

# Toward the Toxicology of Some Nitro-Compounds

Bisheng Tan<sup>1\*</sup>, Longyu Liao<sup>1</sup>, Yang Zhou<sup>1</sup>, Xinping Long<sup>2\*</sup>, Jinshan Li<sup>1</sup>

<sup>1</sup>Institute of Chemical Materials, China Academy of Engineering Physics (CAEP), Mianyang, P. R. China 621900; <sup>2</sup>China Academy of Engineering Physics (CAEP), Mianyang, P. R. China 621900.  
Email: tanbs\_my@caep.cn

**Abstract:** Nitro-compounds are widely used in medicine, agriculture and industry. Their toxicity issues attract more and more attention. There are a lot of factors influencing toxicity, and the degrees are different from one another. Some physical properties of compounds, such as the surface properties, may play crucial roles in the toxicity of these compounds. Twenty seven parameters of twenty eight nitro-compounds, including molecular size related parameters, molecular surface electrostatic potential based parameters, solubility parameters, molecular cohesive energies, surface tensions, dielectric constants and Mulliken charges of nitro groups, were considered to correlate with toxicity (semi-lethal dose,  $LD_{50}$ ) of the nitro-compounds. Fourteen parameters with higher correlation coefficients were selected to join in the modelling process of heredity and variation (genetic function approximation), further screening toxicity related parameters, the screened parameters are molecular surface electrostatic potentials based  $\sigma_+^2$ ,  $\sigma_-^2$ ,  $\nu\sigma_{tot}^2$ ,  $A_S^+$ ,  $\bar{V}_S$ , Log Pow, and nitro group's Mulliken charges  $q_{NO_2}$ . Building the linear relation between toxicity and these screened parameters, and quantitatively studying the toxicity of nitro-compounds, this work may help us evaluate health risks and approach the toxicology of nitro-compounds.

**Keywords:** Acute toxicity test; semi-lethal dose; electrostatic potentials; genetic function approximation; toxicology

## 1 Introduction

Nitroaromatic compounds are widely used in medicine, industry and agriculture. Nitroaromatic pesticides and explosive residues are considered as being toxic environmental pollutants [1]. Therefore, it is very important to study the toxicity of nitro containing compounds.

The toxicity studies cover a wide field, ranging from carcinogenesis, the whole body system (reproductive system, immune system, nervous system, digestive system, respiratory system, cardiovascular system, dermal system, endocrine system, the individual viscera (liver, kidney, belly, et al.), to acute toxicity test.

Acute toxicity test, also called single dose acute toxicity test, is a kind of toxic reaction of the animal subject one or many times tests per 24 hr (6-8hr interval between two tests), including the general behaviours, the changes of appearance, the changes of gross morphology and death effects, which is characterized half lethal dose ( $LD_{50}$ , in unit of mg/kg). The higher is the  $LD_{50}$ , the lower is the toxicity.

The toxicology of nitro-compounds is not well known so far, some investigators argued that covalent addition reactions between metabolic intermediates of nitro-compounds and cell proteins is the mechanism of toxication [2-4].

The cytotoxic, mutagenic and carcinogenic properties of nitroaromatic environmental pollutants are frequently related to their electron-accepting properties [1,5]. Chung et al explored the influences of nitro group on genic mutation and toxicity [6].

In the past few years, quantitative structure-activity relationship (QSAR) [7-9] plays more and more important role in the study of the relationship between the molecular structures of chemicals and their bioactivities, which can be used to quickly predict biotoxicities of newly found or synthesized compounds.

Hansch et al. proposed Hansch-Fujita model and turned a new page of QSAR or QSPR [10,11] in the research of activities of compounds. By the beginning of twentieth century, it is commonly believed that bioactivities of compounds are mainly determined by their physical properties, including vapor pressure,

Henry's law constants, water solubility, octanol/water partition coefficients, heats of formation and ionization potentials of explosive TNT [12], acidity and basicity of hydrogenbond, solubility, surface tension, dipole moment, refractive index and dielectric constant [13], solid, liquid and gaseous enthalpies of formation in terms molecular electrostatic potentials [14], density, vaporization enthalpy, heat capacity, surface tension, isothermal compressibility and dielectric constant [15~18], the role of polarization in the interaction between chemistry and biology [19]. Nano toxicology also begins to attract more and more attention with the fast development of nano technology in recent years [20].

In this work the correlation between toxicity of 28 kinds of nitro compounds and their properties were studied, which include molecular volume, superficial area, enthalpy of vaporization, density of cohesive energy, solubility parameter, polarizability, dipole moment, dielectric constant, surface tension, charge distribution of nitro groups, molecular surface electrostatic potential based functions, and solubility parameters, surface tension, dipole moment and molecular surface electrostatic potentials based parameters were screened to build the relationship with  $LD_{50}^{\text{exp}}$ .

## 2 Theory

Molecular electrostatic potential and related equations proposed by Politzer [21] were displayed in formulas (1) to (8):

$$V(\mathbf{r}) = \sum_A \frac{Z_A}{|\mathbf{R}_A - \mathbf{r}|} - \int \frac{\rho(\mathbf{r}')d\mathbf{r}'}{|\mathbf{r}' - \mathbf{r}|} \quad (1)$$

where  $V(\mathbf{r})$ ,  $Z_A$  and  $\rho(\mathbf{r})$  denote electrostatic potential, charge on  $A$  nucleus located at  $\mathbf{R}_A$  and electron density, respectively. The relative properties are defined as  $P = f [A_s, A_s^+, A_s^-, \bar{V}_s^+, \bar{V}_s^-, \bar{V}_s, \Pi, \sigma_+^2, \sigma_-^2, \sigma_{\text{tot}}^2, \nu, \nu\sigma_{\text{tot}}^2, V_{S,\text{min}}, V_{S,\text{max}}]$ , where  $A_s$ ,  $A_s^+$  and  $A_s^-$  are molecular total surface area, electropositive surface area and electronegative surface area, respectively.  $V_{S,\text{min}}$ ,  $V_{S,\text{max}}$  and  $\Pi$  are the minimum surface electrostatic potential, maximum surface electrostatic potential and average deviation of surface electrostatic potential at  $r$  point, respectively [22].

$$\sigma_{\text{tot}}^2 = \sigma_+^2 + \sigma_-^2 = \frac{1}{r} \sum_{i=1}^r [V_s^+(r_i) - \bar{V}_s^+]^2 + \frac{1}{s} \sum_{j=1}^s [V_s^-(r_j) - \bar{V}_s^-]^2 \quad (2)$$

$$\bar{V}_s^+(r_i) = \frac{1}{r} \sum_{i=1}^r V_s^+(r_i), \quad \bar{V}_s^- = \frac{1}{s} \sum_{j=1}^s V_s^-(r_j) \quad (3)$$

where  $\sigma_+^2$  and  $\sigma_-^2$  are positive and negative standard deviation of molecular electrostatic potential respectively,  $\sigma_{\text{tot}}^2 = \sigma_+^2 + \sigma_-^2$ .  $V_s^+(r_i)$  and  $V_s^-(r_j)$  are positive and negative electrostatic potential located at  $r_i$  and  $r_j$ , respectively.  $\Pi$  is the average deviation of  $V(\mathbf{r})$  on the molecular surface, interpreted as the local polarity, or internal charge separation.

$$\nu = \frac{\sigma_+^2 \sigma_-^2}{[\sigma_{\text{tot}}^2]^2} \quad (4)$$

$$\Pi = \frac{1}{2} \sum_{i=1}^n |V(r_i) - \bar{V}_s| \quad (5)$$

Enthalpy of vaporization, coefficient of diffusion and water/oil partition coefficient [23~25] are derived from molecular surface electrostatic potentials, expressed as formulas (6)~(8).

$$\Delta_{\text{vap}} H^\circ = 1.355 A_s^{0.5} + 1.176 (\nu \sigma_{\text{tot}}^2)^{0.5} - 10.433 \quad (6)$$

$$D \times 10^7 (\text{cm}^2/\text{s}) = 533.5 (A_s)^{-1} - 0.03168 \sigma_+^2 + 0.01425 \sigma_-^2 - 1.620 \quad (7)$$

$$\log P_{\text{ow}} = 0.03 A_s - 0.00472 N \sigma_-^2 - 0.000963 A_s \Pi - 0.504 \quad (8)$$

$$N = n_N + 2n_O$$

The cohesive energy  $E_{\text{coh}}$  [26] of a substance in a condensed state is defined as the increase in internal energy  $U$  (in J/mol) per mole of substance if all the intermolecular forces are eliminated:

$$\text{The cohesive energy} \equiv E_{coh} = \Delta U \quad (9)$$

$$\text{Solubility parameter } \delta = \left( \frac{E_{coh}}{V} \right)^{0.5} = \left( \frac{\Delta_{vap} H - RT}{V} \right)^{0.5} \quad (10)$$

where  $V$  is van der Waals volume of a specific molecule.

Molecular polarizability proposed by Hansch [27] is defined as Equ. (11):

$$a(0)[\text{\AA}^3 / \text{molecule}] = 0.27 (\pm 0.011) NVE \quad (11)$$

where  $\alpha(0)$  and  $NVE$  are volume of polarization and molecular total valence electrons, respectively. The relationship between surface tension and solubility parameter [28] of a compound can be expressed as Equ. (12):

$$\gamma = a\delta^2 V_m^{0.45} + b \quad (12)$$

where empirical parameter  $a$  and  $b$  are 0.0145 and -24.283, obtained from linear fitting method.

Dielectric constants ( $\epsilon^{cal}$ ) of the compounds are obtained from the fitting method in terms of electrostatic potential parameters and solubility parameters.

$$\epsilon^{cal} = f(\delta, \delta^2 \sigma_{tot}^{0.4}) \quad (13)$$

Mulliken charges of nitro groups were computed according to Equ. (14).

$$q_{NO_2} = q_N + q_{O(1)} + q_{O(2)} \quad (14)$$

### 3 Computational Details

Molecular structure optimization were carried out by hybrid density function theory B3LYP/6-31G(d,p) [29,30], molecular van der Waals volumes, surface areas and surface electrostatic potentials were calculated by multifunctional wave function code *Multiwfn* [31]. Surface tensions and slubility parameters were fitted with the combined parameter  $\delta^2 V_m^{0.45}$  in terms of the literature method [28], the fitted squared- $R$  (correlation coefficient) reaches 0.9803, which were displayed in Table 1.

**Table 1.** The calculated electrostatic potential based parameters ( $\sigma_{tot}^2, \sigma_+^2, \sigma_-^2, v, \Delta_{vap} H^\circ$ ), solubility parameters ( $\delta$ ), volumns ( $V_m$ ), molecular areas ( $A_s$ ), cohesive energies ( $E_{coh}$ ) and the predicted surface tensions ( $\gamma$ ).

	$V_m$	$A_s$	$\sigma_{tot}^2$	$\sigma_+^2$	$\sigma_-^2$	$v$	$\Delta_{vap} H^\circ$	$E_{coh} \times 10^{-4}$	$\delta$	$\delta^2 V_m^{0.45}$	$\gamma$
Et	39.300	83.755	3.592	3.156	0.441	0.1079	2.700	1.378	18.722	1828.863	1.034
Propane	53.669	105.309	3.409	2.844	0.565	0.1383	4.279	2.038	19.488	2279.870	7.571
Butane	67.601	126.571	3.146	2.589	0.558	0.1460	5.608	2.594	19.590	2555.923	12.530
Benzene	69.486	125.463	36.835	10.041	26.794	0.1983	7.923	3.563	22.644	3457.483	28.800
BA	78.725	139.236	147.932	101.752	46.180	0.2147	12.183	5.345	26.057	4842.833	44.880
BP	75.077	134.099	151.855	112.261	39.594	0.1928	11.621	5.110	26.089	4752.181	40.900
MeB	83.468	146.282	38.282	8.291	29.991	0.1697	8.953	3.994	21.874	3503.809	28.540
PD	65.709	120.416	127.074	24.746	102.328	0.1568	9.685	4.300	25.582	4303.286	37.120
NB	86.085	150.292	155.002	48.976	106.026	0.2161	12.985	5.185	24.542	4472.365	43.900

Note: Parameters  $V_m, A_s, \sigma_{tot}^2, \sigma_+^2, \sigma_-^2, \Delta_{vap} H^\circ, E_{coh}, \delta, \gamma$  are in unit of  $\text{cm}^3/\text{mol}, \text{\AA}^2, (\text{kcal}/\text{mol})^2, (\text{kcal}/\text{mol})^2, (\text{kcal}/\text{mol})^2, \text{kcal}/\text{mol}, \text{J}/\text{mol}, \text{J}/\text{cm}^3)^{1/2}, \text{mN}/\text{m}$ , respectively.

The experimental surface tensions in Table 1 were taken from the data of 20°C [32]. Dielectric constants of these compounds were calculated according to the fitted genetic function approximation method, and the fitted equation was expressed as follows:

$$\epsilon^{cal} = -3.861 * X1 - 14.859 * \hat{R} (23.757 - X1) + 33.657 * \hat{R} (23.316 - X1) - 0.034 * \hat{R} (5492.795 - X2) + 163.068, \quad X1 = \delta, \quad X2 = \delta^2 \sigma_{tot}^{0.4}$$

The experimental dielectric constants [32] were listed in Table 2, and the square of the fitted linear correlation coefficient reaches 0.9979.

$$\epsilon^{\text{cal}} = -3.861 * X_1 - 14.859 * \hat{R} (23.757 - X_1) + 33.657 * \hat{R} (23.316 - X_1) - 0.034 * \hat{R} (5492.795 - X_2) + 163.068, X_1 = \delta, X_2 = \delta^2 \sigma_{\text{tot}}^{0.4}$$

**Table 2.** The calculated electrostatic potential based parameters, solubility parameters, molecular volumes, cohesive energies, the number of valence electrons, dipole moments, Mulliken charges of nitro groups and the predicted dielectric constants.

	m-DNB	m-NTul	NB	NEt	NMe	o-NTul	p-NBA	p-NTul	TNT
$V_m$	102.942	99.791	86.085	56.530	42.563	99.085	95.339	99.864	132.754
$A_s$	175.830	171.182	150.292	110.544	89.812	167.152	163.927	171.128	216.994
$\sigma_{\text{tot}}^2$	96.386	158.003	155.002	101.578	107.300	158.479	361.630	165.486	91.350
$\sigma_+^2$	49.823	33.540	48.976	35.642	47.327	35.360	188.916	35.673	61.362
$\sigma_-^2$	46.563	124.463	106.026	65.936	59.973	103.119	172.714	129.813	29.989
$v$	0.2497	0.1672	0.2161	0.2278	0.2465	0.1452	0.2495	0.1691	0.2205
$\Delta_{\text{vap}} H^\circ$	13.304	13.340	12.985	9.470	8.456	12.727	18.086	13.514	14.805
$E_{\text{coh}} \times 10^{-4}$	5.318	5.334	5.185	3.714	3.290	5.077	7.319	5.406	5.946
$\delta$	22.730	23.119	24.542	25.633	27.803	22.636	27.708	23.267	21.164
NVE	62	52	46	30	24	52	52	52	84
$\alpha(0)$	16.74	14.04	12.42	8.10	6.48	14.04	14.04	14.04	22.68
$\mu$	4.198	4.889	4.557	3.599	3.488	4.304	7.577	5.237	1.546
$\epsilon$	2.8	23.8	35.7	19.7	39.4	27.4	56.3	22.2	22.0
$q_{\text{NO}_2}$	-0.372	-0.410	-0.406	-0.310	-0.303	-0.425	-0.462	-0.417	-0.355

Note:  $V_m$ ,  $A_s$ ,  $\sigma_{\text{tot}}^2$ ,  $\sigma_+^2$ ,  $\sigma_-^2$ ,  $\Delta_{\text{vap}} H^\circ$ ,  $E_{\text{coh}}$ ,  $\delta$ ,  $\alpha(0)$ ,  $\mu$ ,  $\epsilon$ ,  $q_{\text{NO}_2}$  are in unit of  $\text{cm}^3/\text{mol}$ ,  $\text{\AA}^2$ ,  $(\text{kcal}/\text{mol})^2$ ,  $(\text{kcal}/\text{mol})^2$ ,  $(\text{kcal}/\text{mol})^2$ ,  $\text{kcal}/\text{mol}$ ,  $\text{J}/\text{mol}$ ,  $(\text{J}/\text{cm}^3)^{1/2}$ ,  $\text{\AA}^3$ , Debye, a.u., respectively.

The molecular electrostatic potential related parameters derived from Eqs. (1)~(8) were carried out by *Multiwfn* code [31]. The correlation between  $LD_{50}^{\text{exp}}$  and these parameters was computed by Equ. (15).

$$\Omega_{x,y} = \frac{\text{Cov}(X, Y)}{\sigma_x \sigma_y} \quad (15)$$

where  $\Omega_{x,y}$ ,  $\text{Cov}(X, Y)$ ,  $\sigma_x$  and  $\sigma_y$  are correlation coefficient, covariance, standard deviation of array  $x$  and array  $y$ , respectively.

All of these parameters, those with low correlation coefficient ( $< 0.3$ ) were eliminated, the remained ones including molecular electrostatic potential related parameters  $\sigma_{\text{tot}}^2$ ,  $\sigma_+^2$ ,  $\sigma_-^2$ ,  $V_{s,\text{min}}$ ,  $A_s^+$ ,  $\bar{V}_s$ ,  $v\sigma_{\text{tot}}^2$ ,  $\text{Log } P_{\text{ow}}$ , solubility parameter  $\delta$ , dipole moment  $\mu$ , dielectric constant  $\epsilon$ , surface tension  $\gamma$ , combining function  $\delta^2 V_m^{0.45}$  and Mulliken charge of nitro groups were employed to join the genetic function approximation modelling, seven parameters were preserved in the  $LD_{50}^{\text{cal}}$  related model, including  $\sigma_+^2$ ,  $\sigma_-^2$ ,  $q_{\text{NO}_2}$ ,  $A_s^+$ ,  $\bar{V}_s$ ,  $v\sigma_{\text{tot}}^2$ ,  $\text{Log } P_{\text{ow}}$ .

Genetic algorithm (GA) is a compiled computational program that simulates natural evolution of heredity, mutation, selection and crossover of active organisms [33].

## 4 Results and Discussion

A series of physical parameters in terms of formula in theoretical and computational part of 28 nitro-compounds were obtained and displayed in Table 3, and the correlation coefficients between  $LD_{50}^{\text{exp}}$  and the calculated parameters were listed at the end of Table 3 to Table 6.

**Table 3.** The correlation prediction between  $LD_{50}^{\text{exp}}$  [34] and 6 parameters.

	$LD_{50}^{\text{exp}}$	$V_m$	$\sigma_{tot}^2$	$\sigma_+^2$	$\sigma_-^2$	v	$\Delta_{\text{vap}} H^\circ$
1-Cl-2-NB	0.27	98.169	150.470	56.752	93.718	0.2349	14.009
1-Cl-4-NB	0.81	98.723	138.575	44.362	94.213	0.2176	13.636
23-DNTul	1.12	116.538	103.441	49.110	54.330	0.2494	14.324
24-DNBP	0.035	107.659	101.031	49.080	51.951	0.2498	13.750
24-DNTul	0.27	115.928	90.376	38.501	51.874	0.2445	13.911
25-DNTul	0.71	115.882	75.370	29.208	46.162	0.2374	13.356
26-DNTul	0.18	115.462	94.799	49.013	45.786	0.2497	13.980
2-NI	0.08 <sup>a</sup>	70.698	271.968	169.513	102.456	0.2348	14.466
34-DNTul	1.07	116.849	108.690	49.041	59.649	0.2476	14.649
TNBP	0.6 <sup>c</sup>	124.621	134.646	96.680	37.966	0.2025	15.205
<i>m</i> -DNB	0.01 <sup>c</sup>	102.942	96.386	49.823	46.563	0.2497	13.304
<i>m</i> -NBA	0.54	95.209	278.126	150.506	127.620	0.2483	16.693
<i>m</i> -NTul	1.07	99.791	158.003	33.540	124.463	0.1672	13.340
NB	0.75-1.0 <sup>c</sup>	86.085	155.002	48.976	106.026	0.2161	12.985
NBu	0.50-0.75 <sup>b</sup>	84.602	95.743	26.386	69.357	0.1996	11.507
NEt	1.10	56.530	101.578	35.642	65.936	0.2278	9.470
NMe	1.44 <sup>a</sup>	42.563	107.300	47.327	59.973	0.2465	8.456
NPr	0.50-0.75 <sup>b</sup>	70.383	93.627	25.681	67.945	0.1990	10.231
<i>o</i> -NBA	3.56	94.143	235.101	105.549	129.552	0.2474	15.711
<i>o</i> -NBP	2.828	91.571	311.656	160.509	151.147	0.2498	16.968
<i>o</i> -NTul	0.89	99.085	158.479	35.360	103.119	0.1452	12.727
<i>p</i> -DNB	0.0294 <sup>d</sup>	102.687	82.999	39.628	43.371	0.2495	12.874
<i>p</i> -NBA	3.25	95.339	361.630	188.916	172.714	0.2495	18.086
<i>p</i> -NBP	0.616	92.006	297.564	182.109	115.455	0.2374	16.536
<i>p</i> -NTul	2.14	99.864	165.486	35.673	129.813	0.1691	13.514
Tetryl	0.5 <sup>c</sup>	159.537	144.080	109.412	34.668	0.1827	17.118
TNT	0.48 <sup>d</sup>	132.754	91.350	61.362	29.989	0.2205	14.805
LLM-105	2.000	118.130	187.285	109.731	77.554	0.2426	16.486
Corr.	<b>1.000</b>	<b>-0.1852</b>	<b>0.5623</b>	<b>0.3569</b>	<b>0.6814</b>	<b>0.0439</b>	<b>0.2911</b>

Note:  $LD_{50}^{\text{exp}}$ ,  $V_m$ ,  $A_s$ ,  $\sigma_{tot}^2$ ,  $\sigma_+^2$ ,  $\sigma_-^2$ ,  $\Delta_{\text{vap}} H^\circ$  are in unit of g/kg, cm<sup>3</sup>/mol, Å<sup>2</sup>, (kcal/mol)<sup>2</sup>, (kcal/mol)<sup>2</sup>, (kcal/mol)<sup>2</sup>, kcal/mol, respectively. a, b, c,d denote, mouse, rabbit, dog and cat, respectively.

**Table 4.** 8 parameters in relation to  $LD_{50}^{\text{exp}}$ .

	$E_{\text{coh}} \times 10^{-4}$	$\delta$	NVE	$\alpha(0)$	$\mu$	$\varepsilon$	$\delta^2 V_m^{0.45}$	$\gamma$
1-Cl-2-NB	5.613	23.913	52	14.04	5.032	28.79	4504.604	41.034
1-Cl-4-NB	5.457	23.512	52	14.04	2.922	17.45	4365.836	39.022
23-DNTul	5.745	22.204	68	18.36	6.586	12.82	4195.395	36.550
24-DNBP	5.505	22.613	68	18.36	3.378	6.47	4198.934	36.602
24-DNTul	5.572	21.924	68	18.36	4.843	11.05	4080.603	34.886
25-DNTul	5.340	21.467	68	18.36	0.885	10.76	3911.559	32.435
26-DNTul	5.601	22.026	68	18.36	2.956	11.57	4111.202	35.329
2-NI	5.805	28.654	42	11.34	5.544	52.42	5579.608	56.621
34-DNTul	5.881	22.435	68	18.36	7.308	11.98	4288.283	37.897
TNBP	6.114	22.149	84	22.68	1.786	25.30	4302.534	38.104
<i>m</i> -DNB	5.318	22.730	62	16.74	4.198	2.80	4157.819	36.005
<i>m</i> -NBA	6.736	26.600	52	14.04	5.996	60.35	5497.54	55.431
<i>m</i> -NTul	5.334	23.119	52	14.04	4.889	23.80	4241.595	37.220
NB	5.185	24.542	46	12.42	4.557	35.70	4472.365	43.900

NBu	4.567	23.233	42	11.34	3.855	3.965	3976.783	33.380
NEt	3.714	25.633	30	8.10	3.599	19.70	4037.61	34.262
NMe	3.290	27.803	24	6.48	3.488	39.40	4180.689	36.337
NPr	4.033	23.937	36	9.72	3.757	4.18	3885.974	32.064
<i>o</i> -NBA	6.326	25.921	52	14.04	4.726	62.98	5194.074	51.031
<i>o</i> -NBP	6.852	27.354	52	14.04	5.822	57.44	5712.586	58.550
<i>o</i> -NTul	5.077	22.636	52	14.04	4.304	27.40	4053.246	34.489
<i>p</i> -DNB	5.139	22.370	62	16.74	0	1.56	4022.666	34.046
<i>p</i> -NBA	7.319	27.708	52	14.04	7.577	56.30	5968.733	62.264
<i>p</i> -NBP	6.671	26.926	52	14.04	5.341	59.10	5547.036	56.149
<i>p</i> -NTul	5.406	23.267	52	14.04	5.237	22.20	4297.489	38.031
Tetryl	6.914	20.818	106	28.62	3.352	44.61	4247.816	37.310
TNT	5.946	21.164	84	22.68	1.546	22.00	4041.727	34.322
LLM-105	7.145	24.594	80	21.60	5.402	48.295	4905.232	46.843
Corr.	<b>0.2912</b>	<b>0.4566</b>	<b>-0.2346</b>	<b>-0.2346</b>	<b>0.4411</b>	<b>0.5473</b>	<b>0.5100</b>	<b>0.5060</b>

Note:  $E_{\text{coh}}$ ,  $\delta$ ,  $\alpha(0)$ ,  $\mu$ ,  $\gamma$ ,  $q_{\text{NO}_2}$  are in unit of J/mol,  $(\text{J}/\text{cm}^3)^{1/2}$ ,  $\text{\AA}^3$ , Debye, dyne/cm, a.u., respectively.

**Table 5. 7** electrostatic potential parameters in relation to  $LD_{50}^{\text{exp}}$ .

	$LD_{50}$	$V_{S,\text{min}}$	$V_{S,\text{max}}$	$A_S$	$A_S^+$	$A_S^-$	$\bar{V}_S$	$\bar{V}_S^+$
1-Cl-2-NB	0.27	-32.190	26.761	165.851	103.118	62.733	1.809	12.018
1-Cl-4-NB	0.81	-30.247	25.312	168.939	111.684	57.256	2.936	10.969
23-DNTul	1.12	-30.132	30.378	192.176	116.302	75.874	2.063	15.414
24-DNBP	0.035	-28.017	35.737	181.908	109.672	72.235	4.239	15.591
24-DNTul	0.27	-27.936	30.561	192.820	120.242	72.578	3.801	15.381
25-DNTul	0.71	-26.020	26.231	192.792	122.262	70.530	4.030	14.540
26-DNTul	0.18	-25.924	29.404	190.292	117.537	72.755	3.309	14.332
2-NI	0.08	-39.949	56.771	130.884	72.305	58.580	1.752	19.135
34-DNTul	1.07	-31.012	30.539	196.228	117.035	79.192	2.811	17.348
TNBP	0.6	-23.403	41.362	207.047	116.117	90.930	5.942	19.533
<i>m</i> -DNB	0.01	-26.105	31.540	175.830	103.652	72.178	3.952	16.800
<i>m</i> -NBA	0.54	-36.170	47.384	164.022	81.670	82.351	1.101	15.956
<i>m</i> -NTul	1.07	-33.993	22.297	171.182	114.510	56.672	2.034	10.779
NB	0.85	-32.983	25.334	150.292	100.930	49.362	1.785	10.861
NBu	0.65	-32.282	24.942	153.706	110.197	43.508	3.325	12.194
NEt	1.10	-31.882	25.038	110.544	67.801	42.743	2.412	15.773
NMe	1.44	-30.789	29.713	89.812	47.532	42.280	2.028	20.278
NPr	0.65	-32.066	25.315	132.338	89.159	43.179	3.084	13.782
<i>o</i> -NBA	3.56	-36.470	46.908	160.667	86.379	74.288	1.153	13.262
<i>o</i> -NBP	2.828	-38.030	61.879	157.862	93.308	64.584	1.169	15.022
<i>o</i> -NTul	0.89	-33.789	22.057	167.152	110.826	56.325	1.563	9.801
<i>p</i> -DNB	0.0294	-24.801	28.378	175.599	105.341	70.258	4.312	16.254
<i>p</i> -NBA	3.25	-40.397	50.522	163.927	85.016	78.911	1.151	17.195
<i>p</i> -NBP	0.616	-35.396	64.590	158.990	99.666	59.324	1.938	13.161
<i>p</i> -NTul	2.14	-34.575	21.802	171.128	114.284	56.844	2.176	11.221
Tetryl	0.5	-24.627	43.449	252.176	134.305	117.872	5.583	19.850
TNT	0.48	-21.892	35.556	216.994	125.037	91.956	5.674	17.784
LLM-105	2.000	-38.131	44.554	196.467	108.710	87.756	3.206	19.441
Corr.	<b>1.0000</b>	<b>-0.5745</b>	<b>0.2846</b>	<b>-0.2131</b>	<b>-0.3005</b>	<b>-0.0576</b>	<b>-0.5374</b>	<b>-0.1135</b>

Note:  $V_{S,\text{min}}$ ,  $V_{S,\text{max}}$ ,  $A_S$ ,  $A_S^+$ ,  $A_S^-$ ,  $\bar{V}_S$ ,  $\bar{V}_S^+$ ,  $\bar{V}_S^-$ ,  $\nu\sigma_{\text{tot}}^2$ ,  $\Pi$  are in unit of kcal/mol, kcal/mol,  $\text{\AA}^2$ ,  $\text{\AA}^2$ ,  $\text{\AA}^2$ , kcal/mol, kcal/mol, kcal/mol,  $(\text{kcal}/\text{mol})^2$ , kcal/mol, respectively.

**Table 6.** 3 electrostatic potential parameters and 4 other parameters in relation to  $LD_{50}^{\text{exp}}$ .

	$\bar{V}_S^-$	$v\sigma_{tot}^2$	$\Pi$	$D \times 10^7$	$N$	Log $P_{\text{OW}}$	$q_{\text{NO}_2}$
1-Cl-2-NB	-14.974	35.347	12.735	1.134	5	0.226	-0.391
1-Cl-4-NB	-12.733	30.160	10.796	1.475	5	0.584	-0.402
23-DNTul	-18.402	25.794	16.183	0.374	10	-0.298	-0.350
24-DNBP	-12.995	25.237	13.901	0.498	12	-0.424	-0.396
24-DNTul	-15.383	22.099	14.551	0.666	10	0.130	-0.384
25-DNTul	-14.189	17.889	13.460	0.880	10	0.602	-0.379
26-DNTul	-14.499	23.672	13.716	0.283	10	0.530	-0.392
2-NI	-19.704	63.859	19.243	-1.454	7	-2.388	-0.425
34-DNTul	-18.674	26.914	17.382	0.395	10	-0.717	-0.359
TNBP	-11.414	27.261	15.731	-1.565	17	-0.476	-0.344
<i>m</i> -DNB	-14.498	24.069	15.276	0.499	5	1.085	-0.372
<i>m</i> -NBA	-13.632	69.061	14.822	-1.317	6	-1.539	-0.417
<i>m</i> -NTul	-15.638	26.420	11.830	2.202	5	-0.256	-0.410
NB	-16.774	33.501	12.331	1.889	5	-0.282	-0.406
NBu	-19.138	19.114	12.773	2.003	5	0.580	-0.325
NEt	-18.782	23.136	16.429	3.016	5	-0.493	-0.310
NMe	-18.386	26.452	19.293	3.675	5	-0.894	-0.303
NPr	-19.006	18.637	14.470	2.566	5	0.018	-0.324
<i>o</i> -NBA	-12.927	58.162	13.068	0.203	6	-1.375	-0.496
<i>o</i> -NBP	-18.853	77.844	16.421	-1.172	7	-3.258	-0.418
<i>o</i> -NTul	-14.646	27.471	10.999	1.921	5	0.306	-0.425
<i>p</i> -DNB	-13.594	20.708	14.486	0.781	10	0.267	-0.374
<i>p</i> -NBA	-16.135	90.226	16.680	-1.889	6	-3.110	-0.462
<i>p</i> -NBP	-16.917	70.658	14.262	-2.388	7	-1.732	-0.430
<i>p</i> -NTul	-16.009	27.983	12.228	2.217	5	-0.449	-0.417
Tetryl	-10.672	26.326	15.636	-2.476	21	-0.172	-0.131
TNT	-10.793	20.144	14.33	-0.678	15	0.888	-0.355
LLM-105	-16.906	45.439	18.068	-1.276	16	-3.885	-0.3925
Corr.	<b>-0.1735</b>	<b>0.5444</b>	<b>0.0630</b>	<b>-0.03381</b>		<b>-0.6047</b>	<b>-0.3860</b>

Note:  $D$  is in unit of  $\text{cm}^2/\text{s}$ .**Table 7.** The arrangement of correlation coefficients in descending order.

<i>Para.</i>	$\sigma_-^2$	Log $P_{\text{OW}}$	$V_{\text{S,min}}$	$\sigma_{tot}^2$	$\varepsilon$	$v\sigma_{tot}^2$	$\bar{V}_S^-$	$\delta^2 V_m^{0.45}$	$\gamma$
<i>corr.</i>	0.6814	0.6047	0.5745	0.5623	0.5473	0.5444	0.5374	0.5100	0.5060
<i>Para.</i>	$\delta$	$\mu$	$q_{\text{NO}_2}$	$\sigma_+^2$	$A_S^+$	$E_{\text{coh}}$	$\Delta_{\text{vap}} H^\circ$	$V_{\text{S,max}}$	$NVE$
<i>corr.</i>	0.4566	0.4411	0.3860	0.3569	0.3005	0.2912	0.2911	0.2846	0.2346
<i>Para.</i>	$\alpha(0)$	$A_S$	$V_m$	$\bar{V}_S^-$	$\bar{V}_S^+$	$\Pi$	$A_S^-$	$\mathbf{v}$	$D$
<i>corr.</i>	0.2346	0.2131	0.1852	0.1735	0.1135	0.0630	0.0576	0.0439	0.03381

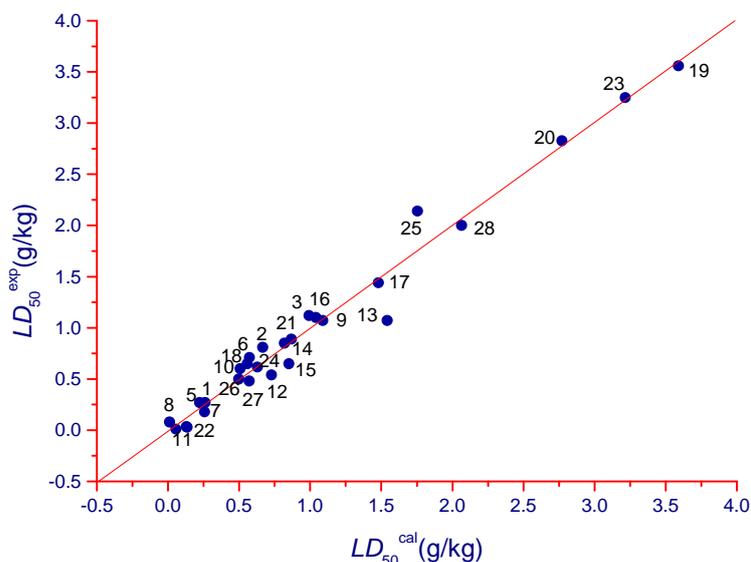
The first columns in Table 3 and Table 5 are experimental values of  $LD_{50}^{\text{exp}}$ , derived from the samples of rats (majority), mice, rabbits, cats and dogs. The correlations between  $LD_{50}^{\text{exp}}$  and the parameters in Table 3 and Table 5 according to Equ. (15) were displayed in the last column in Table 3 to Table 6, which were expressed in Table 7 in descending order, some electrostatic potentials based parameters, dielectric constants, surface tensions, solubility parameters, dipole moment make more contribution to the toxicity. The 9 parameters ranked high (correlation coefficient  $\geq 0.3$ ) in Table 7 were considered in the screening process of genetic function approximation,  $\sigma_+^2$ ,  $\sigma_-^2$ ,  $q_{\text{NO}_2}$ ,  $A_S^+$ ,  $\bar{V}_S^-$ ,  $v\sigma_{tot}^2$ , Log  $P_{\text{OW}}$  were selected to build the relationship (Equ. (16)) with  $LD_{50}^{\text{exp}}$ .

$$LD_{50}^{cal} = -0.012X_1 + 0.024X_2 + 38.855X_3 + 0.164X_4 + 0.028X_5 - 0.227X_6 + 1.017\hat{R}(0.068 - X_7) - 74.386(\hat{R}(X_3 + 0.494))^2 + 346.992(\hat{R}(-0.364 - X_3))^2 + 0.0002(\hat{R}(117.057 - X_5))^2 + 17.241 \quad (16)$$

where  $X_1, X_2, X_3, X_4, X_5, X_6$  and  $X_7$  represent  $\sigma_+^2, \sigma_-^2, q_{NO_2}, A_S^+, \bar{V}_S, \nu\sigma_{tot}^2, \text{Log } P_{ow}$ , respectively,  $\hat{R}$  is ramp function [35], the square of correlation coefficient is 0.9724. The experimental and predicted results were displayed in Table 8 and Figure 1.

**Table 8.** The comparison of predicted semi-lethal doses ( $LD_{50}^{cal}$ , g/kg) and experimental ones ( $LD_{50}^{exp}$ , g/kg).

order	name	$LD_{50}^{exp}$	$LD_{50}^{cal}$	residual	order	name	$LD_{50}^{exp}$	$LD_{50}^{cal}$	residual
1	1-Cl-2-NB	0.27	0.261	-0.009	15	NBu	0.50-0.75	0.850	0
2	1-Cl-4-NB	0.81	0.667	-0.143	16	NEt	1.10	1.040	-0.06
3	23-DNTul	1.12	0.992	-0.128	17	NMe	1.44	1.480	0.04
4	24-DNBp	0.035	0.129	0.094	18	NPr	0.50-0.75	0.558	-0.092
5	24-DNTul	0.27	0.223	-0.047	19	<i>o</i> -NBA	3.56	3.589	0.029
6	25-DNTul	0.71	0.573	-0.137	20	<i>o</i> -NBP	2.828	2.769	-0.059
7	26-DNTul	0.18	0.258	0.078	21	<i>o</i> -NTul	0.89	0.867	-0.023
8	2-NI	0.08	0.012	-0.068	22	<i>p</i> -DNB	0.0294	0.135	0.1056
9	34-DNTul	1.07	1.088	0.018	23	<i>p</i> -NBA	3.25	3.216	-0.034
10	TNBP	0.6	0.507	-0.093	24	<i>p</i> -NBP	0.616	0.630	0.014
11	<i>m</i> -DNB	0.01	0.056	0.046	25	<i>p</i> -NTul	2.14	1.755	-0.385
12	<i>m</i> -NBA	0.54	0.729	0.189	26	Tetryl	0.5	0.498	-0.002
13	<i>m</i> -NTul	1.07	1.542	0.472	27	TNT	0.48	0.572	0.092
14	NB	0.75-1.0	0.820	-0.03	28	LLM105	2.00	2.064	0.064



**Figure 1.** The relationship between experimental semi-lethal doses ( $LD_{50}^{exp}$ ) and predicted ones ( $LD_{50}^{cal}$ ).

It is found from Figure 1 and Table 5 that the calculated semi-lethal doses ( $LD_{50}^{cal}$ ) according to Equ. (12) is in good agreement with experimental ones ( $LD_{50}^{exp}$ ), and the squared-correlation coefficient reaches 0.9282.

The screened parameters, the positive, negative and total variances-,  $\sigma_+^2$  and  $\sigma_-^2$  are effective index to extract the information contained in the electrostatic potential pattern over an entire molecular surface. These quantities indicate the molecule's capacity for noncovalent interactions through the regions of positive and negative potential on its surface. A variety of liquid, solid and solution phase

properties that depend upon molecular interactions can be represented analytically in terms of these quantities plus the surface area. The product  $\nu\sigma_{tot}^2$ , is especially important for representing properties that are related to the interactions of a molecule with others of its own kind [36].  $A_s^+$  represents the positive superficial area of a molecular, which reflects the size of the molecule, and  $\bar{V}_s$  represents the average molecular surface electrostatic potential.

At one time Mulliken charge of nitro group was applied to measure the sensitivity of nitro containing explosives, which reflects the detonation ability of self-oxidation reduction reactions [37], and was considered to evaluate the ability of self-oxidation reduction reactions in the organism, the more negative the  $q_{NO_2}$  is, the more difficultly the self-oxidation reduction reactions initiate. Solubility parameter  $\delta$  reflects the extent of the similarity of the same type or different type molecules, the smaller the change ( $\Delta\delta$ ), the more similar the molecules, abiding by the rule of “like dissolves like” or “like seeks like” [38]. Log  $P_{OW}$  is the logarithm of oil/water partition coefficient for a compound, which reflects the relative size of water-solubility and fat-solubility. These multidimensional knowledges will help us to further understand the toxicity of the nitro containing compounds and reveal the toxicology and provide scientific basis for the design, the toxicity reduction and control of novel nitro-compounds.

## 5 Conclusion

Twenty seven parameters of twenty eight nitro-compounds were computed, which covered the areas of molecular surface properties, solubility, dielectric properties, polarizability and diffusibility. The correlation coefficients between the acute toxicity (semi-lethal doses) of 28 kinds nitro-compounds and these parameters were computed and sequenced in descending order. The results indicate that molecular surface electrostatic potentials based  $\sigma_-^2$ ,  $\sigma_+^2$ ,  $\sigma_{tot}^2$ ,  $\nu\sigma_{tot}^2$ ,  $V_{S,min}$ ,  $\bar{V}_s$ ,  $A_s^+$ , solubility related Log  $P_{OW}$ ,  $\delta^2V_m^{0.45}$ ,  $\delta$ , dielectric constant  $\epsilon$ , surface tension  $\gamma$ , dipole moment  $\mu$ , Mulliken charges related  $q_{NO_2}$  were arranged in front. Genetic function approximations, which model heredity, variation, natural selection and survival of the fittest, were performed to screen these parameters,  $\sigma_+^2$ ,  $\sigma_-^2$ ,  $\nu\sigma_{tot}^2$ ,  $A_s^+$ ,  $\bar{V}_s$ ,  $q_{NO_2}$ , Log  $P_{OW}$  seven parameters were preserved to build the linear relation with toxicity ( $LD_{50}$ ). This work will not only lay a foundation for the toxicity of nitro-compounds, but also for other compounds, and it will provide basic references for the toxicology studies of compounds.

## Acknowledgement

We will acknowledge the financial support of National Natural Science Foundation of China (11372289); Development Fund of CAEP: 2014-1-075. Some computations were carried out in Institute of Computational Science, CAEP.

## References

1. V. Purohit and A. K. Basu, “Mutagenicity of nitroaromatic compounds,” *Chem. Res. Toxicol.*, vol. 13, pp. 673–692, 2000.
2. Y. Y. Liu, A. Y. H. Lu and R. A. Stearns, “In vivo covalent binding of [<sup>14</sup>C] trinitrotoluene to proteins in the rat,” *Chem.Bio. Inter.*, vol. 82, pp.1–19, 1992.
3. G. Sabbioni, “Hemoglobin binding of nitroarenes and quantitative structure-activity relationships,” *Chem. Res. Toxicol.*, vol. 7, pp.267–274, 1994.
4. G. Sabbioni and O. Sepai, “Comparison of hemoglobin binding, mutagenicity and carcinogenicity of arylamines and nitroarenes,” *Chimica*, vol. 49, pp.374–380, 1995.
5. N. Č. Aušra, M. Valė, Š. Jonas, M. Evaldas and Č. Narimantas, “Chemical aspects of cytotoxicity of nitroaromatic explosives: a review,” *CHEMIJA*, vol. 17, pp.34–41, 2006.
6. K.T. Chung, C. A. Murdock, Y. Zhou, S. E. Stevens, Y. S. Li, C. Wei, S.Y. Fernando and M. W. Chou, “Effects of the nitro-group on the mutagenicity and toxicity of some benzamines,” *Enviro.Mol. Mutagen.*, vol. 27, pp.67–74, 1996.

7. A. Colombo, E. Benfenati and M.Karelson, "The proposal of architecture for chemical splitting to optimize QSAR models for aquatic toxicity," *Chemosphere*, vol. 72, pp. 772–780, 2008.
8. C. Hansch, P. P. Maloney, T. Fujita and R. M. Muir, "Correlation of biological activity of phenoxyacetic acids with hammett substituent constants and partition coefficients," *Nature (London)*, vol. 194, pp.178–180, 1962.
9. C. Hansch and A. Kurup, "QSAR of chemical polarizability and nerve toxicity," *J. Chem. Inf. Comput. Sci.*, vol. 43, pp.1647–1651, 2003.
10. A. R. Katritzky, M. Kuanar, S. Slavov and C. D. Hall, "Quantitative correlation of physical and chemical properties with chemical structure: utility for prediction," *Chem. Rev.*, vol. 110, pp. 5714–5789, 2010.
11. S. Sild and M. Karelson, "A general QSPR treatment for dielectric constants of organic compounds," *J. Chem. Inf. Comput. Sci.*, vol. 42, pp. 360–367, 2002.
12. M. Qasim, Y. Kholod, L. Gorb, D. Magers, P. Honea and J. Leszczynski, "Application of quantum-chemical approximations to environmental problems: Prediction of physical and chemical properties of TNT and related species," *Chemosphere*, vol. 69, pp. 1144–1150, 2007.
13. T. J. Sheldon, C. S. Adjiman and J. L. Cordiner, "Pure component properties from group contribution: Hydrogen-bond basicity, hydrogen-bond acidity, Hildebrand solubility parameter, macroscopic surface tension, dipole moment, refractive index and dielectric constant," *Fluid Phase Equilibria*, vol. 231, pp. 27–37, 2005.
14. P. Politzer, Y. Ma, P. Lane and M. C. Concha, "Computational prediction of standard gas, liquid, and solid-phase heats of formation and heats of vaporization and sublimation," *Inter. J. Quantum Chem.*, vol. 105, pp. 341–347, 2005.
15. T. Singh and A. Kumar, "Static dielectric constant of room temperature ionic liquids: internal pressure and cohesive energy density approach," *J. Phys. Chem. B*, vol. 112, pp. 12968–12972, 2008.
16. S. J. Suresh and V. M. Naik, "Theory of dielectric constant of aqueous solutions," *J. Chem. Phys.*, vol. 116, pp. 4212–4220, 2002.
17. V. Vasilyev, "Determination of the effective dielectric constant from the accurate solution of the poisson equation," *J. Comput. Chem.*, vol. 23, pp. 1254–1265, 2002.
18. C. Caleman, P. J. van Maaren, M. Hong, J. S. Hub, L. T. Costa, and D. van der Spoel, "Force field benchmark of organic liquids: density, enthalpy of vaporization, heat capacities, surface tension, isothermal compressibility, volumetric expansion coefficient, and dielectric constant," *J. Chem. Theory Comput.*, vol. 8, pp. 61–74, 2012.
19. C. Hansch, W. E. Steinmetz, A. J. Leo, S. B. Mekapati, A. Kurup and D. Hoekman, "On the role of polarizability in chemical-biological interactions," *J. Chem. Inf. Comput. Sci.* Vol. 43, pp. 120–125, 2003.
20. Y. Zhao and Z. Chai, "Nanotoxicology-safe use foundation of nanomaterials," Beijing: Science Press, pp.1–297, 2010.
21. P. Politzer and J. S. Murray, "Computational prediction of condensed phase properties from statistical characterization of molecular surface electrostatic potentials," *Fluid Phase Equilibria*, vol. 185, pp. 129–137, 2001.
22. J. S. Murray, T. Brinck and P. Politzer, "Relationships of molecular surface electrostatic potentials to some macroscopic properties," *Chem. Phys.*, vol. 204, pp. 289–299, 1996.
23. P. Politzer, J. S. Murray and P. Flodmark, "Relationship between measured diffusion coefficients and calculated molecular surface properties," *J. Phys. Chem.*, vol. 100, pp. 5538–5540, 1996.
24. P. Politzer, Y. Ma, P. Lane and M. C. Concha, "Computational prediction of standard gas, liquid, and solid-phase heats of formation and heats of vaporization and sublimation," *Inter. J. Quantum Chem.*, vol. 105, pp. 341–347, 2005.
25. T. Brinck; J. S. Murray and P. Politzer, "Octanol/water partition coefficients expressed in terms of solute molecular surface areas and electrostatic potentials," *J. Org. Chem.*, vol. 58, pp. 7070–7073, 1993.
26. D. W. van Krevelen and K. te Nijenhuis, "Properties of polymers," Beijing: Science Press, pp.190–319, 2010.
27. C. Hansch, W. E. Steinmetz, A. J. Leo, S. B. mekapati, A. Kurup and P. Hoekman, "On the role of polarizability in chemical- biological interactions," *J. Chem. Inf. Comput. Sci.*, vol. 43, pp. 120–125, 2003.
28. T. J. Sheldon, C. S. Adjiman and T. L. Cordiner, "Pure component properties from group contribution, hydrogen-bond basicity, hydrogen-bond acidity, Hildebrand solubility parameters, macroscopic surface tension, dipole moment, refractive index and dielectric constant," *Fluid Phase Equilibria*, vol. 231, pp. 27–37, 2005.
29. A. D. Becke, "Density-functional thermochemistry. III. The role of exact exchange," *J. Chem. Phys.*, vol. 98, pp. 5648–5652, 1993.
30. C. Lee, W. Yang and R. G. Parr, "Development of the Colle-Salvetti correlation-energy formula into a functional of the electron density," *Phys. Rev. B*, vol. 37, pp. 785–789, 1988.
31. T. Lu and F. Chen, "Multiwfn: A multifunctional wavefunction analyzer," *J. Comput. Chem.*, vol. 33, pp. 580–592, 2012.

32. G. Liu, L. Ma and S. Xiang, "Physical Properties Data Handbook in Chemical and chemical Industry (Organic)," Beijing: Science Press, pp.226, pp. 465, pp.499, 2012.
33. J. H. Holland, "Adaption in natural and atificial systems," The University of Michigan Press, 1<sup>st</sup> ed, 2<sup>nd</sup> ed. Cambridge, MA: NIT Press, 1992.
34. Y. Wen, "Toxicity data of Medicines and Chemicals," Tianjin China: Tianjin Science and Technology Press, pp.1-458,1989.
35. <http://mathworld.wolfram.com/RampFunction.html>.
36. J. S. Murray and P. Politzer, "Statistical analysis of the molecular surface electrostatic potential: an approach to describing noncovalent interactions in condensed phases," *J. Mol. Struct. (Theochem)*, vol. 425, pp. 107-114, 1998.
37. C. Zhang, "Review of the establishment of nitro group charge method and its applications," *J. Hazar. Mater.* , vol. 161, pp. 21-28, 2009.
38. C. M. Hansen, "50 Year with solubility parameters-past and future," *Progress in organic Coating*, vol. 51, pp. 77-84, 2004.

## Appendix

**Table 9.** The full names and Abbreviated names of the related nitro compounds.

Abbreviated name	Systematic nomenclature
1-Cl-2-NB	1-chloro-2-nitrobenzene
1-Cl-4-NB	1-chloro-4-nitrobenzene
23-DNTul	2,3-dinitrotoluene
24-DNBP	2,4-dinitrophenol
24-DNTul	2,4-dinitrotoluene
25-DNTul	2,5-dinitrotoluene
26-DNTul	2,6-dinitrotoluene
2-NI	2-nitroimidazole
34-DNTul	3,4-dinitrotoluene
TNBP	2,4,6-trinitrophenol
m-DNB	1,3-dinitrobenzene
m-NBA	3-nitrobenzenamine
m-NTul	1-methyl-3-nitrobenzene
NB	nitrobenzene
NBu	1-nitrobutane
NEt	nitroethane
NMe	nitromethane
NPr	1-nitropropane
o-NBA	2-nitrobenzenamine
o-NBP	2-nitrophenol
o-NTul	1-methyl-2-nitrobenzene
p-DNB	1,4-dinitrobenzene
p-NBA	4-nitrobenzenamine
p-NBP	4-nitrophenol
p-NTul	1-methyl-4-nitrobenzene
Tetryl	N-2,4,6-Tetranitro-N-methylaniline
TNT	2,4,6-trinitrotoluene
LLM-105	2,6-diamino-3,5-dinitropyrazine-1-oxide