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# NUCLEAR MAGNETIC RESONANCE SPECTRA OF HETEROCYCLIC SYSTEMS: THE $^{15}N$ PARAMETERS OF A SUBSTITUTED PYRIDONE

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Abstract--The $^{15}N$ coupling constants to $^{13}C$ and to $^{1}H$ are reported for 2-hydroxymethyl-5-methoxy-1-phenyl-4-pyridone (1). The one-bond $^{15}N$-$^{13}C$ coupling constants are consistent with $sp^2$ hybridized nitrogen. The $^{13}C$ chemical shifts do not change much on protonation, but the $^{15}N$ chemical shift undergoes a large change. The nmr data are discussed with regard to the question of the aromaticity of 4-pyridones. An improved synthesis of 1 is reported.

$^{15}N$ will undoubtedly become one of the most important methods for study of nitrogen heterocycles, particularly for molecules having several nitrogens, e.g. triazoles.[1] Since the trailblazing work of Roberts and co-workers,[2] an increasingly large number of heterocycles have been studied by $^{15}N$ nmr. These studies were recently reviewed by Levy and Lichter.[3]

As in many molecules of the pyridone class, some question exists as to the degree of aromaticity.[4] Beak, Flygare and co-workers summarize the data on a related class of molecules, the pyrones, but conclude from their magnetic susceptibility measurements that pyrones have no aromatic character.[5] Furthermore, the non-localized contribution to the magnetic susceptibility of 1-methyl-4-pyridone is similar to other molecules considered by these workers to be non-aromatic.

The present work concerns the nmr parameters of a substituted 4-pyridone (1), derived from kojic acid. The $^{15}N$ nmr chemical shift of 1 is 149 ppm downfield from ammonia,[6] compared to 184 ppm for the protonated form 1'. The protonated form has a greater probability of aromatic character.[4] The difference is surprisingly large, as the $^{13}C$ and $^{1}H$ resonances did not change substantially upon protonation (cf. Chart I).[7] The natural abundance $^{15}N$ spectrum of 1-phenyl-2,6-dimethyl-4-pyridone (2) also exhibited a substantial downfield shift on protonation ($\Delta\delta$ + 29 ppm). The change in chemical shift on protonation is about the same as for methylamine (+ 25 ppm), but larger and of opposite sign than for aniline (- 9 ppm).[3,6] It has been suggested that the large change in nitrogen chemical shift (but not $^{13}C$ or $^{1}H$) reflects the importance of resonance forms with a positive charge on nitrogen in the cation.[8]

The chemical shift of 1 (also 2, ca. 166 ppm) are roughly similar to the $^{14}N$ chemical shift of the parent molecule, 4-pyridone (ca. 179 ppm).[6] The latter is considered by

Chart I lists the $^{13}C$ *chemical shifts and the coupling constants observed between* $^{15}N$ and $^{13}C$ (or $^{1}H$) in the enriched substrate. The carbonyl in 1 is certainly not similar to other ketones or even to molecules in which α,β-unsaturation plus an electron donating substituent in the β-position are present, e.g. 4-oxo-2-penten-2-ol ($\delta_{CO}$ = 191 ppm).[9] On protonation, the carbonyl shifts upfield to a value similar to a phenolic ipso carbon. The chemical shifts of the phenyl group in 1 are not indicative of nitrogen lone pair delocalization into phenyl (if such delocalization did occur, the ortho and para carbons would exhibit chemical shifts in the 116-119 ppm range).[9] The lone pair must therefore be delocalized in the heterocyclic ring.

The significance of $^{1}J(^{15}N-^{13}C)$, vis-a'-vis hybridization of these nuclei, has been the *source of considerable controversy*.[10] However, in 1 and 1', the magnitude of the coupling constant (presumed to be negative) is similar to a group of molecules having unquestioned $sp^2$ hybridization at nitrogen and at carbon, e.g. pyrrole [$^{1}J(^{15}N-^{13}C)$ = -10.3 Hz] or nitrobenzene (-15 Hz). The similarity of the $^{1}J$ values for all three bonds to nitrogen is suggestive of similar hybridization and probable planarity at nitrogen (cf. Wasylishen[10]).

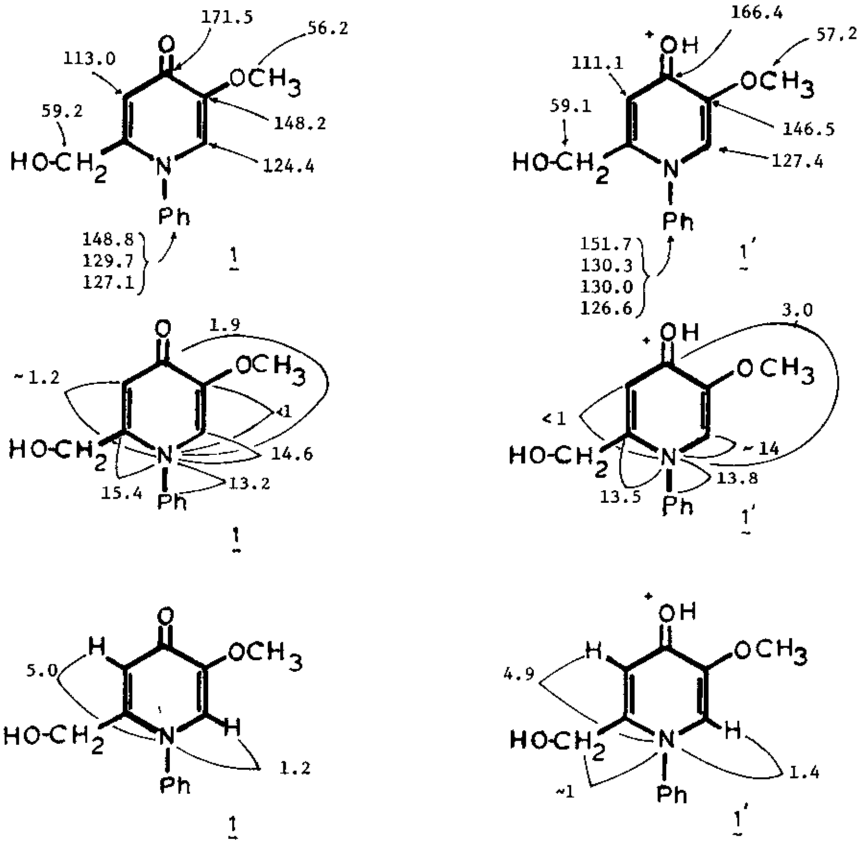
Protonation has little effect on $^{n}J(^{15}N-^{13}C)$, except for the $^{3}J$ involving carbonyl, which is enhanced upon protonation, similar to literature examples.[3] Nitrogen compounds that lack lone pairs or have delocalized lone pairs often show very small $^{2}J(^{15}N-^{13}C)$, and 1 is no exception. Similarly, $^{2}J(^{15}N-^{1}H)$ is small and similar to pyridinium salts (ca. -2Hz).

In conclusion, the $^{15}N$ chemical shifts are interpretable in terms of a high charge density on nitrogen in 1', but not in 1.[11] However, the situation is complex and requires further study.[11] In other respects, the molecule resembles a hybrid between an aromatic system and an α,β-unsaturated ketone, although in our opinion, a definite bias toward aromatic character exists. In particular, the lack of change of $^{1}J(^{15}N-^{13}C)$ on protonation (and therefore a small change in bond order)[12], the general similarity of the $^{15}N$ chemical shift to nitrogen heterocycles of unquestioned aromaticity, the lack of lone pair delocalization in phenyl, and the highly anomalous $^{13}C=O$ would suggest either substantial aromatic character, or at minimum, an extensive resonance involvement of nitrogen. No way seems evident to reconcile these data with the magnetic susceptibility data.[5]

Compound 1 was prepared by placing kojic acid monomethyl ether[13] (1.2 g) in 25 ml of water and adding 1 g of anilinium chloride-$^{15}N$.[14] The mixture was heated under reflux for 24 h, cooled, basified with $K_2CO_3$ until near neutral, and evaporated to dryness. Addition of methanol, removal of inorganic salts, and evaporation to dryness gave the crude pyridone, 1, which was recrystallized from ethyl acetate-methanol (5:1), mp 227-228°; yield 0.520 g.

Witanowski and Webb to lie on the high end of the amide scale in chemical shift. Most N-aryl amides show chemical shifts in the 125-140 ppm range.[3] However, a more direct comparison would exist between 1 and 2 and enaminoketones. In the latter, the $^{15}N$ chemical shifts occur at 81-110 ppm, which is substantially less than 1 or 2, even allowing for the presence of phenyl.[3] The chemical shifts of 1 and 2 are roughly similar to aromatic nitrogen heterocycles (specifically, to pyrrole-like cases, in which the nitrogen lone pair is highly delocalized, e.g. pyrrole itself, 149 ppm).[3] Similarly, 1' and 2' are comparable to N-methylpyridinium salts (ca. 179 ppm), although an allowance for the effect of phenyl in 1' and 2' must be made. Variations in $^{15}N$ chemical shift from compound to compound are larger than in $^{13}C$ nmr, reflecting the larger overall range (ca. 900 ppm) in $^{15}N$.[6]

Chart I



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4. R. F. M. White, and H. Williams, "Physical Methods in Heterocyclic Chemistry," A. R. Katritzky ed., Vol. IV, Academic Press, London, 1971, p. 201 ff, also p. 259 and Vol. II, p. 146. Protonation is shown to occur on oxygen. However, for other ideas on aromaticity, see J. A. Elvidge and L. M. Jackman, *J. Chem. Soc.*, 1961, 859.
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6. The chemical shift of $^{14}$N and $^{15}$N molecules are directly comparable (in ppm), cf. Witanowski and Webb, "Nitrogen NMR," Plenum Press, London, 1973.

   The small variability caused by the use of an external standard (this study used neat labelled nitromethane, taken as 380 ppm from ammonia)[3] is regarded as minor. The solvent used for 1 was DMSO-$d_6$ (concentration 3% w/v). The spectrum of **2** was determined in CDCl$_3$ (saturated) with Cr(acac)$_3$ present.
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