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Calculation of retention indices by molecular topology

III*. Chlorinated dibenzodioxins

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ABSTRACT

A model is developed, based entirely on chemical structure, for the accurate prediction of the retention of chlorinated dibenzodioxins (PCDDs) on a non-polar stationary phase (DB-5) and for reproducing their experimental elution sequence. The first-order molecular connectivity index ($^1\chi$) and six other topological properties, the specific mono-, di- and trichloro substitution patterns, were used as structural descriptors. Thus, one can predict the retention index for any given PCDD having only a knowledge of its chlorine substitution pattern. The agreement between observed and calculated retention indices (the average residual of 1.8 units) indicates that this model works fairly well to describe the retention indices of all analysed PCDDs (37 tetra- to octachlorinated congeners). The developed model was successfully validated by extrapolation on a small set of retention indices determined for di- and trichlorinated PCDD congeners and by interpolation on a set of sixteen retention indices determined for tetra- to octachlorinated PCDDs on a low-polarity HP-5 capillary column. The regression analysis shows that the PCDD retention indices are primarily influenced by their bulk properties, *i.e.*, the size of these molecules. This property, described best by the $^1\chi$ index, accounts for more than 97% of the variation in the retention index data. The other factors that control the magnitude of the retention indices are various chlorine substitution patterns, having either a positive or a negative effect on the magnitude of the retention indices. Finally, a mechanism for the interaction of PCDDs with the non-polar stationary phase is also discussed.

INTRODUCTION

Polychlorinated dibenzodioxins (PCDDs) are xenobiotic contaminants of great concern [1]. Owing to their persistence in the environment, they can be transported over long distances and they are widespread contaminants in the atmospheric and aquatic ecosystems. Residues of polychlorinated dibenzodioxins are found in most organisms sampled in natural aquatic and terrestrial environments. In addition, high toxicity has been associated with many of the individual congeners in these series. As a result, many countries monitor chlorinated dibenzodioxins in the environment. Despite considerable efforts during the last decade, analytical standards are still needed for many of the 75 dioxin congeners. Isomer-specific measurement information is necessary because of the major toxicological differences between individual congeners. Hence it would be very helpful to have a structural model that can predict the retention indices of any particular isomer. Such a method would be useful for identifying chlorinated dioxins found during environmental monitoring efforts.

Many investigators have noted [2] a very good correlation between the experimental retention indices and structural characteristics of molecules by either the application of DARC topological system [3–6] or topological indices such as molecular connectivity indices [2,7–13] and Wiener numbers [2,12,14–16]. Previously, we have demonstrated that the molecular connectivity model [17,18] suc-

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cessfully predicts gas chromatographic (GC) retention indices (I) and elution sequences of series of chlorinated alkanes [19] and chlorinated benzenes [20] on non-polar and polar stationary phases. As a continuation of our research on harmful organochlorine compounds in the environment [21–24], this paper reports on the ability of a molecular connectivity model to describe, in quantitative terms, the GC retention behaviour of PCDDs on a non-polar DB-5 capillary column. The ring structure of polychlorinated dibenzodioxins and the numbering scheme for available chlorination positions are shown in Fig. 1.

In this study, models based on the molecular characteristics of PCDDs will be developed for calculating GC retention indices and for predicting elution sequences of PCDDs. The molecular connectivity indices, which are calculated exclusively on the basis of information such as the number and type of atoms and bonds and the number of all electrons and valence electrons in each non-hydrogen atom, will be used as molecular descriptors. Such data are readily available for all chemicals, synthesized or hypothetical, from their structural formulae and from the Periodic Table. In addition, if necessary, other simple topological properties, such as the presence or absence of particular structural features, may also be tested as potential molecular descriptors. As in our earlier studies [19,20], two criteria will be used to test the quality of fit between observed and calculated retention indices: (i) a very high correlation coefficient and (ii) the correctly predicted elution sequence.

METHOD OF CALCULATION

Several extensive reviews of the theory and method of calculation of molecular connectivity indices have been published [17,18,25–27]. Therefore, only a description of the calculation of the first-order molecular connectivity index used in this study is given here. Information used in the calculation of molecular connectivity indices is the number and type of atoms and bonds in a molecule and the numbers of all electrons and valence electrons in each non-hydrogen atom. These data are readily available for all chemicals, synthesized or hypothetical, from their structural formulae and the Periodic Table. All molecular connectivity indices are calculated for the non-hydrogen part of the molecule. In the non-valence approximation each non-hydrogen atom is described by its atomic δ value, which is equal to the number of adjacent non-hydrogen atoms. The first-order molecular connectivity index ($^1\chi$) is calculated from the atomic δ values by the equation:

$$^1\chi = \Sigma\,(\delta_i\delta_j)^{-0.5} \quad (1)$$

where i and j correspond to the pairs of adjacent non-hydrogen atoms and the summation is over all bonds between non-hydrogen atoms. The $^1\chi$ index has been used extensively in various quantitative structure–property relationship (QSPR) and quantitative structure–activity relationship (QSAR) studies [17,18,25–27]. It has been found in several studies [21,22,28] that this index correlates extremely well with the molecular surface for various classes of chemicals and consequently correlates well with most of molecular surface-dependent properties and processes.

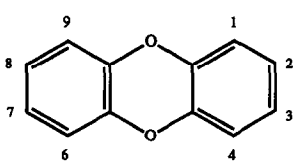

Fig. 1. Structural formula of substituted dibenzodioxins.

Other structural descriptors, *i.e.*, the presence of a specific substitution pattern, used in this study are the following: the number of *meta* chlorine substituents (Cl_M), the number of pairs of *ortho/meta* chlorine substituents (Cl_{OM}), the number of pairs of chlorine substituents in positions 1 and 3 or analogous relative positions (Cl_{13}), the number of pairs of chlorine substituents in positions 1 and 4 or analogous relative positions (Cl_{14}), the number of sequences of three consecutive chlorine substituents (Cl_{SEQ3}) and the simultaneous presence of chlorine substituents in positions 1 and 9 or 4 and 6 (ClOCl). All possible combinations of substituents for those structural descriptors are listed below:

Cl_M: substituents on positions 2, 3, 7 and 8;

Cl_{OM}: pairs of substituents on positions 1–2, 3–4, 6–7 and 8–9;

Cl_{13}: pairs of substituents on positions 1–3, 2–4, 6–8 and 7–9;

Cl_{14}: pairs of substituents on positions 1–4 and 6–9;

Cl_{SEQ3}: sequences of substituents on positions 1–2–3, 2–3–4, 6–7–8 and 7–8–9;

ClOCl: pairs of substituents on positions 1–9 and 4–6.

The numbering scheme for chlorine substituents is presented in Fig. 1. The *ortho* and *meta* positions of chlorine substituents are defined relative to the ring oxygen atoms. All variables, except the ClOCl variable, have an identical and linear weights system. Thus, for each occurrence of a specific substitution pattern the corresponding variable increases by 1. For the ClOCl variable, the presence of one pair of substituents has a weight of 1 and the presence of two pairs of substituents has a weight of 1.5. The non-linear weights for the ClOCl variable are based on earlier experimental findings [29].

The molecular connectivity indices used in this study were calculated with the GRAPH III computer program for microcomputers on an Apple Macintosh SE/30 personal computer. [The GRAPH III program is now fully operational and it is distributed by MacAda, Apple Center Ljubljana, Parmova 41, 61000 Ljubljana, Slovenia. Tables of molecular connectivity indices (up to 6th order), other structural variables and retention indices (measured and/or predicted) for 75 chlorinated dibenzodioxins may be obtained on diskette (Macintosh or IBM PC format) at a small cost from the corresponding author.] The GRAPH III computer program can calculate molecular connectivity indices up to the tenth order for the molecules with 36 non-hydrogen atoms or less. Regression analysis was carried out using a statistical analysis system (SYSTAT, version 5.0) on an Apple Macintosh SE/30 personal computer. To test the quality of the generated regression equation, the following statistical parameters were used: the correlation coefficient (r), the standard error of estimate (s), a test of the null hypothesis (F-test) and the amount of explained variance (EV).

The I values used in this study were taken from a study by Donnelly *et al.* [29]. A Hewlett-Packard Model 5880A gas chromatograph equipped with a flame ionization detector was used with a 60 m × 0.252 mm I.D. (0.25 μm film thickness) DB-5 fused-silica capillary column (J & W Scientific, Rancho Cordova, CA, USA) to determine the retention indices of available PCDDs. The gas chromatograph was programmed from 170 to 340°C at 2°C/min with an initial hold of 1 min. Helium was used as the carrier gas with a flow-rate at 340°C of 20.2 cm/s. C_{20}–C_{44} n-alkanes were used to measure retention indices.

RESULTS

A list of 37 polychlorinated dibenzodioxins (PCDDs) with four to eight chlorine substituents is shown in Table I together with their I values, the first-order molecular connectivity indices and other structural descriptors.

By modelling the retention behaviour of chlorinated alkanes [19] and chlorinated benzenes [20], we found that the combination of global and local structural descriptors is needed to describe their elution sequences correctly. It was reasonable to assume that a similar combination of structural properties will also be important for chromatographic behaviour of PCDD congeners. Therefore, we concentrated our initial search for structural descriptors on molecular connectivity indices and other parameters that describe primarily the size of molecules. The single-variable linear models were calculated for the simple and valence zero- and first-order molecular connectivity indices, molecular mass of the PCDDs, the number of non-hydrogen atoms and bonds, plus the sums of ${}^0\chi$ and ${}^0\chi^v$ or ${}^1\chi$ and ${}^1\chi^v$ indices. The first-order molecular connectivity index (${}^1\chi$) was found the most successful (correlation coefficient 0.988). The same index was also found to be the most successful in describing the chromatographic behaviour of chlorinated benzenes on a non-polar stationary phase [20]. However, as all other global structural descriptors also exhibit very high correlations with the PCDD retention indices, we decided to continue the modelling process with the ${}^1\chi$ index, as the most promising global descriptor, and to re-evaluate the successful model with other global structural descriptors listed above. Most of the calculated connectivity indices were unavailable for statistical evaluation in the multivariable models with the ${}^1\chi$ index because they intercorrelate strongly. Therefore, additional structural variables, describing the presence of specific substitution patterns such as the number of *ortho* and *meta* chlorine substituents, the number and types of pairs of chlorine substituents and the presence of longer sequences of adjacent chlorine sub-

TABLE I

MEASURED RETENTION INDICES (*I*) FOR 37 CHLORINATED DIBENZODIOXIN DERIVATIVES (PCDDs)

The values of the structural descriptors ($^1\chi$, Cl_M, Cl_{OM}, Cl_{13}, Cl_{14}, Cl_{SEQ3}, ClOCl) used in the modelling procedure are also listed.

Compound	*I*	$^1\chi$	Cl_M	Cl_{OM}	Cl_{13}	Cl_{14}	Cl_{SEQ3}	ClOCl
1234-PCDD	2379	8.592	2	2	2	1	2	0
1236-PCDD	2378	8.575	2	1	1	0	1	0
1237-PCDD	2382	8.559	3	1	1	0	1	0
1238-PCDD	2382	8.559	3	1	1	0	1	0
1239-PCDD	2392	8.575	2	1	1	0	1	1
1246-PCDD	2346	8.575	1	1	1	1	0	1
1247-PCDD	2340	8.559	2	1	1	1	0	0
1248-PCDD	2340	8.559	2	1	1	1	0	0
1249-PCDD	2346	8.575	1	1	1	1	0	1
1267-PCDD	2408	8.575	2	2	0	0	0	0
1268-PCDD	2349	8.559	2	1	1	0	0	0
1269-PCDD	2378	8.575	1	1	0	1	0	1
1278-PCDD	2400	8.559	3	1	0	0	0	0
1279-PCDD	2364	8.559	2	1	1	0	0	1
1289-PCDD	2428	8.575	2	2	0	0	0	1
1368-PCDD	2290	8.542	2	0	2	0	0	0
1369-PCDD	2315	8.559	1	0	1	1	0	1
1378-PCDD	2340	8.542	3	0	1	0	0	0
1379-PCDD	2304	8.542	2	0	2	0	0	1
1469-PCDD	2341	8.575	0	0	0	2	0	1.5
1478-PCDD	2353	8.559	2	0	0	1	0	0
2378-PCDD	2386	8.542	4	0	0	0	0	0
12347-PCDD	2573	8.986	3	2	2	1	2	0
12367-PCDD	2604	8.986	3	2	1	0	1	0
12378-PCDD	2587	8.969	4	1	1	0	1	0
12389-PCDD	2623	8.986	3	2	1	0	1	1
12468-PCDD	2501	8.969	2	1	2	1	0	1
12479-PCDD	2501	8.969	2	1	2	1	0	1
123467-PCDD	2812	9.414	3	3	2	1	2	1
123468-PCDD	2742	9.397	3	2	3	1	2	1
123478-PCDD	2781	9.397	4	2	2	1	2	0
123678-PCDD	2788	9.397	4	2	2	0	2	0
124679-PCDD	2713	9.397	2	2	2	2	0	1.5
124689-PCDD	2713	9.397	2	2	2	2	0	1.5
1234678-PCDD	2994	9.824	4	3	3	1	3	1
1234679-PCDD	2949	9.824	3	3	3	2	2	1.5
12346789-PCDD	3196	10.252	4	4	4	2	4	1.5

stituents, were tested in multivariate regression analysis. The simultaneous presence of two chlorine substituents in either positions 1 and 9 or positions 4 and 6 (Fig. 1) was also found [29] to have a large influence on the resulting *I* values of PCDD congeners. Therefore, a structural descriptor describing this particular substitution patterns was also tested in multivariate regression analysis. All these specific structural descriptors are shown in Fig. 2 for octachlorodibenzodioxin.

To generate the experimental elution sequence for all 37 PCDD congeners, seven-variable regression equation was necessary. The following structural descriptors have been found to be important in a multiple linear regression with the $^1\chi$ index: the number of *meta* chlorine substituents (Cl_M), the number of pairs of *ortho/meta* chlorine substituents (Cl_{OM}), the number of pairs of chlorine substituents in positions 1 and 3 or analogous relative positions (Cl_{13}), the number of pairs of chlorine substituents

in positions 1 and 4 or analogous relative positions (Cl_{14}), the number of sequences of three consecutive chlorine substituents (Cl_{SEQ3}), and the simultaneous presence of chlorine substituents in positions 1 and 9 or positions 4 and 6 (ClOCl). All variables are statistically significant above the 99.95% level (Student's t -test).

$$I = -1580.2 + 457.5^{1}\chi + 14.8Cl_{M} + 19.9Cl_{OM} - 35.4Cl_{13} - 12.9Cl_{14} + 22.1Cl_{SEQ3} + 15.3ClOCl \quad (2)$$
$$N = 37,\ r = 1.000,\ s = 3.2,\ F^{7,29} = 26\,016,\ EV = 100\%$$

The statistical parameters show that eqn. 2 is statistically significant above the 99.9% level and it accounts for all of the variation in the I data. It is also very accurate in calculating I data of PCDDs and the average residual of calculated values was only 2.4 units. This topological model was also effective in predicting the correct elution sequence for all 37 PCDD congeners. However, the residual analysis shows that 1,2,3,8,9-PCDD, 1,2,3,4,6,7-PCDD and octachlorodibenzodioxin are outliers which exert an undue influence on the regression

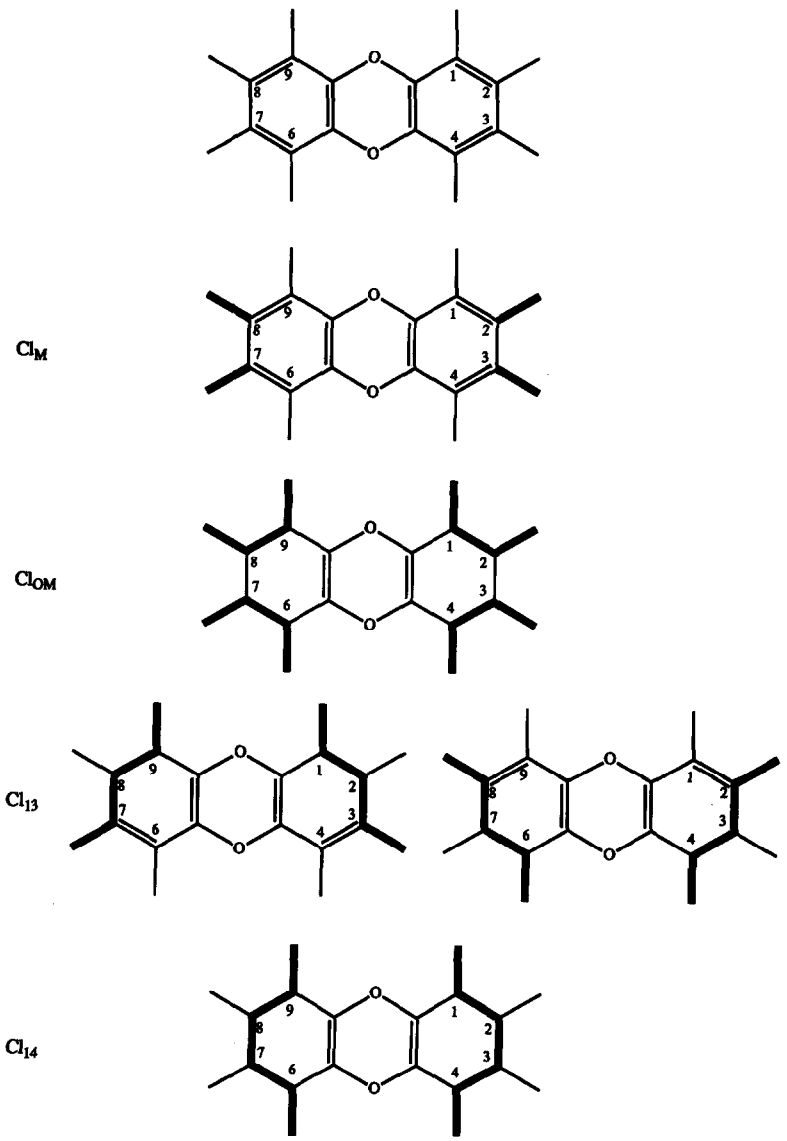

Fig. 2.

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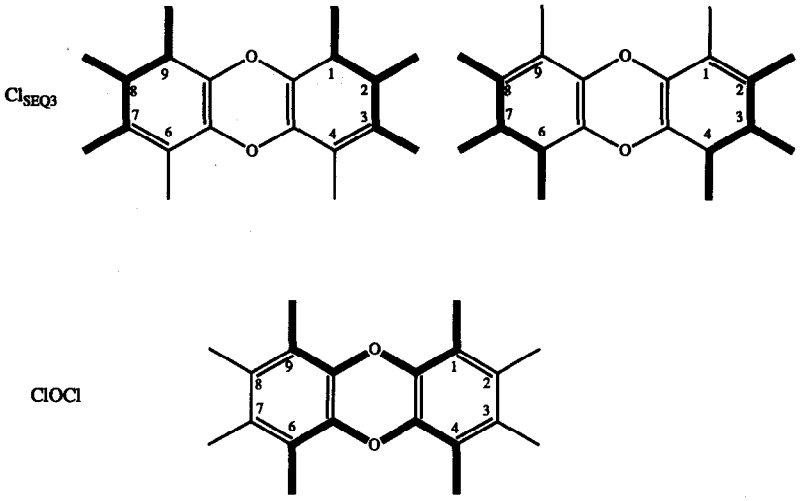

Fig. 2. Structural formulae of octachlorodibenzodioxin with outlined specific substitution patterns, used in this study as local structural descriptors: the four *meta* chlorine substituents (Cl_M), the four pairs of *ortho* and *meta* chlorine substituents (Cl_{OM}), the four pairs of chlorine substituents in positions 1 and 3 or analogous relative positions (Cl_{13}), the two pairs of chlorine substituents in positions 1 and 4 or analogous relative positions (Cl_{14}), the four sequences of three consecutive chlorine substituents (Cl_{SEQ3}), and the simultaneous presence of chlorine substituents in positions 1 and 9 or 4 and 6 (ClOCl).

model since their I values are all underestimated by 3.6–6.2 units. Eliminating them from the regression analysis resulted in an improved correlation and also in a statistically more reasonable and meaningful quantitative model described by eqn. 3 and its statistical parameters:

$$I = -1586.4 + 458.4^1\chi + 14.3Cl_M + 19.1Cl_{OM} - 34.9Cl_{13} - 12.5Cl_{14} + 21.3Cl_{SEQ3} + 13.5ClOCl$$
$$N = 34,\ r = 1.000,\ s = 2.4,\ F^{7,26} = 29\,350,\ EV = 100\% \quad (3)$$

Eqn. 3 is also very accurate in calculating I data of PCDDs and in predicting their correct elution sequence. The average residual of calculated values is now only 1.8 units. The high accuracy of the molecular connectivity model in predicting the I values of PCDDs is also shown in Fig. 3, where the observed *vs.* predicted (eqn. 3) retention indices are plotted.

Because of its high statistical significance and ability to explain all variations in the measured retention indices, the developed model (eqn. 3) was used to estimate the I values for the PCDD congeners with two to six chlorine substituents whose GC retention data have not yet been measured. The results are presented in Table II.

The experimental control of the predicted I values of several selected PCDDs with different degrees of chlorination should afford a constructive challenge to the molecular topology approach and the quantitative model described by eqn. 3.

Finally, an attempt was made to test the other

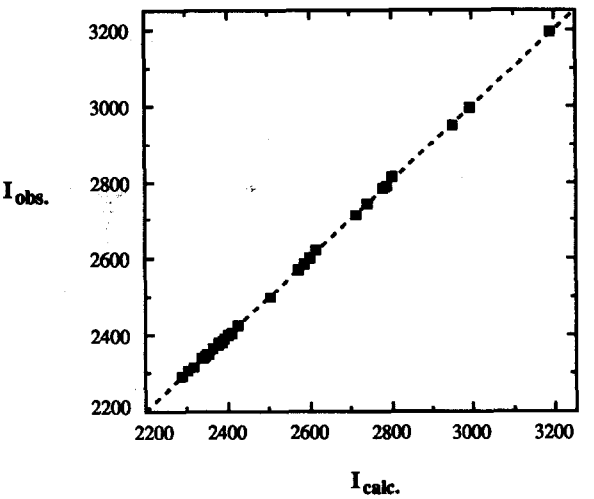

Fig. 3. Plot of calculated *vs.* observed retention indices of 37 PCDDs shown in Table I. The broken line corresponds to the molecular connectivity model, eqn. 3.

TABLE II

CALCULATED RETENTION INDICES (*I*) FOR 36 CHLORINATED DIBENZODIOXIN DERIVATIVES (PCDDs) WITH TWO TO SIX CHLORINE SUBSTITUENTS BY THE MOLECULAR TOPOLOGY MODEL, (EQN. 3)

The values of the structural descriptors ($^1\chi$, Cl_M, Cl_{OM}, Cl_{13}, Cl_{14}, Cl_{SEQ3}, ClOCl) used in the estimation procedure are also listed.

Compound	I_{CALC}	$^1\chi$	Cl_M	Cl_{OM}	Cl_{13}	Cl_{14}	Cl_{SEQ3}	ClOCl
13-PCDD	1940	7.737	1	0	1	0	0	0
14-PCDD	1956	7.754	0	0	0	1	0	0
16-PCDD	1968	7.754	0	0	0	0	0	0
17-PCDD	1975	7.737	1	0	0	0	0	0
18-PCDD	1975	7.737	1	0	0	0	0	0
27-PCDD	1981.4[a]	7.720	2	0	0	0	0	0
28-PCDD	1981.4[a]	7.720	2	0	0	0	0	0
19-PCDD	1982	7.754	0	0	0	0	0	1
23-PCDD	1989[a]	7.737	2	0	0	0	0	0
12-PCDD	2002	7.754	1	1	0	0	0	0
136-PCDD	2128	8.148	1	0	1	0	0	0
137-PCDD	2135	8.131	2	0	1	0	0	0
138-PCDD	2135	8.131	2	0	1	0	0	0
139-PCDD	2142	8.148	1	0	1	0	0	1
124-PCDD	2143[a]	8.165	1	1	1	1	0	0
147-PCDD	2151	8.148	1	0	0	1	0	0
146-PCDD	2158	8.165	0	0	0	1	0	1
236-PCDD	2177	8.148	2	0	0	0	0	0
237-PCDD	2184	8.131	3	0	0	0	0	0
126-PCDD	2190	8.165	1	1	0	0	0	0
123-PCDD	2191	8.165	2	1	1	0	1	0
127-PCDD	2197	8.148	2	1	0	0	0	0
128-PCDD	2197	8.148	2	1	0	0	0	0
129-PCDD	2204	8.165	1	1	0	0	0	1
12469-PCDD	2527	8.986	1	1	1	2	0	1.5
12368-PCDD	2539	8.969	3	1	2	0	1	0
12478-PCDD	2540	8.969	3	1	1	1	0	0
12379-PCDD	2552	8.969	3	1	2	0	1	1
12467-PCDD	2566	8.986	2	2	1	1	0	1
12489-PCDD	2566	8.986	2	2	1	1	0	1
12369-PCDD	2568	8.986	2	1	1	1	1	1
12346-PCDD	2581	9.003	2	2	2	1	2	1
123679-PCDD	2755	9.397	3	2	2	1	1	1
123689-PCDD	2755	9.397	3	2	2	1	1	1
123469-PCDD	2764	9.414	2	2	2	2	2	1.5
123789-PCDD	2803	9.397	4	2	2	0	2	1

[a] The measured *I* values [29] for these four PCDDs are as follows: 27-PCDD and 28-PCDD, 1985; 23-PCDD, 1993; and 124-PCDD, 2152.

size descriptors such as the $^0\chi$, $^0\chi^v$ and $^1\chi^v$ indices, the molecular mass of the PCDDs, the number of non-hydrogen atoms and bonds and the sums of $^0\chi$ and $^0\chi^v$ or $^1\chi$ and $^1\chi^v$ indices in place of the first-order molecular connectivity index in eqn. 3. However, those models were unsuccessful in reproducing the experimental elution sequence for all 37 PCDD congeners.

DISCUSSION

Model description

QSAR analysis with topological features shows that the retention indices of PCDDs are primarily influenced by their bulk properties, *i.e.*, the size of the molecules. In the model developed this property is described best by the $^1\chi$ index, whose numerical

values are directly proportional to the number of bonds in the PCDD congeners, and it accounts for more than 97% of the variation in the I data. However, all parts of a PCDD do not contribute equally to its retention index. The highest contribution stems from the chlorine–carbon bonds, followed by the bonds between unsubstituted carbon atoms, and the lowest from the bonds between substituted carbon atoms. The other factors that control the magnitudes of the retention indices can be collectively termed the chlorine substitution pattern. It is possible to subdivide this general term into three more specific structural features: (1) the absolute position of chlorine atoms on each ring (Cl_M, Cl_{OM}), (2) the relative position of chlorine atoms on each ring (Cl_{13}, Cl_{14}, Cl_{SEQ3}) and (3) the absolute position of chlorine atoms on both aromatic rings (ClOCl). Some of these structural features (Cl_M, Cl_{OM}, Cl_{SEQ3}, ClOCl) have a positive effect on the magnitude of retention indices whereas the others (Cl_{13}, Cl_{14}) have a negative effect. The regression coefficients in eqn. 3 can be used as quantitative estimates for the effects of those chlorination patterns.

Model validation

There was a possibility of validating our model both by extrapolation and by interpolation. The extrapolation test was performed with a small number of reported [29] retention indices for di- and trisubstituted PCDDs which were not included in the regression analysis. The calculated and observed retention indices for 2,3-, 2,7-, 2,8- and 1,2,4-chlorinated PCDDs are presented in Table II. A comparison of these observed and calculated indices clearly demonstrates that the developed model (eqn. 3) is accurate in predicting I data even in this extrapolation region. The average difference between the predicted and observed retention indices is only 5 units, their elution sequence is predicted correctly and the relative differences in retention indices within dichlorinated PCDDs are reproduced very well. Unfortunately, it must be pointed out that our model underestimated the retention indices for all four test compounds used in this extrapolation procedure.

The interpolation test was performed with recently reported [30] retention indices for sixteen tetra- to octachlorinated PCDDs determined on a low-polarity HP-5 capillary column, which is very similar to the DB-5 column used in the study by Donnelly et al. [29] (Table I). The calculated and observed [29,30] retention indices for the second set of test compounds are presented in Table III. The retention indices obtained on the HP-5 column [30] are systematically lower than those obtained earlier on the DB-5 column [29]. This is due mainly to the different stationary phases used and to the different operating conditions. However, there is a very high correlation between the two sets of reported retention indices ($r^2 = 1.000$). The set of calculated retention indices (eqn. 3) also correlates to a high degree with the retention indices obtained on the HP-5 column ($r^2 = 1.000$). Further, the developed model (eqn. 3) generates the correct elution sequence for all sixteen PCDD congeners obtained on the HP-5 column and also for the so-called "window" isomers, *i.e.*, the first and last isomer eluting in each isomeric group. Consequently, the reliable retention indices on the HP-5 column can be calculated for the remaining 33 tetra- to hexachlorinated isomers by a simple linear relationship from the retention indices calculated by our model (eqn. 3). Hence it is fair to conclude that the developed model (eqn. 3) was very successful in predicting the retention

TABLE III

COMPARISON OF MODEL (EQN. 3) PREDICTIONS TO MEASURED RETENTION INDICES ($I1$ [30] AND $I2$ [29]) FOR SIXTEEN TETRA- TO OCTACHLORINATED DIBENZODIOXIN DERIVATIVES (PCDDs)

Compound	I_{calc}	$I1_{obs}$ [30]	$I2_{obs}$ [29]
1368-PCDD	2288	2262.3	2290
2378-PCDD	2387	2353.1	2386
1289-PCDD	2425	2393.8	2428
12468-PCDD	2504	2464.3	2501
12479-PCDD	2504	2464.3	2501
12378-PCDD	2588	2554.8	2587
12389-PCDD	2614	2579.5	2623
124679-PCDD	2714	2668.3	2713
124689-PCDD	2714	2668.3	2713
123478-PCDD	2777	2741.8	2781
123678-PCDD	2790	2746.9	2788
123789-PCDD	2803	2762.0	–
123467-PCDD	2803	2762.0	2812
1234679-PCDD	2950	2893.9	2949
1234678-PCDD	2992	2937.2	2994
12346789-PCDD	3189	3132.6	3196

indices of PCDDs in both the interpolation region and the extrapolation region and that this model can be recommended as a reliable means for calculating retention indices.

The results in Table III indicate that the retention index system introduced by Kováts [31] to minimize the influence of operating conditions on measured retention indices are still influenced to a certain extent by the type of stationary phase and the column temperature or temperature cycle. Thus, strictly, the model developed in this study (eqn. 3) is valid only for retention indices obtained on a DB-5 column and with the temperature cycle used in the study by Donnelly *et al.* [29]. However, it has been demonstrated [31–33] that retention indices are linearly dependent on temperature and that in most instances the temperature coefficients are very small. Further, for stationary phases where the non-specific interaction forces control the retention process, the measured retention indices are linearly dependent and highly correlated [29,30]. This is also demonstrated in our study (see Table III) for two capillary columns, DB-5 and HP-5. Retention indices obtained for chlorinated dibenzodioxins on this two columns correlate above the 99.9% level. Hence it seems that our model can be adapted very rapidly in order to be used for other column types or temperature cycles, provided that two or three reference points are available for its calibration to a particular type of stationary phase and/or temperature cycle.

In the following section, as a part of the validation process, we compare our model with those already published. At present, there are two quantitative models [29,34] that are available for the comparison procedure (an attempt was also made to model the retention indices of PCDDs for tetrachlorinated isomers by solubility parameters [35]). The first model [34] is based on three calculated physical properties as parameters: molecular polarizabilities, ionization potentials and dipole moments. The second model [29] is based on an empirical additive scheme with eleven parameters (ten fragments and one correction factor). For the first model [34] the standard error of the estimate is above 32 units. Hence this model can estimate the retention indices of PCDDs only on a semi-quantitative level, *i.e.*, neither the generation of experimental elution sequences nor reliable isomer-specific estimations are possible with this model.

The second model [29], based on an empirical additive scheme, has an average residual of 3.1 units for the calculated retention indices of 37 tetra- to octachlorinated isomers. This result is comparable to the estimation performance of our model (average residual 2.4 units). However, our model was superior in estimating the retention indices of di- and trichlorinated PCDDs. The average residual for calculated retention indices was only 5 units, while the empirical additive scheme has an average residual of 9 units for this group of PCDD congeners. An additional advantage of the structural model developed in this study is the smaller number of parameters that are needed to attain (a) the same level of precision in estimating retention indices and (b) the experimental elution sequence for PCDD congeners. The introduction of the first-order molecular connectivity index made it possible to reduce the number of necessary structural parameters from eleven to seven and the possibility of a chance correlation.

Mechanism of interaction of PCDDs with non-polar stationary phase

The retention process of PCDDs is primarily influenced by their bulk properties, *i.e.*, the size of these molecules. In the model developed, their size is described best by the $^1\chi$ index. It has been found in several studies [21,22,28] that the $^1\chi$ index correlates extremely well with the molecular surface of various classes of hydrocarbons, halogenated hydrocarbons and similar compounds. Therefore, it was logical to find that this structural descriptor accounts for more than 97% of the variation in the PCDD *I* data, *i.e.*, correlates well with this molecular surface-dependent process.

The six local structural parameters that control the magnitude of retention indices can be classified into two groups: (i) parameters that increase the magnitude of retention indices (Cl_M, Cl_{OM}, Cl_{SEQ3}, ClOCl) and (ii) parameters that decrease the magnitude of retention indices (Cl_{13}, Cl_{14}). From the mechanistic point of view, the first group of parameters describes structural features that have attractive interactions with the stationary phase while the second group of parameters describes structural features that either have repulsive interactions with the stationary phase or interfere with a possible favourable interaction.

From our results, it is also possible to speculate about the mechanism of interaction of PCDD congeners and non-polar stationary phases in gas chromatography. It seems that the *meta* chlorine substituents interact more strongly with a stationary phase than the *ortho* substituents. Further, the accumulation or adjacent substitution also has a positive effect on the magnitude of retention indices described by positive contributions of the pairs of *ortho* and *meta* chlorine substituents and the sequences of three consecutive substituents. The positive effect of the simultaneous presence of chlorine substituents in positions 1 and 9 or 4 and 6 can be rationalized as the two chlorines blocking the repulsive interactions of the polar ether oxygens with the non-polar stationary phase, *i.e.*, the shielding effect. Finally, the negative effects of two types of non-neighbouring substitutions (Cl_{13} and Cl_{14}) can be rationalized as the steric hindrance of possible favourable interactions between PCDD congeners and the non-polar stationary phase. However, in a recent study [36] with similar solutes, chlorinated dibenzofurans, it was suggested that the formation of local dipoles has a strong influence on their interaction with a non-polar stationary phase, *i.e.*, local dipoles reduce the positive interaction between the solute molecules and the stationary phase. Hence it is also possible that in chlorinated dibenzodioxins the presence of substitution patterns such as Cl_{13} and Cl_{14} stimulates the formation of local dipoles which interfere with the positive interaction between the solute molecules and a non-polar stationary phase and consequently reduce the magnitude of the retention indices.

CONCLUSIONS

We have demonstrated that a relatively simple model, based on topological properties of molecules, can be used to predict successfully the retention indices of chlorinated dibenzodioxins on a non-polar stationary phase. The agreement between the observed and calculated retention indices, the r^2 value of 1.000 and the standard deviation of 2.4 all indicate that this model works well to describe the retention indices of all the PCDDs analysed. To reproduce the experimental elution sequence of 37 PCDD congeners the seven-variable model was necessary. Those variables account for (i) the number of chlorine atoms present, *i.e.*, the molecular size of the PCDD congeners, (ii) the position and the relationship of chlorine atoms on each aromatic ring and (iii) the relationship of chlorine atoms on both aromatic rings. Hence one can predict the retention index for any given PCDD having only a knowledge of its chlorine substitution pattern.

The developed mathematical model, which describes the pattern in PCDD retention data from the chlorine substitution patterns, will be of great analytical value. It could be used to verify the observed retention data because of the difficulties associated with preparing and then positively identifying any particular PCDD. In any case, with this model, it is possible to narrow greatly the range to search for and identify a given PCDD. Further, the developed model can predict the retention characteristics of PCDDs which have not yet been synthesized (see Table II).

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