A ^1H and ^{13}C Nuclear Magnetic Resonance and X-Ray Diffraction Study of the Tautomerism of 2-Hydroxy- and 2,3-Dihydroxy-pyridine *N*-Oxides. X-Ray Molecular Structure of 2-Hydroxypyridine *N*-Oxide

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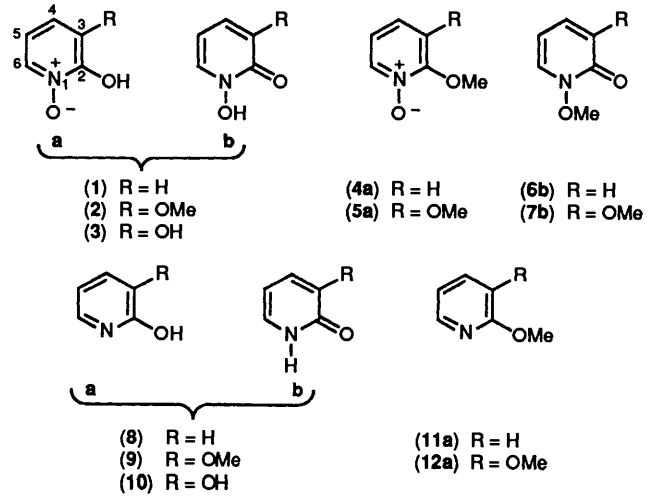
From a ^1H and ^{13}C NMR study, in dimethyl sulphoxide, of twelve 2-hydroxy-, 2,3-dihydroxy-pyridines, 2,3-dihydroxypyridine *N*-oxides, and their methoxy derivatives it is possible to conclude that both pyridin-2-ones and 1-hydroxypyridine-2-ones exist in solution as 2-oxo tautomers. The molecular structure of 2-hydroxypyridine *N*-oxide has been determined by X-ray diffraction methods; as in solution, this compound exists in the crystal state as the 1-hydroxypyridin-2-one tautomer.

Early studies on the tautomerism of 2- and 4-hydroxypyridine *N*-oxides were developed mainly in the fifties.[1] In spite of some molecular calculations showing that the tautomeric equilibria were displaced towards the 2- and 4-hydroxy forms (herein called series **a**),[2] the work done by Gardner and Katritzky,[3] using UV and IR spectroscopy, showed that 2-hydroxypyridine *N*-oxide exists in solution mainly as 1-hydroxypyridine-2-one tautomer (**b** series).

More recently, NMR spectroscopy was introduced as a valuable diagnostic tool to assess the preferred tautomer. Chemical shifts and coupling constants of protons and carbons were used to determine the tautomeric equilibria of 2- and 3-hydroxypyridines.[4–6] This technique was also applied to the study of 3-hydroxypyridine *N*-oxide and a zwitterionic structure was proposed.[7]

To our knowledge, no other systematic NMR work has been done with hydroxy- and polyhydroxy-pyridine *N*-oxides to assign unambiguously the hydroxypyridine *N*-oxide **a** or the *N*-hydroxypyridone **b** structures. In this work we have studied the 2-hydroxy- and 2,3-dihydroxy-pyridine *N*-oxides, the hydroxypyridines, and pyridones depicted by ^1H and ^{13}C NMR spectroscopy.



Model compounds (**4a**) and (**5a**) have a fixed *N*-oxide structure and compounds (**6b**) and (**7b**) a fixed pyridin-2-one structure. ^1H and ^{13}C NMR spectroscopy of both types of compound has been undertaken to establish the characteristics which can be used to distinguish between the tautomeric forms.

Simultaneously an X-ray study of compound (**1**) was undertaken in order to determine its tautomeric structure in the crystal phase.

Experimental

Materials.—Compounds (**9**), (**10**), and (**11a**) were purchased from commercial sources and were used without further purification. The following compounds were prepared according to literature procedures: (**1**);[8] (**4a**);[3] (**2**) and (**5a**);[9] (**12a**).[10] Compound (**3**) was obtained from the ether (**2**) (0.8 g, 7 mmol) by heating it with 49% HBr (16 ml) at 120 °C for 17 h. Evaporation of solvent to dryness under reduced pressure gave a crude sample of compound (**3**) (47%). Subsequent sublimation gave a solid, which was crystallized from butan-1-ol to afford pure compound (**3**), m.p. 182–184 °C (lit.,[11] 188–190 °C). Compounds (**6b**) and (**7b**) were prepared by thermal rearrangement of *N*-oxides (**4a**) and (**5a**) at 120 °C for 6 h. They were isolated as oils by column chromatography on silica gel with methylene dichloride as solvent. Compound (**1**) was sublimed and recrystallized from benzene–ethanol to obtain crystals suitable for X-ray diffraction analysis.

X-Ray Diffraction.—The crystallography analysis is summarized in Table 1 and the final atomic co-ordinates are present in Table 2. Lists of thermal components and hydrogen parameters have been deposited with the Cambridge Crystallographic Data Centre.†

† See 'Instructions for Authors,' January issue, section 5.6.3.

Table 1. Crystal analysis parameters for compound (**1b**) at room temperature.

Crystal data	
Formula	$C_5H_5NO_2$
Crystal habit	Transparent prisms
Crystal size (mm)	0.40 × 0.23 × 0.10
Symmetry	Monoclinic, *C2/c*
Unit-cell determination:	Least-squares fit from 61 reflections ($\theta < 45°$)
Unit-cell dimensions	8.321 0(3), 11.040 5(4), 11.313 4(4) Å, β 103.307(3)°
Packing: V (Å^3), Z	1 011.3(1), 8
D_c(g cm^{-3}), M, F(000)	1.459, 111.10, 464
μ (cm^{-1})	9.30
Experimental data	
Technique	Four-circle diffractometer Bisecting geometry Graphite-oriented monochromator: Cu-K_α ω/2θ scans, scan width 1.6° Detector apertures 1.0 × 1.0°
Total measurements	Up to 65° in θ
Speed	1 min/reflection
Number of reflections:	
Independent	863
Observed	712 [3σ(I) criterion]
Standard reflections:	2 reflections every 90 min No variation
Solution and refinement	
Solution	Direct methods
Refinement	L.S. on F_{obs}, full matrix
Parameters:	
Number of variables	93
Degrees of freedom	619
Ratio of freedom	7.7
H-atoms	Difference synthesis
Final shift/error	0.03
Weighting scheme	Empirical so as to give no trends in $\langle w\Delta^2F\rangle$ *vs.* $\langle\|F_{obs}\|\rangle$ or $\langle\sin\theta/\lambda\rangle$
Max. thermal value	U_{33}[O(7)]0.071(1) Å^2
Final ΔF peaks	0.18 e Å^{-3}
Final R and R_w	0.044, 0.046
Computer and programs	VAX 11/750 XRAY76 System;[a] MULTAN80[b]
Scattering factors	Int. Tables for X-Ray Crystallography[c]

[a] J. M. Stewart, P. A. Machin, C. W. Dickinson, H. L. Ammon, H. Heck, and H. Flack, 'The X-Ray System,' Technical Report TR-446, Computer Science Center, University of Maryland, USA, 1976. [b] P. Main, S. J. Fiske, S. E. Hull, L. Lessinger, G. Germain, J. P. Declercq, and M. M. Woolfson, 'MULTAN 80 System,' University of York, England, 1980. [c] International Tables for X-Ray Crystallography, Kynoch Press, Birmingham, England, 1974, vol. IV.

Table 2. Final fractional atomic co-ordinates (with e.s.d.s in parentheses) for compound (**1b**).

Atom	x	y	z
N(1)	0.072 3(2)	0.198 1(1)	0.079 5(1)
C(2)	0.191 4(2)	0.143 4(2)	0.168 7(2)
C(3)	0.283 7(2)	0.052 9(2)	0.123 9(2)
C(4)	0.259 6(2)	0.028 1(2)	0.004 5(2)
C(5)	0.138 9(3)	0.089 8(2)	−0.080 8(2)
C(6)	0.044 (2)	0.174 6(2)	−0.040 7(2)
O(7)	−0.019 8(2)	0.290 3(1)	0.114 3(1)
O(8)	0.211 4(2)	0.173 5(1)	0.277 8(1)

NMR Measurements.—NMR spectra were recorded on a Bruker AC-250 spectrometer (E.N.S.C.M.) with $(CD_3)_2SO$ solutions. The solvent ^2H signal was used for the field/frequency lock, and the spectrum reference was measured on $SiMe_4$ in pure $(CD_3)_2SO$. Experimental conditions were, for ^1H: concentration 0.05 mol dm^{-3}, spectrometer frequency 250.133 MHz, digital resolution 0.076 Hz; for ^{13}C: concentration 1 mol dm^{-3}, spectrometer frequency 69.896 MHz, digital resolution 0.44 Hz, with either broad-band decoupling in CPD mode or gated decoupling of protons. Attributions of ^{13}C signals were made, when necessary, with the help of ^1H–^{13}C COSY spectra. Simulations and iterative calculations, involving non-first-order ^1H and ^{13}C spectra, were performed using Bruker PANIC software. In the following discussion, we will assume the conservative criterion that the error in the coupling constants is the digital resolution and not the much lower error of PANIC calculations.

Table 3. Selected geometrical parameters (A, °) for compound (**1b**).

N(1)–C(2)	1.380(2)	N(1)–C(6)	1.351(3)
N(1)–O(7)	1.384(2)	C(2)–C(3)	1.423(3)
C(2)–O(8)	1.252(2)	C(3)–C(4)	1.347(3)
C(4)–C(5)	1.400(3)	C(5)–C(6)	1.355(3)
C(6)–N(1)–O(7)	117.2(2)	C(2)–N(1)–O(7)	117.7(2)
C(2)–N(1)–C(6)	125.0(2)	N(1)–C(2)–O(8)	121.0(2)
N(1)–C(2)–C(3)	113.7(2)	C(3)–C(2)–O(8)	125.2(2)
C(2)–C(3)–C(4)	122.2(2)	C(3)–C(4)–C(5)	120.7(2)
C(4)–C(5)–C(6)	118.5(2)	C(5)–C(6)–N(1)	119.9(2)
N(1)–O(7)–H(7)	103(2)		
O(7)–H(7)	1.00(4)		
O(7)···O(8)(i)	2.567(2)		
H(7)···O(8)(i)	1.57(4)		
O(7)–H(7)···O(8)(i)	174(4)		

$i = -x, y, \frac{1}{2} - z$

Results and Discussion

X-Ray Diffraction.—A search in the Cambridge Structural Database (CSD)[12] yielded many references for structures containing the anion of compound (**1**), a common bidentate ligand in co-ordination chemistry, but none for the free ligand. Two other *N*-hydroxypyridin-2-one structures have been determined, those of 1-hydroxy-5-methoxy-6-methylpyridin-2-one (HMOPRO, CSD code) (without co-ordinates)[12] and 1-hydroxy-*N*,*N*-dimethyl-2-oxodihydropyridin-6-carboxamide (DAHBAP, CSD code).[12,13] In both cases, they are in the 1-hydroxy-2-one tautomeric form **b**.

Table 3 gives the main geometrical parameters describing the structure of compound (**1b**). The bond lengths correspond to double bonds localized at C(3)–C(4), C(5)–C(6), and C(2)–O(8), although this last one is a little elongated due, perhaps, to its implication in a hydrogen bond. Among the angular values, note that N(1) is planar and its substitution is symmetric, the C(2)–N(1)–C(6) angle being larger than 120°. On the other hand, at C(2) the substitution is asymmetric, the angle opposite to the double bond having a lower value than 120°. The OH group is involved in an intermolecular hydrogen bond, with a quite small N–O—H angle and with a C(2)/C(6)–N(1)–O(7)–H(7) torsion angle of −70(2)/115(2)°. The H-bond seems to be quite strong[14] and makes angular dimers through a binary axis parallel to *b* (see Figure 1).[15]

The pyridin-2-one structure (**1b**) is characterized by the ring single/double bond alternation and by the C=O bond length. The localized system of bonds in the ring is also found in the 6-$CONMe_2$ derivative[13] and in pyridones,[16,17] but is not found in either 2-hydroxypyridines[16] or in pyridine *N*-

oxides.[18] The short exocyclic C=O bond is shared by other pyridones[13,16,17] and is different from that in true 2-hydroxypyridines [C–O bond 1.330(5) Å].[16] Finally, the N–O bond is not sensitive to (**1a**) ⇌ (**1b**) tautomerism since it is always a single bond [in pyridine *N*-oxide it is 1.33(2)–1.35(2) Å].[18] Assuming a relationship between bond orders and bond lengths, and assuming that bond orders are indicative of a canonical form, the experimental geometry of compound (**1b**) corresponds to the 'neutral' form we have used to represent 1-hydroxypyridin-2-ones.

An important aspect of the structure of tautomer (**1b**) is the nature of the hydrogen bonds. As we have indicated, the compound is a cyclic dimer, similar to that observed for pyridones/hydroxypyridines,[16,17] but different from the structure of the two other *N*-hydroxypyridin-2-ones (see Figure 2), where an intramolecular bond is observed. Thus, it is possible that, in solution, even compound (**1b**) exists as a monomer with an intramolecular H-bond, as was assumed by Gardner and Katritzky.[3]

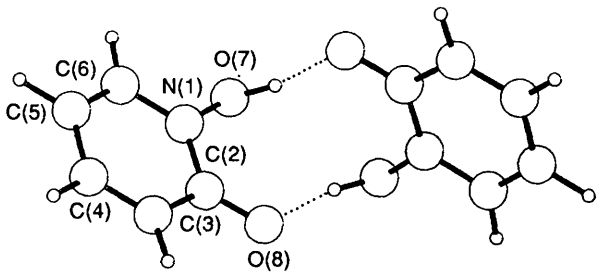


Figure 1. Molecular structure of 1-hydroxypyridin-2-one (**1b**) with numbering system used in the crystallographic work.

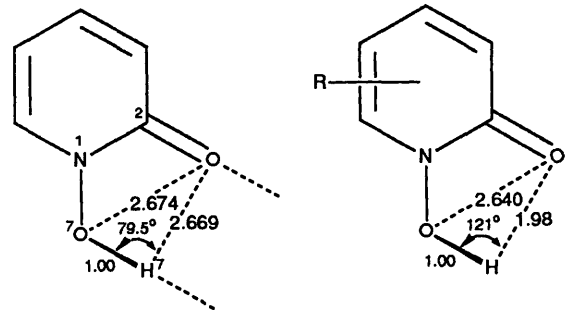


Figure 2. O–H • • • O bonds in 1-hydroxypyridin-2-ones: intermolecular in compound (**1**) and intramolecular in previously reported examples.[12]

^{1}H *NMR Study.*—The chemical shifts and coupling constants were iteratively determined by computer simulation and are shown in Tables 4 and 5. To compare tautomeric compounds (**1**)–(**3**) and (**8**)–(**10**) with fixed structures (**4a**), (**5a**), (**6b**), (**7b**), (**11a**), and (**12a**), it is necessary to select the most abundant tautomer. To avoid cumbersome discussions, we will consider only the pyridone tautomer **b** which, as we will show later on, is indeed the most stable in all cases.

Chemical shifts. Analysis of the chemical shifts (Table 4) of compounds (**4a**), (**5a**), (**6b**), and (**7b**) revealed that generally the protons of the *N*-oxide structure appear downfield compared with those of the pyridones and that, in the former structures, protons 3-H, 4-H, and 5-H resonate over a narrower range of frequencies than do the corresponding protons in pyridones. This behaviour is especially remarkable in compound (**5a**) where the coincidence of resonances for protons 4-H and 5-H led to the appearance of 6-H as a triplet which, for this reason, was previously misassigned to 5-H.[9] Protons 4-H, 5-H, and 6-H gave, in $(CD_3)_2SO$ solution, an ABX system with a *deceptively simple AB portion* (only 5 instead of 8 transitions). This pattern is also observed in [$^2H_7$]dimethylformamide

Table 5. H–H coupling constants (Hz) of compounds (**1**)–(**12a**) in $(CD_3)_2SO$ solution.

Compound	$^3J_{34}$	$^4J_{35}$	$^5J_{36}$	$^3J_{45}$	$^4J_{46}$	$^3J_{56}$
(**1**)	9.06	1.71	0.55	6.73	2.03	6.94
(**2**)				7.44	1.57	7.24
(**3**)				7.39	1.78	7.11
(**4a**)	8.34	1.78	0.42	7.58	1.60	6.46
(**5a**)				8.66	1.6[a]	6.4[a]
(**5a**)[b]				8.45	1.39	6.68
(**6b**)	9.20	1.72	0.52	6.62	2.04	7.08
(**7b**)				7.47	1.68	7.31
(**8**)	9.25	1.17	0.80	6.54	2.21	6.53
(**9**)				7.30	1.68	6.58
(**10**)				7.17	1.77	7.11
(**11a**)	8.45	0.90	0.85	7.10	2.00	5.05
(**12a**)				7.77	1.50	5.00

[a] Probable error on these couplings ±0.6 Hz (ABX system with deceptively simple AB part, RMS error 0.02 Hz). [b] In [$^2H_8$]toluene solution.

Table 4. ^{1}H chemical shifts (δ-values) of compounds (**1**)–(**12a**) in $(CD_3)_2SO$ solution.

Compound	3-H	4-H	5-H	6-H	2-OMe	3-OMe	N-OMe
(**1**)	6.517	7.383	6.205	7.904			
(**2**)		6.823	6.129	7.471		3.728	
(**3**)		6.695	6.069	7.349			
(**4a**)	7.212	7.350	7.026	8.221	3.971		
(**4a**)[a]	6.22–6.29	6.49	6.22–6.29	8.07	4.25		
(**5a**)		7.117	7.111	7.852	3.939	3.856	
(**5a**)[a]		6.220	6.411	7.965	4.357	3.470	
(**6b**)	6.534	7.436	6.238	7.976			3.950
(**7b**)		6.810	6.152	7.531		3.718	3.927
(**8**)	6.314	7.419	6.156	7.359			
(**9**)		6.790	6.093	6.930		3.677	
(**10**)		6.723	6.078	6.863			
(**11a**)	6.804	7.681	6.955	8.182	3.860		
(**12a**)		7.259	6.918	7.687	3.859	3.778	

[a] In [$^2H_8$]toluene solution.

Table 6. ^{13}C chemical shifts (δ-values) of compounds (**1**)–(**12a**) in $(CD_3)_2SO$ solution.

Compound	C-2	C-3	C-4	C-5	C-6	2-OMe	3-OMe	N-OMe
(**1**)	157.69	118.98	137.82	104.17	135.59			
(**2**)	153.35	149.67	112.21	102.04	127.00		55.70	
(**3**)	154.21	147.52	113.84	103.23	125.91			
(**4a**)	158.23	109.03	126.79	117.83	139.36	56.92		
(**5a**)[a]	150.19	149.74	110.35	119.63	132.24	58.89	56.52	
(**6b**)	157.18	121.52	139.28	104.87	136.66			64.22
(**7b**)	152.98	150.72	112.64	102.90	127.11		55.80	64.10
(**8**)	162.36	119.91	140.89	104.79	135.40			
(**9**)	157.42	149.60	114.13	104.16	125.39		55.13	
(**10**)	158.30	147.18	115.58	105.46	123.87			
(**11a**)	163.42	110.41	138.67	116.68	146.67	52.67		
(**12a**)	153.75	143.70	117.86	116.93	136.39	52.69	55.18	

[a] In $[^2H_8]$toluene, carbons C-4, C-5, and C-6 appear at δ_C 109.18, 119.35, and 134.04, respectively. A 2D(^1H–^{13}C) COSY spectrum correlates these values with the corresponding proton chemical shifts of Table 4.

Table 7. Δ_1 (δ pyridine *N*-oxides − δ pyridines) and Δ_2 (δ 1-hydroxypyridin-2-ones − δ pyridin-2-ones).

	C-2	C-3	C-4	C-5	C-6
Δ_1 (**4a**)/(**11a**)	−5.19	−1.38	−11.88	+1.15	−7.31
Δ_1 (**5a**)/(**12a**)	−3.56	+6.04	−7.51	+2.70	−4.15
Δ_2 (**1b**)/(**8b**)	−4.67	−0.93	−3.07	−0.62	+0.19
Δ_2 (**2b**)/(**9b**)	−4.07	+0.14	−1.92	−2.12	+1.61
Δ_2 (**3b**)/(**10b**)	−4.09	+0.34	−2.00	−2.23	+2.04

solution. On the other hand, when the spectrum was recorded in $[^2H_8]$toluene, the chemical shift of each proton was different and a first order analysis of the signals was easily carried out. It should be pointed out that in this solvent proton 4-H resonates at higher field than proton 5-H, due to the aromatic-solvent-induced shift (ASIS). This effect was not observed in compound (**4a**), which behaved similarly in $(CD_3)_2SO$ and in $[^2H_8]$toluene (same spectral pattern). It seems that the 3-methoxy group modifies the spatial relationship between substrate and aromatic solvent in the collision complex.

Coupling constants. Considering the coupling constants (Table 5) of the 2-methoxy derivatives (**4a**) and (**11a**), it was observed that the presence of the *N*-oxide group in compound (**4a**) does not significantly affect $^3J_{34}$, while $^3J_{45}$ and $^3J_{56}$ slightly increase (for a similar effect in the case of pyridine *N*-oxide, see ref. 6). The pyridin-2-one (**6b**) showed, as previously described for compound (**8b**),[6] an increase in $^3J_{34}$ and $^3J_{56}$, the last one being larger for compound (**8b**) than for compound (**6b**). In contrast, $^3J_{45}$ decreases more in (**6b**) than in (**8b**). This fact, which was also observed in compound (**1b**), makes $^3J_{45}$ always smaller than $^3J_{56}$.

Coupling constants $^3J_{45}$ of 2,3-dimethoxypyridine (**12a**) and the corresponding *N*-oxide (**5a**) increased with respect to those of the 2-methoxy analogues (**11a**) and (**4a**). There is an interaction between the *N*-oxide and the 3-methoxy group which modifies the electronic distribution, localizing the C(4)–C(5) double bond. From compound (**5a**) to its isomer (**7b**), $^3J_{45}$ decreases and $^3J_{56}$ increases, similarly to the pyridin-2-ones mentioned above. This effect was also observed in compounds (**2b**), (**3b**), (**9b**), and (**10b**). The presence of the 3-methoxy group always makes $^3J_{45}$ larger than $^3J_{56}$.

^{13}C *NMR Study.*—Chemical shifts and coupling constants were obtained from an iterative computer simulation and are listed in Tables 6, 8, and 9.

Chemical shifts. In general, the strong electron-donor behaviour of the *N*-oxide functionality[19] produces a shielding at the 2-, 4-, and 6-position and a slight deshielding at the 3- and 5-position (Δ_1-values of Table 7). In the case of the (**4a**)–(**11a**) pair, a small shielding is observed at C(3) whereas for the (**5a**)–(**12a**) pair the deshielding at C(3) is abnormally high. As we have stated in the ^1H NMR discussion, in compound (**5a**) there is an interaction between the *N*-oxide and the 3-methoxy group.

The effect of the N–OH functionality in pyridin-2-ones (series **b**, Δ_2-values in Table 7) is rather homogeneous; however, the effect depends on the presence or absence of an OMe or OH group at position 3 (compare values of lines four and five with those of line three).

Comparison between model compounds, 2-methoxypyridine *N*-oxides and 1-methoxypyridones, reveals that when there is no substituent at position 3, (**4a**)–(**6b**), the most sensitive carbons are C(3), C(4), and C(5). The first two atoms resonate downfield whereas C(5) resonates upfield in the pyridone structure **b** compared with the pyridine structure **a**. For 3-methoxy derivatives, (**5a**)–(**7b**), the only observable effect remains that for C(5). Finally, the pyridone effect, previously reported for compound (**8b**),[6] is also observed in compounds (**1b**), (**2b**), (**9b**), and (**10b**).

^{13}C–^1H *Coupling constants.* As was previously established for simple pyridones,[6] the results in Table 8 confirm that ^1J coupling constants are rather insensitive to tautomeric changes with the possible exception of $^1J_{C\text{-}4,4A}$ where the averaged values for tautomeric compounds (**1**)–(**3**), for fixed *N*-oxides (**4a**) and (**5a**), and for fixed pyridones (**6b**) and (**7b**) are 160.5, 168.9, and 161.8 Hz, respectively. The same problem arises from long-range ^{13}C–^1H coupling constants (Table 9) where the effect of the 3-methoxy group overcomes the tautomeric differences (see, for instance, $^3J_{C\text{-}2,6\text{-}H}$ and $^3J_{C\text{-}6,4\text{-}H}$). Only $^3J_{C\text{-}4,6\text{-}H}$ shows systematically lower values for compounds of the **a** series (7.6 Hz) than for pyridones **b** (8.8 Hz). In the *N*-oxide series, these variations made $^3J_{C\text{-}3,5\text{-}H}$ larger than $^3J_{C\text{-}4,6\text{-}H}$ for the hydroxypyridines **a** whereas the reverse is true for pyridones **b**. The very large values of $^2J_{C\text{-}5,6\text{-}H}$ in compounds (**11a**) and (**12a**), *ca.* 7.8 Hz, compared with an averaged value of 3.1 Hz for the remaining compounds, correspond to the reported observation that this coupling constant is much lower in pyridones and in pyridines *N*-oxides than in pyridines.[4]

Conclusions from the NMR Study.—Concerning the tautomerism **a** ⇌ **b** of compounds (**1**), (**2**), and (**3**), the most useful criteria to confirm that these compounds exist in $(CD_3)_2SO$ as 1-hydroxypyridin-2-one tautomers **b** are:

(i) Concerning ^1H chemical shifts, the signals corresponding to protons 3-H, 4-H, and 5-H appear, in the pyridone structures **b**, more separated and at smaller δ-values than do those in the corresponding *N*-oxides **a**.

Table 8. $^1J(^{13}C-^1H)$ coupling constants (Hz) of compounds (1)–(12a) in $(CD_3)_2SO$ solution.

Compound	C-3/3-H	C-4/4-H	C-5/5-H	C-6/6-H	2-OMe	3-OMe	N-OMe
(1)	165.7	158.3	169.8	179.6			
(2)		162.2	171.2	187.4		144.9	
(3)		161.0	169.9	187.4			
(4a)	167.9	168.6	169.1	186.7	147.2		
(5a)		169.2	169.3	189.5	147.4	146.0	
(6b)	167.5	162.5	173.6	186.2			146.5
(7b)		161.1	171.8	188.2		144.9	146.5
(8)	165.7	158.3	169.8	179.6			
(9)		162.2	171.2	187.4		144.9	
(10)		158.9	167.8	181.7			
(11a)	165.6	162.1	165.0	178.2	145.5		
(12a)		161.1	159.6	179.7	145.8	144.9	

Table 9. Long-range $^{13}C-^1H$ coupling constants (Hz) of compounds (1)–(12a) in $(CD_3)_2SO$ solutions.

Compound	C-2/ 3-H	C-2/ 4-H	C-2/ 6-H	C-3/ 4-H	C-3/ 5-H	C-3/ 6-H	C-4/ 3-H	C-4/ 5-H	C-4/ 6-H	C-5/ 3-H	C-5/ 4-H	C-5/ 6-H	C-6/ 3-H	C-6/ 4-H	C-6/ 5-H
(1)	2.0	4.2	10.6	1.8	8.0	*a*	*a*	*a*	9.0	9.3	1.3	2.3	1.2	7.8	5.1
(2)		4.6	7.6	*b*	*b*	*b*		*a*	8.8		*a*	2.5		8.1	4.5
(3)		*c*	*c*	*a*	8[d]	*a*		*c*	*c*		*a*	2.6		8.3	4.4
(4a)	*b*	*b*	*b*	1.3	8.8	*a*	1.5	*a*	7.7	9.0	1.2	3.6	*a*	8.0	5.1
(5a)		*b*	*b*	*b*	*b*	*b*		*a*	8.0		1.5	4.2		6.1	6.1
(6b)	2.3	3.8	10.5	*a*	7.8	*a*	*a*	0.8	9.2	9.6	*a*	3.2	1.2	8.4	5.2
(7b)		*c*	*c*	*b*	*b*	*b*		*a*	8.9		*a*	2.1		8.1	4.6
(8)	1.9	6.7	9.2	1.4	7.1	*a*	*a*	1.5	8.5	8.1	0.8	3.3	*a*	8.0	4.8
(9)		7.0	7.0	*a*	*a*	*a*		1.6	8.9		*a*	3.7		8.2	4.1
(10)[e]		7.0	7.0	1.3	9.0	*a*		1.0	8.7		*a*	3.7		8.3	4.1
(11a)	*b*	*b*	*b*	1.3	6.8	1.3	*a*	1.8	7.2	6.3	0.8	7.1	*a*	7.7	3.9
(12a)		*b*	*b*	*b*	*b*	*b*		1.8	7.6		1.4	8.5		7.9	3.2

[a] Coupling was not observed. [b] Couplings with the OMe protons do not permit measurement of this. [c] Broad signal. [d] Poorly resolved signal. [e] $^3J_{C\text{-}3,NH}$ 3.9 Hz.

(ii) Concerning $^1H-^1H$ coupling constants, $^3J_{56}$ is larger in structures **b** than in structures **a**, and the reverse is true for $^3J_{45}$ (taking into account the enhancement of *ca.* 0.9 Hz produced by a methoxy group or a hydroxy group at position 3).

(iii) Concerning ^{13}C chemical shifts, the signal corresponding to C(5) always resonates at higher field in pyridones **b** than in *N*-oxides **a** (*ca.* 103 and 119 ppm, respectively).

(iv) Finally, concerning $^{13}C-^1H$ coupling constants, only $^1J_{C\text{-}4,4\text{-}H}$ and $^3J_{C\text{-}4,6\text{-}H}$ are useful for tautomerism assignment.

Conclusions.—In $(CD_3)_2SO$ as well as in the solid state, the only observed tautomer is the 1-hydroxypyridin-2-one **b**; even if the results reported herein do not allow us to conclude if this tautomer is a little less favoured than in the corresponding 'non-oxides,' in our opinion the relative difference in stability cannot be considerable.[1,3] Another conclusion from this study concerns 2,3-dihydroxypyridine (**10**) and its *N*-oxide (**3**): owing to the similarity of their NMR behaviour with that of the corresponding 3-methoxy compounds, (**9**) and (**2**), a zwitterionic structure cannot contribute significantly to the tautomeric mixture. In both cases the 2-oxo-3-hydroxy tautomer **b** is more stable than both the 2,3-dihydroxy **a** and the zwitterion forms, in agreement with reported experimental data in solution[1] [theoretical calculations, CNDO/2[20] favour the 2,3-dihydroxypyridine tautomer (**10a**)].

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