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Synthesis, physicochemical and antimicrobial properties of rhenium (I) tricarbonyl complexes of isatin Schiff bases

Adebomi A. Ikotun[1*], Abimbola A. Owoseni[2] and Gabriel O. Egharevba[3]

[1]Industrial Chemistry Programme, College of Agriculture, Engineering and Sciences, Bowen University, Iwo, Nigeria.
[2]Microbiology Programme, College of Agriculture, Engineering and Sciences, Bowen University, Iwo, Nigeria.
[3]Department of Chemistry, Obafemi Awolowo University, Ile-Ife, Nigeria.

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The Schiff base of isatin and sulphanilamide (L1; $C_{14}H_{11}N_3O_3S$) was prepared and reacted with $Re(CO)_5X$ (X = Cl and Br) in toluene to give $[Re(C_{14}H_{10}N_2O)(CO)_3X]$ (X = Cl, 1 and X = Br, 2). The prepared Schiff base of isatin and 4-methoxyaniline (L2; $C_{15}H_{12}N_2O_2$) was reacted with $Re(CO)_5X$ in toluene to give $[Re(C_{14}H_{10}N_2O)(CO)_3X]$, where X = Cl, 3 and X = Br, 4. L2 and $Re(CO)_5Br$ were refluxed in dry toluene under nitrogen and recrystallized to give $[Re(C_{15}H_{12}N_2O_2)(CO)_3Br].^1/_2C_2H_5OH$ (5). Spectroscopic characterization of compounds was done using FTIR, UV-Visible, NMR and Mass spectra analyses. Magnetic susceptibility measurements and melting points were also determined. Elemental analysis of 5 revealed it was a solvate molecule of 4. The *in-vitro* antimicrobial activities of compounds were evaluated against *Staphylococcus aureus, Bacillus subtilis,* Haemolytic *Staphylococcus aureus*, *Pseudomonas aeruginosa, Escherichia coli, Klebsiella* sp., *Aspergillus niger*, *Trichoderma viride* and *Penicillium citrinum*. Spectroscopic analyses revealed new terminal carbonyl bands formed between 1900 and 2030 cm^{-1}, as L1 and L2 coordinated through their azomethine nitrogen and keto oxygen donor atoms towards Re(I). Results of the antimicrobial studies revealed immerse improved activities upon coordination against tested microorganisms especially gram-negative bacteria, therefore they are recommended for further studies in cell imaging.

Key words: Isatin Schiff bases, rhenium (I) tricarbonyl complexes, antimicrobial, antifungal.

INTRODUCTION

Indole-2,3-dione (isatin) is a versatile starting material in syntheses. Its Schiff bases and complexes have been found to possess several pharmacological effects including anticonvulsant, antimicrobial and antiviral activities, inhibition of monoamine oxidase (Sridhar et. al., 2002; Adetoye et al., 2009), behavioural effects (Chohan et al., 2006) and activities against human immune-deficiency virus (Sriam et al., 2005). Isatin is an endogenous compound found in the brains and some tissues of mammals (Sridhar et al., 2002). It was first

*Corresponding author. E-mail: ikotunadebomi@gmail.com or adebomi.ikotun@bowen.edu.ng. Tel: +234 803 585 6562.

isolated from the fruits and flowers of the Cannon ball tree (*Couroupita gueanensis*), thereafter its good antioxidant, antibacterial and anticancer properties have also been established (Premanathan et al., 2012; Guo, 2019; Ding et al., 2020). Coogan et al. (2009) and Azzarelli et al. (2019) have also shown that heavy metals are not just "poisonous", but also possess great biological importance through the synthesis of several novel d^6 transition organometallic based agents, which were also used to target specific biological entities. Therefore, the coordination of Re(I) to isatin Schiff bases is promising with prospective biological activities which could even target biological entities of cancerous cells and could also possess some therapeutic anticancer effects. Presently, there is little or no report on Re(I) complexes of isatin derivatives. All these primarily motivated this research, which aimed at preparing new biologically active Re(I) tricarbonyl complexes of isatin derivatives. Previously, the Re(I) tricarbonyl complexes of the Schiff base of isatin and aniline with good antimicrobial activities were reported (Ikotun et al., 2019a). In this paper, the successful preparations of Re(I) tricarbonyl complexes of the Schiff bases of isatin with sulfanilamide and isatin with 4-methoxyaniline as well as its antimicrobial activities were reported.

EXPERIMENTAL

Chemicals

Isatin, 4-methoxyaniline, sulphanilamide, $Re(CO)_5Cl$ and $Re_2(CO)_{10}$ were obtained from Aldrich. $Re(CO)_5Br$ was prepared from $Re_2(CO)_{10}$ according to literature (Angelici, 1990). The solvents methanol, ethanol, chloroform and *N,N*-dimethylformamide (DMF) were all purchased from Sigma-Aldrich and SAARChem.

Instrumentation

The Infrared spectra were recorded on a Shimadzu IRAffinity-1 spectrometer with a pike MIRacle ATR system (diamond crystal) in the range of 4000 to 400 cm^{-1}. The ^1H NMR and ^{13}C NMR (400 MHz) spectra were recorded at room temperature on Bruker Spectrometer. The UV-Visible spectra were recorded on a Shimadzu UV-1800 spectrometer. Mass spectra were determined using a Fisons VG Quattro Spectrometer, a MicromassZabspec instrument (FAB) or an Applied Biosystem STR Voyager (MALDI-TOFMS) instrument, equipped with a nitrogen laser (337 nm, 3 ns pulse, 20 Hz maximum firing rate). Room temperature magnetic susceptibility measurements were measured using Johnson Matthey Magnetic Susceptibility balance. The monitoring of the reactions and the purity of the compounds were checked by Thin-Layer Chromatography (TLC) carried out on Silica Gel 60 F254 alumina plates (E Merk) using appropriate solvent mixtures of chloroform: diethyl ether (either 5:5 or 6:4) and visualized in UV chamber (365 nm). The melting points of compounds were determined using a Gallenkemp variable heater apparatus or an OptiMelt MPA 100 apparatus, which possesses a digital image processing technology. Microanalysis of compounds was carried out at University of Notre Dame, Notre Dame, Indiana, United States.

Syntheses

Preparation of the ligands

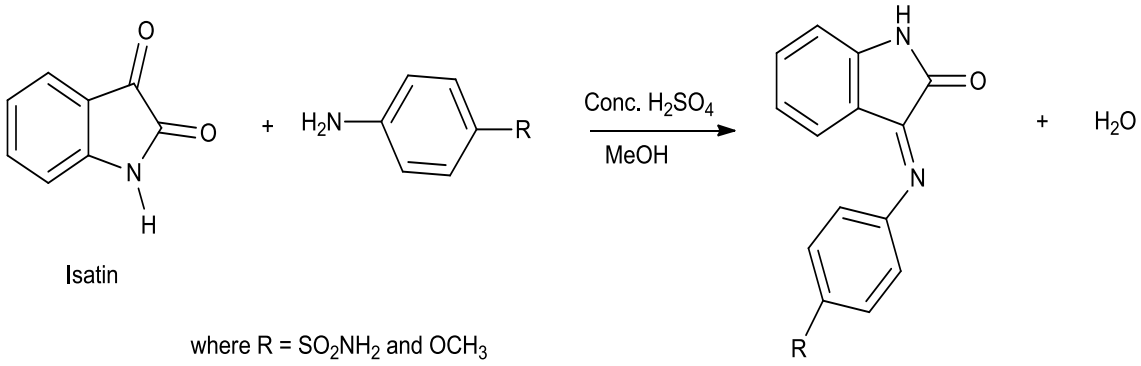
The ligands were prepared according to literature (Adetoye et al., 2009). L1 ($C_{14}H_{11}N_3O_3S$) was prepared by completely dissolving isatin (5 g; 339.8 mmol) in 200 ml methanol. Sulphanilamide (5.85 g; 339.8 mmol) was added while stirring at room temperature with the addition of 8 drops of concentrated H_2SO_4. Stirring was done at room temperature for $1^1/_2$ h. The precipitated yellow solid was filtered out and recrystallized in ethanol: chloroform (70: 30). The yield was 9.43 g (92%). Likewise, L2 ($C_{15}H_{12}N_2O_2$) was prepared by completely dissolving isatin (3 g; 20.40 mmol) in 120 ml methanol, 4-methoxyaniline (2.51 g; 20.40 mmol) was added and it was stirred at room temperature with the addition of 6 drops of concentrated H_2SO_4 for $2^1/_2$ h. The light yellow solid was filtered and recrystallized in ethanol: chloroform (7:3). The yield was 4.53 g (88%).

Preparations of rhenium complexes

The rhenium (I) tricarbonyl complexes were prepared according to literature (Ikotun et al., 2019a,b). Complex 1, $[Re(C_{14}H_{11}N_3O_3S)(CO)_3Cl]$ was prepared with 0.04 g (0.14 mmol) of L1 and 0.05 g (0.14 mmol) of $Re(CO)_5Cl$ stirred in 20 ml toluene at 100°C for $4^1/_2$ h. The light purple solids were filtered out under suction after cooling in the oil and this weighed 0.07 g (87%). Likewise, $[Re(C_{14}H_{11}N_3O_3S)(CO)_3Br]$ (2) was prepared by stirring $Re(CO)_5Br$ (0.2 g; 0.4931 mmol) and 0.14 g (0.4931 mmol) of L1 in 20 ml of hot toluene at 100°C for 20 h. The purple precipitate was filtered out under vacuum after cooling. This weighed 0.2797 g (92% yield). Also, $[Re(C_{15}H_{12}O_2N_2)(CO)_3Cl]$ (3) was prepared by stirring L2 (0.037 g; 0.14 mmol) and $Re(CO)_5Cl$ (0.05 g; 0.14 mmol) in 20 ml of toluene 3 h at 100°C. The solution was allowed to cool in oil, the light purple precipitate was filtered under vacuum and it weighed 0.04 g (49%). Similarly, $[Re(C_{15}H_{12}O_2N_2)(CO)_3Br]$ (4) was prepared by stirring L2 (0.0621 g; 0.2465 mmol) to complete dissolution in 10 ml toluene at 100°C and then adding $Re(CO)_5Br$ (0.1 g; 0.2465 mmol) to the solution. Stirring was done for 29 h in the hot solvent, the solvent was then removed under vacuum to yield purple amorphous solids (0.1461 g; 98%). The preparation of $[Re(C_{15}H_{12}O_2N_2)(CO)_3Br].^1/_2\ C_2H_5OH$ (5) was done by refluxing L2 (0.062 g; 0.2465 mmol) and $Re(CO)_5Br$ (0.1 g; 0.2465 mmol) in 15 ml dry toluene under nitrogen for 1 h. Cooling was done outside the oil bath and the pale purple amorphous solids formed were filtered under vacuum. Recrystallization was done in ethanol: chloroform (5:5) solution and the weight was 0.1078 g (70% yield). Suitable x-ray crystals could not be obtained for the complexes. All reactions were monitored by TLC.

Antimicrobial activity

Mueller-Hinton agar (MHA) and Potato dextrose agar (PDA) were the media used during the *in vitro* antibacterial and antifungal studies. Antibacterial activities were evaluated against three Gram-positive bacteria (*Staphylococcus aureus, Bacillus subtilis* and Haemolytic *Staphylococcus aureus*) and three Gram-negative bacteria (*Pseudomonas aeruginosa, Escherichia coli* and *Klebsiella* species). Antifungal activities of the compounds were evaluated against three fungi (*Trichoderma viride, Aspergillus niger* and *Penicillium citrinum*). Preliminary identification of the bacteria was done at Bowen University, Iwo, Nigeria, using the methods by Cheesbrough (2002). Tetracycline (30 µg; antibiotic test kit) was used as a standard drug for the bacteria, while dimethylformamide (DMF) was used as control.



Scheme 1. Scheme of reaction for preparations of L1 and L2.

Antibacterial test

Each test bacterium was prepared according to the methods by CLSI (2016). Also, the antibacterial susceptibility test was carried out according to CLSI (2016) procedures. Disc diffusion method (Emeruwa, 1982) was used to evaluate the antimicrobial activities of the compounds using filter paper discs of diameter 8 mm and synthesized compounds at a concentration of 100 µg/mL dissolved in dimethylformamide (DMF). Antibacterial activities were evaluated by measuring the diameters of zones of growth inhibition in triplicates and the mean of three results of each data set was taken (Owoseni and Sangoyomi, 2014; Mostafa et al., 2018).

Minimum inhibitory concentration (MIC)

The MIC was carried out for only the compound with the highest zone of inhibition for each of the tested bacteria. This was determined by adding 10, 5.0, 2.5, 1.25, 0.625, and 0.3125 µg/ml of each complex into test tubes containing sterile nutrient broth. The organisms that showed susceptibility to the complex initially were then introduced into the broths containing different concentrations of the complex. The tubes were then incubated for 24 h at 37°C. The MIC was taken as the lowest concentration of the compounds that did not permit any visible growth (CLSI, 2016; Mogana et al., 2020).

Antifungal test

The fungal isolates were allowed to grow on Potato dextrose agar (PDA) (LabM) at 25°C for 5 to 7 days to sporulate. After sporulation, the fungal spores were harvested by pouring a mixture of sterile glycerol and distilled water onto the surface of the plate. A sterile glass rod was used to scrape the spores. Standardization of the harvested fungal spores was done to 10^6 spores/ml. One millilitre of the standardized spore suspension was evenly spread on solidified PDA (LabM) plates using a glass spreader. The plates were left for 1 h for the spore suspension to diffuse into the agar. The sterile discs were impregnated with the test compounds and placed aseptically using sterile forceps on the surface of the agar plates. The plates were then allowed to stand on the laboratory bench for 1 h to allow for proper diffusion of the compounds into the media. Plates were incubated at 25°C for 96 h and observed for zones of inhibition. Activity was evaluated by measuring the diameters of zones of growth inhibition in triplicates and the mean of three results were taken.

RESULTS AND DISCUSSION

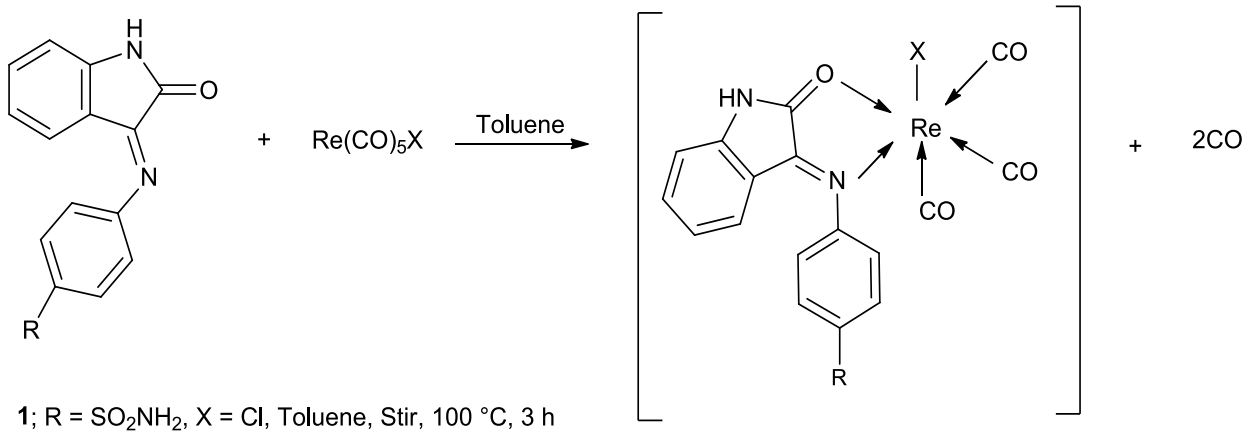
Isatin was separately condensed with sulfanilamide (L1) and 4-methoxyaniline (L2) at room temperature (Adetoye et al., 2009; Ikotun et al., 2019 b). The scheme of preparation is presented as Scheme 1 (Adetoye et al., 2009).

New rhenium (I) complexes of L1 and L2 were also prepared similar to our previous report (Ikotun et al., 2019a) with slight modifications. The general equation for their preparations is presented as Scheme 2.

The physical properties of these complexes and their ligands are presented as Table 1.

Infra-red spectra

The comparison of the distinctive vibrational frequencies of the prepared complexes with those of the isatin ligands L1 and L2 (Chohan et al., 2006; Ikotun et al., 2019a) have been presented in Table 2. The new and diagnostic υ(CO) bands appeared as terminal carbonyl bands ascertaining the formation of these complexes (Angelici, 1990). In spectrum 1, $[Re(C_{14}H_{11}N_3O_3S)(CO)_3Cl]$, the new υ(CO) bands appeared as a strong band at 1906 cm^{-1}, a shoulder band at 1932 cm^{-1} and a medium band at 2021 cm^{-1}. In spectrum 2, $[Re(C_{14}H_{11}N_3O_3S)(CO)_3Br]$, they were observed as a strong band at 1906 cm^{-1}, a shoulder band at 1929 cm^{-1} and a medium band at 2014 cm^{-1}. In spectrum of complex 3, $[Re(C_{15}H_{12}O_2N_2)(CO)_3Cl]$, they appeared as a strong band at 1899 cm^{-1} and two medium bands at 1924 and 2029 cm^{-1}. In spectrum 4, $[Re(C_{15}H_{12}O_2N_2)(CO)_3Br]$, they appeared as two new strong bands at 1906 and 2029 cm^{-1}, as well as a new shoulder band at 1924 cm^{-1}. In spectrum 5, $[Re(C_{15}H_{12}O_2N_2)(CO)_3Br].^1/_2C_2H_5OH$, they appeared as a new strong band at 1899 cm^{-1} and two medium bands at 1921 and 2029 cm^{-1}. These confirm the formation of these rhenium (I) tricarbonyl complexes of these isatin derivatives. The spectrum of L1 ($C_{14}H_{11}N_3O_3S$) showed a medium band at 3325 cm^{-1} attributable to O-H stretching



1; R = SO_2NH_2, X = Cl, Toluene, Stir, 100 °C, 3 h

2; R = SO_2NH_2, X = Br, Toluene, Stir, 100 °C, 20 h

3; R = OCH_3, X = Cl, Toluene, Stir, 100 °C, 3 h

4; R = OCH_3, X = Br, Toluene, Stir, 100 °C, 29 h

$[Re(C_{15}H_{12}O_2N_2)(CO)_3Br].^1/_2C_2H_5OH$ (**5**); R = OCH_3, X = Br, Toluene, Reflux, 1 h, N_2, Recrystallized in Ethanol: Chloroform (50: 50)

Scheme 2. Scheme of reaction for preparation of rhenium(I) tricarbonyl complexes.

Table 1. Physical Properties of L1, L2 and their rhenium(I) tricarbonyl complexes.

Compound	Formula (g/mol)	Colour	Melting point (°C)	% Yield
L1 ($C_{14}H_{11}N_3O_3S$)	301	Light Yellow	267 - 268	92
$[Re(C_{14}H_{11}N_3O_3S)(CO)_3Cl]$ (1)	607	Light Purple	298*	87
$[Re(C_{14}H_{11}N_3O_3S)(CO)_3Br]$ (2)	651	Purple	202 - 204	92
L2 ($C_{15}H_{12}N_2O_2$)	252	Light Yellow	229*	88
$[Re(C_{15}H_{12}N_2O_2)(CO)_3Cl]$ (3)	558	Light Purple	300*	49
$[Re(C_{15}H_{12}N_2O_2)(CO)_3Br].^1/_2C_2H_5OH$ (5)	625	Pale purple	301 - 302	70

*To decomposition.

band. This band moved to higher wavenumbers of 3447 and 3395 cm^{-1} in complexes 1 and 2, respectively. This band was absent in the spectra of L2 and its complexes. The medium band at 3233 cm^{-1} in the spectrum of L1 has been assigned to $\upsilon(NH_2)$ stretching vibration of the sulphonamide and it shifted to higher wavenumbers of 3279 and 3287 cm^{-1} in complexes 1 and 2, respectively. This signifies the involvement of the sulphonamide moiety of the ligand in coordination (Adetoye et al., 2009). The medium band at 3102 cm^{-1} in the spectrum of L1 and at 3156 cm^{-1} in the spectrum of L2 is attributable to the N-H stretching vibration of the amido group. This band has moved to higher wavenumbers of 3256 and 3171 cm^{-1} in the spectra of 1 and 2, respectively, while shifting to lower frequencies of 3102, 3132 and 3125 cm^{-1} in 3, 4 and 5, respectively. The strong band appearing at 1744 cm^{-1} in the spectrum of L1, while appearing at 1736 cm^{-1} in the spectrum of L2 appeared as a weak band at 1750 cm^{-1} in the spectrum of 1 and disappeared in 2, 3, 4 and 5. This has been assigned as the $\upsilon(C=O)$ frequency of the amido group. It signifies the involvement of the oxygen of the $\upsilon(C=O)$ bond in coordination. The uncoordinated C=N and C=C stretching vibrations appeared as overlapping bands at 1659 and 1528 cm^{-1} (Chohan et al., 2006) in L1, while appearing as a strong band at 1605 cm^{-1} and a weak band at 1643 cm^{-1} in L2. These bands have moved to higher frequencies of 1682 and 1612 cm^{-1} in the spectra of both complexes 1 and 2, appearing at 1674 and 1614 cm^{-1} in complex 3, at 1674 and 1713 cm^{-1} in complex 4 and at 1674 and 1605 cm^{-1} in

Table 2. Relevant infrared spectral data of L1, L2 and their rhenium(I) tricarbonyl complexes.

Compound	υ(OH) (cm^{-1})	υ(NH_2) (cm^{-1})	υ(NH) (cm^{-1})	υ(CO) (cm^{-1})	υ(C=O) (cm^{-1})	υ(C=N+C=C) (cm^{-1})	υ(SO_2)^{as} (cm^{-1})	υ(SO_2)^{s} (cm^{-1})	υ(C-N+C-C) (cm^{-1})	υ(S-N) (cm^{-1})	υ(C-S) (cm^{-1})	υ(M-N) (cm^{-1})	δ(M-C-O) (cm^{-1})
L 1 ($C_{14}H_{11}N_3O_3S$)	3325m	3233m	3102m	-	1744s	1659m, 1528s	1319s	1142s	1096s	910s	841s	-	-
Complex1; [Re($C_{14}H_{11}N_3O_3S$)$(CO)_3$Cl]	3447m	3279w	3156m	1906s, 1932sh, 2021m	1750w	1682m, 1612m	1337s	1157s	1096m	902m	837m	640s	544m
Complex 2; [Re($C_{14}H_{11}N_3O_3S$)$(CO)_3$Br]	3395m	3287m	3171m	1906s, 1929sh, 2014s	-	1682m, 1612m	1335s	1157s	1103m	-	895m	640s	540s
L2 ($C_{15}H_{12}N_3O_2$)	-	-	3156m	-	1736s	1643m, 1605s	-	-	1034s	-	-	-	-
Complex 3; [Re($C_{15}H_{12}N_3O_2$)$(CO)_3$Cl]	-	-	3102w	1899s, 1924m, 2029m	-	1674w, 1614w	-	-	1099w	-	-	641m	546m
Complex 4; [Re($C_{15}H_{12}N_3O_2$)$(CO)_3$Br]	-	-	3132w	1906s, 1924sh, 2029s	1713w	1674s	-	-	1096m	-	-	679m	548w
Complex 5; [Re($C_{15}H_{12}N_3O_2$)$(CO)_3$Br].$^1/_2C_2H_5OH$	-	-	3125w	1899s, 1921m, 2029m	1682s	1675m, 1605m	-	-	1103w	-	-	679s	548w

υ, Stretching; δ, deformation; m, medium; w, weak; b, broad; s, shoulder, and s, strong.

complex 5 on coordination to the Re(I) ion. The $\upsilon_{assymm}(SO_2)$ band appeared as a strong band at 1319 cm^{-1} in the spectrum of L1. This underwent a shift to higher frequencies of 1337 cm^{-1} and 1335 cm^{-1} in the spectra of 1 and 2 respectively. Likewise, the $\upsilon_{assymm}(SO_2)$ band appeared as a strong band at 1142 cm^{-1} and this underwent a shift to a higher frequency of 1157 cm^{-1} in both complexes 1 and 2. The uncoordinated C-N and C-C stretching vibrations appeared as overlapping strong, medium or weak bands at 1096 cm^{-1} in both L1 and 1, 1103 cm^{-1} in both complexes 2 and 5, 1034 cm^{-1} in L2, 1099 cm^{-1} in 3 and 1096 cm^{-1} in 4. The υ(S-N) band appeared as a strong band at 910 cm^{-1} in the spectrum of L1 and it underwent a shift to a lower frequency of 902 cm^{-1} in complex 1, while it disappeared in the spectrum of complex 2. The υ(C-S) band appeared as a strong band at 841 cm^{-1} in the spectrum of L1 and it underwent a shift to a lower frequency of 837 cm^{-1} in 1, while it moved to a higher frequency of 895 cm^{-1} in the spectrum of complex 2. The new strong or medium bands at 640 cm^{-1} in complexes 1 and 2, 641 cm^{-1} in complex 3, and 679 cm^{-1} in complexes 4 and 5 are attributable to the υ(M-N) bands. Also, the new medium or strong band that appeared at 544, 540, and 546 cm^{-1} in complexes 1, 2, and 3, respectively, also appeared at 548 cm^{-1} in complexes 4 and 5.

These have been assigned to δ(M-C-O) bending mode. All these confirm the formation of these new rhenium (I) tricarbonyl complexes of L1 and L2.

Table 3. Electronic spectra data of L1 and its Re(I) tricarbonyl complexes.

Compound	Band position (nm)	Molar Absorptivity (E; M^{-1}, cm^{-1})	Band position (cm^{-1})	Band Assignment
L1 ($C_{14}H_{11}N_3O_3S$)	406	2,720	24,631	n-π*
	298	6,887	33,557	π-π*
	249	28,550	40,161	π-π*
Complex 1 $[Re(C_{14}H_{11}N_3O_3S)(CO)_3Cl]$	461	9,874	21,692	MLCT
	261	16,194	38,314	π-π*
Complex 2 $[Re(C_{14}H_{11}N_3O_3S)(CO)_3Br]$	478	6,332	20,921	MLCT
	332	8,668	30,120	π-π*
	252	31,739	39,683	π-π*

Electronic spectra

The electronic spectra data of L1 and its rhenium(I) tricarbonyl complexes 1 and 3 as determined in methanol are presented in Table 3. The maximum absorption bands (λ_{max}) for these compounds have also been determined in methanol. The λ_{max} for L1 is 24,631 cm^{-1} (406 nm) with a molar absorptivity value (E) of 2,720 $M^{-1}cm^{-1}$. This is expected due to the extended conjugation which could also include the C=N after deprotonating nitrogen in the indole ring of isatin, thus also presenting the tautomeric enol form of L1 in solution (Adetoye et al., 2009; Ikotun et al., 2019a). The λ_{max} for complex 1 is 21,692 (461 nm) with the molar absorptivity value of 9,874 $M^{-1}cm^{-1}$. The λ_{max} for complex 2 is 20,931 cm^{-1} (478 nm) with the molar absorptivity value of 6,332 $M^{-1}cm^{-1}$.

The ultraviolet spectrum of L1 showed absorption bands at 33,557 and 40,161 cm^{-1} which have been assigned to π – π* transition (Sutton, 1968). The band at 24,631 cm^{-1} is attributable to n – π* transition. The interpretations of ultraviolet spectra of metal complexes of isatin derived Schiff bases revealed that charge – transfer bands occur in the same region with π – π* transitions (Chohan et al., 2006). The ultraviolet spectra of the rhenium carbonyl complex 1; $[Re(C_{14}H_{11}N_3O_3S)(CO)_3Cl]$ was therefore characterized by the absorption band at 38,314 cm^{-1} assigned to ligand π – π* transitions (Sutton, 1968). The absorption band at 21,692 cm^{-1} has been assigned to MLCT {dπ(Re) – π*} transition. Complex 2 $[Re(C_{14}H_{11}N_3O_3S)(CO)_3Br]$ was also characterized by absorption bands at 30, 120 and 39,683 cm^{-1} assigned to ligand π – π* transitions (Scherer, 2009). The absorption band at 20,921 cm^{-1} has been assigned to MLCT {dπ(Re) – π*} transition. All these are consistent with the magnetic moment of 0 as determined for these complexes and a low spin octahedral configuration.

Molecular weight determinations

The exact mass spectrum of L1 showed a relative abundant peak at 302.059, which corresponds to the (M+1) peak. These prepared complexes of L1 and L2 are halides, thus their mass spectra are expected to display peaks such as $(M+2)^+$, $(M+4)^+$, $(M+6)^+$, etc (Adetoye et al., 2009). The spectrum of complex 1; $[Re(C_{14}H_{11}N_3O_3S)(CO)_3Cl]$ showed the highest peak at $^m/_z$ (ESI) 613 (45%), which corresponds to the $[M+6]^+$ peak. This also signifies that the ratio of the reaction for the formation of compound 1, that is, metal: ligand is 1:1 as expected. This ion at $^m/_z$ 613 fragments via two routes is as follows:

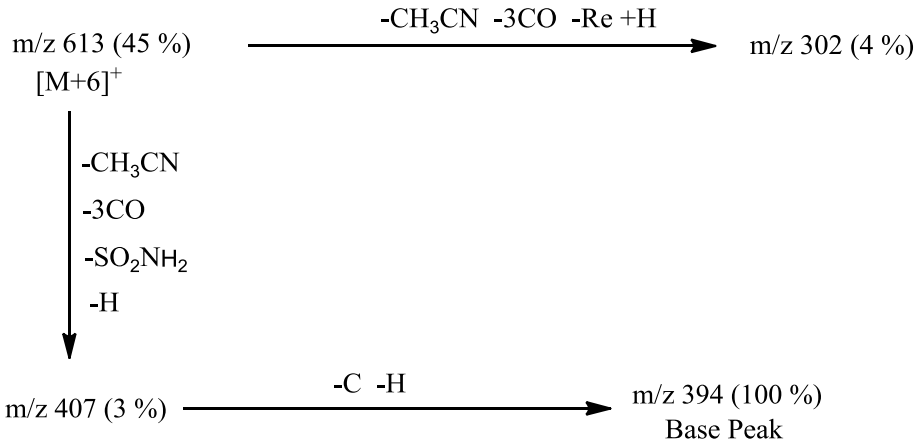
(i) The ion at $^m/_z$ 613 fragments by the loss of 3CO (84 mass units), CH_3CN (41 mass units), SO_2NH_2 (80 mass units) and H (1 mass unit) to give the ion at peak $^m/_z$ 407 (3 %) corresponding to $[M\text{-}Cl\text{-}3CO\text{-}SO_2NH_2\text{-}H]^+$. This ion fragments by loss of C (12 mass units) and H (1 mass unit) to give the ion at the base peak $^m/_z$ 394 (100%) corresponding to $[M\text{-}Cl\text{-}3CO\text{-}SO_2NH_2\text{-}H\text{-}C\text{-}H]^+$. This ion equally corresponds to $[M\text{-}Cl\text{-}2CO\text{-}C_6H_5SO_2NH_2]^+$.
(ii) The ion at $^m/_z$ 613 fragments by the loss of CH_3CN (41 mass units), 3CO (84 mass units) and Re^+ ion (186 mass units) to give the ion at the peak $^m/_z$ 302 (4%) corresponding to $[M\text{-}Cl\text{-}3CO\text{-}Re+H]^+$. This peak also corresponds to the ligand peak ($C_{14}H_{11}N_3O_3$; L1). The spectra data analyses for complex 1 are presented in Table 4, while the fragmentation pattern is shown in Scheme 3.

In the mass spectrum of L2 ($C_{15}H_{12}N_2O_2$), the expected molecular ion appeared at $^m/_z$ (ESI) 253 (22 %) corresponding to $[M+H]^+$. The mass spectrum of Compound 4, $[Re(C_{15}H_{12}N_2O_2)(CO)_3Br]$ revealed that the expected molecular ion, $[M[^+$ appeared at $^m/_z$ (MALDI) 602 (25%). This also confirms the formation of the complex, thus the complexation is 1:1. The $[M+2]^+$ also appeared at 604. The molecular ion fragments via two routes as follows:

(i) The molecular fragments by loss of $Br^·$ radical (80 mass units), Re (186 mass unit) and H_2 (2 mass units) to

Table 4. Mass spectral data of complex 1; $[Re(C_{14}H_{11}N_3O_3S)(CO)_3Cl]$.

$^{M}/_{Z}$	Fragment
613	$[M+6]^+$
407	$[M\text{-}Cl\text{-}3CO\text{-}SO_2NH_2\text{-}H]^+$
394	$[M\text{-}Cl\text{-}3CO\text{-}SO_2NH_2\text{-}H\text{-}C\text{-}H]^+$ OR $[M\text{-}2CO\text{-}C_6H_5SO_2NH_2]^+$
302	$[M\text{-}Cl\text{-}3CO\text{-}Re+H]^+$



Scheme 3. Fragmentation Pattern of Complex 1; $[Re(C_{14}H_{11}N_3O_3S)(CO)_3Cl]$.

Table 5. Mass spectral data of complex 4; $[Re(C_{15}H_{12}N_2O_2)(CO)_3Br]$

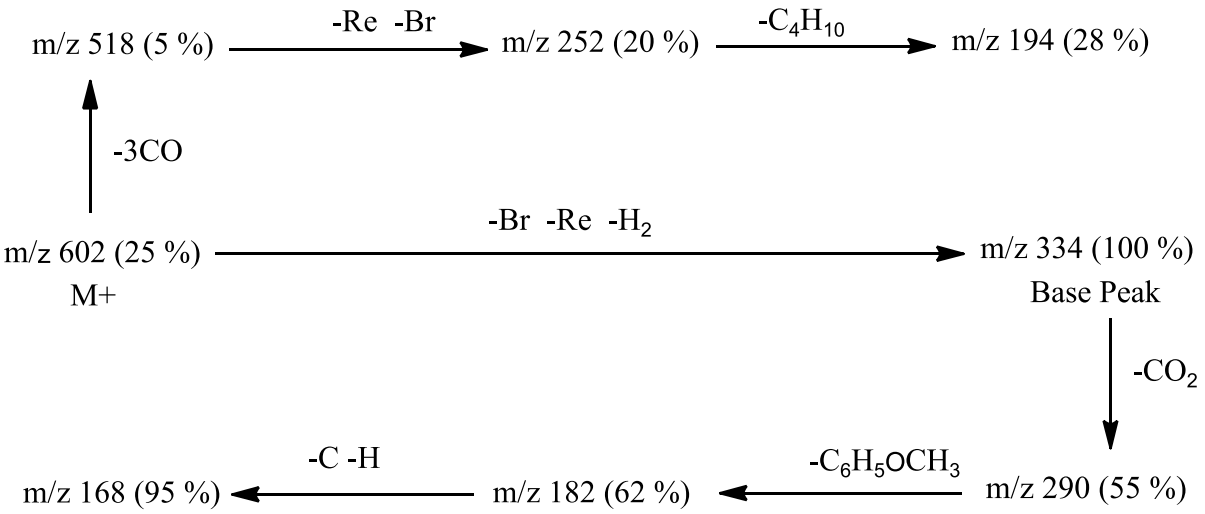
$^{M}/_{Z}$	Fragment
602	$[M]^+$
518	$[M\text{-}3CO]^+$
334	$[M\text{-}Br\text{-}Re\text{-}H_2]^+$
290	$[M\text{-}Br\text{-}Re\text{-}H_2\text{-}CO_2]^+$
252	$[M\text{-}3CO\text{-}Br\text{-}Re]^+$
194	$[M\text{-}3CO\text{-}Br\text{-}Re\text{-}C_4H_{10}]^+$
182	$[M\text{-}Br\text{-}Re\text{-}H_2\text{-}CO_2\text{-}C_6H_5OCH_3]^+$
168	$[M\text{-}Br\text{-}Re\text{-}H_2\text{-}CO_2\text{-}C_6H_5OCH_3\text{-}C\text{-}H]^+$

give the ion at the base peak $^{m}/_{z}$ 334 (100 %), corresponding to $[M\text{-}Br^{\cdot}\text{-}Re\text{-}H_2]^+$. This ion fragments by loss of CO_2 (44 mass units) to yield another ion at $^{m}/_{z}$ 290 (55%) corresponding to $[M\text{-}Br^{\cdot}\text{-}Re\text{-}H_2\text{-}CO_2]^+$. This ion fragments by loss of $C_6H_5OCH_3$ (108 mass units) to yield another ion at peak $^{m}/_{z}$ 182 (62%) corresponding to $[M\text{-}Br^{\cdot}\text{-}Re\text{-}H_2\text{-}CO_2\text{-}C_6H_5OCH_3]^+$. The ion at $^{m}/_{z}$ 182 then loses C (12 mass units) and H (1 mass unit) concomitantly to yield the ion at $^{m}/_{z}$ 168 (95%) corresponding to $[M\text{-}Br^{\cdot}\text{-}Re\text{-}H_2\text{-}CO_2\text{-}C_6H_5OCH_3\text{-}C\text{-}H]^+$.

(ii) The molecular ion fragments by loss of 3CO (84 mass units) to yield the ion at $^{m}/_{z}$ 518 (5%) corresponding to $[M\text{-}3CO]^+$. This ion then loses $Br^{\cdot}$ Radical (80 mass units) and also Re (186 mass units) to give the ion at $^{m}/_{z}$ 252 (20%) corresponding to $[M\text{-}3CO\text{-}Br^{\cdot}\text{-}Re]^+$. This ion also corresponds to the ligand ion (L2). This ion further loses C_4H_{10} (58 mass units) to give the ion at $^{m}/_{z}$ 194 (28%) corresponding to $[M\text{-}3CO\text{-}Br^{\cdot}\text{-}Re\text{-}C_4H_{10}]^+$. The spectral data are collected in Table 5, while the fragmentation pattern is shown in Scheme 4.

Magnetic susceptibility measurement

The magnetic moments for the prepared complexes were measured at room temperature. The value was 0 B.M for the rhenium carbonyl adducts. This value signifies the following:



Scheme 4. Fragmentation pattern of compound 4; $[Re(C_{15}H_{12}N_2O_2)(CO)_3Br]$.

(a) these complexes are diamagnetic;
(b) since Re(I) is in the d^6 electronic state, the complexes will assume an octahedral shape;
(c) L1 and L2 are strong field ligands; and
(d) these rhenium carbonyl adducts are low spin.

Elemental analyses

The results of the elemental analyses carried out for complex 5 are presented subsequently. These results revealed that this compound recrystallized as a solvate compound (Egharevba et al., 1982).

Compound 5: $[Re(C_{15}H_{12}O_2N_2)(CO)_3Br\ ].^1/_2\ C_2H_5OH$
Calculated values: C, 36.5; H, 2.42; N, 4.48; O, 14.1%
Found: C, 36.9; H, 4.76; N, 4.79; O, 13.49

^{1}H- and ^{13}C-NMR spectra

The spectrum of L1 showed two resonance signals due to indole-NH at δ 10.95 and 11.06 ppm in a ratio 1:3, indicating that the isatin Schiff base (ligand) exists in DMSO as two stereoisomers (E and Z). The ^{1}H-NMR signals of the two isomers appear as shown in Figure 1. The numbering system for the ligand is presented in Figure 1.

The major stereoisomer showed the following signals (δ, ppm): 7.90 (2H, d, J = 8.4 Hz, H-13 and H-15), 7.41 (4H, m, H-5, H-6 and $SONH_2$), 7.19 (2H, d, J = 8.8 Hz, H-12 and H-16), 6.75 (1H, t, 7.6 Hz, H-7) and 6.35 (1H, d, J = 7.6 Hz, H-8). 10 signals were observed as expected. The minor stereoisomer showed the following signals (δ, ppm): 7.61 (1H, d, J = 7.6 Hz), 7.74 (2H, d, J = 8.8 Hz), 7.48 (1H, t, J = 0.8 Hz), 7.10 (3H, m) and 6.93 (4H, m). This is in agreement with published work (Adetoye et al., 2009). The ^{1}H-NMR spectrum of complex 1, $[Re(C_{14}H_{11}N_3O_3S)(CO)_3Cl]$ is completely different from that of its ligand, L1, thus providing evidence of metal chelation with significant changes in the chemical shifts. The ^{1}H-NMR spectrum of $[Re(C_{14}H_{10}N_2O)(CO)_3Cl]$ showed the following 11 signals as expected (δ, ppm): 11.05 (1H, s, CONH), 7.60 (1H, t, J = 7.6 Hz), 7.46 (1H, d, J = 7.6 Hz), 7.44 (2H, d, J = 8.8 Hz), 7.07 (1H, t, J = 7.6 Hz), 6.90 (3H, d, J = 8.0 Hz), 6.60 (2H, d, J = 8.8 Hz). In the ^{13}C-NMR spectrum of L1, 25 signals were observed as follows (δ, ppm): 163.6 (C =O), 158.9 (C = O), 155.7 (C = N), 154.1 (C =N), 153.7 (Cq), 152.9 (Cq), 147.7 (Cq), 146.5 (Cq), 140.7 (Cq), 139.7 (CH), 135.7 (CH), 135.1 (CH), 127.9 (CH), 126.6 (CH), 125.8 (CH), 123.6 (CH), 122.8 (CH), 122.8 (CH), 121.2 (CH), 119.0 (CH), 118.0 (CH), 115.9 (CH), 112.8 (CH), 112.1 (CH) and 111.3 (CH). 25 signals mean that the carbon atoms of both the E and Z stereoisomers have produced these signals, with the overlap of 3 carbon atoms. The 3 overlapping atoms are most likely quaternary carbons, since 12 signals are expected within the region, but only 9 appeared. This is not too surprising given the antecedent of the peculiar nature of isatin Schiff bases (Adetoye, 2010; Ikotun et al., 2019a). In the ^{13}C-NMR spectrum of 1, the new carbonyl signals appeared as follows (δ, ppm): 196.7 (C ≡ O), 193.0 (C ≡ O), 184.8 (C ≡ O). These new carbonyl bands support the formation of this complex. All other carbon signals from the ligand appear as follows (δ, ppm): 159.8 (C = O), 151.4 (Cq), 151.0 (Cq), 138.7 (Cq), 131.1 (CH), 127.8 (CH), 123.1 (CH), 125.1 (CH), 118.2 (CH), 113.4 (CH), and 112.6 (CH). This collapses to 11 carbon signals from the ligand instead of 15, thus 4 carbon atoms are overlapping. This is quite similar to previously reported Re(I) complexes of the Schiff base of isatin and aniline (Ikotun et al., 2019a).

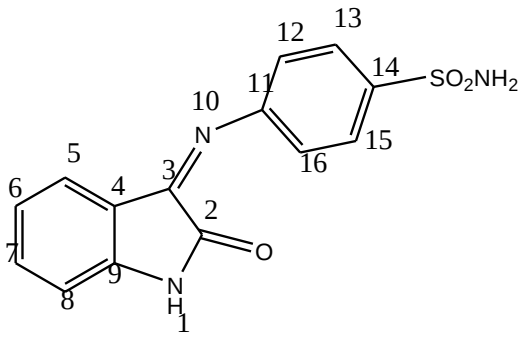


Figure 1. Numbering of atoms in $C_{14}H_{10}N_3O_3S$ (L1).

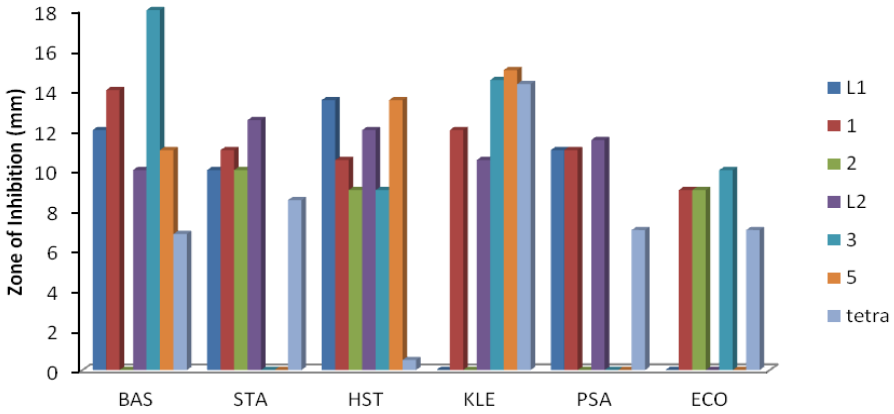


Figure 2. Antibacterial activities of L1, L2 and their rhenium(I) tricarbonyl complexes. BAS = *Bacillus subtilis,* STA= *Staphylococcus aureus,* HST = Haemolytic *Staphylococcus aureus,* KLE = *Klebsiella* spp., PSA = *Pseudomonas aeruginosa,* ECO = *Escherichia coli.* L1 = $C_{14}H_{10}N_2O$, 1 = $[Re(C_{14}H_{11}N_3O_3S)(CO)_3Cl$, L2 = $C_{15}H_{12}O_2N_2$, 2 = $[Re(C_{14}H_{11}N_3O_3S)(CO)_3Br]$, 3 = $[Re(C_{15}H_{12}O_2N_2)(CO)_3Cl]$, 5 = $[Re(C_{15}H_{12}O_2N_2)(CO)_3Br].{}^1/_2C_2H_5OH$.

Antibacterial studies

The results from the antibacterial activities of ligands and the rhenium tricarbonyl complexes are presented in Figure 2.

Complex 1 had a broad spectrum and therefore can be developed as a broad spectrum antibiotic with better activities than the ligand, L1 and tetracycline. L1 was active against all tested Gram positive bacteria with better activities than tetracycline, suggesting that it would be a good grAm positive drug. Compound 2 was active against both *Staphylococcus* bacteria and *E. coli* with a higher zone of inhibition than tetracycline, thus it could be a potential anti-staphylococcal drug. L2 can be developed as a strong anti-enteric bacteria drug due to its high zones of inhibition against *Klebsiella* spp. and *E. coli*. Compound 3 can also be a target anti-enteric bacteria drug. This compound also has the highest zone of inhibition against *S. aureus* (much higher than that of tetracycline). It is also active against *B. subtilis.* Complex 5 had the highest active against Haemolytic *S. aureus*, which even tetracycline was only weakly active against. This compound was also active against *B. subtilis* (better than tetracycline). It had the greatest activity against *Klebsiella* spp. out of all these tested compounds (and also tetracycline), thus it could be a potential drug against *Klebsiella* spp. These results are consistent with previous studies, involving the Schiff base of isatin and aniline with $Re(CO)_5X$ (where X = Cl and Br) (Ikotun et al., 2019a).

Minimum inhibitory concentration (MIC)

The MIC was carried out for only the compound with the highest zone of inhibition for each of the tested bacteria. Complex 5 had the MIC value of 10 µg/ml against *Klebsiella* spp. and compound L2 had the MIC value of 10 µg/ml against *E. coli.*

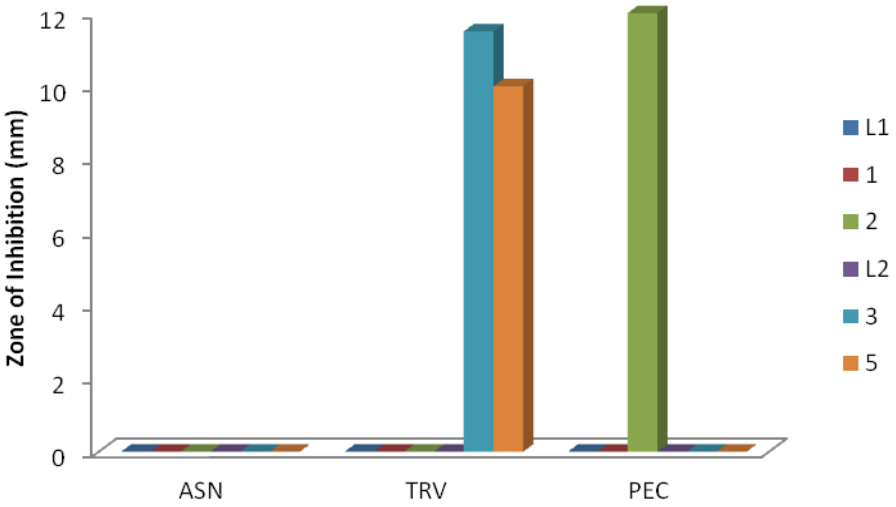


Figure 3. Antifungal activities of L1, L2 and their rhenium(I) tricarbonyl complexes. ASN = *Aspergillus niger,* TRV = *Trichoderma viride,* PEC = *Penicillium citrinum,* L1 = $C_{14}H_{11}N_3O_3S$, 1 = $[Re(C_{14}H_{11}N_3O_3S)(CO)_3Cl]$, 2 = $[Re(C_{14}H_{11}N_3O_3S)(CO)_3Br]$, L2 = $(C_{15}H_{12}O_2N_2)$, 3 = $[Re(C_{15}H_{12}O_2N_2)(CO)_3Cl]$, 5 = $[Re(C_{15}H_{12}O_2N_2)(CO)_3Br].^1/_2C_2H_5OH$.

Antifungal studies

The results from the antifungal activities of ligands and their rhenium(I) tricarbonyl complexes are presented in Figure 3.

Antifungal studies revealed that compound 2 was active against *P. citrinum* while compounds 3 and 5 were active against *T. viride*. All other tested compounds were not active against the tested fungi.

Conclusion

The rhenium (I) tricarbonyl complexes $[Re(C_{14}H_{11}N_3O_3S)(CO)_3Cl]$ (1), $[Re(C_{14}H_{11}N_3O_3S)(CO)_3Br]$ (2), $[Re(C_{15}H_{11}N_2O_2)(CO)_3Cl]$ (3), $[Re(C_{15}H_{11}N_2O_2)(CO)_3Cl]$ (4) and $[Re(C_{15}H_{12}O_2N_2)(CO)_3Br].^1/_2\ C_2H_5OH$ (5) of the prepared isatin Schiff bases, 4-((2-oxoindolin-3-ylidene) amino)benzenesulfonamide (L1) and 3-((4-methoxyphenyl)imino)indolin-2-one (L2) were successfully prepared in good yields. Physicochemical properties of the prepared complexes were determined by spectroscopic means, as well as by magnetic susceptibility and melting point determinations. The spectral data confirmed the complexation of L1 and L2 in ratio metal: ligand = 1:1. The IR spectra of these complexes showed new carbonyl bands identified as terminal carbonyl bands. L1 and L2 have acted in a bidentate manner towards Re(I) coordinating through the azomethine nitrogen and keto oxygen. The prepared complexes were found to be diamagnetic, thus revealing that the ligands are strong field ligands. Results of the antimicrobial studies showed significant inhibitory activities against the growth of tested Gram negative bacteria in the decreasing order 1>3>5>2, therefore they can be recommended for further applications in cell imaging in consistence with literature (Varma et al., 2020).

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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REFERENCES

Adetoye AA, Egharevba GO, Obafemi CA, Kelly DR (2009). Synthesis and physicochemical properties of Co(II), Cu(II), Fe(III), Mn(II) and Ni(II) complexes of the isatin derivative of sulphanilamide. Toxicological & Environmental Chemistry 91(5):837-846.

Angelici RJ (1990). Inorganic Syntheses: Reagents for Transition Metal Complexes and Organometallic Syntheses. John Wiley &Sons, Inc. 28:160-163, (online version 2007).

Azzarelli N, Ponnala S, Aguirre A, Dampf S, Davis M, Ruggiero M, Lopez Diaz V, Babich J, Coogan M, Korter T, Doyle R, Zubieta J (2019). Defining the origins of multiple emission/excitation in rhenium-bisthiazole complexes. Inorganica Chimica Acta 489:301-309.

Cheesbrough M (2002). Biochemical tests to identify bacteria. In: Laboratory practice in tropical countries. Cheesbrough M (ed.). Cambridge Edition 2:63-87.

Chohan ZH, Shaikh AU, Naseer MM (2006). Metal-based isatin-bearing Sulfonamides: their synthesis, characterization and biological properties. Applied Organometallic Chemistry 20(11):729-739.

Clinical and Laboratory Standards Institute (CLSI) (2016). Methods for antimicrobial dilution and disk susceptibility testing of infrequently isolated or fastidious bacteria. 3rd Ed. CLSI guideline M45-A3. Clinical and Laboratory Standards Institute. Wayne, Pennslvania.

Coogan MP, Fernandez-Moreira V, Hess JB, Pope SJA, Williams C (2009). Rhenium fac-tricarbonyl bisimine complexes: luminescence modulation by hdrophobically driven intermolecular interactions. New Journal of Chemistry 33(5):1094-1099.

Ding Z, Zhou M, Zeng C (2020). Recent advances in isatin hybrids as potential anticancer agents. Archiv der Pharmazie 353(3):e1900367.

Egharevba GO, Megnamisi-Belombe M, Endres H, Rossato E (1982). Hexaaquacobalt(II)Bis[dibromobis(ethanedialdioxamato)cobaltate(III)] Acetone solvate. Acta Crystallographica B38(11):2901-2903.

Emeruwa KC (1982). Antimicrobial substances from Cacaya papaya fruit extracts. Journal of Natural Products 45(2):123-127.

Guo H (2019). Isatin derivatives and their anti-bacterial activities. European Journal of Medicinal Chemistry 15(164):678-688.

Ikotun AA, Coogan MP, Owoseni AA, Egharevba GO (2019a). Design, synthesis, physicochemical and antimicrobial properties of rhenium(I) tricarbonyl complexes of 3-(phenylimino)indole-2-one. Journal of Chemical Society of Nigeria 44(5):948-958.

Ikotun AA, Oladimeji AO, Oluranti OO (2019b). Synthesis, Physicochemical and Antimicrobial Properties of Co(II) and Ni(II) metal complexes of the Schiff base of isatin and 4-methylaniline. Journal of Applied Sciences and Environmental Management 23(11):1957-1962.

Mogana R, Adhikari A, Tzar MN, Ramliza R, Wiart C (2020). Antibacterial activities of the extracts, fractions and isolated compounds from *Canarium patentinervium* Miq. against bacterial clinical isolates. BMC Complimentary Medicine and Therapies 20(1):55-65.

Mostafa AA, Al-Askar, AA, Almaary, KS, Dawoud TM, Sholkamy EN, Bakri MM (2018). Antimicrobial activity of some plant extracts against bacteria strains causing food poisoning diseases. Saudi Journal of Biological Sciences 25(2):361-366.

Owoseni AA, Sangoyomi TE (2014). Effect of solvent extracts of some plants on *Ralstonia solanacearum*. British Microbiology Research Journal 4(1):85-92.

Premanathan M, Radhakrishnan S, Kulangiappar K, Singaravelu G, Thirumalaiarasu V, Sivakumar T, Kathiresan K (2012). Antioxidant & anticancer activities of isatin (1H-indole-2,3-dione), isolated from the flowers of Couroupita guianensis Aubl. Indian Journal of Medical Research 136(5):822-826.

Scherer A (2009). Ph.D Thesis, Friedrich-Alexander Universität, Erlangen-Nürnberg, Germany.

Sriam D, Bal TR, Yogeeswari P (2005). Newer aminopyrimidimino isatin abalogues as non-nucleoside HIV-1 reverse transcriptase inhibitors for HIV and other opportunistic infections of AIDS: design, synthesis and biological evaluation. Il Farmaco 60(5):377-384.

Sridhar SK, Pandeya SN, Stables JP, Ramesh A (2002). Anticonvulsant activity of hydrazones, Schiff and Mannich bases of isatin derivatives. European Journal of Pharmaceutical Sciences 16(3):129-132.

Sutton D (1968). Electronic Spectra of Transition Metal Complexes, McGRAW-HILL, London.

Varma RR, Pursuwani BH, Suresh E, Bhatt BS, Patel MN (2020). Single crystal, DNA interraction and cytotoxicity studies of rhenium (I) organometallic compounds. Journal of Molecular Structure 1200:127068.