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SYNTHESIS OF SUBSTITUTED HETEROCYCLIC WITH THEIR COBALT(II) COMPLEXES FROM 2-AMINOTHIAZOLES AND EVALUATION OF THEIR BIOLOGICAL ACTIVITY

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ABSTRACT. In this research, acetophenone and thiourea reacted in the presence of iodine to produce 2-amino-4-phenylthiazoles (**1**, **2**). These compounds were then used in three different reactions to create substituted Schiff-bases (**3**-**5**) by further reactions with substituted benzaldehyde. To produce thiazole, they were first reacted with sodium azide (**6**). After adding maleic anhydride, they interacted with thioglycolic acid to yield oxazepine (7), and lastly, thiazolidine (**8**). The synthesised compounds (**1-8**) were confirmed to have their structures clarified by CHNS and spectroscopic methods such as infrared, ^{1}H NMR and ^{13}C NMR. After being produced (**1-4**, **6-8**), these compounds were used in 2:1 ratio reaction with $CoCl_2.6H_2O$ to generate cobalt complexes (**9-15**). These complexes' magnetic characteristics, thermal analysis (TGA), and differential thermal analysis (DTA) were investigated. Several produced compounds were also tested against the growth of four different types of bacteria.

KEY WORDS: Schiff-bases, Thiazole, Oxazepine, Thiazolidine, Cobalt complexes

INTRODUCTION

Heterocyclic compounds are regularly working as catalysts in organic reactions. For example, five-membered heterocycles present efficacy as catalysts around different transformations, raising the development of sustainable and effective synthetic methodologies. Additionally, these compounds are frequently used as ligands in coordination chemistry. Heterocyclic compound complexes with metal ions, find applications in catalysis, materials science, and the making of coordination polymers [1].

Cobalt organo complexes have gained significant interests in the field of biological activity. An exemplary instance is the utilization of cobaltocene, a cobalt organo complex comprising a cobalt atom positioned between two cyclopentadienyl anions. The potential of cobaltocene has been investigated for its antiviral properties, with a focus on combating specific strains of the herpes simplex virus (HSV) [2].

As a promising applicant for antiviral drug development, research has shown that cobaltocene able to inhibit the replication of HSV by interfering with its DNA synthesis machinery Figure 1[3, 4].

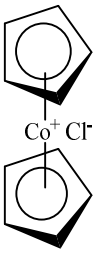

Figure 1. Bioactive cobalt catalyst.

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In this research we synthesised novel organic ligands (**1-8**) and confirmed their structures by their physical properties and FTIR, ^{1}H NMR and ^{13}C NMR spectroscopies. These ligands (**1-4**, **6-8**) were used to prepared novel complexes. These new complexes can be used as catalyst, electro optoelectronics, cancer treatment and understanding molecular interactions.

EXPERIMENTAL

Materials and methods

All chemicals and solvents were obtained from established, commercially available sources and utilized them without additional purification. We verified the IR spectra (ν_{max} in cm^{-1}) using Bruker Alpha FTIR, Germany, Tensor_27. Additionally, ^{1}H-NMR spectroscopy was performed on a Bruker instrument operating at 400 MHz, employing DMSO-d_6 as the solvent and TMS as a standard for chemical shift referencing.

*Synthesis of 2-amino thiazoles derivatives (**1, 2**)*

In a round-bottom flask equipped with a magnetic stirrer, (4 mmol, 0.66 g or 0.61 g) of 4-nitro acetophenone or 4-chloro acetophenone, respectively, was mixed with (2 mmol, 0.15 g) of thiourea and (0.4 mmol, 0.05 g) of iodide. The mixture was dissolved in (20 mL) of dimethyl sulfoxide DMSO, and the round-bottom flask was sealed with a rubber stopper. The mixture was stirred for 12 hours at a temperature of 80 °C. After the reaction was complete, the mixture was cooled to room temperature, and 20 mL of ethyl acetate was added along with a saturated solution of $NaHCO_3$ (20 mL). The organic layer was separated from the aqueous layer and washed with a saturated solution of NaCl. It was then dried using $MgSO_4$ and the solvent was removed under reduced pressure. The formed precipitate was filtered, washed with water, and recrystallized using ethanol [5].

*4-(4-Nitrophenyl) thiazol-2-amine (**1**)*. This compound result in 83% yield as an orange powder (m.p. 75 ºC), FT-IR (KBr, ν, cm^{-1}) 3396 (N-H), 3300, 3109, 1684 (C=N), 1593 (C-NO_2 asym), 1317 (C-NO_2 sym), 1106 (C-S-C asym), 1008 (C-S-C sym). ^{1}H NMR (ppm): (DMSO d_6, 400 MHz) δ: 8.21–8.02 (m, 2H), 7.76–7.73 (m, 2H), 6.80 (s, 1H), 5.45 (s, 2H). CHNS elemental analysis calculated for $C_9H_7N_3O_2S$: C, 48.68%; H, 3.19%; N, 18.99%; S, 14.49%. Found: C, 48.65%; H, 3.01%; N, 18.76%; S, 14.14%.

*4-Chlorophenyl) thiazol-2-amine (**2**)*. This compound result in 52% yield as a yellow powder, (m.p. 100 ºC), FT-IR (KBr, ν, cm^{-1}) 3388 (N-H), 33120, 3092, 1689 (C=N), 1100 (C-S-C asym), 821 (C-S-C sym), 725 (C-Cl). ^{1}H NMR (ppm): (DMSO d_6, 400 MHz) δ: 8.22–8.00 (m, 2H), 7.89–7.77 (m, 2H), 6.76 (s, 1H), 5.42 (s, 2H). CHNS elemental analysis calculated for $C_9H_7ClN_2S$: C, 51.31%; H, 3.35%; N, 13.30%; S, 15.22%. Found: C, 51.02%; H, 3.12%; N, 13.18%; S, 14.99%.

*Synthesis of Schiff-Base (**3-5**)*

A mixture of (0.03 mol) of 2-aminothiazole compounds, (**1-2**) with (0.03 mol) of 4-nitro benzaldehyde or 3-nitro benzaldehyde, was dissolved in 25 mL of absolute ethanol. The mixture was stirred for 3 hours, and a few drops of glacial acetic acid were added to it. After the reaction was completed, the solution was concentrated to half its volume, and crushed ice was added to it. The formed precipitate was filtered, washed with water, and recrystallized using ethanol [6].

*N-(4-(4-Nitrophenyl) thiazol-2-yl)-1-phenylmethanimine (**3**)*. This compound result in 77% yield as a pale orange (m.p. 250-253 ºC), FT-IR (KBr, ν, cm^{-1}) 3093 (C-H arom.), 1681 (C=N), 1643, 1593 (C-NO_2 asym), 1336 (C-NO_2 sym), 1166 (C-S-C asym), 1009 (C-S-C sym). ^{1}H NMR (ppm):

(DMSO d_6, 400 MHz) δ: 8.23 (S, 1H), 7.23-8.19(m, 9H). ^{13}C NMR (ppm): (DMSO d_6, 400 MHz) δ: 112.92 (s, 1C), 125.64, 127.46, 129.92, 133.92, 153.26, 138.65, 147.31, 160.18, 162.25. CHNS elemental analysis calculated for $C_{16}H_{11}N_3O_2S$: C, 62.12%; H, 3.58%; N, 13.58%; S, 10.36%. Found: C, 61.98%; H, 3.23%; N, 13.27%; S, 10.12%.

*1-(3-Nitrophenyl)-N-(4-(4-nitrophenyl) thiazol-2-yl)methanimine (**4**)*. This compound result in 73% yield as an orange (m.p. 130-133 ºC), FT-IR (KBr, ν, cm^{-1}) 3072, (C-H arom.) 1691 (C=N), 1608, 1542 (C-NO_2 asym), 1312 (C-NO_2 sym), 1163 (C-S-C asym), 1009 (C-S-C sym). ^{1}H NMR (ppm): (DMSO d_6) δ: 8.23 (S, 1H), 7.23-8.20 (m, 8H), 7.89 (S, 1H). CHNS elemental analysis calculated for $C_{16}H_{11}N_3O_2S$: C, 62.12%; H, 3.58%; N, 13.58%; S, 10.36%. Found: C, 61.98%; H, 3.23%; N, 13.27%; S, 10.12%.

*N-(4-(4-Chlorophenyl) thiazol-2-yl)-1-phenylmethanimine (**5**)*. This compound result in 42% yield as an yellow (m.p. 187-189 ºC), FT-IR (KBr, ν, cm^{-1}) 2961 (C-H arom.), 1682 (C=N), 1160 (C-S-C asym), 1002 (C-S-C sym), 732 (C-Cl). ^{1}H NMR (ppm): (DMSO d_6) δ: 8.23 (S, 1H), 7.23-8.20 (m, 8H), 7.89 (S, 1H). CHNS elemental analysis calculated for: $C_{16}H_{11}ClN_2S$: C, 64.32%; H, 3.71%; N, 9.38%; S, 10.73%. Found: C, 61.01%; H, 3.52%; N, 9.08%; S, 10.53%.

*Synthesis of 4-(4-nitrophenyl)-2-(5-phenyl-2,5-dihydro-1H-tetrazol-1-yl)thiazole (**6**)*. A mixture of (0.3 mmol, 0.093 g) of prepared Schiff-bases (**3**) dissolved in (15 mL) of dry tetrahydrofuran (THF), was prepared and mixed with (0.3 mmol, 0.019 g) of sodium azide (NaN_3) for 16 hours. Upon completion of the reaction, the solution was concentrated to half its volume, cooled, and then filtered. The formed precipitate was recrystallized using ethanol [7].

This compound result in 71% as a brown (m.p. 283-284 ºC), FT-IR (KBr, ν, cm^{-1}) 3409 (N-H tetrazol), 3301, 1683 (C=N), 1645, 1515 (N=N), 1136 (C-S-C asym), 1107 (C-S-C sym). ^{1}H NMR (ppm): (DMSO d_6) δ, 7.87-8.11 (m, 9H), 7.56 (S, 1H), 6.50 (S, 1H), 5.48 (S, 1H). ^{13}C NMR (ppm): (DMSO d_6, 400 MHz) δ: 112.88, 123.63, 126.69, 127.10, 129.99, 132.83, 138.12, 140.45, 144.45, 153.1. CHNS elemental analysis calculated for: $C_{16}H_{12}N6O_2S$ C, 54.54%; H, 3.43%; N, 23.85%; S, 9.10%. Found: C, 54.12%; H, 3.12%; N, 23.54%; S, 9.02%.

*Synthesis of 3-(4-(4-nitrophenyl)thiazol-2-yl)-2-phenyl-2,3-dihydro-1,3-oxazepine-4,7-dione (**7**)*. A mixture of (0.001 mol, 0.3 g) of prepared Schiff-bases (3) was combined with (0.001mol, 0.098 g) maleic anhydride dissolved in 25 mL of dry benzene for 4 hours. After the reaction was completed, the solution was concentrated to half its volume under reduced pressure. The formed precipitate was cooled, filtered, and recrystallized using ethanol [8].

This compound result in 73% yield as an orange (m.p. 230-232 ºC), FT-IR (KBr, ν, cm^{-1}) 3109 (C-H arom.), 2933 (C-H alph.), 1716 (C=O lacton), 1645 (C=O lactame), 1595 (C=N), 1504 (C-NO_2 asym), 1340 (C-NO_2 sym), 1280 (C-O-C). ^{1}H NMR (ppm): (DMSO d_6) δ 8.31-7.91 (m, 9H), 8.1 (s, 1H), 7.54-7.40 (d, 1H), 7.25 (S, 1H), 6.43-6.29 (d, 1H). CHNS elemental analysis calculated for: $C_{20}H_{13}N_3O_5S$: C, 58.96%; H, 3.22%; N, 10.31%; S, 7.87%. Found: C, 58.39%; H, 3.04%; N, 10.12%; S, 7.58%.

*Synthesis of 3-(4-(4-nitrophenyl) thiazol-2-yl)-2-phenylthiazolidin-4-one (**8**)*. Equimolar amounts of (3 mmol) of prepared Schiff bases (**3**) were mixed with (3 mmol, 0.2 mL) of thioglycolic acid in 25 mL of absolute ethanol. To this mixture, (0.01 mol, 1.36 g) of zinc chloride ($ZnCl_2$) were added. The mixture was stirred for 8 hours. After the reaction was completed, the solution was concentrated to half its volume under reduced pressure to remove the solvent. The formed precipitate was washed with a sodium bicarbonate solution and recrystallized using ethanol [9].

This compound result in 73% yield as a pale yellow (m.p. 285-286 ºC), FT-IR (KBr, ν, cm^{-1}) 3109 (C-H arom.), 2933 (C-H alph.), 1716 (C=O), 1645 (C=N), 1595 (C-NO_2 asym), 1340 (C-NO_2 sym), 1115 (C-S-C). ^{1}H NMR (ppm): (DMSO d_6) δ 7.24-8.31 (m, 8H), 7.07 (s, 1H), 6.90

(s, 1H), 3.64 (s, 2H). CHNS elemental analysis calculated for: $C_{18}H_{13}N_3O_3S_2$: C, 65.38%; H, 3.42%; N, 10.96%; S, 16.72%. Found: C, 56.12%; H, 3.32%; N, 10.72%; S, 16.59%.

Synthesis of complexes in a ratio of (2:1)(L:M)

A mixture of (0.002 mol) of the prepared ligand (**1-4**, **6-8**) was dissolved in 25 mL of absolute ethanol and add to it a solution consisting of dissolving (0.001 mol) of the metal salt ($CoCl_2.6H_2O$) (10 mL) of absolute ethanol and add (0.001 mol, 0.060 g) to the mixture of tri ethyl amine dissolved in 10 mL of absolute ethanol. The mixture was heated with stirring for two hours. The solution was cooled and the resulting precipitate was filtered and recrystallized with ethanol. All complexes were prepared in this way, using special weights for each ligand according to its molecular weight, of the prepared complexes [10].

Complex (**9**) was synthesized using ligand (**1**), yielding an orange product with a (m.p. of 283 °C). The FT-IR spectrum (KBr, ν, cm^{-1}) displayed peaks at 3554 (N-H), 3410, 1646 (C=N), 1595 (C-NO_2 asym), 1333 (C-NO_2 sym), 1124 (C-S-C asym), 1108 (C-S-C sym), 459 (Co-N) and 422 (Co-N). CHNS elemental analysis yielded the following calculated and found percentages for $C_{18}H_{14}N_6O_4S_2Co$: C, 37.74%; H, 2.44%; N, 14.67%; S, 11.18%; Co, 10.30%. Found: C, 37.31%; H, 2.65%; N, 14.12%; S, 10.90%; Co, 9.81%.

Complex (**10**) was prepared from ligand (**2**) and result in 52% yield as an brown (m.p. 250-253 ºC), FT-IR (KBr, ν, cm^{-1}) 3345 (N-H), 3210, 1653 (C=N), 1542 (C-NO_2 asym), 713, 435 (Co-N) and 413 (Co-N). CHNS elemental analysis calculated for $C_{18}H_{14}C_{l2}N_4S_2Co$: C, 37.71%; H, 2.54%; N, 10.61%; S, 11.70%; Co, 10.30%. Found: C, 38.78%; H, 2.38%; N, 10.12%; S, 10.91%; Co, 10.13%.

Complex (**11**) was prepared from ligand (**3**) and result in 66% yield as a dark green (m.p. 180-182 ºC), FT-IR (KBr, ν, cm^{-1}) 3141 (C-H arom.), 2933 (C-H alph.), 1643 (C=N), 1595, 1517 (C-NO_2 asym), 1407 (C-NO_2 sym), 1161 (C-S-C asym), 1103, (C-S-C sym) 462 (Co-N) and 415 (Co-N). CHNS elemental analysis calculated for $C_{32}H_{22}N_6O_4S_2Co$: C, 51.30%; H, 2.39%; N, 11.22%; S, 8.55%; Co, 7.88%. Found: C, 51.01%; H, 2.27%; N, 10.96%; S, 8.13%; Co, 7.31%.

Complex (**12**) was prepared from ligand (**4**) and result in 47% yield as a dark orange (m.p. 289d ºC), FT-IR (KBr, ν, cm^{-1}) 3072 (C-H arom.), 1652 (C=N), 1595, 1532 (C-NO_2 asym), 1320 (C-NO_2 sym), 1142 (C-S-C asym), 1010 (C-S-C sym), 425 (Co-N) and 414 (Co-N). CHNS elemental analysis calculated for$C_{32}H_{20}N_8O_8S_2Co$: C, 45.79%; H, 2.54%; N, 10.61%; S, 11.61%; Co, 7.88%. Found: C, 44.53%; H, 2.38%; N, 10.91%; S, 10.91%; Co, 10.13%.

Complex (**13**) was prepared from ligand (**6**) and result in 44% yield as an orange (m.p. 290d ºC), FT-IR (KBr, ν, cm^{-1}) 3372 (N-H), 3210, 1658 (C=N), 1540 (C-NO_2 asym), 1136 (C-NO_2 sym), 1107 (C-S-C), 583 (Co-N), 479 and 438 (Co-N). CHNS elemental analysis calculated for $C_{32}H_{24}N_{12}O_4S_2Co$: C, 46.01%; H, 2.87%; N, 20.13%; S, 7.66%; Co, 7.07%. Found: C, 45.78%; H, 2.43%; N, 19.90%; S, 7.35%; Co, 6.85%.

Complex (**14**) was prepared from ligand No. 7 and result in 39% as an orange (m.p. 283d ºC), FT-IR (KBr, ν, cm^{-1}) 3010 (C-H arom.), 2920 (C-H alph.), 1710, (C=O lacton), 1632 (C=O lactame), 1540 (C-NO_2 asym), 1340 (C-NO_2 sym), 1110 (C-S-C), 583 (Co-O), 479 (Co-N). CHNS elemental analysis calculated for $C_{40}H_{26}N_6O_{10}S_2Co$: C, 50.81%; H, 2.75%; N, 8.89%; S, 6.77%; Co, 6.24%. Found: C, 50.48%; H, 2.53%; N, 8.62%; S, 6.45%; Co, 5.92%.

Complex (**15**) was prepared from ligand (**8**) and result in 43% yield as an orange (m.p. 250-253 ºC), FT-IR (KBr, ν, cm^{-1}) 3040 (C-H arom.), 2920 (C-H alph.), 1710 (C=O), 1659, 1632 (C=N), 1592 (C-NO_2 asym), 1342 (C-NO_2 sym), 1120 (C-S-C asym), 1003 (C-S-C sym), 460 (Co-O), 412 (Co-N). CHNS elemental analysis calculated for $C_{36}H_{26}Cl_2N_4O_2S_4Co$: C, 49.33%; H, 2.96%; N, 6.39%; S, 14.61%; Co, 6.73%. Found: C, 49.05%; H, 2.73%; N, 6.02%; S, 14.25%; Co, 6.52%.

Biological study

The effect of several prepared compounds on four types of bacteria, both Gram-negative and Gram-positive, has been studied. These bacteria are *Escherichia Coli*, *Staphylococcus aureus*, *Klebsiella pneumonia* and *Salmonella typhi.* The Gram-negative and Gram-positive bacteria were obtained from the laboratories of the Department of Life Sciences, College of Pure Science, University of Mosul.

Inhibition activity test

The Levne method [11], which is based on the Vandepitte method [12], was followed. Nutrient saline medium was injected with individual colonies of the mentioned bacteria separately. The bacteria were then incubated at a temperature of 37 ºC for 18-24 hours. Subsequently, a series of dilutions were made with normal saline solution to obtain a concentration equivalent to 10^8 cells/cm^3, compared to tube number 1 of Macferland standard tubes.

To studying the antibacterial effect of the prepared compounds, filter paper discs with a diameter of 6 mm were saturated with specific concentrations of the compounds dissolved in DMSO, which were selected. Then, the discs were placed on the surface of agar plates using sterilized forceps and incubated at a temperature of 37 ºC for 18-24 hours. Afterward, the inhibition zone diameter was measured and compared to some plates with standard antibiotics (Amoxicillin and Ciprofloxacin) as control samples.

RESULTS AND DISCUSSION

*Synthesis of thiazole compounds and their cobalt complexes (**1**, **2** and **9**, **10**)*

Thiazole compounds (**1**, **2**), specifically 2-amino-4-phenylthiazoles, were prepared by reacting acetophenone or 3-nitro benzaldehyde with thiourea in the presence of dimethyl sulfoxide. Confirmation of resulted compounds proved by their distinctive peaks in IR were observed at the frequency (3300- 3396) cm^{-1} and (1645, 1684) cm^{-1}, they were attributed to the stretching vibration of the two bands belonging to NH_2 and (C=N) functional groups, respectively. In addition, the (^{1}H NMR) spectrum of compounds revealed distinct peaks at positions (5.45-5.42 ppm), attributed to the (NH_2) proton groups, and another peak at (6.80-6.76 ppm) corresponding to the carbon proton of the thiazole ring adjacent to the sulphur. Additionally, there were peaks in the range of (8.22-7.73 ppm) associated with the protons of the aromatic ring [13]. Furthermore, upon interaction with cobalt metal ions (9-10) a shift in frequency towards a longer wavelength was observed [14] (Figure 2). The CHNS technique was used to diagnose the prepared ligands and some of their solid complexes, and when comparing the values obtained practically with those calculated theoretically, the great convergence between them was clearly revealed, which confirms the correct proportions of the elements in the complexes.

*Schiff base compounds and their cobalt complexes (**3-5**, **11-12**)*

Schiff base compounds were prepared through the condensation of 2-amino-4-phenylthiazole compounds with benzaldehyde and its derivatives in absolute ethanol. These compounds were characterized using infrared spectroscopy, which provided distinctive bands at the frequency range [15] of (1643-1691) cm^{-1} which belonged to the (C=N) functional groups, and after coordination with cobalt metal (11-12), a shift in the band towards a shorter wavelength was observed by (2-8 cm^{-1}) approximately [16]. Similarly, the formula of these compounds was confirmed using ^{1}H NMR spectroscopy, which showed a signal around (8.82 ppm) attributed to the 1H proton of imine carbon. Multiple medium-intensity signals were observed at (7.23-8.19

ppm), corresponding to the aromatic protons of the rings (Figure 2). Additionally, ^{13}C NMR of compound (**3**) revealing a signal at (112.92 ppm) assigned to the carbon atom adjacent to the sulfur in the thiazole ring. Signals were also observed at the following positions: (125.64, 127.46, 129.97, 133.92, 153.26, 138.65 ppm), corresponding to the carbon atoms in the aromatic rings. Another signal appeared at (147.31 ppm) assigned to the carbon atom adjacent to nitrogen in the thiazole ring linked to the phenyl group (Figure 3). Furthermore, the elemental analysis CHNS percentage values support the structures of these compounds [17-18].

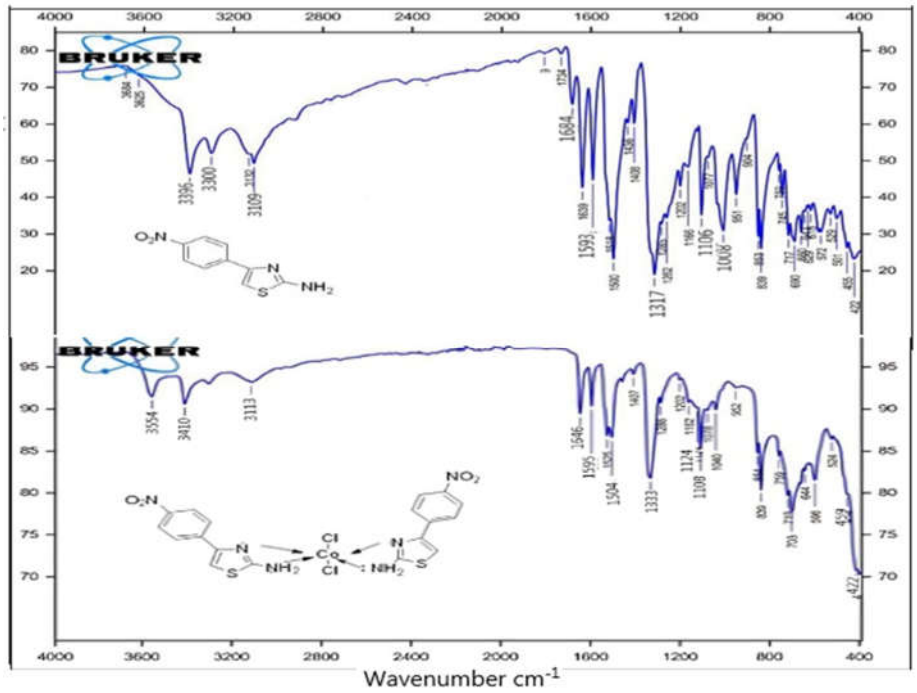


Figure 2. IR spectra of ligand (**1**) and its cobalt complex (**9**).

*Tetrazole (**6**, **13**)*

In the next step, the derivatives of tetrazole (**6**) were prepared from the equimolar reaction of previously prepared Schiff base (**3**) with excess sodium azide in the presence of dry tetrahydrofuran (THF) as a solvent. The reaction occurs through the addition of the (**1**, **3**) dipolar type, and the following (Scheme 1) illustrates the transition state for the addition of excess sodium azide [19].

This compound was characterized using infrared (IR) spectroscopy, where bands observed in the range of (1515) cm^{-1} corresponding to the azo group (N=N), and a distinct band at the location (1350) cm^{-1} due to the stretching of the (C=N) group. After coordination with the metal ion (**13**), the frequency was shifted towards a longer wavelength [20]. Additionally, distinctive bands were observed in the range of (3409) cm^{-1}, attributed to the secondary amine group (NH). After coordination, the frequencies shifted towards longer wavelengths, indicating coordination with the metal ion [21].

The (^{1}H-NMR), of compound (**6**) revealing a singlet signal at (5.48 ppm), attributed to the (1H) proton of the carbon atom in the tetrazole ring linked to the phenyl ring. Another singlet signal at (6.50 ppm) was observed, assigned to the (1H) proton of the carbon atom linked to the sulphur atom in the thiazole ring. Additionally, singlet signal at (7.56 ppm) corresponded to the (1H) proton of the NH group in the tetrazole ring. Multiple signals in the range of (7.87-8.11 ppm) were observed, attributed to the (9H) protons of the two aromatic rings.

The (^{13}C-NMR) of compound (**6**) exhibited a peak at (112.88 ppm), corresponding to the carbon atom adjacent to sulphur in the thiazole ring. Several peaks were observed at the following positions: (123.63, 126.69, 127.10, 129.99, 132.83, 138.12, 140.45 ppm), attributed to the carbon atoms in the aromatic rings. Additionally, a peak at (144.12 ppm) was assigned to the carbon atom in the thiazole ring linked to the phenyl group, and another peak at (148.80 ppm) was associated with the carbon atom in the phenyl ring linked to the nitro group (Figure 4). Furthermore, a peak at (153.17 ppm) corresponded to the carbon atom in the thiazole group linked to the nitrogen atom of the tetrazole ring [22]. Furthermore, the element analysis CHNS percentage values support the structures of this compound.

*Compounds 3,1-oxazepine (7, **14**)*

This compound was prepared through a cyclization reaction, which involved the addition of prepared Schiff bases to maleic anhydride. The reaction proceeds through a nucleophilic attack mechanism of the electron pair of Schiff base nitrogen atom to the carbonyl group of maleic anhydrides, resulting in an intermediate compound with a double charge. This intermediate then undergoes ring formation to produce the oxazepine ring after dehydrated [23].

The infrared (IR) spectra of these compounds exhibited characteristic bands within the range of (1716 cm^{-1}) corresponding to the carbonyl group (C=O) of the lactone, and bands within the range of (1645 cm^{-1}) corresponding to the carbonyl group (C=O) of the lactam. These frequencies shifted towards longer wavelengths after dissociation from the metal ion (**14**) indicating the occurrence of dissociation. Additionally, distinctive bands appeared at frequencies of (1201-1105 cm^{-1}), attributed to both symmetric and asymmetric (C-O-C) nitro group [24].

In the nuclear magnetic resonance spectrum (^{1}H-NMR) of compound (**7**), gave two doublet signals at (7.40-7.54 ppm) and (6.29-6.43 ppm), corresponding to the (2H) protons of the methylene group (CH=CH) in the oxazepine ring. Another signal was observed in the range of (7.25 ppm), attributed to the (1H) proton of the thiazole ring. While the aromatic rings gave multiple signals between (8.2-7.8) [25]. Furthermore, the element analysis CHNS percentage values support the structures of this compound.

*Preparation of thiazolidine-4-one (**8**, **15**)*

This compound was prepared by reaction of Schiff base, previously prepared (**3**), with thioglycolic acid. The reaction involves the electron pair of the sulphur atom in thioglycolic acid attack the carbon atom of the imine group of the Schiff base. Subsequently, the ring formed after the dehydration of water molecule [26].

Thiazolidine (**8**) was characterized using infrared (IR) spectroscopy, which revealed distinctive bands at frequencies ranging from (1645 cm^{-1}) corresponding to the carbonyl group (C=O) of the lactam ring. these frequencies shifted towards shorter wavelengths, indicating coordination with the metal ion [27], as well as distinctive bands at frequencies at (1595 cm^{-1}), attributed to the C=N Which witnessed a clear decrease in frequency towards the lower frequency, which indicates the participation of the nitrogen atom (C=N) and the oxygen (C=O) group in the coordination. This was confirmed by marking the bands belonging to the ν (M-N) and ν (M-O) connections in (A15), which appeared at (420-531 cm^{-1}). In addition, marking the bands belonging to the ν (M-Cl) bond of the prepared complex at about (312 cm^{-1}). It is clear from this that the

binding of the ligand with the metal ion Co in a chelating form to a stable hexagonal ring is achieved through the nitrogen of the (C=N) group and the oxygen in the (C=O) group [26].

Compound **8** was also characterized using proton nuclear magnetic resonance spectroscopy (^{1}H-NMR). It exhibited a single signal at (3.64 ppm), corresponding to methylene protons adjacent to the carbonyl group in the thiazolidine ring. Additionally, a singlet signal was observed at (6.90 ppm), attributed to the (1H) proton of the carbon atom in the thiazolidine ring linked to the phenyl group. Furthermore, multiple signals in the range of (7.24-8.31 ppm) were observed, corresponding to the (8H) protons of the two aromatic rings [28-29] (Scheme 2 and Figure 5).

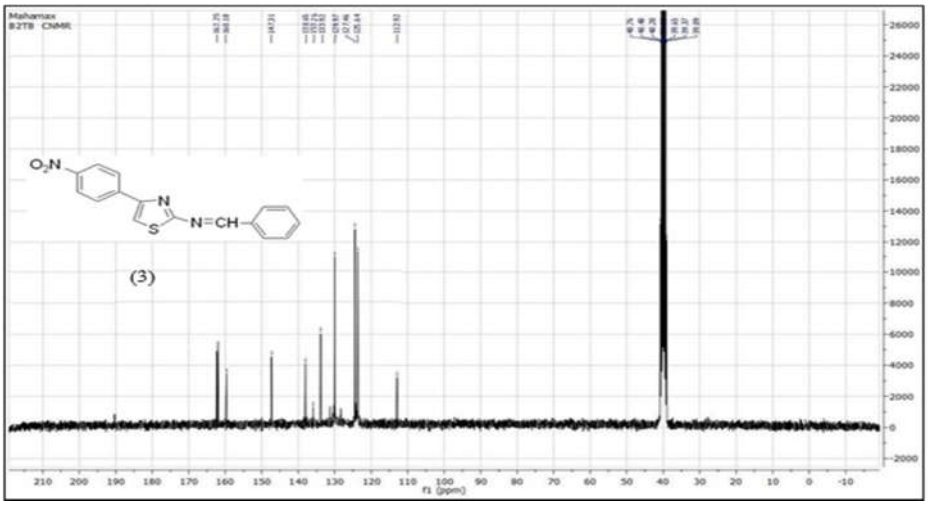


Figure 3. ^{13}C NMR spectrum of (**3**).

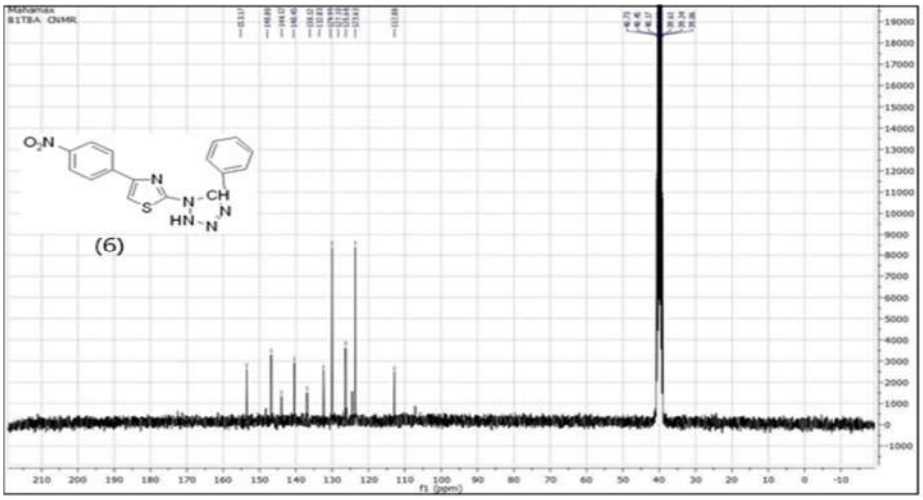
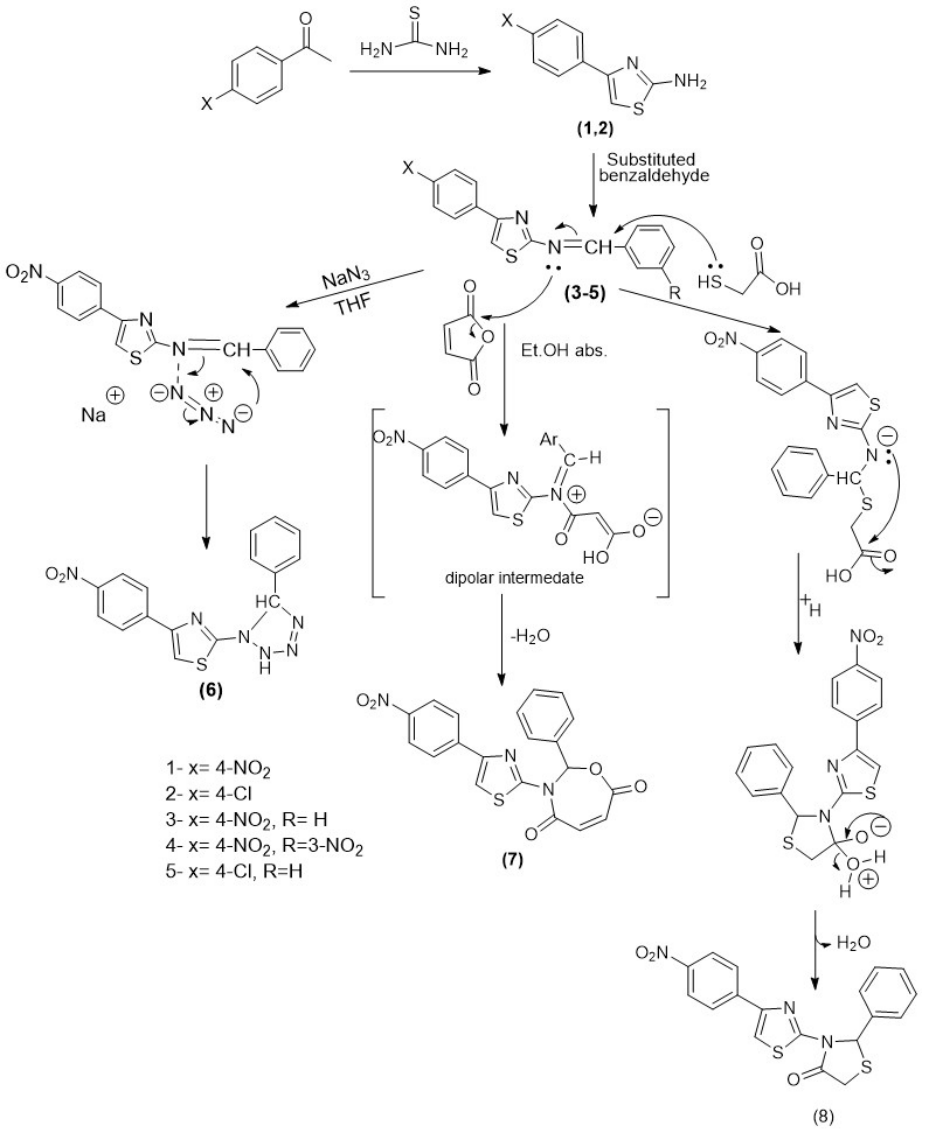


Figure 4. ^{13}C NMR spectrum of (**6**).



Scheme 1. Synthesis of (**1-8**).

Magnetic measurements and electronic spectra

The prepared cobalt(II) complexes with a cobalt(II) (d^7) electronic configuration having the electron arrangement $t2g^5$ eg^2, exhibited magnetic moments ranging from (4.28-5.60) Bohr magnetons (B.M.), which correspond to the presence of three unpaired electrons in the (d^7) system (Table 1). The highest observed magnetic moment value, which exceeds the theoretically

calculated value, is attributed to the orbital contribution. This is consistent with the magnetic moment values for hexacoordinate cobalt(II) complexes with high-spin octahedral geometry [30].

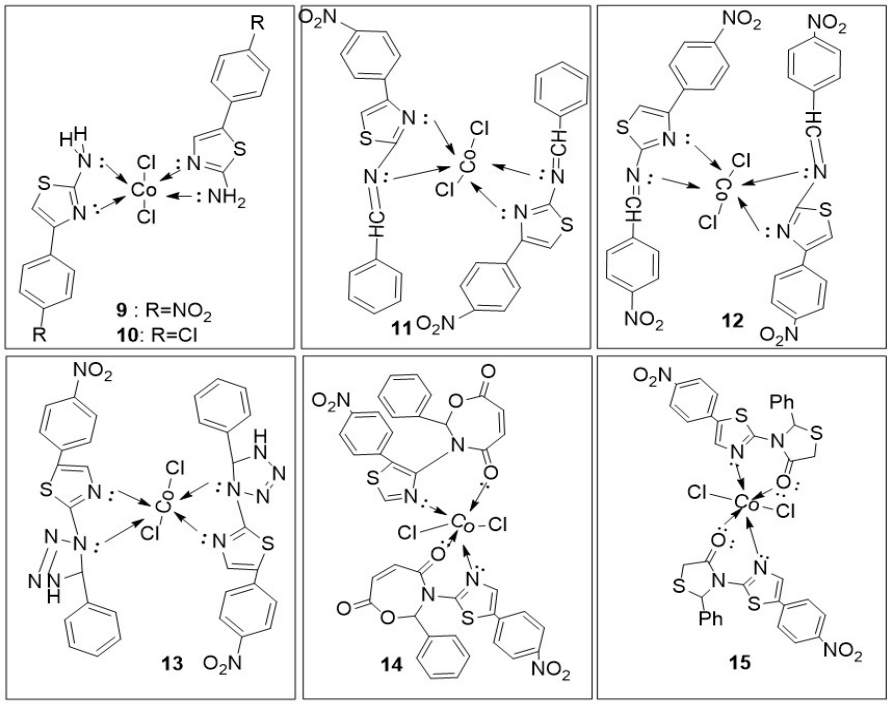


Figure 5. Complex (**9-15**).

The electronic spectra of the cobalt complexes shown in the table below indicate that complexes (A9-A15) exhibit three bands. The first band, ν_1, falls in the range (10988-12345) cm^{-1}, the second band, 2ν, falls in the range (18456-19247) cm^{-1}, and the third band, ν3, falls in the range (22819-24789) cm^{-1}. The appearance of bands ν_1, ν_2, and ν_3 confirms that these allowed transitions are attributed to the cobalt (II) complexes with octahedral geometry [31] (Figure 6A).

Table 1. Electronic transitions and magnetic properties of cobalt(II) complexes.

Complexes No.	$^4T_1g(F) \rightarrow {}^4T_2g(F)$ ν_1	$^4T_1g(F) \rightarrow {}^4A_2g(F)$ $\nu_{2\rightarrow}$	$^4T_1g(F) \rightarrow {}^4T_1g(P)$ ν_3	C.T. (cm^{-1})	μeff B.M.	Structure
9	12345	19230	23419	35087	4.28	oh
10	11988	19198	23240	35480	4.96	oh
11	12360	19047	24570	35087	4.47	oh
12	12171	18456	24789	34904	5.03	oh
13	11988	19198	23240	35480	5.60	oh
14	10985	19340	24119	34891	4.56	oh
15	12341	18980	23810	34775	4.73	oh

In our study, the molar electrical conductivity of complex solutions was measured at a concentration of (10^{-3} M) using dimethyl sulfoxide as the solvent. The results showed low values for the electrical conductivity of the complex solutions in a neutral medium at concentrations ranging from (0-20), indicating that they are non-conductive and do not produce ions in the solution. Since the complexes contain negatively charged organic ions (Cl), it was assumed that these ions are located within the coordination sphere and directly coordinated to the metal ion with coordination bonds, making them non-dissociable in the solution. This aligns with previously published research. A decrease in the conductivity values between the ranges (0-20). This percentage is in the solvent used DMSO, which means that the solution is not electrically conductive, the solution does not contain ions, and the shape is octahedral [32].

Differential and gravimetric thermal analysis of complexes

From the results of the gravimetric thermal analysis (TGA) for complex (**11**), we observe three main changes. The first change begins within the range of (280-330 ºC), which can be attributed to the loss of two chlorine atoms within this range, with a proportion of approximately 21%. The second loss occurs within the temperature range (330-420 ºC) and is associated with the beginning of ligand decomposition, with a weight loss of approximately 46%. The third decomposition, which falls within the range (420-570 ºC), is due to the complete ligand decomposition, resulting in a total weight loss of around 61% (Figure 6B). It's worth noting that these changes match and align with differential thermal analysis (DTA) (Figure 6C).

Regarding complex (**13**), we notice three main changes as follows: the first begins at (280 ºC) and ends at (315 ºC) and is attributed to the loss of two chlorine atoms within the complex, with a weight loss of about 20%. The second loss occurs within the temperature range (315-355 ºC) and can be linked to the onset of ligand decomposition, with a weight loss of approximately 50%. The change within the temperature range (355-450 ºC) is attributed to the completion of ligand decomposition (Figure 6D). There is clear consistency and alignment between both gravimetric thermal analysis and differential thermal analysis (DTA) (Figure 6E).

Through the thermal analysis of complex (**15**), we note four major thermal changes. The first change can be attributed to the loss of moisture present within the complex, which was about 4%, and it concluded at (150 ºC). The second change falls within the temperature range (250-320 ºC) and can be linked to the loss of two chlorine atoms, both within the complex. The third change is attributed to the beginning of ligand decomposition, which occurred within the temperature range (320-450 ºC). The complete ligand decomposition takes place at (550 ºC), clearly seen within the temperature range (450-550 ºC) (Figure 6F). We observe alignment and consistency between both gravimetric thermal analysis (TGA) and differential thermal analysis (DTA) [33, 34] (Figure 6G).

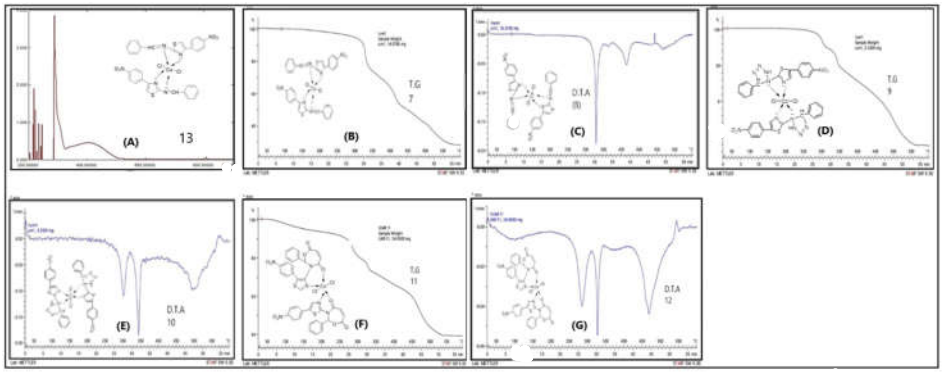


Figure 6. TGA and DTA curves.

Biological activity

The biological impact of several prepared compounds (**1**, **6**, **7**, **8**, **9**, **13**, **14**, **15**) was studied against four types of bacteria, both Gram-positive and Gram-negative: *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumonia*, and *Salmonella typhi* and was compared with Ampicillin as standard antibiotic. These bacteria were selected due to their significance in the medical field, as they are responsible for various diseases and exhibit varying levels of resistance to antibiotics and different drugs. The inhibitory results, as shown in the table, indicate that some of the prepared compounds demonstrated the ability to inhibit the growth of the tested bacteria. The inhibitory activity table reveals that (**6** and **9**) exhibited high effectiveness against the tested bacteria. Table 2 shows the inhibition zones of tested compounds [35].

Table 2. Biological properties of tested compounds.

Comp.* No.	*Staphylococcus aureus* 10 (mg/mL) **ZI mm	*Eschershia coli* 10 (mg/mL) ZI mm	*Klebsiella pneumonia* 10 (mg/mL) ZI mm	*Salmonella typhi* 10 (mg/mL) ZI mm
1	2	1	15	3
6	30	24	13	23
7	8	3	9	1
8	13	1	15	9
9	20	17	17	18
13	8	1	3	2
14	11	7	1	7
15	10	10	9	6
Ampicillin	28	26	20	22

*Inhibition levels are categorized as follows: levels between 1 to 6 mm are classified as low inhibition, those ranging from 6 to 12 mm indicate moderate inhibition, and levels exceeding 12 mm are indicative of high impact and inhibition.** ZI inhibition zone.

CONCLUSION

In this research we have successfully synthesised substituted five membered heterocyclic compounds. These ligands compounds converted to cobalt complexes. From the various physical and spectroscopic studies mentioned earlier, the following conclusions can be drawn. Firstly, the ligands prepared for cobalt chloride complexes exhibit a bidentate ligand behaviour. They coordinate through the nitrogen atom in the thiazole ring and the nitrogen atom in the amino group attached to the ring. As for the Schiff base ligands, they coordinate with cobalt in a bidentate manner through the nitrogen atom in the isothiocyanate group and the nitrogen atom in the thiazole ring. The thiosemicarbazone ligand also coordinates with the metal in the tetradentate form through the nitrogen atom in the tetrazole ring and the sulphur atom in the thiazole ring. Coordination in the oxazepine ligand occurs through the oxygen atom in the carbonyl group and the nitrogen atom in the thiazole ring. Regarding the thiazolidine ligand, coordination takes place in a bidentate manner through the oxygen atom in the carbonyl group in the thiazolidine ring and the sulphur atom in the thiazole ring. Secondly, from the results of magnetic measurements, and spectroscopic studies conducted on the prepared complexes, it can be inferred that they exhibit octahedral geometries. This is attributed to the coordination of the two chlorine atoms with cobalt. These conclusions provided insights into the coordination behaviour and structures of the studied complexes. The biological study of some compounds revealed that number of compounds have excellent inhibition against the bacteria, while others showed moderate to weak activity.

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