A RATHER SIMPLE THEORETICAL CALCULATION OF HEAT OF FORMATION OF SOME AROMATIC NITRO COMPOUNDS

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Abstract

We apply a quite simple approximation to compute enthalpies of formation of some aromatic nitro compounds. The approach lies within the realm of QSPR theory and basic molecular descriptors are atoms and bonds. Higher-order regression polynomial formulae are determined in order to obtain optimal predictions. Results are quite satisfactory since absolute average deviations are similar to experimental uncertainties. Numerical data are compared with other theoretical results derived from the application of AM1 and PM3 semiempirical methods.

Resumen

Se aplica una aproximación simple para calcular las entalpías de formación de algunos nitro-compuestos aromáticos. La aproximación se ubica en el campo de la teoría QSPR y los descriptores moleculares básicos son los átomos y enlaces. Regresiones polinómicas de grado elevado se determinan para obtener las predicciones óptimas. Los resultados son bastante satisfactorios dado que las desviaciones absolutas promedio obtenidas son similares a las incertezas experimentales. Los datos numéricos se comparan con otros resultados teóricos derivados de la aplicación de los métodos semiempíricos AM1 yPM3.

Introduction

The total molecular energy (E_{tot}) is the total electronic energy relative to a situation where the nuclei and electrons are infinitely separated. Within the realm of the Börn-Oppenheimer, E_{tot} is given by

$$E_{tot} = E_{elec} + \sum_{A=1}^{M} \sum_{B=A+1}^{M} \frac{Z_a Z_b}{R_{ab}} \qquad (1)$$

where E_{elec} is the so-called "purely electronic energy" and it is calculated from the stationary Schrödinger equation [1]:

$$H\Psi_{elec} = E_{elec} \Psi_{elec} \qquad (2)$$

The total molecular electronic energy is normally converted to a heat (or enthalpy) of formation, ΔH_f°, by substracting the electronic energy of the isolated atoms which make up the molecular system, and adding the experimental atomic heats of formation [2]:

$$\Delta H_f^o \left(molecule \right) \ = \ E_{tot} - \sum^{atom} E_{elec} \left(atom \right) + \sum^{atom} \Delta H_f^o \left(atom \right) \qquad (3)$$

This conversion is convenient in order to get a more useful quantity for a direct comparison with experiment, since heat of formation, *i.e.* the enthalpy change when one mole of a compound is formed from its constituent elements in their standard states, is a well defined quantity in macroscopic thermodynamic.

Thermochemistry plays a key role in chemical reactions and particularly enthalpies have significant practical applications to explore reactivities and equilibria. Since heats of reactions can be calculated from enthalpies of formation of all reactants and products, it seems desirable to have compiled the largest possible set of data for such a thermochemistry quantity. There are numerous and excellent compilations of available experimental values [3-6] but unfortunately they are not complete. In order to fill these gaps one may resort to theoretical procedures with the proviso they are accurate enough.

The thermochemistry of nitro compounds has not been so intensively studied as that of other homologous series. Because of the scarcity of experimental data, the number of necessary parameters for this sort of calculation was derived from only a reduced number of compounds [7-9]. Nitroaromatic compounds are highly reactive species, which explains why they are of special interest to the chemical and explosives industry. The investigation of their chemical reactivities requires knowing the corresponding thermochemical properties. Regrettably, quantitative information on them is quite limited. Although there are well known experimental techniques to determine heats of formation, some aromatic nitro compounds are somewhat awkard to synthesize and others are extremely unstable. Hence, one is lead to look for reliable theoretical methods to calculate ΔH_f° of nitroaromatic compounds.

The aim of this paper is to employ a rather simple and quite direct procedure to compute enthalpies of formation of nitroaromatic derivatives under the requirement to obtain accurate enough predictions to have a reliable working tool. In case theoretical calculations and available experimental data should reach a trustworthy degree of agreement, some nitroaromatic derivatives which are highly unstable or/and difficult to synthesize could be credibly analyzed and these data should be quite useful to study the physical chemistry properties of those explosives.

The paper is organized in the following way. Next section deals with the theoretical method and computing details. Then we present results for a representative set of nitrobenzenes, nitrotoluenes, nitroanilines, and nitrophenols, analyzing numerical data in comparison with available experimental results and other recently published theoretical values. Finally, we discuss the findings of these calculations and we propose some possible future extensions of this sort of calculations.

Theoretical Method

There is a wide variety of theoretical methods which can be used to compute molecular heats of formation. They have been described and analyzed in a comparative fashion in several previous papers [10-27], so that; for the sake of brevity it is not necessary to repeat this information here. However, some significant points must be discuss now in order to highlight the basis of the method chosen to calculate heats of formation of nitroaromatic derivatives.

Hartree-Fock, MP2 and pBP (perturbative Becke-Perdew model) density functional model provide excellent descriptions of the energetic of bond separation reactions for a number of relatively small molecules. Since thermochemistry data for nearly all molecules which appear on the right of the bond separation reactions are known experimentally or may be determined with very good accuracy from high-level calculations, then heats of formation may be precisely established by combining calculated results and experimental or/and high-level calculated data [28]. For example, the heat of formation of methyl hydrazine may be gotten from the following thermochemical cycle

$$\Delta H_f^\circ(CH_3NHNH_2) = -\Delta E_{rx} - \Delta H_f^\circ(NH_3) + \Delta H_f^\circ(CH_3NH_2) + \Delta H_f^\circ(NH_2NH_2) \quad (4)$$

Here, ΔE_{rx} is the calculated energy of the bond separation reaction and $\Delta H_f^\circ(NH_3)$, $\Delta H_f^\circ(CH_3NH_2)$ and $\Delta H_f^\circ(NH_2NH_2)$ are experimental heats of formation.

Enthalpies of formation determined in this way for somewhat small molecules using HF/1G*, MP2/6-31G* and pBP/DZP (Double Zeta plus Polarization type basis) models are predicted with errors in the range of 2-4 kcal/mol. However, although this methodology resorts to high-level molecular calculations, is not a totally theoretical procedure since it combines computational results with experimental data. Besides, when it is applied to larger molecules has to employ somewhat arbitrary correction factors to achieve satisfactory predictions.

An interesting alternative is the employment of semiempirical models which are specifically parametrized to predict heats of formation. However, these methods although satisfactory for some rather restricted molecular subsets, generally lead to errors of unacceptable magnitude when they are applied to wider molecular sets [29].

Another quite attractive option is the scheme of atom equivalents to relate *ab initio* energies to calculate enthalpies of formation. Different set of atoms and group equivalents have been developed which allow one to perform straightforward thermochemical calculations. These procedures are based on the concept of transferability and they yield a reasonable agreement with available experimental data [30-33]. However, this sort of method combines first-principles *ab initio* calculations with empirically determined parameters, so that it is subjected to the same drawbacks as those pointed out for the first procedure mentioned above (*i.e.* Hartree-Fock or post Hartree-Fock calculations combined with experimental data).

Since for the time being it seems that it is not feasible to have a completely satisfactory and widely applicable only theoretical first-principle procedure to compute molecular heats of formation, we deem suitable to turn to an alternative empirical methodology, such as a QSPR/QSAR (Quantitative Structure Property Relationships

/Quantitative Structure Activity Relationships) approach [34]. In fact, several previous calculations of several physical chemistry properties based on the employment of rather simple and direct molecular and topological descriptors have shown to yield satisfactory enough results, with average absolute deviations of the same order than experimental uncertainties [35-40]. The basic equation for this sort of calculation is

$$\Delta H_f^\circ = f(\{v\}, \{p\}) \tag{5}$$

Where $\{v\}$ is a set of molecular or/and topological descriptors and $\{p\}$ denotes a set of adjustable parameters, while f is any function. The more usual relationships have the linear polynomial structure, *i.e.*

$$\Delta H_f^\circ = p_1 v_1 + p_2 v_2 + \ldots + p \tag{6}$$

although it is also possible to employ higher-order polynomials

$$\Delta H_f^\circ = p_{11}v_1 + p_{21}v_1^2 + \ldots + p_{n1}v_1^n + p_{12}v_2 + p_{22}v_2^2 + \ldots + p_{n2}v_2^n + \ldots + p_{1m}v_m + \ldots + p_{nm}v_m^n + p \tag{7}$$

where m is the number of descriptors and n is the polynomial order.

The most simple and obvious molecular descriptors are atoms and bonds. This choice is in line with the naïve perception of molecules as entities formed by atoms linked together by chemical bonds. At present, standard literature registers a huge number of molecular and topological descriptors currently employed in QSAR/QSPR theory, so that it is not an easy task to determine *a priori* which are the best ones. It is surprising that these "primitive" descriptors have not been used extensively, although they have been proven to be suitable for predicting physical chemistry properties and biological activities [34-40].

In order to employ those simple relationships like (7), we have considered different sort of atoms (*i.e.* primary, secondary, tertiary and quaternary C atoms, etc.) and bonds (i.e. N-O and N=O, etc.). We select the families of nitrobenzene, nitrotoluene, nitroaniline and nitrophenol chosen by Chen and Wu [41] who have calculated their molecular structures and heats of formation by means of the Dewar's AM1 and Stetwart's PM3 methods.

This particular selection is based on four main reasons:
  a) It allows us to make a direct comparison with other theoretical results.
  b) The molecular set comprises 69 compounds and it is quite representative of aromatic nitro derivatives.
  c) Standard literature registers 20 experimental heats of formation for this set (*i.e.* training set) while there is not information for the remaining 49 molecules (*i.e.* test set) which leads us to make a prediction for this thermodynamic property of aromatic nitro compounds whose experimental values are unknown.
  d) Experimental data vary between 4.1 and –29.3 kcal/mol, so that the interval is quite broad (*i.e.* 33.4 kcal/mol) to take into account the chemical differences existing within the whole molecular set.

Calculations were performed resorting to the standard software MATHEMATICA® [42] and the fitting procedure in the multivariate regression analysis was made for first-, second-, and third-order polynomials.

Table 1. *Enthalpies of formation (kcal/mol) (gas phase data) of several nitro aromatic derivatives.* [*] *Average absolute deviation =* $\sum |\Delta H_f°(exp.) - \Delta H_f°(theor.)|/n$, *where n =* *20 (i.e. number of compounds whose experimental heats of formation are known).* [♦] *Hwang, D.R.; Tamura, M.; Yoshida, T.; Tanaka, N.; Hosofa, F. J. Energetic Materials* ***1990***, *8, 85; Akutsu, Y.; Takayama, J.; Tamura, R. J. Energetic Materials* ***1992***, *10, 173.*

Compound	$\Delta H_f°(exp)$[♦]	AM1(calc.)	Abs.Dev.	PM3(calc.)	Abs.Dev.
1. Nitrobenzene	16.1	25.29	9.2	14.54	1.6
2. 1,2-Dinitrobenzene	20.2	38.61	18.4	15.23	5.0
3. 1,3-Dinitrobenzene	11.3	33.13	21.8	9.13	2.2
4. 1,4-Dinitrobenzene	13.3	33.29	20.0	10.13	3.2
5. 1,2,3-Trinitrobenzene	-	53.91	-	18.22	-
6. 1,2,4-Trinitrobenzene	-	50.03	-	13.18	-
7. 1,3,5-Trinitrobenzene	14.9	44.88	30.0	6.94	8.0
8. 1,2,3,4-Tetranitrobenzene	-	73.88	-	23.96	-
9. 1,2,3,5-Tatranitrobenzene	-	68.34	-	18.30	-
10. 1,2,4,5-Tetranitrobenzene	-	69.39	-	18.89	-
11. 1,2,3,4,5-Pentanitrobenzene	-	92.44	-	31.27	-
12. 1,2,3,4,5,6-Hexanitrobenzene	-	117.23	-	45.79	-
13. *o*-Nitrotoluene	9.3	18.92	9.6	8.00	1.3
14. *m*-nitrotoluene	4.1	17.59	13.5	5.07	1.0
15. *p*-Nitrotoluene	7.4	17.25	9.9	4.68	2.7
16. 2,3-Dinitrotoluene	-	31.78	-	8.02	-
17. 2,4-Dinitrotoluene	4.7	26.20	21.5	2.03	2.7
18. 2,5-Dinitrotoluene	-	26.73	-	3.03	-
19. 2,6-Dinitrotoluene	9.6	30.11	20.5	6.38	3.2
20. 3,4-Dinitrotoluene	-	30.46	-	5.29	-
21. 3,5-Dinitrotoluene	-	25.30	-	-0.39	-
22. 2,3,4-Trinitrotoluene	-	46.59	-	10.82	-
23. 2,3,5-Trinitrotoluene	-	42.91	-	5.65	-
24. 2,3,6-Trinitrotoluene	-	45.96	-	9.81	-
25. 2,4,5-Trinitrotoluene	-	42.83	-	5.64	-
26. 2,4,6-Trinitrotoluene	12.3	41.22	28.9	3.36	8.9
27. Trinitrotoluene	-	45.62	-	8.15	-
28. 2,3,4,5-Tetranitrotoluene	-	64.45	-	16.25	-

Results and discussion

Many correlations need not be linear. In general, one should also test multivariate regression analysis for larger than linear polynomial order and if warranted for other functional dependence [43]. We have computed several fitting polynomial-orders and have found that it is not necessary to go beyond third-order to improve significantly the final results.

Table 1. *(cont.)*

Compound	ΔH_f^o(exp)[♦]	AM1(calc.)	Abs.Dev.	PM3(calc.)	Abs.Dev.
29. 2,3,4,6-Tetranitrotoluene	-	63.78	-	14.74	-
30. 2,3,5,6-Tetranitrotoluene	-	65.04	-	15.47	-
31. 2,3,4,5,6-Pentanitrotoluene	-	87.27	-	27.95	-
32. *o*-Nitrophenol	-29.3	-20.17	9.1	-33.24	3.9
33. *m*-Nitrophenol	-28.0	-17.43	10.6	-29.55	1.6
34. *p*-Nitrophenol	-25.4	-16.05	9.4	-28.21	2.8
35. 2,3-Dinitrophenol	-	-5.69	-	-31.33	-
36. 2,4-Dinitrophenol	-30.7	-13.27	17.4	-40.16	9.5
37. 2,5-Dinitrophenol	-	-10.91	-	-36.79	-
38. 2,6-Dinitrophenol	-	-6.29	-	-31.35	-
39. 3,4-Dinitrophenol	-	-4.83	-	-30.08	-
40. 3,5-Dinitrophenol	-	-6.53	-	-32.03	-
41. 2,3,4-Trinitrophenol	-	9.06	-	-29.14	-
42. 2,3,5-Trinitrophenol	-	6.93	-	-32.37	-
43. 2,3,6-Trinitrophenol	-	8.63	-	-32.12	-
44. 2,4,5-Trinitrophenol	-	4.66	-	-35.65	-
45. 2,4,6-Trinitrophenol	-25.9	5.27	31.2	-41.16	15.3
46. 3,4,5-Trinitrophenol	-	11.39	-	-2638	-
47. 2,3,4,5-Tetranitrophenol	-	28.22	-	-22.76	-
48. 2,3,4,6-Tetranitrophenol	-	26.07	-	-27.84	-
49. 2,3,5,6-Tetranitrophenol	-	28.21	-	-25.97	-
50. 2,3,4,5,6-Pentanitrophenol	-	50.51	-	-14.41	-
51. *o*-Nitroaniline	15.2	20.74	5.5	14.41	0.8
52. *p*-Nitroaniline	16.5	24.64	8.1	14.46	2.0
53. *m*-Nitroaniline	16.2	21.65	5.5	13.39	2.8
54. 2,3-Dinitroaniline	-	33.98	-	14.00	-
55. 2,4-Dinitroaniline	12.2	25.42	13.2	5.17	7.0
56. 2,5-Dinitroaniline	-	28.54	-	9.44	-
57. 2,6-Dinitroaniline	-	25.54	-	6.37	-
58. 3,4-Dinitroaniline	-	39.53	-	11.64	-
59. 3,5-Dinitroaniline	-	32.32	-	10.70	-
60. 2,3,4-Trinitroaniline	-	70.77	-	15.51	-
61. 2,3,5-Trinitroaniline	-	45.27	-	11.92	-
62. 2,3,6-Trinitroaniline	-	45.01	-	10.88	-
63. 2,4,5-Trinitroaniline	-	42.17	-	8.24	-
64. 2,4,6-Trinitroaniline	-	34.16	-	-0.11	-
65. 3,4,5-Trinitroaniline	-	50.52	-	14.63	-
66. 2,3,4,5-Tetranitrophenol	-	64.94	-	20.58	-
67. 2,3,4,6-Tetranitrophenol	-	58.00	-	12.84	-
68. 2,3,5,6-Tetranitrophenol	-	62.20	-	17.97	-
69. 2,3,4,5,6-Pentanitroaniline	-	86.66	-	27.94	-
Average absolute deviation[*]	-	-	**15.7**	-	**4.3**

In Table 1 we list the molecular set together with experimental data and other theoretical results computed from the semiempirical AM1 and PM3 methods. Calculated results show that the PM3 method is manifestly better than the AM1 method. However, average absolute deviation arising from the first method is unacceptable since it is rather

large and exceeds the usual experimental uncertainties (*i.e.* 2-4 kcal/mol). Furthermore, AM1 procedure always overestimates enthalpies of formation while the PM3 method underestimates them.

The molecular atom and bond-parameters are presented in Table 2, while final results for first-, and second-order polynomials are given in Table 3 together with absolute deviations and average absolute deviations. Complete results are available upon request to one of us (EAC). Improved Chen and Wu's results are inserted here for comparative purposes.

Table 2. *Fitting parameters in linear and second order equations.*

[*] $\Delta H_f^\circ = p_{1C} n_C + p_{1H} n_H + p_{1N} n_N + p_{1O} n_O + p$ (8)

[**] $\Delta H_f^\circ = p_{1C} n_C + p_{1H} n_H + p_{1N} n_N + p_{1O} n_O + p_{1CC} n_{CC} + p_{1CH} n_{CH} + p_{1CO} n_{CO} + p_{1OH} n_{OH} + p_{1CCarom}$

$n_{CCarom} + p_{1NH} n_{NH} + p_{1CN} n_{CN} + p_{1N-O} n_{N-O} + p_{1N=O} n_{N=O} + p$ (9)

[***] $\Delta H_f^\circ = p_{1C} n_C + p_{2C} n^2_C + p_{1H} n_H + p_{2H} n^2_H + p_{1N} n_N + p_{2N} n^2_N + p_{1O} n_O + p_{2O} n^2_O + p$ (10)

where, for example, n_C means the number of C atoms, p_{1C} is the coefficient corresponding to the number of C atoms, p_{2C} is the coefficient corresponding to the square of the number of C atoms, etc., and p is the independent term. [****] *Computed with the standard statistical software included in the MATHEMATICA® package [42].*

Atom and bond parameters	Linear equation with atoms [*]	Linear equation with atoms and bonds [**]	Quadratic equation with atoms [***]
p_{1C}	78.8057	- 0.3132	14.0624
p_{1H}	-42.9542	4.0256	-35.0357
p_{1N}	43.1735	28.9064	44.5172
p_{1O}	-42.8293	-10.5998	-50.1015
p_{2C}	-	-	5.2947
p_{2H}	-	-	-0.9909
p_{2N}	-	-	-0.3299
p_{2O}	-	-	0.7666
P	-200.8890	-6.9748	-4.100
p_{CC}	-	-14.1530	-
p_{CH}	-	-0.1797	-
p_{CO}	-	-16.8842	-
p_{OH}	-	-16.8842	-
p_{Ccarom}	-	-0.3291	-
p_{NH}	-	-18.0343	-
p_{CN}	-	5.2190	-
p_{N-O}	-	-3.8117	-
$p_{N=O}$	-	-3.8117	-
$R^{2[*]}$	0.99021	0.99193	0.99279
Standard deviation [****]	2.8685	4.1191	2.8764

The analysis of predicted enthalpies of formation reveals that results improve significantly for higher-order polynomials, although differences are no so remarkable when comparing statistical results corresponding to second and third-order formulae. Average absolute deviations are rather low (*i.e.* ~ 2.0 kcal/mol), since experimental uncertainties vary around 2-4 kcal/mol. Besides, just one prediction deviates beyond this interval (*i.e.* 1,3-dinitrobenzene), which may suggest a poor experimental accuracy. In

fact, Verevkin reported thermochemical measurements (transpiration, combustion calorimetry, and DSC) for some nitro compounds [44], and when comparing experimental results for 1,2-dinitrobenzene with other previous data he noted essentially different figures which are not acceptable within the bounds of the experimental uncertainties. Besides, Verevkin published results for 1,2- and 1,4-dinitrobenzene but not for 1,3-dinitrobenzene !!!!

These comments lead us to suppose the predictions for the whole molecular test set are quite promising, so that it is now necessary to wait for the corresponding experimental confirmation.

Table 3. *Heats of formation (kcal/mol) of nitro derivatives (training set).*
* Numbering as in Table 1.

| Molecule *	Eq. (8)	Eq. (9)	Eq. (10)	Eq. (8) /41/	Eq. (10b) /41/	Eq. (9) /41/	Eq. (11b) /41/
1.	14.69	13.70	17.98	15.81	14.95	15.36	14.06
2.	15.16	15.16	14.46	20.11	17.67	20.38	18.57
3.	15.16	15.16	14.46	12.58	13.39	12.49	13.42
4.	15.16	15.16	14.46	13.34	13.51	13.79	14.27
7.	15.63	16.62	14.43	13.96	14.88	13.79	15.49
13	7.59	6.93	7.02	8.72	8.53	8.91	7.89
14.	7.59	6.93	7.02	6.23	7.50	5.33	5.42
15.	6.93	6.93	7.02	5.79	7.23	4.86	5.09
17.	8.06	8.39	7.47	5.36	6.54	5.74	6.76
19.	8.06	8.39	7.47	10.29	9.59	11.06	10.44
26.	8.53	9.84	11.40	11.02	10.59	11.49	11.80
32.	-28.14	-27.57	-28.28	-29.75	-29.33	-29.52	-29.18
33.	-28.14	-27.57	-28.28	-27.08	-27.20	-27.06	-26.06
34.	-28.14	-27.57	-28.28	-25.87	-26.12	-26.16	-24.93
36.	-27.67	-29.03	-28.74	-31.75	-31.63	-30.01	-31.10
45.	-27.20	-27.57	-25.70	-24.85	-24.83	-26.55	-28.03
51.	14.91	15.97	15.58	14.67	15.24	16.22	16.20
52.	14.91	15.97	15.58	17.15	18.29	16.26	16.24
53.	14.91	15.97	15.58	15.25	15.96	15.33	15.34
55.	15.38	12.20	13.38	13.02	11.22	12.29	12.32
Average absolute deviation	**2.1**	**1.9**	**1.7**	**0.8**	**1.0**	**0.8**	**1.2**

Comparison with Chen and Wu's results must be done carefully. As a matter of fact, when one takes into account direct AM1 and PM3 calculations, predictions are rather poor (see columns 3 and 5 in Table 1, ref. 41) and average absolute deviations are 15.7 kcal/mol and 4.7 kcal/mol, respectively. Results improve somewhat when theoretical results are adjusted with respect to experimental data (columns 4 and 6 in Table 1, ref. 41), with average absolute deviation equal to 1.7 kcal/mol and 1.4 kcal/mol, respectively. However, it must be pointed out that such improvement is practically "forced" by the chosen models (Eqs. 1 and 2 in ref. 41). The use of more involved

formulae (*i.e.* Eqs. (8), (9), (10b) and (11b) in ref. 41) yields very good agreements with experimental data (average absolute deviations equal to 0.8, 1.0, 0.8, and 1.2 kcal/mol, respectively), but they resort to a number of fitting parameters to take into account the interaction of the methyl, amino, or hydroxyl groups to the phenyl ring in a completely empirical manner.

Finally, we display in Figure 1 experimental versus theoretical heats of formation computed with the third-order polynomial formula (Eq. 10). Inspection of Figure 1 shows again the quite good agreement between computed and available experimental data of aromatic nitro compounds.

The last Table 4 gives the different predictions of enthalpies of formation for the 40 aromatic nitro molecules whose experimental values are unknown and now these data remain at an expectation position for the thermochemical determinations.
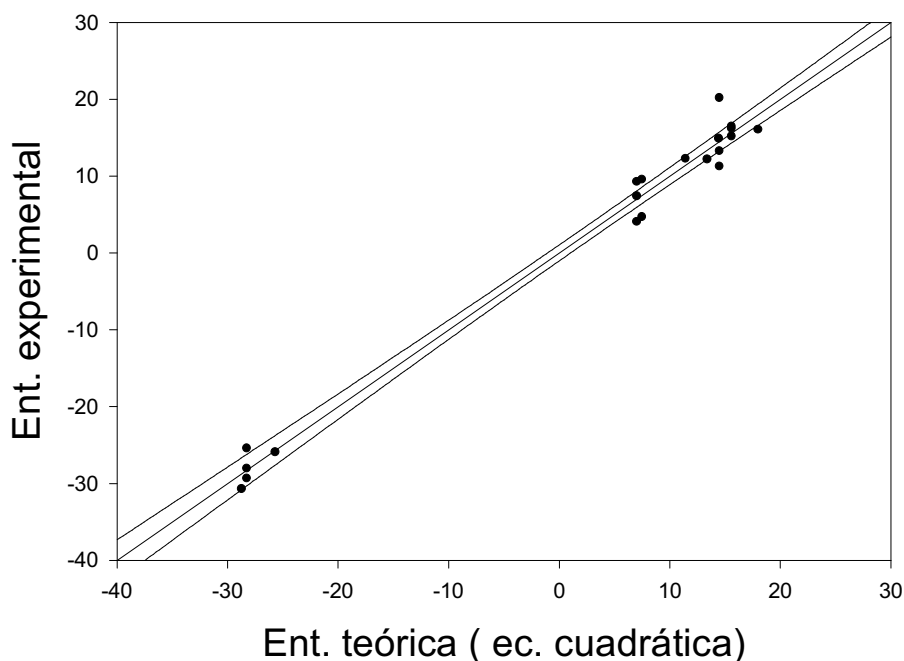
Figure 1: Experimental versus theoretical enthalpy of formation for the test set.

Conclusions

A number of methods for the estimation of thermochemical properties of organic compounds have been developed in recent years. The importance of reliable experimental basis for such methods is widely accepted among both scientists and engineers. At the same time, several theoretical approaches have been proposed in order to complement or/and substitute experimental techniques whenever it is necessary.

Among the different predictive methods, those based on QSPR theory are conceptually straightforward and practically simple and direct. They allow one to study quite different physical chemistry properties with equal easiness. We have calculated the heats of formation of 69 nitrobenzene, nitrotoluene, nitroaniline, and nitrophenol isomers

resorting to the employment of the simplest molecular descriptors, *i.e.* atoms and chemical bonds. Besides, we have taken advantage of using higher-order multivariate regression polynomials in order to improve results. The agreement between experimental results and theoretical predictions for the 20 compounds whose enthalpy of formation values are known is quite satisfactory, since absolute average deviations are similar (although rather lower than) experimental uncertainties. Therefore, the true predictions for the 40 derivatives whose experimental values are unknown are probably correct. Naturally, the last and definitive word about this issue will be given when experimental results will be available.

Table 4. *Predicted heats of formation (kcal/mol) for some nitro aromatic derivatives (i.e. test set). Numbering as in Table 1. (*) Computed as in Table 2.*

Molecule *	Eq.(8)	Eq. (9)	Eq. (10)
5.	15.63	16.62	14.43
6.	15.63	16.62	14.43
8.	-27.08	-10.03	-24.32
9.	-27.08	-10.03	-24.32
10.	-27.08	-10.03	-24.32
11.	16.57	19.53	24.84
12.	17.03	20.99	35.28
16.	8.06	8.38	7.46
18.	8.06	8.38	7.46
20.	8.06	8.38	7.46
21.	8.06	8.38	7.46
22.	8.52	9.84	11.40
23.	8.52	9.84	11.40
24.	8.52	9.84	11.40
25.	8.52	9.84	11.40
27.	8.52	9.84	11.40
28.	8.99	11.30	18.82
29	8.99	11.30	18.82
30.	8.99	11.30	18.82
31.	9.46	12.75	29.74
35.	-27.67	-29.03	-28.74
37.	-27.67	-29.03	-28.74
38.	-27.67	-29.03	-28.74
39.	-27.67	-29.03	-28.74
40.	-27.67	-29.03	-28.74
41.	-27.20	-27.57	-25.71

Present approach based on the use of the most naïve and elementary descriptors (*i.e.* atoms and bonds) within the realm of QSPR theory has a rather serious drawback. In fact, it is incapable to differentiate among isomers. This sort of incapability is not new in QSAR/QSPR theory because many topological and molecular descriptors have this shortcoming. A way to overcome this problem is to introduce suitable descriptors, which are capable to distinguish among isomers. However, this procedure would make the method more involved.

These findings are in line with other previous results reported on biological activities and physical chemistry properties, and all of them seem to show that basic quantities as the number of different atoms and the sort of chemical bonds have found their own niche within the huge universe of topological and molecular descriptors employed within the realm of QSAR/QSPR theory. Besides, it is worth mentioning that we have recently found rather satisfactory results in a similar calculation scheme for a representative set of some aliphatic nitro compounds [45].

In order to apprise suitably this sort of approach, we must point out its direct usefulness for experimentalists and the conceptual simplicity to interpret thermochemical results. Since there is not a large number of theoretical studies devoted to the employment of such fundamental parameters, it seem sensible to apply them to predict other chemical properties and biological activities through the application of this particular theory. It should have been interesting to compare these results with similar ones derived from first-principles methodologies, such as ab-initio calculations or/and Density Functional Theory. Unfortunately, standard literature does not register any data of this kind. At present, we are working along this line and results will be present elsewhere in the forthcoming future.

Table 4.*(cont.)*

Molecule *	Eq.(8)	Eq. (9)	Eq. (10)
42.	-27.20	-27.57	-25.71
43.	-27.20	-27.57	-25.71
44.	-27.20	-27.57	-25.71
46.	-27.20	-27.57	-25.71
47.	-26.73	-26.12	-19.18
48.	-26.73	-26.12	-19.18
49.	-26.73	-26.12	-19.18
50.	-26.26	-24.66	-9.16
54.	15.38	12.20	13.37
56.	15.38	12.20	13.37
57.	15.38	12.20	13.37
58.	15.38	12.20	13.37
59.	15.38	12.20	13.37
60.	15.85	24.10	14.67
61.	15.85	24.10	14.67
62.	15.85	24.10	14.67
63.	15.85	24.10	14.67
64.	15.85	24.10	14.67
65.	15.85	24.10	14.67
66.	-26.73	-26.12	-19.18
67.	-26.73	-26.12	-19.18
68.	-26.73	-26.12	-19.18
69.	16.78	21.79	27.72
$R^{2(*)}$	**0.9902**	**0.9919**	**0.9928**
Standard deviation[(*)]	**2.8685**	**3.3632**	**2.8764**

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