

Modeling Boiling Points of Cycloalkanes by Means of Iterated Line Graph Sequences

Željko Tomović and Ivan Gutman

Faculty of Science, University of Kragujevac, P.O. Box 60, YU-34000 Kragujevac, Yugoslavia

Received January 22, 2001

A class of models for predicting boiling points of cycloalkanes is put forward, based on iterated line graphs L^i , $i = 1, 2, \dots$, of the molecular graph $G = L^0$. Let m_i be the number of edges of L^i , $i = 0, 1, 2, \dots$. The models analyzed are of the form $a_0 m_{i_0} + a_1 m_{i_1} + a_2 m_{i_2} + \dots + a_k m_{i_k} + b$. Our optimal QSPR formulas contain m_0 , m_1 , m_2 , m_3 , and/or m_4 but never m_5 and m_6 . Their precision is as good as or better than the approximations recently reported by Rücker and Rücker (*J. Chem. Inf. Comput. Sci.* **1999**, 39, 788–802).

1. INTRODUCTION

Boiling points of alkanes are traditionally used for testing and/or demonstrating the correlating abilities of topological indices.¹ Boiling points of cycloalkanes have been examined to a much lesser extent (see, for instance, ref 2). Only quite recently Rücker and Rücker³ produced a critical compilation of experimental boiling points of cycloalkanes and reported their correlations with numerous topological indices and (linear) combinations thereof. This work motivated us to extend our earlier QSPR models, based on the iterated line graph sequences, to the boiling points of cycloalkanes.

In a paper⁴ published in 1981 Bertz was the first to propose the use of line graphs of molecular graphs and their invariants for modeling physicochemical properties of organic molecules.⁵ (For definitions see the subsequent section.) Independently of Bertz, line graphs were sporadically used in several, mutually unrelated fields of chemistry.^{8–16} Extensive usage of line graphs in QSPR studies was initiated by Estrada's 1995 article¹⁷ and was eventually followed by a number of researches.^{17–24}

The idea to use not only the line graph but also the first few members of the iterated line graph sequence (for definitions see the subsequent section) was anticipated by Bertz^{25,26} and was eventually implemented by several authors.^{27–31} All QSPR studies based on the iterated line graph sequence, done so far, were concerned with alkanes. The present work seems to be the first where iterated line graphs are used for modeling a physicochemical property of cycloalkanes.³²

2. LINE GRAPHS OF MOLECULAR GRAPHS, ITERATED LINE GRAPH SEQUENCES, AND BERTZ TOPOLOGICAL INDICES BASED ON THEM

The line graph, a standard concept of graph theory,²² is defined as follows. Let G be a graph with $m = m_0$ edges. Let e_1, e_2, \dots, e_m be the edges of G . Each edge connects a pair of vertices. These two vertices are said to be adjacent and to be the endpoints of the respective edge. Two edges are said to be incident if they have an endpoint in common. The line graph $L(G)$ of G is a graph with m vertices, say u_1, u_2, \dots, u_m ; two vertices u_i and u_j of $L(G)$ are adjacent if and

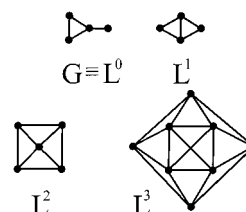


Figure 1. The molecular graph of methylcyclopropane (G) and the first three members of its iterated line graph sequence (L^1, L^2, L^3); for this molecular graph, $m_0 = 4$, $m_1 = 5$, $m_2 = 8$, $m_3 = 18$, $m_4 = 64$, $m_5 = 396$, $m_6 = 4552$, $m_7 = 101024$; for details see text.

only if the edges e_i and e_j of G are incident. By $L^2(G)$ we denote the line graph of $L(G)$, by $L^3(G)$ the line graph of $L^2(G)$, and so on. The graph $L^i(G)$ will be called the i th iterated line graph of the graph G . It is consistent to write $L^0(G)$ and $L^1(G)$ instead of G and $L(G)$, respectively.

An example of a molecular graph and its first three iterated line graphs is shown in Figure 1.

In the case of the path graphs P_n (the molecular graphs of normal alkanes), $L(P_n) = P_{n-1}$. Therefore, the respective iterated line graph sequence is finite and is of the form $\{P_n, P_{n-1}, P_{n-2}, \dots, P_2, P_1\}$. In the case of the cycles C_n (the molecular graphs of unbranched cycloalkanes), $L(C_n) = C_n$. Therefore, the iterated line graph sequence of C_n is of the form $\{C_n, C_n, C_n, \dots\}$.

For all other molecular graphs, the members of the iterated line graph sequence rapidly become enormously large. For instance, in the case of methylcyclopropane the line graphs L^i , $i = 1, 2, \dots, 8$ have 4, 5, 8, 18, 64, 396, 4552, and 101024 vertices, respectively (cf. Figure 1).

The fact that any graph G uniquely determines its line graph $L(G)$ is self-evident. However, if G is a connected graph, then also $L(G)$ uniquely determines G , with the single exception when $L(G)$ is the triangle.³³ If we disregard this exceptional case, then we arrive at the noteworthy conclusion that any member of an iterated line graph sequence fully determines the entire sequence. In other words, any member of the iterated line graph sequence of a graph G contains exactly the same structural information as the graph G itself.

Bertz proposed⁴ the number of edges of the line graph of a molecular graph as a chemically useful structure-descriptor. This quantity is nowadays referred to as the Bertz index.⁵ Each member of an iterated line graph sequence has its Bertz index; the Bertz index of L^i is denoted by m_{i+1} (m_1 is the

* Corresponding author phone: 381-34-331876; fax: 381-34-335040; e-mail: gutman@knez.uis.kg.ac.yu.

Table 1. Correlations Coefficients between the Bertz Indices of Order i and j for Mono- and Bicycloalkanes

	$j = 1$	$j = 2$	$j = 3$	$j = 4$	$j = 5$	$j = 6$
Monocycloalkanes						
$i = 0$	0.809	0.469	0.285	0.188	0.130	0.094
$i = 1$		0.892	0.768	0.674	0.597	0.528
$i = 2$			0.970	0.915	0.851	0.781
$i = 3$				0.983	0.945	0.890
$i = 4$					0.988	0.953
$i = 5$						0.987
Bicycloalkanes						
$i = 0$	0.774	0.387	0.206	0.119	0.066	0.028
$i = 1$		0.877	0.755	0.670	0.600	0.539
$i = 2$			0.973	0.927	0.873	0.817
$i = 3$				0.987	0.955	0.914
$i = 4$					0.990	0.965
$i = 5$						0.992

original Bertz index whereas m_2, m_3, \dots are the higher-order Bertz indices). Figure 1 exemplifies the fact that with increasing i the higher-order Bertz indices increase very rapidly.

It is not known³⁴ whether two nonisomorphic graphs (that are connected and are not regular) may have the same sequence $\{m_0, m_1, m_2, \dots\}$. However, pairs of molecular graphs G_a and G_b for which the equality $m_i(G_a) = m_i(G_b)$ holds for the first few values of i are easily constructed.³⁵

3. QSPR MODELS BASED ON BERTZ INDICES

In what follows BP will denote the boiling point (at normal atmospheric pressure, expressed in Celsius degrees) of a saturated hydrocarbon whose molecular graph is G .³⁶ By bp we denote the approximate value for BP calculated by one of our QSPR models. In this work a class of QSPR models based on Bertz indices is examined

$$BP \approx bp(i_0, i_1, i_2, \dots, i_k) = a_0 m_{i_0} + a_1 m_{i_1} + a_2 m_{i_2} + \dots + a_k m_{i_k} + b \quad (1)$$

where $\{i_0, i_1, i_2, \dots, i_k\}$ is a $(k + 1)$ -element subset of the set $\{0, 1, 2, \dots, p\}$, $m_{i_0}, m_{i_1}, \dots, m_{i_k}$ are the Bertz indices pertaining to $L^{i_0}, L^{i_1}, \dots, L^{i_k}$, respectively, and a_0, a_1, \dots, a_k, b are fitting parameters, obtained by the method of least squares. In this paper $p = 6$ (see below). The value of k was determined by the requirement that a (k) -model is significantly more accurate than the best $(k-1)$ -model and that no $(k+1)$ -model is significantly more accurate than the best (k) -model. What is (statistically) "significant" was established by means of an F-test³⁷ at a 90% confidence level.

The database used are the boiling points of 143 monocycloalkanes (with 3–10 carbon atoms) and of 61 bicycloalkanes (with 4–10 carbon atoms) for which, according to Rücker and Rücker,³ there exist reliable experimental values. Details of this database can be found in ref 3.

For isomers the parameter m_0 (number of edges of the molecular graph G) is constant and therefore instead of the model (1), we employed its modified version:

$$BP \approx bp(i_1, i_2, \dots, i_k) = a_1 m_{i_1} + a_2 m_{i_2} + \dots + a_k m_{i_k} + b \quad (2)$$

where $\{i_1, i_2, \dots, i_k\}$ is now a k -element subset of the set $\{1, 2, \dots, p\}$.

4. NUMERICAL WORK AND RESULTS

Because of rapid increase of the size of the members of an iterated line graph sequence we were able to evaluate m_i of all cycloalkanes from our samples only for i up to 6. Therefore we had to choose $p = 6$. In Table 1 are given the correlation coefficients between various Bertz indices of mono- and bicycloalkanes. These data show that the Bertz indices are only weakly correlated, which justifies the usage of models of the type (1) or (2).

The first database examined was the series of 143 monocycloalkanes with 10 or fewer carbon atoms. For all samples of nonisomeric monocycloalkanes, the one-param-

Table 2. Optimal QSPR Models for Predicting Boiling Points of Monocycloalkanes and Some Statistical Data Indicating Their Precision^a

sample	n	c	N	model	r	AE
monocycloalkanes	3–10	3–6	143	$a_0 m_0 + a_1 m_1 + a_2 m_4 + b$	0.994	3.7
monocycloalkanes	7–10	3–6	123	$a_0 m_0 + a_1 m_2 + a_2 m_3 + b$	0.989	3.4
monocycloalkanes	3–10	3	29	$a_0 m_0 + a_1 m_1 + b$	0.995	3.7
monocycloalkanes	4–10	4	12	$a_0 m_0 + a_1 m_1 + b$	0.998	2.0
monocycloalkanes	5–10	5	46	$a_0 m_0 + a_1 m_1 + a_2 m_3 + b$	0.995	2.1
monocycloalkanes	6–10	6	43	$a_0 m_0 + a_1 m_1 + a_2 m_2 + b$	0.993	2.2
monocyclodecanes	10	3–6	38	$a_1 m_1 + b$	0.908	4.0
monocyclononanes	9	3,5,6	46	$a_1 m_2 + a_2 m_3 + b$	0.945	2.9
monocyclooctanes	8	3–6	24	$a_1 m_2 + a_2 m_3 + b$	0.965	2.6
monocycloheptanes	7	3–6	15	$a_1 m_2 + a_2 m_3 + b$	0.980	1.7
sample	a_0	a_1	a_2	b		
monocycloalkanes	39.381	−9.668	0.012	−100.493		
monocycloalkanes	31.965	−4.120	0.484	−85.250		
monocycloalkanes	34.761	−4.843		−109.966		
monocycloalkanes	37.173	−7.873		−100.360		
monocycloalkanes	39.200	−12.376	0.227	−79.035		
monocycloalkanes	38.643	−15.933	2.394	−66.304		
monocyclodecanes		−6.169		250.934		
monocyclononanes		−4.597	0.568	208.113		
monocyclooctanes		−5.004	0.587	181.545		
monocycloheptanes		−5.439	0.677	148.944		

^a n – number of carbon atoms, c – size of the cycle, N – sample size, r – correlation coefficient, AE – average error (in °C), equal to the arithmetic mean of the absolute values of the absolute errors; a_0, a_1, a_2, b are the coefficients in eqs 1 and 2, obtained by least square fitting.

eter approximation $a_0m_0 + b$ was found to be far better than any of the approximations $a_0m_i + b$, $i = 1, 2, \dots, 6$. For instance, for the sample consisting of monocycloalkanes with 7–10 carbon atoms the correlation coefficient for $a_0m_0 + b$ is 0.91, whereas for $a_0m_i + b$, $i = 1, 2, \dots, 6$ the correlation coefficients are 0.27, 0.14, 0.26, 0.30, 0.31, and 0.31, respectively. The situation with the other samples of non-isomeric monocycloalkanes examined is similar. Therefore, in eq 1 we have fixed $i_0 = 0$ and varied only the indices i_1, i_2, \dots, i_k . We then continued by setting $k = 1, k = 2$, etc. For any given value of k the model (1) was tested for all possible permutations (i_1, i_2, \dots, i_k), and the best such model was selected. The search was ended when no model of the type $bp(0, i_1, i_2, \dots, i_k, i_{k+1})$ was significantly better (as determined by F-test³⁷ at 90% confidence level) than the best model of the type $bp(0, i_1, i_2, \dots, i_k)$.

The optimal QSPR models found by the above-described procedure as well as the statistical data indicating their precision are given in Table 2.

The QSPR model thus obtained (see Table 2) was then applied to the $209 - 143 = 66$ monocycloalkanes for which Rücker and Rücker³ report experimental boiling points, but assume that these are not reliable. (Why these data are classified as not reliable is explained in due detail elsewhere.³) The greatest deviations found were for 1,2-dipropyl-1-methylcyclopropane (19.1 °C), 1-methyl-3-isobutylcyclopentane (17.3 °C), and 1-isopropyl-2-isobutylcyclopropane (16.4 °C). We are inclined to conclude that the experimental boiling points for these compounds are incorrect.

In Table 3 are given the experimental and on the optimal QSPR model calculated values of boiling points of cyclohexane derivatives with 6–10 carbon atoms.

The second database embraces the *BPs* of 61 bicycloalkanes with 4–10 carbon atoms. Also here, in cases of nonisomeric bicycloalkanes the one-parameter approximation $a_0m_0 + b$, was found to be far better than any of the approximations $a_0m_i + b$, $i = 1, 2, \dots, 6$. In all samples of isomeric bicycloalkanes (decanes, nonanes, and octanes), the one-parameter approximation $a_1m_1 + b$ is better than any of the approximations $a_1m_i + b$, $i = 2, 3, \dots, 6$. The optimal QSPR models found for samples of bicycloalkanes are given in Table 4.

A correlation between the experimental and calculated values of boiling points of bicycloalkanes with 4–10 carbon atoms is shown in Figure 2.

Our QSPR model (see Table 4) was then applied to the $127 - 61 = 66$ bicycloalkanes for which Rücker and Rücker³ provide experimental boiling points, but assume that these are not reliable. The greatest deviations found were for 1,1-dimethylspiro[2.5]octane (1.73 °C), 1,4-dimethylbicyclo[2.1.1]hexane (15.0 °C), and 2,6-dimethylbicyclo[3.3.0]octane (14.8 °C). Again, we suspect that the respective experimental values might be incorrect.

5. DISCUSSION AND CONCLUDING REMARKS

For all samples of nonisomeric mono- and bicycloalkanes the optimal QSPR model has $k = 1$ or $k = 2$, which means that besides m_0 only one or two distinct Bertz indices need to be used. As can be seen from Tables 2 and 4, in the optimal QSPR models structure-descriptors appear m_1 – the

Table 3. Experimental and Calculated Boiling Points of Cyclohexane Derivatives with 6–10 Carbons Atoms

compound	experimental	calculated	difference
c6	80.7	84.3	3.6
1mc6	101.0	103.1	2.1
1ec6	131.8	130.6	−1.2
14mc6	121.8	121.8	0.0
13mc6	122.3	121.8	−0.5
12mc6	126.6	124.2	−2.4
11mc6	119.5	120.2	0.7
1pc6	156.7	155.7	−1.0
1ipc6	154.8	149.3	−5.5
1m4ec6	150.8	149.3	−1.5
1m3ec6	150.0	149.3	−0.7
1m2ec6	154.3	151.7	−2.6
135mc6	139.5	140.6	1.1
124mc6	144.8	143.0	−1.8
123mc6	149.4	145.3	−4.1
1m1ec6	152.0	150.1	−1.9
114mc6	136.0	139.0	3.0
113mc6	136.6	139.0	2.4
112mc6	145.1	143.8	−1.3
1bc6	180.9	180.8	−0.1
1ibc6	171.3	172.0	0.7
1m4pc6	173.4	174.4	1.0
1m3pc6	169.0	174.4	5.4
1sbc6	179.3	176.8	−2.5
14ec6	175.5	176.8	1.3
13ec6	172.0	176.8	4.8
1m2pc6	174.5	176.8	2.3
1m4ipc6	170.0	168.1	−1.9
12ec6	176.0	179.2	3.2
1m3ipc6	167.0	168.1	1.1
1e35mc6	168.5	168.1	−0.4
1m2ipc6	171.0	170.5	−0.5
1m1pc6	174.3	175.2	0.9
1tbc6	171.5	166.5	−5.0
11ec6	179.5	180.0	0.5
14m1ec6	168.0	168.9	0.9
1245mc6	167.0	164.1	−2.9
13m1ec6	166.6	168.9	2.3
1235mc6	166.5	164.1	−2.4
1234mc6	172.5	166.5	−6.0
1135mc6	153.0	157.7	4.7
1144mc6	153.0	156.2	3.2
1133mc6	155.0	156.2	1.2

Table 4. Optimal QSPR Models for Predicting Boiling Points of Bicycloalkanes and Some Statistical Data Indicating Their Precision^a

sample	<i>n</i>	<i>N</i>	model	<i>r</i>	AE
bicycloalkanes	4–10	61	$a_0m_0 + a_1m_2 + a_2m_3 + b$	0.995	3.1
bicycloalkanes	7–10	53	$a_0m_0 + a_1m_1 + b$	0.987	3.6
bicyclodecanes	10	18	$a_1m_1 + b$	0.947	3.1
bicyclononanes	9	14	$a_1m_1 + b$	0.908	2.9
bicyclooctanes	8	13	$a_1m_1 + b$	0.875	4.1

sample	<i>a</i> ₀	<i>a</i> ₁	<i>a</i> ₂	<i>b</i>
bicycloalkanes	31.396	−3.352	0.328	−95.539
bicycloalkanes	32.046	−5.708		−85.048
bicyclodecanes		−6.584		281.455
bicyclononanes		−5.929		239.319
bicyclooctanes		−4.662		189.631

^a For details see Table 2.

original Bertz index, m_2 , m_3 , and/or m_4 . In the case of isomeric monocyclic heptanes, octanes, and nonanes the optimal QSPR models contain as structure-descriptors m_2 and m_3 . The optimal QSPR model for isomeric monocyclodecanes is $a_1m_1 + b$, containing only one (independent) variable. Also for all samples of isomeric bicycloalkanes

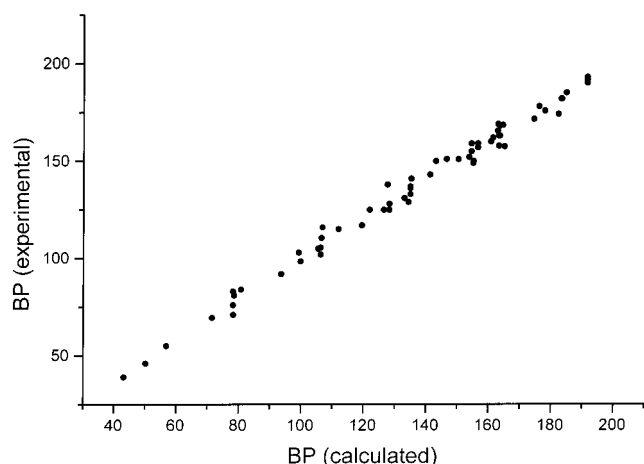


Figure 2. Experimental vs calculated boiling points of bicycloalkanes with 4–10 carbon atoms.

(heptanes, octanes, and decanes) the one-variable model $a_1m_1 + b$ is the optimal one.

In not a single case was the inclusion of the fifth- and/or sixth-order Bertz indices found to be necessary. It is almost certain that the Bertz indices of order higher than 6 play hardly any role in QSPR studies.

In ref 3 the boiling points of cycloalkanes were correlated with a variety of topological indices and linear combinations thereof. By comparing these results with what we obtained in this study, we see that *in all cases examined* the optimal models (1) or (2) give higher correlation coefficients and lower average errors. Such comparisons are, of course, done between regression models possessing the same number of topological indices.

Bearing in mind these encouraging numerical results as well as the straightforward structural interpretation of the topological indices employed in this work (namely the Bertz index and its higher-order analogues), we may conclude that the iterated line graphs, and the Bertz indices based on them, should be considered as a natural basis for designing quantitative structure-property relations. The linear models (1) and (2) may well be an oversimplification, and in the future more sophisticated (nonlinear) QSPR approaches should be attempted.

REFERENCES AND NOTES

- (1) Mihalić, Z.; Trinajstić, N. A Graph-Theoretical Approach to Structure-Property Relationships. *J. Chem. Educ.* **1992**, 69, 701–712.
- (2) Das, A.; Dömötör, G.; Gutman, I.; Joshi, S.; Karmarkar, S.; Khaddar, D.; Khaddar, T.; Khadikar, P. V.; Popović, L.; Sapre, N. S.; Sapre, N.; Shirhatti, A. A Comparative Study of the Wiener, Schultz and Szeged Indices of Cycloalkanes. *J. Serb. Chem. Soc.* **1997**, 62, 235–239.
- (3) Rücker, G.; Rücker, C. On Topological Indices, Boiling Points, and Cycloalkanes. *J. Chem. Inf. Comput. Sci.* **1999**, 39, 788–802.
- (4) Bertz, S. H. The Bond Graph. *J. Chem. Soc. Chem. Commun.* **1981**, 818–820.
- (5) Already in 1947 and 1952 Platt^{6,7} considered a structure-descriptor equal to the sum of the number of bonds adjacent to each of the bonds in the molecule. It is not difficult to verify that Platt's index is equal to the number of edges of the line graph of the molecular graph, thus being equal to the index put forward in 1981 by Bertz. Although this coincidence between the Platt and Bertz indices was noticed by Bertz,²⁵ it escaped the attention of the majority of scientists working in chemical graph theory.
- (6) Platt, J. R. Influence of Neighbour Bonds on Additive Bond Properties in Paraffins. *J. Chem. Phys.* **1947**, 15, 419–420.
- (7) Platt, J. R. Prediction of Isomeric Differences in Paraffin Properties. *J. Phys. Chem.* **1952**, 56, 328–336.
- (8) Gutman, I. Topological Properties of Benzenoid Systems. IX. On the Sextet Polynomial. *Z. Naturforsch.* **1982**, 37a, 69–73.
- (9) Sana, M.; Leroy, G. Graph Theory, Electronic Structures and Reaction Mechanisms. *J. Mol. Struct. (THEOCHEM)* **1984**, 109, 251–269.
- (10) Gutman, I.; El-Basil, S. Topological Properties of Benzenoid Systems. XXXVII. Characterization of Certain Chemical Graphs. *Z. Naturforsch.* **1985**, 40a, 923–926.
- (11) Gutman, I.; Polansky, O. E. *Mathematical Concepts in Organic Chemistry*; Springer-Verlag: Berlin, 1986.
- (12) Polansky, O. E.; Mark, G.; Zander, M. *Der Topologische Effekt an Molekülorbitalen (TEMO)*; Max-Planck-Institut für Strahlenchemie: Mülheim, 1987; pp 379–397.
- (13) Gutman, I.; Cyvin, S. J. *Introduction to the Theory of Benzenoid Hydrocarbons*; Springer-Verlag: Berlin, 1989; pp 108–114.
- (14) Diudea, M. V.; Horvath, D.; Kacso, I. E.; Minailiuc, O. M.; Parv, B. Molecular Topology. VIII: Centricities in Molecular Graphs. The MOLCEN Algorithm. *J. Math. Chem.* **1992**, 11, 259–270.
- (15) Narumi, H.; Kita, H. Equivalent Bond Index. *Commun. Math. Chem. (MATCH)* **1994**, 30, 225–242.
- (16) Diudea, M. V.; Horvath, D.; Bonchev, D. Molecular Topology. 14. Molord Algorithm and Real Number Subgraph Invariants. *Croat. Chem. Acta* **1995**, 68, 131–148.
- (17) Estrada, E. Edge Adjacency Relationships and a Novel Topological Index Related to Molecular Volume. *J. Chem. Inf. Comput. Sci.* **1995**, 35, 31–33.
- (18) Gutman, I.; Estrada, E. Topological Indices Based on the Line Graph of the Molecular Graph. *J. Chem. Inf. Comput. Sci.* **1996**, 36, 541–543.
- (19) Estrada, E. Spectral Moments of the Edge Adjacency Matrix in Molecular Graphs. 1. Definition and Applications to the Prediction of Physical Properties of Alkanes. *J. Chem. Inf. Comput. Sci.* **1996**, 36, 844–849.
- (20) Estrada, E.; Gutman, I. A Topological Index Based on Distances of Edges of Molecular Graphs. *J. Chem. Inf. Comput. Sci.* **1996**, 36, 850–853.
- (21) Estrada, E.; Ramírez, A. Edge Adjacency Relationships and Molecular Topographic Descriptors. Definition and QSAR Applications. *J. Chem. Inf. Comput. Sci.* **1996**, 36, 837–843.
- (22) Estrada, E.; Guevara, N.; Gutman, I. Extension of Edge Connectivity Index. Relationships to Line Graph Indices and QSPR Applications. *J. Chem. Inf. Comput. Sci.* **1998**, 38, 428–431.
- (23) Estrada, E.; Rodríguez, L. Edge-Connectivity Indices in QSPR/QSAR Studies. 1. Comparison to Other Topological Indices in QSPR Studies. *J. Chem. Inf. Comput. Sci.* **1999**, 39, 1037–1041.
- (24) Estrada, E. Edge-Connectivity Indices in QSPR/QSAR Studies. 2. Accounting for Long-Range Bond Contributions. *J. Chem. Inf. Comput. Sci.* **1999**, 39, 1042–1048.
- (25) Bertz, S. H. Branching in Graphs and Molecules. *Discr. Appl. Math.* **1988**, 19, 65–83.
- (26) Bertz, S. H. A Mathematical Model of Molecular Complexity. *Stud. Phys. Theor. Chem.* **1993**, 28, 206–221.
- (27) Gutman, I.; Popović, L.; Mishra, B. K.; Kuanar, M.; Estrada, E.; Guevara, N. Application of Line Graphs in Physical Chemistry. Predicting the Surface Tensions of Alkanes. *J. Serb. Chem. Soc.* **1997**, 62, 1025–1029.
- (28) Gutman, I.; Popović, L.; Estrada, E.; Bertz, S. H. The Line Graph Model. Predicting Physico-Chemical Properties of Alkanes. *ACH Models Chem.* **1998**, 135, 147–155.
- (29) Estrada, E. Generalized Spectral Moments of the Iterated Line Graphs Sequence. A Novel Approach to QSPR Studies. *J. Chem. Inf. Comput. Sci.* **1999**, 39, 90–95.
- (30) Gutman, I.; Tomović, Z. On the Application of Line Graphs in Quantitative Structure–Property Studies. *J. Serb. Chem. Soc.* **2000**, 65, 577–580.
- (31) Gutman, I.; Tomović, Z. More on the Line Graph Model for Predicting Physico–Chemical Properties of Alkanes. *ACH Models Chem.* **2000**, 137, 439–445.
- (32) As pointed out by one of the referees (Dr. Christoph Rücker), the goal of such QSPR studies is not only to describe or predict a particular property for a particular series of compounds as exactly as possible in terms of simple graph invariants but also to find such graph invariants which are useful for a population of compounds as broad as possible and to learn something about the physical interpretation of invariants. In Rücker's opinion, it is to be suspected that the descriptors used here, the numbers of edges of the iterated line graphs, will encounter problems when used for a combined sample of unsubstituted and substituted cycloalkanes or for a sample of straight-chain and branched acyclic alkanes, due to the drastically divergent behavior of these numbers for these closely related groups of compounds. We intend to examine these possible difficulties at a later moment. Another limitation of our structure-descriptors is that they cannot discriminate between isomeric regular graphs.
- (33) Harary, F. *Graph Theory*; Addison-Wesley: Reading, MA, 1969.

- (34) Buckley, F. Mean Distance in Line Graphs. *Congr. Numer.* **1981**, 32, 153–162.
- (35) For instance, the Bertz indices of the following pairs of bicycloalkanes coincide until (at least) seventh order: 1,1'-bicyclopropyl and bicyclo[2.2.0]hexane, dicyclopropylmethane and bicyclo[2.2.1]heptane, 1,1'-bicyclobutyl and bicyclo[3.3.0]octane, dicyclobutylmethane and bicyclo[3.3.1]nonane, etc.
- (36) One should bear in mind that the differences between boiling points of stereoisomeric cycloalkanes may be non-negligible. Yet these

isomers have one and the same molecular graph and, consequently, the same graph-based structure-descriptors. In this work the boiling points used are averaged over stereoisomers, as proposed by Rücker and Rücker.³

- (37) Czerminski, J.; Iwasiewicz, A.; Paszek, Z.; Sikorski, A. *Statistical Methods in Applied Chemistry*; Elsevier: Amsterdam, 1990.

CI010006N