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Azo-azomethine ligands with N_2O_2 donor atom sets and their binuclear UO_2(II) complexes: synthesis, characterization and biological activity

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Two azo-azomethine ligands with N_2O_2 donor atom sets and their binuclear UO_2(II)-complexes were synthesized for therapeutic uses. The ligands were derived from the condensation of 4-(4-hydroxy-3-formyl-1-ylazo)-N-pyrimidin-2-yl-benzenesulfonamide with ethylenediamine and 1,6-hexanediamine. The prepared ligands and their bi-homonuclear uranyl complexes were characterized by thermal analyses (TGA & conventional method), vibrational, electronic, ^{1}H NMR, and mass spectra as well as by different physicochemical techniques. The active coordination centers in the ligands and the geometrical arrangement of the complexes were investigated using the spectral data. Molar conductance measurements in DMSO solution denoted that the complexes are non-electrolytes. The investigated complexes and ligands were screened *in vitro* for their antimicrobial activity against fungi (*Aspergillus flavus* and *Candida albicans*), gram-positive bacteria (*Staphylococcus aureus*) and gram-negative bacteria (*Escherichia coli*). It was observed that the complexes are more potent fungicides and bactericides than the ligands.

Keywords: N_2O_2 azo-azomethine ligands, binuclear UO_2(II)-complexes, biological activity

INTRODUCTION

Azo-azomethine compounds and their metal complexes have found interesting utilities which arise from the importance of such compounds in biological and industrial applications [1, 2], but little work dealt with such subjects [3-5]. Also, sulfa compounds were the first drugs found to act selectively and could be used systematically as preventive and therapeutic agents against different diseases in humans [6]. The vast commercial success of these medicinal agents has made the chemistry of sulfa compounds a major area of research [7]. Sulfur ligands are wide-spread among coordination compounds and are important components of biologically active transition metal complexes [8, 9]. Metal complexes with heterocyclic unsaturated ligands are also of great interest in inorganic and organometallic chemistry, especially due to their unique electrical and magnetic properties [10, 11]. Also, metal complexes containing two or more metal ions per molecule find wide application in biological systems, catalysis, and material science [12–16], beside their peculiar spectroscopic and magnetic properties [17–21]. Complex formation between metal ions and sulfa compounds, combining antibacterial activity of sulfa derivatives and antimicrobial activity of the metal ions, constitutes an important field of research due to their pronounced antimicrobial and fungicidal activities [22–25]. On the other hand, uranium is a symbolic element as it is the last natural element and it is the most common element of actinides. So, it is imperative to look into the structure and biological activity of new bi-homonuclear uranyl complexes with sulfa azo-azomethine ligands, in a continuation of our research work in designing new ligands and complexes [26-31]. The active coordination centers in the ligands and the geometrical arrangement of the complexes will be investigated using the analytical and spectral data.

EXPERIMENTAL

All reagents and solvents used in the present work were reagent grade provided from Merck, Aldrich or Sigma and were used as received.

Synthesis of azo-azomethine ligands

The ligands under interest were prepared according to the following procedures. 4-(4-hydroxy-3-formyl-1-ylazo)-N-pyrimidin-2-yl-benzenesulfonamide was synthesized according to the well-known published procedure [32]. A suspension of 4-amino-N-pyrimidin-2-yl-benzenesulfonamide (2.50 g, 10 mmol) in hydrochloric acid (18 mL) and water (8 mL) was heated to 70°C until complete dissolution. The clear solution was poured into ice water and was

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diazotized below 5°C with sodium nitrite (1.4 g, 20 mmol) dissolved in water (10 mL). The cold diazonium solution was added in the course of 30 min at 0°C to a solution of salicylaldehyde (1.07 mL, 10 mmol) in water (20 mL) containing sodium hydroxide (1.6 g) and sodium carbonate (3.7 g). During the addition process, the solution was vigorously stirred. The product was collected by vacuum filtration and was washed with NaCl solution (25 mL, 10%). Coupling of the diazonium reagent to salicylaldehyde occurred at the *para* position to the hydroxyl group. The azo compound was re-crystallized several times from ethanol.

Schiff base ligands (HL^1 and HL^2) were prepared using a method previously reported in the literature [33]. For each ligand, a mixture of 10 mmol of 4-(4-hydroxy-3-formyl-1-ylazo)-N-pyrimidin-2-yl-benzenesulfonamide (3.83 g) and ethylenediamine (0.60 g) or 1,6-hexanediamine (1.16 g) was dissolved in absolute ethanol (50 mL) with a few drops of glacial acetic acid as a catalyst. The resulting mixture was stirred under reflux for 10–12 h. The product was vacuum-filtered and washed with a small amount of hot ethanol. The various synthetic reactions are summarized in figure 1.

Synthesis of the metal complexes

Complexes of UO_2(II) were synthesized by the reflux-precipitation method. Hot ethanolic solutions of the ligand (1 mmol in 50 mL of ethanol) and uranyl acetate dihydrate [2 mmol in 50 mL of water-ethanol mixture (50%, V/V)] were mixed. The resulting mixture was refluxed on a water bath for 8–10 h. The complexes which precipitated during the reaction were filtered off and washed several times with hot ethanol, then dried in vacuum over anhydrous calcium chloride. The yield of the reaction was found to be 78%—81%. Purities of the complexes were checked by TLC and melting point constancy.

Analytical and physical measurements

The metal contents in the complexes were determined gravimetrically following a standard procedure [34]. A weighed quantity of the complex (0.4~0.5 g) was treated with a few drops of conc. H_2SO_4 and 1 mL of conc. HNO_3. It was heated till the organic matter decomposed and sulfur trioxide fumes came out. The same process was repeated three to four times to decompose the complex completely. Then, it was dissolved in water and the resulting solution was used for determining the metal ion. Uranium was precipitated as ammonium diuranate, followed by ignition to its respective oxide.

The nature and contents of water molecules and acetate groups attached to the central metal ion were determined by conventional thermal decomposition studies. Complexes **1** and **2** were heated at five temperatures (100°C, 200°C, 300°C, 500°C and 1000°C) in a muffle furnace for 40–50 min. The resulting weights were measured. The weight loss at 100°C corresponds to the loss of lattice water from the complexes. The weight loss at 200°C corresponds to the loss of coordinated water. The weight loss at 300°C can be attributed to the removal of acetate groups. On heating at 500°C, the weight indicates loss of parts of the ligand. The weight of the pyrolysis product after heating at 1000°C corresponds to the formation of metal oxide as a final product [35]. Conductance measurements were performed for 10^{-3} mol L^{-1} solution in DMSO at room temperature using a Jenway (model 4070) conductance meter. Matrix Assisted Laser Desorption/Ionization Time-of-Flight (MALDI-TOF) mass spectra were recorded on a BRUKER Auto flex II LRF20 spectrometer using dithranol as a matrix. Fourier transformation infrared (FT-IR) spectra of the free ligands and their UO_2-complexes in KBr pellets were measured using a FT-IR Bruker Tensor 27 spectrophotometer (Germany), within the range 4000-400 cm^{-1} (Central Laboratory, Tanta University, Egypt). UV/Vis spectra were measured on a Shimadzu 240 UV-Visible spectrophotometer in DMF solutions. The magnetic moments were measured at room temperature using the Gouy's method using a magnetic susceptibility balance (Johnson Matthey, Wayne, PA. 19087 USA) at 60 Hz. A Bruker DMX 750 (500MHz) spectrometer was used for obtaining ^{1}H NMR spectra, employing DMSO-d_6 as the solvent and TMS as the internal standard. Chemical shifts of ^{1}H NMR were expressed in parts per million (ppm, δ units), and coupling constant was expressed in units of Hertz (Hz). Thermal gravimetric analysis (TGA) of the complexes was performed on a Shimadzu TG-50 thermal analyzer from ambient temperature up to 800°C with a heating rate of 10°C/min in nitrogen atmosphere.

Biological activity: antifungal and antibacterial screening

In vitro studies of the antifungal and antibacterial activities of the investigated ligands and complexes against *A. flavus*, *C. albicans*, *E. coli*, and *S. aureus* were carried out using the modified Kirby–Bauer disc diffusion method [36] at the micro-analytical unit of Cairo University. Briefly, 100 μL of the test fungi/bacteria were

grown in 10 mL of fresh media until they reached 105 cells mL^{-1} for fungi and 108 cells mL^{-1} for bacteria [37]. Hundred microliters of microbial suspension was spread onto agar plates corresponding to the broth in which they were maintained. Isolated colonies of each organism were selected from the primary agar plates and tested for susceptibility by the disc diffusion method [38]. From the many media available, NCCLS recommends Mueller–Hinton agar since it results in good batch-to-batch reproducibility. The disc diffusion method for filamentous fungi was tested using the approved standard method (M38-A) developed by the NCCLS [39] for evaluating the susceptibilities of filamentous fungi to antifungal agents. The disc diffusion method for yeasts was developed using the approved standard method (M44-P) by the NCCLS [40]. Plates were inoculated with filamentous fungi, *A. flavus*, at 25ºC for 48 h; Gram (+) bacteria, *S. aureus*, and Gram (-) bacteria, *E. coli*. They were incubated at 35–37ºC for 24–48 h. Yeast *C. albicans* was incubated at 30ºC for 24–48 h. Then the diameters of the inhibition zones were measured in millimeters [41]. Standard discs of tetracycline (antibacterial agent) and amphotericin B (antifungal agent) served as positive controls for antimicrobial activity; filter discs impregnated with 10 mL of solvent (distilled water, DMSO) were used as negative controls. The agar used was Meuller–Hinton agar that was rigorously tested for composition and pH. Further, the depth of the agar in the plate is a factor to be considered in the disc diffusion method. This method is well-documented and standard zones of inhibition were determined for susceptible and resistant values. Blank paper discs (Schleicher & Schuell, Spain) with a diameter of 8.0 mm were impregnated with 10 mL of the tested concentration of the stock solutions. When a filter paper disc impregnated with a tested chemical is placed on agar the chemical will diffuse from the disc into the agar. This diffusion will place the chemical in the agar only around the disc. The solubility of the chemical and its molecular size will determine the size of the area of chemical infiltration around the disc. When an organism is placed on the agar it will not grow in the area around the disc if it is susceptible to the chemical. This area of no growth around the disc is known as a ‘‘zone of inhibition’’ or ‘‘clear zone’’. For the disc diffusion, the zone diameters were measured with slipping calipers of the National Committee for Clinical Laboratory Standards. Agar-based methods such as disc diffusion can be good alternatives because they are simpler and faster than broth-based methods [42].

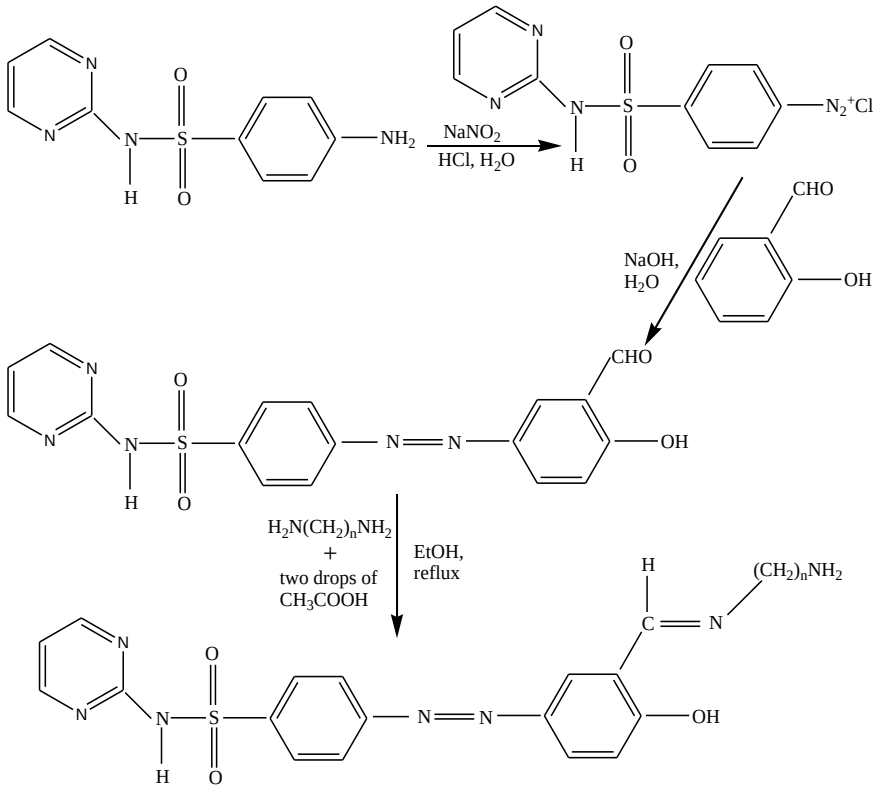

Fig. 1. Preparation of the azo-azomethine ligands [HL^1 (n=2) and HL^2 (n=6)].

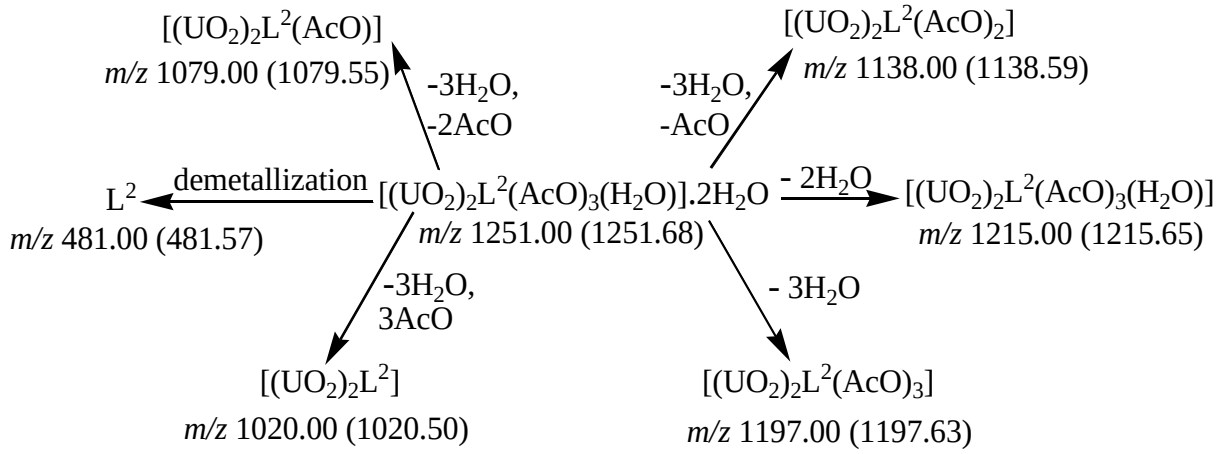

Fig. 2. Fragmentation pathways of $[(UO_2)_2L^2(AcO)_3(H_2O)]\cdot 2H_2O$ (**2**).

Table 1. Analytical and physical data of HL^1, HL^2 and their UO_2(II)-complexes[a] (**1** and **2**).

Molecular formula (Empirical formula)	Mol. Wt. (Cal. Mol. Wt.)	Color (Δ_m)	Analytical data Found % (Calcd.)			
			%Hydrated H_2O	%Coordinated H_2O	%AcO^-	%M
HL^1	425.00	Yellow	—	—	—	—
($C_{19}H_{19}N_7O_3S$)	(425.46)	(—)				
$[(UO_2)_2L^1(AcO)_3(H_2O)]\cdot H_2O$	1177.00	Brown	1.48	1.50	14.88	40.31
($C_{25}H_{31}N_7O_{15}SU_2$) (**1**)	(1177.68)	(6.32)	(1.53)	(1.53)	(15.04)	(40.42)
HL^2	481.00	Yellow	—	—	—	—
($C_{23}H_{27}N_7O_3S$)	(481.57)	(—)				
$[(UO_2)_2L^2(AcO)_3(H_2O)]\cdot 2H_2O$	1251.00	*F.* brown	2.83	1.39	13.93	37.98
($C_{29}H_{41}N_7O_{16}SU_2$) (**2**)	(1251.68)	(6.12)	(2.88)	(1.44)	(14.15)	(38.03)

[a] The yield of the synthesized compounds was 78-81%.
The synthesized complexes decompose without melting above 275 °C.
Mol. Wt. is the molecular weight obtained from mass spectra.
Δ_m is the molar conductance measured in $Ohm^{-1}\ cm^2\ mol^{-1}$.

RESULTS AND DISCUSSION

The ligands (HL^1 and HL^2) and their UO_2(II)-complexes were formulated from the analytical, spectral and molar conductance data which supported the suggested formulae (Table 1). The complexes are highly colored and insoluble in water and common organic solvents such as methanol, ethanol, acetone, ether, $CHCl_3$, CCl_4 and benzene but moderately soluble in highly coordinating solvents such as DMSO and DMF. They are non-hygroscopic and highly stable under normal conditions. The low molar conductance values for the complexes in DMSO indicate them to be non-electrolytes in nature [42].

TOF-mass spectra

The constitutions and purities of the prepared ligands and their UO_2(II)-complexes are confirmed by MALDI-TOF mass spectrometry using dithranol as a matrix. The ligand spectra displayed accurate molecular ion peaks at m/z 425 and 481 for HL^1 and HL^2, respectively, matched with the theoretical values. The mass spectra of $[(UO_2)_2L^1(AcO)_3(H_2O)]\cdot H_2O$ and $[(UO_2)_2L^2(AcO)_3(H_2O)]\cdot 2H_2O$ showed peaks at m/z 1177 and 1251, respectively, corresponding to the molecular weight of the parent ion $[ML]^+$. A further confirmation for the molecular structure of the investigated complexes comes from the appearance of other peaks due to successive degradation of the target compound to various fragments [25]. For example, the mass spectrum of complex **1** displayed peaks at m/z 1177, 1159, 1141, 1082, 1023 and 964 corresponding to $[(UO_2)_2L^1(AcO)_3(H_2O)]\cdot H_2O$ (the molecular weight of the complex cation), $[(UO_2)_2L^1(AcO)_3(H_2O)]$ (loss of the hydrated water molecule), $[(UO_2)_2L^1(AcO)_3]$ (loss of two water molecules) $[(UO_2)_2L^1(AcO)_2]$ (loss of two water

Table 2. Assignment of the IR spectral bands (cm^{-1}) of HL^1, HL^2 and their UO_2(II)-complexes **1** and **2**.

No	ν(OH) [ν(NH)]	ν(NH_2) [ν(CH_{arom})]	ν(CH=N_{arom}) [ν(CH=N_{azom})]	ν(N=N) [ν(S=O)]	ν_{as}(OCO) [ν_s(OCO)]	ν(SO_2N)	ν_{as}(UO_2) [ν_s(C-S]	ν(M-O) [ν(M-N)]
HL^1	3425	3260	1650	1411	—	1326, 1156	—	—
	[3357]	[3039]	[1584]	[1263]	[—]		[686]	[—]
1	3425	3260	1624	1410	1519	1326, 1156	843	664
	[3357]	[3042]	[1582]	[1262]	[1476]		[681]	[421]
HL^2	3425	3259	1652	1409	—	1326, 1156	—	—
	[3356]	[3039]	[1583]	[1262]	[—]		[685]	[—]
2	3425	3262	1621	1409	1495	1326, 1157	844	639
	[3357]	[3042]	[1581]	[1263]	[1442]		[684]	[421]

molecules and one acetate group), $[(UO_2)_2L^1(AcO)]$ (loss of two water molecules and two acetate groups), and $[(UO_2)_2L^1]$ (loss of two water molecules and three acetate groups). Also, UO_2(II)-complexes **1** and **2** decompose *via* abstraction of the ligand, which gives rise to molecular ion peaks attributable to $[L]^+$ (figure 2). This is a common behavior for metal ion complexes containing different ligands (ML) which decompose during spray ionization through cleavage of the metal-ligand bond [44]. This is good evidence confirming the proposed structures of the investigated complexes.

Vibrational (FT-IR) spectra and mode of bonding

Previous studies on metal complexes of Schiff base derivatives of sulfa-drugs indicated that metal ions are bonded to the ligand either through the Schiff base or the sulfonamide part for mononuclear complexes, while for binuclear ones both centers contribute [45]. In order to study the binding mode of HL^1 and HL^2 to the uranyl ion in the complexes, FT-IR spectra of the free ligands were compared with the spectra of the complexes. On examining the infrared spectra of the UO_2(II) chelates in comparison to the corresponding free ligands, the following observations can be made (Table 2);

1. IR spectra of HL^1 and HL^2 displayed strong sharp bands at 3425 cm^{-1} assignable to ν(OH).
2. IR spectra of complexes **1** and **2** displayed broad bands at 3425 cm^{-1}, which can be assigned to ν(OH) of water associated with complexes. The presence of water renders it difficult to confirm the deprotonation of the OH groups on complex formation from the stretching vibration [46].
3. Stretching vibration bands at 1584, 1582 due to aliphatic ν(CH=N) and at 1650 and 1624 cm^{-1} corresponding to aromatic ν(CH=N) in the spectra of HL^1 and HL^2, respectively, were found to be invariable shifts in the spectra of complexes **1** and **2** indicating the coordination of the aromatic and aliphatic azomethine nitrogens to the metal ion in chelate formation [47].
4. In the IR spectra of HL^1 and HL^2, sharp bands appeared at 1326 and 1156 cm^{-1} due to ν_{as}(SO_2N) and ν_s(SO_2N), respectively. These bands slightly shifted to higher or lower frequencies upon coordination to UO_2(II) [47].
5. In the uranyl complexes **1** and **2**, the bands which are observed within the 1519-1495 and 1476-1442 cm^{-1} ranges attributed to ν_{as}(OCO) and ν_s(OCO) of the acetate group, respectively, indicate monodentate coordination of this group [Δ(OCO) = ν_{as}(OCO) - ν_s(OCO) < 100 cm^{-1})] [48].
6. The medium intensity bands appeared around 3357, 3260, 3040, 2939, 1410, 1262 and 685 cm^{-1} can be assigned to ν(NH_2), ν(NH), ν(CH-aromatic), ν(CH_2), ν(N=N), ν(S=O), and ν(C-S), respectively.

This is supported by the appearance of two new bands at 664–639 cm^{-1} and at 420 cm^{-1} due to ν(M–O) and ν(M–N) [22], respectively. Also, the uranyl complexes **1** and **2** show a strong IR band near 843 cm^{-1} assigned to ν_{as}(UO_2) [49]. The assignment of bands of diagnostic importance in the IR spectra of the free ligands and metal complexes under study is collected in Table 2.

From these observations and the previous studies [24, 25, 45, 46], the mode of bonding in UO_2(II)-complexes **1** and **2** can be represented (figure 3).

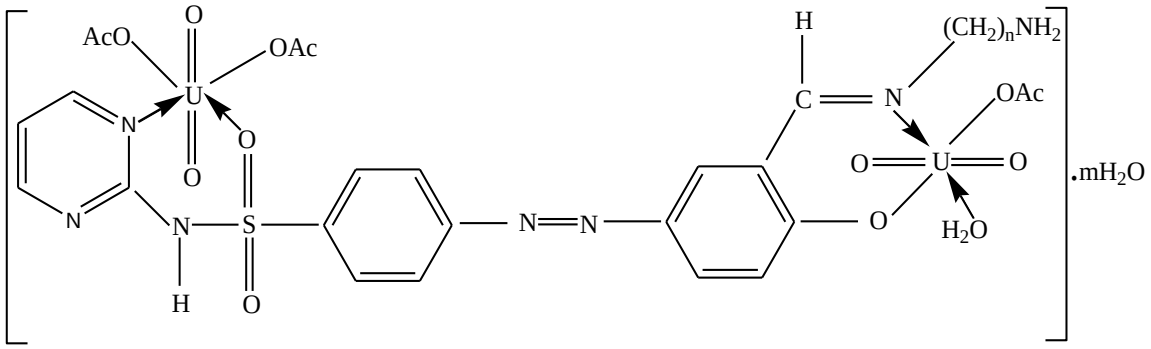

Fig. 3. Representative structures of binuclear UO_2(II)-complexes **1** and **2,** where n=2 and m=1 for complex **1** while n=6 and m=2 for complex **2**.

Table 3. Electronic and ^{1}H NMR spectral data of HL^1, HL^2 and their UO_2(II)-complexes **1** and **2**.

No	Electronic spectra (λ_{max} , nm)	^{1}H NMR spectra						
		δ_{OH}	$\delta_{CH=N}$	$\delta_{Ar—H}$	δ_{NH}	δ_{NH2}	CH_3-protons (CH_3COO)	δ_{H2O}
HL^1	290, 376, 452	11.31	8.47	7.61-6.99	9.55	8.98	—	—
1	293, 405, 481	—	8.49	7.82-7.00	9.56	9.00	3.37	2.51
HL^2	295, 372, 460	11.25	8.48	7.63-6.56	9.56	9.00	—	—
2	305, 380, 479	—	8.49	7.82-7.00	9.58	9.01	3.39	2.50

Table 4. Thermogravimetric analysis of UO_2(II)-complexes **1** and **2**.

Compound	% Loss in weight found (calcd.)	Temperature range (°C)	Assignment (thermal process)
$[(UO_2)_2L^1(AcO)_3(H_2O)]\cdot H_2O$ (**1**)	1.61 (1.53)	50-100	Loss of hydrated H_2O.
$[(UO_2)_2L^1(AcO)_3(H_2O)]$	1.48 (1.53)	120-175	Removal of coordinated H_2O.
$[(UO_2)_2L^1(AcO)_3]$	14.67 (15.04)	230-295	Elimination of coordinated acetate groups.
$[(UO_2)_2L^1]$	33.21 (33.33)	305-1000	Complete decomposition of the complex and formation of metal oxide as a final product.
$[(UO_2)_2L^2(AcO)_3(H_2O)]\cdot 2H_2O$ (**2**)	2.11 (2.88)	60-90	Loss of hydrated H_2O.
$[(UO_2)_2L^2(AcO)_3(H_2O)]$	1.83 (1.44)	136-180	Removal of coordinated H_2O.
$[(UO_2)_2L^2(AcO)_3]$	14.24 (14.15)	220-275	Elimination of coordinated acetate groups.
$[(UO_2)_2L^2]$	35.64 (35.83)	307-1000	Complete decomposition of the complex and formation of metal oxide as a final product.

Table 5. Antimicrobial activities of HL^1, HL^2 and their UO_2(II)-complexes **1** and **2**.

Compound	Inhibition zone diameter (mm mg^{-1} sample)			
	E. coli (G^-)	*S. aureus* (G^+)	*A. flavus* (Fungus)	*C. albicans* (Fungus)
Control: DMSO	0.0	0.0	0.0	0.0
Tetracycline (Antibacterial agent)	33.0	30.0	—	—
Amphotericin B (Antifungal agent)	—	—	20.0	20.0
HL^1	13.0	14.0	0.0	0.0
Complex 1	15.0	15.0	0.0	0.0
HL^2	13.0	15.0	0.0	0.0
Complex 2	18.0	18.0	11.0	0.0

UV-Vis spectra and magnetic moment measurements

The electronic spectral data of the ligands and their UO_2(II) complexes in DMF solution are presented in Table 3. HL^1 and HL^2 displayed mainly three bands; the first band appeared within the 290-295 nm range due to the low energy π—π* transition corresponding to $^1L_b \leftarrow {}^1A$ state of the phenyl ring, while the second band appeared within the 372-376 nm range due to the n—π* transition. The third band appeared in the 452-460 nm range which can be assigned to charge transfer (CT) transitions within the whole molecule [50]. The UO_2(II)-complexes mainly showed a weak band near 480 nm and a highly intense band in the range 293-305 nm which are attributed to $^1\Sigma_g^+ \rightarrow {}^3\pi_u$ transitions and charge transfer being overlapped with π—π* transition, respectively [51]. It may be noted that the band occurring in the 380-405 nm range is due to the uranyl moiety because of apical oxygen→f^o(U) transition being merged with the ligand band due to n→π* transition as evident from broadness and intensity [52]. UO_2(II) complexes **1** and **2** show diamagnetic properties, as expected [53].

^{1}H NMR spectra

In order to determine the center of chelation and replaceable hydrogen upon complex formation, ^{1}H NMR spectra of the free ligands were studied and compared with the spectra of their UO_2(II)-complexes (Table 3). The signals at 11.31 and 11.25 ppm due to δ_{OH} in the spectra of HL^1 and HL^2 disappeared in the ^{1}H NMR spectra of the complexes denoting that complex formation occurs *via* deprotonation of the OH group [54]. The azomethine proton (–CH=N–) appeared as a singlet at 8.47 and 8.48 ppm in the free ligands has downfield shifts upon complex formation, supporting participation of the azomethine nitrogen in coordination to UO_2(II) ion [9]. The signals at 7.63–6.56, 9.56–9.55, and 9.00–8.98 ppm due to δ_{Ar}, δ_{NH} and δ_{NH2} in the free ligand spectra have downfield shifts in the spectra of the complexes due to increased conjugation on coordination, supporting the coordination of the ligands to UO_2(II) ion. The downfield shift of these signals is due to deshielding by UO_2(II) [55]. The ^{1}H NMR spectra of UO_2(II)-complexes displayed two new signals at 2.50-2.51 and 3.37-3.39 ppm for water and CH_3 from acetate, respectively [24]. Thus, the ^{1}H NMR results support the IR inferences.

Thermal analysis

Thermal analysis was used to confirm the molecular structure of the complexes. Also, the thermal stability, properties, nature of intermediates and final products of the thermal decomposition of coordination compounds can be obtained from thermal analysis [56]. From the TGA curves, the mass loss can be calculated for the different decomposition steps and compared with those theoretically calculated for the suggested formula based on analytical and spectral results, as well as molar conductance measurements. TGA indicates the formation of a metal oxide as the end product from which the metal content could be calculated and compared with that obtained from analytical data. The investigated complexes **1** and **2** were subjected to TGA to throw more light on their molecular structures. The obtained results and the thermal decomposition patterns are presented in Table 4. From the tabulated results it can be concluded that the thermal decomposition of the complexes takes place in four steps. The lattice water molecules were volatilized within the temperature range of 50—100°C while the coordinated water molecules were removed within the range of 120—180°C. The number of water molecules was determined from the percentage weight losses at these steps. The removal of coordinated acetate groups was observed within the 220—295°C range [11]. The complete decomposition of the organic ligands occurred at temperatures higher than 305°C. The final product was the metal oxide. The metal content was also determined from the percentage weight of the remaining oxide, which was also used to calculate the molecular weight of the investigated complexes. The values determined were concordant with those obtained from the mass spectral studies.

In-vitro antimicrobial assay

It was reported that the biological and medicinal potency of coordination compounds has been established by antitumor, antiviral, and antimalarial activities, related to the ability of the metal ion to form complexes with ligands containing nitrogen and oxygen donors [57]. The *in vitro* anti-microbial activities of the investigated ligands and complexes were tested against *A. flavus*, *C. albicans*, *E. coli*, and *S. aureus* by the modified Kirby–Bauer disc diffusion method [37]. Standard drugs tetracycline and amphotericin B were also tested for their antibacterial and antifungal activities at the same concentrations and conditions. The complexes had significant antimicrobial activities against the tested

organisms compared with the free ligands (Table 5). Complexes **1** and **2** exhibited high activity against different types of the tested bacteria. Complex **2** displayed moderate activity against *A. flavus*, whereas complex **1** and free ligands are inactive against it. Ligands and complexes are inactive against *C. albicans*. Compared with tetracycline and amphotericin B, the complexes were less active. The data prove the potential of complexes **1** and **2** as broad-spectrum antibacterial agents. Also, complex **2** can be used as an effective antifungal agent against multicellular fungi. It is well known that the activity of any compound is a complex combination of steric, electronic, and pharmacokinetic factors. The action of the compounds may involve the formation of a hydrogen bond through —N=C of the chelate or the ligand with the active centers of the cell constituents resulting in interference with normal cell process [58]. The microbotoxicity of the compounds may be ascribed to the metal ions being more susceptible toward the bacterial cells than the ligands [59]. The improved activities of the metal complexes as compared to the ligand can be explained on the basis of the chelation theory [60]. This theory explains that a decrease in the polarizability of the metal could enhance the lipophilicity of the complexes, which leads to a breakdown of the permeability of the cells, resulting in interference with normal cell processes [61]. This indicates that the chelation tends to make the Schiff bases act as more powerful and potent antimicrobial agents, thus inhibiting the growth of bacteria and fungi more than the parent Schiff bases [62, 63]. Therefore, it is claimed that the process of chelation dominantly affects the biological behavior of the compounds that are potent against microbial and fungal strains. *E. coli* was selected as the backbone of Gram negative bacteria whereas *S. aureus* was selected to represent Gram positive bacteria. Also, *A. flavus* was selected as a higher fungus which represents multicellular fungi whereas *C. albicans* represents the unicellular fungi; they represent a broad spectrum of test organisms. So, the obtained data prove the usefulness of UO_2(II)-complexes as broad-spectrum antimicrobial agents.

CONCLUSION

Two azo-azomethine ligands and their bi-homonuclear uranyl complexes were prepared and characterized. Analytical data, molar conductance measurements, magnetic susceptibility, TOF-mass, IR, UV-Vis, and ^{1}H NMR spectral studies suggest octahedral geometry of the complexes. The ligands coordinate to the metal ions *via* the nitrogen atom of the pyrimidine ring, the oxygen atom of the sulfonamide group, the azomethine-N, and the oxygen atom of OH group in two chelation centers. Conductance data reveal that the complexes are non-electrolytes. The thermal data confirmed the suggested formula based on spectral results. The synthesized complexes were active against bacteria (*E. coli* and *S. aureus*) and fungi (*A. flavus*), thus giving a new thrust of these compounds in the field of metallo-drugs (bio-inorganic chemistry). Also, metal complexes of such type are of interest especially due to their potential as biocides and nematicides with unique electrical and magnetic properties [64].

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ГРУПИ ОТ АЗО-АЗОМЕТИНОВИ ЛИГАНДИ С N_2O_2 –ДОНОРИ И ТЕХНИТЕ ДВУЯДРЕНИ КОМПЛЕКСИ С UO_2(II): СИНТЕЗА, ОХАРАКТЕРИЗИРАНЕ И БИОЛОГИЧНА АКТИВНОСТ

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(Резюме)

Синтезирани са две азо-азометинови лиганди с донор от N_2O_2 и техните двуядрени комплекси с UO2(II) за терапевтични цели Лигандите са получени чрез кондензация на 4-(4-хидрокси-3-формил-1-илазо)-N-пиримидин-2-ил-бензенсулфонамид с етилендиамин и 1,6-хександиамин. Получените лиганди и техните двеномоядрени уранилови комплекси са характеризирани с термични анализи (TGA и конвенционален метод), вибрационни, електронни, 1H NMR и масспектри, както и чрез различни физикохимични техники. Активните координационни центрове в лигандите и геометричното разположение на комплексите са изследвани с помощта на спектрални данни. Измервания на моларната проводимостта в разтвор на DMSO показа, че комплексите са не-електролити. Изследваните комплекси и лиганди бяха скринирани ин витро за тяхната антимикробна активност срещу гъби (Aspergillus flavus and *Candida albicans*), грам-положителни бактерии (*Staphylococcus aureus*) и грам-отрицателни бактерии (*Escherichia coli*). Установено е, че комплексите са по-мощни фунгициди и бактерициди, отколкото лигандите.