/V_N dV_S$ (EQN. 10)

Column	a (°C· μ l)	b (°C)	$T^{**} + 16$ (°C)	S^{***} (°C)	n^{\dagger}	Solute types included ^{§§}
PEG						
(2 m)	409 ± 49*	94.9 ± 2.4*	91	6.8	8	H ₄ , C ₃ , B ₁
	555 ± 50	120.8 ± 2.0	119	8.7	19	H ₅ , C ₆ , B ₇
	570 ± 32	141.5 ± 1.6	146	6.2	21	H ₄ , C ₆ , B ₇ , Py ₄
	532 ± 19	180.5 ± 1.5	181.5	6.3	34	H ₆ , C ₅ , B ₁₀ , Py ₁₃
	672 ± 47	198.8 ± 2.8	181.5	18.6	61	H ₆ , C ₅ , B ₁₀ , Py ₁₃ , An ₁₅ , Ph ₁₂
	534 ± 21	225.6 ± 2.3	222	9.7	55	H ₅ , C ₅ , B ₉ , Py ₁₂ , An ₁₂ , Ph ₁₂
Apiezon						
(2 m)	848 ± 26	202.7 ± 2.0	222	7.3	43	H ₁₀ , C ₈ , B ₁₀ , Py ₁₁ , An ₁ , Ph ₃
Apiezon						
(1 m)	564 ± 28	217.3 ± 1.7	222	7.1	25	H ₃ , B ₁ , An ₁₃ , Ph ₈

* Standard deviation.

** Column temperature.

*** Standard deviation of the regression.

† Total number of data (solutes) used in the correlation.

§§ H = hexanes; C = cyclohexanes; B = benzenes; Py = pyridines; An = anilines; Ph = phenols; the numbers refer to the number of data for each type of solute.

From these results, it can be deduced that, except for the 2-m Apiezon column, eqn. 10 can be reformulated as follows:

$$dV_N/V_N dV_S = (T_b - T - 16)/a \quad (11)$$

where T is the column temperature. From eqn. 11, and using $a = 560^\circ\text{C}\cdot\mu\text{l}$, one finds that a solute with a boiling point 40°C below T will have a $dV_N/V_N dV_S$ value of -0.1 , which means a decrease in V_N of 10% per microlitre of sample size.

From the data for the Apiezon columns in Table IV, it is clear that the column length also has an effect upon the $dV_N/V_N dV_S$ values. This may be essentially the effect of the amount of stationary phase, N_s , in the columns on the factor $1/V_N$ in $dV_N/V_N dV_S$ (V_N is a linear function of N_s). This interpretation is supported by the following observation. As the PEG column gradually lost its stationary phase, the $dV_N/V_N dV_S$ values increased. Therefore, the a and b values (eqn. 10) for the PEG column were calculated after the $dV_N/V_N dV_S$ values had been corrected for this effect (the $dV_N/V_N dV_S$ values used in the correlations were corrected to a time when the column contained 0.47 g of PEG).

In Table IV, two entries at $T = 165.5^\circ\text{C}$ appear. In the second entry, data for the phenols and anilines are included, whereas they are omitted from the first entry. From the standard deviations (Table IV, fifth column), it can be concluded that the $dV_N/V_N dV_S$ values for anilines and phenols at 165.5°C cannot be described well by eqn. 10. A plot of $dV_N/V_N dV_S$ against T_b revealed that most points for anilines and phenols were scattered below the straight line through the points for the other solutes. At 206°C this anomaly had disappeared.

A dependence of V_N on sample size was observed earlier by Martire and Riedl²⁵, who explained the effect by assuming non-linear partition isotherms in the

systems involved. However, this explanation appears to be unlikely: in view of the diversity of the solutes, the large range of column temperatures and the difference in character of the two stationary phases, it cannot be expected that there would be a relationship between the curvature of the partition isotherm and $T_b - T$. The results presented here point to the following (tentative) interpretation.

In general, the dependence of V_N on sample size is not an effect related to partition behaviour, but a result of vaporization phenomena directly after injection of the sample. Positive $dV_N/V_N dV_S$ values ($T_b > T$) are a result of slow warming and slow vaporization of the samples. Negative $dV_N/V_N dV_S$ values ($T_b < T$) are caused by rapid evaporation of the samples, leading to a temporary increase in inlet pressure and thus to an increase in vapour velocity. This higher vapour velocity could be observed in the chromatograms; using solutes with $T_b < T$, the distance between the injection point marker and air-peak maximum (dead-volume marker) was a linear function of the sample size with negative slope. For example, injection of cyclohexane ($T_b/81.4^\circ\text{C}$) at 103°C gave a temporary increase in vapour velocity of about $1\% \cdot \mu\text{l}^{-1}$.

Correlation of gas chromatographic data with substituent constants

The aim of this investigation was to test the validity of eqn. 7. The compounds denoted by XNY are substituted anilines, phenols or pyridines. As an abbreviation for the first term of eqn. 7, $\Delta\log V_N^{\text{An}}$, $\Delta\log V_N^{\text{Ph}}$ or $\Delta\log V_N^{\text{Py}}$ is used. The compounds denoted by XNZ are substituted hexanes, cyclohexanes or benzenes. As an abbreviation for the second term of eqn. 7, $\Delta\log V_N^{\text{H}}$, $\Delta\log V_N^{\text{C}}$ or $\Delta\log V_N^{\text{B}}$ is used. The left-hand side of eqn. 7 is represented by $\Delta\Delta\log V_N^{\text{An,H}}$, $\Delta\Delta\log V_N^{\text{Ph,C}}$, etc.

To test the validity of eqn. 7 at, e.g., a column temperature of 206°C , data on V_N must be available for all compounds in the left-hand side. For the reference compound benzene, the value of $\log V_N^{\text{H,NH}}$ could not be measured at 206°C on the PEG 20,000 column. Therefore, before eqn. 7 can be tested, this value must be calculated, by the extrapolation of data measured at lower temperatures.

In general, estimates of V_N values for a column temperatures other than the investigated temperature T are obtained from the following equation:

$$\log V_N - \log RT/M_S = \Delta\bar{H}^0/2.3RT - \Delta S^0/2.3R \quad (12)$$

where M_S is the molecular weight of the stationary phase, R is the gas constant and $\Delta\bar{H}^0$ and ΔS^0 are the standard partial molar enthalpy and entropy of vaporization, respectively, on the molar fraction scale. This equation can be used only if a plot of $\log V_N - \log T$ versus $1/T$ is linear. In the present case such plots, using the experimental $\log V_N$ values given in Tables I and II, are slightly curved. As the number of temperatures at which measurements were made is too small to justify the use of a quadratic regression equation, another approach to the description of the $\log V_N$ values must be applied. As the $\log V_N$ values at different temperatures, T (or of different compounds, C), are strongly correlated, the method of factor analysis was chosen. Thus, the following equation was applied:

$$\log V_{N(T,C)} = V_{1,T}W_{1,C} + V_{2,T}W_{2,C} \quad (13)$$

where V and W are adjustable parameters, depending only on the temperature and

TABLE V
VALUES OF W FOR USE IN EQN. 13

Compound	W_1	W_2	Compound	W_1	W_2
Anilines:			Cyclohexanes:		
H	7.281	0.007	H	2.212	-0.118
2-CH ₃	7.527	0.010	CH ₃	2.489	-0.049
Phenols:			C ₂ H ₅	3.074	-0.103
H	8.399	-0.012	Cl	4.436	0.046
4-I	11.947	0.120	Br	5.070	0.121
Pyridines:			OCH ₃	3.930	-0.011
H	4.706	0.002	1-X-n-Hexanes:		
2-F	4.863	-0.038	C ₂ H ₅	2.391	-0.258
4-CH ₃	5.251	0.009	F	2.677	-0.149
Benzenes:			Cl	3.822	-0.123
H	3.360	-0.039	Br	4.432	-0.068
CH ₃	3.883	-0.015	OCH ₃	3.254	-0.153
C ₂ H ₅	4.314	-0.032			
F	3.542	-0.077			
Cl	4.773	0.041			
Br	5.440	0.089			
OCH ₃	5.368	0.000			
NO ₂	7.314	0.109			

the compound under consideration, respectively. A selection of compounds for which experimental data are available in Tables I and II at three or more temperatures was made. The data on $\log V_N$ for these compounds were arranged as an (incomplete) data matrix of dimensions 6 (number of temperatures) by 26 (number of compounds). The optimal values of V_1 , V_2 , W_1 and W_2 were calculated by the program NEW-FAC^{14,15,26}. These values were substituted in eqn. 13 to calculate missing values of $\log V_N$ (the values within single parentheses in Table II). To the completed data matrix, factor analysis was applied. Values of W_1 and W_2 resulting from the factor analysis are presented in Table V. Values of V_1 and V_2 found as the regression coefficients of the regression of $\log V_N$ on W_1 and W_2 are presented in Table VI.

TABLE VI

REGRESSION COEFFICIENTS, V , AND STANDARD DEVIATIONS FOR THE REGRESSION OF $\log V_N$ ON W_1 AND W_2 (EQN. 13)

T (°C)	V_1	$S(V_1)$	V_2	$S(V_2)$	S
75	0.5829	0.0006	-0.508	0.012	0.003
103	0.4870	0.0002	-0.197	0.007	0.003
130	0.4139	0.0002	0.104	0.010	0.004
165.5	0.3418	0.0002	0.209	0.020	0.006
206	0.2765	0.0001	0.421	0.012	0.004
231	0.2425	0.0001	0.685	0.017	0.002

As can be judged from these data, the contribution V_2W_2 to $\log V_N$ (see eqn. 13) is mostly small compared with the term V_1W_1 , but still significant. From the standard deviations of the regressions (Table VI), it can be concluded that the description of the data is very satisfactory: an experimental uncertainty of $\pm 1.5\%$ in

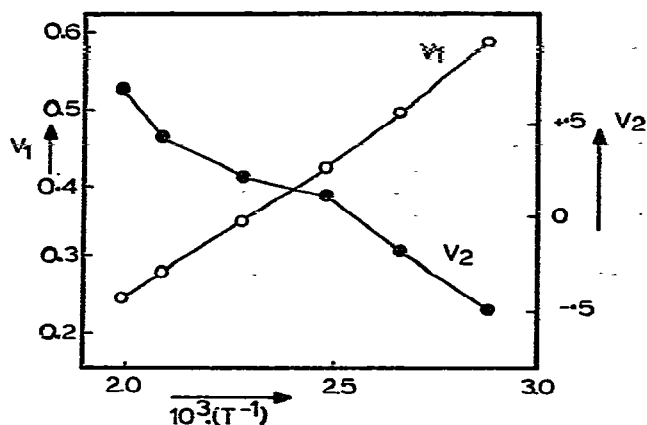


Fig. 1. Factors V_1 and V_2 (eqn. 13) as a function of T^{-1} (K^{-1}).

V_N results in an error of ± 0.006 in $\log V_N$, while the standard deviations in Table VI are between 0.002 and 0.006. V values at arbitrary temperatures can be found by interpolation in the plot of V versus $1/T$ (T measured in Kelvin, see Fig. 1).

Because the most important factor, V_1 , can be described by

$$V_1 = 1650/2.3RT - 2.2/2.3R \quad (14)$$

(from the regression analysis of V_1 on $1/T$, excluding the data at 75°C ; standard deviation of the regression = 0.005) it can be concluded that the gas-liquid partition

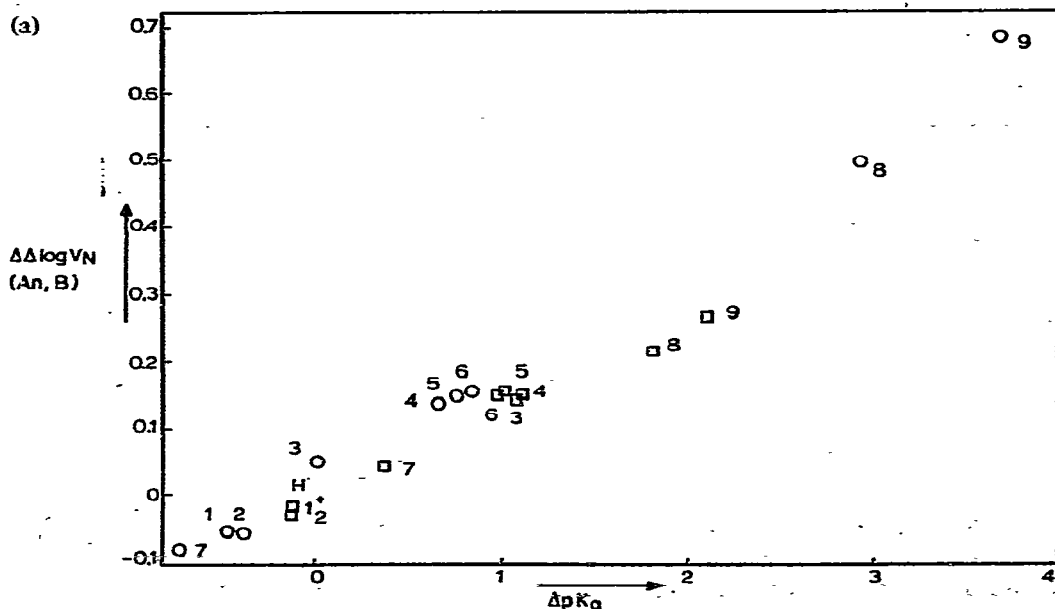


Fig. 2.

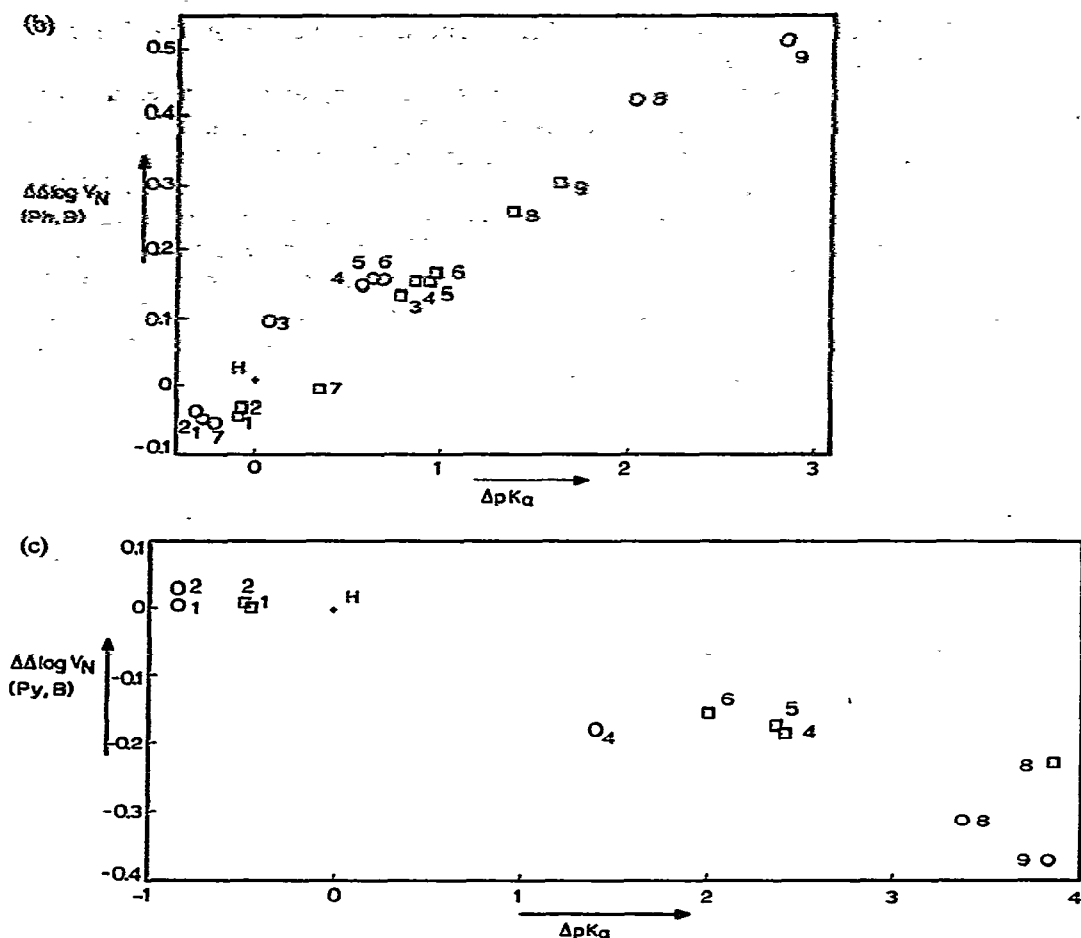


Fig. 2. (a) $\Delta\Delta\log V_N^{XNY,B}$ values on PEG 20,000 as a function of dissociation equilibrium data. The numbers correspond to the substituent numbers in Table I. The symbols \circ and \square refer to substituents in *para*- and *meta*-positions, respectively. XNY = An, $\Delta pK_a = \log(K_X/K_H)$ for the dissociation of substituted anilinium ions in water at 25 °C from refs. 27–29. (b) XNY = Ph, ΔpK_a for the dissociation of substituted phenols in water at 25 °C from refs. 29–32. (c) XNY = Py, ΔpK_a for the dissociation of substituted pyridinium ions in water at 25 °C from refs. 33–35.

on PEG is governed, to a first approximation, by a linear enthalpy–entropy relationship for all compounds.

Values of W for compounds for which experimental data are available at only two temperatures can also be calculated, using the V values in Table VI, by solving two equations such as eqn. 13 with two unknown variables, W_1 and W_2 . However, such W values are not suitable for calculations of $\log V_N$ values for a temperature very far from the experimental temperatures. A number of $\log V_N$ values calculated in this way are given within double parentheses in Tables I and II. Conclusions, based on such data, must be made with caution.

Values of $\Delta\Delta\log V_N^{An,B}$, $\Delta\Delta\log V_N^{Ph,B}$ and $\Delta\Delta\log V_N^{Py,B}$ were calculated from the data in Tables I–III. The $\Delta\Delta\log V_N$ values on PEG 20,000 are shown as a function

of the ΔpK_a values in water at 25°C in Fig. 2 and as a function of the $\Delta\Delta\log V_N$ values on Apiezon M in Fig. 3.

The $\Delta\Delta\log V_N$ values were correlated with the σ_I , σ_R and σ_E values given in Table XII by eqn. 7. The resulting regression coefficients, ρ_I , ρ_R and ρ_E , and the standard deviations of the regressions are presented in Table VII.

The standard deviations of the regressions show that the description of $\Delta\Delta\log V_N$ values by eqn. 7 is in general of a precision comparable to the experimental error in $\Delta\Delta\log V_N$: an experimental uncertainty of $\pm 1.5\%$ in V_N results in an error of ± 0.012 in $\Delta\Delta\log V_N$. Exceptions are the data for *ortho*-substituted phenols (and to a lesser extent for *ortho*-substituted anilines). However, for such data a Hammett-type description cannot be expected. For comparison, we also tested the applicability of the Taft equation, the most widely used two-parameter equation:

$$\Delta\Delta\log V_N = \rho_I\sigma_I + \rho_R\sigma_R \quad (15)$$

In the regression analyses of the $\Delta\Delta\log V_N$ values we tried all sets of σ_R parameters given by Ehrenson *et al.*³⁶, i.e., σ_R^0 , $\sigma_R(\text{BA})$, σ_R^+ and $\sigma_R^-(\text{A})$. For the data for the PEG column the lowest standard deviations of the regressions were obtained with $\sigma_R(\text{BA})$

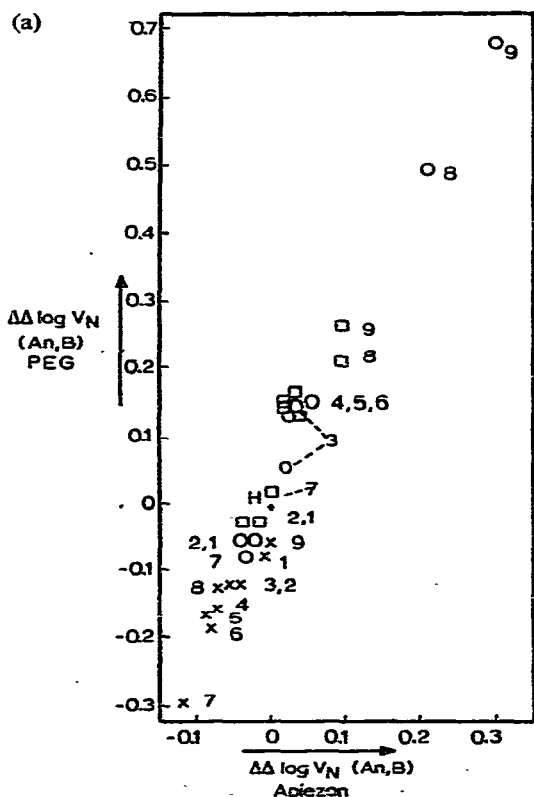


Fig. 3.

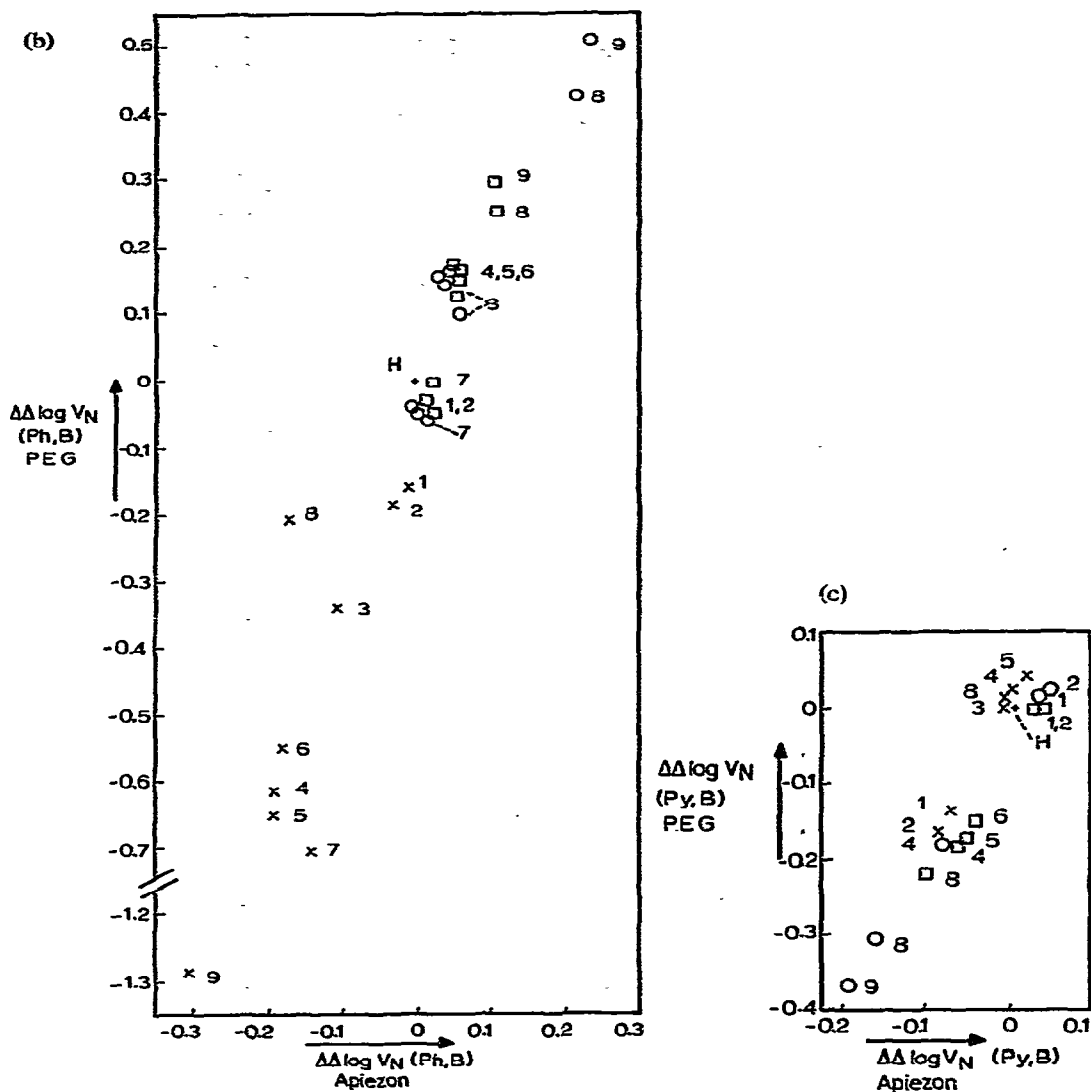


Fig. 3. (a) $\Delta\Delta \log V_N^{XNY,B}$ values on PEG 20,000 as a function of the corresponding data on Apiezon M. The numbers correspond to the substituent numbers of Table I. The symbols \circ , \square and \times refer to substituents in *para*-, *meta*- and *ortho*-positions, respectively. XNY = An. (b) XNY = Ph. (c) XNY = Py.

for *meta*-substituted series*, $\sigma_R^-(A)$ for *para*-substituted series** and σ_R^+ for *ortho*-substituted pyridines. The results of these correlations are presented in Table VIII.

In order to check whether eqn. 7 gave significantly better results than eqn.

* For the data on *meta*-substituted pyridines a distinction between different sets of σ_R values could hardly be made.

** We also tried $\sigma_R^-(P)$ values, but anomalously for the anilines we found lower standard deviations with $\sigma_R^-(P)$ values than with $\sigma_R^-(A)$ values, and for the phenols we found higher standard deviations with $\sigma_R^-(P)$ than with $\sigma_R^-(A)$. We therefore ignored the results obtained with the $\sigma_R^-(P)$ values.

TABLE VII
RESULTS OF THE ANALYSES OF THE REGRESSIONS OF $\Delta \log V_N$ ON σ_I , σ_R AND σ_E (EQN. 7)

Correlated quantity	Column temperature ($^{\circ}\text{C}$)	Position of substituents	Aptezon M														
			σ_I	$S(\sigma_I)$	σ_R	$S(\sigma_R)$	σ_E	$S(\sigma_E)$	S	ρ_I	$S(\rho_I)$	ρ_R	$S(\rho_R)$	ρ_E	$S(\rho_E)$	S	
$\Delta \log V_N^{\text{An,B}}$	165.5	2	-0.258	0.047	0.700	0.117	0.218	0.110	0.053								
		3	0.481	0.015	0.261	0.038	0.054	0.036	0.017								
		4	0.902	0.015	0.860	0.037	-0.313	0.035	0.017								
		2	-0.215	0.043	0.586	0.107	0.203	0.101	0.049	-0.094	0.023	0.202	0.058	0.034	0.055	0.027	
$\Delta \log V_N^{\text{Ph,B}}$	165.5	3	0.387	0.009	0.217	0.022	0.053	0.021	0.010	0.128	0.011	0.114	0.028	-0.010	0.026	0.013	
		4	0.753	0.018	0.719	0.044	-0.309	0.042	0.020	0.304	0.015	0.304	0.038	-0.173	0.035	0.017	
		2	-1.555	0.294	1.257	0.737	1.416	0.692	0.336								
		3	0.515	0.012	0.346	0.030	0.045	0.028	0.014								
206	206	4	0.739	0.011	0.645	0.028	-0.144	0.026	0.013								
		2	-1.277	0.246	1.000	0.617	1.126	0.580	0.281	-0.405	0.036	0.083	0.090	0.143	0.084	0.041	
		3	0.435	0.007	0.309	0.017	0.059	0.017	0.008	0.161	0.015	0.025	0.037	-0.032	0.034	0.017	
		4	0.632	0.010	0.558	0.025	-0.135	0.023	0.011	0.277	0.020	0.156	0.050	-0.160	0.047	0.023	
$\Delta \log V_N^{\text{Ph,B}}$	165.5	2	-0.052	0.040	1.229	0.066	0.962	0.076	0.029								
		3	-0.526	0.019	-0.067	0.071	0.031	0.065	0.014								
		4	-0.685	0.017	-0.041	0.076	0.238	0.057	0.015								
		2	0.001	0.020	1.057	0.033	0.827	0.038	0.015	-0.004	0.016	0.508	0.056	0.397	0.048	0.011	
206	206	3	-0.395	0.009	-0.011	0.034	-0.011	0.031	0.007	-0.155	0.013	-0.279	0.048	-0.136	0.044	0.010	
		4	-0.516	0.007	-0.157	0.031	0.099	0.024	0.006	-0.257	0.011	-0.340	0.050	-0.079	0.037	0.010	

TABLE VIII

RESULTS OF THE ANALYSES OF THE REGRESSIONS OF $\Delta\log V_N$ ON THE TAFT SUBSTITUENT CONSTANTS (EQN. 15)*

Correlated quantity	T (°C)	Position of substituents	ρ_I	S (ρ_I)	ρ_R	S (ρ_R)	S**	S***
$\Delta\log V_N^{An,B}$	165.5	3	0.474	0.019	0.156	0.028	0.021	0.019
		4	0.719	0.017	0.657	0.023	0.021	0.018
	206	3	0.380	0.011	0.122	0.016	0.012	0.011
		4	0.596	0.020	0.572	0.028	0.026	0.022
$\Delta\log V_N^{Ph,B}$	165.5	3	0.507	0.014	0.218	0.021	0.017	0.015
		4	0.609	0.015	0.449	0.021	0.019	0.011
	206	3	0.429	0.010	0.187	0.015	0.012	0.008
		4	0.519	0.010	0.393	0.013	0.012	0.011
$\Delta\log V_N^{Pr,B}$	165.5	2	0.188	0.184	0.461	0.145	0.152	0.030
		3	-0.522	0.024	-0.047	0.059	0.019	0.016
		4	-0.631	0.062	-0.175	0.097	0.047	0.017
	206	2	0.200	0.152	0.387	0.129	0.126	0.015
		3	-0.397	0.011	0.018	0.026	0.009	0.008
		4	-0.471	0.024	-0.138	0.038	0.018	0.003

* For the ρ_R parameters used in the correlations, see the text. The symbols have the same meaning as those in Table VII.

** Standard deviation of the regression (eqn. 15).

*** Standard deviation of the regression (eqn. 7). As ref. 36 gives no data on σ_I and σ_R for C_2H_5 , the experimental data on this substituent were omitted from all correlations in order to obtain a better comparison.

15, we performed *F*-tests on the standard deviations of the regressions in Table VIII, excluding the data on *ortho*-substituted pyridines*. The result was $F = 1.76$, from which it can be deduced that the three-parameter correlation (eqn. 7) is significantly better on the 95% confidence level.

It is clear from Table VIII that eqn. 15 cannot be applied at all to $\Delta\log V_N$ values of *ortho*-substituted pyridines, while eqn. 7 is extremely successful**, as is illustrated by the following example. At 206°C (PEG) we find for *o*-OCH₃-pyridine, from the calculated $\log V_N$ value (Table I, in double parentheses), a $\Delta\log V_N$ value of -0.462, and on the other hand, eqn. 7 applied to the corresponding $\Delta\log V_N$ values for CH₃, C₂H₅, F, Cl, Br and CN predicts a value for $\Delta\log V_N(OCH_3)$ of -0.460. [Eqn. 15 predicts $\Delta\log V_N(OCH_3) = -0.149$]. We also tested the Taft equation on the $\Delta\log V_N$ values for Apiezon. A significant distinction between the applicability of eqns. 7 and 15 could not be assessed for *meta*- and *para*-substituted compounds, presumably because the $\Delta\log V_N$ values for Apiezon are substantially smaller than those for PEG (see Fig. 3): experimental errors are relatively more important in this instance.

* For each equation, pooled variances, S^2 , were calculated according to $S^2 = \Sigma(n-i)S^2 / \Sigma(n-i)$, where the summation includes all the series in the pool, n is the number of $\Delta\log V_N$ values in each series and i is the number of parameters used in the regression (2 or 3). F is then given by S^2 (eqn. 15)/ S^2 (eqn. 7). The number of degrees of freedom, $\varphi = \Sigma(n-i)$, is φ (eqn. 15) = 58, φ (eqn. 7) = 46.

** A similar conclusion can be drawn with respect to the $\Delta\log V_N^{B,C}$ values to be discussed below.

The ρ_E values in Table VII for *meta*- and *para*-substituted anilines and phenols are comparable to the ρ_E values for the dissociation of anilinium ions and phenols^{14,15}: for the *meta* series the ρ_E values are small, while for the *para* series they are negative. Interpretation of the magnitude of ρ_I and ρ_R values is hardly possible for the reasons given in refs. 14 and 15. Some points of interest regarding the sign of the ρ_I or ρ_R values are discussed below.

As shown in Figs. 2 and 3, and by the negative signs of ρ_I and ρ_R for *meta*- and *para*-substituted pyridines and the positive signs of ρ_I and ρ_R for the corresponding anilines and phenols, the substituent effects in pyridines are reversed compared with the effects in anilines and phenols. The polar interactions between the pyridines and the stationary phases are restricted to dipole-dipole and dipole-induced dipole interactions. Therefore, the substituent effects in *meta*- and *para*-substituted pyridines are caused by the antagonism between the dipole moments of the pyridine moiety and the substituent. This antagonism is absent in *ortho*-substituted pyridines. Accordingly, the substituent effects are mostly small: see the points for the halogen and cyano substituents in Fig. 3c.

The positive ρ_I and ρ_R values for phenols and anilines can be explained by assuming the $\Delta \log V_N$ values to represent mainly the effect of the substituent on the intermolecular hydrogen bonding between the hydroxyl or amino group and the stationary phase³⁷⁻³⁹.

In order to show that intermolecular hydrogen bonding is important, even at a temperature as high as 206°C, the association constants for hydrogen bonding of phenol and aniline with PEG are estimated by applying the following equation:

$$[(V_N/V_N^*)_{\text{PEG}} \cdot (V_N^*/V_N)_{\text{Apiezon}} - 1] \cdot x^{-1} = K' \quad (16)$$

In this equation, which is an adaptation of eqn. 8 given by De Ligny in ref. 9, V_N represents a value for the hydrogen donor molecule (phenol or aniline). V_N^* is a datum for a reference molecule that cannot form hydrogen bonds and has about the same dipole moment as the hydrogen donor molecule; in this case chlorobenzene⁴⁰ is taken as the reference compound*. The term x represents the molar fraction of the hydrogen acceptor compound (PEG) in the stationary phase, which is equal to unity in the present case. K' is the apparent equilibrium constant for the association of hydrogen donor and acceptor molecules (molar fraction scale**).

Substitution of the appropriate data of Tables I and II in eqn. 16 results in K' values of 7.9 and 2.3 for phenol and aniline, respectively, at 206°C. A comparison with literature data can be made in the following way.

Diethyl ether, tetrahydrofuran and PEG all have ether oxygen atoms as proton acceptors and will have comparable hydrogen bonding properties. From data on the partial molar enthalpy and the standard partial molar entropy of hydrogen bonding

* Analogously to the pure base method, given by Arnett and co-workers^{41,42} for finding thermodynamic data for hydrogen bonding, methoxybenzene can also be chosen as the reference compound. This hardly alters the conclusion derived from the application of eqn. 16.

** The original version of eqn. 16 was intended for a group of closely related hexadecane-type stationary phases. Therefore, the application to the very dissimilar phases PEG and Apiezon yields only approximate K' values.

of the former two compounds with phenol^{41,43,44} and aniline⁴⁵, it can be calculated that at 206°C the association constants on the molar fraction scale would be 3.8 and 1.3, respectively. These data are in reasonable agreement with the values of the association constants for hydrogen bonding of PEG with phenol and aniline, estimated above.

Eqn. 16 is based on the assumption that hydrogen bonding in Apiezon is absent. However, in view of the good correlation of the $\Delta\Delta\log V_N^{\text{An,B}}$ and $\Delta\Delta\log V_N^{\text{Ph,B}}$ data on Apiezon with the corresponding data on PEG (Figs. 3a and 3b), some hydrogen bonding must occur, presumably with the about 5% aromatic material in Apiezon M. [Literature data on hydrogen bonding with aromatic compounds are as follows: $\Delta\bar{H} \approx -1.5 \text{ kcal}\cdot\text{mole}^{-1}$ (refs. 41, 43 and 46), $\Delta\bar{S}^0 \approx -1.2$ (ref. 43) to $+1.0$ (ref. 46) $\text{cal}\cdot\text{mole}^{-1}\cdot\text{K}^{-1}$ * for phenol, and $\Delta\bar{H} = -1.64 \text{ kcal}\cdot\text{mole}^{-1}$, $\Delta\bar{S}^0 = -3.7 \text{ cal}\cdot\text{mole}^{-1}\cdot\text{K}^{-1}$ * for aniline⁴⁷. At 206°C, $\Delta\mu^0$ would be equal to $-1.5 \text{ kcal}\cdot\text{mole}^{-1}$ for phenol and $+0.1 \text{ kcal}\cdot\text{mole}^{-1}$ for aniline, corresponding to association constants of 5 and 0.9, respectively. K' values of this order of magnitude can be determined experimentally indeed.]

The negative $\Delta\Delta\log V_N$ values for *ortho*-substituted anilines and phenols (see Figs. 3a and 3b) can be explained qualitatively by hindrance of intermolecular hydrogen bonding, caused either by steric effects, or by competition of intramolecular hydrogen bonding. The latter effect is well known for these compounds^{48,49}, e.g., Spencer *et al.*⁵⁰ found that *o*-methoxyphenol does not give a hydrogen bond with ethers because the intramolecular bond is too strong.

The applicability of eqn. 7 for the purpose of predicting $\Delta\Delta\log V_N$ values has some limitations, as is demonstrated below. *m*-Aminophenol can be regarded either as a substituted phenol or as a substituted aniline. Consequently, a $\Delta\Delta\log V_N$ value for this compound should be calculable in two ways:

(1) by substitution of the ρ values for phenols (Table VII) and the σ values for NH_2 (Table XII) in eqn. 7, resulting in $\Delta\Delta\log V_N = -0.125$ for PEG at 206°C;

(2) by substitution of the corresponding ρ values for anilines and σ values for OH in eqn. 7, resulting in $\Delta\Delta\log V_N = -0.002$.

The poor agreement between these results can be explained as follows. In the first case, the substituent effect of OH on the hydrogen bonding of the NH_2 group is neglected and, conversely, in the second case the effect of NH_2 on the hydrogen bonding of the OH group is neglected. Therefore, it must be concluded that eqn. 7 cannot be used for the prediction of the $\Delta\Delta\log V_N$ values of the compounds XNY, when both X and Y can give strong interactions (in the present case hydrogen bonds) with the solvent. On the other hand, by measuring the retention volume of *m*-aminophenol and comparing the experimental $\Delta\Delta\log V_N$ value with the predicted values mentioned above, it would be possible to investigate whether the OH or the NH_2 group is involved in hydrogen bonding with the solvent.

The effect of the column temperature, T , on the ρ values is similar to its effect on $\log V_N$. The latter effect is represented mainly by the values of V_1 in Table IV. In Table IX some values of ρ/V_1 are given. These values show only small variations;

* The original literature data on $\Delta\bar{S}^0$ are on the molarity scale ($\Delta\bar{S}_c^0$). They were re-calculated for the molar fraction scale ($\Delta\bar{S}_x^0$) by using the equation $\Delta\bar{S}_x^0 = \Delta\bar{S}_c^0 + R \ln N$, where N is the number of moles of solvent per litre.

TABLE IX
SOME VALUES OF q/V_1 WITH PEG 20,000

Quantity	Class of compounds	Position of substituents	Column temperature (°C)	
			165.5	206
q_2/V_2	Anilines	3	1.41	-1.40
		4	2.64	2.72
	Phenols	3	1.59	1.57
		4	2.28	2.28
	Pyridines	3	-1.54	-1.43
		4	-2.00	-1.86
q_n/V_1	Anilines	3	0.7	0.8
		4	2.5	2.6
	Phenols	3	1.1	1.1
		4	2.0	2.0
	Pyridines	3	-0.2	0.0
		4	-0.1	-0.6
q_E/V_1	Anilines	3	0.2	0.2
		4	-0.9	-1.1
	Phenols	3	0.1	0.2
		4	-0.4	-0.5
	Pyridines	3	0.1	0.0
		4	0.7	0.4

only for the pyridines are some of the variations significant. Therefore, it can be concluded that temperature does not have a specific effect on the substituent interactions.

A final question to be discussed is whether the cyclohexanes can be used as reference compounds to describe substituent effects in benzenes, and whether the hexanes can be used as reference compounds for the cyclohexanes. From the data in Tables I-III, values of $\Delta\Delta\log V_N^{B,C}$ and $\Delta\Delta\log V_N^{C,H}$ were calculated. These data were correlated with the substituent constants, using eqn. 7 as the regression equation. The results are given in Table X.

It must be realized that we are now not comparing the compounds XNY and XNZ, but the compounds XNH and XMH, where N and M are two different carbon skeletons. Accordingly, eqn. 4 now reads as follows:

$$\log \left[\frac{P_{X(N)}}{P_{X(M)}} \right] - \log \left[\frac{P_{H(N)}}{P_{H(M)}} \right] = \Delta\Delta\log V_N^{B,C}$$

or

$$\Delta\Delta\log V_N^{C,H} = \frac{1}{2.3 RT} (\Delta\mu_{X \leftrightarrow N}^0 - \Delta\mu_{X \leftrightarrow M}^0)$$

For the $\Delta\Delta\log V_N^{B,C}$ values the results of the regression analyses are good. As expected, both inductive and resonance effects contribute to these values. For PEG, the quantity $\log V_N^{\text{benzene}} - \log V_N^{\text{cyclohexane}}$ represents mainly a dipole (PEG)-induced dipole

TABLE X
RESULTS OF THE ANALYSES OF THE REGRESSION OF $\Delta\log V_N^{D,C}$ AND $\Delta\log V_N^{C,H}$ VALUES ON σ_I , σ_R AND σ_H BY EQN. 7

Correlated quantity	Stationary phase	Column temperature (°C)	ρ_I	$S(\rho_I)$	ρ_R	$S(\rho_R)$	ρ_H	$S(\rho_H)$	S	S^* ($\Delta\log V_N$)
$\Delta\log V_N^{D,C}$	PEG	206	-0.421	0.022	-0.316	0.053	-0.491	0.057	0.024	0.178
	Apiezon	206	-0.067	0.012	-0.309	0.030	-0.374	0.032	0.014	0.063
$\Delta\log V_N^{C,H}$	PEG	130	-0.263	0.081	0.263	0.196	0.171	0.210	0.089	0.146
	Apiezon	206	-0.078	0.026	0.106	0.062	0.012	0.067	0.028	0.048

* Standard deviation of the $\Delta\log V_N$ values = $\sqrt{\sum(\Delta\log V_N)^2/n}$, where n is the number of data (= 7).

TABLE XI
RESULTS OF THE ANALYSES OF THE REGRESSIONS OF LITERATURE DATA ON σ_I , σ_R AND σ_{II} BY EQN. 7

Correlated quantity	Position of substituents	Substituents* included in the correlation	e_I	$S(e_I)$	e_R	$S(e_R)$	e_{II}	$S(e_{II})$	S
FCl ₃ B (Carbowax 20M)	3	1, 4, 8, 9	-172	4	-12	24	-13	17	4
	3	1, 4, 8, 9, 10, 11	-164	25	-153	33	-64	44	23
	4	1, 4, 8, 9	-116	8	-5	50	-12	35	7
	4	1, 4, 8, 9, 10, 11	-106	30	-150	39	-57	52	27
FCl ₃ B (Apiezon M)	3	1, 4, 8, 9	-64	8	-42	47	-12	33	7
	3	1, 4, 8, 9, 10, 11	-61	9	-56	11	-7	15	8
	4	1, 4, 8, 9	-50	1	-29	6	6	4	8
	4	1, 4, 8, 9, 10, 11	-48	6	-58	7	-3	10	5

* The numbers correspond to the substituent numbers in Table I; 10 = OH, 11 = NH₂.

TABLE XII

SUBSTITUENT CONSTANTS σ_I , σ_R AND σ_E TO BE USED IN EQN. 7

Substituent	σ_I	σ_R	σ_E
CH ₃	0.0	-0.113	-0.040
C ₂ H ₅	0.0	-0.107	-0.050
<i>i</i> -C ₃ H ₇	-0.009	-0.093	-0.067
<i>tert.</i> -C ₄ H ₉	-0.019	-0.100	0.012
C ₆ H ₅	0.153	-0.086	-0.175
F	0.463	-0.286	0.384
Cl	0.450	-0.177	0.243
Br	0.450	-0.162	0.225
I	0.414	-0.132	0.157
OCH ₃	0.279	-0.412	-0.033
OH	0.274	-0.475	-0.095
NH ₂	0.188	-0.580	-0.468
CF ₃	0.474	0.003	0.270
COCH ₃	0.271	0.139	-0.475
CO ₂ CH ₃	0.282	0.134	-0.226
CN	0.566	0.085	-0.095
NO ₂	0.613	0.152	-0.302

(benzene) interaction. The important conclusion is that eqn. 7 holds not only for substituent effects on hydrogen bonding interactions (PEG and phenols or anilines) and on dipole-dipole interactions (PEG and pyridines), but also for substituent effects on dipole-induced dipole interactions (PEG and benzenes)*.

For the $\Delta \log V_N^{C,H}$ values the results of the regression analyses are poor: the standard deviations of the regressions are of the same magnitude as the standard deviations of the $\Delta \log V_N^{C,H}$ values (compare the entries in the last two columns of Table X). Only inductive effects are expected to contribute to $\Delta \log V_N^{C,H}$, as both the cyclohexane and the hexane systems are saturated. Indeed, only the ρ_1 values are significant (at the 90% probability level).

Relatively few gas chromatographic data in the literature are suitable for correlations according to eqn. 7. Mostly, data for suitable reference compounds are not available. Moreover, the data must be very precise, as four data in the left-hand side of eqn. 7 are combined and as three regression coefficients must be estimated. The only suitable data that were encountered were those of West and Hall¹⁸. Their quantities F for X-substituted chlorobenzenes represent deviations from additivity of retention indices, I :

$$F^{Cl,B} = I_{XNC_1} - I_{XNH} - I_{HNC_1} + I_{HNH} \quad (18)$$

(HNH denotes benzene, etc. This equation is a combination of eqns. 7-9 in ref. 18). As I is proportional to $\log V_N$, the F values are proportional to $\Delta \log V_N$ values (compare eqns. 18 and 7). $F^{Cl,B}$ values for Carbowax 20M (comparable with PEG 20,000) and Apiezon M were calculated according to eqn. 8 in ref. 18. The results

* Other examples are the $\Delta \log V_N^{P,B}$ values in Apiezon and the $F^{Cl,B}$ values in Apiezon (see below).

of the regression analyses on the $F^{Cl,B}$ values by eqn. 7 are presented in Table XI. The standard deviations of 5–8 I units are of the same order as the experimental error. In Table XI it is demonstrated that inclusion of data for the substituents OH and NH_2 (numbers 10 and 11) in the correlation greatly increases the standard deviations for Carbowax, whereas no effect is found for Apiezon. This is in accordance with expectation, as the effects of intermolecular hydrogen bonding will be greater for Carbowax than for Apiezon. The negative ρ_1 and ρ_R values show that the substituted chlorobenzenes have reversed substituent effects of the same type as discussed for the pyridines.

CONCLUSIONS

The deviations, $\Delta\Delta\log V_N$, of the additivity of group contributions to $\log V_N$ can be correlated with Hammett-type substituent constants, using a three-parameter regression equation. The $\Delta\Delta\log V_N$ values for anilines, phenols and pyridines can be described very well by such an equation, with the exception of the values for *ortho*-substituted anilines and phenols. The $\Delta\Delta\log V_N$ values for anilines and phenols represent mainly the effect of the substituents on the intermolecular hydrogen bonding between anilines or phenols and the stationary phase. The substituent effects in *meta*- and *para*-substituted pyridines and chlorobenzenes are the reverse of the effects in the corresponding anilines or phenols and must be explained in terms of dipole-dipole and dipole-induced dipole interactions between the pyridines or chlorobenzenes and the stationary phase. The temperature has no specific effect on $\Delta\Delta\log V_N$ values: the effect is analogous to the temperature effect on $\log V_N$ values. The substituent effects in benzenes relative to the effects in cyclohexanes can also be described fairly well with the same substituent constants. The description of the effects in cyclohexanes, relative to the effects in *n*-hexanes, is less satisfactory.

The effect of sample size on V_N is caused by vaporization phenomena directly after the injection of the sample, rather than by the occurrence of curved partition isotherms.

APPENDIX

The three substituent constants, σ_I , σ_R and σ_E , used in eqn. 7 were generated from 570 literature data on substituent effects for 17 substituents in 76 series of chemical reactions or equilibria. All types of reactions as distinguished by Ehrenson *et al.*³⁶, *i.e.*, σ_I , σ_R^0 , $\sigma_R(BA)$, σ_R^+ , $\sigma_R^-(A)$ and $\sigma_R^-(P)$, were represented in the series. The generation procedure, which was also an optimization procedure, included factor analysis^{14,15}. Values of the substituent constants are given in Table XII.

The constants σ_I and σ_R closely resemble Taft's σ_I and σ_R^0 . The parameter σ_E represents the direct resonance effect in a combination with the inductive and normal resonance effect. If substituent effects are defined in such a way that ρ_I and ρ_R are positive, then ρ_E is negative for σ_R^- -type reactions, zero for σ_R^0 -type reactions and positive for σ_R^+ -type reactions. Thus, the sign of ρ_E identifies a reaction as belonging to one of the reaction types.

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