J IRAN CHEM SOC (2017) 14:2567–2578
DOI 10.1007/s13738-017-1191-0

ORIGINAL PAPER

# Supramolecular homobimetallic *bis*-diorganotin(IV) complexes of ditopic oxygen nitrogen donor ligand: synthesis, spectroscopic characterization, crystal structure and biological screening

**Shaukat Shujah[1] · Saqib Ali[2] · Nasir Khalid[3] · Auke Meetsma[4]**

Received: 20 December 2016 / Accepted: 28 August 2017 / Published online: 26 September 2017
© Iranian Chemical Society 2017

**Abstract** Six new homobimetallic *bis*-diorganotin(IV) complexes: $[Me_2Sn]_2L$ (**1**), $[Et_2Sn]_2L$ (**2**), $[n\text{-}Bu_2Sn]_2L$ (**3**), $[Ph_2Sn]_2L$ (**4**), $[Oct_2Sn]_2L$ (**5**) and $[n\text{-}BuClSn]_2L$ (**6**) (**$H_4L$**=$N^{1\prime}$, $N^{6\prime}$-*bis*(2-hydroxybenzylidene)adipodihydrazide) have been synthesized and structurally characterized by means of elemental analysis, mass spectroscopy, FT-IR, NMR ($^1H$, $^{13}C\{^1H\}$, $^{119}Sn$) and single-crystal X-ray diffraction. Spectroscopic studies indicate coordination of the ligand to the diorganotin(IV) moieties via iminolic oxygen, nitrogen and phenolic oxygen atoms generating pentacoordinated tin centers. Single-crystal X-ray analysis of (**1**) revealed homobimetallic nature of complex with dimethyltin moieties oriented in *trans*-conformation. The ligand is nonplanar with each Sn atom in a distorted square pyramidal coordination geometry. Packing diagrams suggest the essential role of C–H···N and C–H···O interactions in generating supramolecular assembly. The ligand and complexes were screened for in vitro antimicrobial activity and cytotoxicity. Compound (**4**) exhibits highest cytotoxicity.

**Keywords** Homobimetallic · Supramolecular · Antifungal · Antibacterial · Cytotoxicity

✉ Shaukat Shujah
shaukat.shujah@yahoo.com

[1] Department of Chemistry, Kohat University of Science and Technology, Kohat-26000, KPK, Pakistan

[2] Department of Chemistry, Quaid-i-Azam University, Islamabad-45320, Pakistan

[3] Chemistry Division, Pakistan Institute of Nuclear Science and Technology, PO Nilore, Islamabad, Pakistan

[4] Crystal Structure Center, Chemical Physics, Zernike Institute for Advanced Materials, University of Groningen, Nijenborgh 4, 9747 AG Groningen, The Netherlands

## Introduction

Organotin(IV) compounds have been recognized for their therapeutic potential in biocompatible strategy for cancer treatment [1], antimicrobial activities [2], photocatalytic applications [3] as precursors for tin oxide in gas sensors [4, 5], manufacture of organic light emitting diodes [6] and ability to generate well-organized supramolecular architecture through strong metal ligand coordinate bonds and weak cooperative forces like hydrogen bonds and $\pi$–$\pi$ interactions [7–10]. Through careful synthesis control, metal or ligand directed self-assembly can be consciously designed into a synthetic framework with interesting properties and useful applications in various fields like molecular recognition, chiroptical switching devices and gas storage materials. [11–14].

Diacyl hydrazones are a group of flexible nitrogen and oxygen containing ditopic ligands with the ability to ligate with tin in monobasic *bis*-bidentate or tridentate, dibasic *bis*-tridentate or tetrabasic *bis*-tridentate form and yield biologically active species and supramolecular architectures in solid state [15–17]. Among the main group elements, tin complexes have received the most attention because fine-tuning of chemical and structural properties of the molecular system can be made by modulating the organic groups or the ligand attached to the tin atom. Diorganotin(IV) complexes derived from ditopic ligands like dithiocarbamates, dicarboxylates and dihydrazones not only possess pharmacological properties but are known to generate supramolecular architectures, macrocyclic and cage-type structures, which have been examined exhaustively during the past few years [8, 18–21].

In view of all these considerations and as a continuation of our previous studies on *bis*-diorganotin(IV) complexes derived from ONO–ONO donor ligands [22], In

this article, we reported the synthesis, spectroscopic characterization of six *bis*[diorganotin(IV)] derivatives of $N^{1\prime}$, $N^{6\prime}$-*bis*(2-hydroxybenzylidene)adipodihydrazide and their inhibitory activities against various human pathogens. All the synthesized compounds have been characterized by elemental analysis, mass spectroscopy, FT-IR and multinuclear NMR ($^{1}H$, $^{13}C\{^{1}H\}$ and $^{119}Sn$), and crystal structure of **1** was determined by X-ray analysis.

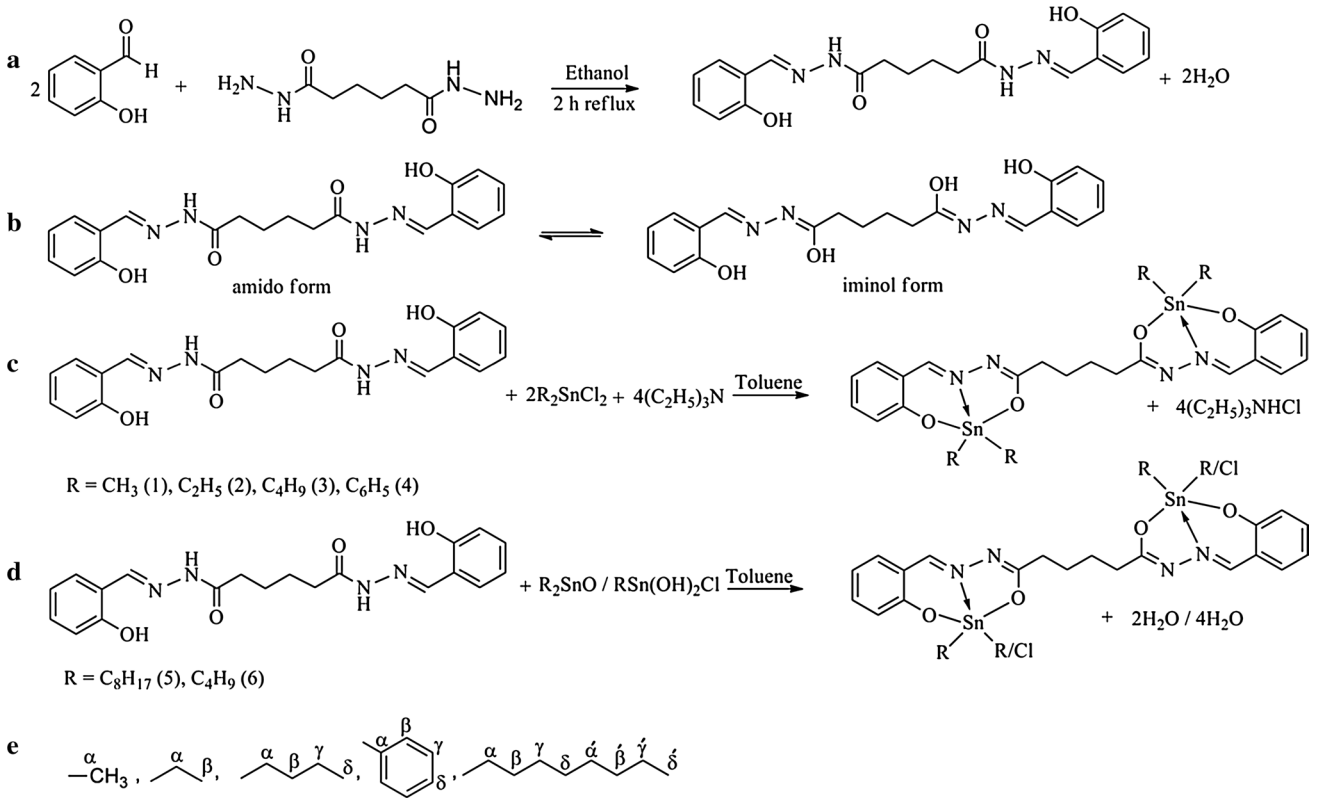
## Experimental

### Materials and methods

Chemical reagents diorganotin(IV) dichlorides, dioctyltin(IV) oxide, butyltin(IV) chloridedihydroxide, adipic hydrazide and 2-hydroxybenzaldehyde were procured from Sigma–Aldrich Co., while the organic solvents used were of Merck, Germany. Chloroform was dried and distilled before use by standard procedure [23]. The melting points were recorded on an electrothermal melting point apparatus, model MP-D Mitamura Rieken Kogyo (Japan) by using capillary tubes and are uncorrected. Elemental analyses for C, H and N were performed on Leco CHNS 932 instrument. The infrared spectra were recorded as KBr disks on a Bio-Rad Excaliber FT-IR, model FTS 300 MX spectrophotometer (USA), in the range 4000–400 $cm^{-1}$. $^{1}H$ and $^{13}C\{^{1}H\}$ NMR spectra were obtained on Bruker ARX 300 MHz-FT-NMR, and $^{119}Sn$ NMR spectra were recorded on Bruker 400 MHz-FT-NMR spectrometer.

**Synthesis of $N^{1\prime}$, $N^{6\prime}$-*bis*(2-hydroxybenzylidene)adipodihydrazide ($H_4L$)** Salicylaldehyde (1.40 g, 11.48 mmol) and adipic dihydrazide (1.0 g, 5.74 mmol) were dissolved in ethanol. The mixture was stirred and refluxed for 2 h to give a white solid product. The solid was isolated, washed three times with ethanol and dried in a vacuum desiccator having anhydrous $CaCl_2$ (Scheme 1a, b).

Yield 78%, m.p. > 300 °C. *Anal.* Calc. for $C_{20}H_{22}N_4O_4$ ($M$ = 382): C, 62.82; H, 5.80; N, 14.65 Found: C, 62.79; H, 5.83; N, 14.61%. EI-MS, m/z(%): $[C_{20}H_{22}N_4O_4]^+$ 382(72.9), $[C_{14}H_{17}N_4O_3]^+$ 289(3.3), $[C_8H_7N_2O_2]^+$ 163(17.7), $[C_7H_5NO]^+$ 119(100.0), $[C_6H_5O]^+$ 93(24.5), $[C_6H_5]^+$ 77(18.4) FT-IR ($cm^{-1}$): 3220 $\nu_{N-H}$, 3442 $\nu_{O-H}$, 1680 $\nu_{C=O}$, 1616 $\nu_{C=N}$. $^{1}H$ NMR (ppm): 8.34 (*s*, 2H, CH=N), 2.26 (*bs*, 4H, $2CH_2$), 1.54 (*bs*, 4H, $2CH_2$), 6. 90 (*d*, 2H, Ar–H, $^{3}J_{H-H}$ = 7.5), 7.27 (*t*, 2H, Ar–H, $^{3}J_{H-H}$ = 7.8), 6.89 (*t*, 2H, Ar–H, $^{3}J_{H-H}$ = 7.2), 7.20 (*d*, 2H, Ar–H, $^{3}J_{H-H}$ = 7.8),




**Scheme 1** Synthesis of N1′,N6′-*Bis*(2-hydroxybenzylidene)adipodihydrazide ($H_4L$) (**a**, **b**) *bis*[diorganotin(IV)] and *bis*[butylchlorotin(IV)] derivatives (**c**, **d**). Numbering scheme of alkyl groups bonded to tin atom in *bis*[dialkyltin(IV)] derivatives of $H_4L$ (**e**)

$^{13}C\{^{1}H\}$ NMR (ppm): 146.9 (CH=N), 168.8 (NCO), 34.2, 25.1 ($-CH_2CH_2$), 157.8, 131.6 129.9, 120.5, 119.7, 116.5 (Ar–C).

***Bis*[dimethyltin(IV)] [N$^{1\prime}$, N$^{6\prime}$-*bis*(2-oxidobenzylidene) adipodihydrazide] (1)** The ligand N$^{1\prime}$, N$^{6\prime}$-*bis*(2-hydroxybenzylidene)adipodihydrazide (0.57 g, 1.5 mmol) **$H_4$L** and triethylamine (0.84 mL, 6.0 mmol) were dissolved in chloroform (50 mL), and the mixture was stirred for 30 min at 298 K. Dimethytin(IV) dichloride (0.66 g, 3.0 mmol) in chloroform (25 mL) was added drop wise and reaction mixture further stirred for 3 h. The solution turned dark yellow and white precipitates of $Et_3NHCl$ formed. The precipitates were filtered, and filtrate was concentrated by rotary evaporator to obtain yellow solid. The product was recrystallized from $CHCl_3$/n-hexane (4:1) mixture (Scheme 1c).

Yield 78%. mp 201–202 °C. *Anal.* Calc. for $C_{24}H_{30}N_4O_4Sn_2$ ($M$ = 678): C, 42.65; H, 4.47; N, 8.29 Found: C, 42.61; H, 4.45; N, 8.31% EI-MS, m/z(%): $[(C_8H_5N_2O_2)_2C_4H_8Sn_2(CH_3)_4]^+$ 678(3.5), $[(C_8H_5N_2O_2)_2C_4H_8Sn_2(CH_3)_3]^+$ 663(85.2), $[(C_8H_5N_2O_2)_2C_4H_8Sn_2(CH_3)_2]^+$ 648(4.3), $[(C_8H_5N_2O_2)\ CNC_4H_8Sn(CH_3)_2]^+$ 393(8.8), $[(C_8H_5N_2O_2)C_4H_8Sn(CH_3)_2]^+$ 367(4.6), $[(C_8H_5N_2O_2)\ CH_2Sn(CH_3)_2]^+$ 325(23.6), $[(C_8H_6N_2O_2)Sn(CH_3)_2]^+$ 312(4.5), $[(C_8H_5N_2O_2)Sn(CH_3)_2]^+$ 311 (16.1), $[(C_8H_6N_2O_2)\ Sn]^+$ 282(100.0), $[C_7H_4NOSn]^+$ 238(46.3), $[(CH_3)_2HSn]^+$ 151 (4.0), $[CH_3Sn]^+$ 135(25.4), $[Sn]^+$ 120(9.6) FT-IR ($cm^{-1}$): 1612 $\nu_{C=N}$, 1084 $\nu_{N-N}$, 576 $\nu_{Sn-O}$, 468 $\nu_{Sn-N}$, $^1$H NMR (ppm): 8.59 (*s*, 2H, CH=N, $^3J(^{119}Sn–^1H)$ = 47 Hz)], 2.35 (*bs*, 4H, $2CH_2$), 1.73 (*bs*, 4H, $2CH_2$), 6. 77 (*d*, 2H, Ar–H, $^3J_{H-H}$ = 8.4), 7.33 (*t*, 2H, Ar–H, $^3J_{H-H}$ = 7.8), 6.74 (*t*, 2H, Ar–H, $^3J_{H-H}$ = 7.5), 7.13 (*dd*, 2H, Ar–H, $^3J_{H-H}$ = 7.8), 0.79 (*s*, 6H, $H_\alpha$, $SnCH_3$, $^2J$ ($^{119/117}Sn–^1H$) = 75, 79. $^{13}C\{^1H\}$ NMR (ppm): 161.0 (CH=N), 175.5 (NCO), 34.2, 26.0 ($-CH_2CH_2$), 166.3, 135.2, 134.2, 121.6, 117.2, 116.5 (Ar–C), 1.3 ($C_\alpha$–$SnCH_3$, $^1J[^{119/117}Sn–^{13}C]$ = 648, 621 Hz), $^{119}$Sn NMR: $\delta$ (ppm) = −154.8.

***Bis*[diethyltin(IV)] [N$^{1\prime}$, N$^{6\prime}$-*bis*(2-oxidobenzylidene)adipodihydrazide] (2)** Compound **2** was prepared in the same way as **1**, using N$^{1\prime}$, N$^{6\prime}$-*bis*(2-hydroxybenzylidene)adipodihydrazide (0.57 g, 1.5 mmol), triethylamine (0.84 mL, 6.0 mmol) and diethyltin(IV) dichloride (0.74 g, 3.0 mmol) in a 1:2:4 ratio. The solid product was recrystallized from a chloroform and *n*-hexane (4:1) mixture.

Yield 72%. mp 144–145 °C. *Anal.* Calc. for $C_{28}H_{38}N_4O_4Sn_2$ ($M$ = 734):C, 45.94; H, 5.23; N, 7.65 Found: C, 45.91; H, 5.22; N, 7.69% EI-MS, m/z(%):$[(C_8H_5N_2O_2)_2C_4H_8Sn_2(C_2H_5)_3]^+$ 705(100.0), $[C_7H_4NOSn]^+$ 238(11.0), $[Sn]^+$ 120(5.4) FT-IR ($cm^{-1}$): 1610 $\nu_{C=N}$, 1088 $\nu_{N-N}$, 570 $\nu_{Sn-O}$, 460 $\nu_{Sn-N}$, $^1$H NMR (ppm): 8.61 (*s*, 2H, CH=N, $^3J(^{119}Sn–^1H)$ = 43 Hz)], 2.36 (*bs*, 4H, $2CH_2$), 1.75 (*bs*, 4H, $2CH_2$), 6. 77 (*d*, 2H, Ar–H, $^3J_{H-H}$ = 8.4), 7.32 (*t*, 2H, Ar–H, $^3J_{H-H}$ = 7.8), 6.71 (*t*, 2H, Ar–H, $^3J_{H-H}$ = 7.4), 7.13 (*dd*, 2H, Ar–H, $^3J_{H-H}$ = 7.8), 1.46 (*q*, 4H, $H_\alpha$–SnEt, $^3J_{H-H}$ = 7.5), 1.27 (*t*, 6H, $H_\beta$–SnEt, $^3J_{H-H}$ = 7.2) $^{13}C\{^1H\}$ NMR (ppm): 160.9 (CH=N), 176.0 (NCO), 34.3, 26.2 ($-CH_2CH_2$), 167.0, 135.1, 134.2, 121.5, 116.9, 116.4 (Ar–C), 14.2 ($C_\alpha$–SnEt, $^1J[^{119/117}Sn–^{13}C]$ = 618, 590 Hz), 9,6 ($C_\beta$–SnEt, $^2J[^{119}Sn–^{13}C]$ = 43 Hz), $^{119}$Sn NMR: $\delta$ (ppm) = −192.5.

***Bis*[di-n-butyltin(IV)] [N$^{1\prime}$, N$^{6\prime}$-*bis*(2-oxidobenzylidene) adipodihydrazide] (3)** Compound **3** was prepared in the same way as **1**, using following precursors quantities: N$^{1\prime}$, N$^{6\prime}$-*bis*(2-hydroxybenzylidene)adipodihydrazide (0.57 g, 1.5 mmol), dibutyltin(IV) dichloride (0.91 g, 3.0 mmol) and triethylamine (0.84 mL, 6.0 mmol) were reacted in a 1:2:4 ratio. Solid product was recrystallized from a chloroform and *n*-hexane (4:1) mixture.

Yield 75%. mp 88–90 °C. *Anal.* Calc. for $C_{36}H_{54}N_4O_4Sn_2$($M$ = 846): C, 51.21; H, 6.45; N, 6.64 Found: C, 51.19; H, 6.41; N, 6.60% EI-MS, m/z(%): $[(C_8H_5N_2O_2)_2C_4H_8Sn_2(C_4H_9)_4]^+$ 846(5.5), $[(C_8H_5N_2O_2)_2\ C_4H_8Sn_2\ (C_4H_9)_3]^+$ 789(100.0), $[(C_8H_5N_2O_2)_2C_4H_8Sn_2(C_4H_9)_2]^+$ 732(4.3), $[(C_8H_5\ N_2O_2)\ Sn]^+$ 281(5.5), $[C_7H_4NOSn]^+$ 238(30.2), $[(C_4H_9)_2Sn]^+$ 234(7.6), $[C_4H_9Sn]^+$ 177 (4.2), $[Sn]^+$ 120(4.3) FT-IR ($cm^{-1}$): 1608 $\nu_{C=N}$, 1076 $\nu_{N-N}$, 568 $\nu_{Sn-O}$, 472 $\nu_{Sn-N}$, $^1$H NMR (ppm): 8.58 (*s*, 2H, CH=N, $^3J(^{119}Sn–^1H)$ = 43 Hz)], 2.35 (*bs*, 4H, $2CH_2$), 1.75 (*bs*, 4H, $2CH_2$), 6. 76 (*d*, 2H, Ar–H, $^3J_{H-H}$ = 8.7), 7.31 (*t*, 2H, Ar–H, $^3J_{H-H}$ = 7.8), 6.71 (*t*, 2H, Ar–H, $^3J_{H-H}$ = 7.5), 7.12 (*dd*, 2H, Ar–H, $^3J_{H-H}$ = 7.8), 1.58–1.65 (*m*, 4H, $H_\alpha$–SnBu), 1.44–1.49 (*m*, 4H, $H_\beta$–SnBu), 1.34 (*q*, 4H, $H_\gamma$–SnBu, $^3J_{H-H}$ = 7.4), 0.88 (*t*, 6H, $H_\delta$–SnBu, $^3J_{H-H}$ = 7.5) $^{13}C\{^1H\}$ NMR (ppm): 160.8 (CH=N), 175.8 (NCO), 34.3, 26.0 ($-CH_2CH_2$), 166.9, 135.0, 134.2, 121.6, 116.8, 116.5(Ar–C), 22.0 ($C_\alpha$–SnBu, $^1J[^{119/117}Sn–^{13}C]$ = 604, 577 Hz), 26.9 ($C_\beta$–SnBu, $^2J[^{119/117}Sn–^{13}C]$ = 36 Hz), 26.5 ($C_\gamma$–SnBu, $^3J[^{119/117}Sn–^{13}C]$ = 94 Hz), 13.6 ($C_\delta$–SnBu), $^{119}$Sn NMR: $\delta$ (ppm) = −192.4.

***Bis*[diphenyltin(IV)] [N$^{1\prime}$, N$^{6\prime}$-*bis*(2-oxidobenzylidene) adipodihydrazide] (4)** Compound **4** was prepared in the same way as **1**, using following precursors quantities: N$^{1\prime}$, N$^{6\prime}$-*bis*(2-hydroxybenzylidene)adipodihydrazide (0.57 g, 1.5 mmol), diphenyltin(IV) dichloride (1.03 g, 3.0 mmol) and triethylamine (0.84 mL, 6.0 mmol) were reacted in a 1:2:4 ratio. The solid product was recrystallized from a chloroform and *n*-hexane (4:1) mixture.

Yield 76%. mp 186–188 °C. *Anal.* Calc. for $C_{44}H_{38}N_4O_4Sn_2$ ($M$ = 926): C, 57.18; H, 4.14; N, 6.06 Found: C, 57.21; H, 4.09; N, 6.08% EI-MS, m/z(%): $[(C_8H_5N_2O_2)_2C_4H_8Sn_2(C_6H_5)_4]^+$ 926(5.6), $[(C_8H_5N_2O_2)_2\ C_4H_8Sn_2(C_6H_5)_3]^+$ 849(100.0), $[(C_8H_5N_2O_2)_2C_4H_8Sn_2(C_6H_5)_2]^+$ 772(3.4), $[(C_8H_5N_2O_2)$

$CNC_4H_8Sn(C_6H_5)_2]^+$ 517(5.5), $[(C_8H_5N_2O_2)C_4H_8Sn(C_6H_5)_2]^+$ 491(3.9), $[(C_8H_5N_2O_2)CH_2Sn(C_6H_5)_2]^+$ 449(10.1), $[(C_8H_6N_2O_2)Sn(C_6H_5)_2]^+$ 436(5.3), $[(C_8H_5N_2O_2)Sn(C_6H_5)_2]^+$ 435(5.3), $[(C_8H_5N_2O_2)Sn]^+$ 281(4.3), $[C_7H_4NOSn]^+$ 238(25.3), $[(C_6H_5)_2Sn]^+$ 274 (3.5), $[C_6H_5Sn]^+$ 197(36.8), $[Sn]^+$ 120(10.6) FT-IR ($cm^{-1}$): 1611 $\nu_{C=N}$, 1080 $\nu_{N-N}$, 578 $\nu_{Sn-O}$, 472 $\nu_{Sn-N}$, $^1$H NMR (ppm): 8.52 (*s*, 2H, CH=N, $^3J(^{119}Sn-^1H) = 52$ Hz)], 2.53 (*bs*, 4H, $2CH_2$), 1.93 (*bs*, 4H, $2CH_2$), 7.11 (*d*, 2H, Ar–H, $^3J_{H-H} = 8.4$), 7.37–7.50 (*m*, 2H, Ar–H), 6.79 (*t*, 2H, Ar–H, $^3J_{H-H} = 7.8$), 7.19 (*d*, 2H, Ar–H, $^3J_{H-H} = 8.7$), 7.82–7.86 (*m*, 4H, $H_\beta$–$SnC_6H_5$), 7.37–7.50 (*m*, 4H, $H_\gamma$–$SnC_6H_5$), 7.37–7.50 (*m*, 2H, $H_\delta$–$SnC_6H_5$) $^{13}C\{^1H\}$ NMR (ppm): 161.0 (CH=N), 175.7 (NCO), 34.4, 26.1 (–$CH_2CH_2$), 167.1, 135.4, 134.4, 122.0, 117.5, 116.6 (Ar–C), 139.0 ($C_\alpha$– $SnC_6H_5$), 136.2 ($C_\beta$– $SnC_6H_5$, $^2J[^{119/117}Sn-^{13}C] = 54$ Hz), 128.9 ($C_\gamma$– $SnC_6H_5$, $^3J[^{119/117}Sn-^{13}C] = 87$, 85 Hz), 130.5 ($C_\delta$–$SnC_6H_5$, $^4J[^{119/117}Sn-^{13}C] = 18$ Hz), $^{119}$Sn NMR: $\delta$ (ppm) = −333.0.

***Bis*[di-n-octyltin(IV)] [N$^{1\prime}$, N$^{6\prime}$-*bis*(2-oxidobenzylidene) adipodihydrazide] (5)** Compound **5** was prepared by refluxing N$^{1\prime}$, N$^{6\prime}$-*bis*(2-hydroxybenzylidene)adipodihydrazide (0.57 g, 1.5 mmol) with di-*n*-octyltin(IV) oxide (1.09 g, 3.0 mmol) in 100 mL dry toluene in 1:2 ratio. The water formed during the reaction was removed by Dean–Stark apparatus. The yellow solution obtained was rotary evaporated under reduced pressure viscous liquid product that was obtained (Scheme 1d).

Yield 72%. mp viscous liquid. *Anal.* Calc. for $C_{52}H_{86}N_4O_4Sn_2$ (*M* = 1070): C, 58.44; H, 8.11; N, 5.24 Found: C, 58.39; H, 8.09; N, 5.27% EI-MS, m/z(%): $[(C_8H_5N_2O_2)_2C_4H_8Sn_2(C_8H_{17})_3]^+$ 957(87.2), $[(C_8H_5N_2O_2)_2C_4H_8Sn_2(C_8H_{17})_2]^+$ 844(4.6), $[(C_8H_5N_2O_2)Sn]^+$ 281(4.3), $[C_7H_4NOSn]^+$ 238 (29.8), $[Sn]^+$ 120(3.4); $[C_4H_9]^+$ 57(100.0) FT-IR ($cm^{-1}$): 1610 $\nu_{C=N}$, 1077 $\nu_{N-N}$, 568 $\nu_{Sn-O}$, 470 $\nu_{Sn-N}$, $^1$H NMR (ppm): 8.57 (*s*, 2H, CH=N, $^3J(^{119}Sn-^1H) = 43$ Hz)], 2.33 (*bs*, 4H, $2CH_2$), 1.74 (*bs*, 4H, $2CH_2$), 6. 75 (*d*, 2H, Ar–H, $^3J_{H-H} = 8.4$), 7.30 (*t*, 2H, Ar–H, $^3J_{H-H} = 7.8$), 6.70 (*t*, 2H, Ar–H, $^3J_{H-H} = 7.5$), 7.11 (*dd*, 2H, Ar–H, $^3J_{H-H} = 7.8$), 1.60–1.68 (*m*, 4H, $H_\alpha$–SnOct), 1.44–1.49 (*m*, 4H, $H_\beta$–SnOct), 1.22–1.31 (*bs*, 16H, $H_{\gamma-\gamma}$–SnOct,), 0.87 (*t*, 6H, $H_{\delta'}$–SnOct, $^3J_{H-H} = 6.9$) $^{13}C\{^1H\}$ NMR (ppm): 160.6 (CH=N), 175.8 (NCO), 34.3, 26.2 (–$CH_2CH_2$), 166.8, 134.9, 134.1, 121.6, 116.8, 116.6 (Ar–C), 22.6 ($C_\alpha$–SnOct, $^1J[^{119/117}Sn-^{13}C] = 649$, 622 Hz), 24.7 ($C_\beta$–SnOct, $^2J[^{119/117}Sn-^{13}C] = 36$ Hz), 33.4 ($C_\gamma$–SnOct, $^3J[^{119/117}Sn-^{13}C] = 78$ Hz), 29.2, 29.1,31.8, 22.3 ($C_{\delta-\gamma'}$–SnOct), 14.1 ($C_\delta$–SnOct), $^{119}$Sn NMR: $\delta$ (ppm) = −198.

***Bis*[n-butylchlorotin(IV)] [N$^{1\prime}$, N$^{6\prime}$-*bis*(2-oxidobenzylidene)adipodihydrazide] (6)** Compound **6** was prepared in the same way as **5**, using following precursors quantities: N$^{1\prime}$, N$^{6\prime}$-*bis*(2-hydroxybenzylidene) adipodihydrazide (0.57 g, 1.5 mmol) and butyldihydroxidetin(IV) chloride (0.73 g, 3.0 mmol) were reacted in a 1:2 ratio. Solid product was recrystallized from a chloroform and *n*-hexane (4:1) mixture.

Yield 75%. mp 130–132 °C. *Anal.* Calc. for $C_{28}H_{36}Cl_2N_4O_4Sn_2$ (*M* = 802): C, 41.99; H, 4.53; N, 7.00 Found: C, 42.01; H, 4.56; N, 6.98% EI-MS, m/z(%): $[(C_8H_5N_2O_2)_2C_4H_8Sn_2(C_4H_9Cl)_2]^+$ 802 (5.05), $[(C_8H_5N_2O_2)_2C_4H_8Sn_2(C_4H_9)_2Cl]^+$ 767(70.5), $[(C_8H_5N_2O_2)_2C_4H_8Sn_2(C_4H_9)Cl_2]^+$ 745(10.7), $[(C_8H_5N_2O_2)CNC_4H_8Sn(C_4H_9)Cl]^+$ 455(3.3), $[(C_8H_6N_2O_2)Sn(C_4H_9)Cl]^+$ 374(7.4), $[(C_8H_5N_2O_2)Sn(C_4H_9)Cl]^+$ 373(8.1), $[(C_8H_5N_2O_2)Sn(C_4H_9)]^+$ 338(5.3), $[(C_8H_5N_2O_2)SnCl]^+$ 316(3.9), $[(C_8H_5N_2O_2)Sn]^+$ 281 (14.6), $[C_7H_4NOSn]^+$ 238 (100.0), $[Sn]^+$ 120(10.5) FT-IR ($cm^{-1}$): 1606 $\nu_{C=N}$, 1077 $\nu_{N-N}$, 568 $\nu_{Sn-O}$, 451 $\nu_{Sn-N}$, $^1$H NMR (ppm): 8.71 (*s*, 2H, CH=N), 2.30 (*bs*, 4H, $2CH_2$), 1.74 (*bs*, 4H, $2CH_2$), 6. 89 (*d*, 2H, Ar–H, $^3J_{H-H} = 8.1$), 7.37 (*t*, 2H, Ar–H, $^3J_{H-H} = 7.8$), 6.82 (*t*, 2H, Ar–H, $^3J_{H-H} = 7.2$), 7.17 (*d*, 2H, Ar–H, $^3J_{H-H} = 7.2$), 1.66–1.76 (*m*, 4H, $H_\alpha$–SnBu), 1.46–1.57 (*m*, 4H, $H_\beta$–SnBu), 1.43 (*q*, 4H, $H_\gamma$–SnBu, $^3J_{H-H} = 7.2$), 0.92 (*t*, 6H, $H_\delta$–SnBu, $^3J_{H-H} = 7.2$) $^{13}C\{^1H\}$ NMR (ppm): 159.3 (CH=N), 166.0 (NCO), 34.2, 26.1 (–$CH_2CH_2$), 162.3, 134.9, 132.0, 122.2, 117.6, 116.6 (Ar–C), 25.6 ($C_\alpha$–SnBu), 28.3 ($C_\beta$–SnBu), 27.4 ($C_\gamma$–SnBu), 14.1 ($C_\delta$–SnBu), $^{119}$Sn NMR: $\delta$ (ppm) = −200.

## Antibacterial activity

The synthesized compounds were tested for antibacterial activity against *Escherichia coli* ATCC 11229, *Bacillus subtilis* ATCC 11774, *Shigella flexenari* ATCC 10782, *Stephlococcus aureus* ATCC 25923, *Pseudomonas aeruginosa* ATCC 10245 and *Salmonella typhi* ATCC 10749 using the agar well diffusion method and imipenem as standard drug [24].

## Antifungal activity

The in vitro antifungal activity of synthesized compounds was also investigated against six fungal strains [*Trichophyton longifusus* ATCC 22397, *Candida albicans* ATCC 2192, *Aspergillus flavis* ATCC 1030, *Microsporum canis* ATCC 9865, *Fusarium solani* ATCC 11712 and *Candida glaberata* ATCC 90030] using the agar tube dilution test [25]. Miconazole and amphotericin B were used as reference drugs.

## Cytotoxicity

The potential cytotoxicity of synthesized compounds was assessed by brine shrimp lethality bioassay, which is a reliable, fast, sensitive and economical method for screening the toxicity of substances before performing detailed cell-based

or in vivo studies [25]. Solutions of test compounds having 1, 10 and 100 μg $mL^{-1}$ concentrations were prepared. Data were analyzed with Finney's probit analysis to determine the $LD_{50}$ [26]. Etoposide was used as the standard drug. Etoposide was also tested as the standard drug.

### X-ray crystallographic studies

A crystal with the dimensions of 0.24 × 0.18 × 0.11 mm was mounted on top of a glass fiber and aligned on a *Bruker* [27] *SMART APEX CCD* diffractometer (platform with full three-circle goniometer). The diffractometer was equipped with a 4 K *CCD* detector set 60.0 mm from the crystal. The crystal was cooled to 100(1) K using the *Bruker KRYO-FLEX* low-temperature device. Intensity measurements were performed using graphite monochromated Mo-Kα radiation from a sealed ceramic diffraction tube (*SIEMENS*). Generator settings were 50 kV/40 mA. *SMART* was used for preliminary determination of the unit cell constants and data collection control. The intensities of reflections of a hemisphere were collected by a combination of three sets of exposures (frames). Each set had a different ϕ angle for the crystal, and each exposure covered a range of 0.3° in *ω*. A total of 1800 frames were collected with an exposure time of 10.0 s per frame. The overall data collection time was 7.9 h. Data integration and global cell refinement were performed with the program *SAINT* [27]. The final unit cell was obtained from the *xyz* centroids of 5187 reflections after integration. Intensity data were corrected for Lorentz and polarization effects, scale variation, for decay and absorption: a multi-scan absorption correction was applied, based on the intensities of symmetry-related reflections measured at different angular settings (*SADABS*) [27], and reduced to $F_o^2$. The program suite *SAINTPLUS* [27] was used for space group determination (*XPREP*).

The unit cell was identified as monoclinic; reduced cell calculations did not indicate any higher metric lattice symmetry. The space group $P2_1/c$ was derived from the systematic extinctions. Examination of the final atomic coordinates of the structure did not yield extra crystallographic or metric symmetry elements. The structure was solved by Patterson methods, and extension of the model was accomplished by direct methods applied to difference structure factors using the program *DIRDIF*-08 [28]. The positional and anisotropic displacement parameters for the non-hydrogen atoms were refined. The hydrogen atoms were generated by geometrical considerations, constrained to idealized geometries, and allowed to ride on the carrier atoms with an isotropic displacement parameter related to the equivalent displacement parameter of their carrier atoms, with $U_{iso}(H) = 1.2U_{eq}(C)$ or $1.5U_{eq}$(methyl C). The methyl groups were refined as rigid groups, which were allowed to rotate freely. Assigned values of bond distances: secondary C–$H_2$ = 0.99 Å, methyl C–$H_3$ = 0.98 Å and aromatic C–H = 0.95 Å. Final refinement on $F^2$ carried out by full-matrix least-squares techniques converged at $wR(F^2) = 0.0648$ for 2691 reflections and $R(F) = 0.0259$ for 2377 reflections with $F_o \geq 4.0\ \sigma(F_o)$ and 156 parameters. The final difference Fourier map was essentially featureless with a few peaks of max. 1.27(10) e/Å$^3$ within 1.0 Å from Sn position, but were neglected/rejected, being artefacts. No other significant peaks having chemical meaning above the general background were observed in the final difference Fourier syntheses. The positional and anisotropic displacement parameters for the non-hydrogen atoms were refined on $F^2$ with full-matrix least-squares procedures minimizing the function $Q = \sum_h [w(|(F_o^2) - k(F_c^2)|)^2]$, where $w = 1/[\sigma^2(F_o^2) + (aP)^2 + bP]$, $P = [\max(F_o^2,0) + 2F_c^2]/3$, $F_o$ and $F_c$ are the observed and calculated structure factor amplitudes, respectively; ultimately the suggested $a$ (=0.0383) and $b$ (=0.0624) were used in the final refinement.

All refinement calculations and graphics were performed on a HP XW6200 (Intel XEON 3.2 Ghz)/Debian-Linux computer at the University of Groningen with the program packages *SHELXL* [29] (least-square refinements), a locally modified version of the program *PLUTO* [30] (preparation of illustrations) and *PLATON* package [31].

## Results and discussion

### Synthesis of ligand ($H_4L$) and diorganotin(IV) complexes (1–6)

Adipic acid dihydrazide was reacted with 2-hydroxybenzaldehyde to get the ditopic Schiff base ligand $H_4L$. Six diorganotin(IV) [$N^{1\prime}$, $N^{6\prime}$-*bis*(2-oxidobenzylidene)adipodihydrazide] complexes were prepared by the reaction of the ligand ($H_4L$) with the selected diorganotin(IV) dichlorides in the appropriate mole ratio in dry chloroform (Scheme 1c, d). The numbering scheme for the organic groups attached to Sn is given in scheme 1e. The compounds 1–6 are soluble in common organic solvents and stable in air. All the compounds were obtained in good yield and purity.

### FT-IR Spectra

The comparison of IR spectra of complexes with that of ligand provides evidence for complexation and donor sites involved in chelation. The absorption bands observed at 3442, 3220 and 1680 $cm^{-1}$ in the IR spectrum of ligand can be assigned to the υO–H, υN–H and υC=O of the amide group, respectively. The IR spectral data confirm the stability of keto form of ligand. The disappearance of these bands in all the complexes suggest the conversion of ligand to enol from followed by deprotonation and coordination of

enolic and phenolic oxygens to the diroganotin(IV) moieties. A decrease in the stretching vibration of C=N to lower frequencies has been observed which provide evidence for the interaction of azomethine nitrogen with Sn atom. The shift in electron density also causes a decrease in repulsion of the lone pairs of electrons on the two nitrogen atoms. As a result band due to υ(N–N) is shifted to higher frequencies at 1076–1088 $cm^{-1}$ in the spectra of organotin(IV) complexes. The appearance of new IR bands in the regions of 568–576 and 451–472 $cm^{-1}$ shows the formation of Sn–O and Sn–N bonds, respectively [32, 33].

## NMR spectra

The absence of resonance signals due to OH and NH groups in $^{1}H$ NMR spectra of *bis*-diorganotin(IV) complexes **1–6** suggests deprotonation and enolization of ligand during complex formation [34]. All the complexes are centrosymmetric because in the $^{1}H$ NMR spectra resonance signals for half of each molecule were observed. The resonance signals for aromatic protons of the ligand which appear at 6.89–7.27 ppm and methylene protons of the alkyl linker at 2.26 and 4.54 ppm remain almost unaffected in the NMR spectra of *bis*-diorganotin(IV) complexes since these groups are not involved in bonding. The signal at 8.34 ppm assigned to the azomethine (CH=N) proton in the ligand after coordination with the diorganotin(IV) moieties undergoes a downfield shift to 8.52–8.71 ppm with $^{3}J(^{119}Sn–^{1}H)$ spin–spin coupling constant of 43–52 Hz. The shift in resonance frequency and appearance of tin satellites affirm the presence of Sn–N bond in solution. The characteristic tin satellites can be clearly seen in the $^{1}H$ NMR spectrum of *bis*[diethyltin(IV)] complex provided in Fig. 1. The chemical shift and coupling constant values are consistent with the literature reports for diorganotin(IV) complexes of *bis*-ONO donor ligands [35]. The alkyl/phenyl groups bonded to the tin center also give characteristic peak pattern. The singlet of methyl protons in complex **1** resonate at 0.79 ppm with characteristic tin satellites with $^{2}J(^{119}Sn–^{1}H)$ coupling constant of 79 Hz. The calculation of C–Sn–C angle using Lockhart–Manders equation, $\theta = 0.016|^{2}J|^{2} - 1.32|^{2}J| + 133.4$, gives an angle of 129°, which suggest pentacoordination around tin center in solution state [36]. The protons of terminal methyl groups of complexes **2**, **3, 5** and 6 resonate at 1.27, 0.88, 0.87 and 0.92 ppm with a $^{3}J(^{1}H–^{1}H)$ coupling constant 7.2, 7.5, 6.9 and 7.2 Hz, respectively. All the other protons resonate in the expected range. In complex **5** the protons of phenyl groups appear as multiplets in the regions 7.82–7.86 and 7.37–7.50 ppm.

The $^{13}C\{^{1}H\}$ NMR spectral data of synthesized complexes reveal a downfield shift in the resonance signals of all carbon atoms as compared to ligand. The changes in resonance signals are caused by the electron density shift from ligand to the diorganotin(IV) moieties. The coupling constant $^{1}J$ [$^{119}Sn$, $^{13}C$] values provided in table for organotin(IV) complexes can be used to assess the coordination around tin atom in solution. The $^{1}J$ [$^{119}Sn$, $^{13}C$] values for compounds **1**, **2**, **4** and **5** are in the range of 604–649 Hz, which suggest pentacoordination around tin [37]. The C–Sn–C angles (°) calculated on the basis of NMR parameters ($^{1}J$ and $^{2}J$) are provided in Table 1.

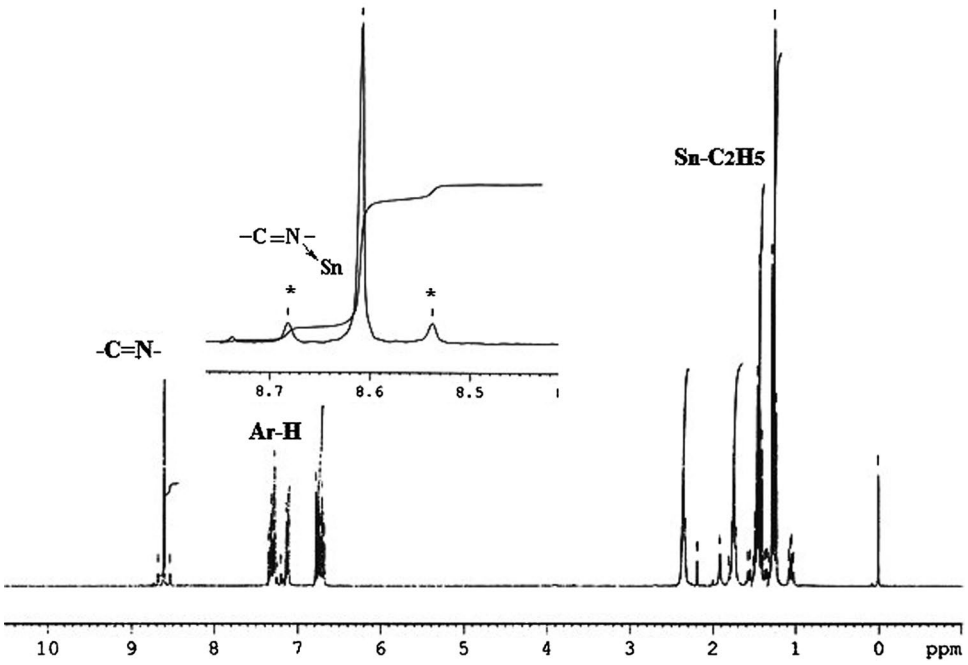



**Fig. 1** $^{1}H$ NMR spectrum of *bis*[diethyltin(IV)] complex (2)

**Table 1** (C–Sn–C) angles (◦) based on NMR parameters of organotin(IV) complexes 1–6

| Comp. No. | Compound | $^{1}J(^{119}Sn, ^{13}C)$ (Hz) | $^{2}J(^{119}Sn, ^{1}H)$ (Hz) | Angle(◦) | |
|---|---|---|---|---|---|
| | | | | $\theta$ ($^{1}J$) | $\theta$ ($^{2}J$) |
| 1. | $(Me_2Sn)_2L$ | 648 | 79 | 133.6 | 129 |
| 2. | $(Et_2Sn)_2L$ | 618 | – | 131.0 | – |
| 3. | $(n\text{-}Bu_2Sn)_2L$ | 604 | – | 135.3 | – |
| 4. | $(Ph_2Sn)_2L$ | – | – | – | – |
| 5. | $(Oct_2Sn)_2L$ | 649 | – | 139.4 | – |
| 6. | $(BuClSn)_2L$ | – | – | – | – |

$^{119}$Sn NMR spectral data also give information regarding the coordination geometry of Sn atom in solution. A sharp single resonance signal observed for all the *bis*-diorganotin(IV) derivatives, demonstrate that both tin atoms in a complex have similar coordination environment.

The $^{119}$Sn NMR signals for 1, 3, 5 and 6 complexes were observed at −154, −192, −198 and −200 ppm, respectively. For *bis*-diphenyl complex, the signal appears at −333 ppm due to pi interactions amplified by anisotropic shielding effects. The chemical shift data suggest pentacoordination around tin atom with trigonal bipyramidal geometry [38–41].

## X-ray crystallographic studies

X-ray crystallography provided the explicit structure for complex **1**. The molecular structure and atomic numbering scheme are depicted in Fig. 2. Pertinent crystallographic data, selected bond lengths and angles are listed in Tables 2 and 3. The asymmetric unit of centrosymmetric binuclear complex 1 comprises of half of the molecule. The ditopic ligand comprises of two dianionic domains in trans-configuration, each coordinating with a dimethyltin(IV) moiety via the ONO donor atoms forming five and six membered chelate rings.

Each of the two tin atoms in the dinuclear complex has a coordination number of five, resulting from the coordination of O1, N1, O2 atoms from the ligand, and two carbon atoms C11, C12 from the methyl groups forming a $O_2NC_2$ core. The coordination of enolic form of tetraanionic ligand is evident from the C=N and C–O bond lengths in complex 1: O2–C8 1.281(–) Å/C8–N2 1.307(–) Å (Fig. 2). The conjugation in C–N–N–C chain is supported by the intermediate values for the bond lengths. The two oxygen atoms from the ligand occupy the axial positions with Sn–O1 and Sn–O2 bond lengths of 2.076(2) and 2.147(2) Å, respectively. The values are less than the sum of the van der Waals radii of Sn and O atoms (3.68 Å) indicating a strong Sn–O bond. The Sn–N(1) bond distance [2.170(2) Å] is comparable to the sum of covalent radii of Sn and N (2.15 Å) and less than the sum of the van der Waals radii (3.75 Å) suggesting a strong tin–nitrogen coordination. The O(1)–Sn–N(1), O(2)–Sn–N(1) and C(11)–Sn–C(12) angles [83.36(8)°, 72.41(8)°, 127.84(10)°] exhibit distortion from 90° and the O(1)-Sn–O(2) angle [154.50(–)°] significantly deviates from linear angle of 180°. The sum of angles [C(11)–Sn–N(1), C(12)–Sn–N(1), C(11)–Sn–C(12)] subtended at the tin atom in the equatorial plane is 359.1, so the atoms which occupy the equatorial positions, are almost in the same plane. The Sn center and O(2), C(8), N(2) and N(1) atoms form a five membered ring, while the Sn center and the O(1), C(1), C(6), C(7) and N(1) atoms form a six membered ring. The steric requirements of these chelate rings make the ligand non-planar. In the solid state, the $R_2Sn$(IV) groups are disposed at trans-position due to packing effects. However, flexibility of butylene linker allows the complexes to adopt different orientations in solution and there is a fast dynamic equilibrium between the different possible conformations [42].

The geometry around Sn atom can be characterized by the index of trigonality $\tau$ which can be calculated using equation $\tau = (\beta - \alpha)/60$, where $\beta$ and $\alpha$ are the consecutive largest of the basal angles around the Sn center. For pentacoordinated Sn $\tau$ value is one for perfect trigonal–bipyramidal geometry whereas zero for a perfect square pyramidal structure. The $\tau$ value 0.5 for a molecule indicates a geometry midway between square–pyramidal and trigonal bipyramidal [43].

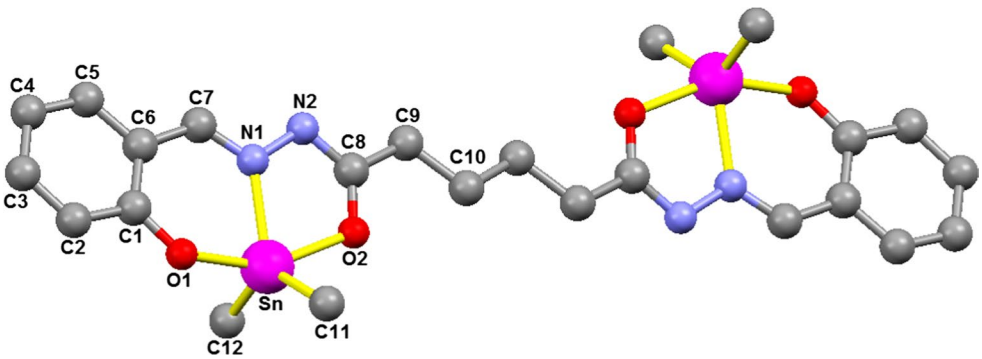



**Fig. 2** Molecular structure of compound **1** with the atomic numbering scheme, and hydrogen atoms are omitted for clarity (symmetry code for the unlabeled atoms:1 − x, −y, 1 − z)

**Table 2** Crystal data and structure refinement parameters for compound (1)

| Empirical formula | $C_{24}H_{30}N_4O_4Sn_2$ |
|---|---|
| Formula mass | 675.94 |
| Crystal system | Monoclinic |
| Space group | $P2_1/c$ |
| $a$ (Å) | 10.298(2) |
| $b$ (Å) | 10.492(2) |
| c (Å) | 12.489(3) |
| β(°) | 109.49(3) |
| $V$ (Å$^3$) | 1272.0(5) |
| $Z$ | 2 |
| Crystal habit | Block |
| Size (mm) | 0.24 × 0.18 × 0.11 |
| T (K) | 100 (1) |
| ρ (g cm$^{-3}$) | 1.765 |
| μ (Mo Kα) (cm$^{-1}$) | 20 |
| $F$(000) | 668 |
| Total reflections | 9979 |
| Independent reflections | 2691 |
| For [$F_o \geq 4.0\,\sigma\,(F_o)$] | 2377 |
| $R(F) = \Sigma(\|\|F_o\|-\|F_c\|\|)/\Sigma\|F_o\|$ For $F_o > 4.0\,\sigma\,(F_o)$ | 0.0259 |
| $wR(F^2) = [\Sigma[w(F_o^2-F_c^2)^2]/\Sigma[w(F_o^2)^2]]^{1/2}$ | 0.0648 |
| Goodness-of-fit | 1.069 |
| $\theta$ Range (deg) | 2.60–29.41 |
| Data/restrictions/params | 2691/0/156 |
| Largest diff. peak and hole (eÅ$^{-3}$) | −0.54 and 1.27(10) |

**Table 3** Selected bond lengths (Å) and bond angles (°) of complex (1)

| | | | |
|---|---|---|---|
| Bond lengths | | | |
| Sn–O(1) | 2.076(2) | Sn–C(12) | 2.100(3) |
| Sn–O(2) | 2.147(2) | N(1)–N(2) | 1.394(3) |
| Sn–N(1) | 2.170(2) | N(1)–C(7) | 1.290(4) |
| Sn–C(11) | 2.097(3) | N(2)–C(8) | 1.307(4) |
| Bond angles | | | |
| O(1)–Sn–O(2) | 154.50(7) | N(1)–Sn–C(12) | 107.15(9) |
| O(1)–Sn–N(1) | 83.36(8) | C(11)–Sn–C(12) | 127.84(10) |
| O(1)–Sn–C(11) | 94.77(10) | Sn–O(1)–C(1) | 131.16(18) |
| O(1)–Sn–C(12) | 100.58(10) | Sn–O(2)–C(8) | 115.11(18) |
| O(2)–Sn–N(1) | 72.41(8) | Sn–N(1)–N(2) | 116.63(15) |
| O(2)–Sn–C(11) | 92.38(10) | Sn–N(1)–C(7) | 127.42(18) |
| O(2)–Sn–C(12) | 94.17(10) | N(2)–N(1)–C(7) | 115.0(2) |
| N(1)–Sn–C(11) | 124.07(10) | N(1)–N(2)–C(8) | 111.2(2) |

The calculated τ value (0.44) for complex **(1)** indicates a structure biased toward square–pyramidal geometry. In the lattice molecules are connected to each other through C7–H7….O1 (2.609 Å) and C11–H11…N2 (2.617 Å) interactions forming supramolecular rings containing four tin atoms belonging to four different molecules (Fig. 3). Consequently in the solid state the molecules are packed together to form a multilayered porous structure (Fig. 4).

## Antibacterial activity

The development of drug resistance by pathogenic microbes mainly due to gene mutation has grown the need for more effective antimicrobial. Thus, the synthesized ligand and *bis*[diorganotin(IV)] complexes (**1–6**) were screened for their antibacterial action against four gram-negative (*Escherichia coli*, *Shigella flexenari, Pseudomonas aeruginosa* and *Salmonella typhi*) and two gram-positive bacteria (*Bacillus subtilis*, *Staphlococcus aureus*). The results of investigated bacterial activity of synthesized compounds are presented in Table 4. The *bis*[diorganotin(IV)] complexes (**1–6**) exhibited elevated inhibitory activity in comparison to the parent ligand. Highest antibacterial activity was shown by *bis*[diphenyltin(IV)] (**4**) against *Bacillus subtilis*, a gram-positive bacteria with a loosely packed polyglycan outer layer allowing the easy penetration of the complex inside the cell where it can then interact with the cytoplasmic membrane. On the other hand, a gram-negative bacterial cell has a bilayer phospholipid structure which guards the inner cytoplasmic membrane to a larger degree against the inhibitory action of the organotin(IV) complex. However, most of the synthesized complexes also have an inhibitory action on the growth of *Shigella flexenari,* a gram-negative bacteria. The *bis*[dibutyltin(IV)] complex (**3**) is unique in the sense that it is active against *Salmonella typhi*, a gram-negative bacteria and *Bacillus subtilis,* a gram-positive bacteria. *Bis*[dioctyltin(IV)] complex (5) showed insignificant antibacterial activity against all tested bacteria. None of the synthesized complex is more active than the reference drug. *Bis*[dimethyltin(IV)] (1), *bis*[diethyltin(IV)] (2) and [Chlorobutyltin(IV)] complex (6) exhibited mild toxicity to selected bacterial strains. *Salmonella typhi* demonstrated resistance against all synthesized compounds except *bis*[dibutyltin(IV)] complex (**3**). The bacterial resistance to some Organotin(IV) compounds is reported in the literature. However, resistance mechanism is yet to be fully explored [44, 45].

Compounds may exhibit bactericidal or bacteriostatic effects but the inhibitory action of organotin(IV) compounds may be due to their ability to inhibit ATP synthesis and can be justified through chelation theory. The ligand on complexation with the diorganotin(IV) moieties partially shares the positive charge on tin atom and decreases its hydrophilic character. The electron density is delocalized over the whole chelate ring causing an increase in the lipophilic nature of the central Sn atom. The high lipophilic character of tin atom facilitates the permeation of complexes through the lipid

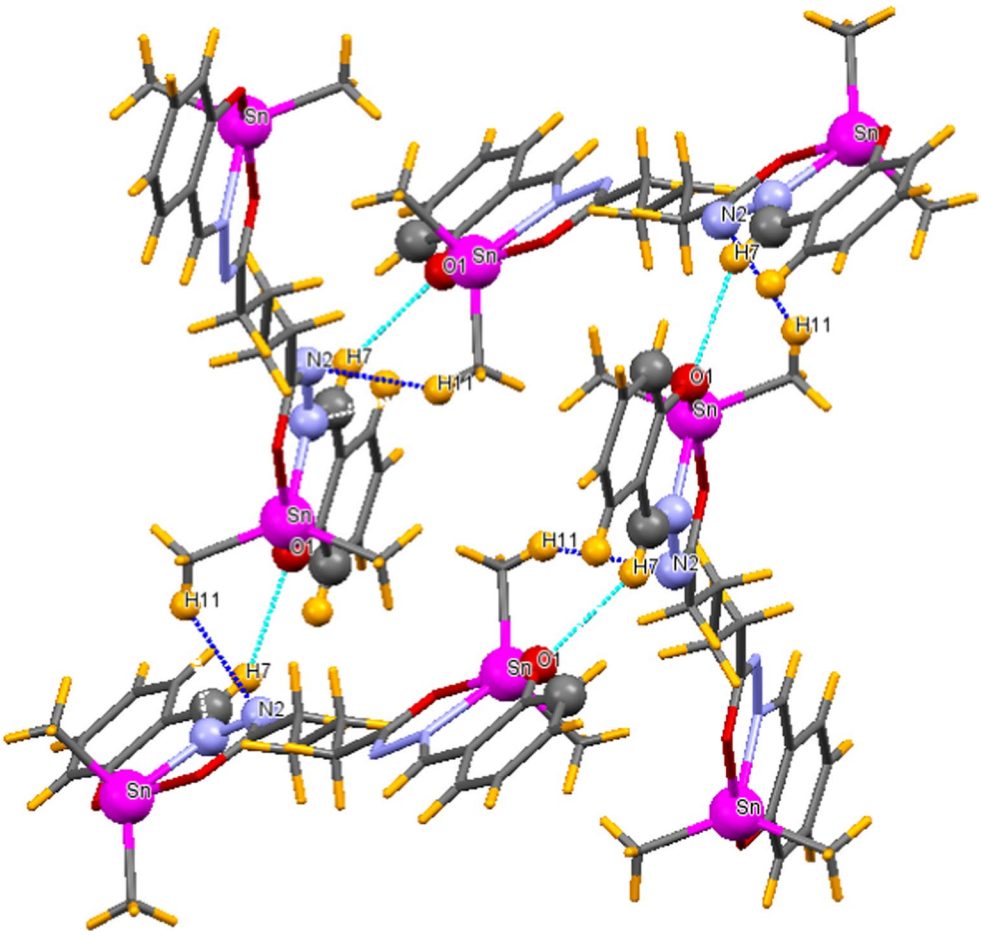



**Fig. 3** Supramolecular cyclic structure of compound **1** mediated by C7–H7…O1 (2.609 Å) and C11–H11…N2 (2.617 Å) interactions

layer of the cell membrane [46]. Once inside the cell then the organotin(IV) complex may block various metabolic pathways by deactivating various enzymes.

The variation in antibacterial activity of the synthesized *bis*[diorganotin(IV)] complexes against the selected bacterial strains may be due to a number of factors including differences in nature and lengths of alkyl groups bonded to tin center and dissimilarities in the construction of cell wall and cell membrane etc. Enhanced lipophilic character result in an increase in antibacterial activity; however, in case of more bulky alkyl group low activity has been observed due to steric factors which favor slow movement through the cell boundary.

## Antifungal activity

Fungal infections of skin, hair, nails and eyes may develop into serious human diseases like aspergillosis, histoplasmosis, candidosis, cryptococcosis and mucormycosis if not properly treated. Antifungal drug resistance is an emerging phenomenon and has amplified the need to design and synthesize potential antifungals to combat pathogens.

The synthesized compounds were studied in vitro for antifungal activity against six pathogenic fungal strains including yeasts (*Candida albicans* ATCC 2192, *Candida glabrata* ATCC 90030), dermatophytes (*Microsporum canis* ATCC 9865, *Trichphyton longifusus* ATCC 22397) and opportunistic molds (*Aspergillus flavus* ATCC 1030 and *Fusarium solani* ATCC 11712) using the agar tube dilution test. Variation in activity against various fungal strains presented in Table 5 indicates different modes of interaction with the microbes. The compounds have the ability to develop noncovalent secondary interaction with bioreceptors within the microbial cells and inhibit DNA synthesis within the nucleus [47, 48].

The ligand ($H_4L$) is inactive against all the investigated fungal strains. Compounds **1** and **4** are highly effective against *Aspergillus flavis*. Compound **2** demonstrates low activity against *Candida albicans* and *Microsporum canis*. Compound **3** exhibited mild activity against *Aspergillus flavis* and *fusarium solani*. Compound **5** is inactive against all the strains, and compound **6** shows low activity against *Aspergillus flavis* and *Microsporum canis*. The highest activity of compound **4** might be due to its high lipophilic

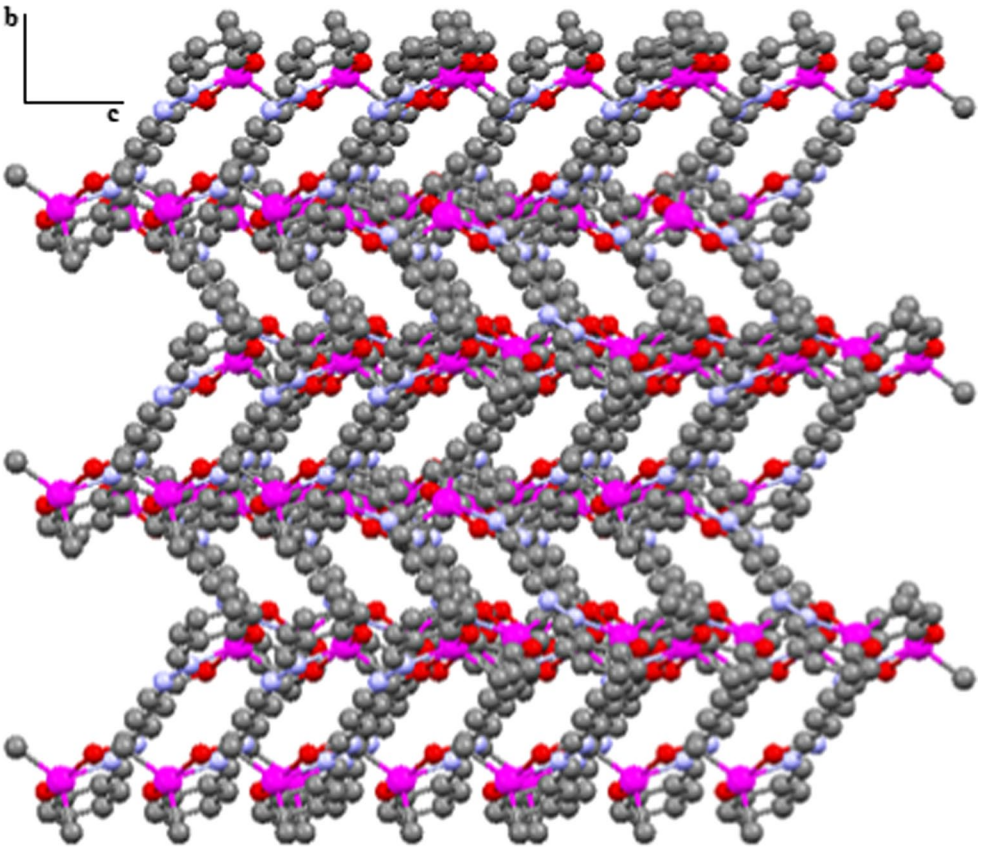



**Fig. 4** A portion of lattice of complex **1** showing multilayered packing of molecules forming porous structure

**Table 4** Antibacterial activity data of *bis*-diorganotin(IV) derivatives of $N^{1\prime}$, $N^{6\prime}$-*bis*(2-hydroxybenzylidene) adipohydrazide[a]

| Bacterium (ATCC No.) | Inhibition zone diameter (mm) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | **$H_4L$** | **1** | **2** | **3** | **4** | **5** | **6** | **Reference drug** |
| *Escherichia coli* (11229) | – | – | – | – | 17 | – | 12 | 30 |
| *Bacillus subtilis* (11774) | – | 15 | 12 | 21 | 21 | 9 | 13 | 37 |
| *Shigella flexnari* (10782) | – | 17 | 10 | 12 | 18 | – | 15 | 36 |
| *Staphlococcus aureus* (25923) | – | 15 | – | 12 | – | – | – | 26 |
| *Pseudomonas aeruginosa* (10145) | – | 15 | 14 | – | – | – | – | 32 |
| *Salmonella typhi* (10749) | – | – | – | 19 | – | – | – | 30 |

[a]Conc. 1 mg/mL of DMSO, Reference drug, Imipenum,—Insignificant activity

**Table 5** Antifungal activity data of *bis*-diorganotin(IV) derivatives of $N^{1\prime}$, $N^{6\prime}$-*bis*(2-hydroxybenzylidene) adipohydrazide[a,b]

| Fungus (ATCC No.) | **Percent Inhibition** | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | **$H_4L$** | **(1)** | **(2)** | **(3)** | **(4)** | **(5)** | **(6)** | Standard drug |
| *Trichophyton longifusus* (22397) | – | – | – | – | – | – | – | 100 |
| *Candida albicans* (2192) | – | – | 20 | – | – | – | – | 100 |
| *Aspergillus flavis* (1030) | – | 85 | – | 40 | 85 | – | 10 | 100 |
| *Microsporum canis* (9865) | – | – | 35 | – | – | – | 20 | 100 |
| *Fusarium solani* (11712) | – | – | – | 50 | 85 | – | – | 100 |
| *Candida glaberata* (90030) | – | – | – | – | – | – | – | 100 |

[a]Conc. 400 µg/mL of DMSO

[b]Standard drug: Amphotericin-B, Miconazole,—no inhibition

**Table 6** Brine shrimp (*Artemia salina*) lethality bioassay data of *bis*-diorganotin(IV) derivatives of $N^{1\prime}$, $N^{6\prime}$-*bis*(2-hydroxybenzylidene) adipohydrazide[a]

| Sample code | $H_4L$ | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|---|
| $LD_{50}$ (μg/mL) | – | – | – | 4.24 | 0.89 | – | – |

[a]Standard drug: Etoposide, $LD_{50}$ 7.46 mg/mL

character. However, none of the compound is more active than the standard drug.

## Cytotoxicity

The cytotoxicity of synthesized compounds (**$H_4L$, 1–6**) was assessed by in vivo lethality to brine shrimp nauplii, and the data are provided in Table 6. Organotin(IV) compounds can exert their cytotoxic effects by interacting with membrane active sites, intracellular proteins, nuclear receptors and DNA. The toxicity of organotin(IV) compounds depends on various factors including the lipophilic character of alkyl groups and can prevent the mitochondrial oxidative phosphorylation, causing apoptosis, necrosis, DNA damage or estrogen receptor blockage [49, 50]. Among the synthesized compounds *bis*-diphenyltin(IV) (**4**) derivative display the highest toxicity with $LD_{50}$ 0.89 μg/mL.

## Conclusions

Six new homobimetallic diorganotin(IV) derivatives compounds of $N^{1\prime}$, $N^{6\prime}$-*bis*(2-hydroxybenzylidene)adipodihydrazide) have been synthesized and characterized by FT-IR, NMR, mass spectroscopy and elemental analysis. Single-crystal X-ray analysis of (**1**) revealed homobimetallic nature of complex with dimethyltin moieties oriented in trans-conformation. The ligand is non-planar with each Sn atom in a distorted square pyramidal coordination geometry due to Sn–N coordination. The noncovalent C–H···N and C–H···O interactions plays a seminal role in generating the porous supramolecular assembly. Some of the compounds were found active against studied bacterial and fungal strains. The highest cytotoxicity was noted for complex **4** with $LD_{50}$ 0.89 μg/mL.

## Supplementary material

CCDC reference number 962696 for $[Me_2Sn]_2L$ (**1**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Center via www.ccdc.ac.uk/data_request/cif.

**Acknowledgements** The corresponding author is thankful to Higher Education Commission of Pakistan for financial support.

## References

1. M.Z. Bulatović, D. Maksimović-Ivanić, C. Bensing, S. Gómez-Ruiz, D. Steinborn, H. Schmidt, M. Mojić, A. Korać, I. Golić, D. Pérez-Quintanilla, M. Momčilović, Angew. Chem. Int. Ed. **53**, 5982 (2014)
2. M. Rizwan, S. Ali, S. Shahzadi, S.K. Sharma, K. Qanungo, M. Shahid, S. Mahmood, J. Coord. Chem. **67**, 341 (2014)
3. S.E. Etaiw, M.M. El-Bendary, Appl. Catal. B-Environ. **126**, 326 (2012)
4. M.K. Atal, R. Sharma, A. Saini, V. Dhayal, M. Nagar, J. Sol–Gel Sci. Technol. **79**, 114 (2016)
5. L. Renard, O. Babot, H. Saadaoui, H. Fuess, J. Brötz, A. Gurlo, E. Arveux, A. Klein, T. Toupance, Nanoscale **4**, 6806 (2012)
6. M.C. García-López, B.M. Muñoz-Flores, V.M. Jiménez-Pérez, I. Moggio, E. Arias, R. Chan-Navarro, R. Santillan, Dyes Pigments **106**, 188 (2014)
7. M. Oh, G.B. Carpenter, D.A. Sweigart, Acc. Chem. Res. **37**, 1 (2004)
8. R. Yadav, M. Trivedi, R. Chauhan, R. Prasad, G. Kociok-Köhn, A. Kumar, Inorg. Chim. Acta **450**, 57 (2016)
9. K. Gholivand, A. Gholami, K.J. Schenk, M.D. Esrafili, K. Farshadfar, RSC Adv. **5**, 98610 (2015)
10. N. Muhammad, S. Zia-ur-Rehman, S. Shujah, A. Ali, A.Meetsma Shah, J. Coord. Chem. **67**, 1110 (2014)
11. K. Xing, R. Fan, J. Fan, X. Du, Y. Song, S. Gao, P. Wang, Y. Yang, Cryst. Growth Des. **16**, 4727 (2016)
12. F. Castet, V. Rodriguez, J.L. Pozzo, L. Ducasse, A. Plaquet, B. Champagne, Acc. Chem. Res. **46**, 2656 (2013)
13. B.M. Muñoz-Flores, R. Santillán, N. Farfán, V. Álvarez-Venicio, V.M. Jiménez-Pérez, M. Rodríguez, O.G. Morales-Saavedra, P.G. Lacroix, C. Lepetit, K. Nakatani, J. Organomet. Chem. **769**, 64 (2014)
14. F. Yu, D.D. Li, L. Cheng, Z. Yin, M.H. Zeng, M. Kurmoo, Inorg. Chem. **54**, 1655 (2015)
15. A.M. Stadler, A.M. Harrowfield, Inorg. Chim. Acta **362**, 4298 (2009)
16. W.H. Hegazy, Y.S. Al-Faiyz, Med. Chem. Res. **23**, 518 (2014)
17. J. Wu, L. Zhao, M. Guo, J. Tang, Chem. Commun. **51**, 17317 (2015)
18. I.P. Ferreira, G.M. de Lima, E.B. Paniago, W.R. Rocha, J.A. Takahashi, C.B. Pinheiro, J.D. Ardisson, Eur. J. Med. Chem. **58**, 493 (2012)
19. S. Hussain, S. Ali, S. Shahzadi, M.N. Tahir, M. Shahid, K.S. Munawar, S.M. Abbas, Polyhedron **117**, 64 (2016)
20. P. Rawat, R.N. Singh, Spectrochim. Acta A **140**, 344 (2015)
21. I.F. Hernández-Ahuactzi, J. Cruz-Huerta, H. Tlahuext, V. Barba, J. Guerrero-Alvarez, H. Höpfl, Cryst. Growth Des. **15**, 829 (2015)
22. S. Shujah, N. Muhammad, A. Shah, S. Ali, A. Meetsma, Z. Hussain, J. Organomet. Chem. **759**, 19 (2014)

23. D.D. Perrin, W.L.F. Armengo, *In Purification of Laboratory Chemicals*, 3rd edn. (Pergamon Press, Oxford, 1988)
24. W. Rehman, M.K. Baloch, A. Badshah, Euro. J. Med. Chem. **43**, 2380 (2008)
25. A. Rahman, M.I. Choudhary, W.J. Thomsen, *Bioassay Techniques for Drug Development* (Harvard Academic Press, The Hague, 2001)
26. D.J. Finney, *Probit Analysis*, 3rd edn. (Cambridge University Press, Cambridge, 1971)
27. Bruker, SMART, SAINTPLUS, XPREP, *Area Detector Control and Integration Software. Smart Apex Software Reference Manuals* (Bruker Analytical X-ray Instruments, Inc., Madison, Wisconsin, USA, 2006)
28. P.T. Beurskens, G. Beurskens, R. Gelder, S. García-Granda, S.R.O. Gould, J.M.M.Smits Israël, *The DIRDIF-99 Program System, Crystallography Laboratory* (University of Nijmegen, Nijmegen, 1999)
29. G.M. Sheldrick, *SHELXL-97, Program for the Refinement of Crystal Structures* (University of Göttingen, Göttingen, 1997)
30. A. Meetsma, *PLUTO, Molecular Graphics Program* (University of Groningen, Groningen, 2007)
31. A.L. Spek, *PLATON, Program for the Automated Analysis of Molecular Geometry* (University of Utrecht, Utrecht, 2006)
32. M. Hong, H.D. Yin, J.C. Cui, Solid State Sci. **13**, 501 (2011)
33. H.D. Yin, M. Hong, Q.B. Wang, S.C. Xue, D.Q. Wang, J. Organomet. Chem. **690**, 669 (2005)
34. S. Shujah, Zia-ur-Rehaman, N. Muhammad, S. Ali, N. Khalid, M.N. Tahir, J. Organomet. Chem. **696**, 2772 (2011)
35. T. Sedaghat, M. Aminian, H.A. Rudbari, G. Bruno, J. Organomet. Chem. **754**, 26 (2014)
36. T.P. Lockhart, W.F. Manders, Inorg. Chem. **25**, 892 (1986)
37. J. Holecek, A. Lycka, Inorg. Chim. Acta **118**, L15 (1986)
38. J. Holecek, M. Nadvornik, K. Handlir, A. Lycka, J. Organomet. Chem. **241**, 177 (1983)
39. M. Nadvornik, J. Holecek, K. Handlir, A. Lycka, J. Organomet. Chem. **275**, 43 (1984)
40. A. Lycka, J. Holecek, M. Nadvornik, K. Handlir, J. Organomet. Chem. **280**, 323 (1985)
41. J. Holecek, M. Nadvornik, K. Handlir, A. Lycka, J. Organomet. Chem. **258**, 2903 (1983)
42. V. Barba, E. Vega, R. Luna, H. Höpfl, H.I. Beltrán, L.S. Zamudio-Rivera, J. Organomet. Chem. **692**, 731 (2007)
43. N. Farfán, T. Mancilla, R. Santillan, A. Gutiérrez, L.S. Zamudio-Rivera, H.I. Beltrán, J. Organomet. Chem. **689**, 3481 (2004)
44. U. Roy, D. Nair, Ecotoxicology **16**, 253 (2007)
45. N. Muhammad, Zia-ur-Rehaman, S. Shujah, A. Shah, S. Ali, A. Meetsma, Z. Hussain, J. Coord. Chem. **65**, 3766 (2012)
46. K. Fukushima, S.K. Dubey, S. Suzuki, J. Gen. Appl. Microbiol. **58**, 283 (2012)
47. P. Chaudhary, M. Swami, D.K. Sharma, R.V. Singh, Appl. Organomet. Chem. **23**, 140 (2009)
48. G.A. Ayoko, J.J. Bonire, S.S. Abdulkadir, P.F. Olurinola, J.O. Ehinmidu, S. Kokot, S. Yiasel, Appl. Organomet. Chem. **17**, 749 (2003)
49. M. Nath, Appl. Organomet. Chem. **22**, 598 (2008)
50. D.B. Shpakovsky, C.N. Banti, E.M. Mukhatova, YuA Gracheva, V.P. Osipova, N.T. Berberova, D.V. Albov, T.A. Antonenko, L.A. Aslanov, E.R. Milaeva, S.K. Hadjikakou, Dalton Trans. **43**, 6880 (2014)