

NOTE

Synthesis and X-Ray Crystal Structure of 3-(Pyrazol-4-yl)propargyl Alcohol

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Abstract The crystal structure of the title compound has been determined by X-ray diffraction. The N and O atoms are involved in chains of hydrogen bonds, running through the whole crystal, which show proton disorder in a 1:1 ratio. This implies an inversion in the sense of the hydrogen bond network and the presence of inversion centers in the structure. Each molecule is engaged in two unconnected chains building sheets of molecules. An analysis of packing modes of NH-pyrazoles containing at least another hydrogen bond donor or acceptor site in the substituents has been performed.

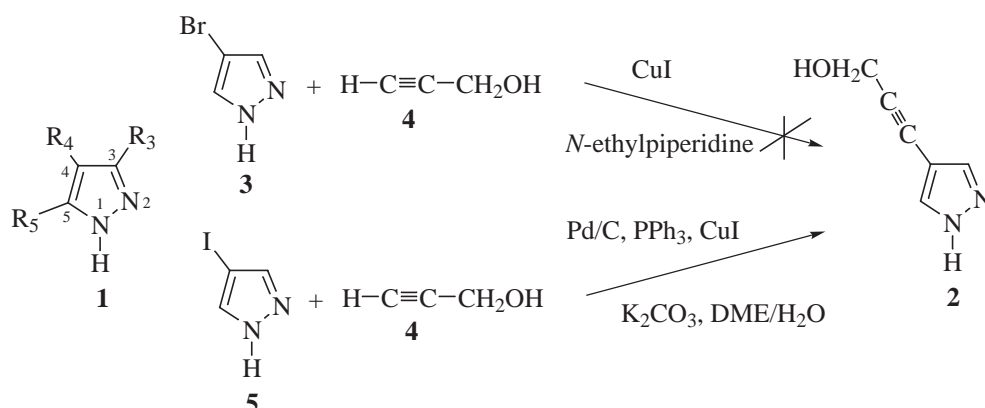
Keywords Pyrazole derivatives, Crystal structure, Hydrogen bond networks

Introduction

We are interested in the systematic exploration of hydrogen-bond (HB) networks of NH-pyrazoles in the solid state [1–4]. NH-Pyrazoles **1** are self-sufficient systems having one HB acceptor site (the N(2) nitrogen atom) and one HB donor site (the NH). They crystallize in two types of sys-

tems: chains and rings; among the latter, dimer, trimers, and tetramers.

When another HB donor or acceptor site is present in the C-substituents of the pyrazole moiety, the HB network becomes much more complex. We have summarized in Table 2 the different situations encountered in the literature including our results.



Results and Discussion

Chemistry

The synthesis of 3-(pyrazol-4-yl)-propargyl alcohol **2** was first attempted starting from 4-bromopyrazole **3** and propargyl alcohol **4** without success.

Then 4-iodopyrazole **5** and different conditions were used and the desired compound was obtained in 60% yield (see Experimental Section). Crystals for the X-ray determination were obtained in ethanol-water 1:1.

X-Ray Crystallography

The bond lengths and angles in the pyrazole moiety display a quite symmetric pattern due to the proton disorder observed between both nitrogen atoms (Table 1, Fig. 1). The ring is not significantly planar ($\chi^2=11.78$ vs a tabulated value of 5.99) [5] and the carbon atoms of the substituent deviate progressively from its least-square plane (0.026(2), 0.042(2), and 0.043(2) Å for C(6), C(7), and C(8) respectively). The oxygen atom is out of the pyrazole plane and the angle between the C(7), C(8), and O(9) least-square plane and the pyrazole one is 86.1(1)°. The C(6)-C(7) bond distance is not significantly different from that reported for the triple bond in organic compounds [6] retrieved from the Cambridge Structural Database (CSD hereinafter) [7],

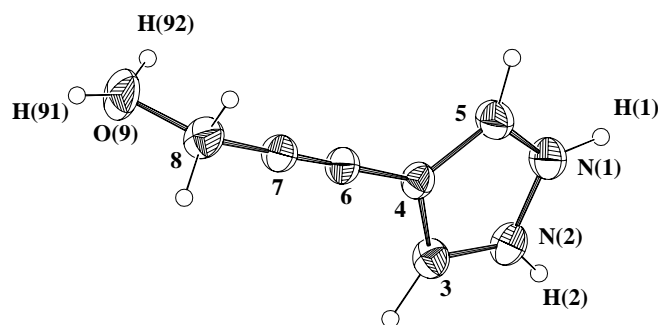


Figure 1 A perspective view of the title compound displaying the numbering scheme. The disordered hydrogen atoms, H(1)/H(2) and H(91)/H(92), are represented at both locations (population parameter: 0.5 for each one). Anisotropic displacement parameters are drawn at 30% probability level

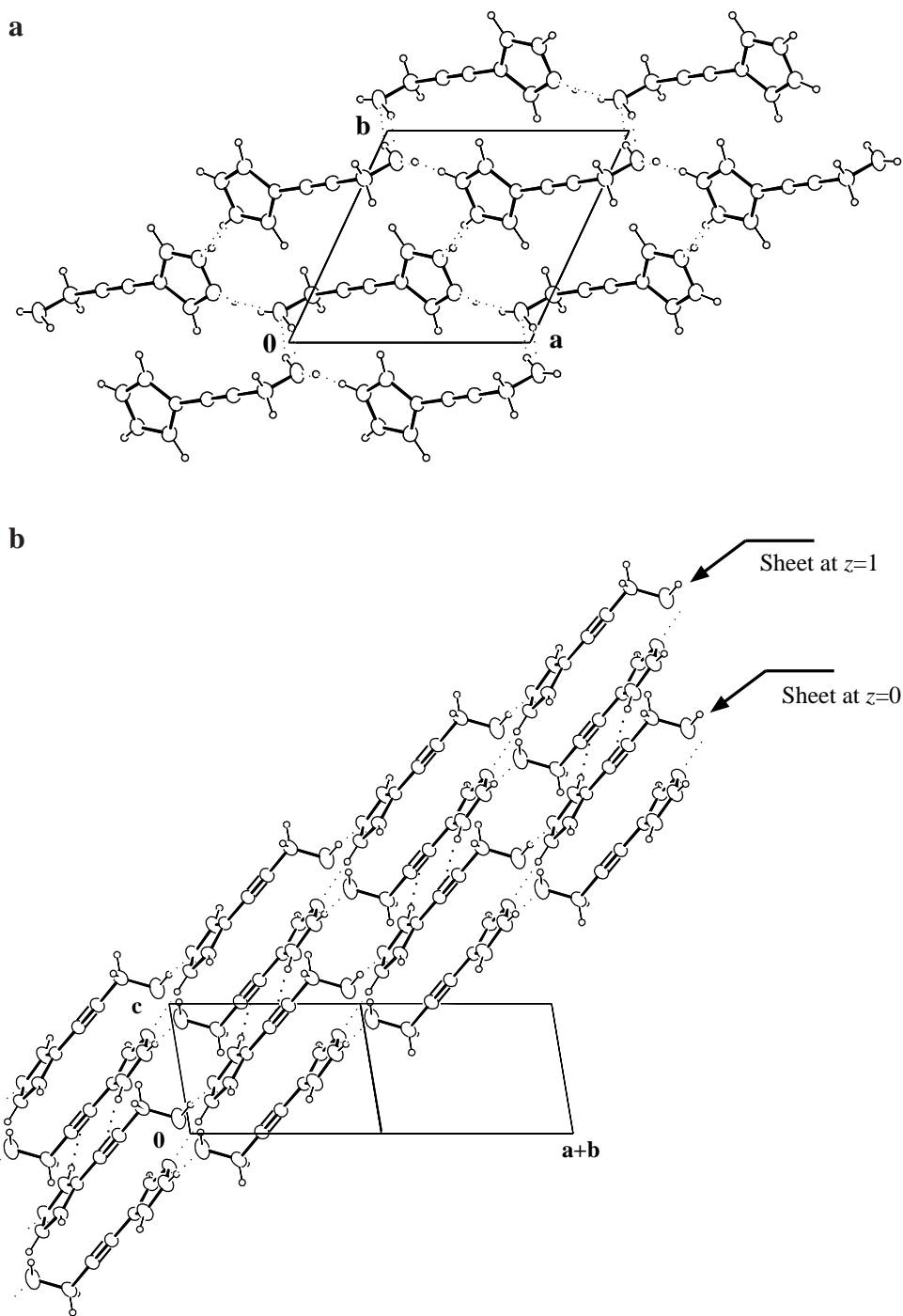
1.181(14) Å for C,H-C≡C-C,H, although the bond length is slightly elongated, following the same tendency reported in the referenced work [6]; 1.189(10) Å for C≡C-C(*sp*²,*ar*) and 1.192(10) Å for C≡C-C≡C where a small amount of electron delocalization could be observed.

The molecules are linked by OH...O, NH...N, OH...N and NH...O hydrogen bonds to form sheets of molecules parallel to the plane defined by the vectors **a**+**c** and **b**+**c** (Table 1, Fig. 2). Each sheet contains monodimensional hydrogen

Table 1 Selected geometrical parameters (Å, °)

N(1)-N(2)	1.345(2)	C(4)-C(6)	1.425(2)
N(1)-C(5)	1.323(3)	C(6)-C(7)	1.193(2)
N(2)-C(3)	1.321(2)	C(7)-C(8)	1.458(3)
C(3)-C(4)	1.387(2)	C(8)-O(9)	1.404(3)
C(4)-C(5)	1.385(2)		
N(2)-N(1)-C(5)	108.6(2)	C(3)-C(4)-C(6)	128.3(1)
N(1)-N(2)-C(3)	108.4(2)	C(5)-C(4)-C(6)	127.9(2)
N(2)-C(3)-C(4)	109.7(1)	C(4)-C(6)-C(7)	179.9(2)
C(3)-C(4)-C(5)	103.9(1)	C(6)-C(7)-C(8)	179.0(2)
N(1)-C(5)-C(4)	109.5(2)	C(7)-C(8)-O(9)	111.7(2)
N(2)-C(3)-C(4)-C(6)	178.8(2)	C(6)-C(7)-C(8)-O(9)	140.4(10)
C(6)-C(4)-C(5)-N(1)	-178.7(2)	C(4)-C(6)-C(7)-C(8)	38.9(8)
Hydrogen interactions			
	D-H	H...A	D...A
O(9)-H(92)...O(9)(-x,-y,-z)	0.99(10)	1.80(9)	2.705(2)
O(9)-H(91)...N(1)(x-1,y,z-1)	0.81(6)	2.00(5)	2.771(2)
N(2)-H(2)...N(2)(1-x,1-y,2-z)	0.89(3)	1.99(3)	2.869(2)
N(1)-H(1)...O(9)(x+1,y,z+1)	0.90(5)	1.88(6)	2.771(2)
C(3)-H(3)...O(9)(-x,1-y,1-z)	1.01(2)	2.84(2)	3.654(2)
C(5)-H(5)...Cent(C6≡C7)(1-x,-y,-z)	0.99(2)	2.78(2)	3.763(2)

Figure 2 a-b **a** A packing diagram down the *c* axis showing two superimposed layers of hydrogen bonded molecules and the disordered chains of hydrogen bonds along the **a–b** direction. **b** Same as **a** but down the **a–b** axis and displaying only one model of disordered positions for the hydrogen atoms. The OH...O hydrogen bond that completes the chain has also been omitted to clarify the drawing. Both layers are interconnected by CH...||| hydrogen contacts that have been explicitly indicated on the figure



bond networks that run along the **a–b** direction. The hydrogens involved in the bonds – H(1)/H(2) and H(91)/H(92) – are disordered (see experimental) giving rise to the inversion of the donor and acceptor behavior of the N and O atoms depending on which disordered position is considered. Furthermore, the individual situation actually present in one chain is independent of the situation in any other. Due to the equal probability of both possible arrangements, the overall result in the crystal is a 50/50% disorder. There are

two additional weak hydrogen contacts; one of the quite well characterized CH...O type [8] between molecules within the same sheet and the other is of the more unusual CH...||| type [9], which is the only directional interaction found that interconnects the sheets of molecules. The CH...O interaction is on the weak side of the distribution according to the H...O distance displayed by CH...OH acceptors [8c], (mean value of 2.52(11) Å; the e.s.d. has been estimated from the mean values of five data subsets). However,

er, the interaction involving the triple bond seems to be on the strong side, as compared with the mean value for the H..Centroid (C≡C) distance, 2.83(18) Å, of 11 reported structures [9] containing C(sp)-H...||| interactions (no data have been found for C(sp²)-H nor C(Ar)-H donor groups). There are no voids in the structure and the total packing coefficient [10] is 0.73 ($C_k^{all} = V_{molecules}/Unit\ Cell\ Volume$).

A search in the CSD (October 1997 release) has been performed to retrieve all NH-pyrazole derivatives bearing a functional group which is involved in hydrogen bonds with the nitrogen atoms of the pyrazole moiety, either as an ac-

ceptor (pz-NH...X) or as a donor (Y-H...N-pz). Our main aim was to classify and describe the main types of HB networks displayed by these compounds. The imposed restrictions were: R factor value less than 0.10 and only one chemical species present in the crystal (this excluded salts, hydrates, and other clathrates or host-guest complexes). Table 2 gathers a summary of the search results together with the description of the hydrogen bond network. Another two new structures have been added to the 13 found in the CSD; one is the corresponding to the title compound and the other (3-nitropyrazole) has been recently reported by us [11]. In

Table 2 Hydrogen-bond networks in crystals of NH-pyrazoles possessing one or more C-functional groups. Atoms involved in hydrogen bonds with the pyrazole moiety are in bold face and the ones they are not are underlined

NH-Pyrazole	REFCODE	Group(s) Description
3(5)-(2'-Hydroxyphenyl)pyrazole	KUFVAI	pz- NH , OH cyclic dimer
3,5-bis(4-Methylpyrazolyl)-4-methylpyrazole	YAXZOM	pz- NH , N(Ar) cyclic dimer
3-Nitropyrazole	Ref. 11	pz- NH , pz- N , - NO₂ classic pyrazole trimer + NH..O inside trimer (bifurcated H bond)
5-(2-Benzylaminoethyl)-3-phenyl	BIWWEJ	pz- NH , - NH - 1-D network
2,7-Dimethyl-6-(pyrazol-3'-yl)pyrazolo (1,5-a)pyrimidine	LEVVAJ	pz- NH , N(Ar) 1-D network
3-(2-Furoyl)-4,5-bis(methoxycarbonyl) pyrazole	BEWLEU ^a	pz- NH , CO , - O -(furan) 1-D network (bifurcated H bond)
4-(Di- <i>t</i> -butylhydroxysiloxy)-5-(2,2- dimethyl-1-oxopropyl)-1 <i>H</i> -pyrazole	KOSFUT	pz- NH , CO ; pz- N , SiOH 2 cyclic dimers => Chain
4-Acetyl-1-(4-cyanopyrazol-3-yl)- 5-methylpyrrole-2-carboxylic acid	BENSES	pz- NH , - COOH , - CN , 1-D network (bifurcated H bond) - COMe 2-D network
beta-(3-Pyrazolyl)-L-alanine	PYRZAL10	pz- NH , COO ⁻ ; pz- N , NH₃⁺ 2-D network
3-(Pyrazol-4-yl)propargyl Alcohol	This work	pz- NH , pz- N , - OH 2-D network
3-Amino-4-acetyl-5-methylpyrazole	VORNIZ	pz- N , NH₂ ; pz- NH , COMe cyclic dimer; 2-D network
3-Methyl-4-bromo-5-carboxamide-pyrazole	MBCPAZ ^a	pz- N , NH₂ ; pz- NH , CONH₂ cyclic dimer; 2-D network
3,5-Di- <i>t</i> -butyl-4-nitropyrazole	WILBAU	pz- NH , pz- N , NO₂ classic pyrazole dimer => 2-D network (bifurcated H bond)
3,5-Pyrazoledimethanol	TARCOE	pz- NH , pz- N , OH 2-D network OH 3-D network
3-Hydroxy-5,5'-dimethyl-4,4'-bi-1 <i>H</i> -pyrazole	HDMPYZ	pz- NH , - O ⁻ ; pz- N , NH(Ar) 3-D network

^a Hydrogen atom coordinates not present in CSD. The hydrogen bond network has been established according to geometrical considerations (bond distances and angles)

spite of the small amount of data available up to now, several remarks can be established. First, it is worth mentioning that all structures display the pz-NH (N_1 in Scheme 1) involved in hydrogen bonds (four of them are bifurcated interactions) while in only nine cases did the pz-N (N_2 in Scheme 1) act as an acceptor of a hydrogen bond. This could be an indication that the donor ability of the pz-NH group is bigger than the acceptor ability of the pz-N. Second, there is a preference for the hydrogen bond network displayed by these molecules, as far as the pyrazole moiety is involved in the network, to be mono- or bi-dimensional rather than tri- or zero-dimensional (five and six cases vs one and three respectively). The title compound fits into the

most populated group, bi-dimensional networks, although the lack of data suggests that more structural studies are needed to reach more general and accurate conclusions.

Experimental Section

General Methods

^1H and ^{13}C NMR spectra were recorded on a Varian Gemini 200 apparatus (^1H at 199.99 MHz and ^{13}C at 50.29 MHz),

Table 3 Crystal analysis parameters at room temperature

Crystal data

Formula	$\text{C}_6\text{H}_6\text{N}_2\text{O}$
Crystal habit	Colourless plate
Crystal size (mm)	$0.50 \times 0.33 \times 0.05$
Symmetry	Triclinic, $P-1$
Unit cell determination:	Least-squares fit from 59 reflections ($\theta < 45^\circ$)
Unit cell dimensions ($\text{\AA}, ^\circ$)	$a = 8.3981(5)$ $\alpha = 102.666(6)$ $b = 8.3419(6)$ $\beta = 92.884(5)$ $c = 4.9252(2)$ $\gamma = 64.908(6)$
Packing: $V(\text{\AA}^3)$, Z	304.52(4), 2
Dc(g/cm ³), M, F(000)	1.332, 122.126, 128
$\mu(\text{cm}^{-1})$	7.84

Experimental data

Technique	Four circle diffractometer: Philips PW1100, Bisecting geometry. Graphite oriented monochromator: $\omega/2\theta$ scans Detector apertures $1 \times 1^\circ$. 1 min/reflect. $\text{CuK}\alpha$ radiation. $\theta_{\text{max}} 65^\circ$, Scan width: 1.6°
Number of reflections:	
Independent	1040
Observed ($3\sigma(I)$ criterion)	956
Standard reflections:	2 reflections every 90 min. No variation
Extinction coeff. ($\times 10^4$)	0.20(4)

Solution and refinement

Solution	Direct methods: Sir92
Refinement:	Least-Squares on F_o , full matrix
Parameters:	
Number of variables	115
Degrees of freedom	841
Ratio of freedom	8.3
H atoms	From difference synthesis
Weighting-scheme	Empirical as to give no trends in $\langle w\Delta^2F \rangle$ vs $\langle F_{\text{obs}} \rangle$ and $\langle \sin\theta/\lambda \rangle$
Max. thermal value (\AA^2)	$U_{33}[\text{O}(9)] = 0.104(1)$
Final ΔF peaks ($\text{e}\text{\AA}^{-3}$)	0.27
Final R and Rw	0.042, 0.043

and chemical shifts are expressed in parts per million (δ) relative to tetramethylsilane.

3-(Pyrazol-4-yl)-propargyl alcohol (2)

To 14 ml of a 50:50 mixture of 1,2-dimethoxy ethane and water previously degassed with argon stream, is added 0.78 g (4 mmol) of 4-iodopyrazole, 1.38 g (2.5 eq.) of potassium carbonate, 46 mg (6%) of cuprous iodide, 126 mg (12%) triphenylphosphine and 128 mg (3%) of 10% palladium over carbon. The resulting suspension is left under argon stream for 15 min. Then 0.6 ml (2.5 mmol) propargyl alcohol is added dropwise via syringe. The reaction mixture is stirred at 80 °C for 24 h, and filtered through a small pad of Celite. The dimethoxyethane is eliminated under reduced pressure. The aqueous solution is acidified with 3 mol/l hydrochloric acid and extracted twice with toluene. Organic extracts are discarded and the aqueous layer is made basic with solid potassium carbonate. Extraction is then performed several times with ethyl acetate. Combined organic extracts are dried over sodium sulfate affording the crude product as a yellow solid. Purification by flash chromatography over silica (ethyl acetate) affords 0.29 g (60% yield) of a white solid. M.P. 171 °C, FAB⁺ (NBA) 123.1 (MH⁺). ¹H NMR (CD₃OD+CF₃CO₂H) : 7.72 (s, 2H), 5.01 (s, 2H), 4.36 (s, 2H). ¹³C NMR (CD₃OD+CF₃CO₂H) : 137.9, 103.9, 89.8, 77.1, 51.6.

Crystal Structure of Compound 2

Table 3 contains the experimental details and the most relevant parameters of the refinement. The structure was solved by direct methods, SIR92 [12]. The non-hydrogen atoms were refined anisotropically and the hydrogen ones, found unambiguously in the Fourier difference synthesis, were included and refined (without restraints) as isotropic. The population parameters for all the disordered hydrogen atoms, H(1)/H(2) and H(91)/H(92), have the value of 0.50, giving rise to the symmetry corresponding to space group P-1. The 50% disorder of the H atoms on the pyrazole ring has also been confirmed by the values of the intra-annular bond angles at both N atoms, which present almost the same value (Table 1) [3]. The structure refinement in P1 was also attempted, but the high correlation found between structural parameters, together with the non-sense geometry presented by the refined model, led us to reject this possibility. The calculations were carried out with the XTAL3.2 [13] PESOS [14] and PARST [5] sets of programs. The atomic scattering factors were taken from the International Tables for X-Ray Crystallography, Vol. IV [15].

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Supplementary Material List of the structure factors, atomic coordinates, and anisotropic displacement compo-

nents for the non-hydrogen atoms, hydrogen atom parameters, bond lengths, and bond angles have been deposited in electronic available format.

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