A study on structural aspects of N'-[1-(2,4-dihydroxyphenyl)ethylidene]benzohydrazide and its metal complexes : Experimental and theoretical approach

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Abstract : N'-[1-(2,4-Dihydroxyphenyl)ethylidene]benzohydrazide (DHPEBH) was synthesized and characterized by IR, mass, ^{1}H NMR, ^{13}C NMR and DEPT. The HyperChem 7.5 software was used for quantum mechanical calculations. The geometry optimization was carried out using *ab initio* method. The theoretical spectral data and QSAR parameters were generated with semi empirical single point PM3 method. The HOMO and LUMO frontier orbital energies were also computed for the optimized molecule. The experimental and theoretical spectral data are nearly comparable. As the title compound has potential electron donor atoms, the metal ion interaction studies were also carried out. The pH-metry studies indicated the presence of three dissociable protons in DHPEBH. The solid complexes of title compound with Cu^{II}, Ni^{II}, Co^{II} and Mn^{II} were synthesized and characterized by elemental analysis, mass, IR, TGA and DTA.

Keywords : DHPEBH, complexes, HyperChem 7.5 software, QSAR, TGA, DTA.

Introduction

Benzoyl hydrazones are widely used as chelating ligands in coordination chemistry[1]. These hydrazones are well known for their coordination with various metal ions, forming stable compounds[2]. The coordination compounds containing hydrazone ligands have been reported to act as inhibitors of enzymes[3] and antifungal/antibacterial agents[4]. Moreover the coordination environment of the ligand (O, N atoms) with the metal ion is similar to the coordination environments of the biological system[5].

In the present investigation we report the structural properties of DHPEBH and its metal complexes envisaged from computational studies, equilibrium studies and spectral analysis.

Experimental

A mixture of aroyl hydrazide and resorsinoacetophenone was dissolved in 25 ml of ethanol by adding a drop of concentrated sulphuric acid. The solution was refluxed, filtered and compound obtained was recrystal-lized. Upon cooling, slowly crystals of DHPEBH developed. The purity of the compound was checked by TLC and the T_m = 228–230 °C.

The IR spectra were recorded on a Perkin-Elmer 435 spectrophotometer and ^{1}H and ^{13}C NMR on Bruker WH (270 MHz) spectrometer, DEPT spectra on ACF 200 Bruker 200m MHz superconductivity magnet spectrometer, mass spectra were recorded on Micro Mass V.G70-70H spectrometer operating at 70 eV using direct inlet system. The metal contents in the complexes were determined on a Perkin-Elmer 2380 atomic absorption spectrophotometer and C, H, N analyses were carried out on a Perkin-Elmer 240C analyser. Thermal behavior of complexes studied by thermo-gravimetrical analysis (TGA) and differential thermal analysis (DTA) techniques were recorded on Mettler Toledo Star System in the temperature range of 0–1000 °C in nitrogen atmosphere (Flow rate 300 ml/mm) at heating rate of 20 °C/min.

The proton-ligand dissociation constant of the ligand was determined potentiometrically using Irving-Rossotti

pH titration technique. The pH measurements were made with a Digisun DI-707 digital pH meter, consisting of a combined glass electrode and calomel electrode.

The metal complexes of Cu^{II}, Ni^{II}, Co^{II} and Mn^{II} were prepared by mixing methanolic solution of N'-[1-(2,4-dihydroxyphenyl)ethylidene]benzohydrazide (DHPEBH) and corresponding metal chloride solution in 1 : 2 molar ratio.

The molecule DHPEBH was built by Hyperchem tools[6-11], then the geometry optimization was carried out by employing *ab initio* optimized semi empirical single point PM3 method. Chemaxon tools were employed for computing theoretical pKa values.

Results and discussion

Spectral studies :

The IR spectrum[12-17] of DHPEBH shows characteristic band at 3495 cm^{-1} attributable to υ_{OH}. A strong band at 1650 cm^{-1} is due to $\upsilon_{C=O}$ and a peak at 1606 cm^{-1} is due to $\upsilon_{C=N}$. Peaks appearing at 3215 cm^{-1} and at 3000–3100 cm^{-1} correspond to υ_{NH} and υ_{CH} aromatic protons respectively.

The mass spectrum[12-17] of the title compound shows a dominant peak at m/z 271, which is in accordance with the expected protonated ion (M+H). The mass spectrum also contains the peak at m/z 293 some 23 mass units higher than the expected molecular mass identified. This is identified as the sodium adduct ion peak (M+Na)$^+$.

^{1}H NMR spectrum[12-17] of DHPEBH was recorded in DMSO-d_6. The signal for -OH proton which is in *ortho* position to a azomethine group is recorded at δ 9.3 ppm (1H, s). Another signal at δ 10.48 ppm is assigned to -OH proton which is in *para* position to azomethine group. The -CONH amide proton appears at δ 13.34 ppm and multiplet due to aromatic protons occurs between 7–7.4 (8H, m). The ^{1}H NMR spectrum of DHPEBH also shows resonance at δ 2.9 ppm due to -CH$_3$ protons. The IR and ^{1}H NMR spectral data obtained experimentally is in accordance with single point PM3 method data (Tables 1 and 2).

^{13}C NMR spectrum[12-17] of DHPEBH showed 12 signals at δ 103.6, 106.9, 108.9, 111.7, 126.5, 127.7, 128.1, 129.2, 129.8, 131.4 and 133.2 ppm indicating the presence of 12 aromatic carbons. It also showed four peaks at

Table 1. IR spectral data of DHPEBH (*ab initio*)/(Experimental)^a

Compd.	$\upsilon_{OH(para)}$	υ_{NH}	$\upsilon_{CH(aro)}$	$\upsilon_{C=O}$	$\upsilon_{C=N}$	$\upsilon_{C-H\ bend}$
DHPEBH	3765.61	3213	3192	1785	1785	1529
DHPEBH^a	3495	3215	3000–3100	1651	1606	1578

Table 2. ^{1}H NMR spectral data of DHPEBH (*ab initio*)/(Experimental)^a

Compd.	$\delta_{OH(ortho)}$	$\delta_{OH(para)}$	δ_{NH}	$\delta_{CH(aro)}$	$\delta_{CH(ali)}$
DHPEBH	9.005	8.248	11.306	7.326	4.173
DHPEBH^a	9.30	10.48	13.34	7–7.4	2.90

δ 159.3, 161.2, 161.7 and 164 ppm corresponding to two carbon atoms of carboxy hydrazone group (C=O and C=N) indicating the existence of both keto and enol forms.

The DEPT 45 of DHPEBH showed signals at δ 13.6, 103.6, 106.9, 108.9, 127.7, 128.1, 129.2, 129.8 and 131.5 ppm corresponding to nine protonated carbons. The comparison of chemical shifts of ^{13}C NMR with DEPT 45, 90 and 135 spectra supports the existence of keto-enol tautomerism in DHPEBH.

QSAR studies and quantum chemical studies :

QSAR properties of DHPEBH were determined by single point PM3 method[18,19] (Table 3).

Table 3. QSAR properties of DHPEBH

Surface area	490.07 A^2
Volume	798.06 A^3
Hydration energy	–16.06 kcal/mol
log P	5.01
Refractivity	77.87 A^3
Polarisability	29.24 A^3
Mass	270.29 amu

This analysis represents an attempt to relate structural descriptors of compounds with their physicochemical properties and biological activities.

Quantum chemical calculations have been widely used to study donor and acceptor properties of molecules. Figs. 1 and 2 shows the values of energy of the highest occupied molecular orbitals (E_{HOMO}), energy of the lowest unoccupied molecular orbitals (E_{LUMO}) and the energy gap between them ($E_{LUMO-HOMO}$). These values of E_{HOMO}, E_{LUMO} and $E_{LUMO-HOMO}$ DHPEBH were found to be –8.684 eV, –0.808 eV and 7.876 eV respectively.

Therefore higher value of E_{HOMO} indicates higher tendency for the donation of electron(s) to the appropriate acceptor molecule with low energy and empty mo-

lecular orbital[20,21]. In DHPEBH HOMO are localized on the C=O, N-H and C=N bonds in the central part of the molecule (Fig. 1).
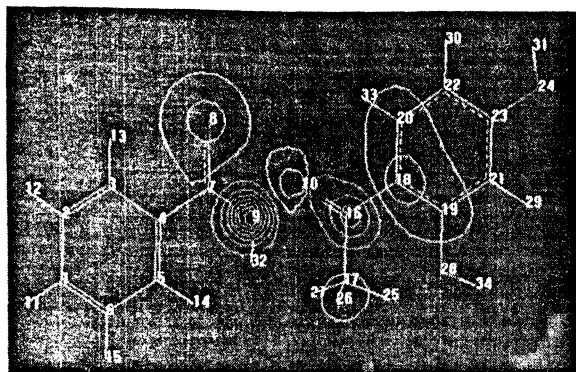

Fig. 1. Highest occupied molecular orbital (HOMO) of N'-[1-(2,4-dihydroxyphenyl)ethylidene]benzohydrazide (DHPEBH) (-8.684 eV).

Fig. 2 shows unoccupied molecular orbital regions that can accept electrons. These orbitals are present mainly on the C=O, N-H, C=N, C=C and C-OH (*para*) bonds (Fig. 2). As HOMO and LUMO frontier orbitals are commonly localized on carboxy hydrazide group, it can affirm that the title compound is a potential donor molecule as well as acceptor molecule.
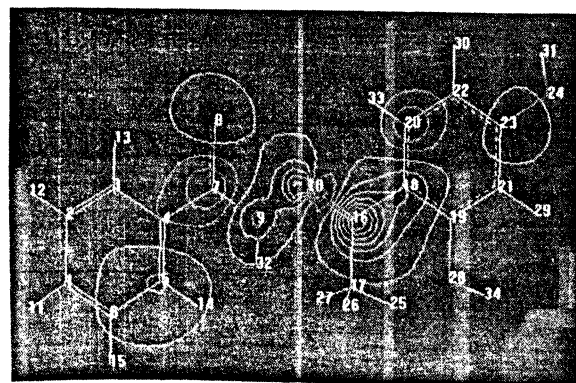

Fig. 2. Lowest unoccupied molecular orbital (LUMO) of N'-[1-(2,4-dihydroxyphenyl)ethylidene]benzohydrazide (DHPEBH) (-0.808 eV).

From the above Figs. 1 and 2, it is evident that HOMO and LUMO orbitals are more localized on carboxy hydrazone moiety of title compound.

Equilibrium studies :

The acid dissociation constants were determined experimentally and compared with computed values.

(i) The acid dissociation constants of the title compound have been determined pH metrically at 30 °C in different 70% v/v aquo-organic solvent mixtures (ethanol, dimethyl formamide). The pKa values of DHPEBH in 70% v/v ethanol-water and 70% v/v DMF-water at 30 °C temperature are shown in the Table 4. These results show that the DHPEBH has three dissociable protons. It is observed that the pKa values are higher in

Table 4. Acid dissociation constants of DHPEBH

Acid dissociation constants (pKa values) of DHPEBH	Chemaxon data	70% v/v ethanol-water	70% v/v DMF-water
$pK_{1a(ortho -OH\ group)}$	8.57	8.7	9.6
$pK_{2a(para -OH\ group)}$	9.93	10.4	11.3
$pK_{3a(amide -CONH\ group)}$	10.72	11.5	12.7

DMF-water than in ethanol-water. The observed lower pKa valnes in ethanol-water are due to relatively high solvation capacity of ethanol-water medium which would breakdown the structuredness of water by organic molecules resulting in the increase of polar character of solvent medium.

The observed high pKa values in DMF-water mixture relative to ethanol-water are thus probably due to low tendency of title compound to intricate itself in hydrogen bonding with DMF than in ethanol[22,23].

(ii) The compound DHPEBH was buîlt by using Chemaxon software[24,25] and the pKa values were computed. These studies indicated the presence of three dissociable protons in DHPEBH with pKa values 8.57 for *ortho* -OH group, 9.93 for *para* -OH group and 10.72 for amide group. Based on this information from Chemaxon software, we could correlate the pKa values obtained from pH metric studies carried out in 70% v/v DMF-water and 70% v/v ethanol-water media (Table 4).

The interaction of DHPEBH with Cu^{II}, Ni^{II}, Co^{II} and Mn^{II} has been studied pH metrically at 30 °C in 70% v/v ethanol-water medium. The titrations carried out with solutions containing metal ion and title compound in 1 : 1 ratio indicated coordination of metal ion through dissociation of two protons in Cu^{II} system and one proton in other metal ion systems under study. Though the compound has three dissociable protons corresponding to *ortho* hydroxy (pKa 8.7), amide (pKa 11.5) and *para* hydroxy

(pKa 10.4) protons, dissociation of *ortho* hydroxyl proton occurs with much ease in presence of metal ion. The second proton dissociation in Cu^{II} system is attributed to dissociation of amide proton through oxygen via enol form[12]. Thus in Cu^{II} system the donor sites attributable are imine nitrogen, oxygen atoms of phenolate and enol in dissociated form. While in Ni^{II}, Co^{II} and Mn^{II} systems the DHPEBH involves phenolate oxygen, carbonyl oxygen atoms and imine nitrogen in complexation. Thus tridentate nature of molecule results in five and six membered chelated rings. The possibility of participation of oxygen of *para* hydroxyl group through dissociation of proton, in the region of pH of complexation, is less probable as it is far from other donor sites.

Characterization of M^{II}-DHPEBH complexes :

The IR spectral data of all the metal complexes shows bands observed in the region of 3614 cm^{-1} ascribed to *para* substituted hydroxyl group as this phenolic -OH was not involved in coordination. A broad band appearing at 3296–3180 cm^{-1} indicates the presence of coordinated water or occluded molecules in the corresponding metal complexes. The aromatic -CH stretching vibrations occur at 2669 cm^{-1}, as observed in the ligand spectra.

The comparison of the spectra of metal complexes with the spectrum of DHPEBH within the range 1650–1250 cm^{-1} clearly indicates electron delocalization due to chelate formation. The $\upsilon_{C=N}$ vibration appearing at 1606 cm^{-1} in the ligand spectrum, is shifted to lower frequency of 1599 cm^{-1} in the complexes[26-28]. This negative shift shows the participation of azomethine nitrogen in coordi-

nation with metal ions[29]. IR frequencies characteristic for υ_{M-O} has been observed[29] in the range of 508–565 cm^{-1}. The band at 1253 cm^{-1} due to phenolic C-O has shifted to higher frequency of 1296 cm^{-1} in all the complexes of DHPEBH. This substantiates the involvement of *ortho* hydroxyl group in coordination with metal ion [29].

Mass spectral data and analytical physical data of DHPEBH and its metal complexes were given in Table 5. The molecular ion peak occurs at *m/z* 592 $[M-2H]^+$ in the mass spectrum of Mn^{II}-DHPEBH complex. The mass spectrum of the Co^{II}-DHPEBH complex contains a base peak at *m/z* 597 which is in accordance with the expected molecular ion $[M^+]$ mass of the metal complex. Analysis by mass spectroscopy gave the molecular ion $[M^+-5H]$ peak of Ni^{II}-DHPEBH complex at *m/z* 592. These observations indicate the existence 1 : 2 ratio of metal ligand composition for Mn^{II}, Co^{II} and Ni^{II} complexes with tridentate nature of the ligand moiety with one ionized donor site O^- and two other donor atoms viz. imine nitrogen and carbonyl oxygen. The mass spectrum of Cu^{II}-DHPEBH complex contains a molecular ion peak at *m/z* 703 $[M-4H]^+$ indicating the dimeric form of copper complex with 1 : 1 metal to ligand composition with coordinated water molecules.

The thermal behaviour of metal complexes were investigated by thermo-gravimetrical analysis (TGA) and differential thermal analysis (DTA) techniques[30-32].

The decomposition of the Mn^{II}-DHPEBH complex occurs in three steps. The first step of weight loss occurs in the temperature range 135 °C to 242 °C which is probably due to loss of occluded water. The second stage

Table 5. Mass spectral data and analytical data of DHPEBH and its metal complexes

Compd.	Empirical formula	Molecular ion	Mass (Calcd.)	Analysis (%) : Found (Calcd.)			
				C	H	N	M
DHPEBH	$C_{15}H_{14}N_2O_3$	271 $[M+H]^+$	270.28	66.48 (66.66)	5.31 (5.18)	10.51 (10.37)	–
[Mn(DHPEBH)$_2$]	[Mn($C_{15}H_{13}N_2O_3$)$_2$]	592 $[M-2H]^+$	594.48	55.28 (60.55)	4.41 (4.37)	8.73 (9.41)	9.40
[Co(DHPEBH)$_2$]	[Co($C_{15}H_{13}N_2O_3$)$_2$]	597 $[M]^+$	597.44	55.12 (60.40)	3.61 (4.35)	8.45 (9.37)	9.85
[Ni(DHPEBH)$_2$]	[Ni($C_{15}H_{13}N_2O_3$)$_2$]	592 $[M-5H]^+$	597.24	56.37 (60.27)	4.08 (4.35)	8.65 (9.37)	9.85
[Cu(DHPEBH(H$_2$O)]$_2$	[Cu($C_{15}H_{12}N_2O_3$)(H$_2$O)]$_2$	703 $[M-4H]^+$	699.69	54.22 (51.44)	3.94 (3.45)	8.25 (8.0)	18.16

of decomposition corresponds to the partial decomposition of ligand with an endothermic peak at $t_{min} = 330\ °C$. The residue of 15% is probably due to formation of metal oxide.

Co^{II}-DHPEBH complex exhibited very little mass loss up to 242 °C indicating high thermal stability of the complex. The third step of decomposition taking place from 564 °C to 992 °C corresponds to the decomposition of coordinated part of the ligand. An endothermic curve was observed at $t_{min} = 880\ °C$ on the DTA curve. These results confirm 1 : 2 metal ligand compositions in Mn^{II} and Co^{II}-DHPEBH complexes.

Ni^{II}-DHPEBH complex displays three stages of weight loss. The first stage of weight loss corresponds to loss of occluded water. The second step of weight loss is due to partial decomposition of metal complex. The third stage of decomposition where maximum weight loss occurred was attributed to total loss of ligand moiety.

The thermogram of Cu^{II}-DHPEBH complex shows mass loss of approximately 5% in the temperature range 135.9 °C to 350 °C accompanied by two endothermic peaks with $t_{min} = 110\ °C$, $t_{min} = 330\ °C$. This loss corresponds to loss of coordinated as well as occluded water. Maximum weight loss during second stage of decomposition from 457 °C to 993 °C and an endothermic peak in this region with $t_{min} = 920\ °C$ indicates decomposition of the complex indicating loss of ligand moiety. In Cu^{II}-DHPEBH complex these results of TGA and DTA studies indicated the presence of two coordinated water molecules and metal ion and ligand in 2 : 2 ratio. The residue left directly corresponds the oxide form of metal ion.

Conclusions : The theoretical and experimental methods of study on title compound is informative in understanding various physicochemical aspects of compound. The NMR studies revealed existence of keto-enol tautomerism in DHPEBH. The computed IR and NMR data are nearly in good agreement with experimental data. The theoretical and experimental studies indicated that the title compound is tribasic acid. The equilibrium studies on title compound in presence of Cu^{II} ion inferred dissociation of two protons upon complexation. While with other metal ions understudy the results revealed release of one proton only. The mass spectral data, ele-

mental analyses and TGA and DTA[30-32] supported the composition of Mn^{II}, Co^{II} and Ni^{II} complexes as 1 : 2 and for Cu^{II} complex as 2 : 2 with coordinated water molecules. The IR spectral data of complexes is informative to understand donor sites. Further the HOMO and LUMO figures computed for neutral molecule inferred the presence of suitable orbitals at carboxy hydrazone moiety for bonding. Thus it may be concluded that theoretical data computed is useful to analyze experimental data.

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