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Intramolecular Hydrogen Bonding and Tautomerism in Schiff Bases: Synthesis, Spectroscopic and Theoretical Studies of *N*-(2,2'-Methylene*bis*(4-methoxyphenyl)salicylidene and *N*-(2,2'-Methylenebis(4-methoxyphenyl)-2-oxonaphthalidene-methylamine

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The new Schiff bases (**4** and **5**) were synthesized respectively from the reaction of 2,2'-methylene*bis*(4-aminomethoxybenzene) (**3**) with salicylaldehyde and 2-hydroxy-1-naphthaldehyde. The products have been characterized by elemental analysis, FTIR, UV-visible and NMR techniques. The tautomeric equilibria of 2-hydroxy Schiff bases were investigated in polar, non-polar, acidic and basic media by using UV-visible absorption spectra. Compound **4** is in, predominantly, phenol-imine (O-H···N) form, whereas compound (**5**) is in tautomeric equilibria (phenol-imine, O-H···N and keto-amine, O···H-N forms) in polar and non-polar solvents, as supported by ^{1}H NMR and UV-visible data. All of the NMR assignments were made using ^{1}H, ^{13}C NMR and aided by 2D COSY, NOESY, HETCOR and HMBC heteronuclear correlation techniques. In addititon, theoretical calculations have been carried out PM6 methods in the MOPAC2009 and Marvinbeans-5_3_01-windows programs. The heat of formation (ΔH_f), enthalpy (ΔH), entropy (ΔS) Gibbs free energy (ΔG), conformations and tautomers of the synthesized compounds are estimated by using MOPAC2009 (PM6) program.

Keywords: Schiff bases, Tautomerism, Hetcor, HMBC, UV-visible, Theoretical calculation.

INTRODUCTION

Schiff bases and their metal complexes have attracted more attention due to their pharmacological properties as antibacterial, antifungal, anticancer and antiviral agents[1-6]. Photochromism is another characteristic of these materials leading to its application in various areas such as electronic display systems, optical switching devices, information storage and optical computers[7-9].

In view of the importance and also the usefulness of these compounds, the chemists are prompted to generate the derivatives by introducing different substituents. The presence of *ortho* hydroxy group, for instance, has been regarded as one of the important elements which favours for the existence of intramolecular hydrogen bonding (O-H···N and O···H-N) and also the tautomerism which accounts for the formation of either phenol-imine or keto-amine tautomers[10-12]. In 2-hydroxy Schiff bases strong hydrogen bonds between the OH groups and the imine nitrogens are formed. In some instances, the hydrogen atom of the OH is completely transferred to the imine nitrogen, causing photochromism[10,13]. In other words, phenol-imine $\rightleftharpoons$ keto amine equilibrium shifts predominantly to the keto-amine side[10,13-16,19,20]. This type of tautomerism in 2-hydroxy Schiff bases have been investigated using IR[10,17,21-23], UV-visible[10,13,14], ^{15}N NMR[17,20,24], ^{1}H NMR [17,18,21-23], ^{13}C NMR[16,18-20,24] and X-ray crystallography techniques[5,10,11,19,22,24] in solution and in solid state. On the other hand, experimental results are supported by theoretical calculations on the tautomeric forms of the *ortho*-hydroxy Schiff bases[25-28].

In this study, we report (i) the synthesis of compounds **3**, **4** and **5** (Fig. 1), (ii) spectroscopic characterizations of the new compounds (**4** and **5**) in order to establish the hydrogen bonding and tautomerism and (iii) theoretical calculations. In addition, total assignments of ^{1}H and ^{13}C NMR spectra for the structure are unambiguously made with the help of H-H correlation spectroscopy (H-H COSY), as well as heteronuclear chemical shift correlation (HETCOR) and heteronuclear multiple-bond correlation (HMBC).

EXPERIMENTAL

2-Hydroxybenzaldehyde, 2-hydroxy-1-naphthaldehyde, 4-nitrophenol, hydrazine hydrate (95 %), NaH, Pd-C (5 %) and iodomethane were purchased from Fluka and used without further purification. Benzene, methanol, THF and DMSO were used by redistallated. Melting points were measured on a Sanyo Gallenkamp apparatus using a capillary tube. Elemental analyses (C, H and N) were performed using a Vario EL III CHNS elemental analyzer. UV-visible spectra were measured with

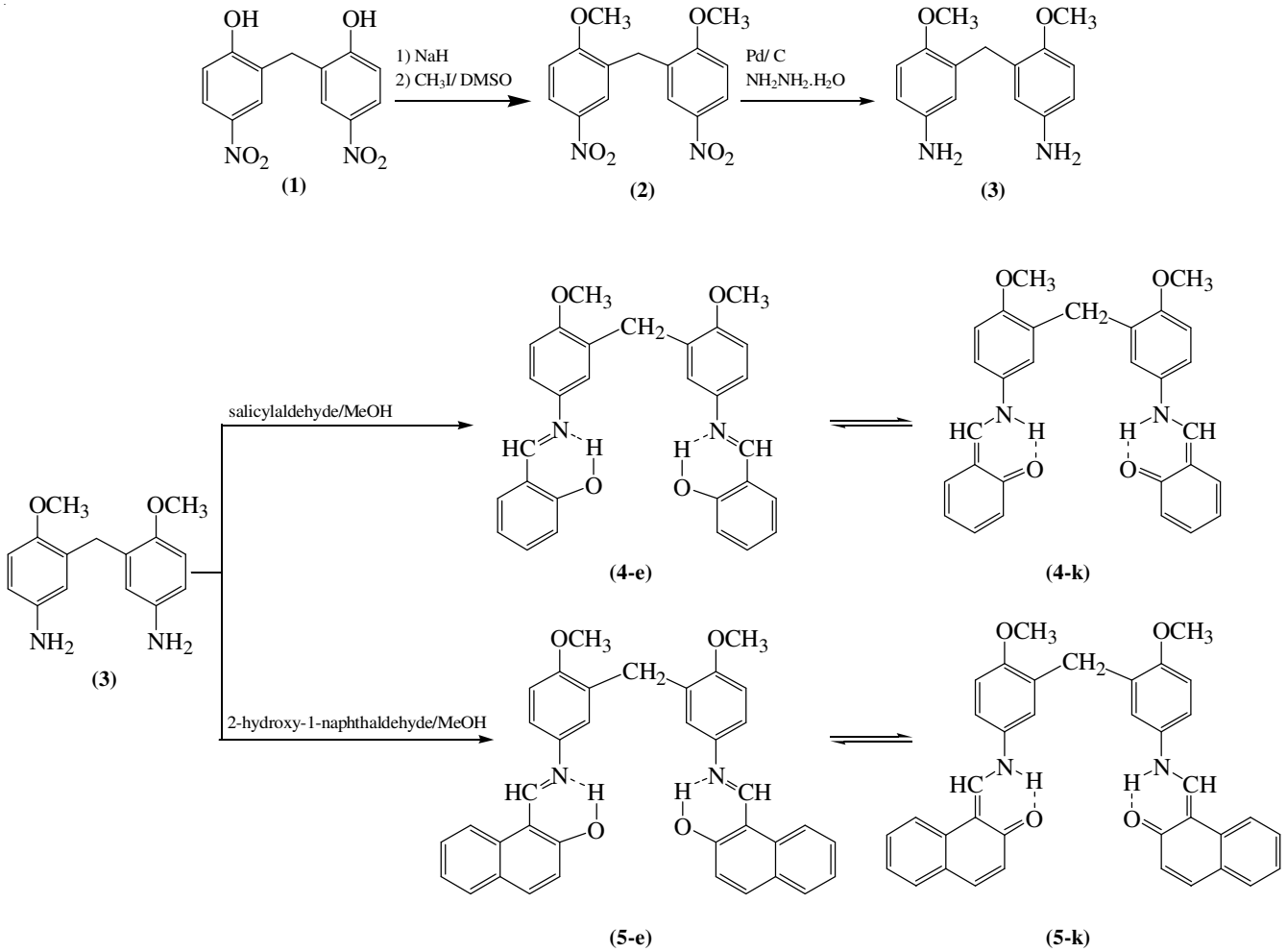


Fig. 1. Synthesis of compound **3**, **4** and **5** (e: Phenol-imine, k: Keto-amine)

Shimadzu 3150 spectrophotometer using 1 cm Quartz cell. ^{1}H and ^{13}C NMR, COSY, HMBC and HETCOR spectra were obtained on a Bruker 500 MHz Ultrashield Spectrometer equipped with a 5 mm PABBO BB-inverse gradient probe. The concentration of solute compounds was ca. 150 mg in 1 mL $CDCl_3$ and DMSO-d_6. Standard Bruker pulse programs[29] were used in the experiments. FTIR spectra were recorded on a Perkin Elmer Spectrum 100 FTIR spectrometer in KBr discs. The CS Chemoffice[30] and the MOPAC2009[31] programs were used for the calculation of the physicochemical properties of the molecules. All the molecules were drawn by the CS ChemDraw and then minimized by the MM2 method in the CS Chem 3D program. Their theoretical calculations in aqueous phase was carried out using the new semiempirical PM6 quantum chemical methods in the MOPAC2009 program.

2,2'-Methylene*bis*(4-nitrophenol) (1): 2,2'-Methylene*bis* (4-nitrophenol) was prepared according to the published procedure[26].

2,2'-Methylene*bis*(4-nitromethoxy benzene) (2): The reaction of **1** (5.32 g; 18 mmol) and NaH (1.44 g, 24 mmol) in THF produced sodium[2,2'-methylene*bis*(4-nitrophenolate)]. A solution of sodium[2,2'-methylene*bis*(4-nitrophenolate)] (3.34 g; 10 mmol) used as prepared in DMSO (100 mL) and then iodomethane (2.84 g; 20 mmol) was added dropwise to this solution with stirring. The reaction mixture was maintained at reflux for 8 h and then cooled to room temperature, forming a yellow precipate.

The yellow residue was filtered and washed with water (50 mL). The white-yellow solid was dried under *vacuo*, yield 3.88 g (67 %), m.p. 186 °C. Elemental analysis calcd. for $C_{15}H_{14}N_2O_6$: C, 56.60; H, 4.43; N, 8.80. Found: C, 56.51; H, 3.72; N, 8.60. IR (KBr, ν_{max}, cm^{-1}): Ar-$H_{(asym.)}$ 3070 w, Ar-$H_{(sym.)}$ 3027 w, C=C 1589 vs, NO_2 1517 s, 1343 vs, C-O-$_{(arom.)}$ 1268 s.

2,2'-Methylene*bis*(4-aminomethoxy benzene) (3): To the mixture of 2,2'-methylene*bis*(4-nitromethoxybenzene) (**2**) (5.01 g; 15 mmol) and Pd-C catalyst (0.25 g) in dry ethanol (150 mL), hiydrazine hydrate (5 mL) was added dropwise with stirring. The mixture was maintained at reflux for 10 h and then allowed to an ambient temperature. The reaction mixture was filtrated and the solvent was removed. The crude white-solid product was crystallized in ethanol. Yield 2.30 g, (57 %), m.p. 128 °C. Elemental analysis calcd. for $C_{15}H_{18}N_2O_2$: C, 69.74; H, 7.02; N, 10.84. Found: C, 69.72; H, 6.47; N, 10.79 IR (KBr, ν_{max}, cm^{-1}): NH_2 3400 m, Ar-$H_{(sym.)}$ 3030 w, 3000 w, Ar-$H_{(asym.)}$ 3080 w, C=C 1600 vs, C-O-$_{(arom.)}$ 1234 s.

***N*-[2,2'-Methylene*bis*(methoxyphenyl)]salicylidene (4):** A solution of 2,2'-methylene*bis*(4-aminomethoxybenzene) (3) (2.58 g; 10 mmol) and 2-hydroxybenzaldehyde (10 mmol, 1.1 mL) in methanol on the ice bath was stirred for 4 h. The precipitated solid was filtrated and then it was recrystallized from methanol. Yield 3.50 g (75%), m.p. 182 °C. Elemental analysis calcd. for $C_{29}H_{26}N_2O_4$: C, 74.66; H, 5.62; N, 6, Found: C, 75.32; H, 5.43; N, 6.15. IR (KBr, ν_{max}, cm^{-1}) NH 3435 s,

Ar-$H_{(asym.)}$ 3056 w, Ar-$H_{(sym.)}$ 3010 w, C=N 1620 vs, C=C 1598 vs, C-O-$_{(arom.)}$ 1252 s. ESI-MS: 467 $[M + H]^+$.

***N*-[2,2'-Methylene*bis*(methoxyphenyl]-2-oxonaphthalidenemethylamine (5):** A solution of 2,2'-methylene*bis*(4-amino methoxybenzene) (**3**) (2.58 g; 10 mmol) and 2-hydroxy-1-naphthaldehyde (1.72 g; 10 mmol) in methanol on the ice bath was stirred for 5 h. The precipitated solid was filtrated and then it was recrystallized from methanol. Yields 4.10 g (72 %), m.p. 193 °C. Elemental analysis calcd. for $C_{37}H_{30}N_2O_4$: C, 78.43; H, 5.34; N, 4.94, Found: C, 78.70; H, 4.92; N, 5.33. IR (KBr, ν_{max}, cm^{-1}) NH 3435 s, Ar-$H_{(asym.)}$ 3046 w, Ar-$H_{(sym.)}$ 3023 w, C=N 1623 vs, C=C 1564 vs, C-O-$_{(arom.)}$ 1250 s. ESI-MS: 567.1 $[M + H]^+$.

RESULTS AND DISCUSSION

The FTIR spectra of compounds **2-5** exhibit two medium intensity absorptions at 3077-3060 and 3030-3000 cm^{-1} attributed to the asymmetric and symmetric stretching vibrations of the aromatic C-H bonds. The characteristic $\nu(NH_2)$ (3400 and 3211 cm^{-1}) stretching bands of compound **3** disappear in the spectra of compounds **4** and **5**.

The characteristic ν(C=N) absorption bands were observed at 1620 and 1623 cm^{-1} for compounds (**4**) and (**5**). The observation of aromatic ν(C-O) at 1305 cm^{-1} and the O-H stretch at 4000-3500 cm^{-1} region was not observed in the IR spectrum for compound (**5**). This observation implies that the H atom from the O-H group in compound migrates to azomethine N atom *via* keto-amine form (N-H···O) intramolecular hydrogen bonding in the solid state.

UV-visible studies: The Schiff bases show absorption in the range greater than 400 nm in polar and nonpolar solvents[10,13,19,28]. The UV-visible spectra of the compounds (**4** and **5**) were found to be useful in understanding the degree of stabilization upon these series of phenol-imine and keto-amine tautomers[10,11].

The UV-visible spectra of the compounds (**4** and **5**) were studied in polar and non-polar solvents in both acidic (CF_3COOH) and basic (NEt_3) media. In solutions, the expected tautomeric species are illustrated in Fig. 2 and the calculated keto-amine forms are given in Table-1, which are estimated from the following equations: $A_2/A_1 = x/(100-x)$ where, A_1 = the absorbance of the phenol-imine tautomer ($\pi\rightarrow\pi^*$), A_2 = the absorbance of the keto-amine tautomer ($n\rightarrow\pi^*$), x = the percentage of keto-amine tautomer. The electronic absorbtion spectra of compound **5** displays four mean bands (Fig. 3). The first (210-234 nm) and the second (240-281 nm) bands are assigned to the $\pi\rightarrow\pi^*$ transitions of aromatic rings. The third band (301-334 nm) also indicates $\pi\rightarrow\pi^*$ transitions

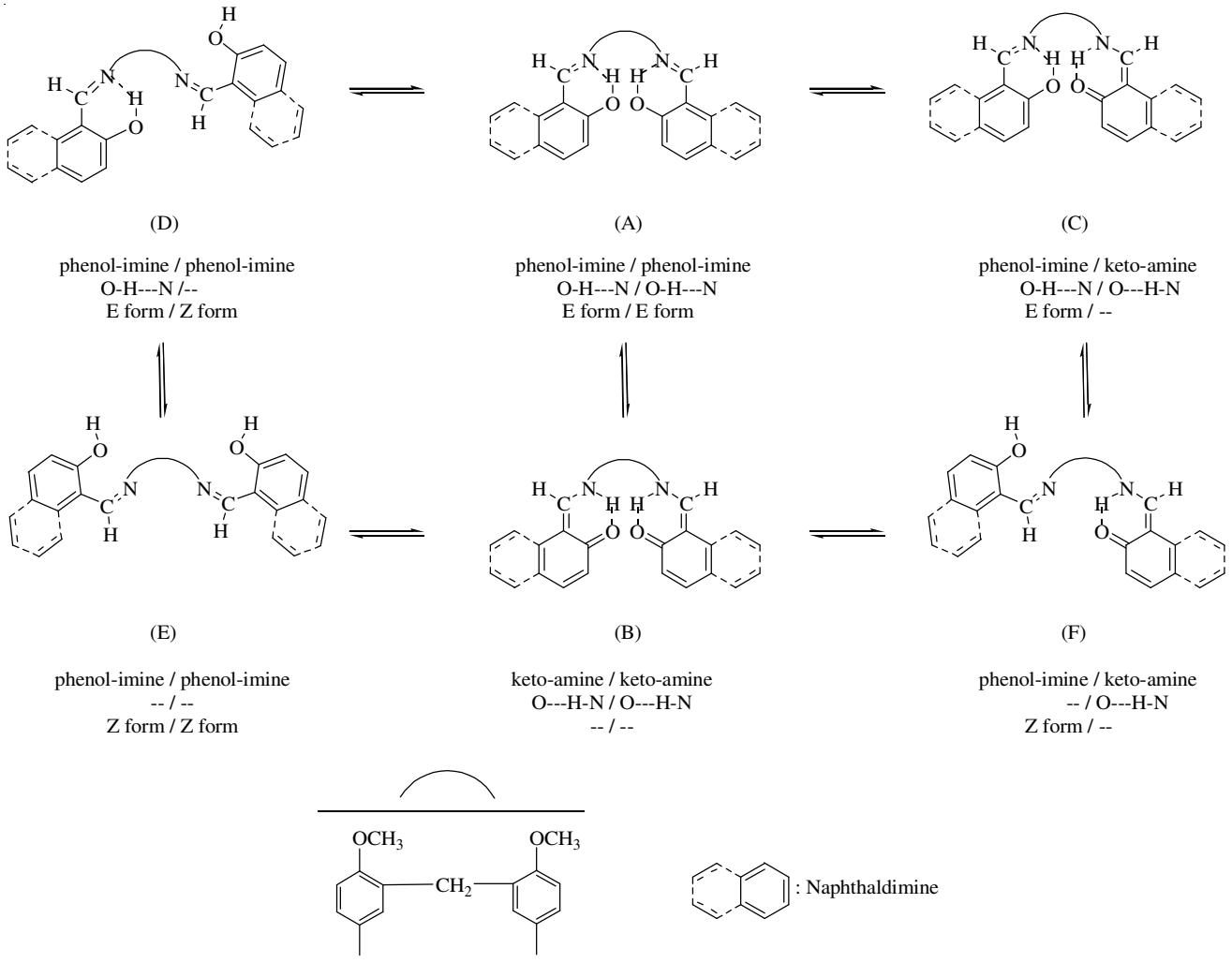


Fig. 2. Expected tautomeric species of **4** and **5** in solutions

TABLE-1
EFFECTS OF SOLVENT, ACIDIC AND BASIC MEDIA ON THE UV SPECTRA OF COMPOUNDS (**4**) AND (**5**)

Comp.	Solvent	λ, nm (ε, $M^{-1}cm^{-1}$)			Keto-amine isomer (%)		
		Solvent media	Acidic media[a]	Basic media[b]	Solvent media	Acidic media[a]	Basic media[b]
(4)	DMSO	354.0(34760)	324.5(22800), 282.0(16160)	Not measured	-	-	-
	EtOH	352.0(38400)	327.5(16120), 282.0(13080)	354.0(60920)	-	-	-
	$CHCl_3$	355.0(40960)	397.5(60960), 277.0(47280)	353.5(50400), 299.0(41240)	-	-	-
	Benzene	354.5(41840), 276.5(25120)	400.0(56040), 279.0(35240)	353.5(46440)	-	-	-
	Cyclohexane	352.0(36080)	Not measured	352.0(31240)	-	-	-
(5)	DMSO	447.5(21760), 395.0(29280) 341.5(20440), 327.5(22600)	355.5(25760), 316.0(31720) 282.5(19960)	Not measured	49.0	-	-
	EtOH	468.0(27000), 449.0(31040) 363.0(21640), 340.0(21680) 324.5(23560)	357.5(10720), 317.5(15040) 273.5(13440)	467.0(14240), 449.0(16400) 394.0(20600), 340.0(15480) 326.0(16680)	59.0	-	47.0
	$CHCl_3$	449.0(30040), 390.5(37840) 340.0(28040), 325.0(30920)	444.5(69320), 378.0(31520)	449.5(30720), 386.0(47160) 340.0(35440), 325.0(39120)	52.0	69.0	51.0
	Benzene	389.0(34440), 342.0(20400) 326.0(20680), 275.5(19760)	442.5(57400), 377.5(27080) 276.0(21920)	386.5(42400), 342.0(24200) 326.0(23760)	-	68.0	-
	Cyclohexane	384.5(36400), 340.0(21880) 323.5(21960)	Not measured	385.5(55640),340.5(32680) 324.5(32200)	-	-	-

$A_2/A_1=x/(100–x)$ where, A_1 = The absorbance of the phenol-imine isomer (π-π^*); A_2= The absorbance of the keto-amine isomer (n-π^*); x = The percentage of keto-amine isomer. [a]CF_3COOH, [b]$(C_2H_5)_3N$

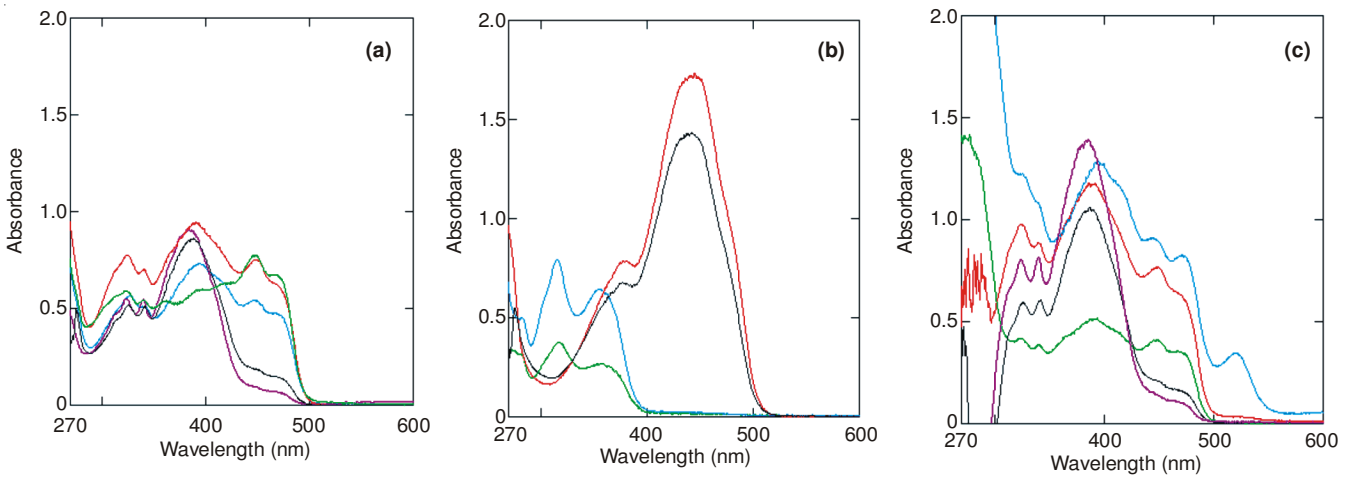


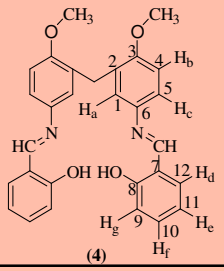
Fig. 3. UV-visible spectra of compound **5**. DMSO, ethanol, chloroform, benzene, cyclohexane. (a) pure solvent, (b) acidic (CF_3COOH) and (c) basic (NEt_3) solutions

of aromatic rings and appears to be splitted two bands in the spectrum of compound **5** where the C=N groups are involved in intramolecular hydrogen bonds. The bands at 325-396 nm can be assigned to an intramolecular $\pi\rightarrow\pi^*$ transitions of the C=N groups. The Schiff bases show absorptions $n\rightarrow\pi^*$ in the range greater than 400 nm in polar and non-polar solvents[23,28]. It should be pointed out that the new band belongs to the keto-amine form of the Schiff bases with OH group in *ortho* position to the imine group[11,14]. The band is observed at > 400 nm in pure solvents (DMSO, EtOH and $CHCl_3$), in $CHCl_3$ and benzene in acidic media and in basic media of solvents EtOH and $CHCl_3$ for compound **5**. Whereas this band is not observed for compound **4** in all of the solutions indicating that the only phenol-imine tautomers are present in the solutions. The keto-amine isomer ratios of compound **5** are given in Table-1. The results imply that the solvent polarities and the addition of CF_3COOH are considerably effective on the tautomeric equilibria.

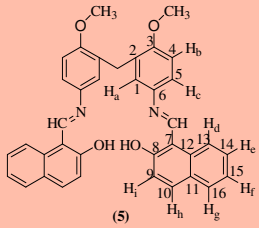
NMR Studies: Proton magnetic resonance spectroscopy is a helpful tool for the identification of organic compounds in conjunction with other spectrometric information. Table-2 lists complete ^1H and ^{13}C NMR assignments in $CDCl_3$ for compounds **4** and **5**. The expected tautomeric species and geometric isomers (E and Z) of the Schiff bases compounds (**4** and **5**) in solutions are depicted in Fig. 2. The ^1H signals were assigned on the basis of chemical shifts, multiplicities and coupling constants. In the solution, the compounds have symmetric structures according to ^1H NMR spectra.

The peaks at 7.10 (d, 2H), 7.03 ppm (d, 2H), 7.20 ppm (dd, 2H), 7.38-7.33 ppm (m, 2H) and 6.90-6.96 ppm (m, 2H) are assigned to be Ha, Hb, Hc, Hd-Hf and He-Hg, respectively, for 4 and 7.17 (d, 2H), 6.98 ppm (d, 2H), 7.27 ppm (dd, 2H), 7.72 ppm (d, 2H), 7.33 (td, 2H), 7.51 (td, 2H), 8.06 (dd, 2H), 7.08 (d, 2H) and 7.77 (d, 2H) are assigned to be Ha, Hb, Hc, Hd, He, Hf, Hg, Hh and Hi respectively, for compound **5**, which have H-H correlation in H-H COSY and NOESY spectra (Figs. 4 and 5). The signals at δ = 13.21 ppm (s, 2H) for compound **4** and at δ = 15.55 ppm (d, 2H) for compound **5** which can not been found any proton-proton correlative signal in H-H COSY spectrum and any proton-carbon signal in HETCOR spectrum (Fig. 6), are assigned to the proton of hydroxy groups. Assign-

TABLE-2
^{1}H NMR AND ^{13}C NMR SPECTRAL DATA IN $CDCL_3$. CHEMICAL SHIFTS (δ) ARE REPORTED IN ppm, AND s: SINGLET, d: DOUBLET, dd: DOUBLE DOUBLET, m: MULTIPLIED, t: TRIPLET



(4)



(5)

Compound	4	5
H_a	7.10 (d, 2H), [$^4J_{Ha\text{-}Hc}$= 2.63 Hz]	7.17 (d, 2H), [$^4J_{Ha\text{-}Hc}$ = 2.71 Hz]
H_b	7.03 (d, 2H), [$^3J_{Hb\text{-}Hc}$= 8.38 Hz]	6.98 (d, 2H), [$^3J_{Hb\text{-}Hc}$ = 8.68 Hz]
H_c	7.20(dd, 2H),[$^3J_{Hc\text{-}Hb}$= 8.38 Hz, $^4J_{Hc\text{-}Ha}$= 2.63 Hz]	7.27 (dd, 2H), [$^3J_{Hc\text{-}Hb}$ = 8.68 Hz, $^4J_{Hc\text{-}Ha}$ = 2.71 Hz]
H_d	7.38-7.33 (m, 2H)	7.72 (d, 2H), [$^3J_{Hd\text{-}He}$ = 7.52 Hz]
H_e	6.90-6.96 (m, 2H)	7.33 (td, 2H), [$^3J_{He\text{-}Hdf}$ = 7.45 Hz, $^4J_{He\text{-}Hg}$ = 1.11 Hz]
H_f	7.38-7.33 (m, 2H)	7.51 (t, 2H), [$^3J_{Hf\text{-}Heg}$ = 7.15 Hz]
H_g	6.90-6.96 (m, 2H)	8.06 (dd, 2H), [$^3J_{Hg\text{-}Hf}$ = 8.44 Hz, $^4J_{Hg\text{-}He}$ = 1.09 Hz]
H_h	-	7.08 (d, 2H), [$^3J_{Hh\text{-}Hi}$ = 9.16 Hz]
H_i	-	7.77 (d, 2H), [$^3J_{Hi\text{-}Hh}$ = 9.16 Hz]
C<u>H</u>	8.57 (s, 2H)	9.32 (d, 2H), [$^3J_{CH\text{-}NH}$ = 4.5 Hz]
C<u>H</u>$_2$	4.05 (s, 2H)	4.12 (s, 2H)
C<u>H</u>$_3$	3.90 (s, 6H)	3.96 (s, 6H)
O<u>H</u>	13.21 (s, 2H)	15.55 (d, 2H)
C1	123.3	122.8
C2	132.6	130.0
C3	156.9	156.6
C4	117.1	111.2
C5	119.8	118.7
C6	131.8	137.9
C7	119.5	108.7
C8	161.0	170.1
C9	118.9	136.2
C10	131.9	122.3
C11	110.9	127.2
C12	129.8	133.2
C13	-	129.3
C14	-	123.3
C15	-	127.9
C16	-	118.9
<u>C</u>H	160.3	153.4
<u>C</u>H$_2$	30.0	30.1
<u>C</u>H$_3$	55.8	55.9

s, singlet; d, doublet; dd, doublet of doublet; t, triplet; m, multiplet

ments of the protons and carbons were made by two dimensional heteronuclear-correlated experiments (HETCOR) using delay values which corresponds to ^{1}J(C, H), HMBC using delay values which corresponds to ^{2}J(C, H) or ^{3}J(C, H) between the carbons and protons (Fig. 7, Table-3). The signals appeared as a singlet at δ = 8.57 ppm for compound **4** and doublet 9.32 ppm (d, 2H, $^3J_{CHNH}$ = 4.5 Hz) for compound **5** can be ascribed to CH=N. The singlets (C<u>H</u>N and O<u>H</u>) are observed for compound **4** in $CDCl_3$ and DMSO show the existence of only phenol-imine tautomer (E/E isomer in Fig. 2, form A). The doublets (C<u>H</u>N and O<u>H</u>) are observed for compound **5** indicate keto-amine tautomer (N-H···O, hydrogen bond) present in the solution (Fig. 2, form B, Fig. 8). A singlet assignable to the chemically and magnetically equivalent protons in methoxy group of phenyl ring were observed at δ = 3.90 ppm for compound **4** and δ = 3.96 ppm for compound **5**. The singlets are observed at δ = 4.05 and δ = 4.12 ppm for the Ar-CH_2-Ar protons of compounds **4** and **5**, indicated that they are equivalent. Ha-Hi protons are easily distinguishable and assignable by using HMBC methods (Table-3, Fig. 7).

All of the possible carbon peaks are observed from the proton decoupled ^{13}C NMR spectra of compounds **4** and **5**. As expected, the compounds seem to have symmetric molecular structures in solution (Table-2). The assignments of aromatic carbon atoms were done in the first step by one-bond proton-carbon correlations observed in HETCOR spectra (protonated carbon atoms) and in the second step by long range correlations found HMBC spectra. Assignments of the protonated carbons were made by two dimensional heteronuclear-corre lated experiments (Figs. 6 and 7) using delay values which correspond to ^{1}J(C, H). As an example, only the HETCOR spectrum of compound **5** is depicted in Fig. 6.

TABLE-3
2D COSY AND NOESY (^{1}H-^{1}H CORRELATION), HETCOR AND HMBC (^{1}H-^{13}C CORRELATION) FOR COMPOUND **5**

Atom	HETCOR (COSY)	HMBC [J(C,H)]				NOESY
	^1J	^2J	^3J	^4J	$^{intra}J$	$^{intra}J$
Ha	C1	-	C3, C5	-	CH	Hh, Ha, CH
Hb	C4 (Hc)	C3	C2, C6	C1	-	Ha, He, Hc
Hc	C5 (Hb)	C6	C3	-	-	Hb, Hg, CH
Hd	C8 (He, Hf)	C16	-	-	-	He, Hf,
He	C9 (Hd,Hf)	C10	-	C15	CH	Hb, Hc, Hd, Hf CH
Hf	C10 (Hg,He)	-	-	-	C16	Hd, He
Hg	C11 (Hf)	C15	C12	-	C7	Hc
Hh	C12 (Hi)	C15	-	C7, C10	-	Ha, Hd, Hi
Hi	C13 (Hh)	C14	C15	C16	C8, C10	Hh
CH	CH	C7	C6, C14, C16	-	C15	Ha, Hc, He

Intra; intramolecular interaction

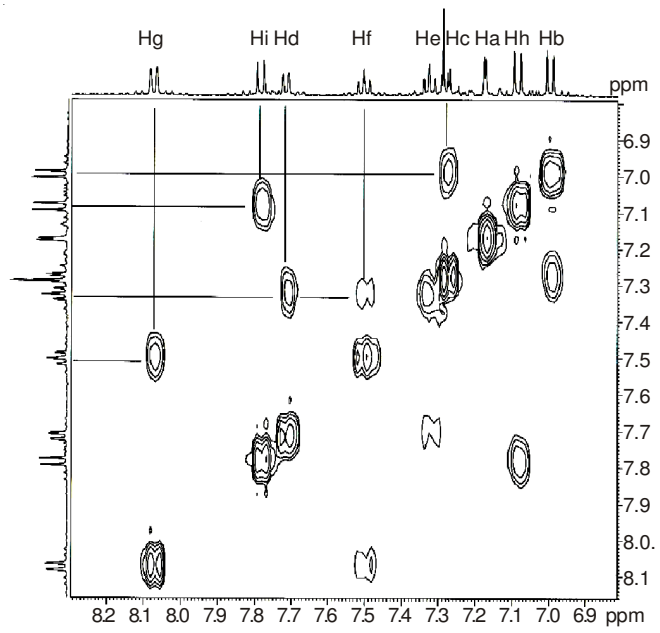


Fig. 4. COSY spectrum of compound **5**

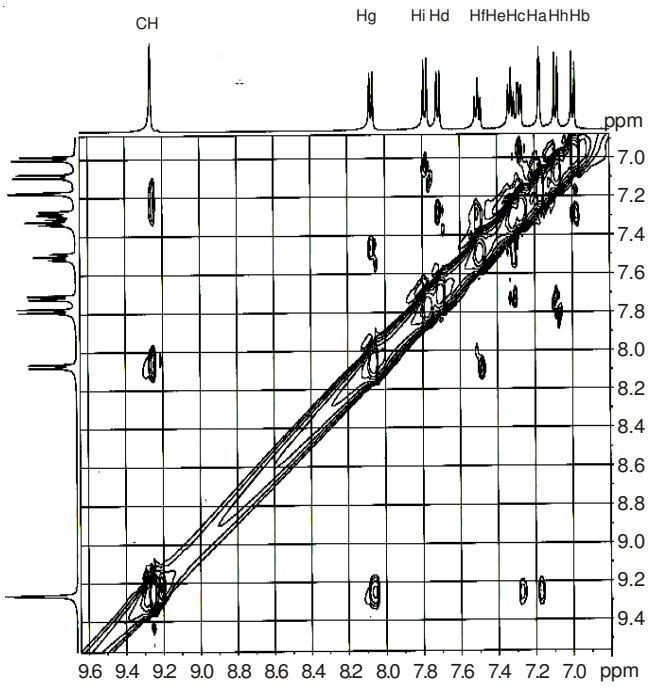


Fig. 5. NOESY spectrum of compound **5**

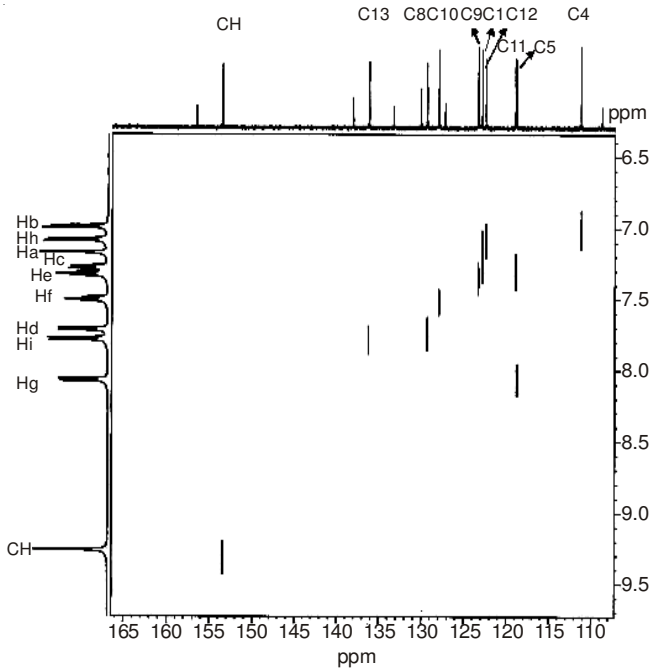


Fig. 6. HETCOR spectrum of compound **5**

The signals at δ 122.8, 111.2, 118.7, 170.1, 136.2, 122.3, 127.2, 133.2, 129.3, 153.4, 30.1 and 55.9 ppm assign them to C1, C4, C5, C8, C9, C10 C11, C12, C13, CH, CH_2 and CH_3 carbon atoms (Table-2). In compound **5**, the absence of any contours at δ 130, 156.6, 137.9, 108.7 and 170.1 ppm assign them to the C2, C3, C6 C7 and C8 carbon atoms, respectively. On the other hand, the nonprotonated carbons C2, C3, C6 C7 and C14 of compound **5** were also determined using delays in the two dimensional HMBC experiment to emphasize the long range coupling, either ^{2}J(C,H) or ^{3}J(C,H) between the carbons and protons (Fig. 7, Table-3).

Theoretical calculation: Theoretical calculations are carried out using PM6 methods in the MOPAC2009[30]. Initial estimates for the geometries of all are obtained by a molecular mechanics program (ChemBioOffice Ultra 2010 for Windows) followed by full optimization of all geometrical variables (bond lengths, bond angles and dihedral angles), without any symmetry constraint[31].

The results of theoretical calculations for compounds **4** and **5** are listed in the Tables 4-6.

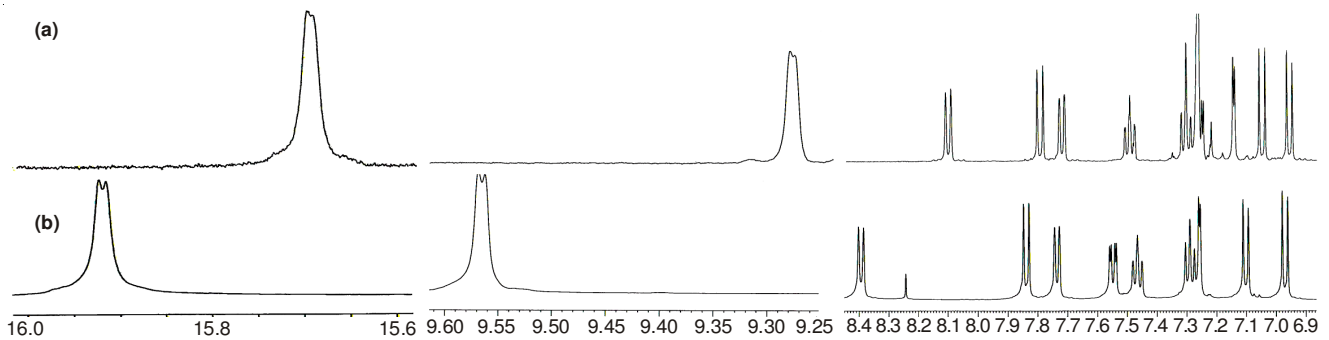


Fig. 8. ^{1}H-NMR spectra of compound **5** at δ 6.8-16.2 ppm, (a) in $CDCl_3$ and (b) in DMSO

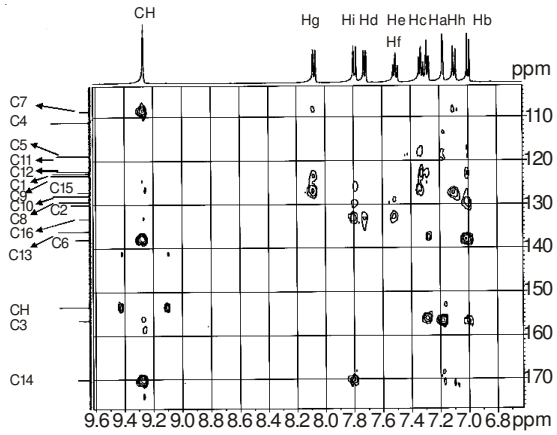


Fig. 7. HMBC spectrum of compound **5**

Tautomer calculation: The effects of the solvents on tautomer equilibria have been examined by the calculatins. Though, it is found out that the experimental results of compound **4** have not been shown the tautomer, it has shown that solvents other than water the phenol-imine and keto-amine tautomer equilibrium in theoretical calculation. It was found to be the predominant form of keto-amine for compound **5** in theoretical calculations (Table-4, Fig. 1).

Isomer calculation: All forms of the isomers in Fig. 2 have been studied for different solvent phases (H_2O, DMSO, EtOH, $CHCl_3$, benzene, cyclohexane) (Tables 5 and 6). The stable isomer forms have been determined by ΔG_f energies. The isomers listed in accordance with ΔG_f stabilities in all solvent phases (Table-6). It is observed that stabilities of the

TABLE-4
PM6 CALCULATION OF TAUTOMERIC EQUILIBRIUM CONSTANTS pK_T IN LIQUID PHASE

Compound	ΔH_f	ΔH	ΔS	ΔG_f[a]	ΔG[b]	$\delta\Delta G_f$[c]	K_T[d]	pK_T[e]
				H_2O				
4e	-53.484	21528.572	225.651	-120.728	-45.715	158.295		
4k	98.466	20657.504	204.358	37.567	-40.241			
5e	-19.221	24933.050	243.882	-91.898	-47.744	-10.659	6.57E+07	-7.820
5k	-31.329	24601.233	239.020	-102.557	-46.627			
				DMSO				
4e	-52.702	21719.700	223.544	-119.318	-44.896	-10.826	8.72E+07	-7.940
4k	-63.651	21529.600	223.129	-130.144	-44.963			
5e	-21.670	25196.000	254.051	-97.377	-50.511	-16.754	1.94E+12	-12.280
5k	-41.350	24690.500	244.233	-114.131	-48.091			
				EtOH				
4e	-52.117	21692.729	223.264	-118.650	-44.840	-10.504	5.06E+07	-7.700
4k	-62.715	21510.285	222.947	-129.153	-44.928			
5e	-21.050	25181.279	254.177	-96.795	-50.563	-16.488	1.24E+12	-12.093
5k	-40.515	24686.990	244.186	-113.282	-48.080			
				$CHCl_3$				
4e	-47.678	21542.510	225.439	-114.859	-45.638	-7.079	1.55E+05	-5.190
4k	-55.762	21398.700	222.067	-121.938	-44.777			
5e	-16.331	25007.170	251.586	-91.304	-49.965	-16.248	8.27E+11	-11.910
5k	-34.256	24664.190	245.957	-107.551	-48.631			
				Benzene				
4e	-42.949	21414.968	225.848	-110.252	-45.888	-5.732	1.60E+04	-4.200
4k	-48.624	21309.743	226.040	-115.984	-46.050			
5e	-11.273	24852.617	250.076	-85.796	-49.670	-15.680	3.16E+11	-11.500
5k	-27.713	24658.970	247.525	-101.475	-49.103			
				Cyclohexane				
4e	-41.910	21390.137	223.884	-108.627	-45.327	-5.094	5.44E+03	-3.730
4k	-47.098	21273.996	223.568	-113.721	-45.349			
5e	-10.158	24821.584	249.394	-84.477	-49.498	-16.202	7.65E+11	-11.880
5k	-26.295	24608.234	249.612	-100.679	-49.776			

[a]$\Delta G_f = \Delta H_f - T\Delta S$; [b]$\Delta G = \Delta H - T\Delta S$; [c]$\delta\Delta G_f = \Delta G_{f(k)} - \Delta G_{f(e)}$; [d]$K_{Tf} = e^{(-\delta\Delta Gf/RT)}$; [e]$pK_{T(f)} = -\log K_{Tf}$; R = 1.987 × 10^{-3} kcal/mol K and T= 298 K

TABLE-5
PM6 CALCULATION OF THE TAUTOMERIC SPECIES OF COMPOUND **5** MOLECULES IN LIQUID PHASE

Compd.	ΔH_f	ΔH	ΔS	ΔG_f	ΔG
			H_2O		
A	-23.872	24971.278	248.4773	-97.918	-49.075
B	-41.818	24816.816	246.9922	-115.422	-48.787
C	-32.7	24877.329	248.1514	-106.649	-49.072
D	-23.73	25025.802	248.9132	-97.906	-49.150
E	50.945	26098.676	259.7981	-26.475	-51.321
F	-33.552	24695.657	240.9281	-105.349	-47.101
			DMSO		
A	-23.557	24917.415	248.592	-97.637	-49.163
B	-41.425	24787.696	247.050	-115.046	-48.833
C	-32.386	25072.149	250.703	-107.095	-49.637
D	-23.380	24964.903	247.160	-97.034	-48.689
E	51.366	26079.158	258.706	-25.728	-51.015
F	-33.239	24698.025	241.084	-105.082	-47.145
			EtOH		
A	-22.951	24898.449	248.242	-96.927	-49.078
B	-40.585	24786.514	248.009	-114.492	-49.120
C	-31.677	25055.435	250.913	-106.449	-49.717
D	-22.612	24961.330	247.201	-96.278	-48.705
E	52.288	26068.051	258.933	-24.874	-51.094
F	-32.557	24691.892	241.318	-104.470	-47.221
			$CHCl_3$		
A	-18.361	24815.974	248.596	-92.443	-49.266
B	-34.276	24736.642	249.497	-108.626	-49.613
C	-26.329	24923.163	251.687	-101.332	-50.080
D	-16.790	24991.491	247.513	-90.549	-48.767
E	59.354	26021.752	263.418	-19.145	-52.477
F	-27.385	24632.318	242.751	-99.725	-47.707
			Benzene		
A	-13.468	24712.820	247.165	-87.123	-48.942
B	-27.672	24671.921	249.785	-102.108	-49.764
C	-20.606	24681.141	249.480	-94.951	-49.664
D	-10.592	24902.684	250.996	-85.389	-49.894
E	67.010	25956.210	264.629	-11.849	-52.903
F	-20.674	24541.178	243.075	-93.110	-47.895
			Cyclohexane		
A	-12.392	24677.381	248.301	-86.386	-49.316
B	-26.236	24640.812	250.668	-100.935	-50.058
C	-19.446	24732.339	250.943	-94.227	-50.049
D	-9.238	24892.044	249.221	-83.506	-49.376
E	68.706	25926.437	264.835	-10.215	-52.994
F	-20.674	24541.178	243.075	-93.110	-47.895

[a]$\Delta G_f = \Delta H_f - T\Delta S$; [b]$\Delta G = \Delta H - T\Delta S$

isomers in all solvents have been in the same parallels. The declining stability of isomer forms in the the same solvent was determined as B > C > F > A > D > E. According to the solvent effect, the stability exhibits the decrease in parallel with decreasing solvent polarity (H_2O > DMSO > EtOH > $CHCl_3$ > benzene > cyclohexane) (Table-6). It was mentioned before that the phenol-imine and keto-amine equilibrium of compound **5** shifts to keto-amine form (Table-4). The B isomer written keto-amine/keto-amine on both sides of the compound forms the most stable isomer compound **5**. Besides, B has two H-bondings. C and F isomers which are the phenol-imine/keto-amine forms of compound **5** are, respectively in second and third place in stability order. C isomer having two H-bondings is more stable than F isomer. On the other hand, two H-bondings having phenol-imine/phenol-imine on both sides in isomer A has been observed for compound **5** and it is rationale to be in fourth place in stability. Though, the molecule is in phenol-imine/phenol-imine structure in isomer D, isomer has one H-bonding and this causes the less stability. Although, the molecule is again in phenol-imine/phenol-imine structure in E isomer form, it has been determined as the least stable isomer since it does not have the H-bonding (Table-6).

Conclusion

The absorption band at 400 nm belongs to the keto-amine form of the Schiff bases. The keto-amine tautomer was always observed when the Schiff base was derived from 1-hydroxy naphthaldehyde and aromatic amine. Whereas, in Schiff bases derived from salicylaldehyde and aromatic amine the keto-amine form was not observed in polar and non-polar solvents, but it was observed in acidic media[13,15]. Compounds **4** and **5** were in tautomeric equilibria (enol-imine, O-H···N keto-amine, O···H-N forms) in solvents, acidic chloroform and benzene solutions and basic dimethyl sulfoxide, chloroform and benzene. ^{1}H NMR data for compounds **4** and **5** show that the tautomeric equilibria favors the phenol-imine and keto-amine forms, respectively, in $CDCl_3$ and DMSO (Fig. 8).

Both of the compounds **4** and **5**, appear to be the tetradentate ligands, having two N and two O donor atoms, for transition metal cations. They can produce coloured complex dye in solutions and solid state. Preliminary results obtained from the reaction of compound **4** and Ni(II) cation can prove this proposal. On the other hand, compounds **4** and **5** illustrated significant antifungal activities against tested yeast strains. But, in general they were inactive against bacteria in exception of S. *aureus* for compound **5**. Consequently, for developing new antifungal agents both of the compounds could be lead for further studies.

In the theoretical calculations, the effects of the solvent on tautomer equilibria and isomer stabilities have been investigated. Except the water phase, compound **4** shows the phenol-imine and keto-amine tautomer equilibria. Compound **5** has the keto-amine tautomer, predominantly in the equilibria accor-

TABLE 6
GIBB'S FREE ENERGIES FOR THE TAUTOMERIC SPECIES OF COMPOUND **5** IN SOLUTIONS

Compound	ΔG_f	Compound	ΔG_f	Compound	ΔG_f	Compound	ΔG_f	Compound	ΔG_f	Compound	ΔG_f
H_2O		DMSO		EtOH		$CHCl_3$		Benzene		Cyclohexane	
B	-115.422	B	-115.046	B	-114.492	B	-108.626	B	-102.108	B	-100.935
C	-106.649	C	-107.095	C	-106.449	C	-101.332	C	-94.951	C	-94.227
F	-105.349	F	-105.082	F	-104.47	F	-99.725	F	-93.110	F	-93.11
A	-97.918	A	-97.637	A	-96.927	A	-92.443	A	-87.123	A	-86.386
D	-97.906	D	-97.034	D	-96.278	D	-90.549	D	-85.389	D	-83.506
E	-26.475	E	-25.728	E	-24.874	E	-19.145	E	-11.849	E	-10.215

ding to the data of theoretical calculations. On the other hand, stable isomer forms have been determined by ΔG_f energies. It is observed that stabilities of the isomers in all solvents have been in the same parallels. The declining stability of isomer forms in the the same solvent was determined as B > C > F > A > D > E. Consequently, the stabilities of the isomers decrease in parallel with decreasing solvent polarities in the order H_2O > DMSO > EtOH > $CHCl_3$ > benzene > cyclohexane.

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