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Cine-Substitution of Nitro Group in 1-Aryl-2-methyl-4-nitroimidazoles by Thiols; X-ray Diffraction Proof for the Product Structure

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1-Aryl-2-methyl-4-nitroimidazoles react with 2-amino- or with 2-hydroxyethanethiols to give products of *cine*-substitution of the nitro group. 5-(2′-Hydroxyethylthio)-2-methyl-1-phenylimidazole has been isolated as a free base, other products in the form of dipicrates. A structure of 5-(2′-aminoethylthio)-2-methyl-1-phenylimidazole dipicrate was proved by X-ray diffraction.

Key words: 1-aryl-4-nitroimidazoles, thiols, *cine*-substitution, X-ray

1-Alkyl- and 1-arylnitroimidazoles reacting with some nucleophiles afford products of the vicarious or oxidative substitution of hydrogen atom at the imidazole ring [1]. Sometimes the substitution reaction is accompanied by reduction of the nitro group [2] or by the imidazole ring opening followed by its transformation [3]. Much more seldom the *ipso* or *cine*-replacement of the nitro group is observed. For several years nitroimidazoles have been intensively investigated as radiosensitizers of hypoxic tumor cells and as veterinary drugs [4]. It is well known that nitro compounds may react with water-soluble thiols present in living cells [5]. Therefore, reactions of nitroimidazoles with thiols are of wide interest.

The *cine*-substitution of the nitro group in the position 4 of the imidazole ring was reported till now only once. 1-(2′-Hydroxyethyl)-2-methyl-4-nitroimidazole subjected to an attack of 2-aminoethanol under drastic alkaline conditions gave 5-(2′-hydroxyethyl)-1-hydroxyethyl-2-methylimidazole in a moderate yield [6]. In contrast to that 1,4-dinitroimidazoles undergo *cine*-substitution with certain *O*-, *N*- and *C*-centered nucleophiles under very mild conditions; a hydrogen atom replacing only the nitro group attached to the ring nitrogen atom; the nitro group in position 4 was always present in the product [7].

This work presents some results of *cine*-substitution of the nitro group in 1-aryl-2-methyl-4-nitroimidazoles.

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RESULTS AND DISCUSSION

Several years ago Goldman and Wuest [6] showed that nucleophilic *cine*-substitution of the nitro group in 1,2-dialkylnitroimidazoles is possible provided a thiol is used as a nucleophile. They also showed that the reaction of 5-nitroimidazole derivatives requires much milder conditions that the one for the isomeric 4-nitro compounds. *Cine*-substitution of the nitro group in the 5-nitroimidazoles was accompanied by its *ipso*-replacement. The latter reaction was not observed in 4-nitroisomers. In contrast to the above results Girard [8] reported only *ipso*-substitution of the nitro group in 1-alkyl-5-nitroimidazoles reacting with cysteine.

We have tried to perform reactions of 2-amino- and 2-hydroxyethanethiols with 1-aryl-4-nitroimidazoles, 1-aryl-2-methyl-4-nitroimidazoles and 1-aryl-5-methyl-4-nitroimidazoles. For a comparison, the reaction of 1,2-dimethyl-4-nitroimidazole with 2-hydroxyethanethiol was also carried out. Only 1-aryl-2-methyl-4-nitroimidazoles and 1,2-dimethyl-4-nitroimidazole afforded products of the nitro group substitution; the remaining starting azoles underwent partial decomposition only. The results of the reaction of 2-hydroxyethanethiol or 2-aminoethanethiol with 1-substituted 2-methyl-4-nitroimidazoles (Scheme 1) performed under nitrogen are collected in Table 1. Some of the products were separated as free bases (**2 a–b**), other (**3 a–e**) in the form of dipicrates. Surprisingly, also a pyridyl derivative **3e** formed a dipicrate instead of the expected tripicrate. The products were characterized by elementary analysis and by spectroscopy. Unfortunately, it is not easy to distinguish definitely between 4- and 5-substituted imidazoles by spectroscopic measurements, particularly when the position 2 is substituted [9]; spectra of both isomers are very similar. To prove that the isolated compounds were indeed the desired products of *cine*-substitution, and not of *ipso*-substitution, of the nitro group namely 1-aryl-5-(2′-hydroxyethylthio)-2-methylimidazoles or 1-aryl-5-(2′-aminoethylthio)-2-methylimidazoles respectively, X-ray diffraction analysis of at least one product was necessary. The analysis led us to the conclusion that *cine*-substitution of the nitro group really takes place in reaction of 1-aryl-2-methyl-4-nitroimidazoles with thiols under the conditions used in this work.

Scheme 1

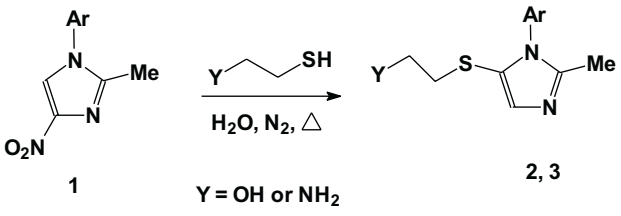


Table 1. Yields of the products from 1-aryl-2-methyl-4-nitroimidazoles reaction with thiols.

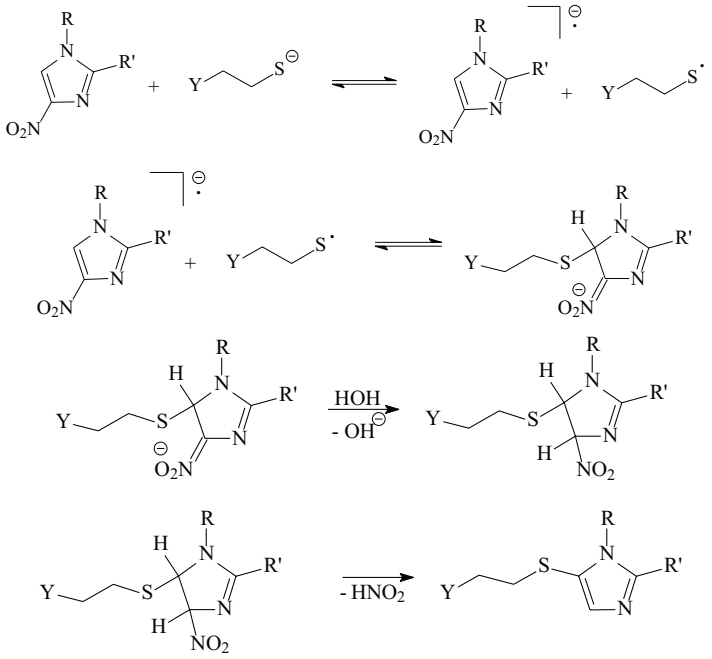
No	Ar (R)	Y	yield [%]
2a	C_6H_5	OH	60
2b	(CH_3)	OH	27
3a	C_6H_5	NH_2	37*
3b	4-MeC_6H_4	NH_2	30*
3c	4-$MeOC_6H_4$	NH_2	45*
3d	4-ClC_6H_4	NH_2	61*
3e	3-pyridyl	NH_2	32*

*a product isolated as dipicrate.

The reaction requires anaerobic conditions; therefore, a mechanism of the *cine*-substitution probably involves SET (Scheme 2) and is similar to that one proposed by Goldman and Wuest [6]. We think, that rather low reduction potential of 4-nitroimidazoles ($E_{1/2} = < -0.5$ V) in comparison with that of 5-nitroisomers ($E_{1/2} > -4.2$ V) [10], is the main reason for necessity of rather drastic conditions of the reaction.

In the first step of the reaction a one-electron transfer from a nucleophile (thiol anion) to a nitroimidazole molecule occurs. The forming *S*-centered thiol radical and nitroimidazole radical-anion recombine in the second step. The third step involves a transfer of the proton from water molecule to an anionic adduct being a product of the recombination. Elimination of a nitrous acid molecule from the protonated adduct leads to the formation of a *cine*-substitution product in the final step.

Scheme 2



To prove our finding concerning the position in the imidazole ring being attacked by thiol anions, X-ray diffraction analysis of 5-(2′-aminoethylthio)-2-methyl-1-phenyl dipicrate (**3a**) was performed. Compound **3a** is bi-protonated on the N3 ring nitrogen atom and on the N2 nitrogen atom of the amino group (Fig. 1 and 2).

Hydrogen atoms H11 and H15 form double hydrogen bonds with the oxygen atoms of picrate anion. An arm of the bond being directed towards the oxygen atom connected directly with the benzene ring is positively stronger (Table 2 and Fig. 3). Second weaker arm of the split hydrogen bond, being directed towards the oxygen atom in the nitro groups, causes their twist in respect to the benzene ring by an angle of 21.3(4)° (bond H11...O2) and on 26.7(2)° (bond H15...O2A). For a comparison the remaining nitro groups are twisted definitely less: 5.9(4)° and 6.4(4)° or 7.5(5)° and 12.1(5)°.

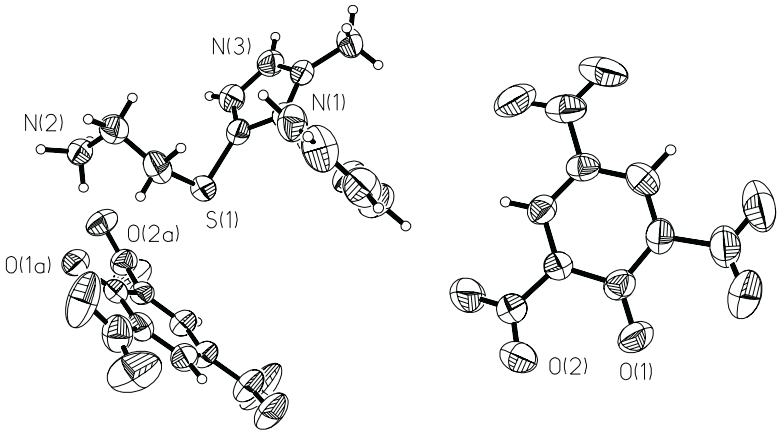


Figure 1. Displacement ellipsoid representation (at the 50% probability level) of 5-(2′-aminoethylthio)-2-methyl-1-phenylimidazole dipicrate (**3a**) [16].

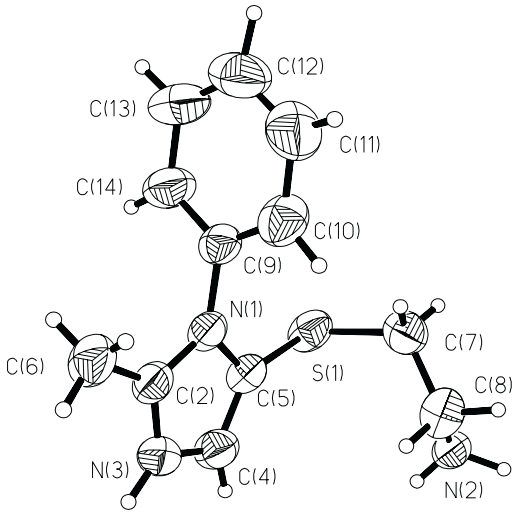


Figure 2. Displacement ellipsoid representation (at the 50% probability level) of imidazole dication of **3a** [16].

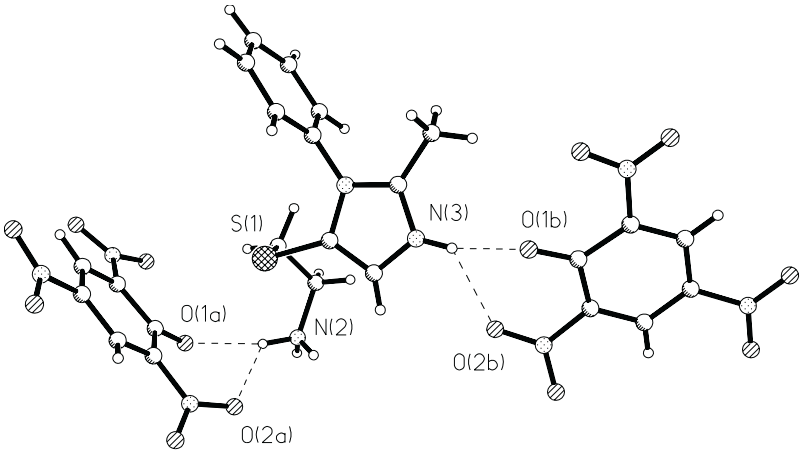


Figure 3. Intermolecular hydrogen bonds in compound **3a** [16].

Table 2. Specified hydrogen bonds (with e. s. d.'s except fixed and riding H).

D–H (A)	H...A (Å)	D...A (Å)	<(DHA) (deg)	
0.89(3)	1.80(4)	2.681(3)	166(3)	N3–H11...O1[a]
0.89(3)	2.52(3)	3.009(4)	115(3)	N3–H11...O2[a]
0.92(4)	1.95(4)	2.819(3)	157(3)	N2–H15...O1A[b]
0.92(4)	2.34(3)	2.969(4)	125(3)	N2–H15...O2A[b]

Symmetry code: a) 1 + x, –1 + y, z; b) x, y, z.

The phenyl substituent at N1 and the imidazole ring are twisted to each other on 88.51(11)°. Both rings are planar. A bond connecting the methyl group with C2 lies in the same plane as the imidazole ring.

EXPERIMENTAL

Melting points were not corrected. NMR spectra were recorded in DMSO-d_6 with TMS as the internal standard by means of Varian XL-300 spectrometer. Mass spectra were taken using Shimadzu GCMS QP-2000 spectrometer. 1,2-Dimethyl-4-nitroimidazole was prepared by alkylation of 2-methyl-4(5)-nitroimidazole sodium salt with dimethyl sulfate [11]. 1-Aryl-2-methyl-4-nitroimidazoles were obtained by treating 1,4-dinitro-2-methylimidazole with anilines [12]. Other starting materials were commercially purchased.

Synthesis of 1-substituted 5-(2′-hydroxyethylthio)-2-methylimidazoles: A nitroimidazole (4 mmole), 2-mercaptoethanol (5 ml) and water (5 ml) were heated for 160 hrs under reflux in the atmosphere of nitrogen. The reaction mixture was poured into aqueous sodium hydroxide solution (50 ml, 20%). The forming emulsion was extracted three times with chloroform and the combined extracts were dried over anhydrous magnesium sulfate. Evaporation of the solvent under reduced pressure at 60°C afforded the oily residue, which was rinsed then with dry diethyl ether to give a product solidifying after a few hours. The solid product was chromatographed on preparative TLC plates (Merck, 20 × 20 cm, silica gel 60 F_{254}, 2 mm) using methanol-chloroform (1:20) mixture as an eluent. The collected main fractions were crystallized from dry diethyl ether.

5-(2′-Hydroxyethylthio)-2-methyl-1-phenylimidazole 2a, yield 60%; m. p. (diethyl ether) 115–116°C; ^{1}H NMR δ (ppm, DMSO-d_6): 7.64–7.30 (m, 5H, Ar), 7.11 (s, 1H, C4-H), 4.77 (br. s, 1H, OH), 3.36 (t, J = 6 Hz, 2H, CH_2), 2.39 (t, J = 6 Hz, 2H, CH_2), 2.13 (s, 3H, CH_3); MS 70 eV (m/z, %) M^+: 234 (96.3), 190 (81.1), 157 (25.3), 148 (97.0), 116 (34.8), 77 (100.0), 56 (81.6); E. A. (%) : $C_{12}H_{14}N_2OS$ requires: C 61.51, H 6.02, N 11.96; found: C 50.75, H 6.09, N 11.53.

1,2-Dimethyl-5-(2-hydroxyethylthio)imidazole 2b, yield 27%; m. p. (diethyl ether) 81–83°C; ^{1}H NMR δ (ppm, DMSO-d_6): 6.95 (s, 1H, C4-H), 4.83 (t, J = 5 Hz, 1H, OH), 3.44 (q, J = 5 Hz, 2H, CH_2), 3.34 (s, 3H, N-CH_3), 2.61 (t, J = 5 Hz, 2H, CH_2), 2.30 (s, 3H, CH_3); MS 70 eV (m/e, %) M^+: 172 (69.3), 128 (100.0), 127 (80.5), 87 (43.9), 57 (76.3), 47 (51.2); E. A. (%): $C_7H_{12}N_2OS$ requires: C 48.81, H 7.02, N 16.26; found: C 49.25, H 7.18, N 16.23.

Synthesis of 5-(2′-aminoethylthio)-1-aryl-2-methylimidazole dipicrates: A nitroimidazole (1 g), 2-aminoethanethiol hydrochloride (2 g), water (20 ml) and dioxane (10 ml) were refluxed under nitrogen for 160 hrs. The solvents were removed then at *ca*. 80°C under reduced pressure and the residue was treated with the saturated aqueous solution of picric acid to give yellow crystals. The crystals were rinsed with water, dried and recrystallized from methanol.

5-(2′-Aminoethylthio)-2-methyl-1-phenylimidazole dipicrate (3a), yield 37%; m. p. (methanol) 17°C dec.; ^{1}H NMR δ (ppm, DMSO-d_6): 8.60 (s, 4H, Ar_{pikr}-H), 8.04 (s, 1H, Ar_{im}-H), 7.78 (br s, 3H, NH_3), 7.71–7.56 (m, 5H, Ar_{Ph}-H), 2.89 (q, J = 6.0 Hz, 2H, CH_2), 2.67 (t, J = 7.5 Hz, 2H, CH_2), 2.40 (s, 3H, CH_3); E. A. (%): $C_{24}H_{21}N_9O_{14}S$ requires: C 41.68, H 3.06, N 18.23; found C 41.89, H 3.09, N 18.17.

5-(2′-Aminoethylthio)-2-methyl-1-(4′′-methylphenyl)imidazole dipicrate (3b), yield 30%; m. p. (methanol) 177^{0}C dec.; ^{1}H NMR δ (ppm, DMSO-d_6): 8.60 (s, 4H, Ar_{pikr}-H), 8.04 (s, 1H, Ar_{im}-H), 7.80 (br s, 3H, NH_3), 7.47–7.46 (m, 4H, Ar_{Ph}-H), 2.91 (q, J = 6 Hz, 2H, CH_2), 2.68 (t, 2H, J = 7.5 Hz, CH_2), 2.44 (s, 3H, CH_{3im}), 2.40 (s, 3H, CH_{3Ph}); E. A. (%): $C_{25}H_{23}N_9O_{14}S$ requires: C 42.56, H 3.29, N 17.87; found: C 42.45, H 3.31, N 17.78.

5-(2′-Aminoethylthio)-1-(4′′-methoxyphenyl)-2-methylimidazole dipicrate (3c), yield 45%; m. p. (methanol) 177°C dec.; NMR δ (ppm, DMSO-d_6): 8.60 (s, 4H, Ar_{pikr}-H,), 7.97 (s, 1H, Ar_{im}-H), 7.75 (br s, 3H, NH_3), 7.48 (d, J = 8.7 Hz, 2H, Ar_{Ph}-H), 7.20 (d, 2H, J = 8.7 Hz, Ar_{Ph}-H), 2.88 (q, J = 6.9 Hz, 2H, CH_2), 2.66 (t, J = 6.9 Hz, 2H, CH_2), 2.50 (s, 3H, OCH_3), 2.37 (s, 3H, CH_3); E. A. (%): $C_{25}H_{23}N_9O_{15}S$ requires: C 41.61, H 3.21, N 17.47; found: C 41.75, H 3.12, N 17.54.

5-(2′-Aminoethylthio)-1-(3-chlorophenyl)-2-methylimidazole dipicrate (3d), yield 61%; m. p. (methanol) 177°C dec.; NMR δ (ppm, DMSO-d_6): 8.60 (s, 4H, Ar_{pikr}-H), 7.79 (s, 1H, Ar_{im}-H), 7.77–7.56 (m, 7 H, Ar_{Ph}-H + NH_3), 2.89 (q, J = 6.6 Hz, 2H, CH_2), 2.66 (t, J = 7.2 Hz), 2H, CH_2), 2.40 (s, 3H, CH_3); E. A. (%): $C_{24}H_{20}N_9O_{14}SCl$ requires: C 39.71, H 2.78, N 17.36; found: C 39.62, H 2.80, N 17.19.

5-(2′-Aminoethylthio)-2-methyl-1-(3-pyridyl)imidazole dipicrate (3e), yield 32%; m. p. (methanol) 177°C dec.; NMR δ (ppm, DMSO-d_6): 8.88 (dd, J = 1.5 Hz, J = 4.8 Hz, 1H, $C5_{pir}$-H), 8.80 (d, J = 2.4 Hz, 1H, $C2_{pir}$-H), 8.60 (s, 4H, Ar_{pikr}-H), 8.09 (ddd, J = 9 Hz, J = 2.4 Hz, J = 1.5 Hz, 1H, $C4_{pir}$-H), 8.03 (s, 1H, Ar_{im}-H), 7.76 (dd, J = 9 Hz, J = 4.8 Hz, 4H, $C5_{pir}$-H + NH_3), 2.89 (q, J = 6 Hz, 2H, CH_2), 2.64 (t, J = 7.2 Hz, 2H, CH_2), 2.43 (s, 3H, CH_3); E. A. (%): $C_{23}H_{20}N_{10}O_{14}S$ requires: C 39.89, H 2.91, N 20.23; found: C 40.01, H 2.99, N 20.12.

Signals of the proton at the nitrogen atom of imidazole ring in the dipicrates were usually not seen in the ^{1}H NMR spectra. It was due to the presence of some amount of water in DMSO-d_6 causing fast exchange of acidic protons with water molecules. The missing signals should appear at *ca*. 3.5 ppm.

X-ray diffraction analysis: X-ray diffraction data were collected on a KUMA KM-4 κ-geometry diffractometer, using graphite-filtered CuK_α (λ = 1.54178 Å) radiation. The unit cell dimensions were calculated from the least-squares fit of 28 reflection. Relevant crystallographic data, together with data collection and structure refinement details, are listed in Table 2. The ω – 2Θ scan method was used. Intensity data were corrected for Lorentz and polarization effect. The determination of the unit cell parameters and the data reduction were performed with KUMA KM4 software program system [13]. The structure was solved by direct method, using SHELXS97 program [14]. Full matrix least-squares refinement was done with the SHELXL97 program [15]. Scattering factors incorporated in SHELXL97 were used [15]. The function $\Sigma w(|F_o|^2 - |F_c|^2)^2$ was minimized, with $w^{-1} = [\sigma^2(F_o)^2 + (0.0941\ P)^2 + 0.72\ P]$, where $P = [(Max(F_o^2, 0) + 2F_c^2)/3]$. Empirical extinction correction were also applied according to the formula $F_c^{'} = kF_c[1 + 0.001 \times F_c^2\lambda^3/\sin 2\Theta]^{-1/4}$, the x value converged at 0.0006(4). At the final stages of refinement four reflection were excluded from the reflection files due to their large $|F_o|^2 - |F_c|^2$ differences. The

non-hydrogen atoms were refined anisotropically, all hydrogen atoms were found in subsequent difference Fourier maps and isotropically refined. Final atomic parameters for the non-hydrogen atoms are listed in Table 4. For the preparation of structural drawings a stereochemical workstation was used [16].

Table 3. Crystal data and structure refinement for compound **3a**.

Empirical formula $C_{24}H_{21}N_9O_{14}S$
Formula weight 691.56 g/mol
Temperature 293(2) K
Wavelength 1.54178 Å
Crystal system Triclinic
Space group $P\bar{1}$

Unit cell dimensions:
a = 7.887(2) Å
b = 12.400(2) Å
c = 15.684(3) Å
α = 80.84(3)°
β = 79.55(3)°
χ = 84.71(3)°
Volume 1486.0(5) Å^3
Z = 2
Density (calculated), 1.572 g/cm^3
Absorption coefficient, 1.756 mm^{-1}
F(000) = 724
Crystal size 0.4 mm × 0.2 mm × 0.2 mm mm
Theta range for data collection, 2.90° to 56.90°.
h k l range –8 <= h <= 8; –13 <= k <= 13; 0 <= l <= 17
Reflections
collected 4143
unique (R_{int}) 3966 (0.01)
observed ($I > 2\sigma$ (I)), 3450
Absorption correction: none
Goodness of fit 1.063
R(F) = 0.0513
wR(F) = 0.1448
Δ_{max} = 0.56 Å^3
Δ_{min} = –0.35 Å^3
three standard reflections
monitored every 100 reflections
intensity decay: 0.6%

Table 4. Atomic coordinates and equivalent isotropic displacement parameters U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U_{eq}
S(1)	0.3310(1)	0.2676(1)	0.3858(1)	0.057(1)
O(1A)	0.372(3)	0.1104(2)	0.5625(1)	0.059(1)
N(1)	0.5154(3)	0.3523(2)	0.2256(1)	0.045(1)
O(2A)	0.3694(3)	0.0611(2)	0.5809(1)	0.064(1)
N(2)	0.2432(4)	0.0147(2)	0.4241(2)	0.051(1)
C(15A)	0.0624(3)	0.2013(2)	0.5819(2)	0.046(1)
N(4A)	0.3482(3)	0.1344(2)	0.6268(2)	0.053(1)
N(3)	0.7506(3)	0.2499(2)	0.2124(2)	0.055(1)
C(20A)	–0.0561(3)	0.2969(2)	0.5749(2)	0.050(1)
C(16A)	0.2141(3)	0.2214(2)	0.6151(2)	0.043(1)
C(17A)	0.2426(4)	0.3194(2)	0.6377(2)	0.049(1)
C(2)	0.6670(4)	0.3367(2)	0.1741(2)	0.049(1)
C(18A)	0.1225(4)	0.4063(2)	0.6269(2)	0.051(1)

Table 4 (continuation)

O(3A)	0.4398(4)	0.1379(2)	0.6810(2)	0.085(1)
C(9)	0.3869(4)	0.4389(2)	0.2053(2)	0.048(1)
C(19A)	–0.0258(4)	0.3959(2)	0.5959(2)	0.053(1)
C(5)	0.5034(4)	0.2720(2)	0.2995(2)	0.047(1)
C(4)	0.6525(4)	0.2090(3)	0.2896(2)	0.055(1)
C(7)	0.1770(4)	0.1985(3)	0.3451(2)	0.060(1)
O(5A)	0.0524(4)	0.5890(2)	0.6323(2)	0.089(1)
N(5A)	0.1517(4)	0.5113(2)	0.6491(2)	0.070(1)
C(10)	0.2646(5)	0.4202(3)	0.1587(2)	0.067(1)
C(14)	0.3950(5)	0.5391(3)	0.2306(2)	0.067(1)
N(6A)	–0.2201(4)	0.2927(2)	0.5455(2)	0.068(1)
O(7A)	–0.2434(4)	0.2152(2)	0.5106(3)	0.109(1)
O(4A)	0.2728(5)	0.5172(2)	0.6854(3)	0.124(1)
C(8)	0.2236(5)	0.0804(3)	0.3390(2)	0.062(1)
O(6A)	–0.3263(4)	0.3687(3)	0.5529(3)	0.121(1)
C(12)	0.1519(6)	0.6058(4)	0.1642(3)	0.085(1)
C(6)	0.7285(6)	0.4035(3)	0.0897(3)	0.069(1)
C(13)	0.2750(6)	0.6227(3)	0.2086(3)	0.082(1)
C(11)	0.1442(6)	0.5070(4)	0.1391(3)	0.086(1)
N(4)	0.0244(4)	0.9652(2)	0.1791(2)	0.063(1)
C(16)	0.1237(4)	1.0073(2)	0.0951(2)	0.048(1)
O(1)	0.0521(3)	1.1936(2)	0.1150(2)	0.089(1)
O(2)	–0.0948(4)	1.0187(2)	0.2139(2)	0.084(1)
C(18)	0.3142(4)	0.9668(2)	–0.0320(2)	0.052(1)
N(5)	0.4235(4)	0.8875(3)	–0.0801(2)	0.069(1)
C(15)	0.1220(4)	1.1247(2)	0.674(2)	0.054(1)
C(17)	0.2206(4)	0.9327(3)	0.478(2)	0.050(1)
O(4)	0.4276(4)	0.7919(2)	–0.0457(2)	0.097(1)
O(5)	0.5081(4)	0.9201(3)	–0.1505(2)	0.100(1)
C(20)	0.2207(4)	1.1514(2)	–0.0188(2)	0.056(1)
C(19)	0.3134(4)	1.0765(3)	–0.0669(2)	0.058(1)
O(3)	0.0693(6)	0.8759(3)	0.2139(2)	0.151(2)
N(6)	0.2284(4)	1.2656(3)	–0.0590(2)	0.084(1)
O(7)	0.1518(6)	1.3353(3)	–0.0237(3)	0.141(2)
O(6)	0.3007(8)	1.2876(3)	–0.1314(4)	0.213(3)

Table 5. Selected bond lengths (Å) and bond angles (deg) with e. s. d.'s in parentheses.

S1–C5	1.734(3)	C2–C6	1.472(5)
S1–C7	1.807(4)	C9–C10	1.366(5)
N1–C2	1.333(4)	C9–C14	1.374(4)
N1–C5	1.398(3)	C5–C4	1.349(4)
N1–C9	1.445(4)	C7–C8	1.490(5)
N2–C8	1.475(4)	C10–C11	1.402(6)
N3–C2	1.327(4)	C14–C13	1.383(5)
N3–C4	1.363(4)	C12–C13	1.342(6)
		C12–C11	1.355(7)
C5–S1–C7	101.56(15)	C4–C5–N1	105.8(2)
C2–N1–C5	109.0(2)	C4–C5–S1	130.4(2)
C2–N1–C9	123.9(2)	N1–C5–S1	123.7(2)
C5–N1–C9	127.0(2)	C5–C4–N3	107.7(3)
C2–N3–C4	109.8(3)	C8–C7–S1	115.1(2)
N3–C2–N1	107.6(2)	C9–C10–C11	117.4(4)

Table 5 (continuation)

N3–C2–C6	126.6(3)	C9–C14–C13	118.7(4)
N1–C2–C6	125.8(3)	N2–C8–C7	113.1(3)
C10–C9–C14	121.8(3)	C13–C12–C11	120.6(4)
C10–C9–N1	119.2(3)	C12–C13–C14	120.6(4)
C14–C9–N1	118.9(3)	C12–C11–C10	120.9(4)

Table 6. Selected torsion angles (deg) with e. s. d.'s in parentheses.

C4–N3–C2–C6	–179.6(0.3)
C9–N1–C2–N3	–179.3(2)
C9–N1–C2–C6	0.2(5)
C2–N1–C9–C10	89.8(3)
C5–N1–C9–C10	–89.5(3)
C9–N1–C5–S1	–4.2(4)
C7–S1–C5–N1	83.4(2)

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REFERENCES

1. Ostrowski S., *Polish J. Chem*., **68**, 2237 (1994).
2. Suwiński J. and Świerczek K., *Khim. Geterotsykl. Soed.*, 1214 (1996).
3. Suwiński J., Pawlus W., Salwińska E. and Świerczek K., *Heterocycles*, **37**, 2237 (1994).
4. Smithen C.E. and Hardy C.R, in *Advanced Topics on Radiosensitizers of Hypoxic Cells*, NY, 1982, p.1.
5. Voogd C.E., *Mutation Research*, **86,** 243 (1981).
6. Goldman P. and Wuest J.D*., J. Am. Chem. Soc*., **103**, 6224 (1981).
7. Suwiński J. and Świerczek K., *Tetrahedron Reports*, a review (in press).
8. Girard M., Clairmont F., Maneckje A., Mousseau N., Dawson B. and Whitehouse L., *Can. J. Chem.*, **71**, 1349 (1993).
9. Boyer J.H., *Nitroimidazoles*, VCH Publishers Inc., Deerfield Beach, Florida 1986.
10. Wardman P. and Clarke E.D., *J. Chem. Soc., Faraday Trans. I*, **72**, 1377 (1976).
11. Cosar C., Crisan C., Horclois R., Jacob R.M., Robert J., Tchelitcheff S. and Vaupré R., *Arzem. Forsch*., **16**, 23 (1966).
12. Salwińska E. and Suwiński J., *Polish J. Chem*., **64**, 813 (1990).
13. KUMA (1991). *Kuma KM-4 User's Guide*. *Version 5.0*. Kuma Diffraction, Wrocław, Poland.
14. Sheldrick G.M., *Acta Cryst. A*, **46**, 467 (1990).
15. Sheldrick G.M., SHELXL97, Program for the Refinement of Crystal Structures, University of Göttingen, Germany (1997).
16. Siemens, *Stereochemical Workstation*, Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA (1989).