



Synthesis and Thermal Behavior of a Fused, Tricyclic 1,2,3,4-Tetrazine Ring System

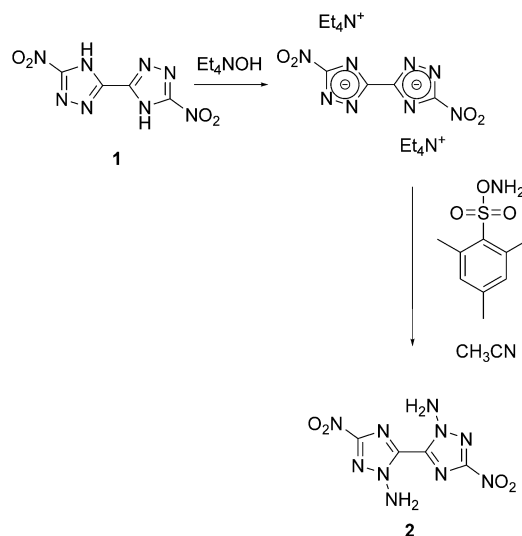
David E. Chavez,* Jeffery C. Bottaro, Mark Petrie, and Damon A. Parrish

Abstract: This study presents the synthesis and characterization of a fused, tricyclic 1,2,3,4-tetrazine ring system. The molecule is synthesized in a three-step process from 5,5'-dinitro-bis(1,2,4-triazole) via a di-N-amino compound. Oxidation to form the azo-coupled fused tricyclic 1,2,3,4-tetrazine is achieved using *tert*-butyl hypochlorite as the oxidant. The di-N-amino compound and the desired fused tricyclic 1,2,3,4-tetrazine display interesting thermal behavior and are predicted to be high-performance energetic materials.

The synthesis of the first 1,2,3,4-tetrazine was reported by Yamaguchi and co-workers in 1988.^[1] While many examples of 1,2,3,4-tetrazine mono- and di-N-oxides have been reported,^[2] very few syntheses of unoxidized 1,2,3,4-tetrazines have been described.^[3] Additionally, neither the synthesis of the parent 1,2,3,4-tetrazine heterocycle, nor any nonfused derivatives have been reported to date. 1,2,3,4-tetrazine-1,3-dioxide heterocycles are a stable class of molecules with decomposition temperatures typically above 200 °C.^[3] This stabilization is known to occur through the zwitterionic nature of the N-oxide functional group as well as conjugation through fused π systems. Interestingly, the fused bicyclic 1,2,3,4-tetrazine reported by Yamaguchi and co-workers displayed relatively poor thermal stability.

Synthetic routes to 1,2,3,4-tetrazines typically make use of just a few methodologies. The method used by Yamaguchi was nitrogen-atom ring-insertion of an N-amino group attached to a 1,2,3-triazole.^[1] An alternate route is through cyclization of an arene diazonium salt with a diazocyclopentadiene unit.^[4] Similarly, arene diazonium salts have been condensed with 3,5-diaminopyrazole to provide a fused 1,2,3,4-tetrazine.^[5]

Our approach involved the possibility of using an azo coupling strategy starting with a di-N-amino compound. Azo coupling of N-amino compounds has been previously reported.^[6] Our efforts began with the double N-amination of 3,3'-dinitro-5,5'-bi-1,2,4-triazole (**1**).^[7] While the N-oxidation of **1** has been reported,^[8] no reports of N-amination have been described.^[9] Recently, we outlined a similar amination



Scheme 1. Synthesis of **2**.

effort.^[10] We began our investigation by studying the amination of a variety of salts of **1**, including the potassium, ammonium, triethylammonium, and diazabicycloundecane salts. The aminating reagents studied included mesitylenesulfonyl-*O*-hydroxylamine^[11] and toluenesulfonyl-*O*-hydroxylamine.^[12] Overall, we found that the reaction could be performed by adding the bis(tetraethylammonium) salt of **1** to a solution of mesitylsulfonyl-*O*-hydroxylamine in acetonitrile (Scheme 1). The desired di-N-amination product **2** was isolated in 75 % yield. The reaction could also be performed using toluene sulfonyl hydroxylamine to give the product in comparable yields.

Compound **2** was found to be thermally stable up to 241 °C, where it began to decompose. Crystals suitable for X-ray diffraction were grown from acetonitrile. The molecule was found to exist in the monoclinic crystal system, and belongs to the $P2_1/n$ space group. The molecule was found to have a density of 1.827 g cm⁻³ at 20 °C and 1.857 g cm⁻³ at -123 °C. The structure is shown in Figure 1. The N-NH₂ bond length is 1.406 Å while the C-NO₂ bond length is 1.450 Å. The N-NH₂ groups are not in conjugation with the ring nitrogen atom, but are rotated 90 °C out of the plane of the ring, as is typical with N-amino moieties. This effect causes the molecules to pack in a complex arrangement.

Oxidation of **2** was investigated using sodium dichloroisocyanurate, trichloroisocyanuric acid, sodium hypochlorite, and *tert*-butyl hypochlorite as the oxidizer. While each oxidant appeared to provide some level of azo-coupled product, we found that *tert*-butyl hypochlorite was the most effective at

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

Dr. J. C. Bottaro, Dr. M. Petrie
SRI International
Menlo Park, CA 94025 (USA)

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

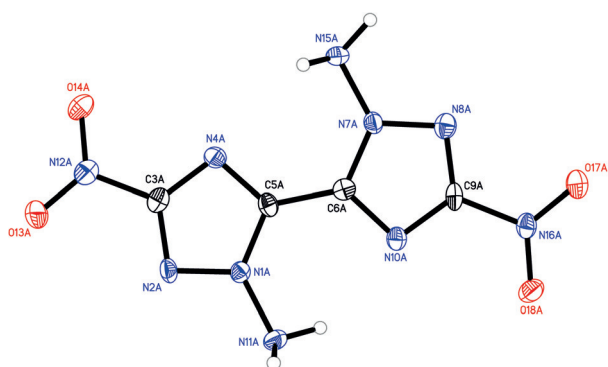
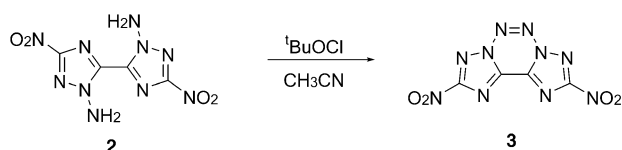


Figure 1. Molecular structure of **2** as it appears in the crystal structure. Nonhydrogen atomic displacement ellipsoids are set at 50% probability.



Scheme 2. Synthesis of **3**.

efficiently converting **2** to the desired fused tricyclic 1,2,3,4-tetrazine **3** in about 80% yield (Scheme 2). The product is a light-yellow solid and begins to decompose at 138 °C.

X-ray crystallographic analysis of **3** shows that the molecule crystallizes as two different polymorphs (α (toluene) and β (acetone)). Both molecules crystallize in the orthorhombic crystal system and the P2(1)2(1)2(1) space group but the packing and unit cell are quite different.^[13] The α polymorph has a density of 1.907 g cm⁻³ at 21 °C while the β polymorph has a density of 1.901 g cm⁻³ at 21 °C. The molecule is nearly planar, but packs in a herringbone pattern. The crystal structure is shown in Figure 2, while the crystal packing of the α and β polymorphs are shown in Figure 3a and 3b, respectively. The N1–N2 bond length is shortened to 1.375 Å compared to the same bond in **1**, while the C–NO₂ bond is extended to 1.464 Å.

The sensitivity data for compounds **2** and **3** are shown in Table 1.^[13] Compound **2** was found to be insensitive to impact,

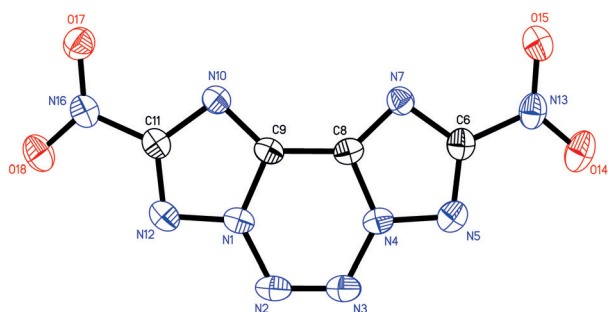


Figure 2. Molecular structure of **3** as it appears in the crystal structure. Nonhydrogen atomic displacement ellipsoids are set at 50% probability.

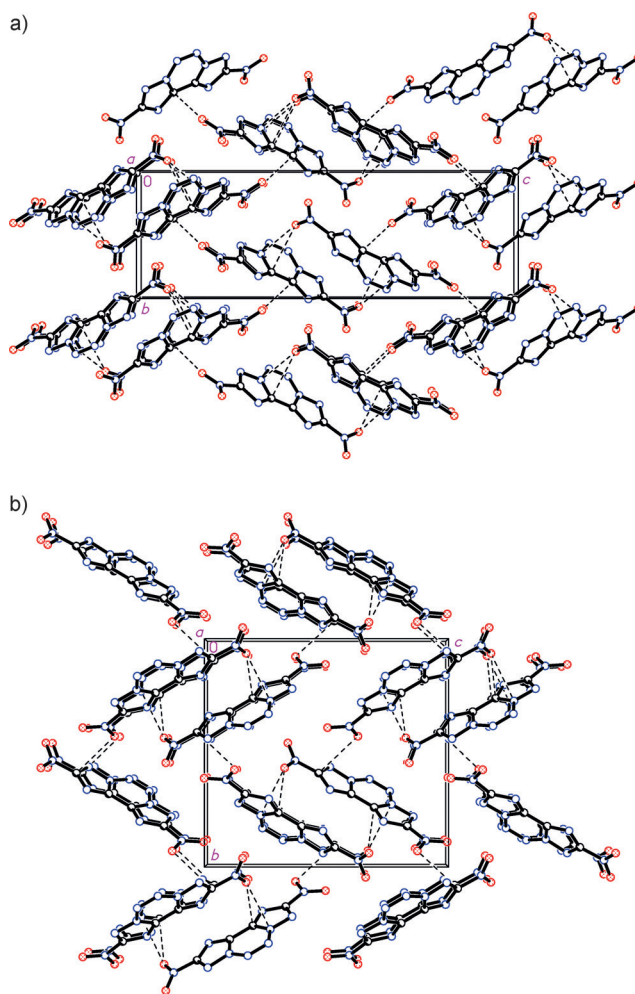


Figure 3. A view of the packing down the *a*-axis of the unit cell for the α (a) and β (b) polymorphs of **3**.

Table 1: Sensitivity data for **2** and **3**.

	Impact [J] ^[a]	Spark [J] ^[b]	Friction [N] ^[c]
2	> 78	0.125	> 360
3	5.3	0.025	92
PETN	2.5	0.062	92
RDX	4.6	0.062	157

[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.

spark, and friction. Compound **3** is similar to RDX (1,3,5-trinitroperhydro-1,3,5-triazine) with respect to impact and electrostatic discharge, and was similar to PETN (pentaerythritol tetranitrate) with respect to friction.

The heats of formation of compounds **2** and **3** were calculated by using the method developed by Byrd and Rice.^[15] The heat of formation of **2** was calculated to be 518 kJ mol⁻¹, while the heat of formation of **3** was calculated to be 787 kJ mol⁻¹. These data, taken together with the crystal densities of **2** and **3**, allow for the prediction of the explosive performance properties for **2** and **3** using the Cheetah thermochemical code.^[16] Compound **2** was predicted to have

a detonation pressure of 32 GPa and a detonation velocity of 8.7 km s⁻¹. The detonation pressure for **3** was predicted to be 38 GPa and the detonation velocity was predicted to be 9.4 km s⁻¹.

In conclusion, we have synthesized a tricyclic 1,2,3,4-tetrazine starting from 5,5'-dinitro-bis-1,2,4-triazole, followed by N-amination and oxidative ring closure. Compound **2** displays excellent thermal stability, good density, is insensitive to impact, spark, and friction, and is predicted to have performance properties approaching RDX. Compound **3** is similar to RDX and PETN with respect to its sensitivity properties and is predicted to be a high performance material.

Experimental Section

Synthesis of 2: Compound **1** (0.70 g, 2.7 mmol) was treated with 1M tetraethylammonium hydroxide in water (0.80 g, 5.4 mmol, 5.4 mL). The mixture was stirred for 30 min and the water was removed by rotary evaporation. Mesitylene sulfonyl *O*-hydroxylamine (2.0 g, 9.3 mmol) was added to acetonitrile (35 mL). The tetraethylammonium salt of **1** was then added to the reaction mixture portionwise over 5 min. The reaction was stirred for 30 min, and then filtered and the solvent was evaporated. The residue was treated with water (5 mL), triturated, and the precipitate filtered and dried to provide **2** (0.64 g, 80%). M.P. 241 °C (dec.). ¹H NMR ([D₆]DMSO): δ = 7.5 ppm (s, 4H). ¹³C NMR ([D₆]DMSO): δ = 140.45, 157.83 ppm. IR (KBr): $\tilde{\nu}$ = 3333, 3300, 3237, 3165, 1627, 1594, 1561, 1474, 1421, 1316, 1217, 1192, 1132, 1045, 1014, 931, 838, 816 cm⁻¹. Elemental analysis calcd for C₄H₄N₁₀O₄: C 18.76, H 1.57, N 54.68; found: C 18.75, H 1.59, N 54.66.

Synthesis of 3: Compound **2** (0.30 g, 1.17 mmol) was added to acetonitrile (5 mL) and was subsequently treated dropwise with *tert*-butyl hypochlorite (0.31 g, 2.93 mmol). The mixture was stirred for 30 min and the reaction poured into ethyl acetate (30 mL). The mixture was washed with water (5 × 7 mL) and the organic layer dried with sodium sulfate, filtered, and evaporated. Compound **3** was isolated as a yellow solid (0.235 g, 80%). M.P. 138 °C (dec.). ¹³C NMR ([D₆]acetone): δ = 138.30, 161.72 ppm. IR (KBr): $\tilde{\nu}$ = 1684, 1574, 1520, 1508, 1459, 1433, 1375, 1330, 1302, 1258, 1221, 1162, 1104, 1089, 1045, 995, 877, 835, 772, 752, 669, 635, 571 cm⁻¹. Elemental analysis calcd for C₄N₁₀O₄: C 19.06, N 55.56; found: C 19.04, N 55.57.

See the Supporting Information for further experimental details, including X-ray crystallographic data.

Acknowledgements

We would like to thank Stephanie Hagelberg (elemental analysis) for characterization, Hongzhao Tian and Jose G. Archuleta, (sensitivity testing), and Mary Sandstrom (thermal analysis). We would also like to thank the Joint Munitions Technology Development Program for funding this work. 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).

Keywords: 1,2,3,4-tetrazines · 1,2,4-triazoles · amination · oxidation · energetic materials

How to cite: *Angew. Chem. Int. Ed.* **2015**, *54*, 12973–12975

Angew. Chem. **2015**, *127*, 13165–13167

- [1] T. Kaihoh, T. Itoh, K. Yamaguchi, A. Ohsawa, *J. Chem. Soc. Chem. Commun.* **1988**, 1608–1609.
- [2] a) A. S. Churakov, O. Yu. Smirnov, Y. A. Strelendo, S. L. Ioffe, V. A. Tartkovsky, Y. T. Struchkov, F. M. Dolgushin, A. I. Yanovsky, *Mendeleev Commun.* **1994**, 4, 122–124; b) A. M. Churakov, V. A. Tartakovsky, *Chem. Rev.* **2004**, *104*, 2601–2616; c) D. G. Piercey, D. E. Chavez, S. Heimsch, C. Kirst, T. M. Klapötke, J. Stierstorfer, *Propellants Explos. Pyrotech.* **2015**, *40*, 491–497.
- [3] a) D. Seebach, D. Enders, B. Renger, W. Bruegel, *Angew. Chem.* **1973**, 85, 504; b) D. Seebach, R. Dach, D. Enders, B. Renger, M. Jansen, G. Brachtel, *Helv. Chim. Acta* **1978**, *61*, 1622–1647; c) S. Mataka, J. P. Anselme, *Chem. Lett.* **1973**, 51–54.
- [4] P. J. Mackert, K. Hafner, N. Nimmerfro, K. Banert, *Chem. Ber.* **1994**, *127*, 1479–1488.
- [5] Z. Li Song, L. Hao, Y. Lu, N.-y. Wu, *Huaxue Shiji* **2013**, *35*, 176–177.
- [6] a) P. Yin, D. A. Parrish, J. M. Shreeve, *Chem. Eur. J.* **2014**, *20*, 6707–6712; b) C. Qi, S. H. Li, Y. C. Li, Y. A. Wang, X. K. Chen, S. P. Pang, *J. Mater. Chem.* **2011**, *21*, 3221–3225; c) Y. C. Li, C. Qi, S. H. Li, H. J. Zhang, C. H. Sun, Y. Z. Yu, S. P. Pang, *J. Am. Chem. Soc.* **2010**, *132*, 12172–12173; d) T. M. Klapötke, D. G. Piercey, J. Stierstorfer, *Dalton Trans.* **2012**, 41, 9451–9459.
- [7] A. A. Dippold, T. M. Klapötke, N. Winter, *Eur. J. Inorg. Chem.* **2012**, 3474–3484.
- [8] A. A. Dippold, T. M. Klapötke, *J. Am. Chem. Soc.* **2013**, *135*, 9931–9938.
- [9] For N-amination and N-oxidation of 5,5'-bis(1,2,3-triazole) < see: C. He, J. M. Shreeve, *Angew. Chem. Int. Ed.* **2015**, *54*, 6260–6264; *Angew. Chem.* **2015**, *127*, 6358–6362.
- [10] M. M. Breiner, D. E. Chavez, D. A. Parrish, *Synlett* **2013**, 519–521.
- [11] L. A. Carpino, *J. Am. Chem. Soc.* **1960**, *82*, 3133–3135.
- [12] J. Mendiola, J. A. Rincon, C. Mateos, J. F. Soriano, O. de Frutos, J. K. Niemeier, E. M. Davis, *Org. Process Res. Dev.* **2009**, *13*, 263–267.
- [13] The differential scanning calorimetry (DSC) and sensitivity data of the α and β polymorphs do not differ significantly.
- [14] CCDC 1406269 (**2**), and CCDC1412792 and CCDC141791 (α and β polymorphs, respectively, of **3**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.
- [15] a) E. F. Byrd, B. M. Rice, *J. Phys. Chem. A* **2006**, *110*, 1005–1013; b) E. F. Byrd, B. M. Rice, *J. Phys. Chem. A* **2009**, *113*, 5813.
- [16] 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.

Received: July 21, 2015

Published online: September 3, 2015