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Research paper

Prediction of the Density of Energetic Co-crystals: a Way to Design High Performance Energetic Materials

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Abstract: For designing a new energetic material with good performance, a knowledge of its density is required. In this study, the relationship between the densities of energetic co-crystals and their molecular structures was examined through a quantitative structure-property relationship (QSPR) method. The methodology of this research provides a new model which can relate the density of an energetic co-crystal to several molecular structural descriptors, which are calculated by Dragon software. It is indicated that the density of a co-crystal is a function of sp , OB , DU , n_{AT} , as well as several non-additive structural parameters. The new recommended correlation was derived on the basis of the experimental densities of 50 co-crystals with various structures as a training set. The R^2 or determination coefficient of the derived correlation was 0.937. This correlation provided a suitable estimate for a further 12 energetic co-crystals as a test set. Meanwhile, the predictive ability of the correlation was investigated through a cross validation method. Moreover, the new model has more reliability and performance for predicting the densities of energetic co-crystals compared to a previous one which was based on an artificial neural network approach. As a matter of fact, designing novel energetic co-crystals is possible by utilising the proposed method.

Keywords: energetic co-crystals, density, MLR method, artificial neural network, molecular design

Nomenclature:

Ant	Anthracene
AA	Anthranilic acid
ABA	Aminobenzoic acid
ANTA	5-Amino-3-nitro-1,2,4-triazole
AP	Ammonium perchlorate
3-AT	3-Amino-1,2,4-triazole
BC	Benzo-18-Crown-6
BL	γ -Butyrolactone
1-BN	1-Bromonaphthalene
9-BN	9-Bromonaphthalene
BPY	4,4'-Bipyridyl
BQN	Benzoquinone
BTF	Benzotrifuroxane
CL-20	2,4,6,8,10,12-Hexanitrohexaazaisowurtzitane
DADP	Diacetonediperoxide
DAT	3,4-Diaminotoluene
DBZ	Dibenzothiophene
DMB	1,4-Dimethoxybenzene
DMDBT	4,6-Dimethyldibenzothiophene
DMF	<i>N,N</i> -Dimethylformamide
DMINON	1,3-Dimethyl-2-imidazolidinone
DNB	1,3-Dinitrobenzene
DNBT	5,5'-Dinitro-3,3'-bi-1,2,4-triazole
DNDAP	2,4-Dinitro-2,4-diazapentane
3,4-DNP	3,4-Dinitropyrazole
DNPP	Dinitropyrazo[4,3-]pyrazole
DOX	1,4-Dioxane
DPYETA	1,2-Di(4-pyridyl)ethane
DPYETE	1,2-Di-4-pyridylethene
EDNA	Ethylenedinitramine
FA	4-Fluoroaniline
HMPA	Hexamethylphosphoramide
HMX	1,3,5,7-Tetranitro-1,3,5,7-tetrazocane
MATNB	1-Methylamino-2,4,6-trinitrobenzene
MHN	<i>D</i> -Mannitol hexanitrate
NAP	Naphthalene
NFQN	Naphthoquinone
NMP	<i>N</i> -Methylpyrrolidone

NNAP	1-Nitronaphthalene
Per	Perylene
Phe	Phenanthrene
Py	2-Pyrrolidone
PA	Phenothiazine
PDA	1,2-Phenylenediamine
PDCA	1,4-Piperazinedicarboxaldehyde
PNox	2-Picoline-N-oxide
PNO	Pyridine-N-oxide
PYDOXD	Pyrazine-1,4-dioxide
T2	Thieno[3,2-b]thiophene
TATB	1,3,5-Triamino-2,4,6-trinitrobenzene
TBTNB	1,3,5-Tribromo-2,4,6-trinitrobenzene
TITNB	1,3,5-Triiodo-2,4,6-trinitrobenzene
TNA	1-Amino-2,4,6-trinitrobenzene
TNAZ	1,3,3-Trinitroazetidine
TNB	1,3,5-Trinitrobenzene
TNP	2,4,6-Trinitrophenol (picric acid)
TNT	2,4,6-Trinitrotoluene
TODAAZ	7 <i>H</i> -tris-1,2,5-Oxadiazolo[3,4-b:3',4'-d:3'',4''-f] azepine
TT	Tetrathiafuvalene

Supporting Information (SI), *i.e.* computed variables of Equation 1 for all tested co-crystals are available at:

http://www.wydawnictwa.ipw.waw.pl/cejem/Vol-17-Number-1-2020/CEJEM_01055_SI.pdf

1 Introduction

Energetic materials (explosives, propellants and pyrotechnics), a class of compounds containing a great mass of stored energy, play a vital role in both military and civilian applications. Making progress in the field of energetic materials, as well as promoting novel high energy materials, is highly significant in the field of material science research. Nevertheless, obtaining a beneficial balance between low sensitivity and high detonation performance is indeed a challenge in the field of energetic materials, in order to remove the limitations placed upon the utilization of these materials and to make them of practical use in civilian and military applications. In order to modify

the properties of energetic materials, certain strategies have been applied, such as recrystallization, synthesizing new compounds or coating them using physical methods, in which each strategy may have its own deficiencies [1, 2]. As a matter of fact, high detonation performance and low sensitivity are not incompatible. The point is that these two properties can coexist using certain techniques or conditions. For instance, a moderate release of detonation heat is desirable with low sensitivity, rather than a large release of detonation heat. Small and planner molecules seem to possess less free space, which results in a reduction in sensitivity and may enhance the density and improve the detonation performance [3].

In recent years, a novel strategy to ameliorate the adverse properties of explosives has been devised, namely co-crystallization, which is also utilized in pharmaceutical science. A co-crystal is typically composed of two or more species in a definite molecular ratio, whose generation depends on noncovalent interactions, such as hydrogen bonding, halogen bonding and π -stacking. As a matter of fact, co-crystallization provides a new compound whose properties differ from those of the pure components in terms of density, melting/decomposition temperature, morphology, *etc.* [4-6]. It should be mentioned that the techniques mainly used for the synthesis of energetic co-crystals include solvent evaporation, solvent/nonsolvent crystallization, spray drying methods and resonant acoustic mixing crystallization [7-10].

According to the literature, some energetic co-crystals have been reported. For instance, Bolton *et al* [11] reported the CL-20:HMX co-crystal in a 2:1 molar ratio, and the results indicated that the sensitivity of the CL-20 was reduced to approximately that of HMX whilst the detonation performance of HMX was elevated to that of CL-20. In other work, by Yang *et al.* [12], the detonation properties of TNT as well as the safety of CL-20 were modified through co-crystallization in a 1:1 molar ratio. In addition, Xu *et al.* [7] reported CL-20:TATB in a 3:1 molar ratio, and the results again showed that the sensitivity of CL-20 was decreased. Zhang *et al.* [13] have successfully reported five energetic co-crystals of benzotrifuroxan (BTF). In other work, by Zhang *et al.* [14], an energetic co-crystal of TNB/NNAP was introduced. A series of nitrogen-rich energetic co-crystals of DNBT was reported by Matzger *et al.* [15]. Landenberger *et al.* [16] have also synthesized some co-crystals of HMX. Three insensitive energetic co-crystals of NNAP with TNT, picric acid and MHN were introduced by Hong *et al.* [17]. A CL-20:DNDAP energetic co-crystal was reported by Zhang *et al.* [18]. Landenberger *et al.* [19] modified the properties of DADP through co-crystallization. On the basis of the Kamlet-Jacobs equations, the detonation

performance of an energetic material, the detonation velocity and the detonation pressure, is related to its density. Thus the detonation pressure corresponds to the square of the density and the detonation velocity is linearly proportional to the density. Since the density is an essential parameter of an energetic material, experts have sought methods for devising high energy density materials [20].

As a matter of fact, identification of the molecular structure is the main target for realizing the performance of a molecule and this is due to the fact that there is a link between the structure and the energetic properties of a compound. Since performing laboratory tasks are usually time consuming and costly, a quantitative structure property relationship (QSPR) provides a method which provides data and information in a minimum of time and cost. In other words, this strategy could successfully predict the physicochemical properties of a compound [21]. There are numerous reports in this field. Zohari *et al.* [22] have predicted the density of azole-based compounds. Fathollahi *et al.* [23] have predicted the densities of energetic co-crystals through the QSPR approach using an artificial neural network. Moreover, Zohari *et al.* [24] have found a link between the densities and molecular structures of energetic azido compounds used as green plasticizers. Keshavarz *et al.* [25] have successfully predicted the densities of energetic compounds through their molecular structures. They have also introduced two novel correlations for the assessment of the crystal densities of hazardous ionic molecular energetic materials [26] and have estimated the properties of energetic materials, including sensitivity, and physical and thermodynamic properties [27]. In addition to the Kamlet-Jacob equations, Keshavarz *et al.* [28] have successfully predicted the detonation performance of CHNOFCl, aluminized and ammonium nitrate explosives. Jafari *et al.* [29] have introduced a model to predict the detonation performances of new tetrazole-based high energy density materials. They have also found a simple method for calculating the detonation pressure of ideal and non-ideal explosives [30]. Rahimi *et al.* [31] have estimated the densities of energetic materials on the basis of their molecular structures.

The purpose of the present work is to propose a novel correlation which can relate the densities of energetic co-crystals to their molecular structures through a multiple linear regression (MLR) method. A comparison is also made between the new model and the previous one [23], which was based on an artificial neural network approach. The correlation introduced in this work can afford a novel insight for designing new energetic co-crystals with good performance.

2 Materials and Methods

2.1 Descriptors, calculation and model building

In this research, the relationship between the densities of energetic co-crystals and their molecular structures was studied by the MLR method. In order to derive the best correlation between the densities and the molecular structures of energetic co-crystals, it is essential to peruse the molecular descriptors. In other words, a molecular descriptor can alter a molecular feature to a numerical variable. In this study, Dragon software was used for the molecular descriptor calculations and more than 1488 descriptors were selected, which included various types such as functional group counts, constitutional and geometrical properties and so forth. It should be mentioned that the molecular structures of the compounds were initially optimized due to the fact that the bond lengths and angles play a vital role in the computation of the descriptors. In addition, the chemical structures of the reported compounds were drawn using Version 16 of Chemdraw, and the MM2 molecular mechanics force field was used for optimizing the compounds [32-36].

The study has revealed that the most reliable correlation was derived utilizing the most relevant, significant influence descriptors on the density of the training set. Hence, the determination coefficient was assessed for predicting the reliability of the model, and the cross validation method was used to evaluate its predictive ability. Ultimately, the model was tested for some energetic co-crystals as a test set. The experimental data of the densities of the energetic co-crystals reported in Table 1 were extracted from the cited references.

The study has also revealed that it is possible to relate the density of an energetic co-crystal to an appropriate combination of the number of atoms, the value of the oxygen balance, the degree of unsaturation in the compound, as well as several non-additive structural parameters. Equation 1 demonstrates the derived relationship between the densities of the studied energetic co-crystals and their molecular descriptors through the multiple linear regression method [45].

$$\rho = 1913 + 0.017sp + 0.003OB + 0.008DU - 0.0128 n_{AT} + 0.136\rho^+ \quad (1)$$

where ρ is the density of the compound in $\text{g}\cdot\text{cm}^{-3}$, sp is sum of the atomic polarizabilities, OB is the value of the oxygen balance, DU is the degree of unsaturation of the compound, n_{AT} is the number of atoms and ρ^+ is a correction factor, which is defined below.

Table 1. Comparison of the predicted densities of energetic co-crystals with experimental data as α training set

No.	Co-formers	Ref.	Molar ratio	ρ_{exp} [g·cm ⁻³]	ρ_{cal} [g·cm ⁻³]	Dev.	ρ_{cal} [g·cm ⁻³] Ref. [23]	Dev.
1	CL-20:HMX	[11]	2: 1	1.945	1.980	-0.035	2.871	-0.926
2	CL-20:TNT	[12]	1:1	1.846	1.850	-0.004	1.872	-0.026
3	CL-20:DNB	[8]	1:1	1.880	1.847	0.033	1.848	0.032
4	CL-20:BTF	[37]	1:1	1.918	1.927	-0.009	1.961	-0.043
5	CL-20:TATB	[7]	3:1	1.960	2.016	-0.056	1.992	-0.032
6	CL-20:TODAAZ	[38]	1:1	1.922	1.836	0.085	1.868	0.054
7	CL-20:BQN	[39]	1:1	1.737	1.821	-0.084	1.774	-0.037
8	CL-20:NFQN	[39]	1:1	1.774	1.793	-0.019	1.765	0.009
9	CL-20:DMF	[39]	1:2	1.675	1.698	-0.023	2.387	-0.712
10	CL-20:BL	[39]	1:1	1.804	1.798	0.005	2.441	-0.637
11	CL-20:DOX	[39]	1:4	1.560	1.597	-0.037	2.378	-0.818
12	CL-20:HMPA	[39]	1:3	1.395	1.547	-0.152	2.410	-1.015
13	EDNA:BPY	[40]	1:1	1.452	1.487	-0.035	1.482	-0.030
14	EDNA:DPYETA	[40]	1:1	1.355	1.428	-0.073	1.481	-0.126
15	EDNA:DPYETE	[40]	1:1	1.434	1.559	-0.125	1.489	-0.055
16	EDNA:PYDOXD	[40]	1:1	1.640	1.692	0.052	2.034	-0.394
17	TNB:NNAP	[14]	1:1	1.492	1.649	-0.157	1.537	-0.045
18	TNB:BTF	[13]	1:1	1.806	1.881	-0.075	1.794	0.012
19	TNB:TIINB	[41]	2:1	2.203	2.132	0.071	2.201	0.002
20	DNB:T:ANTA	[15]	1:2	1.802	1.843	-0.041	2.246	-0.444
21	DNB:T:DNPP	[15]	1:1	1.833	1.876	-0.043	2.268	-0.435
22	DNB:T:3,4-DNP	[15]	1:2	1.824	1.887	-0.063	2.358	-0.534
23	DNPP:3-AT	[42]	1:2	1.700	1.726	-0.026	1.955	-0.255
24	BTF:TNT	[13]	1:1	1.805	1.849	-0.044	2.427	-0.622
25	BTF:TNAZ	[13]	1:1	1.834	1.888	-0.054	2.522	-0.688
26	BTF:TNA	[13]	1:1	1.884	1.874	0.010	2.446	-0.562

No.	Co-formers	Ref.	Molar ratio	ρ_{exp} [g·cm ⁻³]	ρ_{cal} [g·cm ⁻³]	Dev.	ρ_{cal} [g·cm ⁻³] Ref. [23]	Dev.	
27	BTF:MATNB	[13]	1:1	1.804	1.842	-0.038	2.476	-0.672	
28	HMX:PDA	[43]	1:1	1.599	1.653	-0.054	2.155	-0.556	
29	HMX:PDCA	[43]	1:1	1.579	1.655	-0.076	2.236	-0.657	
30	HMX:DMI	[44]	1:1	1.705	1.643	0.062	1.601	0.104	
31	HMX:PNox	[43]	1:2	1.533	1.662	-0.129	2.236	-0.703	
32	HMX:FA	[43]	1:1	1.634	1.676	-0.042	2.218	-0.584	
33	HMX:T2	[43]	1:1	1.709	1.757	-0.048	2.193	-0.484	
34	HMX:Py	[43]	1:1	1.603	1.684	-0.081	2.186	-0.583	
35	HMX:DAT	[43]	1:1	1.604	1.620	-0.016	2.186	-0.582	
36	TNT:1-BN	[43]	1:1	1.661	1.651	0.009	2.031	-0.370	
37	TNT:NAP	[43]	1:1	1.430	1.534	-0.104	1.919	-0.489	
38	TNT:9-BN	[43]	1:1	1.614	1.651	-0.037	2.031	-0.417	
39	TNT:Ant	[43]	1:1	1.449	1.518	-0.069	2.031	-0.582	
40	TNT:Per	[43]	1:1	1.464	1.526	-0.062	1.972	-0.508	
41	TNT:TT	[43]	1:1	1.632	1.778	-0.146	2.081	-0.449	
42	TNT:DBZ	[43]	1:1	1.477	1.593	-0.116	1.961	-0.484	
43	TNT:ABA	[43]	1:1	1.506	1.622	-0.116	2.037	-0.531	
44	TNT:AA	[43]	1:1	1.524	1.622	-0.098	2.039	-0.515	
45	TNT:DMB	[43]	1:1	1.435	1.559	-0.124	1.949	-0.514	
46	TNT:DMDBT	[43]	1:1	1.430	1.544	-0.114	1.950	-0.520	
47	TNT:PA	[43]	1:1	1.496	1.596	-0.100	1.970	-0.474	
48	TNT:T2	[43]	1:1	1.604	1.698	-0.094	1.994	-0.390	
49	TNT:PDA	[43]	1:1	1.509	1.574	-0.065	1.956	-0.447	
50	TNT:Phe	[43]	1:1	1.422	1.518	-0.096	1.936	-0.514	
					<i>RMSD</i> [g·cm ⁻³]				0.077
					<i>AAD</i> [g·cm ⁻³]				0.066

- (i) For an energetic co-crystal with more than 100 atoms, the value of ρ^+ is 1.0.
 (ii) The value of ρ^+ is 0.5 in following situations:
 (a) For the presence of iodine and bromine as halogen substituents.
 (b) If there is a nitrogen atom in a heterocycle with more than 5 members.
 (c) For the presence of the O-(CH₂)₂-O fragment in a ring.

The atomic polarizability is the charge dependent, effective atomic polarizability calculated by an empirical method, as shown in Equation 2.

$$\alpha_i = \alpha_i^0 - \alpha_i q_i \quad (2)$$

where α^0 , α and q_i are the effective atomic polarizability of a neutral atom, the charge coefficient and the net atomic charge, respectively [46]. The oxygen balance is the excess content of oxygen atoms, in percent, after oxidizing all of the atoms in the molecule which can be oxidized to produce H₂O, CO₂, MgO₂, Al₂O₃ and so on [47]. For example the oxygen balance of a molecule with the general formula C_aH_bN_cO_dCl_eS_f is defined by Equation 3.

$$OB = -\frac{32 \times \left\{ (a+f) + \frac{(b-e)}{4} - \frac{d}{2} \right\}}{Mw} \times 100 \quad (3)$$

where Mw is the molecular weight of the compound. The degree of unsaturation of a molecule is calculated by Equation 4.

$$DU = -\frac{\alpha}{2} + \frac{\gamma}{2} + \delta + \frac{3}{2}\varepsilon + 2\xi + 1 \quad (4)$$

where α , γ , δ , ε and ξ are the number of monovalent, trivalent, tetravalent, pentavalent and hexavalent atoms in the molecular formula, respectively [48]. The correlation coefficient matrix of all variables in the proposed model is shown in Table 2. Due to the nonexistence of overlaps between all of the selected descriptors of Equation 1, the selected descriptors are independent variables.

Table 2. The correlation matrix of the variables of Equation 1

Variable	sp	OB	DU	ρ^+	n_{AT}
sp	1	–	–	–	–
OB	0.1481	1	–	–	–
DU	0.04965	0.2121	1	–	–
ρ^+	0.8347	0.2529	0.3697	1	–
n_{AT}	0.8246	0.2248	0.4056	0.8158	1

3 Results and Discussion

3.1 Independent variables with increasing/decreasing functions

As seen in Equation 1, the coefficients of sp , OB and DU have positive signs, indicating that the higher values of these parameters augment the value of the density. It seems that, increasing the number of oxygen atoms in a compound or its degree of unsaturation will enhance the probability of intermolecular interactions and the formation of hydrogen bonds in a co-crystal, so that the value of the density will increase. Moreover, increasing atomic polarizabilities (sp) will enhance the interaction between polar sites with opposite charges, and thus will enhance the density. According to Equation 1, the coefficient of n_{AT} is negative, which indicates that higher values of this parameter diminish the value of the density. It should be mentioned that increasing the number of atoms will result in steric hindrance, so that molecules cannot easily approach each other, resulting in a reduction in density. For the existence of some molecular fragments listed in ρ^+ , this reduction may be augmented. Moreover, the estimated density of an energetic co-crystal by the new proposed correlation is consistent with experimental data.

3.2 Reliability and model validation

In accordance with the results obtained, the R^2 value or coefficient of determination of Equation 1 was 0.937. For an examination of the reliability of Equation 1, the deviation of the predicted densities from the experimental data was calculated. As represented in Table 1, the estimated densities of the energetic co-crystals have a root mean square deviation ($RMSD$) and an average absolute deviation (AAD) of 0.077 and 0.066 $\text{g}\cdot\text{cm}^{-3}$, respectively. In addition, Table 3 indicates the statistical parameters of Equation 1, which permits a comparison of the relative weights of the variables in the model. The standard error illustrates a measure of the precision of a predicted coefficient that can evaluate the precision over repeated measurements. The P-value was considered to assess the magnitude of an observed effect or variation. It must be noted that, for a P-value less than 0.05, this may verify that the observed effect is not due to accidental variations and the effect is of high significance. Hence, appropriate statistical parameters and a fairly good R^2 value, 0.937, confirms that the estimated results of the new correlation are consistent with the experimental data. As illustrated in Table 1, the predicted densities by the new model are compared with the results of the previous one [23], which was based on the artificial neural network. As can be seen from this comparison, the new model has greater reliability than the previous one.

Table 3. Standardized coefficients and some statistical parameters of Equation 1

Variable	Coefficient	Standard error	P-value	Lower 95%	Upper 95%
Intercept	1.913	0.038	$1.97 \cdot 10^{-40}$	1.836	1.990
<i>sp</i>	0.017	0.004	$2.19 \cdot 10^{-4}$	0.008	0.026
<i>OB</i>	0.003	0.000	$3.39 \cdot 10^{-23}$	0.003	0.003
<i>DU</i>	0.008	0.002	$7.30 \cdot 10^{-5}$	0.004	0.013
ρ^+	0.136	0.060	$2.82 \cdot 10^{-2}$	0.015	0.258
n_{AT}	-0.012	0.002	$1.27 \cdot 10^{-6}$	-0.017	-0.008

The cross validation method was utilized for an examination of the predictive ability of the proposed model. The leave-one-out cross validation (Q_{LOO})² and leave-many-out cross validation technique (Q_{LMO})² is applied to describe the internal validation. In this study, the (leave-20%-out) cross-validation was performed to verify the new model [49]. In Table 4 a further 12 energetic co-crystals with various molecular structures were used as a test set in an external validation of the equation obtained. As seen in Table 4, the new model provides relatively good results, which validates the reliability of the new proposed correlation. The estimated densities of energetic co-crystals by the new proposed correlation is compared with a previously reported model.

For the evaluation of the value of Q^2 of the internal validation and to better indicate the power of its predictability, Roy *et al.* [53] proposed two statistical parameters, as r_m^2 and $r_m'^2$ which are defined by Equations 5-8.

$$\overline{r_m^2} = \frac{(r_m^2 + r_m'^2)}{2} \quad (5)$$

$$\Delta r_m^2 = |r_m^2 - r_m'^2| \quad (6)$$

$$r_m^2 = r^2 \times \left(1 - \sqrt{(r^2 - r_0^2)}\right) \quad (7)$$

$$r_m'^2 = r^2 \times \left(1 - \sqrt{(r^2 - r_0'^2)}\right) \quad (8)$$

where r^2 and r_0^2 are the squared correlation coefficients between the cross validation predicted results and the experimental data, with and without intercept, respectively. The parameter $r_0'^2$ has the same meaning as r_0^2 , but uses

Table 4. Comparison of the predicted densities of energetic co-crystals with experimental data as a test set

No.	Co-crystal	Ref.	Molar ratio	$\rho_{\text{exp}} [\text{g}\cdot\text{cm}^{-3}]$	$\rho_{\text{cal}} [\text{g}\cdot\text{cm}^{-3}]$	Dev.	$\rho_{\text{cal}} [\text{g}\cdot\text{cm}^{-3}]$ Ref. [23]	Dev.
1	HMX:DNDAP	[16]	1:2	1.570	1.623	-0.053	1.674	-0.104
2	HMX:NMP		1:1	1.571	1.597	-0.026	1.598	-0.027
3	HMX:DMF			1.612	1.647	-0.035	1.616	-0.004
4	HMX:PNO	[50]		1.700	1.697	0.003	1.600	0.100
5	TNT:NNAP	[17]		1.539	1.548	-0.009	1.577	-0.038
6	TNT:TNB	[51]		1.640	1.735	-0.095	1.703	-0.063
7	NNAP:TNP	[17]		1.530	1.606	-0.076	1.631	-0.101
8	CL-20:DNDAP	[18]		1.871	1.968	-0.097	1.980	-0.109
9	DADP:TBTNB	[19]		1.936	2.014	-0.078	1.959	-0.023
10	DADP:MHN			2.260	2.262	-0.002	2.273	-0.013
11	NNAP:MHN	[17]	2:1	1.824	1.826	-0.002	1.689	0.135
12	AP:BC	[52]	1:1	1.396	1.445	-0.049	1.448	-0.052
	<i>RMSD</i> [$\text{g}\cdot\text{cm}^{-3}$]					0.085		0.331
	<i>AAD</i> [$\text{g}\cdot\text{cm}^{-3}$]					0.074		0.297

the reversed axes. Roy *et al.* [34] showed that for a model with a good power of predictability, the value of Δr_m^2 should be less than 0.2 and \bar{r}_m^2 should be more than 0.5. As can be seen in the Table 5, the values of \bar{r}_m^2 and Δr_m^2 were 0.882 and 0.031, respectively.

Table 5 represents the reliability and validation outcomes of this regression model and indicates that there is little difference between the Q^2_{LOO} , Q^2_{LMO} , Q^2_{EXT} and R^2 values of Equation 1. Therefore, the proposed correlation is a good model and has an ideal predictive power.

Figure 1 demonstrates the relation between the calculated and experimental density values of the energetic co-crystals that are presented in Tables 1 and 4, respectively. From this figure it is apparent that the new model has revealed a suitable linear fit to the experimental data, for both training and test sets.

Table 5. Validation of test results for the regression model obtained

Property	R^2	Q^2_{EXT}	Q^2_{LOO}	Q^2_{LMO}	$RMSD$ [g·cm ⁻³]	AAD [g·cm ⁻³]	\bar{r}_m^2	Δr_m^2
Equation 1	0.937	0.973	0.937	0.940	0.077	0.066	0.882	0.031

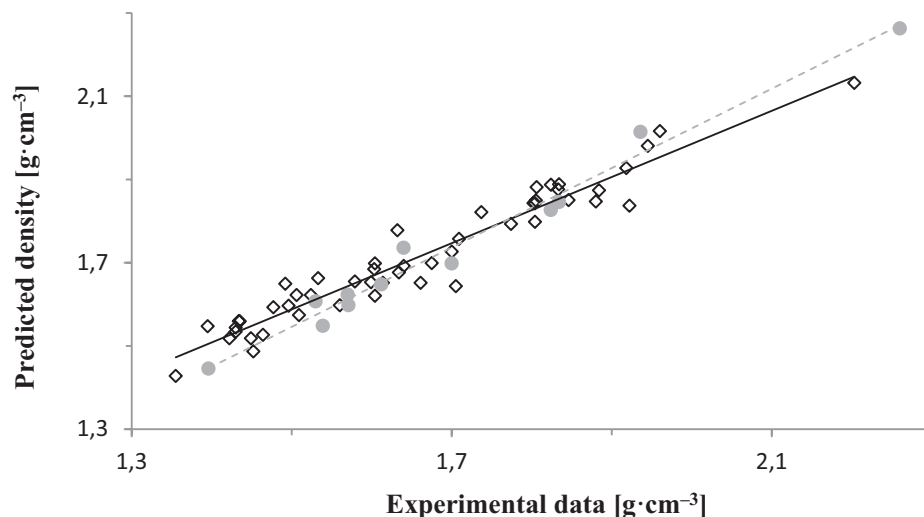


Figure 1. Predicted densities of energetic co-crystals vs. experimental data for both the training (\diamond) and the test (\bullet) sets; trend lines for the test set: solid line, $y = 0.9539x + 0.115$ ($R^2 = 0.9796$), and for training set: dashed line, $y = 0.7951x + 0.3953$ ($R^2 = 0.9341$)

4 Co-crystal Design with the Help of Equation 1

Since increasing the density of an energetic material increases its performance, on the basis of the Kamlet-Jacobs equations, estimation of the density of a designed co-crystal is necessary. For achieving this goal, the role of all variables in Equation 1 should be considered. For example the computed variables of Equation 1 for the seven high density co-crystals with densities greater than $1.90 \text{ g}\cdot\text{cm}^{-3}$, are illustrated in Table 6. Results obtained for 62 co-crystals are shown in Table S1 (see SI).

Table 6. Computed variables of Equation 1 for seven high density co-crystals

Co-crystal	$\rho_{\text{exp}} [\text{g}\cdot\text{cm}^{-3}]$	sp	OB	DU	ρ^+	n_{AT}
CL-20:HMX	1.945	58.16	-13.64	23	1	100
CL-20:BTF	1.918	33.72	-20.86	19	0	54
CL-20:TATB	1.960	78.48	-18.31	34	1	132
CL-20:TODAAZ	1.922	30.53	-55.70	13	0.5	50
TNB:TITNB	2.203	43.20	-33.04	20.5	0.5	54
DADP:TITNB	2.260	32.11	-43.30	8.5	1	40
DADP:TBTNB	1.936	28.19	-53.51	8.5	1	40

5 Conclusions

A novel and reliable correlation was derived to predict the densities of energetic co-crystals through the QSPR approach. It is indicated that the density of a co-crystal is a function of sp , OB , DU , and n_{AT} , as well as several non-additive structural parameters. According to the appropriate statistical results ($R^2 = 0.937$), the correlation has good reliability. The proposed model has $RMSD$ and AAD of 0.077 and $0.066 \text{ g}\cdot\text{cm}^{-3}$, respectively. So the predicted densities of the studied energetic co-crystals have good agreement with experimental data. The validity of the model was also investigated through external and internal validation. However there was little difference between the values of Q^2_{LOO} , Q^2_{LMO} , Q^2_{EXT} and R^2 , and thus the model has ideal predictability. Also by comparing the proposed model with another model which is based on the artificial neural network approach, it was confirmed that the new model has better reliability and power to estimate the densities of energetic co-crystals. The new model should help chemists in designing and developing novel energetic co-crystals with good performance.

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