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A Modified Distance Matrix to Distinguish *Cis*/*Trans* Isomers of Cycloalkanes

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A Modified Distance Matrix to Distinguish *Cis*/*Trans* Isomers of Cycloalkanes[#]

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Abstract

The general distance matrix **D** was modified to distinguish *cis*/*trans* isomers of cycloalkanes. A new topological index, $VDI_{(\pm 1)}$, was derived from the modified distance matrix ($\mathbf{D}_{\text{mod}}$) according to the calculation of *VDI* proposed in a previous paper. This new structural descriptor discriminates all compounds studied in this paper. The regression analysis against the boiling temperatures (t_b) for 53 *cis*/*trans* isomers of cycloalkanes with $VDI_{(\pm 1)}$ and other topological indices gives a high correlation coefficient ($r = 0.9961$) and low standard deviation ($s =$ 3.31 ºC), which is much better than that obtained with $VDI_{(0)}$.

Keywords. Topological index; boiling temperature; quantitative structure–property relationships; QSPR; molecular graph; structural descriptor; distance matrix.

1 INTRODUCTION

Isomerism in organic chemistry can be classified into three types: constitutional, geometrical and conformational isomerism. *Cis*/*trans* isomersim belongs to the second type, in which the atoms connect with each other in the same sequence but distribute differently in space. Cycloalkanes bearing several substituents, generally, have *cis*/*trans* isomers and the different spatial distribution of the substituents on the carbon cycle will result in different physical, chemical properties and biological activities. As we know, molecular graph theory is a powerful tool to encode into numbers the constitutional features of the molecular structure, and many useful topological indices have been recently proposed [1–13]. Since the molecular graphs are planar images of molecules, molecular topological indices are often referred to as two–dimensional (2D) descriptors [14]. Despite many successful applications in QSPR/QSAR with 2D topological descriptors [15,16], they fail to consider the stereospecific properties (or 3D information) of molecules, such as *cis*/*trans* isomerism, and atomic chirality. Recently, more and more chemists have shown interest in the study

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[#] Dedicated to Professor Milan Randić on the occasion of the 70th birthday.

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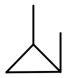
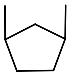
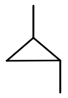
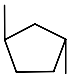
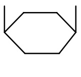
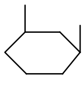
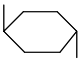
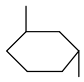
of stereostructural features and some good descriptors have been reported [17–21]. This paper developed a new topological index $VDI_{(\pm1)}$ to distinguish the *cis*/*trans* isomers of cycloalkanes on the basis of Vertex degree–Distance Index (*VDI*) proposed in our previous paper [22]. The calculated $VDI_{(\pm1)}$ for 53 *cis*/*trans* isomers of cycloalkanes are are not degenerated and the regression analysis with $VDI_{(\pm1)}$ against the boiling temperatures of 53 compounds [23] gives better QSPR models than with $VDI_{(0)}$.

2 MATERIALS AND METHODS

The traditional graph theoretical approach neglects the spatial features of molecules [24] and treat a *cis*–isomer in the same way as a *trans*–isomer, which leads to identical topological distance matrices. In order to explore a new graph distance matrix that discriminates *cis*/*trans* compounds, we proposed a modified topological distance, $\mathbf{D}_{\mathrm{mod}\,ij} = \mathbf{D}_{ij} + a$, to quantify the distance between *cis* and *trans* substituents on cycle, where $\mathbf{D}_{ij}$ is the topological length of the shortest path between vertex *i* and *j* [22], and *a* is a parameter that depends on the substituted position and relative spatial direction of the substituents. In order to identify a suitable value for *a*, we explore the relationship between the boiling temperatures [23] and the substituents position for some cycloalkanes (see Table 1).

Table 1. Boiling temperatures (t_b) for some *cis*/*trans* isomers of cycloalkanes

compound	t_b (ºC)	compound	t_b (ºC)
	37.0		90.8
	28.2		91.7
	124.4		120.1
	119.4		124.5

From Table 1, we can see that the boiling temperatures of *cis*–isomers are higher than that of *trans*– isomers for 1,2– and 1,4–substitution, as contrary to 1,3–substitution. This suggests that not only the substituted position but also the relative spatial direction (*cis*– or *trans*–) of groups have effect on the boiling temperatures. Therefore, we define the parameter *a* as follows: if the distance between two substituted sites (carbon atoms) on a ring is odd (such as 1,2–, 1,4–substitution), then *a* = +1 for *cis*–substitution and *a* = –1 for *trans*–substitution; otherwise (for example, 1,3–substitution), *a* = +1 and –1 for *trans*– and *cis*–substitutions, respectively. That is:

$$a=\begin{cases}+1 & \text{odd distance, } \textit{cis}\text{-substituted; even distance, } \textit{trans}\text{-substituted}\\ -1 & \text{odd distance, } \textit{trans}\text{-substituted; even distance, } \textit{cis}\text{-substituted}\end{cases}$$

For example, Figure 1 is the hydrogen–depleted molecular graph of *trans*,*cis*–1–methyl–3–ethyl–4–propylcyclopentane.

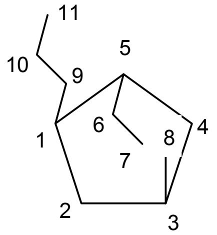


Figure 1. Structure of *trans*,*cis*–1–methyl–3–ethyl–4–propylcyclopentane.

Its modified distance matrix $\mathbf{D}_{\text{mod}}$ is:

$$D_{\text{mod}}=\begin{bmatrix} D_{11} & D_{12} & D_{13} & D_{14} & D_{15} & D_{16} & D_{17} & D_{18} & D_{19} & D_{110} & D_{111}\\ D_{21} & D_{22} & D_{23} & D_{24} & D_{25} & D_{26} & D_{27} & D_{28} & D_{29} & D_{210} & D_{211}\\ D_{31} & D_{32} & D_{33} & D_{34} & D_{35} & D_{36} & D_{37} & D_{38} & D_{39} & D_{310} & D_{311}\\ D_{41} & D_{42} & D_{43} & D_{44} & D_{45} & D_{46} & D_{47} & D_{48} & D_{49} & D_{410} & D_{411}\\ D_{51} & D_{52} & D_{53} & D_{54} & D_{55} & D_{56} & D_{57} & D_{58} & D_{59} & D_{510} & D_{511}\\ D_{61} & D_{62} & D_{63} & D_{64} & D_{65} & D_{66} & D_{67} & D_{68}+a & D_{69}+a & D_{610}+a & D_{611}+a\\ D_{71} & D_{72} & D_{73} & D_{74} & D_{75} & D_{76} & D_{77} & D_{78}+a & D_{79}+a & D_{710}+a & D_{711}+a\\ D_{81} & D_{82} & D_{83} & D_{84} & D_{85} & D_{86}+a & D_{87}+a & D_{88} & D_{89}+a & D_{810}+a & D_{811}+a\\ D_{91} & D_{92} & D_{93} & D_{94} & D_{95} & D_{96}+a & D_{97}+a & D_{98}+a & D_{99} & D_{910} & D_{911}\\ D_{101} & D_{102} & D_{103} & D_{104} & D_{105} & D_{106}+a & D_{107}+a & D_{108}+a & D_{109} & D_{1010} & D_{1011}\\ D_{111} & D_{112} & D_{113} & D_{114} & D_{115} & D_{116}+a & D_{117}+a & D_{118}+a & D_{119} & D_{1110} & D_{1111} \end{bmatrix}$$

$$=\begin{bmatrix} 0 & 1 & 2 & 2 & 1 & 2 & 3 & 3 & 1 & 2 & 3\\ 1 & 0 & 1 & 2 & 2 & 3 & 4 & 2 & 2 & 3 & 4\\ 2 & 1 & 0 & 1 & 2 & 3 & 4 & 1 & 3 & 4 & 5\\ 2 & 2 & 1 & 0 & 1 & 2 & 3 & 2 & 3 & 4 & 5\\ 1 & 2 & 2 & 1 & 0 & 1 & 2 & 3 & 2 & 3 & 4\\ 2 & 3 & 3 & 2 & 1 & 0 & 1 & 4+1 & 3-1 & 4-1 & 5-1\\ 3 & 4 & 4 & 3 & 2 & 1 & 0 & 5+1 & 4-1 & 5-1 & 6-1\\ 3 & 2 & 1 & 2 & 3 & 4+1 & 5+1 & 0 & 4-1 & 5-1 & 6-1\\ 1 & 2 & 3 & 3 & 2 & 3-1 & 4-1 & 4-1 & 0 & 1 & 2\\ 2 & 3 & 4 & 4 & 3 & 4-1 & 5-1 & 5-1 & 1 & 0 & 1\\ 3 & 4 & 5 & 5 & 4 & 5-1 & 6-1 & 6-1 & 2 & 1 & 0 \end{bmatrix}=\begin{bmatrix} 0 & 1 & 2 & 2 & 1 & 2 & 3 & 3 & 1 & 2 & 3\\ 1 & 0 & 1 & 2 & 2 & 3 & 4 & 2 & 2 & 3 & 4\\ 2 & 1 & 0 & 1 & 2 & 3 & 4 & 1 & 3 & 4 & 5\\ 2 & 2 & 1 & 0 & 1 & 2 & 3 & 2 & 3 & 4 & 5\\ 1 & 2 & 2 & 1 & 0 & 1 & 2 & 3 & 2 & 3 & 4\\ 2 & 3 & 3 & 2 & 1 & 0 & 1 & 5 & 2 & 3 & 4\\ 3 & 4 & 4 & 3 & 2 & 1 & 0 & 6 & 3 & 4 & 5\\ 3 & 2 & 1 & 2 & 3 & 5 & 6 & 0 & 3 & 4 & 5\\ 1 & 2 & 3 & 3 & 2 & 2 & 3 & 3 & 0 & 1 & 2\\ 2 & 3 & 4 & 4 & 3 & 3 & 4 & 4 & 1 & 0 & 1\\ 3 & 4 & 5 & 5 & 4 & 4 & 5 & 5 & 2 & 1 & 0 \end{bmatrix}$$

According to the calculation of Vertex degree–Distance Index (*VDI*) presented in the previous paper [22]:

$$VDI = \left(\prod_{i=1}^{N} f_i \right)^{\frac{1}{N}} \tag{1}$$

where f_i is the element of the vector VS obtained by vertex degree matrix (V)–multiply–derivative distance matrix (**S**):

$$VS = [f_1, f_2, \cdots, f_N] \tag{2}$$

In this paper, we substitute the matrix **S** with $\mathbf{D}_{\text{mod}}$ to obtain the modified *VDI*. In order to distinguish the expressions of *VDI* derived from different kind of distance matrix **S** and $\mathbf{D}_{\text{mod}}$, we assigned *VDI* from **S** matrix as $VDI_{(0)}$, while *VDI* from $\mathbf{D}_{\text{mod}}$ as $VDI_{(\pm1)}$. Thus we calculated the $VDI_{(\pm1)}$ of *trans*,*cis*–1–methyl–3–ethyl–4–propylcyclopentane, *i.e.* $VDI_{(\pm1)} = 6.5101$. In comparison, the values of $VDI_{(\pm1)}$ for other three *cis*/*trans* isomers of 1–methyl–3–ethyl–4–propylcyclopentane were also calculated as follows:

cis,*cis*–1–methyl–3–ethyl–4–propylcyclopentane	$\text{VDI}_{(\pm1)} = 6.3857$
cis,*trans*–1–methyl–3–ethyl–4–propylcyclopentane	$\text{VDI}_{(\pm1)} = 6.5024$
trans,*trans*–1–methyl–3–ethyl–4–propylcyclopentane	$\text{VDI}_{(\pm1)} = 6.3147$

Obviously, four *cis*/*trans* isomers of 1–methyl–3–ethyl–4–propylcyclopentane have different $VDI_{(\pm1)}$, while their values of $VDI_{(0)}$ are all equal to 6.3862. The calculated $VDI_{(\pm1)}$ for 53 *cis*/*trans* isomers of cycloalkanes (shown in Figure 2) are listed in Table 2.

3 REGRESSION ANALYSIS AND DISCUSSION

Computed with the above algorithm, $VDI_{(\pm1)}$ has distinct values for all the studied *cis*/*trans* isomers, so it can be expected to reflect the diversity of properties resulted from the different geometric configuration. In this paper, we took the boiling temperatures (t_b, ºC) of 53 *cis*/*trans* isomers of cycloalkanes as the testing property. First, a regression against t_b with two variables, $N^{2/3}$ (N is the number of carbon atoms in a cycloalkane molecule) and $VDI_{(0)}$ was carried out, giving the QSPR model:

$$\begin{gathered} t_b = -159.53 + 90.5446\, N^{2/3} - 13.4083\, VDI_{(0)} \\ r = 0.9909,\ s = 4.96\ ^\circ\text{C},\ \text{F} = 1348.82,\ n = 53 \end{gathered} \tag{3}$$

Taking normal cycloalkanes (*n*–cycloalkanes) as reference compounds, the $VDI_{(0)}$ of each cycloalkane minus that (VDI_{norm}) of the corresponding *n*–cycloalkane bearing the same number of carbon atoms gives a new variable: $\Delta VDI_{(0)} = VDI_{(0)} - VDI_{\text{norm}}$ (the values of VDI_{norm} for *n*–cyclopentane to *n*–cyclodecane are 5.0000, 5.2222, 5.4444, 5.5694, 5.6944 and 5.7744, respectively). For example, for *trans*–1–ethyl–2–methylcyclopropane, $\Delta VDI_{(0)} = 5.5058 - 5.2222 = 0.2836$; for *cis*,*trans*–1,3,5–trimethylcyclohexane, $\Delta VDI_{(0)} = 6.4600 - 5.6944 = 0.7656$. Then in combination with $N^{2/3}$, $VDI_{(0)}$ and $\Delta VDI_{(0)}$ we obtained another regression equation:

$$t_b = -358.40 + 69.2552\, N^{2/3} + 35.2249\, VDI_{(0)} - 37.8404(\Delta VDI_{(0)})^2 \quad (4)$$
$$r = 0.9937,\ s = 4.17\ ^{\circ}\mathrm{C},\ \mathrm{F} = 1280.84,\ n = 53$$

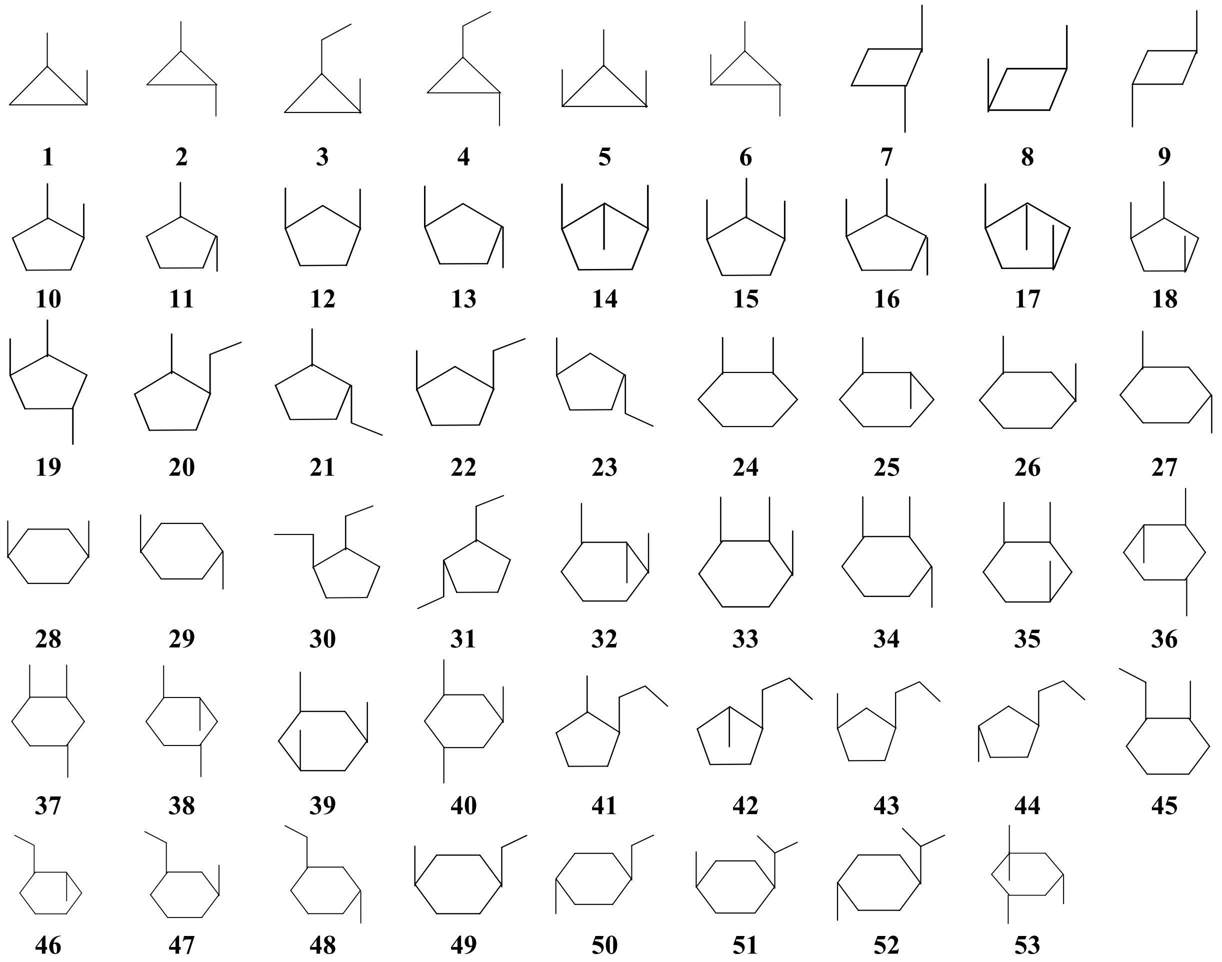


Figure 2. The molecular structures for 53 *cis*/*trans* isomers of cycloalkanes.

From Eq (4), it can be seen that $\Delta VDI_{(0)}$ improves the regression result and the standard deviation s is lower by 0.8 ºC in Eq (4) than that in Eq (3). In comparison, the similar regression analyses with $VDI_{(\pm1)}$ instead of $VDI_{(0)}$ are performed and the following corresponding equations are obtained:

$$t_b = -153.79 + 91.3113\, N^{2/3} - 14.7964\, VDI_{(\pm1)} \quad (5)$$
$$r = 0.9917,\ s = 4.73\ ^{\circ}\mathrm{C},\ \mathrm{F} = 1484.32,\ n = 53$$

$$t_b = -356.40 + 69.1019\, N^{2/3} + 35.0158\, VDI_{(0)} - 35.9089\, (\Delta VDI_{(\pm1)})^2 \quad (6)$$
$$r = 0.9952,\ s = 3.63\ ^{\circ}\mathrm{C},\ \mathrm{F} = 1695.85,\ n = 53$$

where $\Delta VDI_{(\pm1)} = VDI_{(\pm1)} - VDI_{\mathrm{norm}}$. From the above four Eqs (3), (4), (5) and (6), we can see that $VDI_{(\pm1)}$ and $\Delta VDI_{(\pm1)}$ have better correlation with t_b than $VDI_{(0)}$ and $\Delta VDI_{(0)}$. The reason perhaps is that $VDI_{(\pm1)}$ and $\Delta VDI_{(\pm1)}$ contain more details about the molecular geometrical configuration. The different geometrical configuration leads to the various $VDI_{(\pm1)}$ and $\Delta VDI_{(\pm1)}$ which are responsible for the diversity of t_b.

Table 2. Values of N, $VDI_{(0)}$, $VDI_{(\pm1)}$, $\Delta VDI_{(\pm1)}$, $OEI_{(0)}$, t_b (ºC), and n_D for 53 Cycloalkanes

No	N	$VDI_{(0)}$	$VDI_{(\pm1)}$	$\Delta VDI_{(\pm1)}$	$OEI_{(0)}$	t_b (ºC)		n_D	
						$t_{b\ exp}$[a]	$t_{b\ calc}$[b]	$n_{D\ exp}$[c]	$n_{D\ calc}$[d]
1	5	5.4547	5.4303	0.4303	8.2222	37.0	30.21	1.3829	1.3781
2	5	5.4547	5.5236	0.5236	8.2222	28.2	26.91	1.3713	1.3742
3	6	5.5058	5.4669	0.2447	10.0417	58.7	62.90	1.3846	1.3917
4	6	5.5058	5.6071	0.3849	10.0417	59.0	59.63	1.3953	1.3879
5	6	5.9512	5.8896	0.6674	9.6667	66.0	65.70	1.3970	1.4007
6	6	5.9512	6.0462	0.8240	9.6667	59.7	57.04	1.3873	1.3906
7	6	5.7394	5.7968	0.5746	9.6667	58.0	61.29	1.3950	1.3930
8	6	5.6499	5.6706	0.4484	9.3194	60.5	61.32	1.3933	1.3922
9	6	5.6499	5.6402	0.4180	9.3194	57.5	62.29	1.3896	1.3933
10	7	6.0699	6.0523	0.6079	10.6111	99.5	95.50	1.4222	1.4138
11	7	6.0699	6.1195	0.6751	10.6111	91.9	92.30	1.4120	1.4101
12	7	6.0090	6.0270	0.5826	10.2639	90.8	93.03	1.4089	1.4104
13	7	6.0090	6.0006	0.5562	10.2639	91.7	94.15	1.4107	1.4117
14	8	6.4688	6.5717	1.0023	12.1528	110.4	111.40	1.4138	1.4147
15	8	6.4688	6.4534	0.8840	12.1528	123.0	119.68	1.4262	1.4243
16	8	6.4688	6.4899	0.9205	12.1528	117.5	117.23	1.4218	1.4215
17	8	6.4124	6.4651	0.8957	11.8056	109.3	115.50	1.4106	1.4191
18	8	6.4124	6.4285	0.8591	11.8056	116.8	117.89	1.4186	1.4218
19	8	6.4124	6.3819	0.8125	11.8056	116.7	120.77	1.4186	1.4252
20	8	6.0880	6.0584	0.4890	12.1806	128.0	124.25	1.4293	1.4250
21	8	6.0880	6.1649	0.5955	12.1806	121.2	119.97	1.4219	1.4200
22	8	6.0265	6.0567	0.4873	12.0383	121.0	121.34	1.4203	1.4210
23	8	6.0265	6.0117	0.4423	12.0383	121.0	122.89	1.4186	1.4228
24	8	6.1701	6.1548	0.5854	12.5278	129.8	124.86	1.4360	1.4264
25	8	6.1701	6.2131	0.6437	12.5278	123.5	122.21	1.4270	1.4234
26	8	6.1234	6.1391	0.5697	12.1806	120.1	122.53	1.4229	1.4235
27	8	6.1234	6.1162	0.5468	12.1806	124.5	123.48	1.4284*	1.4245
28	8	6.1117	6.1077	0.5383	12.3856	124.4	123.99	1.4230	1.4248
29	8	6.1117	6.1191	0.5497	12.3856	119.4	123.53	1.4185*	1.4243
30	9	6.1199	6.0716	0.3772	13.83	153.6	151.82	1.4355	1.4358
31	9	6.1199	6.2364	0.5420	13.83	147.5	146.21	1.4295	1.4293
32	9	6.5491	6.6394	0.9450	13.9444	144.0	141.95	1.4300	1.4295
33	9	6.5491	6.5356	0.8412	13.9444	151.7	148.83	1.4405	1.4375
34	9	6.5491	6.5676	0.8732	13.9444	151.2	146.79	1.4399	1.4351
35	9	6.4935	6.4902	0.7958	13.8022	146.6	148.86	1.4340	1.4369
36	9	6.4935	6.5226	0.8282	11.8056	142.9	140.66	1.4266	1.4289
37	9	6.4935	6.4797	0.7853	11.8056	146.7	143.23	1.4345	1.4319
38	9	6.4935	6.5531	0.8587	11.8056	142.9	138.76	1.4341	1.4267
39	9	6.4600	6.5023	0.8079	13.25	138.5	145.04	1.4269	1.4325
40	9	6.4600	6.4610	0.7666	13.25	140.5	147.45	1.4307	1.4353
41	9	6.0757	6.0445	0.3501	13.8928	152.6	150.94	1.4343	1.4342
42	9	6.0757	6.1518	0.4574	13.8928	146.4	147.73	1.4274	1.4305
43	9	6.0184	6.0502	0.3558	13.615	148.0	147.57	1.4260	1.4298
44	9	6.0184	6.0021	0.3077	13.615	148.0	148.75	1.4260	1.4312
45	9	6.1929	6.1668	0.4724	14.1772	156.0	152.91	1.4456	1.4377
46	9	6.1929	6.2608	0.5664	14.1772	151.7	149.29	1.4381	1.4335
47	9	6.1449	6.1716	0.4772	14.035	156.0	150.32	1.4432	1.4342
48	9	6.1449	6.1318	0.4374	14.035	150.0	151.67	1.4382	1.4358
49	9	6.1284	6.1210	0.4266	14.1044	152.6	151.56	1.4374	1.4354
50	9	6.1284	6.1416	0.4472	14.1044	149.0	150.89	1.4304	1.4346
51	10	6.4772	6.4671	0.6927	15.3233	172.0	175.52	1.4431	1.4469
52	10	6.4772	6.4950	0.7206	15.3233	170.6	174.05	1.4366	1.4452
53	10	6.9988	7.0251	1.2507	13.8194	152.5	152.00	1.4319	1.4271

[a] from ref. 23; [b] calculated by Eq (8); [c] from ref. 23, values of n_D were obtained at 20ºC except No **27** and **29** (marked with *) which were measured at 25ºC; [d] calculated by Eq (12) in Table 3.

Our previous paper [22] has proved that *OEI*, the odd–even index, is a useful variable to obtain QSPR models for t_b, so in this paper we will use it to correlate the boiling temperatures. The expression of *OEI* is as follows:

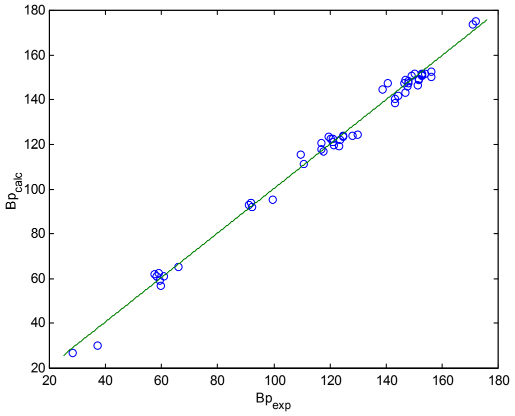
$$OEI = \sum_{i=1}^{N}\sum_{j\neq i}^{N}\left[(-1)^{\mathbf{D}_{ij}-1}\mathbf{S}\right] \tag{7}$$

where **S** is the derivative distance matrix as same as that in Eq (2). With the addition of $OEI_{(0)}$ to Eq (6), we obtain the following regression equation:

$$t_b = -369.15 + 53.6110\,N^{2/3} + 41.0194\,VDI_{(0)} - 37.0755(\Delta VDI_{(\pm1)})^2 + 3.1275\,OEI_{(0)} \tag{8}$$
$$r = 0.9961,\ s = 3.31\ ^{\circ}\mathrm{C},\ \mathrm{F} = 1536.32,\ n = 53$$

Here, $OEI_{(0)}$ is calculated on the basis of the derivative distance matrix **S** (other than the modified distance matrix $\mathbf{D}_{\mathrm{mod}}$) according to Eq (7). As expected, Eq (8) improves the correlation coefficient and lowers the standard deviation further. The calculated boiling temperatures ($t_{b\ \mathrm{calc}}$) with Eq (8) are listed in Table 2.

Eq (8) shows that t_b increases with the increase of $N^{2/3}$, $VDI_{(0)}$ and $OEI_{(0)}$, but decreases with the augmentation of $\Delta VDI_{(\pm1)}$. Because *cis*/*trans* isomers have the same values of $N^{2/3}$, $VDI_{(0)}$ and $OEI_{(0)}$, only the difference for $\Delta VDI_{(\pm1)}$ results in the discrimination of boiling temperatures. Therefore, the larger the value of $\Delta VDI_{(\pm1)}$ or $VDI_{(\pm1)}$ is, the lower is the boiling temperature for *cis*/*trans* isomers, which can be seen in Table 2. Figure 3 shows the plot of $t_{b\ \mathrm{calc}}$ *vs* $t_{b\ \mathrm{exp}}$.



Figue 3. Plot of $t_{b\ \mathrm{calc}}$ *vs* $t_{b\ \mathrm{exp}}$ for 53 *cis*/*trans* isomers of cycloalkanes.

In addition, the refractive index of cycloalkanes is also a property relating with the molecular structure. This paper further takes refractive index n_D [23] as another testing property to investigate the QSPR ability of $VDI_{(\pm1)}$. The regression results between n_D (see Table 2) of 53 *cis*/*trans* isomers of cycloalkanes and the employed variables are shown in Table 3. The replacement of $\Delta VDI_{(0)}$ with $\Delta VDI_{(\pm1)}$ also improved the correlations between n_D and structural descriptors, which gives weight to the rationality of the newly developed topological index $VDI_{(\pm1)}$.

Table 3. Regression for the Refractive Index (n_D) of the 53 Cycloalkanes with Different Descriptors

$$n_D = a_0 + a_1 VDI_{(0)} + a_2(\Delta VDI_{(0)})^2 + a_3(\Delta VDI_{(\pm1)})^2 + a_4 OEI_{(0)}$$

Eq	a_0	a_1	a_2	a_3	a_4	r	s
(9)	0.9285	0.0843	–0.0652			0.9488	0.00564
(10)	0.9417	0.0820		–0.0596		0.9553	0.00528
(11)	1.0273	0.0615	–0.0467		0.0028	0.9561	0.00528
(12)	1.0360	0.0598		–0.0431	0.0029	0.9648	0.00474

4 CONCLUSIONS

The quantitative characterization of geometrical isomers is a challenging subject in QSAR/QSPR studies. When the molecular spatial features are considered, it is necessary to improve the preceding approach of constructing topological index. This paper tried to develop a new topological index $VDI_{(\pm1)}$ to distinguish *cis*/*trans* isomers of cycloalkanes. The regression analysis against boiling temperatures gives high correlation coefficient and low standard deviation, which shows that $VDI_{(\pm1)}$ is an interesting approach to discriminate geometrical isomers. Of course, it is worthy of further investigation the optimum value for a, which was considered ±1 in this study.

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