



Synthesis, studying analytical properties and biological activity of new transition metal complexes with sulfadiazine derivative as reagent

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Abstract

A new of nickel(II) and copper(II) complexes of 4-((4-acetylphenyl)diazanyl)-3-amino-N-(pyrimidin-2-yl) benzenesulfonamide (SDA) derived from sulfadiazine have been prepared and identified by FTIR, NMR, mass spectroscopy, UV-Visible spectroscopy, and elemental analysis. Also tested to evaluated their activities as antibacterial agents. The spectroscopic and analytical data suggest all prepared nickel(II) and copper(II) complexes a square planar geometry. The agar well diffusion method was used to test the target ligand and their Ni(II) and Cu(II) complexes for antibacterial activity against Gram (+) and Gram (-) bacteria.

Keywords: Antibacterial Activity, Sulfadiazine, Azo compound, Complexes.

1. Introduction

Among the dispersed dyes, azo organic dyes are a very important component for printing and the textile industries ^[1,2]. They've also been used in a wide range of applications including food coloring, cosmetics, optical switches, plastics, nonlinear optics, electro-optical devices, and liquid crystal displays ^[3,4]. Furthermore, hetero phenyl-based azo moiety have been investigated for its biological activities applications, for example characteristics of antioxidants ^[5], antitumor ^[6], antimicrobial and antiviral activities ^[7,8] and antidiabetics ^[9]. A diazonium salt generated from a primary aromatic amine acting as an electrophile is generally coupled with a nucleophilic coupling compounds, mostly an amine or phenol, to make an azo dye ^[10]. When compared to simple aromatic derivatives, these azo derivatives yield a wide variety of colors through the visible spectrum because heterocyclic azo compounds have an important bathochromic shifting ^[11], by changing the chemical functional groups integrated into the azo compound, different colors

can be created. Furthermore, compared to other dye molecules, these organic dyes are additional stable and unaffected to light degradation over time ^[12], because of their potential uses in a variety of disciplines, heterocyclic ring systems and its compounds, such as pyrazole, pyridine ^[13,14] thiazole, benzothiazole ^[15], and pyrimidine ^[16] have sparked a lot of interest in azo compounds. The design and prepared of biologically efficient compounds for chemotherapy is one such field ^[17]. The unique biological features of heterocyclic molecules, especially their antiviral ^[18], antimicrobial ^[19], anticancer ^[20], anti-inflammatory ^[21], analgesic properties ^[22] and anti-mycobacterial ^[23] have been intensively explored. The pyrimidine ring is existing in numerous pharmacologically and physiologically active derivatives as well as sulfonamide moiety; hence sulfadiazine and it derivatives are particularly relevant ^[24-26]. The agar well diffusion method was used to screen a novel ligand and its complexes for anti-microorganism activity against two kinds of bacteria Gram (+) and Gram (-) in this work.

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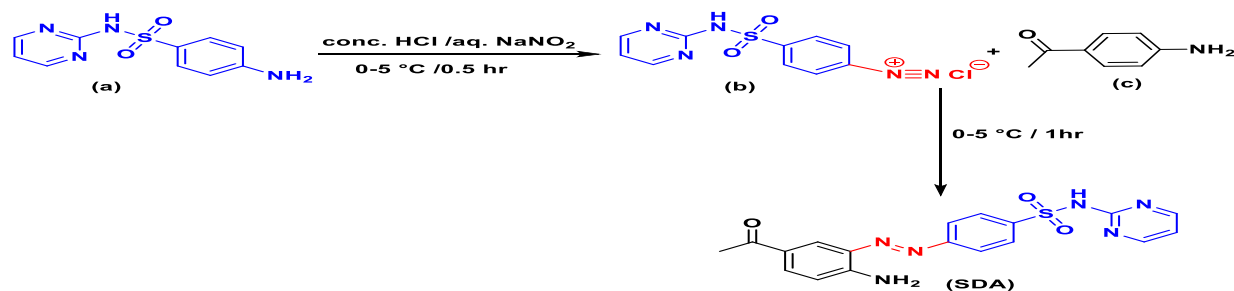
2. Experimental Section

2.1. Materials and methods

All chemical materials and organic solvents were commercially. FTIR spectra was obtained by using FTIR- ATR, Bruker ALPHA FTIR, Elemental analysis (C.H.N.S) were recorded by using EuRo VECTOR elemental analyzer. (UV-Vis) measurements were recorded on Shimaduz 1650PC model, ^{13}C and ^1H NMR were obtained in DMSO on the Bruker spectrometer (400 MHz for ^1H NMR and 100 MHz for NMR ^{13}C , respectively), Mashhad University, Iran. Measurements of pH were recorded by utilize pH meter Hanna model. The metal percentage of the complex was analyzed by Perkin-Elmer model 2280, atomic absorption technique. Molar conductance was measured at room temperature in DMF (10^{-3}M), on conductivity meter, HANNA model 214EC.

2.2. Procedure for synthesis of azo dye

Based on Awale et al. [6] approach was used to synthesized (E)-4-((5-acetyl-2-amino phenyl) diazenyl)-N-(pyrimidin-2-yl) benzenesulfonamide (SDA). with a minor modification (Scheme 1). Put (3



Scheme 1: synthesis of azo dye

2.3. Procedure for synthesis of metal complexes

Synthesis of copper(II) and nickel(II) complexes in (1:2) molar ratio with (E)-4-((5-acetyl-2-aminophenyl) diazenyl)-N-(pyrimidin-2-yl)benzenesulfonamide (SDA). An ethanolic solution (25 mL) that has been heated, (10 mmol) of prepared ligand (SDA) was added to an ethanolic solution in drops (20 mL) of $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ and $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (5 mmol) with continual stirring. After complete addition to the reaction mixture, it was refluxed for 4 hours and then cooled down to room temperature. The dark-colored precipitates were filtered, washed with anhydrous ethanol many times, and dried the target products under reduced pressure. Figure 1 depicts the predicted shape of metal complexes.

mmol) of sulfadiazine in clean beaker and dissolved in (5 mL, H_2SO_4 conc.) and chilled to ($0-5^\circ\text{C}$). Separately, (3 mmol) of (NaNO_2) was dissolved by using (10 mL) distilled water and cooled the solution to ($0-5^\circ\text{C}$) before being added carefully drop by drop to the cold sulfadiazine solution (a). To obtain diazonium salt (b), the end reaction mixture was agitated for 0.5 hour at ($0-5^\circ\text{C}$). (3 mmole) of 4-aminoacetophenone was dissolved in 30 mL of a 5 percent NaOH and cooled to ($0-5^\circ\text{C}$). At a temperature below 5°C , the result diazonium salt (b) was slowly added drop by drop to the 4-aminoacetophenone (c) solution, and the solution was agitated for 1 hour under the same conditions. TLC technique is used to observe the reaction at the same time by using (3:2) mixture of hexane and ethyl acetate as the eluent. The reaction mixture was neutralized after obtaining a dark brown hue precipitate. The precipitate was filtered and washed with water before being dried by using oven. The finished product was refined by recrystallization from methanol.

Table 1 lists all of the physical attributes as well as the (C.H.N.S.) analysis.

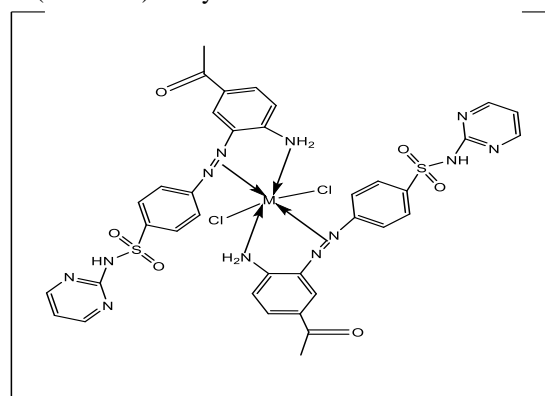


Fig.1: The suggested geometry of prepared complexes $\text{M} = \text{Ni(II)}$ or Cu(II)

2.4. Biological activity

The anti-microorganism activity of organic azo compound (SDA) and its metal complexes (1a, 2a) were investigated against two types of human pathogenic bacterial strains *Bacillus subtilis*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Escherichia coli*. The organic azo dye (SDA) and its metal complexes (1a and 2a) were produced as stock solutions in organic solvent DMSO at a concentration of 100 g/mL, and their antibacterial efficacy was compared to that of the conventional medication Chloramphenicol, which was used as a positive control.

3. Results and Discussion

The organic azo ligand (SDA) was created by combining 4-aminoacetophenone an alkaline solution containing the necessary diazotized. Spectral analyses (FT-IR, ^1H , ^{13}C NMR, and micro elemental analyses and UV-Vis) were used to identify the produced ligand. Metal salts' interactions with the prepared ligand was studied using aqueous-ethanol solutions on a regular basis.

3.1. Spectral data of prepared azo ligand

(E)-4-((5-acetyl-2-aminophenyl)diazenyl)-N-(pyrimidin-2-yl)benzenesulfonamide(SDA). This is

an organic azo dye derivative made from azo coupling reaction of 4-aminoacetophenone with sulfadiazine and the target ligand produce as solid powder and dark brown color. (m.p.= 208-210° C with 91% reaction yield. FTIR (4000-400 cm^{-1}): 3384, 3321 (Ar-NH₂), 3265 (Ar-NH-), 1680 (-C=O), 1608 (-C=N), 1458(N=N), 1381(Ar-C=C), 1332 (SO₂)_{asy}, 1254 (C-O), 1154 (SO₂)_{sy}. FT-IR spectrum of azo dye (SDA) show two absorption peaks at 3384 and 3321 cm^{-1} of the symmetric and asymmetric stretching vibration of amine group and absorption peak at 3265 cm^{-1} due to the stretching vibration sulfonamide(N-H). The important group, its azo stretching vibration (N=N) appeared at 1458 cm^{-1} . On the other hand, it has stretching vibration at 1680 cm^{-1} for (C=O) carbonyl aromatic conjugated ketone. ^1H NMR δ (ppm): 11.37 (1H, s, for -NH sulfonamide), 8.52 (2H, d, $J= 4\text{Hz}$, for 2HC=N pyrimidine ring), 8.02-7.21 (9H, m, ArH), 6.22 (2H, s, ArNH₂), 2.67 (3H, s, CH₃ of acyl groups) (Fig.2). ^{13}C NMR δ (ppm): δ 195.45, 157.74, 154.68, 141.61, 138.32, 137.26, 136.68, 135.24, 129.22, 124.89, 122.84, 119.77, 116.86, 114.84, 34.35(Fig.3). LC-MS: m/z (%) = 396.43 [M+1]⁺ (Fig.4). Analytical data of: C₁₈H₁₆N₆O₃S (%): C, 54.54; H, 4.07; N, 21.20; S, 8.09, Found: C, 54.46; H 4.03; N 21.17; S 8.01.

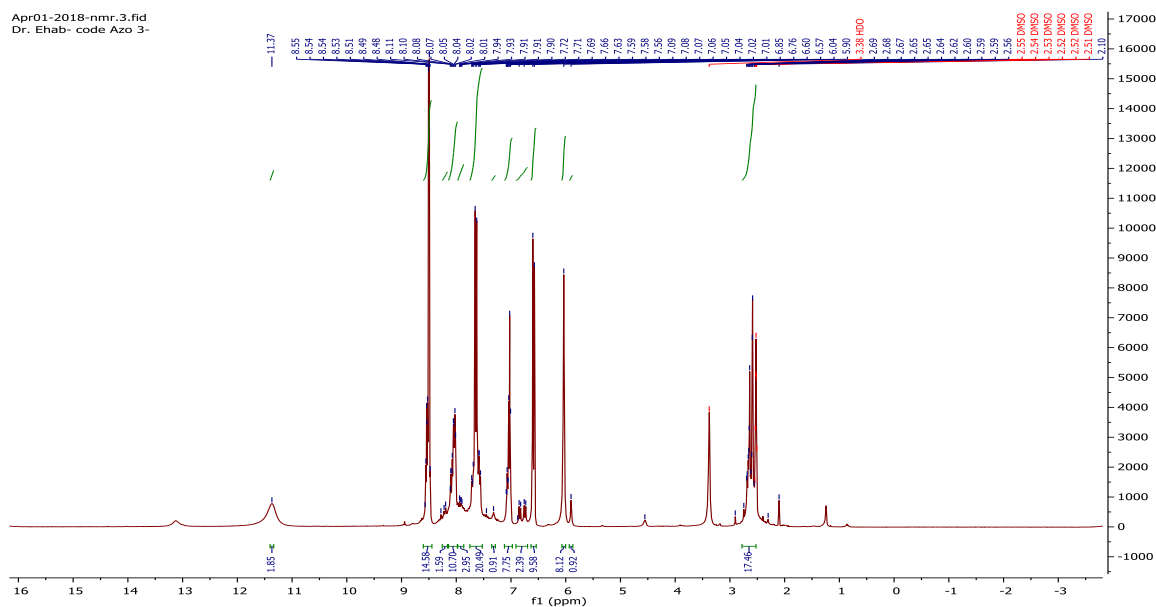


Fig. 2. ^1H NMR spectrum of SDA

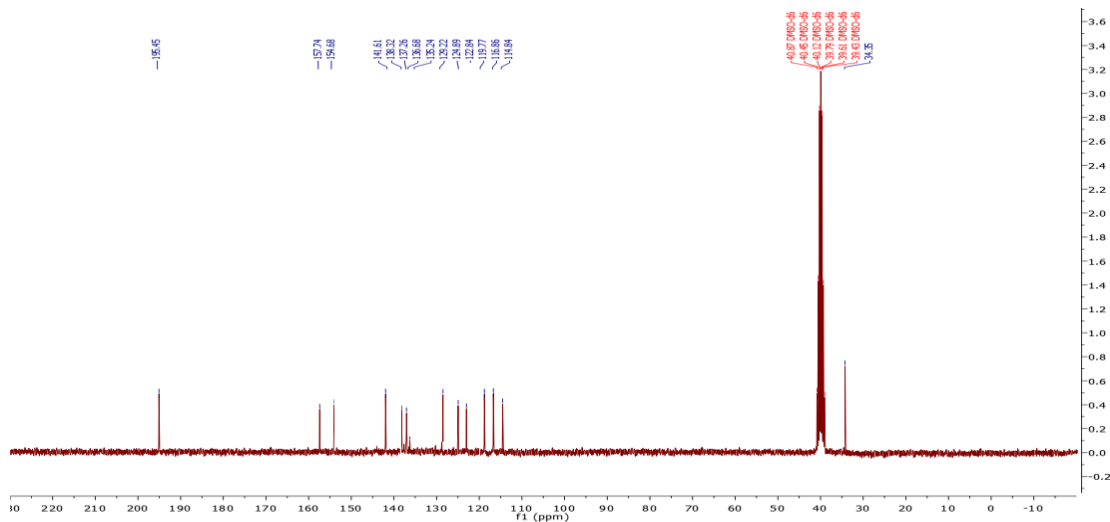


Fig. 3. ^{13}C NMR spectrum of SDA

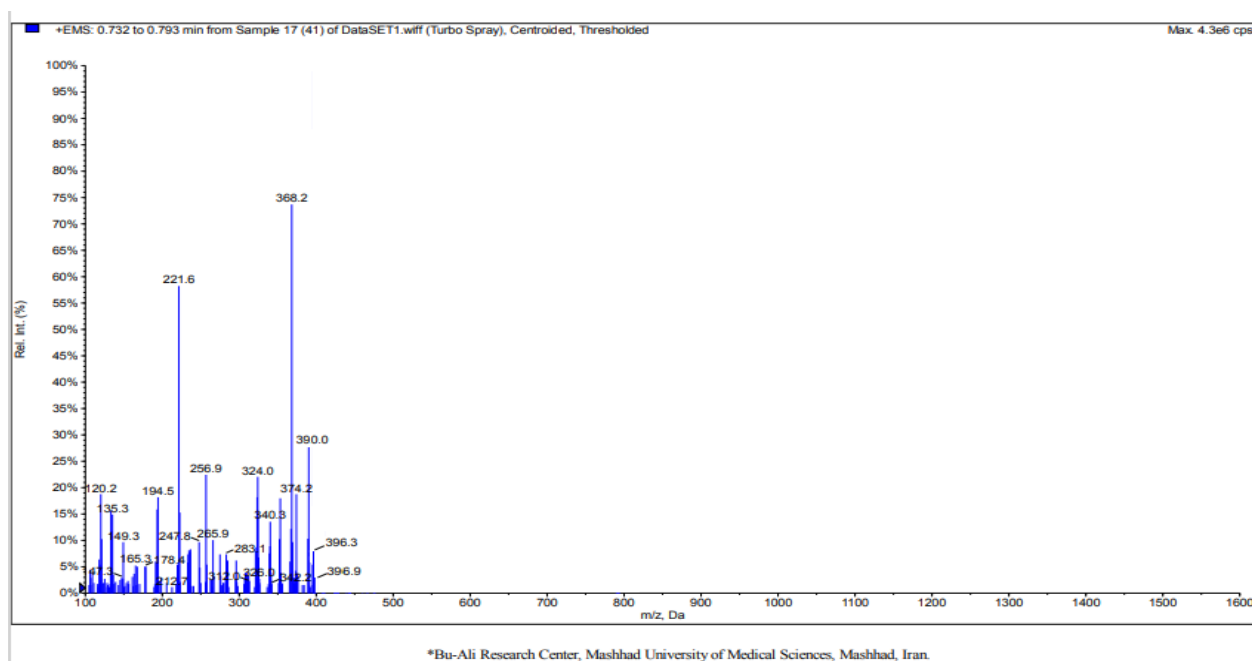


Fig.4. Mass spectrum of SDA

Table 1: UV-Visible, magnetic susceptibility, and conductance measurement datum conditions of the generated chemicals

| Compound | Optimum PH | Optimum molar con. $\times 10^{-4}$ | Max) λ (nm | (L/mol.cm) Max ϵ | μ =(S.cm ² .mol ⁻¹ Λ | μ Eff. (B.M) |
|----------|------------|-------------------------------------|--------------------------|-----------------------------|--|------------------|
| SDA | | | 218 270 396 | 1944 1245 1978 | | |
| Ni | 9 | 2.5 | 220 272 400 466 | 1354 1287 1787 687 | 14.35 | 3.45 |
| Cu | 9 | 2.5 | 220 272 404 470 | 1896 1245 2014 745 | 18.35 | 2.35 |

3.2. Electronic spectra

Table 2. lists the UV-Vis spectra of the ligands and their metal chelates melted in organic solvent ethanol (10^{-3} mol/L) in addition to the datum produced. Peaks at 218, 270, and 396 nm in the UV-Vis spectrum of the azo ligand were return to a mild energy electron transition ($\pi-\pi^*$) [17]. Peaks in the Cu(II) spectra return to charge transfer and ligand field may be found at 220, 272, 404, and 470 nm, and the magnitude of the magnetic moment at 1.72 B.M can be used to support the fact of octahedral geometry [20]. Fourth absorption peaks were observed in the Ni(II) complex at 220, 272, 400, and 466 nm, which were linked to the charge transfer and ligand field. This complex's magnetic moment was discovered to be 3.01 B.M, which was remarkably similar to the octahedral configuration [19].

3.3. Ligand to metal ratio

To appoint the complexes in solutions, mole ratio and job strategies have been tested. In both cases, the results were spread out in a 1:2 (metal to ligand) ratio. Table 2 summarizes the gating outputs as well as the specifications for manufacturing compounds.

3.4. Physical properties

The interaction of a ligand melted in ethanol with metal ions melted in optimum pH and in a (Metal: Ligand) ratio of (1:2) resulted in solid complexes. In terms of well-calculated values, the findings of elemental analysis and metal import from compounds were practically identical. The non-electrolytic

conductivity of prepared ligand and metal copper(II) and nickel(II) chelates melted at dimethylsulphoxide (10^{-3} mol/L) is shown in Table 1.

3.5. Determination of gibbs free energy and stability constant

The equations can be used to get the stability constant (K) for the (1:2) metal to prepared ligand complex.

$$K = \frac{1-\alpha}{4\alpha^3 C^2} ; \quad \alpha = \frac{A_m - A_s}{A_m}$$

Where:

As= absorption in a solution having the same amount of ligand and metal ion.

c = concentration to the compound solution at mole/L.

α = degree of dissociation.

Am= absorption in a solution containing the same amount of metal and surplus for ligand.

Great (K) values indicate high consistency for generated complexes [15].

Gibbs free energy (G) thermodynamic characteristics were also investigated. The G data were calculated using the equation [16].

$$\Delta G = -R T \ln k$$

Where:

T = absolute temperature (Kelvin).

R = gas constant = $8.314 \text{ J.mol}^{-1}\text{K}$.

The reaction between the azo dye ligand (L) and metal ions understudy results in a negative value of (G), as shown in Table 2.

Table 2: The Prepared Complexes' Stability Constant and Gibbs Free Energy.

| Complexes | As | Am | α | $K \cdot 10^6$ | Ln K | $\Delta G \text{ KJ.mol}^{-1}$ |
|-----------------------|-------|-------|----------|----------------|-------|--------------------------------|
| [Ni(L) ₂] | 0.235 | 0.451 | 0.412 | 31.11 | 16.97 | -42.065 |
| [Cu(L) ₂] | 0.101 | 0.112 | 0.401 | 35.05 | 16.89 | -41.867 |

3.6. Antibacterial activity

The prepared compounds (2a and 3a) were tested for antibacterial activity against Gram-positive bacteria (*S. epidermidis*, *B. subtilis*) and Gram negative

bacteria (*E. coli*, *P. aeuroginosa*). The results summarized in Table 3. the results of antibacterial activity show compound (3a) more active all tested microorganisms.

Table 3: Antibacterial activity of newly synthesized compounds

| Compound | Gram-positive bacteria | | | | | | | | | | Gram-negative bacteria | | | | | | | | | |
|-----------------|------------------------------|----|----|-----|----|--------------------|----|----|-----|----|------------------------|----|----|-----|----|----------------------|----|----|-----|----|
| | <i>Staphylococcus aureus</i> | | | | | <i>B. subtilis</i> | | | | | <i>E. coli</i> | | | | | <i>P. aeruginosa</i> | | | | |
| Chloramphenicol | 25 | 50 | 75 | 100 | *C | 25 | 50 | 75 | 100 | *C | 25 | 50 | 75 | 100 | *C | 25 | 50 | 75 | 100 | *C |
| 2a | 9 | 11 | 12 | 15 | 21 | 13 | 17 | 21 | 31 | 35 | 13 | 19 | 22 | 30 | 33 | 11 | 15 | 22 | 28 | 30 |
| 3a | 8 | 10 | 14 | 21 | 33 | 12 | 15 | 25 | 34 | 37 | 11 | 19 | 24 | 28 | 29 | 12 | 14 | 21 | 25 | 31 |

*C: positive control antibacterial drug chloramphenicol (100 μ L)

4. Conclusion

In conclusions, synthesis new copper(II) and nickel(II) complexes with 4-((4-acetylphenyl) diazenyl)-3-amino-N-(pyrimidin-2-yl) benzenesulfonamide (SDA) as ligand. Infrared spectral studies confirmed the copper(II) and nickel(II) metal-ligand coordination at NH₂ and azo group. In addition, by elemental analysis studies, molar conductivity of complexes measurements, electronic absorption, magnetic susceptibilities, the structure for Ni(II), and Cu(II) complexes is assigned as octahedral structure and high spin. The antibacterial activity of ligand and their complexes with Ni(II), and Cu(II) showed high activity when increase concentration.

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