

GAS-LIQUID CHROMATOGRAPHY IN QUALITATIVE ANALYSIS

PART I. AN INTERPOLATION METHOD FOR THE PREDICTION OF RETENTION DATA

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INTRODUCTION

The use of retention data in qualitative analysis is impeded by the difficulty of preparing authentic reference compounds. A logarithmic interpolation method of calculating the retention times of unsymmetrical molecules from those of the symmetrical counterparts has been investigated and is described in this paper. The compounds investigated include *n*-paraffins, olefins, sulphides, disulphides, thiols, *sec.*-alcohols, halides, ketones, ethers and selenides.

EXPERIMENTAL

Apparatus and procedure

Chromatograms were obtained using an apparatus consisting of glass columns (5 ft. long and 4 mm I.D.) with a modified flame ionisation detector^{1,2}. The carrier gas was a 3:1 (by volume) mixture of hydrogen and nitrogen. The columns were packed, with the stationary phases silicone fluid 704 (Hopkin and Williams), squalane (B.D.H.) and polyethylene glycol 400 (Union Carbide) supported on acid-washed (1% phosphoric acid) 60-72 mesh celite (J.J.'s Ewell, Surrey) and in certain cases on 60-72 mesh C.22 brick dust (J.J.'s), by conventional techniques. Samples (approximately 10 γ) for analysis were introduced by means of stainless steel capillary pipettes³. The column efficiencies were between 400 and 500 theoretical plates per foot of column.

Calculation of the relative retention times

Retention times were measured from the time of injection of the sample to the time of appearance of the peak maxima on the recorder chart, and were corrected for the calculated "dead-time"⁴ of the apparatus. *n*-Paraffins were chosen as internal standards for the determination of the relative retention times on silicone fluid and squalane whilst *n*-alcohols were chosen as secondary internal standards for polyethylene glycol (PEG). All values quoted in this paper are relative to theoretical *n*-nonane⁵.

Materials

The compounds used in this work were either purified commercial materials or were prepared by members of N.R.P.R.A. staff. Details of the synthesis of the 2-methyl-pent-2-en-1-yl and 4-methyl-pent-3-en-2-yl sulphides will be published shortly⁶.

RESULTS AND DISCUSSION

The logarithm of the absolute retention volume for a particular substance is directly related to the free energy of solution of the solute molecules in the stationary liquid phase. As the free energy of solution is an approximately additive function of the groups constituting the molecule, linear homologous series plots ($\log R$ against N the carbon number) have been observed for many classes of organic compounds^{7,8}. These plots have been used to predict the retention times of unavailable members of a series. However, it is often neither convenient nor possible to obtain sufficient members of a series in order to determine the required retention time by this method. Retention times can also be calculated by the method of "summation of group contributions"^{9,10}, but except in the most favourable cases the results are not sufficiently precise for qualitative analysis.

A consequence of the additivity of group values of free energy of solution is that, if a molecule can be represented as R-X-R', then

$$\log_{10} R_{1,2} = \frac{1}{2} \{ \log_{10} R_{1,1} + \log_{10} R_{2,2} \}$$

where $R_{1,2}$, $R_{1,1}$ and $R_{2,2}$ are the retention times of R-X-R', R-X-R and R'-X-R', respectively.

The agreement between the observed and calculated values may be expected to be good provided that:

- (i) there is no conjugation across the group X
- (ii) none of the molecules are sterically hindered
- (iii) neither R nor R' are strongly polar
- (iv) the bonds linking R and X and R' and X are symmetrical in polar character or that these bonds are separated by a number of non-conjugated atoms in group X, and
- (v) the retention times of the two symmetrical compounds can be measured with comparable and good accuracy.

The virtues of this method, where applicable, are that only two substances are required to calculate the retention time of the unknown and since only two terms are used in the calculation accumulative errors are minimised. We have found the method particularly useful in cases where the symmetrical compounds are easier to synthesise than the unsymmetrical counterparts, for instance mono- and di-sulphides.

n-Paraffins

Since specific interactions are very weak in this series, excellent agreement may be expected and is indeed obtained between the observed and calculated values, as reflected by a standard deviation of 0.83% (Table II).




TABLE II

Stationary phase and concentration w/w	Solid support	Temperature °C	R	R'	X	Relative retention times			
						R:X-R'	R':X-R'	R:X-R' observed	R:X-R' calculated
Squalane 5%	Celite	20	<i>n</i> -propyl	<i>n</i> -butyl	—(CH ₂) ₂ —	0.40	2.55	1.00	1.02
Squalane 5%	Celite	20	<i>n</i> -propyl	<i>n</i> -butyl	—CH ₂ —	0.177	11.00	0.40	0.40
Squalane 5%	Celite	65	<i>n</i> -butyl	<i>n</i> -amyl	—CH ₂ —	1.00	5.29	2.30	2.30
Squalane 20%	C22	65	<i>n</i> -propyl	<i>n</i> -butyl	—CH ₂ —	0.183	11.00	0.42	0.42
PEG 20%	Celite	65	<i>n</i> -amyl	<i>n</i> -hexyl	—CH ₂ —	3.70	13.66	7.09	7.12
PEG 20%	Celite	65	<i>n</i> -amyl	<i>n</i> -hexyl	—(CH ₂) ₂ —	7.09	26.40	13.66	13.66

Alkyl-aryl hydrocarbons

This series has not been widely investigated, however, preliminary results indicate that *para*-substituted compounds give good agreement (2.7% R.M.S. deviation) whilst the *ortho* compounds give poor agreement (15% error), as shown in Table III.

TABLE III

Stationary phase and concentration w/w	Solid support	Temperature °C	R	R'	X	Relative retention times			
						R:X-R'	R':X-R'	R:X-R' observed	R:X-R' calculated
PEG 20%	Celite	65	H	<i>o</i> -methyl		11.92	9.11	3.58	4.18
PEG 20%	Celite	65	H	<i>p</i> -methyl		11.92	6.73	3.58	3.59
PEG 20%	Celite	65	H	<i>p</i> -ethyl		11.92	19.84	6.40	6.17

A-1 Olefins

The retention times of alk-1-enes may be calculated from those of suitable *n*-alkanes and alk- α,ω -dienes, for instance that of oct-1-ene is obtained using those of *n*-decane and hexa-1,5-diene.

The agreement between calculated and observed values may be expected to be slightly inferior compared with *n*-paraffins owing to the somewhat polar nature of the double bond. As can be seen from Table III a R.M.S. deviation of 2.4% is observed for the three *A-1* olefins measured. In the cases of hept-1-ene and oct-1-ene this:

deviation may in part arise from the large difference in retention time of the two symmetrical compounds.

TABLE III

Stationary phase and concentration w/w	Solid support	Temperature °C	R	R'	X	Relative retention times			
						R-X-R	R'-X-R'	R-X-R' observed	R-X-R' calculated
Squalane 5%	Celite	65	vinyl	ethyl	—(CH ₂) ₂ —	0.053	0.074	0.062	0.063
Squalane 5%	Celite	65	vinyl	<i>n</i> -propyl	—(CH ₂) ₂ —	0.053	0.411	0.152	0.148
Squalane 5%	Celite	65	vinyl	<i>n</i> -butyl	—(CH ₂) ₂ —	0.053	2.45	0.350	0.360

Alkyl and alkenyl monosulphides

The method gives excellent results for alkyl and alkenyl sulphides, provided that *tert.*-alkyl groups are not present, as illustrated in Table IV. The disagreement between observed and calculated values for *tert.*-alkyl sulphides appears to be about 12% with the unsymmetrical compound emerging sooner than calculated. This may be due to steric hindrance. We propose to investigate the anomalous behaviour of *tert.*-butyl sulphides further.

TABLE IV

Stationary phase and concentration w/w	Solid support	Temperature °C	R	R'	X	Relative retention times			
						R-X-R	R'-X-R'	R-X-R' observed	R-X-R' calculated
Silicone 20%	Celite	160	cyclohexyl	cyclohex-2-enyl	—S—	53.6	75.6	63.6	63.7
PEG 20%	Celite	65	ethyl	allyl	—S—	1.42	7.28	3.25	3.22
Silicone 20%	Celite	65	ethyl	allyl	—S—	0.34	1.42	0.69	0.69
PEG 20%	Celite	65	methyl	<i>n</i> -butyl	—S—	0.66	14.07	3.08	3.05
PEG 20%	Celite	65	methyl	allyl	—S—	0.66	7.28	2.20	2.19
Silicone 20%	Celite	65	methyl	allyl	—S—	0.075	1.42	0.35	0.33
PEG 20%	Celite	65	ethyl	<i>tert.</i> -butyl	—S—	1.42	3.39	1.90	2.19
Silicone 20%	Celite	65	ethyl	<i>tert.</i> -butyl	—S—	0.34	1.63	0.67	0.74

R.M.S. deviation (excluding anomalous *tert.*-butyl cases) 2.47%.

Alkyl and alkenyl disulphides

The overall picture of agreement with these compounds is similar to that of the mono-sulphides (Table V).

TABLE V

Stationary phase and concentration w/w	Solid support	Temperature °C	R	R'	X	Relative retention times			
						R-X-R	R'-X-R'	R-X-R' observed	R-X-R' calculated
PEG 20%	Celite	100	isopropyl	allyl	—S·S—	9.61	31.85	17.55	17.50
Silicone 20%	Celite	100	isopropyl	allyl	—S·S—	4.13	7.79	5.75	5.67
PEG 20%	Celite	100	n-butyl	allyl	—S·S—	46.65	31.85	38.32	38.55
Silicone 5%	Celite	138	n-butyl	allyl	—S·S—	15.38	5.21	8.87	8.95
Silicone 5%	Celite	138	ethyl	I	—S·S—	2.2	44.2	9.9	9.9
Silicone 5%	Celite	138	tert.-butyl	I	—S·S—	5.3	44.2	14.6	15.3
Silicone 5%	Celite	138	I	II	—S·S—	44.2	75.8	58.2	57.9

R.M.S. deviation excluding *tert.*-butyl compound 0.76%.

I = 4-methylpent-3-en-2-yl.

II = 2-methylpent-2-en-1-yl.

Alkane-1-thiols

The retention times of alkane-1-thiols have been calculated from those of suitable *n*-paraffins and propane-1,3-dithiol and butane-1,4-dithiol. The somewhat poor agreement between the observed and calculated values may be due to the slightly polar nature of the thiol group and also the difference in the retention times of the paraffin and dithiol, particularly on polyethylene glycol stationary phase. (Table VI).

TABLE VI

Stationary phase and concentration w/w	Solid support	Temperature °C	R	R'	X	Relative retention times			
						R-X-R	R'-X-R'	R-X-R' observed	R-X-R' calculated
Silicone 5%	Celite	65	n-propyl	—CH ₂ -SH	—CH ₂ —	0.21	4.49	0.95	0.97
Silicone 5%	Celite	65	n-butyl	—CH ₂ -SH	—CH ₂ —	1.00	4.49	2.18	2.12
PEG 20%	Celite	65	n-butyl	—CH ₂ -SH	—CH ₂ —	0.95	48.57	6.64	6.79
Silicone 5%	Celite	65	n-amyl	—CH ₂ -SH	—CH ₂ —	5.29	4.49	5.08	4.87
PEG 20%	Celite	65	n-amyl	—CH ₂ -SH	—CH ₂ —	3.79	48.57	12.56	13.56
Silicone 5%	Celite	65	n-hexyl	—CH ₂ -SH	—CH ₂ —	27.8	4.49	11.60	11.18
PEG 20%	Celite	65	n-hexyl	—CH ₂ -SH	—CH ₂ —	13.99	48.57	23.70	26.07
Silicone 5%	Celite	65	ethyl	—CH ₂ -SH	—(CH ₂) ₂ —	0.11	11.96	0.95	1.15
Silicone 5%	Celite	65	n-propyl	—CH ₂ -SH	—(CH ₂) ₂ —	0.45	11.96	2.18	2.32
Silicone 5%	Celite	65	n-butyl	—CH ₂ -SH	—(CH ₂) ₂ —	2.30	11.96	5.08	5.24

R.M.S. deviation 8.0%.

Ketones

Data for these materials are very limited. The results indicate that observed and calculated values should agree to within about 5 % (Table VII).

TABLE VII

Stationary phase and concentration w/w	Solid support	Temperature °C	R	R'	X	Relative retention times			
						R-X-R	R'-X-R'	R-X-R' observed	R-X-R' calculated
PEG 20 %	Celite	65	methyl	ethyl	>C=O	1.09	2.87	1.78	1.77
PEG 20 %	Celite	65	methyl	n-propyl	>C=O	1.09	6.68	2.80	2.70
PEG 20 %	Celite	65	methyl	n-butyl	>C=O	1.09	25.64	5.69	5.28

Selenides

To date only one selenide system has been investigated. The result suggests reasonable agreement should be obtainable (Table VIII).

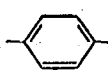
TABLE VIII

Stationary phase and concentration w/w	Solid support	Temperature °C	R	R'	X	Relative retention times			
						R-X-R	R'-X-R'	R-X-R' observed	R-X-R' calculated
PEG 20 %	Celite	65	methyl	allyl	—Se—	0.92	12.98	3.63	3.45

Aromatic ethers

Only one ether system of this type has been studied. The result suggests reasonable agreement in the case of *p*-substituted ethers (Table IX).

TABLE IX

Stationary phase and concentration w/w	Solid support	Temperature °C	R	R'	X	Relative retention times			
						R-X-R	R'-X-R'	R-X-R' observed	R-X-R' calculated
PEG 20 %	Celite	100	H	<i>p</i> -methoxy		1.95	131.5	16.38	16.02

sec.-Alcohols, sec.-thiols, and sec.-sulphides

In the two *sec.*-alcohol systems studied excellent agreement between observed and calculated values has been obtained. The retention times of *sec.*-thiols and *sec.*-sulphides can be calculated similarly (Table X).

TABLE X

Stationary phase and concentration w/w	Solid support	Temperature °C	R	R'	X	Relative retention times			
						R-X-R	R'-X-R'	R-X-R' observed	R-X-R' calculated
PEG 20%	Celite	65	methyl	ethyl	$\begin{array}{c} \text{OH} \\ \\ \text{---CH---} \end{array}$	2.84	8.54	5.21	4.92
Silicone 5%	Celite	65	methyl	ethyl	$\begin{array}{c} \text{OH} \\ \\ \text{---CH---} \end{array}$	0.16	0.53	0.29	0.29
PEG 20%	Celite	65	methyl	ethyl	$\begin{array}{c} \text{SH} \\ \\ \text{---CH---} \end{array}$	0.61	2.17	1.18	1.15
PEG 20%	Celite	65	methyl	ethyl	$\begin{array}{c} \text{C}_2\text{H}_5 \\ \\ \text{S} \\ \\ \text{---CH---} \end{array}$	1.74	5.15	3.16	2.99

prim.-Halides

In this series, if one of the symmetrical compounds contains two halogen atoms, poor agreement may be expected and Table XI confirms this.

TABLE XI

Stationary phase and concentration w/w	Solid support	Temperature °C	R	R'	X	Relative retention times			
						R-X-R	R'-X-R'	R-X-R' observed	R-X-R' calculated
Silicone 20%	Celite	65	<i>n</i> -butyl	$\text{---CH}_2\cdot\text{Br}$	$\text{---CH}_2\text{---}$	1.00	4.54	2.45	2.13

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SUMMARY

A logarithmic interpolation method for the prediction of the retention times of unsymmetrical molecules from those of the symmetrical counterparts is described. The classes of organic compounds to which the method has been successfully applied include *n*-paraffins, olefins, sulphides, disulphides, thiols, *sec.*-alcohols, halides, ketones, ethers and selenides.

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