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NEW PERSPECTIVES IN THE PREDICTION OF KOVÁTS INDICES

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SUMMARY

Sets of Kováts indices corresponding to different chromatographic conditions and/or to different chemical families can be rendered coherent by the use of topology–information correlations established according to the principles of the DARC (Description, Acquisition, Retrieval and Conception) topological system. These correlations are based on the Kováts indices or on data derived from these indices (Kováts index increment, ΔI, and isotopology factor, τI). They serve to demonstrate the prediction potential, the minimization of the number of parameters and of the number of data, and the precision of our approach. Chromatographic retention data banks can be envisaged on the basis of this approach.

INTRODUCTION

In analytical organic chemistry, the methods used for the acquisition and automatic computer processing of mass and nuclear magnetic resonance (NMR) spectroscopic data are advancing rapidly. There are already operational data banks in mass spectroscopy[1], and ^{13}C NMR spectroscopic data banks are currently being set up[2,3]. "File search" or "library search" computer systems are being used successfully in the computer-aided interpretation of mass spectra[2,3]. Nevertheless, from the data processing point of view, the identification of new compounds that have no reference spectrum is still the most difficult problem[4]; thus, current research on the method of asking these banks a question is aimed at discovering resemblances between compound sub-structures[5], rather than determining the identities of the compounds themselves.

Together with the means required to develop and exploit these spectroscopic data processing methods, a preliminary and qualitative chromatographic analysis may be a simple and useful complementary means of identification, provided that there is a rapidly accessible data bank. We shall show how such a data bank can be set up, starting from an in-depth exploitation of a population of Kováts indices which, in gas–liquid chromatography, are recognized as being the most reproducible retention data.

Although very useful collections of chromatographic retention data already exist[6–8], they often appear in handbook form and their use is relatively restricted to establishing whether or not a particular compound has already been studied and, if

so, under what conditions. Thus, an organic chemist often encounters two types of problems:

(1) When synthesizing a new family of compounds there are often no chromatographic data available to identify these products; however, there might be some products already studied whose structures are comparable but whose substituents or chemical functions are different. If so, how can he extrapolate the behaviour of new compounds from already known compounds?

(2) For a known compound, there may be available retention data obtained under certain chromatographic conditions (stationary phase SP_1 and temperature T_1), but not under other chromatographic conditions (SP_2 and T_2). If so, how can he extrapolate the behaviour of a known compound under new conditions (SP_2 and T_2) from already known conditions (SP_1 and T_1)?

The same methodology can be used to solve both of these problems. Indeed, the functional group and each site of the molecular environment of compounds belonging to a same population contribute an additional value to the Kováts indices. The variations in these elementary contributions result either from a structural variation (functional group, environment) or from a variation of the chromatographic conditions (stationary phase, polarity and temperature). These contributions and their variations can be grasped by setting up topology–information correlations[9-11]. We shall show how, with these correlations, it is possible to analyze and extend the information content of already published populations of Kováts indices. We shall also stress the strategy required in choosing the minimum number of pertinent compounds to permit the characterization of a population of compounds.

METHOD AND RESULTS

There are already many works on the establishment of retention–structure relationships, notably for hydrocarbon analysis[12-14], which have been recently reviewed[15-18]. In referring to one of these methods. Souter repeated his opinion "that a method is required, based on a much smaller number of structural terms. These terms would be evaluated by solving an over-determined set of equations expressing retention data for a number of compounds; least-squares methods would probably be applied in this procedure"[19].

We shall give examples of how the DARC* topological system[20,21], which is based on the concept of an Environment which is Limited, Concentric and Ordered (ELCO) (i.e., on a topological description of the molecular environment from an origin taken as a focus), meets these criteria. As the principles of the DARC system as well as its generalization to the processing of polyfunctional compounds, of those with no apparent functional group and the simultaneous processing of different populations, appear elsewhere with chromatographic applications[11], we shall not consider them here.

In order to show how an in-depth exploitation of the Kováts indices could be envisaged so as to extend the information content of already published populations of Kováts indices, we shall deal successively with four chromatographic problems:

(1) the interpolation and extrapolation of structural effects;

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* Description, Acquisition, Retrieval and Conception.

(2) the prediction of indices to be determined on stationary phase SP_2 at temperature T_1 on the basis of indices already determined for the same compounds on SP_1 at the same temperature T_1;

(3) the prediction of indices to be determined on SP_2 at T_2 based on those already determined on SP_1 at T_1;

(4) the perturbations brought about by varying the functional group in different populations whose member compounds have comparable structures (*i.e.*, having the same ELCO).

Also, we shall consider the methodology problems raised by Souter: prediction potential, minimization of the number of parameters and of the number of data, and precision.

Prediction of structural effects: interpolation and extrapolation

Rijks[22,23] determined, on squalane at 50° and 70°, the Kováts indices of 45 alkanes having up to nine carbon atoms. We have re-calculated them at 60° and extended the population by including the first nine reference *n*-alkanes whose value is, by definition, already known. We have treated this population by a degree *n* topology–information correlation[13]. In the given example, we shall illustrate the flexibility in choosing a structural variable and the possibilities of minimizing the number of parameters. This will be done by re-grouping the topological sites located at the same distance from the focus, and having the same degree of ramification. We thus obtain a correlation having only 18 structural parameters. The correlation coefficient, R, is 0.9998 and the Exner ψ test is 0.026. For the 45 compounds analyzed by Rijks, the standard deviation is 3.9 I.U. and the average deviation between the experimental value and the value calculated on the basis of the correlation is 3.1 I.U., *i.e.*, the relative average deviation is $< 0.5\%$.

With this topology–information correlation, it is not only possible to make predictions for the alkanes with nine carbon atoms, but also those having more than nine carbon atoms. Insofar as the methodology is concerned, the extrapolations based on this correlation for alkanes having a greater number of carbon atoms than the alkanes used in establishing this correlation are justified by the degree *n* polyfocalization, thanks to the weight factors attributed to each of the topological sites[11]. As an example, in Table I we show the predictions for alkanes having up to ten carbon atoms, *i.e.*, 150 compounds of which only about 50 were used to establish the correlation (Scheme 1).
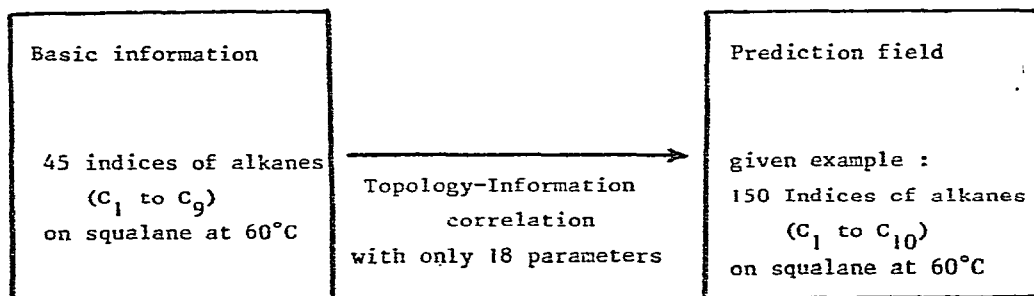
Scheme 1. Example of the prediction potential of a topology–information correlation.

TABLE I

PREDICTION OF KOVÁTS INDICES OF 150 C_1–C_{10} ALKANES ON SQUALANE AT 60°
WITH A TOPOLOGY–INFORMATION CORRELATION LIMITED TO 18 PARAMETERS

With a 23-parameter correlation instead of a 17-parameter correlation, the maximum deviations are
lowered by about half (*i.e.*, to *ca.* 1 %).
The name of the main chain is indicated by the number of carbon atoms it contains (e.g., 6 = hexane,
11 = undecane). The main chain substituents are: M = methyl, DM = dimethyl, TM = trimethyl
or tetramethyl, PM = pentamethyl, ET = ethyl, DET = diethyl, IPR = isopropyl.

Alkane	Kováts indices on squalane at 60°			Difference	
	Exptl. (Rijks) (a)	Calc. (correlation) (b)	Exptl. (Matukuma) (c)	$I_a - I_b$	$I_c - I_b$
1	100.0	100.0		0.0	
2	200.0	199.8		0.2	
3	300.0	297.9		2.1	
4	400.0	404.8		−4.8	
2-M3		360.3			
5	500.0	502.0		−2.0	
2-M4	475.4	478.4		−3.0	
2,2-DM3	412.6	407.1		5.5	
6	600.0	597.1		2.9	
2-M5	569.8	569.5		0.3	
3-M5	584.6	587.1		−2.5	
2,2-DM4	537.6	538.6		−1.0	
2,3-DM4	568.1	566.9		−1.2	
7	700.0	696.6		3.4	
2-M6	666.8	662.6		4.2	
3-M6	676.5	675.8		0.7	
3-ET5	686.6	686.1		0.5	
2,2-DM5	626.3	628.4		−2.1	
2,3-DM5	672.5	669.2		3.3	
2,4-DM5	630.1	633.9		−3.8	
3,3-DM5	660.2	660.4		−0.2	
2,2,3-DM4	641.1	643.6		−2.5	
8	800.0	797.8		2.2	
2-M7	765.0	761.2		3.8	
3-M7	772.6	773.4		−0.8	
4-M7	767.4	769.0		−1.6	
3-ET6		772.6			
2,2-DM6	719.9	715.6		4.3	
2,3-DM6	760.8	756.1		4.7	
2,4-DM6	732.4	738.3		−5.9	
2,5-DM6	728.7	726.7		2.0	
3,3-DM6	744.7	747.9		−3.2	
3,4-DM6	771.6	769.3		2.3	
2-M3-ET5	762.4	761.9		0.5	
3-M3-ET5	775.7	772.7		3.0	
2,2,3-TM5	738.6	744.8		−6.2	
2,2,4-TM5	690.9	694.9		−4.0	
2,3,3-TM5	761.4	759.2		2.2	
2,3,4-DM5	753.7	748.3		5.4	
9	900.0	899.0	900.0		1.0
2-M8		863.3	864.8		1.5

TABLE I (continued)

Alkane	Kováts indices on squalane at 60°			Difference	
	Exptl. (Rijks) (a)	Calc. (correlation) (b)	Exptl. (Matukuma) (c)	$I_a - I_b$	$I_c - I_b$
3-M8	870.4	873.7	870.8	−3.3	−2.9
4-M8		868.3	863.3		−5.0
3-ET7		874.6	867.4		−7.2
4-ET7		863.5	858.2		−5.3
2,2-DM7	815.9	815.6	816.5	0.3	0.9
2,3-DM7		852.7	855.5		2.8
2,4-DM7		830.6	821.2		−9.4
2,5-DM7		836.5	833.7		−2.8
2,6-DM7		819.6	827.5		7.9
3,3-DM7	836.9	839.6	837.3	−2.7	−2.3
3,4-DM7		860.5	858.0		−2.5
3,5-DM7		847.2	834.4		−12.8
4,4-DM7		839.9	828.6		−11.3
2M3-ET6		846.5	844.7		−1.8
2M4-ET6		833.2	824.9		−8.3
3M3-ET6		858.0	856.0		−2.0
3M4-ET6		859.7	855.6		−4.1
2,2,3-TM6	822.9	825.7	823.3	−2.8	−2.4
2,2,4-TM6	790.4	793.4	790.7	−3.6	−2.7
2,2,5-TM6	776.9	774.1	777.3	2.8	3.2
2,3,3-TM6		844.9	841.7		3.2
2,3,4-TM6	850.5	846.5	849.7	4.0	3.2
2,3,5-TM6	812.8	817.1	813.2	−4.3	−3.9
2,4,4-TM6	809.2	812.6	809.7	−3.4	−2.9
3,3,4-TM6		858.1	855.1		−3.0
3,3-DET5	879.8	875.3	880.2	4.5	4.9
2,2-DM-3-ET5	824.2	836.3	824.4	−12.1	−11.9
2,3-DM-3-ET5		865.2	875.0		9.8
2,4-DM-3-ET5	838.2	834.7	838.4	3.5	3.7
2,2,3,3-TM5	854.8	853.4	855.8	1.4	2.4
2,2,3,4-TM5	822.2	826.0	821.9	−3.8	−4.1
2,2,4,4-TM5	774.5	763.2	774.6	11.3	11.4
2,3,3,4-TM5	860.6	855.0	861.1	5.6	6.1
10		1000.2	1000.0		−0.2
2-M9		964.5	963.9		−0.6
3-M9		975.8	969.6		−6.2
4-M9		968.6	960.0		−8.6
5-M9		967.6	957.4		−10.2
3-ET8		976.6	964.0		−12.6
4-ET8		967.2	951.5		−15.7
2,2-DM8		918.6	914.9		−3.7
2,3-DM8		954.0	952.1		−1.9
2,4-DM8		930.8	915.8		−15.0
2,5-DM8		932.3	921.8		−10.5
2,6-DM8		933.0	931.5		−1.5
2,7-DM8		928.8	928.5		−0.3
3,3-DM8		941.4	932.0		−11.2
3,4-DM8		949.0	936.0		−13.0

TABLE I (*continued*)

Alkane	Kováts indices on squalane at 60°			Difference	
	Exptl. (Rijks) (a)	Calc. (correlation) (b)	Exptl. (Matukuma) (c)	$I_a - I_b$	$I_c - I_b$
3,5-DM8		941.2	921.8*		−19.4
3,6-DM8		948.1	929.0*		−19.1
4,4-DM8		933.3	918.0		−15.3
4,5-DM8		953.9	943.1*		−10.8
4-IPR7		935.5	925.0		−10.5
2-M-3-ET7		947.6	941.0		−6.6
2-M-4-ET7		923.2	907.4		−15.8
2-M-5-ET7		936.8	924.8		−12.0
3-M-3-ET7		954.0	953.0		−1.0
3-M-4-ET7		948.7	935.7*		−13.0
4-M-3-ET7		955.3	940.5		−14.8
4-M-4-ET7		947.7	937.6		−10.1
2,2,3-TM7		923.8	914.4		−9.4
2,2,4-TM7		887.2	875.7		−11.5
2,2,5-TM7		885.4	878.1		−7.3
2,2,6-TM7		870.2	873.0		2.8
2,3,3-TM7		935.6	931.7		−3.9
2,3,4-TM7		936.9	933.4*		−3.5
2,3,5-TM7		925.1	912.9*		−12.2
2,3,6-TM7		909.7	919.0		+8.9
2,4,4-TM7		903.7	889.4		−14.3
2,4,5-TM7		920.6	906.7		−13.9
2,4,6-TM7		886.0	870.1		−15.9
2,5,5-TM7		897.2	891.7		−5.5
3,3,4-TM7		943.4	936.6		−6.8
3,3,5-TM7		915.6	907.7		−7.9
3,4,4-TM7		948.2	932.2		−16.0
3,4,5-TM7		949.0	945.0*		−4.0
2-M-3-IPR6		917.4	915.5		−1.9
3,3-DET6		958.3	954.1		−4.2
3,4-DET6		947.8	945.8		−2.0
2,2-DM-3-ET6		914.9	902.1		−12.8
2,2-DM-4-ET6		882.3	881.3		−1.0
2,3-DM-3-ET6		948.5	949.4		0.9
2,3-DM-4-ET6		935.0	930.6		−4.4
2,4-DM-3-ET6		930.6	929.8*		−0.8
2,4-DM-4-ET6		920.7	920.7		0.0
2,5-DM-3-ET6		905.6	891.4		14.2
3,3-DM-4-ET6		947.3	937.8		−9.5
3,4-DM-3-ET6		961.8	964.6		3.0
2,2,3,3-TM6		933.1	928.8		−4.3
2,2,3,4-TM6		918.2	908.8*		−9.4
2,2,3,5-TM6		881.1	873.3		−7.8
2,2,4,4-TM6		875.0	888.6		13.6
2,2,4,5-TM6		866.6	872.1		5.5
2,2,5,5-TM6		811.9	820.2		8.3
2,3,3,4-TM6		952.0	949.1		−2.9
2,3,3,5-TM6		908.0	903.3		−4.7

TABLE I (continued)

Alkane	Kováts indices on squalane at 60°			Difference	
	Exptl. (Rijks) (a)	Calc. (correlation) (b)	Exptl. (Matukuma) (c)	$I. - I_b$	$I_c - I_b$
2,3,4,4-TM6		937.4	935.0		−2.4
2,3,4,5-TM6		922.2	923.1*		0.9
3,3,4,4-TM6		965.5	983.7		18.2
2,4-DM-3-IPR5		904.6	915.1		10.5
2,2,3-TM-3-ET5		958.2	965.7		7.5
2,2,4-TM-3-ET5		911.3	903.9		−7.4
2,3,4-TM-3-ET5		954.6	969.4		14.8
2,2,3,3,4-PM5		951.3	953.4		2.1
2,2,3,4,4-PM5		911.0	921.7		10.7
11		1101.4	1100.0		−1.4

* An average value is given for the two diastereoisomeric compounds analyzed by Matukuma.

The predictions based on the correlation are compared to Matukuma's experimental values[24] on squalane at 60° for alkanes with nine or ten carbon atoms. For the set of compounds having nine and ten carbon atoms the average deviation between the experimental and the calculated values is 7.0 I.U., i.e. ca. 0.8 %. The maximum deviations are less than 2 %.

The above example shows that, contrary to other methods requiring a ca. ten-fold larger number of structural parameters[14], the behaviour of any alkane can be predicted with a limited number of parameters. The number of parameters can be modulated either by re-grouping, or by not re-grouping, fairly equivalent topological sites. By using a 23-parameter correlation (obtained by not re-grouping topological sites in the first environment, E_B^1) instead of an 18-parameter correlation, the structural variable better reflects the molecular behaviour. The precision is also greater. The average deviation between Rijks' experimental value and the calculated value decreases to 2.7 I.U. and the standard deviation decreases to 3.3 I.U. For the particularly hindered 2,2-dimethyl-3-ethylpentane, the absolute deviation decreases from 12 to 6 I.U., i.e., the relative deviation decreases from 1.5 to 0.7 %. However, when establishing the retention–structure correlation, one should seek an optimum between the number of parameters, related to a minimal number of necessary data, and the desired precision in the predictions.

Prediction of the influence of stationary phase variation

Rijks also determined the Kováts indices of about 70 alkenes on squalane (SQ) and acetyltributyl citrate (CIT) at 50°. We shall show that these data can be used to predict the influence of a variation in the stationary phase on the behaviour of a population of compounds, and that these same data verify our predictions, thereby stressing the precision of our approach.

This population of alkenes covers a structural field characterized by the dummy target compound associated to the population (Fig. 1). This dummy target compound is obtained by superposing the characteristic graph of each alkene in the population. In order to characterize the behaviour of a population of compounds while

minimizing the number of experimental data required, it suffices to choose wisely the compounds and introduce progressively each topological site into the ELCO according to the notion of a key population in the DARC/PELCO (Peturbation of an ELCO) strategy[25].
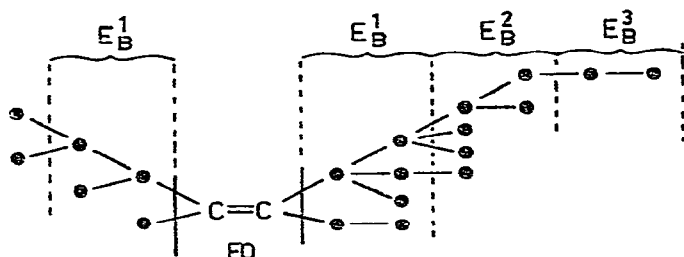

Fig. 1. The dummy target compound associated to the alkene population analyzed by Rijks. This trace is compounded from the sum of the environments (ELCO) of the condensed graph of every alkene.

Thus, from the 29 indices of alkenes on CIT at 50° shown in Table II, we have established a 22-parameter topology–information correlation according to pathway (1) in Scheme 2. This correlation allows us to predict the behaviour of about 70 alkenes
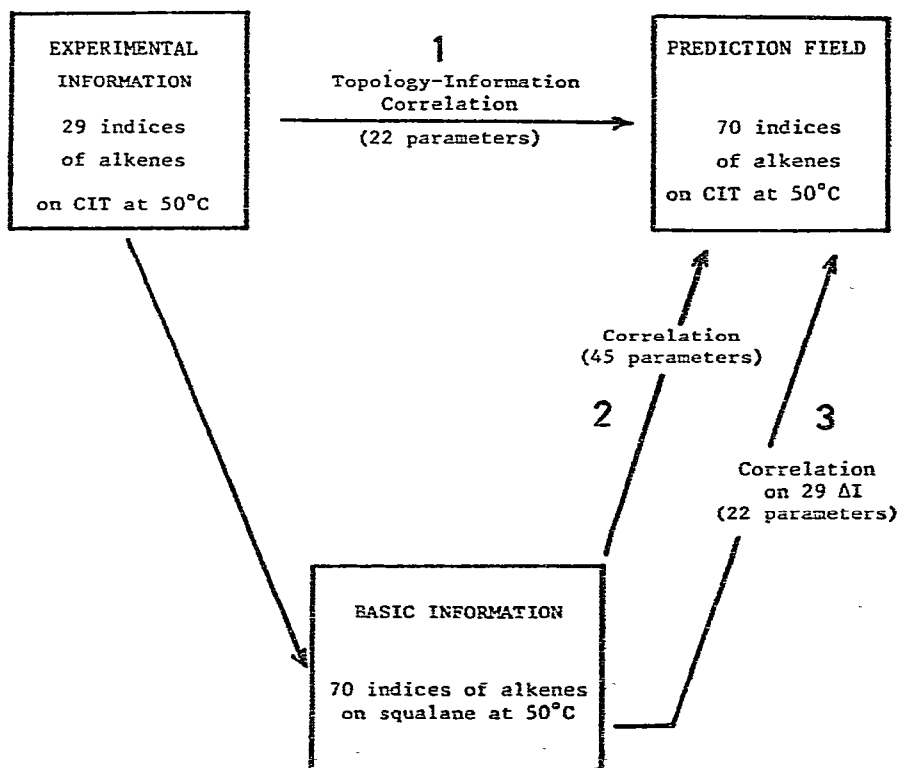
Scheme 2. Possible pathways for predicting the behaviour of at least 70 alkenes on acetyltributyl citrate (CIT) with a minimum of experimental values (29). Pathway (3) offers the greatest precision.

TABLE II

PREDICTION OF KOVÁTS INDICES OF ALKENES AT 50° ON ACETYLTRIBUTYL CITRATE (CIT) (b) BY USING A LARGE AMOUNT OF BASIC INFORMATION ON SQUALANE* AND A MINIMUM OF EXPERIMENTAL INFORMATION ON CIT (a)

Examples of names of alkenes: 1.6 = 1-hexene; c-3,4,4-TM-2.5 = cis-3,4,4-trimethyl-2-pentene; t-3-M-3.6 = trans-3-methyl-3-hexene.
Average deviation = 0.9 I.U., i.e., ca. 0.1%.
Standard deviation = 2.4 I.U.

Alkene	Kováts indices on acetyltributyl citrate at 50°			Difference (c) — (b)
	Used (a)	Calc. (b)	Exptl. (c)	
c-2.4		454.2	454.5	0.3
t-2.4		441.5	440.9	−0.6
1.5	515.5	516.2	515.5	−0.7
c-2.5	542.2	541.9	542.2	0.3
t-2.5	535.1	534.6	535.1	0.5
3-M-1.4				
2-M-1.4	525.2	525.3	525.2	−0.1
2-M-2.4		551.7	551.5	−0.2
1.6	616.9	616.5	616.9	0.4
c-2.6		640.2	640.1	−0.1
t-2.6		631.1	630.4	−0.7
c-3.6		627.9	627.2	−0.7
t-3.6	625.0	625.0	625.0	0.0
2-M-1.5		617.0	616.7	−0.3
3-M-1.5		583.3	582.1	−1.2
4-M-1.5	581.4	581.4	581.7	0.3
2-M-2.5		633.5	634.5	1.0
c-3-M-2.5		642.2	640.0	−2.2
t-3-M-2.5		649.8	649.4	−0.4
c-4-M-2.5		590.7	589.1	−1.6
t-4-M-2.5		594.0	593.5	−0.5
2-ET-1.4	628.0	627.8	628.0	0.2
2,3-DM-1.4	593.7	593.6	593.7	0.1
2,3-DM-2.4	663.4	663.8	663.4	−0.4
3,3-DM-1.4	536.7	537.4	536.7	−0.7
1.7	717.2	716.7	717.2	0.5
t-2.7		732.4	732.1	−0.3
c-3.7		725.2	724.7	−0.5
t-3.7		720.0	719.3	−0.7
2-M-1.6		714.8	715.3	0.5
3-M-1.6		676.5	675.6	−0.9
4-M-1.6		690.1	691.2	1.1
5-M-1.6	685.1	685.1	685.1	0.0
2-M-2.6		725.4	727.2	1.8
c-4-M-2.6		689.1	686.5	−2.5
t-4-M-2.6		688.4	684.2	−4.2
t-5-M-2.6		691.6		
t-2-M-3.6		677.5	676.8	−0.7
c-3-M-3.6		722.3	726.4	4.1
t-3-M-3.6		726.6	720.7	−5.9

TABLE II (continued)

Alkene	Kováts indices on acetyltri-butyl citrate at 50°			Difference (c) — (b)
	Used (a)	Calc. (b)	Exptl. (c)	
2-ET-1.5		717.2	716.7	—0.6
3-ET-1.5	676.0	675.8	676.0	0.2
3-ET-2.5		732.8	733.4	0.6
2,3-DM-1.5		684.8	684.2	—0.6
2,4-DM-1.5		672.5	671.9	—0.6
3,4-DM-1.5	667.1	666.8	667.1	0.3
2,3-DM-2.5		741.8	741.4	—0.4
2,4-DM-2.5		671.3	674.8	3.5
c-3,4-DM-2.5		707.6	713.0	5.4
t-3,4-DM-2.5		712.9	712.9	0.0
2-ET-3-M-1.4	692.3	692.5	692.3	—0.2
3,3-DM-1.5		656.4	656.0	—0.4
4,4-DM-1.5	634.8	634.3	634.8	0.5
c-4,4-DM-2.5		668.2	668.0	—0.2
t-2,2-DM-3.6		721.5	720.7	—0.7
c-3-M-2.6		732.3	729.4	—2.9
t-2,5-DM-3.6	720.6	720.6	720.6	0.0
2,4,4-TM-1.5	736.0	736.5	736.0	—0.5
2,4,4-TM-2.5		746.0	749.7	3.5
c-2,2-DM-3.6		747.8	746.9	—0.9
2,3,3-TM-1.5	768.3	767.3	768.3	1.0
2-M-3-ET-1.5	766.2	766.4	766.2	—0.2
2,3-DM-1.6	773.2	773.6	773.2	—0.4
t-2-M-3.7	769.4	770.1	769.4	0.3
c-3,4,4-TM-2.5	782.0	782.3	782.0	—0.3
2,5-DM-2.6	783.8	783.8	783.8	0.0
2,3,4-TM-2.5	802.2	801.8	802.2	0.4
1.8	816.8	816.8	816.8	0.0
t-4.8	814.3	814.6	814.3	—0.3
2,3-DM-2.6		826.8	825.9	—0.9
t-2.8	831.9	832.4	831.9	—0.5

* These alkene indices on squalane at 50° (from Rijks) are given in Table III.

on CIT at 50°. For the compounds used to establish this correlation, the following values apply: correlation coefficient $R = 0.999$; Exner's ψ test $= 0.06$; standard deviation $= 4.8$ I.U.; average deviation $= 3.6$ I.U. For the entire set of estimated compounds, the average deviation $= 8.8$ I.U., i.e. ca. 1.4%.

In order to increase the precision of the predictions while using the same number of experimental data on CIT, we can exploit the basic information (Scheme 2) corresponding to the behaviour of the same alkene population on squalane. This can be done through pathway (2) or (3).

Pathway (2) entails a 45-parameter topology–information correlation regrouping the basic and the experimental information used. However, the results obtained in this manner are not much better than those obtained through pathway (1). Indeed, the stationary phase variation characterized by the Kováts index increments $\Delta I [I(\text{CIT}, 50°) — I(\text{SQ}, 50°)]$ represents only 5% of the basic information. Thus, in

comparison to the virtually ideal behaviour of alkenes on squalane, this variation is only a second-order one.

So that the errors introduced by the computer processing of the basic information when establishing the topology–information correlation do not partially shadow the structural influence on ΔI, we have envisaged pathway (3). This pathway represents the establishment of a 22-parameter correlation ($R = 0.99$, $\psi = 0.2$, average deviation = 0.3 I.U., standard deviation = 0.4 I.U.) of the Kováts index increments for the 29 key population alkenes. The ΔI estimated on the basis of this correlation are automatically added to the already available "basic information" obtained on squalane and give the calculated values of the Kováts indices for the "prediction field", $i.e.$, for alkenes on CIT at 50°. The results are given in Table II. The average deviation for the set of Kováts indices is 0.9 I.U., $i.e.$, $ca.$ 0.1 %; the relative maximum deviation is $< 1\%$ and the standard deviation = 2.4 I.U.

Although pathways (1) and (3) have the same number of correlation parameters and use the same number of data on CIT at 50°, the prediction of the results obtained with pathway (3) is about 10 times greater than with pathway (1). This stresses the interest that lies in using to the utmost advantage already known data for a structural population before trying to predict new data.

Prediction of the influence of variations in the stationary phase and temperature

The same population of about 70 alkenes studied by Rijks at 50° on squalane and acetyltributyl citrate was also studied by him at 70°. We shall show how the behaviour of these same alkenes on CIT at 70° can be predicted on the basis of their known behaviour on SQ at 50° (Scheme 3).

If, in accordance with their size, we qualify the Kováts index increments, ΔI, as second-order variations, then the variations of the indices with temperature, $\delta I/\delta T$, are third-order variations. The latter data can also be used in establishing topology–information correlations, despite statistical criteria of average quality.
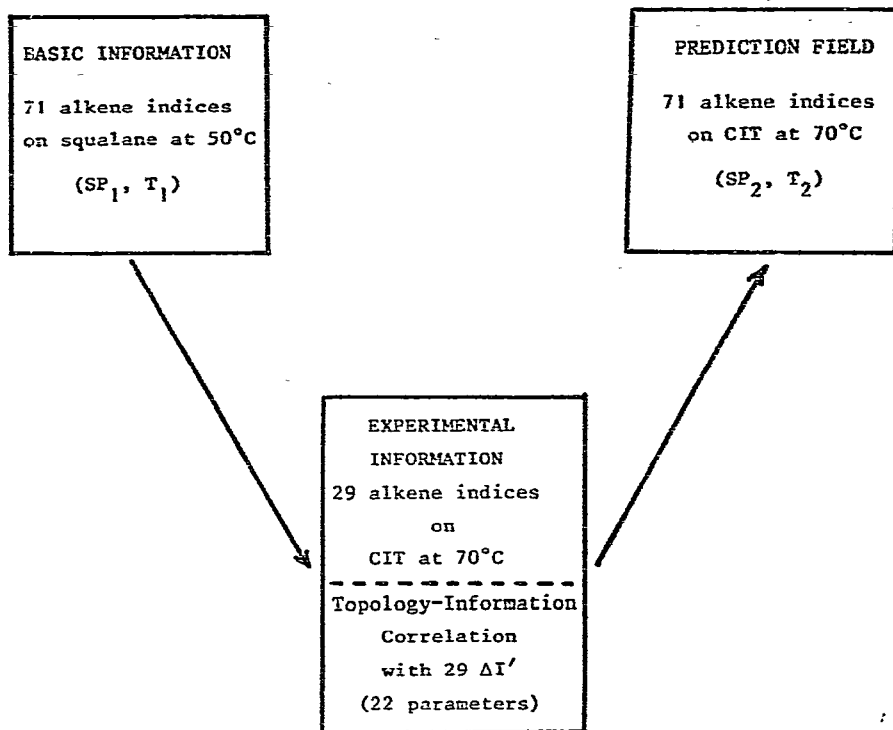
A topology–information correlation is established with the Kováts index increments, $\triangle I'$, corresponding to the difference between new chromatographic conditions (SP_2 and T_2) and already known chromatographic conditions (SP_1 and T_1) for the 29 compounds shown in Table III. Thus:

$$\Delta I' = I(SP_2, T_2) - I(SP_1, T_1)$$
$$= I(CIT, 70°) - I(SQ, 50°)$$
$$= \Delta I + 20\, \delta I/\delta T$$

Then the $\Delta I'$ are estimated for all of the compounds in Table III and added to the corresponding Kováts indices obtained on squalane at 50°, thus yielding the Kováts indices on CIT at 70°. When these calculated values are compared with Rijks' experimental values [$I(CIT, 70°)$], the average deviation for this set of compounds is 1.1 I.U., $i.e.$, $ca.$ 0.15 %, the maximum deviation is $< 0.8\%$ and the standard deviation = 3.0 I.U.

Prediction of the influence of the functional group: exploitation of the isotopology factor

The preceding three paragraphs deal with the interpolation and extrapolation of data pertaining to the behaviour of compounds with the same structural popula-

```
┌────────────────────────┐          ┌────────────────────────┐
│ BASIC INFORMATION      │          │   PREDICTION FIELD     │
│                        │          │                        │
│ 71 alkene indices      │          │   71 alkene indices    │
│ on squalane at 50°C    │          │    on CIT at 70°C       │
│                        │          │                        │
│    (SP₁, T₁)           │          │     (SP₂, T₂)          │
└────────────────────────┘          └────────────────────────┘
```

(SP_1, T_1) and (SP_2, T_2)

```
                  ┌──────────────────────────┐
                  │    EXPERIMENTAL          │
                  │    INFORMATION           │
                  │ 29 alkene indices        │
                  │         on               │
                  │    CIT at 70°C           │
                  │ ─ ─ ─ ─ ─ ─ ─ ─ ─        │
                  │ Topology-Information     │
                  │    Correlation           │
                  │    with 29 ΔI′           │
                  │   (22 parameters)        │
                  └──────────────────────────┘
```

Scheme 3. Prediction of the behaviour of alkenes under new chromatographic conditions (SP_2 and T_2) from already known conditions (SP_1 and T_1).

tion. We shall now demonstrate how complementary data between structurally different populations can be exploited for more general problems such as how the chromatographic behaviour of alkanes can be used in predicting the behaviour of alkenes, and how the chromatographic behaviour of alkenes can be used in predicting the behaviour of dibromoalkanes.

We have used the isotopology factor, τI, which is a generalization of Schomburg's homomorphism factor[26]:

$$\tau I = I_{substance} - I_{isotopologous\ compound}$$

The substance and the isotopologous compound have the same ELCO. The only difference lies either in the nature of the focus (FO) or in the chromaticity of certain topological sites.

In both of the above-mentioned cases the procedure for treating the isotopological factors is the same. A 22-parameter correlation is established on the basis of the τI factors corresponding to each of the compounds: the alkenes in Table IV and the dibromoalkanes in Table V. Then the values of τI are estimated from this correlation and added to the Kováts indices of their corresponding isotopologous compounds.

In the first case, both the alkenes and the alkanes were studied on squalane

TABLE III

PREDICTION OF 71 KOVÁTS INDICES OF ALKENES ON ACETYLTRIBUTYL CITRATE (CIT) AT 70°

Basic information on squalane (SQ) at 50° and a minimum of experimental information on CIT at 70° were used, with the aid of a correlation of topology–information established on $\Delta I' = [I(CIT, 70°) - I(SQ, 50°)]$.

Average deviation = 1.1 I.U., *i.e. ca.* 0.15%. Standard deviation = 3.0 I.U.

Alkene	Kováts indices				$I_{exptl.} - I_{calc.}$
	SQ, 50°	CIT, 70°			
		Used	Calc.	Exptl.	
c-2.4	416.9		453.7	454.3	0.6
t-2.4	406.6		440.6	440.3	−0.3
1.5	481.8	515.6	517.3	515.6	−1.7
c-2.5	504.9	542.0	541.4	542.0	0.6
t-2.5	500.0	534.3	533.7	534.3	0.6
3-M-1.4	450.3		483.0		
2-M-1.4	488.0	524.9	525.1	524.9	−0.2
2-M-2.4	514.3		551.2	551.2	0.0
1.6	582.3	617.1	616.7	617.1	0.4
c-2.6	603.6		641.2	640.2	−1.0
t-2.6	596.9		631.8	629.8	−2.0
c-3.6	592.6		627.2	627.4	0.2
t-3.6	592.1	624.0	624.0	624.0	0.0
2-M-1.5	580.1		618.4	616.7	−1.7
3-M-1.5	551.4		585.2	583.4	−1.8
4-M-1.5	549.4	582.0	582.7	582.0	−0.7
2-M-2.5	597.8		632.9	633.7	0.8
c-3-M-2.5	602.8		642.0	640.1	−1.9
t-3-M-2.5	612.7		649.2	649.2	0.0
c-4-M-2.5	556.2	.	591.0	589.1	−1.9
t-4-M-2.5	561.9		593.9	592.7	−1.2
2-ET-1.4	592.0	627.9	627.6	627.9	0.3
2,3-DM-1.4	558.8	594.3	594.3	594.3	0.0
2,3-DM-2.4	625.1	663.4	663.4	663.4	0.0
3,3-DM-1.4	506.8	537.4	538.4	537.4	−1.0
1.7	681.8	717.3	716.7	717.3	0.6
t-2.7	698.4		732.2	731.7	−0.5
c-3.7	690.4		726.2	724.9	−1.3
t-3.7	687.5		720.5	718.6	−1.9
2-M-1.6	678.1		715.3	715.3	0.0
3-M-1.6	644.7		677.4	676.6	−0.8
4-M-1.6	657.9		690.1	692.2	2.1
5-M-1.6	650.0	685.5	685.5	685.5	0.0
2-M-2.6	691.2		723.7	726.7	3.0
c-4-M-2.6	654.9		690.8	687.4	−3.4
t-4-M-2.6	656.7		689.9	687.1	−2.8
t-5-M-2.6	659.5		692.2		
t-2-M-3.6	647.1		677.3	675.7	−1.6
c-3-M-3.6	684.6		722.1	725.7	3.6
t-3-M-3.6	691.2		725.9	720.5	−5.4
2-ET-1.5	681.8		718.5	716.7	−1.8

TABLE III (*continued*)

Alkene	Kováts indices				$I_{exptl.} - I_{calc.}$
	SQ, 50°	CIT, 70°			
		Used	Calc.	Exptl.	
3-ET-1.5	646.9	677.8	677.7	677.8	0.1
3-ET-2.5	697.2		732.1	733.4	1.2
2,3-DM-1.5	650.4		687.0	685.7	−1.3
2,4-DM-1.5	637.7		673.8		
3,4-DM-1.5	636.9	669.2	668.5	669.2	0.7
2,3-DM-2.5	703.4		741.4	741.8	0.4
2,4-DM-2.5	640.6		669.8	673.5	−3.7
c-3,4-DM-2.5	670.6		708.3	713.0	4.7
t-3,4-DM-2.5	678.3		713.2	712.9	−0.3
2-ET-3-M-1.4	659.1	692.7	693.0	692.7	−0.3
3,3-DM-1.5	626.2		659.0	658.1	−0.9
4,4-DM-1.5	604.6	636.4	636.1	636.4	−0.3
c-4,4-DM-2.5	635.5		669.3	669.7	0.4
t-2,2-DM-3.6	692.8		722.0	719.5	−2.5
c-3-M-2.6	693.3		733.7	729.8	−3.9
t-2,5-DM-3.6	695.1	719.5	719.5	719.5	0.0
2,4,4-TM-1.5	704.3	738.3	738.6	738.3	−0.3
2,4,4-TM-2.5	715.4		744.6	749.9	5.3
c-2,2-DM-3.6	716.8		748.8	748.6	−0.2
2,3,3-TM-1.5	734.6	772.0	770.3	772.0	1.7
2-M-3-ET-1.5	735.0	768.5	768.6	768.5	−0.1
2,3-DM-1.6	739.3	774.5	774.9	774.5	−0.4
t-2-M-3.7	741.1	768.8	768.8	768.8	0.0
c-3,4,4-TM-2.5	747.1	783.1	783.7	783.1	−0.6
2,5-DM-2.6	749.9	783.7	783.7	783.7	0.0
2,3,4-TM-2.5	765.9	802.2	802.2	802.2	0.0
1.8	781.2	817.0	817.0	817.0	0.0
t-4.8	783.6	814.1	814.1	814.1	0.0
2,3-DM-2.6	788.8		827.9	826.4	−1.5
t-2.8	797.7	831.4	832.0	831.4	−0.6

at 50°. The isotopology factors of the Kováts indices are determined from the Kováts indices of 28 isotopologous alkanes. The Kováts index must be measured experimentally for 23 of them, as those of the remaining 5 reference *n*-alkanes are, by definition, already known. When the calculated values are compared with the experimental values obtained by Rijks (Table IV), the average deviation = 3.1 I.U., *i.e.*, *ca.* 0.5%, and the standard deviation = 4.0 I.U.

We wish to stress the prediction potential and the precision afforded by such an approach. The number of τI data can be minimized to, let us say, the 29 compounds of the key population of alkenes in order to establish a topology–information correlation, labelled A. From correlation A, we are able to predict the behaviour of > 70 alkenes. For the purpose of comparison we can establish another correlation, labelled B, by a direct exploitation of the Kováts indices for the same 29 key-population alkene compounds without resorting to the complementary information contributed by the isotopologous alkanes, *i.e.*, by the same procedure indicated in pathway (1) in Scheme 2. The precision of our predictions is clearly better when using correlation A

TABLE IV

CALCULATION OF KOVÁTS INDICES FOR ALKENES FROM INDICES OF ISO-TOPOLOGICAL ALKANES ON SQUALANE AT 50°

A topology–information correlation on τI was used ($\tau I = I_{alkene} - I_{isotopological\ alkane}$).
Average deviation = 3.1 I.U., i.e. *ca.* 0.5%. Standard deviation = 4.0 I.U.

Alkene	τI	$I(SQ, 50°)$		Difference, Exptl. − calc.
		Calc.	Exptl.	
c-2.4	16.9	415.3	416.9	1.6
t-2.4	6.6	415.9	406.6	−9.3
1.5	−18.2	484.9	481.8	−3.1
c-2.5	4.9	502.4	504.9	2.5
t-2.5	0.0	503.1	500.0	−3.1
3-M-1.4	−25.0	447.2	450.3	3.1
2-M-1.4	12.7	485.7	488.0	2.3
2-M-2.4	39.0	516.5	514.3	2.2
1.6	−17.7	580.5	582.3	−1.8
c-2.6	3.6	597.8	603.6	5.8
t-2.6	−3.1	598.4	596.9	−1.5
c-3.6	−7.4	592.6	592.6	0.0
t-3.6	−7.9	593.3	592.1	−1.2
2-M-1.5	10.4	575.4	580.1	4.7
3-M-1.5	−32.8	551.4	551.4	0.0
4-M-1.5	−20.3	552.0	549.4	−2.6
2-M-2.5	28.1	596.6	597.8	1.2
c-3-M-2.5	18.6	607.3	602.8	−4.5
t-3-M-2.5	28.5	608.1	612.7	4.6
c-4-M-2.5	−13.5	554.5	556.2	1.7
t-4-M-2.5	−7.8	555.1	561.9	6.8
2-ET-1.4	7.8	587.3	592.0	4.7
2,3-DM-1.4	−8.5	559.9	558.8	−1.1
2,3-DM-2.4	57.8	613.3	625.1	11.8
3,3-DM-1.4	−30.0	508.7	506.8	−1.9
1.7	−18.2	683.0	681.8	−1.2
t-2.7	−1.6	697.6	698.4	0.8
c-3.7	−9.6	687.9	690.4	2.5
t-3.7	−12.5	688.5	687.5	−1.0
2-M-1.6	11.5	671.5	678.1	6.6
3-M-1.6	−31.5	642.6	644.7	2.1
4-M-1.6	−18.3	657.8	657.9	0.1
5-M-1.6	−16.6	650.0	650.0	0.0
2-M-2.6	24.6	691.3	691.2	−0.1
c-4-M-2.6	−21.3	656.2	654.9	−1.3
t-4-M-2.6	−19.5	656.9	656.7	−0.2
t-5-M-2.6	−7.1	662.4	659.5	−2.9
t-2-M-3.6	−19.5	642.2	647.1	4.9
c-3-M-3.6	8.4	689.5	684.6	−4.9
t-3-M-3.6	15.0	690.3	691.2	0.9
2-ET-1.5	−.5	674.6	681.8	7.2
3-ET-1.5	−39.1	642.9	646.9	4.0
3-ET-2.5	11.2	702.5	697.2	−5.3
2,3-DM-1.5	−21.3	659.6	650.4	−9.2

TABLE IV (continued)

Alkene	τI	$I(SQ, 50°)$		Difference, Exptl. — calc.
		Calc.	Exptl.	
2,4-DM-1.5	7.9	632.9	637.7	4.8
3,4-DM-1.5	−34.8	636.3	636.9	0.6
2,3-DM-2.5	31.7	704.8	703.4	−1.4
2,4-DM-2.5	10.8	644.2	640.6	−3.6
c-3,4-DM-2.5	−1.1	677.1	670.6	−6.5
t-3,4-DM-2.5	6.6	677.9	678.3	0.4
2-ET-3-M-1.4	−12.6	657.0	659.1	2.1
3,3-DM-1.5	−32.7	626.2	626.2	0.0
4,4-DM-1.5	−21.0	611.9	604.6	−7.3
t-4,4-DM-2.5	−10.9	611.1	614.7	3.6
2,3,3-TM-1.4	−11.2	632.4	628.5	−3.9
t-2,2-DM-3.6	−26.6	695.0	692.8	−2.2
c-3-M-2.6	17.1	694.6	693.3	−1.3
t-2,5-DM-3.6	−33.3	691.5	695.1	3.6
2,4,4-TM-1.5	14.4	697.0	704.3	7.3
2,4,4-TM-2.5	25.5	715.4	715.4	0.0
2-M-3-ET-1.5	−26.4	739.0	735.0	−4.0
2,3-DM-1.6	−20.8	747.2	739.3	−7.9
t-2-M-3.7	−23.8	738.3	741.1	2.8
c-3,4,4-TM-2.5	10.0	742.6	747.1	4.5
2,5-DM-2.6	21.5	749.9	749.9	0.0
2,3,4-TM-2.5	13.5	767.8	765.9	−1.9
2-M-3-ET-2.5	17.0	787.1	778.4	−8.7
1.8	−18.8	781.2	781.2	0.0
t-4.8	−16.4	786.3	783.6	−2.7
2,3-DM-2.6	28.7	788.5	788.8	0.3
t-2.8	−2.3	796.5	797.7	1.2

than when using correlation B: with A, the average deviation is about half of that obtained with B (4.9 compared with 8.8 I.U.) and the standard deviation with A is one third of that obtained with B.

However, practical reasons might dictate the choice of the isotopologous series (e.g., filiation in organic synthesis). This can lead to molecules having very different "polarities", as shown in Table V. The behaviour of isomeric and diastereoisomeric dibromoalkanes is calculated from the behaviour of the alkenes that were brominated. The alkene indices, I, were determined on squalane at 50° [22,23] and ultimately completed by other values[24]. The dibromoalkane indices, J, were determined on squalane at 100° with the bromoalkanes serving as the reference series[27]. Although index J is about 316 I.U. less than index I, we shall use these unstandardized data in order to demonstrate that the same methodology is still valid. The correlation coefficient $R = 0.99$ and $\psi = 0.15$ with the correlation established on the basis of the isotopology factors considered in this example. The average deviation between the calculated and experimental values of J is 2.6 I.U., and the standard deviation = 3.6 I.U.

The interest in exploiting the isotopology factor lies not only in the fact that the precision of the predictions is better, but also that there are numerous extrapolation possibilities. Indeed, the isotopologous compound accounts for a large part of the

TABLE V

CALCULATION OF KOVÁTS INDICES OF DIBROMOALKANES AT 100° FROM KOVÁTS INDICES OF ALKENES AT 50°

Stationary phase, squalane. $\tau I = I_{DB, SQ, 100°} - I_{alkene, SQ, 50°}$.
Average deviation = 2.6 I.U. Standard deviation = 3.6 I.U.

Isotopologous alkene	Dibromoalkane*	τI	I_{DB}		Difference, exptl. — calc.
			Calc.	Exptl.	
1.2	1,2-DB2	299.0	473.7	473.7	0.0
1.3	1,2-DB3	238.0	527.2	527.0	−0.2
1.4	1,2-DB4	234.0	631.3	627.1	−4.2
1.5	1,2-DB5	231.2	708.2	712.6	4.4
1.6	1,2-DB6	224.7	801.8	807.5	5.7
1.7	1,2-DB7	220.2	897.9	902.4	4.5
3-M-1.4	1,2-DB-3M4	251.7	703.1	702.2	−9.0
3-ET-1.5	1,2-DB-3ET5	222.1	869.0	869.0	0.0
3,3-DM-1.4	1,2-DB-3,3DM4	276.2	791.8	782.8	−0.9
4-M-1.5	1,2-DB-4M5	211.6	761.5	761.5	0.0
4,4-DM-1.5	1,2-DB-4,4-DM5	214.4	819.3	819.3	0.0
2-M-1.3	1,2-DB-2M3	190.0	577.3	572.5	−4.8
2-M-1.4	1,2-DB-2M4	191.0	682.8	679.1	−3.7
2-ET-1.4	1,2-DB-2ET4	192.0	783.5	783.5	0.0
2,3-DM-1.4	1,2-DB-2,3DM4	210.2	768.3	769.3	1.0
2,3,3-TM-1.4	1,2-DB-2,3,3TM4	249.5	870.6	877.6	7.7
c-2.4	(T) 2,3-DB4	193.1	607.7	610.4	2.7
t-2.4	(E) 2,3-DB4	189.4	593.7	596.2	2.5
c-3.6	(T) 3,4-DB6	191.4	781.2	783.7	1.6
t-3.6	(E) 3,4-DB6	187.9	778.8	780.4	1.6
c-4.8	(T) 4,5-DB8	161.8	948.8	948.3	−0.5
t-4.8	(E) 4,5-DB8	159.4	942.2	942.8	0.6
c-2,5-DM-3.6	(T) 3,4-DB-2,5DM6	218.0	911.9	919.1	7.2
t-2,5-DM-3.6	(E) 3,4-DB-2,5DM6	200.0	903.2	896.0	−7.2
c-2.5	(T) 2,3-DB5	192.1	695.5	697.2	1.7
t-2.5	(E) 2,3-DB5	190.0	686.7	689.8	3.1
c-2.6	(T) 2,3-DB6	177.4	782.3	780.7	−1.6
t-2.6	(E) 2,3-DB6	176.1	772.0	772.6	0.6
c-2.7	(T) 2,3-DB7	165.6	878.1	872.5	−5.6
t-2.7	(E) 2,3-DB7	167.6	866.4	866.3	−0.1
c-2.8	(T) 2,3-DB8	165.5	970.7	968.3	−2.4
t-2.8	(E) 2,3-DB8	162.3	962.4	960.4	−2.0
c-3.7	(T) 3,4-DB7	175.6	868.8	866.0	−2.8
t-3.7	(E) 3,4-DB7	174.5	862.3	861.9	−0.4
t-4-M-2.5	(E) 2,3-DB-4M5	193.1	763.3	755.2	−8.1
t-4,4-DM-2.5	(E) 2,3-DB-4,4-DM5	235.3	848.5	849.9	1.4

* DB = dibromo; diastereoisomers, (E) = erythro and (T) = threo.

data. The further away we move from the focus, the weaker the influence of the isotopology factor, and the weaker its contribution as we move beyond the first layer sites of the second environment (i.e., beyond layer A of E_B^2).

CONCLUSION

We have shown through a series of examples that different sets of Kováts indices, whether obtained for the same population of compounds by a variation in chromatographic conditions, or obtained for different populations of compounds under the same chromatographic conditions, or obtained for different populations of compounds under different chromatographic conditions, can be rendered coherent by using the methodology of the DARC topological system.

The overlapping of sets of Kováts indices of different origins increases the information content of each set and facilitates the interpolation and extrapolation possibilities. Thus, for example, the large amount of data on hydrocarbon analysis can be exploited in order to increase the prediction potential of experimental data relative to populations of alkyl-substituted compounds.

The interest in experimentally determining a new set of Kováts indices does not lie in the number of compounds studied, but rather in the nature and extent of the structural pattern covered by the compound population. The topology–information correlations established according to the principles of the DARC/PELCO strategy show the interest that lies in experimentally determining further sets of Kováts indices on the basis of a minimum number of compounds. This strategy avoids the introduction of redundant data and the presence of gaps in a structural space which would normally arise from the experimental study of lists of commercial compounds.

Rohrschneider[28,29] and McReynolds[30], as well as the resulting recent exploitations of Kováts indices by factorial analysis[31,32] or numerical taxonomy[33,34], chiefly stress stationary phase behaviour. This topological analysis, however, stresses solute behaviour. By thermodynamically exploiting the values attributed to the parameters of the topology–information correlations, established on the basis of the Kováts indices or from their derived data (ΔI and τI), the behaviour of the solutes can be analyzed virtually at the level of each molecular atom[35,36].

Our prediction and physico-chemical studies are currently aimed at the processing of retention data in gas and liquid chromatography. It should be stressed that these two aims are complementary, and that establishing a prediction system without a physico-chemical support is not to be recommended.

REFERENCES

1 S. R. Heller, D. C. Maxwell and A. McCormick, *Advan. Mass Spectrom.*, 6 (1974) 1037.
2 R. Schwarzenbach, J. Meili, H. Könitzer and J. T. Clerc, *Org. Magn. Resonance*, 8 (1976) 11.
3 B. A. Jezl and D. L. Dalrymple, *Anal. Chem.*, 47 (1975) 203.
4 F. W. McLafferty, R. Venkataraghavan, K. S. Kwok and G. Pesyna, *Advan. Mass Spectrom.*, 6 (1974) 999.
5 W. Bremser, M. Klier and E. Meyer, *Org. Magn. Resonance*, 7 (1975) 97.
6 O. E. Schupp and J. L. Lewis, *Gas Chromatographic Data Compilation*, AMD 25 A, A.S.T.M., Philadelphia, Pa., 1967; AMD 25 A-S1, A.S.T.M., Philadelphia, Pa., 1971.
7 W. O. McReynolds, *Gas Chromatographic Retention Data*, Preston Technical Abstracts Co., Niles, Ill., 1966.
8 G. Zweig and J. Sherma, *Handbook of Chromatography*, CRC Press, Cleveland, Ohio, 1972.
9 M. Chastrette, G. Lenfant and J. E. Dubois, *C. R. Acad. Sci., Ser. C*, 265 (1967) 602.
10 G. Lenfant, M. Chastrette and J. E. Dubois, *J. Chromatogr. Sci.*, 91 (1971) 220.
11 J. E. Dubois and J. R. Chrétien, *J. Chromatogr. Sci.*, 12 (1974) 811, and references cited therein.
12 G. Schomburg and G. Dielmann, *J. Chromatogr. Sci.*, 11 (1973) 151.

13 G. Castello, M. Lunardelli and M. Berg, *J. Chromatogr.*, 76 (1973) 31.
14 J. M. Takács, *J. Chromatogr. Sci.*, 11 (1973) 210.
15 J. K. Haken, *J. Chromatogr. Sci.*, 11 (1973) 144.
16 L. S. Ettre, *Chromatographia*, 6 (1973) 489.
17 L. S. Ettre, *Chromatographia*, 7 (1974) 39.
18 L. S. Ettre, *Chromatographia*, 7 (1974) 261.
19 P. Souter, *J. Chromatogr. Sci.*, 12 (1974) 418 and 424.
20 J. E. Dubois, in W. T. Wipkey, S. R. Heller. R. J. Feldmann and E. Hyde (Editors), *Computer Representation and Manipulation of Chemical Information*, Wiley, New York, 1974, p. 239.
21 J. E. Dubois, *Isr. J. Chem.*, 14 (1975) 17.
22 J. A. Rijks, *Thesis*, Eindhoven, 1973.
23 J. A. Rijks and C. A. Cramers, *Chromatographia*, 7 (1974) 99.
24 A. Matukuma, in C. L. Harbourn (Editor), *Gas Chromatography 1968*, Institute of Petroleum, London, 1969, p. 55.
25 J. E. Dubois, D. Laurent and A. Aranda, *J. Chim. Phys.*, 70 (1973) 1608 and 1616.
26 G. Schomburg, *Advan. Chromatogr.*, 6 (1968) 211.
27 J. R. Chrétien, M. Lafosse and M. H. Durand, *Bull. Soc. Chim. Fr.*, (1975) 1013.
28 L. Rohrschneider, *J. Chromatogr.*, 22 (1966) 6.
29 L. Rohrschneider, *J. Chromatogr. Sci.*, 11 (1973) 160.
30 W. O. McReynolds, *J. Chromatogr. Sci.*, 8 (1970) 685.
31 P. H. Weiner and J. F. Parcher, *Anal. Chem.*, 45 (1973) 302.
32 R. B. Selzer and D. G. Howery, *J. Chromatogr.*, 115 (1975) 139.
33 D. L. Massart, M. Lauwereys and P. Lenders, *J. Chromatogr. Sci.*, 12 (1974) 617.
34 A. Eskes, F. Dupuis, A. Dijkstra, H. de Clercq and D. L. Massart, *Anal. Chem.*, 47 (1975) 2168.
35 J. R. Chrétien, *C.R. Acad. Sci., Ser. C*, 281 (1975) 151.
36 J. E. Dubois and J. R. Chrétien, to be published.