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Structure of 2,3-Dihydro-1*H*-imidazo[1,2-*b*]pyrazole (IMPY), an Inhibitor of DNA Synthesis, $C_5H_7N_3$

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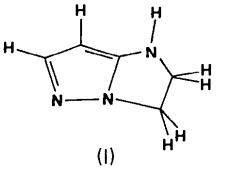
Abstract. $M_r = 109{\cdot}13$, orthorhombic, $P2_12_12_1$, $a = 7{\cdot}098$ (1), $b = 7{\cdot}225$ (1), $c = 10{\cdot}980$ (3) Å, $V = 563{\cdot}09$ Å^3, $Z = 4$, $D_m = 1{\cdot}29$, $D_x = 1{\cdot}29$ Mg m^{-3}, λ(Cu $K\alpha$) = 1·54178 Å, $\mu = 0{\cdot}70$ mm^{-1}. Final $R = 0{\cdot}059$ for 425 significant reflections measured at 298 K. The pyrazole portion is planar, while the dihydroimidazole group has a shallow half-chair conformation with C(4) deviating by 0·136 (4) Å out of the plane of this ring.

Introduction. The title compound (NSC 51143: IMPY, I) is a potent and selective inhibitor of DNA synthesis (Ennis, Möller, Wang & Selawry, 1971), and is currently being evaluated for clinically useful anti-tumour activity (Vogel, Denefrio, Padgett & Silverman, 1980). Evidence has been obtained demonstrating that IMPY acts by inhibiting the ribonucleotide-reductase enzyme system (Cory & Fleischer, 1980), possibly by binding to a non-haem iron site. As a first step in the establishment of structure–activity relationships for IMPY and its congeners, its molecular structure has been established. This is the first reported X-ray study of an imidazo-[1,2-*b*]pyrazole system.



(I)

Experimental. Large prismatic crystals of IMPY obtained from aqueous solution, D_m determined by flotation, crystal *ca* 0·60 × 0·40 × 0·15 mm sealed in glass capillary tube so as to avoid the excessive decomposition noted at an earlier stage, preliminary X-ray photographs showed orthorhombic symmetry, systematic absences $h00$: $h = 2n + 1$; $0k0$: $k = 2n + 1$;

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00*l*: $l = 2n + 1$, accurate cell dimensions obtained by least-squares analysis of 25 θ values, Enraf–Nonius CAD-4 diffractometer, monochromated Cu $K\alpha$ radiation, reflections within range $1{\cdot}5 < \theta < 60{\cdot}0°$ (h: 0 to 7; k: 0 to 8; l: 0 to 12) measured using ω–2θ scans, maximum count time 60s; intensities of three standard reflections (305, $\bar{2}1\bar{1}$ and $41\bar{1}$) monitored at intervals of 3600s had decreased in intensity by ~8% during course of data collection and corrections for crystal decay were applied to data set; 526 total reflections, 425 with $I > 3\sigma(I)$ considered observed; structure solved by direct methods using *MULTAN* 80 (Main *et al.*, 1980) and refined on F by full-matrix least squares, H-atom positions located from difference Fourier syntheses and kept fixed during refinement, final difference map did not show any peaks > 0·15e Å^{-3}, final $R = 0{\cdot}055$, $R_w = 0{\cdot}059$, $w = 1/\sigma(F)^2$, zero shift/error in final least-squares cycle, $F(000) = 232$, atomic scattering factors taken from *International Tables for X-ray Crystallography* (1974), all calculations performed on a PDP11/34A computer using SDP program system (Frenz, 1980).

Discussion. The final atomic parameters are listed in Table 1.* The molecular structure of IMPY is shown in Fig. 1; bond distances and angles are given in Table 2.

* Tables of structure factors, H-atom coordinates and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 38220 (5 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. *Final fractional coordinates* (×10⁴) *and average thermal parameters* (Å² ×10³)

E.s.d.'s are in parentheses.

	x	y	z	$\langle U_{ii} \rangle$
N(1)	2098 (5)	4819 (6)	716 (3)	47
N(2)	1483 (6)	3157 (6)	2384 (4)	50
N(3)	3379 (6)	5817 (6)	66 (4)	54
C(1)	4579 (7)	4969 (8)	1925 (4)	54
C(2)	4850 (7)	5926 (7)	814 (5)	55
C(3)	250 (7)	4072 (7)	459 (5)	58
C(4)	−299 (8)	3388 (8)	1718 (5)	59
C(5)	2775 (6)	4265 (6)	1808 (4)	40

Table 2. *Bond lengths* (Å) *and angles* (°) *for the non*-H *atoms*

E.s.d.'s are in parentheses.

C(5)–C(1)	1·384 (4)	N(3)–N(1)	1·363 (3)
C(5)–N(1)	1·352 (3)	N(1)–C(3)	1·446 (4)
C(5)–N(2)	1·371 (4)	N(2)–C(4)	1·471 (4)
C(1)–C(2)	1·416 (4)	C(4)–C(3)	1·519 (5)
C(2)–N(3)	1·330 (4)		
C(1)–C(5)–N(1)	107·6 (3)	C(5)–N(1)–N(3)	112·6 (2)
C(1)–C(5)–N(2)	142·2 (3)	C(5)–N(1)–C(3)	112·6 (3)
N(1)–C(5)–N(2)	110·1 (2)	N(3)–N(1)–C(3)	134·4 (3)
C(5)–C(1)–C(2)	103·0 (3)	C(5)–N(2)–C(4)	106·2 (2)
C(1)–C(2)–N(3)	113·4 (3)	N(2)–C(4)–C(3)	105·6 (3)
C(2)–N(3)–N(1)	103·4 (2)	N(1)–C(3)–C(4)	100·2 (3)

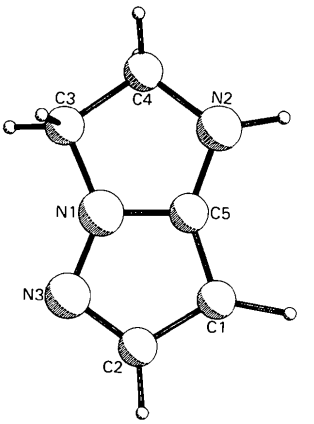

Fig. 1. The molecular structure of IMPY, showing the numbering scheme used.

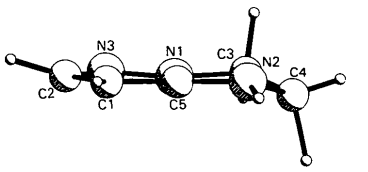

Fig. 2. A view approximately parallel to the molecular best plane.

The analysis has confirmed the structure assigned to the imidazo[1,2-*b*]pyrazole system, with neither N atom of the pyrazole group carrying a proton. It is noteworthy that bonds N(1)–C(5) and N(2)–C(5) have substantial double-bond character, presumably on account of their delocalization with the aromaticity of the pyrazole ring. This portion of the molecule is planar, whereas the dihydroimidazole group is significantly buckled (Fig. 2) into a shallow half-chair, with C(4) deviating by 0·136 (4) Å from the plane of this ring.

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