Nitrolysis of a Highly Deactivated Amide by Protonitronium. Synthesis and Structure of HNFX[1]

Robert D. Chapman,*[,2a] Richard D. Gilardi,[2b] Mark F. Welker,[2c] and Charles B. Kreutzberger[2c]

Naval Aviation Science & Technology Office (Code 4T4220D), Naval Air Warfare Center Weapons Division, China Lake, California 93555, Laboratory for the Structure of Matter (Code 6030), Naval Research Laboratory, 4555 Overlook Avenue SW, Washington, D.C. 20375, and TPL, Inc., 3921 Academy Parkway North NE, Albuquerque, New Mexico 87109

Received September 29, 1998

Efficient N-nitrolysis of highly deactivated 3,3,7,7-tetrakis(difluoramino)octahydro-1,5-bis(4-nitrobenzenesulfonyl)-1,5-diazocine (**1**) has been achieved by the use of protonitronium reagent formed in the system nitric acid−trifluoromethanesulfonic acid, producing 3,3,7,7-tetrakis(difluoramino)-octahydro-1,5-dinitro-1,5-diazocine (HNFX, **2**) in 65% yield in a nonoptimized reaction. The crystal structure of the first morphology of HNFX contains cavities in the form of channels through its unit cell; the observed density is 1.807 g·cm^{-3}.

Introduction and Background

In a previous report,[3] we described a novel strategy to produce a β,β-bis(difluoramino)-substituted nitrogen heterocycle, 3,3,7,7-tetrakis(difluoramino)octahydro-1,5-bis-(4-nitrobenzenesulfonyl)-1,5-diazocine (**1**), by the use of 4-nitrobenzenesulfonyl as a judiciously chosen N-protecting group. A 3,3,7,7-tetrakis(difluoramino)octahydro-1,5-diazocine was desired as a potential precursor to 3,3,7,7-tetrakis(difluoramino)octahydro-1,5-dinitro-1,5-diazocine (HNFX, **2**), the first example of a new class of compounds predicted to be potentially superior explosives or solid propellant oxidizers: *gem*-bis(difluoramino)-substituted heterocyclic nitramines.[4] *vic*-Bis(difluoramino)-substituted primary nitramines[5] and *N*-alkyl-*N*-(difluoraminomethyl)nitramines[6] have been reported in prior literature. However, the synthesis of *gem*-bis(difluoramino)alkanes has required strongly acidic conditions,[7] such as anhydrous sulfuric acid, difluorosulfamic acid, or fluorosulfonic acid, with which most nitramines are incompatible. In the first synthesis of HNFX, for example, the use of 5-(difluoramino)-3,7-dinitro-9-oxa-3,7-diazabicyclo[3.3.1]nonan-1-ol (**3**) in a typical difluoramination reaction (difluoramine−difluorosulfamic acid−sulfuric acid) produced HNFX in only ∼1% yield.[8] Therefore, the N-nitro component is preferably incorporated after difluoramination to produce *gem*-bis(difluoramino)alkyl components. A dilemma encountered in the preparation of a β,β-bis(difluoramino)-substituted heterocycle, such as a 3,3,7,7-tetrakis(difluoramino)octahydro-1,5-diazocine, is that the nitrogen in most aminoacetone derivatives would be more basic than the ketone carbonyl (and oxygen in hemiaminal intermediates), thereby deactivating difluoramination via difluoramino-carbocations, unless the nitrogen is protected with a sufficiently electronegative protecting group to favorably affect this basicity. This was our strategy in the difluoramination producing **1**.[3]

The next dilemma encountered in this approach, however, was the known reluctance of more electronegatively substituted amides and of sterically hindered amides to undergo direct nitrolysis.[9,10] (The nitrogens in diazocine **1** are in a pseudoneopentyl environment.) Reported examples of such unsuccessful nitrolyses include the following. *N*,*N*-Di-*n*-butyltrichloroacetamide failed to be nitrolyzed by nitric acid−trifluoroacetic anhydride, whereas *N*,*N*-di-*n*-butylacetamide gave an 82% yield of *N*,*N*-di-*n*-butylnitramine;[9] with nitronium tetrafluoroborate in acetonitrile, *N*,*N*-diethyltrichloroacetamide failed to react until 40 °C, but *N*,*N*-diethylacetamide could quantitatively yield *N*,*N*-diethylnitramine at 20 °C;[11] and tris{[*N*-(2-cyanoethyl)nitramino]-methyl}amine failed to be nitrolyzed by nitric acid−trifluoroacetic anhydride, whereas tris[(*N*-methylnitramino)methyl]amine underwent nitrolysis (21% yield).[12] Related to nitrobenzenesulfonamide derivatives, the tosyl group of *N*-methyl-*N*-(4-methylbenzenesulfonyl)carbamate methyl ester underwent C-nitration by nitronium tetrafluoroborate, and only *N*-methyl-*N*-(4-methyl-3-nitrobenzenesulfonyl)carbamate methyl ester was recovered, under conditions in which *N*-methyl-*N*-(methanesulfonyl)carbamate methyl ester underwent N-nitrolysis of the methanesulfonyl group to yield *N*-methyl-*N*-nitrocarbamate methyl ester.[13]

(1) Presented in part at the Office of Naval Research Energetic Materials Informal Workshop, Annapolis, MD, 3−6 Dec 1996.

(2) (a) Naval Air Warfare Center Weapons Division. (b) Naval Research Laboratory. (c) TPL, Inc.

(3) Chapman, R. D.; Welker, M. F.; Kreutzberger, C. B. *J. Org. Chem.* **1998**, *63*, 1566.

(4) Miller, R. S. *Mater. Res. Soc. Symp. Proc.* **1996**, *418*, 3.

(5) Sayles, D. C. U.S. Patent 3,636,154, 1972; *Chem. Abstr.* **1972**, *76*, 72002.

(6) (a) Tyler, W. E.; Lovett, J. R. U.S. Patent 3,687,954, 1972; *Chem. Abstr.* **1972**, *77*, 164014. (b) Zheng, Y.; Zhou, J.; Zhou, D.; Zhang, M. *Binggong Xuebao* **1988**, 59; *Chem. Abstr.* **1988**, *109*, 189782.

(7) (a) Baum, K. *J. Am. Chem. Soc.* **1968**, *90*, 7083. (b) Graham, W. H.; Freeman, J. P. *J. Org. Chem.* **1969**, *34*, 2589. (c) Fokin, A. V.; Kosyrev, Yu. M.; Makarov, V. A.; Novoselov, N. P. *Dokl. Chem. Transl. of Dokl. Akad. Nauk* **1969**, *186*, 350.

(8) *Research in Energetic Compounds*; Report ONR-7-1; Final report to the Office of Naval Research (Arlington, VA) on Contract N00014−88-C-0536; Fluorochem Inc.: Azusa, CA, Sept 1991. Described in ref 3.

(9) Robson, J. H.; Reinhart, J. *J. Am. Chem. Soc.* **1955**, *77*, 2453.

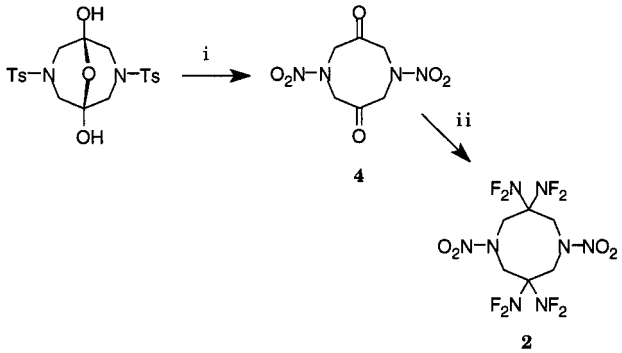
(10) Andreev, S. A.; Novik, L. A.; Lebedev, B. A.; Tselinskii, I. V.; Gidaspov, B. V. *J. Org. Chem. USSR (Engl. Transl.)* **1977**, *14*, 221.

(11) Andreev, S. A.; Lebedev, B. A.; Tselinskii, I. V.; Shokhor, I. N. *J. Org. Chem. USSR (Engl. Transl.)* **1979**, *16*, 1159.

(12) Norris, W. P. *J. Org. Chem.* **1960**, *25*, 1244.

10.1021/jo9819640 CCC: $18.00 © 1999 American Chemical Society
Published on Web 01/15/1999

Scheme 1[a]



[a] Reagents (yield): (i) HNO_3–$(CF_3CO)_2O$, CH_2Cl_2, 0 °C (81%); (ii) F_2NSO_3H–H_2SO_4–CH_2Cl_2, (−16 ± 4) °C (∼1%).

Results and Discussion

Consistent with the difficulties encountered in nitrolyses of the deactivated systems described above, we found that nosylamide derivative **1** proved inert toward the relatively powerful nitrating system nitric acid–trifluoroacetic anhydride. Following the failure of **3** to serve as an efficient precursor to **2** via difluoramination,[8] we made one more attempt to use nitro as a direct N-protecting group by preparing tetrahydro-1,5-dinitro-1,5-diazocine-3,7(2*H*,6*H*)-dione (**4**), rather than transannularly bridged hemiacetal **3**, from a 1,5-ditosyldiazocine by N-nitrolysis with nitric acid–trifluoroacetic anhydride in dichloromethane (Scheme 1). Unfortunately, difluoramination of **4** under various anhydrous conditions (difluorosulfamic acid–sulfuric acid) still produced HNFX (**2**) in only ∼1% yield, comparable to results with **3**.

It therefore became more desirable to convert nosylamide **1** to nitramine **2** after difluoramination. Even harsher nitrolysis conditions were employed to prepare HNFX directly from nosylamide **1**. Mixed (nitric–sulfuric) acid required an elevated temperature of ∼70 °C to effect nitrolysis at any appreciable rate. Even so, this nitrolysis required 6 weeks to consume starting material **1** and mononitrodiazocine intermediates, and the resulting isolated yield of HNFX (**2**) was only 16%. There is crystallographic evidence (vide infra) that these conditions caused competitive C-nitration of the nosyl protecting groups (Scheme 2); resultant 2,4-dinitrobenzenesulfonyl substituents would be even more difficult to remove from the nitrogen by electrophilic substitution. The low recovered yield might be attributable to competitive amide hydrolysis under the harsh conditions. A run held at 50 °C for 54 h, although not carried to complete nitrolysis, produced a 22% crude yield of **2**, suggesting that the slow complete nitrolysis at 70 °C was also due to poor solubility of reactants in mixed acid, requiring gradual dissolution of starting material via nitrolysis in order to achieve complete reaction.

We made an attempt to achieve nucleophilic denosylation of **1** under conditions reported by Fukuyama et al. for other *N*-alkylnosylamides.[14] Thiophenol in the presence of base (K_2CO_3) in HMPA solvent effected drastic changes in reactant **1**, according to ^{19}F NMR analysis. After only 5 min reaction time, absorptions arising from species related to *gem*-bis(difluoramino)-diazocines were already minor; their multiple number suggested that the removal of the two protecting groups in **1** is not concerted but stepwise. In addition to the residual *gem*-bis(difluoramino)diazocine species, which were clearly diminishing, there was evidence of an inorganic fluorine species formed concomitantly (perhaps difluoramine on the basis of its ^{19}F NMR chemical shift). Another aliquot analyzed after 80 min reaction showed no trace of residual *gem*-bis(difluoramino)diazocine species. An apparent byproduct of the degradation is 4-nitrobenzenesulfonyl fluoride (NsF), as indicated by ^{19}F NMR chemical shift and addition of authentic NsF to an NMR sample. In 90:10 DMF–HMPA, changes occurred more gradually; starting material **1** disappeared over the course of ∼1 h, and the spectral evidence indicated relatively simple behavior until *gem*-bis(difluoramino) species eventually disappeared after ∼2.5 h. We surmise that the expected β,β-bis(difluoramino)-substituted unprotected free amine, 3,3,7,7-tetrakis(difluoramino)octahydro-1,5-diazocine, has poor stability. An attempt to quench partially denosylated amide **1** (from sulfolane solvent as well as from DMF–HMPA) directly into acetyl nitrate after a few minutes of reaction produced no evidence of isolable nitramine (HNFX, **2**). The proposed instability of unprotected β,β-bis(difluoramino)alkylamines is also consistent with an observation by Fokin et al. that attempted (nucleophilic) hydrazinolysis of *N*-[2,2-bis(difluoramino)propyl]phthalimide to a free amine resulted in complete degradation of the *gem*-bis(difluoramino)alkyl component.[15]

We therefore reconsidered alternative reagents for the direct N-nitrolysis of amide **1**. The system of nitric acid–trifluoromethanesulfonic (triflic) acid was first recognized decades ago by Coon et al. as an unusually powerful nitrating system for aromatic substrates.[16] Only more recently did Olah et al. propose that such systems involve the protonitronium ion (NO_2H^{2+}) as the reactive nitrating species formed in "superacidic" solvents such as triflic acid.[17] More evidence supporting this proposal has since been obtained by the Prakash–Olah collaboration,[18] and protonitronium has been used for various other C-nitrations of deactivated aromatic systems.[19]

We tested this reagent on recalcitrant amide **1** and found protonitronium (from nitric acid–triflic acid) to be a suitable, efficient reagent for N-nitrolysis.[20] Because of its highly deactivated nature, nosylamide **1** still required more forcing conditions than reported C-nitrations, which typically proceed to completion within minutes at ambient or subambient temperature. The reaction was quite slow at room temperature; only minor (<10%) reaction had occurred within 23 h. At 55 °C,

(13) Luk'yanov, O. A.; Mel'nikova, T. G.; Kriger, L. N.; Tartakovskii, V. A. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1981**, 2138.

(14) Fukuyama, T.; Jow, C.-K.; Cheung, M. *Tetrahedron Lett.* **1995**, *36*, 6373.

(15) Fokin, A. V.; Voronkov, A. N.; Timofeenko, I. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1978**, 2644.

(16) Coon, C. L.; Blucher, W. G.; Hill, M. E. *J. Org. Chem.* **1973**, *38*, 4243.

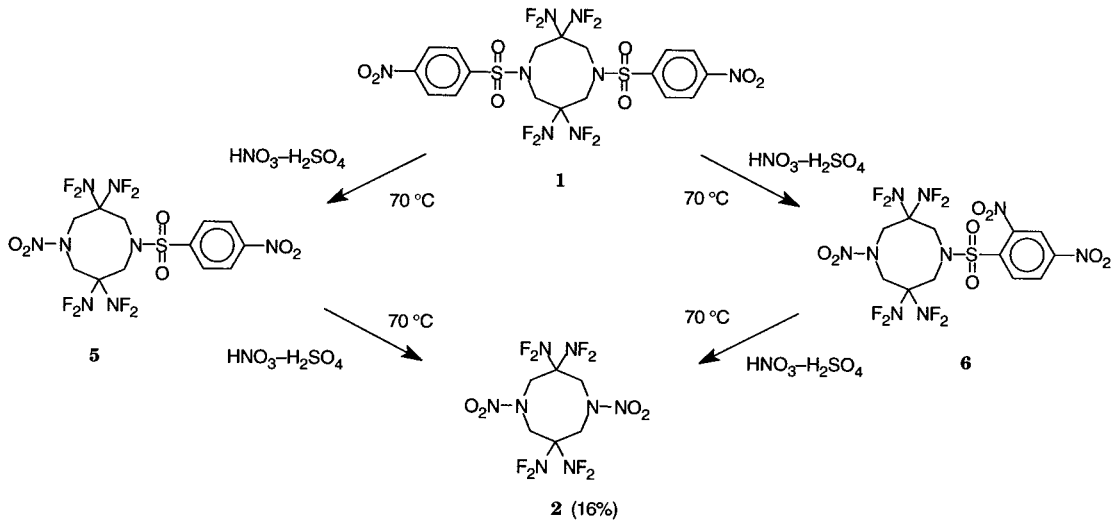
(17) (a) Olah, G. A.; Laali, K. K.; Sandford, G. *Proc. Natl. Acad. Sci. U.S.A.* **1992**, *89*, 6670. (b) Olah, G. A.; Rasul, G.; Aniszfeld, R.; Prakash, G. K. S. *J. Am. Chem. Soc.* **1992**, *114*, 5608.

(18) Prakash, G. K. S.; Rasul, G.; Burrichter, A.; Olah, G. A. *Am. Chem. Soc. Symp. Ser.* **1996**, *623*, 10.

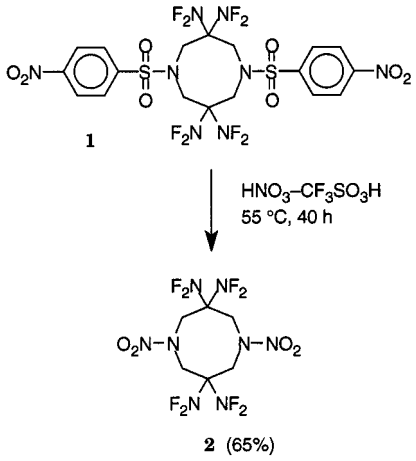
(19) (a) Olah, G. A.; Orlinkov, A.; Oxyzoglou, A. B.; Prakash, G. K. S. *J. Org. Chem.* **1995**, *60*, 7348. (b) Subramanian, G.; Boyer, J. H.; Trudell, M. L.; Koppes, W. M.; Sitzmann, M. E.; Nock, L. A.; Gilardi, R.; Russell, T. P. *J. Org. Chem.* **1996**, *61*, 1898.

(20) The system N_2O_5–HNO_3–$(CF_3SO_2)_2O$ has been used for nitrolysis of *N*-acetyl in 7-acetyl-2,5,9-trinitro-2,5,7,9-tetraazabicyclo-[4.3.0]nonan-8-one: Pagoria, P. F.; Mitchell, A. R.; Jessop, E. S. *Propellants Explos. Pyrotech.* **1996**, *21*, 14.

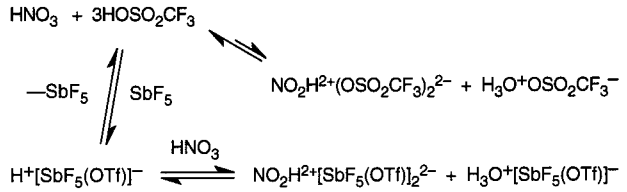
Scheme 2



Scheme 3



Scheme 4



however, the reaction rate became appreciable though still not fast. Monitoring the reaction by ^{19}F NMR showed complete consumption of starting material only after about 40 h (Scheme 3). In the first feasibility test, the isolated, purified yield of HNFX was 65%. Reaction conditions have not been developed to optimization.[21] An interesting aspect of this nitrolysis reaction was that the 4-nitrobenzenesulfonyl substituents themselves appeared *not* to become significantly nitrated during the course of nitrolysis. At 29 h reaction time when most of the nosyl substituent had been removed, the aromatic species in situ clearly was 4-nitrobenzenesulfonyl and not 2,4-dinitrobenzenesulfonyl according to ^{1}H NMR analysis. The presence of 2,4-dinitrobenzenesulfonyl as a byproduct in the mixed-acid nitrolysis but not in the triflic acid nitrolysis might be reasonably explained by the greater extent of protonation of the amide nitrogens in the latter system, which would further deactivate electrophilic C-nitration at the ortho position. Triflic acid clearly is a better solvent for **1** than is mixed acid. The low content of unprotonated amide nitrogen susceptible to electrophilic attack may also account for the lower kinetic reactivity of the N-nitrolysis compared to that of previous C-nitrations.

An attempt was made to improve the kinetics of the nitrolysis by increasing the content of protonitronium ion in the mixture. This ion is usually present only to a small extent in an equilibrium with nitronium (even in strong acids such as fluorosulfonic and triflic). However, Prakash et al. have shown that this equilibrium is affected by the presence of a strong Lewis acid, such as antimony pentafluoride;[18] this should be due to the complexation of the superacid's anion by SbF_5. $SbF_5(OSO_2F)^-$ [22] and $SbF_5(OSO_2CF_3)^-$ [23] have been previously identified; the acidity of HSO_3F-SbF_5 has been quantified.[24] In our case, $H^+[SbF_5(OSO_2CF_3)]^-$, even stronger than the original triflic acid, would drive the equilibrium further toward protonitronium (Scheme 4), producing an even more powerful nitrating mixture. The $HNO_3-HOTf-SbF_5$ system brought the reaction to a ~1:1 mixture of mononitro-mononosyldiazocine (**5**) and HNFX (**2**) within less than 1 h at room temperature. However, competitive C-nitration then ensued. The subsequent displacement of the 2,4-dinitrobenzenesulfonyl protecting group was sufficiently slower such that the complete nitrolysis to HNFX was comparable in reaction time to that found in the simpler HNO_3-HOTf system, which we therefore retained as the preferred system for this transformation in the presence of competitively nitratable components such as phenyl (including nosyl).

Structure of HNFX (2).[25] X-ray crystallographic analysis of HNFX recrystallized from a variety of solvent

(21) The reaction time of 40 h required in the feasibility test was a kinetic limitation only of the concentrations used and is not inherent in the system. Later qualitative tests have shown reaction times to completion in the range of 6−24 h depending on reactant concentrations. Nitrolysis has been observed to proceed cleanly, though so far unquantified, in a concentration as high as 5 w/v% **1** in $HOTf-HNO_3$. It might also be surmised that the use of anhydrous nitronium salts in superacids[17a] would suppress the formation of hydronium triflate byproduct (Scheme 4) and hydrolysis as a possible side reaction.

(22) Thompson, R. C.; Barr, J.; Gillespie, R. J.; Milne, J. B.; Rothenbury, R. A. *Inorg. Chem.* **1965**, *4*, 1641.
(23) Mootz, D.; Bartmann, K. *Z. Naturforsch. B* **1991**, *46b*, 1659.
(24) Gillespie, R. J.; Peel, T. E. *J. Am. Chem. Soc.* **1973**, *95*, 5173.

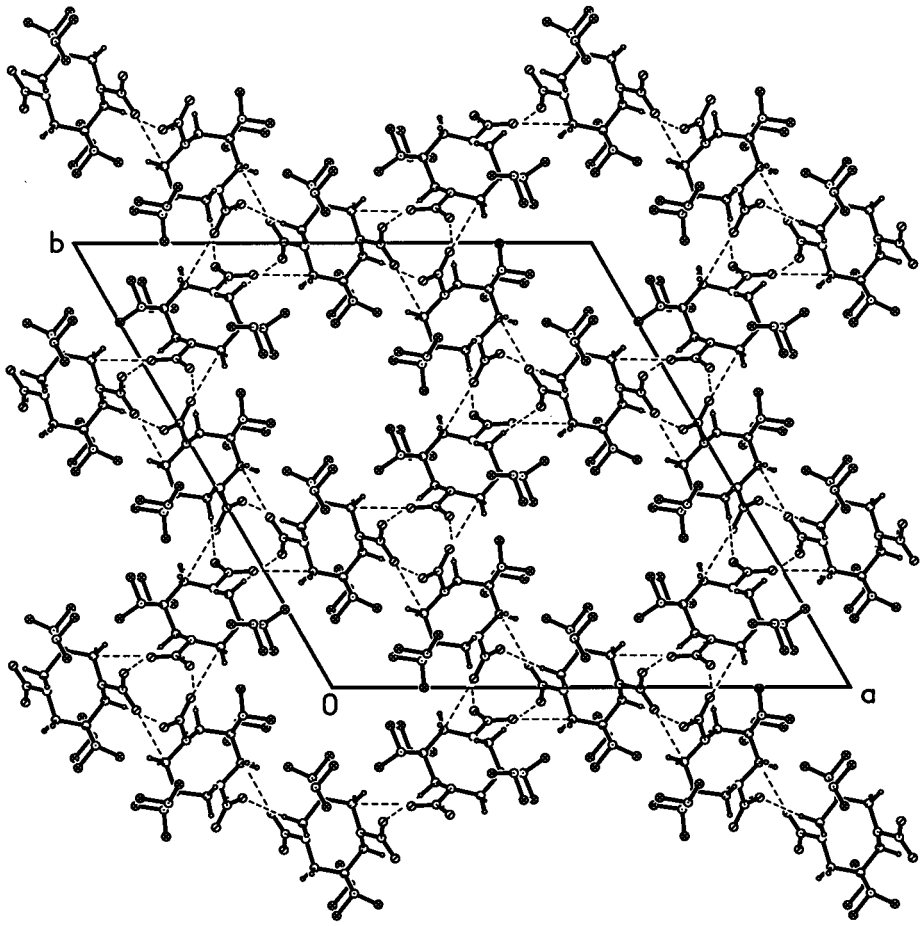


Figure 1. A view down the *c* axis showing the packing of HNFX (**2**) in this trigonal crystal form. Empty channels occur along the 3-fold axes at (0,0,*z*), a corner of the cell, and at ($^1/_3$,$^2/_3$,*z*) and ($^2/_3$,$^1/_3$,*z*) within the cell. Dashed lines indicate short contacts between nitro oxygen atoms and methylene carbon or hydrogen atoms in neighboring molecules; molecules linked by these contacts form 3-fold helices about crystallographic 3-fold screw axes (at, e.g., $^1/_3$,$^1/_3$,*z*).

systems shows an interesting, unpredicted feature (Figure 1): channels, with a 3-fold axis of symmetry surrounded by HNFX molecules, passing through each unit cell. Analysis has sometimes shown the presence of disordered mass due to recrystallization solvent(s). Though solvent-free crystals can be readily prepared by driving out solvent (e.g., by heating under vacuum), all crystals analyzed so far have retained these channels. The crystal density of the form produced so far is 1.807 g·cm^{-3} (21 °C), if a vacuum (i.e., zero mass) is assumed in the channels.

Note, however, that cyclic nitramines, especially those incorporating eight-membered rings, are well known to exhibit polymorphism;[26] octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine (HMX) has four known polymorphs of different densities. The phenomenon of solvent inclusion observed in HNFX crystals is also qualitatively similar to that found in the first polymorph of hexanitrohexaazaisowurtzitane (α-CL-20),[27] which is the lowest-density form.

Interestingly, mono-*N*-nitrodiazocine byproducts of the nitrolysis reaction by mixed acid (Scheme 2) do not include solvent, proving that such inclusion is not inherent in 3,3,7,7-tetrakis(difluoramino)octahydro-1,5-diazocines. A crystal of an impurity retrieved from a sample of HNFX proved to be a cocrystallized mixture of 3,3,7,7-tetrakis(difluoramino)octahydro-1-nitro-5-(4-nitrobenzenesulfonyl)-1,5-diazocine (**5**) and a C-nitrated byproduct, 3,3,7,7-tetrakis(difluoramino)octahydro-1-nitro-5-(2,4-dinitrobenzenesulfonyl)-1,5-diazocine (**6**). On the basis of four molecules with a formula weight of 593.328 occupying a unit cell of volume 2114.8 Å^3 (Figure 2), **6** has a density of 1.863 g·cm^{-3}, higher than that of the symmetrical bisnitramine (**2**).

Conclusion

We have demonstrated that protonitronium ion is an attractive and efficient N-nitrolyzing reagent in addition to its previously reported applicability for C-nitrations. Protonitronium is conveniently and most inexpensively formed from nitronium sources, including nitric acid, in "superacids" like triflic acid and fluorosulfonic acid.[17] With this powerful reagent, even highly deactivated amides, e.g., nosylamide **1**, involving perhaps the most electronegative protecting group to date that has been successfully directly nitrolyzed, can be directly nitrolyzed to the corresponding nitramine in high yield. Protonitronium should also be suitable for N-nitrolysis of other

(25) The authors have deposited atomic coordinates for structures with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, U.K.

(26) (a) Oyumi, Y.; Brill, T. B.; Rheingold, A. L. *J. Phys. Chem.* **1986**, *90*, 2526. (b) Achuthan, C. P.; Jose, C. I. *Propellants Explos. Pyrotech.* **1990**, *15*, 271.

(27) (a) Ryzhkov, L. R.; McBride, J. M. *J. Am. Chem. Soc.* **1997**, *119*, 4826. (b) Nielsen, A. T.; Chafin, A. P.; Christian, S. L.; Moore, D. W.; Nadler, M. P.; Nissan, R. A.; Vanderah, D. J.; Gilardi, R. D.; George, C. F.; Flippen-Anderson, J. L. *Tetrahedron* **1998**, *54*, 11793.

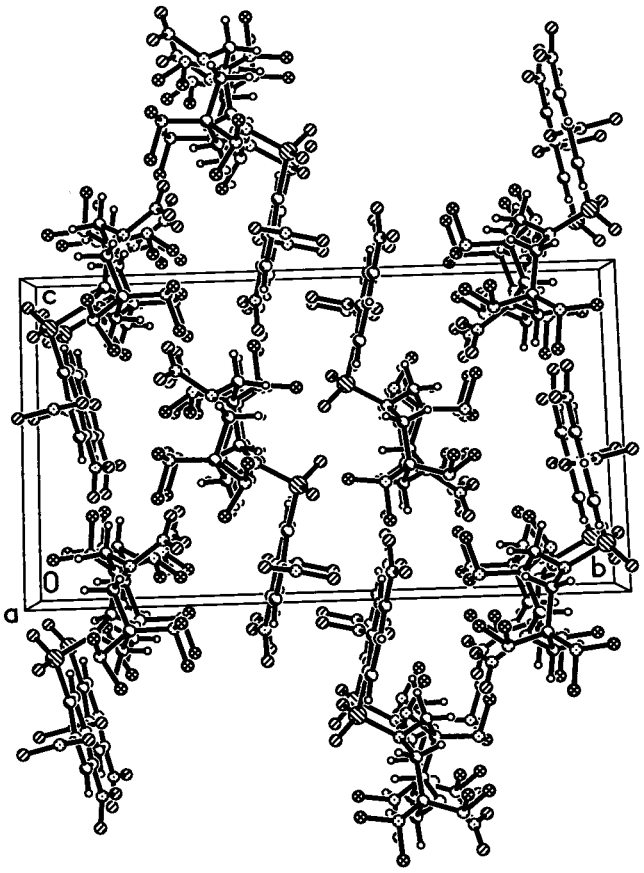


Figure 2. A view down the *a* axis of the crystal structure of **6**. Compound **5** occurs as a random co-occupant, making its presence known by weaker electron density at the ortho-nitro position, indicating its occupation in only ca. 50% of the sites. The unit cell has four molecules of **5** + **6** and no included solvent or channels as in **2**.

electronegative amides in addition to the arenesulfonamides used here.

A straightforward four-step synthesis of HNFX (**2**) from commercial starting materials is now available. The first measured crystal morphology of **2** shows "solvent channels" which prevent attainment of its theoretical density of 1.999 g·cm^{-3}.[4]

Experimental Section

General Experimental Procedures. All chemicals were reagent grade or better, unless specified by source; otherwise, Aldrich Chemical Co. was a typical source. ***WARNING:*** Some organic difluoramine derivatives and some nitramines are sensitive, detonable materials! The first crystal form of HNFX (**2**) reported here is a relatively sensitive high explosive! Such materials should be handled only by appropriately qualified personnel. Adequate shielding should be used to contain a possible detonation.

HRMS data were obtained at the University of New Mexico (Albuquerque) via thermal desorption with a Nicolet FTMS-2000 spectrometer.

Tetrahydro-1,5-dinitro-1,5-diazocine-3,7(2*H*,6*H*)-dione (4). Trifluoroacetic anhydride (91.3 g, 0.434 mol) and "absolute" nitric acid (Spectrum "100%" nitric acid, 24.1 g, 0.38 mol) were carefully mixed in a jacketed addition funnel at −10 °C. (**CAUTION**: Although nitric acid−trifluoroacetic anhydride has been a fairly commonly used nitrating reagent, several incidents of unexpected detonation have occurred in several laboratories.[28a] These may, however, have been due to acetyl nitrate byproduct from nitrolyses of *N*-acetyl compounds.[28b]) The nitrating reagent was added dropwise to a slurry of 3,7-bis(4-methylbenzenesulfonyl)-9-oxa-3,7-diazabicyclo[3.3.1]nonane-1,5-diol[3] (10.0 g, 21.3 mmol) in 50 mL of dichloromethane cooled to −10 °C in a 250-mL round-bottom flask with an overpressure of N_2. After 2 h of stirring at −10 to 0 °C, the sealed reaction mixture was stored in a refrigerator at 0 °C. After 8 days, solid product, **4** (3.65 g), was filtered off and washed (CH_2Cl_2). The mother liquor was returned to the refrigerator for 1 day, producing another 0.36 g of precipitate, **4**, which was filtered off. (In some runs, product **4** contained byproduct 4-methyl-3-nitrobenzenesulfonic acid or 4-methyl-3,5-dinitrobenzenesulfonic acid, which was washed out with cold aqueous $NaHCO_3$.) Total yield of **4**: 4.01 g (81%). Mp: 214−215 °C dec. ^{1}H NMR (200 MHz, DMSO-d_6): δ 4.77 (bs); ^{1}H NMR (300 MHz, DMSO-d_6): δ 4.78, 4.80 (apparent d); ^{1}H NMR (400 MHz, DMSO-d_6): δ 4.76, 4.78 (apparent d). ^{13}C NMR (75 MHz, DMSO-d_6): δ 60.2, 200.9. IR (KBr): ν_{CO} 1760, $\nu_{NO_2(sym)}$ 1520, $\nu_{NO_2(as)}$ 1280 cm^{-1}. HRMS Calcd ($C_6H_8N_4O_6$): 232.04440. Found: 232.09357 ± 0.07525 (M ± s of five).

The ^{1}H NMR spectrum of **4** is interesting in showing an apparent doublet for the CH_2 protons, resolvable at 300 MHz and at 400 MHz but not at 200 MHz. Generic *N*-nitroazocines, e.g., HMX, usually exhibit singlets for methylene protons despite nonplanarity of the ring system (even though C_2N-N segments tend to be planar due to partial sp^2 character of the $N-NO_2$ bond) because of rapid ring inversion of the system.[29] The doublet seen in the spectrum of **4** is presumably part of an AB quartet, from nonequivalent geminal protons, made apparent by hindered inversion of this ring. At lower field and lower $\Delta\nu$, the spectrum approaches AA′ rather than AB.

3,3,7,7-Tetrakis(difluoramino)octahydro-1,5-dinitro-1,5-diazocine (2) by Mixed-Acid Nitrolysis. Fuming sulfuric acid containing 2% SO_3 ("2% oleum") was made by mixing concentrated H_2SO_4 and 30% fuming sulfuric acid. Mixed acid was made from 67 wt % absolute nitric acid (Spectrum "100%") and 33 wt % of 2% oleum; to 100 mL of this was added **1**[3] (1.7 g, 25 mmol), and the mixture was warmed and held at 70 °C with stirring. Aliquots were monitored neat by ^{19}F NMR until **1** and intermediates had converted to HNFX (**2**); complete consumption of starting material and intermediates required 6 weeks at 70 °C. The reaction mixture was then quenched into ice water, neutralized with $NaHCO_3$, and extracted with dichloromethane.

The crude product solution from this reaction was purified in two batches. Each sample in dichloromethane was passed through silica gel. One batch was recrystallized from 1:1 CH_2Cl_2−hexanes, some of which provided the sample in which impurity **6** was found (vide supra). The remainder of this batch and the second batch of crude product were recrystallized from chloroform, yielding colorless needles pure by NMR and identified crystallographically. Total yield of **2**, 161.7 mg (16%); mp 216−218 °C dec.

A variation in the procedure involved quenching the supernatant mixed-acid solution after 54 h at 50 °C (i.e., prior to completion of nitrolysis), followed by neutralization and extraction, which produced a 22% crude yield of **2** of >90% purity by ^{19}F NMR.

In the course of early preparations and isolations of **2**, such as from low-yield nitrolyses of **4**, it was learned that certain solvents, such as acetone, tended to include in isolated crystals of **2**. Included volatile solvents could be driven out by heating under vacuum overnight at 40−60 °C. Recrystallization from certain other solvents, such as chloroform and dichloromethane−hexane, produces solvent-free crystals which still contain channels, as confirmed crystallographically.

3,3,7,7-Tetrakis(difluoramino)octahydro-1,5-dinitro-1,5-diazocine (2) by Protonitronium Nitrolysis. To **1**[3]

(28) (a) Bedford, C. D. *Chem. Eng. News* **1980**, *58*(35), 33. (b) Gilbert, E. E. *Chem. Eng. News* **1980**, *58*(40), 5.

(29) (a) Farminer, A. R.; Webb, G. A. *Tetrahedron* **1975**, *31*, 1521. (b) Bulusu, S.; Axenrod, T.; Autera, J. R. *Org. Magn. Reson.* **1981**, *16*, 52.

(101.6 mg) dissolved in triflic acid (20.07 g) cooled to 0 °C in a 25-mL round-bottom flask was slowly added absolute nitric acid (Spectrum "100%", 2.0 mL) via an addition funnel pressurized with an N_2-purge oil bubbler; the acid was washed from the funnel with another 4.0 mL of triflic acid. To the semisolid HNO_3−HOTf mixture was added another 6.42 g triflic acid (total triflic acid, 33.43 g). After 23 h at room temperature, the flask, initially fitted with an oil bubbler, was warmed to 55 °C in an oven and then stoppered. (Small aliquots were periodically withdrawn for analysis.) After 40 h at 55 °C,[21] the reaction mixture was carefully pipetted into ice water; the solution was basified (saturated aqueous Na_2CO_3) to pH 10 and extracted with CH_2Cl_2 (4 × 50 mL). The residue was recrystallized: $CHCl_3$ gave a first crop, filtered with a small glass frit; addition of an equal volume of CCl_4 to the mother liquor followed by distillation of $CHCl_3$ gave a second crop; evaporation of mother liquor and recrystallization from 1:1 CCl_4−hexanes gave a third crop and undissolved (washed) residue on the flask; total yield of purified **2**, 38.9 mg (65%). Recrystallized samples were effectively pure (≳98%) according to ^{1}H and ^{19}F NMR spectra, matching those of crystallographically analyzed **2** prepared by other nitrolyses (vide supra). ^{1}H NMR (200 MHz, acetone-d_6): δ 5.03 (s). ^{13}C NMR (50 MHz, acetone-d_6): δ 54.2 (quintet, $^3J_{CF}$ = 6.3 Hz), 99.4 (quintet, $^2J_{CF}$ = 5.6 Hz). ^{19}F NMR (188 MHz, acetone-d_6): δ 28.90. ^{19}F NMR (CD_3OD−acetone-d_6): δ 29.19. ^{19}F NMR (HOTf−HNO_3): δ 29.57.

X-ray Diffraction Analyses. The data collection for HNFX (**2**) was carried out on an automated Bruker P4 diffractometer equipped with an incident-beam monochromator. Data collection for the mononitrodiazocine cocrystal (**5** plus **6**) was on a Bruker 1K SMART/CCD system using a 5 kW Rigaku rotating anode source. The area detector was collected and reduced with the Bruker SMART and SAINT computer programs. Space group assignments were based on systematic absences present in the diffraction patterns and were confirmed by structure solution and refinement. All structures were initially determined by direct methods, aided by the program XS, and refined with the full-matrix least-squares program XL, contained in the SHELXTL collection of computer programs. All crystal data are provided in the Supporting Information.[25]

Acknowledgment. The financial support of this work by the Office of Naval Research and the Ballistic Missile Defense Organization under ONR contract N00014-93-C-0126 to TPL, Inc. and Work Order N0001496-WX20101 to NAWCWPNS, managed by Dr. Richard S. Miller and Dr. Judah Goldwasser (ONR), is gratefully acknowledged. We thank Prof. Edward A. Walters (University of New Mexico, Albuquerque) for the HRMS analysis of **4**. We thank Dr. Lawrence Merwin (NAWCWPNS China Lake) for a 400-MHz ^{1}H NMR spectrum of **4**. We thank Dr. Randal Johnson (TPL, Inc.) for assistance in collecting data for this manuscript.

Supporting Information Available: ^{1}H and ^{13}C NMR spectra of compound **4**; tables of crystal data and structure refinements, atomic coordinates, bond lengths and angles, anisotropic displacement parameters, hydrogen coordinates, and ORTEP diagrams for **2** and for the cocrystal of **5** and **6**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO9819640