Heterocycles

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Energetic Trinitro- and Fluorodinitroethyl Ethers of 1,2,4,5-Tetrazines

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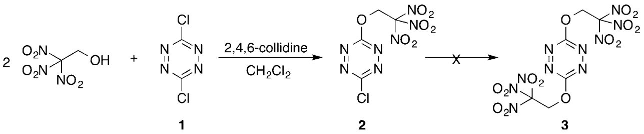
Abstract: *Several new energetic ethyl ethers of 1,2,4,5-tetrazine have been synthesized. These molecules display good thermal stability, good oxygen balance, and high densities. Included in these studies are a 2,2,2-trinitroethoxy 1,2,4,5-tetrazine and two fluorodinitroethoxy 1,2,4,5-tetrazines. One of these compounds was converted into the di-N-oxide derivative. The sensitivity of these materials towards destructive stimuli was determined, and overall the materials show promising energetic performance properties.*

The 1,2,4,5-tetrazine heterocyclic ring system is one of the most versatile and unique nitrogen ring heterocycles known in the literature.[1] The heterocycle displays numerous chemical and physical properties which allow it to be used in a broad range of applications. It is also one of the most electron-deficient ring systems known, and as such, it has a tendency to form stable radical anions.[2] When substituted by the appropriate functional groups at the 3- and 6-positions, the radical anion can be formed reversibly, and in several cases, the fluorescence properties of these materials can be turned on and off on-demand.[2,3] The facile ability to undergo the inverse electron demand hetero-Diels–Alder reaction is another property of the 1,2,4,5-tetrazine and has been employed in a significant number of in vitro and in vivo studies.[4] The process can occur in a bioorthogonal fashion, and has become a very powerful tool in biological studies. Other applications include organic solar photovoltaics,[5] photochemical studies of protein folding,[6] and anion detection.[7]

Over the past several years we have studied tetrazines in energetic materials applications such as propellants, explosives, pyrotechnics, and gas generators. Tetrazines display attractive properties for energetic materials applications because of their high, positive heats of formation, high densities, and interesting sensitivity properties. Klapötke[8] and others[9] have reported the synthesis of the highly energetic compound 3,6-bis (2,2,2-trinitroethylamino)-1,2,4,5-tetrazine. This compound displays promising properties, but suffers from thermal lability often associated with the trinitroethyl group. Our goal was to attempt to synthesize polynitroethyl-ether-substituted tetrazines to determine whether the absence of a free N-H functional group would lead to increased thermal stability.

Our efforts began with the study as to whether 2,2,2-trinitroethanol could act as a nucleophile with certain electrophilic tetrazine ring systems. 2,2,2-Trinitroethyl substitutions generally occur using a Mannich reaction type of an approach.[10] Unfortunately, the desired Mannich reaction coupling partner, 3,6-dihydroxy-1,2,4,5-tetrazine, has not been described in the literature. There are a few examples describing the use of 2,2,2-trinitroethanol as a nucleophile with electrophilic reagents such as acid chlorides.[11] 3,6-dichloro-1,2,4,5-tetrazine (**1**) is a substrate that displays reactivity similar to acid chlorides. Scheme 1 displays the reaction of trinitroethanol with **1** in the presence of 2,4,6-collidine, using methylene chloride as the solvent. The reaction proceeds smoothly to provide the intermediate **2** in excellent yield at room temperature. Unfortunately, the reaction did not proceed to provide the doubly substituted product **3**.



Scheme 1. Nucleophilic reaction of 2,2,2-trinitroethanol with **1**.

Alternative methods were investigated to obtain **3**, including the application of heat and substituting the methylene chloride solvent with higher boiling solvents such as chloroform and dichloroethane. No evidence of **3** was observed in these cases. Heating to higher temperatures in sealed vessels was also unfruitful. The use of more polar solvents is complicated by the fact that 2,2,2-trinitroethanol has a tendency to ionize in polar solvents. The compound **2** was found to melt at 98 °C and was stable until to 168 °C prior to decomposition, and is higher than that of most trinitroethyl-substituted energetic compounds.[12]

Extremely thin crystals of **2** were grown from a variety of solvents. While these crystals were not suitable for publishable X-ray crystallographic data, the structure could be confirmed. The structure of **2** is displayed in Figure 1. The density was measured to be 1.865 $g\,cm^{-3}$ (-123 °C).

We then turned our attention toward other polynitro alcohols and their reaction with **1**. One such alcohol was 2-fluoro-2,2-dinitroethanol (FDNE).[13] Using the same reaction conditions as described for the synthesis of **2**, the reaction proceeded at a faster rate, thus producing the monosubstituted product **4** (Scheme 2). The use of two equivalents of

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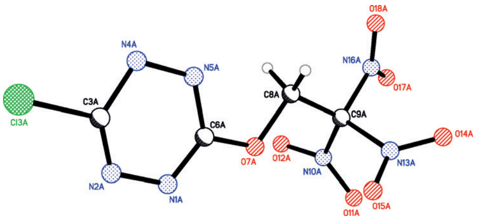
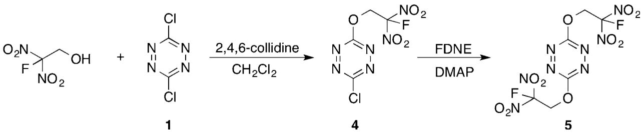


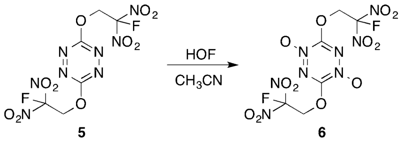
Figure 1. ORTEP drawing of the crystal structure of **2**.



Scheme 2. Synthesis of **4** and **5**. DMAP = 4-(*N*,*N*-dimethylamino)pyridine.

FDNE did result in the production of the disubstituted product, but the reaction was very sluggish. Ultimately we found that the use of 4-dimethylaminopyridine allowed the reaction to progress at a reasonable rate to give the desired disubstituted product in good yield.

In an attempt to introduce more oxygen into **5**, we investigated its oxidation with a variety of oxidizing agents (Scheme 3). Interestingly, while monoamino- and diamino-substituted 1,2,4,5-tetrazines have been reported to provide N-oxide products upon oxidation, there have been no reports of the oxidation of alkoxy-substituted tetrazines. We surmised that oxidation of these substrates would be more challenging because of the electron-deficient nature of the 2-fluoro-2,2-dinitroethoxy substituent. Hypofluorous acid[14] (HOF) proved to be an effective reagent for the oxidation of this substrate. Hypofluorous acid was generated by bubbling a 10% solution of elemental fluorine in nitrogen into a solution of water (10%) in acetonitrile below −5 °C. Concentrations of HOF of 0.35–0.45 M were commonly obtained. The compound **4** was added to the HOF solution and stirred at 0 °C for several hours and allowed to warm to room temperature and stirred for an additional 2 hours. The solution turned from a bright orange to a bright yellow over this time. Upon concentration, a yellow precipitate was formed. The product was determined to be the 1,4-dioxide product **6** (Scheme 3).



Scheme 3. The oxidation of **5** using hypofluorous acid.

X-ray quality crystals of **5** and **6** were grown from slow evaporation of dichloroethane and ethyl acetate, respectively.[15] The compound **5** crystallizes in the monoclinic crystal system and exhibits the $P2_1/n$ space group. The density of **5** was found to be 1.89 g cm^{-3} at 20 °C. The compound **6** also crystallizes in the monoclinic crystal system but belongs to the *C*2/*c* space group. The material has a density of 1.963 g cm^{-3} at 20 °C. The C−O bond from the tetrazine carbon to the ether oxygen is 1.34 Å in **5** and the corresponding bond in **6** has shortened slightly to 1.32 Å. The structures of **5** and **6** are displayed in Figures 2 a and b, respectively.

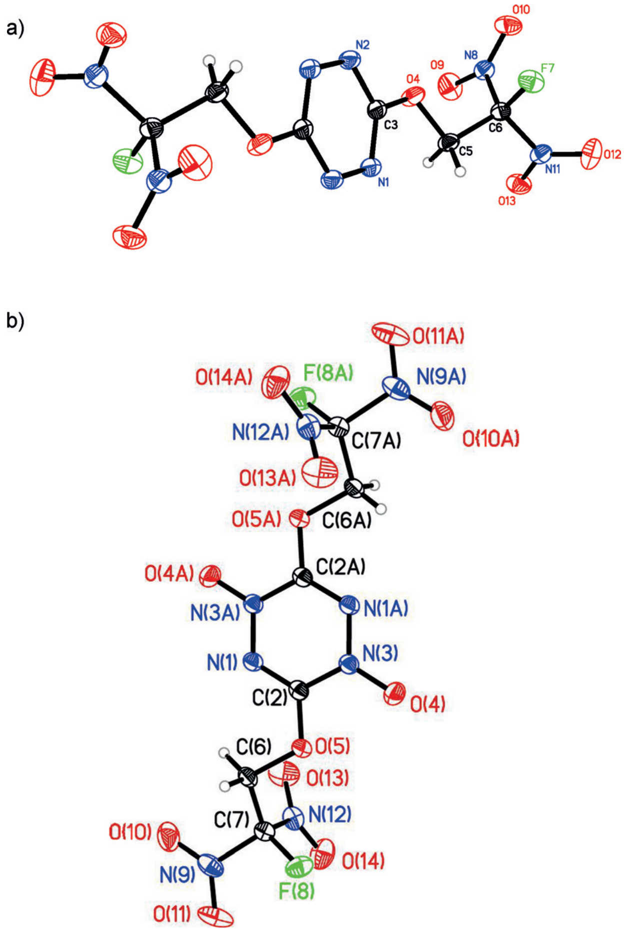


Figure 2. ORTEP representations of the crystal structures of **5** (a) and **6** (b) shown at the 50% probability level.

The thermal stabilities of **4**, **5**, and **6** were determined by differential scanning calorimetry. The compound **4** was found to melt at 78 °C and was thermally stable in the melt until it began to decompose at 209 °C. The compound **5** displayed a melting point of 116 °C and began to decompose at 204 °C. The di-N-oxide did not melt but began to decompose at 174 °C.

The sensitivity data for **2**, **5**, and **6** are shown in Table 1. The compound **2** was found to be very sensitive to impact and friction. The compounds **5** and **6** displayed very similar sensitivity properties, both being less sensitive to impact than RDX while being more sensitive to friction than RDX.

The heat of formation of **5** and **6** were estimated using the method of Klapötke and co-workers.[16] The heat of formation of **5** was calculated to be −303 kJ mol^{-1} while the heat of formation **6** was calculated to be −322 kJ mol^{-1}. By using these data, and the densities of **5** and **6** the explosive

Table 1: Sensitivity data for **2**, **5**, and **6**.[a]

	Impact [J][b]	Spark [J][c]	Friction [N][d]
2	1.9	0.125	49
5	5.4	0.062	104
6	5.6	0.062	104
PETN	2.5	0.062	68
RDX	4.6	0.062	157

[a] Sensitivity values for the PETN an RDX were obtained during the same series of sensitivity experiments for **2**, **5**, and **6**. [b] LANL type 12, 50% drop height, 2.5 kg. [c] ABL spark 3.4% threshold initiation level (TIL). [d] 50% load Bruceton up/down method

performance properties can be predicted using the Cheetah thermochemical code.[17] The compound **5** was predicted to have a detonation pressure of 33.2 GPa and a detonation velocity of $8.4\,\mathrm{km\,s^{-1}}$. The detonation temperature was predicted to be nearly 4000 K. [T_{det} (RDX) = 3436 K]. The detonation pressure for **6** was predicted to be 40.6 GPa and the detonation velocity was predicted to be $8.8\,\mathrm{km\,s^{-1}}$. The detonation temperature was calculated to be 4295 K. The oxygen balance of **5** (OB% = −12.46) and **6** (OB% = −3.6) are also promising when compared to a conventional material such as RDX (OB% = −22.6).

In conclusion, we have synthesized several new polynitroalkoxy 1,2,4,5-tetrazines. We have also reported the first di-N-oxide of an alkoxy tetrazine. These materials have detonation temperatures higher than conventional energetic materials such as RDX and HMX and display a better oxygen balance. These materials have high densities, good thermal stabilities, and promising energetic materials properties, and thus may be useful as ingredients in energetic materials applications.

Experimental Section

Caution! The prepared compounds are explosive with sensitivity towards various stimuli. Although we had no problems during synthesis, proper protective equipment (Kevlar gloves, wrist protectors, face shield, ear protection, and thick leather coat) should be worn. Extra precautions should be taken when working on larger scale. 2-Fluor-2,2-dinitroethanol is a known vessicant and is toxic. Care should be taken when handling this material.

5: Compound **4** (0.268 g, 1.0 mmol) was dissolved in methylene chloride (5 mL) and 2-fluoro-2,2-dinitroethanol (0.154 g, 1.0 mmol) was added. 4-Dimethylaminopyridine (0.122 g, 1.0 mmol) was added. The reaction was stirred at room temperature for 1 hour, filtered through a short column of silica gel and concentrated to give **5** (289 mg, 75%). M.P. 174 °C (dec.). ^{1}H NMR ([D$_6$]acetone) δ = 6.08 ppm (d, 4H). ^{13}C NMR ([D$_6$]acetone) δ = 65.36 (d), 119.47 (d), 165.78 ppm. IR (KBr) $\tilde{\nu}$ = 3050, 2994, 1663, 1453, 1412, 1377, 1346, 1326, 1310, 1246, 1202, 1123, 1088, 1037, 1009, 942, 849, 807, 765, 581 cm^{-1}. C,H,N analysis calcd for $C_6H_4F_2N_8O_{10}$ (MW 386.14): C 18.66, H 1.04, N 29.02; found: C 18.62, H 1.08, N 28.99 %.

6: Acetonitrile (100 mL) and water (10 mL) were mixed in an Erlenmeyer flask and cooled to −5 °C. To this solution was bubbled 10% F_2 in nitrogen for 1.5 hours, thus maintaining the temperature at −5 °C. A 2.5 mL aliquot of the solution was added to a KI/starch solution and titrated with a 0.5 M sodium thiosulfate solution. Compound **5** (0.386 g, 1.0 mmol) was added to acetonitrile (5 mL) and cooled to 0 °C. A solution of the hypoflurous acid (5 mmol) was added. The reaction was stirred at 0 °C for 2 hours and at room temperature for 2 hours. The reaction was concentrated, treated with minimal cold water, and filtered to give the di-N-oxide, 334 mg (80 %) of a bright yellow product. M.P. 174 °C (dec.) ^{1}H NMR ([D$_6$]DMSO) δ = 5.92 ppm (d, 4H).^{13}C NMR ([D$_6$]DMSO) δ = 66.67 (d), 118.71 (d), 148.57 ppm. IR (KBr) $\tilde{\nu}$ = 3047, 2986, 1617, 1590, 1519, 1435, 1402, 1329, 1237, 1116, 1065, 1042, 978, 851, 807 cm^{-1}. C,H,N calcd for $C_6H_4F_2N_8O_{12}$(MW 418.14): C 17.23, H 0.96, N 26.80; found: C 17.25, H 1.00, N 26.78 %.

For experimental details, including the X-ray crystallographic data, please see the Supporting Information.

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[15] CCDC 1456930 (**5**) and 1456931 (**6**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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