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Nitrated Heterocycles

Selective Preparation of 3,4,5-Trinitro-1*H*-Pyrazole: A Stable All-Carbon-Nitrated Arene

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The all-carbon-nitrated azoles, such as 1,2,3,4-tetranitropyrrole (**1**), 2,4,5-trinitroimidazole (**2**), 3,5-dinitro-1,2,4-triazole (**3**), 3,4-dinitro-1,2,3-triazole (**4**), and 5-nitrotetrazole (**5**) are known (Figure 1). They suffer from several prohibitive drawbacks in terms of stability and water sensitivity (hygroscopic) due to their very high acidity ($pK_a < 0$).[1] Compound **1** is unstable at ambient temperature upon storage,[2] and **3** is deliquescent.[2] As a light yellow instable oil, **4** begins to decompose at 100 °C and must be stored in a diethyl ether solution,[2] and **5** decomposes at low temperature after melting (m.p. 101 °C, dec. 115–120 °C).[2] For all these reasons, they cannot be used in any suitable applications as energetic materials unless the corresponding conjugated bases are used.[2]

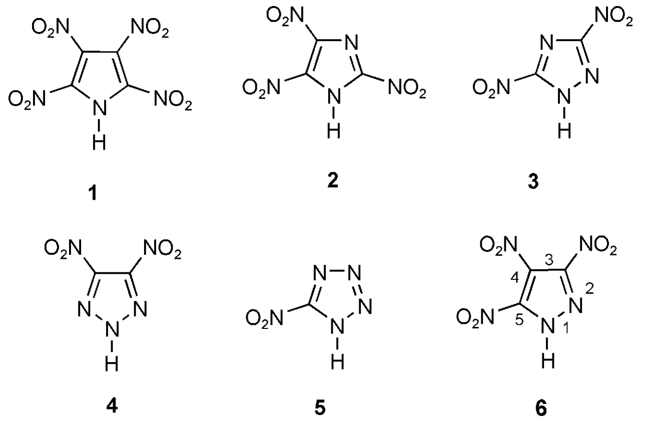

Figure 1. Known all-carbon nitrated azoles **1**–**5** and unknown 3,4,5-trinitro-1*H*-pyrazole (**6**).

Surprisingly, 3,4,5-trinitro-1*H*-pyrazole (**6**; TNP) is the only all-carbon nitrated azole missing in the series (Figure 1). The synthesis of TNP has probably been attempted numerous times in several specialized laboratories. The diazotization of 4-amino-3,5-dinitropyrazole (**7**; see Scheme 1) has been reported in the literature,[3] therefore diazotization of **7** might be a good starting point for obtaining TNP. However, the resulting 4-diazo-3,5-dinitropyrazolate zwitterion undergoes an unusual displacement of one nitro group instead of the diazo (N_2^+) group.[3] The diazotization route must be revisited and original methodologies leading to TNP need to be implemented.

Herein, we describe the selective preparation TNP, which exhibits remarkable and unprecedented properties for a strong electron-deactivated aromatic heterocycle: It is not hygroscopic and it is weakly acidic, and furthermore, it displays low sensitivity to external stimulai[4] and outstanding thermal and chemical stability compared to that of other all-carbon-nitrated azoles. Beyond the scope of the nitroazole chemistry, TNP shows by far the best thermal and chemical stability of any fully nitrated aromatic systems (i.e., polynitroarylenes, furazanes, furoxanes).

Nitroazoles are usually prepared either by direct nitration,[5] or indirectly from the corresponding aminoazoles through either diazotization or oxidation.[6] All these reactions can be potentially employed to introduce nitro groups onto the pyrazole backbone. However, as shown herein, a judicious choice of the starting material is critical to perform such elementary reactions.[7]

Both 4-amino-3,5-dinitropyrazole (**7**) and 5(3)-amino-3(5),4-dinitropyrazole (**8**) could be foreseen to be precursors of TNP. The synthesis of **7** was first reported in 1993[8] and then improved by Pagoria and co-workers.[9] The preparation of the regioisomer **8** was only reported recently by our group (see the Supporting Information).[10] An efficient route to **8** was realized from 1,3,4-trinitropyrazole,[11] which was prepared in a quantitative yield by N nitration of 3,4-dinitropyrazole. 1,3,4-trinitropyrazole was then reacted with the soft azide ion to give 3-azido-4,5-dinitropyrazole. Harder amines[12] (allylamines, bistrimethylsilylamine) or ammonia were found to be highly reactive such that no selective reaction occurred at C5, even at low temperatures. The final reduction of 3-azido-4,5-dinitropyrazole was performed by conventional means (triphenylphosphine or thiolacetic acid) to afford **8** in 30–50 % yield.

Highly deactivated primary amines require severe oxidation conditions depending on their basicity.[13] Caro's acid (H_2SO_5) was prepared in situ, but had insufficient reactivity to give TNP by oxidation of **7** or **8**. A stronger oxidizing agent such as diperoxysulfuric acid ($H_2S_2O_8$), was much more appropriate as the solution turned green (nitroso intermediate formation) indicating the presence of a nitroso group (Scheme 1). The oxidation was monitored by observing the change of the color of the solution from deep green to yellow, indicating the complete transformation of the nitroso into the nitro product (Het-NO → Het-NO_2). However, work-up was

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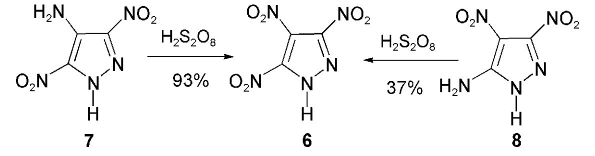
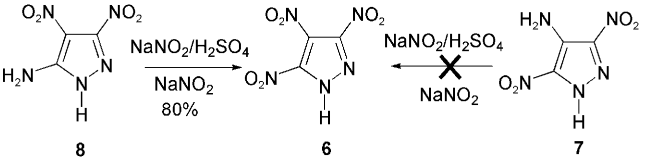


Scheme 1. Oxidation of aminodinitropyrazoles to give TNP (**6**). For experimental details, see the Supporting Information.

very problematic as all our runs, when added to ice, afforded a yellow impure oil after extraction. ^{13}C NMR spectroscopy confirmed that both amino dinitropyrazoles (especially **7**) gave one major symmetric pyrazole (two signals recorded at $\delta = 122.6$ and 143.2 ppm). Purification on silica gel was not successful because of material degradation. This problem was eventually circumvented through selective extraction of the undiluted reaction mixture with dichloromethane. TNP was thus obtained in 93 % and 37 % yields from **7** and **8**, respectively. As a slower reaction (higher temperatures required for **7** versus **8**), the oxidation of **7** was more selective due to the steric bulk of the amino group which inhibits the competitive intermolecular reactions. In contrast, **8** was readily oxidized into TNP with concomitant formation of several minor by-products.[14]

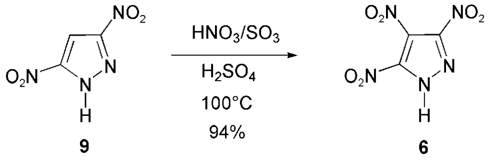
Diazotization of aminodinitropyrazoles **7** and **8** was then evaluated as an alternative pathway to oxidation (Scheme 2). 4-Diazo-3,5-dinitropyrazole was readily obtained from **7** but it did not undergo any nucleophilic displacement at C4, thereby confirming the previously reported observation.[3] In contrast, when **8** was subjected to diazotization in 20 % sulfuric acid impure TNP was obtained in fairly good yield (80 %) and collected as a red, sticky gum.[15]



Scheme 2. Diazotization route to TNP. For experimental details, see the Supporting Information.

Direct oxidation of **7**, or diazotization of **8** and subsequent nucleophilic displacement by NO_2^- are complementary methods to selectively obtain TNP in high yields. On the contrary, direct oxidation of **8** or diazotization of **7** and subsequent nucleophilic displacement by NO_2^- give very poor results.

TNP showed an unexpected and exceptional thermal stability observed by differential scanning calorimetry (DSC; see the Supporting Information). TNP melts at 187.8 °C and boils over the 200–260 °C temperature range. Then a residual decomposition process is recorded from 260–350 °C. As a proof of high stability, its heat of decomposition is only 255 J g^{-1}, which is extremely low for a high energy compound.[16] This observation prompted us to attempt the direct nitration of 3,4-dinitropyrazole or 3,5-dinitropyrazole (**9**).[17] Nitration of 3,4-dinitropyrazole gives 1,3,4-trinitropyrazole under mild conditions (0 °C–20 °C), regardless of the nitrating reagent (nitronium ions, acetyl nitrate.) used. Nitration **9** at C4 looks challenging because of the presence of two adjacent electron-withdrawing nitro groups. Nevertheless, the unsubstituted C4 is unequivocally a favorable position to undergo electrophilic reactions on pyrazoles since the relatively downfield signal at $\delta = 100$ ppm (^{13}C NMR) indicates a likely "residual" nucleophilicity at C4. Nitration at 20–140 °C was therefore attempted on **9** in mixed acids under usual conditions, without any success (^{1}H NMR monitoring). Severe reaction conditions using the assumed nitroprotonium dication,[18] which was generated in situ using 20–30 % sulfuric oleum mixed with nitric acid at 100 °C, afforded after usual work-up (dilution with water and then extraction) TNP as a clean white solid in a very high yield (94 %; Scheme 3). This method is now the preferred one to obtain TNP. NMR, IR, and DSC characterizations were similar to those performed on TNP samples obtained from the oxidation and diazotization routes.



Scheme 3. Direct nitration of 3,5-dinitropyrazole.

^{15}N NMR spectra of TNP shows two sharp peaks at $\delta = -33.4$ and -33.5 ppm for each of the nitro groups. Only one broad peak was observed in the ^{14}N NMR spectrum as a result of the lower ^{14}N NMR resolution. The nitrogen atoms of the pyrazole ring appear as a single down-field peak at $\delta = -136.4$ ppm due to fast proton exchange on the NMR timescale.

The pK_a of TNP was determined by potentiometry to be 2.35, which is worth comparing to those reported in the literature for pyrazole and partially nitrated pyrazoles:[5a,19,20] 1*H*-pyrazole: p$K_a = 14.2$; 3(5)-nitropyrazole: p$K_a = 9.81$; 4-nitropyrazole: p$K_a = 9.67$; 3(5),4-dinitropyrazole: p$K_a = 5.14$; 3,5-dinitropyrazole: p$K_a = 3.14$. The effect of the introduction of a nitro group in position four of the pyrazole ring is strongly dependent upon the presence of flanking nitro groups in the 3- or 3,5-positions. The pK_a change is quite small (0.8 unit) on going from 3,5-dinitropyrazole to TNP. Twisting of the nitro groups when they are situated in close proximity might account for such an unexpected behavior. This twisted conformation was confirmed by X-ray analysis (Figure 2).

X-ray data of TNP revealed that half proton occupancy occurs on the N1 and N2 nitrogen atoms for both molecules crystallized in the unit cell. Such half proton occupancy corresponds to a static disorder between two structures of the same energy. A dynamic disorder, that is, rapid proton transfer, can be excluded because it is observed in cyclamers (cycles) and never in catemers (chains).[21] Forms A and B

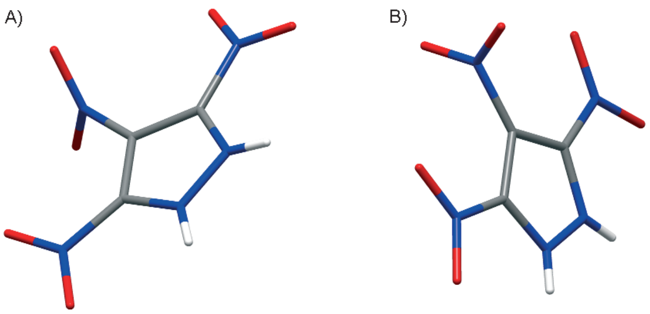


Figure 2. The structure of 3,4,5-trinitro-1*H*-pyrazole (**6**) determined by X-ray analysis.[26] The hydrogen atoms on the nitrogen centers show half occupancy due to a static disorder occurring in the catemers of the two forms (A and B).

differ by the torsion angles of the nitro groups. Selected structural parameters of TNP (**6**) and sodium 3,4,5-trinitropyrazolate (**6′**) are summarized in Table 1.

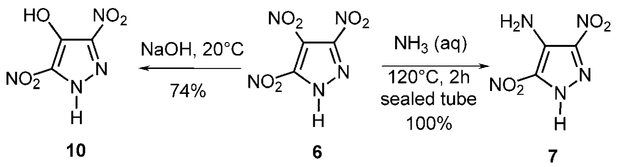
Table 1: Geometry of **6** and its sodium salt **6′**.

TNP	Twist angle of the NO_2 group [°] at:		Bond length [Å]		
	C3 and C5	C4	N1–N2	N2–C3 and N2–C5	C3–C4
6 (A)	9	67	1.336	1.332	1.381
6 (B)	0	81	1.330	1.332	1.380
6′	1–13[a]	82	1.343	1.348	1.386

[a] In the solid state, the twist angles at C(3) and C(5) have distinct values.

The bonds of the sodium salt **6′** are slightly longer due to the negative charge. Surprisingly, the intracyclic bonds of **6** remarkably match those of standard bonds observed in 1*H*-pyrazole and 4-nitropyrazole,[19] along with a perfect ring planarity (see the Supporting Information). Accordingly, all the structural parameters point at an unaffected aromaticity. The nitro groups at C3 and C5, and the ring are almost coplanar, whereas the hindered nitro group at C4 is considerably twisted, preventing the conjugation of this group with the pyrazole ring. The lack of conjugation has an obvious effect upon the acidity of the compound as confirmed by the experimental acidity constant of **6** ($pK_a = 2.35$). TNP appears to be the sole weak acid in these series since the all-carbon nitrated azoles **1**–**5** are unambiguously strong acids ($pK_a < 0$). The low acidity might explain the exceptional thermal stability of TNP recorded by DSC in comparison to the reported instability of the other all-carbon nitrated azoles **1**–**5**. As an illustration of the relationship between acidity and stability, the sodium salt of 3,4,5-trinitropyrazole (**6′**) has an enhanced stability with a decomposition point recorded at 294 °C (very sharp peak, 3000 $J\,g^{-1}$) by DSC. In summary, as is the case for other NH-acidic energetic materials, the more acidic a nitroazole, the less stable it is in terms of thermal, chemical, and mechanical stabilities.

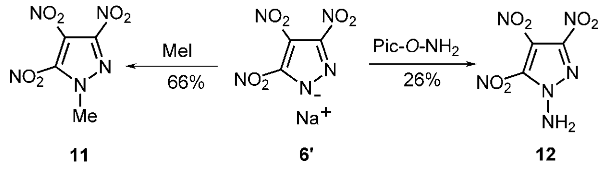
TNP shows also superior thermal and chemical stability compared to the other known fully nitrated aromatic systems such as 3,4-dinitro-oxa-3,5-diazole (DNF, dinitrofurazane), hexanitrobenzene (HNB), and decanitrobiphenyl.[22] As apparently stable explosives, these two latter nitrocarbon compounds show some lowering of melting point and slight decomposition on prolonged storage at room temperature.[22] Dark oils are collected as a result of instability when standing in a dessicator at 0–25 °C. DNF fumes upon storage yielding dinitrofurazanyl ether.[23] Instability is believed to be associated with a facile nitro/nitrite rearrangement of the labile nitro groups producing radicals ($C\text{-}NO_2 \rightarrow C\text{-}ONO \rightarrow CO^{\bullet} + NO^{\bullet}$).[22] As a more stable explosive, TNP can be stored at room temperature without any problems. The ability of the TNP nitro groups to be displaced is quite impaired, and TNP is stable in water unlike all the previous aromatic systems (HNB readily reacts with water).[22] TNP is only hydrolyzed in alkaline water. For a complete displacement of the 4-nitro group to obtain **10**, concentrated sodium hydroxide solutions must be used (Scheme 4). Complete amination at C4 to yield **7** requires the use of concentrated ammonia under pressure (sealed tube). In comparison, HNB readily reacts when bubbling ammonia at room temperature in benzene solution, and decanitrobiphenyl is even more reactive than HNB.[22]



Scheme 4. Nucleophilic substitutions (S_NAr) on TNP. For experimental details, see the Supporting Information.

In addition to thermal and chemical stability, TNP has excellent mechanical resistance against external stimuli and it has much lower impact sensitivity than standard explosives (cyclonitramines; all the safety data are detailed in the Supporting Information). Finally, this highly stable energetic molecule looks very promising since it presents as well a high energetic potential (see the Supporting Information).[4]

Two new derivatives of TNP, presenting a very high thermostability (see DSC in the Supporting Information), are *N*-methyl-3,4,5-trinitropyrazole (**11**) and *N*-amino-3,4,5-trinitropyrazole (**12**).[24] These derivatives can be readily prepared from sodium trinitropyrazolate **6′** in one-step procedures (Scheme 5).



Scheme 5. Electrophilic reactions on sodium trinitropyrazolate 6′. (Pic-O-NH_2 = 2,4,6-trinitrophenyl-*O*-hydroxylamine). For experimental details, see the Supporting Information.

Trinitropyrazoles **11** and **12** each exhibit three distinct aromatic carbon atoms: $\delta = 123.5$ (C4, triplet), 137.7 (triplet), 148.8 (broad signal), and 123.1 (C4, triplet), 136.5 (triplet), 140.8 ppm (broad signal), respectively.[25] Asymmetry in **12** was also revealed by three distinct sharp peaks at $\delta = -31.7$, -33.3, and -36.7 ppm (^{14}N-NMR) attributed to the three nitro functions. Lastly, the N-amino group of **12** was detected by ^{15}N NMR analysis (INEPT) as a triplet at $\delta = -288.7$ ppm ($J_{\mathrm{NH}} = 74$ Hz).

In conclusion, 3,4,5-trinitro-1*H*-pyrazole (**6**) has been prepared according to several appropriate synthetic methods. The unexpected nitration of 3,5-dinitropyrazole has been successfully accomplished with a superelectrophile at elevated temperature. It is evident that this straightforward reaction would not have even been attempted under such drastic conditions if the extraordinary stability of TNP would not have been established before. The remarkable TNP stability (thermal, chemical, and mechanical) is mainly a result of the preservation of the ring geometry and to the specific nitro conformation at C4 which confers a low acidity to the material. The nitro at C4 is therefore strongly linked to the ring so that drastic conditions are required to provoke its displacement. As a weak acid, TNP is today the sole aromatic explosive, that is all-carbon nitrated and can be used in powerful ammunitions or in propellants exhibiting great thermal, chemical, and mechanical stability.[4]

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[25] The broad signals and triplets are due to ^{13}C coupling to the neighboring naturally abundant ^{14}N (J ^{13}C-^{14}NO$_2$).

[26] CCDC 770180 (**6**), CCDC 770181 (**6'**), and CCDC 770182 (**8**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data request/cif.