ISSN 1070-3284, Russian Journal of Coordination Chemistry, 2019, Vol. 45, No. 12, pp. 889–898. © Pleiades Publishing, Ltd., 2019.

Tin(IV) Complexes with Salen Type Schiff Base: Synthesis, Spectroscopic Characterization, Crystal Structure, Antibacterial Screening and Cytotoxicity

S. Ali[a], T. Ara[a], M. Danish[b], S. Shujah[c, *], and A. M. Z. Slawin[d]
[a] *Department of Chemistry, Quaid-e-Azam University, Islamabad, 45320 Pakistan*
[b] *Department of Chemistry, University of Gujrat, Gujrat, 50700 Pakistan*
[c] *Department of Chemistry, Kohat University of Science and Technology, Kohat, 26000 Pakistan*
[d] *Molecular Structure Laboratory, School of Chemistry, University of St Andrews, St Andrews, KY16 9ST UK*
**e-mail: shaukat.shujah@yahoo.com*

Received August 18, 2018; revised November 20, 2018; accepted December 24, 2018

Abstract—A series of six tin(IV) complexes [$SnCl_2$(L) (**I**), Me_2Sn(L) (**II**), Bu_2Sn(L) (**III**), Ph_2Sn(L) (**IV**), Oct_2Sn(L) (**V**), BuSnCl(L) (**VI**)] derived from *N*,*N*'-bis(2-hydroxy-1-naphthylidene)-1,2-diaminobenzene [LH_2] have been synthesized. The obtained compounds were characterized by elemental analysis, mass spectrometry, FT-IR and NMR (^{1}H, ^{13}C) spectroscopy. The crystal structures of compounds (**IV**) and (**VI**) have also been determined by single crystal X-ray analysis (CIF files CCDC nos. 856596 (**IV**) and 856595 (**VI**)). The study revealed that the complexes exist as discrete monomeric species and the tin atom is hexa-coordinated in a distorted octahedral geometry. The two phenyl groups in compound (**IV**) are at *trans*-positions. Similarly, in complex (**VI**) the butyl and chloro groups also adopt *trans*-orientation. The in vitro antibacterial screening and cytotoxicity investigations revealed that the biological activities significantly depend upon the alkyl or others groups present on tin atom. Most of the tin(**IV**) complexes are active against *Escherichia coli* and highest activity is shown by complex (**IV**) against *Bacillus subtilis*. Furthermore, complex (**IV**) has also demonstrated the highest cytotoxicity against brine shrimp with LD_{50} value 0.858 μg/mL.

Keywords: organotin(IV), Schiff base, X-ray structure, antibacterial activity, cytotoxicity

DOI: 10.1134/S1070328419120017

INTRODUCTION

Schiff bases and their metal complexes are famous for their antimicrobial activity [1], use in potentiometric membrane sensors [2], catalytic oligomerization [3], isomerization [4], and metathesis reactions [5]. Schiff bases are being used as starting materials in the preparation of antibiotics containing amine groups, potential pesticides and herbicides, for determining the lysine and arginine quantity in food and the total protein amount in serum samples. Schiff bases can be polymerized to get polymers with superior mechanical, thermal, electrical and dielectric properties. They are being used in photoconductive layers in electrophotographic photoreceptors that show improved chargeability, durability and sensitivity. Organotins are currently famous for their kinetic studies, interaction with DNA and as anticancer agents [6, 7]. Salen type of Schiff bases are chelating agents with ONNO donor sites which exhibit photophysical and thermal protective properties [8, 9], and can be used to obtain organotin derivatives with unique nonlinear optical, catalytic and biological properties [10–14].

In continuation with our previous work and to assess the change in biological properties of Schiff bases after complexation, we have synthesized a series of tin(IV) derivatives of an ONNO donor dibasic tetradentate Schiff base. The synthesized compounds have been structurally characterized through spectrometric techniques and single crystal X-ray analysis.

EXPERIMENTAL

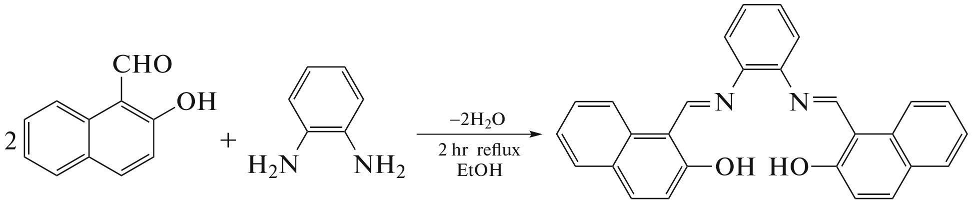
Materials and methods. Organotin(IV) halides, organotin(IV) oxides and hydroxides, salicylaldehyde, 2-hydroxy-1-naphthaldehyde, and *o*-phenylenediamine were purchased from Aldrich Chemicals (USA). All the solvents were purchased from Merck (Germany), and dried before use according to the standard methods [15]. Melting points were determined in a capillary tube using Electrothermal Melting Point Apparatus model MPD Mitamura Riken

Kogyo (Japan) and are uncorrected. The IR-absorption spectra were recorded using KBr pellets on a Bio-Rad Excalibur FT-IR model in the frequency range of 4000–400 cm^{-1}. Multinuclear NMR (^{1}H and ^{13}C) spectra were recorded on a Brüker 300 MHz FT-NMR Spectrometer (Brüker, Switzerland). The elemental analyses were made on Elemental Analyzer, Leco Corporation (USA). The mass spectrometric analyses were carried out on MAT-312, mass spectrometer. The *m/z* values of all fragments containing tin, which show a typical isotopic peak pattern in mass spectrum, are reported by using Sn = 120.

Synthesis of *N*,*N*'-bis(2-hydroxy-1-naphthylidene)-1,2-diaminobenzene (LH$_2$) The synthesis of ligand was carried out by reacting 2-hydroxy-1-naphthaldehyde 1.6 g (9.3 mmol) and *o*-phenylenediamine 0.5 g (4.6 mmol) in ethanol (50 mL). The mixture was refluxed for 2 h with continuous stirring. The solution on cooling afforded yellow precipitates which were collected by filtration and washed several times with ethanol (Scheme 1). The analytically pure product was isolated in a yield of 78% with m.p. 215–217°C.

For $C_{28}H_{20}N_2O_2$			
Anal. calcd., %	C, 80.75	H, 4.84	N, 6.73
Found, %	C, 80.59	H, 5.18	N, 6.75

FT-IR (ν, cm^{-1}): 3376 ν(OH)$_{phenolic}$, 1618 ν(C=N), 1565, 1530, 1473 ν(C=C)$_{arom}$, 1325 ν(C–O). ^{1}H NMR (δ, ppm): 15.14 (s., 1H, OH), 8.45 (d., 2H, naphthyl–H, $^{3}J_{H-H}$ = 8.4), 7.36 (t., 2H, naphthyl–H, $^{3}J_{H-H}$ = 7.2), 7.54 (t., 2H, naphthyl–H, $^{3}J_{H-H}$ = 7.4), 7.33 (d.d., 2H, naphthyl–H, $^{3}J_{H-H}$ = 6.0, 3.3), 7.95 (d., 2H, naphthyl–H, $^{3}J_{H-H}$ = 9.0), 7.03 (d., 2H, naphthyl–H, $^{3}J_{H-H}$ = 9.3), 9.65 (s., 2H,C=NH), 7.818–7.769 (m., 4H, Ph–H). ^{13}C NMR (δ, ppm): 169.2, 109.61, 137.40, 124.18, 127.30, 121.96, 128.0, 129.49, 133.34, 120.08 (naphthyl–C), 157.65 (C=N), 138.7, 120.92, 128.77 (Ph–C).



Scheme 1.

The organotin(IV) complexes were prepared according to reported method [16] with slight modification briefly described here.

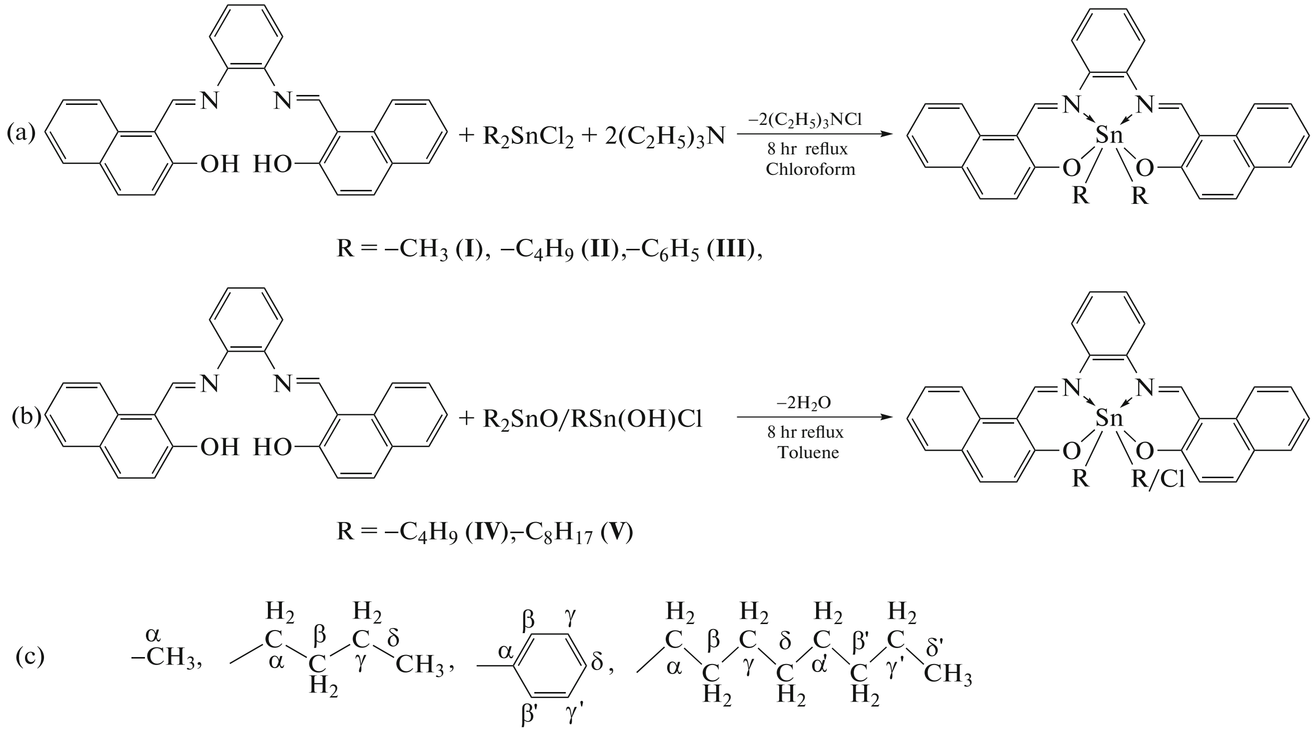
Synthesis of organotin(IV) complexes from tin(IV) chloride or diorganotin(IV) chloride. An appropriate amount of Schiff base ligand LH$_2$ (0.7 mmol) was mixed with triethylamine (1.4 mmol) in a two necked round bottom flask containing dry chloroform (100 mL), a magnetic stirring bar and equipped with a water condenser. The mixture was stirred for 30 min. A chloroform solution of appropriate tin(IV) precursor SnCl$_4$ or R$_2$SnCl$_2$ containing stoichiometric amount of reactant (0.7 mmol) was then added to the Schiff base solution. The mixture was stirred and refluxed for 8 h (Scheme 2a) and then allowed to cool at room temperature. The precipitated triethylammonium chloride salt was filtered off. The solvent was evaporated under reduced pressure and the solid product obtained recrystallized from a chloroform-hexane (9 : 1) mixture.

Synthesis of organotin(IV) complexes from organotin(IV) oxides or organotin(IV) chloride dihydroxide. Stoichiometric amounts of the ligand LH$_2$ and the appropriate organotin(IV) precursor R$_2$SnO or RSn(OH)$_2$Cl were suspended in dry toluene (100 mL) in a two necked round bottom flask (250 mL), equipped with a Dean–Stark apparatus, magnetic bar and reflux condenser. The reaction mixture was refluxed for 8 h (Scheme 2b) and water formed during the condensation reaction was removed at regular intervals. The reaction mixture was brought to room temperature and solvent was removed under vacuum. The obtained solid was recrystallized from a chloroform–hexane (4 : 1) mixture. Synthesis of diorganotin(IV) and chloroorganotin(IV) derivatives of LH$_2$ and numbering scheme of alkyl groups (R) bonded to tin atom are given in Scheme 2a–2c.

Dichlorotin(IV) *N*,*N*'-bis(2-oxido-1-naphthylidene)-1,2-diaminobenzene (**I**): the yield was 75%, m.p. 210–212°C.

For $C_{28}H_{18}N_2O_2Cl_2Sn$			
Anal. calcd., %	C, 55.67	H, 3.00	N, 4.64
Found, %	C, 56.11	H, 3.37	N, 4.60

FT-IR (ν, cm^{-1}): 1616 ν(C=N), 1572, 1535, 1454 ν(C=C)$_{arom}$, 1232 ν(C–O), 556 ν(Sn–O), 475 ν(Sn–N). MS (100 eV; *m/z*, %: 534 ($C_{28}H_{18}O_2N_2Sn^{+}$, 9.2), 414 ($C_{28}H_{18}O_2N_2^{+}$, 8.5), 365 ($C_{17}H_{11}ONSn^{+}$, 4.3), 262 ($C_{10}H_6OSn^{+}$, 100), 120 (Sn^{+}, 51.2). ^{1}H NMR (δ, ppm): 8.52 (d., 2H, naphtyl–H, $^{3}J_{H-H}$ = 8.4), 7.34 (t., 2H, naphtyl–H, $^3J_{H-H} = 7.5$), 7.5 (t., 2H, naphtyl–H, $^3J_{H-H} = 7.5$), 7.44 (d.d., 2H, naphtyl–H, $^3J_{H-H} = 6.3$), 7.96 (d., 2H, naphtyl–H, $^3J_{H-H} = 9.3$), 7.06 (d., 2H, naphtyl–H, $^3J_{H-H} = 9.3$), 9.13 (s., 2H,C=NH, $^3J = 21.68$ Hz), 7.85–7.81 (m., 4H, Ph–H). ^{13}C NMR (δ, ppm): 174.56, 110.69, 138.83, 125.36, 126.58, 122.86, 127.77, 135.36, 137.94, 118.3 (naphthyl–C), 156.95 (C=N), 141.28, 118.99, 129.42 (Ph–C).



Scheme 2.

Dimethyltin(IV) *N*,*N*'-bis(2-oxido-1-naphthylidene)-1,2-diaminobenzene (**II**): the yield was 72%, m.p. 99–102°C.

For $C_{30}H_{24}N_2O_2Sn$

Anal. calcd., %	C, 63.97	H, 4.29	N, 4.97
Found, %	C, 62.08	H, 4.41	N, 4.61

FT-IR (ν, cm^{-1}): 1602 ν(C=N), 1568, 1531, 1455 ν(C=C)$_{arom}$, 1230 ν(C–O), 554 ν(Sn–O), 469 ν(Sn–N). MS (100 eV; *m/z, %*): 549 ($C_{28}H_{18}O_2N_2SnR^+$, 100), 534 ($C_{28}H_{18}O_2N_2Sn^+$, 9.2), 365 ($C_{17}H_{11}ONSn^+$, 10.7), 262 ($C_{10}H_6OSn^+$, 9.8), 120 (Sn^+, 13.4). ^{1}H NMR (δ, ppm): 7.93 (d., 2H, naphtyl–H, $^3J_{H-H} =$ 8.4), 7.32 (t., 2H, naphtyl–H, $^3J_{H-H} = 7.5$), 7.547–7.4 (m, 4H, naphtyl–H), 7.81 (d., 2H, naphtyl–H, $^3J_{H-H} =$ 9.3), 6.94 (d., 2H, naphtyl–H, $^3J_{H-H} = 9.3$), 9.13 (s., 2H,C=NH, $^3J = 18.6$ Hz), 7.54–7.74 (m., 4H, Ph–H), 0.86 (s., 6H, H_α–SnMe, ^2J ($^{119/117}$Sn–^{1}H) = 98, 101). ^{13}C NMR (δ, ppm): 174.56, 110.69, 137.94, 127.77, 128.21, 125.36, 128.29, 129.47, 135.36, 118.33 (naphthyl–C), 156.95 (C=N), 141.28, 122.86, 129.10 (Ph–C), 1.6 (C_α–SnMe).

Dibutyltin(IV) *N*,*N*'-bis(2-oxido-1-naphthylidene)-1,2-diaminobenzene (**III**): the yield was 76%, m.p. 77–80°C.

For $C_{36}H_{36}N_2O_2Sn$

Anal. calcd., %	C, 66.79	H, 5.60	N, 4.33
Found, %	C, 66.81	H, 5.35	N, 4.61

FT-IR (ν, cm^{-1}): 1602 ν(C=N), 1568, 1531, 1457 ν(C=C)$_{arom}$, 1236 ν(C–O), 558 ν(Sn–O), 460 ν(Sn–N). MS (100 eV; *m/z, %*): 591 ($C_{28}H_{18}O_2N_2SnR^+$, 100), 534 ($C_{28}H_{18}O_2N_2Sn^+$, 25.3), 365 ($C_{17}H_{11}ONSn^+$, 22.2), 262 ($C_{10}H_6OSn^+$, 9.8), 120 (Sn^+, 15.3). ^{1}H NMR (δ, ppm): 7.94 (d., 2H, naphtyl–H, $^3J_{H-H} =$ 8.4), 7.32 (t., 2H, naphtyl–H, $^3J_{H-H} = 7.5$), 7.47–7.3 (m., 4H, naphtyl–H), 7.80 (d., 2H, naphtyl–H, $^3J_{H-H} =$ 9.3), 6.97 (d., 2H, naphtyl–H, $^3J_{H-H} = 9.3$), 9.16 (s., 2H,C=NH, $^3J = 15.29$ Hz), 7.52–7.70 (m., 4H, Ph–H), 1.48–1.62 (m., 8H, H_α-,H_β-SnBu), 1.18–1.25 (m, 4H, H_γ-SnBu), 0.72 (t., 6H, H_δ-SnBu, $^3J_{H-H} = 7.2$), ^{13}C NMR (δ, ppm): 174.97, 109.44, 139.76, 126.56, 126.88, 122.68, 127.60, 129.40, 136.71, 118.09 (naphthyl–C), 156.37 (C=N), 141.86, 118.86, 128.13 (Ph–

C), 28.09 (C_{α}-SnBu), 26.52 (C_{β}-SnBu), 25.27 (C_{γ}-SnBu), 13.79 (C_{δ}-SnBu).

Diphenyltin(IV) *N*,*N*'-bis(2-oxido-1-naphthylidene)-1,2-diaminobenzene (**IV**): the yield was 70%, m.p. 235–238°C.

For $C_{40}H_{28}N_2O_2Sn$

Anal. calcd., %	C, 69.89	H, 4.11	N, 4.08
Found, %	C, 69.87	H, 4.13	N, 4.10

FT-IR (ν, cm^{-1}): 1616 ν(C=N), 1593, 1510, 1464 ν$(C=C)_{arom}$, 1247 ν(C–O), 536 ν(Sn–O), 460 ν(Sn–N). MS (100 eV; *m/z, %*): 611 ($C_{28}H_{18}O_2N_2SnR^+$, 100), 534 ($C_{28}H_{18}O_2N_2Sn^+$, 9.5), 365 ($C_{17}H_{11}ONSn^+$, 14.2), 262 ($C_{10}H_6OSn^+$, 14.4), 120 (Sn^+, 19.5). ^{1}H NMR (δ, ppm): 7.90 (d., 2H, naphtyl–H, $^3J_{H-H}$ = 8.4), 7.32 (t., 2H, naphtyl–H, $^3J_{H-H}$ = 7.5), 7.41–7.47 (m., 4H, naphtyl–H), 7.80 (d., 2H, naphtyl–H, $^3J_{H-H}$ = 9.3), 6.96 (d., 2H, naphtyl–H, $^3J_{H-H}$ = 9.3), 9.13 (s., 2H,C=NH, ^3J = 21.92 Hz), 7.68–7.70 (m., 4H, Ph–H), 7.50–7.54 (m., 10H, PhSn), ^{13}C NMR (δ, ppm): 174.54, 110.7, 140.45, 125.32, 126.65, 122.75, 126.82, 135.19, 138.65, 117.84 (naphthyl–C), 156.32 (C=N), 140.32, 118.61, 127.66 (Ph–C), 139.52 (C_{α}-SnPh), 129.32 (C_{β}-SnPh), 128.04 (C_{γ}-,C_{δ}-SnPh).

Dioctyltin(IV) *N*,*N*'-bis(2-oxido-1-naphthylidene)-1,2-diaminobenzene (**V**): the yield was 71% in the form of a viscous liquid.

For $C_{44}H_{52}N_2O_2Sn$

Anal. calcd., %	C, 69.57	H,6.90	N, 3.69
Found, %	C, 69.53	H, 6.95	N, 3.71

FT-IR (ν, cm^{-1}): 1617 ν(C=N), 1570, 1533, 1457 ν$(C=C)_{arom}$, 1232 ν(C–O), 540 ν(Sn–O), 489 ν(Sn–N). MS (100 eV; *m/z, %*): 760 ($C_{28}H_{18}O_2N_2SnR_2^+$, 4.6), 647 ($C_{28}H_{18}O_2N_2SnR^+$, 100), 534 ($C_{28}H_{18}O_2N_2Sn^+$, 25.3), 365 ($C_{17}H_{11}ONSn^+$, 22.3), 262 ($C_{10}H_6OSn^+$, 8.7), 120 ($Sn^+$, 9.4). ^{1}H NMR (δ, ppm): 7.89 (d., 2H, naphtyl-H, $^3J_{H-H}$ = 8.4), 7.27 (t., 2H, naphtyl-H, $^3J_{H-H}$ = 7.5), 7.47–7.3 (m., 4H, naphthyl–H), 7.75 (d., 2H, naphtyl–H, $^3J_{H-H}$ = 9.3), 6.91 (d., 2H, naphtyl–H, $^3J_{H-H}$ = 9.3), 9.2 (s., 2H,C=NH), 7.47–7.65 (m., 4H, Ph–H), 1.60–1.64 (m., 4H, H_{α}-SnOct), 1.06–1.32 (bs., 22H, $H_{\beta-\gamma}$-SnOct,), 0.82 (t., 6H, $H_{\delta'}$-SnOct, $^3J_{H-H}$ = 6.9), ^{13}C NMR (δ, ppm): 174.98, 110.66, 138.58, 126.54, 126.84, 122.60, 127.49, 129.33, 135.49, 118.03 (naphthyl–C), 156.62 (C=N), 141.87, 118.79, 128.06 (Ph-C), 22.59 (C_{α}-SnOct), 25.43 (C_{β}-SnOct), 33.28 (C_{γ}-SnOct), 29.01, 25.68, 31.79, 22.9 ($C_{\delta-\gamma}$-SnOct), 14.1 (C_{δ}-SnOct).

Butylchlorotin(IV) *N*,*N*'-bis(2-oxido-1-naphthylidene)-1,2-diaminobenzene (**VI**): the yield was 79%, m.p. 260–261°C,

For $C_{32}H_{27}N_2O_2ClSn$

Anal. calcd., %	C, 61.42	H, 4.35	N, 4.48
Found, %	C, 61.41	H, 4.39	N, 4.50

FT-IR (ν, cm^{-1}): 1606 ν(C=N), 1578, 1539, 1454 ν$(C=C)_{arom}$, 1241 ν(C–O), 538 ν(Sn–O), 450 ν(Sn–N). MS (100 eV; *m/z, %*): 534 ($C_{28}H_{18}O_2N_2Sn^+$, 25.3), 365 ($C_{17}H_{11}ONSn^+$, 16.3), 262 ($C_{10}H_6OSn^+$, 14.2), 120 (Sn^+, 16.6). ^{1}H NMR (δ, ppm): 7.99 (d., 2H, naphtyl-H, $^3J_{H-H}$ = 8.4), 7.43 (t., 2H, naphtyl–H, $^3J_{H-H}$ = 7.5), 7.55–7.61 (m., 4H, naphtyl–H), 7.91 (d., 2H, naphtyl–H, $^3J_{H-H}$ = 9.3), 6.4 (d., 2H, naphtyl–H, $^3J_{H-H}$ = 9.3), 9.19 (s., 2H,C=NH, ^3J = 60.75 Hz), 7.70–7.79 (m., 4H, Ph–H), 1.56–1.64 (m., 4H, H_{α}-SnBu), 1.42–1.51 (m., 4H, H_{β}-SnBu), 1.06–1.28 (m., 4H, H_{γ}-SnBu), 0.78 (t., 6H, H_{δ}-SnBu, $^3J_{H-H}$ = 7.2), ^{13}C NMR (δ, ppm): 169.16, 109.40, 138.45, 125.64, 127.52, 124.00, 128.62, 129.41, 135.19, 118.09 (naphthyl–C), 158.57 (C=N), 139.40, 120.23, 128.84 (Ph–C), 30.87 (C_{α}-SnBu), 27.94 (C_{β}-SnBu), 27.70 (C_{γ}-SnBu), 13.66 (C_{δ}-SnBu).

X-ray Crystallography

X-ray crystal structure data for complexes **IV** and **VI** were collected at 93(2) K using a Rigaku MM007 high brilliance RA generator (MoK_{α} radiation, confocal optics) and Mercury CCD system. At least a full hemisphere of data was collected using ω scans. Intensities were corrected for Lorentz polarization and absorption effects. The structures were solved by direct methods. Hydrogen atoms bound to carbon were idealized. Structural refinements were performed with full-matrix least-squares based on F^2 using SHELXTL [17]. The crystallographic data of complex **IV** and **VI** is shown in Table 1. Selected bond lengths and bond angles are listed in Table 2.

Supplementary material for structures **IV** and **VI** has been deposited with the Cambridge Crystallographic Data Centre (CCDC nos. 856596 (**IV**) and 856595 (**VI**), respectively; deposit@ccdc.cam.ac.uk or http://www.ccdc.cam.ac.uk).

Antibacterial screening. All the synthesized compounds were evaluated for antibacterial activity against *Escherichia coli* ATCC 11229, *Bacillus subtilis* ATCC 11774, *Shigella flexneri* ATCC 10782, *Staphylococcus aureus* ATCC 25923, *Pseudomonas aeruginosa* ATCC 10245 and *Salmonella typhi* ATCC 10749 employing the agar well diffusion method using Imipenem as standard drug [18]. Six mm diameter wells were dug in the media using sterile metallic borer. Sterile cotton swab was used to spread the eight-hour old bacterial

Table 1. Crystal data and structure refinement for compounds **IV** and **VI**

Parameter	Value	
	IV	**VI**
Crystal shape	Plate	Needle
Crystal colour	Pale orange	Orange
Crystal size, mm	0.100 × 0.100 × 0.100	0.100 × 0.100 × 0.100
Empirical formula	$C_{40}H_{28}N_2O_2Sn \cdot H_2O$	$C_{32}H_{27}ClN_2O_2Sn \cdot 0.25CH_2Cl_2$
Formula weight	705.35	646.93
Crystal system	Orthorhombic	Monoclinic
Space group	*Fdd*2	*C*2/*c*
Radiation used	MoK_α	
Wavelength, Å	0.71073	
Temperature K	93(2)	
Unit cell dimensions		
a, Å	45.690(6)	16.344(4)
b, Å	47.214(6)	28.868(4)
c, Å	12.2303(14)	13.753(3)
$\alpha = \beta, \gamma$	90, 90	90, 123.70(3)
Volume, $Å^3$	26384(6)	5398.1(18)
Z	32	8
F(000)	11456	2612
ρ_{calcd}, mg m^{-3}	1.421	1.592
μ, mm^{-1}	0.82	1.13
Data collection and refinement parameters		
Reflections measured/independent/observed ($I > 2\sigma(I)$)	39151/11563/9796	17936/4901/2850
θ Range, deg	2.5 to 25.4	1.7 to 25.3
GOOF	1.19	1.05
R ($F^2 > 2\sigma(F^2)$), wR (F^2),	0.114, 0.249	0.090, 0.262,
$\Delta\rho_{max}/\Delta\rho_{min}$, e $Å^{-3}$	2.50/−1.54	1.81/−1.54

inoculums containing 10^4–10^6 colony forming units (CFU)/mL on the surface of nutrient agar. The test sample (2 mg/mL in DMSO) was introduced into the respective wells. DMSO and reference antibacterial drug served as negative and positive controls, respectively. The plates were incubated at 37°C for 20 h. Activity was determined by measuring diameter of the inhibition zone in mm.

Cytotoxicity. Brine shrimp lethality bioassay [19] was used to assess the cytotoxicity of synthesized compounds. Brine-shrimp (*Artemia salina*) eggs were hatched in artificial sea water (3.8 sea salt/L) at room temperature (22–29°C). After two days these shrimps were transferred to vials containing 5 mL of artificial sea water (30 shrimp per vial) with 10, 100 and 1000 ppm. Final concentrations of each compound are taken from their stock solutions of 12 mg/mL in DMSO. After 24 h the number of surviving shrimps was counted. All experiments with different concentrations (1, 10, 100 mg/mL) of the test substances were conducted in triplicate and compared with the control. Etoposide was used as the standard drug. Data were analyzed with a finny computer programme (probit analysis) to determine the LD_{50} values [20].

RESULTS AND DISCUSSION

Ligand LH_2 and diorganotin(IV) complexes **I**–**VI** were synthesized by the stoichiometric reaction of respective precursors as shown in Schemes 1 and 2a, 2b. The use of triethylamine facilitates the product formation by removing the HCl generated during the reaction in the form of triethylammonium chloride salt. Organotin(IV) derivatives were recrystallized from chloroform *n*-hexane (4 : 1) mixture and

Table 2. Selected bond distances (Å) and bond angles (deg) for **IV** and **VI**

Bond	*d*, Å	Bond	*d*, Å
Sn(1)–C(35)	2.123(7)	Sn(1)–O(16)	2.194(6)
		IV	
Sn(1)–O(6)	2.125(5)	Sn(1)–N(1)	2.198(6)
Sn(1)–C(29)	2.171(8)	Sn(1)–N(3)	2.258(6)
		VI	
Sn(1)–O(6)	2.020(6)	Sn(1)–N(3)	2.188(8)
Sn(1)–O(16)	2.144(8)	Sn(1)–N(1)	2.195(8)
Sn(1)–C(29)	2.145(11)	Sn(1)–Cl(1)	2.504(3)
Angle	ω, deg	Angle	ω, deg
C(35)Sn(1)O(6)	88.3(3)	C(29)Sn(1)N(1)	95.2(3)
		IV	
C(35)Sn(1)C(29)	164.4(3)	O(16)Sn(1)N(1)	77.7(2)
O(6)Sn(1)C(29)	84.4(3)	C(35)Sn(1)N(3)	97.1(3)
C(35)Sn(1)O(16)	87.8(3)	O(6)Sn(1)N(3)	81.4(2)
O(6)Sn(1)O(16)	126.1(2)	C(29)Sn(1)N(3)	95.4(3)
C(29)Sn(1)O(16)	85.5(3)	O(16)Sn(1)N(3)	152.3(2)
C(35)Sn(1)N(1)	97.1(3)	N(1)Sn(1)N(3)	74.6(2)
O(6)Sn(1)N(1)	155.9(2)	C(35)Sn(1)O(6)	88.3(3)
		VI	
O(6)Sn(1)O(16)	91.8(3)	O(6)Sn(1)N(1)	150.1(3)
O(6)Sn(1)C(29)	94.8(3)	O(16)Sn(1)N(1)	76.1(3)
O(16)Sn(1)C(29)	90.8(4)	C(29)Sn(1)N(1)	112.3(3)
O(6)Sn(1)N(3)	82.1(3)	N(3)Sn(1)N(1)	72.1(3)
O(16)Sn(1)N(3)	95.1(3)	O(6)Sn(1)Cl(1)	103.8(3)
C(29)Sn(1)N(3)	173.4(4)	O(16)Sn(1)Cl(1)	164.00(17)
C(29)Sn(1)Cl(1)	91.2(3)	N(1)Sn(1)Cl(1)	88.5(3)
N(3)Sn(1)Cl(1)	83.9(2)		

single crystals of compounds **IV** and **VI** were obtained and analysed. All the synthesized compounds are stable in air and were obtained in good yield (70–78%). The numbering scheme of alkyl/phenyl groups attached to the Sn center is provided in Scheme 2c.

The infrared spectra of all compounds have been recorded as KBr pellets in the range from 4000–400 cm^{-1}. The important absorption frequencies like ν(C=O), ν(Sn–O), ν(Sn–N), and ν(C=N) have been assigned by comparison of the free ligand spectra with that of the diorganotin(IV) derivatives. In the spectra of the ligands a strong band at 3376 cm^{-1} is assigned to OH stretching vibration. The IR spectra of the complexes do not exhibit any absorption in this region indicating the deprotonation of the OH group, similar to earlier observations [21]. The phenolic C–O stretching vibration of the Schiff base that appeared at 1325 cm^{-1} undergoes a shift towards lower frequencies in the complex confirming the participation of oxygen in the C–O–M bond formation. Also a strong band appears at 1618 cm^{-1} in the free ligand. This band is attributed to the C=N stretching vibration. The C=N stretching vibration of the complexes shift to the lower frequency region as compared to the C=N stretching vibration of the free ligand indicating a donation of the nitrogen's electron lone pair of the azomethine group to the Sn atom [22]. The bands observed in the lower frequency region (538–558 and 450–489 cm^{-1}) are attributed to ν(Sn–O) and ν(Sn–N), respectively [23].

^{1}H NMR spectra of all compounds have been recorded on a 300 MHz NMR spectrometer with $CDCl_3$ as solvent. The expected resonances are assigned by their peak multiplicity, intensity pattern, integration and/or tin satellites [24]. The integration of the spectra are in good agreement with the composition of the compounds. The hydroxyl proton in ligand LH_2 appear at 15.41 ppm indicating the presence of a strong hydrogen bond, however, in the

Table 3. Comparision of selected bond distances (Å) and bond angles (deg) for compound **IV** and reported structure [32]

Bond	Compound **IV**	Reported structure [32]
	d, Å	
Sn–O	2.125, 2.194	2.216, 2.185
Sn–N	2.258, 2.198	2.216, 2.195
Sn–C_{Ph}	2.172, 2.123	2.177, 2.184
Angle	ω, deg	
NSnN	74.62	75.38
OSnO	126.09	124.84
OSnN	81.43, 152.31, 77.73, 155.91	81.82, 157.20, 77.95, 153.30
C_{Ph}SnN	97.06, 97.12, 95.40, 95.19	92.27, 93.07, 97.01, 95.83
C_{Ph}SnO	87.77, 88.27, 84.34, 85.54	89.19, 89.03, 84.89, 86.30
CSnC	164.41	168.50

^{1}H NMR spectra of all complexes this resonance signal is totally absent which suggest the replacement of the phenolic proton by the organotin(IV) moiety. The methyl protons of dimethyltin(IV) derivatives appear as a sharp singlet at 0.86 ppm with characteristic tin satellites and ^2J ($^{119/117}$Sn–^{1}H) coupling constants of 98 and 101 Hz. The protons of the *n*-butyl groups show multiplets in the range of 1.48–1.62, 1.18–1.25 and a sharp triplet at 0.72 ppm. The phenyl moieties show a complex pattern in the range of 7.50–7.70 ppm [25–27]. Similarly, dioctyltin(IV) derivatives give complex multiplets in the range of 1.06–1.64 ppm and a triplet due to terminal methyl group at 0.82 ppm.

The shifting in the peak position of azomethine proton (–C=NH) in complexes show that the lone pair of electrons on N atom is being used in the bond formation with Sn. Aromatic protons of the ligand appeared within the usual range and are almost not affected upon chelation [28].

The ^{13}C NMR spectral data for the R groups (CH_3, C_4H_9, C_6H_5, C_8H_{17}) attached to the tin atom were assigned by comparison with related analogues and their ^nJ[^{119}Sn,^{13}C] coupling constants [29]. The positions of the phenyl and naphthyl carbon signals undergo a minor variation in the complexes as compared to those observed in free ligand. The carbon attached to the OH group shifts to a lower field region in all complexes, indicating participation of the C–O group in the coordination with tin(IV) to form a C–O–M bond [30]. The resonances due to the aromatic carbon atoms do not shift significantly on binding to tin. The highest downfield shift is observed for C–O in the complexes, confirming the binding of the ligand with the tin(IV) moiety. All R-groups give signals in the expected range. The shifting of azomethine carbon resonance in the complexes suggests Sn–N bonding [31].

The mass fragmentation pattern of synthesized compounds follows the established routes and all fragments containing tin exhibit the characteristic isotopic peak pattern in mass spectra. The molecular ion peak of low intensity was observed for compounds **III** and **V**. The loss of first alkyl group leads to the formation of fragments assignable to base peaks, which is followed by loss of second alkyl group, a phenoxy or naphthoxy fragment to form $C_{18}H_{12}N_2OSn^+$, Sn^+ and SnH^+, generating signals with variable intensities for all complexes.

The asymmetric unit of compound **IV** consists of two independent molecules. The bond lengths and bonds angles of **IV** are given in Table 2. Atom Sn(1) is bonded to two phenyl groups occupying the apical position in a *trans* configuration at an angle of 164.41° with a slightly different Sn–C bond lengths (2.123, 2.172 Å). These values are slightly different from a reported structure (168.50°, 2.177 and 2.184 Å) [32], comparison of selected bond lengths and bond angles of compound **IV** and reported structure is provided in Table 3. The nitrogen and oxygen ONNO donor sites of ligand occupy the equatorial coordination sites in *trans* orientation forming a hexa-coordinated tin center. The influence of the strain caused by the organic group attached to the tin atom can be seen in the bite angles O(6)Sn(1)N(3) (81.42°), O(16)Sn(1)N(1) (77.73°), and N(1)SnN(3) (74.62°) as depicted in Fig. 1. The O(6)Sn(1)O(16) angle is 126.1(2)°, that is larger than the reported values [32, 33].

The structure of **VI** depicted in Fig. 2 is composed of discrete monomeric molecules in which the ONNO

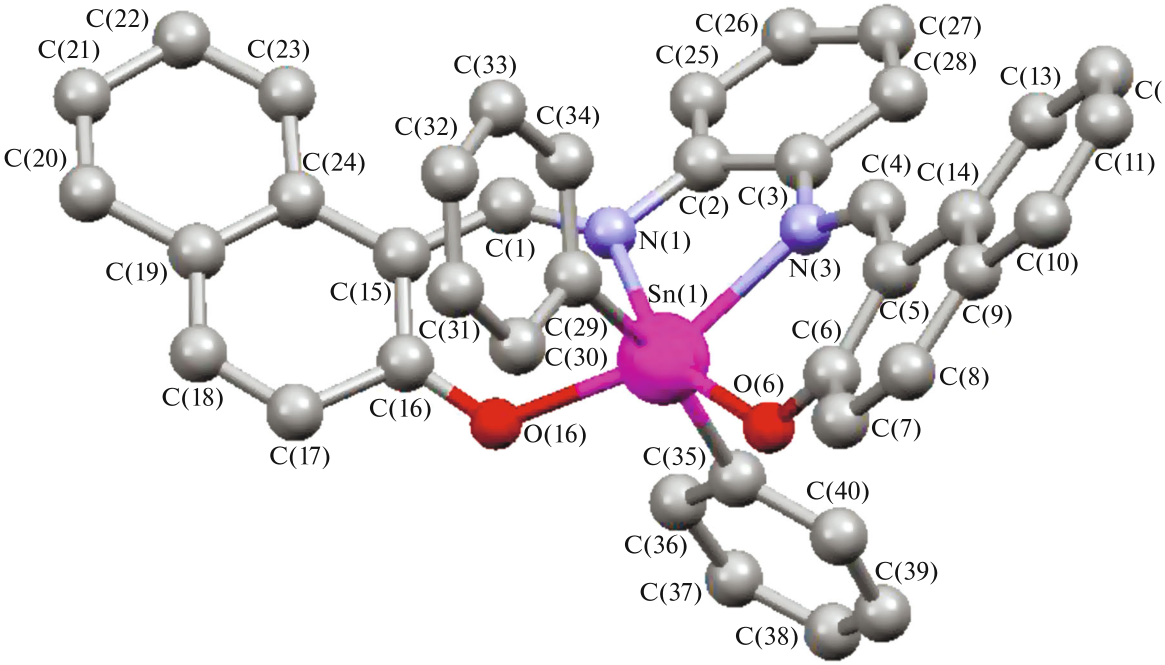


Fig. 1. Molecular structure of compound **IV**. Hydrogen atoms are omitted.

donor atoms of LH_2, the *n*-butyl group, and chloro groups are surrounding the tin atom forming a hexacoordinated metal center. The bond lengths and bond angles of **VI** are given in Table 2.

The Sn atom lies in the same plane as the N and O atoms coordinated to it, and one *n*-butyl group is oriented above the plane. The distorted octahedral geometry around the tin atom is the result of the strain imposed by the six-membered rings Sn–N–C–C–C–O, which is reflected in the equatorial plane with O(6)Sn(1)O(16) angle of 91.8(3)° and correspondingly more acute by the N(3)Sn(1)N(1) angle 71.2(3)°. The distorted geometry can be seen in the deviation from 180° of the angles N(3)Sn(1)C(29) (173.4(4)°). The OSnCl angle of 164.00(17)° is less than the idealized 180°, however, larger than the reported value [33]. The bite angle O(6)Sn(1)N(3) 82.1(3)° and 95.1(3)° are relatively higher and the Sn–C, Sn–O bond lengths are quite similar to other tin compounds, a typical Sn–O bond distance in the SnO_2N_2 system is around 2.02 Å. The Sn–N distances (2.188(8) and 2.195(8) Å) are much shorter than those observed in Sn(IV) systems with Sn←N donor accepter bonds (2.696(2) and 2.595(3) Å) [34].

The synthesized compounds were screened for in vitro antibacterial activity at a concentration level of

Table 4. Antibacterial activity^{a-c} of ligand and its diorganotin(IV) derivatives

Name of bacteria	Zone of inhibition of sample, mm						
	LH_2	**II**	**III**	**IV**	**V**	**VI**	standard
Escherichia coli	–	10	16	13	12	12	30
Bacillus subtilis	–	12	18	20		14	37
Shigella flexnari	–	10	16	–	–	16	36
Staphylococcus aureus	–	–	10	–	–	12	26
Pseudomonas aeruginosa	–	–	–	–	–	–	32
Salmonella typhi	–	–	–	16	13	–	30

[a] Concentration 1 mg/mL of DMSO.
[b] Reference drug, imipenem.
[c] Insignificant activity.

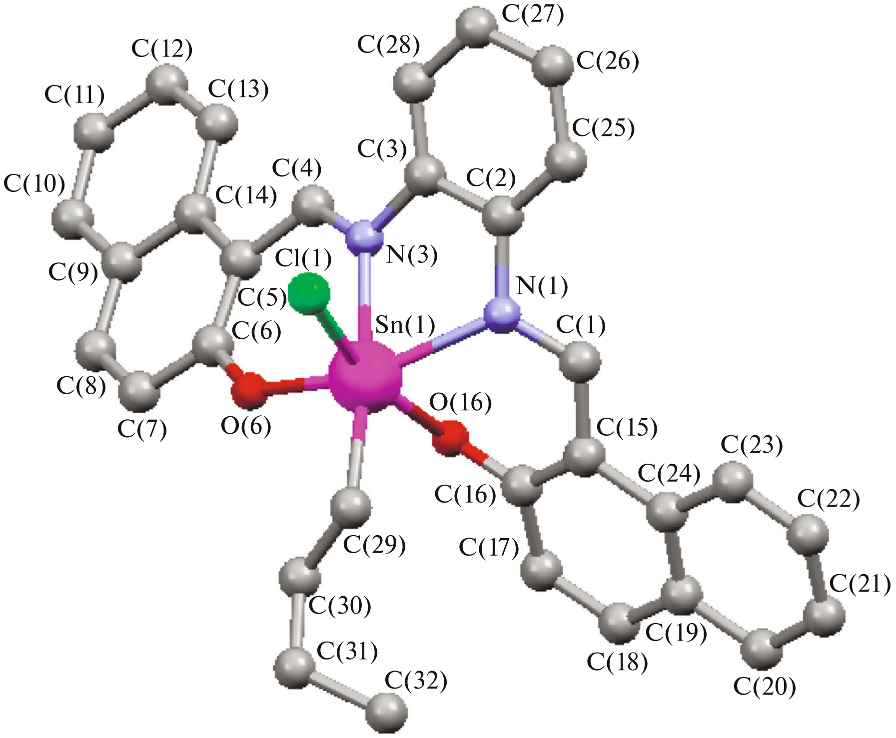


Fig. 2. Molecular structure of compound **VI**. Hydrogen atoms are omitted.

1 mg/mL in 6 mm diameter of well against six pathogenic bacterial strains. The inhibition zones were measured in mm and results are shown in Table 4. The ligand in inactive against all bacterial strains however on complexation a pronounced increase in the antibacterial activity occurs. These observations are consistent with earlier reports [35]. The enhanced bactericidal antibacterial activity of complexes can be attributed to the increase in lipophilic character of tin after complexation which facilitated the movement of complexes through the lipid layer before they can interact with the active sites within the cell [36].

The results indicated that compound **IV** possesses the highest antibacterial activity among all the synthesized compounds. Compounds **III** and **VI** expresses a significant activity against *Bacillus subtilis* and *Shigella flexnari*, respectively. None of the synthesized compounds is active against *Pseudomonas aeraginosa* and more active than the standard drug.

The cytotoxicity of the synthesized compounds was studied by the Brine shrimp lethality method and the results are given in Table 5. The cytotoxicity of organotin compounds can be explained on the basis of their ability to interact with the various active sites within the cell resulting in DNA damage, apoptosis, estrogen receptor blockage or inhibition of the mitochondrial oxidative phosphorylation [37]. The highest cytotoxicity is exhibited by diphenyl derivative **IV** followed by compound **VI** with LD_{50} values 0.858 and 36.812 μg/mL, respectively. Rest of the compounds showed insignificant cytotoxicity.

Thus, six diorganotin(IV) derivatives of *N*,*N*'-bis(2-hydroxy-1-naphthylidene)-1,2-diaminobenzene have been synthesized and characterized by elemental analysis, mass spectrometery, FT-IR, multinuclear NMR (^{1}H and ^{13}C). The ligand coordinates with the dialkyltin(IV) moieties through ONNO donor sites. Single crystal X-ray structure of complex **IV** and **VI** show a hexa-coordination around tin center in solid state. All the complexes exhibited significant inhibitory

Table 5. Brine Shrimp (*Artemia salina*) lethality bioassay data of ligand and its diorganotin(IV) derivatives*

Compound	LD_{50}, μg/mL
LH_2	
II	
III	
IV	0.858
V	
VI	36.812

* Standard drug = Etoposide, LD_{50} = 7.46 μg/mL.

activity against *Bacillus subtilis* and *Shigella flexnari*. Compound **IV** displayed highest cytotoxicity among the synthesized compounds with LD_{50} 0.858 μg/mL.

REFERENCES

1. Singh, K., Kumar, Y., Puri, P., Kumar, M., and Sharma, C., *Eur. J. Med. Chem.*, 2012, vol. 52, p. 313.
2. Gupta, V.K., Singh, A.K., Ganjali, M.R., Norouzi, P., Faridbod, F., and Mergu, N., *Sensors and Actuators B: Chemical*, 2013, vol. 182, p. 642.
3. Mogorosi, M.M., Mahamo, T., Moss, J.R., Mapolie, S.F., Slootweg, J.C., Lammertsma, K., and Smith, G.S., *J. Organomet. Chem.*, 2011, vol. 696, no. 23, p. 3585.
4. Ding, F., Doorslaer, S.V., Cool, P., and Verpoort, F., *Appl. Organomet. Chem.*, 2011, vol. 25, no. 8, p. 601.
5. De Clercq, B. and Verpoort, F., *J. Mol. Catal. A: Chem.*, 2002, vol. 180, no. 1, p. 67.
6. Dubey, R.K., Singh, A.P., and Patil, S.A., *Inorg. Chim. Acta*, 2014, vol. 410, suppl. C, p. 39.
7. Kumari, R. and Nath, M., *Appl. Organomet. Chem.*, 2017, vol. 31, no. 8. e3661.
8. Cheng, J., Wei, K., Ma, X., Zhou, X., and Xiang, H., *J. Phys. Chem., C*, 2013, vol. 117, no. 32, p. 16552.
9. Naik, A.D., Fontaine, G.L., Bellayer, S., and Bourbigot, S., *ACS Applied Materials & Interfaces*, 2015, vol. 7, no. 38, p. 21208.
10. Vandenbergen, A., Cashion, J., Fallon, G., and West, B., *Aust. J. Chem.*, 1990, vol. 43, no. 9, p. 1559.
11. Muñoz-Flores, B.M., Santillan, R., Farfan, N., et al., *J. Organomet. Chem.*, 2014, vol. 769, p. 64.
12. Darensbourg, D.J., Ganguly, P., and Billodeaux, D., *Macromolecules*, 2005, vol. 38, no. 13, p. 5406.
13. Jing, H., Edulji, S.K., Gibbs, J.M., et al., *Inorg. Chem.*, 2004, vol. 43, no. 14, p. 4315.
14. Dey, D.K., Das, M. K. and Noth, H., *Z. Naturforsch., B*, 1999, vol. 54, no. 2, p. 145.
15. Armarego, W.L. and Chai, C.L.L., *Purification of Laboratory Chemicals*, Butterworth-Heinemann, 2013.
16. Labisbal, E., Rodríguez, L., Sousa-Pedrares, A., et al., *J. Organomet. Chem.*, 2006, vol. 691, no. 7, p. 1321.
17. Sheldrick, G., *SHELXTL 6.14,* Madison: Bruker AXS, 2004.
18. Rehman, W., Baloch, M.K., and Badshah, A., *Eur. J. Med. Chem.*, 2008, vol. 43, no. 11, p. 2380.
19. Atta-ur-Rahman, C.M. and Thomsen, W.J., *Bioassay Techniques for Drug Development*, Harwood Academic, 2001.
20. Finney, D., *Probit Analysis*, Cambridge University, 1971.
21. Tan, Y.-X., Zhang, Z.-J., Liu, Y., et al., *J. Mol. Struct.*, 2017, vol. 1149, suppl. C, p. 874.
22. Shujah, S., Zia-Ur-Rehman, Muhammad, N., et al., *J. Organomet. Chem.*, 2014, vol. 759, p. 19.
23. Shujah, S., Khalid, N., and Ali, S., *Russ. J. Gen. Chem.*, 2017, vol. 87, no. 3, p. 515.
24. Shahzadi, S., Ali, S., Shahid, K., et al., *Phosphorus Sulfur.*, 2010, vol. 185, no. 10, p. 2045.
25. Sirajuddin, M., Ali, S., Shah, F.A., et al., *J. Iran. Chem. Soc.*, 2014, vol. 11, no. 2, p. 297.
26. Hong, M., Yin, H., Zhang, X., et al., *J. Organomet. Chem.*, 2013, vol. 724, p. 23.
27. Shujah, S., Ali, S., Khalid, N., and Meetsma, A., *J. Iran. Chem. Soc.*, 2017, vol. 14, no. 12, p. 2567.
28. Muhammad, N., Zia-Ur-Rehman, Shujah, S., et al., *J. Coord. Chem.*, 2012, vol. 65, no. 21, p. 3766.
29. Dey, D.K., Saha, M.K., Das, M.K., et al., *Polyhedron*, 1999, vol. 18, no. 20, p. 2687.
30. Gericke, R. and Wagler, J., *Main Group Met. Chem.*, 2014, vol. 37, p. 1.
31. Wang, Q., Ding, R., Ang, N., et al., *Z. Anorg. Allg. Chem.*, 2010, vol. 636, no. 5, p. 861.
32. Teoh, S.-G., Yeap, G.-Y., Loh, C.-C., et al., *Polyhedron*, 1997, vol. 16, no. 13, p. 2213.
33. Yearwood, B., Parkin, S., and Atwood, D.A., *Inorg. Chim. Acta*, 2002, vol. 333, no. 1, p. 124.
34. Carcelli, M., Corazzari, G., Ianelli, S., et al., *Inorg. Chim. Acta*, 2003, vol. 353, p. 310.
35. Shujah, S., Zia-Ur-Rehman, Muhammad, N., et al., *J. Organomet. Chem.*, 2011, vol. 696, no. 15, p. 2772.
36. Shujah, S., Zia-Ur-Rehman, Muhammad, N., et al., *J. Organomet. Chem.*, 2013, vols. 741–742, p. 59.
37. Nath, M., *Appl. Organomet. Chem.*, 2008, vol. 22, no. 10, p. 598.