SYNTHESIS AND SPECTROSCOPIC STUDIES OF SCHIFF BASES FROM VARIOUSLY SUBSTITUTED BENZALDHYDES AND 2-AMINOMETHYL PYRIDINE

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ABSTRACT

Variously substituted hydroxybenzaldimines have been synthesized from the condensation of salicylaldehyde, o-vanillin, p-vanillin or vanillin with 2-aminomethyl pyridine. The compounds were characterized using elemental analyses, FT-IR, UV-vis. The spectroscopic methods showed the Schiff bases exist as a mixture of tautomer. The electronic effects of the variously substituted hydroxybenzaldehydes were examined in methanol and dimethylformamide (DMF). It was observed that the electronic effects of the substituents and solvents influenced the intramolecular hydrogen bonding via the conjugation of the heterocyclic ring or by modifying the capacity of the nitrogen atom from entering into hydrogen bonding.

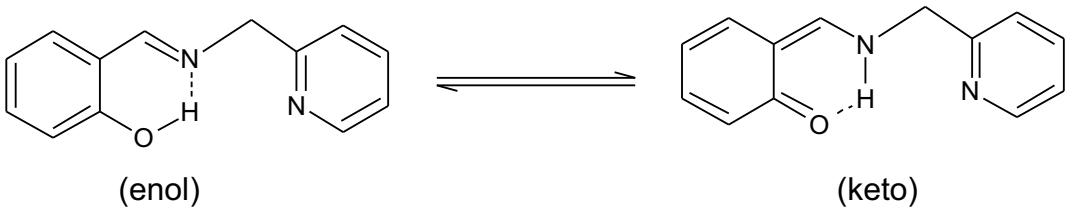
Keywords: Substituted Hydroxybenzaldimines, Tautomerism

INTRODUCTION

Schiff bases are formed when any primary amine reacts with an aldehyde or a ketone (Da Silva *et al*., 2011). Schiff bases have considerable flexible synthetic procedure; consequently a wide variety of them can be prepared. Structurally they are compounds in which the carbonyl group (C=O) has been replaced by an imine or azomethine group (C=N). The imine or azomethine groups are present in various natural, natural derived or artificial compounds such as pigment, dyes, catalysts etc. (Zhou *et al*., 2010). They are also used as intermediates in organic synthesis as well as polymers stabilizers (Sondhi *et al*., 2006). Schiff bases are known to exhibit a broad range of biological activities including antifungal, antibacterial, antimalaria, antiproliferative, anti-inflammatory, antiviral and antipyretic properties (Parekh *et al*., 2005, Sinha *et al*., 2008, Aggarwal *et al*., 2009, Adsule *et al*., 2006).

The physical and biological properties exhibited by Schiff bases are directly related to the presence of intramolecular H-bonding and as well as proton transfer equilibrium (Rozwadowski *et al*., 1993). For instance, photochromism arises from intramolecular proton transfer associated with a change in the π-electron configuration (Ünver *et al*., 2002, Nazir, 2000). Such molecular self-isomerization is associated with a change in the π-electron density distribution within molecule (Hoshino *et al*., 1988). Similarly, in rodopsine, halorodopsine and bacteriorhodopsine, the retinal molecule is connected to peptide through NH_2 group of lysine residue forming a Schiff base. Furthermore, enzymes such as tryptophan synthase, transaminases, transketolases, etc. are observed to contain Schiff bases (Wojciechowski *et al*. 2003).

There are two types of intramolecular H-bonding that are well known and have been intensely studied; these are the enol-imine (N----H-OH) and the keto-amine (N-H----O) (Garnovskii *et al*., 1993). Tautomerism which orginate from the proton transfer process has its equilibrium stabilized by the H-bonding resulting in an inter-conversion between the enol-imine and the keto-amine (Scheme 1) (Elmali *et al*., 1999; Ferringa *et al*., 1993, Yuzawa *et al*., 1993). Garranic *et al*., 1996 claimed that the type of H-bonding formed is not dependent of the stereochemistry of the molecules or the sort of substituent bond to the imine nitrogen but depends rather on the kind of aldehyde used. The Schiff bases derived from salicyaldehyde always form the N···H-O type of hydrogen bonding regardless of the nature of the N substituent (alkyl or aryl) (Elerman and Kabak, 1997; Elmali *et al*., 1998).



Scheme 1: Proton Transfer Equilibrium in Schiff Base.

Only the synthesis and structure of Schiff bases of salicylaldehydes with 2-aminomethylpyridine have been previously reported (Cimerman *et al.*; 1994). This paper reports the synthesis of four Schiff bases derived from the condensation reaction of various substituted hydroxylbenzaldhydes and 2-aminomethylpyridine. It also examined the occurrence of tautomerism via H-bonding using IR and UV-vis spectroscopic techniques. These two techniques -IR (Yildiz *et al.*, 1998; Ledbetter Jr., 1997; Lewis and Sandorfy, 1982) and UV-vis, (Salman *et al.*, 1990; Cohen and Flavian 1967; Ledbetter Jr, 1966; Allen and Roberts, 1980) have been used to study the existence of intramolecular H-bonding tautomerism between these species in solution and or in the solid state (Pierens *et al.*, 2012). However, this study investigates the influence of solvent as well as the effect of aldehyde on the formation of H-bonding that stabilizes the tautomers formed.

EXPERIMENTAL

Materials

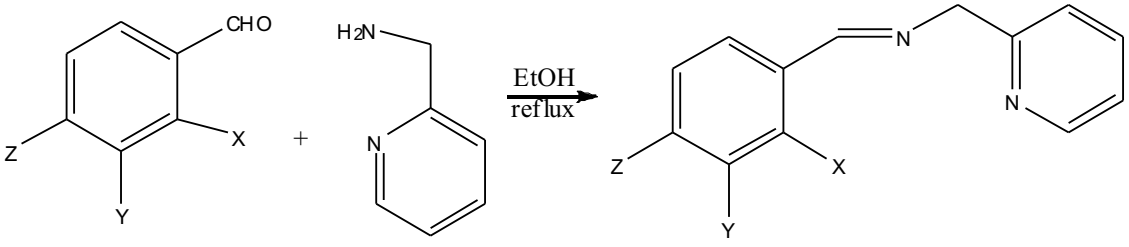
2-aminomethyl pyridine, o-vanillin, p-vanillin and vanillin were purchased from Sigma Aldrich and were used without further purification. Salicyaldehyde was distilled before use. The solvents were distilled and dried according to standard procedures before use.

Physicochemical Measurements

Mid infrared spectra were recorded on a Perkin-Elmer spectrum 2000 FT-IR spectrometer. The spectra were determined using a KBr beam splitter and a DTG detector, in the region 4000 - 400 cm^{-1} with typically 16 scans at an average resolution of 4 cm^{-1}. Samples were run as mulls in Nujol on KBr windows. Carbon, hydrogen and nitrogen combustion microanalyses were carried out using a Fisons Elemental Analyzer 1108 CHNS-O, at University of KwaZulu-Natal, South Africa. Melting points were determined using a Gallenkamp melting point apparatus. The results were uncorrected. The ultraviolet-visible (UV/vis) spectra were recorded on a Varian Cary 500 spectrophotometer. The compounds were dissolved in methanol (≈ 5.0 x 10^{-4} M). Low resolution mass spectra were obtained using a Finnigam Mat LCQ ion trap mass spectrometer equipped with an electrospray ionization source and 2 mg of the Schiff bases (dissolved in chloroform) were used for the analysis.

General Procedure for Schiff Base Synthesis

Equimolar quantities (5 mmol) of each aromatic aldehydes and 2-aminomethyl pyridine were dissolved in 10 ml of warm ethanol and refluxed for 1 hour. After cooling, the crystalline products were filtered and recrystallized from ethanol, and then dried under reduced pressure over silica. The synthetic process for the preparation of the Schiff bases is shown in Scheme 2 while the position of the substituents on the aldehydes used is listed in Table 1. The following Schiff bases were obtained from the condensation of 2-aminopyridine with the various substituted hydroxyl benzaldehyde.



Scheme 2: General Reaction Equation

Table 1: The Position of the Substituents and the Name of the Synthesized Schiff Bases

X	Y	Z		Products of condensation
OH	H	H	GL1a	2-((pyridin-2-ylmethylimino)methyl)phenol
OH	3-OCH_3	H	GL1b	5-methoxy-2-((pyridin-2-ylmethylimino)methyl)phenol
OH	H	4-OCH_3	GL1c	2-methoxy-6-((pyridin-2-ylmethylimino)methyl)phenol
H	3-OCH_3	4-OH	GL1d	2-methoxy-4-((pyridin-2-ylmethylimino)methyl)phenol

RESULTS AND DISCUSSION

The microanalysis and the analytical data for the Schiff bases are given in Table 2. Micro analytical data agree with the theoretical composition of the Schiff bases. Direct reaction of one equivalent of 2-aminomethyl pyridine with one equivalent of appropriate substituted salicyaldehyde in ethanol gave the corresponding Schiff base. Compounds 2, 3 and 4 were isolated as solid with 57, 90 and 81 % yields and each with sharp melting point, while compound 1 was oily with 68 % yield. Mass spectra data of compound GL1a, GL1b and GL1c confirmed the proposed structure of the Schiff bases. The spectra mass of three compounds show the molecular ion peak corresponding to their formulation. The resulting Schiff bases were intensely coloured. The intensities of the colours were attributed to different positions of the auxochromic groups (hydroxyl and methoxy) present as substituents on the asymmetric carbon. The colour of the product of the unsubstituted salicyaldehyde (GL1a) was yellow while those of all the products of methoxy substituted salicyaldehyde were brown. It implies that the presence of methoxy resulted in shifting the colour towards red.

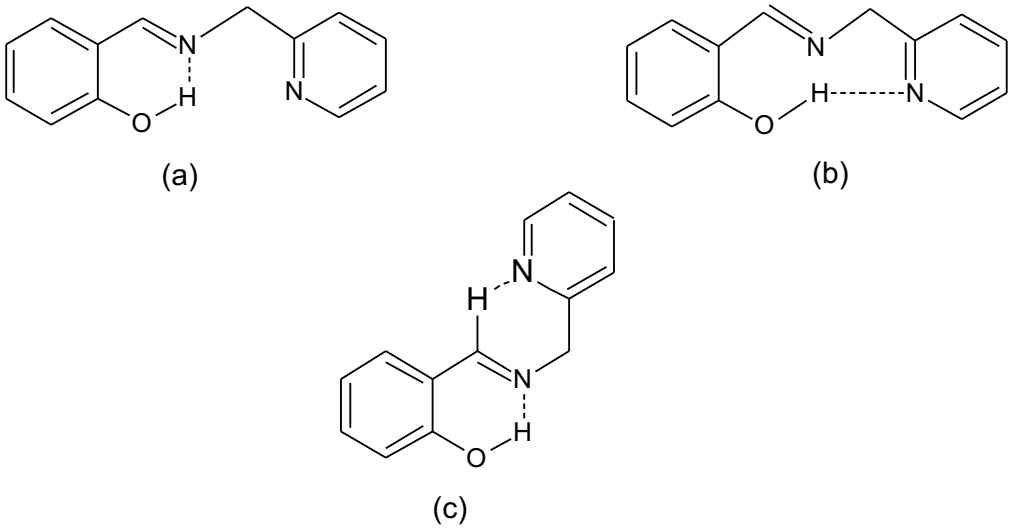
Table 2: Microanalysis and Analytical Data for the Schiff Bases GL1a-GL1d

No.	**Molecular formula**	**% Found (Calculated)**			**Color**	**Yield (%)**	**M.p. (°C)**	**Molar mass**	**M+**
		% C	% H	% N					
GL1a	$C_{13}H_{12}N_2O$	72.31 (72.09)	5.73 (5.60)	13.09 (12.90)	yellow	68	oily	211	211
GL1b	$C_{14}H_{16}N_2O_3$	69.96 (69.41)	6.29 (5.82)	11.52 (11.56)	brown	57	82-84	242	243
GL1c	$C_{14}H_{14}N_2O_2$	68.68 (69.41)	5.88 (5.82)	11.22 (11.56)	brown	90	94-95	242	243
GL1d	$C_{14}H_{14}N_2O_2$	65.03 (64.60)	6.10 (6.20)	10.26 (10.76)	brown	81	102-104	242	-

INFRARED SPECTROSCOPY

Selected bands of diagnostic importance are listed in Table 3 while Figure 1 shows the IR spectra of the Schiff bases under study. The bands assigned to the stretching of $C=N_{(imine)}$ bonds from compound GL1a-GL1d were observed at the frequency range of 1648 – 1617 cm^{-1}. However, as a result of H-bonding between C=N and the *ortho* hydroxyl substituent in GL1a, GL1b and GL1c, it was observed that the C=N bands were shifted to lower wave numbers (1627, 1618, and 1617 cm^{-1} respectively) and these has been attributed to the effect of intramolecular H-bonding between C=N and the *ortho* hydroxyl groups (Curran and Siggia, 1970). The appearance of the $C=N_{(imine)}$ stretching frequency at 1648 cm^{-1} in GL1d implies the absence of intramolecular H-bonding due to the *para* position of the hydroxyl group and therefore intermolecular H-bonding is a possibility. In addition, the presence of the electron donating methoxy groups in GL1b and GL1c produced a further reduction in wavenumber compared to the unsubstituted GL1a. This is because the methoxy substituent pushes delocalized electron density into the phenyl ring therefore increasing the bond order of C=N and consequently lowering $C=N_{(imine)}$ stretching frequency.

While there is interaction between *ortho* hydroxyl and the imine, there is also the possibility of interaction between the *ortho* hydroxyl and the nitrogen of the aminomethylpyridine for the Schiff bases GL1a, GL1b and GL1c. However, the *ortho* hydroxyl-imine hydrogen bond six-membered chelates (Scheme 3a and 3c) are expected to be more stable than the nine-membered imine-amino nitrogen chelate (Scheme 3b). Such associations would lead to a decrease in vibrational frequency of $C=N_{(pyridine)}$ from its range of 1585 – 1590 cm^{-1}. However this is not the case with this compound and as such the association did not occur in these compounds.



Scheme 3: Possible of Hydrogen-bond Configuration

The bands in the region 1303-1232 cm^{-1} have been ascribed to be as a result of stretching vibrations of phenolic C-O, signifying the existence of enol-imine species. However the presence of the stretching frequency around 1730 cm^{-1} also suggests that the products are in the keto form. This means therefore that all the products undergo tautomerism as both bands are present signifying a mixture of keto- and enol- tautomers. The evidence of H-bonding interaction is shown by the presence of medium and broad ν(OH) stretching band that move to lower wavenumber from its monomeric value of approximately 3600 cm^{-1} (Bellamy, 1953).

The presence of six member rings involving O-H-----N was observed as a result of the downward shift of the hydroxyl stretching frequency to 3442-3355 cm^{-1} (Bergmann et al., 1953). The case of GL1d could be as a result of intramolecular interaction between the *meta*-methoxy and the *para* substituted OH groups. In

addition, medium and broad ν(OH) stretching bands are the observed characteristic features for all the Schiff bases reported here. The results suggest associated properties between the *ortho* hydroxyl and the C=N group for all the ligands GLa-GLc or intramolecular association between the *meta*-methoxy and the *para*-substituted OH containing Schiff base 1d respectively. The observed bands within the 870-630 cm^{-1} range are assigned to the out-of-plane deformations of aromatic C-H groups. The stretching vibrations of the aromatic C-H groups give medium to weak bands above 2900 cm^{-1}.

Table 3: Electronic Absorption Spectra Data in Methanol (DMF) (nm) and Mid Infrared Frequencies (cm^{-1}) of the Schiff Bases GL1a-GL1d

S/N	π→π*		π→π*		π→π*	n→π*	νO-H	$\nu C{=}N_{(imine)}$	$\nu C{=}N_{(pyridine)}$	νC-O
GL1a	217	230	260	-	317	365 (**344**)	3417	1627	1589	1303
GL1b	221		266		345	380 (**341**)	3442	1618	1590	1287
GL1c	220		265		325, 336	425 (**332**)	3440	1617	1589	1259
GL1d	215	233		270	(317)	401 (**361**)	3355	1648	1583	1232

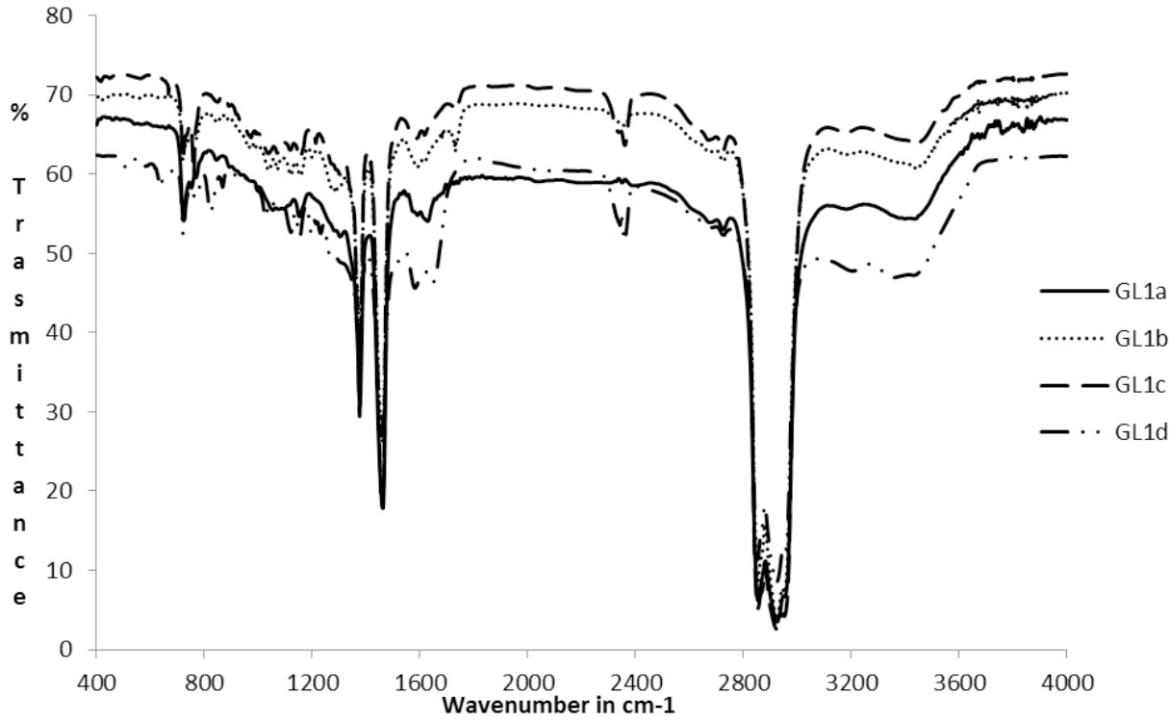


Figure 1: FT-IR Spectra GL1a-GL1d in Nujol on KBr Window

ELECTRONIC ABSORPTION SPECTRA

The electronic spectra data of all Schiff bases are listed in Table 3 while the spectra of all Schiff bases were shown in Figure 2 and 3. Electronic spectra were measured in methanol and Dimethyl formamide (DMF). The electronic absorption spectra of the Schiff bases in methanol produced four main bands. The two bands that are seen on the higher energy side, within the 217-230 nm and 260-265 nm are due to the transitions of the π→π* of the aromatic rings (Bosnich, 1968, Bilghe *et al.*, 2009). The third band within the 315-362 nm is

assigned to the π→π* of the imine (C=N) (Dowing and Urbach, 1966), while the bands appearing within the 380-425 nm is due to the n→π* of the imine. The presence of the band at 425 nm and 401 nm for GL1c and GL1d respectively confirms the predominance of the keto-amine tautomeric form in methanol and this is due to solvation and resonance stabilization caused by the presence of the methoxy group at the *meta* position (Dudek, 1963). The results corroborate the IR wavenumber found at 1730 cm^{-1}.

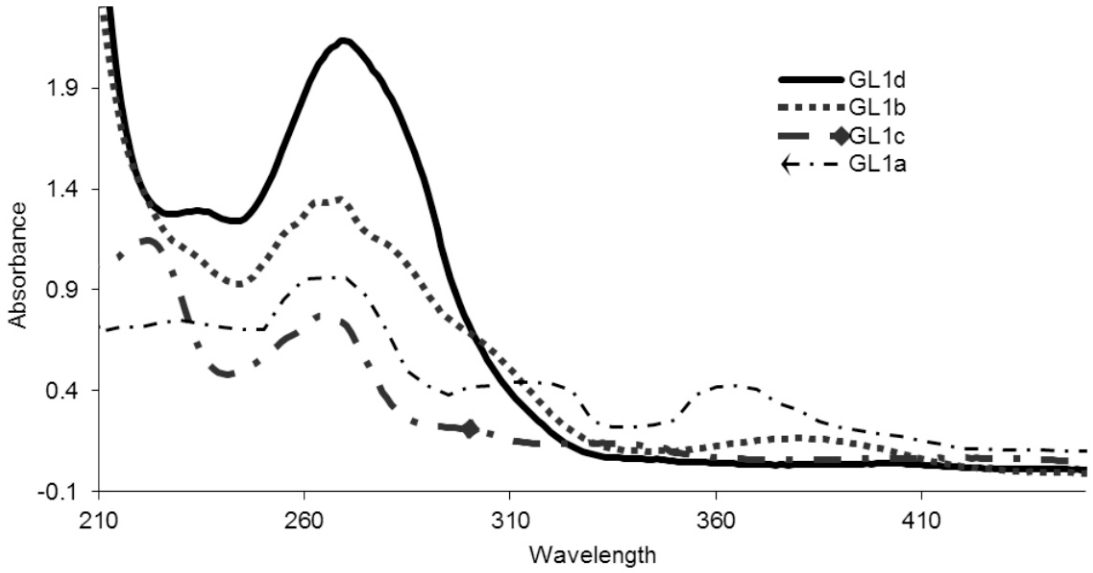


Figure 2: Electronic Spectra of GL1a, GL1b, GL1c and GL1d in Methanol at Concentration of 5 x 10^{-3} mol dm^{-3}

The insertion of methylene between the C=N and the pyridine isolates the pyridine from the conjugated phenyl rings, hence increasing the basicity of the azomethine nitrogen. However there is constant competition between ortho pyridine nitrogen and imine nitrogen to form H-bonding with the ortho hydroxyl hence could be the reason why the keto-amine is not predominant in GL1a and GL1b. Dudek (1963) claimed that the formation of keto-amine tautomer is due to solvation and resonance stabilization. The result confirmed that hydrogen bond type depends neither on the stereochemistry of the molecule nor methanol that we have used, but on the kind of aldehyde used (Gavranic *et al.*, 1996).

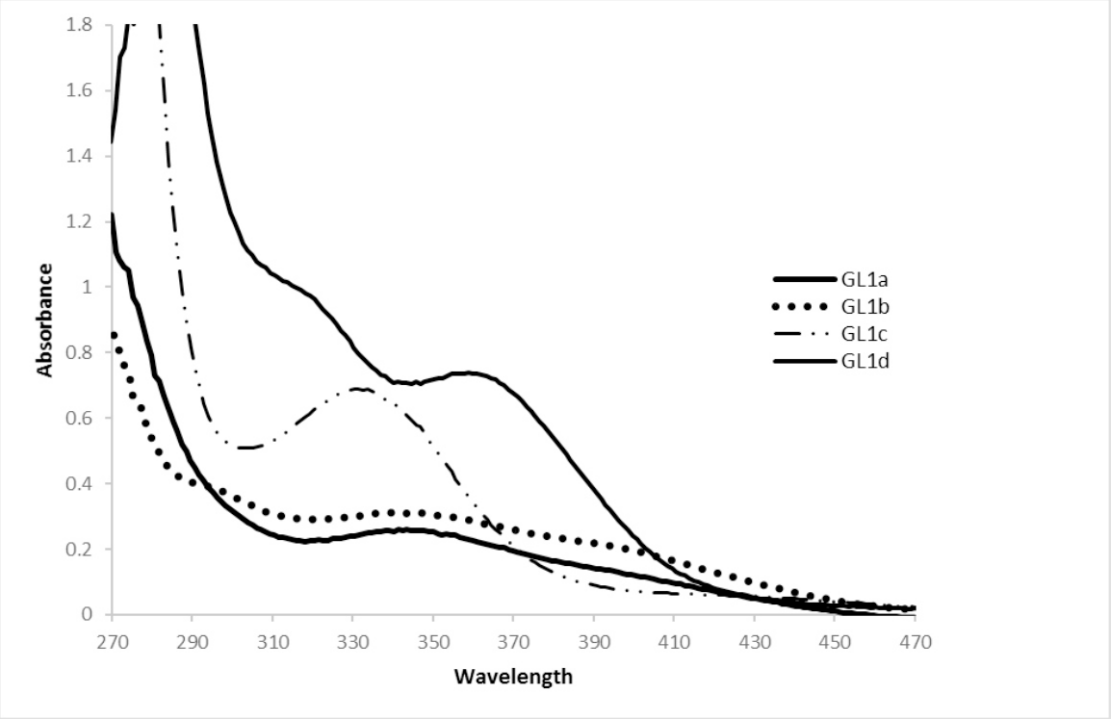


Figure 3: Electronic Spectra of GL1a, GL1b, GL1c and GL1d in DMF at Concentration of 5 x 10^{-3} mol dm^{-3}

It was not possible comparing wavelengths below 270 in DMF since the solvent absorb in this region. However, the band at 400 nm which depicts keto-amine tautomerism that was observed for Schiff bases 1c and 1d in methanol was absent. The bands assigned to $n \rightarrow \pi^*$ of the imine in methanol for the Schiff bases blue shifted in DMF, appearing in the range of 341-361 nm. This observation is ascribed to the solvent polarity (Alexander and Sleet, 1970). The enol-imine predominance in DMF implies that a strong intermolecular hydrogen bond exit between the solvent and the Schiff bases. The polar structures of the Schiff bases are destabilized by the DMF polarity, resulting in the blue shifting of the bands (Ungnade, 1953).

CONCLUSION

On the basis of spectroscopic and analytical data it can be concluded that intramolecular hydrogen bonding prescribes the geometry of Schiff bases **GL1a-Gl1c** while **GL1d** suggest intermolecular hydrogen bonding. The spectra data from the two techniques suggest mixture of tautomers. Comparison of UV/vis and IR spectra results indicated a significant influence of parent aldehyde and solvent on the tautomerization process. The protic and aprotic solvents caused the proton transfer reversible process, i.e., tautomer changing from the OH to NH form or vice versa. Parent aromatic aldehyde as well as solvent obviously plays a more important role in determining the equilibrium position of the tautomers formed.

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