Rediscovering N-Methyltetranitropyrrole – A Versatile High Energy Material *via* Facile Two-step Eco-friendly Synthetic Approach

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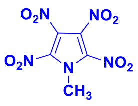
A highly efficient 2-step method was developed as an environmentally benign process for the synthesis of N-methyltetranitropyrrole (1) employing metal nitrate/conc. sulphuric acid as nitrating reagent. This method resulted 1 in high purity having higher thermal stability along with reduced sensitivity, which makes it a versatile high energy material. An over-oxidized high energy product was also isolated during optimization.

Table 1: Comparison of physical and energetic properties of **1** by present and earlier[3a] methods with those of TNT, TNAZ and RDX.



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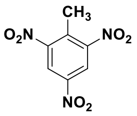
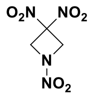
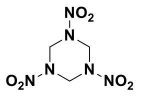


TNT



TNAZ

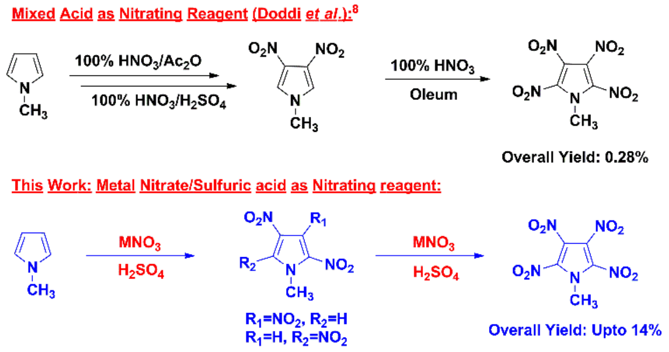


RDX

	1	**TNT[3a]**	**TNAZ[3a]**	**RDX[3a]**
T_m[a] (°C)	**106/100[e]**	81	100	204
T_{dec}[b] (°C)	**273/196[e]**	295	240	230
IS[c] (J)	**>40/30[e]**	15	6	7.4
FS[d] (N)	**>360/240[e]**	>353	324	120
D_v (m s^{-1})[3a]	**8950**	7303	9006	8795
P (GPa)[3a]	**36.9**	21.3	36.37	34.9

[a] Melting point (Open Capillary). [b] Temperature of decomposition (onset) under nitrogen gas (DSC, 5 °C min-1). [c] Impact sensitivity (BAM drophammer, method 1 of 6). [d] Friction sensitivity (BAM friction tester, method 1 of 6). [e] Data from mixed acid method (Ref. 3a).

A major goal in the synthesis of novel energetic materials is the development of insensitive high-energy density materials with excellent performance. They are extensively utilized for military, space and civilian applications. In the last two decades, there is a growing demand from the space and defence sectors towards high performance high energy (HE) formulations. However, the percentage content of the high-performance explosives viz. RDX, HMX, CL-20 are restricted in these HE formulations keeping their sensitive and stability towards handling in mind.[1] For example, Composition B contains ~60% of RDX along with ~40% of TNT as a melt-cast material. Although the melt cast materials are an important integral components of high energy (HE) formulations, they reduce the overall performance. Therefore, one of the most practical ways to enhance the overall performance of the HE formulation is to substitute the lowly-performing TNT, one of the most widely used melt-cast energetic material, with high performing melt-cast materials.[2] In our attempt to replace TNT with a better performing alternative, recently we have reported N-methyltetranitropyrrole **1** as a potential melt castable material, whose energetic properties were much superior than TNT and comparable to those of TNAZ and RDX (Table 1).[3] In last twenty years several new HEMs have been developed for practical applications.[4] However, their utility is severely limited owing to lack of facile synthetic route. Another major shortcoming being their sensitivity. Physical characteristics of a HEM such as crystal/particle size, morphology, shape and purity etc. play a significant role in determining its sensitivity.[5] Controlling the crystal/particle size and morphology of the explosive particles is one of the way to reduce the sensitivity towards external stimuli.[6] For example, 5 µm fine particles of RDX and

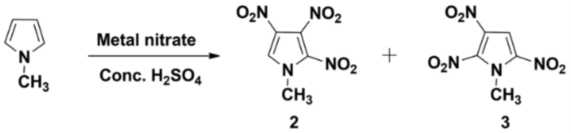


Scheme 1: Comparison of overall yields of **1** by mixed acid and metal nitrate/sulfuric acid as nitrating reagents.

HMX have been found application in the propellant compositions to attain high burning rates.[5c]
The synthesis of **1** was first reported by Doddi *et al*. in 1979 (Scheme 1) by the stepwise nitration of 1-methylpyrrole in a meagre 0.28% overall yield (3-step).[7] After 40 years, in 2019, we reported its synthesis in 4-steps in two different ways: (i) from the stepwise nitration of 1-TIPSpyrrole and (ii) from 1-methylpyrrole *via* iodination, dehalonitration etc.in more than 5% overall yield.[3a] Recently, we developed another route towards the synthesis of **1** via *tert*-butylpyrrole, which provided simple purification methods to reach the precursor 1-methyl-2,3,4-trinitropyrrole in improved yields at the cost of increasing the number of steps.[3e] However, these synthetic methods have significant drawbacks, including the usage of conventional nitration process of mixed acids such as fum. HNO_3/conc. H_2SO_4, 100% HNO_3/oleum, fum. HNO_3/Ac_2O and 100% HNO_3. As a result, lots of acid wastes were generated, causing environmental pollution. Due to the strong oxidizing and hygroscopic nature of 100% HNO_3, its storage and handling is difficult. Additionally, these processes involve stringent chromatographic purifications in the interim steps and the final product must be extracted and purified by column chromatography using benzene (a known carcinogen), which may not be suited in the large-scale production required in energetic formulations. Therefore, establishing a more efficient, scalable and green method for the synthesis of **1** is highly desirable.

In view of the aforementioned shortcomings, herewith, we developed a highly efficient 2-step process for the synthesis of **1** from 1-methylpyrrole by employing metal nitrate and sulfuric acid as nitrating reagent (Scheme 1). In comparison with mixed acid condition, metal nitrate/sulfuric acid brings many advantages.[8] For example, nitrate salts are more cost-effective, since they have longer shelf life, easy to handle and are less hazardous. There is minimal increase in temperature when the nitrate salts mixed with the sulfuric acid compared to the significant exotherm observed when nitric acid is added to sulfuric acid. On heating metal nitrate/sulfuric acid reactions does not produce nitrogen oxides. Therefore, this process is also eco-friendly. The nitration of 1-methylpyrrole was attempted with inorganic metal nitrates like sodium nitrate ($NaNO_3$), potassium nitrate (KNO_3) and lithium nitrate ($LiNO_3$) with conc. sulfuric acid as mild nitrating condition, which produces pure HNO_3 in-situ. The reaction conditions and yields are given in Table 2. The attempted direct synthesis of **1** from 1-methylpyrrole by adding compound to lithium nitrate and sulfuric acid at -15 °C and heating at 65 °C for 0.5 h, did not yield the desired product. Instead, in single step, it resulted in the formation 1-methyl-2,3,4-trinitropyrrole (**2**) as major product (27%) along with 1-methyl-2,3,5-trinitropyrrole (**3**)

Table 2: Reaction conditions of the nitration of 1-methylpyrrole.



Entry[a]	MNO_3[b]	Temperature (°C)	Time (h)	Yield[c] (%)	
				2	3
1[d]	$LiNO_3$	65	0.5	27	10
2	$LiNO_3$	65	0.5	25	10
3	KNO_3	65	0.5	28	8
4	$NaNO_3$	65	0.5	28	10
5	$LiNO_3$	25	5	23	9
6	$NaNO_3$	25	5	25	8
7	KNO_3	25	5	27	10
8	$LiNO_3$	0	5	28	11
9	KNO_3	0	5	35	12
10	$NaNO_3$	0	5	33	11

[a] The amount of 1-methylpyrrole is 12 mmol in all entries. [b] 8 Equivalents of metal nitrate used in all entries. [c] Yields of Isolated product. [d] Reaction Conditions: 1-Methylpyrrole was added to the nitrating mixture at -15 °C (Entry 1): Reaction Conditions: Metal nitrate was added to the 1-methylpyrrole in conc. sulfuric acid at 0 °C (Entry 2-10).

as minor product (10%), which were easily purified by column chromatography. Although this result was disappointing for us, however, it is noteworthy to mention here that this is the first example of direct introduction of three nitro groups exclusively upon any pyrrole derivatives as a substrate. As the reaction was significantly exothermic during this addition and we failed to obtain **1** directly, therefore, we reduced the temperature to optimize the formation of **2** and **3**. When the addition and the reaction were carried at 0 °C, the yields of **2** and **3** improved to 28-35% and 11-12%, respectively compared to the reaction at 65 °C or 25 °C (Table 2, Entry 8-10). The best condition after an extensive screening was nitration of N-methylpyrrole (12 mmol) in 15 mL of conc. sulfuric acid at 0 °C with potassium nitrate (8 equiv.) for 5 h to yield **2** and **3** in 35 and 12%, respectively, after chromatographic purification. Further, to understand the facile synthesis of 2,3,4-trinitro derivative vs its 2,3,5-isomer, the reactivity of 1-methyl-2,4-dinitropyrrole (as it was the major product during dinitration)[3a,7] was examined by performing DFT calculations (B3LYP/6-31+G) to obtain the electrostatic potential charges at its C-3 and C-5 positions (Figure 1).[9] Development of relatively higher negative charge at C-3 compared to that at C-5 supports further preferential electrophilic substitution at C-3, complying with our experimental observation of 1-methyl-2,3,4-trinitropyrrole as the major product.

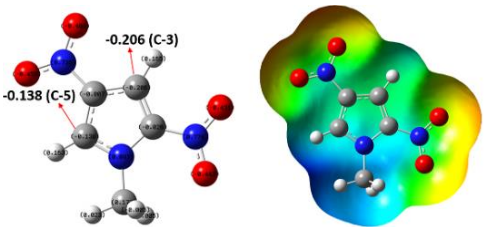
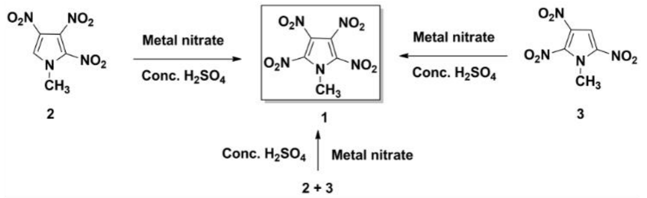


Figure 1: Electrostatic potential charges at C-3 and C-5 positions of 1-methyl-2,4-dinitropyrrole.

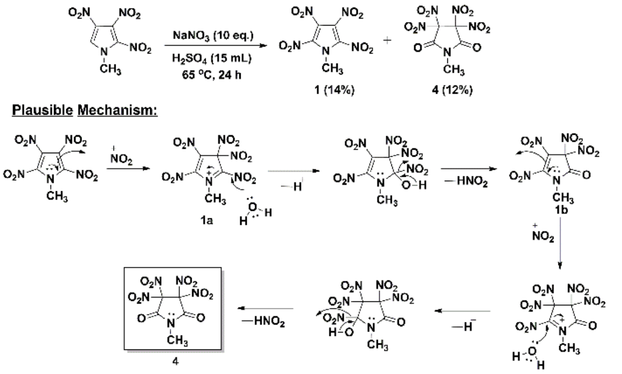
The nitration of **2** was carried out again with the metal nitrate/sulfuric acid at 65 °C for 5 h. Compound **1** was obtained as white precipitate after pouring the reaction mixture onto ice flakes. As this method produced **1** as precipitate, we have optimized the reaction parameters such as temperature and mole ratios of the metal nitrates. Interestingly, both upon decrease or increase of temperature the yield was reduced. Similar trend was observed with more equivalents of metal nitrate. The best yield of 40% was obtained by using 4 equivalents of $LiNO_3$. The less reactive, 1-methyl-2,3,5- trinitropyrrole (**3**) was also further nitrated to **1** by using same metal nitrates. With 4 equivalents of lithium nitrate, the product **1** was obtained in 20% yield only after extraction with ethyl acetate.

Table 3: Reaction conditions of the nitration of 1-methyl-2,3,4-trinitropyrrole (**2**), 1-methyl-2,3,5-trinitropyrrole (**3**) and their mixture (**2** & **3**).



Entry	Substrate[a]	MNO_3[b]	Temperature (°C)	Time (h)	Yield (1)[c] (%)
1	**2**	**$LiNO_3$ (4)**	**65**	**5**	**40**
2	2	$NaNO_3$ (4)	65	5	30
3	2	KNO_3 (4)	65	5	35
4	3	$LiNO_3$ (4)	65	6	20
5	3	$NaNO_3$ (8)	65	6	10
6	3	KNO_3 (8)	65	6	15
7	**2 + 3**	**$LiNO_3$ (4)**	**65**	**6**	**22**
8	2 + 3	$NaNO_3$ (8)	65	6	19
9	2 + 3	KNO_3 (8)	65	6	20

[a] The amount of substrate is 1.8 mmol in all entries. [b] Molar equivalents of nitrate salts are given in parentheses. [c] Yield of Isolated product.



Scheme 2: Nitration of 1-methyl-2,3,4-trinitropyrrole (**2**) with excess equivalents of $NaNO_3$/ Conc. H_2SO_4.

However, with KNO_3/$NaNO_3$ in sulfuric acid as the nitrating agent, the reaction needed additional 4 equivalents of metal nitrate (Table 3, Entry 5-6) to completely convert to **1** in only 10-15% yield. Further, to avoid the column chromatography purification in step 1 for the separation of **2** and **3**,[3e] we performed the nitration of their mixture to obtain **1**. This resulted in the lower yields of 19-22% (Table 3, Entry 7-9). This low yield may be attributed to the decomposition of **1** in excess equivalents of metal nitrate. In order to check this hypothesis, we conducted the nitration of **2** in presence of more equivalents (10 eq.) of sodium nitrate. Surprisingly, we found formation of another compound along with **1** (Scheme 2). This unknown compound was started precipitating in the reaction mixture itself after 4 h of stirring. Hence, we continued stirring for 24 h to complete its precipitation in the reaction mixture. After the reaction was completed, the crystalized solid was directly filtered through Ace-Hirsch filter funnel and washed with sulfuric acid. Single crystals of diffraction quality directly obtained from it and subjected for XRD analysis to resolve its structure as 1-methyl-3,3,4,4-tetranitropyrrolidine-2,5-dione (**4**) (Figure 3). Although similar type of oxidative product formation was recently reported in case of 1-methyl-2,4,5-trinitroimidazole but without gem-nitration.[10] We believe the plausible mechanism proceeds via the formation of **1**, which undergo further nitration at the 3rd position with the assistance of the lone pair in the ring nitrogen to form intermediate **1a** and subsequent attack by water upon the iminium ion, followed by elimination of NO_2^- group resulted in the formation of lactam **1b**. In the presence of excess of NO_2^+, one more nitration occurs at the 4th position of the ring. Similar attack by water and subsequent NO_2^- elimination results in the formation of the product **4** (Scheme 2). The formation of **4** with higher equivalents of metal nitrate may be responsible for the lower yields of **1** in case of nitration of mixture (**2** & **3**) and **3**.

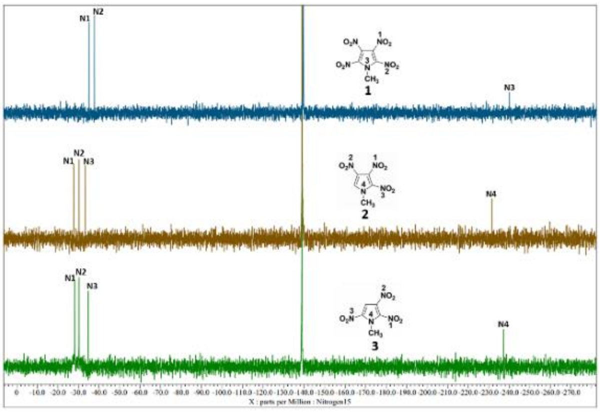
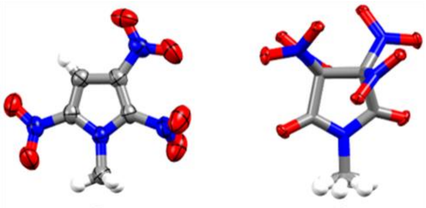


Figure 2: ^{15}N NMR spectra of compounds **1**, **2** and **3**.

All the compounds were completely characterized by NMR (^{1}H, ^{13}C) and IR spectroscopy along with mass spectrometry (HRMS). ^{15}N NMR spectroscopic data for **1**, **2** and **3** were recorded in CD_3CN using nitromethane as an external standard (Figure 2). The nitrogen peaks were assigned on the GIAO NMR calculations using Gaussian 09 program.[9] The ^{15}N peaks (N1/N2/N3) which corresponds to the C-NO_2 resonated downfield in the range of -25 to -40 ppm. The resonances in the range of -230 to -240 ppm correspond to pyrrole ring nitrogen. Suitable crystals of **3** were grown from the slow evaporation of ethyl acetate. Compounds **3** and **4** crystallized in the orthorhombic crystal system with space group *Pbcn* (Z=8) and *Pnna* (Z=4), respectively (Figure 3). Additional crystallographic data are provided in ESI. In comparison to mixed acid nitration approach, this process involves no chromatographic purification in the final step, hence, product **1** was analysed for the thermal decomposition and purity. Compound **1** was found to be very much stable upto 273 °C (by DSC) as compared to 196 °C reported earlier.[3a] This may be attributed to lack of contamination with acid impurities in the present method as it shows more than 95% purity vs that of 84% obtained using the earlier mixed acid condition (DSC and UPLC data in ESI).[3a] This is again reflected in its relatively higher melting point of 106 °C than previous method (100 °C). The scanning electron microscope (SEM) images of the raw 1-methyl-2,3,4,5-tetranitropyrrole obtained by both mixed acid



3 4

Figure 3: ORTEP-POV ray diagrams of **3** and **4** (top view). Thermal ellipsoids are scaled upto at 50% probability level. Color code: grey - C, white - H, blue - N and red - O.

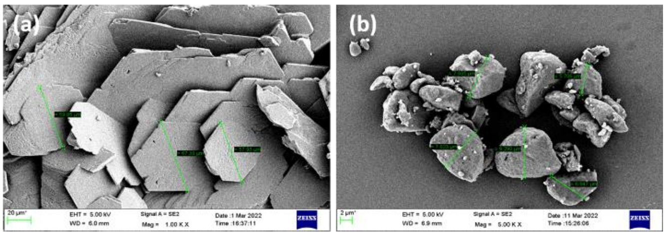


Figure 4: SEM images of raw compound **1** by (a) HNO_3/H_2SO_4 and (b) MNO_3/H_2SO_4 methods.

(HNO_3/sulfuric acid) and metal nitrate/sulfuric acid nitration conditions were recorded. The product obtained via former condition displays large stacked sheets with particle size of 80 µm (Figure 4 (a)), whereas those obtained by the present process are clearly much smaller in particle size of 7.5 µm (Figure 4 (b)). This resulted in further reduced impact and friction sensitivities of **1** making it an insensitive HEM (Table 1) than the product from the earlier method (IS = 30 J; FS = 240 N).[3a] Compound **4** possesses density of 1.917 g/cc at 114 K and stable upto 100 °C (DSC). Further, the detonation performances evaluated by using EXPLO5 (version 6.03),[11] exhibits detonation velocity and pressure of 8.84 km/s and 35.54 GPa, respectively and these values are comparable to RDX (ESI).

In conclusion, we have successfully developed an eco-friendly and highly efficient 2-step synthetic methodology for N-methyltetranitropyrrole **1**. This method yielded **1** with highest purity with smaller particle size through precipitation. This led to enhancement in its thermal stability accompanied with reduce sensitivity. This process is easily scalable, pitching N-methyltetranitropyrrole as a highly promising and versatile high energy density material.

Conflicts of interest

There are no conflicts of interest to declare.

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