RELATIONSHIPS BETWEEN GAS–LIQUID CHROMATOGRAPHIC BEHAVIOUR AND STRUCTURE OF ARYLALIPHATIC ACIDS

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(First received March 28th, 1985; revised manuscript received May 14th, 1985)

SUMMARY

The gas–liquid chromatographic retention behaviour of methyl esters of arylaliphatic acids was studied using the stationary phase Apolane 87. The increments of selected structural fragments were calculated from the Kováts retention indices of the initial group of ten methyl esters of arylaliphatic acids. The intramolecular interactions cause a deviation of the retention indices from the additivity principle; this effect must also be taken into account in the choice of the initial group of compounds. The values of the retention indices of another 21 methyl esters of arylaliphatic acids were calculated from these increments. The regression relationship between calculated and experimental values was characterized by a low standard deviation ($s = 11.0$) and a high correlation coefficient ($r = 0.999$). The relationships between Kováts retention indices and valence connectivity indices, $^1\chi^v$, or molar refractivities, MR, were also evaluated with correlation coefficients between 0.910 and 0.975 and 0.941 and 0.963, respectively, depending on the number of compounds considered. The regression analysis indicated that the dispersion forces and molecular topology were more important than the electrostatic interactions.

INTRODUCTION

The considerable efforts devoted to studies of the dependence of retention behaviour on the structure of solutes in gas–liquid chromatography (GLC) has been characterized by two approaches, as follows.

(1) Utilization of the additivity of the retention indices, which makes possible their calculation from the increments for the individual structural fragments according to

$$I = I_0 + \Sigma n_i \, \delta I_i \tag{1}$$

where n is the number of structural fragments i characterized by the increment δI_i

and I_0 is the retention index of the standard compound. The additivity principle generally holds for a series of structurally similar compounds whose mechanism of separation is not too different. Such a method was applied to substituted alkylbenzenes[1-4] and polysubstituted aromatic compounds[5]. In this connection, the differences among the positional isomers and interactions among the individual substituents, to a restricted extent, were characterized by further increments. A modified Free–Wilson approach was used[6] for the calculation of the retention indices of substituted pyridopyrimidines. The Rohrschneider[7] and Kováts[8] additive theory was the basis for the expression[9] of the Kováts retention index, I, as the sum of the empirical increments of the individual atoms (I_a), bonds (I_b) and interactions of the solute with the stationary phase (I_{int}) according to

$$I = I_a + I_b + I_{int} \tag{2}$$

Such an approach was applied to homologous series of alkanes[10], alkenes, alkylbenzenes[11,12] and simple aromatic compounds[13].

(2) Evaluation of the relationships between the retention indices and suitable structural parameters. From previous results[14-16], Gassiot-Matas and Firpo-Pamies[17] expressed the retention indices as a linear function of two structural parameters. The first is a measure of the molecular volume of the solute; the molar refractivity, MR, was often used for its characterization. As is evident from its definition, MR depends on both the molar volume and the polarizability of the molecule. It was even considered as a measure of the dispersion interactions between the solute and the stationary phase. The second parameter corresponds to the polarity of the solute, which may correlate with the dipole moment, μ.

The retention index, RI, is generally expressed by

$$RI = aMR + b\mu^2 + c \tag{3}$$

The validity of this relationship was proved[17,18] for various series of related compounds. The valence connectivity indices, χ^v, whose linear dependence on MR is known[19] for many series of structurally similar compounds, were used instead of the molar refractivity[14,15,17]. If the polar interactions between stationary phase and solutes are suppressed, the polar parameter can be neglected and the following single-term equation is sufficient for the expression of the retention index[20-23]:

$$RI = k_1 MR (\chi^v) + k_2 \tag{4}$$

The statistical significance of these single-parameter relationships increase with decreasing polarity of the stationary phase.

The dependence of the GLC retention behaviour of arylaliphatic acids I–IV on their structure was evaluated. The additivity of the Kováts retention indices, I,
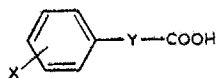
I , Y = CH_2 ; II , Y = CH_2CH_2 ;
III , Y = $CH(CH_3)$; IV , Y = $CH_2CH(CH_3)$

was used for the calculation of the retention increments for the chosen structural fragments in the initial series of suitable acids I–IV. The Kováts retention indices of the group of structurally related acids were calculated from these increments. The values thus obtained were compared with the experimental values. The dependences of the Kováts retention indices on the molar refractivities and the connectivity indices were also evaluated.

EXPERIMENTAL

Method

A Carlo Erba Fractovap 2450 gas chromatograph equipped with a flame-ionization detector was used. A glass column (1 m × 3.5 mm I.D.) was filled with 3% Apolane 87 on Chromosorb W HP (100–120 mesh) (Applied Science Labs., State College, PA, U.S.A.). Helium was used as the carrier gas at a flow-rate of 50 ml/min. The working temperature was 190°C and the ranges 140–155 and 160–180°C were used for extrapolation.

Samples

The preparation of the arylaliphatic acids I–IV has been described elsewhere[24–30]. The compounds were chromatographed as methyl esters in methanolic solution.

Calculations

The molar refractivities were calculated using the values from ref. 31. Methyl esters of the acids I–IV were characterized by the values MR_X (for the substituents X) and MR_Y (for the connecting chain Y). Thus the ΣMR value describes only the variable fragments X and Y. As the mono- and disubstituted derivatives were evaluated together in regression analysis, the increment ΔMR for a hydrogen atom was included in the values of MR_X for the monosubstituted derivatives. The connectivity indices $^1\chi^v$ were calculated using the method of Kier and Hall[19]. The values of δ_i^v for heteroatoms were taken from ref. 14.

Regression coefficients were calculated by multiple regression analysis and were statistically evaluated by a standard procedure. The level of statistical significance α was better than 0.005.

RESULTS AND DISCUSSION

A suitable initial series of the methyl esters of arylaliphatic acids was selected (Table I) for the incremental method of calculation of the Kováts retention indices. The increments ΔI, summarized in Table II, were calculated from the corresponding I values. Comparison of the ΔI values for the methylene group demonstrated the similarity of the increments when this group was located both on the connecting chain between methoxycarbonyl and aromatic nucleus, $\Delta I(CH_2)^R$, and in alkoxy group, $\Delta I(CH_2)^{OR}$ or $\Delta I(CH_2)^O$. The slight increase in the last value might be due to a decline in the steric hindrance of the interaction of the ether oxygen atom in Ib with the stationary phase. This explanation is also supported by the very low value of $\Delta I(CH_3)^r$ for the methyl group on branching of the connecting chain in the prox-

TABLE I

KOVÁTS RETENTION INDICES AND STRUCTURAL PARAMETERS OF ARYLALIPHATIC ACIDS IN THE ORIGINAL SERIES

Compound	X	Y	I_{exp}	$^1\chi^v$	MR_X	ΣMR
Ia	4-i-C$_3$H$_7$O	CH$_2$	1489.4	4.552	18.09	22.71
Ib	4-i-C$_4$H$_9$O	CH$_2$	1606.1	5.013	22.69	27.31
Ic	4-n-C$_5$H$_{11}$O	CH$_2$	1770.0	5.657	27.29	31.91
Id	4-n-C$_6$H$_{13}$O	CH$_2$	1874.2	6.157	31.89	36.51
Ie	4-C$_6$H$_5$CH$_2$O	CH$_2$	2075.3	5.714	32.77	37.39
If	3-Cl-4-C$_6$H$_5$CH$_2$O	CH$_2$	2233.7	6.194	37.77	42.39
Ig	3-CH$_3$O-4-C$_6$H$_5$CH$_2$O	CH$_2$	2185.3	6.243	39.61	44.23
IIa	4-C$_6$H$_5$CH$_2$O	CH$_2$CH$_2$	2178.0	6.214	32.77	42.01
IIb	4-c-C$_6$H$_{11}$CH$_2$O	CH$_2$CH$_2$	2158.6	7.175	34.08	43.32
IVa	3-Cl-4-i-C$_4$H$_9$O	CH$_2$CH(CH$_3$)	1875.3	6.412	27.69	41.55
Is	H	CH$_2$	1070.5*	3.045	2.06	6.68
It	3-Cl	CH$_2$	1304.3*	3.519	7.06	11.68
Iu	4-CH$_3$O	CH$_2$	1364.0*	3.569	8.90	13.52
Iv	3,4-(CH$_3$O)$_2$	CH$_2$	1478.0*	4.097	15.74	20.36
IVg	4-CH$_3$O	CH$_2$CH(CH$_3$)	1484.5*	4.489	8.90	22.76

* Extrapolated values from retention indices measured in the temperature range 140–150°C.

TABLE II

VALUES OF ΔI FROM KOVÁTS RETENTION INDICES OF ACIDS IN THE ORIGINAL SERIES

Parameter	Meaning	Value	Calculation
$\Delta I(CH_2)^{OR}$	CH$_2$ in alkoxy group	104.2	$I(Id) - I(Ic)$
$\Delta I(CH_2)^R$	CH$_2$ in connecting chain	102.7	$I(IIa) - I(Ie)$
$\Delta I(CH_2)^O$	CH$_2$ joined to oxygen	116.7	$I(Ib) - I(Ia)$
$\Delta I(3\text{-Cl})$	3-Cl next to 4-OR	158.4	$I(If) - I(Ie)$
$\Delta I(3\text{-OCH}_3)$	3-OCH$_3$ next to 4-OR	110.0	$I(Ig) - I(Ie)$
$\Delta I(CH_3CH)$	CH$_3$CH in connecting chain	110.8	$I(IVa) - [I(Ib) + I(3\text{-Cl})]$
$\Delta I(CH_3)^r$	CH$_3$ on branching	8.1	$\Delta I(CH_3CH) - \Delta I(CH_2)$

imity of a methoxycarbonyl group. The methyl group hinders the interaction of the methoxycarbonyl group with the stationary phase, causing a decrease in the retention of the corresponding derivatives III and IV.

Each increment was calculated from only one pair of experimental values because of the small number of compounds in the initial series. Nevertheless, the statistical significance of the ΔI values was satisfactory, as is evident from the comparison of the calculated (I_{calc}) and experimental (I_{exp}) values for another 20 methyl esters of acids I–IV (Table III). The mutual relationship between the two values was evaluated by regression analysis and the following equation was obtained:

$$I_{calc} = 0.993 I_{exp} + 17.702 \qquad (5)$$
$$n = 21; \ r = 0.999; \ s = 11.019; \ F = 8293.8$$

The increments for CH$_3$O and Cl in Table II were calculated from 3,4-disubstituted derivatives. Their values were probably influenced by the interactions of these

TABLE III

KOVÁTS RETENTION INDICES AND STRUCTURAL PARAMETERS OF ARYLALIPHATIC ACIDS

Compound X		Y	I_{exp}	I_{calc}*	δI**	$^1\chi^v$	MR_X	ΣMR
Ih	3-Cl-4-c-C$_6$H$_{11}$CH$_2$O	CH$_2$	2224.7	2214.3	−10.4	7.154	39.10	43.72
Ii	3-Cl-4-c-C$_6$H$_{11}$O	CH$_2$	2094.3	2096.1	1.8	6.876	34.48	39.10
Ij	3-Cl-4-C$_6$H$_5$(CH$_2$)$_2$O	CH$_2$	2333.9	2337.9	4.0	6.694	42.39	47.01
Ik	3-CH$_3$O-4-n-C$_6$H$_{13}$O	CH$_2$	1988.7	1984.2	−4.5	6.685	38.73	43.35
Il	3-CH$_3$O-4-c-C$_6$H$_{11}$CH$_2$O	CH$_2$	2165.9	2169.9	4.0	7.203	40.92	45.54
Im	3-Cl-4-n-C$_6$H$_{13}$O	CH$_2$	2036.4	2032.6	−3.8	6.636	36.89	41.51
In	3-Cl-4-n-C$_8$H$_{17}$O	CH$_2$	2233.4	2241.0	7.6	7.886	46.09	50.71
Io	3-Cl-4-C$_6$H$_5$(CH$_2$)$_3$O	CH$_2$	2428.3	2442.1	13.8	7.194	46.97	51.59
Ip	4-c-C$_6$H$_{11}$CH$_2$O	CH$_2$	2059.1	2055.2	−3.9	6.675	34.08	38.70
IIc	3-Cl-4-c-C$_6$H$_{11}$CH$_2$O	CH$_2$CH$_2$	2322.6	2317.0	−5.6	7.654	39.08	48.32
IId	3-Cl-4-C$_6$H$_5$CH$_2$O	CH$_2$CH$_2$	2332.3	2336.4	4.1	6.694	37.77	47.01
IIe	3-CH$_3$O-4-i-C$_3$H$_7$O	CH$_2$CH$_2$	1710.5	1703.1	−7.4	5.579	24.93	34.17
IIf	3-CH$_3$O-4-n-C$_6$H$_{13}$O	CH$_2$CH$_2$	2083.8	2086.9	3.1	7.185	38.73	47.97
IIIa	3-Cl-4-c-C$_6$H$_{11}$CH$_2$O	CH(CH$_3$)	2232.2	2222.3	−9.9	7.601	39.08	48.32
IIIb	3-Cl-4-C$_6$H$_5$CH$_2$O	CH(CH$_3$)	2240.1	2241.8	1.7	6.641	37.77	47.01
IIIc	4-c-C$_6$H$_{11}$CH$_2$O	CH(CH$_3$)	2078.5	2064.0	−14.5	7.122	34.08	43.32
IVb	3-Cl-4-C$_6$H$_5$CH$_2$O	CH$_2$CH(CH$_3$)	2328.0	2344.5	16.5	6.909	37.77	51.63
IVc	4-i-C$_3$H$_7$O	CH$_2$CH(CH$_3$)	1565.3	1600.2	34.9	5.472	18.14	32.00
IVd	3-CH$_3$O-4-i-C$_3$H$_7$O	CH$_2$CH(CH$_3$)	1710.5	1711.6	1.1	6.000	24.98	38.84
IVe	3-CH$_3$O-4-n-C$_6$H$_{13}$O	CH$_2$CH(CH$_3$)	2090.2	2099.5	9.3	7.606	38.73	52.59
IVf	3-CH$_3$O-4-c-C$_6$H$_{11}$CH$_2$O	CH$_2$CH(CH$_3$)	2272.1	2276.6	4.6	7.874	40.92	54.78

* Kováts retention indices of the original series of acids (Table I) and values of ΔI (Table II) were used for calculation.

** $\delta I = I_{calc} - I_{exp}$.

substituents with the alkoxy group. The different values of the increments obtained from the mono- and disubstituted derivatives (Table IV) support the existence of intramolecular interactions. The Kováts retention indices of compounds Is, It and Iu, extrapolated from the values measured over the range 140–155°C, were used for the calculation of the former increments. The mutual interactions among the substituents decrease the retention indices, probably by reducing the interactions of the solutes with the stationary phase. A similar result was observed at 120°C (see Table IV). The esters of acis Is, It and Iu were measured at this temperature and the retention indices for the derivatives Ie, If and Ig were extrapolated from the values measured over the range 160–180°C (Table V).

TABLE IV

COMPARISON OF ΔI VALUES FROM MONO- AND DISUBSTITUTED ARYLALIPHATIC ACIDS

Temperature (°C)	Parameter	Monosubstituted	Disubstituted	$\Delta\Delta I$
190	ΔI(Cl)	233.8 (It − Is)	158.4 (If − Ie)	75.4
	ΔI(CH$_3$O)	293.5 (Iu − Is)	110.0 (Ig − Ie)	183.5
120	ΔI(Cl)	191.9 (It − Is)	146.9 (If − Ie)	45.0
	ΔI(CH$_3$O)	246.6 (Iu − Ie)	116.3 (Ig − Ie)	130.3

TABLE V

KOVÁTS RETENTION INDICES OF ARYLACETIC ACIDS AT 120°C

Compound X		I_{exp}
Ie	4-$C_6H_5CH_2O$	2029.1*
If	3-Cl-4-$C_6H_5CH_2O$	2176.0*
Ig	3-CH_3O-4-$C_6H_5CH_2O$	2145.4*
Is	H	1148.6
It	3-Cl	1340.5
Iu	4-CH_3O	1395.2

* Extrapolated values from retention indices measured in the temperature range 160–180°C.

The dependence of the Kováts retention indices on the connectivity indices $^1\chi^v$ was expressed by

$$I = 246.53 \ ^1\chi^v + 438.69 \tag{6}$$
$$n = 36; \ r = 0.910; \ s = 145.77; \ F = 169.1$$

As is evident from Fig. 1, the arylalkoxy derivatives deviate significantly from eqn. 6. Omission of these compounds yielded eqn. 7, while eqn. 8 was calculated only for the arylalkoxy derivatives.

$$I = 231.48 \ ^1\chi^v + 459.61 \tag{7}$$
$$n = 27; \ r = 0.975; \ s = 77.38; \ F = 502.8$$
$$I = 228.30 \ ^1\chi^v + 775.58 \tag{8}$$
$$n = 9; \ r = 0.958; \ s = 32.89; \ F = 77.2$$

The arylalkoxy derivatives show a systematic deviation towards higher values of the Kováts retention indices. When calculating the connectivity indices of unsaturated compounds, the valence contributions δ_i of the double bonds can be included once[32] or twice[33]. The first, more conventional approach was used in eqns. 6–8. Both methods caused the arylalkoxy derivatives to be shifted from the original regression line. An increase in the retention index seems to be the result of some another interaction with the stationary phase that is not included in the connectivity index.

There is a high correlation between the connectivity indices and molar refractivities in the group of the arylaliphatic acids studied. The correlation is described by

$$^1\chi^v = 0.102 \ \Sigma MR + 2.265 \tag{9}$$
$$n = 36; \ r = 0.966; \ s = 0.333; \ F = 479.0$$

As can be seen from Fig. 2, the arylalkoxy derivatives deviate systematically from eqn. 9 towards higher values of ΣMR. Because of this, the retention indices in this series correlate better with MR than with the connectivity indices:

$$I = 26.84 \ \Sigma MR + 931.76 \tag{10}$$
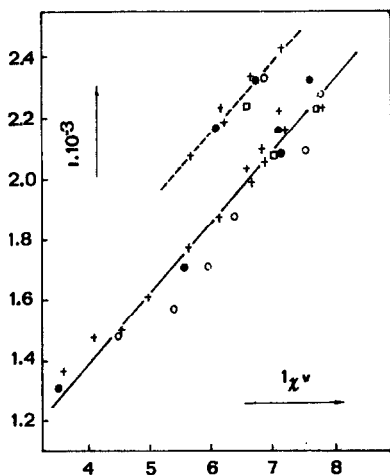$$n = 36; \ r = 0.941; \ s = 118.90; \ F = 271.8$$

Fig. 1. Relationship between Kováts retention indices, I, and connectivity indices, $^1\chi^v$. Dashed line (for arylalkoxy derivatives) calculated from eqn. 8; solid line (for the other derivatives) calculated from eqn. 7. +, Arylacetic; ●, 3-arylpropanoic; □, 2-arylpropanoic; ○, 2-methyl-3-arylpropanoic acid.
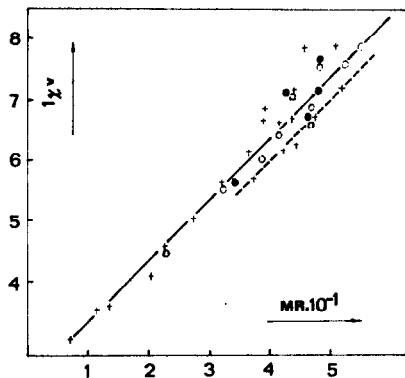
Fig. 2. Relationship between molar refractivity, MR, and connectivity indices, $^1\chi^v$. Dashed line for arylalkoxy derivatives, solid line for the other derivatives. Compounds as in Fig. 1.

Separation of the total value of MR into a contribution of the aromatic substituents, MR_X, and a contribution of the connecting chain Y, MR_Y, yields

$$I = 28.77\ MR_X + 8.57\ MR_Y + 1009.33 \qquad (11)$$
$$n = 36;\ r = 0.963;\ s = 96.54;\ F = 215.7$$

From eqn. 11 it can be concluded that the aromatic substituents and the connecting chains contribute differently to the dispersion interactions with the stationary phase. However, the character of the connecting chain does not have any effect on the correlation of the Kováts retention indices with the connectivity indices. Retention of esters of the arylaliphatic acids seems to be influenced more by the topology of the connecting chain than the dispersion interactions, whereas the opposite seems to apply to the aromatic ring. When the structures differ in the number of aromatic rings, it is probably better to use the molar refractivity for correlation with the retention indices. On the other hand, when structural modifications occur in the connecting chain, the connectivity index seems to be the parameter of choice.

Significant differences were observed when the icremental method was used for the same substituents in the mono- and disubstituted derivatives. These differences were probably due to intramolecular interactions among the substituents. Correlations of the Kováts retention indices with MR or $^1\chi^v$ did not show any significant deviations of the mono- and disubstituted derivatives. It is probable that the effect of these interactions on the retention behaviour is below the value of the standard deviation.

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