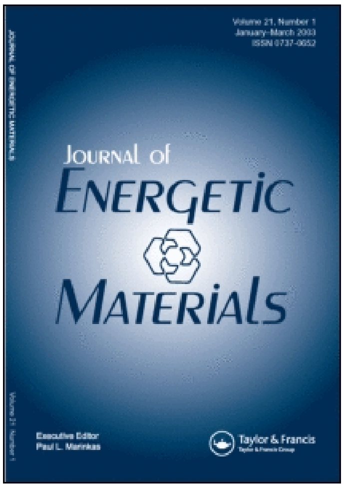

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Improved synthetic routes to polynitroheterocycles

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IMPROVED SYNTHETIC ROUTES TO POLYNITROHETEROCYCLES

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ABSTRACT

The preparations of several explosive precursors utilizing oxidative nitration are described. These include 1,3-di-t-butyl-5,5-dinitrohexahydropyrimidine, 3-t-butyl-5,5-dinitrotetrahydro-1,3-oxazine, 2,2-dinitro-1,3-propanediol (ADIOL) and potassium aci-2,2-dinitroethanol. The former pyrimidine and oxazine precursors were nitrolyzed to 1,3,5,5-tetranitrohexahydropyrimidine (DNNC) and 3,5,5-trinitrotetrahydro-1,3-oxazine (TriNOx). ADIOL, a widely used reagent in explosives preparation, was prepared by the trans-ketalization of 2,2-dimethyl-5,5-dinitro-1,3-dioxane. The dioxane was prepared in high yield by the oxidative nitration of 5-hydroxymethyl-2,2-dimethyl-5-nitro-1,3-dioxane. The little known explosive, 1,3,3,5,5-pentanitropiperidine (PNP), has been prepared from potassium aci-2,2,4,4-tetranitrobutanol and t-butylamine hydrochloride. The vacuum thermal stabilities of DNNC, TriNOx and PNP at 100°C are reported.

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INTRODUCTION AND RESULTS

The oxidative nitration of nitronate salts to gem-dinitro compounds using potassium ferricyanide (Eq.1) has been thoroughly explored[1,2]. This method has also proved useful in the large-scale production of the explosive 1,3,3-trinitroazetidine (TNAZ) largely because the yield is high, the reagents are inexpensive, and the waste is easily disposable[3-5]. It is for these reasons that the authors have adopted this method in the preparation of other gem-dinitro compounds.

$$R_1R_2CH(NO_2) \xrightarrow[NaNO_2,\ Na_2S_2O_8]{NaOH,\ K_3Fe(CN)_6} R_1R_2C(NO_2)_2 \qquad (1)$$

However, oxidative nitration is not nearly so successful for the preparation of some gem-dinitro compounds. One example is the direct synthesis of 2,2-dinitro-1,3-propanediol (ADIOL) by the oxidative nitration of nitromethane/formaldehyde mixture or tris(hydroxymethyl)nitromethane[1]. In these preparations, the ADIOL is extracted by organic solvent after oxidative nitration with only 30-35% recovery. This is attributed to the solubility of ADIOL in water and its ability to undergo deformylation by a retro-Henry reaction under basic conditions (Eq.2). The oxidative nitration reaction is normally performed under basic conditions, with pH values between 8 and 11. Any attempt to shift the deformylation equilibrium by lowering the pH of the reaction solution prior to extraction will only complicate the procedure.

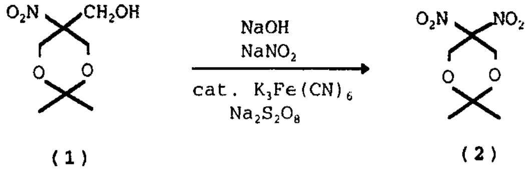
$$\text{ADIOL} + OH^- \longrightarrow HOCH_2C(NO_2)^- + CH_2O + H_2O \qquad (2)$$

ADIOL

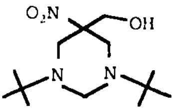
(3)

The oxidative nitration medium contains an excess of nitrite ion which, at low pH, converts to nitrous acid. The acid decomposes into voluminous amounts of nitric oxide and nitrosates the ADIOL to an unstable nitrite ester.

The difficult extraction step was circumvented by isolating the ADIOL as a water insoluble cyclic ketal. This was achieved by treating tris(hydroxymethyl)nitromethane with acetone and boron trifluoride etherate to generate 5-hydroxymethyl-2,2-dimethyl-5-nitro-1,3-dioxane[6] **(1)**, which was converted in excellent yield to 2,2-dimethyl-5,5-dinitro-1,3-dioxane **(2)** by oxidative nitration. ADIOL was nearly quantitatively recovered by treating the cyclic ketal with excess methanol and trace acid. Potassium aci-2,2-dinitroethanol **(3)** was obtained by treating the said methanolic solution with potassium hydroxide.



The explosive, 1,3,5,5-tetranitrohexahydropyrimidine (DNNC), is best prepared by the nitrolysis of 1,3-di-t-butyl-5,5-dinitrohexahydropyrimidine **(4)**. Previous methods of preparing compound **(4)** relied upon a two-step procedure in which ADIOL is first synthesized from nitromethane and later condensed with t-butylamine and formaldehyde in a Mannich reaction[7-10]. The reported yields of the pyrimidine precursor based on ADIOL approach 70%, yet decrease to ca. 20% if the yields are recalculated based on nitromethane. The authors have found that 1,3-di-t-butyl-5-hydroxymethyl-5-nitrohexahydropyrimidine **(5)**, a material that could be easily converted to **(4)** by oxidative nitration, could not be prepared by reacting tris(hydroxymethyl)-nitromethane with t-butyl-amine, or by the condensation of nitromethane with excess formaldehyde and t-butylamine. In these reactions only 3-t-butyl-5-hydroxymethyl-5-nitrotetrahydro-1,3-oxazine **(6)** or a mixture of products was generated[11].



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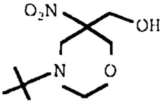

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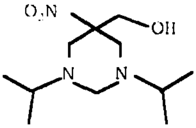
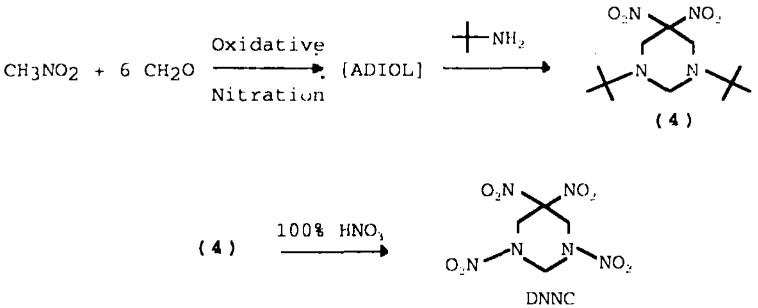


(7)

This is in contrast to the isopropyl analogue of **(5)**, 5-hydroxymethyl-1,3-diisopropyl-5-nitrohexahydropyrimidine **(7)**, which has been prepared by condensing tris(hydroxymethyl)-nitromethane with isopropylamine and formaldehyde[12-14]. However, nitrolysis of the isopropyl analogue of **(4)**, 1,3-diisopropyl-5,5-dinitrohexahydropyrimidine, to DNNC was affected with only 15% yield[13], and is attributed to the less favorable nitrolysis of the isopropyl group compared to the t-butyl group.

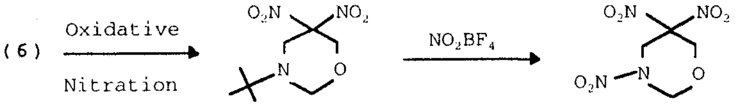
It has been found that compound **(4)** could be more simply prepared by an alternate route. To the reaction medium in which ADIOL was prepared in situ by oxidative nitration was added excess t-butylamine (Eq.3). Yields between 70 and 80% of **(4)** were obtained by this process, which gives strong evidence that ADIOL can be formed in high yields by oxidative nitration.



(3)

The preparation of DNNC was best achieved by an adaptation of the method by Boileau, Piteau and Jacob[10], whereby 100% nitric acid was first frozen before the addition of compound **(4)**. The DNNC obtained was found to be pure with no further recrystallization needed. Similar to the findings reported by Boileau, et al., nitration by mixed acids gave a highly impure product requiring great effort in purification. Our attempt to nitrolyze **(4)** using acetyl nitrate was not successful.

The precursor to TriNOx, 3-t-butyl-5,5-dinitrotetrahydro-1,3-oxazine **(8)**, was prepared by base deformylation of compound **(6)** followed by oxidative nitration (Eq.4). Nitrolysis of **(8)** with 100% nitric was found to be inefficient yet the product obtained was fairly pure. Contrary to that reported by Cichra and Adolph[8], nitrolysis of **(8)** with acetyl nitrate gave impure product with low yield. Nitrolysis with nitronium tetrafluoroborate, a non-acidic nitrolyzing reagent, gave a 69% recrystallized yield. It has been reported that C-nitro-oxazines are very susceptible to ring-opening by acid catalysis[3,15].

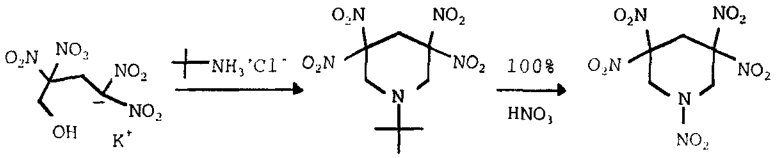


(8) TriNOx

(4)

Two heterocyclic precursors of the polynitro explosive, 1,3,3,5,5-pentanitropiperidine (PNP), have been prepared by the ring-closure of 2,2,4,4-tetranitropentane-1,5-diol with ammonium acetate and by the Mannich condensation of ADIOL, t-butylamine and formaldehyde[8,16]. In both methods the overall yields based on ADIOL are poor. Reacting potassium aci-2,2,4,4-tetranitrobutanol **(9)**, which was derived from the acid catalyzed dimerization of compound **(3)** following the method of Klager, Kispersky and

Hamel[17], with t-butylamine hydrochloride in the presence of excess formaldehyde gave 73% yield of the PNP precursor, 1-t-butyl-3,3,5,5-tetranitropiperidine **(10)** (Eq.5). Nitrolysis of the precursor was easily affected with 100% nitric acid.



(9) (10) PNP (5)

The polynitro explosives, TriNOx, DNNC and PNP, were subjected to small-scale thermal and sensitivity tests. These tests were performed according to standard procedures[18], and the results are reported in Table 1. The procedure for estimating the densities of organic compounds was developed by Stine[19].

TABLE 1

Explosives Testing Data for TriNOx, DNNC and PNP.

Explosive	Density [g/cm^3]	DTA Exotherm [°C]	Drop Weight Impact Height[20] [cm]	Vacuum Stability[21] [mL/g]
TriNOx	1.74(est.)	192	31	1.33
DNNC	1.82	183	21	0.98
PNP	1.82(est.)	181	22	failed

EXPERIMENTAL

Caution The polynitro compounds, DNNC, TriNOx, PNP, ADIOL, and potassium aci-dinitroethanol, are sensitive explosives and should be handled with appropriate care. All starting materials were obtained from commercial sources or prepared from the referenced literature. The ^1H and ^{13}C FT-NMR spectra were obtained on a JEOL GSX-270 spectrometer. Chemical shifts are relative to internal tetramethylsilane. All melting points were determined at 2°C per minute with a Mettler FP1 apparatus and are corrected.

2,2-Dimethyl-5,5-dinitro-1,3-dioxane (2)

To 200 mL of water containing sodium hydroxide (4.2 g, 105 mmol) was added compound **(1)** (10.0 g, 52.4 mmol) and the suspension was stirred until solution was complete. To this solution was added a solution of sodium nitrite (14.4 g, 209 mmol) and potassium ferricyanide (1.7 g, 5.2 mmol) in 30 mL of water. Solid sodium persulfate (13.1 g, 55.0 mmol) was added in portions while the temperature was kept below 30°C by the addition of ice. The cloudy solution was stirred for an additional two hours. The solid was filtered, washed with water and air dried to give 9.25 g (86%) of white product, mp 55.3-56°C (lit. mp 55.5-56°C)[6]. ^{1}H nmr ($CDCl_3$) ∂ 1.45 (s, 6H), 4.65 (s, 4H); ^{13}C nmr ($CDCl_3$) ∂ 22.93, 62.19, 101.01, 111.75.

2,2-Dinitro-1,3-propanediol (ADIOL)

To a solution of **(2)** (10.0 g, 48.5 mmol) in 100 mL of anhydrous methanol was bubbled a catalytic amount of dry HCl gas. The solution was allowed to react for 24 hours at room temperature and tested for completion by TLC. One gram of activated charcoal was added and the mixture warmed, filtered, and stripped of solvent. Several grams of anhydrous magnesium sulfate was mixed into the crude syrupy residue to initiate solidification. Soxhlet extraction of the solid matrix with methylene chloride (60 mL) yielded 6.49 g of product. Evaporation of the methylene chloride solvent afforded an additional 1.37 grams, mp 134.2-134.5°C (combined yield, 98%). Recrystallization from chloroform/heptane mixture gave white needles, mp 137.6-140.0°C (lit. mp 140-2°C).[1]

Potassium aci-2,2-dinitroethanol (3)

A solution composed of 200 mL of anhydrous MeOH, compound **(2)** (20.0 g, 97.1 mmol) and a catalytic amount of dry HCl gas was allowed to react for 24 hours at room temperature and tested for completion by TLC. The mixture was cooled by an ice-bath and treated by dropwise addition of methanolic KOH (14 g 85% KOH in 50 mL MeOH) until the solution was no longer acidic. The suspension was filtered and air dried to recover 19 g of (3) and KCl, explodes 218°C (lit. exp. 220°C)[22]. ^1H nmr (DMSO-d_6) ∂ 4.44 (t, 1H), 4.70 (d, 2H).

1,3-Di-t-butyl-5,5-dinitrohexahydropyrimidine (4)

Nitromethane (10.0 g, 164 mmol), 37% formalin (80 g, 1 mol) and 20 mL of water were combined in a 500 mL flask and cooled by an ice bath. A cooled solution of sodium hydroxide (13.6 g, 340 mmol) in 25 mL of water was added dropwise to the nitromethane mixture and the temperature kept below 15°C. Care was taken with the addition of the first few drops of base since the base-catalyzed condensation of nitromethane with formaldehyde is highly exothermic. After stirring for 10 minutes, aqueous solutions of sodium nitrite (45.0 g, 0.652 mol, in 110 mL water) and potassium ferricyanide (5.40 g, 16.4 mmol, in 20 mL water) were added consecutively. Solid sodium persulfate (40.0 g, 0.168 mol) was added in small portions to keep the reaction temperature below 30°C. After 15 minutes, the flask was removed from the ice bath and the wine-red solution stirred for another 15 minutes at room temperature. The solution pH was adjusted to within 8 and 10 with aqueous sodium hydroxide before t-butylamine (36.0 g, 493 mmol) was added in one portion. The mixture was stirred for 18 hours and filtered to recover a slurry-like solid. The solid was repeatedly triturated with water, filtered and dried to give 35.5 g of crude pale yellow product (75%), mp 68°C (lit. mp 80°C).[10] ^1H nmr (acetone-d_6) ∂ 1.13 (s, 18H), 3.60 (s, 2H), 3.69 (s, 4H); ^{13}C nmr (acetone-d_6) ∂ 26.67, 51.78, 54.75, 64.11, 116.29.

1,3,5,5-Tetranitrohexahydropyrimidine (DNNC)

(Mixed Acid Method) Following the method outlined by Cichra and Adolph[8], compound **(4)** (7.50 g, 26.0 mmol) dissolved in 100 mL of concentrated H_2SO_4 was added dropwise at 0°C to a mixture of 17 mL of 90% HNO_3 and 27 mL of concentrated H_2SO_4. The reaction was allowed to warm to room temperature, stirred for an additional 16 hours, and poured onto ice to yield 5.94 g of crude product. The product was recrystallized twice from 70% nitric acid to obtain 2.80 g (40%) of pure DNNC, mp 154°C (lit. mp 153-4°C).[8] ^1H nmr (acetone-d_6) ∂ 5.46 (s, 4H), 6.31 (s, 2H); ^{13}C nmr (acetone-d_6) ∂ 49.97, 60.31, 108.21.

(100% HNO_3 Method) Freshly distilled 100% HNO_3 (30 mL, 0.73 mol) was placed in a 200 mL flask and frozen by a dry-ice/acetone bath. With the bath still in place, **(4)** (2.00 g, 6.94 mmol) was dispersed over the top of the frozen nitric acid. The frozen mixture was allowed to warm to room temperature, stirred for an additional 18 hours and poured onto ice-water to obtain 1.16 g (63%) of pure DNNC, mp 154°C (lit. mp 153-4°C).[8]

1-t-Butyl-3,3,5,5-tetranitropiperidine (10)

A solution of **(9)** (1.00 g, 3.42 mmol), 37% formalin (10 mL, 120 mmol), t-butylamine hydrochloride (0.50 g, 4.6 mmol) and 25 mL water was stirred at room temperature for 48 hours. The suspension was filtered and dried to give 0.80 g of white solid (73%); recrystallized from MeOH/water, mp 137°C (lit. mp 136-7°C).[8] ^1H nmr (acetone-d_6) ∂ 1.21 (s, 9H), 3.95 (s, 4H), 4.31 (s, 2H); ^{13}C nmr (acetone-d_6) ∂ 26.29, 30.69, 52.05, 56.71, 116.22.

1,3,3,5,5-Pentanitropiperidine (PNP)

To 80 mL of 100% nitric acid at 0°C was added portionwise **(10)** (4.14 g, 12.9 mmol). The solution was taken from the ice bath and allowed to warm to room temperature. After stirring for 16 hours the mixture was poured onto 500 g of ice-water, stirred for one hour, and filtered to obtain 3.5 g of fine white crystals

(88%), mp 153-155°C (dec). Recrystallization from acetone/chloroform yielded 2.5 grams of PNP (63%), mp 158.6-159.5°C (dec) (lit. mp 120-5°C, dec).[16] ^{1}H nmr (acetone-d_6) ∂ 4.63 (s, 2H), 5.43 (s, 4H); ^{13}C nmr (acetone-d_6) ∂ 35.76, 50.43, 120.95.

3-t-Butyl-5-hydroxymethyl-5-nitrotetrahydro-1,3-oxazine (6)

A 5-L 3-necked jacketed flask equipped with an overhead stirrer was charged with 500 mL of water, paraformaldehyde (135 g, 4.5 mol) and one pellet of NaOH. The temperature was brought to 40°C with stirring and nitromethane (61 g, 1 mol) was added over 15 minutes; the temperature increased to ca. 60°C. The bath temperature was brought to 60°C and a small amount of Dow Corning® Antifoam 2210 was added. With vigorous stirring, t-butylamine (73 g, 1 mol) was added dropwise over a period of 1 hour. After stirring for an additional 1.5 hours, the slurry was cooled to room temperature, filtered and thoroughly washed with water and air dried to yield 200 g (92%) of the oxazine, mp 137-138°C (dec) (lit. 147-8°C).[7] ^{1}H nmr (DMSO-d_6) ∂ 1.0 (s, 9H), 2.64 (d, 1H), 3.62 (m, 4H), 3.86 (d, 2H), 4.49 (asym d, 2H), 5.39 (s, 1H); ^{13}C (DMSO-d_6) ∂ 26.17, 48.56, 52.18, 63.81, 67.83, 80.48, 89.01.

3-t-Butyl-5,5-dinitrotetrahydro-1,3-oxazine (8)

A slurry composed of 50 mL of water, **(6)** (4.00 g, 18.4 mmol), and NaOH (2.20 g, 55.0 mmol) was heated to 50°C for 1 hour, filtered hot and cooled to 10°C. A mixture of sodium nitrite (5.1 g, 74 mmol), potassium ferricyanide (0.60 g, 1.8 mmol) and 50 mL water was added consecutively to the above solution. Solid sodium persulfate (5.46 g, 22.9 mmol) was added portionwise while the temperature was kept below 30°C by addition of ice. After stirring for 1 hour, the precipitate was filtered, washed with water and dried to give 2.35 g (55%) of product, mp 86-7°C (lit. mp 90-93°C).[15] ^{1}H nmr (DMSO-d_6) ∂ 1.04 (s, 9H), 3.86 (s, 2H), 4.35 (s, 2H), 4.58 (s, 2H); ^{13}C nmr (DMSO-d_6) ∂ 26.16, 49.57, 52.96, 67.26, 79.77, 112.25.

3,5,5-Trinitrotetrahydro-1,3-oxazine (TriNOx)

(100% HNO_3 Method) Nitric acid (12 mL, 290 mmol) was placed in a 100 mL flask and cooled by a dry-ice/acetone bath until the acid solidified. With the bath still in place, compound **(8)** (2.35 g, 10 mmol) was added and dispersed over the top of the frozen mass. The acid was allowed to warm to room temperature, stirred for 4 hours and poured onto ice water to recover 254 mg (11%) of crude product, mp. 80-81°C, (lit mp 88-89°C).[8] ^{1}H nmr (acetone-d_6) ∂ 4.92 (s, 2H), 5.47 (s, 2H), 5.62 (s, 2H); ^{13}C nmr (acetone-d_6) ∂ 49.67, 69.63, 77.92, 109.04.

(NO_2BF_4 Method) To an ice cooled solution of nitronium tetrafluoroborate (1.46 g, 11.0 mmol) dissolved in 50 mL of acetonitrile was added portionwise over 30 minutes solid **(8)** (2.35 g, 10 mmol). The acetonitrile was evaporated and 30 mL of water was added to initiate precipitation of product. The residue was filtered, washed with water and dried to yield 1.8 g of crude yellow solid. Recrystallization from 45% nitric acid gave 1.54 g of white product (69%), mp 85-6°C, (lit mp 88-89°C).[8]

ACKNOWLEDGEMENT

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