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Water soluble organotin(IV) complexes with Girard-T reagent-based hydrazones: synthesis, spectral characterization, and antibacterial activity

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Two ionic hydrazones, 3-methoxysalicylaldehyde and 4-hydroxysalicylaldehyde Girard-T hydrazinim chloride, (3-OMeH₂SalGT)Cl (**1**) and (4-OHH₂SalGT)Cl (**2**), respectively, and five new water soluble diorganotin complexes R₂Sn((3-OMeSalGT)Cl [R = Ph (**3**), Me (**4**), Bu (**5**)], and R₂Sn(4-OHSalGT)Cl [R = Ph (**6**), Me (**7**)] have been synthesized. Spectroscopic data show that the ligand is deprotonated and coordinated to tin as a zwitterion using the imine nitrogen, and enolic and phenolic oxygens. The *in vitro* antibacterial activity of ligands and complexes has been evaluated against Gram-positive (*Bacillus subtilis* and *Staphylococcus aureus*) and Gram-negative (*Escherichia coli* and *Pseudomonas aeruginosa*) bacteria. The ligands showed low activity while the organotin(IV) complexes exhibited remarkable inhibitory effects and with water solubility, these compounds have excellent potential to be used as drugs.

Keywords: Girard-T; Organotin; Water solubility; Antibacterial activity; Hydrazone

1. Introduction

Schiff bases and their metal complexes have industrial and biological applications [1–3]. In spite of a large number of studies involving the synthesis and characterization of these compounds, there are only a few investigations on ionic Schiff bases. Condensation of Girard's reagents T (trimethylammoniumacetohydrazide chloride), P (pyridiniumacetohydrazide chloride), and others with ketones or aldehydes forming water-soluble ionic hydrazones represents an interesting research subject. Although these Schiff bases are similar to semicarbazones and acid hydrazones, only a few complexes of Girard reagent hydrazones with transition metals have been reported [4–13]. To the best of our knowledge, no attempt has been made to synthesize organotin(IV) complexes with Girard reagent-based ligands. Organotin(IV) complexes have chemical properties, biological significance, industrial importance, and structural variety. Among the non-platinum complexes exhibiting anticancer properties, organotin compounds have received considerable attention. They may show no cross-resistance and possess less or different toxicity than platinum drugs. Many organotin(IV) compounds have been synthesized and tested for their antitumor activities [14–18]. In many

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cases, *in vitro* activity of these compounds was not retained under *in vivo* conditions, frequently from lack of water solubility of these molecules. Solubility in water dominates the *in vivo* testing of compounds with promising *in vitro* properties [19, 20]. As a part of our studies on organotin(IV) complexes [21–25] and to design organotin(IV) complexes with improved water solubility, herein we report synthesis, characterization, and antibacterial activity of two Girard-T hydrazones, (3-OMeH₂SalGT)Cl and (4-OHH₂SalGT)Cl, derived from condensation of Girard's T reagent with 3-methoxysalicylaldehyde and 4-hydroxysalicylaldehyde, respectively, and their diorganotin(IV) complexes.

2. Experimental

2.1. Materials and methods

All starting materials were purchased from Merck while diphenyltin dichloride and Girard-T reagent were supplied from Alfa Aesar and Acros Company, respectively; all were used as received. All solvents were of reagent grade and used without purification. IR spectra were obtained using a FT BOMEM MB102 spectrophotometer. ¹H and ¹¹⁹Sn{¹H} NMR spectra were recorded with a Bruker 400 MHz Avance Ultrashield Spectrometer using TMS and SnMe₄, as references, respectively.

2.2. Synthesis of (3-OMeH₂SalGT)Cl (1)

3-Methoxysalicylaldehyde (0.760 g, 5 mmol) in absolute methanol (5 mL) was added slowly to a solution of Girard-T (0.835 g, 5 mmol) in absolute methanol (7 mL) with constant stirring. The resulting solution was refluxed for 60 min at 80 °C. A white precipitate formed after evaporating the solvent at room temperature. The resulting product was collected, washed with ethanol followed by diethyl ether and dried over CaCl₂.

Yield: 0.869 g (60%); m.p. 110–115 °C; Anal. Calcd for C₁₃H₂₀ClN₃O₃ (%): C, 51.74; H, 6.68; N, 13.92. Found: C, 51.50; H, 6.74; N, 13.46. FT-IR (KBr, cm⁻¹): 3450–3420 br, ν(OH); 3160, ν(NH); 3020, 2930, ν(CH); 1692, ν(C=O); 1612, ν(C=N). ¹H NMR (DMSO-d₆): δ = 13.3 (s, br, NH), 12.06 (s, OH_{enolic}), 10.43, 9.38 (s, OH_{phenolic}), 8.65, 8.46 (s, HC=N), 7.36–6.81 (aromatic protons), 4.81, 4.45 (s, CH₂), 3.82, 3.80 (s, OCH₃), 3.34, 3.31 (s, NCH₃).

2.3. Synthesis of (4-OHH₂SalGT)Cl (2)

Girard-T (0.835 g, 5 mmol) in methanol (7 mL) was added to a solution of 4-hydroxy salicylaldehyde (0.690 g, 5 mmol) in methanol (5 mL) and stirred for 30 min. During this time a white precipitate gradually formed, was collected, washed with ethanol followed by diethyl ether and dried over CaCl₂.

Yield: 1.338 g (93%); m.p. 250 °C; Anal. Calcd for C₁₂H₁₈ClN₃O₃ (%): C, 50.09; H, 6.31; N, 14.60. Found: C, 50.33; H, 6.15; N, 14.84. FT-IR (KBr, cm⁻¹): 3250–3150 br, ν(OH); 3113, ν(NH); 3012, 2905, ν(CH); 1693, ν(C=O); 1618, ν(C=N). ¹H NMR (DMSO-d₆): δ = 12.70 (s, br, NH), 11.73 (s, OH_{enolic}), 10.97, 10.08, 9.97 (s, OH_{phenolic}), 8.42, 8.25 (s, HC=N), 7.54, 7.37 (d, H₆, *J* = 9.0 Hz), 6.41–6.31 (m, H_{3,5}), 4.73, 4.31 (s, CH₂), 3.30, 3.28 (s, NCH₃).

2.4. Synthesis of $\text{Ph}_2\text{Sn}(3\text{-OMeSalGT})\text{Cl}$ (3)

Triethylamine (0.28 mL, 2 mmol) was added to a stirring solution of (3-OMeH₂SalGT)Cl (0.289 g, 1 mmol) in absolute methanol (7 mL). Then a solution of Ph_2SnCl_2 (0.340 g, 1 mmol) in methanol (3 mL) was added. This solution was refluxed for 120 min at 80 °C. During this time, a yellow precipitate gradually formed. The product was filtered, washed with cool ethanol, and dried in vacuum on CaCl_2 . Yield: 0.3 g (52%); m.p. 250 °C; Anal. Calcd for $\text{C}_{25}\text{H}_{28}\text{N}_3\text{O}_3\text{ClSn}$ (%): C, 52.43; H, 4.94; N, 7.34. Found: C, 52.54; H, 4.64; N, 7.29. FT-IR (KBr, cm^{-1}): 1612, 1605, $\nu(\text{C}=\text{N})$; 1212, $\nu(\text{C}-\text{O})$; 548, $\nu(\text{Sn}-\text{O})$; 461, $\nu(\text{Sn}-\text{N})$. ^1H NMR (DMSO- d_6): δ =8.65 [s, 1H, $\text{CH}=\text{N}$, $^3J(^{119}\text{Sn}-^1\text{H})=40.0$ Hz], 7.56 [dd, 4H, H_o in SnPh_2 , $^3J_{\text{HH}}=7.4$, $^4J_{\text{HH}}=1.8$, $^3J(^{119}\text{Sn}-^1\text{H})=86.7$ Hz], 7.31–7.36 (m, 6H, $\text{H}_{m,p}$ in SnPh_2), 7.00–7.06 (m, 2H, $\text{H}_{4,6}$), 6.68 (dd, 1H, H_5 , $J=7.9$, 7.9 Hz), 4.17 (s, 2H, CH_2), 3.77 (s, 3H, OCH_3), 3.12 (s, 9H, $\text{N}-\text{CH}_3$). ^{13}C NMR (DMSO- d_6): δ =53.08 (NCH_3), 55.91 (OCH_3), 65.76 (C9), 115.65 (C1), 116.29 (C4), 117.33 (C5), 126.39 (C6), 127.94 [C_{meta} in SnPh_2 , $^3J(^{119}\text{Sn}-^{13}\text{C})=60.6$ Hz], 128.26 [C_{para} in SnPh_2], 134.20 [C_{ortho} in SnPh_2 , $^2J(^{119}\text{Sn}-^{13}\text{C})=60.0$ Hz], 136.39 [C_{ipso} in SnPh_2], 150.08 (C7), 151.30 (C2), 159.31 (C3), 164.12 (C8). $^{119}\text{Sn}\{^1\text{H}\}$ NMR (DMSO- d_6): δ =−443.2.

2.5. Synthesis of $\text{Me}_2\text{Sn}(3\text{-OMeSalGT})\text{Cl}$ (4)

(3-OMeH₂SalGT)Cl (0.289 g, 1 mmol) was dissolved in MeOH (7 mL) in presence of NEt_3 (0.28 mL, 2 mmol). This solution was stirred for 30 min and then Me_2SnCl_2 (0.220 g, 1 mmol) in methanol (3 mL) was added. The solution was refluxed for 180 min at 80 °C. A yellow precipitate formed after evaporating the solvent at room temperature. This product was collected, washed with cool ethanol, and dried in vacuum on CaCl_2 . Yield: 0.4 g (89%); m.p. 198 °C; Anal. Calcd for $\text{C}_{15}\text{H}_{24}\text{N}_3\text{O}_3\text{ClSn}$ (%): C, 40.17; H, 5.39; N, 9.37. Found: C, 40.29; H, 5.89; N, 9.00. FT-IR (KBr, cm^{-1}): 1619, 1605, $\nu(\text{C}=\text{N})$; 1214, $\nu(\text{C}-\text{O})$; 546, $\nu(\text{Sn}-\text{O})$; 417, $\nu(\text{Sn}-\text{N})$; 610, $\nu_{\text{as}}(\text{Sn}-\text{C})$; 585, $\nu_{\text{s}}(\text{Sn}-\text{C})$. ^1H NMR (DMSO- d_6): δ =8.58 [s, 1H, $\text{CH}=\text{N}$, $^3J(^{119}\text{Sn}-^1\text{H})=22.0$ Hz], 6.94–6.97 (m, 2H, $\text{H}_{4,6}$), 6.61 (dd, 1H, H_5 , $J=7.8$, 7.8 Hz), 4.1 (s, 2H, CH_2), 3.71 (s, 3H, OCH_3), 3.22 (s, 9H, $\text{N}-\text{CH}_3$), 0.68 [s, 6H, $\text{Sn}-\text{CH}_3$, $^2J(^{119}\text{Sn}-^1\text{H})=96.4$ Hz]. ^{13}C NMR (DMSO- d_6): δ =10.57 [SnCH_3 , $^1J(^{119}\text{Sn}-^{13}\text{C})=876.6$ Hz], 53.25 (NCH_3), 55.40 (OCH_3), 65.53 (C9), 115.30 (C1), 115.70 (C4), 116.83 (C5), 126.05 (C6), 151.08 (C7), 156.24 (C2), 160.47 (C3), 164.70 (C8). $^{119}\text{Sn}\{^1\text{H}\}$ NMR (DMSO- d_6): δ =−272.9.

2.6. Synthesis of $\text{Bu}_2\text{Sn}(3\text{-OMeSalGT})\text{Cl}$ (5)

This complex was synthesized as described for **4** from Bu_2SnCl_2 (0.304 g, 1 mmol). Yield: 0.43 g (82%); m.p. 140 °C; Anal. Calcd for $\text{C}_{21}\text{H}_{36}\text{N}_3\text{O}_3\text{ClSn}$ (%): C, 47.35; H, 6.81; N, 7.88. Found: C, 48.00; H, 6.38; N, 7.85. FT-IR (KBr, cm^{-1}): 1622, 1601, $\nu(\text{C}=\text{N})$; 540, $\nu(\text{Sn}-\text{O})$; 423, $\nu(\text{Sn}-\text{N})$. ^1H NMR (DMSO- d_6): δ =8.61 [s, 1H, $\text{CH}=\text{N}$], 6.58–6.94 [m, 2H, $\text{H}_{4,6}$], 6.55 [dd, 1H, H_5 , $J=7.8$, 7.8 Hz], 4.13 (s, 2H, CH_2), 3.71 (s, 3H, OCH_3), 3.24 (s, 9H, $\text{N}-\text{CH}_3$), 0.74 (t, $J=8$ Hz, 6H, H_δ), 1.31–1.34 (m, 4H, H_γ), 1.35–1.43 (m, 8H, $\text{H}_{\alpha,\beta}$). ^{13}C NMR (DMSO- d_6): 13.51 (C_δ in SnBu_2), 25.65 [C_γ in SnBu_2 , $^3J(^{119}\text{Sn}-^{13}\text{C})=126.1$ Hz], 26.87 (C_β in SnBu_2 , $^2J(^{119}\text{Sn}-^{13}\text{C})=34.4$ Hz), 29.21 (C_α in SnBu_2), 53.16 (NCH_3), 55.50 (OCH_3), 65.33 (C9), 115.03 (C1), 115.89 (C4), 116.68 (C5), 126.18 (C6), 150.98 (C7), 157.22 (C2), 161.04 (C3), 165.20 (C8). $^{119}\text{Sn}\{^1\text{H}\}$ NMR (DMSO- d_6): δ =−303.5.

2.7. Synthesis of $\text{Ph}_2\text{Sn}(4\text{-OHSalGT})\text{Cl}$ (**6**)

Complex **6** was synthesized as described for **3** from (4-OHH₂SalGT)Cl (0.287 g, 1 mmol). Yield: 0.34 g (61%); m.p. 272–274 °C (dec.); Anal. Calcd for C₂₄H₂₆N₃O₃ClSn (%): C, 51.60; H, 4.69; N, 7.52. Found: C, 51.53; H, 4.96; N, 8.04, FT-IR (KBr, cm⁻¹): 1623, 1600, $\nu(\text{C}=\text{N})$; 558, $\nu(\text{Sn}-\text{O})$; 450, $\nu(\text{Sn}-\text{N})$. ¹H NMR (DMSO-d₆): δ = 8.54 [s, 1H, CH=N], 7.55–7.57 [m, 4H, H_o in SnPh₂, ³ $J(^{119}\text{Sn}-^1\text{H})$ = 85.7 Hz], 7.34–7.36 (m, 6H, H_{m,p} in SnPh₂), 7.26 (d, 1H, H₆, J = 9.1 Hz), 6.24–6.35 (m, 2H, H_{3,s}), 4.16 (s, 2H, CH₂), 3.16 (s, 9H, N-CH₃). ¹³C NMR (DMSO-d₆): δ = 53.12 (NCH₃), 65.87 (C9), 106.45 (C1), 106.97 (C6), 110.44 (C5), 128.05 [C_{meta} in SnPh₂], ³ $J(^{119}\text{Sn}-^{13}\text{C})$ = 90.1 Hz], 128.46 [C_{para} in SnPh₂], 134.20 [C_{ortho} in SnPh₂], ² $J(^{119}\text{Sn}-^{13}\text{C})$ = 57.3 Hz], 148.90 [C_{ipso} in SnPh₂], 136.91 (C3), 159.01 (C7), 162.76 (C2), 164.26 (C4), 168.73 (C8). ¹¹⁹Sn{¹H} NMR (DMSO-d₆): δ = -433.9.

2.8. Synthesis of $\text{Me}_2\text{Sn}(4\text{-OHSalGT})\text{Cl}$ (**7**)

Complex **7** was synthesized as described for **4** from (4-OHH₂SalGT)Cl (0.287 g, 1 mmol). Yield: 0.31 g (80%); m.p. 237 °C; Anal. Calcd for C₁₄H₂₂N₃O₃ClSn (%): C, 38.69; H, 5.10; N, 9.67. Found: C, 38.49; H, 4.78; N, 9.76. FT-IR (KBr, cm⁻¹): 1605, $\nu(\text{C}=\text{N})$; 621, $\nu_{\text{as}}(\text{Sn}-\text{C})$; 552, $\nu_{\text{s}}(\text{Sn}-\text{C})$; 552, $\nu(\text{Sn}-\text{O})$; 429, $\nu(\text{Sn}-\text{N})$. ¹H NMR (DMSO-d₆): δ = 8.52 [s, 1H, CH=N, ³ $J(^{119}\text{Sn}-^1\text{H})$ = 35.1 Hz], 7.20 (d, 1H, H₆, J = 8.7 Hz), 6.21 [dd, 1H, H₅, J = 8.6, 2.2 Hz], 6.05 (d, 1H, H₃, J = 2.2 Hz), 4.01 (s, 2H, CH₂), 3.17 (s, 9H, N-CH₃), 0.67 [s, 6H, Sn-CH₃, ² $J(^{119}\text{Sn}-^1\text{H})$ = 88.3 Hz]. ¹³C NMR (DMSO-d₆): δ = 7.42 [SnCH₃, ¹ $J(^{119}\text{Sn}-^{13}\text{C})$ = 811.4 Hz], 53.23 (NCH₃), 65.61 (C9), 105.86 (C1), 106.91 (C6), 109.94 (C5), 136.76 (C3), 160.91 (C7), 163.22 (C2), 164.68 (C4), 168.25 (C8). ¹¹⁹Sn{¹H} NMR (DMSO-d₆): δ = -223.4.

2.9. Antibacterial tests

The *in vitro* antibacterial activities of ligands and their corresponding organotin(IV) complexes were investigated against standard strains of two Gram-positive (*Bacillus subtilis* ATCC 12711 and *Staphylococcus aureus* ATCC 6538) and two Gram-negative (*Escherichia coli* ATCC 11,303 and *Pseudomonas aeruginosa* ATCC 27853) bacteria. In order to compare the results, vancomycin (30 mg/disk), streptomycin (10 mg/disk), penicillin (10 mg/disk), nalidixic acid (30 mg/disk), and gentamicin (10 mg/disk) were used as standard antibacterial drugs. Determination of the antibacterial activity was carried out by paper-disk diffusion method. The solutions from **3** and **6** in DMSO and **1**, **2**, **4**, **5**, and **7** in H₂O were prepared at 5, 10, 20, and 40 mg/mL concentration. Muller Hinton broth was used for preparing basal media for the bioassay of the organisms. A lawn culture from 0.5 MacFarland suspension of each strain was prepared on Muller Hinton agar. Blank paper disks (6.4 mm diameter) were saturated with a solution of test compounds (40 μL) and placed on the surface of the agar plates. On one paper disk only DMSO was poured as a control. The plates were incubated at 37 °C for 24 h. The inhibition zone diameters around each disk were measured in mm.

3. Results and discussion

3.1. Synthesis

Condensation of the Girard's T reagent [(NH₂-NH-C(=O)-CH₂N(CH₃)₃]Cl with 3-methoxyisalicylaldehyde and 4-hydroxyisalicylaldehyde gives the corresponding hydrazones as

ammonium quaternary salts, (3-OMeH₂SalGT)Cl (**1**) and (4-OHH₂SalGT)Cl (**2**), respectively. Owing to the existence of ketoamide (NH–C=O) in these compounds two tautomers, keto-amine and enol-imine, are possible. The synthetic pathway and tautomeric forms of **1** and **2** are shown in figure 1. According to the literature [10, 12], in the solid state such compounds are in keto-amine form (I) and associated with the organic cation through a short hydrogen bond with chloride. Organotin(IV) complexes **3–7** were prepared by reaction of R₂SnCl₂ (R = Ph, Me or Bu) with the corresponding hydrazone in methanol in the presence of NEt₃ as a base. The ligands and complexes are stable in air, soluble in DMSO and DMF, less soluble in EtOH and CHCl₃, and insoluble in Et₂O. Compounds **3** and **6** are moderately soluble and the others are readily soluble in water. The ligands and complexes were characterized by elemental analysis and IR and NMR spectroscopy. Attempts to grow single crystals suitable for X-ray crystallography were abortive.

3.2. Spectroscopic studies

IR spectra of ligands NH and C=O stretches indicate tautomeric form I in the solid state. In IR spectra of the complexes disappearance of $\nu(\text{O–H})$ and $\nu(\text{N–H})$ shows deprotonation of ligand and subsequent coordination to tin. The strong and sharp band assigned to $\nu(\text{C=O})$ in the ligand at 1692 cm^{-1} is absent in spectra of complexes supporting ligand coordination in the enol form. The $\nu(\text{C=N})$ at $1612\text{--}1618\text{ cm}^{-1}$ in the spectra of ligands shifts to lower frequency indicating coordination of azomethine nitrogen. The appearance of new bands in the IR spectra of complexes at $417\text{--}461$ and $558\text{--}540\text{ cm}^{-1}$ assigned to $\nu(\text{Sn–N})$ and $\nu(\text{Sn–O})$, respectively, supports bonding of nitrogen and oxygen to tin [26].

In ¹H NMR spectra of free Schiff bases, two groups of signals were observed from presence of tautomeric forms I and II in solution. The ratio of the integrals of the signals provides a reliable measure of ketonic to enolic forms in solution as 55:45 for **1** and 60:40 for **2**. In ¹H NMR spectra of complexes, the absence of signals for two acidic hydrogens suggests deprotonation and coordination of phenolic and enolic oxygens. The signal attributable to imine proton of the free ligands is accompanied by satellites in

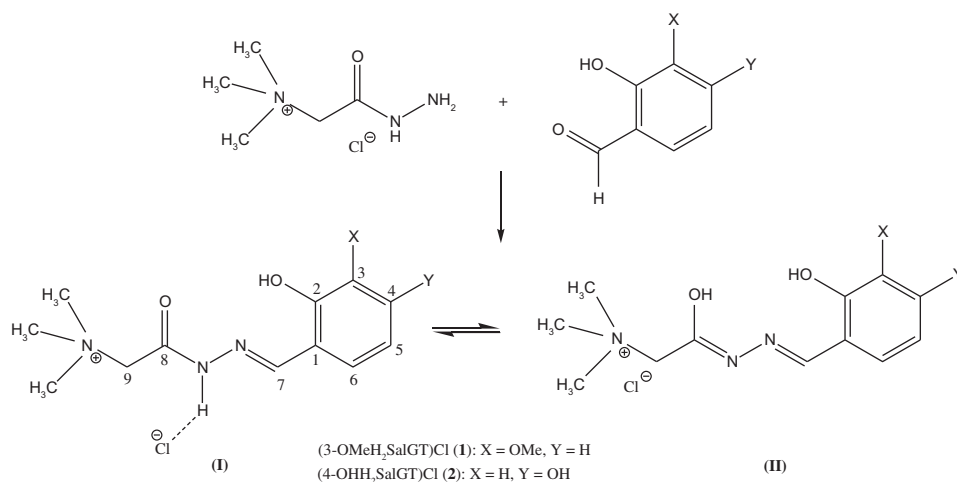


Figure 1. Synthetic pathway and tautomeric forms of ligands.

complexes due to $^3J(^{119}\text{Sn-H})$ coupling, an indication that the imine nitrogen is coordinated to tin(IV). The ^1H NMR spectrum of dimethyl complexes shows a singlet at low frequency for SnMe_2 accompanied by satellites because of $^{119}\text{Sn-H}$ coupling. Substitution of this coupling constant in the Lockhart-Manders equation [27] gives the values 155.8 and 142.4° for the Me-Sn-Me angle in **4** and **7**, respectively, in DMSO.

The $^{119}\text{Sn}\{^1\text{H}\}$ NMR spectra of all complexes show one sharp singlet at lower frequency than SnPh_2Cl_2 (−32 ppm), SnBu_2Cl_2 (+122 ppm), and SnMe_2Cl_2 (+137 ppm). ^{119}Sn NMR chemical shift is strongly dependent on the coordination number of tin, and an increase in coordination number produces a large upfield shift. On the basis of the

Table 1. Antibacterial activity data of ligands and their organotin(IV) complexes.

Compound	Conc. (mg/mL)	Inhibition zone (mm)			
		<i>E. coli</i>	<i>P. aeruginosa</i>	<i>S. aureus</i>	<i>B. subtilis</i>
1	5	7	13	8	7
	10	7	17	9	9
	20	8	17	14	10
	40	16	20	16	12
2	5	7	15	8	7
	10	7	15	8	7
	20	9	18	10	7
	40	16	20	15	9
3	5	23	12	n.c.	29
	10	23	14	n.c.	33
	20	24	17	n.c.	34
	40	24	19	n.c.	34
4	5	22	14	19	30
	10	24	18	23	30
	20	25	24	24	30
	40	27	24	26	31
5	5	10	14	7	17
	10	16	20	8	23
	20	18	24	12	23
	40	20	27	14	31
6	5	8	9	7	19
	10	14	11	7	21
	20	19	19	9	25
	40	25	24	11	30
7	5	22	13	n.c.	28
	10	24	16	n.c.	32
	20	27	18	n.c.	33
	40	28	19	n.c.	38
Vancomycin		19	n.a.	17	24
Streptomycin		16	n.a.	12	22
Penicillin		12	n.a.	19	13
Nalidixic acid		25	n.a.	12	23
Gentamicin		20	20	16	21

Notes: n.a. = no activity; n.c. = no check.

chemical shift ranges proposed empirically for organotin(IV) derivatives [28–32], the coordination number of tin is six for all complexes.

3.3. Antibacterial studies

The *in vitro* antibacterial activities of the Schiff bases and their organotin(IV) complexes were evaluated along with five standard antibacterial drugs, *viz.* vancomycin, streptomycin, penicillin, nalidixic acid, and gentamycin. The micro-organisms used in this work include *B. subtilis* and *S. aureus* (as Gram-positive bacteria) and *E. coli* and *P. aeruginosa* (as Gram-negative bacteria). The results are presented in table 1. Comparing the biological activity of the Schiff bases, organotin(IV) complexes and standard drugs, reveals that the organotin complexes have activity against all bacteria under investigation and show more inhibition than the parent ligands. Enhanced antibacterial activity of the ligand on complexation may be due to electron delocalization over the whole chelate ring increasing the lipophilic character which favors permeation of the complexes through the lipid layer of the cell membrane [33–36] and also because of the intrinsic biological activity of organotin. Bacteria of the genus *Pseudomonas* are a resistant micro-organism that many standard drugs have no activity against [37, 38]. Therefore, it is interesting that *P. aeruginosa* was remarkably inhibited by all complexes. In most cases, toxicity towards *S. aureus* (as Gram-positive bacteria) is more than Gram(–) strains. The reason is the difference in the structures of cell walls. The walls of Gram(–) cells are more complex than those of Gram(+) cells. Lipopolysaccharides form an outer lipid membrane and contribute to the complex antigenic specificity of Gram(–) cells. The antibacterial activities of compounds are due to either killing the bacteria or inhibiting multiplication of them by blocking their active sites. A mechanism postulated for action of antibacterial compounds is deactivation of various cellular enzymes or denaturation of one or more proteins of the cell [39–42]. Lipophilicity is an important factor making the drug more soluble in lipids which facilitate micro-organism membrane crossing. Solubility in water is important for activity *in vivo*. In view of the remarkable biological activities of synthesized complexes with solubility in both water and organic solvents, these compounds have excellent potential as drugs.

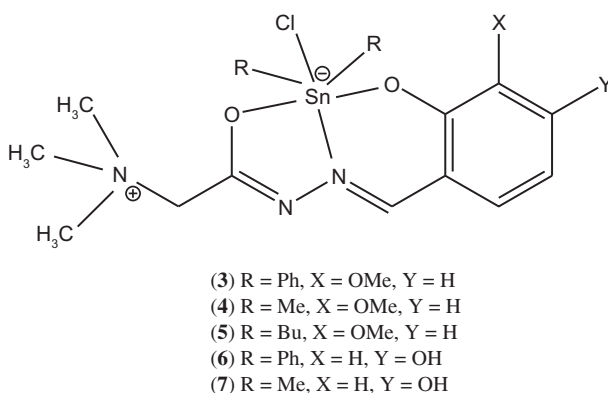


Figure 2. Suggested structures for 3–7.

4. Conclusion

On the basis of the above discussion and with due regard to the structure of transition metal complexes with similar ligands [4, 10, 12], the aforesaid Schiff bases were coordinated as twice-deprotonated using ONO donors. Therefore, the complexes are six-coordinate and neutral (figure 2). The synthesized organotin complexes are remarkable in inhibiting Gram-positive (*B. subtilis* and *S. aureus*) and Gram-negative (*E. coli* and *P. aeruginosa*) bacterial species. These new complexes are the first examples of organotin compounds with Girard reagent-based ligands. In view of the solubility of these complexes in both water and organic solvents, they are good candidates for cytotoxicity studies and solubility in water dominates the *in vivo* testing of compounds with promising *in vitro* properties. This research opens new avenues to study water soluble organotin(IV) complexes with potential biological activities. This project is currently under study in our laboratory.

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