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Effects of nitric acid concentration for nitration of fused [1,2,5]oxadiazolo[3,4-d]pyrimidine-5,7-diamine

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Nitration reactions are very often used for the selective synthesis of novel, high performing nitramine-based materials. Now nitration reactions of the fused 5,7-diamino pyrimidine derivative **1**, under different nitric acid concentrations were examined. Concentrated nitric acid gave selectively *N*-(5-amino-4,5-dihydro-[1,2,5]oxadiazolo[3,4-d]pyrimidin-7-yl)nitramide, **2**, while the fused ring nitrate salt, **4**, and ring open nitrate salt, **3** were obtained using low concentrations of nitric acid (<70%). In addition, the cesium salt of the fused nitramine derivative **5** was synthesized. All new compounds were isolated in high yields and comprehensively characterized by NMR, FTIR spectroscopy, and elemental analyses. The molecular structures of **2**, **3**, and **5** were analyzed by single X-ray crystallographic data. These compounds have high calculated heats of formation and high crystal densities. Detonation properties for compounds **2** and **3** were calculated using EXPLO5 software. Fused ring compound **2** (vD, 8549 m·s^{-1}; P, 29.62 GPa), and nitrate salt, **3** (vD, 8392 m·s^{-1}; P, 29.37 GPa) have superior detonation properties compared with TNT (vD, 7303 m·s^{-1}; P, 21.30 GPa). In addition, electrostatic potentials, two-dimensional (2D)-fingerprints, and Hirshfeld surfaces analysis were used to predict the sensitive properties of compounds **2** and **3**. The experimental sensitives suggest possible applications with insensitive energetic applications.

Introduction

Fused ring compounds have been widely used in the design and synthesis of novel energetic materials (EMs).[1-5] Because of high conjugation, the aromatic skeleton lying in a plane and π−π interactions, fused ring structures are in high demand in the field of EMs.[6,7] They have a planar molecular configuration that provides layer-by-layer compact stacking resulting in lower sensitivity to mechanical stimuli than non-planar energetics. A large number of heteroatoms in fused ring compounds increases the positive enthalpy of formation, and improves density, and energetic performance of the resultant materials. Five membered nitrogen-rich fused heterocycles have been extensively studied and found to have increasingly high density, and good oxygen balance with better detonation properties than traditional nitramine-based explosives.[8-11] However, owing to the energetic functional groups, they are unstable and extremely sensitive to impact and friction.[12,13] Therefore, it is important to design novel energetics with an ideal combination of energy and sensitivity.

2,4,6-Triamino-1,3,5-trinitrobenzene (TATB) is the finest example of a powerful, highly stable, and insensitive energetic molecule due to having strong intermolecular and intramolecular hydrogen bonding interactions which lead to the formation of a closely packed system. It is extremely insensitive to shock, heat, or impact.[14] TATB is less toxic due to having low vapor pressure and low solubility in many organic solvents, which further helps for long-term storage in the design of strategic weapons. Inspired by the excellent stability of TATB, several research communities worldwide focused on developing new planar heterocyclic, insoluble, and hydrogen bond-rich materials.[15] Fused bicyclic compounds with a combination of nitro and amino groups are alternative designs for insensitive high performing materials.[16] In particular, fused compounds such as [5,6]-bicyclic energetic materials have been well studied (Figure 1).[17-21] Most designs are fused bicyclic rings of triazole-triazine, tetrazole-tetrazine, tetrazole-tetrazine, and tetrazine-tetrazine.[22,23] Among these fused energetic materials, a few furazan-pyrazine-based energetic materials have been designed having a tricyclic ring skeleton with a combination of furazan-pyrazine-triazole, furazan-pyrazine-furazan, and furazan-pyridine-tetrazole.[24-27] They are commonly functionalized with amino, *N*-oxide, nitro, and nitramine groups to increase the density and detonation properties. Most of these materials have excellent energetic properties compared with 1,3,5-trinitro-1,3,5- triazacyclohexane (RDX), 1,3,5,7-tetranitro-1,3,5,7-tetrazocane (HMX), but most are less thermostable and highly sensitive to mechanical stimuli.

As shown in Scheme 1, the nitration of the fused [5,6]-bicyclic heterocyclic compounds with di or tri amino groups has been studied using fuming nitric acid, which results in unexpected nitramine products. The amine group at C-7 does not participate in nitration to form nitramine **(b)** or to be

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hydrolyzed to give a deamination product or carbonyl derivative **(d)**.[28,29] Very recently, we have reported a mono-*N*-oxidation of heterocycle-fused pyrimidines, [1,2,5]oxadiazolo[3,4-d]pyrimidine-5,7-diamine (**1**) with improved density, and detonation properties.[30] They have ultrahigh thermostability due to the presence of the fused pyrimidine ring with diamino groups. They display strong hydrogen bonding, which results in high density, and are insensitive to mechanical stimuli. Here, we report the synthesis of a fused pyrimidine with a mono nitramine **2** by the nitration of **1** using 100% nitric acid. Based on the literature reports,[28,29] we expected the amine at the C-5 to be highly reactive and to undergo the formation of C-5 nitramine. Surprisingly, the amine at the C-5 position had not participated in the nitration, which suggests fused-five membered rings may control the reaction to lead the formation of C-7 nitramine. Also, it is interesting that the nitramine derivative **2** that is formed is the structural isomer of carbonyl derivative **d**. The nitration of **1** with less concentrated nitric acid (<70%) gave unexpected energetic salts or fused pyrimidine ring-opened products in quantitative yields. All new derivatives were characterized by advanced spectroscopic techniques. Molecular structures of mono nitramine **2**, nitrate salt **3**, and cesium salt **5** were analyzed by single X-ray structuring. The experimental density, thermostabilities, and calculated energetic properties of all new compounds are discussed in this manuscript.

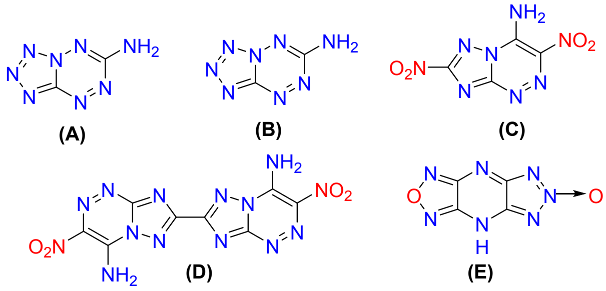
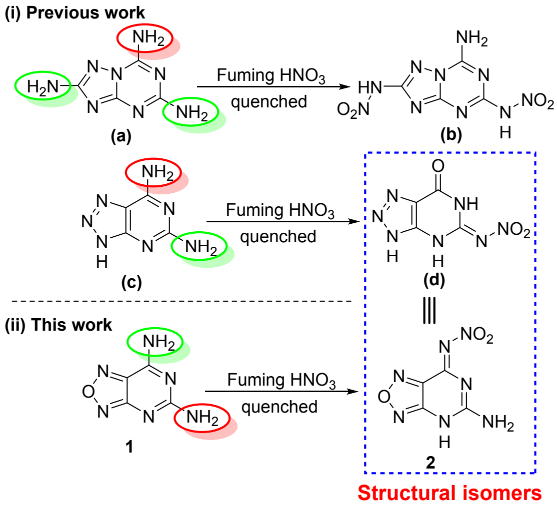


Figure 1. Selected fused [5,6]-bicyclic energetic materials.

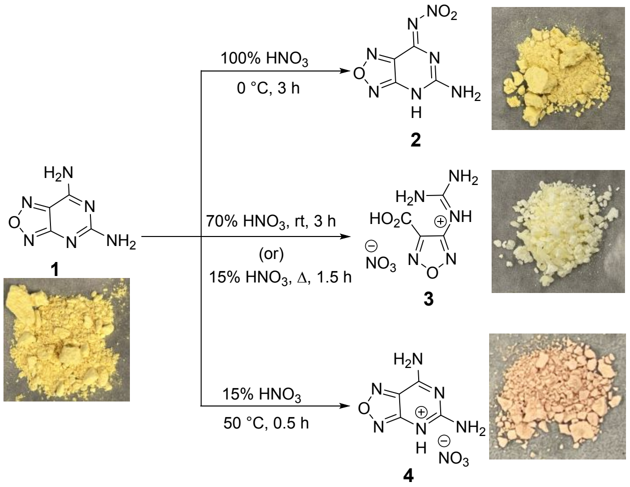


Scheme 1. Fused [5,6]-bicyclic compounds nitramine formation

Results and discussion

Synthesis

The starting compound **1** was prepared by using a literature procedure through the reaction of 6-aminopyrimidine-2,4-diamine with sodium nitrite and acetic acid followed by oxidative cyclization.[31] Then, diamine derivative **1** was reacted with freshly distilled 100% nitric acid at 0°C to give mono nitramine derivative **2** in 88% yield. The reaction of diamine, **1** with 70% concentrated nitric acid at room temperature or with 15% nitric acid at reflux temperature gave an unexpected fused ring open product of nitrate salt, **3** in high yields. The reaction of **1** with 15% nitric acid at reflux for 0.5 h, gave the nitrate salt **4** in 85% yield (Scheme 2).[30] We believe that the concentration of the nitric acid is highly important for the selective outcome of the nitration products from the diamine compound, **1**.



Scheme 2. Synthesis of energetic compounds, **2-4**.

In dilute nitric acid, diamine derivative **1** undergoes nitration and hydrolyzes to give nitrate salt, **3.** We proposed a plausible reaction mechanism to understand the reaction sequence (Scheme 3). In the first step, the nitramine derivative **2** will be formed in 70% nitric acid at room temperature or 15% nitric acid at reflux temperature. Under both reaction conditions, the diamine compound, **1** is converted into nitramide derivative, **2** (**a-c**). Later, it underwent protonation (reaction intermediate, **RMI**) followed by hydrolysis (**RMII**) due to the high amount of aqueous nitric acid in the reaction mixture. Additional protonation (**RMIII**) and hydrolysis release ring-opening product of nitrate salt (**RMIV**), which further undergo rearrangement to give the nitrate salt, **3**.

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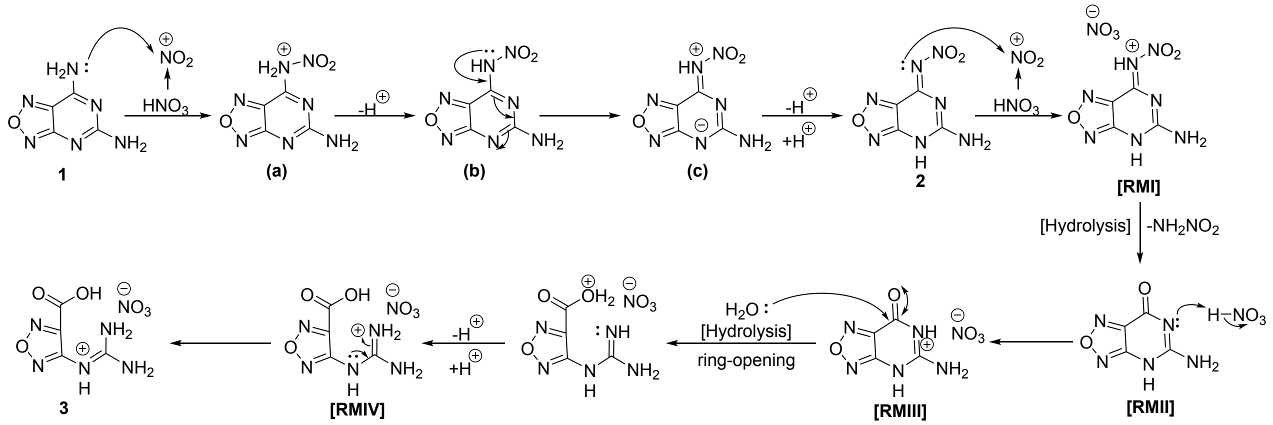
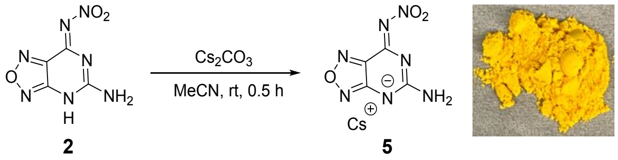


Scheme 3. Proposed reaction mechanism for compound **3** from compound **1**

The nitric acid concentration is critical in obtaining the nitramine compound **2.** Since **2** is isolated by quenching the reaction in ice-cold water, it is stable in an aqueous medium. Reactions with aqueous bases such as 28% aqueous ammonia or 50% hydroxylamine or 80% hydrazine monohydrate led to the formation of extremely unstable or hygroscopic products. Surprisingly, the reaction with an aqueous solution of cesium carbonate in acetonitrile at room temperature gives high yields of the cesium salt of fused nitramine derivative, **5** (Scheme 4). The size of the cesium cation is much larger than the corresponding cations of the ammonium bases, which helps stabilize the fused nitramine anion ring skeleton.



Scheme 4. Synthesis of energetic salt, **5**

Single crystal X-ray analysis

All new molecules were characterized by multinuclear NMR (^1H, ^{13}C, and ^{15}N), FTIR, DSC, and elemental analysis. Molecular structures of **2**, **3**, and **5** were characterized by single crystal X-ray data (Electronic Supplementary Information). All these crystals were obtained by slowly evaporating saturated solutions of acetonitrile-water mixtures, and their structures were obtained neat. Compound **2** crystallized in the form of yellow needles with a calculated density of 1.929 g·cm^{-3} at 100 K, in an orthorhombic space group *Pnma* and with four molecules per unit cell. As is seen in Figure 2a, the amine and nitramide groups are coplanar with the fused-pyrimidine ring skeleton. In contrast, the oxygen atoms of the nitro group are perpendicular to the fused ring skeleton. The torsion angles of N(2)–O(1)–N(3)–C(3) = 0.0 (1), N(2)–C(2)–C(3)–N(4) = 180.0 (1)°, and N(6)–N(5)–C(1)–N(1) = 0.0 (1)°. The bond length of N6–O2 is 1.214 (2) Å, comparable to those reported in the literature. The entire molecule is conjugated with a delocalized electron system accomplished by extensive hydrogen bonding (Figure 2b). The fused-pyrimidine ring molecule has six hydrogen bonds with four adjacent molecules. In the crystal packing structure, fused-ring molecules are held together by intermolecular hydrogen

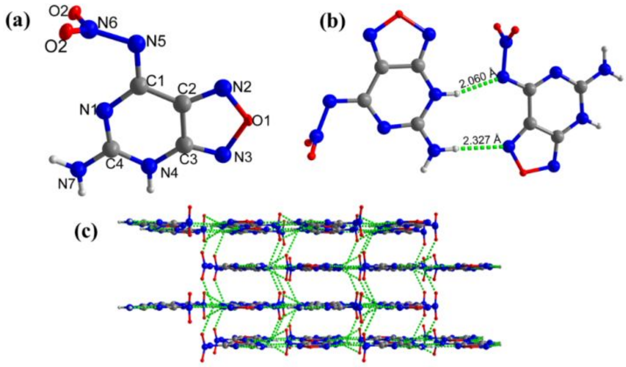


Figure 2. (a) Molecular structure of **2.** (b, c) Intermolecular hydrogen bonding and packing diagram of **2** viewed up the c axis. Green dotted lines indicate strong hydrogen bonding.

bonds in a two-dimensional lattice. Further, their layer-by-layer interactions form a three-dimensional framework (Figure 2c).

Compound **3** crystallized in an orthorhombic space group *Pbca* (Z = 8) symmetry, with a calculated density of 1.814 g·cm^{-3} at 100 K. As depicted in Figure 3a, the crystal structure of **3** is the combination of nitrate and 4-carboxy-*N*-(diaminomethylene)-1,2,5-oxadiazol-3-aminium ions. The bond lengths in the nitrate ion, 1,2,5-oxadiazole ring, and other functional groups are typically single and double bonds. The bond length of C(1)–C(3) = 1.4828 (17), C(2)–N(3) = 1.3829 (17), and both the carboxylic acid and *N*-(diaminomethylene)-aminium groups are coplanar with a 1,2,5- oxadiazole ring. The torsion angles of N(1)–C(1)–C(2)–N(3) = -178.90 (11), N(1)–C(1)–C(3)–O(2) = -0.66 (17), and N(2)–O(1)–N(1)–C(1) = 0.11 (13)°. The planar structure is supported by intramolecular hydrogen bonds, N(3)–H(3)···O(3), and N(3)–H(4B)···N(2). The extensive intermolecular hydrogen bonds of nitrate anion and its corresponding cation results in a two-dimensional layer network (Figure 3b).

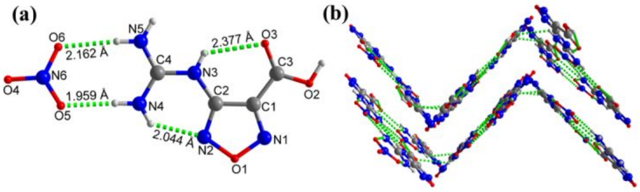


Figure 3. (a) Molecular structure of **3**. (b) Ball-and-stick packing diagram of **3** viewed up the a axis. Green dotted lines indicate strong hydrogen bonding.

Compound **5** crystallizes in the triclinic space group with *P-1* (Z = 2) symmetry with a calculated density of 2.617 g·cm^{-3} at 100 K. The fused pyrimidine ring anion skeleton is nearly planar with amine and nitramide groups. Unlike the structure of **2**, the oxygen atoms in the nitro group are relatively coplanar with the fused-ring skeleton. The torsion angles of O(1)–N(2)–C(4)–C(3) = 178.9 (4), C(3)–N(4)–C(2)–N(3) = 1.3 (6)°, C(3)–N(4)–C(2)–N(5) = -179.4 (3)°, and N(7)–N(6)–C(3)–N(4) = 1.6 (6)°. In the crystal packing, each fused-ring anion skeleton has seven coordination sites with cesium atoms, while one of the Cs atoms is in coordination with O1 (Figure 4a). The hydrogen atoms of amine are in hydrogen bonding with two adjacent molecules, which forms the two-dimensional network. In the crystal packing diagram, the cesium atoms are bound in the expansion of the 2D layer and connect the layers in between to form three-dimensional frameworks (Figure 4b).

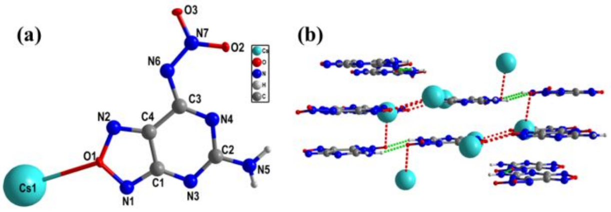


Figure 4. (a) Molecular structure of **5**. (b) Ball-and-stick packing diagram of **5** viewed up the a axis. Green dashed lines indicate strong hydrogen bonds.

Two-dimensional (2D)-fingerprints of the crystals and the Hirshfeld surfaces were analyzed for compounds **2**, **3**, and **5** using the Crystalexplorer17.5 software program (Figure 5).[32] These analyses help understand the characteristics of sensitivity and high energy performance of explosive material. As shown in Figure 5a-c, the red and blue colored areas on the Hirshfeld surfaces denote high and low close contact populations, respectively. The red sites are due to the intermolecular hydrogen bond interactions, and the blue spots for C···O, C···C, and C···N bond interactions, which explain the π–π stacking. In 2D fingerprint plots, sharp spikes for **2** (Figure 5d), **3** (Figure 5e), and **5** (Figure 5f) denote the high contribution of intermolecular hydrogen bonds (O···H and N···H interactions). Compound **3** has a large number of hydrogen bond (HB) interactions (55.8%) between the nitrate ion and its corresponding cation, while the cesium salt **5** (23.7%) has lower HB interactions. Compound **2** also has relatively high HB interactions of 47.0%. The selected molecules of **2**, **3**, and **5** have overall

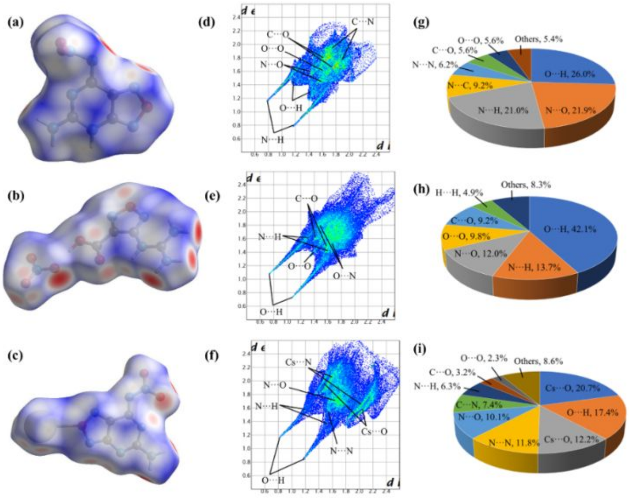


Figure 5. (a,b,c) Hirshfeld surface analysis for the selected molecules of **2**, **3** and **5** (white, distance *d* = van der Waals distance; blue, *d* > van der Waals distance; red, *d* < van der Waals distance). (d,e,f) 2D fingerprint plots in crystal stacking for **2**, **3** and **5** with individual atomic contact percentage contribution of the associated Hirshfeld surfaces (g,h,i). The percentage of atomic contact contributions in **2**, **3** and **5**.

C⋯O, N⋯C, and N⋯N bond interactions of 21.0, 14.5, and 22.4%, respectively, indicating the existence of π–π stacking between the molecules. Owing to the fused ring skeletons in compounds **2** and **5**, there is a high percentage of interactions between the two ring molecules compared with compound **3**. The higher percentages of O⋯O bond interactions in the crystal packing, the sensitivity of the material increases. In the case of compound **3**, it has a slightly higher 9.8% of O⋯O bond interactions compared with compound **2** (4.7%), which suggests an increased sensitivity in compound **3** compared to the fused ring compound **2**.

Physicochemical and detonation properties

The thermal behavior of **2**, **3**, and **5** were analyzed by DSC scans with a heating rate of 5 °C min^{-1} under an N_2-gas atmosphere. The onset exothermic temperature of **2** (T_d = 196.29 °C) is relatively higher than compound **b** (T_d = 189 °C), but it is less stable compared to its structural isomer, **d** (T_d = 242 °C). Compound **5** exhibits excellent thermostability of 250.71 °C due to the planar structure and salt formation. With the planar structure and strong hydrogen bonding between neighboring fused nitrogen atoms of amino groups on the pyrimidine ring, mono nitramine compound **2** has high thermostability compared with the nitrate salt, **3** (T_d = 179.78 °C). Just as for thermostability, mechanical sensitivity experiments toward impact and friction were determined to be insensitive to mechanical stimuli (*IS* >40 J, *FS* > 360 N).[33]

The experimental densities were measured using a gas pycnometer at 25 °C. These materials have excellent densities and are comparable with some well-known materials. Compound **2** has a high density of 1.88 g·cm^{-3}, because of the fused planar structure and strong hydrogen bonding between the amino group of the pyrimidine ring with adjacent molecules. The nitrate salt **3** has a density of 1.77 g·cm^{-3}, which is higher than TNT (1.65 g·cm^{-3}), while compound **5** has a higher density of 2.52 g·cm^{-3}. Heats of formation of **2** and **3** were calculated by using the Gaussian 03 suite of programs with isodesmic reactions (ESI).[34] Compound **2** and **5** have high positive heats of formation of 395.9 kJ·mol^{-1}/1.98 kJ·g^{-1}, and 228.7 kJ·mol^{-1}/0.69 kJ·g^{-1}, while the nitrate salt **3** has a much lower value of 37.9 kJ·mol^{-1}/0.16 kJ·g^{-1}. After determining the densities and heats of formation, the energetic properties were calculated using EXPLO5 (version 6.06).[35] Compound **2** (*v*D, 8549 m ·s^{-1}; P, 29.62 GPa) has high detonation properties compared with nitrate salt, **3** (*v*D, 8392 m ·s^{-1}; P, 29.37 GPa) and both compounds have superior to TNT (*v*D, 7303 m ·s^{-1}; P, 21.30 GPa). Compound **2** with high positive heat of formation and high density, we expected it might have comparable detonation properties with its structural isomer **d**. But, it has relatively low detonation properties comparable with high dense compound **d**. The high density in compound **d** was caused by extensive hydrogen bonding in its crystal packing, which helped increase its thermostability (Table 1).

The molecular electrostatic potential (ESP) is an excellent tool to explain molecular sensitivities. The ESP plots of compounds **2** and **3** were evaluated using Multiwfn 3.8 and VMD 1.9.1 (Figure 6).[36] The impact sensitivity of an energetic compound is closely related to its surface ESP. The larger positive potential areas with higher ESP values often have high sensitivities.[37] The red and blue colored regions indicate the positive and negative potentials, and the orange and cyan spheres indicate the maxima and minima of ESP, respectively. Mononitramine compound **2** has a high electronegative area (blue) due to the nitroamino group and a less electropositive area (red) (Figure 6a). In nitrate salt **3**, the electrostatic potentials are almost equally shared (Figure 6b). Compared with **2**, the nitrate salt, **3** exhibits higher ESP maximum values, especially in amino group areas (+112.0 vs. +55.3). Therefore, nitrate salt **3** is more sensitive toward impact than the fused mono nitramine derivative **2**.

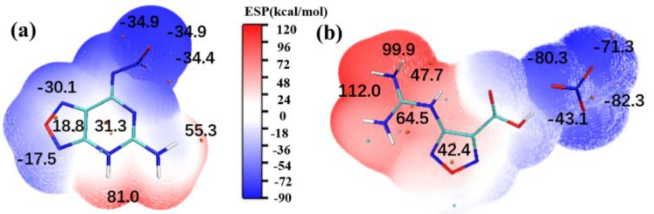


Figure 6. Calculations of ESP for compound **2** (a), and **3** (b).

Table 1. Energetic properties and detonation parameters

Comp	ρ[a] (g·cm^{-3})	*vD* [b] (*m s*$^{-1}$)	*P*[c] (GPa)	ΔH_f[d] (*kJ mol*$^{-1}$/*kJ g*$^{-1}$)	T_{dec}[e] (°C)	IS^f [J]	FS^g [N]
2	1.88	8549	29.62	395.9/1.98	196	>40	>360
3	1.77	8392	29.37	37.9/0.16	179	>40	>360
4[h]	1.82	8563	30.10	346.3/1.61	247	>40	>360
5	2.58	7284	26.44	228.7/0.69	250	>40	>360
b[i]	1.84	8787	34.20	544.9/2.13	189	>40	>360
d[j]	1.94	8845	32.54	223.0/1.13	242	36	348
TNT[k]	1.65	7303	21.30	-59.0/-0.26	295	15	353

[a] Density measured by a gas pycnometer at 25 °C; [b] Calculated detonation velocity; [c] Calculated detonation pressure; [d] Calculated molar enthalpy of formation in solid state; [e] Temperature of decomposition (onset); [f] Impact sensitivity; [g] Friction sensitivity; [h] Ref 30; [i] Ref 24; [j] Ref 31; [k] Ref 7.

Conclusion

In summary, we demonstrated the nitration of diamino fused pyrimidine derivative **1** and isolated a mono nitramine using highly concentrated nitric acid. It is the first example of the nitration of the C-7 amine of fused 5,7-diamino pyrimidine derivatives. Also, the high yields of nitrate salt, **4** and fused ring open nitrate salt **3** were obtained using low 70% or concentrated nitric acid. All new derivatives were characterized using multi-nuclear NMR, FT-IR spectroscopy, and elemental analysis. The molecular structures of **2**, **3**, and **5** were analyzed by a single X-ray crystallography data. These compounds are relatively thermally stable (>179 °C) and insensitive to impact and friction (IS>40 J, FS>360 N) due to planar structures and the inter- and intra-molecular hydrogen bonding interactions between the two molecules. These new compounds with high experimental densities and calculated detonation properties may find useful applications as insensitive and high-performing energetic materials.

Author Contributions

A. K. C. and Y. T. investigation, methodology, and initial characterization of this work. R. J. S. X-ray data collection and solved the structures. A. K. C. and J. M. S. conceptualisation, manuscript writing – review and editing, supervision.

Conflicts of interest

There are no conflicts to declare.

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