SYNTHESIS AND STRUCTURE OF 6-HYDRAZINO-2,4,5-TRICHLORONICOTINONITRILE

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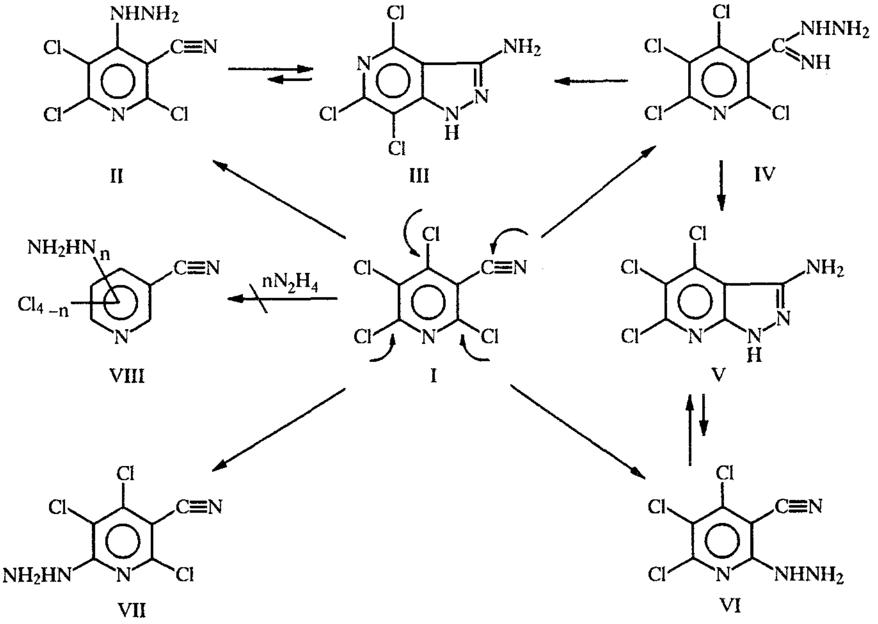
UDC

The reaction of tetrachloronicotinonitrile with hydrazine hydrate has been studied. The structure of the reaction product has been established based on x-ray structural analysis.

In the reaction of polyhalogenated pyridines with N-nucleophiles nucleophilic substitution can occur at either the 2-position or 4-position in the pyridine ring [1-4]. The presence of a cyano group in the 3-position of a halopyridine molecule also makes it possible to obtain the corresponding 3-aminopyrazolo[4,3-c]-pyridine via intramolecular reaction between the nitrile and hydrazine functional groups [5-7]. In the present paper we have studied the reaction of tetrachloronicotinonitrile (I) with hydrazine hydrate.

The molecular structure of compound I contains four electrophilic sites capable of reaction with hydrazine hydrate. It is therefore possible to form under these conditions three different substituted pyridines II, VI, VII, as well as the amidrazone IV. In addition, the possibility of an intramolecular cyclization reaction leading to the formation of condensed bicyclic systems III and V cannot be excluded. Finally, polysubstitution reactions are also possible, resulting in the formation of bis- and tris-hydrazono derivatives, or the corresponding condensed systems illustrated by structure VIII.



We have found that only a 1:1 composition substitution product is obtained upon reaction of compound I with hydrazine hydrate at room temperature or upon cooling to −35°C, in either dioxane, tetrahydrofuran, DMF, or methylene chloride solution, and even in the presence of excess $N_2H_4 \cdot H_2O$. Type VIII compounds can therefore be excluded from consideration.

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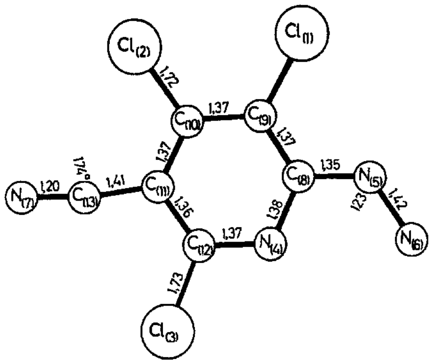


Fig. 1. Molecular structure of 6-hydrazino-2,4,5-trichloronicotinonitrile with bond length values averaged for two independent molecules.

TABLE 1. Bond Length Values for Two Crystallographically Independent Molecules

Bond	d_A, Å	d_B, Å	Bond	d_A, Å	d_B, Å
$Cl_{(1)}—C_{(9)}$	1,73	1,74	$N_{(4)}—C_{(8)}$	1,38	1,38
$Cl_{(2)}—C_{(10)}$	1,72	1,72	$C_{(8)}—C_{(9)}$	1,36	1,37
$Cl_{(3)}—C_{(11)}$	1,72	1,73	$C_{(9)}—C_{(10)}$	1,37	1,37
$N_{(5)}—N_{(6)}$	1,42	1,42	$C_{(10)}—C_{(11)}$	1,37	1,37
$N_{(5)}—C_{(8)}$	1,37	1,34	$C_{(11)}—C_{(12)}$	1,35	1,36
$N_{(7)}—C_{(13)}$	1,21	1,19	$C_{(12)}—N_{(4)}$	1,37	1,38
$C_{(13)}—C_{(11)}$	1,42	1,41			

σd = 0,010...0,015 Å

The molecular weight of the substitution product was determined by mass spectrometry and corresponds to a monosubstitution product containing three chlorine atoms, thus precluding structure IV from consideration as well.

In order to determine the structure of the reaction product obtained from nitrile I and hydrazine we have carried out an x-ray structure investigation. Crystals of the product were grown by slow cooling of a saturated solution in tetrahydrofuran. X-ray analysis revealed that nucleophilic substitution in this case occurs exclusively at the 6-position; the structure of the reaction product corresponds to structure VII (Fig. 1).

The bond length and bond angle values for two crystallographically independent molecules A and B are given in Tables 1 and 2, respectively. The molecules are essentially planar, with the angle between the plane of the pyridine ring and the corresponding $C_{(8)}N_{(5)}N_{(6)}$ plane equal to 3.5 and 2° in molecules A and B, respectively. The hydrazine fragment adopts a cis-conformation relative to the pyridine nitrogen atom. The alternative conformer does not exist, apparently because of the possibility of steric hindrance between the chlorine atom in position 5 and the hydrazino group.

The C−Cl bond lengths are in the 1.742 Å range and fall within the range of values observed in chlorosubstituted benzene derivatives [8]. The geometric parameters for the pyridine rings in the two crystallographically independent molecules coincide with one another with an accuracy exceeding experimental error for their determination. The $N_{(5)}-C_{(8)}$ bond lengths, equal to 1.37 and 1.34 Å, respectively, are short compared to normal single bonds of this type; they are similar to N−C bond length values observed in pyridines. The evidence of N−C bond contraction and the coplanarity of the hydrazine and pyridine fragments in these molecules indicate the existence of significant n-π-conjugation between these fragments. The N−N bond lengths in the hydrazino groups are equal to 1.42 Å, which is a conventional or normal range [9]. Based on literature data for cyanopyridines the C≡N bond length should not exceed 1.15 Å [10-13].

The $N_{(7)}-C_{(13)}$ interatomic distances in the crystal structure we investigated are equal to 1.21 and 1.19 Å, respectively, which correspond to the maximum distances observed in cyanopyridines. The bond lengths between the carbon atoms in the pyridine ring and the cyano group carbon atoms are 1.42 and 1.41 Å, substantially shorter than for analogous bond distances in other cyanopyridine which have been structurally analyzed; the latter bond length values have been reported to be in the

TABLE 2. Bond Angle Values for Two Crystallographically Independent Molecules

Angle	ω_A, deg	ω_B, deg	Angle	ω_A, deg	ω_B, deg
$N_{(6)}N_{(5)}C_{(8)}$	123,5	122,5	$C_{(13)}C_{(11)}C_{(12)}$	117,0	118,7
$N_{(5)}C_{(8)}N_{(4)}$	113,5	114,5	$Cl_{(3)}C_{(12)}N_{(4)}$	112,9	111,6
$N_{(5)}C_{(8)}C_{(9)}$	122,9	123,3	$Cl_{(3)}C_{(12)}C_{(11)}$	123,0	123,3
$Cl_{(1)}C_{(9)}C_{(8)}$	118,7	118,8	$C_{(8)}N_{(4)}C_{(11)}$	114,7	114,9
$Cl_{(1)}C_{(9)}C_{(10)}$	122,6	121,1	$N_{(4)}C_{(8)}C_{(9)}$	123,7	122,1
$Cl_{(2)}C_{(10)}C_{(9)}$	120,5	120,8	$C_{(8)}C_{(9)}C_{(10)}$	118,7	119,9
$Cl_{(2)}C_{(10)}C_{(11)}$	119,5	118,9	$C_{(9)}C_{(10)}C_{(11)}$	120,0	120,3
$N_{(7)}C_{(13)}C_{(11)}$	171,6	176,9	$C_{(10)}C_{(11)}C_{(12)}$	118,9	117,5
$C_{(13)}C_{(11)}C_{(10)}$	124,1	123,8	$C_{(11)}C_{(12)}N_{(4)}$	124,1	125,1

$\sigma\omega = 0{,}8...1{,}5°$

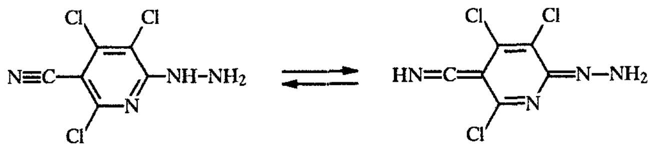
1.44-1.48 Å range [10-13]. The $C_{(11)}-C_{(13)}-N_{(7)}$ group exhibits a significant deviation from linearity which also merits attention; the angle around the $C_{(13)}$ atom is 172°, or 177° for the analogous angle in molecule B.

In general cyano groups do not deviate from linearity by more than 3°, and the deviations are usually attributed to steric or crystal packing factors or forces.

Figure 2 depicts a structural projection of the molecule along the ac plane. As mentioned above, two crystallographically independent molecules have been observed in the crystal structure. One of these molecules (A) is oriented close to the sliding mirror plane C. The second type of molecule (B) is oriented along the 2_1 screw axis. There are no intermolecular distances between molecules of the two types which may be regarded as indicative of hydrogen bonding, while short intermolecular distances which may be interpreted in terms of hydrogen bonding are observed between molecules of the same type. Short intermolecular contact distances appear between the nitrogen atoms in the cyano group and the hydrazino group. The minimum intermolecular contact distance observed between molecules oriented near the sliding reflection plane is 2.92 Å, and occurs between $N_{(7)}...N_{(5)}$. The geometry corresponding to this intermolecular contact also appears to be favorable or suitable for hydrogen bond formation, with the $C_{(13)}N_{(7)}N_{(5)}$ angle equal to 175°, and the nitrile group essentially coplanar with the $c_{(8)}N_{(5)}N_{(6)}$ plane in the adjacent or neighboring molecule. The deviation from coplanarity is only 9°. We conclude, therefore, that in the crystal structure the type A molecules are bound via hydrogen bonds forming an infinite chain in the [001] direction.

The intermolecular distance between the analogous pair of nonbonded atoms in the second group of molecules (B) is equal to 3.05 Å, which is close to the sum of the van der Waals radii for two nitrogen atoms. The $C'_{(13)}N'_{(7)}N'_{(5)}$ angle in this case is 141°, and the deviation from coplanarity is 17°. Nevertheless, we assume that the molecules which are oriented along the screw axis are bound together via hydrogen bonding in this case as well. Our assumption is supported by the observation that the $C'_{(13)}N'_{(7)}$ bond in the nitrile group is clearly elongated. The superposition of all this structural evidence and data taken together leads us to conclude that the crystal structure represents an intermediate structure between two tautomeric forms (1) and (2), with prototropic tautomerism occurring by means of intermolecular hydrogen bonding.

Spectral studies in solution confirm our conclusion concerning the existence of prototropic tautomerism. In particular, studies of the electronic spectra of 6-hydrazinotrichloronicotinonitrile in aqueous alcohol solutions of varying degrees of acidity revealed a pronounced acidometric effect, indicative of proton equilibrium in a system due to NH-acidity. In acidic solution a bathochromic shift of its absorption maxima is observed as the pH is increased, while at pH ≥ 7 a new absorption maximum appears as 323 nm; the intensity of this new band increases with increasing pH of the solution, while λ_{max} remains unchanged in this case. The long-wavelength maximum can be attributed to a contribution from the quinoid form of the compound (2).



(1) (2)

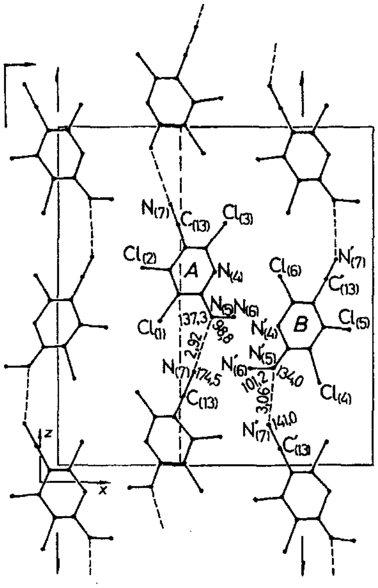


Fig. 2. Projection of a structural fragment along the ac plane.

TABLE 3. Atomic Coordinates ($\times 10^4$)

Atom	*x*	*y*	*z*	Atom	*x*	*y*	*z*
$\mathrm{Cl}_{(1)}$	2069(1)	925(1)	4301(0)	$\mathrm{Cl'}_{(1)}$	5336(1)	0,546(1)	2544(2)
$\mathrm{Cl}_{(2)}$	1681(1)	1268(1)	5933(2)	$\mathrm{Cl'}_{(2)}$	5963(1)	566(1)	4133(2)
$\mathrm{Cl}_{(3)}$	3434(1)	1148(1)	7173(2)	$\mathrm{Cl'}_{(3)}$	4495(1)	-18(1)	5745(2)
$\mathrm{N}_{(4)}$	3209(3)	941(3)	5729(6)	$\mathrm{N'}_{(4)}$	4476(3)	130(3)	4217(5)
$\mathrm{N}_{(5)}$	3083(3)	736(3)	4428(5)	N' (5)	4374(3)	261(3)	2868(5)
$\mathrm{N}_{(6)}$	3559(3)	615(3)	4391(6)	$\mathrm{N'}_{(6)}$	3909(4)	121(3)	2914(6)
$\mathrm{N}_{(7)}$	2251(5)	1458(4)	7867(7)	$\mathrm{N'}_{(7)}$	5671(4)	333(5)	6262(6)
$\mathrm{C}_{(8)}$	2890(3)	895(3)	5099(6)	$\mathrm{C'}_{(8)}$	4665(3)	271(4)	3511(6)
$\mathrm{C}_{(9)}$	2427(4)	996(4)	5139(6)	$\mathrm{C'}_{(9)}$	5122(5)	389(4)	3470(6)
$\mathrm{C}_{(10)}$	2261(4)	1139(3)	5850(7)	$\mathrm{C'}_{(10)}$	5392(4)	406(4)	4164(7)
$\mathrm{C}_{(11)}$	2563(4)	1187(4)	6496(7)	$\mathrm{C'}_{(11)}$	5213(4)	287(4)	4891(7)
$\mathrm{C}_{(12)}$	3023(3)	1094(4)	6414(6)	$\mathrm{C'}_{(12)}$	4767(5)	152(4)	4889(6)
$\mathrm{C}_{(13)}$	2426(6)	1,340(4)	7252(8)	$\mathrm{C'}_{(13)}$	5464(4)	303(4)	5635(7)

In conclusion, nucleophilic substitution of a Cl atom by a hydrazine group in tetrachloronicotinonitrile occurs at the 6-position, in contrast with the behavior in its isomeric substrate tetrachloropicolinonitrile, where the 4-position appears to be more active [14]. This difference may be rationalized in terms of supplementary stabilization of the negative charge by the CN group in the δ-complex formed by nitrile I, and the absence of such a stabilization effect in the δ-complex formed by tetrachloropicolinonitrile.

EXPERIMENTAL

IR spectra were recorded on a Specord M-80 spectrophotometer, UV spectra on a Beckman DI-7 spectrophotometer. Mass spectra were measured on a RIBER-MAG spectrometer at an ionizing energy of 70 eV and with direct sample introduction to the ion source. The course of reactions and the purity of compounds were monitored by TLC on Silufol UV-254 plates using 1:1 benzene–ethyl acetate as the eluent system.

The results of C, H, N elemental analysis agreed with calculations.

X-Ray Structural Analysis of Compound VII. Colorless, clean-edged (faceted) rhombic crystals gave the following unit cell parameters: a = 28.236(7), b = 3.757(3), c = 16.437(5) Å, space group $Pca2_1$, V = 1743.7 Å^3, m = 237.46, d_{calc} = 1.81 g/cm^3, Z = 8. The intensities of 1165 independent nonzero reflections of the type hol-h41 were measured on a DAR

-UM diffractometer using CuKα-radiation. A statistical test for centrosymmetry did not allow us to distinguish between two alternative space groups Pbcm and $Pca2_1$ or to make an unequivocal space group selection. The more probable structure would seem to be the centrosymmetric Pbcm space group with general multiplicity for the 8-position and hence one independent molecule in the unit cell. However, all attempts to solve and refine the structure by direct methods within the framework of this space group proved fruitless. The structure was therefore solved using a direct statistical method after assigning a "manual" working set of coordinates and reference reflections for the $Pca2_1$ space group; this space group assignment was then verified by the subsequent refinement process. The positional and thermal parameters were refined by full matrix least squares using anisotropic thermal approximations and the Roentgen-75 program complex to give a final R factor R = 0.061.

The hydrogen atoms could not be localized. The atomic coordinates are summarized in Table 3.

2,4,5,6-Tetrachloronicotinonitrile (I). Prepared according to a literature procedure [15].

6-Hydrazino-2,4,5-trichloronicotinonitrile (VII, $C_6H_3Cl_3N_4$). To a cooled solution (−35°C) of 2.42 g (10 mmoles) compound I in 60 ml chloroform was added with stirring a similarly cooled solution of 2 ml (20 mmoles) hydrazine hydrate in 10 ml ethyl alcohol. The reaction mixture was stirred for 2 h, and the temperature was then raised gradually to 0°C. The resulting precipitate was filtered rapidly, washed with ether (2 × 15 ml), water (3 × 15 ml), and cold ethyl alcohol (2 × 10 ml), then dried to give chromatographically pure crystalline product, yellow in color (R_f 0.50), mp 183-185°C (dec.). IR spectrum (KBr), cm^{-1}: 3304 ($NHNH_2$); 2224 ($C\equiv N$); 1636, 1580 (C=C, C=N). UV spectrum (C_2H_5OH), λ_{max} (log ε): 289.0 (4.28); 314.0 (4.11, sh). Mass spectrum, m/e: M^+ 236 (100). Yield 2.01 g (84.8%).

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