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TAUTOMERISM AND ROTAMERISM IN 2-(2-PHENYLHYDRAZINO)PYRIDINE

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The title compound is shown by X-ray crystallography and NMR spectroscopy to exist both in the solid state and in solution as such. Deuterium-induced shifts confirm the phenylamino structure for 2-phenylaminopyridine.

Keywords: 2-(2-phenylhydrazino)pyridine, rotamerism, tautomerism, X-ray diffraction analysis.

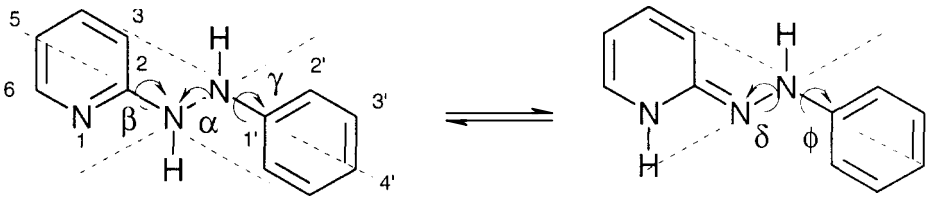
Pyridines with NH–X substituents in the 2-position of the ring are potentially tautomeric. An early review [1] demonstrated that amino-derivatives of six-membered heteroaromatic rings usually exist predominantly in the amino form and discounted various claims to the contrary. Later [2], these conclusions were confirmed for the NH_2 group, while for NHX groups it was shown that the nature of X could have a profound influence and that electron-withdrawing X groups increase the importance of the imino form in the order:

alkyl (little effect) < COR < SO_2R, NO_2, CN (large effect)

This influence was ascribed to a combination of (i) the influence of X on the NHX acidity and (ii) conjugation effects. In several cases both the ring nitrogen atom and also the X substituent can be involved in the formation of tautomers. In 2-NHX substituted pyridines, rotation of the NHX moiety around the ring-N bond, as well as rotation of the X group around the N–X bond, can produce several conformational energy minima.

Since the comprehensive reviews [1, 2] were written, considerable further attention has been paid to the problem of tautomerism and rotamerism in 2-NHX pyridines. Compound classes investigated include those in which X is nitro [3-7], phenylazo [8], SO_3 [9], and acyl [10-12]. Although the UV spectra of 2-acetamido- and 2-benzylamidopyridine were initially interpreted to support the acylimino form [10, 11], the conclusion from the totality of this work [3-12] is that, whereas 2-nitroaminopyridine exists predominantly in the nitroimino form, all 2-acylaminopyridines exist as such.

In the present paper, the tautomerism and rotamerism of 2-(2-phenylhydrazino)pyridine **1** are discussed in detail; 2-phenylaminopyridine **3** is also investigated.



1 **2**

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EXPERIMENTAL

2-(2-phenylhydrazino)pyridine (1) was prepared according to Beyer *et al.* [13]. The ^{1}H and ^{13}C NMR spectra of 2-(2-phenylhydrazino)pyridine **1** were recorded in $CDCl_3$ and DMSO-d_6. DIS measurements were performed using ^{1}H broadband decoupling. The recycling time was set to 10 s and 16 K points were acquired for a typical spectral window of 5200 Hz, recording *ca* 3000 transients. The FID data were zero-filled prior to Fourier transformation, providing a digital resolution of *ca* 5 ppb per point.

Crystallography. A sample of 2-(2-phenylhydrazino)pyridine (**1**) freshly recrystallized from dichloromethane was utilized. All measurements were made at -125°C with a Siemens P4S four-circle diffractometer by using monochromatized MoKα (λ = 0.7107Å) radiation. Throughout data collection the intensities of three standard reflections were monitored at regular intervals and the intensities varied by <2%. Intensities were corrected for Lorentz and polarization effects but not for absorption. The structure was solved by direct methods using SHELXS [14] and refined on F^2 using all data by full-matrix least-squares procedures using SHELXTL [15]. All non-hydrogen atoms were refined with anisotropic displacement coefficients. The NH hydrogen atoms were found from a difference map and their positions refined. The CH hydrogen atoms were included in calculated positions with isotropic displacement coefficients equal to 1.3 times the isotropic equivalent of their carrier carbons. The function minimized was $\Sigma w(F_o^2 - F_c^2)^2$, with $w = [\sigma^2(F_o^2) + 0.0566P^2 + 0.01P]^{-1}$, where $P = [\max(F_o^2) + 2F_c^2]/3$. A final difference map showed no features greater or less than 0.16 $e^-/Å^3$.

Crystal data. $C_{11}H_{11}N_3$, M = 185.2. Monoclinic, a = 9.642(1), b = 11.088(1), c = 9.837(1) Å; β = 113.77(1)°, V = 962.5(2) $Å^3$ (by least-squares refinement on diffractometer angles for 59 accurately centered reflections), space group $P2_1/c$, $F(000)$ = 392, Z = 4, D_c = 1.278 $g \cdot cm^{-3}$. μ(MoKα) = 0.80 cm^{-1}. Colorless block, 0.88 × 0.62 × 0.41 mm, ω scans, $2\theta_{max}$ = 52°, 133 parameters, S = 1.03, wR = 0.0919 for all 1881 data, R = 0.0338 for 1419 data with $F_o > 4\sigma(F_o)$.

RESULTS AND DISCUSSION

The structure of 2-(2-phenylhydrazino)pyridine (**1**) in the solid state was determined by single crystal X-ray crystallography at -125°C. Figure 1 shows a perspective view and atom labelling of the structure. The NH-hydrogen atoms were unambiguously located from Fourier difference maps and their positions refined, thereby confirming the tautomeric structure **1**.

In the solid state, the conformation of the molecule is determined by the torsion angles a = 85.8(2)°, β = 11.0(2)°, and γ = 9.6(2)°, as defined above. Thus, the two aryl substituents are approximately orthogonal and the N(1')–N(2') bond is approximately coplanar with each of the two aryl rings. These features, along with the relatively short N–N [1.386(1) Å] and C–N [1.380(2), 1.392(2) Å] bond lengths, suggest conjugation of the aryl

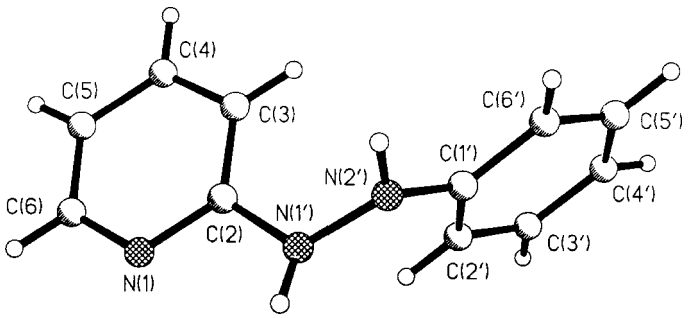


Fig. 1. Perspective view and atom labelling of the crystal structure of 2-(2-phenylhydrazino)pyridine (**1**).

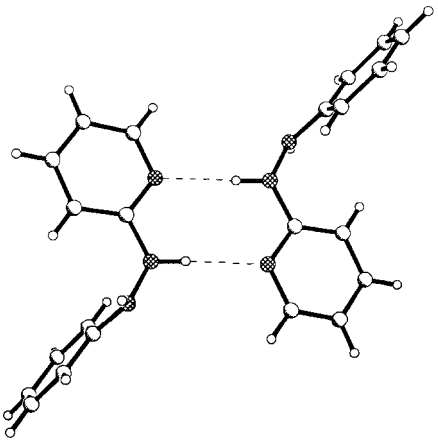
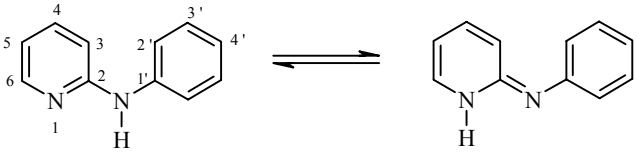


Fig. 2. Perspective view of the 2-(2-phenylhydrazino)pyridine (**1**) dimer.

π-systems with the nitrogen lone pairs. Similar features have previously been noted in the structure of l,2-diphenylhydrazine [16], which is, surprisingly, the only other 1,2-diarylhydrazine in the Cambridge Structural Database. In the solid state, the conformation of the molecule and the molecular packing appear to be controlled by pairs of linear intermolecular hydrogen bonds between N(1')H and N(l) of molecules related by a crystallographic center of inversion, with an N···N separation of 3.047(2) Å.

The existence of tautomer **1** for 2-(2-phenylhydrazino)pyridine and the tautomer **3** for 2-phenylaminopyridine in solution was supported by NMR chemical shifts, including deuterium secondary isotope effects on the ^{13}C chemical shifts (DIS). We have previously demonstrated the utility of DIS in the elucidation of heteroaromatic tautomerism [12, 17]. Briefly, the method relies on the fact that when a proton is replaced by a deuterium, carbons two or three bonds away display a shielding of the order of 0.1 ppm (a positive DIS of *ca.* 100 ppb). A partially deuterated sample of compound **3** was obtained by shaking the $CDC1_3$ solution with a mixture of H_2O:D_2O in a ratio 2:1 and then removing the aqueous layer. The DIS measured for compound **3** in the resulting $CDCl_3$ solution are presented in Table. For compound **1,** the DIS given in Table 1 were measured for a DMSO solution, as fast H–D exchange precluded the use of $CDCl_3$. Table 1 also presents unambiguous assignments of the ^1H and ^{13}C chemical shifts, made on the basis of ^1H–^1H and direct and long-range ^1H–^{13}C correlation spectra.



3 **4**

The DIS clearly demonstrate that compound **3** exists in $CDC1_3$ solution mainly as 2-phenylaminopyridine. DIS values of 89 and 127 ppb at the carbons at positions l' and 2' respectively are expected for the tautomer **3,** and are incompatible with tautomer **4**. Interpretation of the DIS for compound **1** is complicated by the presence of two exchangeable protons. However, similarity of the ^{13}C chemical shifts for the pyridine ring in compounds **1** and **3** also indicates that compound **1** exists in $CDCl_3$ solution mainly as tautomer **1**. Moreover, the fact that both C2 and Cl' experience DIS from two exchangeable protons and the similarity of the DIS values for C2 and Cl' is more compatible with tautomer **1** than with tautomer **2**.

TABLE 1. ^{1}H and ^{13}C Chemical Shifts and DIS Values in Compounds **1** and **3**

Position	**1** in DMSO			**1** in $CDCl_3$		**3** in $CDCl_3$		
	δH (ppm)	δC (ppm)	DIS (ppb)	δH (ppm)	δC (ppm)	δH (ppm)	δC (ppm)	DIS (ppb)
2	—	160.8	55, -10	—	160.6	—	156.3	104
3	6.65	105.7	-52	6.75	106.3	6.85	107.9	—
4	7.50	137.5	—	7.45	138.2	7.38	137.5	—
5	6.71	118.0	-59	6.80	120.1	6.63	114.5	—
6	8.08	147.7	—	8.10	147.8	8.17	148.0	—
NH	8.29, 7.80	—	—	6.30, 5.87	—	8.14	—	—
1'	—	149.6	59,-13	—	148.2	—	140.6	89
2'	6.80	111.8	-51	6.76	112.4	7.28	120.4	127
3'	7.16	128.8	23	7.20	129.3	7.27	129.1	—
4'	6.66	113.7	-42	6.65	115.2	6.99	122.5	—

The results reported in this paper show satisfactory internal consistency and support the general view that tautomeric structures of substituted amino heterocycles XNH–Het generally exist in the amino form except when X is a very strong electron-withdrawing group such as NO_2.

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