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Synthesis and Determination of Stability Constants of a New Bis-1,2,4-triazole Ligand for Complexation with Zinc(II), Copper(II) and Nickel(II) in Acetonitrile

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ABSTRACT

In this work, the synthesis and complexation properties of a new compound, 1,3-bis[5-(2-hydroxyphenyl)-4-phenyl-1,2,4-triazole-3-yl-thio]propane (BTP), towards certain transition metal ions, (M(II) where M = Zn, Cu, Ni) in acetonitrile is reported. A hard-modeling strategy was applied to UV-Visible spectroscopy data obtained from monitoring the reaction between BTP and the selected metal ions to determine the concentration profiles of each species and the corresponding stability constant(s) of the complex(es). The stability constants of complexes are always defined in terms of their free metal, free ligand and complexed forms. These constants are influenced by parameters such as the type of metal, ligand, counterion or solvent. In this study, the formation constants of the complexes were determined for the synthesized ligand with several metallic cations in acetonitrile solvent by UV-Vis spectrophotometry.

Keywords: Zn(II), Cu(II) and Ni(II) Complexes; Triazole Ligand; Spectrophotometry

1. Introduction

The synthesis and metal complex structures of substituted 1,2,4-triazole ligands have gained considerable attention in recent years [1-5]. 1,2,4-triazole and its derivatives are very interesting ligands because they combine the coordination geometry of both pyrazole and imidazole with regard to the arrangement of their three heteroatoms. Many transition metal complexes of 1,2,4-triazoles derivatives can be synthesized [6]. Triazoles are nitrogen-containing organic compounds, and their metal complexes display a broad range of biological activity, acting as antitumor, antibacterial, antifungal and antiviral agents [7]. Substituted 1,2,4-triazoles have been actively studied as bridging ligands between transition metal(II) ions coordinating through their N1 and N2 atoms. The design and construction of coordination ligands using the 1,2,4-triazole moiety as a part of a ligand system has gained great attention in recent years [8]. The complexes of 1,2,4-triazole and its derivatives are also good candidates for the construction of various metal coordination polymers [9-13].

Traditionally, in order to study the complaxation of new synthesized ligand with metallic cations, potentiometry, paper electrophoresis, membrane permeation,

affinity capillary electrophoresis, UV-vis and fluorescence spectroscopy, and mass spectrometry can be used [14-17]. In this study, UV-vis spectroscopy was chosen because of its simplicity, low cost and availability of the UV-vis spectrophotometer in most laboratories.

The development of chelating reagents specific for bivalent metal ions (Zn(II), Cu(II) and Ni(II)) is becoming increasingly important in a wide variety of applications in the medical, pharmaceutical and related fields. In this work the complexation behavior of a newly synthesized BTP ligand with selected metallic cations has been studied using a model-based analysis. The formation constants of the complexes of the synthesized ligand, BTP, with several metallic cations in acetonitrile solvent were determined by UV-vis spectrophotometry and hard model analysis.

2. Experimental

2.1. Materials and Methods

All reagents were of analytical grade, and all solvents were commercially available (from Merck) and used without further purification. 3-(2-Hydroxyphenyl)-4-phenyl-1*H*-1,2,4-triazole-5(4*H*)-thione was prepared according to the literature [18].

The CHNS elemental analyses were performed on a

Leco CHNS 932 elemental analyzer. IR spectra were obtained using a Nexus 670 FT-IR Thermo Nicolet spectrometer using a KBr disk. ^{1}H NMR and ^{13}C-NMR spectra were recorded on a Bruker 300 MHz Ultrashield spectrometer using TMS as an internal standard in CDCl₃. The melting point was determined on an electrothermal digital melting point apparatus and was uncorrected.

Syntheses and characterization of 1,3-*bis*[5-(2-hydroxyphenyl*)-4-phenyl-1,2,4-triazole-3-yl-thio]propane* (*BTP*).

A mixture of 3-(2-Hydroxyphenyl)-4-phenyl-1H-1, 2,4-triazole-5(4H)-thione 5.66 gr (0.021 mol) and 0.84 gr (0.021 mol) NaOH was dissolved in 100 ml 20% aqueous DMF, then 2.02 gr (0.01 mol) of 1,3-dibromopropane was added. The reaction mixture was stirred 12 h; the solution was poured on to crushed ice (100 gr). The precipitate was filtered and crystallized from EtOH. (**Scheme 1**).

Yield: 63%; Mp: 193-195˚C. IR (KBr, cm-1): 3053.7, 2929.2, 2844.3, 2708.9, 2627.3, 1619.3, 1585.2, 1487.2, 1431.9, 1401.3, 1295.7, 1254.1, 1164.3, 752.2, 694.6, 606.7; ^{1}H-NMR (300 MHz, CDCl₃): 2.33 (2H, q, CH₂, *J* = 6.9 and 6.6), 3.37 (4H, t, SCH₂, *J* = 6.9 and 6.6), 6.5 (2H, t, ArH, *J* = 7.5), 6.57 (2H, d, ArH, *J* = 7.8), 7.03 (2H, d, ArH, *J* = 8.1), 7.18 (2H, t, ArH, *J* = 7.5), 7.32 (4H, d, ArH, *J* = 6.3), 7.56 (2H, s, ArH), 7.6 (4H, s, ArH),

11.32 (2H, broad s, OH); ^{13}C-NMR (300 MHz, CDCl₃): 28.66, 30.75, 110.15, 117.90, 118.53, 125.47, 127.62, 130.53, 130.79, 131.35, 134.20, 152.93, 153.41, 157.95; Anal. Calcd for $C_{31}H_{26}N_6O_2S_2$: 64.34 C, 4.53 H, 14.52 N and 11.08% S. Found: 64.39 C, 4.41 H, 14.67 N and 11.16% S.

2.2. Complex Formation

All solutions were prepared using acetonitrile. Small volumes of concentrated metal cation solutions (e.g. 0-150 μL from stock solutions with a concentration of 10^{-3} M) were added to ligand solutions (2 mL of a 10^{-4} M stock solution). The solutions were thermostated at 25˚C. An example of the change in absorbance due to complex formation is given in **Figure 1**. This figure shows the complexation of Cu^{2+} by the BTP ligand. **Scheme 2** represents the possible structure of the M^{2+} in complex with the BTP ligand.

An intramolecular O-H⋯N hydrogen bonds in ligand exists between the hydroxyphenyl group and the triazole N atom, resulting in a nearly planar six-membered ring in the central part of the molecule. Also these hydrogen bonds in complex was exist that indicate with FT-IR spectra of ligand and complex (not shown hear).
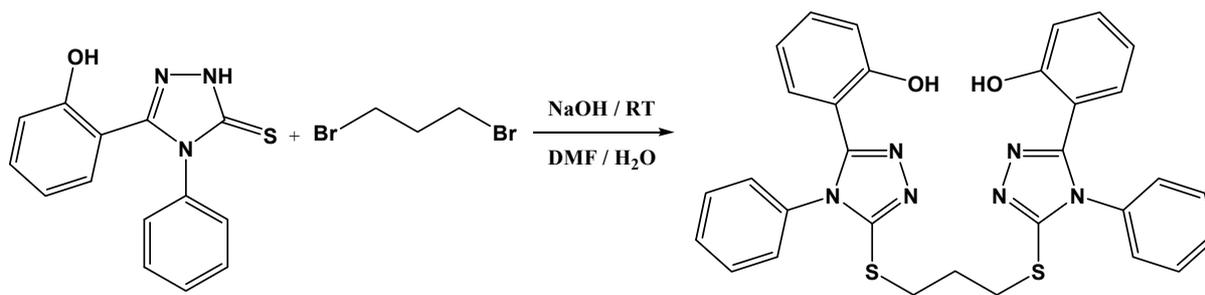
Scheme 1. Synthesis rout of BTP.
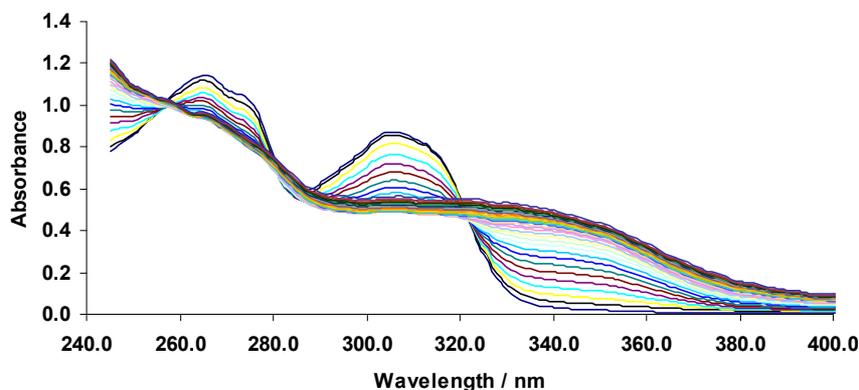
Figure 1. changes in UV-Vis absorption spectra of 1,3-bis[5-(2-hydroxyphenyl)-4-phenyl-4H-1,2,4-triazole-3-yl-thio] propane in acetonitrile (4.76 × 10^{-5} mol/L); arrows indicate a change in the absorbance with increase in the concentration of Cu^{2+}. [Cu^{2+}] mol/L: 0, 4.74 × 10^{-6}, 9.43 × 10^{-6}, 1.41 × 10^{-5}, 1.87 × 10^{-5}, 2.33 × 10^{-5}, 2.78 × 10^{-5}, 3.23 × 10^{-5}, 3.67 × 10^{-5}, 4.11 × 10^{-5}, 4.55 × 10^{-5}, 4.98 × 10^{-5}, 5.41 × 10^{-5}, 5.83 × 10^{-5}, 6.25 × 10^{-5}, 6.67 × 10^{-5}, 7.08 × 10^{-5}, 7.49 × 10^{-5}, 7.89 × 10^{-5}, 8.3 × 10^{-5}, 8.7 × 10^{-5}, 9.09 × 10^{-5}, 9.48 × 10^{-5}, 9.87 × 10^{-5}, 1.03 × 10^{-4}, 1.06 × 10^{-4}, 1.1 × 10^{-4}, 1.14 × 10^{-4}, 1.18 × 10^{-4}, 1.21 × 10^{-4}, and 1.25 × 10^{-4}.

Scheme 2. Possible structure of Cu^{2+} complexed with BTP [$Cu(BTP)_2$].

3. Results and Discussion

3.1. Treatment of the Experimental Data

For the case of a one-step ML_2 complex formation, the following equation could be derived using the ligand concentration [19]:

$$M + 2L \leftrightarrow ML_2 \qquad (1)$$
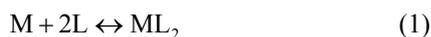
$$K_f = [ML_2]\big/[L]^2[M] \qquad (2)$$

$$C_L = [L] + 2[ML_2] \qquad (3)$$

$$C_M = [M^{n+}] + [ML_2] \qquad (4)$$

$$K_f[L]^3 + (2C_M - C_L)K_f[L]^2 + [L] - C_L = 0 \qquad (5)$$

3.2. Theory of Model-Based Analysis

The theory of model based analysis (hard model analysis) has been presented in the litrtures [20].

Absorption data are governed by Beer-Lambert's law and the measurements are well-described by a matrix equation:

$$D = CS^T + E \qquad (8)$$

where D is a matrix with rows formed by the absorption spectra measured as a function of the progress of the process. The columns of D are the absorption traces measured at different wavelengths. According to Beer-Lambert's law, this matrix can be decomposed into the product of a matrix C containing, column-wise, the concentration profiles of the absorbing species and a matrix S containing, row-wise, their molar absorptivities. Matrix E is a collection of the residuals, the difference between the measurement D and its calculated representation CS^T.

Hard model analysis consists of finding a set of parameters for which the sum over all the squares, *ssq*, over all the elements of the error matrix, E, is minimal [20].

This crucial sum is a function of the measurement, D, the pre-defined model and the parameters:

$$ssq = \sum E_{i,j}^2 = f(D, \text{model, parameters}) \qquad (9)$$

Starting with initial guesses of the equilibrium constants (K_{fl} and K_{f2}), the concentration profiles based on the model proposed are constructed. These equilibrium constants are refined in an iterative approach using the NGL/M algorithm so as to minimize the ssq. If the improvement in ssq in two successive iterations is below a certain threshold, *i.e.* the shift in the parameters resulted in no further improvement of the ssq value, then the process is terminated, and the final values of the parameters leading to the last ssq is reported. It must be mentioned that in each iteration, the matrix of the linear parameters (S^T) is calculated explicitly as $S^T = C^+D$.

To summarize, given the model and the measurement D, Equation (8) can be written as

$$ssq = f(k) = D - CS^T = D - CC^+D \qquad (10)$$

Also it should be noted that the most difficult aspect of the model-based approach is to define the correct chemical model. A soft model process (e.g. multivariate curve resolution-alternative least squares or MCR-ALS) [21-23] can be used prior to applying any equation during any hard model approach.

3.3. Analysis of Experimental Data

The complexometric spectra for the complexation of Cu^{2+} with the ligand BTP was represented in **Figure 1**. The number of spectrophotometrically active components was specified by singular value decomposition (SVD) of data. The results indicated that there are three major components (**Figure 2**). The results of the MCR analysis for this dataset (not shown) support the assumption that the system obeys Equations (1)-(5), therefore the absorbing components in this system could be assumed to be L, CuL_2 and Cu^{2+} (solvated cation).

Hard model analysis was then applied for determination of K_f as well as resolving the system and acquiring the pure spectra. The results are shown in **Figure 3**. The equilibrium constant of the CuL_2 complex was calculated to be $10^{6.01}$ - $10^{6.10}$ using different initial estimates.

The same analysis was done for the complexation of Ni^{2+} with BTP in acetonitrile. **Figure 4** represents the complexometric spectra of BTP with Ni^{2+}. The number of significant components was estimated using the SVD algorithm. **Figure 5** shows that there are 2 significant components in this matrix. Because the investigated wavelength range for this data was from 240 nm to 400 nm and also because the solvated form of Ni^{2+} had no absorbance in this range, it can be concluded that the active spectroscopic components were the ligand itself

and the resulting complex. Model-based analysis of this dataset as a 2:1 complex formed in one step is shown in **Figure 6**. The stability constant of this complex was calculated to be 10^6.

The complexometric spectra for the complexation of Zn^{2+} by the ligand BTP was presented in **Figures 7-8**.
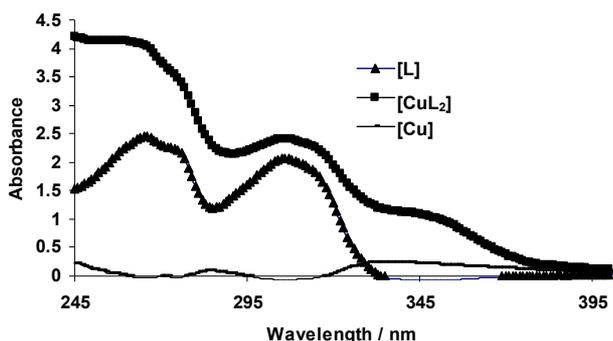
Figure 2. consecutive singular value of singular value decomposition of Cu^{2+}-BTP a function of components.
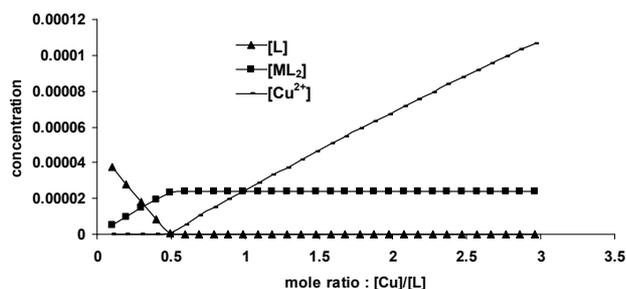
Figure 3. Results of model-based analysis of complexation of Cu^{2+} with 1,3-bis [5-(2-hydroxyphenyl)-4-phenyl-4H-1,2,4-triazole-3-yl-thio] propane in acetonitrile.
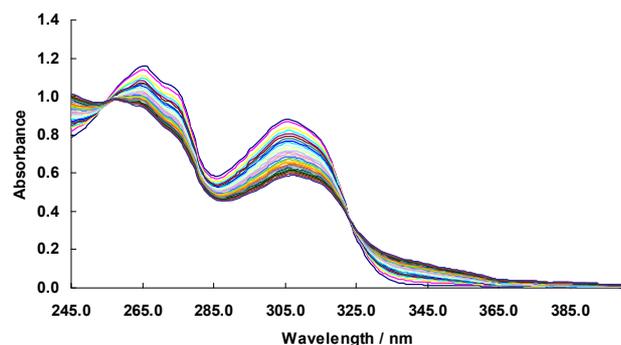
Figure 4. changes in UV-Vis absorption spectra of 1,3-bis-[5-(2-hydroxyphenyl)-4-phenyl-4H-1,2,4-triazole-3-yl-thio] propane in acetonitrile (4.76×10^{-5} mol/L); arrows indicate a change in the absorbance with increase in the concentration of Ni^{2+}. [Ni^{2+}] mol/L: 0, 4.74×10^{-6}, 9.43×10^{-6}, 1.41×10^{-5}, 1.87×10^{-5}, 2.33×10^{-5}, 2.78×10^{-5}, 3.23×10^{-5}, 3.67×10^{-5}, 4.11×10^{-5}, 4.55×10^{-5}, 4.98×10^{-5}, 5.41×10^{-5}, 5.83×10^{-5}, 6.25×10^{-5}, 6.67×10^{-5}, 7.08×10^{-5}, 7.49×10^{-5}, 7.89×10^{-5}, 8.3×10^{-5}, 8.7×10^{-5}, 9.09×10^{-5}, 9.48×10^{-5}, 9.87×10^{-5}, 1.03×10^{-4}, 1.06×10^{-4}, 1.1×10^{-4}, 1.14×10^{-4}, 1.18×10^{-4}, 1.21×10^{-4}, and 1.25×10^{-4}.

Figure 5. Consecutive singular value of singular value decomposition of Ni^{2+}-BTP a function of components.
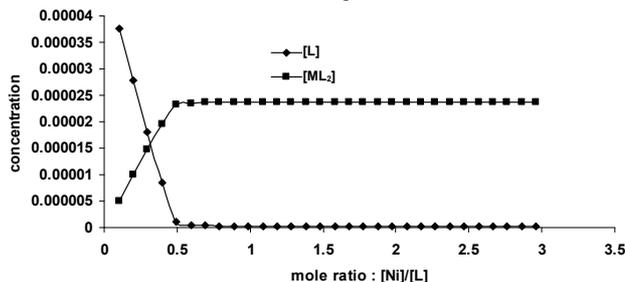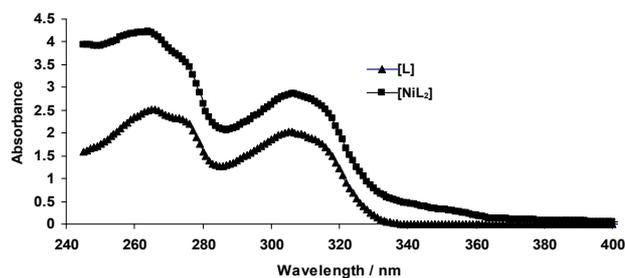
Figure 6. Results of model-based analysis of complexation of Ni^{2+} with 1,3-bis [5-(2-hydroxyphenyl)-4-phenyl-4H-1,2,4-triazole-3-yl-thio] propane in acetonitrile.
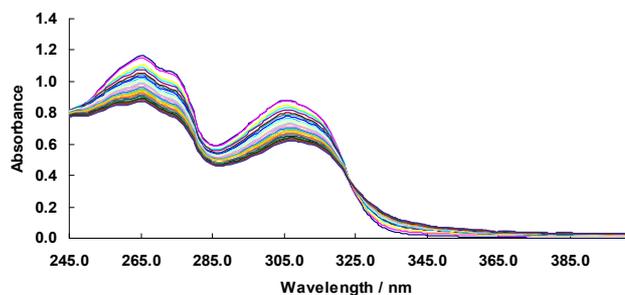
Figure 7. changes in UV-Vis absorption spectra of 1,3-bis-[5-(2-hydroxyphenyl)-4-phenyl-4H-1,2,4-triazole-3-yl-thio] propane in acetonitrile (4.76×10^{-5} mol/L); arrows indicate a change in the absorbance with increase in the concentration of Zn^{2+}. [Zn^{2+}] mol/L: 0, 4.74×10^{-6}, 9.43×10^{-6}, 1.41×10^{-5}, 1.87×10^{-5}, 2.33×10^{-5}, 2.78×10^{-5}, 3.23×10^{-5}, 3.67×10^{-5}, 4.11×10^{-5}, 4.55×10^{-5}, 4.98×10^{-5}, 5.41×10^{-5}, 5.83×10^{-5}, 6.25×10^{-5}, 6.67×10^{-5}, 7.08×10^{-5}, 7.49×10^{-5}, 7.89×10^{-5}, 8.3×10^{-5}, 8.7×10^{-5}, 9.09×10^{-5}, 9.48×10^{-5}, 9.87×10^{-5}, 1.03×10^{-4}, 1.06×10^{-4}, 1.1×10^{-4}, 1.14×10^{-4}, 1.18×10^{-4}, 1.21×10^{-4}, and 1.25×10^{-4}.

Figure 8. consecutive singular value of singular value decomposition of Zn^{2+}-BTP a function of components.
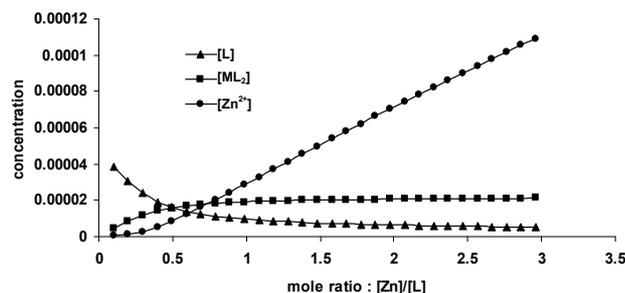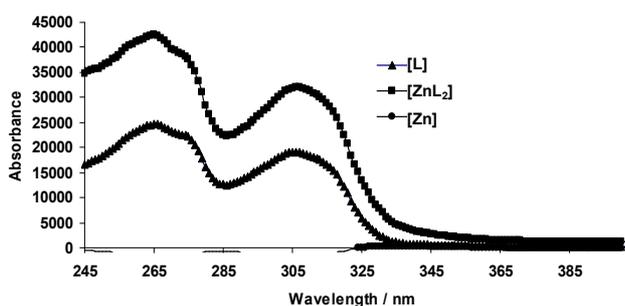
Figure 9. Results of model-based analysis of complexation of Zn^{2+} with 1,3-bis [5-(2-hydroxyphenyl)-4-phenyl-4H-1,2, 4-triazole-3-yl-thio] propane in acetonitrile.

The results of model-based analysis of the complexation of Zn^{2+} by the ligand BTP was presented in **Figure 9**. The stability constant of the ZnL_2 complex was calculated to be $10^{9.11}$ - $10^{9.12}$ using different initial estimates.

4. Conclusion

In this work, the synthesis and complexation properties of a new compound, 1,3-bis[5-(2-hydroxyphenyl)-4-phenyl-1,2,4-triazole-3-yl-thio]propane (BTP), towards certain transition metal ions, (M(II) where M = Zn, Cu, Ni) in acetonitrile is reported. A hard-modeling strategy was applied to UV-Visible spectroscopy data obtained from monitoring the reaction between BTP and the selected metal ions to determine the concentration profiles of each species and the corresponding stability constant(s) of the complex(es). Among the tested metallic cations

Cu(II), Zn(II) and Ni(II). Were formed the most stable complexes with this BTP. Based on the results of this study the new synthesized ligand is introduced as a new active emissive probe to detect Cu(II), Zn(II) and Ni(II) by absorption spectroscopy either directly or after pre-concentration.

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