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Hydrogen halides as nucleophilic agents for 3,4,5-trinitro-1*H*-pyrazoles

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1-R-3,4,5-Trinitropyrazoles (R = H, Me) undergo nucleophilic substitution on treatment with concentrated hydrogen halide solutions to give 5-halo-1-R-3,4-dinitropyrazoles.

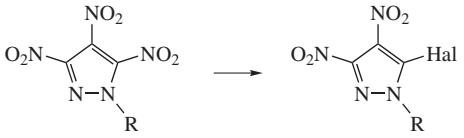
An increasing interest in pyrazoles is due to the fact that they can find use for peaceful[1] and military purposes.[2] Previously, we have shown that replacement of NO_2 group in 3,4- and 3,5-dinitropyrazoles is a versatile approach to molecules containing C(pyrazole)–X(O, S, N) bonds.[3] This reaction pathway is characteristic of dinitropyrazoles containing no additional groups capable of nucleophilic substitution. In 3,4-dinitropyrazoles, irrespective of the capability to undergo ionization under the reaction conditions, *i.e.* in the presence or absence of a substituent at the N^1 ring atom, only the 3-NO_2 group is selectively replaced on treatment with nucleophiles. On the other hand, N^1-substituted 3,5-dinitropyrazoles react with nucleophiles with selective replacement of the 5-NO_2 group, whereas in the case of N^1-unsubstituted analogues the reaction stalls in salt formation due to ionization of the N(ring)–H bond.

Recent studies carried out by our group[4,5] as well as those by Herve *et al.*[6] provided 3,4,5-trinitro-1*H*-pyrazole **1** and its *N*-methyl derivative, namely, 1-methyl-3,4,5-trinitro-1*H*-pyrazole **2**, the first representatives of pyrazoles completely nitrated at the carbon atoms.

We have found that the features of nucleophilic substitution in polynitropyrazoles of this type differ from the previously known behaviour. With O-, S-, N-anionic (RX^-, X = O, S, N) and covalent N-nucleophiles, trinitropyrazole **1** reacts in anionic form due to the high NH-acidity of compound **1** ($pK_a = 0.05$,[5] $pK_a = 2.35$[6]). This involves reactivity reversal, and it is the 4-NO_2 group that undergoes selective nucleophilic substitution.[5,7] On the other hand, the nucleophilic substitution in N^1-substituted compound **2**, conforms to the general regularities for 3,4- and 3,5-dinitropyrazoles described above, *i.e.*, the 3(5)-nitro group is replaced.[8]

To confirm our viewpoint that the regiospecificity of nucleophilic substitution in the trinitropyrazole series is primarily governed by their ionisation capability, we studied the reaction of compounds **1** and **2** with hydrogen halides. Note that trinitropyrazole **1** is not ionised in concentrated hydrogen halide solutions.

In fact, heating of trinitropyrazole **1** at 60–70 °C in concentrated aqueous HCl and HBr solutions gives compounds **3** and **4**; complete conversion is reached within 15 h and the yields are 90 and 60%, respectively (Scheme 1).† ^{13}C NMR data showed that these compounds are 5-chloro-3,4-dinitropyrazole **3** and 5-bromo-3,4-dinitropyrazole **4**, respectively, since they contained three signals at 116–118, 125–127 and 150 ppm, which correspond to three different carbon atoms of unsymmetric structures, two of these signals are broadened (C–NO_2). Furthermore, these spectra were identical to those of the specimens of compounds **3** and **4** that we obtained previously from 5-diazo-3,4-dinitropyrazole.[9] Additional proof of the structures of compounds **3** and **4** was obtained by comparison of their ^{13}C NMR chemical shifts with those in 3,5-dinitro-4-chloropyrazole **7**,‡ *i.e.* 103 and 150 ppm.



1 R = H
2 R = Me

3 R = H, Hal = Cl
4 R = H, Hal = Br
5 R = Me, Hal = Cl
6 R = Me, Hal = Br

Scheme 1 *Reagents and conditions*: HCl (35%) or HBr (48%), 60–70 °C.

N-Methyl-substituted trinitropyrazole **2** reacts with aqueous hydrogen halides in a similar manner and faster than compound **1**: the complete conversion is attained within 5 h of heating at 60–70 °C. The reaction gives 5-chloro-1-methyl-3,4-dinitropyrazole **5** and 5-bromo-1-methyl-3,4-dinitropyrazole **6** in 90% and 80% yields, respectively (Scheme 1).§

The structures of these compounds were established based on the differences in the NMR spectral characteristics of **5** and **6**

† The structures of all the compounds were determined using ^1H and ^{13}C NMR spectroscopy in [$^2H_6$]DMSO (Bruker AC-300) and confirmed by IR (Bruker ALPHA) and mass (Finnigan MAT Incos 50) spectra as well as by elemental analyses. All the compounds have absorption bands at 1325 and 1520 cm^{-1} (NO_2) in the IR spectra and a molecular ion peak $[M]^+$ in the mass spectra.

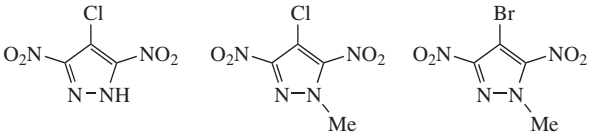
5-Halo-3,4-dinitropyrazoles (general procedure). A solution of 2 mmol trinitropyrazole **1** in 4 ml conc. HCl (d = 1.175 g cm^{-3}) or HBr (d = = 1.48 g cm^{-3}) was heated for 15 h at 60–70 °C with stirring. The mixture was diluted with H_2O (15 ml) and extracted with diethyl ether (3×5 ml); the organic layer was dried with Na_2SO_4. The solvent was removed *in vacuo* and the residue was crystallized from CCl_4.

*5-Chloro-3,4-dinitro-1*H*-pyrazole* **3**: yield 95%, mp 110–111 °C (lit.,[9] mp 110–112 °C). ^{13}C NMR, δ: 148.63 (C^3), 130.68 (C^5), 122.69 (C^4).

*5-Bromo-3,4-dinitro-1*H*-pyrazole* **4**: yield 63%, mp 120–121 °C (lit.,[9] mp 118–120 °C). ^{13}C NMR, δ: 149.97 (C^3), 125.38 (C^4), 117.76 (C^5).

‡ 4-Chloro-3,5-dinitropyrazole was first mentioned in our study,[10] but we did not provide experimental details of its synthesis at that time.

*4-Chloro-3,5-dinitro-1*H*-pyrazole* **7**. Nitric acid (20 ml, d = 1.51 g cm^{-3}) was added dropwise with stirring to a solution of 4-chloropyrazole (15.6 g, 0.12 mol) in H_2SO_4 (190 ml, d = 1.824 g cm^{-3}) at 15–25 °C. The reaction mixture was kept for 5 h with stirring at 100–105 °C, poured into 1 liter of ice water and extracted with ethyl acetate (2×300 ml). The organic layer was washed with water and dried with $MgSO_4$; the solvent was removed *in vacuo* and the residue was crystallized from water to give 16.9 g (70%) of compound **7**. Mp 157–159 °C. ^{13}C NMR, δ: 148.97 ($C^{3,5}$), 103.09 (C^4).



7 **8** **9**

from those of known 4-chloro-1-methyl-3,5-dinitropyrazole **8**¶ and 4-bromo-1-methyl-3,5-dinitropyrazole **9**.[12] A typical distinction consists in the upfield shifts of the ^{1}H (4.02; 3.95 ppm) and ^{13}C NMR signals corresponding to the methyl group of compounds **5** and **6** in comparison with similar shifts (4.25 and 4.33 ppm) in compounds **8** and **9**. Additionally, compound **5** was studied by 2D HMBC NMR experiment, which displayed correlation between NMe protons and carbon atom at 130.6 ppm. Since this signal had no quadrupole broadening typical of nitrogen action, it was assigned to C–Cl.

In summary, the regiospecificity of nucleophilic substitution in trinitropyrazole derivatives on treatment with hydrogen halides does not depend on the presence or absence of a substituent at the N[1] ring atom and obeys the rule of selective substitution at positions 3 or 5 that is common to 3,4- and 3,5-dinitropyrazoles.

This confirms our supposition that regiodirection of nucleophilic substitution in 3,4,5-trinitropyrazoles is determined by whether they are N–H ionized or not.

§ *5-Halo-1-methyl-3,4-dinitropyrazoles (general procedure).* Aqueous HCl (4 ml, d = 1.175 g cm^{-3}) or HBr (4 ml, d = 1.48 g cm^{-3}) were added to a solution of compound **2** (2.62 mmol) in MeOH (4 ml); the reaction mixtures were heated for 5 h at 60–70 °C with stirring. The solvent was removed *in vacuo* and the residue was crystallized from CCl_4.

*5-Chloro-1-methyl-3,4-dinitro-1*H*-pyrazole* **5**: yield 89%, mp 59–61 °C. ^{1}H NMR, δ: 4.02 (s, 3H, Me). ^{13}C NMR, δ: 146.59 (C^3), 130.61 (C^5), 123.20 (C^4), 38.47 (NMe).

*5-Bromo-1-methyl-3,4-dinitro-1*H*-pyrazole* **6**: yield 79%, mp 53–55 °C. ^{1}H NMR, δ: 3.95 (s, 3H, Me). ^{13}C NMR, δ: 147.20 (C^3), 125.32 (C^4), 119.76 (C^5), 39.38 (NMe).

¶ *4-Chloro-1-methyl-3,5-dinitro-1*H*-pyrazole* **8**. Compound **7** (0.58 g, 3 mmol) was added to a solution of $NaHCO_3$ (0.51 g, 6 mmol) in H_2O (10 ml). The reaction mixture was stirred for 10 min, then Me_2SO_4 (0.34 ml, 3.6 mmol) was added. The mixture was stirred for 4 h at room temperature. The precipitate formed was filtered off and dried with P_2O_5 to give 0.54 g (87%) of compound **8**. Mp 101–103 °C (lit.,[11] mp 101.5–102.5 °C). ^{1}H NMR, δ: 4.25 (s, 3H, Me). ^{13}C NMR, δ: 148.10 (C^3), 143.15 (C^5), 105.92 (C^4), 43.83 (NMe).

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