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Synthesis of New Ligands Containing Azomethine Group and Investigation of Antioxidant, Antiurease Activities

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Highlights

- As standard antioxidant, Trolox (6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid) was used.
- The reducing power activities of the compounds were compared with BHT.
- Values were the means of three replicates ± Standard deviation .

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Abstract

A series of Schiff base ligands containing 1,2,4-triazole ring were obtained by the addition of aldehydes to the amino compound under mild conditions in 80–82% yields. A reduction of these ligands with sodium borohydride resulted in Schiff base reduction products. New ligands were investigated for their antioxidant activities such as DPPH (2,2-diphenyl-1-picrylhydrazyl), ABTS (2,2'-azino-bis (3-ethylbenzo-thizoline-6-sulphonic acid) diammonium salt) radical scavenging and reducing power. ^{1}H and ^{13}C-NMR spectra (δ, ppm) were observed on a Varian Mercury 200 MHz spectrophotometer as standard substance using tetramethylsilane Match constants (J values) were given as Hertz. NMR coefficients are truncated as follows: s=singlet, d=dublet, t=triplet, m=multiplet signal. Combustion analysis was performed on a Carlo Erba 1106 elemental analyzer. All the compounds gave C, H, and N analysis results within ±0.6 % of the theoretical values. The IR spectra (υ, cm^{-1}) were viewed with a Perkin-Elmer 1600 FTIR spectrometer in KBr pellets.

1. INTRODUCTION

Schiff bases are used for obtaining thermotropic liquid crystallized polymers as salat ligands in coordination chemistry, as a dioxygen carrier for metal treatment as radiopharmacologies, modeling systems for biological macromolecules and in catalytic reactions [1-3]. Also, Schiff bases containing phenyl in aldehyde or amine structures in acidic ambiance are corrosion inhibiting for aluminum [4-6]. The geometrical structures of Schiff bases can give us an idea about the complexity of the complexes. The complexes obtained with Schiff bases having a more rigid structure are more likely to form a polymeric structure [7].

It has been reported that structurally modified derivatives of Schiff bases can be used in the pharmaceutical industry as a bioactive substance in drugs with metal coordinated complexes. Bonding with metals thanks to nitrogen and sulfur donor atoms due to its antitumor, antibacterial, antimicrobial and antifungal properties and their effects on the reproductive system of the thiosemicarbazones potentially present in the presence of nitrogen and sulfur donor atoms, the heterocyclic complexes obtained by B (III), Pd (II), and Pt (II). The researches on these issues are widely included in the literature [8-11].

Studies on Schiff bases that can reduce the effects of radiation have been made. Researchers have found that azobenzene Schiff bases can absorb UV radiation with cis-trans change; thus, they suggested that the harmful effect of radiation could be transformed [12]. Surgical procedures and chemotherapy drugs are currently used in the treatment of cancer cells. These drugs have many side effects as well as healing effects.

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Studies on new metal-based anticancer drugs to reduce these side effects of drugs continue rapidly. Also, it has been observed that all polymer-metal complexes have high thermal stability [13, 14].

Oxidative agents play a significant role in plays an important role in various diseases, such as carcinogenesis, atherosclerosis, diabetes, nefritisis, cardiovascular diseases and neurodegenerative diseases [15-17]. For these reason, new synthetic antioxidants are requested from exterior sources [18]. The urease (urea amidohydrolase EC 3.5.1.5) is a nickel-dependent enzyme which catalyzes the hydrolysis of urea to carbon dioxide and ammonia. Ureases are widely found in various plants, algae, fungi and bacteria [19, 20]. In human, excess urease activity can be harmful to health like kidney stones, peptic and duodenal ulcers, urinary catheter encrustation, hepatic coma, gastric cancers and pyelonephritis [21]. Urease is well known for the pathologies caused by Gram (-) bacterium Helicobacter pylori which is play a crucial role in the pathogenesis of especially ulcer and cancer (gastric and peptic) [22]. In the past decades, various urease inhibitors have been studied such as phosphorodiamidates, boric acid, humic acid, citric acid, hydroxamic acid etc. [23, 24]. As a result, in this research urease inhibitors with good activity are expected.

Keeping in view the importance of Triazol, Shiff's bases, and reduction products our aimed is to the develop hybrid molecules through the combination of different pharmacophores in one frame to utilize as ligands and to study the ligands and their metal complexes from a structural point of view. Metal chelates of Schiff bases hold exciting possibilities for the future concerning their wide applications viz. in designing new catalytic systems, in formulating new synthetic route, in developing new analytical reagents and in metal-based antimicrobial agents etc., In addition, the synthesis of a compound can be used in a selective extraction of the metal is of great importance for the environment and the metal industry.

In current research, synthesized new ligands containing Azomethine group with high efficiency. Antioxidant and antiurease activities of new ligands were determined by in vitro assay and compared to the activity of standard compounds.

2. EXPERIMENTAL

2.1. General

All synthesized compounds were sensitive to air humidity and oxygen, so all experiments were carried out in an inert atmosphere and Schlenk technique was used in the reactions. Glass materials used in reactions before use, a vacuum was applied and heated to remove the moisture and oxygen contained and then filled with argon gas. Ethyl p-methylbenzimidate hydrochloride 1 was synthesized benefiting a published method [25]. Antioxidant activities of compounds were measured spectrophotometrically (UV-1240, Shimadzu, Japan).

2.2. *Ethyl N'-Furan-2-Carbonyl-p-methylbenzohydrazonate (2)*

To the solution of ethyl p-methyl benzimidate hydrochloride 1 (0.01 mol) in dry ethanol and the solution of furan-2-carboxylic acid hydrazide (0.01mol) in dry ethanol were mixtured and stirred at 0 °C for 6 h. Then, ammonium chloride was separated by filtration. Finally a white solid matter was obtained, purified by ethylacetate to determined compound 2. "Yield, 1.74 g (64.00 %)"; " white powder, mp 162-163 °C (EtOH)"; IR (cm^{-1}): [699-771, 851 (mono, 1, 4 di substitute arom. ring); 1616 (ν C=N); 1674 (ν C=O); 3316 (ν NH)]; ^{1}H NMR (J, Hz): 1.32 (3H, t, J=6.90, CH_2CH_3); 2.38 (3H, s, Ar-CH_3); 4.26 (2H, q, J=6.90, CH_2CH_3); Ar–H [7.30 (2H, d, H-1, J=7.80, p-tolyl); 7.95 (2H, d, H-2, J=7.80, p-tolyl); 8.08-8.71 (3H, m, H-3,4,5, furyl)]; 10.76 (1H, s, NH); ^{13}C NMR (δ, ppm): 10.04 (CH_3); 21.16 (Ar-CH_3); 63.01 (OCH_2); Ar–C [124.72 (C); 131.65 (2CH); 132.13 (2CH); 133.02 (CH); 134.19 (C); 139.26 (CH); 145.90 (C); 150.32 (CH)]; 167.18 (C=N); 170.04 (C=O); Anal.calcd. Found, %: C 66.21; H 5.87; N 10.26. $C_{15}H_{16}N_2O_3$. Calculated, %: C 66.17; H 5.92; N 10.29.

2.3. *4-Amino-3-Furan-2-yl-5-p-methylphenyl-1, 2, 4-Triazole (3)*

A hydrazine hydrate solution (0.01 mol) and compound 2 (0.005 mol) were dissolved in 1-hydroxy propan (50 mL), after the mixture was refluxed for 18h, left to cool. Then removed from the precipitate formed. The product was purified with ethylacetate to obtained compound 3. "Yield, 2.02 g (84.13%)"; "white powder, mp 183-184 °C (CH_3COOEt)''; IR (cm^{-1}): [706-770, 838 (mono, 1,4 di substitue arom. ring); 1615, 1617 (ν 2C=N); 3194-3321 (ν NH_2)]; ^{1}H NMR (J, Hz): 2.39 (3H, s, Ar-CH_3), 6.28 (2H, s, NH_2), Ar–H [7.56 (2H, d, H-1, J=7.80, p-tolyl), 7.89 (2H, d, H-2, J=7.80 p-tolyl), 8.05-8.75 (3H, m, H-3,4,5, furyl)]; ^{13}C NMR (δ ppm): 20.82 (Ar-CH_3); Ar–C [123.88 (CH); 124.90 (C, Ph); 127.42 (2CH, Ph); 128.15 (2CH, Ph); 134.56 (C, Ph); 138.90 (CH); 147.01(C); 149.98 (CH)]; 153.11, 155.00 (2C, triazole C_5, C_3); Anal.calcd. Found, %: C 64.98; H 5.05; N 23.29. $C_{13}H_{12}N_4O$. Calculated, %: C 64.99; H 5.03; N 23.32.

2.4. *Synthesis of Arylidenamino Compounds (4a–c)*

The aldehyde compound (1 mmol) was dissolved completely in ethyl alcohol (30 mL) and the amine compound (1 mmol) was added. Half of alcohol was removed in vacuum after boiling for 4 hours in inert atmosphere and crystallized by addition of diethylether. The resulting crystals were cleaned with diethylether and dried in vacuo.

2.4.1. *3-Furan-5-(p-methylphenyl-4-yl)-4-(2-Hydroxy-1-benzylidenamino)-4H-1,2,4-Triazole (4a)*

"Yield, 2.80 g (81.44 %)"; "white powder, mp 148-149 °C (EtOH)"; IR (cm^{-1}): [695-768, 743, 819 (mono, 1,2, 1,4 di substitue) arom. ring], 1530, 1595 (ν 2C=N), 3309 (ν OH); 1H NMR (J, Hz): 2.34 (3H, s, Ar-CH_3), Ar–H [7.30 (2H, d, H-1, J=7.80, p-tolyl), 7.60 (1H, t, H-8, J=7.02, 2-hydroxyphenyl), 7.71 (2H, d, H-2, J=7.80, p-tolyl), 7.75 (1H, t, H-7, J=7.02, 2-hydroxyphenyl), 7.80-8.07 (4H, m, H-6, 9, 10, 11, 2-hydroxyphenyl), 8.10-8.51 (3H, m, H-3,4,5, furyl)]; 8.69 (1H, s, N=CH), 10.30 (1H, s, OH); ^{13}C NMR (δ, ppm): 21.11 (Ar-CH_3); Ar–C [120.08 (CH); 121.23; (2CH, Ph); 122.54 (CH); 123.36 (CH), 125.34 (CH); 127.45 (2CH); 129.13 (CH); 129.98 (C); 130.12 (CH); 135.80 (C); 137.40 (C); 138.67 (C); 139.23 (C); 149.10 (CH); 150.12, 152.75 (2C, triazole C_5, C_3); 171.52 (N=CH); Anal.calcd. Found, %: C 69.73; H 4.66; N 16.29. $C_{20}H_{16}N_4O_2$. Calculated, %: C 69.76; H 4.68; N 16.27.

2.4.2. *3-Furan-5-(p-methylphenyl-4-yl)-4-(1-Naphthylidenamino)-4H-1,2,4-Triazole (4b)*

"Yield, 3.03 g (80.16 %)"; "white powder, mp180-181 °C (EtOH)''; IR (cm^{-1}): [690-728, 699-773, 813 (2 mono, 1,4 di substitue) arom. ring], 1593, 1629 (ν 2C=N); ^{1}H NMR (J, Hz): 2.33 (3H, s, Ar-CH_3), Ar–H [6.90-7.04 (3H, m, H-3,4,5, furyl), 7.06-7.18 (m, 1H, H-8, 1-naphthyl), 7.36 (2H, d, H-1, J=7.80, p-tolyl), 7.48-7-60 (2H, m, H-7, 11, 1-naphthyl), 7.86-8.00 (2H, m, H-2, p-tolyl), 8.06 (1H, d, H-12, J=8.76, 1-naphthyl), 8.34 (1H, d, H-6, J=8.76, 1-naphthyl), 8.60-8.89 (2H, m, H-9, 10, 1-naphthyl)]; 9.20 (1H, s, N=CH); ^{13}C NMR (δ, ppm): 20.22 (Ar-CH_3); Ar–C [109.43 (C); 116.11 (CH); 122.04 (2CH); 123.00 (C); 123.16 (CH); 123.75 (CH); 124.07 (C); 125.04 (CH); 126.55 (CH); 127.66 (2CH); 129.87 (CH); 133.12 (CH); 135.89 (CH); 137.12 (CH), 138.77 (C); 148.70 (C); 149.24 (CH); 150.87 (CH); 160.99 (C)]; 151.24, 153.76, (2C, triazole C_5, C_3), 167.02 (N=CH); Anal.calcd. Found, %: C 76.15; H 4.78; N 14.84. $C_{24}H_{18}N_4O$. Calculated, %: C 76.18; H 4.79; N 14.80.

2.4.3. *3-Furan-5-(p-methylphenyl-4-yl)-4-(2-Hydroxy-1-Naphthylidenamino)-4H-1,2,4-Triazole (4c)*

"Yield, 3.22 g (81.78 %)''; "white powder, mp191-192 °C (EtOH)''; IR (cm^{-1}): [695-771, 747, 832 (mono, 1,2, 1,4 di substitue) arom. ring]; 1626, 1640 (ν 2C=N); 3318 (ν OH); 1H NMR (J, Hz): 2.33 (3H, s, Ar-CH_3); Ar–H [7.25 (2H, d, H-1, J=7.80, p-tolyl); 7.39 (2H, d, H-2, J=7.80, p-tolyl); 7.44 (1H, t, J=8.65, H-8, 2-hydroxy-1-naphthyl); 7.56-7.69 (2H, m, H-6, 9, 2-hydroxy-1-naphthyl); 7.73 (1H, t, J=8.65, H-7, 2-hydroxy-1-naphthyl); 7.75-8.05 (2H, m, H-10, 11, 2-hydroxy-1-naphthyl); 9.22 (1H, s, N=CH); 10.04 (1H, s, OH); ^{13}C NMR (δ, ppm): 20.45 (Ar-CH_3); Ar–C [113.24 (C); 117.36 (CH); 119.14 (C); 121.33 (2CH); 123.00 (C); 124.35 (CH); 124.55 (CH); 124.91 (CH); 127.88 (2CH); 128.09 (CH); 128.46 (CH); 130.05 (C); 134.58 (C); 136.12 (CH); 138.09 (CH); 142.55 (C); 150.02 (CH); 160.13 (C)]; 149.77, 150.54 (2C, triazole C_5, C_3); 164.56 (N=CH); Anal. calcd. Found, %: C 73.03; H 4.65; N 14.22. $C_{24}H_{18}N_4O_2$. Calculated, %: C 73.09; H 4.60; N 14.20.

2.5. *Synthesis of Arylamino Ligands (5a–c)*

The arilidenamino ligands (4a–c) (0.005 mol) and pured methanol (30 mL) were mixed, and sodium borohydride (0.01 mol) was attended carefully to the solution. The solution was boiled for 25 min and then left to warm. After being evapora, the resulting solid product was washed with water for three times. After the moisture of the substance is dried, the matter was purified with a suitable solvent.
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2.5.1. *3-Furan-5-(p-methylphenyl-4-yl)-4(2-Hydroxy-1-benzylamino)-4H-1,2,4-Triazole (5a)*

"Yield, 3.01 g (87.00 %)"; "white powder, mp 176-177 °C (EtOH)''; IR (cm^{-1}): [746, 691-774, 857 (1,2 di, mono, 1,4 di substitue) arom. ring]; 1568, 1612 (ν 2C=N); 3278 (ν NH); 3304 (ν OH); ^{1}H NMR (J, Hz): 2.39 (3H, s, Ar-CH_3); 3.92 (2H, d, J=4.56, -$NHCH_2$); 6.74 (1H, t, J=4.56, -$NHCH_2$); Ar–H [6.95 (2H, m, H-2, p-tolyl); 7.17 (2H, d, H-1, J=7.80, p-tolyl); 7.25 (2H, m, H-7, 8, 2-hydroxyphenyl); 7.48-7.55 (3H, m, furyl); 7.87–7.89 (2H, m, H-6, 9, 2-hydroxyphenyl)]; 10.36 (s, 1H, OH); ^{13}C NMR (δ, ppm): 20.96 (Ar-CH_3); 52.47 (CH_2); Ar–C [120.31 (CH); 121.66 (CH); 122.99 (2CH); 125.89 (CH); 126.54 (2CH); 127.23 (C); 129.76 (C); 130.32 (C); 138.67 (CH); 142.56 (CH); 143.90 (C); 144.26 (CH);151.06 (C); 152.12 (CH)]; 150.45, 151.18 (2C, triazole C_5, C_3); Anal.calcd. Found, %: C 69.34; H 5.21; N 16.22. $C_{20}H_{18}N_4O_2$. Calculated, %: C 69.35; H 5.24; N 16.17.

2.5.2. *3-Furan-5-(p-methylphenyl-4-yl)-4-(1- Triazole (5b)*: *Naphthylamino)-4H-1,2,4-Triazole (5b)*

"Yield, 3.14 g (82.78 %)"; "white powder, mp 184-185 °C (EtOH)''; IR (cm^{-1}): [692-771, 698-763, 854, (2 mono, 1,4 di substitue) arom. ring], 1535, 1626 (ν 2C=N), 3213 (ν NH); ^{1}H NMR (J, Hz): 2.41 (3H, s, Ar-CH_3); 4.29 (2H, d, -$NHCH_2$, J=4.56); 6.80 (1H, t, $NHCH_2$, J=4.56); Ar–H [7.14 (2H, d, J=7.80, p-tolyl); 7.32 (2H, t, H-8, 11, J=8.76, 1-naphthyl); 7.41-7.60 (3H, m, furyl); 7.77 (2H, d, J=7.80, p-tolyl); 7.81-7.95 (2H, m, H-10, 12, 1-naphthyl); 8.00-8.35 (3H, m, H-6, 7, 9, 1-naphthyl)]; ^{13}C NMR (δ, ppm): 20.96 (Ar-CH_3); 46.88 (CH_2); Ar–C [112.55 (C); 118.32 (C); 122.12 (2CH); 123.17 (CH); 123.66 (C); 126.30 (C); 127.04 (2CH); 127.85 (CH); 128.66 (CH); 129.40 (CH); 129.23 (CH); 133.09 (CH); 137.91 (CH); 138.32 (C); 138.70 (CH); 149.01 (C); 149.18 (CH); 149.76 (CH); 156.42 (C)]; 152.50, 154.89 (2C, triazole C_5, C_3); Anal.calcd. Found, %: C 75.71; H 5.34; N 14.76. $C_{24}H_{20}N_4O$. Calculated, %: C 75.77; H 5.30; N 14.73.

2.5.3. *3-Furan-5-(p-methylphenyl-4-yl)-4-(2-Hydroxy-1-Naphthylamino)-4H-1,2,4-Triazole (5c)*

"Yield, 3.46 g (87.41 %)"; "white powder, mp 191-192 °C (EtOH)''; IR (cm^{-1}): [725-707, 738, 810 (mono, 1,2, 1,4 di substitue) arom. ring]; 1588, 1619 (ν 2C=N); 3293 (ν NH); 3314 (ν OH); ^{1}H-NMR (J, Hz): 2.44 (3H, s, Ar-CH_3); 4.12 (2H, d, J=4.56, -$NHCH_2$); 6.85 (1H, t, J=4.56, -$NHCH_2$); Ar–H [7.31 (2H, d, H-1, J=7.80, p-tolyl); 7.40 (2H, d, H-2, J=7.80, p-tolyl); 7.50 (1H, t, J=8.65, H-8, 2-hydroxy-1-naphthyl); 7.55-7.64 (2H, m, H-6, 9, 2-hydroxy-1-naphthyl); 7.70 (1H, t, J=8.65, H-7, 2-hydroxy-1-naphthyl); 7.80-8.00 (2H, m, H-10, 11, 2-hydroxy-1-naphthyl)]; 10.21 (1H, s, OH); ^{13}C NMR (δ, ppm): 21.07 (Ar-CH_3); 42.87 (CH_2); 60.26 (C); Ar–C [107.99 (C); 115.80 (C); 118.90 (C); 121.99 (2CH); 123.16 (C); 123.77 (CH); 124.88 (CH); 126.50(CH); 127.65 (2CH); 128.19 (CH); 128.22 (C); 129.00 (CH); 129.81 (CH); 138.89 (CH); 139.55 (CH); 149.15 (C); 152.00 (CH), 160.26 (C)]; 150.08, 151.32 (2C, triazole C_5, C_3); Anal.calcd. Found, %: C 72.74; H 5.06; N 14.09. $C_{24}H_{20}N_4O_2$. Calculated, %: C 72.71; H 5.09; N 14.13.

2.6. Antioxidant and Urease Inhibitory Activity Assays

The DPPH and ABTS radical scavenging activities of the compounds contain triazole moiety were determined using the method described by Williams et al. [26] and Arnao et al. [27], respectively. The reducing power activities of the compounds were examined considering Oyaizu method [28]. Antiurease activities of compounds were assayed according to the procedure of Van Slyke and Archibald [29].

3. RESULTS AND DISCUSSION

In current research, the hydrazone compound **2** was obtained from the reaction of ethyl p-methylbenzimidate hydrochloride **1**, which was synthesized according to reference [25], with furan-2-carbohydrazide and the content of the compound is lightened by FT-IR, ^{1}H-NMR, ^{13}C-NMR and elemental analysis techniques. The compound **3** was synthesized by adding hydrazine hydrate to the compound **2**. The reaction was refluxed for 24 hours using 1-propanol as solvent and the 4- amino-3-furan-2-yl-5-p-methylphenyl-1,2,4-triazole **3** was formed. IR spectrum of compound **3** was determined the $–NH_2$ bands between 3321–3194 cm^{-1} area. The ^{1}H-NMR characteristic signal of **3** was observed at δ 6.28 (s, 2H, NH_2).

The Carbon-NMR signals for the triazole C_3, C_5 were observed at δ 150-155. Synthesis of Schiff bases obtained from the reaction of carbonyl compounds with primary amines takes place in two main steps as separation and addition steps. Firstly, a carbonylamine intermediate compound is formed from the condensation of the carbonyl group with the primary amine, then a Schiff base is obtained from the dehydration of this intermediate compound [30]. Figure **1** shows the formation of synthesized Schiff bases. Synthesized Schiff bases were obtained in high yields by activation of amines and aldehydes in ethanol (% 80-82). Compounds **(4a−c)** composed of compound **3** by refluxing with 2-hydroxy-1-benzaldehyde, 1-naphthaldehyde and 2-hydroxy-1-naphthaldehyde in acetic acid solvent.

Firstly, we synthesized the ariliden compounds. IR spectra showed the imine peaks of **(4a–c)** in the 1530-1640 cm^{-1} area. When the Proton-NMR spectra of Schiff bases are examined, the most important peak to be considered is the peak belonging to the azomethine proton, which is the characteristic peak of this type of compounds. The proton bound to the azomethine group is generally resonance in the range of δ = 8-9 ppm. When the ^{1}H-NMR spectrum of the obtained Schiff base compounds was examined, the peaks of azomethine hydrogens were observed as δ = 8.69-9.22 ppm and singlet as expected in all three compounds. Peaks of imine carbons are seen in the ^{13}C-NMR spectrum between δ = 164.6-171.5 ppm. Imine peak emerged as a singlet. It was observed that the NMR results supported the formation of the compound and were consistent with the literature [31]. Reduction in reduced products **(5a–c)** was took place only the non-ring C=N bond of the ariliden compounds **(4a–c) (Figure 1)**. These degradation reactions were happening in fairly moderate conditions.

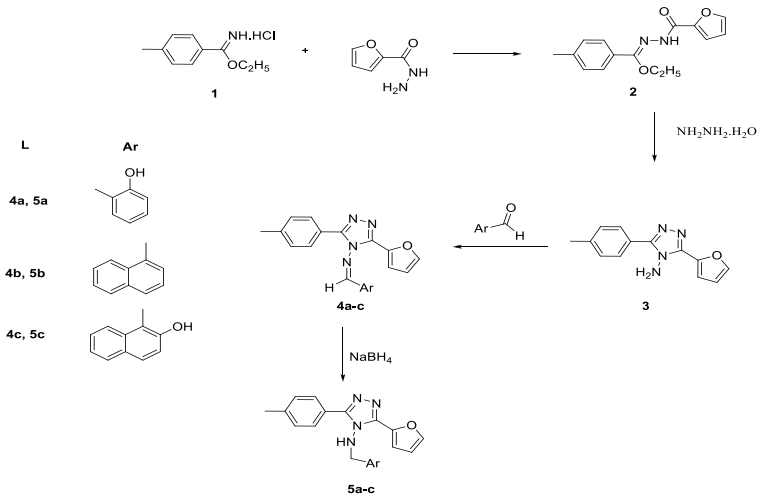

Figure 1. *Synthesized ligands*

Reduction products **(5a–c)** represent IR peaks between 3250–3320 cm^{-1} (υNH). The proton-NMR characteristic signals of **(5a–c)** were observed as a triplet at δ 6.74–6.85 (t, 1H, NH) and as a doublet at δ 3.92–4.29 (d, 2H, CH_2). The $–CH_2–$ signals of compounds **(5a–c)** were observed between δ 43–52. These results were consistent with the literature [31]. The reducing capacity of a compound may serve as a significant indicator for its potential antioxidant activity [32]. The reducing power activities of the compounds contain azomethine group were viewed at various concentrations (50-200 μg/mL), and findings were compared with BHT (Table 1).

Table 1. *The reducing power antioxidant activity of new ligands (2, 3, 4a–c, 5a-c)*

Comp.	Ligands Concentration µg/mL)	Reducing Power Absorbance*	Comp.	Reducing Power Absorbance*
	50	0.018±0.004		0.037±0.003
2	100	0.032±0.004	5a	0.054±0.007
	150	0.046±0.007		0.072±0.009
	200	0.059±0.001		0.089±0.006
	50	0.193±0.026		0.137±0.002
3	100	0.276±0.012	5b	0.146±0.004
	150	0.311±0.014		0.161±0.009
	200	0.469±0.024		0.192±0.004
	50	0.075±0.004		0.068±0.004
4a	100	0.088±0.009	5c	0.082±0.006
	150	0.112±0.013		0.113±0.016
	200	0.155±0.009		0.174±0.012
	50	0.044±0.008		0.162±0.012
4b	100	0.079±0.005	BHT	0.205±0.018
	150	0.121±0.001		0.274±0.021
	200	0.137±0.008		0.311±0.025
	50	0.067±0.002		
4c	100	0.079±0.004	-	-
	150	0.118±0.008		
	200	0.137±0.006		

**Values were the means of three replicates ± Standard deviation (SD).*

In this study, the reducing power capacity of newly synthesized compounds rised with increasing concentration of samples. Compounds 4b and 4c showed similar results. In the same concentrations, compounds 3 and 2 showed the highest (0.469±0.024) and lowest (0.059±0.001) activities, respectively. Compound 3 showed higher activity than BHT at all concentration.

Gumrukcuoglu et al. (2013) have synthesized new 1,4-butylene bridged bis-1,2,4-triazole derivatives and their reducing power antioxidant capacity absorbance values found between 0.121-0.143 [33]. In this study, the reducing power absorbance values of triazole derivatives are between 0.059-0.469 in the range of.

Table 2. *The antioxidant and antiurease activities of new ligands and standards (2, 3, 4a–c, 5a–c)*

Compounds	DPPH SC_{50} (µM)*	ABTS SC_{50} (µM)*	Antiurease IC_{50} µM)*
2	12809.28±2502.59	2877.73±287.07	0.99±0.013
3	5071.17±382.07	1119.6±95.72	0.12±0.009
4a	9737.89±699.02	1874.72±127.68	0.15±0.004
4b	5334.98±207.39	1628.28±25.73	0.14±0.001
4c	11749.17±431.96	1299.17±108.79	0.14±0.013
5a	5324.36±582.73	2421.09±398.41	0.16±0.011
5b	4542.71±197.44	806.02±1.43	0.22±0.027
5c	6512.24±981.80	1063.63±43.41	0.29±0.039
Trolox	132.03±9.75	214.55±24.56	-
Thiourea	-	-	0.11±0.004

*Values were the means of three replicates ± Standard deviation (SD).

DPPH and ABTS radical scavenging assays have been used to evaluate the antioxidant activity of compounds due to the simple, rapid, and reproducible procedures of compounds. The DPPH and ABTS radical scavenging activities of new ligands are presented in Table 2. As standard antioxidant, Trolox (6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid) was used. Their comparable scavenging efficiency were stated in SC50 (50% of radicals in the discarded activity) value. Compound 5b (SC50 = 4542.71 ±

197.44 μM for DPPH; SC50 = 806.02±1.43 μM for ABTS) and 2 (SC50 = 12809.28 ± 2502.59 μM for DPPH; SC50 = 2877.73±287.07 μM for ABTS) exhibited the highest and the lowest scavenging activities among all the tested compounds, respectively. Scavenging activity values of the compounds were lower than Trolox. DPPH is a free radical compound that has been widely used to determine the free radical scavenging ability of various samples. DPPH decreases significantly upon exposure to proton radical scavenger [34]. Bilgin Sokmen et al. (2015) have synthesized newly 1,2,4-bis triazole derivatives and their DPPH SC50 values found between 4376.08- 13337.95 μM [35]. Bilgin Sokmen et al. (2013) have synthesized some new methoxy substitued bis-1,2,4-triazole derivatives and their ABTS radical scavenging activities values (SC50) determined between 3274.88- 8734.22 μg/mL [36].

As seen in Table 2, the original compounds showed moderate urease inhibitory activity. Inhibition values were increased with increasing sample concentration. Higher enzyme inhibitory activity shows low IC50 value. The highest and lowest enzyme inhibition activities were found at compounds 3 (IC50=0.12±0.009 μM) and 2 (IC50=0.99±0.013 μM), respectively. Triazoles have been regarded as structural type inhibitors of urease. 1,2,3 - Triazole and 1,3,4-thiadiazole derivatives were synthesized by Khan et al. showed potent urease inhibitor activity between IC50=45.60- 459.56 μM [37]. Gumrukcuoglu et al. reported that of the antiurease IC50 values of the 1,2,4-triazole derivatives were between 2.44 – 2.62 μM [33].

4. CONCLUSION

In current study, the results exhibit that the obtained new ligands containing azomethine group had antioxidant and an effective antiurease activities. Consequently, these substances are considered to be antioxidant agents in technology such as medicine uses, food additives, industrial uses as stabilizers in fuels and lubricants to prevent oxidation.

Recently, many scientist are showing a great interest in the synthesis and physico-chemical properties of transition metal complexes with substituted 1,2,4-triazoles. Triazoles and their derivatives have been evidenced to be effective bactericides, pesticides, fungicides and insecticides [38, 39]. Many Schiff bases obtained from either heterocyclic amines or aldehydes possess excellent ability to synthesis transition metals complexes [40].

Thus the main idea of our present research work is to synthesize triazole derived Schiff bases as well as to synthesis variety of metal complexes with various transition metal ion.

CONFLICTS OF INTEREST

No conflict of interest was declared by the authors.

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