Synthesis, characterization and antimicrobial evaluation of diorganotin(IV) complexes containing 1,2,4-triazole derivative as Schiff base ligands

Devi Jai* and Yadav Jyoti
Department of Chemistry, Guru Jambheshwar University of Science and Technology, Hisar, INDIA
*jaya.gju@gmail.com

Abstract

In the present work, 1,2,4-triazole based new diorganotin(IV) complexes of type R_2SnL^{1-2} (3-10) has been synthesized using tridentate (ONS) chelating Schiff base ligands (H_2L^{1-2}) where H_2L^1 = 2-(((3-mercapto-5-phenyl-4H-1,2,4-triazol-4-yl)imino) methyl)-4-nitrophenol and H_2L^2 = 2-(((3-mercapto-5-phenyl-4H-1,2,4-triazol-4-yl)imino)methyl)-6-methoxy -4-nitrophenol. The structure elucidation of compounds (1-10) was done by using various spectroscopic techniques like: FT-IR, Mass, ^1H, ^{13}C and ^{119}Sn NMR. Characterization data concluded that complexes exhibited pentacoordinated environment around the tin metal with tridentate Schiff bases (ONS) which were coordinated to the metal with the azomethine nitrogen, phenolic oxygen and thiolic sulfur.

Compounds were screened for their in vitro antibacterial (gram positive bacteria, gram negative bacteria) and antifungal activities to examine the biological profile of metal complexes in comparison to Schiff base ligands by using serial dilution method. From the calculation of activity data, it was found that organotin complexes were more effective than free ligands and compound 10 (Ph_2SnL^2) was most active as compared to clinical available drugs.

Keywords: Pharmacophore, triazole, thiol, salicylaldehyde.

Introduction

Metallo-organic chemistry is becoming an emerging area of research due to the tremendous increase in the resistance microbes, so as to overcome that problem, the discovery and developing of non-resistant drug are very important. Many studies suggested that phenolic, nitrogen and sulfur containing compounds form a large group of bioactive compounds which have the ability to scavenge microbes. They have the ability to form the complex with metal and rendering them inactive and also increase the activity of free compound [26,30,37].

1,2,4 triazole is a heterocyclic compound known for its biological activity like antimicrobial, anticancer, antitubercular, antiviral, anti-inflammatory, antimalarial, anti-HIV, antidiabetic, anti-oxidant, antiallergic etc.; industrial and catalytic application[8,19,22,24,31]. 1,2,4 triazole unit is present in various commercially available drugs like letrozole, vorozole and anasterozole which are used in the treatment of cancer, likewise trazodone is antidepressant drug and fluconazole is antifungal drug; both contain triazole as one unit. 3-aminocarbonyltriazole containing drug ribavirin is used as antiviral agent[2,5,9,21,27]. The triazoles containing Schiff bases are used as plant growth-regulating, antifungal, antitumor, antibacterial, and antituberculer agents[3,4,20,23].

It is revealed from the literature that any compound which is already biologically active, when coordinated to metal, its activity increases according to overtones concept and tweedy's chelation theory [10,33]. Tin is unmatched by other metals in the variety of its organometallic compounds which places organotin(IV) compounds as most strongest area in the field of organometallics [11-15]. Organotin(IV) complexes extended its coordination number due to low lying 5d orbitals and have prominent electron acceptor ability of tin atom, making it suitable for novel drugs. The biological activity of organotin(IV) compounds arises due to presence of hydrolysable groups, geometrical and electronic properties and the number of tin-carbon bond [29].

In the present study, we report the synthesis of triazole Schiff base ligands from the reaction of 4-amino-5-phenyl-1,2,4-triazole-3-thiol with salicylaldehyde derivatives. The above synthesized triazole Schiff bases further react with diorganotindichloride to form their respective diorganotin(IV) complexes and it is expected that they will form a biologically potent compound and reduce the microbial growth. The synthesized compounds are well characterized by using FT-IR, Mass, ^1H, ^{13}C, and ^{119}Sn NMR spectroscopy. The synthesized compounds are evaluated for *in vitro* antimicrobial activity against gram positive bacteria ((*Staphylococcus aureus and Bacillus subtillus*; gram-negative bacteria (*Escherichia coli and Pseudomonas aeruginosa*) and two fungal strain (*Aspergillus niger* and *Candida albicans*)].

Material and Methods

Materials and Instrumentation

Chemicals like 4-amino-5-phenyl-1,2,4-triazole-3-thiol, 5-nitrosalicylaldehyde, 3-methoxy-5-nitrosalicylaldehyde and different diorganotin dichloride derivatives were purchased from Sigma-Aldrich Company. All solvents were of analytical grade and used after drying with standard procedure[38]. The chemicals and apparatus were free from moisture. FT-IR spectra was recorded using Shimadzu IR affinity-I 8000 FT-IR spectrophotometer by KBr pellets

method in the range of 400-4000 cm^{-1}. The NMR spectra (^1H, ^{13}C and ^{119}Sn) of Schiff base ligands and their diorganotin(IV) complexes were recorded on Bruker Avance II 400 MHz NMR spectrometer using DMSO-d_6 and $CDCl_3$ solvent and tetramethylsilane (TMS) and tetramethyltin as internal standard.

Chemical shifts (δ) and coupling constants (J) value were reported in ppm and Hz. Electronic spectra were recorded in DMSO at room temperature using UV- Vis-NIR Varian Cary – 5000 spectrometer. Molar conductance was recorded using conductivity bridge type model- 306 Systronic in DMF at room temperature. Mass spectra of Schiff base ligands and complexes were carried on SCIEX-QTOF in methanol solvent.

Synthesis of Schiff base ligands (1-2): 30 mL methanolic solution of 4-amino-5-phenyl-1,2,4-triazole-3-thiol (0.961g, 5 mmol) was added into the 10 mL methanolic solution of 5-nitrosalicylaldehyde/3-methoxy-5-nitrosalicylaldehyde (0.835g/0.985g, 5 mmol) and refluxed for 20-30 min by adding 2–3 drops of glacial acetic acid. The reaction progress was checked by thin layer chromatography (TLC). A solid product formed, was filtered, recrystallized by methanol and dried.

[1] 2-(((3-mercapto-5-phenyl-4H-1,2,4-triazol-4-yl) imino)methyl)-4-nitrophenol, H_2L^1: Yield: 94%, Yellow solid; M.p.: 223-225°C, Conductivity: (ohm^{-1} cm^2 mol^{-1}) in DMF: 12.32, MS: m/z (M^+) Cacld. for $C_{15}H_{11}N_5O_3S$: 341.34; found: 342.06 $(M+H)^+$. ^1H NMR [400 MHz, DMSO-d_6 δ(ppm)]: 14.257 (s, 1H, SH), 12.13 (s, 1H, OH), 10.22 (s, 1H,- N=C-H), 8.628-8.621 (1H, d, C_6-Ar-H, $^4J_{HH}$ = 2.8Hz), 8.32-8.29 (1H, dd, C_4-Ar-H, $J_{otho,\ meta}$ = 9.2Hz, 2.8Hz), 7.883-7.885 (2H, m, $C_{2',6'}$-Ar-H), 7.58-7.52 (3H, m, $C_{3',4',5'}$ -Ar-H), 7.20-7.18 (1H, d, C_2 - Ar-H, $^3J_{HH}$ = 9.2Hz): ^{13}C NMR [100 MHz, DMSO-d_6, δ(ppm)]: 162.76 (HC=N), 159.73, (C-SH), 152.32 (C-OH), 150.32 (C-NO_2). FT-IR (ν, cm^{-1}): 3429 (O-H, br), 2367 (S-H), 1605 (C=N, m).

[2] 2-(((3-mercapto-5-phenyl-4H-1,2,4-triazol-4-yl) imino)methyl)-6-methoxy-4-nitrophenol, H_2L^2: Yield: 94%, Yellow solid; M.p.: 223-225°C, Conductivity: (ohm^{-1} cm^2 mol^{-1}) in DMF: 12.33, MS: m/z (M^+) Cacld. for $C_{16}H_{13}N_5O_4S$: 371.07; found: 372.06 $(M+H)^+$. ^1H NMR [400 MHz, DMSO-d_6 δ(ppm)]: 14.907 (s, 1H, SH), 12.22 (s, 1H, OH), 10.34 (s, 1H,- N=C-H), 8.672-8.666 (1H, d, C_6-Ar-H, $^4J_{HH}$ = 2.4Hz), 8.40-8.36 (1H, dd, C_4-Ar-H, $J_{otho,\ meta}$ = 9.0Hz, 2.4Hz), 7.93-7.90 (2H, m, $C_{2',6'}$-Ar-H), 7.62-7.58 (3H, m, $C_{3',4',5'}$ -Ar-H) : ^{13}C NMR [100 MHz, DMSO-d_6, δ(ppm)]: 163.08 (HC=N), 161.08, (C-SH), 154.38 (C-OH), 150.73(C-NO_2). FT-IR (v, cm^{-1}): 3415 (O-H, br), 2371 (S-H), 1602 (C=N, m).

Synthesis of diorganotin(IV) complexes (3-10): The tetrahydrofuran (20 mL) solution of above formed Schiff base ligand H_2L^1 (0.341g, 1 mmol) was stirred for 20 minutes after adding triethylamine (0.278 mL, 2 mmol). Dimethyltin dichloride (2.19g, 1 mmol) was added to above solution and refluxed for 5-6 h. The white colored Et_3NHCl salt was formed which was then filtered and solvent was evaporated under reduced pressure. The yellow colored product was obtained after the complete evaporation of solvent which was then recrystallized from the dry hexane. After that the product was dried in a moisture free environment. The other complexes of tin were prepared by using suitable ligands, H_2L^2 (0.371g, 1 mmol) in 1:1 molar ratio according to the above described procedure.

[3] Me_2SnL^1: Yield: 72%, yellow solid; M.p.: 135-142°C, Conductivity: (ohm^{-1} cm^2 mol^{-1}) in DMF: 11.75, MS: m/z (M^+) Cacld. for $C_{17}H_{15}N_5O_3SSn$: 488.11; found: 489.16 $(M+H)^+$. ^1H NMR [400 MHz, $CDCl_3$, δ(ppm)]: 10.85 (s, 1H,- N=C-H), 8.466 (1H, S, C_6-Ar-H), 8.27-8.26 (1H, dd, C_4-Ar-H, $J_{otho,\ meta}$ = 9.2Hz, 2.8Hz), 7.72 (2H, s (br) $C_{2',6'}$-Ar-H), 7.53 (3H, s(br), $C_{3',4',5'}$ -Ar-H), 7.21-6.99 (1H, d, C_2 - Ar-H, $^3J_{HH}$ = 8.8Hz), 0.878 (6H, s, Sn-CH_3): ^{13}C NMR [100 MHz, $CDCl_3$. δ(ppm)]: 166.45 (HC=N), 160.07, (C-SH), 154.14 (C-OH), 10.11 (Sn-CH_3). ^{119}Sn NMR [400 MHz, $CDCl_3$, δ(ppm)]: −132.16. FT-IR (ν, cm^{-1}): 1595 (C=N, m), 525 (Sn-N), 644 (Sn-O).

[4] Et_2SnL^1: Yield: 73%, dark yellow solid; M.p.: 143–145°C, Conductivity: (ohm^{-1} cm^2 mol^{-1}) in DMF: 11.70, MS: m/z (M^+) Cacld. for $C_{19}H_{19}N_5O_3SSn$: 516.16; found: 517.16 $(M+H)^+$. ^1H NMR [400 MHz, $CDCl_3$, δ(ppm)]: 10.87 (s, 1H,- N=C-H), 8.479-8.472 (1H, d, C_6-Ar-H, $^4J_{HH}$ = 2.8Hz), 8.27-8.24 (1H, dd, C_4-Ar-H, $J_{otho,\ meta}$ = 9.2Hz, 2.4Hz), 7.75-7.73 (2H, m, $C_{2',6'}$-Ar-H), 7.53-7.52 (3H, m, $C_{3',4',5'}$ -Ar-H), 7.03-7.01 (1H, d, C_2 - Ar-H, $^3J_{HH}$ = 9.2Hz), 1.375-1.338 (10H, m, Sn- CH_2CH_3):. ^{13}C NMR [100 MHz, $CDCl_3$. δ(ppm)]: 166.43 (HC=N), 160.12, (C-SH), 154.19 (C-OH), 32.22 (Et-C), 9.05 (Et-C). ^{119}Sn NMR [400 MHz, $CDCl_3$, δ(ppm)]: −162.43. FT-IR (ν, cm^{-1}): 1597 (C=N, m), 527 (Sn-N), 646 (Sn-O).

[5] Bu_2SnL^1: Yield: 75%, orange solid; M.p.: 140–144°C, Conductivity: (ohm^{-1} cm^2 mol^{-1}) in DMF: 12.34, MS: m/z (M^+) Cacld. for $C_{23}H_{27}N_5O_3SSn$: 572.27; found: 573.28 $(M+H)^+$. ^1H NMR [400 MHz, $CDCl_3$, δ(ppm)]: 10.86 (s, 1H,- N=C-H), 8.475-8.468 (1H, d, C_6-Ar-H, $^4J_{HH}$ = 2.8Hz), 8.27-8.24 (1H, dd, C_4-Ar-H, $J_{otho,\ meta}$ = 9.2Hz, 2.4Hz), 7.74-7.71 (2H, m, $C_{2',6'}$-Ar-H), 7.53-7.51 (3H, m, $C_{3',4',5'}$ -Ar-H), 7.02-7.00 (1H, d, C_2 - Ar-H, $^3J_{HH}$ = 9.2Hz), 1.373-1.345 (12H, m, Sn- CH_2CH_3), 1.09-1.06 (6H, t, Sn-CH_2, J = 7.6Hz). ^{13}C NMR [100 MHz, $CDCl_3$. δ(ppm)]: 166.78 (HC=N), 160.17, (C-SH), 154.38 (C-OH), 45.14 (Bu-C), 39.68 (Bu-C), 22.19 (Bu-C), 10.16 (Bu-C). ^{119}Sn NMR [400 MHz, $CDCl_3$, δ(ppm)]: −217.52. FT-IR (ν, cm^{-1}): 1596 (C=N, m), 527 (Sn-N), 648 (Sn-O).

[6] Ph_2SnL^1: Yield: 79%, yellow solid; M.p.: 165-167°C, Conductivity: (ohm^{-1} cm^2 mol^{-1}) in DMF: 12.67, MS: m/z (M^+) Cacld. for $C_{27}H_{19}N_5O_3SSn$: 612.35; found: 613.33 $(M+H)^+$. ^1H NMR [400 MHz, $CDCl_3$, δ(ppm)]: 10.86 (s, 1H,- N=C-H), 8.476-8.469 (1H, d, C_6-Ar-H, $^4J_{HH}$ = 2.8Hz),

8.27-8.24 (1H, dd, C_4-Ar-H, $J_{otho,\ meta}$ = 9.2Hz, 2.4Hz), 7.74-7.71 (2H, m, $C_{2',6'}$-Ar-H), 7.50-7.49 (3H, m, $C_{3',4',5'}$ -Ar-H), 7.21-7.17 (8H, m, Sn-Ar-H), 7.02-7.00 (1H, d, C_2 - Ar-H, $^3J_{HH}$ = 9.2Hz), 6.78-6.76 (2H, m, Sn-Ar-H). ^{13}C NMR [100 MHz, $CDCl_3$. δ(ppm)]: 167.17 (HC=N), 161.78, (C-SH), 155.09 (C-OH), 122-118 (Ph-C). ^{119}Sn NMR [400 MHz, $CDCl_3$, δ(ppm)]: −336.17. FT-IR (ν, cm^{-1}): 1593 (C=N, m), 533 (Sn-N), 652 (Sn-O).

[7] Me_2SnL^2: Yield: 80%, red solid; M.p.: 137-140°C, Conductivity: ($ohm^{-1}\ cm^2\ mol^{-1}$) in DMF: 12.11, MS: m/z (M^+) Cacld. for $C_{18}H_{17}N_5O_4SSn$: 518.13; found: 519.14 $(M+H)^+$. ^{1}H NMR [400 MHz, $CDCl_3$, δ(ppm)]: 10.35 (s, 1H,- N=C-H), 8.671-8.665 (1H, d, C_6-Ar-H, $^4J_{HH}$ = 2.4Hz), 8.40-8.36 (1H, dd, C_4-Ar-H, $J_{otho,\ meta}$ = 9.0Hz, 2.4Hz), 7.90-7.87 (2H, m, $C_{2',6'}$-Ar-H), 7.60-7.56 (3H, m, $C_{3',4',5'}$ -Ar-H), 1.09 (s, 6H, Me). ^{13}C NMR [100 MHz, $CDCl_3$. δ(ppm)]: 165.12 (HC=N), 161.98, (C-SH), 154.79 (C-OH), 9.11 (Me). ^{119}Sn NMR [400 MHz, $CDCl_3$, δ(ppm)]: −149.02. FT-IR (ν, cm^{-1}): 1599 (C=N, m), 568 (Sn-N), 670 (Sn-O).

[8] Et_2SnL^2: Yield: 81%, red solid; M.p.: 143-145°C, Conductivity: ($ohm^{-1}\ cm^2\ mol^{-1}$) in DMF: 11.94, MS: m/z (M^+) Cacld. for $C_{20}H_{21}N_5O_4SSn$: 546.19; found: 547.19 $(M+H)^+$.^{1}H NMR [400 MHz, $CDCl_3$, δ(ppm)]: 10.34 (s, 1H,-N=C-H), 8.670-8.663 (1H, d, C_6-Ar-H, $^4J_{HH}$ = 2.8Hz), 8.42-8.38 (1H, dd, C_4-Ar-H, $J_{otho,\ meta}$ = 9.0Hz, 2.8Hz), 7.90-7.88 (2H, m, $C_{2',6'}$-Ar-H), 7.62-7.58 (3H, m, $C_{3',4',5'}$ -Ar-H), 1.22-1.19 (m, 4H), 0.80-0.78 (t, 6H, $^3J_{HH}$ = 7.6 Hz). ^{13}C NMR [100 MHz, $CDCl_3$. δ(ppm)]: 165. 21 (HC=N), 161.77, (C-SH), 154.15 (C-OH), 23.17 (Et-C), 8.77 (Et-C). ^{119}Sn NMR [400 MHz, $CDCl_3$, δ(ppm)]: −159.09. FT-IR (ν, cm^{-1}): 1595 (C=N, m), 569 (Sn-N), 668 (Sn-O).

[9] Bu_2SnL^2: Yield: 81%, red solid; M.p.: 143-145°C, Conductivity: ($ohm^{-1}\ cm^2\ mol^{-1}$) in DMF: 13.02, MS: m/z (M^+) Cacld. for $C_{24}H_{29}N_5O_4SSn$: 602.29; found: 603.30 $(M+H)^+$. ^{1}H NMR [400 MHz, $CDCl_3$, δ(ppm)]: 10.35 (s, 1H,- N=C-H), 8.672-8.666 (1H, d, C_6-Ar-H, $^4J_{HH}$ = 2.4Hz), 8.41-8.35 (1H, dd, C_4-Ar-H, $J_{otho,\ meta}$ = 9.0Hz, 2.4Hz), 7.88-7.85 (2H, m, $C_{2',6'}$-Ar-H), 7.55-7.52 (3H, m, $C_{3',4',5'}$ -Ar-H), 1.23-1.20 (m, 14H, Sn-CH_2CH_3), 1.01-0.98 (t, 4H, $^3J_{HH}$ = 7.6Hz). ^{13}C NMR [100 MHz, $CDCl_3$. δ(ppm)]:. 165.22 (HC=N), 161.74, (C-SH), 154.15 (C-OH), 34.23 (Bu-C), 26.89 (Bu-C), 9.04 (Bu-C). ^{119}Sn NMR [400 MHz, $CDCl_3$, δ(ppm)]: −237. FT-IR (ν, cm^{-1}): 1593 (C=N, m), 568 (Sn-N), 663 (Sn-O).

[10] Ph_2SnL^2: Yield: 82%, red solid; M.p.: 200-202°C, Conductivity: ($ohm^{-1}\ cm^2\ mol^{-1}$) in DMF: 12.22, MS: m/z (M^+) Cacld. for $C_{28}H_{21}N_5O_4SSn$: 642.37; found: 643.38 $(M+H)^+$.^{1}H NMR [400 MHz, $CDCl_3$, δ(ppm)]: 10.38 (s, 1H,-N=C-H), 8.665-8.659 (1H, d, C_6-Ar-H, $^4J_{HH}$ = 2.4Hz), 8.43-8.40 (1H, dd, C_4-Ar-H, $J_{otho,\ meta}$ = 9.0Hz, 2.4Hz), 7.93-7.90 (2H, m, $C_{2',6'}$-Ar-H), 7.65-7.62 (3H, m, $C_{3',4',5'}$ -Ar-H), 7.40-7.37 (dd, 10H, Sn-Ar-H, J_{ortho}= 7.42, 5.80 Hz). ^{13}C NMR [100 MHz, $CDCl_3$. δ(ppm)]: .165.26 (HC=N), 161.70, (C-SH), 154.15 (C-OH), 120-118 (Ph-C). ^{119}Sn NMR [400 MHz, $CDCl_3$, δ(ppm)]: −342.20. FT-IR (ν, cm^{-1}): 1595 (C=N, m), 579 (Sn-N), 671 (Sn-O).

Pharmacology

Antimicrobial activity: All compounds were tested for *in vitro* antimicrobial activity against bacterial and fungal strains *viz.* two gram positive bacteria (*Staphylococcus aureus* (NCIM 5021) and *Bacillus subtillus* (NCIM 2063); two gram-negative bacteria (*Escherichia coli* (MTCC 723) and *Pseudomonas aeruginosa* (MTCC 7093)); two fungal strains like *Aspergillus niger* (MTCC 9933) and *Candida albicans* (MTCC 227) using ciprofloxacin and fluconazole as positive and DMSO as a negative control using serial dilution method and minimum inhibitory concentration (MIC) was calculated. For carrying out the experiment, tested compounds were prepared by dissolving 5 mg of compounds in 5 mL of DMSO. The concentration of 100 µg/mL of stock solution was prepared by taking 9 mL of DMSO in 1 mL of above prepared solution.

Stock solution (1 mL) was added into each test tube containing 1 mL of nutrient broth for bacteria or 1 mL of PDB for fungus. Each test tube was serially diluted up to 3.125 µg/mL concentration and further 1 mL of bacterial/fungal strains was inoculated into each test tube. The bacterial/fungal test tubes were incubated at 37°C/31°C for 24h/7days and MICs value were calculated [17,18].

Results and Discussion

Synthetic aspect: In the present research, 1,2,4-triazole Schiff base ligands (1-2) were prepared and obtained as different colored solids by the reaction of 4-amino-5-phenyl-1,2,4-triazole-3-thiol with the salicylaldehyde derivatives in methanol followed by synthesis of diorganotin(IV) complexes (3-10) with R_2SnCl_2 (R= methyl, ethyl, butyl and phenyl) in 1:1 molar ratio and using tetrahydrofuran as solvent. The synthesized complexes were soluble in DMSO, chloroform, methanol, ethylacetate, DMF, acetonitrile and insoluble in hexane and water.

The value of molar conductivity depicts the non-electrolytic nature of the compounds. Spectroscopic data suggests that complexes have pentacoordinated geometry and Schiff base ligands act as a tridentate (ONS) which is bound to the metal through phenolic oxygen, thiol sulfur and nitrogen of azomethine group.

Electronic spectra: The absorption spectra of ligands (1-2) and diorganotin(IV) complexes (3-10) were taken in DMSO solvent. A band appeared at 410 and 297 nm was assigned to n-π* and π-π* transition of azomethine group present in Schiff base ligands. In diorganotin(IV) complexes, red shift was observed at 417 and 289 nm due to formation of coordinated bond between metal and azomethine nitrogen of ligands [7].

IR spectra: The vibrational frequencies were recorded in 4000-400 cm^{-1} range and the coordination of Schiff base

ligands with tin metal was confirmed by comparing their vibrational frequencies. A distinctive broad band for hydroxyl group (*v*-OH) in Schiff base ligands was at 3415-3429 cm^{-1} which got disappeared on complexation, this indicates the deprotonation and binding of oxygen with tin metal. A sharp stretching vibration band at 2367-2371 cm^{-1} was due to the thiol group (*v*-SH), gets disappeared on complexation suggesting the coordination of sulfur with the metal[6]. The diagnostic band due to azomethine group *v*(C=N) was at 1602-1605 cm^{-1} which shifted to lower value in complexes due to donation of electron density by nitrogen to tin metal[34].

Additionally, some bands appeared at 644-671 cm^{-1} and 525-579 cm^{-1} due to *v*(Sn–O) and *v*(Sn-N) stretching frequencies respectively which confirm the coordination of oxygen and nitrogen with the metal. The further investigation of formation of Schiff base ligands and their diorganotin(IV) complexes was by ^{1}H, ^{13}C and ^{119}Sn NMR studies[35].

NMR spectra

^{1}H NMR spectra: The ^{1}H NMR spectra of Schiff base ligands and diorganotin(IV) complexes was recorded in DMSO-d_6 and $CDCl_3$. The denticity and bonding of Schiff base ligands with tin metal are revealed by appearance and disappearance of signals in ^{1}H NMR spectra (figure 1 and 2). In the ^{1}H NMR spectra, singlet at δ 14.25-14.90 ppm was due to thiol (S-H) proton and singlet at δ 12.13-12.22 ppm was due to hydroxyl (OH) proton, get disappeared on complexation indicating the chelation of sulfur and oxygen with the metal atom [1].

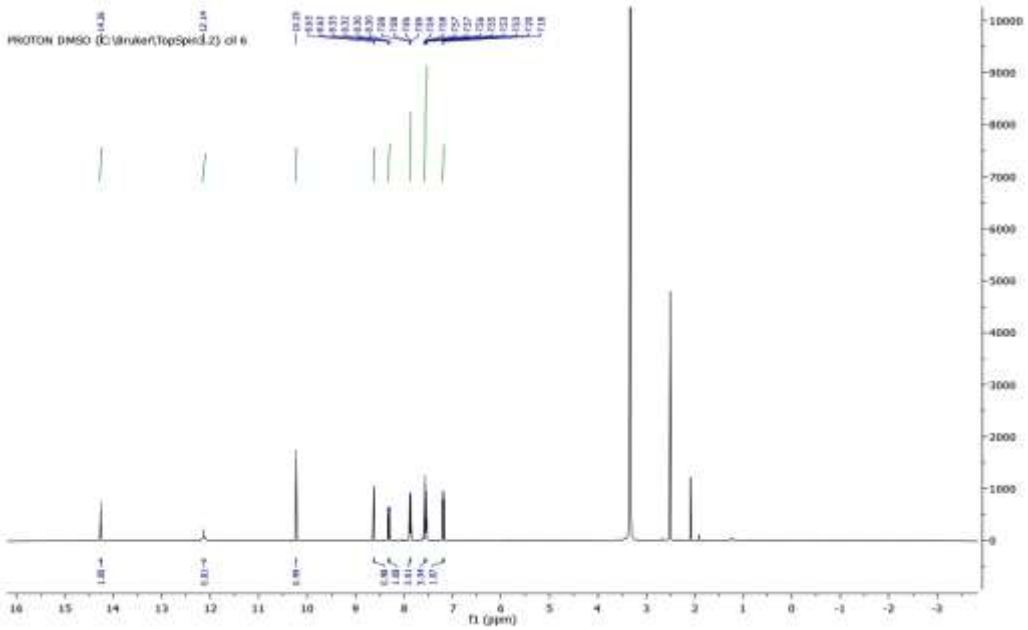


Figure 1: ^{1}H NMR of Schiff base ligand 1 (H_2L^1)

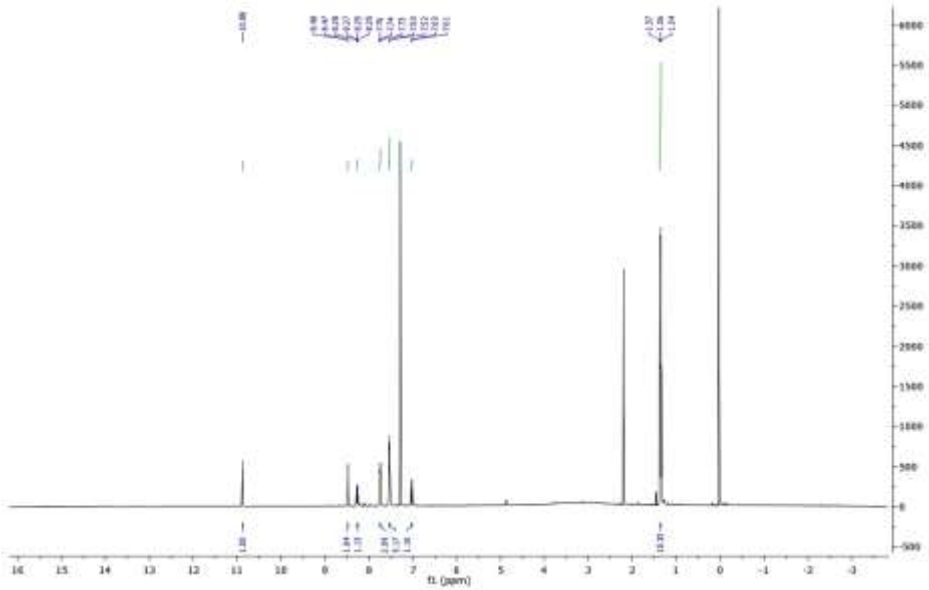


Figure 2: 1H NMR of diethyltin(IV) complex 3 (Et_2SnL^1)

A characteristic singlet signal at δ 10.22-10.34 ppm appeared due to azomethine proton (CH=N) which gets shifted downfield to δ 10.34-10.85 ppm in complexes, confirming the involvement of azomethine group in bond formation[25]. The aromatic protons signals were in the range of δ 8.68-7.20 ppm in Schiff base ligands and remain unaltered on complexation indicating the non- involvement of aromatic protons.

Some additional signals appeared in diorganotin(IV) complexes due to presence of alkyl and aryl groups. The presence of methyl group was confirmed by the presence of singlet of six hydrogen at δ 0.87-1.09 ppm and signal of ten protons as multiplet in the range of δ 0.78-1.37 ppm due to ethyl group directly attached to tin. The butyl proton signals resonate at δ 0.98-1.09 ppm and δ 1.23-1.37 ppm as triplet and multiplet and signals of phenyl protons are in the range of δ 6.76-7.40 ppm respectively. These signals in proton spectra confirmed the complexation.

^{13}C NMR spectra: In Schiff base ligands, signal at δ 160.23-163.08 ppm assigned to azomethine (– CH=N–) carbon, signals at δ 159.73-161.08 ppm and δ 152.32-154.38 ppm due to sulfur and hydroxyl carbon get shifted to lower value in complexes indicating their coordination with tin metal as observed in IR and proton NMR spectra[32]. Additionally, signal at δ 9.11-10.11 due to carbon of methyl group, ethyl carbon signal signals at δ 23.17-32.22 and δ 8.77-9.05, signal at δ 39.68-34.23, 22.19-26.89 and 10.16-9.04 ppm due to carbon of butyl group and phenyl carbon signal appeared at δ 118-122 ppm.

^{119} Sn NMR spectra: ^{119}Sn NMR gives the information regarding the coordination number. A singlet at δ -132.16 to -149.02 ppm for methyl, - 159.09 to – 162.43 ppm for ethyl, -217.52 to -237 ppm for butyl, -336.17 to -342.20 ppm for phenyl complexes appeared respectively. The value of chemical shifts indicated the penta coordinated structure around the tin metal in complexes[28]. In each spectra, a sharp singlet is present which confirmed the existence of single species.

Mass spectra: The further confirmation of structure of synthesised compounds was done by mass spectrometry. The experimental molecular mass is in close agreement with the calculated mass. Figure 3 shows the mass spectra of Schiff base ligand 1 (H_2L^1) and scheme 2 shows its possible fragmentation pattern. The base peak and molecular ion peak in (H_2L^1) are present at m/z= 342.06 which appeared as positive mode. The mass peak at m/z= 267.12 is due to the removal of phenyl group directly attached with triazole ring from parent compound. The peaks at m/z= 217.08 and m/z= 174.12 were due to the further fragmentation of m/z= 267.12 by the removal of hydroxyl, thiol group and nitro group. A peak at m/z= 503.35 was due to the removal of hydroxyl and phenyl group and the formation of its binuclear compound takes place.

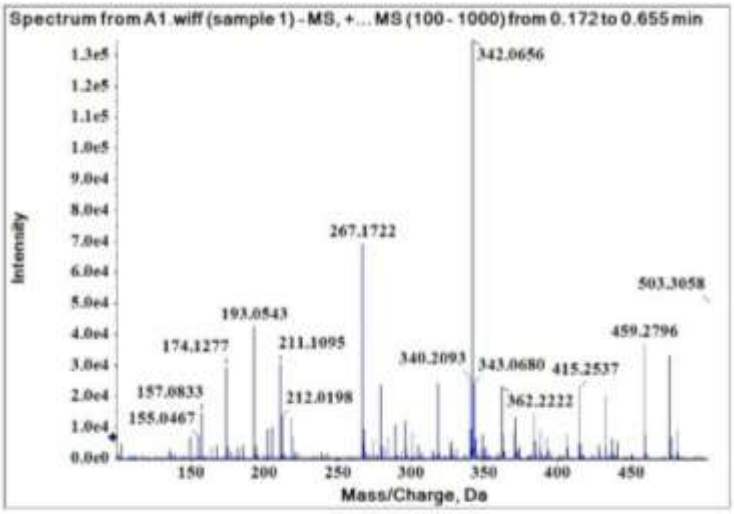
In the mass spectra of complexes, [Me_2SnL^1] has molecular ion peak at m/z= 489.11 due to [M + H] ion and peak at m/z= 458.11 is due to of two methyl group. Other molecular ion peaks present in the complexes were same as the ligand and follows the same fragmentation pattern as ligand. From the mass spectra data it is found that the Schiff base ligands are bound with the tin metal in the mononuclear manner or in 1:1 molar ratio which was also diagnosed from other spectral techniques.

Antimicrobial activity: The Schiff base ligands and their complexes are screened for *in vitro* antimicrobial activity against two gram positive bacteria (*Staphylococcus aureus and Bacillus subtillus*); two gram-negative bacteria (*Escherichia coli and Pseudomonas aeruginosa*) and two fungus (*Aspergillus niger* and *Candida albicans*) using serial dilution method and their MIC values are calculated.

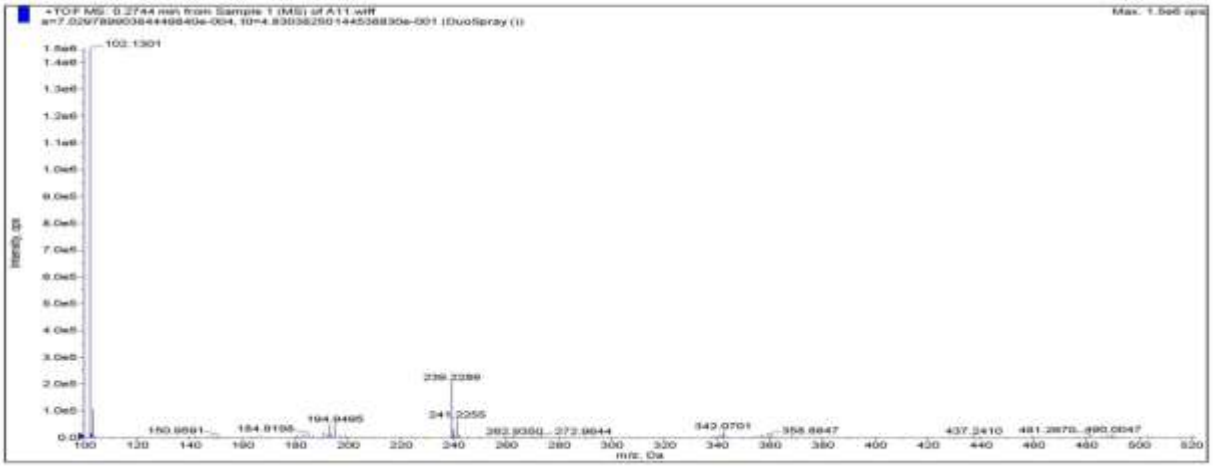
Table 1
Minimum inhibitory concentration (MIC in µM/mL) of compounds (1-10) against bacterial and fungal strains

Compounds	MIC in µM/mL					
	Gram +ve bacteria		Gram –ve bacteria		Fungi	
	S.aureus	*B.subtilis*	*E. coli*	*P.aeruginosa*	*A.niger*	*C.albicans*
1	0.072	0.036	0.018	0.018	0.036	0.018
2	0.066	0.016	0.033	0.016	0.016	0.033
3	0.050	0.025	0.012	0.012	0.025	0.025
4	0.048	0.024	0.024	0.012	0.024	0.024
5	0.042	0.021	0.010	0.021	0.021	0.021
6	0.040	0.020	0.020	0.020	0.020	0.010
7	0.048	0.024	0.048	0.024	0.012	0.024
8	0.044	0.022	0.011	0.022	0.022	0.005
9	0.010	0.020	0.010	0.020	0.010	0.020
10	0.009	0.009	0.004	0.004	0.004	0.004
Ciprofloxacin	0.0047	0.0047	0.0047	0.0047	-	-
Fluconazole	-	-	-	-	0.0102	0.0051

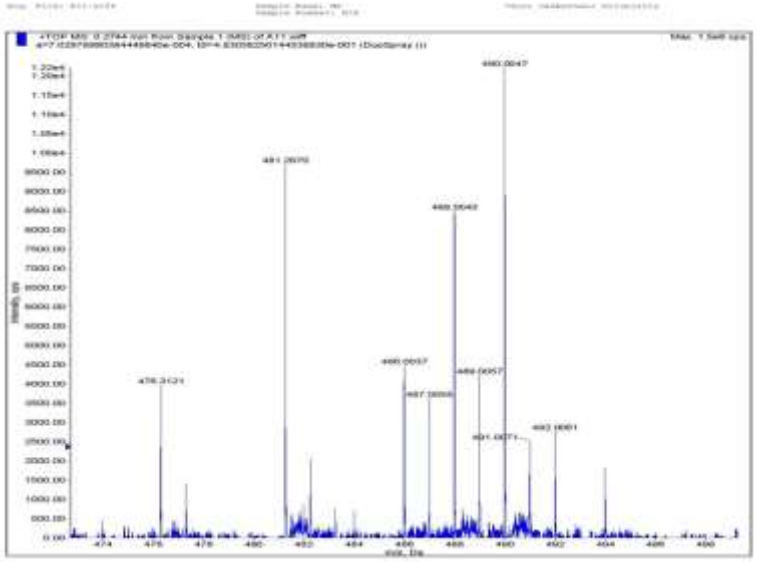
*****4-amino-5-phenyl-1,2,4-triazole-3-thiol MIC value = 0.035 µM/mL



(a)



(b)



(c)

Figure 3: Mass spectra a) Schiff base ligand 2 (H_2L^2) b) dimethyltin(IV) complex 5 (Me_2SnL^2) c) expanded form of dimethyltin(IV) complex (Me_2SnL^2).

Ciprofloxacin and fluconazole are used as positive control for antibacterial and antifungal activity and DMSO as negative control. The results of microbial activity are summarized in table 1 and figure 4.

The results of microbial activity suggested that Schiff base ligands were found to be biologically potent but on complexation with the tin metal, the activity was significantly enhanced. So, it is known that chelation with tin metal makes the Schiff base ligands more potent microbial agent and inhibits the growth of microbes more effectively as compared to free Schiff base ligands[33]. It is considered that coordination number, solubility and cell permeability play a key role in increasing the activity.

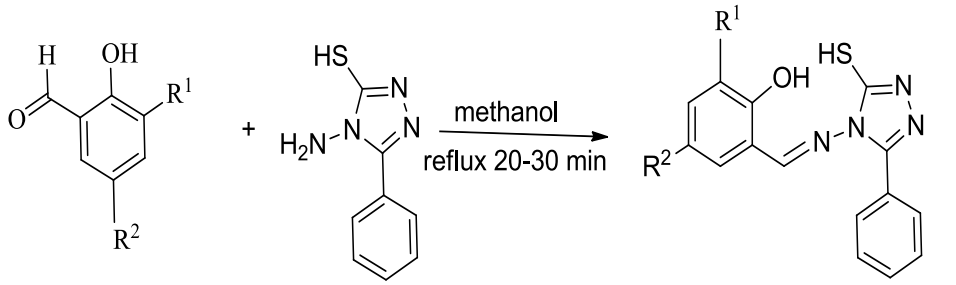
From the antibacterial studies, it is found that Schiff base ligands are active against bacteria and fungus compared to their starting precursor and the presence of electronegative group in benzene ring and azomethine group enhanced the activity due to increase in lipophilicity of compounds[16]. The order of antimicrobial activity of Schiff base ligands is:

$H_2L^2 > H_2L^1$.

On complexation, activity increases due to chelation which was explained by tweedy chelation theory. In all the synthesized complexes, diphenyltin complexes are found to be more active because of the deloacalisation of π electron cloud to whole the chelate ring which results in increasing the lipophilicity of complexes[39]. The general trend for the antimicrobial activity is:

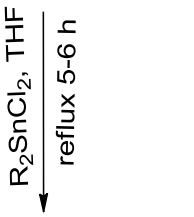
Ph > Bu > Et ≥ Me.

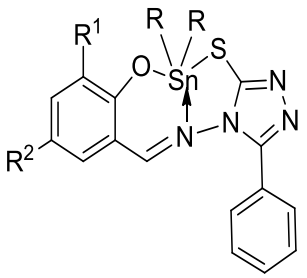
Compounds 10 was found to be more active in all the synthesized compounds having MIC values 0.009 µM/mL which was most active than the standard fluconazole.



Schiff base ligands (**1-2**)

	R^1	R^2
(**1**) H_2L^1 =	H	NO_2
(**2**) H_2L^2 =	OMe	NO_2

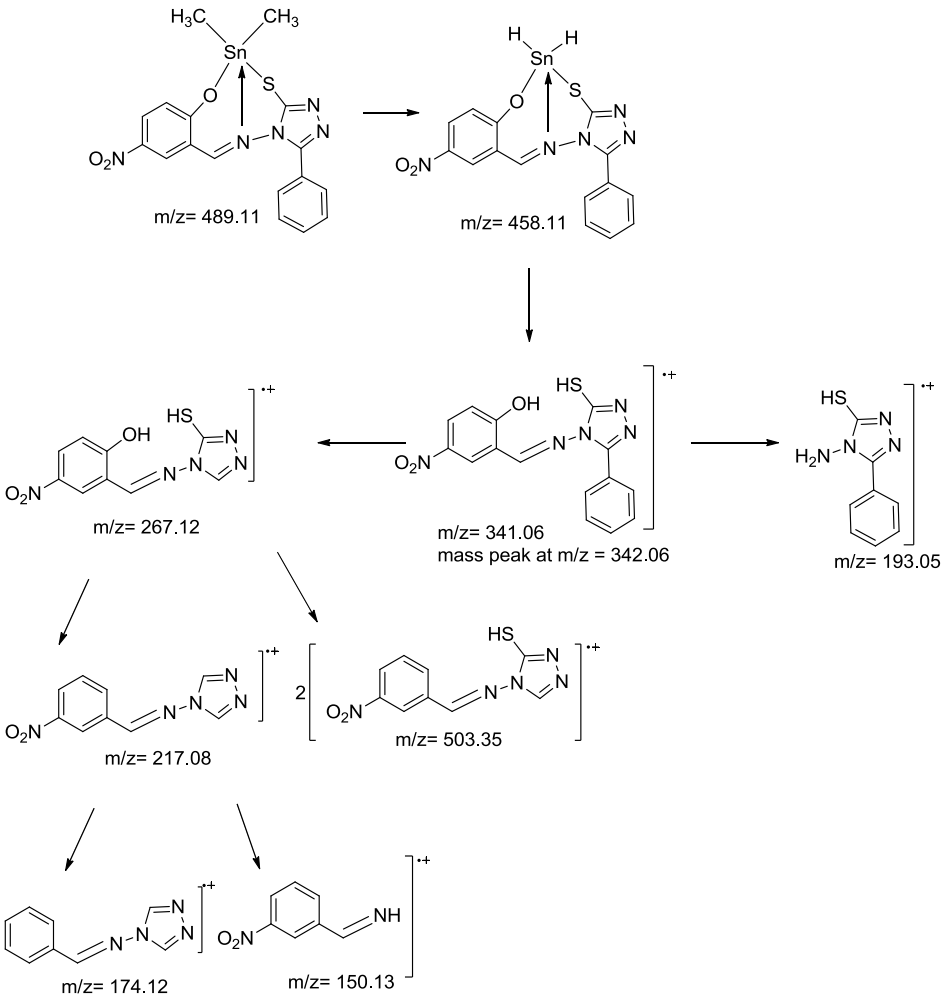




Diorganotin(IV) complexes (**3-10**)

(**3**)	R^1 = H	$R^2 = NO_2$	R= Me	(**7**)	R^1 = OMe	$R^2 = NO_2$	R= Me
(**4**)	R^1 = H	$R^2 = NO_2$	R= Et	(**8**)	R^1 = OMe	$R^2 = NO_2$	R= Et
(**5**)	R^1 = H	$R^2 = NO_2$	R= Bu	(**9**)	R^1 = OMe	$R^2 = NO_2$	R= Bu
(**6**)	R^1 = H	$R^2 = NO_2$	R= Ph	(**10**)	R^1 = OMe	$R^2 = NO_2$	R= Ph

Scheme 1: Synthesis of Schiff base ligands (1-2) and their diorganotin(IV) complexes (3-10).



Scheme 2: Possible mass fragmentation of ligand 1 (H_2L^1) and its dimethyltin(IV) complex 3 (Me_2SnL^1)

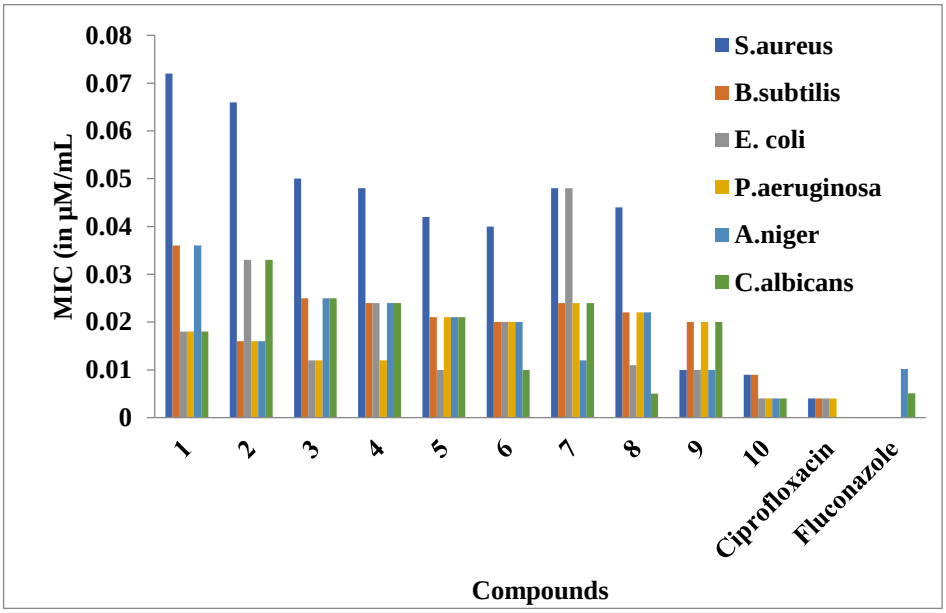


Figure 4: Graph showing minimum inhibitory concentration (in µM/mL) against different bacterial and fungal strain of Schiff base ligands (1-2) and their diorganotin(IV) complexes (3-10)

Conclusion

In the present work we successfully reported the synthesis of 1,2,4 triazole based Schiff bases ligands (1-2) and their diorganotin(IV) complexes (3-10). The geometry and coordination mode of compounds were studied by using spectroscopic techniques which revealed that Schiff bases

are bound to metal in tridentate manner with azomethine nitrogen and phenolic oxygen and thiolic sulfur groups (ONS) and formed pentacoordinated complexes. The *in vitro* antimicrobial and antioxidant studies of the compounds exhibited that on complexation, activity enhanced as compared to the free Schiff base ligands. The compound 10 (Ph_2SnL^2) displayed promising antimicrobial activity.

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