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TAUTOMERISM IN SCHIFF BASES DERIVED FROM SUBSTITUTED 2- AMINO PYRIDINES AND 2-HYDROXY 1-NAPHTHALDEHYDE - ^{1}H NMR EVIDENCE FOR TAUTOMERISM AND CONJUGATION

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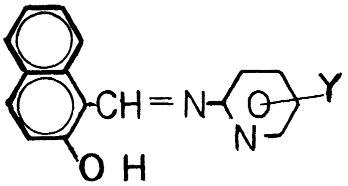
Data showing the direct influence of substituents in the pyridine ring on the electron density at the azomethine function in 2- aminopyridine derivatives and their contrasting behaviour as compared to the aniline analogoues are presented. Results point out tautomeric equilibration and extended conjugation in title compounds.

Although Schiff-bases existing in either ketoenamine or enolimine form has now been widely accepted, discussions do exist as to whether these tautomeric forms are found as an equilibrium mixture or not$^{(1-7)}$. Further Tabei and Saitou $^{(6)}$ demonstrated by means of a study of the Schiff-bases of the type Ar-CH=N-Ar-Y that substituents, Y, in the aniline ring did not influence greatly the electron density and bond-order of azomethine function and this is believed to be the general phenomenon in this class of compounds. We have now investigated ^{1}H NMR spectra of the Schiff-bases derived from substituted 2-aminopyridines and 2-hydroxy 1-naphthaldehyde. We report here nmr evidence for the existence of an equilibrium mixture as well as a direct relationship between nature of the substituent in the pyridine ring and electron density at the azomethine function in our systems, which is very much unlike the case with aniline based derivatives.

Several Schiff-bases of the formulation (1) were isolated by condensing 2-hydroxy 1-naphthaldehyde with a variety of substituted 2-aminopyridines by refluxing a methanolic solution of the corresponding amine and aldehyde at <u>ca</u>. 60°C in 1:1 mole ratio for half an hour. The products were recrystallised from a mixture of methanol and petroleum ether and characterized by elemental analyses and infra-red spectra to be as in (1).



(1)

(Where Y = H, 3-methyl, 4-methyl, 5-methyl, 6-methyl, 5-chloro, 4,6-dimethyl, 3-nitro and 5-nitro).

Room temperature ^{1}H NMR data of the Schiff-bases in $CDCl_3$ (with TMS as internal standard) were recorded. The doublets observed for azomethine protons -C$\underline{H}$ = N- (at δ=9. 96 ± 0.06 ppm) and the broadening of phenolic -C-O$\underline{H}$ provide main evidence for strong hydrogen bonding between phenolic hydroxyl and azomethine nitrogen. A partial transfer of proton from phenolic OH to azomethine nitrogen leading to the formation of ketoenamine tautomer with -CH - NH- linkage leads to a doublet for azomethine proton at δ =9.96±0.06 ppm as shown in Table 1. The field invariance of the splitting (whether 60 MHZ or 100 MHZ instrument was used) emphasises its true coupling nature as against the presence of isomers such as syn and anti with varied chemical shifts.

Table 1. ^1H NMR Spectral Data of Schiff-bases from Substituted 2- Aminopyridines and 2- Hydroxy 1-naphthaldehyde (δ values in ppm at room temperature in $CDCl_3$).

Y	H	3-methyl	4-methyl	5-methyl	6-methyl	5-chloro	4,6-dimethyl	3-nitro	5-nitro
-C<u>H</u>=N-(a)	9.99	10.02	9.95	9.91	9.90	9.94	9.94	10.75(d)	10.76(d)
-O<u>H</u> (b)	15.45	15.69	15.46	15.46	15.46	15.40	15.46	13.08	13.10
pK_a of(c) amino.py.	6.70	7.24	7.48	7.22	7.41	4.83	7.84	2.33	2.78
Coupling const.,J,	7	8	8	7	8	6	8	-	-

<u>a</u>. Doublets, <u>b</u>. Broad, <u>c</u>. Data from reference 8, <u>d</u>. Sharp singlets, Coupling const. in HZ.

The relatively large magnitude of the coupling constants (<u>viz</u>. 6-8 HZ) is indicative of the coupling arising from two adjacent protons rather than due to any long range coupling. In D_2O, the doublets due to -C<u>H</u>=N- collapse into sharp singlets indicating that the coupled proton undergoes rapid H - D exchange. The rapidity of this exchange (nmr time scale) is suggestive of phenolic hydrogen being coupled to the azomethine proton through keto-enamine tautomer. With basic solvent like C_5D_5N, the collapse of the doublets into singlets observed, is possibly due to either base catalysed intermolecular exchange or high favourability of enolimine form in basic solvents. The dependence of coupling constants, J, on temperature and solvent (whether $CDCl_3$ or C_6H_6) lends support to the view that equilibrium amounts of tautomers exist depending on temperature and solvent polarity. Further the coupling constants observed with our Schiff-bases are much smaller than 12 HZ reported for benzoylacetaldehyde where a total conversion to ketoenamine form has been invoked(5).

A systematic variation of J values depending on inductive effects of the substituents on the pyridine ring is apparent from Table 1. Strongly electron releasing groups tend to stabilise ketoenamine form. With electron withdrawing groups like NO_2, either exclusive presence of enolimine form or a rapid intermolecular exchange (even in $CDCl_3$) can be inferred from Table 1 providing compelling evidence for the effects of pyridine ring substituents on the azomethine group. While the deshielding effect of NO_2 function on -CH=N- is derived mainly from its electron withdrawing nature, 3-methyl substituent in pyridine ring seems to exert steric influence on -CH=N-, which is similar to the effect of ortho substituent in aldehydic ring already reported(7). In view of the stronger basicity of aminopyridines compared to anilines, stronger hydrogen bonding tendencies in Schiff-bases derived from 2-hydroxy 1-naphthaldehyde and aminopyridines is as to be expected. This does indeed lead to markedly different properties of Schiff-bases from aminopyridines when compared with those from aromatic amines(9).

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