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### New synthetic route to diaminonitropyrazoles as precursors of energetic materials

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Abstract—Treatment of nitropyrimidine derivatives with (*N*-substituted) hydrazines (2 equiv.) gave 1-(substituted)-3,5-diamino-4nitropyrazole, providing a very mild conversion of pyrimidines into pyrazoles. This reaction provided a convenient route to precursors for new efficient and insensitive explosives.

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Currently, in the field of explosives research, emphasis is given to high quality simple compounds with high energy, high density, heat resistance and low sensitivity. Synthesis and structural characterization of new insensitive energetic compounds with these properties is the focus of studies in our laboratory.<sup>1</sup>

A literature survey reveals that many energetic compounds containing pyrimidine<sup>1</sup> and pyrazole<sup>2</sup> rings are of multi-purpose interest since the heterocyclic skeleton with nitrogen content confers a high enthalpy of formation and thermal stability. Many papers were devoted to reactions of substituted pyrimidines with nucleophiles causing ring contraction<sup>3–5</sup> such as conversion of urazil into pyrazolone and urea<sup>4</sup> by hydrazine, conversion of 4-methoxy-5-nitropyrimidine into 3-amino-4nitropyrazole<sup>5</sup> by the same reagent, and transformation of 2-substituted-4-chloropyrimidine into 2-substituted4-methyl-s-triazine by potassium amide in liquid ammonia.<sup>6</sup>

In this paper, we describe the reaction of *N*-substituted hydrazines with 4-(substituted)-6-chloro-5-nitropyrimidines in order to discover new precursors of energetic compounds (Scheme 1).

The attack on 4,6-dichloro-5-nitropyrimidine by (*N*-substituted)-hydrazines gave the dihydrazino compounds  $A_1$ ,  $A_2$  and  $A_4$  with low to moderate yields, except with the benzylhydrazine  $A_3$  (Table 1). In this latter case, only one chlorine atom was substituted by benzylhydrazine. The action of (*N*-substituted)-hydrazines on 4-amino-substituted pyrimidines derivatives led to ring opening and 1-substituted-3,5-diamino-4-nitropyrazoles were obtained. This ring transformation proceeded by a mechanism not get reported in pyrim-



### Scheme 1.

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R <sub>1</sub>	$R_2$	<b>R</b> <sub>3</sub>	Product	Time (min)	Yield (%)	Mp (°C)	Temperature of decomposition (°C)
Cl	Cl	Н	<b>A</b> <sub>1</sub> <sup>7</sup>	30	54		186
Cl	C1	CH <sub>3</sub>	A <sub>2</sub>	30	11		189
Cl	Cl	Bn	A <sub>3</sub>	30	97		225
Cl	C1	SO <sub>2</sub> Ph	A <sub>4</sub>	60	37		212
$N(CH_3)_2$	Cl	н	$B_{1}^{8}$	80	57	260-262	
N(CH <sub>3</sub> ) <sub>2</sub>	C1	CH <sub>3</sub>	B <sub>2</sub>	180	54	186–188	
Morpholino	Cl	Н	B <sub>1</sub>	60	21		
NH(CH <sub>2</sub> ) <sub>3</sub> CH <sub>3</sub>	Cl	Н	A <sub>5</sub>	40	27	255-256	
$N(CH_3)_2$	OMe	Н	B <sub>1</sub>	60	61		

 
 Table 1. Synthesis of 4,6-di(substituted)hydrazino-5-nitropyrimidines and 1-substituted-3,5-diamino-4-nitropyrazoles from 4-(substituted)-6-chloro-5-nitropyrimidines

idine chemistry (Scheme 2). The yields of pyrazoles obtained from 4-N,N-dimethyl substituted pyrimidines showed that this is the better leaving group used.

Moreover, with a butylamino group in position 4, the reaction stopped at the first step of the rearrangement, i.e. the substitution of hydrazine in position 6. The butylamino group may stabilize the pyrimidine system to prevent the second attack of hydrazine in position 2. The rearrangement of 4-N,N-dimethyl-5-nitro-6-methoxypyrimidine with hydrazine hydrate shows that a methoxy group instead of a chlorine atom in position 6 does not affect the yield of 3,5-diamino-4-nitropyrazole that much. Therefore, a chlorine atom and a methoxy group have the same reactivity in this rearrangement.

The opening of the pyrimidine ring involves a nucleophilic attack by hydrazine on position 2 of the hydrazino derivatives, with scission of the 2–3 bond and generation of a cyano group. The resulting acyclic intermediate undergoes an intramolecular nucleophilic attack on the cyano group by the 6-hydrazino group, which results in the formation of a pyrazole ring.

Differential Scanning Calorimetric (DSC) analyses of  $A_1$  and  $A_4$  have shown that compound  $A_1$  exhibits a broad exothermic peak at 186°C, while compound  $A_4$  exhibits a high energetic single sharp exothermic peak at 212°C.

In view of these results, the impact sensitivity of  $A_1$  and  $A_4$  was measured with a drop weight impact test (11 kg). Under these test conditions, Octogene<sup>9</sup> (HMX) was readily detonated with a hammer's height of 12 cm. Compounds  $A_1$  and  $A_4$  could not be detonated with this test despite numerous attempts, and are thus less sensitive to impact than Pentrite or Octogene.<sup>9</sup>

In conclusion, we have described the reactivity of *N*-substituted hydrazines with nitropyrimidines. The reaction between 4-(substituted)-6-(chloro or methoxy)-pyrimidines and hydrazine hydrate leads, in one step with a previously undescribed mechanism, to 1-(substituted)-3,5-diamino-4-nitropyrazoles. As a result, this reaction provides a convenient route to some precursors for new insensitive explosives.

### **Experimental section**

Melting points were determined on a Kofler melting point apparatus and are uncorrected. Differential Scanning Calorimetric (DSC) analyses were recorded with a DSC 822 Mettler apparatus by heating a sample at a rate of 10°C/min in the presence of static air. IR spectra were recorded on a Perkin–Elmer Spectrum One FT-IR spectrometer with a Perkin Elmer Universal ATR sampling accessory. NMR spectra were recorded on a Brüker Avance 200 MHz NMR. The chemical shifts in CDCl<sub>3</sub> and DMSO- $d_6$  are reported in  $\delta$  (ppm). Mass spectra were recorded on a HP 5973 mass spectrometer in the Faculty of Pharmacy of Tours, France.



# General procedure for the synthesis of dihydrazino compounds:

To a solution of a 4,6-dichloro-5-nitropyrimidine (500 mg, 2.6 mmol) in methanol was added dropwise hydrazine hydrate (0.63 mL,  $4.5 \times 2.6$  mmol). The mixture was stirred at room temperature for 30 min. The precipitate obtained was filtered off and purified by recrystallization from isopropanol.

4,6-Dimethylhydrazino-5-nitropyrimidine  $A_2$  ( $R_4 = R_5 =$  NHNHCH<sub>3</sub>). Orange needles, mp 189°C;  $v_{max}/cm^{-1}$  3335, 3285, 1630, 1567, 1521, 1506, 1484, 1398, 936, 863;  $\delta_H$  (200 MHz, DMSO- $d_6$ ) 3.20 (s, 6H, 2×CH<sub>3</sub>), 4.62 (s, 4H, 4×NH), 7.91 (s, 1H, H<sub>arom</sub>).

4-Benzylhydrazino-5-nitro-6-chloropyrimidine A<sub>3</sub> (R<sub>4</sub>= NHNHBn, R<sub>5</sub>=Cl). Yellow needles, mp 225°C;  $\nu_{max}$ / cm<sup>-1</sup> 3333, 2921, 1643, 1565, 1531, 1495, 1465, 1454, 1407, 1345, 1300, 1255, 1027;  $\delta_{\rm H}$  (200 MHz, CDCl<sub>3</sub>) 3.65 (s, 2H, CH<sub>2</sub>Ph), 5.02 (s, 2H, 2×NH), 7.18–7.39 (m, 5H, H<sub>arom</sub>), 8.33 (s, 1H, H<sub>arom</sub>); m/z 279 (M<sup>+</sup>, 4%), 216 (9), 91 ([CH<sub>2</sub>Ph]<sup>+</sup>, 100), 65 (25).

4,6-Dibenzylsulfonylhydrazino-5-nitropyrimidine  $A_4$ ( $R_4 = R_5 = NHNHSO_2Ph$ ). Yellow needles, mp 212°C;  $v_{max}/cm^{-1}$  3338, 3254, 3061, 1576, 1521, 1497, 1448, 1408, 1350, 1301, 1229, 1212, 1180, 1167, 1090;  $\delta_H$  (200 MHz, DMSO- $d_6$ ) 7.28 (s, 1H,  $H_{arom}$ ), 7.45–7.86 (m, 10H,  $H_{arom}$ ), 10.28 (br s, 4H, 4×NH);  $\delta_C$  (50.47 MHz, DMSO- $d_6$ ) 128, 129, 133, 139, 144, 156, 158;  $\delta_N$  (30.42 MHz, DMSO- $d_6$ ) -14, -151, -213, -257.

4-Butylamino-5-nitro-6-hydrazinopyrimidine  $A_5$  ( $R_4$  = NHNH<sub>2</sub>,  $R_5$  = NH(CH<sub>2</sub>)<sub>3</sub>CH<sub>3</sub>). Orange needles, mp 255–256°C;  $\nu_{max}/cm^{-1}$  3334, 3272, 2953, 2935, 2871, 1587, 1553, 1525, 1506, 1477, 1458, 1366, 1347, 1262, 1245, 1223, 1159, 1122, 1076, 967, 946, 782;  $\delta_{\rm H}$  (200 MHz, CDCl<sub>3</sub>) 0.98 (t, 3H, CH<sub>3</sub>), 1.43 (sextuplet, 2H, CH<sub>2</sub>), 1.57 (s, 2H, NH<sub>2</sub>); 1.68 (sextuplet, 2H, CH<sub>2</sub>), 3.67 (quadruplet, 2H, CH<sub>2</sub>-N), 8.24 (s, 1H, H<sub>arom</sub>), 9.37 (d, 1H, NH-CH<sub>2</sub>), 12.37 (s, 1H, NH-NH<sub>2</sub>);  $\delta_{\rm C}$  (50.47 MHz, CDCl<sub>3</sub>) 14, 20, 31, 42, 149, 160.

## General procedure for the synthesis of pyrazole compounds:

To a warm solution of 4,6-substituted-5-nitropyrimidine (2 mmol) in ethanol was dropwise added hydrazine hydrate  $(4.5\times2 \text{ mmol})$ . The mixture was stirred under reflux until the starting material was fully converted (TLC). After cooling the mixture, the precipitate obtained was filtered off, and washed with hot ethanol.

1-Methyl-3,5-diamino-4-nitropyrazole **B**<sub>2</sub> (R<sub>6</sub>=CH<sub>3</sub>). Yellow needles, mp 186–188°C;  $v_{max}$  (cm<sup>-1</sup>) 3411, 3293, 1614, 1571, 1493, 1413, 1380, 1225, 1166, 1126, 1087;  $\delta_{\rm H}$  (200 MHz, DMSO- $d_6$ ) 3.34 (s, CH<sub>3</sub>), 5.87 (s, 2H, NH<sub>2</sub>), 7.20 (s, 2H, NH<sub>2</sub>);  $\delta_{\rm C}$  (50.47 MHz, DMSO- $d_6$ ) 34, 108, 145, 149; 160 *m*/*z* 157 (M<sup>+</sup>, 55%), 127 (M<sup>+</sup>–[NO], 9), 96 (M<sup>+</sup>–[NO<sub>2</sub>+Me], 20), 65 (100), 43 (41).

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