Nitropyrazoles

19.* Selective nucleophilic substitution of a nitro group in 3,4-dinitropyrazoles

I. L. Dalinger,[a] I. A. Vatsadze,[a] T. K. Shkineva,[a] I. O. Kortusov,[b] G. P. Popova,[a] V. V. Kachala,[a] and S. A. Shevelev[a]*

[a]N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences,
47 Leninsky prosp., 119991 Moscow, Russian Federation.
Fax: +7 (499) 135 5328. E-mail: dalinger@ioc.ac.ru
[b]D. I. Mendeleev University of Chemical Engineering,
9 Miusskaya pl., 125047 Moscow, Russian Federation

N-Substituted 3,4-dinitropyrazoles, 1,5-dimethyl-3,4-dinitropyrazole and 1-methoxymethyl-5-methyl-3,4-dinitropyrazole, undergo nucleophilic substitution when reacted with S-, O-, and N-nucleophiles. The substitution occurs regioselectively at the 3-position, affording products in good yields. Anions of N-unsubstituted 3,4-dinitropyrazoles, 1*H*-3(5)-methyl-4,5(3)-dinitropyrazole and 1*H*-4,5(3)-dinitropyrazole, also react in water with S-nucleophiles with regioselective substitution of the nitro groups in the position 3(5).

Key words: pyrazole, nitro group, nitropyrazoles, 3,4-dinitropyrazoles, nucleophilic substitution, nucleophiles, protective group.

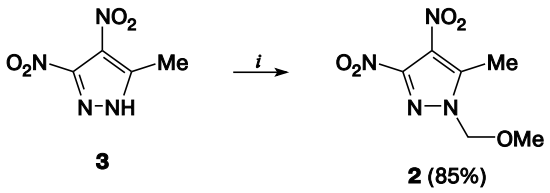
Previously[2—4] we have demonstrated that S-, O-, and N-nucleophiles react with N-substituted 4-R-3,5-dinitropyrazoles to selectively replace the nitro group at the position 5. However, under rather severe conditions and when the pyrazole position 3 is activated by an electron-withdrawing group in the position 4, such as CN group, the substitution of the nitro group at the 3-position may occur.[5] Notably, in the case of N-substituted 3,4-dinitropyrazoles in which both replaced and the second nitro group are in the *ortho*-positions, only few examples of nucleophilic substitution of 3-NO_2 are known, namely, reactions with hydrazine[6] and with aqueous ammonia with the latter run under pressure at 190 °C (see Ref. 7). As a next step in our studies of the modification of nitropyrazoles, more research on the replacement of the 3-NO_2 group in 3,4-dinitropyrazoles appeared important.

We have studied in detail the reactions of the model dinitropyrazoles, 1,5-dimethyl-3,4-dinitropyrazole (**1**) and 1-methoxymethyl-5-methyl-3,4-dinitropyrazole (**2**), with S-, O-, and N-nucleophiles. Pyrazole **1** was chosen as a model because of its availability by a direct one-step nitration of 1,5-dimethylpyrazole.[8]

Dinitropyrazole **2** was synthesized by alkylation of 3(5)-methyl-4,5(3)-dinitropyrazole[9] with methoxymethyl chloride in acetonitrile in the presence of K_2CO_3.

The structure of **2** as a 3,4- rather than 4,5-dinitropyrazole derivative was assigned based on 2D correlation $^1H—^{13}C$ HMBC and $^1H—^1H$ NOESY techniques. In the HMBC spectrum, spin-spin coupling between CH_3 protons and $C\underline{H}_2OCH_3$ protons was found at only one pyrazole carbon (δ 143.95), and additionally, the correlation NOESY spectrum shows spin-spin coupling between CH_3 protons and $C\underline{H}_2OCH_3$ protons, which is only possible if the pyrazole CH_3 group is in the 5-position.

Scheme 1



i. $MeOCH_2Cl$, K_2CO_3, MeCN, 25 °C, 1 h.

Studying nucleophilic substitution reactions of nitropyrazole **2** is important since, as we have demonstrated earlier,[3] *N*-methoxymethyl group is easily removable through acid hydrolysis, yielding N-unsubstituted nitropyrazoles. At the same time, dinitropyrazolate anion, like nitrite anion, is known to be a potential leaving group, so the orientation of nucleophilic substitution in dinitropyrazole **2** cannot be predicted precisely.

We chose ethylthioglycolate, *p*-methyl-, *p*-chlorothiophenol, and *p*-chlorobenzyl mercaptan as S-nucleophiles. The reaction was run in acetonitrile at room temperature in the presence of K_2CO_3 as a base. The substitution products formed in 65—86% yield, with the full con-

* For Part 18, see Ref. 1.

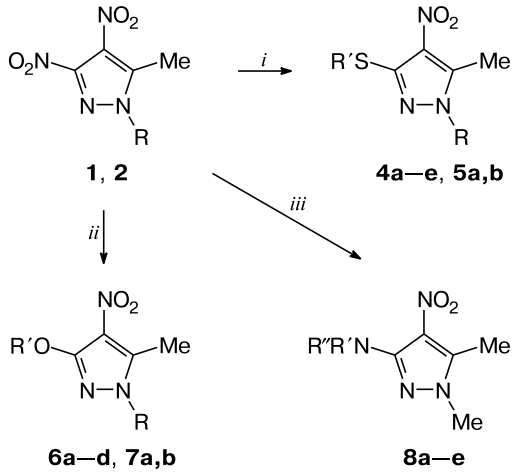
Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 9, pp. 1739—1743, September, 2010.

version taking 7 h for dinitropyrazole **1** and 3 h for dinitropyrazole **2**. It should be noted that 3,4-dinitropyrazoles **1** and **2** are much more reactive towards the above S-nucleophiles compared with the isomeric 1,4-dimethyl-3,5-dinitropyrazole and 1-methoxymethyl-4-methyl-3,5-dinitropyrazole that we have studied earlier. The reaction of the latter in acetonitrile either cannot go to completion at all or requires heating at reflux for 15 h to complete.[2]

It is also noteworthy that the above 3,5-dinitropyrazoles do not react with nucleophiles of the different type, such as N- and O-nucleophiles.[2]

However, we have found that 3,4-dinitropyrazoles **1** and **2** can react with N- and O-nucleophiles, but under more severe conditions than those needed with S-nucleophiles (Scheme 2).

Scheme 2



1: R = Me; **2:** R = CH_2OMe; **4:** R = Me, R′ = Et (**a**), CH_2CO_2Et (**b**), $CH_2C_6H_4Cl$-*p* (**c**), C_6H_4Me-*p* (**d**), C_6H_4Cl-*p* (**e**); **5:** R = CH_2OMe, R′ = Et (**a**), C_6H_4Me-*p* (**b**); **6:** R = Me, R′ = Ph (**a**), 3,4-$Me_2C_6H_3$ (**b**), CH_2CF_3 (**c**), Me (**d**); **7:** R = CH_2OMe, R′ = Ph (**a**), CH_2CF_3 (**b**); NR′R″ =  (**8a**),  (**8b**),  (**8c**), $N(CH_3)NH_2$ (**8d**), $NHNH_2$ (**8e**)

i. R′SH/K_2CO_3, MeCN, 25 °C, 7 h; *ii*. R′OH/K_2CO_3, MeCN, reflux, 15 h for **6a**—**c**, **7a**,**b** and CH_3ONa/MeOH, reflux for **6d**; *iii*. NHR′RI (3 equiv), Pr^{i}OH, reflux, 7 h.

We used sodium methylate, trifluoroethanol, phenol, and 3,4-dimethylphenol as O-nucleophiles. The reaction was run in acetonitrile in the presence of K_2CO_3 as a base, and in methanol in the case of sodium methylate. Note that in contrast to reactions with S-nucleophiles, full conversion requires refluxing for 10—15 h and yields are in the range 50—83%. The only exception is the reaction with sodium methylate, in which the substitution product is formed in a quantitative yield, probably owing to the employment of a presynthesized O-anion rather than having it being generated *in situ* in heterophase.

As to reactions with N-nucleophiles, several examples of these, as was mentioned above, have been known before. Yet the available data are clearly not sufficient to understand the general rules of nucleophilic substitution of the 3-NO_2 group. It also appeared important to characterize the structure of the substitution products with the modern NMR correlation techniques.

As N-nucleophiles we used aliphatic amines and hydrazines, *i.e.*, morpholine, pyrrolidine, hexamethylene imine, hydrazine, and methylhydrazine. The reaction was run in refluxing isopropanol (*cf.* Ref. 6a), for 7 h, with N-nucleophile in a 3-fold excess affording the substitution products in 50—76% yield. Thus we have demonstrated that the substitution of the 3-NO_2 group can be successfully effected using secondary amines along with hydrazine.

The substitution pattern for reactions with S-, O-, N-nucleophiles was determined on example of compounds **4a**, **6d**, **8c** using correlation HMBC and HSQC experiments. NMR spectra of nitropyrazoles are known[10,11] to contain carbon signals in the order C(3) ≥ C(5) > C(4). In the NMR spectra of above compounds, the C(4) carbon gives a broadened signal due to quadrupole relaxation of the nitro-group ^{14}N nuclei, and consequently is attached to NO_2 group. Furthermore, the cross peaks due to the coupling of C(3) carbon with the functional-group protons ($SC\underline{H}_2CH_3$, OCH_3, $N\underline{H}NH_2$), and the cross peaks due to coupling of C(5) with the methyl protons in the HMBC spectrum provide a confirming evidence for the nucleophilic substitution of the 3 rather than 4 position.

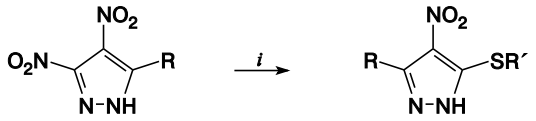
Previously, the 4-NO_2 group was believed to be entirely unreactive towards nucleophilic substitution[11,12] because of the enhanced electron density of this position in nitropyrazoles, which is supported by the widely known examples of an electrophilic attack on the 4-position. However, as demonstrated in our recent studies,[13] in the case of 1*H*-3,4,5-trinitropyrazole under conditions providing formation of trinitropyrazolate anion, interaction with S-, N-, O-nucleophiles does occur to selectively replace the nitro group in the 4-position.

Considernig the above, it seemed interesting to investigate interaction of 1*H*-3,4-dinitropyrazoles with nucleophiles. We chose as model systems the reactions of 1*H*-3(5)-methyl-4,5(3)-dinitropyrazole **3** and 1*H*-4,5(3)-dinitropyrazole **9** (see Ref. 9) with S-nucleophiles as the most reactive of heteroatomic anionic nucleophiles.

The reaction was run in water in the presence of NaOH (2 equivalents) and the appropriate thiol (1.2 equivalents), that is, under conditions of two interacting anions, at room temperature for 5 h. The following acidification with diluted H_2SO_4 afforded substitution products **10** and **11a**—**c** (Scheme 3) in high yields (72—94%).

The ^{13}C NMR spectra of compounds **10** and **11a**—**c** contain, along with the signals from carbons of R and R′ moieties, three signals of the pyrazole carbons broadened

Scheme 3



3, 9 **10, 11a—c**

R = Me (**3**); R = H (**9**); **10:** R = Me, R′ = Et; **11:** R = H, R′ = Et (**a**); Ph (**b**); *p*-MeC_6H_4 (**c**)

i. NaOH (2 equiv)/R′SH (1.2 equiv), H_2O, 25 °C, 2 h.

due to the NH proton exchange. Application of correlation HMBC, HSQC, and NOESY techniques is therefore complicated. To exclude affecting of ^{13}C NMR spectra by the NH exchange, we prepared the sodium salt of pyrazole **10** by reacting **10** with MeONa (1 equivalent) in absolute methanol followed by removing methanol *in vacuo*. The ^{13}C NMR spectra of this salt show three signals with chemical shifts at δ 128.18, 144.97, and 146.38. Of these, the only broadened one (due to quadrupole relaxation) is at δ 128.18, corresponding to C(4) carbon, so the latter is bonded to the nitro group. Additionally, in HMBC spectrum, the same atom produces the resonance featuring a cross peak with the protons of the methyl group in the 3(5)-position. These data in combination with the absence of coupling between methyl and $SC\underline{H}_2CH_3$ protons in the NOESY spectrum unambiguously indicate that, as in the case of N-substituted 3,4-dinitropyrazoles, nucleophilic substitution occurs regioselectively at the 3(5)-position, at least in reactions with S-nucleophiles in water.

Experimental

^1H and ^{13}C NMR spectra were recorded on Bruker AC-300 and Bruker DRX-500 spectrometers, respectively in [$^2H_6$]DMSO (unless otherwise stated) at 298 K. Chemical shifts for ^1H and ^{13}C are referred to Me_4Si. IR spectra were measured on a Specord M-80 spectrometer from KBr pellets. Mass spectra were recorded using a Finnigan MAT INCOS 50 instrument (direct insertion probe, EI, electron energy 70 eV). TLC (Silufol UV-254) was used to control reaction evolution and product purity. Elemental analysis was performed with a Perkin—Elmer Series II 2400 analyzer.

1-Methoxymethyl-5-methyl-3,4-dinitro-1*H*-pyrazole (2). To a solution of 5-methyl-3,4-dinitropyrazole (**3**) (5.0 g, 0.030 mol) in acetonitrile (200 mL) was added K_2CO_3 (4.5 g, 0.033 mol) and methoxymethyl chloride (2.38 g, 0.030 mol). The mixture was stirred for 1 h, poured into water (500 mL) and extracted with ethyl acetate (2×70 mL). The solvent was removed *in vacuo* to yield the product (5.4 g, 85%). M.p. 62—63 °C (CCl_4). Found (%): C, 33.15; H, 3.89; N, 26.12. $C_6H_8N_4O_5$. Calculated (%): C, 33.34; H, 3.73; N, 25.92. ^1H NMR, δ: 5.61 (s, 2 H, CH_2); 3.33 (s, 3 H, OCH_3); 2.66 (s, 3 H, Me_{Pz}). ^{13}C NMR, δ: 147.79 (C(3)); 143.95 (C(5)); 124.63 (C(4)); 81.38 (OCH_3); 56.73 (CH_2); 10.62 (CCH_3). IR, ν/cm^{-1}: 1556, 1512, 1488, 1368, 1336 (NO_2). MS, *m/z* (I_{rel} (%)): 216 $[M]^+$.

Interaction of 1-R-3,4-dinitropyrazoles with S-nucleophiles (general procedure). A mixture of 1,5-dimethyl-3,4-dinitropyrazole (**1**) or 1-methoxymethyl-5-methyl-3,4-dinitropyrazole (**2**) (2.7 mmol), the appropriate thiol (2.9 mmol), and K_2CO_3 (3 mmol) in acetonitrile (15 mL) was stirred vigorously for 7 h in the case of **1** and for 3 h in the case of **2** at 20—25 °C, then poured into water (70 mL). The precipitate that formed was filtered off, washed with water, dried *in vacuo* over P_2O_5, and crystallized from CCl_4.

1,5-Dimethyl-3-(ethylthio)-4-nitro-1*H*-pyrazole (4a). Yield 78%, m.p. 124—125 °C. Found (%): C, 42.11; H, 5.42; N, 21.04. $C_7H_{11}N_3O_2S$. Calculated (%): C, 41.78; H, 5.51; N, 20.88. ^1H NMR, δ: 3.70 (s, 3 H, CH_3); 3.16 (q, 2 H, $C\underline{H}_2CH_3$, J = 7.1 Hz); 2.61 (s, 3 H, CH_3); 1.44 (t, 3 H, $CH_2C\underline{H}_3$, J = 7.1 Hz). ^{13}C NMR, δ: 144.94 (C(3)); 142.03 (C(5)); 133.09 (C(4)); 37.20; 24.09; 14.05; 11.21. IR, ν/cm^{-1}: 1552, 1472, 1388, 1336 (NO_2). MS, *m/z* (I_{rel} (%)): 201 $[M]^+$.

Ethyl[(1,5-dimethyl-4-nitro-1*H*-pyrazol-3-yl)thio]acetate (4b). Yield 86%, m.p. 110—112 °C. Found (%): C, 41.80; H, 4.91; N, 16.47. $C_9H_{13}N_3O_4S$. Calculated (%): C, 41.69; H, 5.05; N, 16.21. ^1H NMR, δ: 4.16 (q, 2 H, J = 7.2 Hz); 3.94 (s, 2 H); 3.73 (s, 3 H); 2.61 (s, 3 H); 1.23 (t, 3 H, J = 7.1 Hz). IR, ν/cm^{-1}: 1710 (CO); 1576, 1560, 1384, 1320 (NO_2). MS, *m/z* (I_{rel} (%)): 259 $[M]^+$.

3-[(4-Chlorobenzyl)thio)]-1,5-dimethyl-4-nitro-1*H*-pyrazole (4c). Yield 86%, m.p. 88—89 °C. Found (%): C, 48.59; H, 3.99; N, 14.25. $C_{12}H_{12}ClN_3O_2S$. Calculated (%): C, 48.40; H, 4.06; N, 14.11. ^1H NMR, δ: 7.50 (d, 2 H, J = 8.0 Hz); 7.36 (d, 2 H, J = 8.0 Hz); 4.30 (s, 2 H); 3.84 (s, 3 H); 2.59 (s, 3 H). ^{13}C NMR, δ: 144.30 (C(3)); 142.22 (C(5)); 136.55; 133.22 (C(4)); 131.75; 130.95 (CH); 128.24 (CH); 37.31; 33.05; 11.18. IR, ν/cm^{-1}: 1548, 1488, 1476, 1396, 1336 (NO_2).

1,5-Dimethyl-3-[(4-methylphenyl)thio)]-4-nitro-1*H*-pyrazole (4d). Yield 76%, m.p. 161—162 °C. Found (%): C, 54.95; H, 5.11; N, 16.23. $C_{12}H_{13}N_3O_2S$. Calculated (%): C, 54.74; H, 4.98; N, 15.96. ^1H NMR, δ: 7.47 (d, 2 H, J = 8.1 Hz); 7.22 (d, 2 H, J = 8.1 Hz); 3.65 (s, 3 H); 2.60 (s, 3 H); 2.35 (s, 3 H). ^{13}C NMR, δ: 144.11 (C(3)); 142.17 (C(5)); 138.81; 134.05 (CH); 133.29 (C(4)); 129.94 (CH); 125.28; 37.29; 20.76; 11.23. IR, ν/cm^{-1}: 1548, 1472, 1392, 1340 (NO_2). MS, *m/z* (I_{rel} (%)): 263 $[M]^+$.

3-[(4-Chlorophenyl)thio)]-1,5-dimethyl-4-nitro-1*H*-pyrazole (4e). Yield 65%, m.p. 147—148 °C. Found (%): C, 46.72; H, 3.67; N, 14.98. $C_{11}H_{10}ClN_3O_2S$. Calculated (%): C, 46.56; H, 3.55; N, 14.81. ^1H NMR, δ: 7.62 (d, 2 H, J = 8.9 Hz); 7.50 (d, 2 H, J = 8.8 Hz); 3.72 (s, 3 H); 2.62 (s, 3 H). ^{13}C NMR, δ: 142.89 (C(3)); 142.28 (C(5)); 135.19 (CH); 133.84; 133.40 (C(4)); 129.24 (CH); 128.21; 37.36; 11.21. IR, ν/cm^{-1}: 1552, 1476, 1376, 1340 (NO_2). MS, *m/z* (I_{rel} (%)): 283, 285 (2 : 1) $[M]^+$.

3-Ethylthio-1-methoxymethyl-5-methyl-4-nitro-1*H*-pyrazole (5a). Yield 82%, m.p. 75—76 °C. Found (%): C, 41.74; H, 5.79; N, 18.42. $C_8H_{13}N_3O_3S$. Calculated (%): C, 41.55; H, 5.67; N, 18.17. ^1H NMR, δ: 5.46 (s, 2 H); 3.31 (s, 3 H); 3.15 (q, 2 H, J = 7.9 Hz); 2.65 (s, 3 H); 1.34 (t, 3 H, J = 7.9 Hz). IR, ν/cm^{-1}: 2964; 2928; 1552, 1484, 1396, 1344 (NO_2); 1092. MS, *m/z* (I_{rel} (%)): 231 $[M]^+$.

1-Methoxymethyl-5-methyl-3-[(4-methylphenyl)thio)]-4-nitro-1*H*-pyrazole (5b). Yield 78%, m.p. 82—83 °C. Found (%): C, 53.53; H, 5.31; N, 14.54. $C_{13}H_{15}N_3O_3S$. Calculated (%): C, 53.23; H, 5.15; N, 14.32. ^1H NMR, δ: 7.49 (d, 2 H, J = 8.0 Hz);

7.23 (d, 2 H, J = 8.0 Hz); 5.34 (s, 2 H); 3.21 (s, 3 H); 2.65 (s, 3 H); 2.43 (s, 3 H). IR, ν/cm^{-1}: 2960; 1556, 1488, 1336 (NO_2); 1096. MS, m/z (I_{rel} (%)): 293 $[M]^+$.

Interaction of 1-R-3,4-dinitropyrazoles with O-nucleophiles (general procedure). A mixture of 1,5-dimethyl-3,4-dinitropyrazole (**1**) or 1-methoxymethyl-5-methyl-3,4-dinitropyrazole (**2**) (2.7 mmol), the appropriate hydroxyl-containing compound (phenol, alcohol) (2.9 mmol), and K_2CO_3 (3 mmol) in acetonitrile (15 mL) was refluxed with vigorous stirring for 15 h in the case of **1** and for 10 h in the case of **2**, then poured into water (70 mL). The formed precipitate was filtered off, washed with water, dried *in vacuo* over P_2O_5, and crystallized from CCl_4.

1,5-Dimethyl-4-nitro-3-phenoxy-1*H*-pyrazole (6a). Yield 83%, m.p. 119—120 °C. Found (%): C, 56.80; H, 4.84; N, 18.32. $C_{11}H_{11}N_3O_3$. Calculated (%): C, 56.65; H, 4.75; N, 18.02. ^{1}H NMR, δ: 7.39 (m, 2 H); 7.19 (m, 3 H); 3.72 (s, 3 H); 2.60 (s, 3 H). IR, ν/cm^{-1}: 1564, 1476, 1376 (NO_2); 1200. MS, m/z (I_{rel} (%)): 233 $[M]^+$.

3-(3,4-Dimethylphenoxy)-1,5-dimethyl-4-nitro-1*H*-pyrazole (6b). Yield 71%, m.p. 145—146 °C. Found (%): C, 59.92; H, 5.84; N, 16.23. $C_{13}H_{15}N_3O_3$. Calculated (%): C, 59.76; H, 5.79; N, 16.08. ^{1}H NMR, δ: 7.15 (m, 1 H); 6.93 (s, 1 H); 6.83 (m, 1 H); 3.71 (s, 3 H); 2.62 (s, 3 H); 2.21 (s, 6 H). IR, ν/cm^{-1}: 1560, 1480, 1396, 1340 (NO_2); 1204. MS, m/z (I_{rel} (%)): 261 $[M]^+$.

1,5-Dimethyl-4-nitro-3-(2,2,2-trifluoroethoxy)-1*H*-pyrazole (6c). Yield 70%, m.p. 64—65 °C. Found (%): C, 35.41; H, 3.29; N, 17.79. $C_7H_8F_3N_3O_3$. Calculated (%): C, 35.16; H, 3.37; N, 17.57. ^{1}H NMR, δ: 4.95 (q, 2 H, J = 8.4 Hz); 3.71 (s, 3 H); 2.60 (s, 3 H). IR, ν/cm^{-1}: 2960; 1568, 1364 (NO_2); 1268; 1204; 1160. MS, m/z (I_{rel} (%)): 239 $[M]^+$.

1-Methoxymethyl-5-methyl-4-nitro-3-phenoxy-1*H*-pyrazole (7a). Yield 57%, m.p. 71—72 °C. Found (%): C, 54.80; H, 4.89; N, 16.15. $C_{12}H_{13}N_3O_4$. Calculated (%): C, 54.75; H, 4.98; N, 15.96. ^{1}H NMR, δ: 7.42 (m, 2 H); 7.21 (m, 3 H); 5.35 (s, 2 H); 3.37 (s, 3 H); 2.65 (s, 3 H). IR, ν/cm^{-1}: 2988; 2932; 2832; 1564, 1484, 1380, 1368 (NO_2); 1204; 1180. MS, m/z (I_{rel} (%)): 263 $[M]^+$.

1-Methoxymethyl-5-methyl-4-nitro-3-(2,2,2-trifluoroethoxy)-1*H*-pyrazole (7b). Yield 50%, m.p. 54—55 °C. Found (%): C, 35.93; H, 3.80; N, 15.79. $C_8H_{10}F_3N_3O_4$. Calculated (%): C, 35.70; H, 3.74; N, 15.61. ^{1}H NMR, δ: 5.47 (s, 2 H); 4.95 (q, 2 H, J = 8.4 Hz); 3.31 (s, 3 H); 2.62 (s, 3 H). IR, ν/cm^{-1}: 2986; 2932; 1568, 1488, 1396 (NO_2); 1268; 1204; 1162. MS, m/z (I_{rel} (%)): 269 $[M]^+$.

3-Methoxy-1,5-dimethyl-4-nitro-1*H*-pyrazole (6d). A solution of NaOMe (0.194 g, 3.6 mmol) in MeOH (10 mL) was treated with a solution of pyrazole **1** (0.56 g, 3 mmol) in MeOH (5 mL) at 20—25 °C. The mixture was heated at reflux for 5 h, cooled. The precipitate that formed was filtered off and air-dried. Yield 98%, m.p. 130—131 °C. Found (%): C, 42.31; H, 5.42; N, 24.76. $C_6H_9N_3O_3$. Calculated (%): C, 42.10; H, 5.30; N, 24.55. ^{1}H NMR, δ: 3.91 (s, 3 H); 3.69 (s, 3 H); 2.54 (s, 3 H). ^{13}C NMR, δ: 155.86 (C(3)); 141.50 (C(5)); 117.96 (C(4)); 56.20; 36.55; 11.30. IR, ν/cm^{-1}: 1552, 1484, 1388, 1344 (NO_2). MS, m/z (I_{rel} (%)): 171 $[M]^+$.

Interaction of 1-R-3,4-dinitropyrazoles with N-nucleophiles (general procedure). A mixture of 1,5-dimethyl-3,4-dinitropyrazole (**1**) (1.6 mmol) and the appropriate amine (4.8 mmol) in isopropanol (15 mL) was refluxed for 7 h. The solvent was removed *in vacuo*. Compounds **8a**, **8d**, **8e** were crystallized from EtOH—H_2O (2 : 3). Products **8b,c** were chromatographed on silica eluting with $CHCl_3$—MeOH (10 : 1).

4-(1,5-Dimethyl-4-nitro-1*H*-pyrazol-3-yl)morpholine (8a). Yield 54%, m.p. 132—133 °C. Found (%): C, 48.07; H, 6.47; N, 25.10. $C_9H_{14}N_4O_3$. Calculated (%): C, 47.78; H, 6.24; N, 24.77. ^{1}H NMR ($CDCl_3$, δ): 3.89 (m, 4 H); 3.77 (s, 3 H); 3.24 (m, 4 H); 2.56 (s, 3 H). IR, ν/cm^{-1}: 1564, 1496, 1372, 1360 (NO_2). MS, m/z (I_{rel} (%)): 226 $[M]^+$.

1,5-Dimethyl-4-nitro-3-(pyrrolidin-1-yl)-1*H*-pyrazole (8b). Yield 69%, oil. Found (%): C, 51.60; H, 6.82; N, 26.96. $C_9H_{14}N_4O_2$. Calculated (%): C, 51.42; H, 6.71; N, 26.65. ^{1}H NMR, δ: 3.64 (s, 3 H); 3.31 (m, 4 H); 2.54 (s, 3 H); 1.83 (m, 4 H). IR, ν/cm^{-1}: 1552, 1376, 1360 (NO_2). MS, m/z (I_{rel} (%)): 210 $[M]^+$.

1-(1,5-Dimethyl-4-nitro-1*H*-pyrazol-3-yl)azepine (8c). Yield 76%, oil. Found (%): C, 55.58; H, 7.72; N, 23.78. $C_{11}H_{18}N_4O_2$. Calculated (%): C, 55.44; H, 7.61; N, 23.51. ^{1}H NMR, δ: 3.62 (s, 3 H); 3.30 (m, 4 H); 2.53 (s, 3 H); 1.72 (m, 8 H). IR, ν/cm^{-1}: 1564, 1484, 1380 (NO_2). MS, m/z (I_{rel} (%)): 238 $[M]^+$.

1,5-Dimethyl-3-(1-methylhydrazino)-4-nitro-1*H*-pyrazole (8d). Yield 52%, m.p. 111—112 °C. Found (%): C, 39.15; H, 6.20; N, 38.32. $C_6H_{11}N_5O_2$. Calculated (%): C, 38.91; H, 5.99; N, 37.82. ^{1}H NMR, δ: 4.52 (br.s, 2 H); 3.73 (s, 3 H); 2.92 (s, 3 H); 2.53 (s, 3 H). ^{1}H NMR ($CDCl_3$, δ): 4.25 (br.s, 2 H); 3.33 (s, 3 H); 3.05 (s, 3 H); 2.62 (s, 3 H). IR, ν/cm^{-1}: 3352; 2968; 1556, 1360 (NO_2); 1220. MS, m/z (I_{rel} (%)): 185 $[M]^+$.

1,5-Dimethyl-3-hydrazino-4-nitro-1*H*-pyrazole (8e). Yield 74%, m.p. 157—158 °C (*cf.* Ref. 6a: m.p. 152—154 °C). ^{1}H NMR, δ: 7.23 (br.s, 1 H); 4.19 (br.s, 2 H); 3.66 (s, 3 H); 2.52 (s, 3 H). ^{13}C NMR, δ: 153.74 (C(3)); 140.24 (C(5)); 118.10 (C(4)); 36.47; 11.22.

Interaction of 1*H*-3(5)-R-4,5(3)-dinitropyrazoles with S-nucleophiles (general procedure). A solution of 3(5)-methyl-4,5(3)-dinitro-1*H*-pyrazole (**3**) or 4,5(3)-dinitro-1*H*-pyrazole (**9**) (2 mmol) in H_2O (10 mL) was treated with NaOH (4 mmol) and after 5 min with the appropriate thiol (4 mmol), stirred for 3 h at 20—25 °C, and acidified with 20% H_2SO_4 to pH 2—3. The formed precipitate was filtered off, washed with water, dried *in vacuo* over P_2O_5, and crystallized from EtOH—H_2O (2 : 3).

5-Ethylthio-3-methyl-4-nitro-1*H*-pyrazole (10). Yield 78%, m.p. 107—108 °C. Found (%): C, 38.66; H, 4.92; N, 22.63. $C_6H_9N_3O_2S$. Calculated (%): C, 38.49; H, 4.85; N, 22.44. ^{1}H NMR, δ: 13.7 (br.s, 1 H); 3.04 (q, 2 H, J = 7.1 Hz); 2.56 (s, 3 H); 1.30 (t, 3 H, J = 7.1 Hz). ^{13}C NMR, δ: 145.87; 142.44; 129.13; 23.62 (CH_2); 14.10 (Me); 11.54 (Me_{Pz}). IR, ν/cm^{-1}: 3376; 1568, 1480, 1376, 1348 (NO_2). MS, m/z (I_{rel} (%)): 187 $[M]^+$.

Sodium salt of 5-ethylthio-3-methyl-4-nitro-1*H*-pyrazole. To a solution of NaOMe (0.108 g, 2 mmol) in absolute MeOH (5 mL) was added pyrazole **10** (0.374 g, 2 mmol). After stirring for 30 min at 20—25 °C, the solvent was removed *in vacuo*, washed with ether, dried *in vacuo* over P_2O_5. Yield 98%, T_{decomp} 256 °C. Found (%): Na, 38.36. $C_6H_8N_3NaO_2S$. Calculated (%): Na, 38.49. ^{1}H NMR, δ: 3.00 (q, 2 H, J = 7.2 Hz); 2.32 (s, 3 H); 1.25 (t, 3 H, J = 7.1 Hz). ^{13}C NMR, δ: 146.38; 144.97; 128.18 (C(4)); 23.38 (CH_2); 14.72 (Me); 14.59 (Me).

5-(Ethylthio)-4-nitro-1*H*-pyrazole (11a). Yield 72%, m.p. 73—74 °C. Found (%): C, 34.79; H, 4.12; N, 24.48. $C_5H_7N_3O_2S$. Calculated (%): C, 34.67; H, 4.07; N, 24.26. ^{1}H NMR, δ: 14.0 (br.s, 1 H); 8.86 (br.s, 1 H); 3.12 (q, 2 H, J = 7.1 Hz); 1.35 (t, 3 H, J = 7.1 Hz). ^{13}C NMR, δ: 144.28; 132.29; 131.89; 24.24; 14.16. IR, ν/cm^{-1}: 1560, 1472, 1376, 1340 (NO_2). MS, m/z (I_{rel} (%)): 173 $[M]^+$.

4-Nitro-5-(phenylthio)-1*H*-pyrazole (11b). Yield 90%, m.p. 218—219 °C. Found (%): C, 49.12; H, 3.30; N, 19.35. $C_9H_7N_3O_2S$. Calculated (%): C, 48.86; H, 3.19; N, 18.99. ^{1}H NMR, δ: 13.9 (br.s, 1 H); 8.85 (br.s, 1 H); 7.59 (m, 2 H); 7.45 (m, 3 H). ^{13}C NMR, δ: 143.25; 133.34; 132.23; 131.61; 129.28; 128.79. IR, ν/cm^{-1}: 1564, 1472, 1368 (NO_2). MS, m/z (I_{rel} (%)): 221 $[M]^+$.

5-[(4-Methylphenyl)thio]-4-nitro-1*H*-pyrazole (11c). Yield 94%, m.p. 175—176 °C. Found (%): C, 50.86; H, 3.99; N, 18.02. $C_{10}H_9N_3O_2S$. Calculated (%): C, 51.05; H, 3.86; N, 17.86. ^{1}H NMR, δ: 13.8 (br.s, 1 H); 8.90 (br.s, 1 H); 7.49 (d, 2 H, J = 8.1 Hz); 7.21 (d, 2 H, J = 8.1 Hz); 2.33 (s, 3 H). IR, ν/cm^{-1}: 1564, 1476, 1368 (NO_2). MS, m/z (I_{rel} (%)): 235 $[M]^+$.

References

1. I. L. Dalinger, I. A. Vatsadze, T. K. Shkineva, G. P. Popova, B. I. Ugrak, S. A. Shevelev, *Izv. Akad. Nauk, Ser. Khim.*, 2010, 1589 [*Russ. Chem. Bull., Int. Ed.*, 2010, 1631].
2. A. A. Zaitsev, T. I. Cherkasova, I. L. Dalinger, V. V. Kachala, Yu. A. Strelenko, I. V. Fedyanin, V. N. Solkan, T. K. Shkineva, G. P. Popova, S. A. Shevelev, *Izv. Akad. Nauk, Ser. Khim.*, 2007, 2004 [*Russ. Chem. Bull., Int. Ed.*, 2007, **56**, 2074].
3. A. A. Zaitsev, I. O. Kortusov, I. L. Dalinger, V. V. Kachala, G. P. Popova, S. A. Shevelev, *Izv. Akad. Nauk, Ser. Khim.*, 2009, 2054 [*Russ. Chem. Bull., Int. Ed.*, 2009, **58**, 2118].
4. (a) A. A. Zaitsev, I. L. Dalinger, A. M. Starosotnikov, V. V. Kachala, Yu. A. Strelenko, T. K. Shkineva, S. A. Shevelev, *Zh. Organ. Khimii*, 2005, **41**, 1538 [*Russ. J. Org. Chem.* (*Engl. Transl.*), 2005, **41**, 1507]; (b) A. A. Zaitsev, I. A. Vatsadze, I. L. Dalinger, V. V. Kachala, Yu. V. Nelyubina, S. A. Shevelev, *Izv. Akad. Nauk, Ser. Khim.*, 2009, 2045 [*Russ. Chem. Bull., Int. Ed.*, 2009, **58**, 2109]; (c) A. A. Zaitsev, D. V. Zaiko, I. L. Dalinger, V. V. Kachala, T. K. Shkineva, S. A. Shevelev, *Izv. Akad. Nauk, Ser. Khim.*, 2009, 2058 [*Russ. Chem. Bull., Int. Ed.*, 2009, **58**, 2122].
5. I. L. Dalinger, A. A. Zaitsev, T. K. Shkineva, S. A. Shevelev, *Izv. Akad. Nauk, Ser. Khim.*, 2004, 553 [*Russ. Chem. Bull., Int. Ed.*, 2004, **53**, 580].
6. (a) L. I. Baryshnenkova, V. P. Perevalov, V. A. Polyakov, *Khimiya Geterotsikl. Soedinenii*, 1997, 1272 [*Chem. Heterocycl. Compd.* (*Engl. Transl.*), 1997, **33**, 1113]; (b) WO 2006/070198 A1 (2006); *Chem. Abstr.*, 2006, **145**, 124562.
7. V. P. Perevalov, M. A. Andreeva, L. I. Baryshnenkova, Yu. A. Manaev, G. S. Yamburg, B. I. Stepanov, V. A. Dubrovskaya, *Khimiya Geterotsikl. Soedinenii*, 1983, 1676 [*Chem. Heterocycl. Compd.* (*Engl. Transl.*), 1983, **19**, 1326].
8. M. A. Andreeva, Yu. A. Manaev, R. Ya. Mushii, V. P. Perevalov, V. I. Seraya, B. I. Stepanov, *Zh. Obshch. Khimii*, 1980, **50**, 2106 [*J. Gen. Chem. USSR* (*Engl. Transl.*), 1980, **50**].
9. J. W. A. M. Janssen, H. J. Koeners, C. G. Kruse, C. L. Habraken, *J. Org. Chem.*, 1973, **38**, 1777.
10. L. Larina, V. Lopyrev, *Nitroazoles. Synthesis, Structure and Applications*, Springer, LLC, 2009, 196.
11. A. A. Zaitsev, I. L. Dalinger, S. A. Shevelev, *Успехи химии*, 2009, **78**, 643 [*Russ. Chem. Rev., Int. Ed.*, 2009, **78**].
12. J. H. Boyer, *Nitroazoles: The C-Nitro Derivatives of Five-membered N- and N,O-Heterocycles, in Organic Nitro Chemistry Series*, Vol. **1**, VCH, Essen, 1986, 368 pp.
13. I. L. Dalinger, I. A. Vatsadze, T. K. Shkineva, G. P. Popova, S. A. Shevelev, *Mendeleev Commun.*, 2010, **20**, 253.

Received June 9, 2010;
in revised form July 12, 2010