Commun. Fac. Sci. Univ. Ank. Series B
V.51 (2). pp. 21-30 (2005)

SOLVENT EFFECTS ON THE ELECTRONIC ABSORPTION SPECTRA AND DISSOCIATION CONSTANTS OF SOME SULFA DRUGS

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(Received Sept. 25, 2005; Accepted Octb. 20, 2005)

ABSTRACT

Aryl Schiff bases compounds derived from sulpha drug derivatives (sulphonamide I, sulphadiazine II and sulphamethaxazole III) with salicylaldehyde were prepared and investigated by different spectroscopic techniques (Uv - vis. IR, ^{1}H- NMR) and elemental analysis. The effect of solvent polarity parameters, metal ion and electron acceptor were studied, the study was extended to evaluate the dissociate constants (pK_a) values of these compounds using spectrophotometric studies.

Keywords: Sulfa drug, Solvent effects, pk_a determination

INTRODUCTION

Schiff bases compounds are important due to their potential application as precursors for materials in different area of science and technology such as ceramic, glasses and catalysis. In the area of bioinorganic chemistry, interest in Schiff base complexes stems from using them as models for metalloprotein and metalloenzymes [1]. The effect of solvent and temperature on the dissociation of some indazole Schiff base derivatives of O- hydroxy azo- methine was studied. The thermodynamic metal- ligand stability constant of Be^{+2}, Mg^{+2}, Sr^{+2} and Ba^{+2} ions with azomethine indazole Schiff bases have been determined, furthermore, proton - ligand dissociation constant was calculated potentiometrically[2]. A large number of Schiff bases and their complexes have been studied because of their interesting and important properties, catalytic activation in hydrogenation of olefins[3,4].

The electronic absorption spectra of Schiff bases derived from Aryl amines in organic solvents and buffer solutions have been studied [5]. Molecular complexes of charge transfer of some 4-(2-hydroxy -4'- substituted benzylidene amino)-2-methyl quinoline with fluoranil and 2,4-dinitrofluorobenzene have been investigated by IR, ^{1}H-NMR, electronic absorption and ESR spectroscopy [6].

Issa et al. [7] studied the electronic absorption spectra of some hydroxyl aryl Schiff bases in organic solvents of different polarity. Also the pK_a values of the investigated compounds were determined from spectral measurements in buffer solutions of varying pH.

In the present paper the electronic absorption spectra of some Schiff base compounds derived from sulfa drugs have studied in organic solvents of varying polarity and buffer solutions of different pH. Furthermore molecules charge transfer complexes, the main IR and ^1H NMR signals were assigned .

Experimental

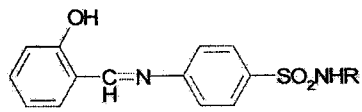
Chemical

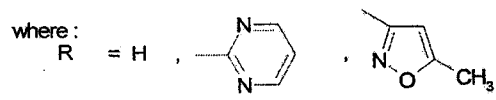
Reagent grade salicylaldehyde (Merck), sulphonamide, sulphadiazine (Tiba), sulphamethoxazole (Luna Co.), 5,5- diethyl barbituric acid, boric acid and citric acid anhydrous (Fluka) were used. The organic solvents ethanol (EtOH), methanol (MeOH), chloroform ($CHCl_3$), dimethylformamide (DMF), acetone, n-propanol (Pr-OH), dichloroethane ($Cl_- CH_2 - CH_2 - Cl$), carbon tetrachloride (CCl_4) and n-hexane ($C_6 H_{14}$) were obtained as pure grade material from (BDH).

Preparation of sulphonamide Schiff bases compounds:

The preparation of Schiff base compounds depends on the condensation of the sulphonamide, sulphadiazine and sulphamethoxazole (0.01 mole) with the salicyaldehyde (0.01 mole) under reflux in ethanol [8,9] for 4-6 h. On allowing the reaction mixture to cool, the solid is separated out, then filtered off and recrystallized several times from ethanol and preserved in a desiccator over dried silica gel. The purity of the resulting compounds was checked by melting point constancy and the structures of presented compounds were conformed by IR spectra ^1H-NMR and elemental analysis [7].

The formula of the compounds have the following structure:-





(I) (II) (III)

Preparation of solutions

Solutions

Stock solutions of 1×10^{-3} M of the Schiff base compounds were prepared by dissolving the accurate weight of the solid compound in the required of ethanol. The required concentration was obtained by accurate dilution.

Universal buffer solutions

Universal buffer solutions of pH values ranging between 2-12 were prepared as recommended by Britton[10]. It consisted of an acid mixture which was 0.04 M of each of acetic acid, boric acid and phosphoric acid .A series of buffer solutions of pH 2-12 was prepared by mixing 75 ml of the acid mixture in 250 ml measuring flask with the appropriate volume of 0.4 M sodium hydroxide and completed to the mark with twice distilled water. The pH of each buffer solution was checked using a Digital ORION pH-meter Model 201 accurate to ± 0.05 pH units.

Results and Discussion

ELECTRONIC ABSORPTION SPECTRA IN ORGANIC SOLVENTS

The electronic absorption spectra of the aryl azomethine compounds under investigation involve the absorption bands due to various electron transitions liable to occur within the molecules such as:

a) Bands due to localized excitation of the in-electrons within the aromatic moieties attached to the azomethine group which generally lies in the Uv-region.

b) Bands corresponding to localized electronic transitions within the azomethine group namely the excitation of the π and n- electrons which lie in the visible region.

From the localization point of view the absorption of an organic molecule is the summation of the absorption bands of different fragments. Accordingly, for an azomethine compound the absorption spectrum should contain the bands due to electronic transitions within the aromatic moieties as well as the -N=CH- group. The possible interaction between the -N=CH- group and the aromatic rings will leads to the phenomenon of intramolecular charge transfer interaction (CT band), which in turn leads to the following possibilities:-

i) The appearance of new bands.

ii) The shift of absorption bands due to electronic transitions within the molecular parts influenced by the charge migration.

Spectrophotometric studies of substituted azomethine sulphonamide derivatives had pointed out that the intense bands due to the π-π^* transition of the -N=CH- linkage mask almost totally the weak band due to $n \rightarrow \pi^*$ transition, based on this, the latter band was reported only in few investigations. The π-π^* transitions of the –N=CH-

group are also influenced by one type of interaction with the π-electron of the phenyl rings, i,e. involve partial charge transfer character which occurs in the direction of azomethine group (ϕ--»N=CH-) if the phenyl group has an electron donating substitutents, while the reverse direction (ϕ«--N=CH-) takes place when the phenyl ring carries an electron with drowning group Fig.(1).

From which it is clear that their electronic absorption spectra should comprise bands due to electronic excitation within the phenyl, sulphonamide and azomethine groups along with these hands due to charge transfer interactions. The electronic spectra in ethanol display four absorption bands as summarized, the first band (A lies at 192-220 nm) while the second one (B) is found at (220-260 nm). These two bands are characterized by high molar absorptivities and are assigned. The moderate and low energy π-π* transitions within the aromatic moieties are corresponded to (`La «---'A) and (`Lb «--- 'A) states respectively. The third band (C) located at~ 270 nm is due to the π-π* transition of the –N=CH- of the azomethine linkage. The broad, composite band (D) located at longer wavelength side (λ_{max} > 348 nm) is due to a charge transfer migration (CT) involving the whole molecule. This band originates, most probably, from the sulphonamide moiety as a donor part to the azomethine linkage as an acceptor one. This can be supported of calculating the energy of the charge transfer E_{CT}, using the relation [11]:

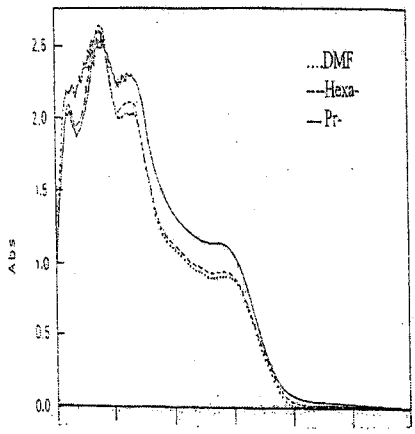


Fig.(1):Electronic absorption spectra of compound II in solvent (DMF,Hexa and Pr-).

Hexa-).

$$E_{CT}\,(eV) = 1243.6 / \lambda_{max}\,(nm)$$

Inspection of the spectral curves shows that, the bands due to local excitation within the aromatic moieties (π-π* transitions) display irregular solvent shifts, though the general trend is a red shift with increased solvent polarity. This behavior is characteristics of the π-π* transition of substitutuent, where the solvent substitutent interaction would be additive or counter acts the solvent shift of the aromatic moiety. This is in agreement with the ease of charge migration taking place from the hydroxylated moiety as discussed above.

Attempts have been made to assess the influence of solvents on the CT band using variety of experimental conditions, this gives some empirical values to different solvents which are the microscopic and macroscopic solvent polarity parameters.

Microscopic Solvent Polarity Parameters

The first empirical parameters is the so called Z-value introduced by Kosower[12,13] who was the first to set up comprehensive scale for solvent polarity. He termed the molar transition energy calculated from the position of the absorption maximum, Z-value:

$$Z = 2.8259 / \lambda_{(nm)} \quad (K\ Cal\ mole^{-1})$$

Reichardt and Dimroth[14,15] applied Kosower's technique to a series of pyridinium-N-phenol betamine which are perhaps the most solvent dependent spectra known. The molar transition energies of the betamines termed E_T value and can be calculated using the following relation:

$$E_T(K.Cal.mole^{-1}) = 2.829 \times 10^{-3}\ \nu\ (cm^{-1})$$

Macroscopic solvent polarity parameters:

Solvent properties which show a reasonable degree of correlation with the transition energy are the dielectric constant (D) and the refractive index (n). The relation governing them was given by Gati and Szalay [16] in the following form:

$$\Delta\bar{\nu} = (a-b)(n^2-1\ /2n^2+1) + b(D-1/D+1)$$

where (a) and (b) are constants depending on the nature of solute.

The more precise relations are the functions of dielectric constant given by Suppan [17] of the type:

$$F(D) = 2(D-1)/(2D+1) \text{ and } \phi\ (D) = (D-1)/(D+2)$$

So, it is clear that the macroscopic solvent polarity parameters are not the main factors affecting the position of the CT band, it is more possible to suggest that some sort of specific solute-solvent interaction (solvating or more effectively hydrogen bonding between solute and solvent molecules) may also contribute to the solvent shift. Hence, the shift in CT band position is actually the resultant effect of; (i) the changed solvent polarity, (ii) the shift due to intermolecular hydrogen bond formed between solvent molecules and OH or most probably the -CH = N- group and (iii) the shift due to intermolecular hydrogen bonding. It must be also noted that, red shift of the CT band with increased solvent polarity denotes the increased solvent stabilization of the excited state since this would be a more polar structure.

Determination of the dissociation constant values

The absorption spectra of the sulpha drug under investigation were studied in buffer solutions of varying pH values (2.5-11.7) and scanned along the visible range 200-500 nm. In each run, a known volume of the sulpha drug was diluted to 10 ml using the desired buffer solutions, the measurements were carried out at room temperature (25 ^{0}C) to determine the dissociation constants of (NH) or (OH) protons of the sulpha drug compounds.

The absorption spectra of $5x10^{-5}$ of the sulpha drugs (I, II and III) investigated in solutions of varying pH values are shown in Fig.(2). The variation of absorbance with pH has been utilized in calculating the pK_a of NH group and hydroxyl group.

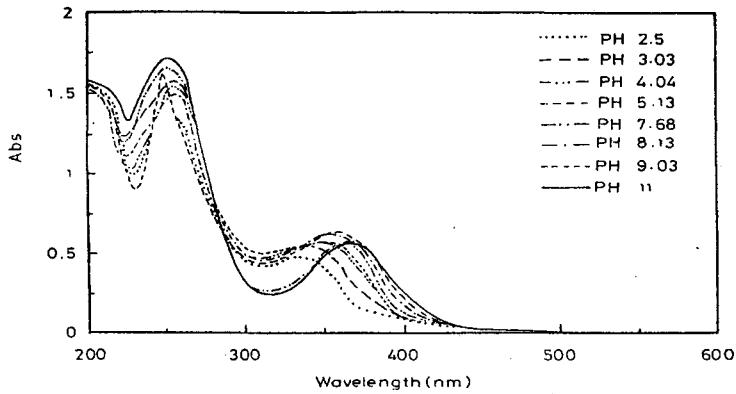


Fig.(2):Absorption spectra of compound (I) in buffer solution of different pH values

Table (1): The ionization constant (pK_a) for the Schiff base compounds (I-II)

Compound	λ nm	Method (1)	Method (2)	Method (3)	Mean value
I	270	5.45	5.6	7.4	6.15
	340	5.65	6.5	8.2	6.78
II	277	9.6	7.4	8.2	8.40
	323	9.6	7.39	8.8	8.59
III	274	9.45	7.05	7.8	8.10
	326	9.55	7.1	7.6	8.08

The method applied for the pK_a values are the half-height, the limiting absorbance and the modified limiting absorbance Figs.(3,4). The pK_a values are calculated at different wavelength and listed in Table (1). The electronic absorption spectra of the sulpha drug compounds under consideration in buffer solutions of varying pH values (2.5 - 11.7) exhibited two bands. The first band at 270-340 nm, and the second one at 277-323 nm. The first band is due to the local excitation of the π-π^* transition within the aromatic moity. While the second band is due to charge transfer interaction within the whole

molecule taking place from the azomethine (CH=N) group as a source to the aromatic ring.

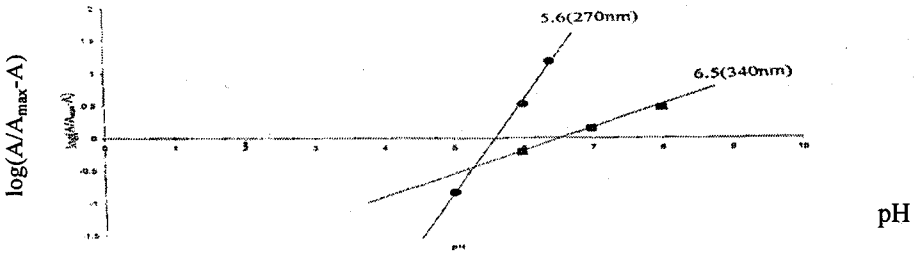


Fig.(3): The limiting absorbance method for determining the pKa for compound (I)

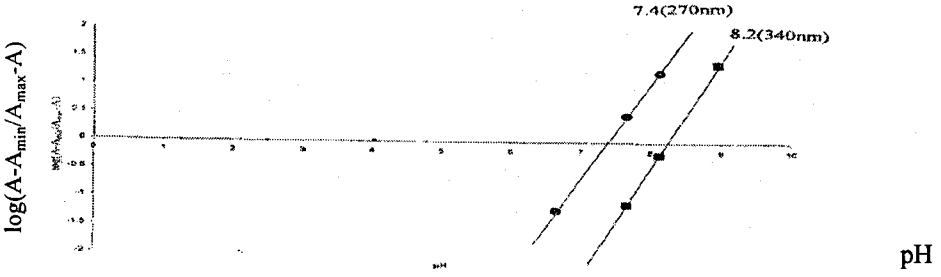
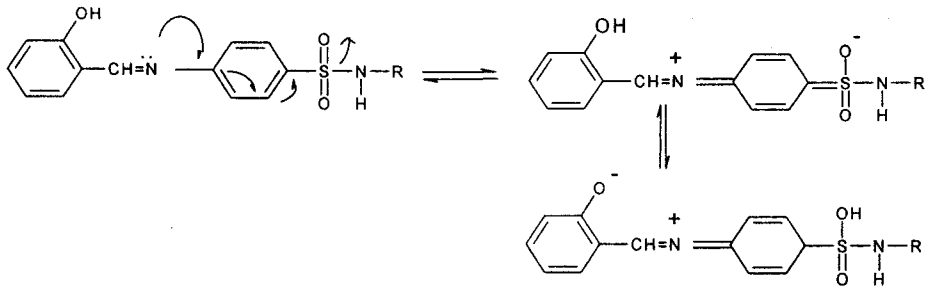


Fig.(4): The modified limiting absorbance method for determining the pKa for compound (I)

Although the first band for sulpha drugs I, II and III is less sensitive to both medium and substituents but it was found to exhibit a small blue shift on going from acidic to alkaline medium, on the other hand, the CT band of these compounds, being sensitive to both substituents medium and suffers a markedly blue shift as the pH of solution is turned alkaline.

So a clear isobestic point is obtained indicating the presence of two different species in equilibrium, leading to the formation of imine form as follows:



Effect of Metal ions:-

The absorption spectra of the original compounds show maximum wavelength at 352, 381 and 380.5 nm for compounds I, II and III respectively, whereas the complexes appear at λ_{max} 301-394 nm as shown in Fig.(5).

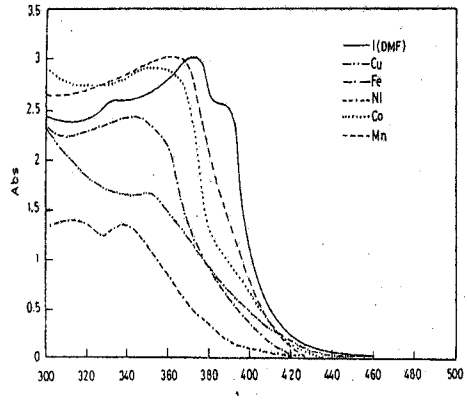


Fig.(5): Electronic absorption spectra of compound (I) with different metal ions.

In the presence of metal ions there is a change in the location and intensity of the absorption band, a small bathochromic shift was observed compared those of the ligands with the different metal ions[18,21] . The results indicated that at least 1.5 ml of $5x10^{-3}M$ of the compounds (reagents) was sufficient to achieve maximum colour intensity. The absorbance of the formed complexes using different amounts of the reagent showed that complete stabilization and clarify of solution within at least 3.0 min at room temperature and remain constant for at least 12 hrs.

The highest absorbance was obtained in the following order (Ni^{2+}< Cu^{2+} <Fe^{3+}<Co^{2+} < Mn^{2+}) buffer reagent, this order was applied for further studies, the essential for analytical studies is to increase the absorbance of the formed complex.

3.4 Effect of electron acceptors:-

The association constant (K) and molar extinction coefficient (ε) of the CT complexes studied have been determined by utilizing rearranged form of the Bensi-Hildebrand equation [22]:

$$[A] + [D] = \frac{\varepsilon L[A][D]}{d} - \frac{1}{k_{CT}}$$

where [A] and [D] are initial molor concentration of the acceptor and the donor respectively, L the path length in centimeters, and d the absorption, this equation enables one to determined (K) and (ε) independently for the formed complexes under the condition of constant [A] and [D]>> [A]. The values of ε and k are determined from the gradient and negative intercept of the linear plots of [A] + [D] against [A] [D]/d as shown in Fig. (6). in which both K and ε were evaluated.

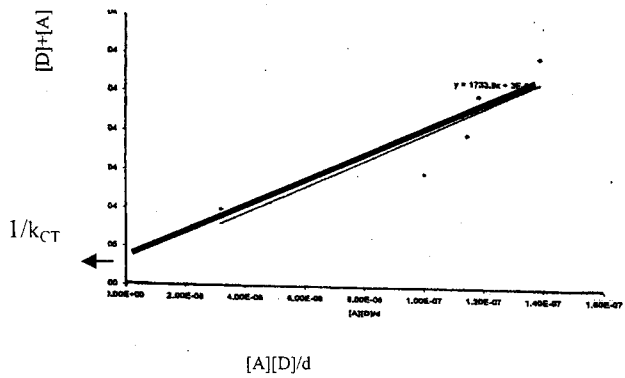


Fig.(6):The relation between [A]+[D] and [A][D]/ d for compound (II) with different electron acceptors (Bensi- Hildebrand equation)

ÖZET: Sülfa ilaç türevleri (sülfamit I sulfadiazine II ve sülfametaksazol III) ile salisilaldehitten atil schff bazı bileşikleri hazırlanmış ve farklı spektroskopik teknikler (uv-görünür, IR, HNMR) ve element analiziyle incelenmiştir. Çözücü polarlık parametreleri, metal iyonu ve electron akseptör etkileri araştırılmış, çalışma spektrometrik yöntemler kullanılarak bu bileşiklerin ayrışma sabitlerini (pKa) değerlendirmeye de uygulanmıştır.

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