

CRYSTAL AND MOLECULAR STRUCTURE
OF CARBONYLCYANIDE-4-CHLOROPHENYLHYDRAZONE
(4-CHLOROPHENYLHYDRAZONOPROPANEDINITRILE)

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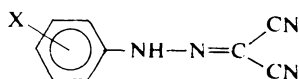
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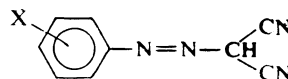
The crystal structure of carbonylcyanide-4-chlorophenylhydrazone was solved by the single crystal X-ray diffraction method and interpreted by the heavy atom method. The compound crystallizes in the $P2_1/c$ monoclinic group with 4 molecules per unit cell and with lattice parameters: $a = 1.1843(3)$, $b = 0.5944(1)$, $c = 1.4922(3)$ nm and $\beta = 117.92(2)^\circ$. The structure was refined by the least squares method for 1 078 observed reflections to a final value of $R = 4.9\%$. The crystal structure consists of monomeric units, where hydrogen bonds were observed between atoms $N3...H5$ 0.2193 nm and $N3...H3$ 0.2404 nm between two molecules transformable through centre of symmetry $-x, -y, -z$. The name 4-chlorophenylhydrazonopropanedinitrile is recommended for the studied compound on the basis of this X-ray structural analysis.

Carbonylcyanidephenylhydrazones are biologically active substances¹⁻⁴, best known for their uncoupling effect on oxidative phosphorylation⁵⁻⁷. This property depends on their ability to decouple mitochondrial oxidation from phosphorylation, leading to interruption of the synthesis of adenosinetriphosphate. Although these substances have long been used as a very valuable tool in the study of bioenergetic processes⁷⁻¹⁰, the molecular mechanism of their action has not yet been elucidated^{11,12}.

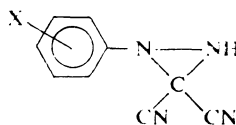
Elucidation of the mechanism of the uncoupling effect of carbonylcyanidephenylhydrazones on oxidative phosphorylation would be useful not only from the point of view of description of the chemical basis for the formation of adenosinetriphosphate, but also for explanation of the biological effect of these substances in general. However, a necessary condition for study of the mechanism of biochemical reactions is knowledge on the structure and physicochemical properties of the reactants. Carbonylcyanidephenylhydrazones are generally considered to have a structure of the phenylhydrazone type² I or of the azobenzene type¹ II.



I



II



III

X = Cl, OCF₃, CH₃, NO₂, COCH₃

It has also been suggested that carbonylcyanidephenylhydrazones have a structure of the diaziridine type¹³ III. ¹³C, ¹H and ¹⁵N NMR analyses have demonstrated¹⁴ that these substances are present in solution as phenylhydrazones.

This work summarizes the results obtained from X-ray structural analysis of carbonylcyanidephenylhydrazones.

EXPERIMENTAL

Carbonylcyanide-4-chlorophenylhydrazone was obtained by diazotation of *p*-chloroaniline with NaNO₂ and subsequent coupling of the diazone salt formed with malonodinitrile^{1,14,15}. The purity of the product formed was verified chromatographically and by elemental analysis. The

TABLE I

Basic crystallographic data of carbonylcyanide-4-chlorophenylhydrazone

Empirical formula	C ₉ H ₅ N ₄ Cl
Relative molecular weight	204.6
Crystallographic system	monoclinic
Space group	<i>P</i> 2 ₁ / <i>c</i>
Dimensions of the unit cell	<i>a</i> = 1.1843(3) nm <i>b</i> = 0.5944(1) <i>c</i> = 1.4922(3) <i>β</i> = 117.93(3)
Volume of the unit cell	<i>V</i> = 927.9 · 10 ⁻³ (4) nm ³
Number of formula units per unit cell	<i>Z</i> = 4
Number of electrons per unit cell	F(000) = 416
Measured crystal density	<i>D</i> ₀ = 1.454 Mg m ⁻³
Calculated crystal density	<i>D</i> _c = 1.464 Mg m ⁻³
Linear absorption coefficient	<i>μ</i> = 0.38 mm ⁻¹
Monochromatic radiation	MoK _{α1} = 0.070926 nm

crystal density at room temperature was found pycnometrically in hexane. A single crystal shaped like a rhombohedral prism with dimensions of $0.5 \times 0.3 \times 0.3$ mm was selected for intensity measurements. The integral intensities were measured on a four-circle automatic control Syntex P2₁ diffractometer. Graphite monochromatized MoK α radiation was used for the measurements. The crystal was recentred after each 200 measured intensities. The integral intensities were measured in the range $0^\circ < 2\theta \leq 55^\circ$, of which only those with $I \geq 1.96\sigma(I)$ (1 073) were classified as observed and these were used for final structure refinement. All the intensities were corrected for the Lorentz and polarization factors. Correction for absorbance was neglected.

The crystal structure was solved by the heavy atom method. The position of the chlorine atom was found from the three-dimensional Patterson function. The positions of the other nonhydrogen atoms, C and N, were found by gradual application of Fourier synthesis of the electron density. After determination of the positions of all the atoms, the structure was refined in three cycles by the least squares method using diagonal approximation, isotropic thermal parameters and a unit weighing scheme. In the next 5 refinement cycles, anisotropic thermal vibration of all the nonhydrogen atoms was assumed, which were refined together with the positional parameters by the least squares method using the minimization function $\sum w(|F_0| - |F_c|)^2$, in a 9×9 block diagonal approximation, where the *R* factor, defined as $\sum ||F_0| - |F_c|| / |F_c|$, decreased to a value of 0.057.

TABLE II

Positional parameters ($\cdot 10^4$) of the atoms of the carbonylcyanide-4-chlorophenylhydrazone molecule (standard deviations in brackets)

Atom	<i>x/a</i>	<i>y/b</i>	<i>z/c</i>
Cl	2 678(1)	2 626(1)	2 645(1)
C1	1 152(2)	3 689(4)	1 895(1)
C2	1 018 (2)	5 808(3)	1 459(1)
C3	0 107(2)	2 421(4)	1 737(1)
C4	-1 110(2)	3 236 (3)	1 133 (1)
C5	-0 215(2)	6 653(3)	0 865(1)
C6	-1 256(2)	5 361(3)	0 717(1)
C7	-3 870(2)	8 912(3)	-0 820(1)
C8	-4 961(2)	7 884(3)	-0 813(1)
C9	-4 020(2)	11 030(3)	-1 332(1)
N1	-2 517(1)	6 181(3)	0 146(1)
N2	-2 714(1)	8 082(3)	-0 339(1)
N3	-5 754(2)	7 011(3)	-0 720(1)
N4	-4 122(2)	12 722(3)	-1 722(3)
H1	1 787	6 798	1 676
H2	0 047	1 052	1 759
H3	-2 013	2 867	1 174
H4	-0 220	8 166	0 536
H5	-3 040	5 293	0 391

Introduction of hydrogen atoms into the structure, with positions determined in the differential Fourier map of a residual electron density of $1.04 \cdot 10^3 \text{ e nm}^{-3}$ reduced the *R* factor to a final value of 0.049. The final refinement was carried out by fixing the isotropic thermal and positional parameters of the hydrogen atoms.

TABLE III

Interatomic bonding distances (nm) and their standard deviations in the carbonylcyanide-4-chlorophenylhydrazone molecule

Bond	Bond length	Bond	Bond length
Cl—C1	0.1738(2)	C7—C8	0.1434(3)
C1—C2	0.1392(3)	C7—C9	0.1439(3)
C1—C3	0.1372(3)	C8—N3	0.1137(3)
C2—C5	0.1399(3)	C9—N4	0.1131(3)
C3—C4	0.1382(3)	C2—H1	0.1003(2)
C4—C6	0.1382(3)	C3—H2	0.0819(2)
C5—C6	0.1379(3)	C4—H3	0.1121(3)
C6—N1	0.1415(2)	C5—H4	0.1023(2)
N1—N2	0.1303(2)	N1—H5	0.1004(2)
N2—C7	0.1309(2)	N3—H3 ^a	0.2404(2)
		N3—H5 ^a	0.2193(2)

^a Intermolecular interaction; symmetry code $-x, -y, -z$.

TABLE IV

Valence angles ($^\circ$) and their standard deviations in the carbonylcyanide-4-chlorophenylhydrazone molecule

Atoms	Angle	Atoms	Angle
Cl—C1—C2	119.12(14)	C7—C8—N3	173.85(20)
Cl—C1—C3	119.52(16)	C7—C9—N4	178.10(21)
C1—C2—C5	118.52(17)	C7—N2—N1	120.05(15)
C1—C3—C4	120.08(19)	C8—C7—C9	119.29(16)
C2—C1—C3	121.35(17)	C8—C7—N2	123.37(18)
C2—C5—C6	119.44(18)	C9—C7—N2	117.26(16)
C3—C4—C6	119.09(18)	C4—H3...N3 ^a	158.48(11)
C4—C6—N1	117.37(16)	C8—N3—H5 ^a	166.83(17)
C5—C6—N1	121.14(17)	C8—N3...H3 ^a	144.53(17)
C6—N1—N2	119.79(15)	N1—H5...N3 ^a	170.69(10)

^a Intermolecular angles; symmetry code $-x, -y, -z$.

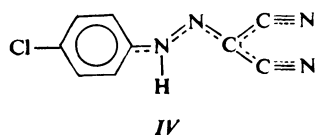
The basic crystallographic data for carbonylcyanide-4-chlorophenylhydrazone are given in Table I. The refined positional parameters of the nonhydrogen atoms and the determined positional parameters of the hydrogen atoms in the differential Fourier map are given in Table II. The interatomic bonding distances and valence angles are given in Tables III and IV, the anisotropic thermal parameters of the nonhydrogen atoms are listed in Table V. The scattering curves for the neutral atoms were taken from the tables¹⁶.

The calculations were carried out on a Syntex P2₁, XTL module and on a Siemens 4004/150 computer using the NRC crystallographic programs for the IBM/360 system¹⁷.

STRUCTURE DESCRIPTION AND DISCUSSION

The atomic distribution in the unit cell projected onto the (010) plane is shown in Fig. 1. The four chlorine atoms are approximately located in the centres of the quarters of the unit cell.

The crystal structure consists of discrete molecules; the shortest intermolecular distances between atoms N3, H3 and H5 (0.2193 and 0.2404 nm) for two molecules transformable through the centre of symmetry (symmetry code $-x, -y, -z$) reflect the presence of hydrogen bonds. The bonding distances and angles (Tables III and IV) between the carbon and nitrogen atoms in the molecule lie in an interval between the sum of the Pauling covalent radii¹⁸ corresponding to single and multiple bonds (C—C 0.154 nm, C=C 0.134 nm, N—N 0.146 nm, N=N 0.126 nm, C—N 0.146 nm, C=N 0.123 nm, and C≡N 0.115 nm), indicating considerable delocalization of the π -electrons over the whole molecule. To determine the degree of coplanarity of the molecule, 5 planes were constructed through selected atoms by the least squares method (Table VI); deviations of selected atoms from these planes are listed in Table VII. The molecules in the unit cell are oriented so that the H3 and H5 hydrogen atoms interact with the N3 nitrogen atom in the neighbouring molecule, leading to formation of twelve-membered and six-membered chelate rings. The geometry of both chelate rings is almost planar, in good agreement with the correlation of the bonding distances and angles given in Tables III and IV. On the basis of this data, the structural formula of carbonylcyanide-4-chlorophenylhydrazone can be expressed by the canonical form IV:



Solution of the crystal and molecular structure confirmed one of three possible forms of the structural formula. It follows from the results of X-ray structural analysis that this substance exists in crystalline form as a phenylhydrazone type of substance. It was unambiguously demonstrated by study of the differential Fourier map of the residual electron density that the H5 hydrogen atom is localized close

TABLE V

Anisotropic temperature parameters for the nonhydrogen atoms ($\cdot 10^4$) in the 4-chlorophenylhydrazonepropanedinitrile molecule

Atom	<i>B</i> 11	<i>B</i> 22	<i>B</i> 33	<i>B</i> 23	<i>B</i> 13	<i>B</i> 12
Cl	77(1)	465(2)	70(1)	64(2)	65(1)	94(2)
C1	69(2)	310(7)	47(1)	-15(5)	54(3)	51(6)
C2	62(2)	290(7)	52(1)	-42(5)	53(3)	-68(6)
C3	85(2)	231(6)	47(1)	-29(5)	60(3)	-34(6)
C4	74(2)	259(7)	46(1)	13(5)	51(2)	10(6)
C5	77(2)	246(7)	49(1)	4(5)	71(3)	38(6)
C6	63(1)	215(6)	215(6)	26(4)	47(2)	-3(5)
C7	65(2)	244(7)	48(1)	7(5)	53(2)	-38(6)
C8	76(2)	247(7)	46(1)	-6(5)	59(2)	-13(6)
C9	53(1)	255(7)	56(1)	-5(5)	52(2)	-20(5)
N1	77(2)	226(5)	52(1)	26(4)	60(2)	-31(5)
N2	59(1)	263(6)	43(1)	-11(4)	45(2)	-45(5)
N3	90(2)	359(8)	80(1)	-56(5)	92(3)	36(6)
N4	91(2)	321(6)	80(1)	85(5)	54(3)	-10(6)

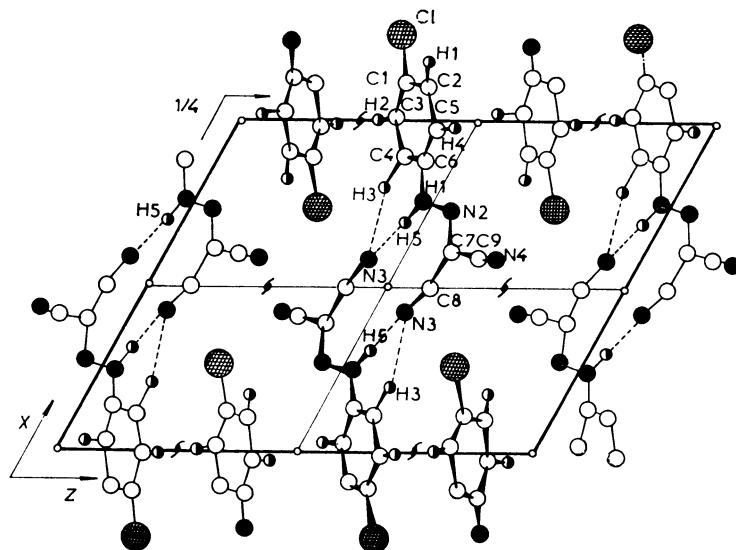


FIG. 1

Projection of the structure of 4-chlorophenylhydrazonepropanedinitrile onto the (010) plane

to the N1 nitrogen atom. This type of structural form was also found in solutions by NMR analysis¹⁴. Thus we recommend that the studied compound be called 4-chlorophenylhydrazone propanedinitrile.

TABLE VI

Planes constructed, by the least squares method through selected atoms of the carbonylcyanide-4-chlorophenylhydrazone molecule and angles (°) between planes (1) to (5)

Plane number	Atoms defining the plane	Planes	Angle
(1)	Cl, C2, C3, C4 C5, C6	(1)–(2)	8.04
		(1)–(3)	38.69
(2)	C6, N1, N2, C7	(1)–(4)	30.44
(3)	N1, N2, C7, N1 ^a N2 ^a , C7 ^a	(1)–(5)	42.71
		(2)–(3)	30.77
(4)	C4, C6, N1, N3 ^a	(3)–(4)	8.29
(5)	Cl, C1, C6, N1	(4)–(5)	23.79

^a Atoms of the molecules transformed through symmetry code $-x, -y, -z$.

TABLE VII

Deviations (nm · 10⁴) of some atoms from planes (1) to (5)

Atom	(1)	(2)	(3)	(4)	(5)
Cl	-72	—	—	—	-1
C1	-52	—	—	-10 377	2
C2	90	—	—	-13 343	-8 149
C3	-54	—	—	-3 458	8 091
C4	122	—	—	754	8 298
C5	-23	—	—	-9 325	-8 150
C6	-83	-194	-4 487	-2 425	-1
C7	-798	-210	-1 480	2 690	-7 354
C8	-3 859	-1 295	7 842	7 135	-1 501
C9	—	-302	-1 731	—	-15 019
N1	-589	193	282	1 473	0
N2	434	211	-2 237	-178	-6 688
N3	-6 978	-2 854	12 188	9 923	2 856
N4	—	-724	-4 611	—	-21 351
H3	—	—	—	2 378	—
H5	-4 393	-2 299	2 753	2 559	—

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