The authors gratefully acknowledge financial support from USPHS Grant 5RO1 GM 19643 and the excellent technical typing by Rowena Gilstrap.

References

DHANESWAR, N. N., TAVALE, S. S. & PANT, L. (1974). *Acta Cryst.* **30**, 583–587.

FERRIER, R. J. (1978). *Adv. Carbohydr. Chem. Biochem.* **35**, 31–80.

GUPTA, A., KIRFEL, A., WILL, G. & WULFF, G. (1977). *Acta Cryst.* B**33**, 637–641.

HAGEMAN, J. H. & KUEHN, G. D. (1992). *Practical Protein Chromatography*, edited by A. KENNEY & S. FOWELL, pp. 45–71. Totowa, NJ: Humana Press.

MAESTAS, R. R., PRIETO, J. R., KUEHN, G. D. & HAGEMAN, J. H. (1980). *J. Chromatogr.* **189**, 225–231.

RETTIG, S. J. & TROTTER, J. (1977). *Can. J. Chem.* **55**, 3071–3075.

SAKORE, T. D., TAVALE, S. S. & PANT, L. M. (1967). *Acta Cryst.* **22**, 720–725.

Siemens Analytical X-ray Instruments (1990). *SHELXTL-Plus*. Siemens Analytical X-ray Instruments, Inc., Germany.

SOUNDARARAJAN, S. (1984). MSc. Thesis. New Mexico State Univ., USA.

SOUNDARARAJAN, S., BADAWI, M., KOHLRUST, C. M. & J. H. HAGEMAN. (1989). *Anal. Biochem.* **178**, 125–134.

TORSSELL, K. (1957). *Ark. Kemi*, **10**, 473–482.

ZVONKOVA, Z. V. & GLUSHKOVA, V. P. (1958). *Sov. Phys. Crystallogr.* **3**, 564–568.

Acta Cryst. (1993). C**49**, 693–695

Structure of 4(5)-Nitroimidazole at 100 K

BY HENDRIK L. DE BONDT,* E. RAGIA, N. M. BLATON, O. M. PEETERS AND C. J. DE RANTER†

Laboratorium voor Analytische Chemie en Medicinale Fysicochemie, Instituut voor Farmaceutische Wetenschappen, Katholieke Universiteit Leuven, Van Evenstraat 4, *B*-3000 *Leuven, Belgium*

(*Received* 21 *January* 1992; *accepted* 23 *October* 1992)

Abstract. 4(5)-Nitroimidazole, $C_3H_3N_3O_2$, M_r = 113.08, monoclinic, $P2_1/n$, $a = 6.9559$ (4), $b = 9.9130$ (6), $c = 7.3045$ (4) Å, $\beta = 119.41$ (4)°, $V = 438.8$ (4) Å^3, $Z = 4$, $D_m(293\ \mathrm{K}) = 1.64$, $D_x = 1.7117\ \mathrm{Mg\ m^{-3}}$, $\lambda(\mathrm{Mo}\ K\alpha) = 0.71069$ Å, $\mu = 0.1367\ \mathrm{mm^{-1}}$, $F(000) = 232$, $T = 100$ K. Final $R = 0.024$ for 633 unique observed $[F \geq 4\sigma(F)]$ reflections. The molecules are planar and are stacked in planes almost parallel to the *bc* plane. These molecular layers are built up by three hydrogen bonds. 4–5-tautomerism is discussed.

Introduction. Nitroimidazoles are generally known as antiprotozoic and antibiotic drugs (Edwards, 1981). The investigation of 4(5)-nitroimidazole is part of an extensive structure–activity study which includes conformational analysis on low-temperature data as well as charge density analysis on high-resolution low-temperature data sets.

Experimental. The title compound was supplied by Aldrich–Europe (Beerse, Belgium). Colourless crystals were obtained from a standard 2:1 dimethyl sulfoxide/methanol solution and were used for density measurements by flotation in $CCl_4/CHBr_3$. A prismatic crystal, with approximate dimensions 0.25 × 0.26 × 0.2 mm, was mounted for X-ray diffraction data collection on a Stoe STADI-4 four-circle diffractometer with graphite-monochromated Mo $K\alpha$ (reflection 200) radiation. The space group, $P2_1/n$, was determined from observed symmetry and systematic absences $h0l$ $(h + l = 2n + 1)$, $0k0$ $(k = 2n + 1)$. Unit-cell dimensions were obtained by least-squares refinement of accurately determined 2θ values of 28 reflections with $20 \leq 2\theta \leq 50°$. X-ray intensities were collected in the $\omega/2\theta$ scan mode up to maximal $(\sin\theta)/\lambda = 0.65$ Å^{-1} $(2\theta_{\max} = 55°)$ and for $-8 \leq h \leq 7$, $-11 \leq k \leq 11$, $0 \leq l \leq 8$. For all reflections, peak profiles of 96 steps were stored. Intensities of three standard reflections ($\bar{2}22$, 301 and $\bar{1}03$), monitored every hour of radiation, showed an average decrease in intensity of 3.2% in 66 h radiation. The reflection intensities were rescaled using a cubic regression curve. A total of 1657 reflections were measured. Symmetry-related reflections were averaged to give 828 unique reflections of which 633 were considered observed with $F \geq 4\sigma(F)$. $R_{\mathrm{int,\ observed,}\ F}$ is 0.015. Data reduction with the peak profile analysis program *DREAM* (Blessing, 1987). Lorentz and polarization corrections were applied. Structure factors were calculated with scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV, Table 2.2B) and contracted hydrogen form factors from Stewart, Davidson & Simpson (1965). Anomalous-dispersion corrections were performed for all non-H atoms (Ibers &

---

* Present address: Department of Chemistry and Lawrence Berkeley Laboratory, University of California at Berkeley, CA 94720, USA.

† Author to whom correspondence should be addressed.

Hamilton, 1964). The phase problem was successfully solved by direct methods using *MULTAN*82 (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1982) which revealed the positions of all non-H atoms. Full-matrix least-squares refinements were performed on F, first isotropically and next anisotropically. All H atoms were located in a difference map and were given an isotropic temperature factor U of 1.9×10^{-2} Å^2 during the refinement of their positions. An isotropic extinction parameter, $g = 1.6\ (1) \times 10^{-6}$, defined as $F_c(\text{corrected}) = F_c(\text{uncorrected})/[1 + g\text{Lp}F_c^2(\text{uncorrected})]$ was also refined. Final $R = 0.024$, $wR = 0.031$, $w = 4F^2/[\sigma^2(F^2) + (0.02F^2)^2]$, with $S = 1.583$. Largest parameter shift/e.s.d. = 0.02. The residual electron density varies between −0.16 and 0.18 e Å^{-3}. The number of reflections per refined parameter (633/83) = 7.6. All calculations were performed on a Digital PDP-11/73 and MicroVAX 2000 microcomputer using *SDP*/*VAX* (Frenz, 1985) and *PARST* (Nardelli, 1983).

Discussion. Recently, a room-temperature investigation on this compound was published by Segalas, Poitras & Beauchamp (1992). The low-temperature results reported below should be considered as more reliable (1) because the present structural analysis suffers from smaller absorption errors ($\mu_{\text{Mo}} = 0.1367$ *versus* $\mu_{\text{Cu}} = 1.18$ mm^{-1}), (2) because errors due to thermal vibration are considerably smaller at 100 K and consequently (3) the final model fits the measurements much better ($R = 2.4$ instead of 4.8%). The main differences between these results and the almost simultaneously published room-temperature results can be seen in the more intensely vibrating nitro group. Indeed, thermal vibration shortens most of the room-temperature bond lengths (Segalas, Poitras & Beauchamp, 1992) so that they are systematically shorter than those determined at 100 K. Therefore, the low-temperature bond lengths are closer to the correct bond lengths. The stacked molecules have similar dynamic properties at both temperatures since corresponding atomic displacement parameters at 293 and 100 K correlate well, $U_{\text{eq}}(293\ \text{K}) = 2.66\ (9) \times U_{\text{eq}}(100\ \text{K})$.

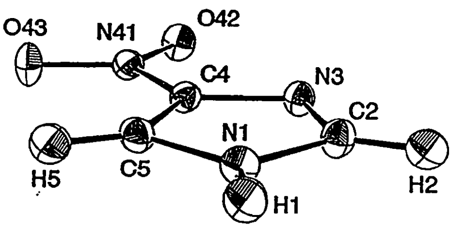

Fig. 1. An *ORTEP* (Johnson, 1976) plot of the title compound with the atomic numbering scheme. The ellipsoids are drawn at the 50% probability level.

Table 1. *Atomic coordinates and isotropic or equivalent isotropic temperature factors* (Å^2 × 10^2)

$U_{\text{eq}} = (1/3)\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j$. Fixed U_{iso} for H atoms.

	x	y	z	U
N1	0.7619 (2)	−0.0101 (1)	0.6960 (2)	1.46 (2)
C2	0.7581 (2)	0.1019 (1)	0.8011 (2)	1.57 (2)
N3	0.7666 (2)	0.2132 (1)	0.7071 (2)	1.51 (2)
C4	0.7757 (2)	0.1673 (1)	0.5350 (2)	1.37 (3)
C5	0.7724 (2)	0.0303 (1)	0.5238 (2)	1.48 (3)
N41	0.7865 (2)	0.2595 (1)	0.3902 (2)	1.52 (2)
O42	0.7881 (2)	0.3815 (1)	0.4241 (1)	2.02 (2)
O43	0.7937 (2)	0.2128 (1)	0.2368 (1)	2.17 (2)
H1	0.751 (2)	−0.098 (2)	0.735 (2)	1.9
H2	0.746 (2)	0.096 (2)	0.925 (2)	1.9
H5	0.777 (2)	−0.028 (2)	0.425 (2)	1.9

Table 2. *Bond lengths* (Å), *bond angles* (°) *and hydrogen-bond geometry* (Å, °)

N1—C2	1.357 (2)	C5—N1	1.355 (2)	N1—H1	0.93 (2)
C2—N3	1.317 (2)	C4—N4	1.428 (2)	C2—H2	0.95 (2)
N3—C4	1.367 (2)	N41—O42	1.234 (2)	C5—H5	0.94 (2)
C4—C5	1.360 (2)	N41—O43	1.236 (2)		

C2—N1—C5	107.9 (1)	C2—N3—C4	103.6 (1)
C2—N1—H1	125 (1)	N3—C4—C5	112.4 (1)
C5—N1—H1	127 (1)	N3—C4—N41	120.7 (1)
N1—C2—N3	111.9 (1)	C5—C4—N41	126.9 (1)
N1—C2—H2	122 (1)	N1—C5—C4	104.3 (2)
N3—C2—H2	126 (1)	N1—C5—H5	124.7 (9)
C4—C5—H5	131 (1)	C4—N41—O43	118.2 (1)
C4—N41—O42	118.5 (1)	O42—N41—O43	123.3 (1)

D—H···A	D—H*	D···A	H···A	D—H···A
N1—H1···N3$^{\text{i}}$	1.01	2.864 (2)	1.857 (1)	174.2 (1)
C2—H2···O43$^{\text{ii}}$	1.08	3.260 (2)	2.322 (2)	144.2 (1)
C5—H5···O42$^{\text{iii}}$	1.08	3.421 (2)	2.392 (2)	159.0 (1)

Symmetry code: (i) $-x + \frac{3}{2}$, $y - \frac{1}{2}$, $-z + \frac{3}{2}$; (ii) x, y, $z + 1$; (iii) $-x + \frac{3}{2}$, $y - \frac{1}{2}$, $-z + \frac{1}{2}$.

* H-atom positions normalized to N—H = 1.01 Å and C—H = 1.08 Å (Allen, Kennard, Watson, Brammer, Orpen & Taylor, 1987).

An *ORTEP* view (Johnson, 1976) of the title compound with the atomic numbering scheme is shown in Fig. 1. The final atomic coordinates and equivalent isotropic thermal parameters are given in Table 1*. Bond lengths and bond angles are given in Table 2.

The title compound crystallizes as its 4-nitro tautomer which could be anticipated since, in the imidazolium cation, deprotonation of the N atom closest to the nitro substituent is sterically more favourable due to steric repulsion by the nitro group. Grimison, Ridd & Smith (1960) derived a predomination factor of 400 in favour of the 4-nitro tautomer over the

---

* Lists of structure factors, anisotropic thermal parameters and least-squares-planes data have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 55736 (12 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: HH1003]

5-nitro tautomer. They determined a pK_a difference of 2.6 for the conjugated acids of 1-methyl-4-nitroimidazole and its 5-nitro isomer in aqueous solutions. The title compound with its nitro group in the 4 position still has one sterically repulsive intramolecular interaction, *i.e.* C5—C4—N41 [126.9 (1)°] is substantially larger than N3—C4—N41 [120.7 (1)°]. This steric effect can be observed in all 4-nitroimidazole structures (Cook & Bugg, 1975; Puig-Torres, Martin, Larson & Simonsen, 1984; Dupont, Dideberg & Jamoulle, 1984; Kulkarni, Grimmett, Hanton & Simpson, 1987; Glass, Blount, Butler, Perrotta & Oliveto, 1972; Kalman, van Meurs & Toth, 1980; Solans & Font-Altaba, 1981, 1982; Taira & Uchi, 1988).

The ring deformation patterns in polysubstituted benzene derivatives (Domenicano & Murray-Rust, 1979; Domenicano, Murray-Rust & Vaciago, 1983) are also valid for the title compound. The angular changes occurring at the *ipso* and *ortho* positions of the aromatic ring are controlled primarily by the inductive effects of the substituents. In particular, the σ-electron-withdrawing nitro substituent increases the *ipso* ring angle from 109.8 (1)° in unsubstituted imidazole (McMullan, Epstein, Ruble & Craven, 1979) to 112.4 (1)°. An opposite effect can often be found for the *ortho* angles 103.6 (1)° at N3 and 104.3 (2)° at C5 instead of 105.1 (1) and 106.0 (1)°, respectively, in unsubstituted imidazole.

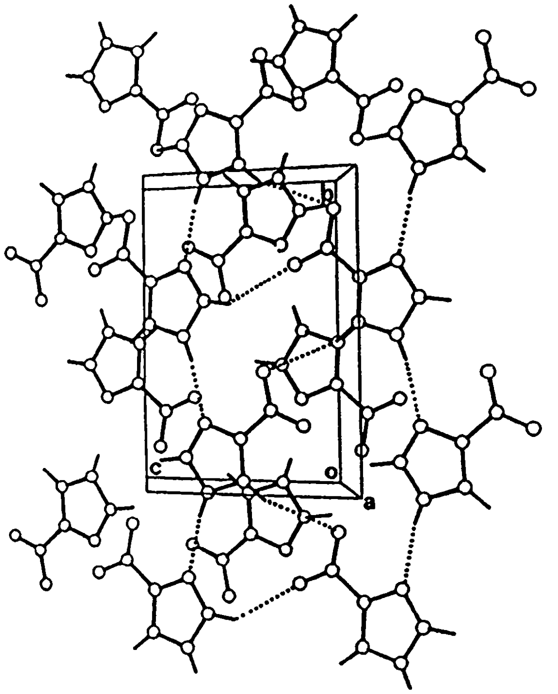

Fig. 2. A *PLUTO* (Motherwell & Clegg, 1978) plot of the crystal showing the packing along **a**. Hydrogen bonds are indicated by dashed lines.

The imidazole ring is planar with a maximum deviation from the best fitting plane of 0.001 (2) Å. The nitro group forms a dihedral angle of 0.2 (1)° with the least-squares plane through the imidazole ring atoms.

The stacking of the molecule along the *a* axis is shown in Fig. 2. The molecules are stacked in planes almost parallel to the *bc* plane [2.84 (5)°]. Inspection of non-bonding distances shorter than the sum of the van der Waals radii reveals the hydrogen bonds summarized in Table 2. Since two of these hydrogen bonds (H2···O43 and H5···O42) are almost parallel to the *c* axis and one (H1···N3) is parallel to the *b* axis, all molecules stacked in the same plane are linked through hydrogen bonds.

References

Allen, F. H., Kennard, O., Watson, D. G., Brammer, L., Orpen, A. G. & Taylor, R. (1987). *J. Chem. Soc. Perkin Trans.* 2, pp. S1–S19.

Blessing, R. H. (1987). *Crystallogr. Rev.* **1**, 3–58.

Cook, W. J. & Bugg, C. E. (1975). *J. Pharm. Sci.* **64**, 221–225.

Domenicano, A. & Murray-Rust, P. (1979). *Tetrahedron Lett.* **24**, 2283–2286.

Domenicano, A., Murray-Rust, P. & Vaciago, A. (1983). *Acta Cryst.* B**39**, 457–468.

Dupont, L., Dideberg, O. & Jamoulle, J. Cl. (1984). *Acta Cryst.* C**40**, 1269–1271.

Edwards, D. I. (1981). *Prog. Med. Chem.* **18**, 87–116.

Frenz, B. A. (1985). *Enraf–Nonius SDP-Plus Structure Determination Package.* Enraf–Nonius, Delft, The Netherlands.

Glass, R. S., Blount, J. F., Butler, D., Perrotta, A. & Oliveto, E. P. (1972). *Can. J. Chem.* **50**, 3472–3477.

Grimison, A., Ridd, J. H. & Smith, B. V. (1960). *J. Chem. Soc.* pp. 1352–1356.

Ibers, J. A. & Hamilton, W. C. (1964). *Acta Cryst.* **17**, 781–782.

Johnson, C. K. (1976). *ORTEP*II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.

Kalman, A., van Meurs, F. & Toth, J. (1980). *Cryst. Struct. Commun.* **9**, 709–712.

Kulkarni, S., Grimmett, M. R., Hanton, L. R. & Simpson, J. (1987). *Aust. J. Chem.* **40**, 1399–1413.

Main, P., Fiske, S., Hull, S. E., Lessinger, L., Germain, G., Declercq, J.-P. & Woolfson, M. M. (1982). *MULTAN*82. *A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data.* Univs. of York, England, and Louvain, Belgium.

McMullan, R. K., Epstein, J., Ruble, J. R. & Craven, B. M. (1979). *Acta Cryst.* B**35**, 688–691.

Motherwell, W. D. S. & Clegg, W. (1978). *PLUTO.* Program for plotting molecular and crystal structures. Univ. of Cambridge, England.

Nardelli, M. (1983). *Comput. Chem.* **7**, 95–98.

Puig-Torres, S., Martin, G. E., Larson, S. B. & Simonsen, S. H. (1984). *J. Heterocycl. Chem.* **21**, 155–159.

Segalas, I., Poitras, J. & Beauchamp, A. (1992). *Acta Cryst.* C**48**, 295–298.

Solans, X. & Font-Altaba, M. (1981). *Acta Cryst.* B**37**, 2111–2114.

Solans, X. & Font-Altaba, M. (1982). *Acta Cryst.* B**38**, 627–629.

Stewart, R. F., Davidson, E. R. & Simpson, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.

Taira, Z. & Uchi, J. (1988). *Acta Cryst.* C**44**, 2002–2004.