

RELATION OF GAS CHROMATOGRAPHIC BEHAVIOUR AND CHEMICAL STRUCTURE

THE APPLICATION OF ENERGY PARAMETERS

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(Received January 25th, 1967)

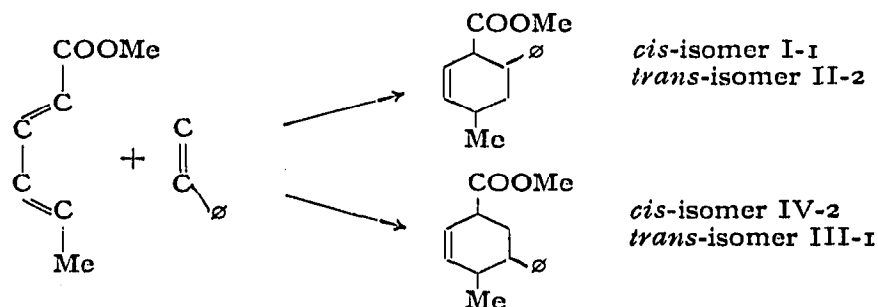
INTRODUCTION

There is a growing interest in the correlation of behaviour in gas-liquid chromatography and chemical structure. The methods proposed so far are based on the model of hard sphere^{1, 2} molecules. With these methods, however, it is difficult to account for many of the structural variations of organic chemistry.

An alternative method, using energy parameters or using the partition functions of statistical mechanics, in principle does not have any such limitations because the energy of the molecule is a function of both the nature and the coordinates of its components. In order to be able to show some basic simple rules of the proposed method we studied a number of model compounds composed of component groups that are constant in the sense of quantum theory³.

MODEL COMPOUNDS COMPOSED OF QUASI FUNDAMENTAL SYSTEMS

The Diels-Alder reaction of methyl sorbate and styrene⁴ produces a set of four racemic* mixtures of addition products.



We have been able to determine the configuration of each addition product by means of I.R., N.M.R. and mass spectrometry.

The absence of temperature effects in the N.M.R. spectra up to 150° indicates that the cyclohexene conformations 1 and 2 are fixed and rigid and do not interchange

* Each racemic mixture is considered as one compound.

into each other. The phenyl group determines the conformation by taking an equatorial position (Fig. 1).

Performing the same Diels-Alder reaction with a *meta* or a *para* substituted styrene⁵ results each time in an analogous set of four substituted adducts. This reaction therefore is a convenient way of obtaining model compounds in which the parent* groups and the substituent* groups can be varied independently from each other. The substituted ethylbenzenes give another set of corresponding model

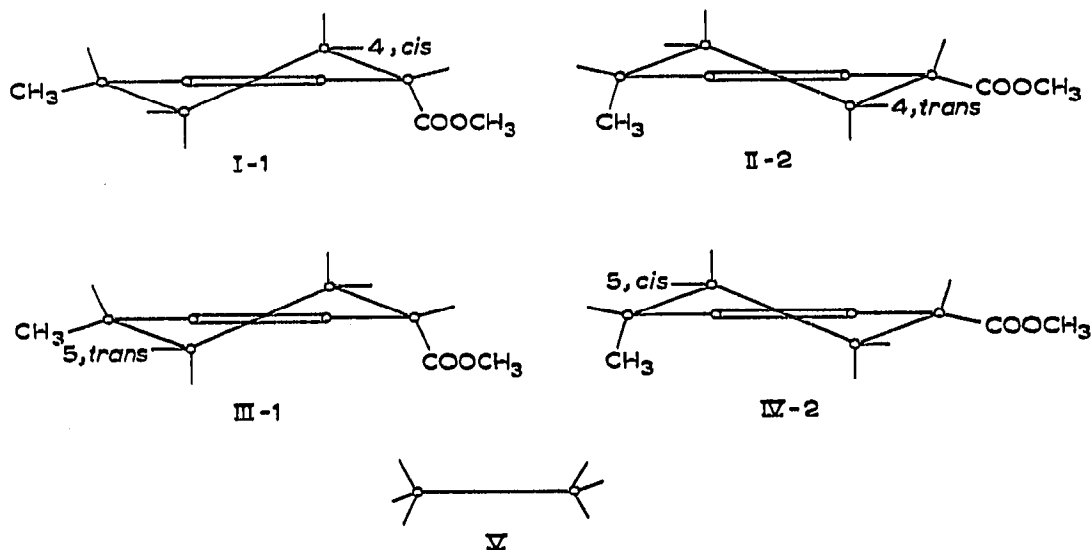


Fig. 1. The conformations of the "parent groups" of the model compounds: 3-carbomethoxy-*cis*-4-phenyl-*cis*-6-methylcyclohexene-1; 3-carbomethoxy-*trans*-4-phenyl-*cis*-6-methylcyclohexene-1; 3-carbomethoxy-*trans*-5-phenyl-*cis*-6-methylcyclohexene-1; 3-carbomethoxy-*cis*-5-phenyl-*cis*-6-methylcyclohexene-1; and ethylbenzene.

compounds. For our investigation, forty model compounds were thus obtained. All parent groups and all substituent groups are constant, in the sense of quantum theory, throughout all combinations of the forty model compounds.

THEORY

Empirical relations between structure and gas chromatographic data of organic compounds were formulated by WEHRLI AND KOVÁTS^{7**}. The adherence to additivity rules of the retention indices of KOVÁTS, which in effect are logarithmic functions of relative retention volumes, suggested to us the idea that the increments of the retention indices, or the increments of the logarithms of the relative retention volumes, should be directly related to the partition functions of statistical mechanics.

When a non-polar liquid is taken as the stationary phase our model compounds should obey additivity rules of the energy function^{3,8} (see also the mathematical consequences of the theory).

* This terminology, introduced by ANDERSEN, BEYER AND WATSON⁶, is a convenient and concise way to differentiate between two series of component groups. The parent groups are shown in Fig. 1, the substituted phenyl groups are regarded as substituent groups.

** By way of simplification WEHRLI AND KOVÁTS⁷ neglected conformational and some other stereomeric aspects of chemical structure.

Some mathematical consequences of the theory

The partition coefficient of gas-liquid chromatography can be regarded as an equilibrium constant of the phase transformation reaction of the solute between the gas phase and the liquid phase⁹. Taking the energy^{3,8} of the solute in the gas phase as the level of zero energy, the equilibrium constant for our model compounds can simply be written as the product of the partition functions of the component groups:

$$K_{P,S} = e^{-(\varepsilon_P + \varepsilon_S)/RT} = e^{-\varepsilon_P/RT} \cdot e^{-\varepsilon_S/RT} = Q_P \cdot Q_S \quad (1)$$

K = equilibrium constant of the phase transformation reaction.

ε = energy of a component group in the liquid phase, its energy in the gas phase taken as the level of zero energy.

Q = partition function.

Subscripts "P" and "S" refer to "Parent group" and "Substituent group" respectively.

R = gas constant.

T = absolute temperature.

It may be derived from known gas chromatographic formulas⁹ that the ratio of the retention volumes of a pair of compounds will give the same numerical value as the ratio of their equilibrium constants. This value is a function of three variables (chemical structure of solutes, type of stationary phase and temperature) only; all other parameters drop out, therefore with the stationary phase and the temperature chosen

$$\frac{V_{R1,1}}{V_{R2,2}} = \frac{K_{P1,S1}}{K_{P2,S2}} = \frac{Q_{P1} \cdot Q_{S1}}{Q_{P2} \cdot Q_{S2}} \quad (2)$$

V_R = retention volume corrected for "Air peak".

Subscripts refer to component groups.

When one component group of a series of model compounds is kept constant, the partition functions associated with the constant component group can be completely eliminated according to eqn. (2). The resultant ratio is a function of the structural variation in the other component group only (see also Tables I to IV).

$$\frac{V_{R1,1}}{V_{R2,1}} = \frac{Q_{P1} \cdot Q_{S1}}{Q_{P2} \cdot Q_{S1}} = \frac{Q_{P1}}{Q_{P2}} \quad (3)$$

The free energy difference of the molecules is an additive function of the contributions of its component parts.

Its relation to the relative retention volumes is found by combination of eqns. (1) and (2):

$$\Delta F_{1,1} - \Delta F_{2,2} = (\varepsilon_{P1} - \varepsilon_{P2}) + (\varepsilon_{S1} - \varepsilon_{S2}) = -2.303RT \log \left(\frac{V_{R1,1}}{V_{R2,2}} \right) \quad (4)$$

ΔF = free energy of the molecule in the liquid phase, its energy in the gas phase taken as the level of zero energy. Indices and subscripts refer to component groups.

At moderate temperatures the energy function⁸ can be split into external and internal parts.

The internal part can be split into still smaller parts representing the vibrational and rotational group contributions. For pairs of stereoisomers, by approximation all energy contributions will be equal, the rotational* contributions excepted:

$$\frac{V_{R1,1}}{V_{R1',1}} = \frac{Q_{P1, \text{vibr.}} \cdot Q_{P1, \text{rot.}}}{Q_{P1', \text{vibr.}} \cdot Q_{P1', \text{rot.}}} = \frac{Q_{P1, \text{rot.}}}{Q_{P1', \text{rot.}}} \quad (5)$$

Testing the theory

We are now in a position to test some mathematical consequences of the theory.

A. Taking the compounds with parent group "I-I" as the reference in every series, the contributions of the substituent groups are completely eliminated.

According to eqn. (3), the relative retention volumes show the influence of the parent groups only and they are therefore independent of the substituent groups (Tables I and II).

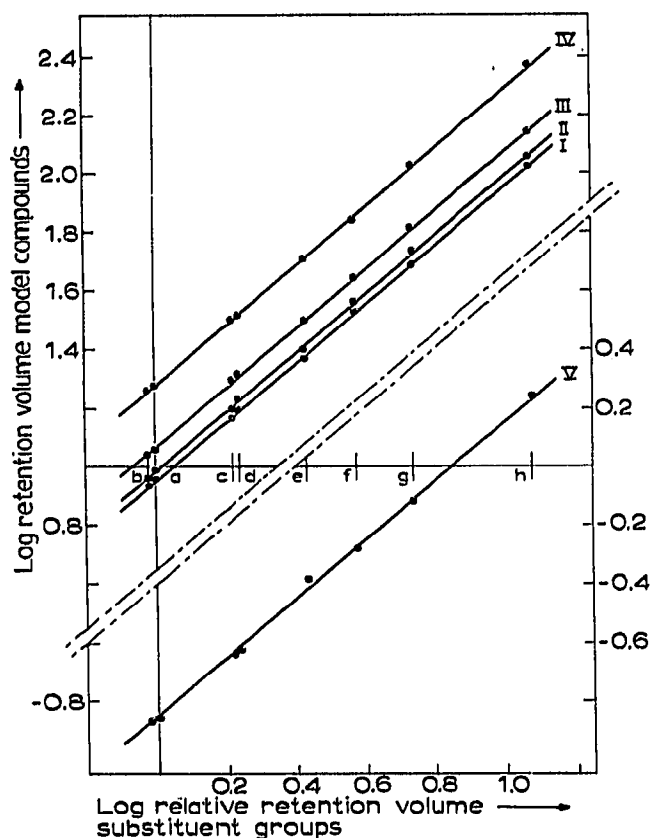


Fig. 2. Plots of logarithms of retention volumes (calculated from values of Table V) of model compounds against logarithms of relative retention volumes (calculated from mean values of Table III) of substituent groups. (The theory predicts straight lines with a slope of 1. The lines were calculated, with the theoretical condition for the slope, with the method of least squares.)

B. In Tables III and IV the compounds with substituent group "a" are taken as reference, therefore in these tables the contribution of the parent groups are eliminated.

According to eqn. (3), the relative retention volumes now show the influence of

* A detailed study of this aspect of the theory is in progress.

TABLE I

INFLUENCE OF PARENT GROUPS

Relative retention volumes on Apiezon L at 125°. Parent group "I-1" taken as reference. Mean values and probable errors calculated.

Parent group*	Substituent group								Mean	P.E.
	a H-ø	b pF-ø	c mMe-ø	d pMe-ø	e mCl-ø	f pMeO-ø	g pBr-ø	h pNO ₂ -ø		
I-1	I	I	I	I	I	I	I	I	I	—
II-2	1.076	1.051	1.067	1.083	1.066	1.071	1.085	1.077	1.072	0.004
III-1	1.280	1.271	1.341	1.323	1.338	1.294	1.336	1.310	1.312	0.009
IV-2	2.071	2.102	2.150	2.088	2.162	2.038	2.183	2.227	2.128	0.021
V	0.01517	0.01558	0.01549	0.01516	0.01749	0.01556	0.01566	0.01662	0.01584	0.0027

* See Fig. 1.

TABLE II

INFLUENCE OF PARENT GROUPS

Relative retention volumes on Apiezon L at 150°. Parent group "I-1" taken as reference. Mean values and probable errors calculated.

Parent group*	Substituent group								Mean	P.E.
	a H-ø	b pF-ø	c mMe-ø	d pMe-ø	e mCl-ø	f pMeO-ø	g pBr-ø	h pNO ₂ -ø		
I-1	I	I	I	I	I	I	I	I	I	—
II-2	1.048	—	1.034	1.050	1.041	1.046	1.055	1.052	1.047	0.003
III-1	1.256	1.242	1.248	1.239	1.278	1.235	1.265	1.280	1.255	0.006
IV-2	1.929	1.964	1.894	1.917	2.062	1.874	1.972	2.054	1.958	0.023
V	0.0250	0.0254	0.0267	0.0232	0.0263	0.0245	0.0252	0.0267	0.0254	0.0004

* See Fig. 1.

TABLE III

INFLUENCE OF SUBSTITUENT GROUPS a-h

Relative retention volumes on Apiezon L at 125°. Substituent group "a" taken as reference. Mean values and probable errors calculated.

Parent group*	Substituent group							
	a H-ø	b pF-ø	c mMe-ø	d pMe-ø	e mCl-ø	f pMeO-ø	g pBr-ø	h pNO ₂ -ø
I-1	I	0.947	1.616	1.709	2.568	3.707	5.303	11.44
II-2	I	0.933	1.617	1.736	2.567	3.722	5.395	11.55
III-1	I	0.964	1.736	1.811	2.753	3.843	5.676	12.00
IV-2	I	0.969	1.691	1.737	2.703	3.675	5.634	12.41
V	I	0.973	1.650	1.708	2.961	3.803	5.473	12.54
Mean	I	0.957	1.662	1.740	2.710	3.750	5.496	11.99
P.E.	—	0.007	0.021	0.017	0.065	0.028	0.063	0.20

* See Fig. 1.

TABLE IV

INFLUENCE OF SUBSTITUENT GROUPS a-h

Relative retention volumes on Apiezon L at 150°. Substituent group "a" taken as reference. Mean values and probable errors calculated.

Parent group*	Substituent group							
	a H- σ	b pF- σ	c mMe- σ	d pMe- σ	e mCl- σ	f pMeO- σ	g pBr- σ	h pNO ₂ - σ
I-1	1	0.945	1.449	1.726	2.484	3.223	4.575	9.14
II-2	1	—	1.430	1.729	2.466	3.217	4.603	9.16
III-1	1	0.934	1.440	1.703	2.529	3.169	4.609	9.32
IV-2	1	0.962	1.423	1.715	2.655	3.131	4.678	9.73
V	1	0.960	1.550	1.602	2.612	3.159	4.602	9.76
Mean	1	0.950	1.458	1.695	2.549	3.180	4.613	9.42
P.E.	—	0.006	0.021	0.021	0.033	0.016	0.015	0.12

* See Fig. 1.

the substituent groups only and are completely independent of the parent groups.

C. The sensitivity of the energy function to variations of chemical structure and the precision of the additivity rules are also demonstrated in a plot of logarithm of retention volumes of model compounds against logarithm of relative retention volumes of substituent groups (see Fig. 2).

D. At moderate temperatures the energy function can be split into external and internal parts. The internal part can be split into still smaller parts representing the vibrational and rotational group contributions⁸.

For pairs of stereoisomers, by approximation all energy contributions will be equal, the rotational contributions excepted.

Considering the rotational degrees of freedom in our Diels-Alder adducts it is to be expected that the pairs of isomers containing the parent groups "I-1" and "III-1" will be eluted in the same order as the pairs containing "II-2" and "IV-2", which is indeed the case (Tables I and II, eqn. (4)).

EXPERIMENTAL

Diels-Alder adducts were prepared by the method given in refs. 4 and 5. Ethylbenzenes were commercially available or were prepared by conventional methods.

Gas chromatographic conditions

Chromatograph: F & M, model 810-15.

Detector: hydrogen flame ionization.

Recorder: Honeywell, -0.05 to 1 mV, 1 sec.

Column dimensions: 2 m \times 0.5 cm I.D. copper coiled tube.

Solid support: Diatoport S (60/80 mesh).

Stationary phase: Apiezon L (6:94).

Temperature: 125° and 150°.

Carrier gas: He at 100 ml/min measured at exit at atmospheric pressure.

Column efficiency: about 2000 theoretical plates.

Sample size: 0.0001 to 0.05 mg.

TABLE V

RETENTION VOLUMES OF MODEL COMPOUNDS ON APIEZON L AT 125°
The volumes were measured in litres at 1 atm and 20°.

Parent group*	Substituent group							
	a H-ø	b pF-ø	c mMe-ø	d pMe-ø	e mCl-ø	f pMeO-ø	g pBr-ø	h pNO ₂ -ø
I-1	9.19	8.70	14.85	15.71	23.60	34.08	48.75	105.2
II-2	9.80	9.15	15.86	17.02	25.16	36.49	54.35	113.3
III-1	11.48	11.07	19.93	20.79	31.59	44.10	65.13	137.8
IV-2	18.89	18.31	31.95	32.81	51.06	69.43	106.44	234.4
V	0.1394	0.1356	0.2300	0.2381	0.413	0.530	0.763	1.748

* See Fig. 1.

TABLE VI

RETENTION VOLUMES OF MODEL COMPOUNDS ON APIEZON L AT 150°
The volumes were measured in litres at 1 atm and 20°.

Parent group*	Substituent group							
	a H-ø	b pF-ø	c mMe-ø	d pMe-ø	e mCl-ø	f pMeO-ø	g pBr-ø	h pNO ₂ -ø
I-1	2.816	2.660	4.080	4.860	6.996	9.076	12.88	25.72
II-2	2.952	—	4.220	5.104	7.280	9.496	13.59	27.05
III-1	3.536	3.304	5.092	6.020	8.944	11.204	16.30	32.94
IV-2	5.432	5.225	7.728	9.316	14.424	17.008	25.41	52.84
V	0.0704	0.0676	0.1091	0.1128	0.1839	0.2224	0.324	0.687

* See Fig. 1.

Analysis time: 0.7 to 2350 min.

Precautions and correction factors

Sample size was adjusted until symmetrical peaks were observed, showing that Henry's law is obeyed⁹. In practice sample volumes for the Diels-Alder adducts were kept less than 3 % of calculated volume of stationary phase in one theoretical plate. The ethylbenzenes require considerably smaller sample sizes to produce symmetrical peaks, air saturated with their vapour was injected by means of a 10 µl syringe.

A silanized support was used.

Ample time was given for the column to reach stationary conditions. Samples were injected at least one hour after oven temperature reading showed constant value.

The retention volumes of a series of even-numbered normal alkanes (C-6, C-8, C-10, C-12, C-14, and C-16) were determined at the two analysis temperatures.

The dead volume of the apparatus or the "air peak" for each analysis temperature was determined from the retention volumes of these normal alkanes according to the method of GOLD¹⁰.

In order to avoid frequent repetition of elaborate precision measurements of carrier-gas flow, column inlet and outlet pressure, effect of the bleeding of the stationary phase, effect of slight differences of oven temperature, etc., a number of suitable

normal alkanes were injected simultaneously with each sample. An overall correction factor for each analysis was calculated from the retention times of the internal standards. The corrected retention volumes are shown in Tables V and VI.

SUMMARY

Energy parameters are used to obtain a relation between gas chromatographic behaviour and chemical structure. The sensitivity of the energy function to variations of chemical structure and the precision of the additivity rules are demonstrated with a number of model compounds composed of component groups that are constant in the sense of quantum theory.

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