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# Synthesis of 4-(*N*-azolyl)-3,5-dinitropyrazoles

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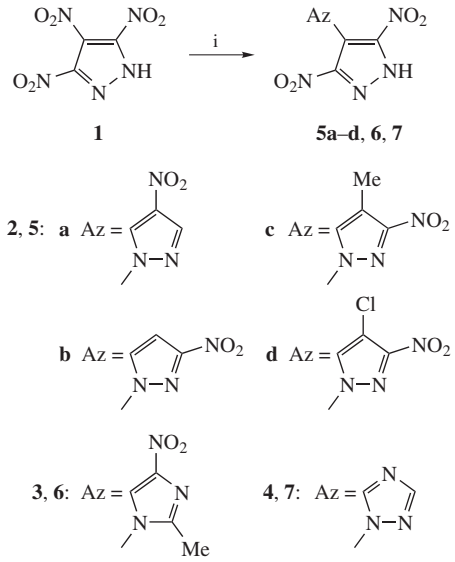
**NH-Azoles selectively substitute 4-positioned nitro group in 3,4,5-trinitro-1*H*-pyrazole in aqueous NaOH to furnish 4-(*N*-azolyl)-3,5-dinitropyrazoles.**

4-(*N*-Azolyl)pyrazoles represent an interesting family of compounds due to their diverse biological activity[1] as well as potential use as polydentate ligands in Pd-catalysed amination reactions.[2] At the same time, most of their syntheses are based on the cyclization of 2-(*N*-azolyl)-1,3-dioxopropanes or their precursors with hydrazines.[3]

Recently, we have shown[4] that 3,4,5-trinitro-1*H*-pyrazole **1** anion extremely easily reacts with aliphatic amines in water at room temperature to undergo regiospecific nucleophilic substitution of 4-positioned $NO_2$-group and to afford 4-amino-3,5-dinitropyrazoles. This finding was a good challenge to develop a similar approach to 4-(*N*-azolyl)-3,5-dinitro-pyrazoles.

In fact, the reactions of pyrazole **1** with NH-azoles (pyrazoles **2a–d**, nitroimidazole **3** and triazole **4**) in water in the presence of 2 equiv. NaOH (80–90 °C, 9 h) gave the expected 4-(*N*-azolyl)-3,5-dinitropyrazoles **5–7** (Scheme 1).† In the presence of only 1 equiv. NaOH, the transformation did not occur, which could indicate that the process involves anions of both azole‡ and substrate **1** ($pK_a = 0.05$[4]).

The regiodirection of substitution was established using $^{13}C$ NMR spectroscopy. $^{13}C$ NMR spectra of all the products contained only two signals assigned to the $C^4$ and $C^{3,5}$ atoms. This is due to the fast exchange of NH protons in the pyrazole system producting thus a symmetrical structure. The signals of the $C^{3,5}$ atoms bearing the $NO_2$ groups have typical quadrupole broadening. All these data as well as comparison to the $^{13}C$ NMR spectra of other known N-unsubstituted 4-R-3,5-dinitropyrazoles[4] clearly show that substitution occurs at 4-position in substrate **1**. The assignment of other singnals was based on literature data.[6]




**Scheme 1** *Reagents and conditions*: i, 1 equiv. AzH (**2a–d**, **3**, **4**), 2 equiv. NaOH, $H_2O$, 80–90 °C, 9 h, then 20% $H_2SO_4$.

The structures of all products were confirmed by $^1H$ and $^{13}C$ NMR, IR and mass spectra. All compounds have characteristic

† $^1H$ and $^{13}C$ NMR spectra were recorded in DMSO-$d_6$ solutions on a Bruker DRX-500 or Bruker AC-300 spectrometer. IR spectra were measured with a Bruker ALPHA spectrometer and mass spectra with a Bruker MicroOTOF II instrument.

*General procedure for the synthesis of 4-(*N*-azolyl)-3,5-dinitropyrazoles* **5a–d**, **6**, **7**. A solution of trinitropyrazole **1**[4] (3 mmol), NH-azole (3 mmol) and NaOH (6 mmol) in water (10 ml) was stirred at 80–90 °C for 9 h. The mixture then was cooled and acidified with 20% $H_2SO_4$ to reach pH 1. The precipitate formed was filtered off, washed with cold water and dried over $P_2O_5$. Recrystallization from EtOH–$H_2O$ (1:1) gave analytically pure samples.

**5a**: yield 61%, mp 215–216 °C. $^1H$ NMR, $\delta$: 9.24 (s, 1H), 8.45 (s, 1H). $^{13}C$ NMR, $\delta$: 149.52 ($C^{3,5}$), 136.69 (CH), 135.92 ($C^{4'}NO_2$), 133.77 (CH), 110.66 ($C^4$). IR (KBr, $\nu$/cm$^{-1}$): 3138 (NH), 1625, 1536, 1515, 1417, 1325 ($NO_2$). MS (ESI), *m*/*z*: 268.0064 [M – H]$^-$. Calc. for $C_6H_2N_7O_6^-$: 268.0072.

**5b**: yield 52%, $T_{decomp.}$ 290 °C. $^1H$ NMR, $\delta$: 8.31 (s, 1H), 7.23 (s, 1H). $^{13}C$ NMR, $\delta$: 156.55 ($C^{3'}NO_2$), 149.45 ($C^{3,5}$), 137.64 (CH), 110.78 ($C^4$), 103.78 (CH). $^{14}N$ NMR (acetone-$d_6$) $\delta$: –21.62, –24.72 ($NO_2$), –76.27 (br., $N^2$). IR (KBr, $\nu$/cm$^{-1}$): 3162, 3139 (NH), 1628, 1557, 1389, 1342 ($NO_2$). MS (ESI), *m*/*z*: 268.0060 [M – H]$^-$. Calc. for $C_6H_2N_7O_6^-$: 268.0072.

**5c**: yield 63%, mp 150–151 °C. $^1H$ NMR, $\delta$: 8.12 (s, 1H), 2.31 (s, 3H, Me). $^{13}C$ NMR, $\delta$: 154.56 ($C^{3'}NO_2$), 148.95 ($C^{3,5}$), 136.31 (CH), 114.28 ($C^{4'}$), 110.94 ($C^4$), 9.39 (Me). IR (KBr, $\nu$/cm$^{-1}$): 3578, 3333 (NH), 1629, 1551, 1528, 1351, 1333 ($NO_2$). MS (ESI), *m*/*z*: 282.0207 [M – H]$^-$. Calc. for $C_7H_4N_7O_6^-$: 282.0218.

**5d**: yield 80%, mp 135–136 °C. $^1H$ NMR, $\delta$: 8.73 (s, 1H). $^{13}C$ NMR, $\delta$: 151.11 ($C^{3'}NO_2$), 149.31 ($C^{3,5}$), 135.57 (CH), 110.21 ($C^4$), 105.97 ($C^{4'}Cl$). IR (KBr, $\nu$/cm$^{-1}$): 3573, 3422 (NH), 1628, 1562, 1545, 1507, 1337 ($NO_2$), 837 (CCl). MS (ESI), *m*/*z*: 301.9678, 303.9648 (3:1) [M – H]$^-$. Calc. for $C_6HClN_7O_6^-$: 301.9671, 303.9643.

**6**: yield 71%, mp 230–232 °C. $^1H$ NMR, $\delta$: 8.20 (s, 1H), 2.35 (s, 3H, Me). $^{13}C$ NMR, $\delta$: 146.70 ($C^{3,5}$), 144.73 ($C^{2'}Me$), 123.75 ($C^4$), 118.97 (CH), 13.68 (Me). $C^{4'}NO_2$ signals were not observed. IR (KBr, $\nu$/cm$^{-1}$): 3162 (NH), 1627, 1506, 1379 ($NO_2$), 1102. MS (ESI), *m*/*z*: 268.0227 [M – H]$^-$. Calc. for $C_7H_4N_7O_6^-$: 268.0218.

**7**: yield 89%, mp 245–247 °C. $^1H$ NMR, $\delta$: 8.82 (s, 1H), 8.20 (s, 1H). $^{13}C$ NMR, $\delta$: 151.86 (CH), 148.62 ($C^{3,5}$), 144.57 (CH), 142.71 ($C^4$). $^{14}N$ NMR (acetone-$d_6$) $\delta$: –24.55, –29.80 ($NO_2$), –71.21 (br., $N^2$), –140.73 (br., $N^1$). IR (KBr, $\nu$/cm$^{-1}$): 3456, 3138 (NH), 1624, 1533, 1448, 1333 ($NO_2$). MS (ESI), *m*/*z*: 226.0325 [M – H]$^-$. Calc. for $C_5H_2N_7O_4^-$: 226.0319.

‡ For azoles **2a–d**, **3**, **4** $pK_a \leq 10$ (see ref. 5).

of $NO_2$ group IR bands. All mass spectra show molecular ions peaks $[M]^+$.

In conclusion, a new useful method of synthesis of the previously unknown 4-(*N*-azolyl)-3,5-dinitropyrazoles has been elaborated.

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