

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 ^1H 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 ^1H 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 ^1H) 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 ^1H) 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 ($\delta_{\text{CO}} = 191 \text{ ppm}$).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 $^1J(^{15}\text{N}-^{13}\text{C})$, 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 [$^1J(^{15}\text{N}-^{13}\text{C}) = -10.3 \text{ Hz}$] or nitrobenzene (-15 Hz). The similarity of the 1J values for all three bonds to nitrogen is suggestive of similar hybridization and probable planarity at nitrogen (cf. Wasylshen¹⁰).

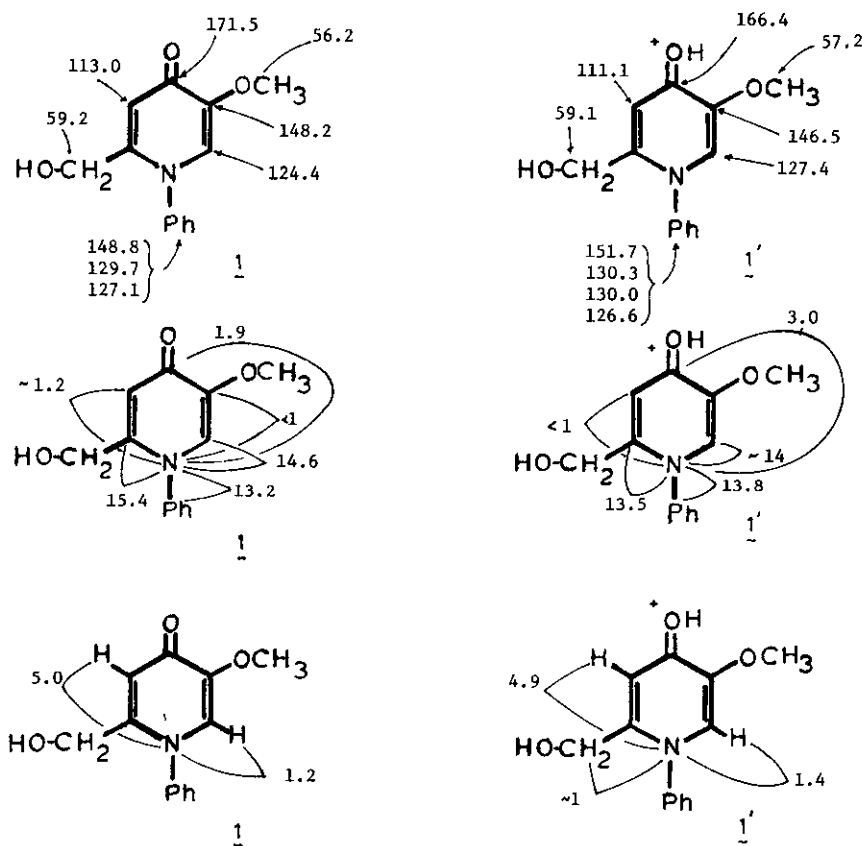
Protonation has little effect on $^nJ(^{15}\text{N}-^{13}\text{C})$, except for the 3J involving carbonyl, which is enhanced upon protonation, similar to literature examples.³ Nitrogen compounds that lack lone pairs or have delocalized lone pairs often show very small $^2J(^{15}\text{N}-^{13}\text{C})$, and 1 is no exception. Similarly, $^2J(^{15}\text{N}-^1\text{H})$ 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 $^1J(^{15}\text{N}-^{13}\text{C})$ 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 $^{13}\text{C}=\text{O}$ 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 ether¹³ (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 ¹⁵N 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 ¹⁵N chemical shift from compound to compound are larger than in ¹³C nmr, reflecting the larger overall range (ca. 900 ppm) in ¹⁵N.⁶

Chart I



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