Synthesis of 4-Amino-3,5-dinitro-1*H*-pyrazole Using Vicarious Nucleophilic Substitution of Hydrogen

Robert D. Schmidt*, Gregory S. Lee, Philip F. Pagoria and Alexander R. Mitchell

Energetic Materials Center, Lawrence Livermore National Laboratory
P.O. Box 808 (L-282), Livermore, CA 94551

Richard Gilardi

Laboratory for the Structure of Matter
Naval Research Laboratory, Washington, DC 20375-5341
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A novel synthesis of the title compound was achieved by direct amination using Vicarious Nucleophilic Substitution (VNS) methodology. Reaction of 1,1,1-trimethylhydrazinium iodide with 3,5-dinitropyrazole in DMSO produces 4-amino-3,5-dinitro-1*H*-pyrazole as a 1:1 crystal solvate with DMSO. Recrystallization from water yields the monohydrated crystal. Recrystallization of the monohydrate from butyl acetate yields the compound in pure form.

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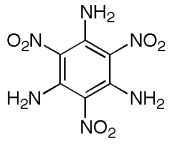
The compound 1,3,5-triamino-2,4,6-trinitrobenzene (TATB, **1**) is an explosive material with a remarkably low detonation sensitivity to impact, friction and spark, and an explosive power comparable to that of 2,4,6-trinitrotoluene (TNT). The unique insensitivity of TATB has been attributed to the high degree of hydrogen bonding afforded by its alternating amino and nitro functional groups, along with the molecular symmetry, which allows the molecule to form a graphite-like crystal structure [1]. It has also been suggested that the thermal stability of TATB may be, at least in part, due to alternating ortho amino and nitro groups, which allow the formation of benzofurazan and benzofuroxan rings in the first step of decomposition [2].



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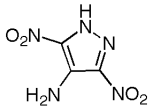


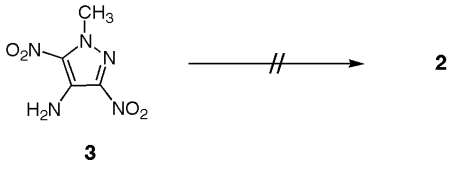
2

By analogy, many ideas for new insensitive explosive compounds have been based upon the assumption that introduction of amino groups into nitroaromatic molecules might decrease the sensitivity of the product relative to the unaminated starting material [3]. It is also generally true that the explosive power of solid explosives is increased by increasing the density, oxygen balance and/or heat of formation of the material [4].

With this in mind, one goal of our group's effort has been to synthesize compounds that may be considered as high-energy analogues of TATB. One target molecule that features the alternating amino-nitro aromatic moiety is 4-amino-3,5-dinitro-1*H*-pyrazole (**2**). Relative to TATB, **2** has a better oxygen balance and, because of its smaller ring size and the presence of nitrogen atoms in the ring, should have a higher density and heat of formation. Until recently, no reports of the successful synthesis of **2** have been published, although the existence of **2** was suggested as early as 1993 [5]. However, Shevelev makes a footnote mention of an approach to the synthesis of **2** [6]. In this paper, we report a novel approach to **2** using the technique of amination by Vicarious Nucleophilic Substitution of hydrogen (VNS) [7].

Our original efforts at preparing **2** were based on the attempted deprotection of *N*-protected analogues of **2**, including 4-amino-3,5-dinitro-1-methylpyrazole (**3**) [8] (Scheme 1). Oxidation followed by decarboxylation [9] was unsuccessful. Attempts to prepare the 1-*t*-butyl analogue of **3** for subsequent deprotection were also unsuccessful.

Scheme 1



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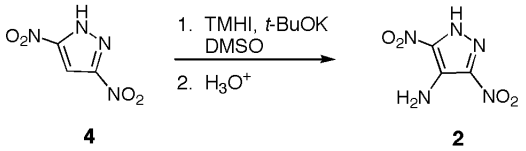
At about this same time, we discovered a powerful new VNS reagent for the direct amination of nitrobenzenes, 1,1,1-trimethylhydrazinium iodide (TMHI) [7]. Although TMHI had never been tested on a nitroheterocyclic compound, we were encouraged by successes with other VNS aminating reagents on heterocycles [10]. The synthesis of TATB by amination of 1,3,5-trinitrobenzene with TMHI suggested a mechanism in which each nitro group is available to stabilize a negative charge formed by reaction with the TMHI nucleophile, allowing the formation of an intermediate, tri-anionic species. This mechanism led us to investigate the amination of 3,5-dinitropyrazole (**4**) [11], which carries an acidic hydrogen, to give 4-amino-3,5-dinitropyrazole (**2**). We reasoned that the acidic proton on **4** would initially react with one equivalent of base to form

a stable nitronate anion leaving the second nitro- group available to participate in the VNS amination. This would allow the synthesis of **2** without the need of a protecting group for the pyrazole proton. We found the reaction of **4** with TMHI in the presence of excess potassium *tert*-butoxide gave **2** in 70% yield (Scheme 2). This reaction proceeds rapidly at room temperature, producing after acidic work-up a good yield of flat, golden crystals.

Scheme 2



4 **2**

X-ray crystallography [12] revealed that the product recovered from this reaction is actually a 1:1 solvate of **2** with DMSO, with a crystal density of 1.608 g/cc. Recrystallization from acetonitrile yielded, surprisingly, the same 1:1 DMSO solvate, whereas recrystallization from water resulted in a 1:1 hydrate. After some experimentation, it was discovered that recrystallization of the monohydrate from butyl acetate/heptane yielded pure crystals of **2**, the structure of which was confirmed by X-ray crystallography (Figure 1 and Table 1). The pure compound **2** is a yellow crystal formed of aggregates of plates, which melts at 175-8 °C (uncorrected), and which has a density (X-ray) of 1.900 g/cc.

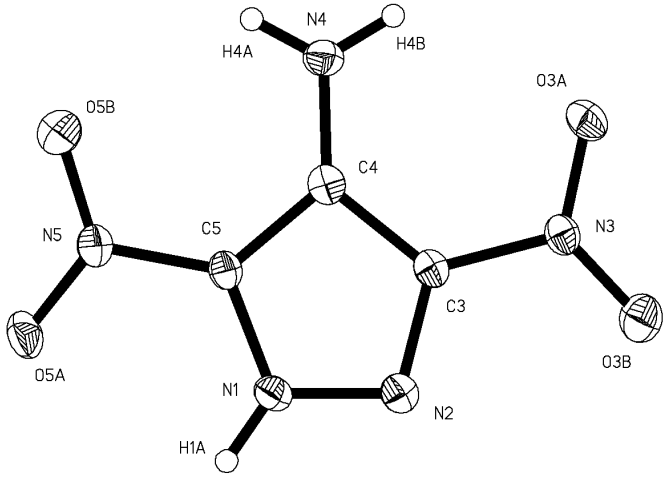


Figure 1. ORTEP drawing of neat **2** from X-ray analysis.

All atoms in **2** are essentially coplanar, with an average deviation from the plane of only 0.03 Å. This facilitates a dense packing scheme, shown in Figure 2, which resembles that of TATB insofar as there are two strong hydrogen bonds within each molecule and six strong intermolecular hydrogen bonds about the perimeter of each molecule. However, it also differs. TATB forms endless, essentially flat two-dimensional sheets in its crystals [13] through amino-nitro hydrogen bonding. These sheets then stack on top of, and parallel to, one another, leading to an assembly of all-parallel molecules resembling graphite. The crystal assembly in **2** contains sub-elements of parallel-molecule stacking (see Figure 2), described here as stacked-ribbons, but the ribbons in adjacent stacks are decidedly not parallel, and a view down the c axis of the crystal through two or more stacks would show an almost orthogonal grid of criss-crossed "ribbons". This difference in the supramolecular assembly patterns would be expected to lead to differences in the mechanical properties of the two materials.

Table 1

Crystal Data and Structure Refinement for 4-Amino-3,5-dinitropyrazole (**2**)

Identification code	ADNP	
Empirical formula	$C_3H_3N_5O_4$	
Formula weight	173.10	
Temperature	294(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 4.7257(5) Å	α= 90°.
	b = 4.7312(6) Å	β= 90°.
	c = 27.063(4) Å	γ = 90°.
Volume	605.07(13) $Å^3$	
Z	4	
Density (calculated)	1.900 Mg/m^3 at 21 °C	
Absorption coefficient	1.555 mm^{-1}	
F(000)	352	
Crystal size	.03 x .28 x .25 mm^3	
Theta range for data collection	3.27 to 57.97°.	
Index ranges	$-5 \le h \le 5, 0 \le k \le 5, 0 \le l \le 29$	
Reflections collected	1036	
Reflections 'observed'	835 [I>2sigma(I)]	
Independent reflections	851 [R(int) = 0.0174]	
Completeness to theta = 57.97°	100.0 %	
Absorption correction	Integration	
Max. and min. transmission	0.9474 and 0.6735	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	851 / 0 / 111	
Goodness-of-fit on F^2	1.100	
Final R indices [I>2sigma(I)]	R1 = 0.0329, wR2 = 0.0868	
R indices (all data)	R1 = 0.0338, wR2 = 0.0880	
Absolute structure parameter	-0.1(7)	
Extinction coefficient	0.013(2)	
Largest diff. peak and hole	0.157 and -0.170 $e.Å^{-3}$	

EXPERIMENTAL

Melting points were measured on a Mel-Temp instrument and are uncorrected. Unless otherwise noted, proton and ^{13}C nmr spectra were recorded on a Bruker 300MHz nmr Spectrometer using DMSO-d_6 as the solvent with tetramethylsilane as the internal standard. The infrared spectra were obtained using a Nicolet 730 ftir spectrophotometer. The starting material 3,5-dinitropyrazole was prepared according to the method of

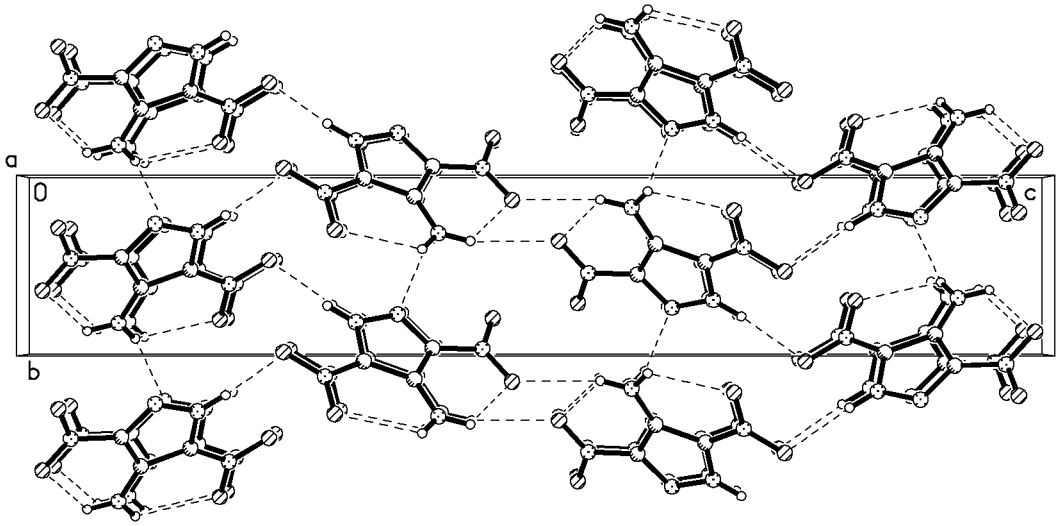


Figure 2. A view down unit cell axis **a**, with **b** (vertical) and **c** (horizontal) in the plane of the paper. The molecules in vertical columns, along b, are parallel, and resemble, from the side, stacked ribbons. Molecules in adjacent columns differ in their inclination out of the plane of the paper, and so are not parallel, but all molecules are hydrogen bonded across each column junction. The strong hydrogen bonds listed in Table 2, and their symmetry equivalents, are shown here as dashed lines.

Table 2

Hydrogen Bonding Parameters [a]

Donor	Acceptor	Symmetry op. (A)	[D–H···A] °	[H···A] Å	[D···A] Å
N4-H4a	O5b	intramolecular	116.9	2.258	2.860
N4-H4b	O3a	intramolecular	116.5	2.238	2.836
N1-H1a	O5a	(1 - x, y - ?, ? - z)	165.7	1.922	2.910
N4-H4a	N2	(x -1, y + 1, z)	163.3	2.468	3.446
N4-H4b	O3a	(x - ?, 1? - y, - z)	146.6	2.256	3.148

[a] Only the shortest H-bonds are tabulated here, those for which H…A is at least 0.2 Å less than the sums of the vdW radii [14], which are 2.72 Å for H…O, 2.75 Å for H…N). For the calculations in this Table, the experimental N-H distances were first normalized to match the average neutron diffraction distance, 1.009 Å, used in Ref. 14 to derive the van der Waals radii from the CCDC X-ray database.

Habraken [11]. Trimethylhydrazinium iodide was prepared as previously reported [7]. Dimethyl sulfoxide (anhydrous, 99.8%) and solid potassium *t*-butoxide (95%) were obtained from Aldrich, and were used as received. Elemental analysis was performed by Midwest Microlab LLC, Indianapolis, Indiana.

4-Amino-3,5-dinitropyrazole (**2**).

3,5-Dinitropyrazole (**4**) (0.355 g, 2.25 mmol) and 1,1,1-trimethylhydrazinium iodide (0.504 g, 2.49 mmol) were dissolved in 12.0 mL DMSO. Solid potassium *t*-butoxide (0.741 g, 6.60 mmol) was then added in one portion with stirring. The clear yellow solution immediately turned to a dark crimson red color as the base dissolved, and the odor of trimethylamine was noted. The reaction mixture was stirred at room temperature for 4 hours, after which it was poured onto 12 g of ice and acidified to pH 3 with 10% HCl. The resulting solids were suction filtered, washed with cold water and air dried to yield 0.382 g of a yellow powder (DMSO monosolvate of **2**). The product was soluble in DMSO, hot water, methanol, ethanol and hot acetonitrile. ^{1}H nmr: δ 7.13 (broad s, 2H, NH_2), 2.51 (s, 6H, DMSO CH_3). ^{13}C nmr: δ 137.8 (s), 128.8 (s), 39.5 (septet). ir (KBr): 3446(s), 3255(m), 3200(m), 3145(w), 3009(w), 1641(s), 1510(s), 1486(s), 1463(s), 1327(s), 1309(s), 1141(w), 1018(m), 936(m).

Recrystallization of crude product from acetonitrile produced small, yellow needles, which were washed with diethyl ether and air-dried (mp 160-162 °C, with decomposition). NMR and IR spectra were identical to those of the starting crude product. Crystallographic analysis confirmed the structure **2**-DMSO (monosolvate).

When the crude **2**-DMSO (0.10g) was placed in water (2 mL), heated until dissolved and cooled overnight, small, yellow irridescent plates formed (mp 169-171 °C). ^{1}H nmr (90MHz): δ 7.15 (very broad s, NH_2). ir (KBr): 3437(s), 3327(s), 3172(s, br), 1641(s), 1577(m), 1513(s), 1477(s), 1438(m), 1323(s), 1236(w), 1214(w), 1095(w), 945(m). Crystallographic analysis confirmed the structure **2**-H_2O (monosolvate).

When **2**-H_2O was recrystallized from hot butyl acetate/heptane, pure **2** recrystallized as yellow plates (mp 175-178 °C). ^{1}H nmr: δ 7.13 (broad s, 2H, NH_2). ^{13}C nmr: δ 131.7 (s), 128.3 (s). ir (KBr): 3437(m), 3325(m), 1641(s), 1581(w), 1510(s), 1476(s), 1440(w), 1328(s), 1237(w), 1208(w), 847(m), 831(w). Differential Scanning Calorimetry (10 °C/minute): endotherm @ 175.70-176.97 °C (66.51 J/g), exotherm (peak) @ 183.63 °C (996.1 J/g).

Anal. Calcd for $C_3H_3N_5O_4$: C, 20.81; H, 1.75; N, 40.46. Found: C, 20.91; H, 1.84; N, 39.94.

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[12] Crystallographic data for the structures of **2** and its DMSO monosolvate have been deposited with the Cambridge Crystallographic Data Centre as supplemental publications CCDC 152129 and 152130. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (e-mail: deposit@ccdc.cam.ac.uk).

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