

The Crystal and Molecular Structure of 3-Amino-4,5-dicyano-1-methylpyrazole

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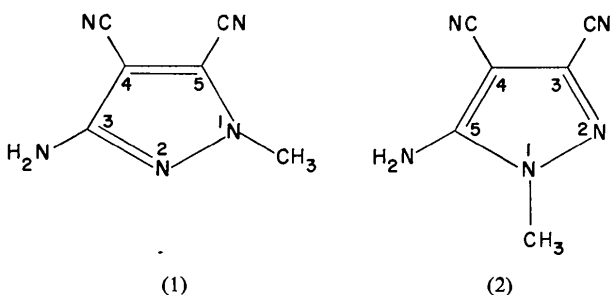
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A single-crystal X-ray analysis of aminodicyanomethylpyrazole, $C_6H_5N_5$, has unequivocally established the site of *N*-methylation to be N(1) rather than N(2). The compound crystallizes in space group $P2_1/c$ with $a=6.199$, $b=15.168$, $c=7.646$ Å, $\beta=91.95^\circ$, $Z=4$. The structure possesses a pseudo mirror plane along c , suggested by the systematically weak and strong intensities for l odd and l even respectively. The substructure with half c was first solved by direct methods with l even reflections. The full structure in $P2_1/c$ was subsequently solved by the method of key shifts. The structure was refined by the full-matrix least-squares method with anisotropic temperature factors for the non-hydrogen and isotropic for the H atoms. The final R for 1058 reflections is 0.07.

Introduction

N-Methylated pyrazoles have attracted considerable attention because they are precursors for the medicinally important pyrazolopyrimidines. There are two isomers of the title compound which differ in the site of methylation. The object of this study was to establish the isomeric state of the molecule.



Experimental

Small crystals of the compound were obtained by slow evaporation of 1:1 ethanol-water solution over a period of several days. Photographs showed the crystals to be monoclinic with systematic absences $h0l$, $l=2n+1$; $0k0$, $k=2n+1$, indicating the space group $P2_1/c$. The cell dimensions $a=6.199$ (3), $b=15.168$ (2), $c=7.646$ (3) Å, $\beta=91.95$ (1) $^\circ$ were determined by a least-squares refinement of 2θ , ω and χ for 12 reflections measured in the 2θ range of 40–60 $^\circ$ on a Picker FACS-1 diffractometer. The observed (1.358 in CCl_4 /cyclohexane) and calculated (1.360 g cm $^{-3}$) densities are consistent with $Z=4$.

Intensities were collected by the θ - 2θ scan technique with Ni-filtered Cu $K\alpha$ radiation ($\lambda=1.5418$ Å) up to $2\theta_{max}=127^\circ$, and corrected for background, Lorentz

and polarization factors. 1058 independent reflections were recorded, and 940 were greater than $1.5\sigma(I)$, where $\sigma(I)$ is based on counting statistics (Evans, 1961).

Structure determination

Analyses of the intensities showed that $\langle E^2 \rangle = 0.2$ for l odd and $\langle E^2 \rangle = 1.6$ for l even suggesting that the molecular planes were separated by $c/2$. We believed that the pseudo mirror plane in (1) produced a pseudo symmetry in the structure. Attempts to solve the structure by direct methods with all the reflections failed owing to the fact that there were very few strong l odd reflections. The substructure with half c was finally solved in $P2_1/m$ with Long's (1965) direct-method program. The asymmetric unit in the substructure contains only six non-hydrogen atoms. The phases of 84 reflections with $E > 1.50$ were obtained through reiterative applications of Sayre's (1952) equation. The seven initial reflections ($\bar{2}12$, $\bar{1}15$, 570, $\bar{1}01$, 361, 382 and 1,13,1) produced 16 possible solutions. The solution chosen was that which converged in the least number of cycles and which gave the highest value of C (0.94), where

$$C = \langle |E_A \sum (E_B E_C)| \rangle / \langle E_A | \sum |E_B| |E_C| \rangle.$$

The sum is over all the terms in the Sayre equations. An E map revealed the six non-hydrogen atoms of the asymmetric unit of the substructure with N(2) on the mirror plane at $y = \frac{1}{4}$.

Starting from the substructure, the complete structure was obtained by the key shift method (Ito, 1973). 200 reflections containing the strongest 100 reflections with l even and l odd were used. The asymmetric unit of the complete structure in $P2_1/c$ consists of one molecule of (1), which had the exact mirror symmetry before shifts. N(1), C(1), C(3) and N(3), of which

the atomic species were not known, were assumed to be N at the start. An overall temperature factor of 3.5 \AA^2 was assumed. R before shifts was 0.25 for the 200 reflections. Key shifts of atoms in the extension from the substructure to the complete structure were examined by varying independently each coordinate of individual atoms by ± 0.1 , ± 0.2 and $\pm 0.3 \text{ \AA}$ from the starting value, and calculating the corresponding R values.

There are two different ways of extending the substructure (Fig. 1) to the complete structure; in setting *A* the origins of the two structures coincide, while in *B* the origin of the complete structure is shifted by $c/4$. *A* was first tried but after two cycles with two shifts reduction of R stopped at a relatively high value of 0.20. *B* was next tried. In the R maps of the first cycle, the lowest R of 0.20 was indicated for $\pm 0.2 \text{ \AA}$ shifts of the y coordinate of N(2). In this case, choice of the sign of the shift is arbitrary from symmetry; a -0.1 \AA shift, *i.e.*, the indicated shift multiplied by a damping factor of 0.5, was adopted with an R of 0.22. In the second cycle, the shift in y of -0.1 \AA for N(51) was the most significant with an R of 0.20. After an additional cycle with shifts in y of -0.1 \AA for C(51) and N(41), R was 0.17. These key shifts of the atoms were sufficient to give approximately correct signs for the reflections.

Structure refinement

The structure was refined initially by the block-diagonal least-squares method with individual isotropic temperature factors to an R of 0.08 for the 200 reflections. The atomic species of N(4), C(1), C(3) and N(3) could be readily discerned from comparison of the B values. The atoms that had the lower B values of 3.0 and 3.1 \AA^2 were assigned as N(1) and N(3), and the atoms with $B=4.5$ and 4.4 \AA^2 as C(1) and C(3), from consideration of the chemical structure (1). The 11 non-hydrogen atoms with isotropic temperature factors were subjected to several cycles of refinement

with the full-matrix least-squares program of Busing, Martin & Levy (1962). R was 0.13 for all 1058 reflections, and dropped to 0.093 on further refinement with anisotropic temperature factors. A difference map revealed all five H atoms. Additional cycles of aniso-

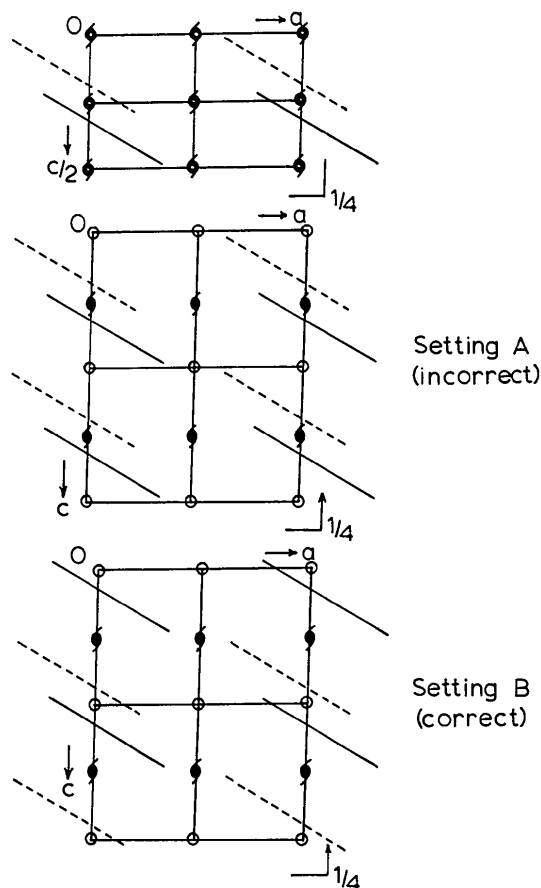


Fig. 1. The relation between the substructure (top) and the two possible full structures, setting *A* and setting *B*.

Table 1. Atomic coordinates in 3-amino-4,5-dicyano-1-methylpyrazole

Positional parameters of non-hydrogen atoms have been multiplied by 10^4 . Positional parameters of hydrogen atoms have been multiplied by 10^3 . Anisotropic thermal parameters have been multiplied by 10^4 . Anisotropic temperature factor is of the form $\exp[-(\beta_{11}h^2 + \dots + 2\beta_{12}hk + \dots)]$. Standard deviations in parentheses refer to the least significant digits.

	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
N(2)	3699 (4)	2477 (2)	2393 (3)	219 (7)	32 (1)	163 (5)	1 (3)	-61 (5)	3 (2)
N(1)	2467 (4)	3157 (2)	1828 (3)	237 (8)	35 (1)	167 (5)	2 (3)	-25 (5)	0 (2)
C(1)	3209 (7)	4052 (2)	2167 (7)	273 (12)	26 (2)	249 (10)	-8 (3)	-21 (8)	-8 (3)
C(5)	627 (5)	2886 (2)	994 (4)	177 (8)	44 (2)	121 (5)	4 (3)	-34 (5)	1 (2)
C(51)	-931 (5)	3477 (2)	247 (4)	232 (9)	45 (2)	163 (7)	3 (3)	-19 (6)	1 (3)
N(51)	-2162 (5)	3954 (2)	-359 (4)	316 (10)	63 (2)	250 (8)	41 (4)	-50 (7)	20 (3)
C(4)	666 (5)	1975 (2)	1020 (4)	189 (8)	36 (1)	134 (6)	-9 (3)	-19 (5)	-1 (2)
C(41)	-867 (5)	1371 (2)	293 (4)	197 (9)	44 (2)	168 (7)	-1 (3)	-36 (6)	-1 (3)
N(41)	-2029 (5)	860 (2)	-290 (5)	306 (10)	58 (2)	275 (8)	-27 (4)	-99 (7)	-9 (3)
C(3)	2597 (4)	1759 (2)	1898 (4)	180 (8)	28 (1)	135 (6)	-7 (3)	-23 (5)	-6 (2)
N(3)	3361 (6)	926 (2)	2340 (5)	301 (11)	33 (1)	279 (8)	1 (3)	-83 (7)	2 (3)
H(11)	331 (10)	415 (4)	324 (9)	12.6 (2.3)					
H(12)	441 (9)	418 (3)	144 (7)	10.4 (1.6)					
H(13)	224 (8)	441 (3)	203 (6)	7.8 (1.4)					
H(31)	273 (8)	45 (3)	185 (6)	8.8 (1.4)					
H(32)	481 (9)	87 (3)	261 (7)	10.1 (1.6)					

Table 2. *Least-squares planes for the base and deviations of atoms from the plane (Å)*

$$\text{Plane: } 0.496X - 0.04Y - 0.869Z = -0.496.$$

Atoms defining plane are marked with an asterisk.

N(1)	-0.001*	N(51)	0.053	N(3)	-0.059
N(2)	-0.001*	C(4)	-0.001*	H(11)	-0.702
C(1)	-0.007	C(41)	0.024	H(12)	0.854
C(5)	0.001*	N(41)	0.064	H(13)	-0.214
C(51)	0.024	C(3)	0.001*	H(31)	0.081
				H(32)	0.203

Planarity of the base

Table 2 shows the deviations of the atoms from the least-squares plane through the pyrazole ring. The ring is planar within experimental error. The substituent atoms, with the exception of the methyl C(1), are significantly displaced from the plane. The amino N(3) is displaced on the opposite side to the cyano groups. The terminal N atoms of the cyano groups show larger displacements from the ring plane than the C atoms. The amino group is twisted by 25° to the base plane.

Hydrogen bonding

A view of the hydrogen bonding along c^* is shown in Fig. 3. Each base is hydrogen bonded to three surrounding bases. There are two independent hydrogen bonds per molecule which involve the amino H atoms and the N atoms of the cyano groups. N(3) is hydrogen bonded to N(41) of an inversion-center related molecule and N(51) of a glide-plane related molecule. Both these hydrogen bonds which involve cyano groups are weak. The methyl groups are nestled between the adjacent cyano N atoms making intermolecular contacts to them of 3.378 and 3.492 Å. The methyl H atoms are separated by more than 2.5 Å from the cyano N atoms.

Base stacking

The glide-plane related molecules are stacked on top of each other with partial overlap of the rings (Fig. 4) which is typical of crystal structures of nucleic acid constituents (Bugg, Thomas, Sundaralingam & Rao, 1971). The interplanar separation between adjacent bases is 3.383 Å. The closest contacts ranging from 3.436 to 3.445 Å are observed between adjacent ring atoms. The cyano groups are not involved in any stacking interactions.

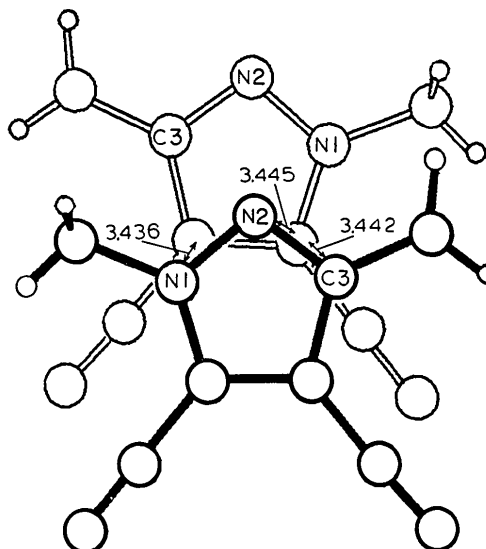


Fig. 4. The stacking of adjacent bases showing the closest contacts.

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