Short communication

Influence of conformation on the accuracy of quantitative–structure retention relationship calculations in gas chromatography

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Abstract

The influence of the conformation of alkenens on quantitative structure–retention relationship calculations was studied. Previously published experimental data obtained by adsorption gas chromatography on graphitized carbon black were used to determine the accuracy of derived predictive equations. © 1997 Elsevier Science B.V.

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1. Introduction

The values of quantum chemical indices (QC) used in modelling of chromatographic retention are usually calculated for optimized molecular geometry, i.e., at minimum molecule energy. At a given distance between the surface of the phase stationary and a solute molecule, Van der Waals forces begin to act. If the interaction energy is higher than the conformation energy barrier, conformational changes have to occur at the moment of sorption and hence, an influence on retention is expected. This hypothesis was initially proposed in Refs. [1,2] and was extended in Ref. [3]. If used in the quantitative structure–retention relationships (QSRR) QC indices will be calculated at a higher molecule energy state, the accuracy of derived predictive equations for conformation-rich compounds should be improved and the supposed hypothesis can be considered as

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correct. The task of the present investigation is to check this possibility.

Adsorption gas chromatography on a carbon black stationary phase, which has flat surface domains, is the most suitable chromatographic mode for this investigation, because the adsorption forces are stronger than in solutions. The realizable Van der Waals forces are strongly dependent on the kind of "landing" of the solute molecule on the stationary phase surface. Alkenes are the best examples, because they have both a rigid flat $>C=C<$ moiety and conformational-rich saturated chains bound to it.

2. Experimental

The calculations were performed with the experimental data obtained on graphitized carbon black GTCB at 150°C and which are cited in Ref. [4]. The new version of the software product OASIS [5,6] allows the calculation of QC index values by PM3 software for many conformation states. The total

energy (E_T) of the studied molecules was used as retention descriptor in the present investigation for two reasons: (i) it is a conformation dependent descriptor and according to the scheme for descriptor selection, given in Ref. [4], pertains to the important group. Hence, it can be used as basic parameter; (ii) E_T was already used in QSRR, although with success only for the homologous series of alkenes [7].

3. Results and discussion

E_T values of different rotamer clusters for a given alkene were calculated with the OASIS program. To avoid the influence of the conformation state, a set of alkenes with only one or almost equal E_T values was selected for the first step of modelling. The obtained regression equation is:

$$RI_{calc} = 298.8(\pm 26.0) - 0.0579(\pm 0.0061) \cdot E_T \quad (1)$$

with variance $v = 696$, S.D. $= \pm 26$, correlation coefficient $r = 0.944$ and maximum error of -48 i.u. The calculated indices RI_{calc} (Table 1) are so faulty, that evidently they have to be tuned (see Ref. [4]). The best tuning parameter was found to be a binary indicator variable accounting for the presence (1) or absence (0) of quaternary C atoms in the alkene molecule – n_q (see Table 1). Unfortunately, none of

the studied 30 QC or topological indices describes adequately the presence of quaternary C atoms in alkene molecules. Thus, the n_q descriptor cannot be exchanged by a calculable index.

It is supposed, that the bulky $(CH_3)_3C$ group greatly repels the flat $>C=C<$ moiety of alkene molecule from the flat stationary phase domains and so decreases the possible maximum interaction.

When the value of RI_{calc}, calculated from Eq. (1), was corrected by addition of the n_q tuning descriptor, a statistically significant improvement of variance of Eq. (1) was achieved. The new equation is:

$$RI_{calc} = 248.2(\pm 7.6) + 0.0763(\pm 0.0021) \cdot E_T$$
$$- 70.40(\pm 1.8) \cdot n_q \quad (2)$$

where $r = 0.9963$, $v = 52$ and S.D. $= \pm 7.2$. The RI_{calc} values calculated according to Eq. (2) are compared with RI_{exp} in Table 1. The significance of the new parameter was proved by F-test, applied to the variances of Eqs. (1) and (2): $F_{13,13} = 13.4 \gg F_{tabl}$.

It is now possible to study the influence of the conformation state under more clear conditions. Alkenes with many conformation states (rotamers) were added to the starting matrix (Table 2). It could be observed from the data in columns 3 and 4 of Table 2, that the greater the number of conformation states, the greater the discrepancy between extreme E_T values – the correlation coefficient is above 0.7 and is statistically significant.

Table 1
Experimental RI_{exp} and calculated according to Eqs. (1) and (2) retention indices RI_{calc} of alkenes for which there exists only one E_T value

No	Alkene (n_q)	E_T	RI_{exp}	RI_{calc} Eq. (1)	RI_{calc} Eq. (2)
1	*cis*-2-Butene (0)	-2190	406	426	414
2	*trans*-2-Butene (0)	-2150	418	423	411
3	*cis*-2-Pentene (0)	-3151	486	481	489
4	1-Pentene (0)	-3086	480	478	484
5	2-Methyl-2-butene (0)	-3109	494	479	486
6	3,3-Dimethyl-1-butene (1)[a]	-4256	497	545	502
7	3-Methyl-*cis*-2-pentene (0)	-4192	569	542	569
8	3-Methyl-*trans*-2-pentene (0)	-4140	572	539	565
9	2,3,3-Trimethyl-1-butene (1)	-5472	591	616	596
10	4,4-Dimethyl-1-pentene (1)	-5383	597	611	590
11	4,4-Dimethyl-*cis*-2-pentene (1)	-5478	600	616	597
12	2,3-Dimethyl-1-pentene (0.5)[b]	-5365	613	610	612
13	5-Methyl-*cis*-2-hexene	-5227	643	602	649

[a] One quaternary C atom.
[b] Two neighbour tertiary C atoms.

Table 2
Number of calculated conformation states, differences, Δ, between their extremum E_T, differences between RI_{exp} and RI_{calc}, obtained from the predictive equations created with, E_{Tmin}, E_{Tmax} and E_{Topt}

No	Alkene	Conformational states	Δ	E_{Tmin} Δ	E_{Tmax} Δ	E_{Topt} Δ
1	cis-2-Butene	1		−7	−8.6	−6.9
2	trans-2-Butene	1		8.3	6.6	8.3
3	cis-2-Pentene	2	0	−5.2	−3.2	−3.4
4	1-Pentene	3	14	−5.9	−4.7	−4.3
5	2-Methyl-2-butene	1		6.2	8.0	7.9
6	3,3-Dimethyl-1-butene	1		0.3	−3.6	−1.6
7	3-Methyl-cis-2-pentene	2	0	−7.0	−1.1	−3.4
8	3-Methyl-trans-2-pentene	2	0	−0.3	5.9	3.7
9	2,3,3-Trimethyl-1-butene	1		−4.7	−4.1	−4.4
10	4,4-Dimethyl-1-pentene	1		8.6	8.8	8.6
11	4,4-Dimethyl-cis-2-pentene	1		3.9	4.4	4.0
12	2,3-Dimethyl-1-pentene	4	3	−16.2	−10.9	−13.3
13	5-Methyl-cis-2-hexene	2	0	−17.2	−7.5	−11.8
14	1-Hexene	8	80	8.2	7.1	4.8
15	4-Methyl-1-pentene	5	35	−24.6	−21.3	−5.0
16	trans-3-Hexene	2	5	11.2	5.6	3.4
17	1-Heptene	29	177	20.5	16.1	11.7
18	5-Methyl-1-hexene	8	43	−11.6	−13.2	−6.3
19	1-Octene	50	197	30.3	13.0	5.9
20	cis-4-Octene	3	54	11.9	11.5	5.0
21	trans-4-Octene	17	279	10.9	4.0	−2.8
22	cis-4-Nonene	9	164	−6.0	−1	−3.2
23	cis-5-Decene	12	256	−15.0	−12	−3.3

The modelling was repeated, now for the extended set of compounds, first with E_T calculated for molecules at lowest energy level – E_{Tmin}. The equation obtained for twenty-three alkenes is:

$$RI_{calc} = 236.1(\pm17.8) - 0.0813(\pm0.0030) \cdot E_{Tmin}$$
$$- 85.4(\pm14.4) \cdot n_q \qquad (3)$$

where $r = 0.9957$, $v = 159$ and S.D. $= \pm13.6$. The differences between RI_{exp} and RI_{calc} are presented in column 5 of Table 2.

Next, RI_{calc} were calculated with E_{Tmax} – the energy at the molecule's maximum energy level. The equation obtained for twenty-three alkenes is:

$$RI_{calc} = 244.4(\pm13.8) - 0.0777(\pm0.0030) \cdot E_{Tmax}$$
$$- 74.5(\pm11.4) \cdot n_q \qquad (4)$$

with $r = 0.9973$, $v = 99.4$ and S.D. $= \pm10.0$. The differences between RI_{exp} and RI_{calc} are presented in column 6 of Table 2. Although no statistically significant improvement can be fixed, a decrease in

the differences between RI_{exp} and RI_{calc} can be observed for most alkenes.

It was assumed further, that for the strongest intermolecular interaction a suitable conformation state is necessary. Its corresponding total energy E_{Topt} value must be located between the values of E_{Tmax} and E_{Tmin}. The E_{Topt} value was searched stepwise, supposing that to its value corresponds the least discrepancy between RI_{exp} and RI_{calc}. The following equation with the found E_{Topt} values was obtained:

$$RI_{calc} = 238.5(\pm9.9) - 0.0796(\pm0.0020) \cdot E_{Topt}$$
$$- 78.9(\pm8.0) \cdot n_q \qquad (5)$$

with $r = 0.9987$, $v = 49.6$ and S.D. $= \pm7$. The improvement is statistically significant according to the F-test: variances of Eqs. (3) and (5) give $F_{23,23}^{exp} = 3.2$, while $F_{23,23}^{tabl} = 2.0$.

It is assumed, that by calculation the total energy value of the corresponding rotamers, for which the discrepancy between RI_{exp} and RI_{calc} is minimum,

the real conformation state (rotamer) in which the solute molecule is adsorbed on the carbon stationary phase surface is resembled. However, further investigations will be needed to determine whether this approach exhibits advantages relative to conventional QSRR calculations. Although the approach is still only a crude attempt to mimic the real situation in the studied case, we hope that it certainly adds to the chromatographic science lore.

Acknowledgments

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