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Substituted O-Vanillin Schiff Base Derived Organotin (IV) Complexes: Synthesis, Characterization, Antimicrobial Evaluation and QSAR Studies

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Abstract

The synthesis and *in vitro* antimicrobial activity of new Schiff bases and their organotin(IV) complexes has been tested against pathogenic Gram positive bacteria (*viz. Klebsiella pneumoniae, Staphylococcus aureus*) Gram negative bacteria (*viz. Escherichia coli*, *Enterobacter aerogenes*) and fungi (*viz. Aspergillus niger* and *Candida albicans*). The QSAR studies of these synthesized compounds has been carried out which indicate that antimicrobial activity of target compounds is governed by topological descriptors and electronic energy of molecule.

Keywords: Schiff bases; Organotin (IV) complexes; Antimicrobial activity; QSAR

Introduction

Schiff base molecules obtained by the condensation of amine with an aldehyde or ketone have been studied widely due to their structural resemblance with natural biological substances and the presence of azomethine group (-N=CH-) which is responsible for the wide range of biological activities including anti-malarial, anti-bacterial, anti-fungal, anti-viral [1-6]. Anti tubercular and anti HIV activity. The Schiff bases are the versatile ligands, when combined with organometallic tin form compounds of high stability with varied stereochemistry [7] and having variety of biological applications [8-10].

Quantitative Structure Activity Relationship (QSAR) is one of the most important areas in computational chemistry which can extensively be used as valuable tool in drug design and medicinal chemistry. The statistically valid QSAR model is to predict the activities of the molecules and to identify the structural feature that play an important role in biological processes [11] QSAR approach is based on the assumption that the behavior of a compound expressed by any measured activities is correlated with the molecular features of the compound [12]. In the present study we have synthesized some new biologically active Schiff bases and studied their ligational behaviour towards dichloro diorganotin (IV) along with their antimicrobial evaluation and QSAR analysis.

Results and Discussion

Chemistry

The reaction of substituted o-vanillin with p-toluic hydrazide or benzhydrazide in equimolar molar ratio afforded four air and moisture stable Schiff base ligands HL_1–HL_4. These ligands were soluble in dimethyl sulfoxide and dimethyl formamide at room temperature and soluble in methanol and ethanol on heating. These bidentate ligands reacted with R_2SnCl_2 (where R = Me, Et, Bu or Ph) in methanol under dry nitrogen atmosphere to form their Sn (IV) complexes (Scheme 1). All the synthesized metal complexes were coloured and insoluble in organic solvents except DMSO. The spectral data and elemental analysis of the synthesized ligands and their metal complexes were well in agreement with their proposed structure (Table 1).

Sr. No.	Compounds	Molecular formula	Molecular mass	Yield (%)	Analysis (%) Found (Calc.)				
					C	H	N	Cl	Sn

1	HL_1	$C_{23}H_{22}N_2O_3$	374.16	82	73.78(73.84)	5.92(6.14)	7.48(7.27)	-	-
2	HL_2	$C_{22}H_{19}N_3O_5$	405.13	86	65.18(65.43)	4.72(4.21)	10.37(9.92)	-	-
3	HL_3	$C_{24}H_{24}N_2O_3$	388.18	83	74.21(74.47)	6.23(6.36)	7.21(9.95)	-	-
4	HL_4	$C_{23}H_{21}N_3O_5$	419.15	79	65.86(66.11)	5.05(5.33)	10.02(10.31)	-	-
5	$Me_2Sn(L_1)Cl$	$C_{25}H_{27}ClN_2O_3Sn$	558.07	74	53.84(54.13)	4.88(5.13)	5.02(5.23)	6.36(6.41)	21.29(20.75)
6	$Et_2Sn(L_1)Cl$	$C_{27}H_{31}ClN_2O_3Sn$	586.10	72	55.37(55.62)	5.33(5.77)	4.78(5.16)	6.05(5.81)	20.27(20.42)
7	$Bu_2Sn(L_1)Cl$	$C_{31}H_{39}ClN_2O_3Sn$	642.17	66	58.01(57.86)	6.12(6.34)	4.36(4.63)	5.52(5.88)	18.50(18.11)
8	$Ph_2Sn(L_1)Cl$	$C_{35}H_{31}ClN_2O_3Sn$	682.10	73	61.66(61.42)	4.58(4.16)	4.11(5.94)	5.20(5.41)	17.41(17.22)
9	$Me_2Sn(L_2)Cl$	$C_{24}H_{24}ClN_3O_5Sn$	589.04	77	48.97(49.12)	4.11(4.22)	7.14(6.87)	6.02(6.31)	20.17(19.87)
10	$Et_2Sn(L_2)Cl$	$C_{26}H_{28}ClN_3O_5Sn$	617.07	81	50.64(50.83)	4.58(4.97)	6.81(6.45)	5.75(5.86)	19.25(19.41)
11	$Bu_2Sn(L_2)Cl$	$C_{30}H_{36}ClN_3O_5Sn$	673.14	75	53.56(53.27)	5.39(5.58)	6.25(6.11)	5.27(5.15)	17.64(17.29)
12	$Ph_2Sn(L_2)Cl$	$C_{34}H_{28}ClN_3O_5Sn$	713.07	68	57.29(56.96)	3.96(3.59)	5.90(5.51)	4.97(5.03)	16.65(16.26)
13	$Me_2Sn(L_3)Cl$	$C_{26}H_{29}ClN_2O_3Sn$	572.09	74	54.62(54.24)	5.11(4.78)	4.90(4.85)	6.20(6.08)	20.77(20.86)
14	$Et_2Sn(L_3)Cl$	$C_{28}H_{33}ClN_2O_3Sn$	600.12	69	56.07(56.34)	5.55(5.99)	4.67(4.73)	5.91(6.11)	19.79(19.63)
15	$Bu_2Sn(L_3)Cl$	$C_{32}H_{41}ClN_2O_3Sn$	656.18	73	58.60(58.89)	6.30(6.11)	4.27(4.55)	5.41(5.45)	18.10(18.27)
16	$Ph_2Sn(L_3)Cl$	$C_{36}H_{33}ClN_2O_3Sn$	696.12	79	62.14(62.55)	4.78(5.12)	4.03(4.34)	5.10(5.23)	17.06(17.35)
17	$Me_2Sn(L_4)Cl$	$C_{25}H_{26}ClN_3O_5Sn$	603.06	67	49.82(49.38)	4.35(4.88)	6.97(7.25)	5.88(5.63)	19.70(19.93)
18	$Et_2Sn(L_4)Cl$	$C_{27}H_{30}ClN_3O_5Sn$	631.09	71	51.42(51.84)	4.79(4.44)	6.66(6.24)	5.62(5.84)	18.82(19.19)
19	$Bu_2Sn(L_4)Cl$	$C_{31}H_{38}ClN_3O_5Sn$	687.15	68	54.21(54.13)	5.58(5.76)	6.12(6.59)	5.16(5.34)	17.28(17.55)
20	$Ph_2Sn(L_4)Cl$	$C_{35}H_{30}ClN_3O_5Sn$	727.09	75	57.84(57.51)	4.16(4.31)	5.78(5.65)	4.88(4.93)	16.33(16.42)

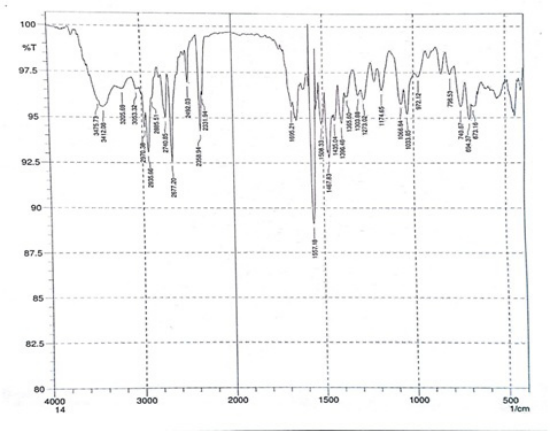
Table 1: Physicochemical characterization and elemental analysis of synthesized compounds.

Electronic Spectra

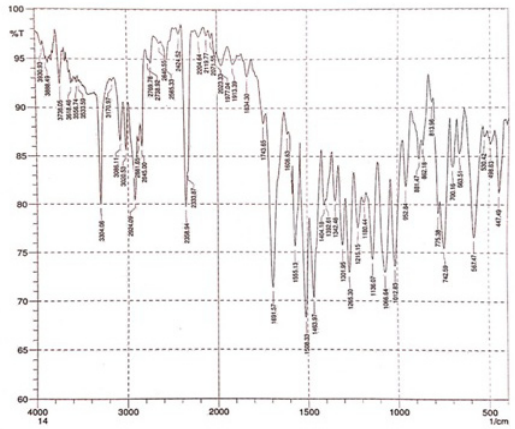
The electronic spectral data of the ligands and their tin complexes were recorded by dissolving these compounds in dry DMSO. The absorption spectra of HL_1–HL_4 were characterized by observing absorption bands at 387-393 nm which is attributed to transition between n-π^* localized on the central azomethine bond. The polarization within the >C=N- group resulting in metal-ligand interaction was shown by the blue shift in the complexes, revealed the involvement of azomethine nitrogen. The π- π^* transition of benzene ring of Schiff base ligands was attributed to bands of medium intensity at 243 nm, 246 nm and 262 nm, which remain unchanged in the complexes.

IR Spectra

The IR spectra of ligands and their complexes were recorded using KBr pellets in the range of 400-4000 cm-1 and is given in experimental part. These ligands can coordinate through the nitrogen of azomethine and oxygen atom after the deprotonation. The ligands HL_1–HL_4 displayed band at 1615-1695 cm-1 [13] and 3412–3373 cm^{-1} due to ν (C=O) and ν (N-H) vibrations, respectively indicating their ketonic nature in the solid state. These bands disappeared in the complexes suggesting enolization of the ligand after deprotonation on coordination. The azomethine ν (C=N) group of Schiff base ligands exhibited a sharp band around 1546-1557cm^{-1} which shifted to lower frequency in the complexes, thereby suggesting the involvement of nitrogen of this group in coordination with metal. Further confirmation of the complexes was supported by appearance of some new bands in the range 447-497 cm^{-1} [14] and 555-567 cm^{-1} [15] which were assigned to ν(Sn-N) and ν(Sn-O) modes respectively.



IR of HL_2

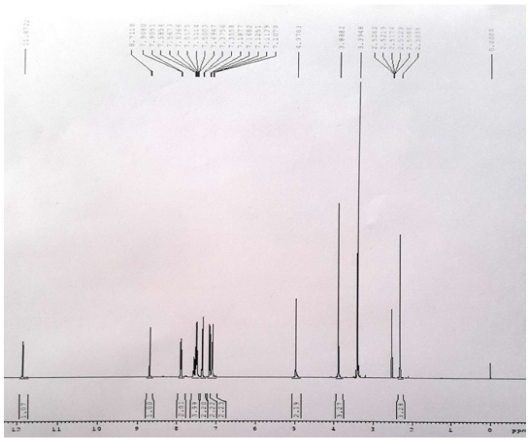


IR of Et_2SnL_2

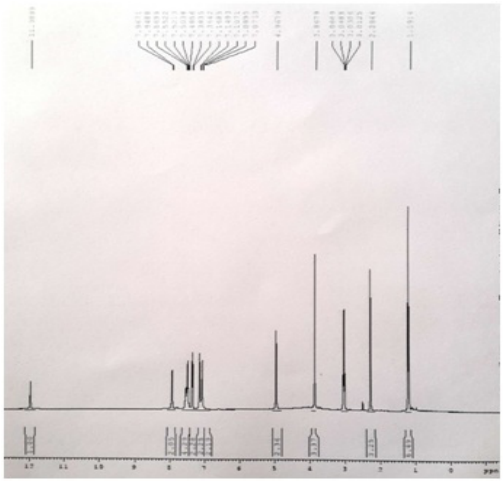
^{1}H NMR

^{1}H NMR spectra of the Schiff bases ligand and their complexes were recorded in DMSO-d_6 and their chemical shifts (δ) are given the experimental part. The ^{1}H NMR spectra of the Schiff base ligands HL_1–HL_4 showed a characteristic NH proton at δ 8.70-8.74 ppm [15] which disappeared in the spectra of the complexes after deprotonation of NH (via enolization). The azomethine proton of these ligands appeared as a sharp singlet around δ 11.78-11.87 ppm [16]. The downfield shifting of this azomethine proton signal in the complexes was observed as a consequence of coordination through nitrogen of this group. The aromatic and aliphatic protons of ligands exhibited signals in the range δ 7.12-7.92 ppm and δ 2.30-5.16 ppm respectively which remain unaltered in the spectra of the complexes indicated non participation of the atoms in bonding to which these protons are attached. The signals present at δ 1.19-1.26 ppm, δ 1.21-3.11 ppm, δ 1.00-3.11 ppm and δ 6.66-7.50 ppm were related to the methyl, ethyl, butyl and phenyl protons directly attached to tin atom. Integrated proton ratios confirmed the formation of complexes of type $R_2Sn(L)C_1$.

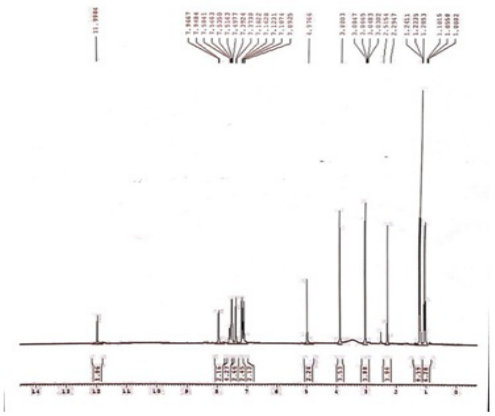
Supplementary material



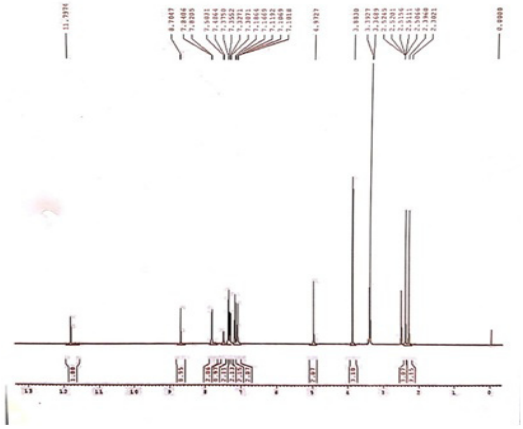
^{1}H-NMR of HL_1



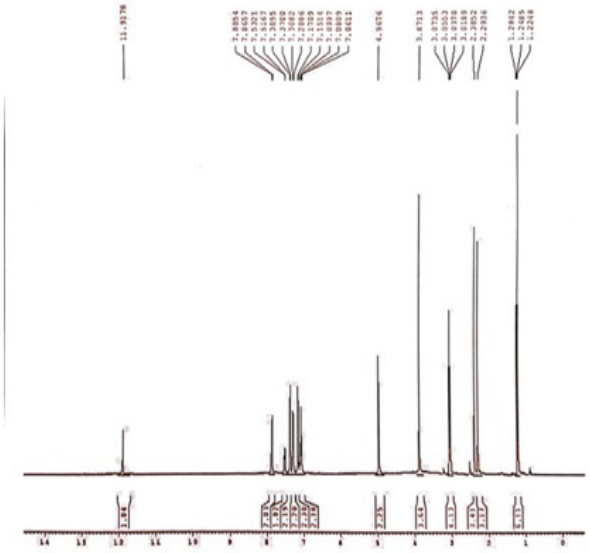
^{1}H-NMR of Me_2SnL_1



^{1}H NMR of Bu_2SnL_1



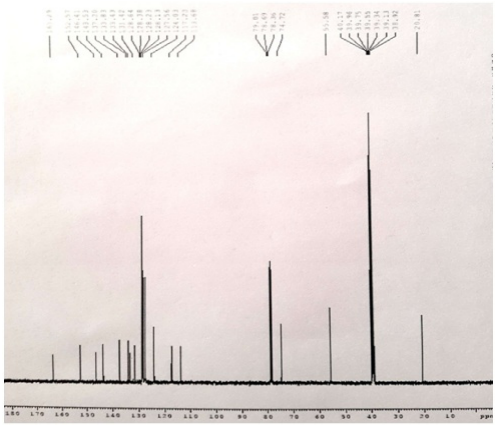
^{1}H NMR of HL_3



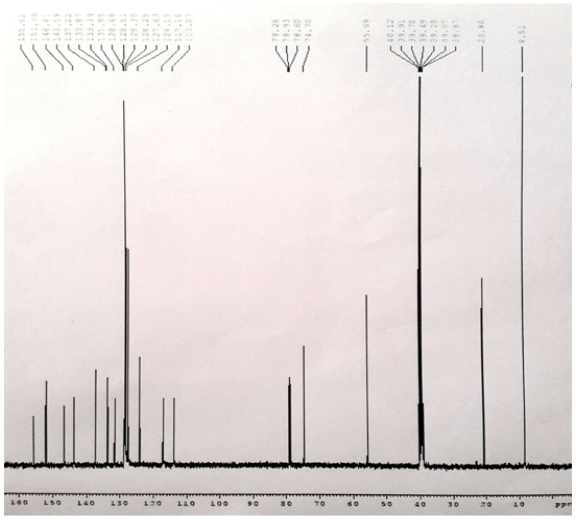
^{1}H NMR of Et_2SnL_3

^{13}C NMR

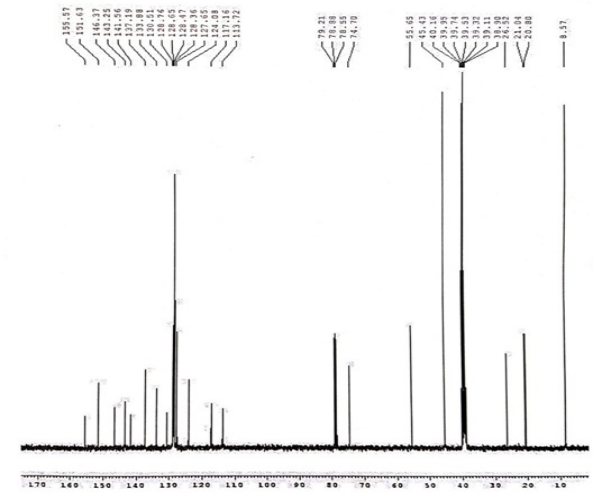
^{13}C NMR spectra of the Schiff bases ligand and their complexes were recorded in DMSO-d_6 and are given in the experimental part. The ligands HL_1–HL_4 displayed characteristic signal of carbon of carbonyl and azomethine (CH=N) groups at δ 163.2–163.3 ppm and δ 152.3– 152.6 ppm respectively [17].Which shifted towards lower values in the complexes, revealed the participation of carbonyl and azomethine carbon in coordination. The signals at δ 113.5-147 ppm and δ 20.8-74.7 ppm were assigned to carbons of aromatic and aliphatic regions of ligands, respectively. The signals at δ 8.5-8.6 ppm, δ 8.5-13.2 ppm and δ 8.2-28.4 ppm revealed the attachment of methyl, ethyl and n-butyl groups with the central metal atom. Similarly the signal at δ 128.1-129.2 ppm were assigned to the phenyl group attached to the tin.



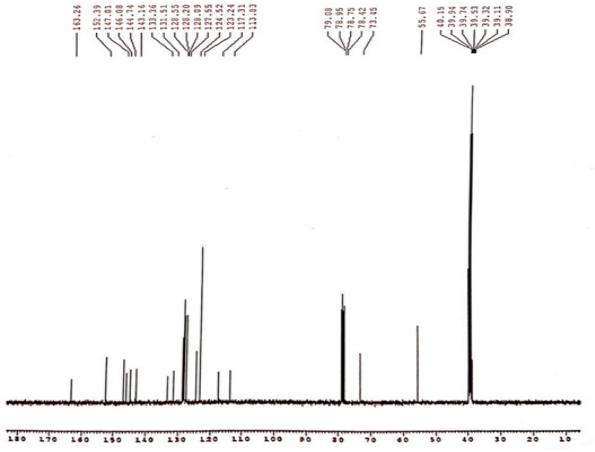
^{13}C-NMR of HL_1



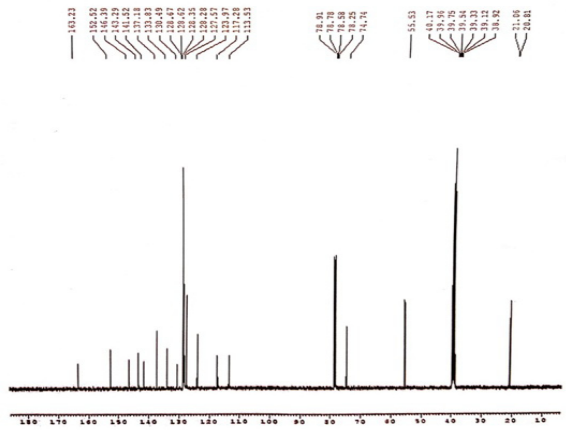
^{13}C-NMR of Me_2SnL_1



^{13}C NMR of Bu_2SnL_1



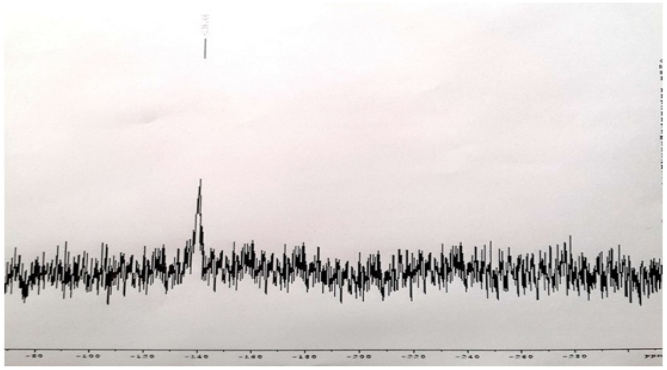
^{13}C NMR of HL_2



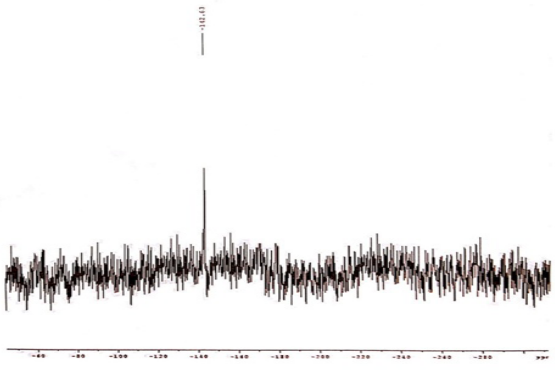
^{13}C NMR of HL_3

^{119}Sn NMR

^{119}Sn NMR is a influential technique to find the coordination number of the central tin atom. The characteristic resonance peaks in the ^{119}Sn NMR spectra of all of the complexes were recorded in $CDCl_3$ and DMSO-d_6. The ^{119}Sn chemical shifts of organotin (IV) derivatives were in the range of -138.5 to -147.6 ppm [18] indicating penta-coordinated environment around tin atom.



^{119}Sn-NMR of Me_2SnL_1



^{119}Sn NMR of Ph_2SnL_3

Antimicrobial activity

The Schiff base ligands and their organotin (IV) complexes were screened for their in vitro antimicrobial activities along with conventional bactericide norfloxacin and fungicide fluconazole for comparing the activity of the compounds. The microorganisms used in the present study include *S. aureus, K. pneumonia, E. coli E. aerogenes*, *Fungi C. albicans* and *A. niger*.

The antimicrobial activity test results of all the tested compounds revealed their ability to act against bacterial and fungal strains appreciably and some of the compounds exhibited better activity than the standard drugs used in the assay. In the entire series, the pMIC of the compounds ranged between 0.874–2.066 µmol/mL and 0.890–2.066 µmol/mL against Gram-positive and Gram-negative bacteria, respectively. Compounds 12, 16 and 20 showed highest antibacterial activity followed by compounds 7, 8, 11, and 19 in the entire series. Similarly, antifungal data suggested that almost same results were obtained as in the antibacterial assay and compounds 11,12,15,16,19 and 20 displayed better activities than other compounds of the series and pMIC for antifungal activity of the entire series ranged from 0.890–2.066 µmol/mL.

The antimicrobial data reveals that the organotin (IV) complexes were found to be better antimicrobial agent as compared to their respective free ligands. The enhancement in the antimicrobial activity of complexes may be due to the delocalization of electron over the whole chelate ring, thereby increasing the lipophilicity of the target compound. This increased lipophilicity of the drug molecule favours its permeation through the cell membrane of microorganism [19]. The other factors which may affect the bioactivity of metal complexes include the number and the nature of the organic groups/halogen atoms directly bound to tin atom. The mode of action of metal complexes may be linked with the formation of hydrogen bond with the active centers of the cell constituents by interfering with normal cell processes.

QSAR analysis

Quantitative structure activity relationship (QSAR) studies between the in vitro antimicrobial activity and descriptors coding for lipophilic, electronic, steric and topological properties of four substituted o-vanillin Schiff bases and their sixteen organotin(IV) complexes were performed to find out the relationship between structural variants and antimicrobial activity using the Linear Free Energy Relationship model (LFER) described by Hansch and Fujita [20]. The dependent variable pMIC (i.e. –log MIC) used as in QSAR study was obtained by taking negative logarithm of observed antimicrobial activities (Table 2).

Comp.	pMICsa	pMICkp	pMICec	pMICea	pMICca	pMICan
1	0.874	1.175	1.175	1.175	1.175	1.175
2	1.210	1.511	1.511	1.210	1.210	1.511
3	0.890	1.191	1.191	0.890	0.890	1.191
4	1.224	1.224	1.224	1.224	1.224	1.224
5	1.349	1.349	1.349	1.349	1.349	1.349
6	1.370	1.671	1.671	1.370	1.370	1.671
7	1.711	1.711	2.012	1.711	1.711	2.012
8	1.737	2.038	2.038	1.737	2.038	2.038
9	1.372	1.673	1.673	1.673	1.372	1.673
10	1.392	1.693	1.693	1.693	1.392	1.693
11	1.731	2.032	2.032	1.731	1.731	2.032
12	2.057	2.057	2.057	1.756	2.057	2.057
13	1.058	1.360	1.360	1.360	1.360	1.360
14	1.380	1.380	1.380	1.380	1.380	1.681
15	1.720	1.720	1.720	1.720	1.720	2.021
16	1.746	2.047	1.746	1.746	2.047	2.047
17	1.382	1.382	1.683	1.382	1.382	1.683
18	1.402	1.703	1.703	1.402	1.402	1.703
19	1.740	1.740	2.041	1.740	1.740	2.041
20	1.765	2.066	2.066	1.765	1.765	2.066
Std.	2.61[#]	2.61[#]	2.61[#]	2.61[#]	2.64[$]	2.64[$]

Norfloxacin[#], Fluconazole[$]

Table 2 : Antimicrobial activity of synthesized derivatives (μM/ml).

The different independent variables (molecular descriptors) like log of octanol–water partition coefficient (log P), Molar Refractivity (MR), Kier's molecular connectivity ($^{0}\chi$, $^{0}\chi^{v}$, $=\chi$, $^{1}\chi^{v}$, $^{2}\chi$, $^{2}\chi^{v}$) and shape (κ_1, κ_2, κ_3, $\kappa\alpha_1$, $\kappa\alpha_2$, $\kappa\alpha_3$) topological indices, Randic topological index (R), Balaban topological index (J), Wiener topological index (W), Total energy (Te), energies of Highest Occupied Molecular Orbital (HOMO) and Lowest Unoccupied Molecular Orbital (LUMO), dipole moment (μ), Nuclear repulsion Energy (Nu.E) and Electronic Energy (Ele.E), calculated for ligands and their organotin (IV) complexes are presented in (Table 3) [21-26].

Comp.	$^{0}\chi$	$^{0}\chi v$	$^{1}\chi$	$^{1}\chi v$	$^{2}\chi$	$^{2}\chi^{v}$	κ_1	κ_2	R	J	W	Te	Ele.E	LUMO	HOMO
1	19.769	15.885	13.669	8.909	11.533	6.218	22.680	12.000	13.669	1.340	2340.000	-4619.890	-34474.400	-0.373	-8.813
2	21.347	16.148	14.580	8.998	12.432	6.156	24.639	12.889	14.580	1.343	2874.000	-5294.900	-38715.000	-1.129	-9.014
3	20.640	16.807	14.063	9.320	12.155	6.718	23.659	12.143	14.063	1.338	2602.000	-4775.780	-36833.800	-0.346	-8.722
4	22.217	17.071	14.974	9.409	13.054	6.656	25.620	13.032	14.974	1.342	3172.000	-5450.770	-41019.800	-1.099	-8.997
5	22.977	22.418	15.354	21.079	14.080	22.782	26.602	13.185	15.354	1.427	3257.000	-5403.110	-44837.300	-1.198	-8.664
6	24.391	23.832	16.475	20.507	14.037	22.697	28.569	14.667	16.475	1.463	3803.000	-5714.770	-50240.500	-1.151	-8.682
7	27.219	26.661	18.475	22.507	15.537	22.999	32.514	17.734	18.475	1.511	5137.000	-6338.010	-60132.100	-1.289	-8.724
8	29.202	27.192	20.564	21.510	17.695	20.872	33.366	17.066	20.564	1.154	6399.000	-6736.740	-64539.200	-1.613	-8.737
9	24.554	22.682	16.264	21.168	14.979	22.720	28.569	14.074	16.264	1.425	3917.000	-6078.150	-48713.100	-1.314	-8.980
10	25.968	24.096	17.386	20.596	14.936	22.635	30.540	15.556	17.386	1.459	4531.000	-6389.760	-54736.100	-1.473	-8.856
11	28.797	26.925	19.386	22.596	16.436	22.937	34.490	18.617	19.386	1.506	6013.000	-7013.010	-65764.100	-1.437	-8.846
12	30.780	27.455	21.475	21.598	18.594	20.810	35.311	17.953	21.475	1.143	7415.000	-7411.790	-70322.400	-1.713	-8.888
13	23.847	23.341	15.747	21.490	14.702	23.282	27.585	13.347	15.747	1.436	3550.000	-5558.990	-46990.900	-1.177	-8.607
14	25.261	24.755	16.869	20.918	14.659	23.197	29.554	14.810	16.869	1.476	4114.000	-5870.110	-52360.700	-1.653	-8.711
15	28.089	27.584	18.869	22.918	16.159	23.499	33.502	17.840	18.869	1.529	5490.000	-6493.950	-63949.400	-1.140	-8.621
16	30.073	28.114	20.958	21.920	18.317	21.372	34.338	17.237	20.958	1.166	6790.000	-6892.650	-68649.100	-1.670	-8.747
17	25.424	23.605	16.658	21.579	15.601	23.220	29.554	14.235	16.658	1.433	4246.000	-6233.990	-51156.700	-1.388	-8.853
18	26.838	25.019	17.779	21.007	15.558	23.135	31.527	15.700	17.779	1.471	4878.000	-6545.590	-56548.600	-1.531	-8.844
19	29.667	27.847	19.779	23.007	17.058	23.437	35.479	18.726	19.779	1.523	6402.000	-7168.880	-68278.600	-1.420	-8.779
20	31.650	28.378	21.868	22.009	19.216	21.310	36.285	18.123	21.868	1.155	7842.000	-7567.630	-71255.100	-1.810	-8.914

Table 3: Value of selected descriptors used in the regression analysis.

Mol. Descriptor	pMICsa	pMICkp	pMICec	pMICea	pMICca	pMICan
$^{0}\chi$	0.934	0.903	0.896	0.889	0.911	0.943
$^{0}\chi^{v}$	0.870	0.811	0.829	0.876	0.852	0.906
$^{1}\chi$	0.933	0.924	0.887	0.872	0.936	0.933
$^{1}\chi^{v}$	0.712	0.638	0.696	0.790	0.677	0.750
$^{2}\chi$	0.900	0.880	0.848	0.859	0.910	0.889
$^{2}\chi^{v}$	0.605	0.532	0.599	0.705	0.557	0.651
$^{3}\chi$	0.363	0.274	0.354	0.469	0.321	0.367
$^{3}\chi^{v}$	0.253	0.167	0.262	0.407	0.228	0.266
κ_1	0.935	0.887	0.908	0.900	0.890	0.955
κ_2	0.929	0.870	0.915	0.887	0.872	0.958
κ_3	0.772	0.635	0.786	0.809	0.669	0.820
R	0.933	0.924	0.887	0.872	0.936	0.933
B	-0.235	-0.372	-0.157	-0.113	-0.396	-0.142
W	0.923	0.911	0.883	0.856	0.916	0.917
Te	-0.923	-0.895	-0.912	-0.887	-0.859	-0.922
Ele.E	-0.941	-0.901	-0.896	-0.897	-0.917	-0.954
Nu.E	0.940	0.899	0.893	0.896	0.919	0.954
LUMO	-0.784	-0.739	-0.706	-0.758	-0.730	-0.754
HOMO	-0.023	-0.094	-0.096	-0.012	0.099	0.039
M	0.226	0.204	0.319	0.304	0.004	0.272

Table 5 : Correlation of molecular descriptors with antimicrobial activity of synthesized derivatives.

High collinearity (r > 0.8) was observed between different parameters i.e. molecular descriptors. The high interrelationship was observed between κ_1 and Ele.E (r = 0.996), W and $^{1}\chi$ (r = 0.995), $^{0}\chi$ and Ele.E (r = 0.995) and low interrelationship was observed between HOMO and W (r = 0.022) and HOMO and $^{1}\chi$ (r = 0.028). The correlation matrix indicated that the antimicrobial activity of synthesized ligands and their organotin (IV) complexes are governed by topological parameters like molecular connectivity, shape indices and electronic energy.

The antifungal activity of synthesized derivatives against *A. niger* is governed by the second order shape attribute (Kappa shape indices), κ_2 (Eq. 1).

QSAR model for antifungal activity against A. niger

$$pMICan = 0.134\ \kappa_2 - 0.358 \qquad \text{Eq. 1}$$

n = 20 r = 0.958 r^2 = 0.918 q^2 = 0.898 s = 0.095 F = 201.482

Here and thereafter, n - number of data points, r - correlation coefficient, r^2 -squared correlation coefficient, q^2 - cross validated r^2 obtained by leave one out method, s - standard error of the estimate and F - Fischer statistics.

The QSAR model represented by Eq. 1 for antifungal activity against *A. niger* demonstrated the importance of second order Kappa shape indices (κ^2). According to Kier, the shape of a molecule may be partitioned into attributes, each describable by the count of bonds of various path lengths [27]. The basis for devising a relative index of shape is given by the relationship of the number of path of length l in the molecule i, lPi, to some reference values based on molecules with a given number of atoms, n, in which the values of lP are maximum and minimum, lPmax and lPmin [28]. The second order shape attribute, κ_2, is given by the following expression:

$$\kappa_2 = (n\text{-}1)(n\text{-}2)^2/(^2Pi)^2$$

The equation 1 highlighted the positive correlation between second order Kappa shape indices (κ_2) for the synthesized compounds and antifungal activity against *A. niger* which depicts that compounds having high κ_2 values (Table 3) will have high antifungal potential and the results presented in the Table 6 are in concordance with the model expressed by Eq. 1.

The linear regression model expressed by Eq. 1 was cross validated by its high q^2 values (q^2 = 0.898) obtained with Leave One Out (LOO) method. The basic requirement for becoming a QSAR model to be valid one is that it must possess q^2 value higher than 0.5 thus supporting the fact that model expressed by Eq. 1 is valid one [29]. The comparison of observed and predicted antifungal activities is presented in (Table 6).

Comp.	pMICan			pMICsa			pMICca			pMICkp			pMICec			pMICea		
	Obs	Pre	Res	Obs	Pre	Res	Obs	Pre	Res	Obs	Pre	Res	Obs	Pre	Res	Obs	Pre	Res
1	1.175	1.250	-0.075	0.874	0.952	-0.078	1.175	1.055	0.120	1.175	1.201	-0.026	1.175	1.241	-0.066	1.175	1.083	0.092
2	1.511	1.369	0.142	1.210	1.059	0.151	1.210	1.163	0.047	1.511	1.303	0.208	1.511	1.351	0.160	1.210	1.191	0.019
3	1.191	1.269	-0.078	0.890	1.011	-0.121	0.890	1.101	-0.211	1.191	1.245	-0.054	1.191	1.259	-0.068	0.890	1.137	-0.247
4	1.224	1.388	-0.164	1.224	1.117	0.107	1.224	1.209	0.015	1.224	1.347	-0.123	1.224	1.369	-0.144	1.224	1.246	-0.022
5	1.349	1.408	-0.059	1.349	1.213	0.136	1.349	1.254	0.095	1.349	1.389	-0.040	1.349	1.387	-0.038	1.349	1.300	0.049
6	1.671	1.607	0.064	1.370	1.349	0.021	1.370	1.387	-0.017	1.671	1.515	0.156	1.671	1.570	0.101	1.370	1.409	-0.039
7	2.012	2.018	-0.006	1.711	1.598	0.113	1.711	1.624	0.087	1.711	1.739	-0.028	2.012	1.948	0.064	1.711	1.628	0.083
8	2.038	1.928	0.110	1.737	1.709	0.028	2.038	1.872	0.166	2.038	1.972	0.066	2.038	1.866	0.172	1.737	1.675	0.062

9	1.673	1.528	0.145	1.372	1.310	0.062	1.372	1.362	0.010	1.673	1.491	0.182	1.673	1.497	0.176	1.673	1.409	0.264
10	1.693	1.726	-0.033	1.392	1.462	-0.070	1.392	1.495	-0.103	1.693	1.617	0.076	1.693	1.680	0.013	1.693	1.519	0.174
11	2.032	2.136	-0.104	1.731	1.740	-0.009	1.731	1.732	-0.001	2.032	1.840	0.192	2.032	2.057	-0.025	1.731	1.738	-0.007
12	2.057	2.047	0.010	2.057	1.855	0.202	2.057	1.980	0.077	2.057	2.074	-0.017	2.057	1.975	0.082	1.756	1.783	-0.027
13	1.360	1.430	-0.070	1.058	1.267	-0.209	1.360	1.301	0.059	1.360	1.434	-0.074	1.360	1.407	-0.047	1.360	1.355	0.005
14	1.681	1.626	0.055	1.380	1.402	-0.022	1.380	1.434	-0.054	1.380	1.559	-0.179	1.380	1.588	-0.208	1.380	1.464	-0.084
15	2.021	2.032	-0.011	1.720	1.694	0.026	1.720	1.671	0.049	1.720	1.783	-0.063	1.720	1.961	-0.241	1.720	1.683	0.037
16	2.047	1.951	0.096	1.746	1.813	-0.066	2.047	1.918	0.129	2.047	2.016	0.031	1.746	1.887	-0.141	1.746	1.729	0.017
17	1.683	1.549	0.134	1.382	1.372	0.010	1.382	1.409	-0.027	1.382	1.535	-0.153	1.683	1.517	0.166	1.382	1.464	-0.082
18	1.703	1.745	-0.042	1.402	1.508	-0.106	1.402	1.542	-0.140	1.703	1.661	0.042	1.703	1.697	0.006	1.402	1.573	-0.171
19	2.041	2.151	-0.110	1.740	1.803	-0.063	1.740	1.779	-0.039	1.740	1.884	-0.144	2.041	2.071	-0.030	1.740	1.792	-0.052
20	2.066	2.070	-0.004	1.765	1.878	-0.113	1.765	2.026	-0.261	2.066	2.118	-0.052	2.066	1.996	0.070	1.765	1.837	-0.072

Table 6: Comparison of observed and predicted antibacterial and antifungal activity obtained by QSAR model.

The results of observed and predicted antifungal activities lie close to each other as evidenced by their low residual values (Table 6) which again supported the validity of model expressed by Eq. 1. The statistical validity of QSAR model was also cross checked by plotting the graphs of observed, predicted and residual pMIC activity values. The plot of predicted pMICan against observed pMICan (Figure 1).

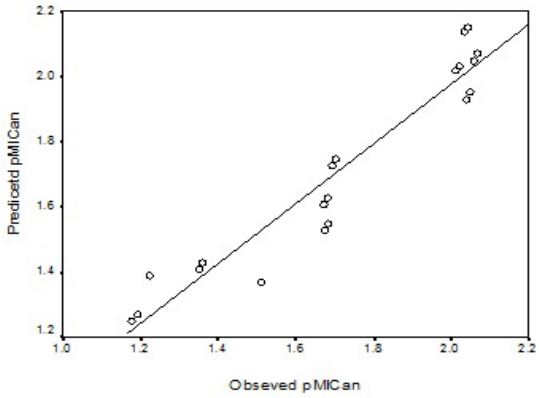


Figure 1: Plot of observed pMICan against the predicted pMICan for the linear regression model developed by Eq. 1 also supported the validity of model expressed by Eq. 1.

The propagation of error was observed on both sides of zero while plotting the observed pMICan Vs residual pMICan (Figure 2)

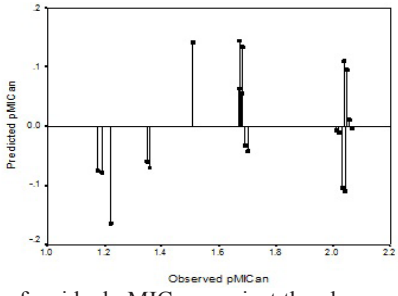


Figure 2: Plot of residual pMIC an against the observed pMICan for the linear regression model developed by Eq. which depicted that there was no systemic error in model development [30].

QSAR models 2 – 8 were obtained by linear regression of the antibacterial and antifungal activity of synthesized derivatives against *S. aureus, C. albicans, K. pneumoniae, E. coli, and E. aerogenes* with molecular descriptors.

QSAR model for antibacterial activity against S. aureus

$pMIC_{sa}$ = - 0.000025 Ele.E + 0.083 Eq. 2

n = 20 r = 0.941 r^2 = 0.886 q^2 = 0.855 s = 0.109 F = 140.08

QSAR model for antifungal activity against C. albicans

$pMIC_{ca}$ = 0.119 $^1\chi$ - 0.565 Eq. 3

n = 20 r = 0.936 r^2 = 0.877 q^2 = 0.830 s=0.115 F=127.974

QSAR model for antifungal activity against C. albicans

$pMIC_{ca}$ = 0.119 R - 0.565 Eq. 4

n = 20 r = 0.936 r^2 = 0.877 q^2 = 0.830 s=0.115 F=127.974

QSAR model for antibacterial activity against K. pneumoniae

$pMIC_{kp}$ = 0.112 $^1\chi$ – 0.327 Eq. 5

n = 20 r = 0.924 r2 = 0.853 q2 = 0.825 s = 0.120 F = 104.331

QSAR model for antibacterial activity against K. pneumoniae

$pMIC_{kp}$ = 0.112 R – 0.327 Eq. 6

n = 20 r = 0.924 r^2 = 0.853 q^2 = 0.825 s=0.120 F=104.331

QSAR model for antibacterial activity against E. coli

pMICec = 0.123 κ_2 – 0.239 Eq. 7

n = 20 r = 0.915 r^2 = 0.837 q^2 = 0.804 s = 0.128 F = 92.54

QSAR model for antibacterial activity against E. aerogenes

pMICea = 0.056 κ1 – 0.175 Eq. 8

n = 20 r = 0.900 r^2 = 0.811 q^2 = 0.764 s = 0.115 F = 77.022

The linear regression model represented by Eq. 2 revealed that the antibacterial activity against *S. aureus* is governed by the Electronic Energy of the molecule (Ele.E). As the coefficient of electronic energy is negative, therefore the antibacterial activity against *S. aureus* will increase with decrease in Ele.E values, that can be checked from the results presented in Table 3 and 6.

Eq. 3 and 4 were obtained for the regression model describing the antifungal activity of the synthesized derivatives against *C. albicans* both of which indicated that first order molecular connectivity index ($^1\chi$) and Randic (R) topological parameter were equally affecting the antifungal activity against *C. albicans* as all the statistical parameters for both these equations were same. The positive coefficient of first order molecular connectivity index ($^1\chi$) and Randic (R) parameter in Eq. 3 and 4 demonstrated that the antifungal of the synthesized derivatives will increase with increase in value of first order molecular connectivity index ($^1\chi$) and Randic (R) parameter.

Similarly the regression analysis for antibacterial activity of synthesized derivatives against *K. pneumoniae* came out with two models represented by Eq. 5 and 6 thus indicating the fact that antibacterial activity against *K. pneumoniae* is governed by two parameters viz. first order molecular connectivity index ($^1\chi$) and Randic (R) parameter to an equal extent. Both of these models have same statistical parameters and thus indicated that the predicted antibacterial activity against *K. pneumoniae* will be same whatever the parameter we use for prediction of activity out of these two molecular descriptors. The outcome of QSAR models represented by Eq. 3 to 6 revealed the fact that K. pneumoniae and *C. albicans* may have similar type of binding site in their target receptor to which these molecules are binding.

QSAR model represented by Eq. 7 indicated the importance of second order Kappa shape indices (κ_2) in describing the antibacterial activity against *E. coli*. The positive correlation of the molecular descriptor second order Kappa shape indices (κ_2) with antibacterial activity revealed that increase in the value of κ_2 will lead to an increase in antibacterial activity against *E. coli*.

The antibacterial activity of synthesized derivatives against *E. aerogenes* was governed by first order Kappa shape indices (κ_1) as demonstrated by Eq. 8. The QSAR models represented by Eq. 2-8 have got high r, r^2, q^2 and F values and low s values which indicated that that the models are valid one. The low residual values obtained after prediction of activity using these models (Table 6) confirmed the fact that models expressed by Eq. 2 – Eq. 8 were also valid ones.

	$^0\chi$	$^0\chi^v$	$^1\chi$	$^1\chi^v$	$^2\chi$	$^2\chi^v$	κ_1	κ_2	R	B	W	Te	Ele.E	HOMO	pMICan
$^0\chi$	1.000														
$^0\chi^v$	0.939	1.000													
$^1\chi$	0.990	0.905	1.000												
$^1\chi^v$	0.774	0.929	0.707	1.000											
$^2\chi$	0.979	0.913	0.976	0.766	1.000										
$^2\chi^v$	0.671	0.864	0.592	0.985	0.662	1.000									
κ_1	0.992	0.951	0.971	0.799	0.951	0.703	1.000								
κ_2	0.947	0.903	0.932	0.725	0.871	0.620	0.972	1.000							
R	0.990	0.905	1.000	0.707	0.976	0.592	0.971	0.932	1.000						
J	-0.270	-0.043	-0.381	0.172	-0.389	0.276	-0.155	-0.071	-0.381	1.000					
W	0.986	0.881	0.995	0.676	0.975	0.556	0.966	0.926	0.995	-0.395	1.000				
Te	-0.980	-0.894	-0.959	-0.746	-0.956	-0.651	-0.978	-0.928	-0.959	0.230	-0.966	1.000			
Ele.E	-0.995	-0.948	-0.984	-0.781	-0.960	-0.679	-0.996	-0.969	-0.984	0.215	-0.977	0.969	1.000		
HOMO	0.043	0.302	0.028	0.374	0.031	0.399	0.067	0.083	0.028	0.279	-0.022	0.115	-0.094	1.000	
pMICan	0.943	0.906	0.933	0.750	0.889	0.651	0.955	0.958	0.933	-0.142	0.917	-0.922	-0.954	0.039	1.000

Table 4: Correlation matrix for antibacterial activity of synthesized derivatives against K. *pneumoniae*

Experimental

Materials and methods

The chemicals used were of analytical grade (Aldrich) and solvents were purified according to standard procedures. The complexes were synthesized under anhydrous condition in inert atmosphere. The molar conductance was measured in dry DMSO using Systronics conductivity bridge model-306. The IR spectra were recorded using a Spectrum BX Series FT-IR spectrophotometer in the range 400-4000 cm^{-1}, using KBr pellets. Multinuclear magnetic resonance spectra (^1H, ^{13}C, ^{119}Sn) were recorded on a Bruker Avance II 400 MHz NMR Spectrometer and all chemical shifts

δ were reported in ppm relative to Tetra Methyl Silane (TMS) as an internal standard in $CDCl_3$ and DMSO- d_6. Elemental analyses were carried out on a Perkin Elmer 2400 analyzer. Tin/chlorine was estimated gravimetrically. Bacterial and fungal strain was procured from Microbial Type Culture Collection (MTCC), IMTECH, Chandigarh.

Synthesis of Schiff base Ligands

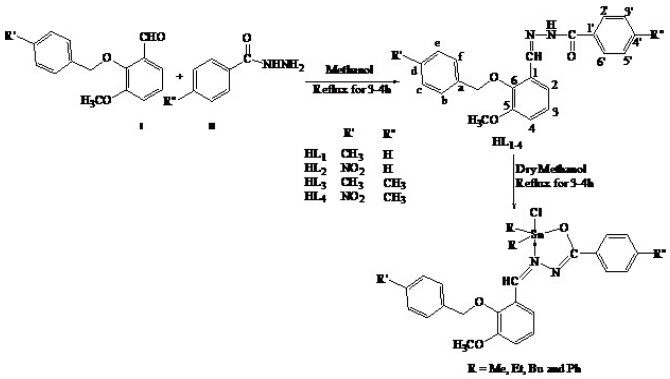
Synthesis of ligands (HL_1-HL_4) were carried out in the following two steps:-

Synthesis of 2-(4-methyl/nitro-benzyloxy)-3-methoxy-benzaldehyde (I).

The solution of o-vanillin (10 mmol) and K_2CO_3 (20 mmol) in 26 ml of DMF was stirred and p-methyl benzyl bromide (10 mmol) was added slowly. The mixture was allowed to stir overnight. Benzylation of o-vanillin with p-methyl benzyl bromide took place through Williamson ether formation resulted in the formation of 2-(4-methyl-benzyloxy)-3-methoxy-benzaldehyde. The reaction mixture was then quenched with ice followed by the addition of 50 ml of water. The solid product obtained was filtered over the vaccum pump and dried. The same procedure was adopted for the synthesis of 2-(4-nitro-benzyloxy)-3-methoxy-benzaldehyde.

Synthesis of Schiff base ligands (HL_1–HL_4)

Ligands HL_{1-4} were synthesized by reacting substituted o-vanillin (I) with p-toluic Hydrazide or benzhydrazide (II) in equimolar ratio in dry methanol. The solid product obtained after refluxing the reaction mixture for about 3-4 hrs was filtered and recrystallized in methanol. The same procedure was adopted for the synthesis of other Schiff base ligands.



Scheme 1. Synthetic route for HL1-4 and their tin complexes

Benzoic acid [3-methoxy-2-(4-methyl-benzyloxy)-benzyledene]-hydrazide [(HL_1, $C_{23}H_{22}N_2O_3$), (1)]

Yield: 82 %; m.p.: 170-171 ^{0}C; IR (KBr): ν = 3385 (NH), ν = 1689 (C=O), ν = 1550 (C=N) cm^{-1}; ^{1}H NMR (DMSO-d_6 and $CDCl_3$): δ = 11.87 (s, 1H, -CH=N), 8.71 (s, 1H, -NH), 7.90-7.92 (d, 2H, C_2'-H & , C_6'-H), 7.49-7.58 (m, 4H, C_3'-H, C_4'-H , C_5'-H & C_2-H), 7.35-7.37 (d, 2H, C_b-H & C_f-H), 7.16-7.18 (d, 2H, C_c-H & C_e-H), 7.10-7.12 (m, 2H, C_3-H & C_4-H), 4.97 (s, 2H, -OCH_2), 3.88 (s, 3H, -OCH_3), 2.30 (s, 3H, -CH_3) ppm; ^{13}C NMR: δ = 163.3 (C=O), 152.6 (C=N), 146.4 (C-6), 143.5 (C-5), 137.2 (C-a), 133.8 (C-d), 133.4 (C-1'), 131.4 (C-4'), 128.6 (C-c & C-e), 128.4 (C-3' & C-5'), 128.2 (C-2 '& C-6'), 128.1 (C-b & C-f), 127.6 (C-2), 124 (C-3), 117.2 (C-1), 113.7 (C-4), 74.7 (OCH_2), 55.3 (OCH_3), 20.8 (CH_3 at Ph ring) ppm.

4-Nitro-Benzoic acid [3-methoxy-2-(4-methyl-benzyloxy)-benzyledene]-hydrazide [(HL_2, $C_{22}H_{19}N_3O_5$), (2)]

Yield: 86 %; m.p.: 174-175 °C; IR (KBr): ν = 3412 (NH), ν = 1695 (C=O), ν = 1557 (C=N) cm^{-1}; ^{1}H NMR (DMSO-d_6 and $CDCl_3$): δ = 11.86 (s, 1H, -CH=N), 8.73 (s, 1H, -NH), 8.25-8.27 (d, 2H, C_c-H & C_e-H), 7.89-7.91 (d, 2H, C_2'-H & , C_6'-H), 7.77-7.79 (d, 2H, C_b-H & C_f-H), 7.49-7.58 (m, 4H, C_2-H, C_3'-H, C_4'-H & C_5'-H), 7.14-7.17 (m, 2H, C_3-H & C_4-H), 5.16 (s, 2H, -CH_2), 3.87 (s, 3H, -OCH_3) ppm; ^{13}C NMR: δ = 163.3 (C=O), 152.4 (C=N), 147 (C-6), 146.1 (C-5), 144.7 (C-d), 143.2 (C-a), 133.4 (C-1'), 131.5 (C-4'), 128.6 (C-3' & C-5'), 128.2 (C-b & C-f), 128.1 (C-2 '& C-6'), 127.6 (C-c & C-e), 124.5 (C-2), 123.2 (C-3), 117.3 (C-1), 113.8 (C-4), 73.5 (OCH_2), 55.7 (OCH_3) ppm.

4-Methyl-Benzoic acid [3-methoxy-2-(4-methyl-benzyloxy)-benzyledene]-hydrazide [(HL_3, $C_{24}H_{24}N_2O_3$), (3)]

Yield: 83 %; m.p.: 164-165 °C; IR (KBr): ν = 3373 (NH), ν = 1687 (C=O), ν = 1546 (C=N) cm^{-1}; ^{1}H NMR (DMSO-d_6 and $CDCl_3$): δ = 11.79 (s, 1H, -CH=N), 8.70 (s, 1H, -NH), 7.82-7.84 (d, 2H, C_2'-H & C_6'-H), 7.48-7.50 (d, 1H, C_2-H), 7.35-7.37 (d, 2H, C_3'-H & C_5'-H), 7.30-7.32 (d, 2H, C_b-H & C_f-H), 7.16-7.18 (d, 2H, C_c-H & C_e-H), 7.10-7.11 (m, 2H, C_3-H & C_4-H), 4.97 (s, 2H, -OCH_2), 3.88 (s, 3H, -OCH_3), 2.39 (s, 3H, -CH_3 at Hydrazide ring), 2.30 (s, 3H, -CH_3 at Ph ring) ppm; ^{13}C NMR: δ = 163.2 (C=O), 152.5 (C=N), 146.4 (C-6), 143.3 (C-5), 141.5 (C-4'), 137.2 (C-a), 133.8 (C-d), 130.5 (C-1'), 128.7 (C-c & C-e), 128.6 (C-3' & C-5'), 128.4 (C-2 '& C-6'), 128.3 (C-b & C-f), 127.6 (C-2), 124 (C-3), 117.3 (C-1), 113.5 (C-4), 74.7 (OCH_2), 55.5 (OCH_3), 21.1 (CH_3 at Hydrazide ring), 20.8 (CH_3 at Ph ring) ppm.

4-Methyl-Benzoic acid [3-methoxy-2-(4-nitro-benzyloxy)-benzyledene]-hydrazide [(HL_4, $C_{23}H_{21}N_3O_5$), (4)]

Yield: 79 %; m.p.: 169-170 °C; IR (KBr): ν = 3394 (NH), ν = 1692 (C=O), ν = 1553 (C=N) cm^{-1}; ^{1}H NMR (DMSO-d_6 and $CDCl_3$): δ = 11.78 (s, 1H, -CH=N), 8.74 (s, 1H, -NH), 8.24-8.27 (d, 2H, C_c-H & C_e-H), 7.77-7.80 (d, 4H, C_2'-H, C_6'-H, C_b-H & C_f-H), 7.54-7.55 (d, 1H, C_2-H), 7.28-7.30 (d, 2H, C_3'-H & C_5'-H), 7.10-7.17 (m, 2H, C_3-H & C_4-H), 5.16 (s, 2H, -OCH_2), 3.87 (s, 3H, -OCH_3), 2.39 (s, 3H, -CH_3 at Hydrazide ring) ppm; ^{13}C NMR: δ = 163.3 (C=O), 152.4 (C=N), 146.8 (C-6), 145.2 (C-5), 144.6 (C-d), 142 (C-a),

140.3 (C-4'), 135.2 (C-1'), 129.4 (C-3' & C-5'), 128.4 (C-b & C-f), 128.1 (C-2 '& C-6'), 127.6 (C-c & C-e), 122.4 (C-2), 123.2 (C-3), 117.4 (C-1), 113.6 (C-4), 73.5 (OCH2), 55.6 (OCH_3), 21 (CH_3 at Hydrazide ring) ppm.

General procedure for the synthesis of organotin complexes (5-20)

The sodium salt of Schiff base ligand was prepared by reacting ligand HL^1 (4.56 g, 10 mmol) and sodium metal (0.225 g, 10 mmol) in 30 mL dry methanol followed by the slow addition of Me_2SnCl_2 (2.19 g, 10 mmol) and then the reaction mixture was refluxed for 4h. The precipitated NaCl was filtered and solvent was evaporated on rotary evaporator under reduced pressure. The final product obtained was recrystallized from dry methanol and hexane and finally dried under reduced pressure. The other tin complexes were synthesized by reacting the ligands, $HL_2/HL_3/HL_4$ with R_2SnCl_2 in 1:1 molar ratio by the same procedure.

[($Me_2Sn(L_1)Cl$, $C_{25}H_{27}ClN_2O_3Sn$), (5)]

Yield: 74 %; m.p.: 126-127 ^{0}C; IR (KBr): ν = 1548 (C=N) cm^{-1}; ^{1}H NMR (DMSO-d_6 and $CDCl_3$): δ = 11.98 (s, 1H, -CH=N), 7.94-7.96 (d, 2H, C_2'-H & , C_6'-H), 7.48-7.56 (m, 4H, C_3'-H, C_4'-H , C_5'-H & C_2-H), 7.36-7.38 (d, 2H, C_b-H & C_f-H), 7.14-7.16 (d, 2H, C_c-H & C_e-H), 7.07-7.10 (m, 2H, C_3-H & C4-H), 4.96 (s, 2H, $-OCH_2$), 3.86 (s, 3H, $-OCH_3$), 2.28 (s, 3H, $-CH_3$), 1.19(s, 6H, $-CH_3$) ppm; ^{13}C NMR: δ = 155.6 (C=O), 151.4 (C=N), 146.4 (C-6), 143.6 (C-5), 137.2 (C-a), 133.9 (C-d), 133.4 (C-1'), 131.6 (C-4'), 128.7 (C-c & C-e), 128.5 (C-3' & C-5'), 128.3 (C-2 '& C-6'), 128.4 (C-b & C-f), 127.6 (C-2), 124.2 (C-3), 117.2 (C-1), 113.9 (C-4), 74.7 (OCH_2), 55.7 (OCH_3), 20.8 (CH_3 at Ph ring), 8.5 (Me) ppm.

[($Et_2Sn(L_1)Cl$, $C_{27}H_{31}ClN_2O_3Sn$), (6)]

Yield: 72 %; m.p.: 124-125 °C; IR (KBr): ν = 1545 (C=N) cm^{-1}; ^{1}H NMR (DMSO-d_6 and $CDCl_3$): δ = 11.84 (s, 1H, -CH=N), 7.89-7.91 (d, 2H, C_2'-H & , C_6'-H), 7.50-7.56 (m, 4H, C_3'-H, C_4'-H, C_5'-H & C_2-H), 7.33-7.35 (d, 2H, C_b-H & C_f-H), 7.15-7.17 (d, 2H, Cc-H & C_e-H), 7.08-7.11 (m, 2H, C3-H & C4-H), 5.01 (s, 2H, $-OCH_2$), 3.87 (s, 3H, $-OCH_3$), 2.28 (s, 3H, $-CH_3$), 3.06-3.11 (m, 4H,$-CH_2$), 1.23-1.26 (t, 6H,$-CH_3$) ppm; ^{13}C NMR: δ = 155.6 (C=O), 151.6 (C=N), 147.3 (C-6), 144.3 (C-5), 141.7 (C-a), 138.2 (C-d), 134.9 (C-1'), 130.6 (C-4'), 129.9 (C-c & C-e), 129.1 (C-3' & C-5'), 128.6 (C-2 '& C-6'), 128.1 (C-b & C-f), 127.6 (C-2), 123 (C-3), 117.3 (C-1), 113.3 (C-4), 74.9 (OCH_2), 55.4 (OCH_3), 21 (CH_3 at Ph ring), 12.6 (Et), 8.6 (Et) ppm.

[($Bu_2Sn(L_1)Cl$, $C_{31}H_{39}ClN_2O_3Sn$), (7)]

Yield: 66 %; m.p.: 121-122 ^{0}C; IR (KBr): ν = 1549 (C=N) cm-1; ^{1}H NMR (DMSO-d_6 and $CDCl_3$): δ = 11.99 (s, 1H, -CH=N), 7.94-7.96 (d, 2H, C_2'-H & , C_6'-H), 7.49-7.58 (m, 4H, C_3'-H, C_4'-H, C_5'-H & C_2-H), 7.37-7.39 (d, 2H, C_b-H & C_f-H), 7.16-7.18 (d, 2H, C_c-H & C_e-H), 7.09-7.12 (m, 2H, C_3-H & C_4-H), 4.97 (s, 2H, $-OCH_2$), 3.88 (s, 3H, $-OCH_3$), 2.29 (s, 3H, -CH3), 3.07-3.11 (m, 4H,-CH2), 1.20-1.24 (m, 8H,$-CH_2$), 1.00-1.10 (t, 6H,$-CH_3$) ppm; ^{13}C NMR: δ = 155.6 (C=O), 151.6 (C=N), 146.4 (C-6), 143.3 (C-5), 141.6 (C-a), 137.2 (C-d), 133.9 (C-1'), 130.5 (C-4'), 128.8 (C-c & C-e), 128.7 (C-3' & C-5'), 128.5 (C-2 '& C-6'), 128.4 (C-b & C-f), 127.7 (C-2), 124.1 (C-3), 117.2 (C-1), 113.7 (C-4), 74.7 (OCH_2), 55.7 (OCH_3), 26.4 (Bu), 24.5 (Bu), 20.8 (CH_3 at Ph ring), 12 (Bu), 8.6 (Bu) ppm.

[($Ph_2Sn(L_1)Cl$, $C_{35}H_{31}ClN_2O_3Sn$), (8)]

Yield: 73 %; m.p.: 139-140 ^{0}C; IR (KBr): ν = 1548 (C=N) cm^{-1}; ^{1}H NMR (DMSO-d_6 and $CDCl_3$): δ = 11.87(s, 1H, -CH=N), 8.76-8.90 (d, 2H, C_2'-H & , C_6'-H), 8.11-8.51 (m, 4H, C_3'-H, C_4'-H, C_5'-H & C_2-H), 7.85-7.95 (d, 4H, C_b-H, C_f-H, C_c-H & C_e-H), 6.66-7.50 (m, 10H Ph and 2H, C_3-H & C_4-H), 4.97 (s, 2H, $-OCH_2$), 3.87 (s, 3H, $-OCH_3$), 2.38 (s, 3H, $-CH_3$) ppm; ^{13}C NMR: δ = 155.7 (C=O), 151.5 (C=N), 146.4 (C-6), 143.3 (C-5), 140.4 (C-a), 134.7 (C-d), 133.9 (C-1'), 131.1 (C-4'), 128.8 (Ph), 128.7 (Ph), 128.6 (Ph), 128.5 (Ph), 128.4 (C-c & C-e), 128.2 (C-3' & C-5'), 127.7 (C-2 '& C-6'), 127.6 (C-b & C-f), 127.2 (C-2), 124.1 (C-3), 117.1 (C-1), 113.8 (C-4), 74.7 (OCH_2), 55.7 (OCH_3), 21.1 (CH_3 at Ph ring) ppm.

[($Me_2Sn(L_2)Cl$, $C_{24}H_{24}ClN_3O_5Sn$), (9)]

Yield: 77 %; m.p.: 128-129 ^{0}C; IR (KBr): ν = 1553 (C=N) cm^{-1}; ^{1}H NMR (DMSO-d_6 and $CDCl_3$): δ = 11.85 (s, 1H, -CH=N), 8.24-8.27 (d, 2H, C_c-H & C_e-H), 7.86-7.88 (d, 2H, C_2'-H & , C_6'-H), 7.72-7.74 (d, 2H, C_b-H & C_f-H), 7.52-7.57 (m, 4H,C_2-H, C_3'-H, C_4'-H & C_5'-H), 7.13-7.17 (m, 2H, C_3-H & C_4-H), 5.01 (s, 2H, $-OCH_2$), 3.87 (s, 3H, $-OCH_3$), 1.23 (s, 6H, $-CH_3$) ppm; ^{13}C NMR: δ = 155.4 (C=O), 151.4 (C=N), 146.9 (C-6), 145.9 (C-5), 144.9 (C-d), 142.9 (C-a), 133.4 (C-1'), 131.6 (C-4'), 128.8, (C-3' & C-5'), 128.1 (C-b & C-f), 127.9 (C-2 '& C-6'), 127.7 (C-c & C-e), 124.5 (C-2), 123.3 (C-3), 117.5 (C-1), 113.8 (C-4), 73.6 (OCH_2), 55.7 (OCH_3), 8.6 (Me) ppm.

[($Et_2Sn(L_2)Cl$, $C_{26}H_{28}ClN_3O_5Sn$), (10)]

Yield: 81 %; m.p.: 126-127 $_0$C; IR (KBr): ν = 1555 (C=N) cm^{-1}; ^{1}H NMR (DMSO-d_6 and $CDCl_3$): δ = 11.86 (s, 1H, -CH=N), 8.25-8.28 (d, 2H, C_c-H & C_e-H), 7.85-7.87 (d, 2H, C_2'-H & , C_6'-H), 7.73-7.75 (d, 2H, C_b-H & C_f-H), 7.51-7.56 (m, 4H,C_2-H, C_3'-H, C_4'-H & C_5'-H), 7.12-7.15 (m, 2H, C_3-H & C_4-H), 4.98 (s, 2H, $-OCH_2$), 3.85 (s, 3H, $-OCH_3$), 3.08-3.11 (m, 4H,$-CH_2$), 1.22-1.26 (t, 6H,$-CH_3$) ppm; ^{13}C NMR: δ = 155.3 (C=O), 151.5 (C=N), 145.3 (C-6), 142.3 (C-5), 135.9 (C-d), 132.9 (C-a), 132.2 (C-1'), 131.3 (C-4'), 129.7, (C-3' & C-5'), 128.7 (C-b & C-f), 128.2 (C-2 '& C-6'), 128 (C-c & C-e), 127.5 (C-2), 125 (C-3), 117.1 (C-1), 113.5 (C-4), 74.7 (OCH_2), 55.5 (OCH_3), 13.2 (Et), 8.8 (Et) ppm.

[($Bu_2Sn(L_2)Cl$, $C_{30}H_{36}ClN_3O_5Sn$), (11)]

Yield: 75 %; m.p.: 123-124 ^{0}C; IR (KBr): ν = 1554 (C=N) cm^{-1}; ^{1}H NMR (DMSO-d_6 and $CDCl_3$): δ = 11.84 (s, 1H, -CH=N), 8.23-8.26 (d, 2H, C_c-H & C_e-H), 7.84-7.86 (d, 2H, C_2'-H & , C_6'-H), 7.72-7.74 (d, 2H, C_b-H & C_f-H), 7.54-7.57 (m, 4H,C_2-H, C_3'-H, C_4'-H & C_5'-H), 7.11-7.16 (m, 2H, C_3-H & C_4-H), 4.99 (s, 2H, -OCH_2), 3.88 (s, 3H, -OCH_3), 3.08-3.11 (t, 4H,-CH_2), 1.62-1.66 (m, 8H,-CH_2), 1.21-1.24 (t, 6H, -CH_3) ppm; ^{13}C NMR: δ = 155.4 (C=O), 151.5 (C=N), 146.8 (C-6), 145.7 (C-5), 144.7 (C-d), 142.8 (C-a), 133.5 (C-1'), 131.5 (C-4'), 128.7, (C-3' & C-5'), 127.9 (C-b & C-f), 127.3 (C-2 '& C-6'), 127.2 (C-c & C-e), 124.5 (C-2), 123.3 (C-3), 117.4 (C-1), 113.6 (C-4), 73.6 (OCH_2), 55.8 (OCH_3), 28.4 (Bu), 26.4 (Bu), 13.2 (Bu), 7.9 (Bu) ppm.

[($Ph_2Sn(L_2)Cl$, $C_{34}H_{28}ClN_3O_5Sn$), (12)]

Yield: 68 %; m.p.: 144-145 ^{0}C; IR (KBr): ν = 1555 (C=N) cm^{-1}; ^{1}H NMR (DMSO-d_6 and $CDCl_3$): δ = 11.86 (s, 1H, -CH=N), 8.26-8.29 (d, 2H, C_c-H & C_e-H), 7.82-7.91 (d, 4H, C_2'-H , C_6'-H, C_b-H & C_f-H), 7.53-7.56 (m, 4H,C_2-H, C_3'-H, C_4'-H & C_5'-H), 7.03-7.21 (m, 10H Ph and 2H, C_3-H & C_4-H), 4.97 (s, 2H, -OCH_2), 3.86 (s, 3H, -OCH_3) ppm; ^{13}C NMR: δ = 155.4 (C=O), 151.5 (C=N), 146.8 (C-6), 145.6 (C-5), 144.8 (C-d), 142.8 (C-a), 133.5 (C-1'), 131.5 (C-4'), 129.2 (Ph), 128.8 (Ph), 128.4 (Ph), 128.1 (Ph), 128.6, (C-3' & C-5'), 128 (C-b & C-f), 127.3 (C-2 '& C-6'), 126.9 (C-c & C-e), 124.5 (C-2), 123.3 (C-3), 117.2 (C-1), 113.8 (C-4), 73.5 (OCH_2), 55.9 (OCH_3) ppm.

[($Me_2Sn(L_3)Cl$, $C_{26}H_{29}ClN_2O_3Sn$), (13)]

Yield: 74 %; m.p.: 127-128 ^{0}C; IR (KBr): ν = 1545 (C=N) cm^{-1}; ^{1}H NMR (DMSO-d_6 and $CDCl_3$): δ = 11.78 (s, 1H, -CH=N), 7.83-7.85 (d, 2H, C_2'-H & , C_6'-H), 7.47-7.49 (d, 1H,C_2-H), 7.34-7.36 (d, 2H, C_3'-H & C_5'-H), 7.28-7.30 (d, 2H, C_b-H & C_f-H), 7.18-7.20 (d, 2H, C_c-H & C_e-H), 7.08-7.11 (m, 2H, C_3-H & C_4-H), 5.01 (s, 2H, -OCH_2), 3.87 (s, 3H, -OCH_3), 2.37 (s, 3H, -CH_3 at Hydrazide ring), 2.30 (s, 3H, -CH_3 at Ph ring), 1.23 (s, 6H, -CH_3) ppm; ^{13}C NMR: δ = 155.4 (C=O), 151.6 (C=N), 146.4 (C-6), 143.3 (C-5), 141.5 (C-4'), 137.3 (C-a), 133.8 (C-d), 129.9 (C-1'), 128.5 (C-c & C-e), 128.4 (C-3' & C-5'), 128.2 (C-2 '& C-6'), 128.2 (C-b & C-f), 127.6 (C-2), 123.9 (C-3), 117.3 (C-1), 113.4 (C-4), 73.6 (OCH_2), 55.4 (OCH_3), 21.2 (CH_3 at Hydrazide ring), 20.8 (CH_3 at Ph ring), 8.6 (Me) ppm.

[($Et_2Sn(L_3)Cl$, $C_{28}H_{33}ClN_2O_3Sn$), (14)]

Yield: 69 %; m.p.: 124-125 ^{0}C; IR (KBr): ν = 1542 (C=N) cm^{-1}; ^{1}H NMR (DMSO-d_6 and $CDCl_3$): δ = 11.91 (s, 1H, -CH=N), 7.86-7.88 (d, 2H, C_2'-H & , C_6'-H), 7.51-7.53 (d, 1H,C_2-H), 7.37-7.38 (d, 2H, C_3'-H & C_5'-H), 7.28-7.30 (d, 2H, C_b-H & C_f-H), 7.15-7.17 (d, 2H, C_c-H & C_e-H), 7.06-7.09 (m, 2H, C_3-H & C_4-H), 4.9 (s, 2H, -OCH_2), 3.87 (s, 3H, -OCH_3), 2.37 (s, 3H, -CH_3 at Hydrazide ring), 2.29 (s, 3H, -CH_3 at Ph ring), 3.01-3.07 (m, 4H,-CH_2), 1.22-1.28 (t, 6H,-CH_3) ppm; ^{13}C NMR: δ = 155.3 (C=O), 151.7 (C=N), 145.4 (C-6), 143.4 (C-5), 141.6 (C-4'), 137.3 (C-a), 133.6 (C-d), 130.1 (C-1'), 128.8 (C-c & C-e), 128.4 (C-3' & C-5'), 128.3 (C-2 '& C-6'), 128.2 (C-b & C-f), 127.8 (C-2), 123.7 (C-3), 117.2 (C-1), 113.4 (C-4), 74.6 (OCH_2), 55.4 (OCH_3), 21.1 (CH_3 at Hydrazide ring), 20.6 (CH_3 at Ph ring), 12.8 (Et), 7.6 (Et) ppm.

[($Bu_2Sn(L_3)Cl$, $C_{32}H_{41}ClN_2O_3Sn$), (15)]

Yield: 73 %; m.p.: 120-121 °C; IR (KBr): ν = 1545 (C=N) cm^{-1}; ^{1}H NMR (DMSO-d_6 and $CDCl_3$): δ = 11.87 (s, 1H, -CH=N), 7.88-7.90 (d, 2H, C_2'-H & , C_6'-H), 7.53-7.55 (d, 1H,C_2-H), 7.35-7.37 (d, 2H, C_3'-H & C_5'-H), 7.25-7.27 (d, 2H, C_b-H & C_f-H), 7.16-7.18 (d, 2H, Cc-H & Ce-H), 7.08-7.11 (m, 2H, C_3-H & C4-H), 5.00 (s, 2H, -OCH_2), 3.88 (s, 3H, -OCH_3), 2.38 (s, 3H, -CH_3 at Hydrazide ring), 2.29 (s, 3H, -CH_3 at Ph ring), 3.01-3.07 (m, 4H,-CH_2), 1.61-1.66 (m, 8H, -CH_2),1.21-1.26 (t, 6H, -CH_3) ppm; ^{13}C NMR: δ = 155.2 (C=O), 151.6 (C=N), 145.4 (C-6), 142.2 (C-5), 135.8 (C-4'), 132.8 (C-a), 132.6 (C-d), 130.9 (C-1'), 129.8 (C-c & C-e), 128.5 (C-3' & C-5'), 128.2 (C-2 '& C-6'), 127.6 (C-b & C-f), 127.3 (C-2), 124.2 (C-3), 117.2 (C-1), 113.3 (C-4), 74.6 (OCH_2), 55.4 (OCH_3), 28.4 (Bu), 24.4 (Bu), 21.1 (CH_3 at Hydrazide ring), 20.3 (CH_3 at Ph ring), 13.1 (Bu), 8.2 (Bu) ppm.

[($Ph_2Sn(L_3)Cl$, $C_{36}H_{33}ClN_2O_3Sn$), (16)]

Yield: 79 %; m.p.: 139-140 ^{0}C; IR (KBr): ν = 1543 (C=N) cm^{-1}; ^{1}H NMR (DMSO-d_6 and $CDCl_3$): δ = 11.78 (s, 1H, -CH=N), 7.86-7.88 (d, 2H, C_2'-H & C_6'-H), 7.50-7.51 (d, 1H, C_2-H), 7.37-7.46 (d, 4H, C_3'-H, C_5'-H, C_b-H & C_f-H), 7.33-7.35 (d, 2H, C_c-H & C_e-H), 7.01-7.23 (m, 10H, Ph & m,2H, C_3-H & C_4-H), 4.97 (s, 2H, -OCH_2), 3.84 (s, 3H, -OCH_3), 2.38 (s, 3H, -CH_3 at Hydrazide ring), 2.30 (s, 3H, -CH_3 at Ph ring) ppm; ^{13}C NMR: δ = 155.3 (C=O), 151.7 (C=N), 145.2 (C-6), 143.5 (C-5), 141.5 (C-4'), 137.3 (C-a), 133.7 (C-d), 129.9 (C-1'), 128.8 (Ph), 128.7 (C-c & C-e), 128.6 (Ph), 128.5 (C-3' & C-5'), 128.4 (Ph), 128.3 (C-2 '& C-6'), 128.2 (C-b & C-f), 128.2 (Ph), 127.7 (C-2), 123.9 (C-3), 117.3 (C-1), 113.4 (C-4), 74.6 (OCH_2), 55.3 (OCH_3), 21.2 (CH_3 at Hydrazide ring), 20.7 (CH_3 at Ph ring) ppm.

[($Me_2Sn(L_4)Cl$, $C_{25}H_{26}ClN_3O_5Sn$), (17)]

Yield: 67 %; m.p.: 129-130 ^{0}C; IR (KBr): ν = 1550 (C=N) cm^{-1}; ^{1}H NMR (DMSO-d_6 and $CDCl_3$): δ = 11.76 (s, 1H, -CH=N), 8.22-8.26 (d, 2H, C_c-H & C_e-H), 7.78-7.81 (d, 4H, C_2'-H, C_6'-H, C_b-H & C_f-H), 7.53-7.56 (d, 1H, C_2-H), 7.24-7.26 (d, 2H,C_3'-H & C_5'-H), 7.12-7.18 (m, 2H, C_3-H & C_4-H), 5.16 (s, 2H, -OCH_2), 3.87 (s, 3H, -OCH_3), 2.37 (s, 3H, -CH_3 at Hydrazide ring), 1.26 (s, 6H, -CH_3) ppm; ^{13}C NMR: δ = 155.3 (C=O), 151.7 (C=N), 146.8 (C-6), 145.9 (C-5), 144.6 (C-d), 143 (C-a), 141.5 (C-4'), 130.5 (C-1'), 128.7 (C-3' & C-5'), 128.5 (C-b & C-f), 128 (C-2' & C-6'), 127.6 (C-c & C-e), 124.5 (C-2), 123.0 (C-3), 117.3 (C-1), 113.8 (C-4), 73.3 (OCH_2), 55.7 (OCH_3), 22.9 (CH_3 at Hydrazide ring) ppm.

[($Et_2Sn(L_4)Cl$, $C_{27}H_{30}ClN_3O_5Sn$), (18)]

Yield: 71 %; m.p.: 127-128 ^{0}C; IR (KBr): ν = 1552 (C=N) cm^{-1}; ^{1}H NMR (DMSO-d_6 and CDCl3): δ = 11.75 (s, 1H, -CH=N), 8.24-8.27 (d, 2H, C_c-H & C_e-H), 7.77-7.80 (d, 4H, $C_{2'}$-H, $C_{6'}$-H, C_b-H & C_f-H), 7.52-7.55 (m, 1H, C_2-H), 7.23-7.25 (d, 2H,$C_{3'}$-H & $C_{5'}$-H), 7.13-7.16 (m, 2H, C_3-H & C_4-H), 5.0 (s, 2H, -OCH_2), 3.85 (s, 3H, -OCH_3), 2.38 (s, 3H, -CH_3 at Hydrazide ring), 3.06-3.10 (m, 4H,-CH_2), 1.21-1.25 (t, 6H,-CH_3) ppm; ^{13}C NMR: δ = 155.3 (C=O), 151.8 (C=N), 146.3 (C-6), 145.9 (C-5), 144.6 (C-d), 143 (C-a), 141.6 (C-$_{4'}$), 130.5 (C-$_{1'}$), 128.7 (C-$_{3'}$ & C-$_{5'}$), 128.5 (C-b & C-f), 128 (C-$_{2'}$ & C-$_{6'}$), 127.7 (C-c & C-e), 124.3 (C-2), 123.1 (C-3), 117.3 (C-1), 113.8 (C-4), 73.4 (OCH_2), 55.6 (OCH_3), 23 (CH_3 at Hydrazide ring), 12.9 (Et), 8.7 (Et) ppm.

[($Bu_2Sn(L_4)Cl$, $C_{31}H_{38}ClN_3O_5Sn$), (19)]

Yield: 68 %; m.p.: 124-125 ^{0}C; IR (KBr): ν = 1551 (C=N) cm-1; 1H NMR (DMSO-d_6 and $CDCl_3$): δ = 11.74 (s, 1H, -CH=N), 8.21-8.25 (d, 2H, C_c-H & C_e-H), 7.76-7.80 (d, 4H, $C_{2'}$-H, $C_{6'}$-H, C_b-H & C_f-H), 7.51-7.55 (m, 1H, C_2-H), 7.24-7.26 (d, 2H,$C_{3'}$-H & $C_{5'}$-H), 7.12-7.15 (m, 2H, C_3-H & C_4-H), 4.98 (s, 2H, -OCH_2), 3.89 (s, 3H, -OCH_3), 2.37 (s, 3H, -CH_3 at Hydrazide ring), 3.07-3.11 (t, 4H,-CH_2), 1.61-1.65 (m, 8H,-CH_2), 1.23-1.26(t, 6H,-CH3) ppm; ^{13}C NMR: δ = 155.3 (C=O), 152 (C=N), 146.2 (C-6), 145.9 (C-5), 144.6 (C-d), 143.1 (C-a), 141.4 (C-4'), 130.5 (C-1'), 128.7 (C-3' & C-5'), 128.5 (C-b & C-f), 127.9 (C-$_{2'}$ & C-$_{6'}$), 127.6 (C-c & C-e), 124.4 (C-2), 123 (C-3), 117.3 (C-1), 113.8 (C-4), 73.5 (OCH_2), 55.5 (OCH_3), 27.4 (Bu), 25.4 (Bu), 23.2 (CH_3 at Hydrazide ring), 12.2 (Bu), 8.2 (Bu) ppm.

[($Ph_2Sn(L_4)Cl$, $C_{35}H_{30}ClN_3O_5Sn$), (20)]

Yield: 75 %; m.p.: 141-142 ^{0}C; IR (KBr): ν = 1554 (C=N) cm^{-1}; ^{1}H NMR (DMSO-d_6 and $CDCl_3$): δ = 11.75 (s, 1H, -CH=N), 8.22-8.24 (d, 2H, C_c-H & C_e-H), 7.73-7.81 (d, 4H, C_2'-H, C_6'-H, C_b-H & C_f-H), 7.48-7.50 (d, 1H, C_2-H), 7.27-7.29 (d, 2H,C_3'-H & C_5'-H), 7.12-7.24 (m, 10H, Ph & m,2H, C_3-H & C_4-H), 5.00 (s, 2H, -OCH_2), 3.88 (s, 3H, -OCH_3) , 2.38 (s, 3H, -CH_3 at Hydrazide ring) ppm; ^{13}C NMR: δ = 155.3 (C=O), 151.5 (C=N), 145.4 (C-6), 142.4 (C-5), 136.2 (C-d), 132.4 (C-a), 132.3 (C-4'), 131.2 (C-1'), 129.8 (C-3' & C-5'), 129 (Ph), 128.7 (Ph), 128.7 (C-b & C-f), 128.4 (Ph), 128.1 (Ph), 127.9 (C-2' & C-6'), 127.6 (C-c & C-e), 127.4 (C-2), 123.9 (C-3), 117.4 (C-1), 113.3 (C-4), 74.4 (OCH_2), 55.4 (OCH_3), 20.4 (CH_3 at Hydrazide ring) ppm.

Antimicrobial activity

Test Microorganisms

Gram positive bacteria (viz. *Klebsiella pneumoniae* [NCDC No. 138], *Staphylococcus aureus* [MTCC No. 3160] Gram-negative bacteria (viz. *Escherichia coli* [MTCC No. 443], *Enterobacter aerogenes* [NCDC No. 106) and fungus (*Aspergillus niger* [MTCC No. 282] and *Candida albicans* [MTCC No. 227] were used for antimicrobial assay. All the microbial strains were procured from Microbial Type Culture Collection (MTCC), Institute of Microbial Technology (IMTECH), Chandigarh.

Ligands and their tin complexes were screened for in-vitro antimicrobial activity using serial dilution technique to find out their Minimum Inhibitory Concentration (MIC) value. The medium was prepared by dissolving weighed amount of nutrient broth/ sabouraud dextrose broth in 1L of distilled water and 1 ml of nutrient medium was transferred to each test tube. The test tubes having nutrient medium were autoclaved for 30 minutes at 120 °C. The solution of test compounds was prepared by dissolving 1.0 mg of synthesized compounds in dry DMSO which was further diluted to give a stock solution of 100 µg/ml. The solution of test compounds was transferred to test tubes having sterilized nutrient medium to get a set of five dilutions of test compounds having concentrations 50, 25, 12.5, 6.25 and 3.125 µg/ml. The inoculation of test strains was done with the help of micropipette with sterilized tips as 100 µL of freshly cultured strain was transferred in to test tubes and incubated at 37 °C for 24 hours for bacterial strains, 48 hours for *C. albicans* and 7 days at 25 °C for *A. niger*. The DMSO was taken as negative control whereas norfloxacin and fluconazole were taken as positive control for antibacterial and antifungal activity, respectively. The experiments were performed in triplicates and the mean values were observed.

QSAR studies

The structures of 1-20 were first pre-optimized with the Molecular Mechanics Force Field (MM) procedure included in Hyperchem 6.03 [31] And the resulting geometries were further developed by means of the semiempirical method PM3 (Parametric Method-3). A gradient norm limit of 0.01 kcal/A° ´was taken into consideration for the geometry optimization. The lowest energy structure was used for each individual molecule to calculate physicochemical properties using TSAR 3.3 software for Windows [32]. Further, the regression analysis was performed using the SPSS software package [33].

Conclusion

A series of novel compounds was synthesized and characterized using elemental analyses, various spectroscopic techniques like UV, IR and (^{1}H, ^{13}C and ^{119}Sn) NMR. The substituted o-vanillin Schiff bases and their organotin(IV) complexes were screened for antimicrobial activity against representative microorganisms and the compounds evaluated had inhibited the growth of all the tested bacterial and fungal strains. The complexes were found to be more active antimicrobial agent in comparison to the Schiff bases. The QSAR studies were carried out to find out the relationship between structural features and antimicrobial activity of synthesized deriv-

atives which revealed the fact that antimicrobial activity of these derivatives is governed by topological descriptors and electronic energy of the molecules.

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Conflict of interest

The authors declare that they have no conflict of interest.

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