Preparation of 2,5-Diamino-3,6-Dinitropyrazine (ANPZ-i): A Novel Candidate High Energy Insensitive Explosive

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Darstellung von 2,5-Diamino-3,6-Dinitropyrazin (ANPZ-i): Ein neuer Kandidat für einen unempfindlichen Hochenergie-Sprengstoff. 2,5-Diamino-3,6-Dinitropyrazin (ANPZ-i) wurde durch elektrophile Nitrierung von 2,5-Diethoxypyrazin unter Verwendung von Nitroniumtetrafluoroborat in Sulfolan und sukzessiver Aminolyse im Autoklaven dargestellt. Die Ergebnisse rechnergestützter Untersuchungen deuten darauf hin, daß ANPZ-i eine ähnliche Leistung wie Hexogen bei einer zu erwartenden höheren Unempfindlichkeit aufweisen sollte. ANPZ-i (**1**) ist deshalb ein neuer Kandidat für einen unempfindlichen Hochenergie-Sprengstoff.

Préparation de la 2,5-diamino-3,6-dinitropyrazine (ANPZ-i): Un nouveau candidat pour un explosif énergétique insensible

La 2,5-diamino-3,6-dinitropyrazine (ANPZ-i) a été préparée par nitration électrophile de 2,5-diéthoxypyrazine en utilisant du tétrafluoroborate de nitronium dans du sulfolane, suivie d'une aminolyse dans l'autoclave. Les résultats des simulations numériques indiquent que l'ANPZ-i devrait donner des performances semblables à celles de l'hexogène pour une insensibilité escomptée plus élevée. L'ANPZ-i (**1**) est donc un nouveau candidat pour un explosif énergétique insensible.

Summary

2,5-Diamino-3,6-dinitropyrazine (ANPZ-i) has been prepared via the electrophilic nitration of 2,5-diethoxypyrazine using nitronium tetrafluoroborate in sulpholane and subsequent amination under autoclave conditions. Molecular modelling studies have been carried out which indicate that ANPZ-i should have a similar performance to RDX but with an expected higher insensitivity. ANPZ-i (**1**) is therefore a novel candidate high energy insensitive explosive.

1. Introduction

Existing explosives such as TNT or RDX are very powerful, but suffer from a high sensitivity (thermal and mechanical). Several approaches can be adopted in order to render the system insensitive, e.g. by the use of inert and energetic binders. An alternative approach is the incorporation of amino groups into the explosive, for example TATB (1,3,5-triamino-2,4,6-trinitrobenzene) is very insensitive, however lacks sufficient power output. It has been postulated that the insensitivity in TATB arises from intramolecular hydrogen bonding between adjacent amino and nitro groups.

The aim of this research was therefore to prepare high energy compounds, with a similar performance to RDX, but with also a high insensitivity. Nitrogen heterocyclic compounds are considered to be ideal for this application since they inherently contain nitrogen in the form of the ring heteroatoms. Additionally, functionalisation with nitro and amino groups should impart insensitivity to the molecule. This work was carried out within DERA Chemical Technology Department, where highly integrated research is carried out drawing from disciplines such as molecular modelling, physical and chemical characterisation, hazard assessment, formulation, scale-up and of course bench synthetic chemistry.

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2. Results and Discussion

The preparation of ANPZ (2,6-diamino-3,5-dinitropyrazine) and PZO (2,6-diamino-3,5-dinitropyrazine-N-oxide) has been reported by researchers at LLNL, Livermore, California (USA)[1]. The synthesis of these explosive molecules was repeated and found to be relatively straightforward. Consequently, it was decided that the isomer of ANPZ: 2,5-diamino-3,6-dinitropyrazine (ANPZ-i, **1**) and its dioxide derivative: 2,5-diamino-3,6-dinitropyrazine-1,4-dioxide (PZDO, **2**) would be attractive target explosive molecules (Scheme 1).

Initially, the ethylation of piperazine-2,5-dione (**3**) was found to be problematic[2]. It is thought that commercially available triethyloxonium tetrafluoroborate or Meerwein's salt is contaminated with fluoroboric acid. The fluoroboric acid protonates **3** forming an unreactive salt.

Triethyloxonium tetrafluoroborate was therefore generated *in situ*, by the reaction between epichlorohydrin and boron trifluoride diethyl etherate, and then used in the alkylation of piperazine-2,5-dione. It is essential that the Meerwein's salt is prepared in dry conditions and therefore all the reagents were freshly distilled and the reaction was kept under nitrogen at all times. The Meerwein's salt is formed in quantitative yield and is kept in the reaction vessel

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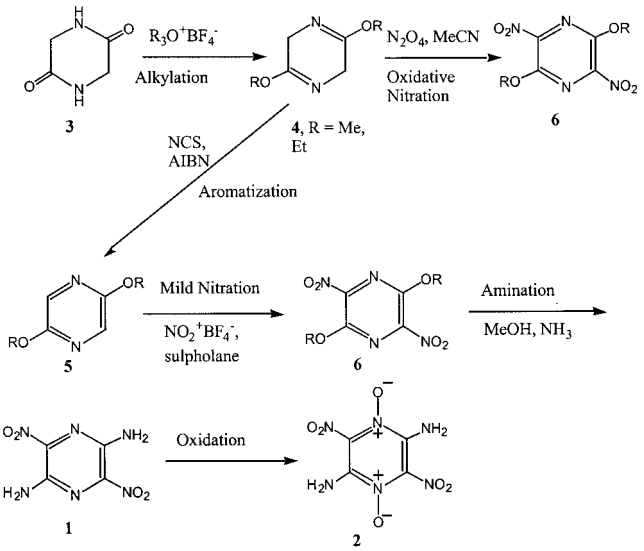

Scheme 1. Proposed preparation of 2,5-diamino-3,6-dinitropyrazine-1,4-dioxide (PZDO) via ANZP-i

where it is used to alkylate **3** in dichloromethane solvent again in very high yield. Aromatization of 2,5-diethoxy-3,6-dihydropyrazine (**5**) also proceeds very smoothly and 2,5-diethoxypyrazine (**6**) is produced in high yield[3]. Both the 2,5-dimethoxy-3,6-dihydropyrazine and 2,5-dimethoxypyrazine were also prepared.

The oxidative nitration of 2,5-diethoxy-3,6-dihydropyrazine (**4**) was attempted a number of times using N_2O_4, as detailed in the literature[4]. For each reaction a decomposition product was obtained and it is the author's opinion that this reaction is not repeatable.

The electrophilic nitration of 2,5-diethoxypyrazine (**5**) was attempted with a wide range of conditions (Table 1). Mixed acid nitration of **5** resulted in an extremely violent reaction where decomposition of the starting material was instantaneous above a specific temperature (*c*. −10 °C). Therefore, it was thought that a milder nitrating agent would be more effective for the nitration of this highly activated aromatic species.

Table 2. Reaction Conditions Used in the $NO_2^+BF_4^-$/Sulpholane Nitration of 2,5-Diethoxypyrazine

No.	Reaction length	Reaction Temperature (°C)	Stoichiometry (substrate: salt)	Reaction yield (%)
1	15 h	r.t.	1:2	30–35
2	5 d	r.t.	1:2	35
3	2–5 d	40	1:2	35–40
4	3 d	r.t.	1:4	< 5
5	2–3 h	100	1:2	20
6	15 h	75	1:2	20

The use of nitronium tetrafluoroborate in sulpholane was found to be effective in dinitrating **5**, typically with a yield of 30–40%. A range of conditions were used in order to optimize this reaction (Table 2), however, the optimum yield appears to be *c*. 35–40%. It is thought that the relatively low reaction yield with the tetrafluoroborate salt may be due to decomposition of the salt.

2,5-Diethoxypyrazine was also successfully nitrated using nitronium hexafluoroantimonate (V) in dry sulpholane with a reaction yield of ∼35%, however a large excess of the nitrating agent was required in order to achieve this reaction yield.

The amination of 2,5-diethoxy-3,6-dinitropyrazine (**6**) was attempted using aqueous ammonia in acetonitrile at atmospheric pressure, however, unreacted starting material was recovered. Therefore, amination of the substrate was attempted with an ammonia saturated solution of methanol under autoclave conditions; 2,5-diamino-3,6-dinitropyrazine (**1**) was obtained in 95% yield.

Both HPLC and IR analysis indicated the presence of a pure compound and the 60 MHz ^{1}H NMR spectrum showed only the presence of amino protons, which collapsed and formed a doublet on D_2O addition, with no ethoxy proton signals present. ^{13}C NMR analysis has also been carried out.

Detonics studies using MOLPAK and Cheetah calculations have given the following predicted data (Table 3) for ANPZ-i (**1**) and PZDO (**2**).

Table 1. Nitrating Systems Employed in the Attempted Nitration of 2,5-Diethoxypyrazine

No.	Nitrating System	Result
1	*c*. HNO_3, 30% oleum, r.t.	Violent decomposition
2	*c*. HNO_3, *c*. H_2SO_4, 0 °C	Decomposition
3	69% aq. HNO_3, 0 °C	Decomposition
4	*c*. HNO_3, −10 °C	Decomposition
5	N_2O_5, CH_2Cl_2, −20 °C < T < +10 °C	Several breakdown products
6	100% HNO_3, Ac_2O	No reaction
7	100% HNO_3, AcOH	Decomposition
8	i-Pr-ONO_2, Δ	No reaction
9	$NO_2^+BF_4^-$, NO_2Me	No reaction
10	$NaNO_2$, aq. HCl, 2 h, 0 °C	Decomposiion
11	BzCl, $AgNO_3$, MeCN	Decomposition
12	$NO_2^+BF_4^-$, sulpholane (high concentration)	Decomposition
13	$NO_2^+BF_4^-$, sulpholane (0.5 M commercial grade)	Successful dinitration
14	$NO_2^+SbF_6^-$, sulpholane	Successful dinitration

Table 3. Comparison of Calculated Performance Data for ANPZ-i and PZDO Versus Empirical Data for TATB and RDX

Compound	Calculated Performance Data (From Molecular Modelling)
ANPZ-i **(1)**	$V_D = 8.63$ km.s^{-1}, $P_{C\text{-}J} = 34.9$ GPa (at density $= 1.88$ g.cm^{-3})
PZDO **(2)**	$V_D = 9.04$ km.s^{-1}, $P_{C\text{-}J} = 40.2$ GPa (at density $= 1.92$ g.cm^{-3})
	Empirical Performance Data
TATB	$V_D = 7.62$ km.s^{-1}, $P_{C\text{-}J} = 25.9$ GPa (at density $= 1.85$ g.cm^{-3})
RDX	$V_D = 8.64$ km.s^{-1}, $P_{C\text{-}J} = 33.8$ GPa (at density $= 1.77$ g.cm^{-3})

Therefore, ANPZ-i has a predicted performance roughly equal to that of RDX but with an envisaged higher insensitivity.

A number of attempted oxidations of 2,5-diamino-3,6-dinitropyrazine (**1**) were carried out using 30% hydrogen peroxide and trifluoroacetic acid (*in situ* generation of trifluoroperacetic acid). Typically upon work-up of the reaction mixture no product could be obtained since the starting material/product could not be extracted from the aqueous acidic layer. Also, only negative ferric chloride tests were observed[6]. Further oxidation systems were used in the attempted oxidation of **1** including MCPBA (*meta*-chloroperbenzoic acid), DMD (dimethyldioxirane)[5] and HF/MCPBA all without success.

By comparison of the structures of ANPZ (2,6-diamino-3,5-dinitropyrazine) and ANPZ-i (2,5-diamino-3,6-dinitropyrazine), the former is readily oxidized to the mono-N-oxide since the oxide is flanked by two amino groups and hence stabilized by intramolecular hydrogen bonding. Conversely, with the structure of ANPZ-i, both mono- and di-oxidation would lead to an N-oxide group being flanked by one amino group and one nitro group. It is suspected that this change in electronic environment of the oxide group is responsible for the difficulty in oxidising ANPZ-i when compared to ANPZ.

To summarize 2,5-diamino-3,6-dinitropyrazine (ANPZ-i), which is a novel explosive compound, has been prepared and fully characterized. ANPZ-i was prepared via the electrophilic nitration of 2,5-diethoxypyrazine using nitronium tetrafluoroborate in sulpholane and subsequent diamination under autoclave conditions. The N-oxidation of ANPZ-i was not achieved despite the use of a wide selection of oxidation systems.

Molecular modelling of ANPZ-i has shown it to have approximately equal performance to RDX but with an envisaged higher insensitivity. Additionally, its calculated performance is significantly higher than that of TATB. It is hoped that in the future larger amounts of ANPZ-i will be produced for hazard testing.

3. Experimental

Commercial chemicals were supplied by the Aldrich Chemical Co. at the highest purities available (generally $> 98\%$) and were used as received. ^{1}H and ^{13}C NMR spectra were recorded on either a Bruker MSL-300 FT-NMR spectrometer (300 MHz) or a Varian EM 360A spectrometer (60 MHz) at ambient temperature using TMS as the internal reference for. Mass spectral (MS) analysis was carried out using a VG 7070EQ mass spectrometer. Spectra were acquired in +EI mode between masses 10 and 400 at 1 decade s^{-1} while the probe was heated at 5 °C s^{-1} from ambient temperature to 650 °C. IR spectral measurements were carried out using a Nicolet 710 FT-IR spectrometer equipped with MCT(A) detector. Liquids were characterized as films between KBr plates and solids as KBr discs. HPLC analyses were performed on an ATJ Unicam Diamond 600 system using 22 cm × 5 mm i.d. columns with Lichrosorb RP18 (7 μm) packings (Merck); the eluent was acetonitrile-water 50:50 v/v at flow rate 1.0 ml min^{-1}, and monitoring wavelength 254 nm.

3.1 Triethyloxonium Tetrafluoroborate (Meerwein's salt)

To a stirring solution of boron trifluoride diethyl etherate (freshly distilled over CaH_2) (140 ml, 157 g, 1.39 mol) in dry diethyl ether (freshly distilled over sodium) (300 ml) was added drop by drop epichlorohydrin (freshly distilled over $MgSO_4$) (66 ml, 78.1 g, 1.03 mol). The addition was carried out at such a rate that the reaction mixture gently refluxed and would typically take 15 minutes. Throughout the addition of reagents the reaction must be kept under a constant stream of nitrogen so as to ensure very dry conditions. The reaction mixture was then refluxed for 1.5 hours and left to stand at room temperature overnight. The condenser was replaced with a filtration stick (inside a rubber septum) and whilst still under a positive pressure the liquid was removed from the reaction vessel by vacuum suction, The white solid that remained in the reaction vessel was washed with cold, dry diethyl ether (3 × 250 ml) with the solvent each time removed via the filtration stick. Approximately 145 g of pure white solid, triethyloxonium tetrafluoroborate, was left in the reaction vessel. M.Pt. = 92 °C. (Lit. 91–92 °C, decomposition)[7].

*3.2 2,5-Diethoxy-3,6-Dihydropyrazine (**4**, R = Et)*

To the Meerwein's salt ($\sim$145 g) from the previous experiment was added freshly distilled dichloromethane

(350 ml) and then piperazine-2,5-dione (dried overnight) (32.9 g, 0.29 mol). The resulting mixture was then stirred at room temperature and under nitrogen for 5 days; after the first day a large amount of sticky white solid is generated in the reaction vessel and the liquid changes from colourless to light brown. After the 5 days the reaction mixture was quenched with aqueous sodium hydroxide solution (2.5 M) and the organic layer separated. The aqueous layer was washed with dichloromethane (2×125 ml) and the organic layers combined, dried over $MgSO_4$, filtered and concentrated *in vacuo* to yield a light brown fluffy solid (28.0 g, 0.160 mol, 71% yield).

M.Pt.: 83–85 °C (lit. 84 °C)[3]

δ^1H (60 MHz, $CDCl_3$): 1.30 (6H, t, $2 \times$ Me), 4.10 (4H, s, $2 \times NCH_2$), 4.15 (4H, q, $2 \times CH_2O$).

δ^{13}C (75 MHz, $CDCl_3$): 14.30 (CH_3), 46.65 (C-3 and C-6), 61.00 (OCH_2), 162.70 (C-2 and C-5).

ν_{max}(cm^{-1}): 1690 (C═N), 2350 (C-H).

3.3 2,5-Diethoxypyrazine (**5**, R = Et)

A stirring suspension of 2,5-diethoxy-3,6-dihydropyrazine (2.00 g, 12.0 mmol), NCS (1.80 g, 13.0 mmol) and AIBN (0.03 g, catalytic amount) in carbon tetrachloride (40 ml) was slowly heated under an atmosphere of nitrogen to 80 °C. At around 70 °C the suspension changed to a homogeneous mixture, indicating that the reaction had commenced. The stirring mixture was heated under reflux overnight (15 h), whereupon it was allowed to cool to 0 °C. The succinimide was filtered off and washed with carbon tetrachloride (25 ml). The organic layers were then combined and the solvent removed *in vacuo* to yield a pink liquid (1.83 g, 10.9 mmol, 90.5% yield).

δ^1H (60 MHz, $CDCl_3$): 1.35 (6H, t, $2 \times CH_3$), 4.30 (4H, q, $2 \times OCH_2$), 7.75 (2H, s, Ar-H).

δ^{13}C (75 MHz, $CDCl_3$): 15.00 (CH_3), 62.80 (OCH_2), 128.75 (C-3 and C-6), 156.28 (C-2 and C-5).

ν_{max}(cm^{-1}): 1685 (C═N), 2900 (C-H).

2,5-dimethoxy-3,6-dihydropyrazine and 2,5-dimethoxypyrazine were prepared in a similar manner.

3.4 2,5-Diethoxy-3,6-Dinitropyrazine (**6**, R = Et)

To a stirring 0.5 M solution of nitronium tetrafluoroborate in sulpholane (7 ml) was added quickly 2,5-diethoxypyrazine (0.500 g, 2.90 mmol). Stirring was continued overnight at room temperature, then the orange/red solution was poured onto crushed ice (30 ml). The resulting precipitate was filtered off to give a bright yellow solid (0.23 g, 0.90 mmol, 30% yield).

M.Pt. = 112 °C (lit. 118 °C)[4].

δ^1H (60 MHz, $CDCl_3$): 1.50 (m, 6H, $2 \times CH_3$) 4.55 (q, 4H, $2 \times CH_2$).

δ^{13}C (75 MHz, $CDCl_3$): 14.65 (CH_3), 66.10 (OCH_2), 139.61 (C-3 and C-6), 144.41 (C-2 and C-5).

ν_{max}(cm^{-1}): 2986 (C-H), 1554 (NO_2 asymm.), 1335 (NO_2 symm.).

m/z: 258 (M^+), 259 ($M^+ + 1$).

3.5 2,5-Diamino-3,6-Dinitropyrazine (**1**)

Ammonia gas was bubbled through dry MeOH (35 ml) in an autoclave vessel for 5 minutes then 2,5-diethoxy-3,6-dinitropyrazine (350 mg, 1.40 mmol) was added. The reaction mixture was heated in the sealed autoclave system for 4 hours (150 °C, 1.72 MPa). The autoclave was then allowed to cool down to room temperature whereupon the reaction mixture was added to acetonitrile, but a precipitate did not form as expected. Therefore, the ammonia saturated acetonitrile/methanol solvent was allowed to evaporate at room temperature to leave a dark yellow solid, 2,5-diamino-3,6-dinitropyrazine (270 mg, 1.40 mmol, ~98% yield).

M.Pt. = 288 °C (decomposition point).

δ^1H (60 MHz, $CDCl_3$): 2.00 (bs, 4H, $2 \times NH_2$).

δ^{13}C (75 MHz, $CDCl_3$); 149.49 (C-NO_2), 150.30 (C-NH_2).

ν_{max}(cm^{-1}): 3387; 3316 (NH_2), 1632 (NO_2 asymm.), 1248 (NO_2 symm.).

m/z: 200 (M^+).

CHN Analysis, calculated: C, 24.08; H, 2.02; N, 42.00; O, 31.99. Found: C, 23.79; H, 2.99; N, 42.00; O, 31.22.

3.6 Attempted Oxidation of 2,5-Diamino-3,6-dinitropyrazine (**1**)

To a stirring suspension of 2,5-diamino-3,6-dinitropyrazine (100 mg, 0.500 mmol) in trifluoroacetic acid, TFA (15 ml) at a temperature of between 0 °C and 5 °C, with cooling by an acetone/dry ice bath, was added gradually 30% aqueous hydrogen peroxide solution (3 ml). The reaction mixture was then allowed to warm to room temperature and stirred for 3 days. After this period further 30% aq. H_2O_2 (2 ml) solution was added and stirring continued for 24 hours. The reaction mixture was then added to water and the acid neutralized with solid $NaHCO_3$; any excess $NaHCO_3$ was filtered off. The aqueous layer was then left to evaporate at atmospheric pressure and the solid that remained washed with acetone. The mixture was then filtered of any insoluble inorganic material and the acetone layer concentrated *in vacuo* to yield a brown solid. Mass spectral analysis of this solid showed it to be a decomposition product. Additionally, a negative ferric chloride test was observed[6].

4. References

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