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Synthesis, Characterization and Biological Activities of Some Organotin(IV) Complexes

WAJID REHMAN*, BAKHTIAR MUHAMMAD, ZONERA HASSAN†, JAMIL KHAN‡, NADIA BASHIR, ABDULLAH KHAN¶ and GULZAR HAMMED§
Department of Chemistry, Hazara University, Mansehra, Pakistan
E-mail: sono_waj@yahoo.com

Organotin(IV) complexes with the general formulae R_3SnL (R: alkyl and L: Schiff base) have been prepared and the bonding in these complexes were studied through various spectral techniques like IR, ^1H and ^{13}C NMR. The alkyl and phenyl groups attached to the tin(IV) atom have been assigned by the comparison of experimental chemical shifts with those calculated data. The novel complexes and the ligand, soluble in dimethyl sulphoxide have been screened against various types of bacteria for their antibacterial activity.

Key Words: Organotin, Schiff base, Spectroscopic studies, Antibacterial activity.

INTRODUCTION

The first organotin compound was diethyltindiiodide, discovered by Frankland in 1849[1]. Recently, there has been a great deal of public attention focused on the toxicological and ecotoxicological aspects of organotins. Organometallic compounds containing lead, tin and mercury are all commercially significant. A large number of organotin compounds, for example, are used as pharmaceuticals, pesticides, stabilizers and fire retardants. Organotins with three organic groups can be powerful fungicides and bactericides, depending on the organic group R. Tin has a large number of organometallic derivatives that are used commercially. Their demand increased the worldwide production of organotin compounds during the last 50 years. Unlike their carbon analogues, tin compounds can also be coordinated to 5 and even 6 atoms instead of the regular four[2]. Organotins compounds have wide agricultural and industrial applications. These may accumulate in the food chain and induce imposex in several marine species as well as neurotoxic and immunotoxic effects in higher animals. The discovery of several new organotin species and new applications has led to renewed interest in organotin complexes.

†Department of Biochemistry, Hazara University, Mansehra, Pakistan.
‡Department of Chemistry, Comsats University, Tobe Camp, Abbottabad, Pakistan.
¶Department of Environmental Sciences, Haripur Campus, Hazara University, Mansehra, Pakistan.
§Department of Chemistry, Gomal University, Dera Ismail Khan, NWFP, Pakistan.

In order to spread the scope of study on the coordination conduct of various donor ligands including Schiff base towards organotins, we carried out the several experiments and established their bioactivities[3-9]. As an extension of this research field, we are now interested in the development of the chemistry of some novel organotin compounds obtained by the interaction of a number of diorganotin(IV) halides with the Schiff base derived from salicylaldehyde and urea. Furthermore, it was also intended to screen these complexes for wide spectrum antibactericidal activities against *Staphylococcus aureus*, *Escherichia coli* and *Mycobacterium leprae*.

EXPERIMENTAL

Analytical grade solvents (methanol, chloroform, petroleum ether, acetone and benzene) supplies by Merck, Germany were used. Organotin chlorides and NaOH were obtained from Aldrich Chemicals, dimethyl sulphoxide from Fluka chemicals and were used according to the standard methods[10]. The melting points were measured on a Reichert thermometer. IR Spectra were obtained while using a FTIR-1605 spectrophotometer, Bio-Rad Marlin. Elemental analysis was carried out on a Yanaco MT-3 high-speed CHN analyzer with antipyrene as a reference compound and ^{1}H and ^{13}C NMR spectra were recorded on a Brucker AM 270 instrument at 50 MHz probe. The conductance of the complexes was measured on a Conductometer HANNA equipped with microprocessor HI 9835 at 17.4 °C.

Synthesis of Schiff base: The 1,3-*bis*(2-hydroxybenzylidene)urea derived from urea and salicyaldehyde was prepared from urea 10 mmol and salicyaldehyde 20 mmol. This mixture was refluxed in benzene for 0.5 h. The water formed during the reaction was removed by a Dean/Stark trap to yield yellow solid product. The product was thoroughly washed with chloroform. The solid complexes were recrystallized from a 1:2 (v/v) mixture of methanol and petroleum ether/chloroform.

Synthesis of complexes: The ligand 10 mmol was dissolved in 25 mL methanol in a three-necked round bottom flask equipped with a reflux condenser, thermometer and a drying tube. Stoichiometric amount of NaOH was added, followed by the appropriate amount of triorganotin(IV)chloride in 25 mL methanol drop wise with constant stirring for 0.5 h. The reaction mixture was then refluxed for 5 h under nitrogen. The reaction was centrifuged and filtered to remove the NaCl. The filtrate was concentrated under vacuum. Some complexes obtained were liquid and some were solids. The solid complexes were recrystallized from a 1:2 (v/v) mixture of methanol and chloroform.

RESULTS AND DISCUSSION

1,3-*Bis*(2-hydroxybenzylidene)urea: The working solutions of the reactants used were 10 mmol of urea and 20 mmol of salicyldehyde. Physical state: amorphous solid. Recrystallization solvent: acetone/petroleum ether. m.p. 129 °C; yield: 70 %; molecular mass; 268.27; molar conductance: 10.04 μS cm^{-1} at 17.4 °C;

elemental analysis (%) for $C_{15}H_{12}N_2O_3$ calcd. (found) C: 67.22 (67.16); H: 4.51 (4.24); N: 10.44 (10.24); O: 18.89 (18.40).

1,3-*Bis*(2-(triethylstannyloxy)benzylidene)urea: The amounts of reactants used were 10 mmol of Schiff base, 20 mmol of NaOH and 20 mmol of triethyltin chloride. Physical state: amorphous solid; recrystallization solvent: acetone/petroleum ether; m.p. 149 °C; yield: 75 %; molecular mass: 625; molar conductance: 17.4 μS cm^{-1} at 17.4 °C; elemental analysis (%) for $C_{25}H_{39}NO_2Sn_2$ calcd. (found) C: 48.83 (48.50); H: 5.95 (5.24); N: 4.29 (4.24); O: 7.08 (7.02); Sn: 35.02 (35.10).

1,3-Bis(2-(triphenylstannyloxy)benzylidene)urea: Quantities of the reactants used were 10 mmol of Schiff base, 20 mmol of triphenyltin chloride and 20 mmol of NaOH. Physical state: amorphous solid. Recrystallization solvent: THF. m.p. 138 °C; yield: 75 %; molecular mass: 913; molar conductance: 132.80 μS cm^{-1} at 17.4 °C; elemental analysis: (%) for $C_{49}H_{39}NO_2Sn_2$ calcd. (found) C: 63.42 (63.40); H: 4.33 (4.27); N: 2.89 (2.53); O: 3.15 (3.90); Sn: 24.58 (24.64).

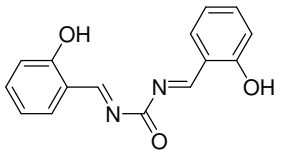
1,3-*Bis*(2-(tribenzylstannyloxy)benzylidene)urea: Quantities of the reactants used were 10 mmol of Schiff base; 20 mmol of tribenzyltin chloride and 20 mmol of NaOH. Physical state: Amorphous solid; Recrystallization solvent: THF; m.p.: 138°C; Yield: 75%. Molecular Mass: 997; Molar Conductance 1328 μS cm^{-1} at 17.4°C. Elemental analysis (%) for $C_{35}H_{51}N_2O_2Sn_2$ calcd. (found) C: 65.39 (65.29); H: 4.58 (4.51); N: 4.68 (4.62); O: 3.52 (3.48); Sn: 22.75 (24.69).

Molar conductance: Molar conductances of the organotin(IV) complexes have been measured in methanol or DMSO depending upon the solubility[11]. Molar conductance values of the complexes and Schiff bases show very low values of molar conductance[12].

IR Spectroscopy: The IR spectral vibrations in the range of 1735-1640 cm^{-1} assigned to ν(C=N) and ν(C=O) in the ligand and complexes[13]. These two peaks lie in the same region, so it is difficult to distinguish between them which are the characteristics of Schiff base. The IR spectra in Schiff base of ν(OH) shows strong band in the 3315 cm^{-1}, which was found absent in the complexes indicating deprotonation. The peaks lie in the range 1750-1700 and 2964 cm^{-1} in the ligand and complexes confirm the presence of C=O and C-H group, respectively[13]. When spectra of Schiff base and complex were compared, more bands were observed in the complexes. The IR spectra of the synthesized compounds substantiate that the absorption bands of Sn-O and Sn-C are in consistence with the earlier reported work[14]. The explicit feature in the spectra of complexes is the presence of bands at 400-500 cm^{-1} for (Sn-O) and (Sn-C) indicating the complex formation[15]. The ν(Sn-C) and ν(Sn-O) vibrations were observed in the range of 555-520 and 578-470 cm^{-1}, respectively.

^{1}H and ^{13}C NMR Spectroscopy: In ligand ^{1}H and ^{13}C NMR spectra -OH peaks observed at 5 and 161 ppm which are absent in complexes, this indicates the deprotonation of alcoholic proton and the complexation of the ligand, respectively[16]. The C=N and C=O peaks are at 163 and 191-193 ppm in ligand and complexes

which indicate that these bonds are not involved in the bonding, respectively[17]. The prediction of geometry can be (Figs. 1-8) assigned by coupling such coupling are not observed in complexes due to overlapping of signals[17]. ^{119}Sn values for complexes are in –ive unknown zone which are similar to those obtained for tetrahedral complexes[18].



1,3-bis(2-hydroxybenzylidene)urea

Fig. 1. Proposed structure of ligand

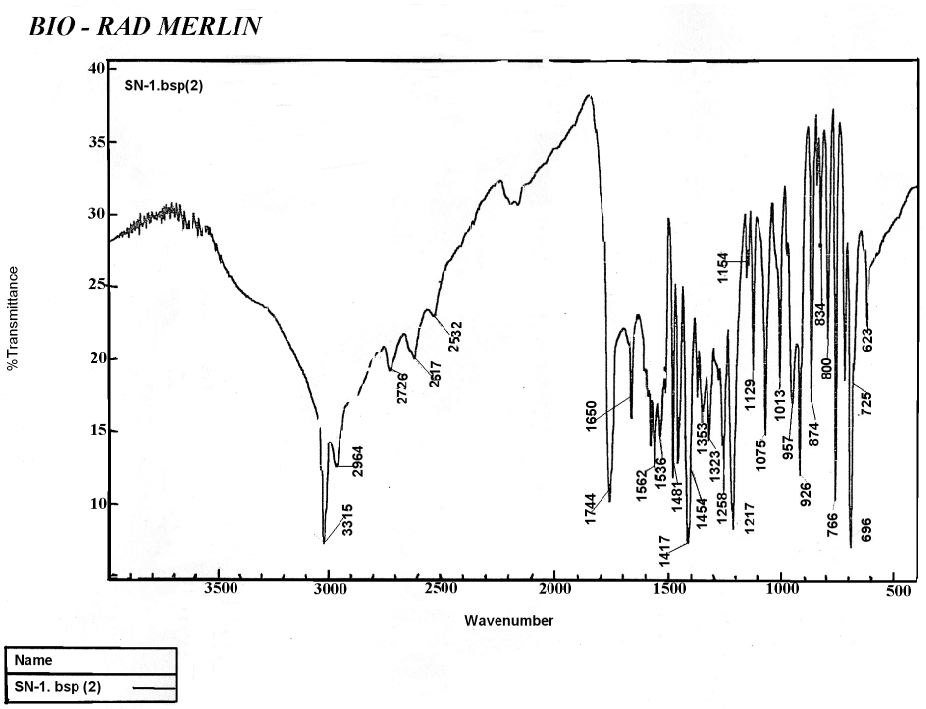
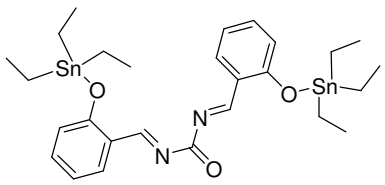


Fig. 2. IR Spectra of ligand



1,3-bis(2-(triethylstannyloxy)benzylidene)urea

Fig. 3. Structure of complex-**I**

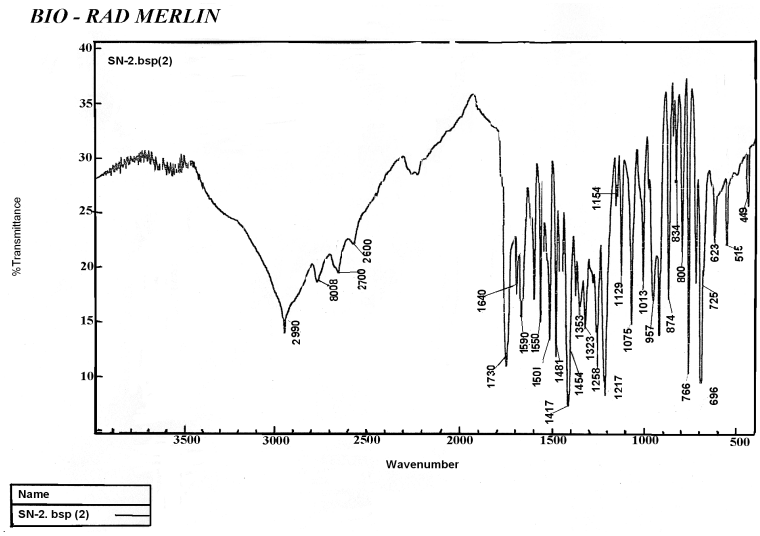
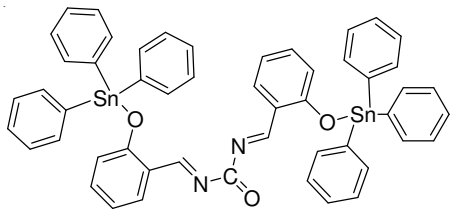


Fig. 4. IR Spectra of complex-**II**



1,3-bis(2-(triphenylstannyloxy)benzylidene)urea

Fig. 5. Structure of complex-**II**

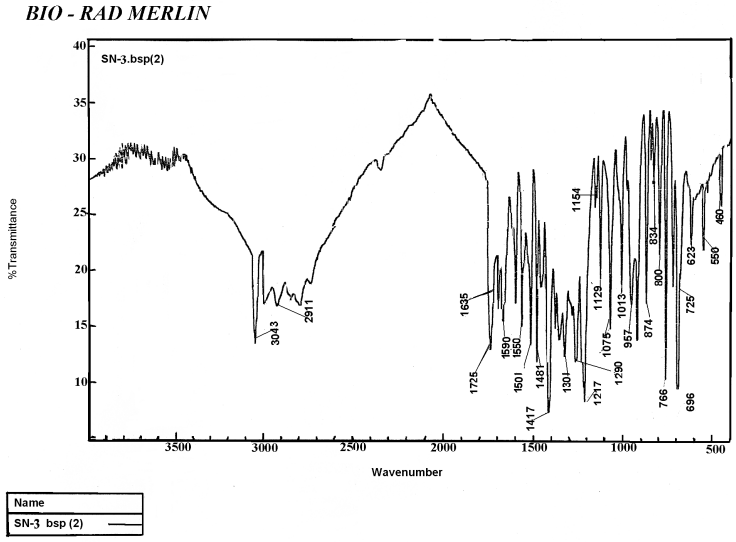
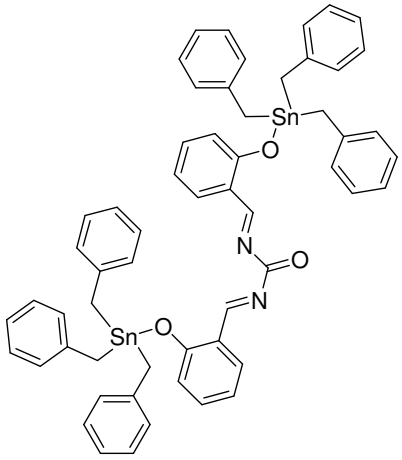


Fig. 6. IR Spectrum of complex-**II**



1,3-bis(2-(tribenzylstannyloxy)benzylidene)urea

Fig. 7. Structure of complex-**III**

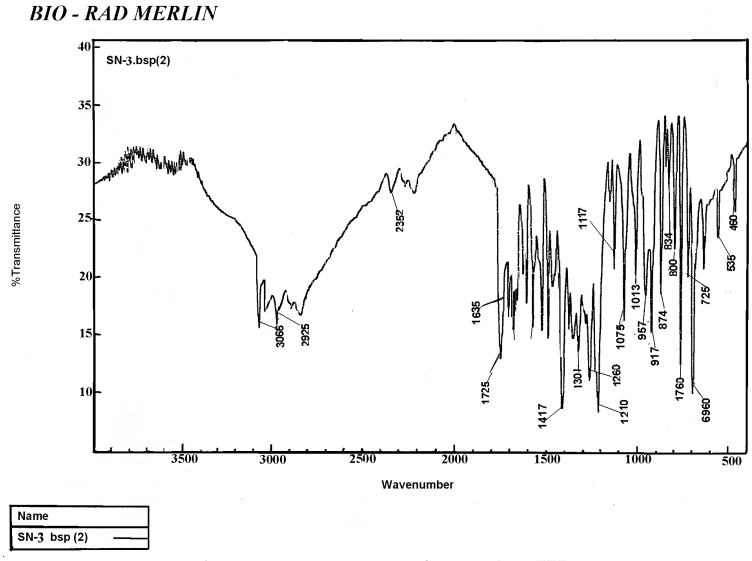


Fig. 8. IR Spectrum of complex-**III**

^{1}H NMR spectrum of ligand: Element/chemical shifts, -OH: 5, CH-aromatic: 6.8-7.4, C=N: 8.1, ^{13}C NMR spectrum of ligand:elements/chemical shifts. CH-aromatic: 118-129, -OH: 161, C=N:163, C=O: 193, IR spectrum of ligand:element/wave number, -OH: 3315, CH: 2964, C=O: 1744, C=N: 1650.

^{1}H NMR: element/chemical shift, -OH: absent, C-H aromatic: 6.4-8, C=N: 8.1.6, Sn-C: -ive unknown zone, CH_2-aliphatic: 1.4, CH_3-aliphatic: 0.9, ^{13}C NMR: element/chemical shift, CH-aromatic: 121-142, C-OH: absent, (C=N): 162. C=O: 191. Sn-C: -ive unknown zone, CH_2-aliphatic: 2.1, CH_3-aliphatic: 8.6, IR: element/wave number. OH: absent, CH: 2990, C=O: 1730, C=N: 1648, Sn-C: 515, Sn-O: 449.

^{1}H NMR: element/chemical shift, -OH: absent, C-H aromatic: 7.1-7.3, CH=N: 8.2, Sn-CH: -ive unknown zone, CH-O: 6.8 ^{13}C NMR: element/chemical shift, CH-aromatic: 118-140, OH: absent, C=N: 160, C=O: 190, Sn-C: 129, C-O: 168, C-H: 128, Sn-O: -ive unknown zone. IR element/wave number, -OH: absent, CH: 3043, C=O: 1725, C=N: 1635, Sn-C: 550, Sn-O: 460.

^{1}H NMR: element/chemical shift, -OH: absent, C-H benzylidene: 6.4-8, C=N: 8.16, Sn-CH: 10.71, CH_2-aliphatic: 1.4, CH-benzene: 7.06-7.14, Sn-O: -ive unknown zone, ^{13}C NMR: element/chemical shift, CH-aromatic: 102-132, C-O: 128, C=N: 161, C=O: 191, Sn-C: unknown zone, Sn-O: -ive zone, CH_2: 12.5-14.12. IR: element/wave number, OH: absent, CH: 3066, C=O: 1735, C =N: 1649, Sn-C: 480, Sn-O: 535).

Antibacterial activity: The antibacterial activity was determined by using the agar well diffusion method[19]. The well was dug in the media with a sterile borer and 8 h bacterial inoculum containing *ca.* 10^4-10^6 colony-forming units (CFU)/mL was spread on the surface of the nutrient agar using a sterile cotton swab. The recommended concentration of the best sample (2 mg/mL in DMSO) was introduced into respective wells. Other wells containing DMSO and the reference antibacterial drug served as negative and positive controls, respectively. The plates were incubated immediate at 37 °C for 20 h. The activity was determined by measuring the diameter of the inhibition zone (in mm) showing complete inhibition. Growth inhibition was calculated with reference to the positive control. Agar well diffusion method has substantiated the activity of Schiff base ligand and complexes against *Staphylococcus aureus*, *Escherichia coli* and *Mycobacterium leprae*, respectively. Data revealed that the ligand and complexes have significant activities against the pathogenic bacteria[20]. This activity is more in the complexes than in the ligand. The results compared with standard drug (imipinem) have indicated that compounds are active but activity is less than the standard drug[20]. Growth inhibition studies of the standard drug (imipinem) the synthesized ligand and their tin complexes against the different species are as follow.

The data in Table-1 indicates that the Schiff base ligand and their complexes have a profound antibacterial activity against the two species; namely *Mycobacterium leprae* and *Staphyllococcus aureus*. The results in Table-1 reveal that the activity of the synthesized compounds is lower than that of the imipinem, the standard drug[21]. The data also apparently show that the antibacterial activities of the complexes are higher than that of the ligand. Among the complexes, the activity of the complex **I** remained lower than that of the complex **II** and complex **III**. The results also substantiated that the bactericidal effect of ligand and its complexes on *E. coli* has been minimal. The data show that the diameter of growth inhibition zone of complexes **2** and **3** remained high, the diameter being 25 mm. This indicates that the toxicity of the complex **II** and complex **III** remained high for *Mycobacterium leprae* and *Staphyllococcus aureus*, respectively. *Bis*(tributyltin) oxide (TBTO) has previously been reported[21] to have an effective control against *Staphyllococcus aureus* (Figs.

9-11). Like wise, the activity of TBTO is similar to the compounds synthesized during this study. The novel synthesized compounds are cost effective and are easy in synthesizing. Although, the toxicity of the standard drug is high, the side effects of the drug are also high. The synthesized complexes can be regarded as novel and these complexes have never been reported previously and whose properties are yet to be discovered. It is likely that the new complexes might be more environments friendly and better use as compared to the standard drug[22-23].

TABLE-1
GROWTH INHIBITION ZONE (DIAMETER IN MILLIMETER)

Species	Ligand	Complex **I**	Complex **II**	Complex **III**	Standard drug
Mycobacterium leprae	15	20	25	23.5	30
Staphylococcus aureus	18	21	22	25.0	31
Escherichia coli	5	9	7.5	8.0	23

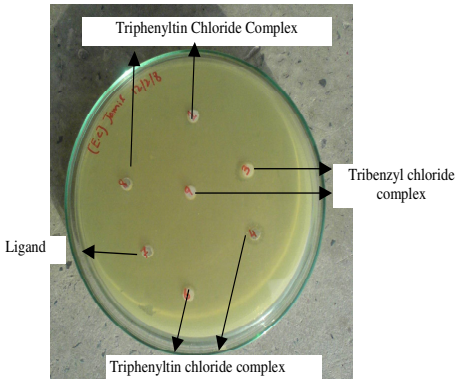


Fig. 9. *Antiescherichia coli* activities

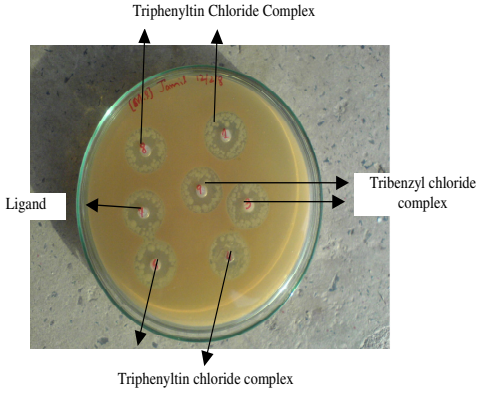


Fig. 10. *Antimicrobacterium leprae* activities

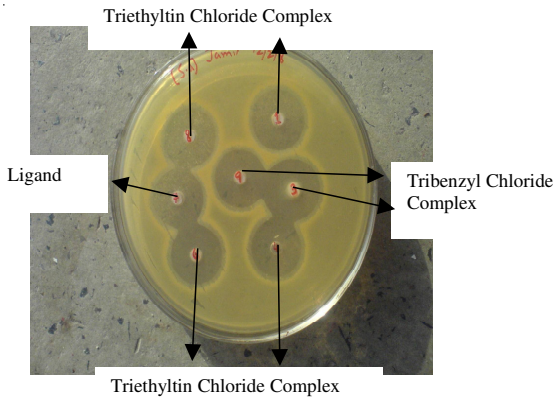


Fig. 11. *Antistaphylococcus aureus* activities

Conclusion

Controlling resistant bacteria is an increasingly challenging endeavor and is a major concern for specialists around the world. The goal of this paper was to focus specifically on the scientific challenges of antibacterial research from the pharmaceutical companies' perspective. Data of paper shows synthesized new antibacterial complexes that can be used as *Antistaphylococcus aureus* and *Antiescherichia coli* drugs.

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