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RELATIONSHIPS BETWEEN GAS CHROMATOGRAPHIC RETENTION INDEX AND MOLECULAR STRUCTURE

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SUMMARY

A relationship between the gas chromatographic retention index and molecular structure of the solute, based on the electrostatic interaction, has been found. The solute structure can be defined by the "molecular connectivity" and dipole moment. Good correlations between these theoretical parameters and the retention index values have been found. The mean relative error of the correlations is less than 1% and the regression coefficients are better than 0.99. These results have allowed the empirical expression $RI = \theta + a_f \mu^2$ to be obtained and this is discussed theoretically.

INTRODUCTION

In previous articles^{1,2} an attempt was made to establish a relationship between the molecular structure of different substances and their retention indices, obtained under isothermal conditions from the retention indices of a family of *n*-alkanes³. The structure of the molecule, and its functional groups, were represented by means of two semi-empirical parameters: total electronic energy, E , as the steric contribution to the retention index; and the sum of the net electrostatic charges (Q_i) localized on each of the principal atoms of the molecules, as the contribution of the electrostatic interactions to the retention index.

The retention index can be related to the molecular structure by means of the equation of a multilinear

$$RI = aE + \sum Q_i c_i + b \quad (1)$$

which may be solved by using the least squares method¹⁻⁵. The results obtained with several families of compounds are very interesting, taking into account the relevant governing factors and the degree of error (see Table I).

However, the above model is useless for those substances which cannot be

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TABLE I
 STATISTICAL REGRESSION ANALYSIS OF EQN. 1 FOR DIFFERENT COMPOUND FAMILIES^{1,2,4,5}

<i>Parameter</i>	<i>Sterol acetates</i>	<i>Ethylcyclopentane derivatives</i>	<i>Cyclohexane derivatives</i>
No. of compounds	55	44	27
No. of variables	13	7	7
Regression coefficient	0.9892	0.9869	0.9974
<i>R</i> signification	>99.99	>99.99	>99.99
Exner's function	0.094	0.072	0.043
Mean relative error (%)	0.29	0.15	0.89

derived from a structural base serving as fundamental nucleus, and to the atoms of which an electrostatic charge may be assigned having a physical significance.

Therefore, a more general model has been formulated.

THEORETICAL

The following postulates are employed:

(a) the electrostatic interactions between the solute molecules and the stationary phase contribute to the retention index through the general equation

$$RI = \vartheta + B$$

where ϑ is a steric term related to the molecular volume (mol.wt., "energy", "bond contribution", "vapour pressure", etc.) and B is a term related to the polar interactions with the stationary phase ("interaction index", "enthalpy component of the activity coefficient", etc.).

(b) ϑ and B should be easily and unequivocally determinable for any molecule.

Steric term ϑ

A study has been made of the best way to represent the "steric term" using a physical variable which characterizes the molecule. To do this, a family of hydrocarbons with different degrees of branching, for which RI on squalane is described in the literature⁶, has been selected. Under such conditions, the minimal interaction between the solutes and the stationary phase is known, we can assume that the interactive term B is negligible, thus, the variable representing the "steric factor" must yield a linear correlation with the retention index:

$$RI = \vartheta \tag{2}$$

Of all the functions studied, only the empirical parameter named "molecular connectivity of the bonding orders", χ , and defined by Randić⁷, and Kier, Hall and Murrey⁸⁻¹² is able to describe such a behaviour⁵. Adjusting eqn. 2, by the least squares method, we obtain:

TABLE II

EXPERIMENTAL⁶ AND CALCULATED RETENTION INDICES FOR SATURATED HYDROCARBONS

No. of compounds	15
No. of variables	1
Regression coefficient	0.99942
R^2	0.99884
R signification	99.99
Exner's function	0.009
ϵ , absolute error (i.u.)	
Mean absolute error (i.u.)	4.39
Mean relative error (%)	0.85
Equation	$RI = 199.34\chi + 21.88$

Compound	χ	RI	RI (calc.)	ϵ	Error (%)
Propane	1.4142	300	303.8	3.79	1.26
<i>n</i> -Butane	1.9142	400	403.5	3.46	0.86
<i>n</i> -Pentane	2.4142	500	503.1	3.13	0.62
<i>n</i> -Hexane	2.9142	600	602.8	2.81	0.47
<i>n</i> -Heptane	3.4142	700	702.5	2.48	0.35
<i>n</i> -Octane	3.9142	800	802.1	2.15	0.27
<i>n</i> -Nonane	4.4142	900	901.8	1.82	0.20
<i>n</i> -Decane	4.9142	1000	1001.5	1.49	0.15
Isobutane	1.7320	366	367.1	1.14	0.31
Isopentane	2.2700	476	474.4	1.60	0.33
Neopentane	2.0000	414	420.5	6.56	1.58
Isohexane	2.7700	570	574.0	4.06	0.71
3-Methylpentane	2.8080	585	581.6	3.36	0.57
2,2-Dimethylbutane	2.5606	539	532.3	6.66	1.23
2,3-Dimethylbutane	2.6427	570	548.7	21.31	3.74

$$RI = 199.34\chi + 21.88$$

Table II shows the statistical analysis of the adjustment, as well as the RI values calculated by means of this equation, comparing them with the values given in the literature.

Using the same parameter to relate the retention of an acyclic isoprenoid family with their structures, the equation obtained is:

$$RI = 188.63\chi + 53.32$$

In Table III the again calculated retention indices are compared with those in the literature, and the result of the statistical analysis of the population is also given.

In both cases, the equation obtained appears to be very significant, as it is able to account for over 99.9% of the total variance of the data, and the absolute errors appearing in the re-calculation were small, considering the extreme simplicity of the method applied.

Similarly, it is to be noted that Randic⁷ and Kier *et al.*⁸ have related the parameter χ to different molecular properties, the most interesting of which seems to be

TABLE III

EXPERIMENTAL¹³ AND CALCULATED RETENTION INDICES OF ACYCLIC ISOPRENOIDS

No. of compounds	15
No. of variables	1
Regression coefficient	0.99975
R^2	0.99950
R signification	99.99
Exner's function	0.0062
Mean absolute error (i.u.)	4.78
Mean relative error (%)	0.52
Equation	$RI = 188.63\chi + 53.32$

Compound	χ	RI	$RI\ calc.$	ϵ
2-Methylbutane	2.2700	478.6	481.52	2.92
2-Methylpentane	2.7700	570.8	575.83	5.03
2-Methylhexane	3.2700	667.8	670.15	2.35
2-Methylheptane	3.7700	766.4	764.46	1.94
2-Methyloctane	4.2700	867.6	858.78	8.82
2,6-Dimethylheptane	4.1259	829.7	831.60	1.94
2,6-Dimethyloctane	4.6639	937.4	933.08	4.32
2,7-Dimethyloctane	4.6259	931.8	925.91	5.95
2,6-Dimethylnonane	5.1639	1021.9	1027.40	5.43
2,7-Dimethylnonane	5.1639	1036.8	1027.40	9.40
2,6-Dimethyldecane	5.6639	1119.8	1121.71	1.91
2,6-Dimethylundecane	6.1639	1218.2	1216.03	2.13
2,6,9-Trimethyldecane	6.0197	1178.9	1188.03	9.11
2,6,10-Trimethylundecane	6.5197	1276.8	1283.14	6.37
2,6-Dimethyldodecane	6.6639	1313.6	1310.34	3.30

the molecular polarizability. Indeed, if there is a linear relationship between the volume of the molecule and its polarizability, the connectivity, χ , will describe more comprehensively the interactions between non-polar molecules, which is the case studied here.

Interactive term B

In order to study the interactive term easily and independently from the "steric term", a series of linear aliphatic alcohols was chosen, since they can be chromatographed on different stationary phases and RI data for them may be found in the literature.

Fig. 1 shows the retention indices of the saturated linear alcohols, as well as those of n -alkanes, on two stationary phases of different polarity: the two sets of three straight lines obtained on Carbowax 20M (polar) and squalane (non-polar) are very similar; the additional variable required to convert the three lines into a single reference plane (common to both sets) is what we call the "interactive term".

In order to express this "interactive term" by means of a physical variable, we use the electrostatic theory of molecular interaction. Given that the total charge on any solute molecule is zero, its ability to interact with the stationary phase may be differentiated through the electrostatic moments (dipole, quadrupole, etc.) providing

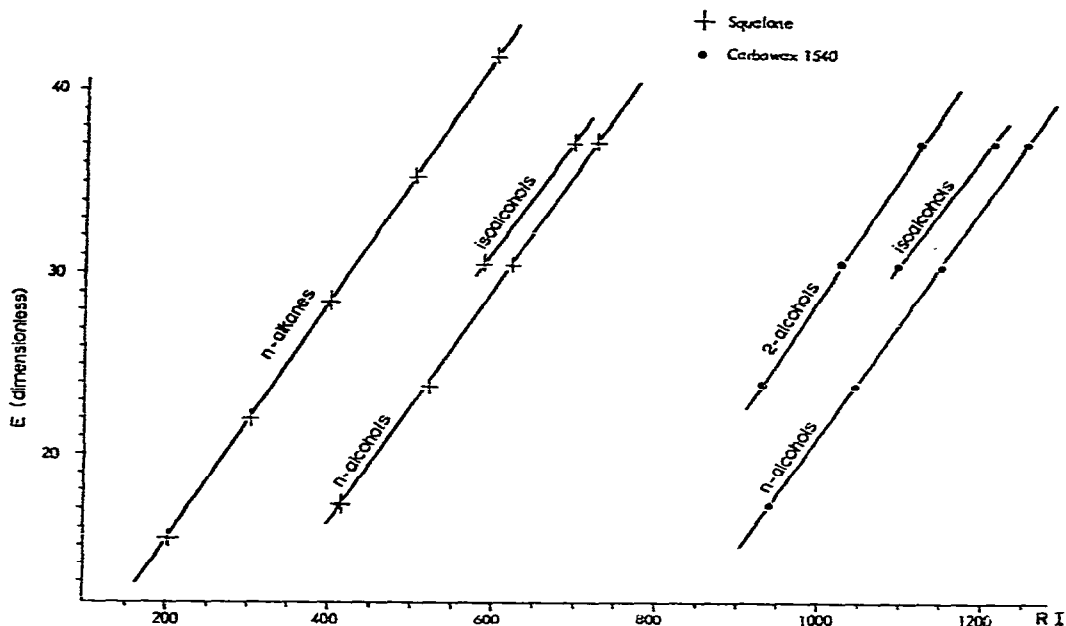


Fig. 1. Retention indices of saturated linear alcohols and *n*-alkanes against the steric factor *E*.

that the stationary phase is considered as a substratum of two-dimensional and undefined electrical charge distribution, common to all solutes the retention of which is being studied. To a first approximation, the degree of electrostatic molecular interaction may be expressed using the dipole moment of the molecule.

There is a precedent, in the literature, where the retention index is related to the dipole moment. Thus, in 1958, Kováts proposed the expression

$$\Delta RI = 6\delta Rd + 50\mu$$

where the index increment on a polar column relative to a non-polar column is related to the solute polarity via its dipole moment μ . The first term δRd has a physical significance which parallels that of the "steric term" in our equation: δRd is the increment of molar refractivity due to the solute's functional group, and therefore reflects the real volume of the solute molecules, as well as their polarizability.

Thus, the complete equation for the calculation of the retention index is:

$$RI = a\chi + b\mu^2 + c \quad (3)$$

This equation has been applied to the retention indices of a family of aliphatic alcohols and hydrocarbons (Table IV) and to olefinic and paraffinic hydrocarbons (Table V), taking the dipole moment values as given in the literature. In both cases, the equation succeeds in explaining over 99.9% of the total variance of the data. All the

TABLE IV

EXPERIMENTAL⁶ AND CALCULATED RETENTION INDICES OF OLEFINIC AND PARAFFINIC HYDROCARBONS ON SQUALANE AT 80°Bibliographic values of dipole moment are used¹⁴.

No. of compounds	20
No. of variables	2
Regression coefficient	0.99986
R^2	0.99972
R signification	99.99
Exner's function	0.0057
Mean absolute error (i.u.)	1.83
Mean relative error (%)	0.39
Equation	$RI = 200.13\chi + 217.45\mu^2 + 16.89$ (3.1)

Compound	χ	μ (D)	RI	
			exptl.	calc.
Propane	1.4142	0	300	299.9
<i>n</i> -Butane	1.9142	0	400	399.9
<i>n</i> -Pentane	2.4142	0	500	500.0
<i>n</i> -Hexane	2.9142	0	600	600.1
<i>n</i> -Heptane	3.4142	0	700	700.2
<i>n</i> -Octane	3.9142	0	800	800.2
<i>n</i> -Nonane	4.4142	0	900	900.3
<i>n</i> -Decane	4.9142	0	1000	1000.3
2-Methylpropane	1.7320	0.13	366	367.2
2-Methylbutane	2.2700	0.13	476	474.8
2,2-Dimethylpropane	2.0000	0*	414	417.1
2-Methylpentane	2.7700	0.13*	570	574.9
3-Methylpentane	2.8080	0.17*	585	585.1
2,2-Dimethylbutane	2.5606	0.21*	539	539.0
1-Propene	1.2071	0.35	287	285.1
2-Butene	1.7071	0.34	384	383.6
2-Methyl-1-propene	1.5629	0.50	383	384.0
2-Methyl-2-butene	2.2700	0.44*	514	514.0
<i>cis</i> -2-Butene	1.9142	0.33	417	423.6
<i>trans</i> -2-Butene	1.9142	0	405	400.0

* Calculated through a previous adjustment of the other values.

statistical terms and variables have a very high degree of significance and the absolute error obtained from the re-calculation is small, considering the simplicity of the method.

General equation

We conclude that the dipole moment of the solute molecule can be used to estimate the degree of interaction with the stationary phase, and that the equation proposed here describes the phenomenon of retention in a quite satisfactory manner.

It should be pointed out that in all the cases studied the values of the coefficients a and c of the variables adjusted are close to those given by eqn. 3 for the theoretical straight line relating the retention index of *n*-alkanes to their connectivity:

$$RI = 200\chi + 17.16$$

(4)

TABLE V

EXPERIMENTAL¹⁵ AND CALCULATED RETENTION DATA FOR ALIPHATIC HYDROCARBONS

No. of compounds	17	14
No. of variables	2	2
Regression coefficient	0.999905	0.999993
R ²	0.999815	0.999987
Exner's function	0.0052	0.0015
Mean absolute error (l.u.)	3.05	0.40
Mean relative error (%)	0.37	0.06
Equations		
Carbowax	$RI = 201.92x + 221.42\mu^2 + 11.17$	
Squalane	$RI = 200.06x + 41.24\mu^2 + 16.95$	

Compound	Carbowax		Squalane	
	exptl.	calc.	exptl.	calc.
Propane	300.00	296.71	300.00	299.88
n-Butane	400.00	397.67	400.00	399.91
n-Pentane	500.00	498.63	500.00	499.94
n-Hexane	600.00	599.59	600.00	599.97
n-Heptane	700.00	700.55	700.00	700.00
n-Octane	800.00	801.50	800.00	800.03
n-Nonane	900.00	902.46	900.00	900.06
n-Decane	1000.00	1003.42	1000.00	1000.09
Ethanol	942.8	951.89	421.5	421.91
1-Propanol	1044.9	1050.30	521.8	521.47
1-Butanol	1151.3	1148.89	621.5	621.06
1-Pentanol	1256.3	1249.16	722.7	720.96
2-Propanol	931.4	934.85	—	—
2-Butanol	1028.6	1027.90	—	—
2-Pentanol	1122.5	1118.36	—	—
Isobutanol	1095.5	1095.20	584.5	584.90
2-Methylbutanol	1211.4	1207.55	694.4	695.98

For molecules differing from the linear hydrocarbons, the retention may be based on eqn. 4, but a polarity term, function of μ^2 , should be added. An attempt to generalize the equations obtained by correlation is now made.

Suppose that, for a nonpolar molecule, a constant retention index on any stationary phase is observed, its value depending exclusively on the steric contribution of the molecule, which we shall call θ and which can be derived from eqn. 4, according to:

$$\theta = 200x + 17.16 \quad (5)$$

For a non-polar substance we can therefore write:

$$RI = \theta \quad (6)$$

In the case of polar molecules, eqn. 6 must be adjusted to allow for the corresponding interactive term. The latter is related to the value of the solute dipole moment and transforms the retention index equation into the form:

$$RI = \theta + a_F \mu^2 \quad (7)$$

The validity of eqn. 7 has been verified as follows. Starting from experimental RI and μ data for a given substance X , it is possible to obtain the value of a_F associated with the gas chromatographic conditions

$$a_F = \frac{RI_{XF} - \theta_X}{\mu_X^2} \quad (8)$$

where RI_{XF} = retention index of solute X on the stationary phase F , θ_X = steric term of solute X , calculated according to eqn. 5, μ_X = value of the dipole moment of solute X and a_F = factor associated with the stationary phase and working conditions. Under identical experimental conditions, the "chromatographic dipole moment", μ_i , of the other molecules belonging to the same chemical series may be calculated using:

$$\mu_i = \sqrt{\frac{RI_{iF} - \theta_i}{a_F}} \quad (9)$$

If a_F represents the interaction capacity of the stationary phase F with the standard dipole, and if μ_i is a function of the dipole moment value of the solute i , then it should be possible to use the μ_i values obtained with this method to predict the RI values on any stationary phase F_j , whose a_{F_j} value is known:

$$RI_{i,F_j} = \theta_i + a_{F_j} \mu_i^2 \quad (10)$$

This method has been applied to several families of chemicals, and the results obtained are now presented and commented upon.

RESULTS

In order to be able to test the validity of eqn. 9, μ_i values were calculated for a number of saturated alcohols, whose retention indices on four different stationary phases are known [squalane, OV-17, 1,2,3-triscyanoethoxypropane (TCEP) and Carbowax 4000] a given temperature and degree of impregnation (Table VI). Starting from the bibliographic value¹⁴ of the dipole moment of ethanol ($\mu = 1.70D$), and of the retention indices of ethanol on each of the stationary phases, it is possible to calculate the a_{F_j} factor corresponding to each stationary phase and temperature used.

It is seen that the "chromatographic dipole moment" values obtained, for the wide range of stationary phase polarities selected, vary by up to 6%, which is acceptable, since this is an *a priori* calculation of the μ_i of polar solutes. Therefore μ_i can be considered as being independent of the nature of the stationary phase. The values of μ_i obtained show good agreement with those described in the literature¹⁴.

The methyl esters of fatty acids

The methyl esters of fatty acids, possessing different degrees of unsaturation and of branching, were chromatographed on two stationary phases ethylene glycol succinate (EGS) and SE-30. Methyl decanoate was taken as base molecule for the calculations, assigning to it a dipole moment of 1.70 D, and the a_F factors associated with each stationary phase were calculated from it. Starting with the experimental

TABLE VI

VALUES OF "CHROMATOGRAPHIC DIPOLE MOMENT" OBTAINED WITH DIFFERENT STATIONARY PHASES

 μ_{sq} in squalane, μ_{ov} in Silicone OV-17, μ_{tcep} in 1,2,3-triscyanoethoxypropane and μ_{cw} in Carbowax.

Compound	μ_{sq}	μ_{ov}	μ_{tcep}	μ_{cw}	$\bar{\mu}$	Δ	Error (%)
1-Propanol	1.6867	1.7183	1.7026	1.7057	1.7033	0.031	1.85
1-Butanol	1.7240	1.7474	1.7022	1.7178	1.7228	0.045	2.62
1-Pentanol	1.7662	1.7759	1.6976	1.7291	1.7422	0.078	4.50
2-Propanol	1.4672	1.6271	1.6188	1.5936	1.5767	0.159	10.14
2-Propanol	—	1.6271	1.6188	1.5936	1.6132	0.033	2.07
2-Butanol	1.5234	1.6057	1.6058	1.5842	1.5798	0.082	5.22
2-Pentanol	1.5211	1.5939	1.5947	1.5813	1.5728	0.073	4.67
Isobutanol	1.6711	1.6968	1.6668	1.6806	1.6788	0.030	1.78
Isopentanol	1.7322	1.7253	1.6710	1.6977	1.7066	0.061	3.58

retention indices on EGS, the "chromatographic dipole moments" for the other molecules of the family were calculated, and these values used to calculate the theoretical retention on the SE-30 column. The calculation procedure is explained in detail in Table VII, which also composes the theoretical values obtained with the experimental ones. The proposed model is able to explain 99.94% of the total variance of the data, with absolute errors sufficiently small to make it viable for identification purposes.

Aldehydes and ketones

Some bibliographic data¹⁵ for a number of aldehydes and ketones, on two stationary phases of different polarity (squalane and Carbowax) are available. Butanal, whose dipole moment is 2.50 D¹⁴, is taken as base molecule for the calculation. When the chromatographic dipole moments of the other molecules of the group considered were calculated, it could be seen that this value is practically constant for each homologues series, which is perfectly reasonable. Using the described procedure (eqn. 10), values of the retention index for each member of the family, on the squalane phase, were predicted and compared with the experimental data (for details, see Table VIII). The statistical analysis shows that, in spite of the smaller number of molecules present and the disparity of structures considered, one of which is furfural, 99.89% of the total variance of the data can be explained. The mean absolute value of the error is of the same order as the reproducibility of the chromatographic data and hence the prediction of the retention index values for these molecules, for which the experimental values are unknown, seems to be valid.

Esters

From the literature¹⁷ a number of experimental retention indices for esters, larger than those of the previous groups and also on two stationary phases (SE-30 and Carbowax), were obtained. A number of acetates and methyl esters were selected, as well as some molecules having different conformations (methyl benzoate, methyl phenylacetate, ethyl butyrate, isobutyl isobutyrate), in order to examine the possibilities of generalization. In the case of linear esters the dipole moment values recommended in the literature, constant for all the homologues with more than five carbons

TABLE VII

EXPERIMENTAL¹⁶ AND CALCULATED RETENTION DATA FOR FATTY ACID METHYL ESTERS

Base molecule for the calculation: methyl decanoate; dipole moment, 1.70 D⁴; retention indices, 1328.30 i.u. on SE-30 (at 200°), 1805.02 i.u. on EGS (at 170°); α_F factors (eqn. 8), 40.1958 for SE-30 (at 200°), 205.1508 for EGS (at 170°).

Compound	Chromatographic dipole moment calculation for the solutes (eqn. 9):			
	RI _{EGS}	α	θ	μ
Methyl decanoate	1805.02	5.97487	1212.13	1.700
Methyl dodecanoate	1983.9	6.97487	1412.13	1.669
Methyl tetradecanoate	2156.84	7.97487	1612.13	1.629
Methyl hexadecanoate	2325.96	8.97487	1812.13	1.583
Methyl heptadecanoate	2410.92	9.47487	1912.13	1.559
Methyl octadecanoate	2495.86	9.97487	2012.13	1.535
Methyl tetradeca-9-enoate	2230.5	7.79137	1575.43	1.787
Methyl hexadeca-9-enoate	2387.5	8.79137	1775.43	1.727
Methyl octadeca-9-enoate	2547.71	9.79137	1975.43	1.670
Methyl octadeca-9,12-dienoate	2621.40	9.60786	1938.73	1.824
Methyl octadeca-9,12,15-trienoate	2712.49	9.42436	1902.03	1.987
Methyl isooctadecanoate	2463.64	9.8307	1983.30	1.530
Methyl anteisononadecanoate	2566.11	10.3687	2090.90	1.522
Methyl isoeicosanoate	2638.02	10.8307	2183.30	1.489
Methyl anteisouncosanoate	2739.64	11.3687	2290.90	1.479
	Calculation of retention index on SE-30:			
	Calc.	Exptl.	ϵ	
Methyl decanoate	1328.29	1328.3	0.0	
Methyl dodecanoate	1524.10	1518.3	5.8	
Methyl tetradecanoate	1718.80	1712.7	6.1	
Methyl hexadecanoate	1912.80	1911.5	1.3	
Methyl heptadecanoate	2009.85	2012.2	2.35	
Methyl octadecanoate	2106.93	2113.0	6.10	
Methyl tetradeca-9-enoate	1703.77	1700.3	3.47	
Methyl hexadeca-9-enoate	1895.36	1892.6	2.76	
Methyl octadeca-9-enoate	2087.56	2111.4	23.89	
Methyl octadeca-9,12-dienoate	2072.49	2074.0	1.54	
Methyl octadeca-9,12,15-trienoate	2060.82	2076.1	15.31	
Methyl isooctadecanoate	2077.42	2076.2	1.1E	
Methyl anteisononadecanoate	2184.01	2184.9	0.94	
Methyl isoeicosanoate	2272.39	2277.8	5.45	
Methyl anteisouncosanoate	2378.82	1285.3	6.49	
<i>Statistical analysis</i>				
No. of compounds	15			
No. of variables	2			
Regression coefficient	0.99973			
R ²	0.99945			
Mean absolute error (i.u.)	6.09			
Mean relative error (%)	0.31			

TABLE VIII

EXPERIMENTAL¹⁵ AND CALCULATED RETENTION DATA FOR ALDEHYDES AND KETONES

Base molecule for the calculation: butanal; dipole moment, 2.50 D¹⁴; retention indices¹⁵, 540.7 i.u. on Squalane (at 62°), 890.7 i.u. on Carbowax (at 70°); a_F factors, 19.0112 for Squalane (62°), 75.0112 for Carbowax (70°).

Compound	Chromatographic dipole moment calculation for the solutes (on Carbowax):			
	RI	χ	θ	μ
Butanal	890.7	2.0236	421.88	2.50
Hexanal	1092.4	3.0236	621.88	2.50
Heptanal	1191.4	3.5236	721.88	2.50
Octanal	1292.8	4.0236	821.88	2.50
Nonanal	1392.0	4.5236	921.88	2.50
Decanal	1492.2	5.0236	1021.88	2.50
Pentanal	992.7	2.5236	521.88	2.50
Isopentanal	933.7	2.3794	493.04	2.424
Nonanone-3	1300.5	4.4749	912.13	2.275
Furfural	1459.8	2.5581	528.78	3.523

	Retention index calculation (on squalane)		
	Calc.	Exptl.	ϵ
Hexanal	741.08	746.5	5.42
Heptanal	840.89	844.8	3.91
Octanal	941.17	—	—
Nonanal	1040.98	—	—
Pentanal	641.18	644.0	2.82
Isopentanal	604.74	608.5	3.76
Nonanone-3	1010.53	—	—
Furfural	764.74	762.0	2.74

Statistical analysis	
No. of molecules	5
No. of variables	2
Regression coefficient	0.99946
R^2	0.99893
Mean absolute error (i.u.)	3.73
Mean relative error (%)	0.52

in the chain, have been used in all instances. Nonyl acetate was selected for the calculation of the factors associated with the stationary phases used.

The results obtained are shown in Table IX. The calculated values are near to the experimental ones, representing on both stationary phases, over 99.99% of the total variance of the data, with a relative error not exceeding 0.5%. With structurally different molecules, no discrimination was observed.

Cyclic alcohols

The aim here was to try and see whether the described method could deal with molecules of various structures which were sufficiently complex to make them un-

TABLE IX

EXPERIMENTAL¹⁷ AND CALCULATED RETENTION DATA FOR ESTERS

When the esters are linear, a dipole moment of 1.10 D has been taken. The dipole moment for the iso-esters has been taken as 1.61 D. In the other cases, marked with an asterisk, a previous calculation employing the experimental RI on Carbowax has been used.

Compound	δ	μ	Carbowax		SE-30	
			exptl.	calc.	exptl.	calc.
Propyl acetate	600.00	1.779*	—	1009.4	704	704.0
Isopropyl acetate	571.16	1.509*	866	866.0	—	646.0
Butyl acetate	700.00	1.700	1065	1074.0	802	795.0
Isobutyl acetate	671.16	1.599*	1002	1002.0	—	755.2
Amyl acetate	800.00	1.700	1169	1174.0	896	895.0
Iscamyl acetate	771.17	1.632*	1116	1116.0	853	858.7
Hexyl acetate	900.00	1.700	1264	1274.0	993	995.0
Ischexyl acetate	871.16	1.613*	1208	1208.0	—	956.7
Heptyl acetate	1000.00	1.700	—	1374.0	1096	1095.0
Nonyl acetate	1200.00	1.700	1569	1574.0	1296	1295.0
Decyl acetate	1300.00	1.700	1674	1674.0	1395	1395.0
Dodecyl acetate	1500.00	1.700	—	1874.0	1595	1595.0
Methyl butyrate	612.13	1.700	971	986.1	—	707.1
Methyl isobutyrate	588.68	1.610	903	924.1	—	678.1
Methyl valerate	712.13	1.700	1081	1086.1	808	807.1
Methyl isovalerate	683.30	1.610	1013	1018.7	—	768.5
Methyl hexanoate	812.13	1.700	1183	1186.1	907	907.1
Methyl isohexanoate	783.30	1.610	1094	1118.7	—	868.5
Methyl heptanoate	912.13	1.700	1282	1286.1	1008	1007.1
Methyl octanoate	1012.13	1.700	1378	1386.1	1109	1107.1
Methyl nonanoate	1112.13	1.700	1484	1486.1	1211	1207.1
Methyl decanoate	1212.13	1.700	1584	1586.1	1310	1307.1
Methyl undecanoate	1312.13	1.700	1694	1686.1	1410	1407.1
Methyl dodecanoate	1412.13	1.700	1800	1786.1	1513	1507.1
Methyl myristate	1612.13	1.700	2002	1986.1	1714	1707.1
Methyl hexadecanoate	1812.13	1.700	2190	2186.1	1911	1907.1
Methyl octadecanoate	2012.13	1.700	—	2386.1	2098	2107.1
Methyl benzoate	862.46	2.437*	1631	1631.0	1080	1057.1
Ethyl butyrate	712.13	1.572*	1032	1032.0	787	793.4
Isobutyl isobutyrate	859.84	1.334*	1090	1090.0	901	918.3
Methyl phenylacetate	957.08	2.489*	1759	1759.0	1156	1160.8
			<i>Carbowax</i>	<i>SE-30</i>		
No. of molecules			28	24		
No. of variables			2	2		
Regression coefficient			0.999627	0.99974		
R ²			0.999253	0.99948		
Mean absolute error (i.u.)			6.16	5.24		
Mean relative error (%)			0.46	0.44		

suitable for calculation by any of the other systems proposed in the different theories of retention and structure. Heintz *et al.*¹⁸ have recently published a table of retention indices for bicyclic alcohols and esters, on two stationary phases: Carbowax and EGSS-X (ethylene succinate - methysilicone copolymer (low silicone content, U.S. Patent 3,263,401)). From this table, those molecules which possess only the alcohol function have been selected.

The only suitable dipole moment value found in the bibliographic tables¹⁴,

was 1.65D for bicyclo [2.2.2]octan-1-ol and we took it as the base for calculations. From the experimental retention index data on Carbowax, it was possible to calculate the chromatographic dipole moment for each of the molecules of the family considered, and these values were then used for the calculation of the retention indices on the other two stationary phases for which are available data, namely, SE-30 and EGSSX. The results obtained, as well as their comparison with the experimental values, are shown in Table X. The results obtained on the SE-30 phase are very similar to those in the previous tables (mean error 6 i.u., regression coefficient 0.99) while the results obtained with EGSSX phase are less satisfactory. This difference is also observable in the case of the methyl esters (Table VII) and suggests a particular interaction mechanism.

TABLE X

EXPERIMENTAL¹⁸ AND CALCULATED RETENTION DATA FOR CYCLIC ALCOHOLS

Base molecule for the calculation: bicyclo[2,2,2]octan-1-ol; dipole moment, 1.65 D⁶; retention index, 1660 i.u. on Carbowax (140°); a_F factor, 339.23 for Carbowax (140°).

Compound	Chromatographic dipole moment calculation for the solutes (on Carbowax):			
	RI_{CW}	χ	θ	μ
A Bicyclo[3,3,0]octan-1-ol	1660	3.31228	679.62	1.70
B Bicyclo[2,2]heptan-1-ol	1495	2.7854	574.24	1.64
C Bicyclo[2,2,2]octan-1-ol	1598	3.2854	674.24	1.65
D <i>endo</i> -Bicyclo[2,2,1]octan-2-ol	1544	2.8602	589.20	1.678
E <i>exo</i> -Bicyclo[2,2,1]octan-2-ol	1558	2.8602	589.20	1.69
F <i>endo</i> -2-Methyl-bicyclo[2,2,1]heptan-2-ol	1471	3.1834	653.84	1.55
G <i>exo</i> -2-Methyl-bicyclo[2,2,1]heptan-2-ol	1469	3.1834	653.84	1.55
H <i>endo</i> -7-Dimethyl-2-methyl-bicyclo[2,2,1]heptan-2-ol	1574	3.9443	806.02	1.50
I <i>exo</i> -7-Dimethyl-2-methyl-bicyclo[2,2,1]heptan-2-ol	1600	3.9443	806.02	1.53

a_F factors, 142.06 for SE-30 (from C retention data), 408.39 for EGSSX (from F retention data)

	RI			
	SE-30		EGSSX	
	Calc.	Exptl.	Calc.	Exptl.
A	1090	1310	1859	—
B	956	942	1672	1669
C	1061	1061	1786	1775
D	989	—	1739	1704
E	995	—	1755	1711
F	996	998	1635	1635
G	995	999	1635	1636
H	1125	1133	1730	1719
I	1139	1146	1762	1755

Alcohols

Starting from the a_F values calculated from ethanol, once the series of μ_i values for a particular stationary phase have been calculated (for this purpose, the retention indices on Carbowax were employed) it is possible to calculate *a priori* the $RI_{i(F)}$ of any of these solutes on any other stationary phase, at a given temperature (eqn. 10).

TABLE XI

EXPERIMENTAL¹⁹ AND CALCULATED RETENTION DATA FOR ALIPHATIC ALCOHOLS

Base molecule for calculation: ethanol; dipole moment, 1.70 D; retention indices, 384.43 i.u. on Squalane (90°), 937.04 i.u. on Carbowax (90°), 535.26 i.u. on OV-17 (90°), 1202.21 i.u. on TCEP (90°); a_{ff} factors (90°), 29.214 for Squalane, 220.429 for Carbowax, 81.405 for OV-17, 312.182 for TCEP.

Compound	Chromatographic dipole moment calculation for the solutes (on Carbowax)			
	RI_{cw}	χ	θ	μ
Ethanol	937.04	1.4142	300.00	1.70
1-Propanol	1041.32	1.9142	400.00	1.7057
1-Butanol	1150.43	2.4142	500.00	1.7178
1-Pentanol	1256.01	2.9142	600.00	1.7291
2-Propanol	923.37	1.7320	363.56	1.5936
2-Butanol	1024.37	2.2700	471.16	1.5842
2-Pentanol	1122.37	2.7700	571.16	1.5813
Isobutanol	1093.77	2.2700	471.16	1.6806
Isopentanol	1214.06	2.8080	578.76	1.6977

	RI					
	SQ		OV-17		TCEP	
	calc.	exptl.	calc.	exptl.	calc.	exptl.
1-Propanol	484.99	483.12	636.84	640.35	1308.3	1305.02
1-Butanol	586.21	586.83	740.21	748.55	1421.2	1404.58
1-Pentanol	687.34	691.14	843.40	856.76	1533.4	1499.7
2-Propanol	437.75	425.45	570.30	570.07	1156.4	1181.7
2-Butanol	544.48	538.96	675.46	681.06	1254.6	1277.2
2-Pentanol	644.21	638.76	774.71	777.97	1351.8	1365.1
Isobutanol	553.67	552.75	701.08	705.54	1352.9	1338.5
Isopentanol	662.96	666.42	813.40	820.49	1478.5	1450.5

	SQ	OV-17	TCEP
No. of molecules	8	8	8
No. of variables	2	2	2
Regression coefficient	0.99926	0.99940	0.9960
F^2	0.99853	0.9988	0.9920
Mean absolute error (i.u.)	4.12	6.80	19.64
Mean relative error (%)	0.72	0.93	1.45

The results of such a calculation are shown in Table XI where they are compared with the experimental values previously obtained¹⁹.

Except for the case of TCEP, where the experimental *RI* error range was large (10–15 i.u.), the adjusted experimental data are quite acceptable. It can be seen that eqn. 10, in every instance, accounts for over 99% of the total variance of the data, all the statistical parameters being significant.

Derivatives of cyclohexane

The same calculation procedure was used as in the previous case, applied to a group of 36 derivatives of cyclohexanes and cyclohexenes (methyl, 1,4-dimethyl, isopropyl and 1-methyl-1-isopropyl) in order to obtain the retention indices on capillary

columns. The stationary phases were squalane, methylsilicone (SE-30) and phenylcyanopropylmethylsilicone (OV-225)²⁰. Methylcyclohexane ($\chi = 3.393$) was used as the base molecule.

Using eqn. 3.1 in Table V, in order to make a correction for hydrocarbons, olefins and paraffins, we obtain $\theta = 696.9$ for methylcyclohexane. The retention indices found for methylcyclohexane were:

Carbowax 20 M	795.2	$\alpha_F(\text{CW})$	= 600.12
squalane	731.9	$\alpha_F(\text{SQ})$	= 217.45
OV-225	771.5	$\alpha_F(\text{OV-225})$	= 456.78
SE-30	730.9	$\alpha_F(\text{SE-30})$	= 211.40

From eqn. 3.1 we calculated the α_F values for each phase and the chromatographic dipole moments associated with each substance (see Table V).

Table XII shows the statistical results for the 36 alkyl derivatives of cyclohexane and cyclohexene using three different stationary phases.

TABLE XII

CYCLOHEXANE AND CYCLOHEXENE ALKYL DERIVATIVES

Statistical summary of calculated and experimental (20) retention indices. *RI* on Carbowax 20 M are used to obtain the "chromatographic dipole moment".

	<i>SQ</i>	<i>OV-225</i>	<i>SE-30</i>
No. of compounds	36	36	36
Regression coefficient	0.9968	0.9972	0.9963
R^2	0.9937	0.9945	0.9926
Mean relative error (%)	0.77	0.83	0.93
Mean absolute error (i.u.)	6.74	7.94	8.18
<i>Equations</i>			
Squalane	$RI = \theta_i + 217.45 \mu_i^2$		
OV-225	$RI = \theta_i + 456.78 \mu_i^2$		
SE-30	$RI = \theta_i + 211.40 \mu_i^2$		

DISCUSSION

The plot of the α_F coefficients obtained for each stationary phase against the retention index increments (as defined by McReynolds) for 1-butanol (ΔRI_b) for each exhibits a linear relationship (Fig. 2). This seems to suggest a similar relation for any other stationary phase and thus it would appear to be possible to predict, *a priori*, the *RI* value of any molecule of the family on any of the phases described by McReynolds²¹.

The hypothesis of a linear relationship between α_F and ΔRI_b is based on the resemblance between the polarity profiles of the stationary phases as described by McReynolds. This suggests that an interaction mechanism common to most of the commercial stationary phases exists. Apiezon, Nujol and polyester phases are exceptions to this rule (Fig. 3).

This method shows great potential for predicting the retention index for compounds which contain the same functional group, but without substitution of any elements by heteroatoms. The molecular connectivity parameter as defined by Randic⁷ and Hall *et al.*⁹ cannot distinguish between different atoms in the same topological structure.

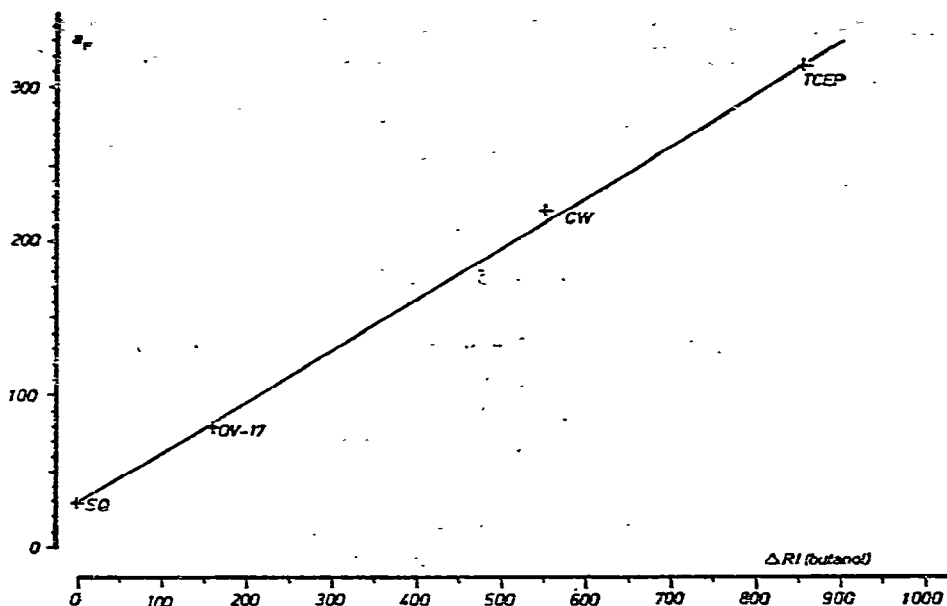


Fig. 2. α_F coefficients for different stationary phases against the retention index increments for 1-butanol.

A theoretical explanation for the empirical relation 10 can be found, taking as a basic theory that of "field-flow fractionation" by Giddings²², in which the normal field of the carrier gas flow is caused by the electrostatic interactions at large distances between the stationary phase and the eluted molecules. According to Hirschfelder *et al.*²³, the potential energy of interaction averaged over orientations may be expressed by:

$$\varphi = \varphi^{es} + \varphi^{ind} + \varphi^{dis}$$

The induction effect is never important²³ in interactions between neutral molecules, while the dispersion effect is important even in the interactions between molecules with large dipole moments. Using this theory and omitting terms divided by r with an exponent of more than 6, we obtain

$$\varphi = -\frac{2}{3} \cdot \frac{1}{r^6} \cdot \frac{\mu_a \mu_b}{kT} - \frac{3}{2} \cdot \frac{\alpha_a \alpha_b}{r^6} - \frac{I_a^0 I_b^0}{I_a^0 + I_b^0} \quad (11)$$

for the averaged interaction energy between two molecules a and b (stationary phase and solute) where μ = dipole moment, k = Boltzmann constant, T = absolute temperature, r = distance of the interaction, α = polarizability and $I^0 \equiv h\nu^0$ = first ionization energy.

From the classical expression for the retention index

$$RI \equiv 100n + 100 \left(\frac{\log V_{g_{n+1}} - \log V_{g_n}}{\log V_{g_{n+1}} - \log V_{g_n}} \right)$$

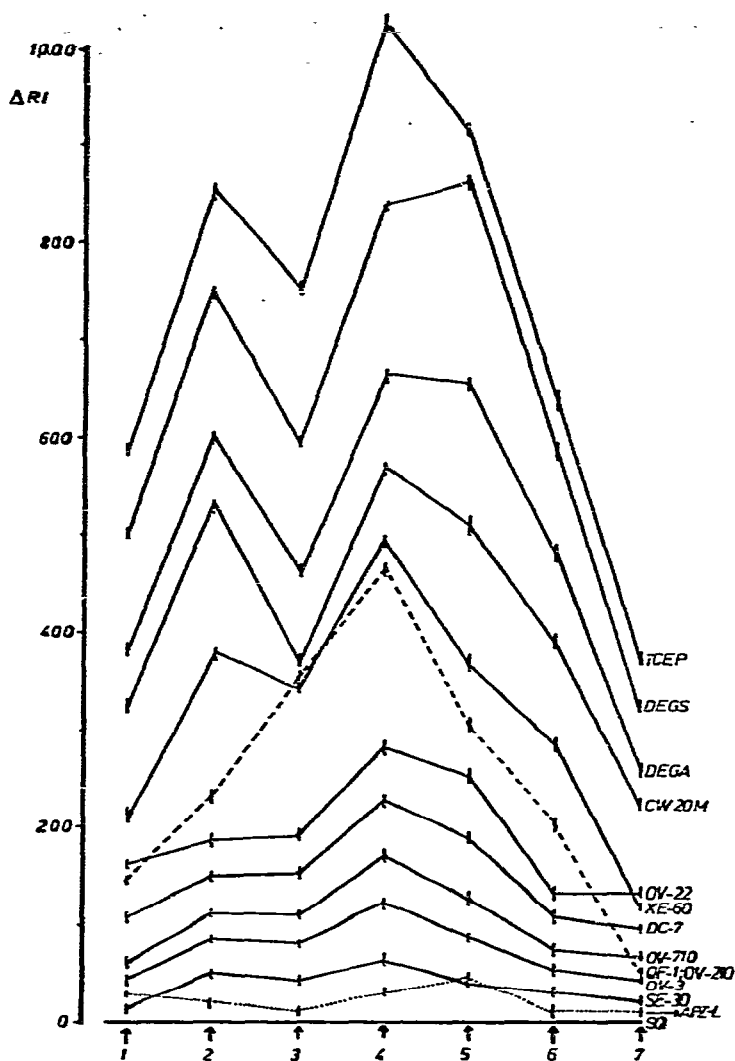


Fig. 3. McReynolds retention index increments² for some stationary phases. Solutes: 1 = benzene; 2 = 1-butanol; 3 = 2-pentanone; 4 = 1-nitropropane; 5 = pyridine; 6 = 2-methyl-2-pentanol; 7 = 2-9ctyne. Stationary phases: TCEP = 1,2,3-Tris(cyano ethoxy)propane; DEGS = diethylene glycol succinate; DEGA = diethylene glycol adipate; CW 20M = Carbowax 20M; APZ-L = Apiezon L; SQ = squalane.

we take only the function between brackets as an expression of retention I :

$$I = \frac{\log V_{g_x} - \log V_{g_n}}{\log V_{g_{n+1}} - \log V_{g_n}}$$

Taking into account the relationship between V_g , k and ΔG° :

$$I_1 = \frac{(\Delta H^\circ)_2 - (\Delta H^\circ)_1}{(\Delta H^\circ)_2 - (\Delta H^\circ)_3}$$

Then to a first approximation it is possible to assume that, when dealing with systems of regular solutions, $(\Delta S^0)_1 \approx (\Delta S^0)_2 (\approx (\Delta S^0)_3)$ where the subscript 1 \equiv X, the eluted substance with index function I_1 , 2 \equiv n, the hydrocarbon that precede 1, and 3 \equiv n+1, the hydrocarbon that follows 1.

We assume that:

$$\Delta H^0 = \varphi N; \quad I_1 = \frac{\varphi_2 - \varphi_1}{\varphi_2 - \varphi_3}$$

Replacing the interaction energies φ_1 , φ_2 and φ_3 by their corresponding values given in eqn. 11 and taking into account the fact that the first ionization energies are very similar, we obtain the following expression (Table XIII)

$$I_1 = \frac{8\mu_0^2}{9kTI_0\alpha_0(\alpha_3 - \alpha_2)} \cdot \mu_1^2 + \frac{\alpha_1 - \alpha_2}{\alpha_3 - \alpha_2} \quad (12)$$

where μ_1 = dipole moment of the substance, μ_0 = dipole moment of the stationary phase, I_0 = ionization energy of stationary phase, α_0 = polarizability of stationary phase, α_1 = polarizability of the substance and $\alpha_3 - \alpha_2$ = polarizability difference between two homologous and consecutive hydrocarbons.

TABLE XIII
ENERGY OF FIRST IONIZATION²⁴

Compound	Energy (eV)
n-C ₄ H ₁₀	10.55-10.79
n-C ₆ H ₁₄	10.43
(CH ₃) ₂ CH-CH(CH ₃) ₂	10.24
C ₆ H ₆	9.2
CHCl ₃	11.4
iso-C ₄ H ₉ OH	10.17
CH ₃ COOC ₂ H ₅	10.09
(CH ₃) ₂ CO	9.7-9.9

In eqn. 12, the term in μ^2 depends only on the nature of the stationary phase and the absolute temperature. The difference $\alpha_3 - \alpha_2$ can be considered as a constant, and corresponds to the α_F factor in the empirical relation¹⁰. In the other hand, the second term of the expression depends only on the polarizability (steric molecular parameter) of the substance, and according to Kier *et al.*⁸, the polarizability is directly related to the molecular connectivity; in other words as θ of the equation 10.

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