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Review on Organic Ligands with Their Various Applications

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ABSTRACT

There are many types of organic ligands in coordination chemistry according to type of involving functional groups [1- 9] in each structure of ligand like (- N=N-, CH=N, CH=CH-CO, -N=N-C=N, -C=C-N, etc…),in the present review some of organic ligands with methods of their preparation : 1. Imine Ligands Imine (Schiff base, Anil, Aldamine, Ketamine, Azomethine) compounds have been synthesized via the condensation reaction of primary aromatic amine group and carbonyl groups of aldehyde or ketone to formation imine compounds like (Figure 1). A mixture of primary aromatic amine [42, 43] with aldehyde or ketone then a few drops was added of glacial acetic acid, the mixture was dissolved in ethanol as a solvent after that allow to refluxed for (1- 4) hrs, the product were poured into ice water then filtered, dried and recrystallization from ethanol solvent via thermal method, (Figure 2). A number of imine compounds [10-19] have been synthesized via the condensation reaction of primary amine group and carbonyl groups of aldehyde or ketone to formation anil (imine compounds) as a macro ligands like (Figure 3). There are two methods to preparation of Schiff base: Thermal Method- reflux)) and Microwave Method in (Figure 4). Its applications as a ligand in coordination chemistry [20, 21] with ion in complex (Figure 5). Other applications of Schiff base in tumors in medical fields (Figure 6). 2. Azo Ligands Azo compounds are considered as type of organic pigments [22-33] which consist of atleast a conjugated chromophore azo (-N=N-) group in link with one or more aromatic or heterocyclic compound.

1. Introduction

Studies of multidentate ligands have experienced a tremendous upsurge because such ligands mimic the environment of metal ions in biological systems [1]. These ligands provide various coordinating sites to the guest metal ions, which can fulfill the primary valency and result in novel structural motifs. Multidentate ligands can have cyclic, linear, branched, and tripodal nature [2]. Cyclic ligands offer high selectivity but slower metalation kinetics. Linear and branched ligands show faster metalation kinetics but less selectivity and easy demetalation. The tripods show the advantages of both types.

Due to such advantages and, also, for the ease of formation, work has been done on the synthesis of tripodal ligand(s), especially the Schiff base tripodal ligand(s). Moreover, the tren based Schiff bases have drawn special interest as they offer a number of applications: chemosensing and fluorosensing, in chelation therapy for the treatment of metal overload, clinical diagnosis, and chemotherapy [3–5]. The metal complexation of such ligands has been extensively studied with trivalent metal ions such as Fe(III), Cr(III), and Al(III) and is found to form uncharged complexes with high thermodynamic stability and kinetic inertness [6–13]. The coordination chemistry with Fe(III) with tripod systems has been explored with respect to their potential application in iron overload treatment [14–17]. The search to develop new effective chelators for the treatment of aluminium intoxication [18, 19] leads to the complexation study of Al(III) with tripodal chelators. Removal of Cr(III) is also extremely necessary as it leads to formation of Cr(VI), a highly toxic form and known to have mutagenic and carcinogenic properties [20, 21]. Such tripodal chelators are known to form strong complexes with Cr(III) and hence can be explored for Cr(III) removal.

2. Experimental

2.1. Materials and Measurements

All chemicals and solvents were of analytical grade available commercially. Potassium hydroxide and hydrochloric acid were obtained from Fisher Scientific. 2-Hydroxynaphthaldehyde and Tris (2-amino ethyl) amine (tren) were obtained from Sigma Aldrich. Anhydrous ferric chloride, aluminium sulphate, and chromium chloride were procured from Qualigens Fine Chemicals (Fisher Scientific). Tetrahydrofuran and dimethyl sulfoxide were purchased from Merck. Chemicals were used as purchased without purification. Solvents were dried using standard methods [22].

Melting points (MP) were determined on a microsil (India) MP apparatus and are uncorrected. They are given in degree centigrade (°C). Electronic spectra were taken on Hitachi spectrophotometer U 0080D. Infrared (IR) spectra were recorded on a Perkin-Elmer RX 1 FT-IR spectrometer using KBr discs. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance II 400 NMR spectrometer, at SAIF, Panjab University, Chandigarh, using tetramethylsilane (TMS) as an internal reference. The chemical shifts are mentioned in parts per million (ppm). The mass spectrum was performed on Waters Micromass Q-TOF Micro with electron spray ionization (EI) technique at SAIF, Panjab University, Chandigarh. C, H, N, S, and O analysis was carried out on EURO EA 3000. Potentiometric studies were carried on Sension 02 pH meter.

2.2. Synthesis of 1-[(E)-2-[Bis[2-[(2-hydroxy-1-naphthyl)methyleneamino]ethyl]amino]ethyl iminomethyl]naphthalen-2-ol (trenhynaph)

In a round bottom flask 10 mL of THF was taken, added to it 3 g (0.0174 mol) of 2-hydroxynaphthaldehyde, and the contents were stirred till complete dissolution. A solution of 0.0846 g of tren in 10 mL of THF was added dropwise. Solution was allowed to stir for 1 hr. Very thick and bright yellow coloured precipitates were obtained, which were filtered, washed with diethyl ether, and dried in vacuum. Yield (2.28 g, 76%), MP: (185–

189)°C, colour (yellow), IR (KBr pellet, cm^{-1}): 3055 (Ar=C–H), 2940(–CH_2, asymmetric), 2821(–CH_2, symmetric), 1622(–C=N), 1350(–C–O), 764(=C–H, OOP); ^{1}H NMR (DMSO-D_6, δ ppm) 3.00 (t, , 6H, H-12), 3.75 (t, , 6H, H-13), 6.68 (d, , 3H, H = 3), 7.13 (d, , 3H, H = 6), 7.32 (t, , 3H, H = 7), 7.53 (d, , 3H, H = 5), 7.60 (d, , 3H, H = 4), 7.98 (t, , 3H, H = 8), 9.04 (d, , 3H, H = 11), 14.11 (d, , 3H, H = 14); ^{13}C NMR (DMSO-D_6, δ ppm) 177.26, 159.05, 136.76, 134.14, 128.58, 127.53, 125.07, 125.33, 121.87, 118.58, 105.77, 38.93, 40.18; mass spectrum (ESI) molecular ion [M+2] peak , [M+1] peak ; anal. calcd. for $C_{39}H_{36}O_3N_4$ (608.27); C,77; H,9; N,9.2; O,7.9; found: C,77.23; H,9.36; N,9.35; O,7.98.

2.3. Titration Procedure

Potentiometric titrations were carried out in order to find out the protonation constant of the ligand and formation constant of the metal complexes. The temperature for the experiment was maintained at. A titration cell which has double glass walls was used and attached to circulatory bath to maintain the consistency of temperature. Sension 02 pH meter in combination with glass electrode was used to measure the pH. The whole equipment set was calibrated according to the standard methods [23].

Doubly distilled deoxygenated and deionized water was used to prepare all the solutions used in the experiment. KOH solution (0.1 M) was prepared in 5 : 95 ratio of DMSO/water. HCl solution (0.1 M) was prepared in water. Ionic strength of the solution was maintained 0.1 M by adding 1 M KCl solution. The solution of ligand of strength 0.01 M was prepared in DMSO and solution of metal 0.01 M in water. The final concentration of ligand and metal in titration cell was maintained at 0.001 M. The ratio of DMSO/water in the resulting titration cell was maintained at 5 : 95 by adding appropriate solutions. Following titrations in which metal to ligand ratios C_M/C_L (0 : 1) and C_M/C_L (1 : 1) were carried out. The data obtained from the experiment is fed into the least square fitting program HYPERQUAD 2006 and manual fitting of experimental and theoretical data was done to obtain the protonation constant of the ligand and the formation constants of metal complexes. The whole titration procedure is carried out twice to confirm the results.

3. Results and Discussions

3.1. Synthesis and Characterization

The ligand trenhynaph was synthesized by condensation of triamine (tren) and aldehyde (2-hydroxynaphthaldehyde) as per the scheme shown in the Figure 2. It is bright yellow in colour and found to be soluble completely in DMSO and DMSO/water ratio above 5 : 95. It is also partially soluble in methanol and ethanol but insoluble in other solvents like chloroform, ether, acetonitrile, acetone, and so forth.

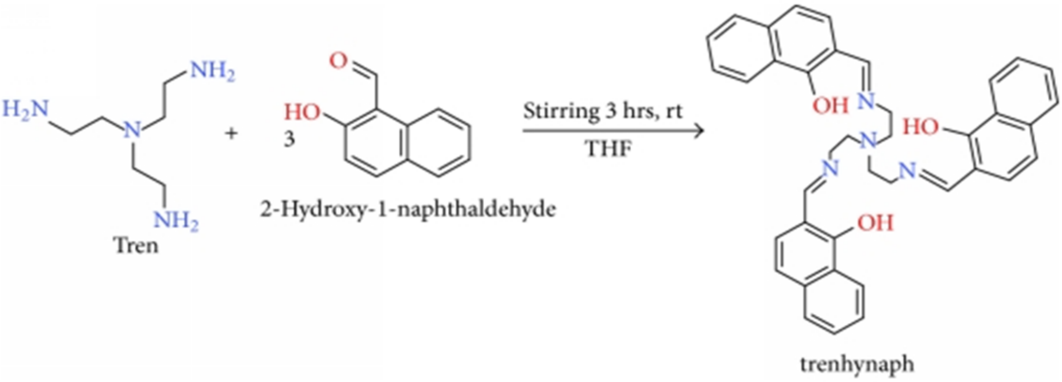
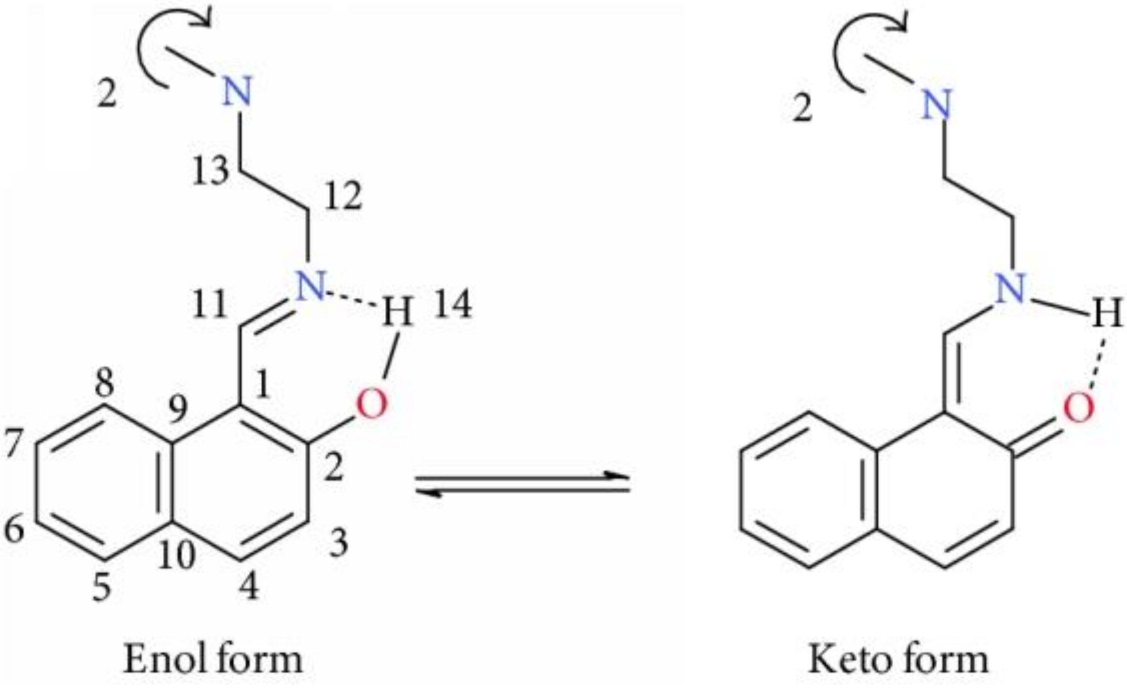


Figure 2

Scheme for the synthesis of trenhynaph.

The ligand was characterised on the basis of elemental analysis, UV-VIS, IR, ^{1}H NMR, ^{13}C NMR, and MASS spectra. It has been studied earlier that the presence of ortho hydroxyl group in Schiff bases favours the existence of intramolecular hydrogen bonds and the tautomerism, which accounts for the formation of either phenol-amine or keto-amine tautomer (Scheme 1). For the Schiff bases of salicylaldehyde with amines (–NH) form is found to be less stable. The salicylaldimines exist predominantly in –OH tautomeric form in crystalline state and the reason behind this is the loss of ring aromaticity [26]. But 2-hydroxynaphthylidenes derivatives show the presence of both the tautomers, i.e., keto-amine and enolimine. In naphthalimides (–NH) form is expected to be more stable due to resonance and delocalization in the retained aromatic structure [27, 28].



Scheme 1

Keto-enol forms of trenhynaph

Matijević-Sosa et al. investigated a number of 2-hydroxy-1-naphthaldehyde Schiff bases through various spectroscopic techniques like IR, one and two dimensional, homo-heteronuclear ^{1}H, and ^{13}C NMR. It was established that in solution (DMSO) the (–NH) tautomer predominates while the IR spectra of solid samples (KBr) suggest that the Schiff bases exist in solid state as (–OH) isomer [29, 30]. Considering these previous observations we investigated the spectra of our ligand and found that the above same trend is being followed in our case also. IR spectra suggest the predominance of the (–OH) isomer and ^{1}H and ^{13}C NMR (DMSO-d_6) suggest the (–NH) tautomer. Electronic spectrum of trenhynaph exhibits three peaks. Peaks obtained at 254.9 nm and 315.99 nm can be attributed to the transitions due to naphthyl ring and 365.99 nm transitions associated with the imine bond, Figure 3(b). Similarly the calculated electronic spectra also give three peaks, Figure 3(a). Although the calculated electronic signals are not the same as the theoretical one, still they follow the same trend as that of the experimental one.

Conclusions

The solution studies of trenhynaph by potentiometric and spectrophotometric methods revealed that three protonation constants can be assigned to hydroxyl group of naphthol moiety. The formation constants of its metal complexes with Fe(III), Cr(III), and Al(III) were determined in solution under similar adopted experimental conditions showing the formation of ML as the single major species at physiological pH. The calculated log values are 29.37, 20.94, and 20.49 for Fe(III)-L, Cr(III)-L, and Al(III)-L, respectively. Nine unit higher log values for Fe(III)-L indicate the admirable affinity of the ligand towards Fe(III) than Cr(III) and Al(III), rendering it as more potent iron chelators at physiological pH. Further, the pM values at for Fe(III) complex with trenhynaph are found to be 2 to 3 units more as compared to structurally similar chelators, deferiprone (medically applied drug for the iron intoxication) and transferrin (the main Fe binding protein in plasma) indicating higher selectivity of the ligand towards iron in its trivalent state. The high binding affinity of the ligand towards Fe(III) metal ion can be utilized for the removal of Fe(III) in iron overload chelation therapy. Also, the noticeable electronic spectral changes of the complex at pH7 with the variation in pH support the ligand for potential application as an optical sensor towards Fe(III) metal ion in biological systems. Hence, synthesis of such ligands and their derivatives will open up a perspective towards the development of new optical biosensors.

Supplementary Materials

Supplementary material consists of two figures. Figure 1 represents the 1H NMR spectra of the ligand trenhynaph. It shows peaks at 3.0039 ppm (t, 6H) and 3.7633 ppm (t, 6H) which can be attributed to the methylene protons. The signal obtained at 9.0615 ppm (d, 3H) shows the presence of imine proton. The peaks obtained at 6.698 (d, 3H), 7.6177 (d, 3H), 7.547 (d, 3H), 7.1334 (t, 3H), 7.3272 (t, 3H), and 7.9926 (d, 3H) corresponds to the naphthyl protons. A peak at 14.1123 ppm (d, 3H) is also obtained corresponding to the proton of imine nitrogen when ligand exists in keto-imine form. Figure 2 represents the mass spectrum of the ligand. It shows molecular ion peak at m/z 609.3, which was expected at 608.27. [M+2] peak is obtained at 610.4.The base peak with 100% intensity is obtained at m/z 455.2 which corresponds to the fragment $C_{28}H_{30}N_4O_2$ (454.2). One more important peak at m/z 281.1 corresponds to the fragment $C_{13}H_{23}N_3$.

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