The Journal of Organic Chemistry

Subscriber access provided by Bibliothèque de l'Université Paris-Sud

Article

Intermolecular weak hydrogen-bonding (Het-H-N/O): an effective strategy for the synthesis of monosubstituted 1,2,4,5-tetrazine-based energetic materials with excellent sensitivity

Yingle Liu, Gang Zhao, Qiong Yu, Yongxing Tang, Gregory
H Imler, Damon A. Parrish, and Jean'ne M. Shreeve

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.9b02484 • Publication Date (Web): 21 Nov 2019

Downloaded from pubs.acs.org on November 23, 2019

Just Accepted

"Just Accepted" manuscripts have been peer-reviewed and accepted for publication. They are posted online prior to technical editing, formatting for publication and author proofing. The American Chemical Society provides "Just Accepted" as a service to the research community to expedite the dissemination of scientific material as soon as possible after acceptance. "Just Accepted" manuscripts appear in full in PDF format accompanied by an HTML abstract. "Just Accepted" manuscripts have been fully peer reviewed, but should not be considered the official version of record. They are citable by the Digital Object Identifier (DOI®). "Just Accepted" is an optional service offered to authors. Therefore, the "Just Accepted" Web site may not include all articles that will be published in the journal. After a manuscript is technically edited and formatted, it will be removed from the "Just Accepted" Web site and published as an ASAP article. Note that technical editing may introduce minor changes to the manuscript text and/or graphics which could affect content, and all legal disclaimers and ethical guidelines that apply to the journal pertain. ACS cannot be held responsible for errors or consequences arising from the use of information contained in these "Just Accepted" manuscripts.

is published by the American Chemical Society. 1155 Sixteenth Street N.W.,
Washington, DC 20036

Published by American Chemical Society. Copyright © American Chemical Society.
However, no copyright claim is made to original U.S. Government works, or works
produced by employees of any Commonwealth realm Crown government in the course
of their duties.

Intermolecular weak hydrogen-bonding (Het-H-N/O): an effective strategy for the synthesis of monosubstituted 1,2,4,5-tetrazine-based energetic materials with excellent sensitivity

Yingle Liu,[a,b], Gang Zhao, [b] Qiong Yu,[b] Yongxing Tang,[b] Gregory H. Imler,[c] Damon A. Parrish,[c] Jean'ne M. Shreeve*[b]*

[a] School of Chemistry and Environmental Engineering, Sichuan University of Science & Engineering, 180 Xueyuan Street, Huixing Lu, Zigong, Sichuan 643000 (China)

[b] Department of Chemistry, University of Idaho, Moscow, ID 83844-2343, USA.

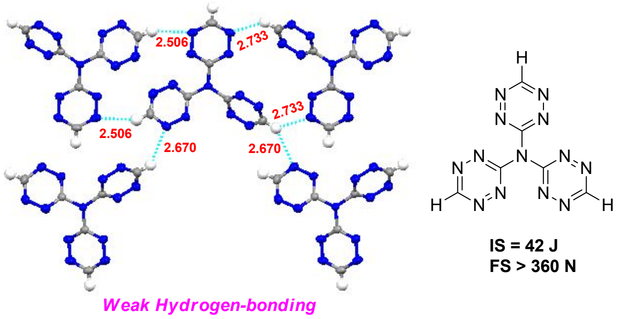
[c] Naval Research Laboratory, Code 6910, 4555 Overlook Ave., Washington, DC 20375 USA.

E-mail: liuyingleyou@163.com; jshreeve@uidaho.edu

ABSTRACT: A series of monosubstituted 1,2,4,5-tetrazine-based energetic materials were effectively synthesized, and fully characterized with IR, multinuclear NMR, and elemental analysis. Heats of formation and detonation performances were determined using Gaussian 03 and EXPLO5 v6.01 programs, which show that **5** and **9** as secondary explosives have detonation velocities superior to the current secondary-explosive benchmark, TATB. Importantly, compounds **2**, **5** and **9** were first characterized with single-crystal X-ray diffraction and Hirshfeld surface calculations, and some intermolecular weak hydrogen bonding (Het-H-N/O) among these compounds illustrate the relationship between these weak interactions and excellent sensitivity of energetic materials. This design method for next-generation energetic materials by incorporating intermolecular weak hydrogen bonds may be of future importance.

KEYWORDS: Energetic materials, Tetrazine, Weak hydrogen-bonding, Sensitivity, N-oxide.

Abstract graphic



Intermolecular weak hydrogen-bonding improve the sensitivity of energy materials.

INTRODUCTION

Over many years, nitrogen-rich energetic compounds have attracted significant interest from many researchers because they can be widely used as propellants,[1,2] explosives,[3-6] airbag inflators[7-8] and pyrotechnics[9] in satisfying the growing demand for military and civilian uses. The combination of highly endothermic heterocycles with energetic units has become a widely accepted concept for the design of nitrogen-rich energetic compounds in the past few decades.[10,11] Among them, energetic units, including nitro, nitroamino, dinitromethyl, and trinitromethyl groups, can greatly enhance the oxygen balance and the density of materials which leads to an increase in detonation performance. However, compounds with these explosophoric groups nearly always exhibit high sensitivities towards destructive stimuli and have low thermal decomposition temperatures. A major challenge for designing modern nitrogen-rich energetic materials is to overcome the sensitivity versus performance trend observed for conventional explosives. [12,13]

1,2,4,5-Tetrazines, also known as *s*-tetrazines, has been studied for more than a hundred years.[14-16] Some 1,2,4,5-tetrazine-based energetic materials which contain various substituents at positions 3 and 6 show desirable properties associated with high N-atom content, positive heats of formation, and thermal stabilities.[17,18] Particularly, some N-oxide 1,2,4,5-tetrazine-based nitrogen-rich energetic compounds, including 6-aminotetrazolo[1,5-b]-1,2,4,5-tetrazine-7-N-oxide,[19,20] 2,4-di-N-oxide 1,2,4,5-tetrazine,[21] 6-amino-[1,5-b]tetrazolo-1,2,4,5-tetrazine mono-N-oxide and di-N-oxide,[22,23] have excellent detonation performance. In addition, in recent years, some 1,2,4,5-tetrazine-based fused rings with outstanding density, insensitivity and detonation performance due to the larger conjugated system and better stacking efficiency have been synthesized and have attracted the wide attention of researchers.[24,25] In contrast, while a considerable amount of work has demonstrated that monosubstituted 1,2,4,5-tetrazine is a suitable starting material for the synthesis of heterocyclic compounds that can be used as biologically active agents for bioorthogonal chemistry, very limited studies on monosubstituted 1,2,4,5-tetrazine-based energetic materials have been reported.[26,27] Recently fused ring-based energetic materials that were synthesized from monosubstituted 1,2,4,5-tetrazine, **III**, show excellent insensitivity toward external stimuli (IS = 31 J, FS > 240 N) which is much better than the value for **I** (IS = 3 J, FS > 5 N) and **II** (IS = 1 J, FS > 40 N) which were obtained from disubstituted 1,2,4,5-tetrazine (Fig 1).[28]

Considering that different substituents on the 1,2,4,5-tetrazine ring have important effects on the mechanical sensitivity of energetic materials and that we were inspired by the excellent thermal behavior of monsubstituted tetrazine-based energetic compounds,[26] we now report the synthesis of 4,4'-(diazene-1,2-diyl)bis(N-(1,2,4,5-tetrazin-3-yl)-1,2,5-oxadiazol-3-amine) (**2**), 1,2-bis(4-((1,2,4,5-tetrazin-3-yl)amino)-1,2,5-oxadiazol-3-yl)diazene oxide (**3**), N-6-amino-1,2,4,5-tetrazine 1,5-dioxide (**5**), and tri(1,2,4,5-tetrazin-3-yl)amine (**9**) (Figure 1). Some of them show good detonation velocities and pressures, and excellent decomposition temperatures and sensitivities. More importantly, we obtained three monosubstituted 1,2,4,5-tetrazine crystals containing no solvent molecules which illustrate the relationship between the intermolecular weak

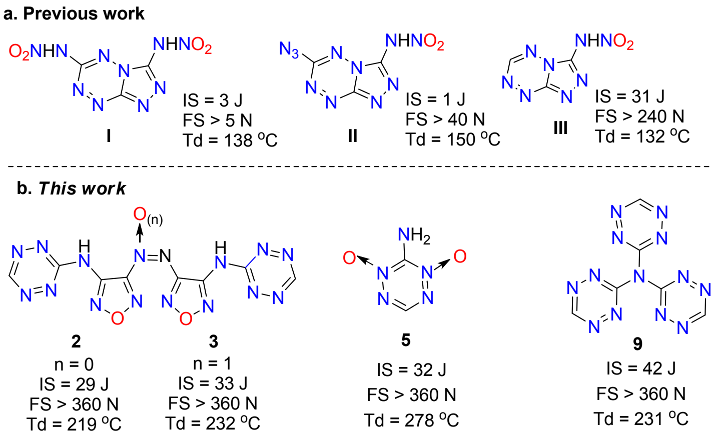


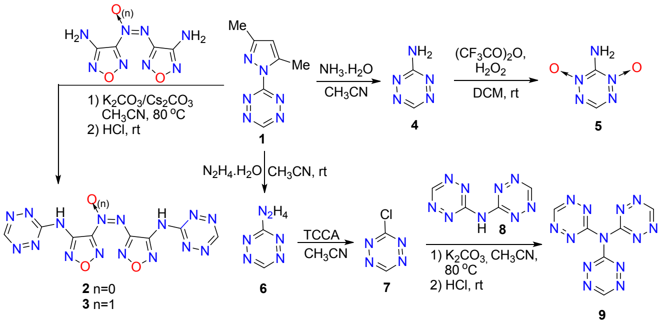
Figure 1. Monosubstituted tetrazine-based energetic materials in previous studies and this study.

hydrogen-bonding and mechanical sensitivity of energetic materials. It is our intention to provide more information for designing next-generation energetic materials with excellent sensitivity and thermal stability.

RESULTS AND DISCUSSION

Synthesis

The synthetic pathways to monosubstituted energetic materials **2, 3, 5** and **9** are shown in Scheme 1. 3-(3,5-Dimethyl-1H-pyrazol-1-yl)-1,2,4,5-tetrazine (**1**) was synthesized according to the literature.[26] It was treated with 4,4'-(diazene-1,2-diyl)bis(1,2,5-oxadiazol-3-amine) or 1,2-bis(4-amino-1,2,5-oxadiazol-3-yl)diazene oxide in acetonitrile with K_2CO_3 or Cs_2CO_3 as base, respectively, to obtain the corresponding 4,4'-(diazene-1,2-diyl)bis(N-(1,2,4,5-tetrazin-3-yl)-1,2,5-oxadiazol-3-amine) (**2**) and 1,2-bis(4-((1,2,4,5-tetrazin-3-yl)amino)-1,2,5-oxadiazol-3-yl)diazene oxide (**3**). Compounds **5** and **9** were first synthesized by Hiskey[21] and Rudakov,[26] respectively, but crystal structures, and the physicochemical and energetic properties



Scheme 1. Preparation of monosubstituted 1,2,4,5-tetrazine energetic materials **2**, **3**, **5** and **9.**

of these compounds have not been reported until now. Now we have improved the synthetic methods for **5** and **9**. As shown in Scheme 1, via replacing the hard-to-obtain compound peroxytrifluoroacetic acid with a mixture of the common compounds trifluoroacetic acid anhydride and hydrogen peroxide, 1,2,4,5-tetrazin-3-amine was easily oxidized to the yellow N-6-amino-

1,2,4,5-tetrazine 1,5-dioxide (**5**) in high yield. In addition, taking into account the toxicity of chlorine gas and the inconvenience of its use, trichloroisocyanuric acid (TCCA) was used as a chlorinating reagent to transform 3-hydrazinyl-1,2,4,5-tetrazine (**6**) into 3-chloro-1,2,4,5-tetrazine (**7**). Finally, **7** was reacted with di(1,2,4,5-tetrazin-3-yl)amine (**8**) to give the desired tri(1,2,4,5-tetrazin-3-yl)amine (**9**).

Spectral studies of compounds

Compounds **2**, **3**, **5** and **9** were fully characterized by ^{1}H and $^{13}C\{^{1}H\}$ NMR and IR spectral analysis as well as by elemental analysis. In the $^{13}C\{^{1}H\}$ NMR spectra of compounds **2**, **3** and **9**, two signals were observed in the range of 162.6–164.6 ppm for C3 and 150.7–158.2 ppm for C6 corresponding to the different types of carbon atoms in the monosubstituted 1,2,4,5-tetrazine rings. However, due to the electron-donating effect of the oxygen atoms, the carbon signals for the monosubstituted 1,2,4,5-tetrazine ring in **5** shifts to high field. The carbon resonance of C3 in **5** was observed at 144.5 ppm and the carbon resonance of C6 at 149.4 ppm.

Single crystal X-ray diffraction studies

Single-crystals suitable for X-ray diffraction studies were obtained by slow evaporation of a mixed solution of DMSO (**2, 5**), DMF (**5**) or CH_3CN (**9**). Crystal structures of these compounds are given in Figure 2-5. The detailed crystallographic refinement parameters and structural data for these compounds can be found in the SI.

Compound **2** crystallizes in the monoclinic space group $P2_{1/}c$ with a density of 1.665 g cm^{-3} at 20 °C (Figure 2). The two furazan rings, two secondary amino groups and the azo group are nearly coplanar, which is shown by the torsion angles N(7)–C(8)–C(12)–N(13) = 4 .07(3)° and N(13)–N(13)–C(12)–C(8) = -1.12(2)°. However, there is a twist angle between the plane of two

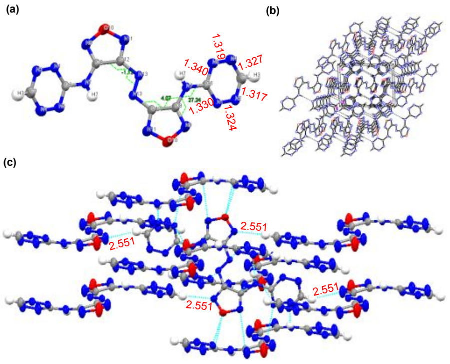


Figure 2. (a) Molecular structure of **2**. (b) Packing diagram of **2**. (c) Weak hydrogen-bonding of **2**.

monosubstituted tetrazine rings and two furazan rings, which is seen by the torsion angle C(6)–N(7)–C(8)–N(9) = 27.24(2)°. The lengths of the N–C, N=C, N-N or N=N bonds in the tetrazine ring (C(6)–N(5): 1.340 Å; N(5)-N(4): 1.319 Å; N(4)-C(3): 1.327 Å; C(3)–N(2): 1.317 Å; N(2)-N(2): 1.317 Å; N(2)-N(1): 1.324 Å; N(1)-C(6): 1.330 Å) are slightly different, and the average bond length in the monosubstituted 1,2,4,5-tetrazine ring is 1.326 Å which is shorter than the values of all the other 3,6-disubstituted tetrazines. For example, 1.335 Å in N^3, N^6-di(1H-1,2,4-triazol-5-yl)-1,2,4,5-tetrazine-3,6-diamine perchlorate salt[17] and 1.336 Å in N^3,N^6-bis(3-azido-1H-1,2,4-triazol-5-yl)-1,2,4,5-tetrazine-3,6-diamine.[18] Unexpectedly, in addition to the hydrogen bond formed by the secondary amine with nitrogen atoms and weak interaction formed among C, N and O atoms in different molecules, a weak hydrogen bond (Het-H-N)[29,30] exists between the C-H of a monosubstituted 1,2,4,5-tetrazine and a nitrogen atom belonging to the furan ring of another molecule. From this view, the monosubstituted tetrazine ring should be more aromatic and less sensitive toward external stimuli than the 3,6-disubstituted tetrazine.

A colorless crystal of **5**•DMSO was obtained by slow evaporation of a DMSO solution that contained **5** (Figure 3). **5**·DMSO crystallizes in the orthorhombic $P2_12_12_1$ space group with four molecules in the unit cell with a calculated density of 1.567 g cm^{-3} at 293 K. Considering the weak interactions and the arrangement of the molecules in space are very important parameters for understanding the properties of energetic materials. A crystal which contains no solvent molecules is often very important in determining the properties of energetic materials.[31] Subsequently, **5** was dissolved in various other solvents, including MeOH, CH_3CN or DMF, and a single crystal was grown by slowly evaporating the corresponding solvent. Ultimately, a yellow crystal of **5** which contained no solvent was successfully obtained from the solution of DMF (Figure 4).

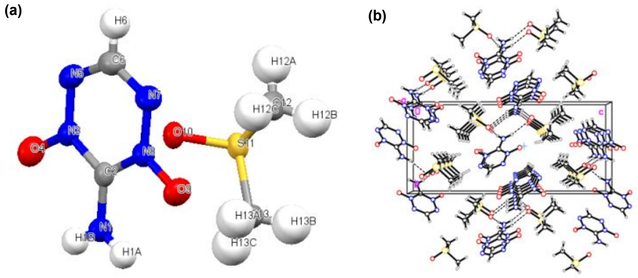


Figure 3. (a) Molecular structure of **5·DMSO**. (b) Packing diagram of **5·DMSO**.

Compound **5** is in the orthorhombic Iba2 space group with eight molecules in the unit cell and a crystal density of 1.770 g cm^{-3} at 20 °C. The H, O, C and N atoms in **5** are all nearly planar, which is supported by the torsion angles H(4A)–N(4)–C(3)–N(5) = -0.1(0)°, C(3)–N(5)–N(7)–C(8) = 0.3(4)°, H(8)-C(8)-N(9)-N(2) = -179.5(6)° and O(1)-N(2)-C(3)-N(4) = 1.6(5)°. The average length of the N–C, N=C, N-N or N=N bonds in the monosubstituted 1,2,4,5-tetrazine ring are 1.339 Å, falling within the range of similar 3,6-disubstituted 1,2,4,5-tetrazine rings (1.335 Å -1.344 Å). However, the average length of the N-oxide bond (1.271 Å) in **5** is longer than all of the reported similar N-oxide bonds in 3,6-disubstituted 1,2,4,5-tetrazine rings (1.259 Å -1.269 Å).[22, 23]

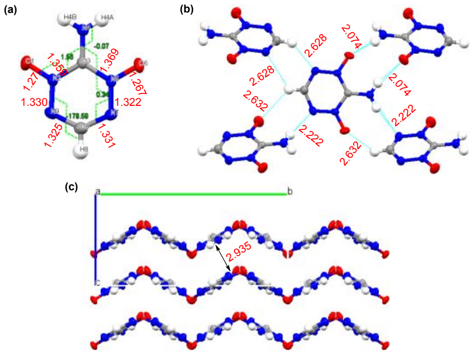


Figure 4. (a) Molecular structure of **5**. (b) Hydrogen bond and weak hydrogen bonds in the crystal of **5**. (c) Packing diagram of **5**.

It is easy to speculate that the electron density in monosubstituted 1,2,4,5-tetrazine 1,5-oxides is higher than the corresponding value in 3,6-disubstituted 1,2,4,5-tetrazine 1,5-oxides. Additionally each NH_2 group interacts with H(4), O(6), N(9) in two other molecules through hydrogen-bonding, and C-H in the monosubstituted 1,2,4,5-tetrazine ring interacts with the N or the O atom in the other two molecules via two intermolecular weak hydrogen bonds (Het-H-N/O). The lengths of these two Het-H-N/O bonds are 2.632 Å and 2.628 Å, which are longer than the values of other normal hydrogen bonds (2.074 Å - 2.222 Å). Under the influence of these interactions, five molecules create a wave-like stacking arrangement (interlayer distance = 2.935 Å) (Fig. 4). As a result, the packing coefficient of **5** is 0.73.

Tri(1,2,4,5-tetrazin-3-yl)amine (**9**) crystallizes in the monoclinic P21/c space group with four formula units per cell and a crystal density of 1.729 g cm^{-3} at 293 K (Figure 5). The lengths of the N–C, N=C, N-N or N=N bonds in the monosubstituted 1,2,4,5-tetrazine ring (C(8)–N(13): 1.329 Å; N(13)-N(12): 1.324 Å; N(12)-C(11): 1.321 Å; C(11)–N(10): 1.322 Å; N(10)-N(9): 1.321 Å; N(9)-C(8):1.331 Å) are nearly the same, so this compound should possess very good aromaticity. Unexpectedly, the three 1,2,4,5-tetrazine rings interact with each other with strong intramolecular N–N interactions in the range of 2.749-2.910 Å. Because of this kind of directional interaction, the three 1,2,4,5-tetrazine rings are distorted with a dihedral angle C(8)–

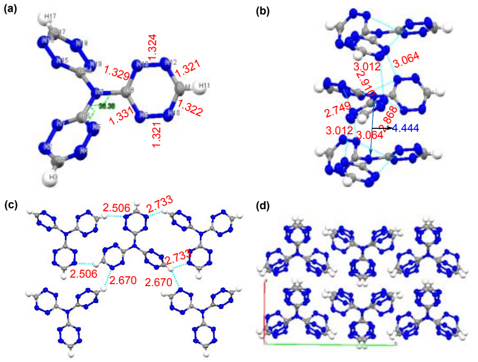


Figure 5. (a) Molecular structure of **9**. (b) N–N interactions in the crystal of **9**. (c) N-H weak hydrogen-bonding in crystal of **9**. (c) Packing diagram of **9**.

N(7)–C(6)–N(5) = 36.38(3)°. In the vertical direction, there are four N–N interactions between the monosubstituted 1,2,4,5-tetrazine ring of one molecule and two other molecules in the range of 3.012-3.064 Å, and the distance between two center nitrogen atoms is 4.444 Å. In the horizontal direction, there are six Het-H···N weak hydrogen bonds between the 1,2,4,5-tetrazine ring of one molecule and other four molecules in the range of 2.506-2.733 Å. Based on these weak interactions, the crystal **5** is stacked like a superimposed flower with a packing coefficient of 0.72.

Physicochemical and energetic properties

The onset decomposition temperatures and thermal stabilities of compounds **2**, **3**, **5** and **9** were evaluated using differential scanning calorimetric (DSC) measurements with a heating rate of 5 °C min^{-1} (Table 1). All of compounds (**2**, **3**, **5** and **9**) decomposed without melting. Among them, the monosubstituted 1,2,4,5-tetrazine-1,5-dioxide (**5)** exhibits the best thermal stability with an onset decomposition temperature of 278 °C, which is higher than the corresponding values of all reported 3,6-disubstituted 1,2,4,5-tetrazine-1,5-dioxides (T_d: 110-252 °C)[22,23] and N-oxide 1,2,4,5-tetrazine-based fused rings (T_d: 140-185 °C).[19,20] This can be explained by the higher electron density and better aromaticity in monosubstituted 1,2,4,5-tetrazine-1,5-dioxides

Table 1. Energetic properties of compounds **2, 3, 5 and 9.**

Comp.	$T_{\text{dec}}{}^{a}$ (°C)	P^{b} (g cm^{-3})	$\Delta H_f{}^{c}$ (kJ mol^{-1}/kJ g^{-1})	Dv^{d} (m s^{-1})	P^{e} (GPa)	IS^{f} (J)	FS^{g} (N)
2	219	1.67	1654.3/4.65	8075	25.1	29	>360
3	232	1.75	1517.6/4.08	8401	28.3	33	>360
5	278	1.77	237.2/1.84	8640	30.2	32	>360
9	231	1.73	1386.2/5.39	8322	26.4	42	>360
TNT[h]	295	1.65	-59.4/-0.26	6881	19.5	15	>353
TATB[i]	360	1.930	-154.2/-0.60	8114	31.2	50	360
LLM-116[j]	178	1.90	96.3/0.56	8488	34.2	>40	360
RDX [k]	204	1.80	70.3/0.36	8795	34.9	7.4	120

[a] Decomposition temperature (onset). [b] Density measured by a gas pycnometer at 25 ℃. [c] Calculated molar enthalpy of formation in solid state. [d] Calculated detonation velocity. [e] Calculated detonation pressure. [f] Impact sensitivity. [g] Friction sensitivity. [h] Ref.32. [i] Ref. 33. [j] Ref. 34. [k] Ref. 35.

than the corresponding value in 3,6-disubstituted 1,2,4,5-tetrazine-1,5-dioxides. Other compounds have thermal decomposition temperatures which fall between 219 °C and 232 °C.

The experimental densities of all monosubstituted 1,2,4,5-tetrazine compounds were obtained by using a gas pycnometer (25 °C) and found to range between 1.67 and 1.77 g cm^{-3}. These are higher than the density of TNT (1.65 g cm^{-3})[32] which is a classic explosive, and the density (1.77 g cm^{-3}) of 6-amino-1,2,4,5-tetrazine-1,5-dioxide, **5**, is comparable to the currently used typical HEDMs, such as RDX (1.80 g cm^{-3}). The remarkably higher density of **5** may be attributed to its planar conjugated system and a wave-like stacking arrangement. Heats of formation of **2**, **3**, **5** and **9** were calculated with Gaussian 03 software[36] based on isodesmic reactions (SI). Due to the presence of a large number of N–N or C–N bonds in the monosubstituted 1,2,4,5-tetrazine rings, all compounds have relatively high positive heats of formation (≥ 1.84 kJ g^{-1}) exceeding the values for TNT (-0.26 kJ g^{-1}),[32] TATB (-0.60 kJ g^{-1}),[33] LLM-116 (0.56 kJ g^{-1})[34] and RDX (0.36 kJ g^{-1})[35] markedly.

Based on the measured densities and calculated heats of formation, detonation performances of **2**, **3**, **5** and **9** were calculated by using EXPLO5 (v 6.01).[37] As shown in Table 1, the calculated detonation velocities are found in the range 8075 to 8640 m s^{-1}. Among them, **5** has the highest detonation velocity (8640 m s^{-1}) which exceeds that of LLM-116 (8488 m s^{-1}) and is comparable to RDX (8795 m s^{-1}). The detonation pressures fall between 25.1 and 30.2 GPa with values in some cases exceeding TNT (19.5 GPa) and approaching TATB (31.2 GPa). Sensitivities toward impact (IS) and friction (FS) were obtained using BAM technology.[38] Not surprisingly these four monosubstituted 1,2,4,5-tetrazine compounds exhibit low impact and friction sensitivities (IS, 29–42 J; FS > 360 N) because of the good aromaticity of the monosubstituted 1,2,4,5-tetrazine rings and intermolecular weak hydrogen bonds. It should be noted that tri(1,2,4,5-tetrazin-3-yl)amine (**9**) has the lowest sensitivities (IS = 42 J; FS > 360 N), and the monosubstituted 1,2,4,5-tetrazine-1,5-oxide, **5**, shows lower sensitivities (IS = 32 J; FS > 360 N) than the corresponding values of all reported 3,6-disubstituted 1,2,4,5-tetrazine-1,5-dioxides (IS: 3-27 J; FS: 10-360 N)[22] and N-oxide 1,2,4,5-tetrazine-based fused rings (IS: 1.5-10 J; FS: 10-160 N),[19,20] but it is slightly higher than 3-amino-6-(3,5-dimethylpyrazol-l-yl)-1,2,4,5-tetrazine 2,4-dioxide (IS = 35 J; FS > 360 N)[11a] and the recently reported polycyclic N-oxides based on 3,6-disubstituted-1,2,4,5-tetrazine (IS: 18.5-78.4 J; FS>360 N).[23]

To gain further information about sensitivity of this series of compounds, weak interactions in representative compounds **5** and **9** were investigated via Hirschfeld surfaces and 2D fingerprint plots.[39] As shown in Fig. 6a and b, the surface of **5** is approximately horizontal and the surface of compound **9** is slightly distorted**.** Furthermore, some red dots mainly caused by the intermolecular normal hydrogen bonding and/or weak hydrogen bonding (Het-H-N) were found on the edges of each surface. The populations of these weak interactions can also be directly achieved by the 2D fingerprint plots. From Fig. 6c and d, the normal hydrogen bonding and weak hydrogen bonding possess 56.0% of the total weak interactions for **5** (Figure S22), and weak hydrogen bonding possesses 44.3% of the total weak interactions for **9.** Remembering that the intermolecular hydrogen bonding has a stabilizing action toward impact and friction,[28,40] it is readily understood that **5** and **9** have good sensitivities (IS ≥ 32 J, FS > 360 N). In addition, the sum of proportions of N/N, N/C and C/N for **9** is 50.6% which mainly comes from the intramolecular interaction a a among three monosubstituted 1,2,4,5-tetrazine rings and intermolecular interactions caused by different monosubstituted 1,2,4,5-tetrazine rings. Mechanical stimuli toward **9** from any orientation can be buffered. So it is not surprising that the **9** exhibits superior sensitivity values (IS = 42J; FS > 360N).

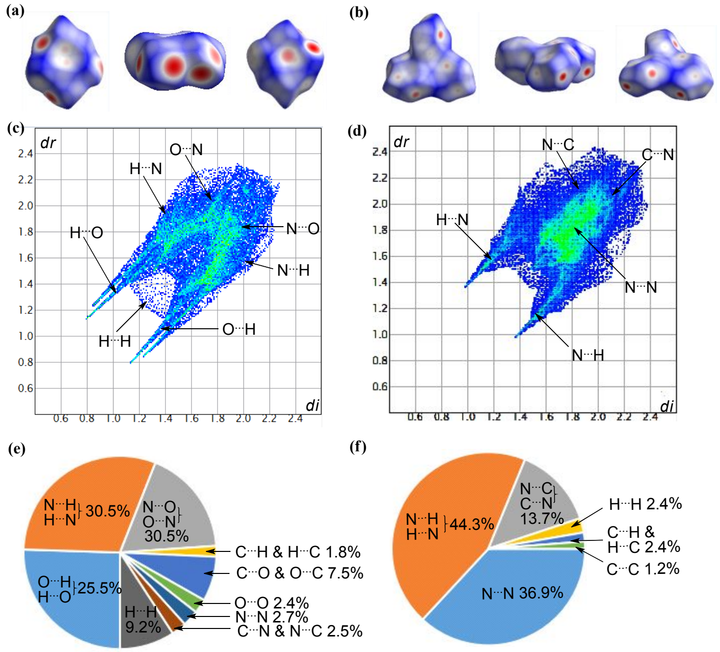


Figure 6. Two-dimensional fingerprint plots in crystal stacking for **5** and **9** as well as the associated Hirshfeld surfaces. Images (a) and (b) show the Hirshfeld surfaces that use color coding to represent the proximity of close contacts around **5** and **9** molecules (white, distance *d* equals the van der Waals distance; blue, *d* exceeds the van der Waals distance; red, *d* is less than the van der Waals distance). The fingerprint plots in crystal stacking for **5** (c) and **9** (d). In images (e) and (f), the individual atomic contacts percentage contribution to the Hirshfeld surface are shown in the pie graphs for **5** and **9**, respectively.

CONCLUSION

In conclusion, a series of monosubstituted 1,2,4,5-tetrazine-based energetic materials was synthesized. All the new compounds were fully characterized with IR, multinuclear NMR, and elemental analysis. Three monosubstituted 1,2,4,5-tetrazine structures were confirmed via X-ray diffraction. Some intermolecular weak hydrogen bonds (het-H-N/O) among these compounds have been discovered. Based on this weak hydrogen bonding, these derivatives of monosubstituted 1,2,4,5-tetrazine exhibit excellent low sensitivity. Especially, **9**, similar to TATB, is insensitive to mechanical stimuli and its calculated detonation velocities and pressures are comparable to the current secondary-explosive benchmark TATB. The monosubstituted 1,2,4,5-tetrazine 1,5-dioxide (**5)** was found to possess good density, excellent thermal stability, and good detonation performance which outperform commonly used explosives, for example, TNT, TATB, and LLM-116. Compounds **5** and **9** have significant application potential as secondary explosives.

EXPERIMENTAL SECTION

General methods

All reagents were purchased from AKSci, VWR or Alfa Aesar in analytical grade and were used as supplied. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker 300 MHz NMR spectrometer or 500 MHz (Bruker AVANCE 500) nuclear magnetic resonance spectrometer. Chemical shifts for ^{1}H, and ^{13}C NMR spectra are reported relative to $(CH_3)_4Si$. $[D_6]$DMSO was used as a locking solvent unless otherwise stated. Infrared (IR) spectra were recorded on an FT-IR spectrometer (Thermo Nicolet AVATAR 370) as thin films using KBr plates. Density was determined at room temperature by employing a Micromeritics AccuPyc II 1340 gas pycnometer. Melting and decomposition (onset) points were recorded on a differential scanning calorimeter (DSC, TA Instruments Q2000) at a scan rate of 5

^{o}C min^{-1}. Elemental analyses (C, H, N) were performed on a Vario Micro cube Elementar Analyser. Impact and friction sensitivity measurements were made using a standard BAM Fall hammer and a BAM friction tester. A Waters Q-Tof Premier mass spectrometer was used for HRMS determination.

Computational methods

The gas phase enthalpies of formation were calculated based on isodesmic reactions (Scheme S1). The enthalpy of reaction is obtained by combining the MP2/6-311++G** energy difference for the reactions, the scaled zero point energies (ZPE), values of thermal correction (HT), and other thermal factors. The solid state heats of formation of **2**, **3**, **5** and **9** were calculated with Trouton's rule according to eqn (1) (T represents either the melting point or the decomposition temperature when no melting ^{o}C occurs prior to decomposition).[41]

$$\triangle H_{sub} = 188/\mathrm{J\ mol^{-1}\ K^{-1}} \times T \qquad (1)$$

Experimental methods

Compounds **4**, **6**, **8** and **9** were synthesized according to the reported method and the spectral data of ^{1}H NMR are the same as reported literature.[26] ^{1}H and ^{13}C{H} NMR spectra of compound **5** are identical with the data reported in the literature.[21]

4,4'-(Diazene-1,2-diyl)bis(N-(1,2,4,5-tetrazin-3-yl)-1,2,5-oxadiazol-3-amine) (2).

A mixture of 4,4'-(diazene-1,2-diyl)bis(1,2,5-oxadiazol-3-amine) (3.0 mmol, 0.59 g), 1,2,4,5-tetrazine **1** (6.0 mmol, 1.06 g), K_2CO_3 (6.0 mmol, 0.83 g) and MeCN (15 mL) was heated at reflux (80 ^{o}C) in an oil bath, checking the efficiency of the reaction by TLC, until the starting material **1** had totally disappeared (~ 4 h). The reaction mixture was cooled and diluted with ice water (30 mL). The mixture was acidified to a pH of 1 by dropwise addition of 5% HCl to generate a fine red precipitate that was collected by vacuum filtration. The red precipitate was washed with cold water (3 × 10 mL) and dried overnight under high vacuum to provide pure red solid **2** (0.91 g) in 85% yield. T_d 219 ^oC; ^1H NMR (300 MHz, [D6]DMSO) δ 12.13 (s, 2H), 10.28 (s, 2H) ppm; $^{13}C\{^1H\}$ NMR (75 MHz, [D6]DMSO) δ 162.8, 159.2, 156.8, 145.6 ppm; IR (KBr pellet): ṽ 3193, 3068, 3024, 2435, 1597, 1455, 1399, 1251, 1122, 1043, 936, 821, 604 cm^{-1}. Crystal structure confirmation is given.

1,2-Bis(4-((1,2,4,5-tetrazin-3-yl)amino)-1,2,5-oxadiazol-3-yl)diazene oxide (3).

A mixture of 1,2-bis(4-amino-1,2,5-oxadiazol-3-yl)diazene oxide (3.0 mmol, 0.64 g), 1,2,4,5-tetrazine **1** (6.0 mmol, 1.06 g), Cs_2CO_3 (6.0 mmol, 1.96 g) and MeCN (15 mL) was heated to reflux (80 ^oC) in an oil bath, checking the efficiency of the reaction by TLC, until the starting material **1** had totally disappeared (~ 6 h). The reaction mixture was cooled and diluted with ice water (30 mL). The mixture was acidified to a pH of 1 by dropwise addition of 5% HCl to generate a fine red precipitate that was collected by vacuum filtration. This red precipitate was washed with cold water (3 × 10 mL) and dried overnight under high vacuum to leave a pure red solid **3** (0.87 g) in 78% yield. T_d 232 ^oC; ^1H NMR (300 MHz, [D6]DMSO) δ 12.25 (s, 2H), 10.29 (s, 1H), 10.25 (s, 1H) ppm; $^{13}C\{^1H\}$ NMR (75 MHz, [D6]DMSO) δ 162.9, 162.6, 157.0, 156.9, 148.4. 146.6 pm;. IR (KBr pellet): ṽ 3102, 3030, 2852, 2788, 2543, 2438, 1519, 1420, 1345, 1265, 1201, 1138, 1074, 1013, 935, 764, 608 cm^{-1}; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_8H_5N_{16}O_3$: 373.0550; Found 373.0737.

6-Amino-1,2,4,5-tetrazine 1,5-dioxide (5). Trifluoroacetic anhydride (4 mL, 28 mmol) was added to a slurry of 50% hydrogen peroxide (1.3 mL, 25 mmol) in methylene chloride (20 mL) with stirring at <10 ^oC. The tetrazine compound **4** (7 mmol) was added at 0 ^oC and stirred for 30 min;

then for 12 hours at room temperature. The solvent was removed and the residue was washed with ether and then air-dried to give a yellow solid **5** (0.68 g) in 75% yield. T_d 278 °C; ^{1}H NMR (d_6-DMSO) δ 8.62 (s, 2H), 8.52 (s, 1H) ppm. ^{13}C{^{1}H} NMR (d_6-DMSO) δ 149.4, 144.5 ppm. IR (KBr pellet): ṽ 3259, 3092, 3048, 3007, 2429, 1874, 1592, 1493, 1450, 1387, 1259, 1121, 1050, 934, 807, 608 cm$^{-1.}$ ^{1}H NMR spectra given in SI.

3-Chloro-1,2,4,5-tetrazine (7). A slurry of 3-hydrazinyl-1,2,4,5-tetrazine (8 mol, 0.90 g) in acetonitrile (16 mL) was cooled to 0 °C. After cooling, excess trichloroisocyanuric acid (9.6 mol, 2.23 g) dissolved in acetonitrile (20 mL) was added to the slurry dropwise. During the addition, the solvent changed to a bright orange color, and gas evolution was observed. After the addition, the system was warmed to room temperature and then stirred for an additional 30 min. The precipitate was removed by vacuum filtration, and the solvent was removed from the filtrate via rotary evaporation (the temperature of the bath should be < 25 °C) leaving behind an orange powder **7** (0.59 g) in 64% yield. The product was utilized without further purification since the NMR spectral data are the same as reported literature.[26] ^{1}H NMR (d6-DMSO) δ 10.30 (s, 1H) ppm; ^{13}C{^{1}H} NMR (d6-DMSO) δ157.8, 170.8 ppm.

Tri(1,2,4,5-tetrazin-3-yl)amine (9) was obtained according to the literature.[26] Red solid (60%); T_d 231 °C; ^{1}H NMR (d_6-DMSO) δ 10.82 (s, 3H) ppm. ^{13}C{^{1}H} NMR (d_6-DMSO) δ 158.2, 164.6 ppm. IR (KBr pellet): ṽ 3012, 1427 cm$^{-1.}$ ^{1}H NMR spectrum provided in SI.

ASSOCIATED CONTENT

Supporting Information.

The Supporting Information is available free of charge on the ACS Publications website at DOI: xxxxxxxxxxxxxx. NMR spectra and CIF files; Theoretical calculations, X-ray crystallography of **2**, **5·DMSO, 5** and **9**.

AUTHOR INFORMATION

Corresponding Authors

* (Y. L) E-mail: liuyingleyou@163.com.

* (J. M. S.) E-mail: jshreeve@uidaho.edu

Notes

The authors declare no competing financial interest.

Caution!

Although no explosions were observed during the syntheses and handing of these compounds in this study, all manipulations should be carried out in a hood behind a safety shield. Mechanical actions involving scratching or scraping must be avoided. Eye protection and leather gloves should be worn. All of the energetic compounds must be synthesized on a small scale.

ACKNOWLEDGMENTS

This work was supported by the Office of Naval Research (N00014-16-1-2089), the Defense Threat Reduction Agency (HDTRA 1-15-1-0028), Science and Technology Department of Sichuan Province (No. 2016JY0246), Education Department of Sichuan Province (No. 16ZB0247) and Open Project Program of Chemical Synthesis and Pollution Control Key Laboratory of Sichuan Province (No. CSPC201906).

REFERENCES

(1) (a) Tanver, A.; Huang, M.; Li, Y. Energetic Interpenetrating Polymer Network (EIPN): Enhanced Thermo-Mechanical Properties of NCO-fMWCNTs/HTPB PU and Alkyne-fMWCNTs/acyl-GAP

Based Nanocomposite and its Propellants. *RSC Adv.* **2016**, *6*, 49101–49112; (b) Hiskey, M. A.; Chavez, D. E.; Naud, D. L. Propellant Containing 3; 6-Bis (1H-1, 2, 3, 4-Tetrazol-5-ylamino)-1, 2, 4, 5-tetrazine or Salts thereof. U.S. Pat. 6, 458, 227, 2002.

(2) Zhang, X.; Shen, L.; Luo, Y.; Jiang, R.; Sun, H.; Liu, J.; Fang, T.; Fan, H.; Liu, Z. Synthesis and Ignition Properties Research of 1,5-Diazabicyclo[3.1.0]Hexane Type Compounds as Potential Green Hypergolic Propellants. *Ind. Eng. Chem. Res.* **2017**, *56*, 2883–2888.

(3) (a) Zhang, W.; Zhang, J.; Deng, M.; Qi, X.; Nie, F.; Zhang, Q. A Promising High-energy-density Material. *Nat. Commun.* **2017**, *8*, 181- 187; (b) Hiskey, M. A.; Chavez, D. E.; Robert, L. B.; John, F. K.; Kinkead, S. A. Use of 3,3'-Diamino-4,4'-Azoxyfurazan and 3,3'-Diamino-4,4'-Azofurazan as Insensitive High Explosive Materials. U.S. Pat. 6,358, 339, 2002.

(4) (a) Wang, Y.; Liu, Y.; Song, S.; Yang, Z.; Qi, X.; Wang, K.; Liu, Y.; Zhang, Q.; Tian, Y. Accelerating the Discovery of Insensitive High-energy-density Materials by a Materials Genome Approach. *Nat. Commun.* **2018**, *9*, 2444-2454; (b) Chavez, D. E.; Hiskey, M. A.; Gilardi, R. D. Novel High-Nitrogen Materials Based on Nitroguanyl-Substituted Tetrazines. *Org. Lett.* **2004**, *6*, 2889-2891.

(5) (a) Xu, Z.; Cheng, G.; Yang, H.; Ju, X.; Yin, P.; Zhang, J.; Shreeve, J. M. A Facile and Versatile Synthesis of Energetic Furazan-Functionalized 5-Nitroimino-1, 2, 4-Triazoles. *Angew. Chem., Int. Ed.* **2017**, *56*, 5877–5881; (b) Huynh, M. H. V.; Hiskey, M. A.; Hartline, E. L.; Montoya, D. P.; Gilardi, R. D. Polyazido High-Nitrogen Compounds: Hydrazo and Azo-1,3,5-triazine. *Angew. Chem. Int. Ed.* **2004**, *43*, 4924 –4928.

(6) (a) Yin, P.; Zhang, J.; Imler, G. H.; Parrish, D. A.; Shreeve, J. M. Polynitro-Functionalized Dipyrazolo-1, 3, 5-triazinanes: Energetic Polycyclization toward High Density and Excellent Molecular Stability. *Angew. Chem., Int. Ed.* **2017**, *56*, 8834–8838; (b) Huynh, M. H. V.; Hiskey, M. A.; Chavez, D. E.; Naud, D. L.; Gilardi, R. D. Synthesis, Characterization, and Energetic Properties of Diazido Heteroaromatic High-Nitrogen C-N Compound. *J. Am. Chem. Soc.* **2005**, *127*, 12537-12543.

(7) Date, S.; Sugiyama, T.; Itadzu, N.; Nishi, S. Burning Characteristics and Sensitivity Characteristics of Some Guanidinium 1,5′-bis-1H-Tetrazolate/Metal Oxide Mixtures as Candidate Gas Generating Agent. *Propellants, Explos., Pyrotech.* **2011**, *36*, 51–56.

(8) Mei, X.; Yang, H.; Li, X.; Li, Y.; Cheng, Y. Study of Some Low Temperature Gas-Generating Compositions. *Propellants, Explos., Pyrotech.* **2015**, *40*, 526–530.

(9) (a) Chavez, D. E.; Hiskey, M. A.; Naud, D. L.; Parrish, D. Synthesis of an Energetic Nitrate Ester. *Angew. Chem., Int. Ed.* **2008**, *47*, 8307–8309; (b) Hiskey, M. A.; Chavez, D. E. High-nitrogen energetic material based pyrotechnic compositions. U.S. Pat. 5, 917, 146, 1999.

(10) Badgujar, D. M.; Talawar, M. B.; Asthana, S. N.; Mahulikar, P. P. Advances in Science and Technology of Modern Energetic Materials: an overview. *J. Hazard. Mater.* **2008**, *151*, 289−305.

(11) Klapötke, T. M. Chemistry of High-Energy Materials, 2nd ed. Walter de Gruyter, Berlin, **2012**.

(12) Yin, P.; Zhang, Q.; Shreeve, J. M. Dancing with Energetic Nitrogen Atoms: Versatile N-Functionalization Strategies for N-Heterocyclic Frameworks in High Energy Density Materials. *Acc. Chem. Res.* **2016**, *49*, 4-16.

(13) Klapötke, T. M. Chemistry of High Energy Materials, **2017**.

(14) Pinner, A. Ueber die Einwirkung von Hydrasin auf Imidoather. *Ber. Dtsch. Chem. Ges*. **1893**, *26*, 2126 –2135.

(15) Ryu, S.; Stratt, R. M.; Baeck K. K.; Weber, P. M. Electron Diffraction of Molecules in Specific Quantum States: A Theoretical Study of Vibronically Excited s-Tetrazine. *J. Phys. Chem. A* **2004**, *108*, 1189– 1199.

(16) Kaim, W. The Coordination Chemistry of 1, 2, 4, 5-Tetrazines. *Coord. Chem. Rev.* **2002**, *230*, 127 –139.

(17) Aizikovich, A.; Shlomovich, A.; Cohen, A. Gozin, M. The Nitration Pattern of Energetic 3, 6-diamino-1, 2, 4, 5-tetrazine Derivatives Containing Azole Functional Groups. *Dalton Trans.* **2015**, *44*, 13939-13946.

(18) Shlomovich, A.; Pechersky, T.; Cohen, A.; Yan, Q. L.; Kosa, M.; Petrutik, N.; Tal, N.; Aizikovich, A.; Gozin, M. Energetic Isomers of 1, 2, 4, 5-Tetrazine-bis-1, 2, 4-triazoles with Low Toxicity. *Dalton Trans.* **2017**, *46*, 5994-6002.

(19) Wei, H.; Zhang, J.; Shreeve, J. M. Synthesis, Characterization, and Energetic Properties of 6-Amino-tetrazolo[1,5-b]-1,2,4,5-tetrazine-7-N-oxide: A Nitrogen-Rich Material with High Density. *Chem. Asian J.* **2015**, *10*, 1130-1132.

(20) Chavez, D. E.; Parrish, D. A.; Mitchell, L.; Imler, G. H. Azido and Tetrazolo 1, 2, 4, 5-Tetrazine N-Oxides. *Angew. Chem. Int. Ed.* **2017**, *56*, 3575 –3578.

(21) Chavez, D. E.; Hiskey, M. A. 1, 2, 4, 5-Tetrazine Based Energetic Materials. *J. Energ. Mater.* **1999**, *17*, 357-377.

(22) Wei, H.; Gao, H.; Shreeve, J. M. N-Oxide 1,2,4,5-Tetrazine-Based High-Performance Energetic Materials. *Chem. Eur. J.* **2014**, *20*, 16943-16952.

(23) Snyder, C. J.; Wells. L. A.; Chavez, D. E.; Imler, G. H.; Parrish, D. A. Polycyclic N-oxides: High Performing, Low Sensitivity Energetic Materials. *Chem. Commun.* **2019**, *55*, 2461-2464.

(24) Hu, L.; Yin, P.; Zhao, G.; He, C.; Imler, G. H.; Parrish, D. A.; Gao, H.; Shreeve, J. M. Conjugated Energetic Salts Based on Fused Rings: Insensitive and Highly Dense Materials. *J. Am. Chem. Soc*. **2018,** *140*, 15001–15007.

(25) Wang, G.; Lu, T.; Fan, G.; Yin, H.; Chen, F.-X. Synthesis and Properties of Insensitive [1, 2, 4] Triazolo [4, 3-b]-1, 2, 4, 5-tetrazine Explosives. *New J. Chem.* **2019**, *43*, 1663-1666.

(26) Rudakov, G. F.; Moiseenko, Y. A.; Spesivyseva, N. A. Synthesis of Mmonosubstituted 1,2,4,5-Tetrazines - 3-amino-1,2,4,5-tetrazines. *Chem. Heter. Com.* **2017**, *53*, 802-810.

(27) Qu, Y.; Sauvage, F.-X.; Clavier, G.; Miomandre, F.; Audebert, P. Metal - Free Synthetic Approach to 3-Monosubstituted Unsymmetrical 1, 2, 4, 5-Tetrazines Useful for Bioorthogonal Reactions. *Angew. Chem. Int. Ed.* **2018**, *57*, 12057-12061.

(28) Liu, Y.; Zhao, G.; Tang, Y.; Zhang, J.; Hu, L.; Imler, G. H.; Parrish, D. A.; Shreeve, J. M. Multipurpose [1, 2, 4] Triazolo [4, 3-b][1, 2, 4, 5] tetrazine-based Energetic Materials. *J. Mater. Chem. A* **2019**, *7*, 7875–7884.

(29) Nichol, G. S.; Clegg, W. Classical and Weak Hydrogen Bonding Interactions Between 4, 4′-bipyridine and Organic Acids: From Co-crystal to Organic Complex. *Cryst. Growth Des*. **2009**, *9*, 1844-1850.

(30) Kunieda, M.; Nakaoka, K.; Liang, Y.; Miranda, C. R.; Ueda, A.; Takahashi, S.; Okabe, H.; Matsuoka, T. Self-Accumulation of Aromatics at the Oil−Water Interface through Weak Hydrogen Bonding. *J. Am. Chem. Soc.* **2010**, *132*, 18281-18286.

(31) Yin, P.; Mitchell, L. A.; Parrish, D. A.; Shreeve, J. M. Energetic N-Nitramino/N-Oxyl-Functionalized Pyrazoles with Versatile π–π Stacking: Structure–Property Relationships of High-Performance Energetic Materials. *Angew. Chem. Int. Ed.* **2016**, *55*, 14409 –14411.

(32) Ravi, P.; Badjujar, D. M.; Gore, G. M.; Tewari, S. R.; Sikder, A. K. Review on Melt Cast Explosives. *Propellants Explos. Pyrotech.* **2011**, *36*, 393-403.

(33) Pagoria, P. F.; Mitchell, A. R.; Schmit, R. D. A. 1,1,1-Trimethylhydrazinium Iodide: A Novel, Highly Reactive Reagent for Aromatic Amination via Vicarious Nucleophilic Substitution of Hydrogen. *J. Org. Chem.* **1996**, *61*, 2934-2935.

(34) Robert, D. S.; Gregory, S. L.; Philip, F. P.; Alexander, R. M.; Richard, G. Synthesis of 4-Amino-3,5-dinitro-1H-pyrazole Using Vicarious Nucleophilic Substitution of Hydrogen. *J. Het. Chem.* **2001**, *38*, 1227-1230.

(35) Bachmann, W. E.; Sheehan, J. C. A New Method of Preparing the High Explosive RDX. *J. Am. Soc. Chem.***1949**, *71*, 1842-1845.

(36) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D. ; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. Gaussian 03, revision E.01; Gaussian, Inc.: Wallingford, CT, **2003**.

(37) Sucéska, M. EXPLO5, *Version 6.01*, Brodarski Institute, Zagreb, Croatia, **2013**.

(38) (a) U. M. Regulations, *UN Recommendations on the Transport of Dangerous Goods, Manual of Tests and Criteria*, 5th edn, United Nations Publication, New York, **2009**; (b) 13.4.2 Test 3 (a) (ii) BAM Fallhammer, p. 75; c) 13.5.1 Test 3 (b)(i): BAM friction apparatus, p. 104.

(39) Wolff, S. K.; Grimwood, D. J.; McKinnon, J. J.; Turner, M. J.; Jayatilaka, D.; Spackman, M. A. CrystalExplorer, version 3.1; University of Western Australia: Crawley, Australia, **2012**.

(40) Zhang. J.; Zhang. J.; Parrish, D. A.; Shreeve, J. M. Desensitization of the Dinitromethyl Group: Molecular/crystalline Factors that Affect the Sensitivities of Energetic Materials. *J. Mater. Chem. A* **2018**, *6*, 22705-22712.

(41) Westwell, M. S.; Searle, M. S.; Wales, D. J.; Williams, D. H. Empirical correlations between thermodynamic properties and intermolecular forces. *J. Am. Chem. Soc.* **1995**, *117*, 5013-5015.