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Novel High-Nitrogen Materials Based on Nitroguanyl-Substituted Tetrazines

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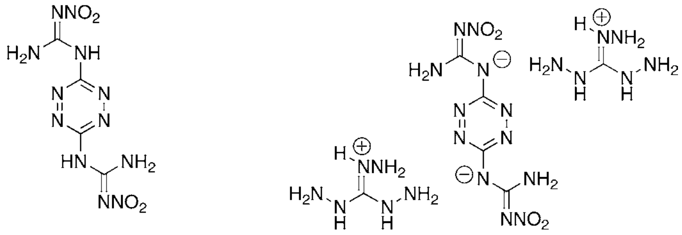
ABSTRACT



The synthesis and properties of several novel high-nitrogen materials based on nitroguanyl-substituted tetrazines are described. An optimized procedure provides straightforward access to these materials in multigram quantities.

Recently there has been considerable interest in the study of the reactivity and properties of 1,2,4,5-tetrazine heterocycles.[1−7] The high degree of attention given to this heterocyclic system stems from the unique and interesting properties displayed by 1,2,4,5-tetrazines. For example, tetrazines have demonstrated powerful synthetic utility through their ability to participate in inverse electron demand Diels−Alder reactions,[1] providing access to a wide range of other heterocycles and natural products.[2] In addition, the 1,2,4,5-tetrazine ring system displays unique materials properties as well. This electroactive, colored ring system typically exhibits high electron affinity, low lying π^* orbitals and n-π^* transitions in the visible light region, attractive properties for optical and electroactive materials applications.[3] Furthermore, tetrazines also possess high positive heats of formation and crystal densities, properties important in energetic materials applications.[4] Most of the recent reports on the chemistry of tetrazines have focused on the development of methods for preparing difficult-to-access nonsymmetrically substituted tetrazines.[5] The majority of successful methods use soft, neutral heteroatom nucleophiles for the displacement of leaving groups at the 3 and 6 positions of the tetrazine.[6] The use of hard carbanion nucleophiles results in unusual azaphilic addition to the tetrazine core.[5b] Only a few reports have documented the reactivity of tetrazines toward anionic heteroatom nucleophiles.[5a,7] In these cases, the reported yields are typically low and undesired side reactions are generally observed.

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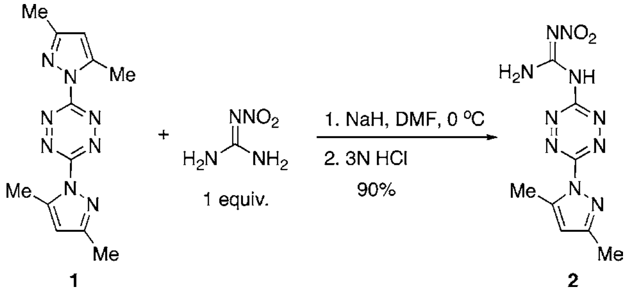
Scheme 1. Reactivity of Sodium Nitroguanidine with **1**



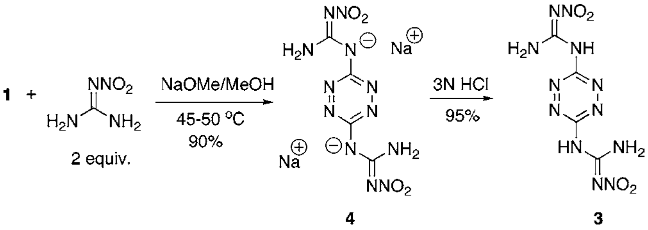
At the Los Alamos National Laboratory we have been interested in the development of novel heterocyclic materials for applications in a wide variety of fields[4,8] In particular, we have studied heterocycles with high nitrogen content. In our continuing efforts in this area, we now report on the reactivity of tetrazines with the anion of nitroguanidine.

The low level of nucleophilicity displayed by nitroguanidine itself is not sufficient to allow participation in nucleophilic displacements on tetrazines, even at elevated temperatures. However, it has been demonstrated that nitroguanidine has a pK_a in the range of 14−15 and forms a stable and isolable potassium salt.[9] Unfortunately, only two references in the literature report the use of a metal salt of nitroguanidine as a nucleophile.[9,10]

We began our investigations by focusing on the readily available 3,6-bis(3,5-dimethylpyrazol-1-yl) tetrazine (**1**) as our starting material.[11] In our preliminary experiments we prepared the sodium salt of nitroguanidine in situ through the use of NaH in DMF. After gas evolution ceased, **1** was added in portions at reduced temperature (Scheme 1). TLC analysis indicated the complete consumption of **1** and the formation of a single, new product after several minutes. Quenching of the reaction mixture with water and acidification resulted in the precipitation of the monosubstitution product **2**.

Having successfully prepared a mononitroguanyl tetrazine derivative, we turned our attention toward the preparation of 3,6-bis-nitroguanyl tetrazine (**3**). In the few previous reports on the reactivity of delocalized anionic heteroatom nucleophiles with tetrazines, difficulty was encountered in preparing doubly substituted products.[5,7] We were concerned that higher reaction temperatures may be required to achieve double displacement, which would likely result in unwanted side reactions.[12] Much to our surprise, the use of 2 equiv of the sodium salt of nitroguanidine resulted in the clean formation of the 3,6-bis-nitroguanyl tetrazine **3** at temperatures below 23 °C leading to a >85% isolated yield.

Scheme 2. Optimized Route for Preparation of **3**



To better examine the materials properties of this novel high nitrogen compound, we required an optimized method to (1) prepare multigram quantities of **3** and (2) eliminate the use of DMF as the solvent. It is known that sodium methoxide can act as base for the deprotonation of nitroguanidine.[9] We thus prepared a methanolic solution of sodium nitroguanidine and found that a temperature of >40 °C was required to prevent the sodium nitroguanidine from precipitating from solution. Portionwise addition of **1** to the methanol solution at a constant temperature range of 45−50 °C and stirring for 2 h resulted in the precipitation of a reddish brown solid. This material was determined to be 3,6-bis-nitroguanyl tetrazine, disodium salt (**4**). Suspending **4** in water and subsequent neutralization with aqueous HCl resulted in the formation of **3** in excellent yield on a 30-g scale (Scheme 2).[13]

To confirm the proposed structure of **3**, an X-ray crystallographic analysis of a crystal grown from dimethyl sulfoxide (DMSO) was performed.[14] Indeed, the X-ray crystal structure demonstrates that **3** exists in the nitrimino form (Figure 1).

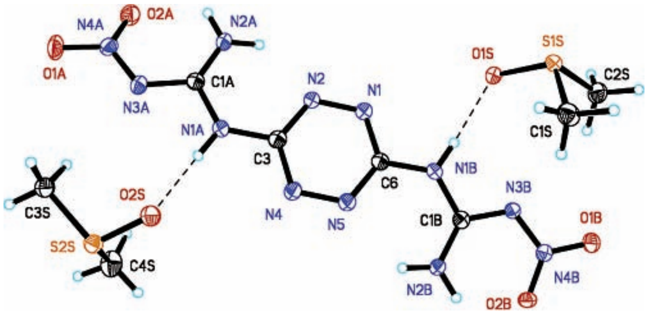


Figure 1. Ortep drawing of **3**·2DMSO.

In addition, the molecule crystallizes in a highly planar geometry. Solvate-free crystals were not attainable, but gas pycnometry indicates that the crystal density of **3** is near 1.76 g/cm^3.

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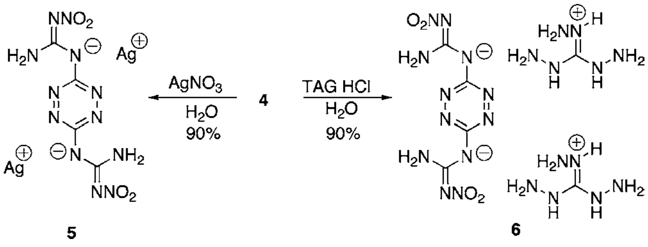
(11) Compound **1** is prepared on the pound scale in two steps at Los Alamos National Laboratory, starting from acetylacetone and triaminoguanidine hydrochloride. Coburn, M. D.; Buntain, G. A.; Harris, B. W.; Hiskey, M. A.; Lee, K.-Y.; Ott, D. G. *J. Heterocycl. Chem.* **1991**, *28*, 2049.

(12) Side reactions in a similar system have been described; see ref 7.

(13) KOMe was also used as a base and provided the more soluble potassium salt of nitroguanidine. which was an equally effective nucleophile.

(14) CCDC 239345 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB21EZ, UK; fax (+44)1223-336-033; deposit@ccdc.cam.ac.uk).

Scheme 3. Transformations of Intermediate **4**



The disodium salt **4** is a useful intermediate as it allows access to a variety of other derivatives of **3** (Scheme 3). For example, dissolution of **4** in warm water, followed by treatment with a solution of silver nitrate in water, results in the formation of the bis-silver salt **5**. Similarly, treatment with a solution of triaminoguanidinium hydrochloride (TAG•HCl) in water results in the formation of the bis-triaminoguanidinium salt **6**. Gas pycnometry indicates a crystal density near 1.61 g/cm^3 for **6**.

Compounds **3** and **6** were further evaluated to determine their corresponding heat of formation values. Compound **3** was found to have a heat of formation of +93 ± 2 kcal/mol by combustion calorimetry. This is quite impressive, considering that the heat of formation of nitroguanidine itself is reported to be −23 kcal/mol,[15] and is a clear indication of the degree of energy imparted to the overall molecule by the tetrazine ring. Compound **6** was found to have a very high heat of formation of +300 ± 2 kcal/mol. The above properties of these high-nitrogen materials make them attractive candidates for energetic materials applications.

We have demonstrated that the sodium salt of nitroguanidine can serve as a excellent nucleophile for reaction with **1**. An optimized method of preparation was developed using methanol as a solvent that allows compounds **3** and **6** to be prepared in multigram quantities. We have further discovered that **3** and **6** exhibit potentially useful energetic materials properties.[16] Current efforts are directed toward the study of combustion behavior of **3**−**6**. Preliminary results indicate that these materials display unique burn rate properties. These studies will be communicated in due course.

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Supporting Information Available: Experimental procedures and characterization data for the products. This material is available free of charge via the Internet at http://pubs.acs.org.

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[16] Compounds **3**−**6** are explosives and should be handled appropriately.