

Synthesis, Characterization and Catecholase Activities of Azo Containing Schiff Base Ligands and Their Transition Metal Complexes

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(Alınış / Received: 20.05.2022, Kabul / Accepted: 18.07.2022, Online Yayınlanma / Published Online: 23.08.2022)

Keywords

Schiff base, metal complexes, synthesis.

Abstract: Schiff bases are also known as a good nitrogen donor ligand ($>C=N-$). Since azo compounds containing two phenyl rings separated by the azo group ($-N=N-$) are versatile molecules, they are of great importance in both scientific and application fields. In this study, three types of azo-azomethine ligands have been synthesized from the reaction of (E)-2-hydroxy-5-((4-methoxyphenyl)diazonyl)benzaldehyde with aniline derivatives. Structures of the synthesized ligands (**2-4**) and complexes (**7-12**) were characterized with ^{13}C -NMR, 1H -NMR, UV-Visible spectroscopy, elemental analysis, and FT-IR. It was understood that metal is bound by N and O atoms in the ligands. The catalytic activities of complexes were investigated. The catecholase enzyme-like activity of the complexes was studied for $3,5\text{-DTBC} \rightarrow 3,5\text{-DTBQ}$ conversion in the presence of air oxygen.

Azo İçeren Schiff Bazı Ligandları ve Geçiş Metal Komplekslerinin Sentezi, Karakterizasyonu ve katekolaz aktiviteleri

Anahtar Kelimeler

Schiff bazı
Metal kompleksleri
sentez

Öz: Schiff bazları ayrıca iyi bir nitrojen donör ligandı olarak bilinir ($>C=N-$). Azo grubu ($-N=N-$) ile ayrılmış iki fenil halkası içeren azo bileşikleri çok yönlü moleküller olduklarından hem bilimsel hem de uygulama alanlarında büyük önem taşırlar. Bu çalışmada, (E)-2-hidroksi-5-((4-metoksifenil)diazonyl)benzaldehitin anilin türevleri ile reaksiyonundan üç tip azo-azometin ligandı sentezlenmiştir. Sentezlenen ligandların (**2-4**) ve komplekslerin (**7-12**) yapıları ^{13}C -NMR, 1H -NMR, UV-Görünür spektroskopi, element analizi ve FT-IR ile karakterize edildi. Metalin ligandlarda N ve O atomları ile bağlı olduğu anlaşılmıştır. Komplekslerin katalitik aktiviteleri araştırılmıştır. Komplekslerin katekolaz enzim benzeri aktivitesi, hava oksijen varlığında $3,5\text{-DTBC} \rightarrow 3,5\text{-DTBQ}$ dönüşümü için incelenmiştir.

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1. Introduction

Schiff base structures obtained from the condensation reactions of aldehydes or ketones with amines were first synthesized by Hugo Schiff in 1964. Schiff base is an organic compound containing an azomethine group and is a nitrogen analog of an aldehyde or ketone in structure [1].

Schiff base structures can be used in many applications thanks to the azomethine group and a wide variety of functional groups that can be added to the structure. Schiff base ligands are used in biological applications or inorganic and analytical chemistry experiments [2], optical and electrochemical fields [3], textile industry and as catalysts in catalytic applications [4]. Schiff base ligands can be coordinated to the metal atom, over the nitrogen of the azomethine group, and can also be attached to the metal through the presence of groups such as OH, which are close to the azomethine group in the ligand structure. In this way, a more stable complex can be formed [5].

These complexes can act as both heterogeneous and homogeneous catalysts in the reaction medium. The factors affecting these properties depend on the ligand type, metal type and coordination sites in the ligand. [6].

Among the complexes of Schiff base ligands with copper metal, especially tetradentate copper(II) complexes are preferred structures in biological systems due to their many properties.[7]. The copper and cobalt complexes of Schiff bases ligands have been used in many application areas such as; epoxidation of olefins [8], alkylation, and arylation [9].

In this study, Schiff base ligands containing azo groups derived from (E)-2-hydroxy-5-((4-methoxyphenyl)diazanyl)benzaldehyde and their copper and cobalt metal complexes were synthesized. The structures of the compounds have been characterized by various spectral and analytical methods. Also, the catecholase activity of the complexes was studied for 3,5-DTBC \rightarrow 3,5-DTBQ conversion in the presence of air oxygen.

2. Material and Method

The chemicals and the reagents were purchased from Sigma, Aldrich, Merck and Fluka. The solvents were dried using established procedures and immediately distilled under nitrogen atmosphere prior to use. Waters Synapt G1 was used for HRMS analyses performed in Middle East Technical University, Instrumental Analysis Laboratory. FT-IR spectra of the synthesized compounds were collected on a Perkin Elmer Spectrum 400 spectrophotometer (4000–400 cm^{-1}) using KBr discs. Perkin Elmer Lambda 45 spectrophotometer was used for UV-Vis. spectra in the range of 200–900 nm. Varian XL-300 NMR was used for the collection of NMR spectra. CDCl_3 was used as the solvent and TMS was an internal standard.

2.1. Synthesis of azo aldehyde 1

The azo aldehydes were synthesized according to the literature [10].

2.2. General procedure for the synthesis of ligands 2-4

The 25 mL methanolic solution of an azo aldehyde (**1**) (2.00 mmol) was added to 2 mmol aniline solution in methanol (5 mL) and refluxed for 3 h. The solution was concentrated on air for two days to give ligand (**2-4**) as a colorful solid.

Ligand 2: Yield: 0.296 g (58%). Color: Dark cherry. Elemental analysis: Calcd. for $\text{C}_{20}\text{H}_{17}\text{N}_3\text{O}_3$ C, 69.15; H, 4.93; N, 12.10. Found: C, 69.14; H, 4.41; N, 12.34. FT-IR (KBr, cm^{-1}): 3425, 2920, 1614 and 1593. UV-vis (λ_{max} , nm): 406, 372, 346. (in 10^{-4} M DMF). ^1H NMR (400 MHz, DMSO) δ 14.17 (s, 1H), 9.79 (s, 1H), 9.09 (s, 1H), 8.17 (d, $J = 2.2$ Hz, 1H), 7.92 (dd, $J = 8.8, 2.4$ Hz, 1H), 7.86 (d, $J = 8.9$ Hz, 2H), 7.39 (d, $J = 8.7$ Hz, 2H), 7.14 (s, 1H), 7.12 – 7.06 (m, 2H), 6.86 (d, $J = 8.7$ Hz, 2H), 3.86 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 163.52, 161.96, 160.08, 157.75, 146.59, 145.16, 138.89, 127.45, 126.73, 124.60, 123.30, 119.77, 118.16, 116.48, 115.02, 56.03.

Ligand 3: Yield: 0.307 g (60%). Color: Dark Orange. Elemental analysis: Calcd. for $\text{C}_{20}\text{H}_{17}\text{N}_3\text{O}_2$ C, 72.49; H, 5.17; N, 12.68. Found: C, 72.45; H, 5.14; N, 12.70. FT-IR (KBr, cm^{-1}): 3434, 2959, 1615 and 1578. UV-vis (λ_{max} , nm): 411, 362, 347 (in 10^{-4} M DMF). ^1H NMR (400 MHz, CDCl_3) δ 13.82 (s, 1H), 8.76 (s, 1H), 8.03 (dd, $J = 4.5, 2.3$ Hz, 2H), 7.92 (d, $J = 8.9$ Hz, 2H), 7.48 (t, $J = 7.7$ Hz, 2H), 7.36 – 7.32 (m, 3H), 7.18 – 7.13 (m, 1H), 7.04 (d, $J = 8.9$ Hz, 2H), 3.91 (s,

3H). ^{13}C NMR (101 MHz, CDCl_3) δ 163.46, 162.20, 161.69, 147.82, 146.85, 145.58, 129.49, 127.40, 127.27, 124.42, 121.21, 118.86, 118.03, 115.21, 55.55.

Ligand 4: Yield: 0.287 g (56%). Color: Dark red. Elemental analysis: Calcd. for $\text{C}_{20}\text{H}_{17}\text{N}_3\text{O}_3$ C, 69.15; H, 4.93; N, 12.10. Found: C, 69.12; H, 4.22; N, 12.25. FT-IR (KBr, cm^{-1}): 3444, 3034, 1615 and 1573. UV-vis (λ_{max} , nm): 405, 363, 340 (in 10^{-4} M DMF). ^1H NMR (400 MHz, DMSO) δ 13.83 (s, 1H), 9.74 (s, 1H), 9.09 (s, 1H), 8.24 (d, $J = 2.2$ Hz, 1H), 7.96 (dd, $J = 8.9, 2.3$ Hz, 1H), 7.86 (d, $J = 8.9$ Hz, 1H), 7.27 (t, $J = 8.0$ Hz, 1H), 7.16 – 7.12 (m, 2H), 7.11 (d, $J = 2.0$ Hz, 2H), 6.90 (d, $J = 7.9$ Hz, 1H), 6.84 (s, 1H), 6.76 (d, $J = 8.0$ Hz, 1H), 3.86 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 163.65, 163.07, 162.00, 158.82, 149.01, 146.57, 145.20, 130.73, 128.06, 127.10, 124.63, 119.60, 118.31, 115.02, 114.89, 112.60, 108.65, 56.03.

2.3. General procedure for the synthesis of complexes 11-15

Ligands (**2-4**) (20 mmol) dissolved in 25 cm^3 absolute EtOH were mixed with 10 mmol metal salts in 10 cm^3 EtOH. The stirred mixture was refluxed for 24 h, then evaporated to 15–20 cm^3 in a vacuum and left to cool to room temperature. The products were filtered in a vacuum and washed with a small amount of MeOH and water.

Complex 7: Yield: 0.38 g (55%). m.p. 250-252 °C. Color: Dark brown. Elemental analysis: Calcd. for $\text{C}_{40}\text{H}_{32}\text{CoN}_6\text{O}_6$ C, 63.35; H, 4.39; N, 11.43. Found: C, 65.33; H, 4.38; N, 11.44. FT-IR (cm^{-1} 15, KBr): 3062 (s), 1602 (s), 1576 (s), 610 (w), 420 (w). UV-Vis (λ , nm): 235, 280, 348, 366, 545, μ_{eff} (BM):4.6.

Complex 8: Yield: 0.42 g (61%). m.p. 196-198 °C. Color: Dark red. Elemental analysis: Calcd. for $\text{C}_{40}\text{H}_{32}\text{CuN}_6\text{O}_6$ C, 63.92; H, 4.29; N, 11.18. Found: C, 63.62; H, 4.19; N, 11.97. FT-IR (cm^{-1} 20, KBr): 3057 (s), 1592 (s), 1575 (s), 663 (w), 420 (w). UV-Vis (λ , nm): 237, 279, 346, 363, 401, 639, μ_{eff} (BM):1.8.

Complex 9: Yield: 0.36 g (55%). m.p. 250-252 °C. Color: Dark red. Elemental analysis: Calcd. for $\text{C}_{40}\text{H}_{32}\text{CoN}_6\text{O}_4$ C, 66.76; H, 4.48; N, 11.68; Found: C, 66.33; H, 4.38; N, 11.44. FT-IR (cm^{-1} , KBr): 3038 (s), 1613 (s), 1585 (s), 594 (w), 418 (w). UV-Vis (λ , nm): 237, 279, 348, 366, 458, 552, μ_{eff} (BM):4.5.

Complex 10: Yield: 0.37 g (56%). m.p. >250°C, decompose. Color: Brown. Elemental analysis: Calcd. for $\text{C}_{40}\text{H}_{32}\text{CuN}_6\text{O}_4$ C, 66.33; H, 4.45; N, 11.60. Found: C, 66.62; H, 4.19; N, 11.97. FT-IR (cm^{-1} , KBr): 3041 (s), 1602 (s), 1528 (s), 599 (w), 457 (w). UV-Vis (λ , nm): 236, 275, 335, 366, 425, 642, μ_{eff} (BM):1.8.

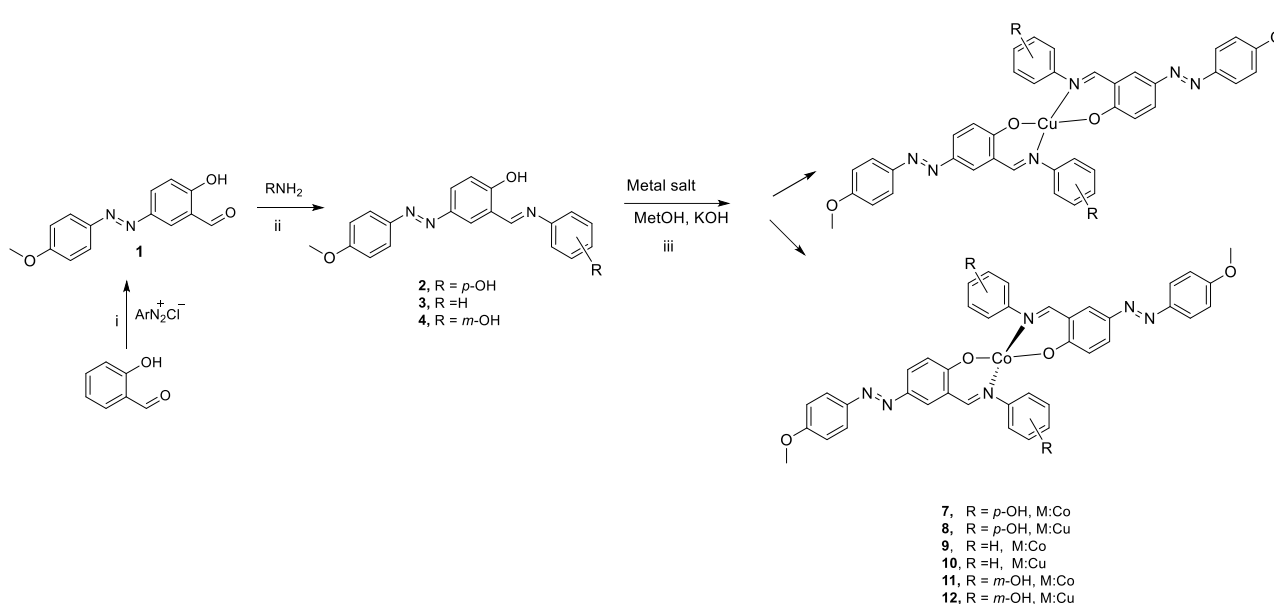
Complex 11: Yield: 0.38 g (55%). m.p. 250-252 °C. Color: Dark red. Elemental analysis: Calcd. for $\text{C}_{40}\text{H}_{32}\text{CoN}_6\text{O}_6$ C, 63.35; H, 4.39; N, 11.43. Found: C, 65.28; H, 4.21; N, 11.41. FT-IR (cm^{-1} 15, KBr): 3062 (s), 1601 (s), 1576 (s), 610 (w), 420 (w). UV-Vis (λ , nm): 235, 275, 348, 366, 541, μ_{eff} (BM):4.7.

Complex 12: Yield: 0.42 g (61%). m.p. 196-198 °C. Color: Dark red. Elemental analysis: Calcd. for $\text{C}_{40}\text{H}_{32}\text{CuN}_6\text{O}_6$ C, 63.92; H, 4.29; N, 11.18. Found: C, 63.83; H, 4.20; N, 11.87. FT-IR (cm^{-1} 20, KBr): 3058 (s), 1595 (s), 1575 (s), 663 (w), 420 (w). UV-Vis (λ , nm): 237, 280, 347, 363, 401, 629, μ_{eff} (BM):2.0.

3. Results and Discussion

The Schiff base ligands (**2-4**) have been synthesized in EtOH from synthetic azo aldehyde **1** and aniline derivatives. Also, their Cobalt and Copper (II) complexes (**7-12**) were prepared with the reaction of Schiff base ligands and transition metal salts in EtOH. All ligands are soluble in common organic solvents like as DMF, DMSO, EtOH and MeOH. Characterization of the ligands was done by FT-IR, UV-visible spectroscopies, ^1H - ^{13}C -NMR, elemental analysis, and melting point techniques. Due to paramagnetism, NMR analyses could not be done for the characterization of complexes. All the mentioned analyses were done to characterize the complexes too.

The data showed that the complexation ratio [Metal: Ligand] is 1:2 as shown in Scheme 1.



Scheme 1. Synthesis route of ligand and Co & Cu (II) complexes. Reagent and conditions: (i) NaNO₂, NaOH, H₂O, 0-5 °C; (ii) EtOH, reflux, 3 h; (iii) EtOH, reflux, 4 h.

When the ¹H-NMR spectra of the ligands are examined, it is seen that ligands (**2-4**) ¹H NMR spectra show singlets in the 14.17-13.83 ppm range can be referred to as the salicylidene phenolic proton (OH). Within ligands **2** and **4**, the signals of the OH groups originating from the amine structure were observed at 9.79 and 9.74 ppm, respectively [11]. In addition, the singlets in the 9.09-8.03 ppm range can be attributed to the proton resonance of the azomethine group (CH=N). In both ligand spectra, multiple signals corresponding to aromatic protons are seen in 8.24-6.76 ppm range [12]. The methoxy groups signals are seen as singlet signals at 3.91 for ligand **3** and -3.86 ppm for ligands **2** and **4**.

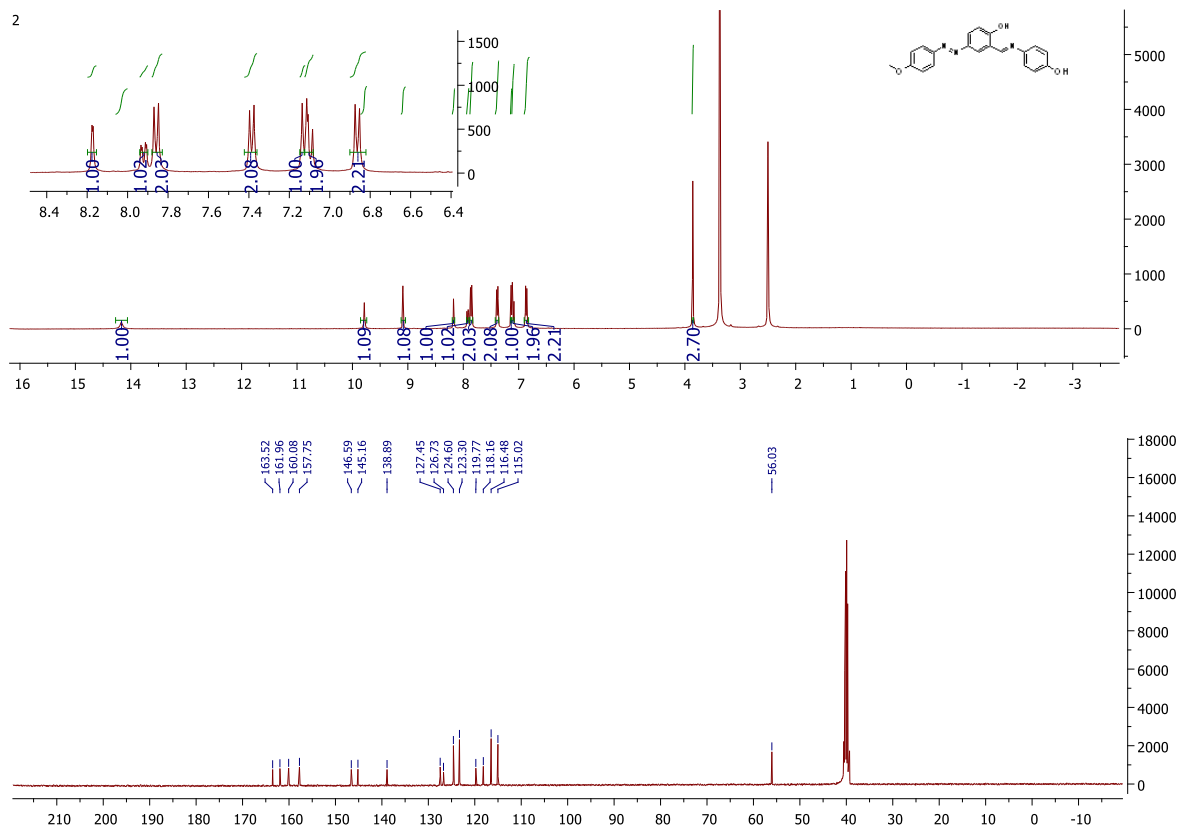


Figure 1. ¹H and ¹³C-NMR spectrum of 2

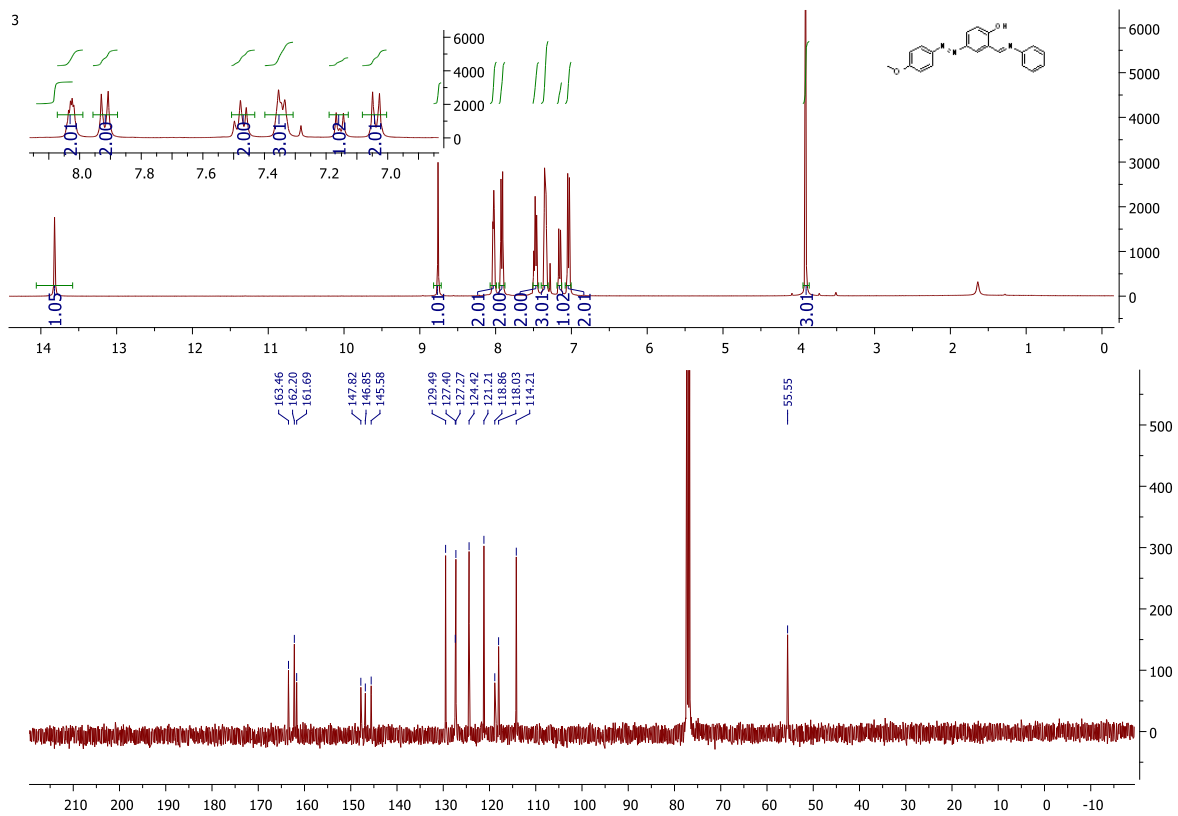


Figure 2. ¹H and ¹³C-NMR spectrum of 3

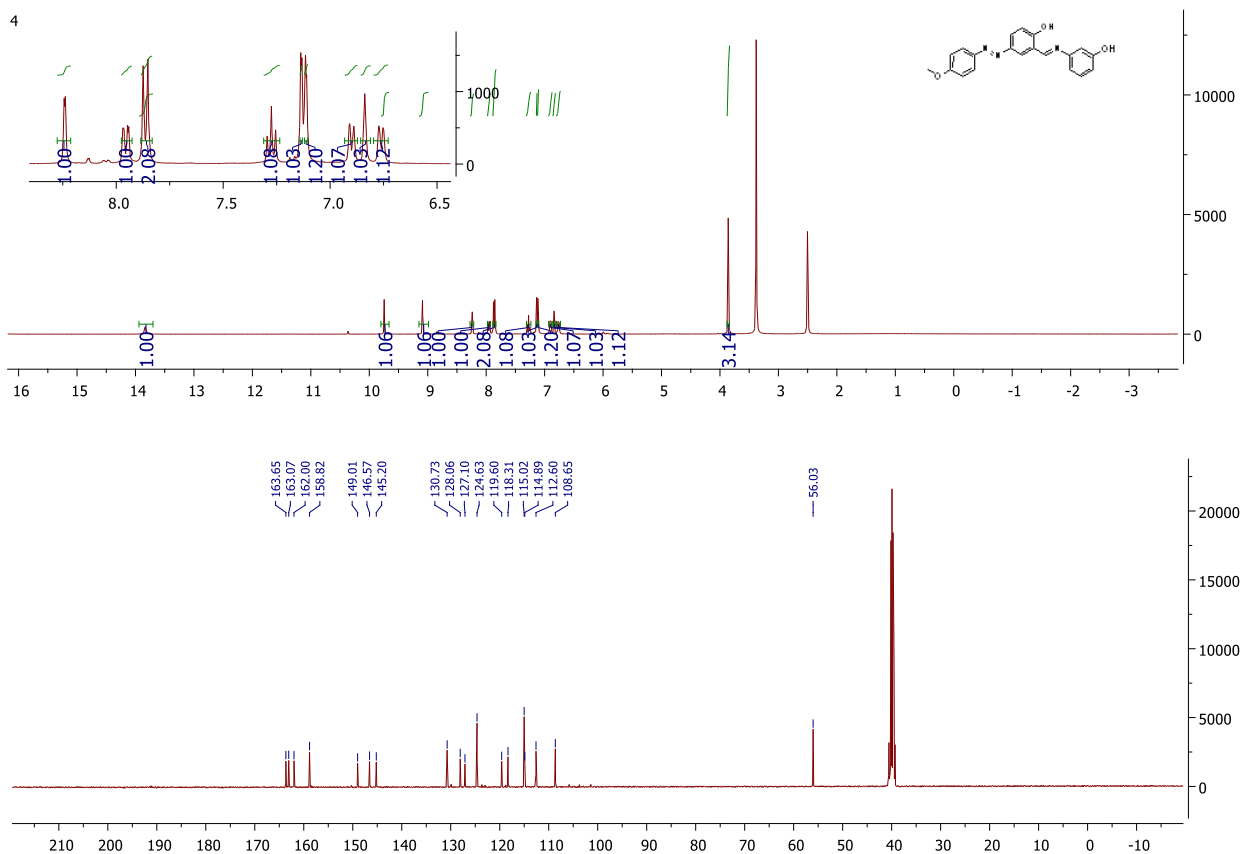


Figure 3. ^1H and ^{13}C -NMR spectrum of **4**

In the ^{13}C NMR spectra of Schiff base ligands, the carbon signal of the azomethine group was observed in the range of 163.46–114.21 ppm. [13]. The signals for the aliphatic carbons in the methoxy groups in ligands **3** and **4** were observed at 2, 55, 55 and 55.79 ppm, and the signal for the carbon in the methyl group was observed at 29.72 ppm.

The characteristic FTIR data of the azo-azomethine ligands and their complexes are listed in the experimental section. To explain the binding of Schiff base ligands to the metal in the complex structures, the FTIR spectra of the free ligands were compared with those of the transition metal complexes. In the complex spectra, the bands at 3425–3444 cm^{-1} which belong to $\nu(\text{OH})$ vibration for ligands, disappeared confirming the coordination of phenolic oxygen to the metal center. The complexes showed shifts of the bands assigned to $\nu(\text{C}=\text{N})$ stretching frequencies however, the $\nu(\text{C}=\text{N})$ stretching frequency shifted from around 1614–1615 cm^{-1} to the lower frequency of 1592–1613 cm^{-1} for the complexes. The shift in the $\nu(\text{C}=\text{N})$ may be attributed to the electron-withdrawing effects from the coordinated metal, which weakens the $(\text{C}=\text{N})$ bond and thus pushes the stretching frequency to a lower frequency [14]. The characteristic bands in the range of 1528–1593 cm^{-1} can be attributed to the $\text{N}=\text{N}$ group for the ligands and their metal complexes[15].

The electronic absorption spectral data for the compounds were obtained in 10^{-4} M DMF solutions at room temperature and data are given in the experimental section (Fig. S9-S16). The absorption bands between 235 and 642 nm are the measured bands for metal complexes at the UV-visible spectra in DMF. The shift in the absorption maxima (λ_{max}) was determined by taking the contrast between the absorption maxima of the metal complexes and ligands. The spectra of the complexes that show intense bands in the high-energy region can be assigned to the ligand-to-metal charge transition (LMCT) [16]. The Co(II) complexes **7**, **9**, and **11** show bands at 458–552 nm. This indicates tetrahedral geometry for the Co(II) complexes. Electronic spectra of the Cu(II) complexes display bands at 629 and 642 nm [17]. These values suggest square planar geometry for Cu(II) complex.

The magnetic moment values of the Cu(II) complexes are 1.8, 1.8, and 2.0 B.M., respectively. was measured. These values are close to the BM of 1.73 calculated for d^9 metal ions, which, as expected, corresponds to an unpaired electron. Here, the complex cannot be said to be square-plane or tetrahedral. However, it has been stated in the

literature that the Cu(II) complexes of Schiff bases are in a square planar structure. Likewise, the magnetic moment values of Co(II) complexes are 4.6, 4.5, and 4.7 B.M., respectively, was measured. This value is close to the BM of 3.87 calculated for d7 metal ions, which, as expected, corresponds to three unpaired electrons. This value shows that the Co(II) complex has sp^3 hybridization and is in tetrahedral geometry [18].

The enzyme catechol oxidase, which is a redox enzyme containing a pair of copper ions (connected by hydroxyl bridges) in its active site, is also known as O-diphenol oxidase. The enzyme structure could only be determined by X-ray diffraction in 1988 [19]. Catechol oxidase enzyme is commonly found in fruits, vegetables, shellfish, and the oxidation of phenols to quinones in the presence of molecular oxygen. Synthetic enzyme studies have focused on Cu(II) and Co(III) complexes due to the presence of binuclear Cu(II) in the active site of the natural enzyme [20]. For this reason, in this study, Cu(II) and Co(II) complexes' catecholase mimetic properties were investigated and 3,5-ditert-butyl catechol (3,5-DTBC) was chosen as the substrate. The catalytic performance of the complexes for the conversion of 3,5-ditert-butyl catechol (3,5-DTBC) to 3,5- di-tert-butylbenzoquinone (3,5-DTBQ) in the presence of air oxygen was investigated (Figure 4).

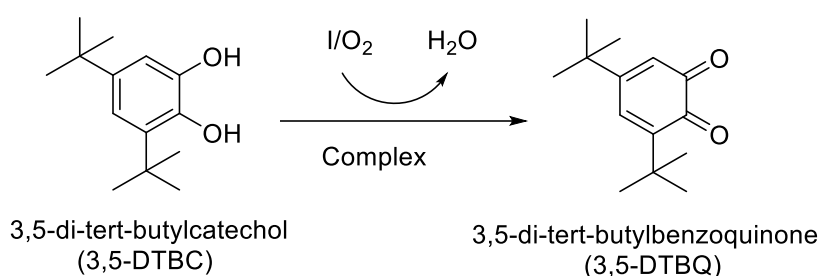


Figure 4. A schematic representation of catechol oxidation

The 3,5-DTBQ compound gives a characteristic absorption maximum at 400 nm in methanol and, this conversion can be followed by the absorbance change at 400 nm. Before performing the kinetic study, the ability of the complexes to mimic catechol oxidase enzyme was checked by reacting 1×10^{-5} M solutions (in MeOH) of the triazine-based complexes with 1×10^{-3} M (100 equivalents) of 3,5-DTBC in the presence of air. Before each experiment, 3,5-DTBC solutions were saturated with air for 30 min. Complex 12 was found to catalyze the oxidation of 3,5-DTBC to the 3,5-DTBQ in the presence of air oxygen (Figure 5).

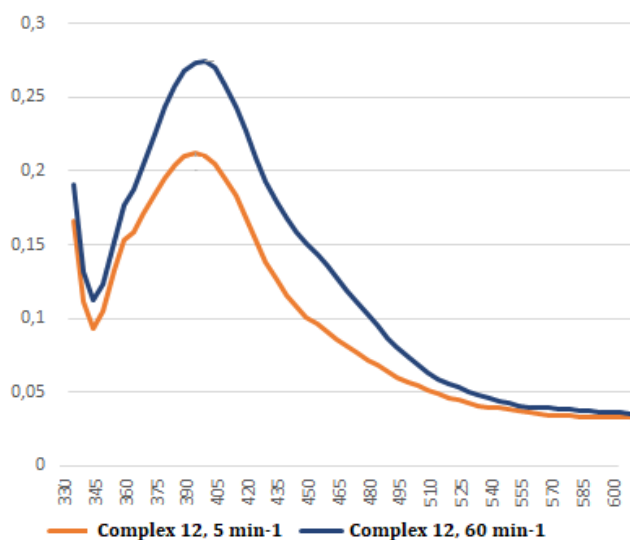


Figure 5. Increase of quinone band (3,5-DTBQ) at 400 nm after addition of 100-fold 3,5- DTBC (10^{-3} M) to complex (12) in MeOH.

In the light of the data obtained as a result of the experiments, it was determined that complex **12** showed the best catalytic efficiency. Other Cu(II) complexes (**8**, **10**) were observed to show relatively low activity. While complexes **7** and **11** showed even lower activity, it was determined that complex **9** did not show any activity.

4. Conclusion

In this study, three types of azo-azomethine ligands have been synthesized from the reaction of (E)-2-hydroxy-5-((4-methoxyphenyl)diazenyl)benzaldehyde with aniline derivatives. Structures of the synthesized ligands (**2-4**) and complexes (**7-12**) were characterized with ¹³C-NMR, ¹H-NMR, UV-Visible spectroscopy, elemental analysis and FT-IR. It was understood that metal is bound by N and O atoms in the ligands.

The catalytic activities of complexes were investigated. The catecholase enzyme-like activity of the complexes was studied for 3,5-DTBC → 3,5-DTBQ conversion in the presence of air oxygen. In the light of the data obtained as a result of the experiments, it was determined that complex **12** showed the best catalytic efficiency.

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