# Hydrogen Bonding & Tautomeric Equilibria in Schiff Bases Derived from 2-Aminopyridines: Electronic Spectral Evidence for Substituent Effects

(MRS) HEMALATHA RANGANATHAN[a], T RAMASAMI[*], D RAMASWAMY & M SANTAPPA[b]

Central Leather Research Institute, Adyar, Madras 600 020

Schiff bases of the type $C_6H_3(R)(OH) CH = NC_5H_3N(Y)$ [where R = H, 3-OCH$_3$, 5,6-benzo, 3-CHO-5-CH$_3$, 5-Cl, 5-Br, 5-CH$_3$, 4-CH$_3$, 3-nitro and 5-nitro and Y = H, 3-CH$_3$, 4-CH$_3$, 5-CH$_3$, 6-CH$_3$, 4,6-dimethyl and 5-Cl] have now been synthesised and evidence sought for the electronic interaction between the substituents R (in the benzene ring) and Y (in the pyridine ring) in the molecule. The effects of substituents R and Y on the strength of hydrogen bond between OH and CH = N, is coupled to ketoenamine $\rightleftharpoons$ phenolimine equilibrium. The groups which increase the acidity of the phenolic hydroxyl and the basicity of the azomethine nitrogen facilitate quinonoid structures with characteristic visible absorption bands in the region 400-600 nm. In those compounds where R = 5,6-benzo, the intensity and the energy of band $\sim$400 nm show a correlation with the electron releasing tendency of Y. Thus there appears an electronic communication between the substituents R and Y causing deviations from the generally accepted model for schiff base structures.

The role of metal complexes of schiff bases derived from heterocyclic amines, in biological processes such as transamination is well documented[12]. Our earlier work[3] indicated that schiff bases derived from 2-aminopyridines behaved differently in comparison to those derived from aromatic amines. In the PMR spectrum, the azomethine proton showed spin-spin coupling with the proton of the phenolic hydroxyl[3]. We also showed that deviations from the well known and generally accepted Brocklehurst model[4,5] for schiff bases were not unlikely in the case of schiff bases derived from 2-aminopyridines[3]. Both experimental and theoretical studies[6,7] have shown that as Brocklehurst model would predict that substituents R and Y in the aromatic rings in 1 do not communicate electronically. The amine-ring substituents do not seem to influence either the electron density or the bond order of the azomethine group, possibly due to the orbital overlap resulting from the non-planar arrangement of the molecule 1. However, in the case of 2, which was formed by replacing aniline in 1 by 2-



aminopyridine, the electronic interaction between the substituents R and Y was possible[3,8,9]. We present here the synthesis and electronic spectral studies on a series

---

(a) Present address: Queen Mary's College, Mylapore, Madras 600 004
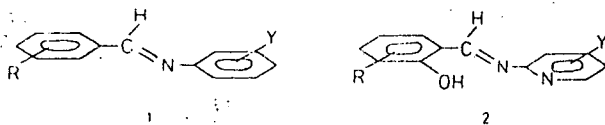
(b) INSA Senior Scientist, Anna University, Madras 600 025.

of schiff bases (2), derived from 2-aminopyridine, to show that (a) there is an electronic communication between R and Y in 2 and (b) the deviations from Brocklehurst model may be more general than originally believed.

## Materials and Methods

Schiff bases of the type (2) were synthesised by the following general procedure: Equimolar proportions of o-hydroxyaldehyde and the required heterocyclic amine were heated under reflux in methanol for 1 hr, and the solid obtained was recrystallised from a methanol-pet ether (40-60°) mixture. The schiff bases obtained were found to give single spots on TLC and were fully characterised by their elemental analyses and mass spectral data. The electronic spectra were recorded using a Pye-Unicam SP 1800D double beam spectrophotometer.

## Results and Discussion

The melting point behaviour of the schiff bases studied indicated the presence of weak intermolecular attractive forces[10]. In the case of schiff bases of the type (2), a pyridine nucleus and phenolic moiety may well form centres for association. Such intermolecular hydrogen bonding between phenols and pyridines has already been reported[11,12]. The analysis of the melting point data of the present series of compounds revealed that the electron donating substituents in the pyridine moiety and electron withdrawing groups in the phenolic moiety increase the tendency for intermolecular association and therefore the melting points, if other steric considerations were not a complicating feature. For example, when Y = H and R = H, 5,6-benzo and

3-nitro, the observed melting points are 70°, 175° and 193° respectively. On the other hand, when R = H and Y = H, 3-methyl, 4-methyl, 5-methyl, 6-methyl, and 4,6-dimethyl, the melting points observed are 70°, 78°, 98°, 101°, 65° and 92° respectively. The steric influence of 6-methyl substituents in the pyridine moiety on the intermolecular association is evident from the lower melting points of 6-methyl derivatives. The existence of intermolecular hydrogen bonds between pyridine and phenolic centres raises questions as to whether there could be other intra- and inter-molecular hydrogen bonds.

Since the schiff bases of the type (2), in addition to R, contain phenolic hydroxyl *ortho* to azomethine group, an intramolecular hydrogen bonding between phenolic hydroxyl and azomethine nitrogen as well as quinonoid formation will have to be considered. Three possible structures (3, 4 and 5) may be visualized especially when R = 5,6-benzo. Earlier PMR evidence[3] does point out that ketoenamine structure (5) predominates such that a strong spin-spin interaction

between $H_b$—C—N—$H_a$ might be detected. The observed magnitude of the coupling constant ($J = 6 - 8\,Hz$) and its dependence on the substituents Y were better discussed in terms of spin interaction in structures of the type (5) rather than due to any vicinal coupling in (3) (ref.3). The formation of both 4 and 5 involves interaction between phenolic hydroxyl and azomethine nitrogen. Therefore the basicity of the 2-aminopyridine and the acidity of the phenolic hydroxyl in the aldehydic moiety are expected to influence the ease of formation of 4 and 5. As far as the azomethine proton signal in PMR is concerned, 4 and 5 differ only in the strengths of interaction and the observed PMR results do not rule out 4. The electronic spectra, on the other hand, are believed to be useful diagnostic tools[13] in distinguishing between structures 4 and 5.

The quinonoid compounds, in general, exhibit $n \rightarrow \pi$ transition at much lower energies (viz. 400-600 nm) compared to the phenolate derivatives (330-350 nm)[13,14]. The UV-visible spectra of schiff bases (2) in chloroform exhibited a set of four bands in the region between 230 and 500 nm. For the purpose of this discussion, only the lowest energy bands are listed in Table 1. Typically when R = H, two bands at 244 and in the region 260-276 nm were observed. The UV bands for benzene (and its derivatives) have been previously[15] attributed to $^1E_{1u}$, $^1B_{1u}$ and $^1B_{2u}$ type $\pi$-$\pi^*$ transitions. On similar analysis, the bands observed for schiff bases (2) in the region 260-276 nm may be attributed to $\pi$-$\pi^*$ transitions within the aromatic
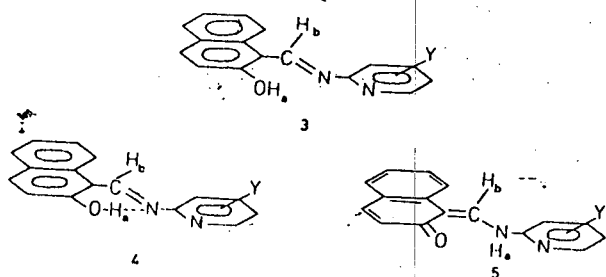


Table 1 —Lowest Energy Electronic Spectral Band in Schiff Bases (2) [Numbers in brackets give molar absorptivity in litre mol⁻¹cm⁻¹]

| R | $\lambda_{max}$ when Y = | | | | | | |
|---|---|---|---|---|---|---|---|
| | H | 3-CH$_3$ | 4-CH$_3$ | 5-CH$_3$ | 6-CH$_3$ | 4,6-dimethyl | 5-Cl |
| H | 332 (11500) | 352 (13700) | 350 (10900) | 350 (12500) | 350 (12650) | 350 (12900) | 356 (12150) |
| 3-OCH$_3$ | 480 (740) | 480 (650) | 480 (805) | 480 (750) | 480 (900) | 480 (705) | 470 (310) |
| 5,6-Benzo | 460 (15400) | 462 (18400) | 460 (17700) | 462 (19800) | 462 (20300) | 460 (19000) | 464 (16200) |
| 3-Formyl- | 488 (800) | 488 (1200) | 488 (1000) | 488 (990) | 488 (1250) | 488 (880) | 488 (690) |
| 5-Methyl- | 362 (9200) | — | — | 360 (10600) | — | — | 360 (15000) |
| 5-Cl | 360 (4250) | — | — | 360 (2260) | — | — | 360 (2645) |
| 5-Br | 362 (10600) | — | 360 (2620) | 360 (12500) | — | — | 360 (15000) |
| 5-CH$_3$ | 354 (14500) | — | — | 340 (10900) | — | — | 340 (12700) |
| 4-CH$_3$ | 446 (1050) | — | — | — | — | — | — |
| 3-Nitro | 446 (930) | — | — | — | — | — | — |

nucleus. The molar absorption coefficients $(1.0\ 1.3) / 10^4$ litre mol$^{-1}$cm$^{-1}$ are also in keeping with such an assignment.

The compounds (2) are expected to show sharp bands in the region of 288-314 nm, possibly due to the $\pi$-$\pi$* bands in the pyridine moiety. Although the electronic spectra of 2 in the region 260-314 nm were expected to be complicated due to the overlapping $\pi \to \pi$* transitions arising from both aromatic and pyridine nuclei, it was evident that the bands in the region 288-314 nm were much more influenced by the nature of the substituent (Y) in the pyridine moiety. Therefore, it is tempting to assign the bands in the region 288-314 nm to $\pi \to \pi$* transition in pyridine nucleus. In addition to these bands in the regions 260-276 nm and 288-314 nm, additional shoulders have been observed between 300 and 326 nm in the spectra of all the schiff bases (2) investigated in this study.

It seems reasonably to assign the shoulders at 300, 326, 314, 320, 322, 320 and 326 nm in the spectra of the schiff bases with R =H, Y =H, 3-methyl, 4-methyl, 5-methyl, 6-methyl, 4,6-dimethyl and 5-chloro, respectively to $n \to \pi$* transitions in the phenolic moiety. Employing usual procedures, the distinction between $n \to \pi$* and $\pi \to \pi$* transitions may be made taking into account the energy and intensity differences. Nevertheless, the contributions from $n \to \pi$* on the pyridine ring and/or symmetry-forbidden transitions from the aromatic nucleus[17] may not be easily ruled out. Further, the schiff bases (2) are expected to show more than one $n \to \pi$* transition; the one arising from the azomethine group is of special interest.

· It is generally believed that the expected bands due to $n \to \pi$* transitions of the azomethine group are not readily observed because these are relatively weak in intensity as compared to $\pi \to \pi$* type transitions. In fact, the long wavelength absorption of N-benzylidenealkylamine is a subject of conflicting reports[18]. Therefore, in the present study, no effort has been made to identify unambiguously the transition of the azomethine function. Nevertheless, the band observed around 400 nm in the visible region is of special interest and data obtained in the present study in this spectral region are included in Table 1.

Earlier workers[13,14] have assigned the absorption band around 400 nm in the quinonoid compounds to $n \to \pi$* transition. In the case of schiff bases, this band centered around 400 nm is also presumed to give information regarding inter- and intra-molecular hydrogen bonds. It is, therefore, meaningful to analyse the variations in the energy and the intensity of the corresponding band at 400 nm in the spectra of schiff bases (2) in terms of possible contributions from intramolecular hydrogen bonding as well as quinonoid structures. Electron withdrawing substituents may be

expected to render the phenolic hydroxyl group more acidic such that hydrogen bonding interactions in which the phenol is the conjugate-acid will be made more favourable. If suitable substituents are present in the aldehydic moiety, the interaction will lead to a ketoenamine $\rightleftharpoons$ phenolimine tautomeric equilibrium. Therefore, the stabilisation of quinonoid structures in respect of substituent R, when Y =H (on the basis of electron withdrawing effect of R), follows the order 5,6-benzo > 5-nitro > 3-nitro > 3-methoxy > 3-formyl-5-methyl. On the other hand, substituents (R) such as 4-methyl and 5-methyl are expected to suppress quinonoid formation even with respect to the unsubstituted derivative due to their electron releasing tendency. Therefore, the substituents may be classified into two groups, viz. those which are capable of stabilising quinonoid structures and those which are not. The data given in Table 1 show that only when R = 5,6-benzo, 5-nitro, 3-nitro, 3-formyl-5-methyl and 3-methoxy, a band in the visible region 400-490 nm is observed. With R = 5-chloro, 5-bromo, 4-methyl and H, the lowest energy transition occurs only in the region 300-360 nm. In such cases, on the basis of electronic spectra, structure represented by 4 seems more likely since $n \to \pi$* transition is observed at lower energy. For those cases where R is an electron withdrawing substituent, the data in Table 1 show that the energy and the intensity of the band around 400 nm are in the order of their electron withdrawing effects,
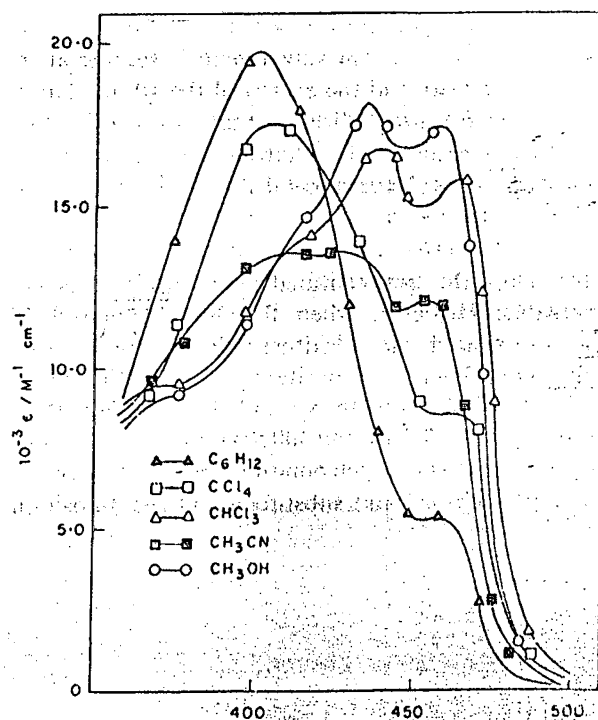


Fig. 1—Solvent-dependence of visible spectra of the schiff base (2) having Y = 5—Cl, R = 5,6-benzo, in C$_6$H$_{12}$ (n-hexane) (▲), CCl$_4$(□), CHCl$_3$(Δ), CH$_3$CN(◙) and CH$_3$OH(O).

viz. 5,6-benzo >5-nitro >3-nitro. suggesting greater ease of formation of quinonoid structures. In the case of 3-OCH₃ and 3-formyl-5-methyl compounds, secondary hydrogen bonding between phenolic proton and the methoxyl or formyl oxygen is likely to stabilise hydrogen bonded structures, in which azomethine is not involved. Indeed the azomethine proton in those cases do not show spin interaction with phenolic hydrogen[19] and meaningful conclusions on such systems on the origin of band ⁓400 nm may be difficult. When R = 5,6-benzo, the spectral pattern in the region of 400-600 nm is somewhat complex and in view of the various possible equilibria and isomeric structures, complexities of the electronic spectra are not surprising. The bands arising from singlet-triplet transitions are expected in the spectral region around 530 nm for such compounds.

The compelling evidence for quinonoid structures, at least when R = 5,6-benzo, is also obtained by the analysis of the solvent-dependence of bands ⁓400 nm. Typically, the dependence of the electronic spectra of 2 when R = 5,6-benzo and 5-chloro on the polarity of the solvent is shown in Fig.1. The pronounced dependence of the energy and intensity of band ⁓400 nm on the solvent polarity argues in favour of (a)the band being $n \to \pi^*$ in origin and (b)the existence of phenolimine and ketoenamine tautomerism in which the equilibrium is in favour of ketoenamine tautomer in CHCl₃.

The influence of pyridine group substituents (Y) on the tautomeric equilibrium when R = 5,6-benzo is evident from Table1. The substituents Y seem to alter both the intensity and the energy of the 400 nm band when R = 5,6-benzo indicating that in this case, the substituents R and Y do electronically communicate with each other. Experimental difficulties precluded synthesis of wide variety of 2-aminopyridine derived schiff bases (2) with various Y and R = 5-nitro and 3-nitro. Only the unsubstituted case (Y=H) was investigated. However, when R = 3-methoxy and 3-formyl-5-methyl, the substituents Y did not seem to influence the energy and position of band ⁓400 nm. In cases where R = 3-methoxy and 3-formyl-5-methyl, the bands observed around 400 nm may well arise from the (secondary) hydrogen bonding interaction between phenolic hydroxyl and substituents in the 3-position

viz methoxy or formyl, rather than with azomethine nitrogen.

From the foregoing results it may be concluded that the electronic spectra do provide firm evidence for (a)quinonoid structures for schiff bases when R = 5,6-benzo, 3-nitro and 5-nitro, (b)phenolimine structures, when R = 5-chloro, 5-bromo, 5-methyl, 4-methyl, etc., (c)intramolecular hydrogen bonding between azomethine nitrogen and phenolic hydroxyl and (d)an electronic interaction between the substituents R and Y when R = 5,6-benzo, indicating that Brocklehurst model would need reassessment in the cases of some schiff bases derived from heterocyclic amines such as 2-aminopyridines.

## References

1 Jenkins W T, J biol chem, 239 (1964) 1742.
2 Maley J R & Bruice J C, J Am chem Soc, 90 (1968) 2843.
3 Hemalatha Ranganathan, Ramasami T, Ramaswamy D & Santappa M, Chem Lett, (1979) 1201.
4 Brocklehurst P, Tetrahedron, 18 (1962) 299.
5 Burgi H B & Dunitz J D, Chem Commun, (1969) 472; Helv Chim Acta, 53 (1970) 1747.
6 Brown N M D & Nonhebel L, Tetrahedron, 24 (1968) 5655.
7 Tabei & Saitou E, Bull chem Soc Japan, 42 (1969) 1440.
8 Hemalatha Ranganathan, Ph D Thesis, University of Madras, 1980.
9 Hemalatha Ranganathan & Ramaswamy D, Curr Sci, (1978) 330.
10 Patai S, The chemistry of carbon-nitrogen double bond (Interscience, New York) 1970.
11 Gold V, Prog Stereochem, 3 (1962) 172.
12 Dudek G O & Holm R H, J Am chem Soc, 83 (1961) 3914.
13 Chatterjea K K & Douglas S E, Spectrochim Acta, 21 (1965) 1625.
14 Dudek G, J org chem, 32 (1967) 2016.
15 Matsen F A, Becker R S & Scott D R in Chemical applications of spectroscopy edited by W West (Interscience, New York) 1968, 258.
16 Mason S F, J chem soc, (1959) 1204, 1247.
17 Matsen F A, Robertson W W & Chouke, Chem Rev, 41 (1947) 273.
18 Bonnett R in The chemistry of carbon-nitrogen double bond edited by S Patai (Interscience, New York) 1970, pp.181.
19 Hemalatha Ranganathan, Rasasami T, Ramaswamy D & Santappa M, Indian J chem (to be submitted).