

Sensitivity of Topological Indices to Methyl Group Branching in Octanes and Azulenes, or What Does a Topological Index Index?

E. C. Kirby

Resource Use Institute, 14 Lower Oakfield, Pitlochry, Perthshire PH16 5DS, Scotland, U.K.

Received June 30, 1993*

The performance of several topological indices in modeling phenomena exhibited by the octanes and by a group of azulenes is examined. It is concluded that in many cases there is considerable potential for improving the quality of linear regression by introducing supplementary descriptors based on elementary aspects of branching.

INTRODUCTION

Many topological indices (TIs) have values that depend primarily upon the size of a molecule and, because it is on this simple quantity that important physicochemical properties often depend, this accounts for many successful correlations. Just a few examples chosen at random are boiling points, densities, heats of formation, sound velocities, and many others. References 1-4 are among several good reviews available.

However, if attention is restricted to groups of molecules of the same molecular weight, things are not so straightforward. A function of one or more indices, plotted against some property, may well give a plot having an excellent predictive value when the sample covers a wide range of molecular sizes, and the residual deviations about the regression line, if the correlation is a good one, will seem of little account. But often, if a small section of the curve is "magnified" and examined in detail, it will be seen that points associated with a particular molecular size have a (relatively) wide and unexplained scatter. "Unexplained" should be taken in a quantitative sense here. It is widely recognized that such a scatter may be caused by variation of quantities (such as "shape", "branching", "compactness", "similarity", and so on) that are much more difficult than size to quantify. Randić⁵ has described molecular shape as "an ambiguous and elusive concept", and remarks that "Only recently it was shown that apparent interrelatedness of numerous molecular properties does not necessarily extend to isomers when attention is restricted to molecules of the same size." It seems reasonable to describe shape as the distribution of a molecule's volume in 3D space, but such a definition is of rather little help in the practical task of devising mathematical tools for comparison. Of branching, which is distinct from shape but nevertheless affects it, and which is perhaps one of the more easily apprehended concepts, Rouvray⁶ has written, "The treatment of branching in chemical species has presented numerous problems. The fundamental problem here is that there is no reliable measure of the amount of branching present in graphs of chemical interest. In spite of several attempts by chemists⁷ to overcome this problem, there is still some uncertainty as to the best way of dealing with branching. Moreover, since correlations with physicochemical properties for branched species are in general not as good as those for unbranched species, the question arises: can indices be developed which offer an effective means of correlating the branched species?" With pessimism but probable realism he also wrote,³ "...ultimately any definition of branching must rest on an intuitive basis. Because of this circumstance, the use of sophistry in

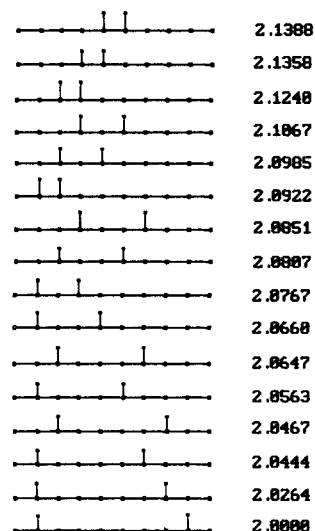


Figure 1. Dimethyldecanes in decreasing order of their largest eigenvalue.

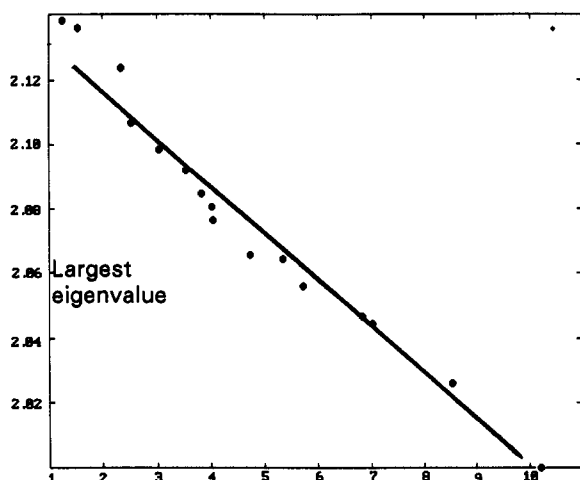
defining the concept of chemical branching appears unlikely to lead to a more viable definition."

Whatever branching actually "is"—and some of its components are discussed briefly in the following section—apart from "cyclicality", it is the only structural variable or group of variables exhibited by a set of compounds with the same molecular formulas that can be detected *directly* using a graph-theoretical analysis. In this paper we use a small sample from each of two unrelated classes of structure, and examine the sensitivity of some better known topological indices toward certain phenomena. These are (1) the boiling points, densities, and motor octane numbers of octanes and (2) the visible absorption spectra of methylazulenes.

CONCEPT OF BRANCHING

A number of writers (e.g. see refs 1-22) have studied and analyzed branching, some in passing and some in considerable detail, and it is widely accepted that it comprises several structural variables, such as the number of branches, their valencies, their distances apart, their distance from the graph center, and the lengths of branches. Not all of these are truly "orthogonal" and therefore easily distinguished (for example, in a tree, if separation is varied, so then is distance from the center; see Figures 1 and 2), but, nevertheless, these variable components are clearly apprehendable and quantifiable. There is not, then, anything elusive or ambiguous about such *components* of branching; rather it is in an appropriate selection and mixing of them, in order to manufacture a single scalar

* Abstract published in *Advance ACS Abstracts*, March 15, 1994.



Distance apart + (1/10) Sum (distance from centre)² of two methyl groups in the dimethyldecane (in edges).

Figure 2. Example of How Substitution Affects Branching, As Measured by the Largest Eigenvalue ($r = -0.982$, $s = 0.075$). See Figure 1.

branching index, that intuition and judgment comes in. Perhaps it is time to reconsider whether branching *should* be considered as a single unified concept. Or at least, whether it is always *useful* to do so. The question is especially pertinent now that techniques for a rational and sequential application of descriptors while ensuring orthogonality have been developed.^{23,24}

A very rough measure of the relative importance of some of the elements can be gained from Table 1, which shows the average behavior of some indices with respect to 12-vertex structures. For each index, the average change in index value from that of a linear polyene, as the number of symmetrically substituted methyl groups is increased to the maximum possible (keeping to 12 vertices in total), is defined as 100: This confirms that when there is no change in size, this is usually the factor that has the most effect. In passing, it is interesting to note that, in contrast to the largest eigenvalue, and the Wiener and Balaban indices, the Randić index shows not only different ratios but also a difference in sign between some elements; it is no wonder therefore that the modeling strengths and weaknesses of different indices vary considerably.

OCTANES

At first sight, many topological indices in use appear quite unhelpful when applied to a single group of isomers. The Randić index ($^1\chi$), for example, appears quite capricious and random in its relationship to densities (see Figure 3), and there is scarcely any correlation between the two ($r = -0.069$).

However, an apparently random scatter *may* be merely the result of mixing several sequences that in themselves are ordered. An intriguing observation was noted some years ago,²⁵ namely, that when motor octane numbers are plotted in order of their "compacted maximal adjacency codes" (a

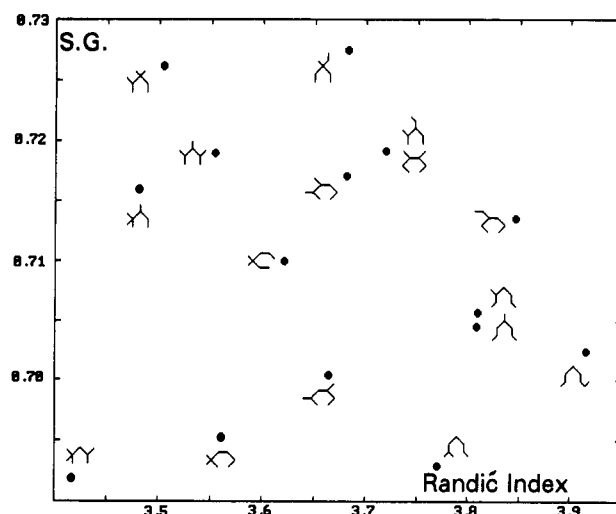


Figure 3. Octanes: Randić index ($^1\chi$) vs density.

measure of the maximum binary number that can represent the upper triangle of an adjacency matrix—and consequently related to branching), the points fall near to two almost parallel lines. Using a simple (though rather ad hoc) supplementary branching index, a poor overall correlation (0.877) was improved to a good one (>0.99). In the same way the predictive power of the Balaban index (J), hitherto the best one available for this purpose,²⁶ could also be improved a little.

So two questions to be asked are: do other indices exhibit similar behavior, and can such simple techniques be applied to other phenomena, such as the densities mentioned above, besides the (conceptually rather complex) motor octane number? The answer to both questions is yes, as Figures 4–6 and the examples in Table 2 demonstrate.

Curiously though, motor octane number (MON)—which is a measure of a hydrocarbon's ability to resist premature detonation under compression in an internal combustion engine and which might be expected to show rather complicated relationships—seems to be more simply related to some TIs than are many other quantities. The previously-mentioned maximal adjacency code,²⁵ the largest eigenvalue (Figure 4), the Wiener index (W), and the Balaban index (J) all show a moderate linear correlation with MON (Table 2), and these can all in varying degrees be improved by "correcting" the values of a subset with added constants to yield correlations in the range 0.97–0.99.

The Randić index ($^1\chi$) with MON shows greater complexity: there are more near collinear subsets of points, and their slope varies. Nevertheless, and despite the fact that this index²⁷ is said to reflect branching only poorly³ (it is amusing, and indicative of the problems encountered in this area, to note that the original paper²⁷ in which this index is discussed is entitled "On Characterization of Molecular Branching"), a simple formula which takes into account the numbers and

Table 1. Sensitivity of Some Indices with Respect to 12-Vertex Structures

variation of "branching" or "compactness"	average effect (percentage comparison; one extra branch = 100)							
	x_{\max}	Dx_{\max}	W	J	$^1\chi$	$^2\chi$	$^3\chi$	$^4\chi$
one to five symmetrically placed methyl groups	100	-100	-100	100	-100	100	100	100
distance between branches in near-symmetrical dimethyldecane	36	-26	-29	30	14	-36	44	102
distance from the center of the branch of a methylundecane	24	-21	-24	21	9	-21	21	114
cyclization of the 12-chain to the 12-ring	90	-454	-412	-268	79	167	208	2116
size reduction 12-chain to 11-chain	-16	-266	-388	13	-463	-143	-96	-667
size reduction 12-ring to 11-ring	0	-200	-300	6	-463	-143	-96	-667

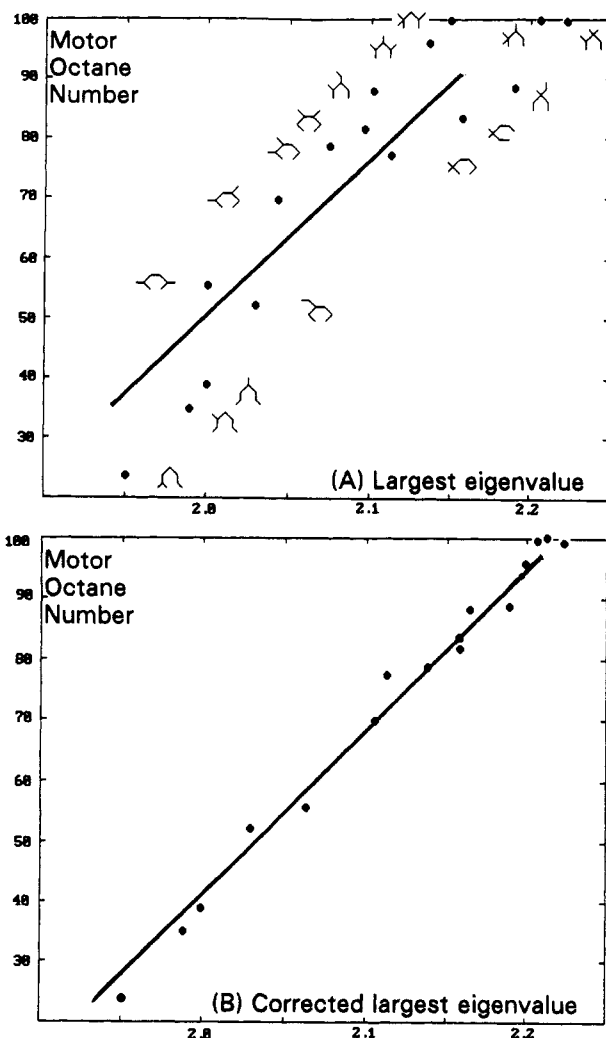


Figure 4. Octanes: (A) the largest eigenvalue vs motor octane number ($r = 0.925$, $s = 9.07$); (B) the same after correction of eigenvalues by $0.0625B$ ($r = 0.994$, $s = 2.81$), where $B = 1$ if there are two or more branching vertices that are either more than one edge apart or are of the same degree; otherwise $B = 0$.

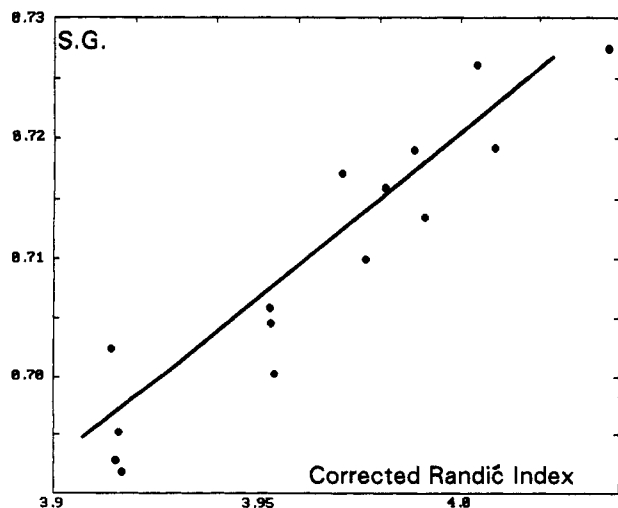


Figure 5. Octanes: Randić index ($^1\chi$) vs density (see Figure 3, where $r = -0.069$), after correction of index values by $0.355V_4 + 0.145V_3$ (V_i is the number of vertices of degree i). Correlation $r = 0.939$, $s = 0.0046$.

degrees of the branching vertices provides an appreciable improvement (Table 2). A small additional improvement (to reach $r = 0.96$) can be made by adding a nonlinear term to the equation.

With boiling point also, $^1\chi$ can be "corrected" to raise the correlation coefficient (see Table 2) from 0.817 ($s = 3.61$) to

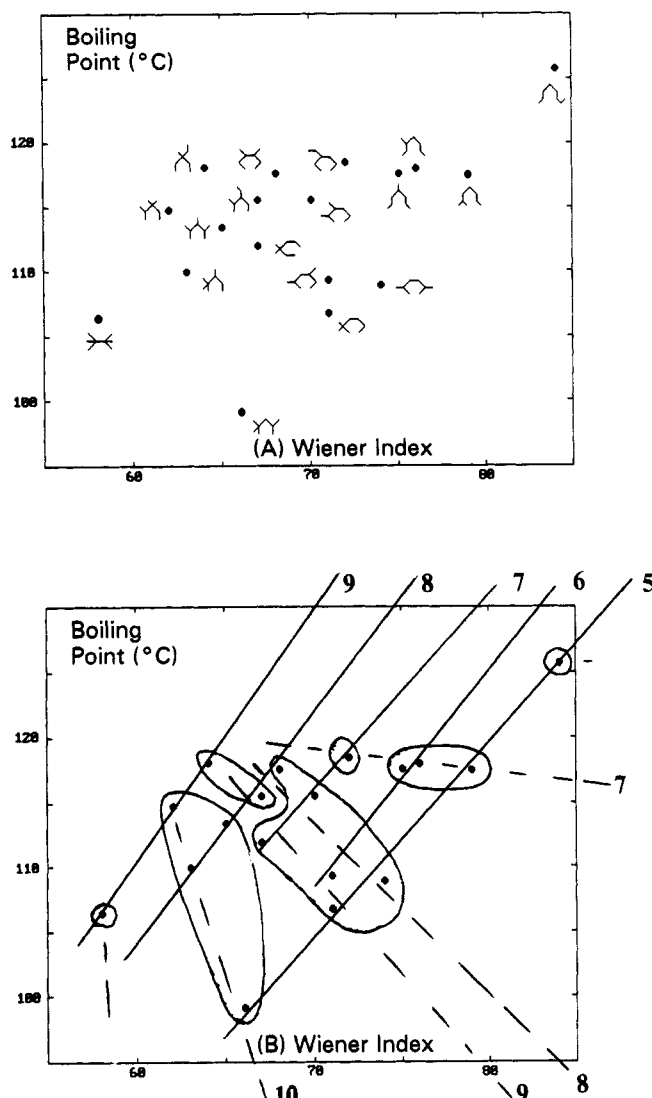


Figure 6. Octanes: (A) the Wiener index vs boiling point with points identified; (B) the same plot with contours shown for equal numbers of P_3 paths (lines), P_2 paths (dotted lines), and equal values for the Balaban centric index (outlined islands).

0.918 ($s = 2.48$). However, it is octane densities that provide a particularly interesting example of the behavior of the Randić index. As was mentioned above, the initial linear correlation coefficient gives no indication of any relationship; yet when the actual structure of the graph (Figure 3) is examined, and individual plot positions are identified, regularities emerge, and it is not difficult to devise a supplementary index in terms of branching which yields a quite respectable correlation coefficient (Figure 5).

The formulas and correlation coefficients reported in Table 2 (from data in Table 3) are, it should be emphasised, only roughly optimized and are unlikely to represent the best obtainable. They are given, not as recommended recipes, but to show that considerable improvement is possible by very simple means. The formulas themselves involve elements of branching, usually though not always in a linear relationship, and generally dominated by the number and degrees of branching vertices. The weakness at present, and this point has not yet been fully addressed, is the variation of form obtained in these trials: further study is needed to determine how far it is possible to devise simple correction formulas (or algorithms for deriving formulas) with a wide range of application.

The behavior of the Wiener index with respect to octane boiling points may be used to demonstrate that there is more

Table 2. Improvement of Linear Index-versus-Observed-Property Relationships for Octanes by Adding a Simple Correction to Certain Index Values^a

	<i>r</i>	<i>s</i>	→	<i>r</i>	<i>s</i>	correction applied
(1) Motor Octane Numbers						
largest eigenvalue (x_{\max})	0.925	9.07		0.994	2.81	0.0625 <i>B</i>
Wiener index (<i>W</i>)	-0.957	7.40		-0.977	5.49	-2 <i>B</i>
Balaban index (<i>J</i>)	0.928	9.52		0.967	6.14	0.17 <i>B</i>
Randić index (RI)	0.778	16.01		0.947	8.18	0.45(<i>V</i> ₄ + <i>V</i> ₃ - 1) + 0.6 <i>V</i> ₄
				0.960	7.17	0.45(<i>V</i> ₄ + <i>V</i> ₃ - 1) + 0.6 <i>V</i> ₄ + 2(RI) ^{1/2}
(2) Density						
x_{\max}	0.531	0.010		0.919	0.0046	-0.135 <i>V</i> ₄ - 0.075(<i>V</i> ₄ + <i>V</i> ₃)(11 - <i>V</i> ₄ - <i>V</i> ₃)/10
<i>W</i>	-0.599	0.009		-0.850	0.0062	11 <i>V</i> ₄ + 4.3 <i>V</i> ₃
<i>J</i>	0.642	0.009		0.926	0.0043	-0.6 <i>V</i> ₄ - 0.2 <i>V</i> ₃
RI	-0.069	0.012		0.939	0.0046	0.355 <i>V</i> ₄ + 0.145 <i>V</i> ₃
(3) Boiling Point						
x_{\max}	-0.548	5.23		-0.864	3.15	0.18(<i>V</i> ₄ + <i>S</i>)
<i>W</i>	-0.533	5.29		-0.837	3.42	8.2 <i>C</i> ^{1/2}
				0.988	0.94	3.65(<i>P</i> ₃ - 5)
<i>J</i>	-0.477	5.50		-0.820	3.58	0.68(<i>V</i> ₄ + <i>S</i>)
RI	0.817	3.61		0.918	2.48	-0.15(<i>V</i> ₄ + <i>S</i>)

^a *B* = 1 if there are two or more branching vertices of the same degree, or 0 otherwise. *V*₃, *V*₄ = number of 3- or 4-valent atoms/vertices, respectively. *S* = the separation (as the number of 2-valent vertices) of the two branching vertices that are furthest apart. *C* = the Balaban centric index. *P*₃ = number of paths of length 3.

than one route to improved correlation. The structure of the primary plot (Figure 6A) is quite complicated. There is evidence of the familiar "banding" of structures, but in a fairly complicated way, and this approach yielded a modest improvement to the regression. One can see though (Figure 6B) that there are also regularities in the plot with respect to the Balaban centric index, and the numbers of paths of lengths 2 and 3 (cf. ref 28), and these too can be used to improve matters. Inspection of Figure 7A suggests that the manner in which the centric index was used, see Table 2, while it does improve the linear regression, gives also a possibly nonlinear plot, but this was not examined further. Lines joining structures with equal numbers of two-paths are not parallel, but those for three-paths are, almost. This latter basis for correction therefore provides the best results (*r* = 0.988, *s* = 0.944).

Other recent approaches to improving the performance of topological indices with isomers have included indices based on graph eigenvalues,²⁹ the derivation of graphical bond orders *P'*/*P* and other modified descriptors,^{5,30} and descriptors derived from the newly introduced "Hosoya matrix".³¹ In this latter paper a regression equation using novel indices ¹*Z* and ²*Z* for octane boiling points is given, which by coincidence is very close (*r* = 0.912, *s* = 2.66) to the result shown here for the Randić index modified to take account of *v*₄ vertices and the separation between branching vertices (*r* = 0.918, *s* = 2.48; Table 2), although the best one so far does appear to be the Wiener index with allowance made for *P*₃ paths, as mentioned above. Earlier work in Japan³² also examined these questions and reported some improvements; for example, the Hosoya index *Z*³³ correlates modestly (0.749) with the boiling points of nonane isomers. This figure was improved to 0.886 by combining *Z* with 0.9*A*₃ (*A*₃ is the half-sum of the off-diagonal elements of the cube of the adjacency matrix).

METHYLAZULENES

The term azulene was applied by Piesse in 1864³⁴ to the blue colors frequently seen in certain plant oils when they are distilled or treated with acids or oxidizing agents. The structure of azulene itself (its graph is shown in Figure 8) was finally confirmed by synthesis in 1936,³⁵ and five years later one of the authors (Plattner) pointed out the remarkable constancy and additivity of shifts in the visible spectrum of

azulene induced by alkylation.^{36,37} As Table 4 shows, positive or negative changes in the wavelength of maximum absorption occur, depending on the position of substitution. This is in marked contrast to the behavior of benzenoids. The shifts were found to be almost additive in polysubstituted azules and to be almost independent of the an alkyl group's size.

For the practical purposes of monitoring reactions and separations, and, historically (before the advent of NMR), structural identification, the observed shifts, known as the "Plattner rules" are very useful, and remarkably accurate, so that it is unlikely that topological indices will be useful in themselves. It is, however, of interest to see what their behavior is in relation to the rather subtle structural variation associated with different substitution positions around the azulene ring system.

Figure 9A shows a plot of the position of the longest wavelength visible absorption band against the largest eigenvalue (the eigenspectrum of the graph representing the simple carbon skeleton was used, and no weighting was introduced. In fact, rather similar *relative* results are obtained by treating C≡H₃ as an extra bond, by considering only the azulene graph with the substitution position(s) weighted, or by deleting each methyl group and the atom it is attached to). Here again, as with octanes, there is a wide scatter, but with regularities being apparent on closer examination. These have several points of interest. Considering azulene itself and the five possible monomethylazulenes, it can be seen that azulene and 1- and 5-methylazulene are collinear, while 2- and 4-methylazulene form a near parallel line displaced to the right. A simple lateral displacement will give what looks like a smooth curve. These lateral displacements are evident (with some "noise") in the polysubstituted species too and enable a corrected and more linear plot to be drawn. (Figure 9B; note that in itself this is of no special value, for in effect it is just a restatement of the original Plattner rules with rather less precision.) The uppermost sequence azulene and 5-methyl-, 1-methyl-, 1,5-dimethyl-, 1,3-dimethyl-, and 1,3,5-trimethylazulene are approximately on a straight line (*r* = 0.996, *s* = 2.49 for the six points). Obviously, arguments based on the slender evidence of such a small sample must be treated with caution, but the fact that the first three points *are* on a straight line suggests that size (molecular weight) is not important (i.e. that this index is not being "distracted" by the irrelevance of size) and that it is the accumulation of branches beyond

Table 3. Octane Data and Indices

		BPt	MON	D	x_{\max}	W	$^1\chi$	J
1		125.7		0.7025	1.8794	84	3.9142	2.5301
2		117.6	23.8	0.6929	1.9499	79	3.7701	2.7158
3		118.0	35.0	0.7058	1.9890	76	3.8081	2.8621
4		117.7	39.0	0.7046	2.0000	75	3.8081	2.9196
5		118.5	52.4	0.7136	2.0285	72	3.8461	3.0744
6		109.0	55.7		2.0000	74	3.6259	2.9278
7		109.4	69.9	0.7004	2.0421	71	3.6639	3.0988
8		106.8	77.4	0.6953	2.1120	71	3.5607	3.1118
9		115.6	78.9	0.7171	2.0743	70	3.6807	3.1708
10		117.7	81.7	0.7192	2.0953	68	3.7187	3.2925
11		112.0	83.4	0.7100	2.1566	67	3.6213	3.3734
12		115.6	88.1	0.7193	2.1010	67	3.7187	3.3549
13		118.2	88.7	0.7274	2.1889	64	3.6820	3.5832
14		113.4	95.9	0.7191	2.1358	65	3.5534	3.4642
15		114.7	99.4	0.7262	2.2216	62	3.5040	3.7083
16		110.0	99.9	0.7160	2.2059	63	3.4814	3.6233
17		99.2	100.0	0.6919	2.1490	66	3.4165	3.3889
18		106.5			2.3028	58	3.2500	4.0204

one methyl group that gives rise to the later kinks in the line. (A standard correction of +0.01 for each methyl group more than one gives $r > 0.999$, $s = 0.76$.) The plot also shows that, here at least, the difference in magnitude of wavelength shift as between azulene-5-methylazulene and azulene-1-methylazulene is fully accounted for in the largest eigenvalue. This linearity of the first three members is evident with the Balaban index J too, but not with other indices such as W and $^1\chi$, and is consistent with the view that x_{\max} and J are less size dependent.

The plot of corrected eigenvalues against wavelength (Figure 9B) was mentioned above as being a correction based on substitution position. Although this is itself a graphical or topological invariant, it seems somehow unsatisfactory, for it offers no new insight. At present though it is the best one available, for, so far, most other supplementary indices tried have not been helpful. One giving partial help is based on the difference between the two distances, by opposite routes, from

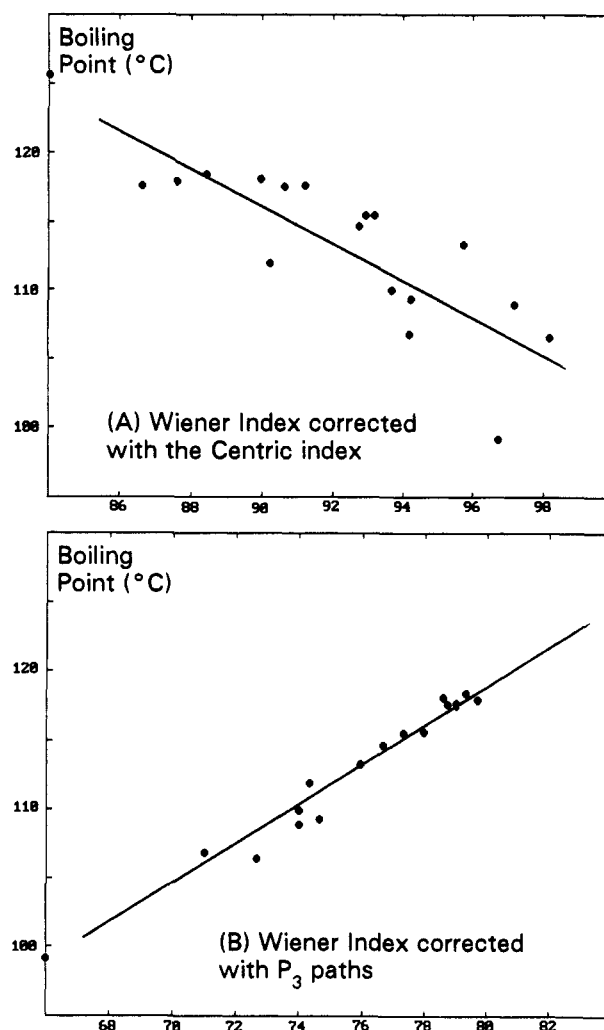


Figure 7. Octanes: (A) the Wiener Index vs boiling point with W corrected by adding 8.2 (centric index) $^{1/2}$ ($r = -0.837$, $s = 3.42$); (B) the same with W corrected by 3.65 ($P_3 - 5$), where P_3 is the number of paths of length 3 ($r = 0.988$, $s = 0.944$).

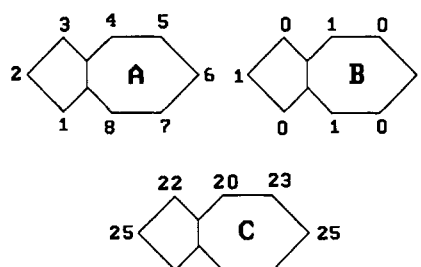


Figure 8. (A) Conventional numbering of the azulene system. (B) Values for the XOR Boolean image (1 and 0 interchanged) of $1/2$ -[(difference in distances to the azulene bridge) MOD 4]. (C) Values for Seybold index.

Table 4. Shifts in the Position of the Overall Visible Band Absorption Maximum Associated with a Methyl Substituent³⁷ (Millimicrons)

compd	wavelength	shift
azulene	580	0
1-methylazulene	608	+28
2-methylazulene	566	-14
4-methylazulene	568	-12
5-methylazulene	592	+12
6-methylazulene	565	-15

the substituent position to the azulene bridging bond. Taken to MOD 4, this distinguishes the 1(3) and 5(7) from the 2, 4(8), and 6 positions and does enable the regression to be improved. For best results however, a distinction between

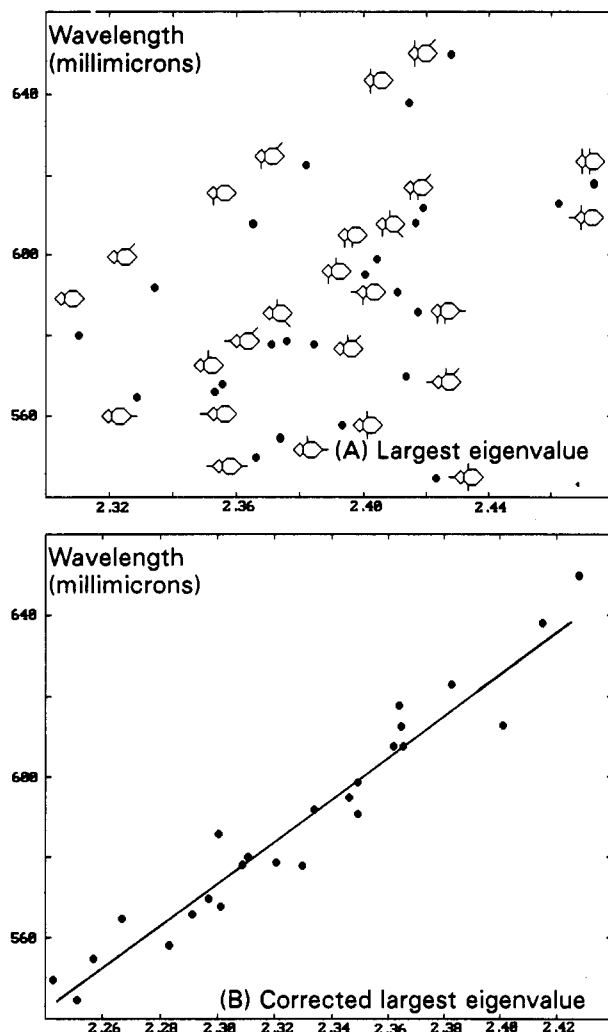


Figure 9. Azulene and 24 methylazulenes: (A) the largest eigenvalue vs visible absorption maximum; (B) the same after correction (see text) by -0.062 for 2(6) and $+0.05$ for 4-substitution ($r = 0.970$, $s = 6.57$).

4(8) and 2 or 6 substitution needs to be made. The Seybold index gives a better resolution but not in a quantitatively helpful way.^{38,39}

CONCLUDING REMARKS

This paper has reported some examples where the performance of topological indices can be raised from the poor or mediocre to "definitely promising" by simple means that take into account elementary aspects of branching. The results are suggestive rather than useful and definitive, and they raise (or reemphasize some previously stated) points and questions of general interest. For example:

(1) A linear regression coefficient alone is completely unreliable as a guide to how much it may be possible to "improve" an index with supplementary descriptors.

(2) Similarly, estimates of what an index reflects (in the proportion of size and shape) give no guidance about how potentially useful it may be for rationalizing properties within a set of isomers, although, obviously, such information is relevant when molecules of different size are being compared.

(3) How widely applicable are the methods reported here, and can more standardized formulas and algorithms be devised?

(4) A long debated question is: can a single branching index that is useful be formulated, or should it be accepted that several separately applied elements of branching may be necessary? This question is more relevant now that Randić has developed systematic techniques for orthogonalization.⁵

REFERENCES AND NOTES

- Balaban, A. T.; Motoc, J.; Bonchev, D.; Mekenyan, O. Topological Indices for Structure-Activity Correlations. *Top. Curr. Chem.* **1983**, *114*, 23.
- Kier, L. B.; Hall, L. H. *Molecular Connectivity in Structure-Activity Analysis*; Research Studies Press Ltd.: Letchworth, England, 1986.
- Rouvray, D. H. The Modelling of Chemical Phenomena using Topological Indices. *J. Comput. Chem.* **1987**, *8*, 470.
- Trinajstić, N. *Chemical Graph Theory*, 2nd ed.; CRC Press: Boca Raton, FL, 1992; Chapter 10, p 225.
- Randić, M. Search for Optimal Molecular Descriptors. *Croat. Chem. Acta* **1991**, *64*, 43.
- Rouvray, D. H. Topological Indices as Chemical Behavior Descriptors. *Congr. Numer.* **1985**, *49*, 161.
- Hässelbarth, W. Die Verzweigkeit von Graphen. *Math. Chem.* **1984**, *16*, 3.
- Lovász, L.; Pelikán, J. *Period. Math. Hung.* **1973**, *3*, 175.
- Bonchev, D.; Trinajstić, N. *J. Chem. Phys.* **1977**, *67*, 4517.
- Cvetković, D.; Gutman, I. Note on Branching. *Croat. Chem. Acta* **1977**, *49*, 115.
- Motoc, I.; Balaban, A. T. *Rev. Roum. Chim.* **1981**, *26*, 593.
- Motoc, I.; Balaban, A. T.; Mekenyan, O.; Bonchev, D. *Math. Chem.* **1982**, *13*, 369.
- Edward, J. T. The relation of physical properties to connectivity indices: a molecular explanation. *Can. J. Chem.* **1982**, *60*, 480.
- Rouvray, D. H.; Pandey, R. B. The fractal nature, graph invariants, and physicochemical properties of normal alkanes. *J. Chem. Phys.* **1986**, *85*, 2286.
- Gutman, I. *Z. Phys. Chem. (Leipzig)* **1986**, *267*, 1152.
- Gutman, I.; Rušić, B.; Trinajstić, N.; Wilcox, C. F. Graph Theory and Molecular Orbitals. XII. Acyclic Polyenes. *J. Chem. Phys.* **1975**, *62*, 3399.
- Rouvray, D. H. The limits of applicability of topological indices. *J. Mol. Struct. (THEOCHEM)* **1989**, *185*, 187.
- Caputo, J. F.; Cook, K. J. A Graph-Theoretical Approach to the Prediction of Physical Properties of Alkanes Based on the Distance Matrix. *Pharm. Res.* **1989**, *6*, 809.
- Diudea, M. V.; Minailiuc, O.; Balaban, A. T. Molecular Topology. IV. Regressive Vertex Degrees (New Graph Invariants) and Derived Topological Indices. *J. Comput. Chem.* **1991**, *12*, 527.
- Mihalić, Z.; Nikolić, S.; Trinajstić, N. Comparative Study of Molecular Descriptors Derived from the Distance Matrix. *J. Chem. Inf. Comput. Sci.* **1992**, *32*, 28.
- Horvat, D.; Graovac, A.; Plavšić, D.; Trinajstić, N.; Strunje, M. On the intercorrelation of topological indices in benzenoid hydrocarbons. *Int. J. Quantum Chem., Quantum Chem. Symp.* **1992**, *26*, 401.
- Randić, M. In Search of Structural Invariants. *J. Math. Chem.* **1992**, *9*, 97.
- Randić, M. Resolution of Ambiguities in Structure-Property Studies by Use of Orthogonal Descriptors. *J. Chem. Inf. Comput. Sci.* **1991**, *31*, 311.
- Randić, M. Fitting of Nonlinear Regressions by Orthogonalized Power Series. *J. Comput. Chem.* **1993**, *14*, 363.
- Kirby, E. C. Can a structural code be a topological index? A short test of a "computed maximal adjacency code." In *MATH/CHEM/COMP 1988, Proceedings of an International Course and Conference on the Interface between Mathematics, Chemistry and Computer Science*, Dubrovnik, June 20-25, 1988; Graovac, A., Ed.; Studies in Physical and Theoretical Chemistry; Elsevier: Amsterdam, 1989; Vol. 63, p 185.
- Balaban, A. T. Topological Indices based on Topological Distances in Molecular Graphs. *Pure Appl. Chem.* **1983**, *55*, 199.
- Randić, M. On Characterization of Molecular Branching. *J. Am. Chem. Soc.* **1975**, *97*, 6609.
- Randić, M.; Wilkins, C. L. On a Graph Theoretical Basis for Ordering of Structures. *Chem. Phys. Lett.* **1979**, *63*, 332.
- Balaban, A. T.; Ciubotariu, D.; Medeleanu, M. Topological Indices and Real Number Vertex Invariants Based on Graph Eigenvalues or Eigenvectors. *J. Chem. Inf. Comput. Sci.* **1991**, *31*, 517.
- Randić, M. Generalized molecular descriptors. *J. Math. Chem.* **1991**, *7*, 155.
- Randić, M. Hosoya Matrix-A Source of New Molecular Descriptors. *Croat. Chem. Acta*, submitted for publication.
- Gao, Y.; Hosoya, H. Topological Index and Thermodynamic Properties. IV. Size Dependency of the Structure-Activity Correlation of Alkanes. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 3093.
- Hosoya, H. Topological Index. A Newly Proposed Quantity Characterizing the Topological Nature of Structural Isomers of Saturated Hydrocarbons. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 2332.
- Piess, D. *Compt. Rend.* **1864**, *57*, 1016.
- St. Pfau, A.; Plattner, P. A. *Helv. Chim. Acta* **1936**, *19*, 858.
- Plattner, P. A. *Helv. Chim. Acta* **1941**, *24*, 283E.
- Heilbronner, E. In *Non Benzenoid Aromatic Compounds*; Ginsburg, D., Ed.; Interscience Publishers: 1959; Chapter V, p 224.
- Bonchev, D.; Balaban, A. T. Topological Centric Coding and Nomenclature of Polycyclic Hydrocarbons. 1. Condensed Benzenoid Systems (Polyhexes, Fusenes). *J. Chem. Inf. Comput. Sci.* **1981**, *21*, 223.
- Seybold, P. G. Topological Influences on the Carcinogenicity of Aromatic Hydrocarbons. I. The Bay Region Geometry. *Int. J. Quantum Chem., Quantum Chem. Symp.* **1983**, *10*, 95.