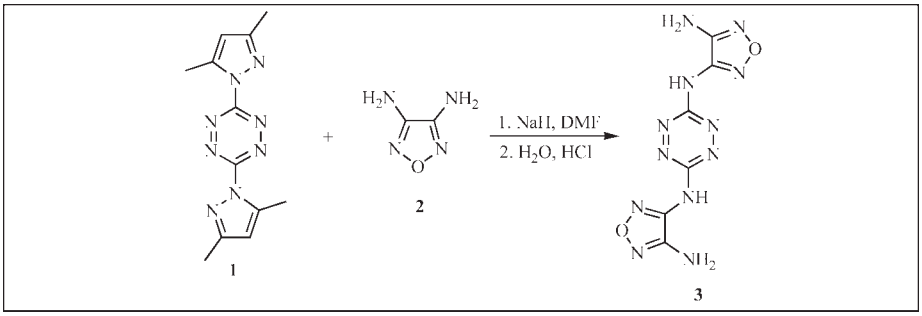
David E. Chavez[a]* and Damon A. Parrish[a,b]

[a]High Explosives Science and Technology (DE-1), Los Alamos National Laboratory, MS C920, Los Alamos, New Mexico 87545
[b]Naval Research Laboratory, 4555 Overlook Avenue, Washington, DC 20375
*E-mail: dechavez@lanl.gov

Received April 24, 2008
DOI 10.1002/jhet.7
Published online 4 February 2009 in Wiley InterScience (www.interscience.wiley.com).



The reactivity of 3,4-diamino-1,2,5-oxadiazole (**2**) toward nucleophilic substitution of 3,6-bis(3,5-dimethylpyrazol-1yl)-1,2,4,5-tetrazine (**1**) was studied. A new class of high nitrogen heterocyclic systems was prepared. It was determined that 3,4-diamino-1,2,5-oxadiazole did not display the required nucleophilicity to be reactive. However, the anion of 3,4-diamino-1,2,5-oxadiazole, prepared by treatment with strong base, was sufficiently reactive to act as a nucleophile.

J. Heterocyclic Chem., **46**, 88 (2009).

INTRODUCTION

High nitrogen heterocyclic systems have seen increasing interest over the past decade due to their potential utility in numerous applications, such as propellants, explosives, and pyrotechnics [1–4]. We have primarily focused on the investigation of tetrazines [5–9] and 1,2,5-oxadiazoles [9] in the past, but had not combined the two heterocycles into a new heterocyclic system. Nucleophilic substitutions of tetrazines, in particular 3,6-bis(3,5-dimethylpyrazol-1yl)-1,2,4,5-tetrazine (**1**), have been studied extensively by us [10] and others [11,12]. Additionally, the nucleophilicity of 3,4-diamino-1,2,5-oxadiazole (**2**) has been studied as well [13], but there exist no literature examples describing the reactivity of **1** with **2** or any other tetrazine. We began our investigations by studying the substitution reaction of **1** with **2**. We wish to report here that we have been successful in identifying conditions that allow us to prepare the desired tetrazine-oxadiazole heterocyclic systems in good yield. We have also confirmed the structure through X-ray crystallography.

RESULTS AND DISCUSSION

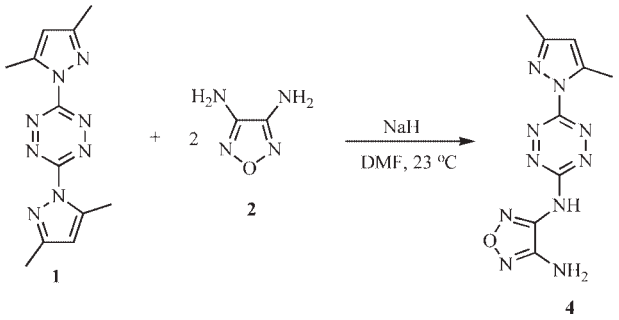
Our initial efforts toward the synthesis of **3** involved the reaction of **1** and **2** in refluxing acetonitrile (Scheme 1). Unfortunately, no reaction was observed even after 2 days. More polar solvents, such as dimethylformamide (DMF) were also investigated, but only trace amounts of product was observed by thin layer chromatography. Because of these setbacks, we focused on an approach we employed recently [5]. In this approach, we reported the synthesis of some new high nitrogen materials by reacting with the anion of nitroguanidine with **1** in methanol. The success of this chemistry led us to investigate whether similar conditions might be applicable with **1** and **2**.

As shown in Scheme 1, our strategy involved the deprotonation of **2** with sodium hydride in DMF. Our ultimate goal was to prepare **3** and as such, we employed two equivalents of **2**. When the reaction was performed at ambient temperature, we observed the complete conversion of **1** to a new product after a few hours as analyzed by thin layer chromatography. Isolation and analysis of the product showed that the material isolated was the mono-substituted product **4**.

It was believed that as the product **4** began to form, an acidic proton was generated, in the form of the oxadiazol-ylamino proton. This acidic proton serves to neutralize the anion of **2**, thus resulting in an unreactive form of **2**. We subsequently reasoned that the addition of more equivalents of the anion of **2** would allow for complete conversion of the intermediate **1** to **3**.

Indeed, when four equivalents of the anion of are generated in DMF by the reaction of sodium hydride and **2**, followed by the addition of **1** at ambient temperature, complete conversion of intermediate **4** to product **3**

Scheme 1



was observed. To isolate the product, the reaction was quenched by pouring into ice water and acidifying to pH = 1 (Scheme 2). Compound **3** was determined to be very thermally stable and doesn't begin to decompose until 280°C. An alternative approach that was equally successful was the use of two equivalents of **2** and four equivalents of sodium hydride.

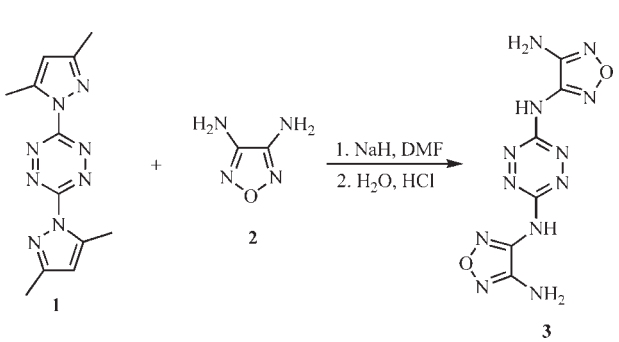
X-ray quality crystals were grown from DMSO with slow diffusion of water. A crystal structure was determined for bis-substituted product **3** and is shown in Figure 1. The crystals obtained were a DMSO solvate containing two DMSO molecules and one molecule of **3**.

Interestingly, as shown in Scheme 3, a bis-tetrazine substituted 1,2,5 oxadiazole can be prepared by using two equivalents of **1** and only one equivalent of **2**. Although these new heterocycles contain a large percentage of nitrogen, they are not energetic materials. They are insensitive to impact, spark and friction. Each of these new heterocyclic molecules will now be investigated as potential starting materials for new high-nitrogen energetic materials.

EXPERIMENTAL

3-(3,5-Dimethylpyrazol-1yl), 6-(3-amino-1,2,5-oxadiazol-4-ylamino)-1,2,4,5-tetrazine (4). To dimethylformamde (10 mL) was added 70 mg of NaH (60% dispersion in oil, 1.7 mmol), and 100 mg of 3,4-diamino-1,2,5-oxadiazole (1 mmol). The

Scheme 2



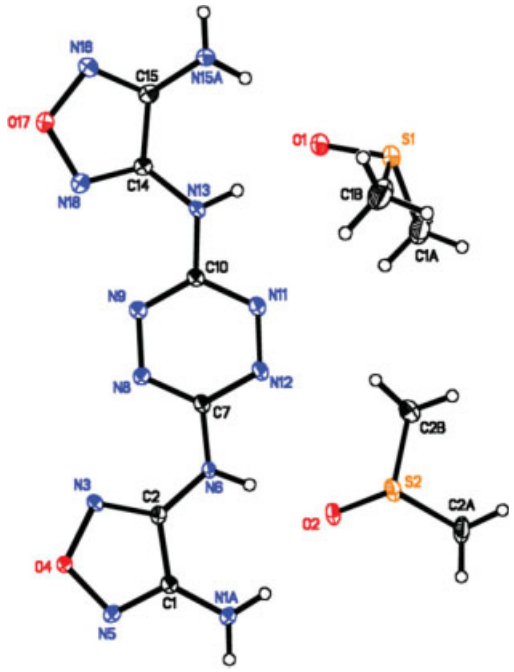
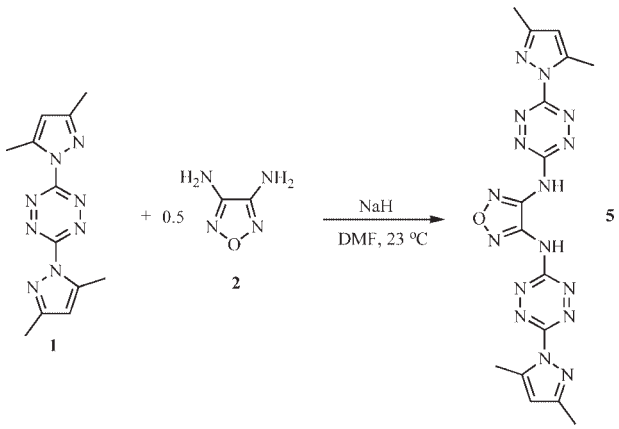


Figure 1. View of **3** showing the labeling of the nonhydrogen atoms. Thermal ellipsoids are shown at the 50% probability level. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

mixture was stirred at 23°C for 30 min. To the reaction mixture, 135 mg of **1** (0.5 mmol) was added. The reaction was then stirred at 23°C for 30 min. After this time **1** was completely consumed. The reaction mixture was then poured into ice water and acidified to pH = 1. The reaction was allowed to stand at 5°C for 16 h and a red precipitate formed. The material was collected by filtration, washed with water and air dried to provide 200 mg (73%), mp 87–89°C; IR (ν, cm^{-1}) 3477, 3354, 3227, 2925, 2851, 1646, 1609, 1581, 1558, 1527, 1450, 1417, 1323, 1262, 1082, 1049, 1025, 976, 955, 833, 800, 563. ^{1}H NMR (deuteriochloroform, ppm): δ 2.23 (s, 3H), 2.43 (s, 3H), 6.2 (s, 2H), 6.25 (s, 1H), 11.42 (s, 1H); ^{13}C NMR (deuteriodimethyl sulfoxide): δ 12.84, 13.37, 109.58,

Scheme 3



142.01, 143.37, 151.13, 152.36, 157.88, 159.98. *Anal*. Calcd. for $C_9H_{10}N_{10}O$: C, 39.43; H, 3.68; N, 51.07. Found: C, 39.47; H, 3.65; N, 51.04.

3,4-Bis[6-(3,5-dimethylpyrazol-1yl)-1,2,4,5-tetrazin-6-ylamino]-1,2,5-oxadiazole (5). To a mixture of 540 mg of **1** (2.0 mmol) and 100 mg of 3,4-diamino-1,2,5-oxadiazole (1 mmol) in 5 mL of DMF was added 140 mg of NaH (60% dispersion in oil, 3.4 mmol) at 23°C. The reaction mixture was allowed to stir for 1 h. The reaction mixture was poured into 20 mL of water, acidified to pH = 1, the solid collected by filtration and washed with water to give a orange product 202 mg (45%), mp 196°C (dec); IR (ν, cm^{-1}) 3228, 3056, 2986, 2933, 1577, 1480, 1421, 1274, 1077, 1047, 1027, 971, 951, 801, 568. ^{1}H NMR (deuterioacetonitrile, ppm): δ 2.27 (s, 6H), 2.52 (s, 6H), 6.20 (s, 2H), 9.63 (bs, 2H). ^{13}C NMR (deuterioacetonitrile): δ 13.72, 13.74, 111.20, 143.97, 147.01, 153.69, 159.81, 161.06. *Anal*. Calcd. for $C_{16}H_{14}N_{16}O$: C, 43.05; H, 3.16; N, 50.20. Found: C, 43.06; H, 3.17; N, 50.19.

3,6-Bis(3-amino-1,2,5-oxadiazol-4-ylamino)-1,2,4,5-tetrazine (3). To a solution of 3.0 g (60% dispersion in oil, 75 mmol) of NaH in 50 mL of DMF was added 2.0 g (20 mmol) of **2**. The mixture was allowed to stir at 25°C for 30 min. A total of 1.35 g (5.0 mmol) of **1** was then added in one portion and the reaction allowed to stir at 25°C for 1 h. The reaction mixture was then poured into 200 mL of water and acidified to pH = 1. A red precipitate formed, the mixture was cooled in an ice bath, the solid collected by filtration and the orange-red solid was washed with water and air-dried to give 1.27 g (91%), mp 280°C (dec); IR (ν, cm^{-1}) 3391, 3329, 3260, 3080, 2953, 2921, 2851, 1642, 1634, 1511, 1446, 1421, 1307, 1262, 1074, 1008, 980, 861, 812. ^{1}H NMR (deuteriodimethylsulfoxide): δ 6.15 (bs, 4H), 10.8 (s, 2H); ^{13}C NMR (deuteriodimethylsulfoxide): δ 143.71, 151.76, 158.78. *Anal*. Calcd. for $C_6H_6N_{12}O_2$: C, 25.9; H, 2.17; N, 60.42. Found: C, 25.5; H, 2.19; N, 60.44.

Single-crystal X-ray diffraction analysis of 3. $C_{10}H_{18}N_{12}O_4S_2$, FW = 434.48, monoclinic, $P2_1/c$, a = 10.1881(8) Å, b = 19.4198(15) Å, c = 9.9515(8) Å, α = 90°, β = 114.649(2)°, γ = 90°, V = 1789.5(2) Å^3, Z = 4, ρ_{calc} = 1.613 mg/m^3, μ = 0.186 mm^{-1}, $F(000)$ = 904, R_1 = 0.0456 for 3369 observed ($I > 2\sigma I$) reflections and 0.0545 for all 3680 reflections, Goodness-of-fit = 1.095, 253 parameters.

A thin red/orange plate of dimensions 0.56 mm × 0.21 mm × 0.007 mm was mounted on glass fiber using a small amount of Cargille immersion oil. Data were collected at the Advanced Photon Source in Argonne National Laboratory. A Bruker three-circle platform diffractometer equipped with a SMART 6000 CCD detector was used to collect the data. An Oxford Cryojet low temperature device was used to keep the crystals at a constant 103(2) K during data collection.

Data collection was performed and the unit cell was initially refined using *SMART* v5.625 [14]. Data reduction was performed using *SAINT* v6.36A [15] and *XPREP* v6.12 [16]. Corrections were applied for Lorentz, polarization, and absorption effects using *SADABS* v2.03 [17]. The structure was solved and refined with the aid of the programs in the *SHELXTL-plus* v6.10 system of programs [18]. The full-matrix least-squares refinement on F^2 included atomic coordinates and anisotropic thermal parameters for all non-H atoms. The H atoms were included using a riding model.

CCDC 685362 contains the supplementary crystallographic data for this article. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

Acknowledgments. The authors thank the Joint DoD/DOE munitions technology development program for financial support. They also thank Stephanie Hagelberg and Gabriel Avilucea for analytical services. ChemMatCARS Sector 15 is principally supported by the National Science Foundation/Department of Energy under grant number CHE-0535644. The use of the Advanced Photon Source was supported by the US Department of Energy, Office of Science, Office of Basic Energy Sciences, under Contract no. DE-AC02-06CH11357.

REFERENCES AND NOTES

[1] Singh, R. P.; Verma, R. D.; Meshri, D. T.; Shreeve, J. M. Angew Chem 2006, 45, 3584.

[2] Klapoetke, T. M.; Steinhauser, G. Angew Chem 2008, 47, 3330.

[3] Guo, Y.; Haixing, G.; Twamley, B.; Shreeve, J. M. Adv Mat 2007, 19, 2884.

[4] Klapoetke, T. M.; Sabate, C. M. Chem Mater 2008, 20, 1750.

[5] Chavez, D. E.; Hiskey, M. A.; Gilardi, R. D. Org Lett 2004, 6, 2889.

[6] Talawar, M. B.; Sivabalan, R.; Senthilkumar, N.; Prabhu, G.; Asthana, S. N. J. Hazard Mater 2004, 113, 11.

[7] Chavez, D. E.; Hiskey, M. A.; Naud, D. L. Prop Expl Pyro 2004, 29, 209.

[8] Chavez, D. E.; Hiskey, M. A.; Gilardi, R. D. Angew Chem Int Ed Engl 2000, 39, 1791.

[9] Chavez, D. E.; Hiskey, M. A. J Heterocycl Chem 1998, 35, 1392.

[10] Chavez, D.; Hill, L.; Hiskey, M.; Kinkead, S. J Energ Mater 2000, 18, 219.

[11] Audebert, P.; Sadki, S.; Miomandre, F.; Clavier, G.; Verniere, M. C.; Saoud, M.; Hapiot, P. New J Chem 2004, 28, 387.

[12] Novak, Z.; Bostai, B.; Csekei, M.; Loerincz, K.; Kotschy, A. Heterocycles 2003, 60, 2653.

[13] Willer, R.; Moore, D. W. J Org Chem 1985, 50, 5123.

[14] Bruker, SMART v5.625; Bruker AXS, Inc.: Madison, WI, 2001.

[15] Bruker, SAINT v6.36A; Bruker AXS, Inc.: Madison, WI, 2002.

[16] Bruker, XPREP v6.12; Bruker AXS, Inc.: Madison, WI, 2001.

[17] Bruker, SADABS v2.03; Bruker AXS, Inc.: Madison, WI, 2000.

[18] Bruker, SHELXTL v6.10; Bruker AXS, Inc.: Madison, WI, 2000.