Synthesis, characterization, and antioxidant studies on4-phenyl-1,3,5-triazine-2,6diamine Schiff bases and their nickel(II), copper(II) and zinc (II) complexes

Abdulaziz Ali[1], Norbani Abdullah[1] and Mohd Jamil Maah[1]

1. Faculty of Science, Department of Chemistry, University Malaya, Malaysia

Abstract

The synthesis, characterization, thermogravimetric and antioxidant activity studies of Schiff bases derived from 4-phenyl-1,3,5-triazine-2,6-diamine and 3,5-di-*tert*-butylsalicyladehyde (H_2L) with their nickel (II) , copper(II) and zinc (II) complexes are reported. The structures of the Schiff bases and the metal complexes wer characterized by elemental analyses (CHN), Fourier transform infrared spectroscopy (FT-IR), and ultraviolet-visible spectroscopy (UV-vis). Additionaly, ^{1}H- and ^{13}C- nuclear magnetic resonance spectroscopy (NMR) were recorded for the Schiff bases, while thermogravimetric analysis (TGA) was recorded for the complexes. Spectral studies reveal that the ligands were acting as tetradentate chelating agents and coordinated to the metal center via deprotonated phenolate oxygen and azomethine nitrogen atoms in a 1:1 ligand to metal ratio. The antioxidant activities of the ligand and complexes were examined using the DPPH radical scavenging method. The results show that the ligand exhibit higher radical scavenging ability than the complexes.

Introduction

Schiff bases are organic compounds which contain the azomethine group (-C=N-). These compounds are synthesized by the reaction of a primary amine and an active carbonyl compound (aldehyde or ketone) [1-3].

A great deal of information regarding the properties of synthetic Schiff bases of potential biological interest has arisen during the last few years [4-5], Different classes of organic compounds containing rich conjugated system can be observed when these compounds contain hydroxyl groups attached to aromatic rings. For example, compounds containing an azomethine group (-CH=N-) known as Schiff bases are formed by the condensation of a primary amine with carbonyl compounds. Schiff bases obtained from aromatic aldehydes and aromatic amines have an effective conjugation system and quite stable. Schiff bases are important compounds owing to their wide range of biological activities and industrial application. They have been found to posses the pharmacological activities such as anticancer [6], antimicrobial [7], anti-inflammatory [8] and antioxidants [9,10]. Such activities may be related to the structural arrangements of the ligands, and to the nature of the substituent groups [11].

In this work, we are encouraged to synthesize triazine Schiff bases containing hydroxyl groups attached to the aromatic ring (Figure 1), along with their nickel , copper and zinc complexes. The novel compounds were characterized on the bases of elemental analysis, IR, ^{1}H and ^{13}C NMR spectroscopy, UV-Vis as well as thermogravimetric analysis (TGA) with a view to further investigating the radical scavenging abilities of these novel compounds using the DPPH method.

Experimental

Materials:

4-phenyl-1,3,5-triazine-2,6-diamine ($C_6H_9N_5$, FW 187.21), 3,5-di-*tert*-butylsalicylaldehyde ($C_{15}H_{22}O_2$, FW 234.34) , triethylamine, copper(II) acetate monohydrate ($CuC_4H_6O_4.H_2O$; FW 199.65), nickel(II) acetate tetrahydrate

($NiC_4H_6O_4.4H_2O$; FW 248.86) ,zinc acetate dihydrate ($C_4H_6O_4Zn.2H_2O$, FW 219.50) and DPPH. These chemicals and common organic solvents were commercially available and used as received.

Physical measurements:

IR spectra were recorded with a Perkin-Elmer FT-IR spectrophotometer model Spectrum 2000 using KBr pellets as support in the range 4000-370 cm^{-1}. ^1H and ^{13}C-NMR spectra were recorded at room temperature on a JEOL ECA-400 spectrometer, operating with a frequency of 400 MHz, using DMSO-d_6 as solvent. Electronic spectra, in DMSO solution, were obtained using a Varian 50 Conc UV-visible spectrophotometer over the wavelength range 200-800 nm. Thermogravimetric analysis was carried out on Perkin Elmer Precisely TGA 4000 thermogravimetric analyzer. The instrument was adjusted at a heating rate of 20°C/min. The heating was performed from 50-900 °C.

The DPPH free radical scavenging assay was performed in triplicate and the average value was obtained. All determinations were made using the Infinite® 200 PRO plate reader (TECAN, Männedorf, Switzerland).

Synthesis of the ligand:

1. H_2L

A solution of 3,5-di-*tert*-butylsalicylaldehyde (2g, 8.53 mmol) and 4 phenyl-1,3,5-triazine-2,6-diamine (0.79g, 4.21 mmol) was mixed and stirred under reflux for 2 hours. The pale yellow powder formed was filtered and recrystallized from ethanol. It was dried in an oven at 80 ^oC for 30 min.

Selected FT-IR data (KBr, cm^{-1}): 3329 (m, -OH), 2923 (m, C-H), 1612 (s, C=N), 1273 (s, C-O).

General method for synthesis of the complexes:

A solution of H_2L(0.50g, 0.81 mmol)) in ethanol (40 cm^3) was added to equimolar quantity of the metal acetate in ethanol. Few drops of triethylamine were then added. The mixture was magnetically stirred and refluxed for 3 hours. The product formed was filtered and recrystallized from DMSO.

$NiL.2H_2O$, selected FTIR data (KBr, cm^{-1}): 3054 (C-H, m), 1606 (C=N, s), 1239 (C-O, s), 550 (Ni-O, w)

CuL. H_2O, selected FTIR data (KBr, cm^{-1}): 2345 (C-H, s), 1605 (C=N, s), 1241 (C-O, s), 546 (Zn-O, w).

$ZnL.2H_2O$, selected FTIR data (KBr, cm^{-1}): 2532 (C-H, m), 1608 (C=N, s), 1240 (C-O, s), 548 (Zn-O, w).

Anti-oxidant activity of the ligand and complexes by DPPH method:

Free radical scavenging activity of the test compounds were determined by the 1,1-diphenyl picrylhydrazyl (DPPH) assay method [12]. Each of the Schiff bases and complexes were dissolved in DMSO to obtain concentration of 1 mg/ml. These stock solutions were then diluted to 5, 10, 25, 50, and 100 µg / ml. Then, 200 µl of each sample solution were combined with 50 µl of DPPH (0.3 mml) in triplicate in a 96- well microtitre plate. Final concentrations of the Schiff bases were 4, 8, 20, 40, and 80 µg/ml. The microtitre plate was incubated for 30 min at room temperature. The plate was then read at 515 nm for 3 hours with 20 minutes intervals to reach a steady state against DMSO as a blank. The percentage DPPH quenched was calculated according to the equation:

DPPH quenched (%) = (Abs. blank – Abs. sample)/ Abs. blank × 100.

The percentage free radical scavenging activity (% inhibition) was plotted against concentration in μg/ml.

Results and discussion

The physical properties of the ligands and their complexes were listed in table 1. Elemental analyses for the complexes confirm 1:1 metal to ligand stoichiometry. The compounds are very stable at room temperature in the solid state. The ligands are soluble in ethanol, methanol, acetone, and high boiling point solvents like DMSO and DMF, whereas the complexes dissolves only in DMSO and DMF and not soluble in either ethanol or methanol.

I.R spectra:

The main stretching frequencies of the IR spectra of the ligand and complexes were shown in table 2

For the ligand, the spectra show the characteristics strong peak due to C=N stretching at 1612 cm^{-1}, indicating the formation of the Schiff base. Another strong peak at 1273 cm^{-1} is assigned to C-O phenolic stretching, while a sharp weak peak at 3329 cm^{-1} is characteristic of free -OH group [13]. Other peaks bands in the region 1000 - 1500 cm^{-1} arise from benzene ring skeletal vibrations. The results strongly support the formation of the Schiff base [14].

The IR spectra of the nickel complexes differ from that of the ligand. It is further noted that the -OH peak, observed for H_2L at 3329cm^{-1}, is now observed at 3401 cm^{-1}, and is assigned to coordinated H_2O molecules in agreement with the results from the elemental analyses . The peaks for C=N at 1612 cm^{-1} and C-O at 1273 cm^{-1} observed for H_2L have shifted to lower energy at 1606cm^{-1} and 1239cm^{-1} respectively in NiL. These suggest that the phenolic oxygens and imino nitrogens are coordinated to Ni(II). Additionally, a new peak observed at 550 cm^{-1} may be assigned to Ni-O bond [13].

The IR spectra for Cu(II) complexes shows the expected functional groups as previously discussed for the corresponding Ni(II) complex. The C=N, C-O and Cu-O peaks for [CuL6].H_2O are at 1605 cm^{-1}, 1241 cm^{-1} and 546 respectively. These are almost similar to those of the corresponding Ni(II) complex, suggesting similar bond strength.

The IR spectra for Zn(II) complexes shows the presence of all the expected functional groups. The wavenumbers of C=N (1608 cm^{-1}) and C-O (1240 cm^{-1}) groups are almost the same as for [CuL6(H_2O)] (1605cm^{-1} and 1241 cm^{-1} respectively.

^{1}H NMR spectra:

The ^{1}H NMR spectra for H_2L is consistent with the expected structural formula in Fig 1. The singlet at 9.96ppm is due to phenolic hydrogen; a singlet at 8.24 ppm is due to imino hydrogen; and a multiplet in the range 6.70 - 7.61 ppm is due to the aromatic hydrogens. Furthermore a singlet at 1.33 ppm is due to tertiary butyl protons. The integration ratio for these hydrogens is 1:1:5.5 respectively (expected ratio =1:1:5.5), and supports the molecular symmetry for the Schiff base [15].

^{13}C NMR spectra:

Further evidence for the proposed structure in Fig 1 can be drawn from^{13}C NMR spectra. The spectra shows 15 peaks, assigned as follows: 29 ppm (tertiary carbon atoms in the tert-butyl groups), 31.8 ppm for the six methyl groups, 159.4 ppm C-OH, 167.91 ppm C=N, The aromatic carbons lie between 120.6 – 141.9 ppm. However, the expected number of peaks, after taking account of the symmetry of the structure, is 15.

UV-Vis spectra:

The UV-Vis spectral data of the ligand and their complexes in DMSO are listed in table 3. The UV-Vis spectra for H_2L shows two moderately intense absorption bands at 288 nm (ε =2.1 x 10^4 $M^{-1}cm^{-1}$) and 351 nm (ε =2.2 x 10^4 $M^{-1}cm^{-1}$). The bands are assigned to π - π^* transition of the aromatic ring and n - π^* transition of the azomethine chromophores, respectively. These values are in agreement with other Schiff bases reported in the literatures [16-17].

For nickel complexes the UV-Vis spectra exhibits weak *d-d* bands 902 (ε_{max} = 550 $M^{-1}cm^{-1}$), and 736 nm (ε_{max} = 257 $M^{-1}cm^{-1}$). These are consistent with an octahedral configuration at Ni(II), and using the Tanabe-Sugano diagram for d^8 complex, these bands are assigned to the transitions $^3A_{2g} \rightarrow {}^3T_{2g}$, $^3A_{2g} \rightarrow {}^3T_{1g}(F)$ respectively[18].
The peak at410 nm (ε = 0.5 x 10^4 $M^{-1}cm^{-1}$) is assigned to metal-ligand charge transfer (MLCT). The spectrum is also compared with that of H_2L. It is noted that the π - π^* band observed for H_2L (288 nm) remains shifted in the complex (274 nm) (ε =2.4x 10^4 $M^{-1}cm^{-1}$). However, the n - π^* band may be hidden under the strong MLCT band at 348 nm(ε = 0.7 x 10^4 $M^{-1}cm^{-1}$). Thus, this band is significantly red-shifted from about 300 nm to about 400 nm as a result of complexation to the Ni(II). These results are in agreement with literature result indicating the formation of the complexes [19].

The UV-Vis spectra of the copper complexes shows a broad *d-d* peak at 670 nm (ε_{max} = 200 $M^{-1}cm^{-1}$). Thus, [CuL (H_2O)] is a mononuclear square pyramidal complex. The π - π^* and MLCT bands are at 297 nm(ε = 2.5 x 10^4 $M^{-1}cm^{-1}$) and 402 nm (ε = 1.02 x 10^4 M^-

^{1}cm^{-1}) respectively, which are almost the same as for the corresponding Ni(II) complex (274 nm, 410 nm), and may be similarly explained.

The UV-Vis spectra of the zinc complexes shows shows that the MLCT and π - π^*peaks 390 nm(ε = 1.7 x 10^4 M^{-1}cm^{-1}) and 275 nm(ε = 2.5 x 10^4 M^{-1}cm^{-1}) are at almost the same energy as the corresponding peaks for [CuL (H_2O)] (402 nm, 297 nm. Thus, both metal ions have insignificant effect on the electronic transitions of the organic moiety. The MLCT peak is normally observed from 348 nm to 323 nm for Zn(II) complexes, involving electronic transitions from the full *d* orbitals of the metal ion ($3d^{10}$) to antibonding orbitals of the ligand [20].

Thermal analysis (TGA):

The thermal decomposition process for Ni(II) , Cu(II) and Zn(II) complexes were examined and assessed in the temperature range 50 – 900°C. The obtained themo-analytical data from the thermogravimetric curves were summarized in table 4.

The data obtained indicate that nickel complexes are thermally stable up to 246°C. The first weight loss of 2.7% at 130°C corresponds to the loss of coordinated H_2O molecules (expected, 5.3%). The next step represents a total weight loss of 87.4% and is assigned to the decomposition of the ligand (expected, 87%). The amount of residue at 875°C is 9.6%. Assuming that the residue is NiO [Mehmet, TGA], the expected value is 10.4%, which is within the acceptable experimental error.

The data obtained indicate that copper complexes are thermally stable up to 250°C. Thus, it is as themally stable as [NiL $(H_2O)_2$] (246°C).

The first weight loss of 3.5% at 140°C corresponds to the loss of coordinated H_2O molecule (expected, 2.5%). The next step represents a total weight loss of 83.3% and is assigned to the decomposition of the ligand (expected, 88.6%). The amount of residue at about 650^{o}C is 13.2%. Assuming that the residue is CuO [Mehmet, TGA], the expected value is 11.1%. Thus, the thermal properties of [CuL (H_2O)] is similar from that of [NiL (H_2O)$_2$].

The data obtained indicate that zinc complexes are thermally stable up to 245^{o}C. Thus, it is as themally stable as [CuL (H_2O)] (250^{o}C).

The first weight loss of 3.7% at 150^{o}C corresponds to the loss of coordinated H_2O molecules (expected, 5.1%). The next step represents a total weight loss of 86.1% and is assigned to the decomposition of the ligand (expected, 86.2%). The amount of residue at 850^{o}C is 10.2%. Assuming that the residue is ZnO [Mehmet, TGA], the expected value is 11.3%, which is within the acceptable experimental error.

Antioxidant activity:

The antioxidant activity of the ligand and their nickel, copper and zinc complexes was measured in terms of their hydrogen donating or radical scavenging ability by UV-Vis spectrophotometer using the stable DPPH radical.

It has been shown that the free radical scavenging ability of the novel Schiff bases is dependent on the chemical substituents attached to the aromatic rings, and generally the antioxidant activity of all compounds was increased with increase of their concentration.

The prepared Schiff bases seem to have a very efficient conjugated system, which means that this type of compounds may play important role as antioxidant agents. In addition, the presence of hydroxyl groups, which are attached to aromatic rings can increase the conjugated systems and consequently increase the antioxidant activity of the corresponding Schiff bases. It is known that the antioxidant activity in phenolic compounds can take place through either of two mechanisms: hydrogen atom transfer, and electron donating ability [21]. The mechanism, which occurs here could be similar to that mechanism, which occurs in hydroxy chalcones and hydroxy flavonoids derivatives [22- 23].

Conclusion:

Schiff base ligand derived from 4-phenyl-1,3,5-triazine-2,6-diamine and3,5-di-*tert*-butylsalicylaldehyde with their nickel, copper and zinc complexes have been synthesised and characterized. The antioxidant studies of the compounds reveal that the ligands are more effective antioxidants than their metal complexes. They mainly act as a hydrogen atom transferring antioxidants in an oxidative process. However, chelating to the metal ions suppresses this property through coordination to the metal centre, thus hampers hydrogen atom abstraction through deprotonation.

Acknowledgments

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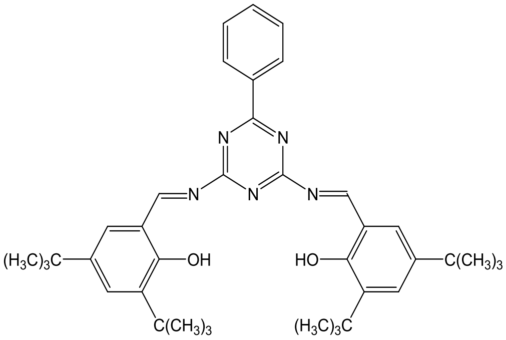

Figure 1: proposed structures of the ligand H_2L

Table1:Physical properties of the ligand and complexes

Compound	Formula	Yield (%)	Colour	Formula wt	Found (Calcd.) %		
					C	H	N
H_2L	$C_{39}H_{49}N_5O_2$	79	Yellow	619.89	75.49	7.90	11.29
					(76.35)	(7.21)	(11.87)
NiL.$2H_2O$	NiC39H51O4N5	75	Green	712.58	65.67	7.15	9.82
					(66.57)	(6.46)	(10.15)
CuL.H2O	CuC39H49O3N5	78	Green	699.43	66.91	7.01	10.01
					(66.13)	(6.34)	(10.79)
ZnL.$2H_2O$	ZnC39H51O4N5	75	Yellow	719.28	65.06	7.09	9.73
					(66.14)	(6.78)	(10.03)

Table 2: IR spectral data of ligand and complexes, wave numbers expressed in cm^{-}

Compound	υ O-H	υ C-H Aliphatic	υ C=N	υ C-O	υ M-O	υ M-N
H_2L	3329	2923	1612	1273	-	-
NiL.2H_2O	3401(H_2O)	3054	1606	1239	550	523
CuL.H2O	3400 (H_2O)	2345	1605	1241	546	496
ZnL.2H_2O	3422(H_2O)	2532	1608	1240	548	500

Table 3: UV-Vis of the ligand and complexes

Compound	λ_{max} (nm)	ε ($M^{-1}cm^{-1}$)	Tentative assignment
H_2L	288	2.1×10^4	$\pi - \pi^*$
	351	2.2×10^4	$n - \pi^*$
NiL.2H_2O	902	550	$^3A_{2g} \rightarrow\ ^3T_{2g}$
	736	257	$^3A_{2g} \rightarrow\ ^3T_{1g}(F)$
	410	0.5×10^4	CT
	274	2.4×10^4	$\pi - \pi^*$
	348	0.7×10^4	$n - \pi^*$
CuL.H2O	402	1.02×10^4	CT
	297	2.5×10^4	$\pi - \pi^*$
ZnL.2H_2O	390	1.7×10^4	CT
	275	2.5×10^4	$\pi - \pi^*$

Table 4: Thermal analysis data for the complexes

Compound	Step	Decomposition T_{max} (°C)	Eliminated species
$NiL.2H_2O$	First	130	$2H_2O$
	Second	300	Ligand
	Third	875	Residue (NiO)
$CuL. H_2O$	First	140	H_2O
	Second	310	Ligand
	Third	650	Residue (CuO)
$ZnL.2H_2O$	First	150	$2H_2O$
	Second	340	Ligand
	Third	850	Residue (ZnO)