

Synthesis and Characterization of the Potential Melt-Castable Explosive 3-(1,2,4-Oxadiazolyl)-5-Nitratomethyl Isoxazole

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The synthesis of 3-(1,2,4-oxadiazolyl)-5-nitratomethyl isoxazole ($C_6H_4N_4O_5$), its physical properties, and its theoretical performances are described. This energetic material was found to have a melting point range of 76.6–79.2 °C, and a thermal onset decomposition temperature of 184.5 °C. These thermal features put this material into the standalone melt-castable explosive class. The material was found to have TNT performance, and was found to be insensitive to impact, friction, and electrostatic discharge, despite having a nitric ester functionality. A critical reaction in making this molecule was the desymmetrization of diaminoglyoxime. The optimization of this transformation is described. Previous reports of this desymmetrization were found to be inaccurate, as the desymmetrization reaction produces a co-crystal of mono- and bi-1,2,4-oxadiazole products.

The development of high-energy-density materials (HEDMs)^[1] with high performance and reasonable sensitivity is an overarching goal in the field of energetic materials. A main thrust of our ongoing research efforts lies in the areas of melt-castable explosives, and we have discussed the characteristics that make a good melt-cast explosive in previous publications.^[2] For CHNO materials, density is critical in maximizing performance, and a common way to maximize density is to incorporate high heat of formation-based heterocycles into a rigid structure with little floppiness that can then be nitrated to further increase the oxygen balance of a molecule. Such rigid energetic molecules with a high degree of symmetry are usually associated with

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	Supporting information for this article is available on the WWW under https://doi.org/10.1002/cplu.202100175

having the highest densities and therefore, the best performances. $^{\left[3\right] }$

Yet many highly symmetrical and rigid molecules are also typically associated with materials that have high melting points. While materials that have excessively high melting points are satisfactory for pressable secondary explosives, high melting points tend to be frowned upon for materials that are to be used as standalone melt-castable explosives. Temperatures of 70–95 °C are ideal for melt-castable materials,^[2a] since materials in this range can be melted with steam. Materials that exhibit melting points >95–125 °C can still be classified as melt-castable materials, but are typically combined with other materials to form a eutectic and depress the melting point, in hopes of bringing it down to the 70–95 °C range.

While symmetrical *bis*-nitratomethyl-*bis*-isoxazole^[2b] was recently been found to serve as a potential melt-castable explosive, it was believed that the floppiness of the nitratomethyl moiety assisted in lowering the melting point by lowering the overall rigidity of the molecule. With this information in hand, it was felt that developing a nonsymmetrical isoxazole/1,2,4-oxadiazole hybrid energetic material containing the nitratomethyl functionality would also lead to materials containing some interesting properties (Figure 1).

In synthesizing **2**, we first needed to desymmetrize diaminoglyoxime (DAG).^[4] DAG, in the presence of 1.50 eq. of triethyl orthoformate and catalytic $BF_3:Et_2O$ heated to 75–80 °C for 10 min was reported by Andrianov et al. to proceed in 80% yield after filtration and recrystallization from hot water to give mono 1,2,4-oxadiazole **3**.^[5] However, when we attempted to reproduce this reaction, it led to only a 33% yield of monocyclic product **3** being obtained. Under the conditions detailed by Andrianov et al., significant amounts of bis-1,2,4-oxadiazole **4** (55%) were obtained (Scheme 1).

In our hands, we found that 1.30 eq. of triethyl orthoformate was the optimal amount in order for good yields of **3** to be obtained. After stirring this reaction for 1 h at 75 °C in the presence of catalytic BF_3 :Et₂O, the reaction mixture was first cooled to ambient temperature and then further to 0 °C. The voluminous solid that appeared was filtered. At this stage, the



Figure 1. Molecular structures of synthesized energetic dinitrate 1 and proposed mononitrate 2.

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IS^[i] [J]

FS^[j] [N]

876

ESD^[k] [J]



Scheme 1. Synthesis of mononitric ester 2.

solid product obtained was determined to be a co-crystal of 3 and 4. Heating this co-crystal in a beaker of water to 50°C to dissolve the solid, and then letting it cool to ambient temperature set the stage for a second filtration. This time, however, it was discovered that the bulk of 4 was retained on the filter, while the bulk of 3, contaminated with a small amount of 4, was present in the mother liquor. Ultimately, it was found that this second filtration was not needed. Treatment of the cocrystal of 3/4 to conditions with sodium nitrite and concentrated HCl afforded hydroximoyl chloride 5, isolated as a white solid of high purity that matched the characterization data outlined by Andrianov et al.^[5] Treatment of **5** with propargyl alcohol in a [3+2] cycloaddition reaction yielded hydroxymethyl isoxazole 6, which was purified by triturating the crude solid in diethyl ether. Nitration of 6 with 98% HNO3 proceeded uneventfully and in high yield to give nitric esters 2. Overall, 2 was synthesized from glyoxal in a 10 gram quantity in 5 steps, and in 16% overall yield.

As shown by the DSC trace in Figure 2, **2** was found to have a lower melting point compared to the *bis*-isoxazole dinitrate 1,^[2b] and exhibited a melting point close to TNT. In fact, **2** was found to have very similar properties to TNT with respect to density, detonation pressure and detonation velocity (Table 1). Despite the presence of the widely perceived sensitive nitric



Figure 2. DSC trace of nitric ester 2.

Table 1. Physical and explosive properties of nitric ester 2 as compared to TNT and dinitrate 2 **TNT**^[5] Data category 1 2 T_m [°C]^[a] 80.4 92.0 76.6 $T_{dec} [^{\circ}C]^{[b]}$ 184.5 295 189.2 $\Omega_{\rm CO2}~[\%]^{\rm [c]}$ -74 -61.5-67.9 $\Omega_{\rm CO}~[\%]^{\rm [d]}$ -24.7 -16.8 -22.6 $ho~[gcm^{-3}]^{[e]}$ 1.65 1.61 1.641 P_{ci} [GPa]^[f] 20.5 19.3 21.0 $V_{det} \ [ms^{-1}]^{[g]}$ 6950 7060 7087 $\Delta_{\rm f}{\sf H}^\circ$ [kJ mol⁻¹]^[h] -59.3-139 -5.8

15

> 360

> 0.25

[a] T_m = onset temperature of melting; [b] T_{dec} = onset temperature of decomposition; [c] Ω_{CO2} =CO₂ oxygen balance; [d] Ω_{CO} =CO oxygen balance; [e] ρ = experimentally determined density. TNT was determined by gas pycnometry. 1 and 2 were determined by single crystal x-ray crystallography; [f] P_j = detonation pressure; [g] V_{det} =detonation velocity; [h] $\Delta_t H^{\circ}$ =molar enthalpy of formation; [i] IS=impact sensitivity; [j] FS=friction sensitivity; [k] ESD=electrostatic discharge sensitivity.

11.2

0.25

> 360

>15

> 360

> 0.20

ester functionality, **2** was found to possess a lower sensitivity to impact and friction compared to TNT.

Single crystal x-ray diffractometry helped identify unequivocally the molecular conformation of 2, as well as reveal its key intermolecular interactions. The Supporting Information provides details on the data acquisition, structure solution, and structure refinement.^[6] A crystallographic analysis of 2 (Deposition Number 2077647) reveals one molecule in the asymmetric unit (Figure 3a). The molecule consists of an oxadiazole ring [r.m.s. deviation = 0.002 Å], an isoxazole ring [r.m.s. deviation = 0.002 Å], and a near planar alkyl nitric ester group [C6/O3/N4/ O4/O5; r.m.s. deviation = 0.019 (1) Å] bonded to the isoxazole ring. The 10 C, N, and O ring- atoms adopt a near planar geometry [r.m.s. deviation = 0.037 (2) Å] with a maximum outof-plane deviation of 0.037 (2) Å for the N3 atom, and the isoxazole ring subtends a dihedral angle of 59.3 (2) $^{\circ}$ with respect to the alkyl nitric ester plane. The molecule's bond length and angles are in the usual range, consistent with those reported for other isoxazoles, oxadiazoles and their derivatives.^[2c,7]

Intermolecular interactions play a key role in the crystal packing of 2.^[7, 8] The interatomic contact distances range between 2.574 (3) and 3.236 (3) Å with the N···H and O···H dominating the van der Waals intermolecular interactions. Specifically, 2 presents short contacts between atoms N3 and atoms H6 A of adjacent molecules and atoms N1 and atoms H4 of adjacent molecules [N3···H6Aⁱ=2.547 (4) Å; N1···H4ⁱ=2.574 (4) Å; symmetry code (i): (x, -1+y, z)]. Also, atoms O2 are in close proximity to atoms H6 A of nearby molecules [O2--H6Aⁱⁱ = 2.659 (3) Å; symmetry code (ii): (-x, -1+y, z)], as are the H1 atoms of the oxadiazole ring with O3 atoms of nearby molecules [H1...O3Aⁱⁱ = 2.635 (3) Å; symmetry code (ii): (1x, -y,1-z)]. The contact distances between the atoms C2 and N3 of adjacent molecules measure 3.236 (3) Å [C2--N3ⁱⁱⁱ=3.236 (3) Å; symmetry code (iii): (-x, -1+y, z)]. Figure 3b shows the crystal stacking of 2 along the *a*-axis. The molecule's 10-atom ring planes are nearly parallel to the *b*-axis and stack in the vicinity

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Figure 3. a) Molecular configuration and atom-numbering scheme for **2**. Non-hydrogen atoms are shown as 50% probability displacement ellipsoids; b) Crystal packing for **2** along the *a*-axis direction; Atoms C, H, O, and N are shown in grey, white, blue, and red, respectively. Blue and red dashed lines depict N--H and O---H intermolecular contacts.

of the *b*-axis. Crystal **2** contains four S1 molecules in its unit cell and belongs to the monoclinic system, P2₁/n space group. Based on its molecular mass and lattice constants of *a*= 6.4077(8) Å, *b*=5.7834 (6) Å, *c*=23.183 (2) Å, *a*= γ =90°, and β =91.724 (8)°, we obtain a density of 1.641 g/cc at 298 K.

In summary, heterocyclic nitric ester **2** was synthesized in a 5 step, 16% overall yielding process from glyoxal. A key to the synthesis was the desymmetrization of diaminoglyoxime (DAG) to yield mono-1,2,4-oxadiazole **3**. Interestingly, conversion of **3** to hydroximoyl chloride **5** via the Sandmeyer reaction was found to yield the desired product in a clean fashion by means of filtration. **2** was found to exhibit standalone melt-castable properties, with a similar density, melting point, detonation velocity, and detonation pressure as compared to TNT.

Experimental Section

General Methods: Chemicals and solvents were used as received from Sigma-Aldrich. ¹H and ¹³C NMR spectra were recorded using a Bruker 400 MHz instrument. The chemical shifts quoted in parts per million in the text refer to typical standard tetramethyl silane in CDCl₃ as the solvent. Infrared spectra were measured with a Bruker Alpha-P FTIR instrument. Melting and decomposition temperatures were measured at a heating rate of 10 °C/min using a TA Instruments Q10 DSC instrument in aluminium pans containing a pinhole. Single-crystal X-ray diffraction studies were performed with a SuperNova Dualflex diffractometer containing an EosS2 charge-coupled device detector and a Mo K α radiation source (λ = 0.71073 Å).⁽⁷⁾ Deposition Number 2077647 for **2** contains the

supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service www.ccdc.cam.ac.uk/structures. **Caution**! Although we did not experience any problems handling the compounds described in this paper, when handling energetic materials such as 2, proper laboratory precautions should be taken. Laboratories and personnel should be properly grounded, and safety equipment such as heavy Kevlar/steel gloves, reinforced Kevlar coat, ballistic face shield, ear plugs, and blast shields are necessary.

3-(1,2,4-oxadiazolyl)-hydroximoyl chloride (5): To 1 1 L roundbottom flask equipped with a stir bar was added diaminoglyoxime (118 g, 1.00 mol, 1 eq), 221 mL of 98% triethyl orthoformate (196.5 g, 1.30 mol, 1.30 eq), and 12.3 mL of BF₃ diethyl etherate (14.2 g, 0.100 mol, 0.100 eq) . The reaction mixture was immersed in an oil bath, heated to 75–80 °C, and stirred for 1 h. The reaction mixture was first cooled to ambient temperature, and then to 0 °C by immersing the round-bottom flask into an ice bath. The resulting solid was collected by Büchner filtration, rinsing the flask with a minimal amount of cold triethyl orthoformate. The solids were transferred to a crystallization dish, and was dried overnight in a fume hood to afford 128 g of a white solid. This solid contains a mixture of monocyclized- and dicyclized-1,2,4-oxadiazole products.

128 g of this white solid and a stir bar was added to a 2 L-threeneck-round-bottom flask, and 700 mL of concentrated HCl was added. The reaction mixture was immersed into an ice-water bath, and was chilled to 0-5 °C. 700 mL of distilled water was added, and the reaction mixture was stirred for 30 minutes until a temperature of 0-5 °C was reached. 104 g of NaNO₂ was dissolved in 250 mL, and was added over 4 hours via a 500 mL addition funnel. During this addition, the temperature was monitored and was not allowed to rise above 10 °C. After the addition was complete, the reaction mixture was stirred overnight for 16 h, during with time the icewater bath melted, and the temperature rose to 20 °C. The reaction mixture was re-cooled to 0 °C by means of an ice-water bath, the solids were collected by Büchner filtration, and the solid was washed with distilled water (3×500 mL). The solid was transferred to a crystallization dish, and was dried overnight in a fume hood to afford 51.6 grams (35% from DAG) of hydroximoyl chloride 5 as a white solid. 5 matched the analytical characteristics as described by Andrianov et al.^[5]

3-(1,2,4-oxadiazolyl)-5-(hydroxymethyl)-isoxazole (6): To a 2 L round-bottom flask equipped with a stir bar were sequentially added 1 L of EtOH, 48.9 mL of propargyl alcohol (47.5 g, 0.850 mol, 5.00 equiv), and NaHCO₃ (42.8 g, 0.509 mol, 3.00 equiv). The reaction mixture was cooled to $0\,^\circ\text{C}$, and the flask was fitted with a pressure-equalizing liquid addition funnel. 5 (25.0 g, 0.170 mol, 1.00 equiv) was dissolved in 300 mL of EtOH, and was added dropwise over 6 h, during which time the temperature was not allowed to rise above 10°C. After the addition was complete, the ice bath was removed, and the reaction mixture was stirred overnight at ambient temperature. The reaction mixture was filtered and the solid was discarded. The mother liquor was transferred to a 2 L round-bottom flask and was concentrated in vacuo to afford a crude dark brown solid. The crude solid was triturated with 200 mL of Et₂O for 4 h. The solid was collected by Büchner filtration and was dried under suction overnight to afford 20.39 g (72%) of isoxazole **6** as a light brown powder. T_{melt} (onset) = 115.8 °C; T_{melt} (peak) = 120.6 T_{dec} = 172.9 °C (onset), 207.2 °C (peak); ¹H NMR (400 MHz, DMSO-d₆) δ 9.88 (s, 1H), 6.93 (s, 1H), 5.81 (s, 1H), 4.68 (s, 2H); ¹³C NMR (100 MHz, DMSO-d₆) δ 175.3, 168.4, 160.1, 151.9, 101.3, 54.6; IR (neat) cm⁻¹ 3370 (m), 3113 (m), 1569 (s), 1528 (s).



3-(1,2,4-oxadiazolyl)-5-(nitratomethyl)-isoxazole (2): To a 100 mL round-bottom flask immersed in an ice bath was added 30 mL of 98% HNO₃. After the nitric acid was chilled to 0°C, alcohol 2 (10.0 g, 59.9 mmol, 1.00 equiv) was added in four equal portions over 1 h, during which time the temperature did not exceed 10 $^\circ\text{C}.$ After the addition was complete, the reaction mixture was stirred for 4 h, during which time the ice bath was allowed to melt, and the reaction mixture was allowed to warm to ambient temperature. The reaction mixture was poured onto crushed ice with stirring. After 3 h, the solid was collected by Büchner filtration and was airdried in a well-ventilated fume hood to afford nitrate 2 as a crude light yellow solid. Crude 2 was recrystallized from boiling isopropanol to afford 10.3 g (81%) of the pure product as a white solid. T_{melt} (onset) = 76.6 °C; T_{melt} (peak) = 79.2 °C T_{dec} = 184.5 °C (onset), 209.7 $^{\circ}$ C (peak); ¹H NMR (400 MHz, Acetone- d_6) δ 9.57 (s, 1H), 7.25 (s, 1 H), 5.94 (s, 2H), $^{13}\mathrm{C}$ NMR (100 MHz, Acetone- d_6 δ 168.5, 167.3, 161.3, 153.8, 106.1, 64.8; IR (neat) cm⁻¹ 3139 (w), 3111 (w), 1737 (s), 1637 (s), 1530 (m).

Acknowledgements

The authors thank the U.S. Army for financial support in carrying out this work.

Conflict of Interest

The authors declare no conflict of interest.

Keywords: Cycloaddition Reactions • Energetic Materials • Explosives • Heterocycles • Nitric Esters

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Manuscript received: April 16, 2021 Revised manuscript received: May 18, 2021