High-Nitrogen Compounds

DOI: 10.1002/ange.201302128

Electroactive Explosives: Nitrate Ester-Functionalized 1,2,4,5-Tetrazines**

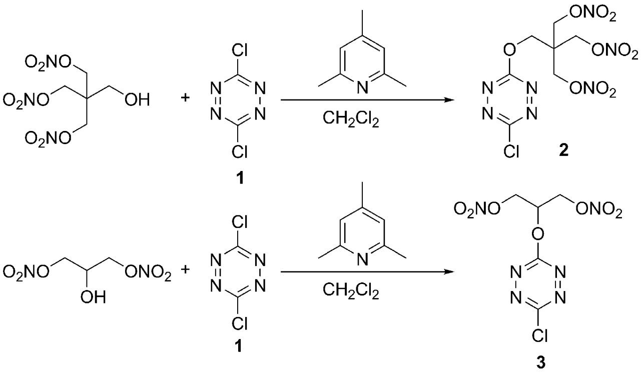
David E. Chavez, Susan K. Hanson, Jacqueline M. Veauthier, and Damon A. Parrish*

Due to their unique optical and electrochemical properties, 1,2,4,5-tetrazine heterocycles have been the focus of intense recent research. The useful photophysical properties of tetrazines have led to their application in the labeling of cellular components through bioorthogonal inverse electron demand hetero Diels–Alder reactions[1] and in the study of protein folding dynamics.[2] Additionally, the extreme electron deficiency of tetrazines has been used in the development of ion sensors,[3] photovoltaics,[4] and fluorescence switches.[5]

During the past decade, Los Alamos National Laboratory has focused much attention on the development of high-nitrogen materials, due in large part to the ideal properties these materials possess as explosives and propellants.[6] For energetic materials applications, tetrazine-based high nitrogen molecules display large positive enthalpies of formation, high densities, good thermal stability, and desirable safety properties compared to conventional energetic materials such as RDX, HMX, and PETN.[7] There has been an ever-increasing interest in the development of explosive technologies that lead to materials that are safer to handle and have tailored properties. One way to increase safety in an explosive device would be to develop alternatives to traditional thermal initiation. This includes photoinitiation or other electroactive pathways that involve control of chemical reactions in a material. Development in this field has been hindered by the lack of suitable molecules that are electroactive and retain desired explosive performance properties.[8]

Conventional energetic materials, such as RDX, HMX or PETN typically are not capable of being electroactive, nor can they reversibly form stable radical anions. Additionally, energetic materials such as 1,1-diamino-2,2-dinitro ethylene (FOX-7) and derivatives of furazans are unstable toward redox electrochemistry.[9] However, the nitrogen-rich tetrazine ring system is redox active and capable of reversible formation of stable radical anions, as demonstrated recently in elegant work by Audebert and co-workers.[5,10] Furthermore, the group showed that it was possible to have on-demand control of the fluorescence properties of certain types of tetrazines. Inspired by this work, we chose tetrazine as a platform to develop hybrid systems of conventional explosives. We now report the synthesis and characterization of nitrate ester derivatized tetrazines. The characterization of the optical and electrochemical properties of these new energetic materials is a critical first step in the development of a new class of electroactive explosives with tailored initiation properties.

As our target materials, we chose to prepare tetrazines substituted by derivatives of pentaerythritol tetranitrate (PETN) and nitroglycerin. The strong electrophile 3,6-dichlorotetrazine (**1**) was employed to prepare the PETN derivative (**2**), through the nucleophilic reaction of Petrin (pentaerythitol trinitrate),[11] using 2,4,6-collidine as a base. The reaction proceeded smoothly under ambient conditions, using methylene chloride as the solvent to afford **2** in 70% yield (Scheme 1). Similarly, the nitroglycerin-derivatized tetrazine (**3**) was prepared in an analogous procedure with 1,3-dinitroxy-2-hydoxy-propane[11] as the nucleophile. The UV/Vis spectra are shown in Figure 1. Molecules **2** and **3** each have absorption bands near 500 nm which correspond to n–π* transitions for the tetrazine ring systems. This absorbance is not significantly altered from the n–π* absorbance for the non-energetic derivative, **1**. However, the more intense transition near 300 nm (π–π*) is red-shifted for **2** and **3** compared to **1**. Both **2** and **3** exhibit fluorescence activity in solution and in the solid state upon exposure to both long- (365 nm) and short-wavelength (254 nm) UV radiation.



Scheme 1. Syntheses of **2** and **3**.

---

[*] Dr. D. E. Chavez, Dr. S. K. Hanson, Dr. J. M. Veauthier
Los Alamos National Laboratory
Los Alamos, NM 87545 (USA)
E-mail: dechavez@lanl.gov

Dr. D. A. Parrish
Laboratory for the Structure of Matter, Naval Research Laboratory
4555 Overlook Ave., Washington, DC 20375 (USA)

[**] The authors would like to thank the DOE Science Campaign 2 for funding, Anna Giambra, Daniel Preston, Mary Sandstrom, Jose Archuleta for performing the sensitivity characterization and testing, and David Morris for helpful discussions. Los Alamos National Laboratory is operated by Los Alamos National Security (LANS, LLC) under contract No. DE-AC52-06A25396 for the U.S. Department of Energy. The authors also thank the Office of Naval Research (Award No. N00014-11-AF-0-0002).

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201302128.

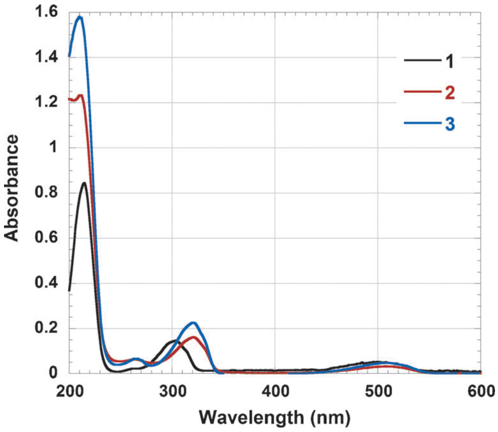


Figure 1. Absorption spectra of **1**, **2**, and **3** at room temperature in CH_3CN.

Crystals of compound **2** suitable for X-ray diffraction were obtained by recrystallization from chloroform. The crystal structure is displayed in Figure 2.[12,13] The crystal density was calculated from the X-ray data and was determined to be 1.77 $g\,cm^{-3}$ at −123 °C, and 1.73 $g\,cm^{-3}$ at 20 °C. The tetrazine moiety of **2** is slightly distorted from planar (e.g., N1-N2-C3-N4 is 7.40(2)°) but the N−N and C−N bond lengths which average 1.328(2) and 1.334(2) Å, respectively, compare well with similar 3,6-alkoxy derivatized tetrazine molecules[14] as does the C−O bond for the O atom adjacent to the tetrazine ring (1.329(2) Å). However, the C-O-C bond angle is somewhat contracted (116.79(9)°) compared to the angle 123.5° found in other 3,6-alkoxytetrazines.[14a] The PETN portion of the molecule compares well with that of the parent PETN compound.[15] Compound **3** remained a liquid at room temperature and we were unable to obtain crystals, even upon cooling to lower temperatures.

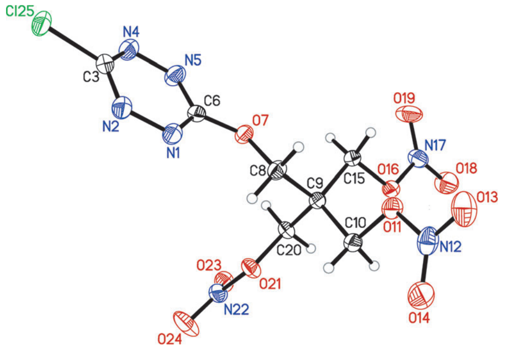


Figure 2. Thermal ellipsoid plot of **2** shown at the 50 % probability level.

As compound **2** was a solid and easier to work with, we continued to characterize **2** with respect to its sensitivity to destructive stimuli such as impact, spark and friction. The data collected are provided in Table 1. The data show that the sensitivity of the compound **2** is very similar to the parent explosive compound PETN. The heat of formation was estimated using a group additivity method[16] and was predicted to be $-69\ kJ\,mol^{-1}$. With the crystal density and heat of formation data in hand, we turned our attention to predicting the explosive performance of compound **2** using the Cheetah thermochemical code.[17] The results of our calculations are displayed in Table 2, and show that compound **2** has explosive performance approaching that of PETN with respect to detonation velocity and detonation pressure.

Table 1: Sensitivity properties of **2**.

	Impact [J][a]	Spark [J][b]	Friction [N][c]	DSC [°C][d]
2	2.6	0.025	94	156
PETN	2.8	0.0625	89	168

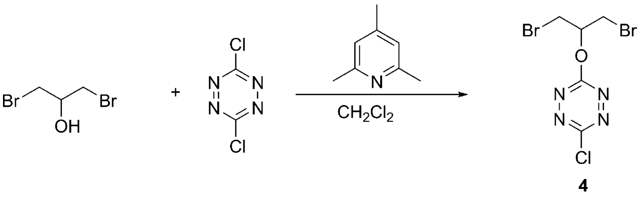
[a] LANL type 12, 50 % drop height, 2.5 kg. [b] ABL spark 3.4 % threshold initiation level (TIL). [c] 50 % load Bruceton up/down method. [d] 10 °C heating ramp rate.

Table 2: Predicted performance properties of **2**.

	$V_{Det.}$ [$km\,s^{-1}$]	P_{CJ} [GPa]
2[a]	7.76	25.4
PETN[b]	8.26	33.2

[a] Cheetah code. [b] Livermore Explosives Handbook.

Our next step was to determine whether compound **2** was capable of reversibly forming a stable radical anion using electrochemical reduction. Compound **2** is more highly functionalized than any of the previously reported tetrazines studied by the Audebert group. Furthermore, the close proximity of the nitrate ester functional groups to the incipient radical anion core of the tetrazine ring could lead to a reactive intermediate and result in the inability to cycle back to the starting oxidation state, due to potential side reactions. A further complicating factor is that PETN is known to undergo electrochemical reduction to the tri-, di- and mononitrate products.[18] In order to determine whether reactive functional groups on the pendant sidechains might pose problems during electrochemical reduction, we chose to study a model system (**4**) that had two bromo substituents (Scheme 2).[19] To our delight, we found that compound **4** did undergo reversible formation of a stable radical anion.[20] With this result in hand, we characterized the electrochemical reduction of **2** and **3** and additionally we found that they were also capable of reversible formation of a radical anion (Figure 3).[20] The redox potential data for tetrazines **1**–**4** are displayed in Table 3. The redox potential is somewhat more negative for the explosive derivatives **2**–**3** compared to **1**.



Scheme 2. Synthesis of **4**.

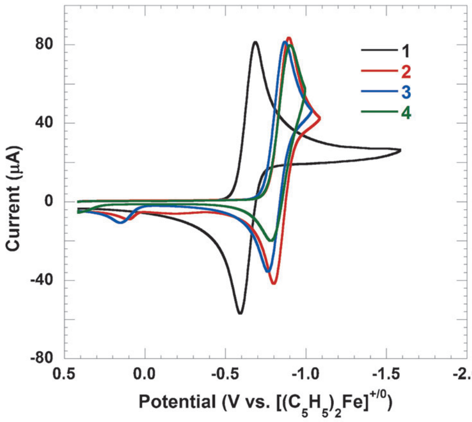


Figure 3. Cyclic voltammograms of **1**–**4** at room temperature in 0.1 M $[(n\text{-}C_4H_9)_4N]PF_6/CH_3CN$ on a glassy carbon working electrode at 0.2 V s^{-1}.

Table 3: Redox potential data for tetrazines **1**–**4**.

Species	$E_{1/2}$(red) [V][a]
1	−0.64
2	−0.85
3	−0.82
4	−0.84

[a] Potentials in volt versus $[(C_5H_5)_2Fe]^{+/0}$.

Compounds **2**–**4** are similar to compounds studied by Audebert and co-workers in that the tetrazine ring is substituted by a chloro and an alkoxy substituent. In Audebert's studies, that class of tetrazine derivatives were capable of on/off fluorescence switching through reversible oxidation/reduction chemistry. It is very likely that compounds **2** and **3** will display the same behavior.

In conclusion we have demonstrated that tetrazine-derivatized explosives are capable of reversible oxidation state control. Compounds **2** and **3** form stable radical anions in the presence of labile nitrate ester functional groups. These molecules are the first members of a new class of energetic materials that will aid the development of new explosive technologies through the exploitation of the unique characteristics of the tetrazine ring system. Further work is ongoing to find optimal conditions for reversible electronic switching at all scan rates and for bulk material samples.

Experimental Section

Caution! Although no problems have occurred during the synthesis and handling of **2** and **3**, the materials are explosive. Laboratories and personnel should be properly grounded and safety equipment such as Kevlar gloves, blast shields, and ear plugs are necessary, especially when working with large-scale reactions. Full synthesis and characterization data for **3** and **4** are available in the Supporting Information.[19]

2: Petrin (2.71 g, 10 mmol), along with 3,6-dichloro-1,2,4,5-tetrazine (1.51 g, 10 mmol) were added to CH_2Cl_2 (50 mL). The reaction mixture was stirred at 25 °C and 2,4,6-collidine (1.21 g, 10 mmol) was added portionwise over 10 min. The reaction was monitored by thin-layer chromatography (TLC) using CH_2Cl_2 as the eluent. When the reaction was complete, the reaction was diluted with CH_2Cl_2 (50 mL) and washed with water. The organic layer was dried with $MgSO_4$, filtered, concentrated and the residue purified by column chromatography to provide **1** (2.66 g, 70 %). M.p. 77 °C. ^{1}H NMR ([D$_6$]acetone): $\delta = 4.95$ (2 H, s), 5.00 ppm (2 H, s). ^{13}C NMR ([D$_6$]acetone): $\delta = 42.87$, 68.30, 71.05, 165.27, 167.55 ppm. IR (KBr): $\tilde{\nu} = 2974$, 2907, 1658, 1644, 1482, 1466, 1455, 1385, 1353, 1278, 1198, 1033, 1012, 1003, 927, 862, 800, 757, 723, 710 cm^{-1}. UV/Vis λ_{max}, nm (log ε) 212 (4.5), 266 (3.0), 321 (3.6), 508 (2.9). Elemental analysis calcd for $C_7H_8N_7O_{10}Cl$: C 21.80, H 2.09, N 25.42; found: C 21.79, H 2.10, N 25.44.

Received: March 13, 2013

Keywords: electroactive compounds · explosives · fluorescence · heterocycles · tetrazines

---

[1] a) M. L. Blackman, M. Royzen, J. M. Fox, *J. Am. Chem. Soc.* **2008**, *130*, 13518 – 13519; b) N. K. Devaraj, R. Weissleder, S. A. Hilderbrand, *Bioconjugate Chem.* **2008**, *19*, 2297 – 2299.

[2] M. Abdo, S. P. Brown, J. R. Courter, M. J. Tucker, R. M. Hochstrasser, A. B. Smith, *Org. Lett.* **2012**, *14*, 3518 – 3521.

[3] Y. Zhao, Y. Li, Z. Qin, R. Jiang, H. Liu, Y. Li, *Dalton Trans.* **2012**, *41*, 13338 – 13342.

[4] Z. Li, J. Ding, N. Song, J. Lu, Y. Tao, *J. Am. Chem. Soc.* **2010**, *132*, 13160 – 13161.

[5] a) G. Clavier, P. Audebert, *Chem. Rev.* **2010**, *110*, 3299 – 3314; b) J. Malinge, C. Allain, A. Brosseau, P. Audebert, *Angew. Chem.* **2012**, *124*, 8662 – 8665; *Angew. Chem. Int. Ed.* **2012**, *51*, 8534 – 8537.

[6] a) D. E. Chavez, M. A. Hiskey, R. D. Gilardi, *Angew. Chem.* **2000**, *112*, 1861 – 1863; *Angew. Chem. Int. Ed.* **2000**, *39*, 1791 – 1793; b) D. E. Chavez, M. A. Hiskey, M. H. V. Huynh, D. L. Naud, S. F. Son, B. C. Tappan, *J. Pyrotech.* **2006**, *23*, 70 – 80; c) D. E. Chavez, B. C. Tappan, B. A. Mason, *Propellants Explos. Pyrotech.* **2009**, *34*, 475 – 479; d) M. A. Hiskey, D. E. Chavez, R. L. Bishop, J. F. Kramer, S. A. Kinkead, U.S. Patent 6 358 339, **2002**.

[7] a) D. E. Chavez, M. A. Hiskey, D. L. Naud, *Propellants Explos. Pyrotech.* **2004**, *29*, 209 – 215; b) D. E. Chavez, B. C. Tappan, M. A. Hiskey, S. F. Son, H. H. Harry, D. Montoya, S. Hagelberg, *Propellants Explos. Pyrotech.* **2005**, *30*, 412 – 417.

[8] a) E. D. Aluker, A. G. Krechetiv, A. Mitrofanov, A. Zverev, M. Kuklja, *J. Phys. Chem. C* **2012**, *116*, 24482 – 24486; b) E. D. Aluker, A. G. Krechetov, A. Yu. Mitrofanov, Yu. P. Sakharchuk, *Russ. J. Phys. Chem. B* **2011**, *5*, 821 – 823.

[9] a) L. Šimková, J. Klíma, P. Sazama, J. Ludvík, *J. Solid State Electrochem.* **2011**, *15*, 2133 – 2139; b) M. B. Talawar, R. Sivabalan, N. Senthilkumar, G. Prabhu, S. N. Asthana, *J. Hazard. Mater.* **2004**, *113*, 11 – 25.

[10] Y. Kim, E. Kim, G. Clavier, P. Audebert, *Chem. Commun.* **2006**, 3612 – 3614.

[11] K. Lange, A. Koenig, C. Roegler, A. Seeling, J. Lehmann, *Bioorg. Med. Chem. Lett.* **2009**, *19*, 3141 – 3144.

[12] $C_7H_8ClN_7O_{10}$, FW = 385.65, monoclinic, $C2/c$, $a = 23.517(6)$, $b = 7.7687(18)$, $c = 19.609(5)$ Å, $\alpha = 90$, $\beta = 126.052(5)$, $\gamma = 90°$, $V = 2896.4(12)$ Å^3, $Z = 8$, $\rho_{calcd} = 1.769$ Mg m^{-3}, $\mu = 0.339$ mm^{-1}, $F(000) = 1568$, $R_1 = 0.0258$ for 2700 observed ($I > 2\sigma I$) reflections and 0.0293 for all 3011 reflections, Goodness-of-fit = 1.049, 226 parameters.

[13] CCDC 922579 (**2**) contains 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.

[14] a) R. Duddu, P. R. Dave, R. Damavarapu, R Surapaneni, R. Gilardi, D. Parrish, *Synth. Commun.* **2008**, *38*, 767 – 774; b) C.

Krieger, H. Fischer, F. A. Neugebauer, F. Guckel, D. Schweitzer, *Acta Crystallogr. Sect. C* **1987**, *43*, 1412 – 1415; c) M. Yu. Antipin, T. V. Timofeeva, D. S. Yufit, I. Sauer, *Izv. Akad. Nauk* **1995**, 2443 – 2450.

[15] E. A. Zhurova, A. I. Stash, V. G. Tsirelson, V. V. Zhurov, E. V. Bartashevich, V. A. Potemkin, A. A. Pinkerton, *J. Am. Chem. Soc.* **2006**, *128*, 14728 – 14734.

[16] J. R. Stine, Materials Research Society, Syposium Proc. 296 (Structure and Properties of Energetic Materials) **1993**, 3 – 12.

[17] L. A. Fried, W. M. Howard, S. Bastea, K. Glaesmann, P. C. Souers, P. A. Vitello, L. F. Kuo, *CHEETAH Thermochemical Code*, Lawrence Livermore National Laboratory, Livermore, CA.

[18] U. Hess, H. Brosig, G. Konig, M. Stoeter, D. Stalleicken, *Pharmazie* **2002**, *57*, 460 – 464.

[19] See Supporting Information.

[20] Some chemical transformation of the tetrazine radical is observed and becomes more prominent at scan rates slower than 0.2 $\mathrm{V\,s^{-1}}$.