Direct Evidence for the Existence of Both Tautomeric Forms of 4-Hydroxypyridines in the Solid State

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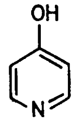
Summary Single-crystal X-ray diffraction studies have shown that 3,5-dichloro-2,6-dimethyl-4-hydroxypyridine exists in the pyridone (oxo) form in the solid, while tetrachloro-4-hydroxypyridine exists as the pyridinol (hydroxy) tautomer.

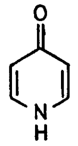
I.r. and u.v. evidence[1] shows that 2- and 4-hydroxypyridines exist predominantly as pyridone tautomers and this is supported by the crystal structure of 2-pyridone.[2] We report the unexpected observation that tetrachloro-4-hydroxypyridine (I) exists in the solid as the pyridinol tautomer (a), whereas the closely related compound 3,5-dichloro-2,6-dimethyl-3-hydroxypyridine (II)[3] is found as the pyridone in the crystalline state.

The primary evidence for this result is the location of the hydrogen atoms in the two crystal structures. Compound (I) forms O–H···N hydrogen bonds of length 2·740 Å, with d(O–H) = 0·93 Å, d(H···N) = 1·88 Å and the angle O–H···N of 153°. In (II), the hydrogen bonds are of the N–H···O type and of length 2·755 Å, with d(N–H) = 0·81 Å, d(H···O) = 1·96 Å, and the angle N–H···O = 167°. Errors in the hydrogen positions are of the order of 0·1 Å.)

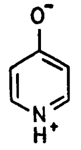
Different types of hydrogen-bonded chains occur in the two structures. In (II), the hydrogen bonds are nearly collinear with the carbonyl bonds [the angle C = O···N(H) is 174·7°] resulting in linear chains parallel to the a-axis. The crystal structure of (I) contains C–O(H)···N angles of 135·5° and helical chains generated by the b-glide of the space group.



(a)



(b)



(c)

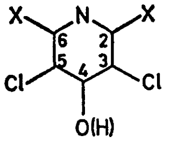
The bond distances and angles (Table) also support the presence of hydroxy- and oxo-tautomers in the respective species. Chatar Singh[4] has noted that, for six-membered rings, the internal angle at a nitrogen with an extra-annular hydrogen is significantly larger (greater than 120°) than at a

TABLE

Selected bond distances and angles

Distances	Compound (I)	Compound (II)	Angles	Compound (I)	Compound (II)
N–C(2)	1·330(6)	1·353(8)	C(2)–N–C(6)	116·6(5)	123·0(6)
C(2)–C(3)	1·364(7)	1·352(8)	N–C(2)–C(3)	124·9(5)	118·3(6)
C(3)–C(4)	1·395(7)	1·446(9)	C(2)–C(3)–C(4)	118·5(5)	123·5(6)
C(4)–C(5)	1·402(7)	1·421(9)	C(3)–C(4)–C(5)	117·3(5)	113·0(6)
C(5)–C(6)	1·373(7)	1·351(8)	C(4)–C(5)–C(6)	119·2(5)	123·5(6)
C(6)–N	1·336(6)	1·370(8)	C(5)–C(6)–N	123·4(5)	118·6(6)
C(4)–O	1·321(6)	1·253(7)			
C(2)–CH_3		1·490(8)			
C(2)–Cl	1·726(5)				
C(3)–Cl	1·715(5)	1·738(7)			
C(5)–Cl	1·717(5)	1·733(6)			
C(5)–CH_3		1·495(9)			
C(5)–Cl	1·717(5)				

nitrogen without an attachment (less than 120°). Here the angle C–N–C clearly suggest the presence of an N–H function in (II), and its absence in (I). In addition, the C–O bond length in (II) (1·253 Å) approaches the value of 1·215 Å in aldehydes and ketones,[5] while the 1·321 Å distance in (I) is closer to 1·36 Å characteristic of C–O bonds in aromatic alcohols.[5] Finally, the ring distances (Table) show that the localized valence structure (b) plays an important role in (II), whereas the bonds in (I) are generally similar to those of pyridine[6] [N–C(2), 1·340; C(2)–C(3), 1·394; C(3)–C(4), 1·394).[6]



(I) X = Cl
(II) X = Me

The intensities of 1797 [compound (I)] and 679 [compound (II)] unique reflections were measured on a 4-circle diffractometer using monochromatized Mo-K_α radiation. The crystal structure of compound (I) was solved by symbolic addition, and that of (II), where the molecules lie in the mirror planes at $y = 1/4$ and $y = 3/4$, by Patterson techniques. Each structure was refined by full-matrix least-squares assuming thermal anisotropy for non-hydrogen atoms and including anomalous scattering coefficients for Cl. Final R factors were: (I); $R_1 = 6{\cdot}5\%$, $R_2 = 8{\cdot}2\%$ (1400 reflections above background); (II); $R_1 = 4{\cdot}4\%$, $R_2 = 3{\cdot}5\%$ (421 reflections above background).

Crystal Data: Compound (I); C_5HCl_4NO, $M = 232{\cdot}90$, orthorhombic, $a = 12{\cdot}439(7)$, $b = 12{\cdot}775(6)$, $c = 9{\cdot}882(6)$ Å, $U = 1570{\cdot}3 \times 10^{-24}$ cm^3, $Z = 8$, $D_X = 1{\cdot}970$, space group $Pbca$, μ (Mo-K_α) = 14·3 cm^{-1}. Compound (II); $C_7H_7Cl_2NO$, $M = 192{\cdot}06$, monoclinic, $a = 6{\cdot}795(9)$, $b = 6{\cdot}932(13)$, $c = 8{\cdot}746(15)$ Å, $\beta = 103{\cdot}56(7)°$, $U = 400{\cdot}4 \times 10^{-24}$ cm^3, $Z = 2$, $D_X = 1{\cdot}593$, space group $P2_1/m$, μ (Mo-K_α) = 4·1 cm^{-1}.

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[2] B. R. Penfold, *Acta Cryst.*, 1953, **6**, 591.

[3] Compound (II) is the active ingredient in COYDEN® anticoccidials, The Dow Chemical Company, Midland, Michigan, U.S.A.

[4] Chatar Singh, *Acta Cryst.*, 1965, **19**, 759, 767, 861.

[5] L. E. Sutton, *Chem. Soc., Special Publ.*, 1965, **18**, S16s—S21s.

[6] B. Bak, L. Hansen-Nygaard, and J. Rastrup-Andersen, *J. Mol. Spectroscopy*, 1958, **2**, 361.