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Maximum Topological Distances Based Indices as Molecular Descriptors for QSPR. 4. Modeling the Enthalpy of Formation of Hydrocarbons from Elements

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Abstract: The enthalpy of formation of a set of 60 hydroarbons is calculated on the basis of topological descriptors defined from the distance and detour matrices within the realm of the QSAR/QSPR theory. Linear and non-linear polynomials fittings are made and results show the need to resort to higher-order regression equations in order to get better concordances between theoretical results and experimental available data. Besides, topological indices computed from maximum order distances seems to yield rather satisfactory predictions of heats of formation for hydrocarbons.

Keywords: QSPR theory, Detour matrix, Enthalpy of formation, Hydrocarbons, Topological indices

1. Introduction

Graphs have found considerable employment in several chemistry fields, particularly in modeling molecular structure [1-10]. The applications of graphs to the study of structure-property relationships implies the representation of molecules by selected molecular descriptors, often referred to as topological indices [11,12]. These topological indices, which often have a direct structural interpretation, are defined in terms of selected structural parts and hopefully should help one in building molecular models for structure-property relationships. Among hundreds of possible descriptors a few have arisen again and again as the most useful for characterization of molecules [13-16]

The graph theoretical characterization of molecular structure is realized by means of various matrices, polynomials, spectra, spectral moments, sequences counting distances, paths and walks. The molecular matrices represent an important source of structural descriptors. Usually, a small number of matrices is used to characterize the molecular topology, namely the adjacency, the distance and sometimes, the Laplacian matrix. Novel matrices were developed in recent years, encoding in various ways the topological information [17]. However, distance matrices remain being the most relevant ones within the realm of the ***Q***uantitative ***S***tructure ***A***ctivity (***P***roperty) ***R***elationships (QSAR/QSPR) theory.

Any matrix, the elements of which satisfy the axioms of distance, can be referred to as a distance matrix $\mathbf{D} \equiv \{D_{ij}\}$ [18]. The axioms of distance require that

a) Distance is a positive quantity, $D_{ij} \geq 0$, assigned to a pair of elements (points in an n-dimensional vector space).
b) $D_{ii} = 0 \ \forall i = 1, 2, ...N$; N = number of elements
c) Distance does not depend on the direction of measurement, *i.e.* $D_{ij} = D_{ji}$
d) Distance satisfies the triangular inequality, *i.e.* $D_{ij} \leq D_{ik} + D_{kj}$

Two distance matrices are particularly important, both of them based on the topological distance for vertices within a graph: the distance matrix and the detour matrix. The detour matrix, together with the distance matrix, was introduced into the mathematical literature in 1969 by Frank Harary [19]. Both matrices were also briefly discussed in 1990 by Buckley and Harary [20]. The detour matrix was introduced into the chemical literature in 1994 under the name *"the maximum path matrix of a molecular graph"* [21,22]. The graph-theoretical detour matrix have found some interest in chemistry [23] and a valuable variation pertaining to the definition of the diagonal elements was proposed by Rücker and Rücker [24]. They found this matrix in combination with the Wiener index W is more useful than Hosoya's Z index for regression of the boiling points of a large sample of compounds containing all acyclic and cyclic alkanes with known boiling points from methane up to polycyclic octanes.

In three previous papers [25-27] we have analyzed the relative merits of these distances when they are used to define molecular descriptors in order to calculate physical chemistry properties within the realm of QSAR/QSPR theory. The aim of this paper is to continue with this sort of discussion resorting to the calculation of heats of formation for a representative set of 60 hydrocarbons.

The paper is organized as follows: next section deals with some basic mathematical definitions and the computational procedure; then we present the results and discuss them; and finally we state the conclusion of the present study as well as some possible extensions.

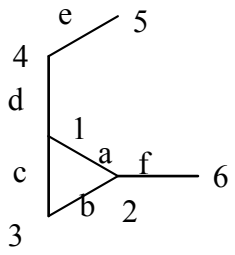
2. Basic Definitions

The adjacency matrix: The adjacency matrix $\mathbf{A} = \mathbf{A}(G)$ of a graph G with N vertices is the square N x N symmetric matrix whose entry in the *i* th row and *j* th column is defined as [19]

$$A_{ij} = \begin{cases} 1 \text{ if } i \neq j \quad \text{and } (i,j) \in \mathbf{E}(G) \\ 0 \text{ if } i = j \quad \text{or } (i,j) \notin \mathbf{E}(G) \end{cases} \qquad \textbf{(1)}$$

where **E**(G) represents the set of edges of G. The sum of entries over row *i* or column *j* in **A**(G) is the degree of vertex *i*, deg_i.

An example of molecular graph and the adjacency matrix is given below for the 1-ethyl-2-methylcyclopropane. The vertices and edges are labeled from 1 to 6 and from *a* to *f*, respectively.



$$\mathbf{A} = \begin{bmatrix} 0 & 1 & 1 & 1 & 0 & 0 \\ 1 & 0 & 1 & 0 & 0 & 1 \\ 1 & 1 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 \end{bmatrix}$$

<u>The distance matrices</u>

The distance matrix **D**(G) can be defined for G with elements Dij, the distance, or the number of *<u>least</u>* steps from vertex *i* to vertex *j*. Similarly, the detour matrix **Δ**(G) of a labeled connected graph G is a real symmetric N x N matrix whose (*i*,*j*) entry is the length of the *<u>longest</u>* path from vertex *i* to vertex *j* (i.e., the *maximum* number of edges in G between vertices *i* and *j* [23]).

For example, for the previous graph corresponding to 1-ethyl-2-methyl cyclopropane molecule, matrices **A** and **Δ** are:

$$\mathbf{A} = \begin{bmatrix} 0 & 1 & 1 & 1 & 2 & 2 \\ 1 & 0 & 1 & 2 & 3 & 1 \\ 1 & 1 & 0 & 2 & 3 & 2 \\ 1 & 2 & 2 & 0 & 1 & 3 \\ 2 & 3 & 3 & 1 & 0 & 4 \\ 2 & 1 & 2 & 3 & 4 & 0 \end{bmatrix} \qquad \mathbf{\Delta} = \begin{bmatrix} 0 & 2 & 2 & 1 & 2 & 3 \\ 2 & 0 & 2 & 3 & 4 & 1 \\ 2 & 2 & 0 & 3 & 4 & 3 \\ 1 & 3 & 3 & 0 & 1 & 4 \\ 2 & 4 & 4 & 1 & 0 & 5 \\ 3 & 1 & 3 & 4 & 5 & 0 \end{bmatrix}$$

Topological molecular descriptors

We present the basic definitions related to the topological descriptors chosen for the present study.

Wiener index [28] $W = 0.5 \sum_{i,j} Dij$ **(2)**

Harary index [29] $H = 0.5 \sum_{i,j} D_{ij}^{-1}$ **(3)**

MTI index [30, 31] $MTI = \sum_{i} e_i$ **(4)**

where e_i are elements of the row matrix $v[\mathbf{A} + \mathbf{D}] = [e_1, e_2, e_3, ..., e_N]$. **v** is the so-called *valence matrix*.

Balaban index [32, 33] $J = [q/(\mu + 1)] \sum_{i,j} (d_i\, d_j)^{-1/2}$ **(5)**

where $d_i = \sum_{j} D_{ij}$, q is the number of edges and μ the number of cycles in the graph. The summations in formulas (2), (3) and (5) are over all edges i-j in the hydrogen-depleted graph.

Zero order connectivity index [34,35] $^{0}\chi = \sum_{i} (\delta_i)^{-1/2}$ **(6)**

where $\delta_i = \sum_{j} A_{ij}$ is the degree of the *i*-th vertex.

Randic's connectivity index [32] $^{1}\chi = \sum_{i,\,j} (\delta_i \delta_j)^{-1/2}$ **(7)**

Generalized connectivity index [35] $^{h}\chi = \sum_{paths} (\delta_{vo}\, \delta_{v1}\, ...\delta_{vh})^{-1/2}$ **(8)**

where the summation is taken over all possible paths of lengths 0, 1, ..., h.

The Zagreb group indices [36,37] $M1 = \sum_{i} \delta_i^2$ **(9)**

$$M2 = \sum_{i,j} \delta_i \delta_j \qquad \textbf{(10)}$$

The employment of these topological descriptors has proven to be extremely useful in QSAR/QSPR studies giving simple correlations between the selected properties and the molecular structure [39-40]. Multiple regression analysis is often employed in such studies in the hope that it might point to structural factors that influence a particular property. Naturally, regression analysis results do no establish any sort of causal relationships between structural components and molecular properties. However, it may be helpful in model building and be useful in the design of molecules with prescribed desirable properties [41].

An interesting alternative to the previous definitions based upon distance matrix **D** is replace it by the detour matrix **Δ**, defining the associated topological indices W*, H*, etc. on the basis of this last matrix in a similar fashion as done in Eqs. (2-5).

3. Results and Discussion

We have employed two sets of topological descriptors; a) {N_c, $^0\chi$, $^1\chi$, $^2\chi$, M1, M2, W, H, H, J, MTI} and b) {N_c, $^0\chi$, $^1\chi$, $^2\chi$, M1, M2, W, H, J, MTI, W*, H*, J*, MTI*}. N_c stands for the number of C atoms. This particular choice was made since we want to know the relative merits of topological indices defined on the basis of the two distance matrices (i.e. **D** and **Δ**). A way to assess it is via this choice, although there are other options.

The molecular set comprises 60 hydrocarbons containing from 1 to 18 carbon atoms and they are presented in Table 1 together with their corresponding topological parameters.

Table 1. Topological parameters for hydrocarbons.

Hydrocarbon	N_c	$^0\chi$	$^1\chi$	$^2\chi$	*M1*	*M2*	*W*	*H*	*J*	*MTI*	*W**	*H**	*J**	*MTI**
1. ethane	2	2.000	2.000	0.000	2	2	1	1.000	1.000	4	1	1.000	1.000	4
2. propane	3	2.707	2.828	1.414	6	8	4	2.500	1.633	16	4	2.500	1.633	16
3. butane	4	3.414	3.828	2.000	10	16	10	4.333	1.975	38	10	4.333	1.975	38
4. 2-methylpropane	4	3.577	3.464	3.464	12	18	9	4.500	2.324	36	9	4.500	2.324	36
5. pentane	5	4.121	4.828	2.707	14	24	20	6.417	2.191	74	20	6.417	2.191	74
6. 2-methylbutane	5	4.284	4.540	3.604	16	28	18	6.667	2.540	68	18	6.667	2.540	68
7. 2,2-dimethyl-propane	5	4.500	4.000	6.000	20	32	16	7.000	3.024	64	16	7.000	3.024	64
8. hexane	6	4.828	5.828	3.414	18	32	35	8.700	2.339	128	35	8.700	2.339	128
9. 2-methylpentane	6	4.992	5.540	4.365	20	36	32	9.000	2.627	118	32	9.000	2.627	118
10. 3-methylpentane	6	4.992	5.616	3.843	20	38	31	9.083	2.754	114	31	9.083	2.754	114
11. 2,2-dimethyl-butane	6	5.207	5.121	5.828	24	44	28	9.500	3.168	106	28	9.500	3.168	106
12. 2,3-dimethyl-butane	6	5.155	5.285	4.976	22	42	29	9.333	2.993	108	29	9.333	2.993	108
13. heptane	7	5.536	6.828	4.121	22	40	56	11.150	2.447	204	56	11.150	2.447	204
14. 3-methylhexane	7	5.699	6.616	4.604	24	46	50	11.617	2.832	182	50	11.617	2.832	182
15. 2,2-dimethyl-pentane	7	5.914	6.121	6.621	28	52	46	12.083	3.154	170	46	12.083	3.154	170

16. 2,2,3-trimethylbutane	7	6.077	5.887	7.041	30	60	42	12.500	3.541	156	42	12.500	3.541	156
17. 3-methylheptane	8	6.406	7.616	5.311	28	54	76	14.267	2.862	276	76	14.267	2.862	276
18. 4-methylheptane	8	6.406	7.616	5.365	28	54	75	14.317	2.920	272	75	14.317	2.920	272
19. 2,2-dimethylhexane	8	6.621	7.121	7.328	23	60	71	14.767	3.112	260	71	14.767	3.112	260
20. 2,3-dimethylhexane	8	6.569	7.361	6.020	30	60	70	14.733	3.171	254	70	14.733	3.171	254
21. 2,4-dimethylhexane	8	6.569	7.328	6.286	30	58	71	14.650	3.099	258	71	14.650	3.099	258
22. 2,5-dimethylhexane	8	6.569	7.252	6.730	30	56	74	14.467	2.928	270	74	14.467	2.928	270
23. 3,3-dimethylhexane	8	6.621	7.243	6.536	32	64	67	15.033	3.373	244	67	15.033	3.373	244
24. 1,3-dimethylbenzene	8	5.983	7.575	6.754	36	76	61	16.083	2.231	268	123	7.833	1.071	516
25. 1,2-dimethylbenzene	8	5.983	7.609	6.478	36	78	60	16.167	2.279	264	124	7.810	1.061	520
26. 1,4-dimethylbenzene	8	5.983	7.575	6.730	36	76	62	16.033	2.192	272	122	7.867	1.082	512
27.1-methyl-3-ethylbenzene	9	6.690	8.651	7.092	40	86	88	19.150	2.232	373	164	10.295	1.153	677
28.1-methyl-4-ethylbenzene	9	6.690	8.651	7.068	40	86	90	19.067	2.180	381	162	10.52	1.171	669
29. 1,2,3-trimethylbenzene	9	6.853	8.430	7.489	42	94	82	19.667	2.413	349	164	10.102	1.152	677
30. 1,2,4-trimethylbenzene	9	6.853	8.397	7.746	42	92	84	19.533	2.346	357	162	10.160	1.168	669
31. 1,3,5-triethylbenzene	9	6.853	8.363	8.045	42	90	84	19.500	2.341	357	162	10.150	1.167	669
32. 1,3-triethylbenzene	10	7.397	9.727	7.430	44	96	121	22.383	2.246	500	213	12.882	1.224	868
33. 1,4-diethylbenzene	10	7.397	9.727	7.406	44	96	125	22.243	2.174	516	209	12.981	1.254	852
34.1,2,3,4-tetramethylbenzene	10	7.724	9.252	8.500	48	110	109	23.367	2.516	452	209	12.595	1.249	852
35. 1,2,3-triethylbenzene	12	8.975	11.658	8.679	54	124	190	30.233	2.524	760	338	18.192	1.343	1352
36. 1,2,4-triethylbenzene	12	8.975	11.625	8.848	54	122	198	29.876	2.413	792	330	18.365	1.379	1320
37. 1,3,5-triethylbenzene	12	8.975	11.591	9.060	54	120	198	29.800	2.405	792	330	18.339	1.377	1320
38.1,2,3,4-tetraethylbenzene	14	10.55	13.556	10.116	64	150	287	38.543	2.674	1124	483	24.252	1.504	1908
39.1,2,3,5-tetraethylbenzene	14	10.55	13.522	10.309	64	148	291	38.326	2.631	1140	479	24.326	1.517	1892
40.1,2,4,5-tetraethylbenzene	14	10.55	13.522	10.289	64	148	295	38.186	2.592	1156	475	24.425	1.530	1876
41. 1-methylnaphthalene	11	7.682	10.754	9.233	56	130	140	27.850	1.993	646	426	8.024	0.626	1898
42. 2-methylnaphthalene	11	7.682	10.720	9.446	56	128	144	27.633	1.932	664	424	8.049	0.629	1890
43. 1-ethylnaphthalene	12	8.389	11.830	9.615	60	140	182	31.533	1.987	816	518	10.444	0.662	2280
44. 2-ethylnaphthalene	12	8.389	11.796	9.748	60	138	190	31.176	1.895	852	514	10.489	0.667	2264
45. 1,2-dimethylnaphthalene	12	8.552	11.575	10.244	62	146	178	31.917	2.027	800	516	10.166	0.664	2270
46. 1,3-dimethylnaphthalene	12	8.552	11.542	10.525	62	144	179	31.833	2.015	804	515	10.175	0.665	2266
47. 1,4-dimethylnaphthalene	12	8.552	11.575	10.288	62	146	176	32.000	2.055	790	516	10.161	0.664	2270
48. 1,5-dimethylnaphthalene	12	8.552	11.575	10.308	62	146	175	32.050	2.066	786	517	10.150	0.663	2274
49. 1,6-dimethylnaphthalene	12	8.552	11.542	10.501	62	144	180	31.783	2.003	808	514	10.186	0.667	2262
50. 1,7-dimethylnaphthalene	12	8.552	11.542	10.501	62	144	181	31.750	1.992	812	515	10.175	0.665	2266
51. 2,3-dimethylnaphthalene	12	8.552	11.542	10.461	62	144	182	31.700	1.976	818	514	10.191	0.667	2262
52. 2,6-dimethylnaphthalene	12	8.552	11.508	10.713	62	142	185	31.533	1.944	830	511	10.225	0.671	2250
53. 2,7-dimethylnaphthalene	12	8.552	11.508	10.713	62	142	186	31.510	1.936	834	512	10.211	0.669	2254
54. 1-propylnaphthalene	13	9.096	12.830	10.376	64	148	236	35.110	1.940	1036	622	13.111	0.695	2712
55. 2-propylnaphthalene	13	9.096	12.790	10.545	64	146	248	34.654	1.837	1090	616	13.173	0.702	2688
56. 2-ethyl-3-methylnaphthalene	13	9.259	12.618	10.843	66	154	232	35.493	1.965	1020	616	12.714	0.701	2682

57. 2-ethyl-6-methylnaphthalene	13	9.259	12.584	11.051	66	152	238	35.219	1.915	1044	610	12.776	0.708	2658
58. 2-ethyl-7-methylnaphthalene	13	9.259	12.584	11.051	66	152	240	35.177	1.902	1052	612	12.751	0.706	2666
59. 1-butylnaphthalene	14	9.803	13.830	11.083	68	156	303	38.646	1.876	1310	739	15.957	0.726	3198
60. 2-butylnaphthalene	14	9.803	13.796	11.252	68	154	319	38.117	1.772	1382	731	16.033	0.734	3166

Although at first sight this rather specialized set includes molecules with only C and H atoms, this option does not necessarily implies a lack of molecular variation within such particular choice. As a matter of fact, the hydrocarbon set includes examples of planar, non-planar, alternant and non-alternant aromatic hydrocarbons, alkyl- and alkenyl-substituted benzene derivatives, acyclic and polycyclic alkanes, strained and unstrained olefins and disparate structures combined with aromatics like benzene and naphthalene, which do not require separate parametrizations for different types of C and H atoms. This molecular set has been used in previous studies on QSPR theory [42-44].

Enthalpy (or heat) of formation is a fundamental thermodynamical key for predicting the compound's thermochemical behavior. Thus, enthalpies of formation are important in the investigation of bond energies, resonance energies, the nature of the chemical bond, the calculation of equilibrium constants of reaction, etc. [45]. Therefore, it is not surprising that considerable endeavor has been directed towards the determination of heats of formation in the past [46-51]. Although a wide variety of procedures to calculate heats of formation theoretically have indeed been introduced, based on such different concepts as isodesmic and homodesmic reactions, atom and group equivalents, transferability and additivity of Fock matrix elements, etc. [52-60] the calculation through QSPR theory has not attracted so much attention.

We have performed a complete analysis to find the best one-, two-, ..., five-variables fittings at first, second and third polynomial orders. Statistical results are given in Table 2 for both molecular sets, while in Table 3 we display some theoretical results together with the experimental data. We have inserted the best five-variables third-order correlations for both topological indices sets a) and b). Complete results are available and can be obtained upon request to one of us (E.A.C.) at the above address.

Table 2. Statistical results for the best fitting equations.

Descriptors	***First order***			***Second order***			***Third order***		
Molecular set 1	**R**	**s**	**F**	**R**	**s**	**F**	***R***	***s***	***F***
J	0.77724	17.5335	89	0.80464	16.8340	52	0.88161	13.4999	65
$^0\chi$, M1	0.97498	6.1944	548	0.97904	5.8789	317	0.98079	5.7355	223
$^0\chi$, $^1\chi$, M1	0.98938	4.0506	865	0.99807	1.8269	2279	0.99817	1.8316	1511
N_c, $^1\chi$, M1, H	0.99210	3.4968	859	0.99675	2.4147	975	0.99728	2.3017	716
N_c, $^0\chi$, M1, H, MTI	0.99637	2.3729	1479	0.99849	1.6802	1618	0.99941	1.1113	2470
Molecular set 2									
J*	0.95134	8.5866	553	0.98210	5.3400	774	0.98346	5.1812	550
$^1\chi$, H*	0.97910	5.6678	660	0.98620	4.7786	487	0.98733	4.6685	341
M1, H*, J*	0.99409	3.0262	1564	0.99652	2.4500	1263	0.99710	2.3052	952
W, J, MTI, J*	0.99719	2.0868	2438	0.99779	1.9920	1436	0.99891	1.4588	1790
N_c, $^0\chi$, M1, J, J*	0.99906	1.2103	5715	0.99937	1.0811	3914	0.99959	0.9292	3534

Table 3. Experimental and theoretical heats of formation (kcal/mol) for a set of 60 hydrocarbons. The numbering of molecules corresponds to the molecular listing of Table 1.

Molecule	ΔH^o_f(exp) *[45/*	ΔH^o_f(theor)$^{(1)}$	ΔH^o_f(theor)$^{(2)}$
1.	-20.24	-20.27	-19.89
2.	-24.82	-24.90	-25.25
3.	-30.15	-29.43	-30.31
4.	-32.15	-32.97	-32.28
5.	-35.00	-34.48	-34.75
6.	-36.92	-37.05	-37.49
7.	-39.67	-39.31	-38.72
8.	-39.96	-40.11	-38.86
9.	-41.66	-41.93	-41.76
10.	-41.02	-41.51	-42.63
11.	-44.35	-43.44	-43.62
12.	-42.49	-43.76	-44.38
13.	-44.88	-45.80	-42.77
14.	-45.96	-46.38	-46.75
15.	-49.27	-48.23	-48.17
16.	-48.95	-49.64	-48.74
17.	-50.82	-50.68	-50.48
18.	-50.69	-50.45	-50.75
19.	-53.71	-52.66	-52.41
20	-51.13	-51.22	-53.31
21.	-52.44	-51.46	-53.22
22.	-53.21	-52.19	-52.69
23.	-52.61	-51.63	-52.30
24.	4.12	5.31	4.15
25.	4.54	5.79	4.64
26.	4.29	4.83	3.61
27.	-0.46	-0.78	-0.40
28.	-0.78	-1.56	-1.25
29.	-2.29	-4.03	-2.30
30.	-3.33	-4.83	-2.76
31.	-3.84	-4.83	-2.73
32.	-5.22	-6.46	-4.81
33.	-5.32	-7.63	-6.14
34.	-10.02	-11.66	-11.32

35.	-16.25	-14.98	-16.55
36.	-16.99	-16.52	-17.25
37.	-17.86	-16.52	-17.17
38.	-29.46	-28.32	-29.42
39.	-29.36	-29.52	-29.32
40.	-29.46	-30.76	-29.34
41.	27.93	30.08	27.71
42.	27.75	29.97	26.88
43.	23.10	22.41	23.74
44.	22.92	22.69	22.41
45.	19.97	20.38	20.34
46.	19.55	20.04	20.18
47.	19.72	19.59	20.62
48.	19.55	19.93	20.76
49.	19.72	19.70	19.99
50.	19.55	19.36	19.92
51.	19.97	20.49	19.68
52.	19.72	19.49	19.17
53.	19.72	19.16	19.12
54.	17.85	16.66	18.89
55.	17.65	17.78	17.22
56.	15.72	15.76	14.99
57.	14.65	14.23	14.15
58.	14.65	13.72	14.02
59.	12.68	11.73	13.53
60.	12.50	13.91	11.65
Average absolute deviation	-	0.76	0.62

(1) Best five-variables fitting for molecular set a).

(2) Best five-variables fitting for molecular set b).

Analysis of results from Tables 2 and 3 shows the better predictive power arising from the fitting equations derived on the basis of set b) of topological descriptors than those corresponding to the set a). The statistical parameters (Table 2) and the correlations between experimental data and theoretical predictions (Table 3) makes clear the convenience of resorting to the use of the detour matrix instead of the standard distance matrix in order to define the pertinent topological parameters. Besides, it seems recommendable to employ higher-order polynomials to get a better degree of prediction. These conclusions are in line with other previous ones in some studies on the usefulness of the application of the detour matrix [25-27].

In order to properly judge the value of the predictions is interesting to note the low average absolute deviations (0.76 and 0.62 kcal/mol, respectively). It must be taken into account that usually the theoretical predictions give an average absolute deviation around 2 kcal/mol, which is the degree of uncertainty in the experimental determinations. Furthermore, there is not any "pathological" prediction and the maximum deviation for the results presented in Table 3 is 2.31 kcal/mol.

4. Conclusions

We have employed some usual topological indices to study the heat of formation of a set of hydrocarbons comprising 60 structurally diverse molecules. In those cases were the definition demands the employment of the distance matrix we have also defined similar indices on the base of the detour matrix (*i.e.* maximum distance) in order to assess the relative merits of both distance definitions. Results show that resorting to the detour matrix for defining the topological indices yields better correlations to predict enthalpies of formation. These results agree with other similar ones to study other physical chemistry properties, which seems to support the use of detour indices in structure-property modeling [25-27, 61-63]. We conclude that the obtained results are good enough for the chosen set to validly infer that the detour matrix Δ represents a convenient topological device to be employed in the QSAR/QSPR analysis and it constitutes a valuable molecular descriptor which verily adds to the set of topological matrices. In order to arrive to more significant and definite conclusions on this issue, we deem it is necessary to extend the calculations to quite different molecular sets and other physical chemistry properties and biological activities. Research along this line is being carried in our laboratories and results will be presented elsewhere in the near future.

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