Synthesis, Characterization and Bioactivity of Diorganotin(IV) Schiff Base Complexes as Potential Antimalarial and Antioxidant Agents: Insight through Cytotoxicity and Molecular Docking

Jai Devi*[1], Bharti Taxak[1], Binesh Kumar[1], Swati Rani[1]

[1]Department of Chemistry, Guru Jambheshwar University of Science & Technology, Hisar-125001, Haryana, India

Email-Id –jaya.gju@gmail.com, bhartitaxak007@gmail.com, bineshchemistry131@gmail.com, spahwa999@gmail.com

*Corresponding author - Jai Devi, Department of Chemistry, Guru Jambheshwar University of Science and Technology, Hisar-125001, Haryana, India

Email id - jaya.gju@gmail.com

Institutional Email id - jaidevi2005@gjust.org

Tel +911662263152, Fax: +911662276240, Phone No: +91-9416789379 (M)

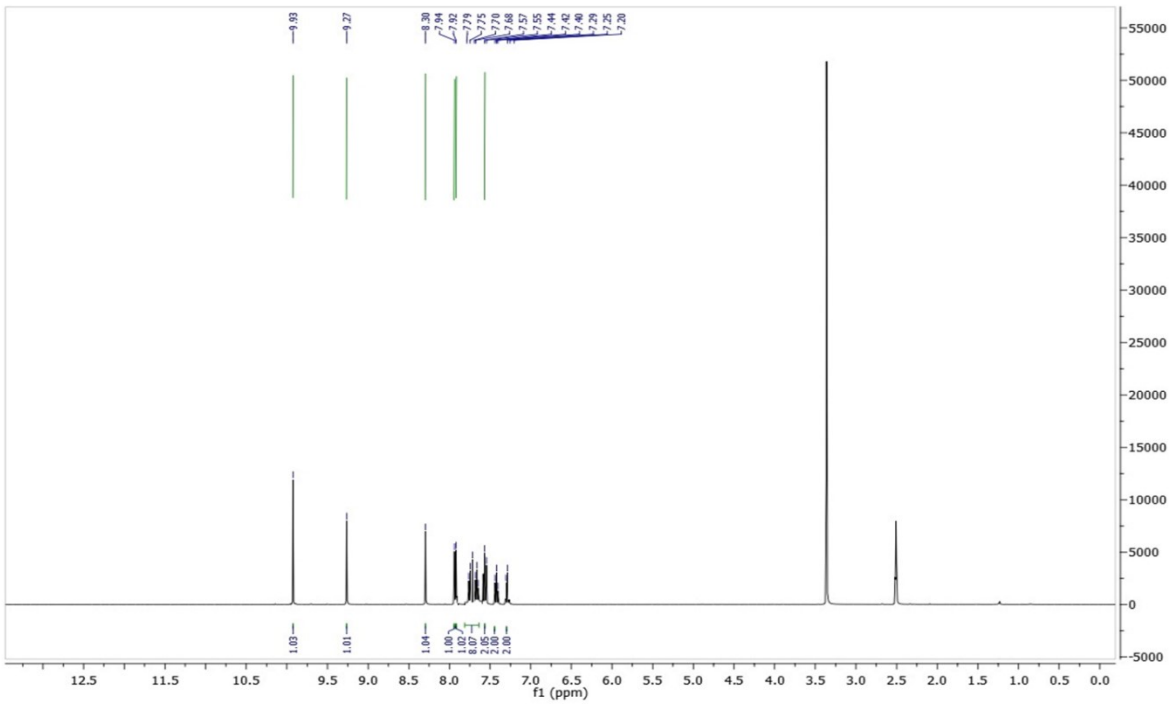

Fig. S01. ^{1}H NMR spectrum of ligand [H_2L^1] (1)

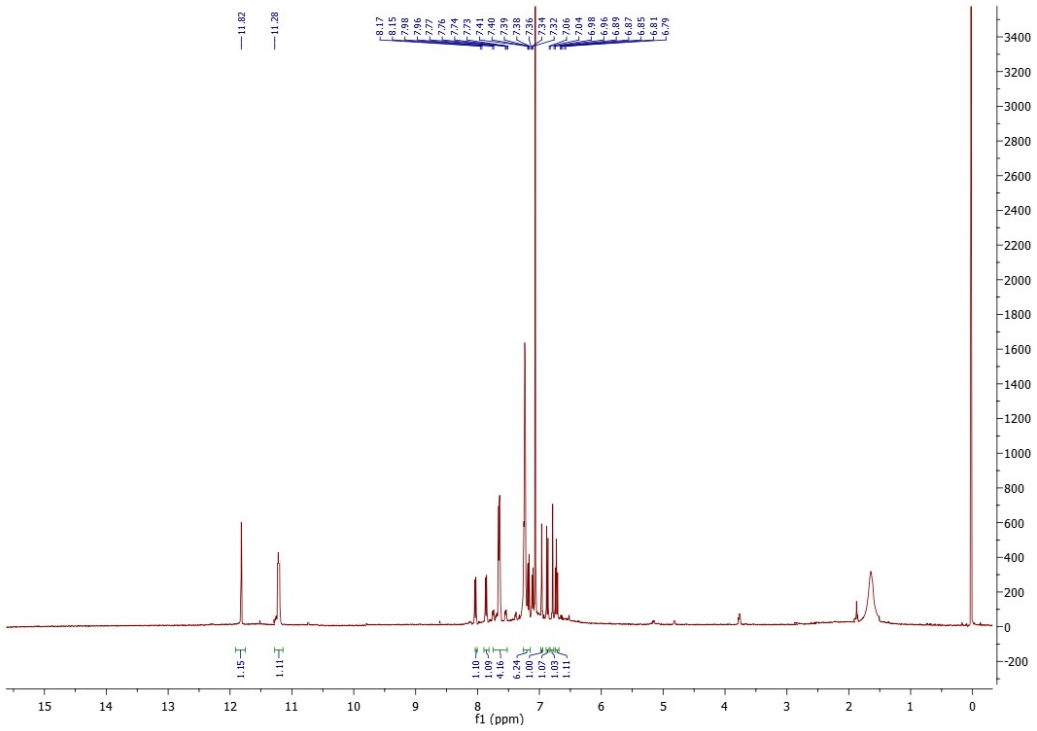

Fig. S02. ^{1}H NMR spectrum of ligand [H_2L^2] (2)

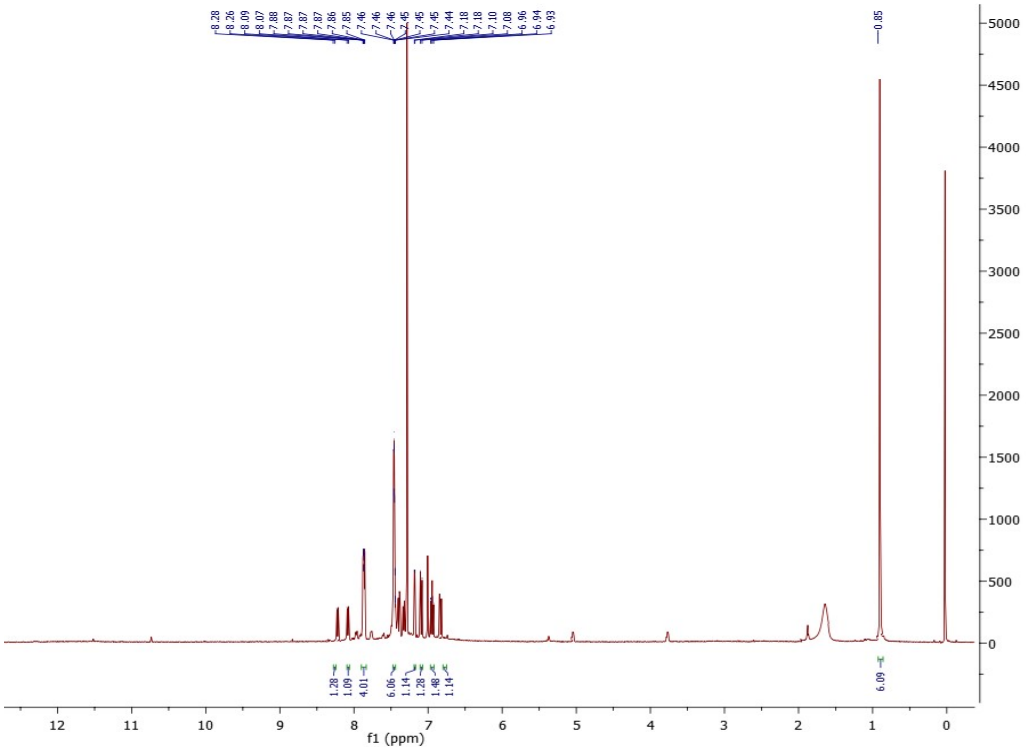

Fig. S03. ^{1}H NMR spectrum of complex [Me_2SnL^1] (3)

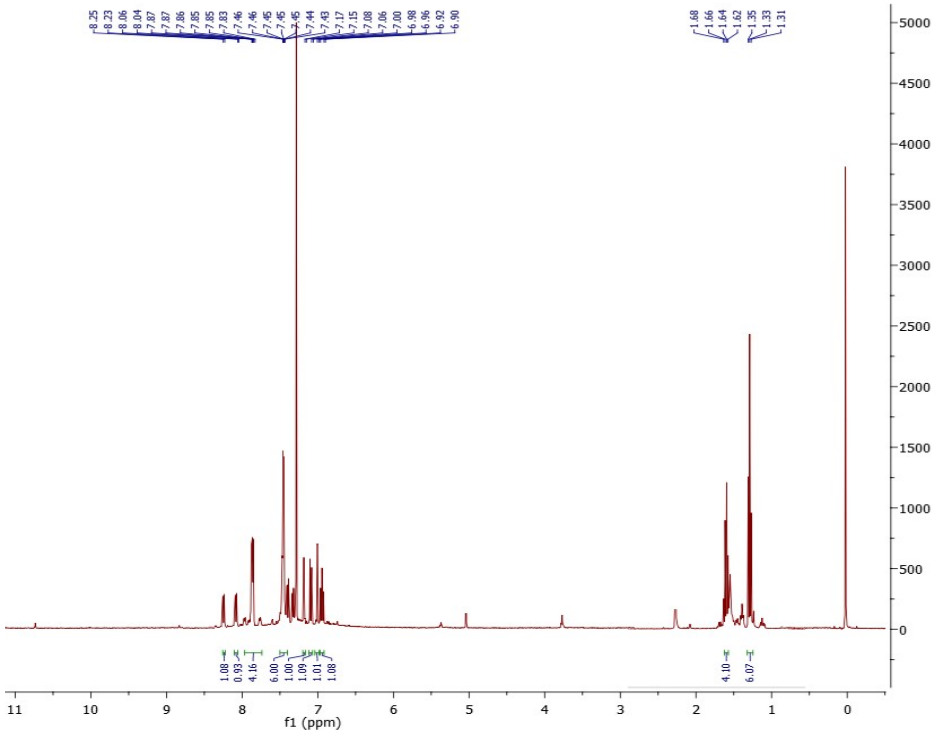

Fig. S04. ^{1}H NMR spectrum of complex [Et_2SnL^1] (4)

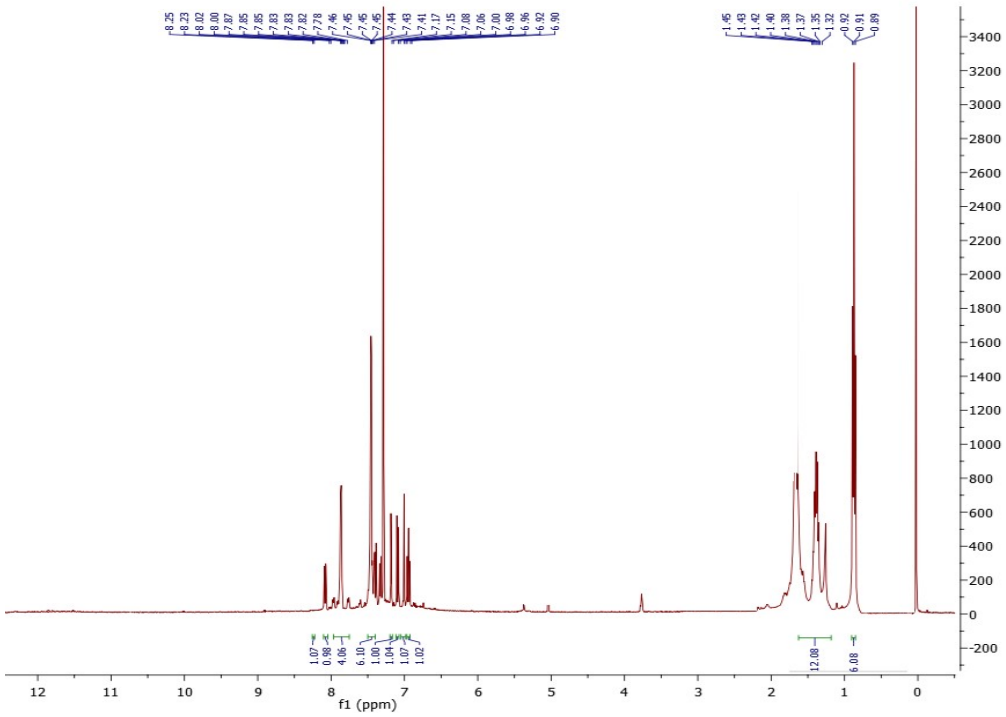

Fig. S05. ^{1}H NMR spectrum of complex [Bu_2SnL^1] (5)

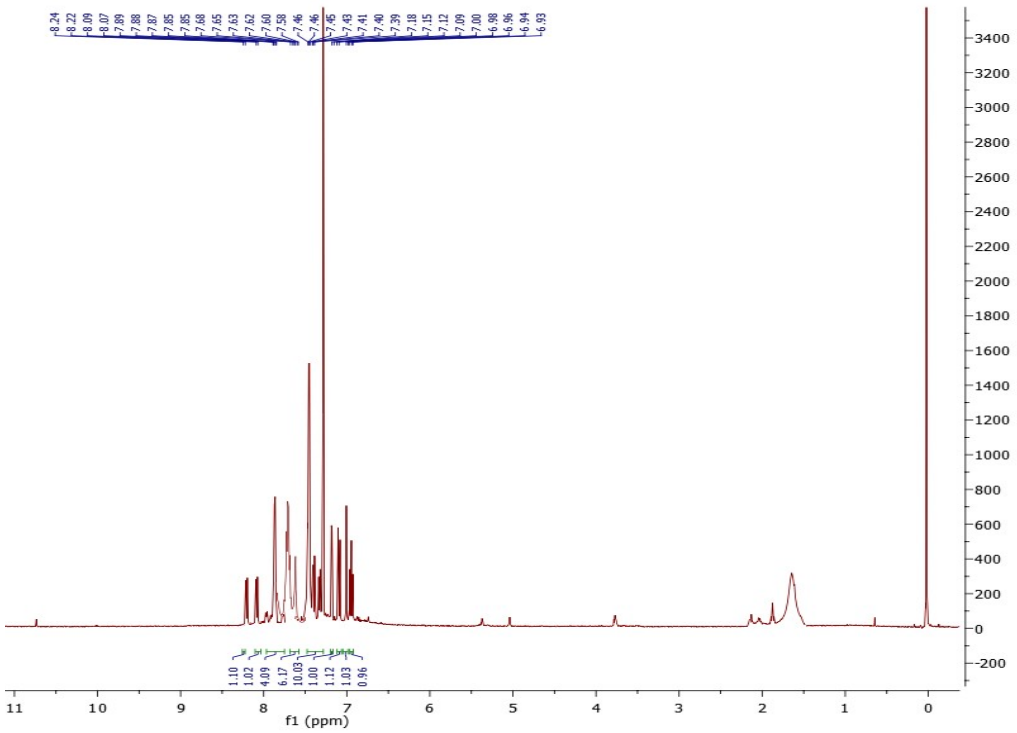

Fig. S06. ^{1}H NMR spectrum of complex $[Ph_2SnL^1]$ (6)

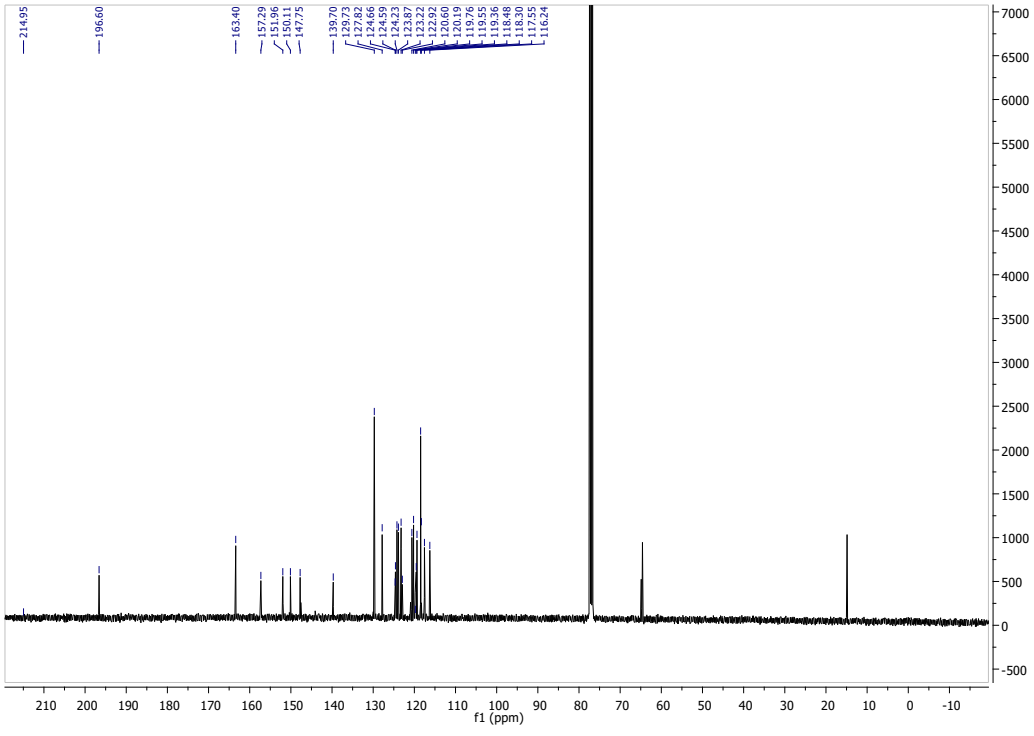

Fig. S07. ^{13}C NMR spectrum of ligand $[H_2L^1]$ (1)

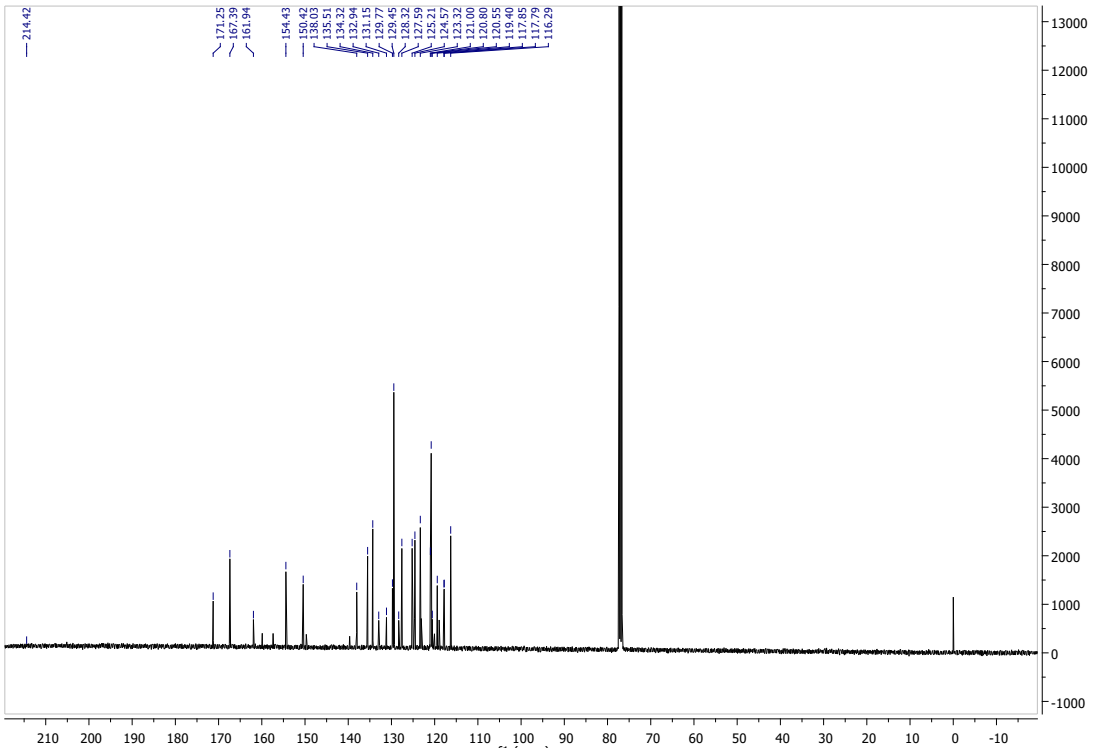

Fig. S08. ^{13}C NMR spectrum of ligand [H_2L^2] (2)

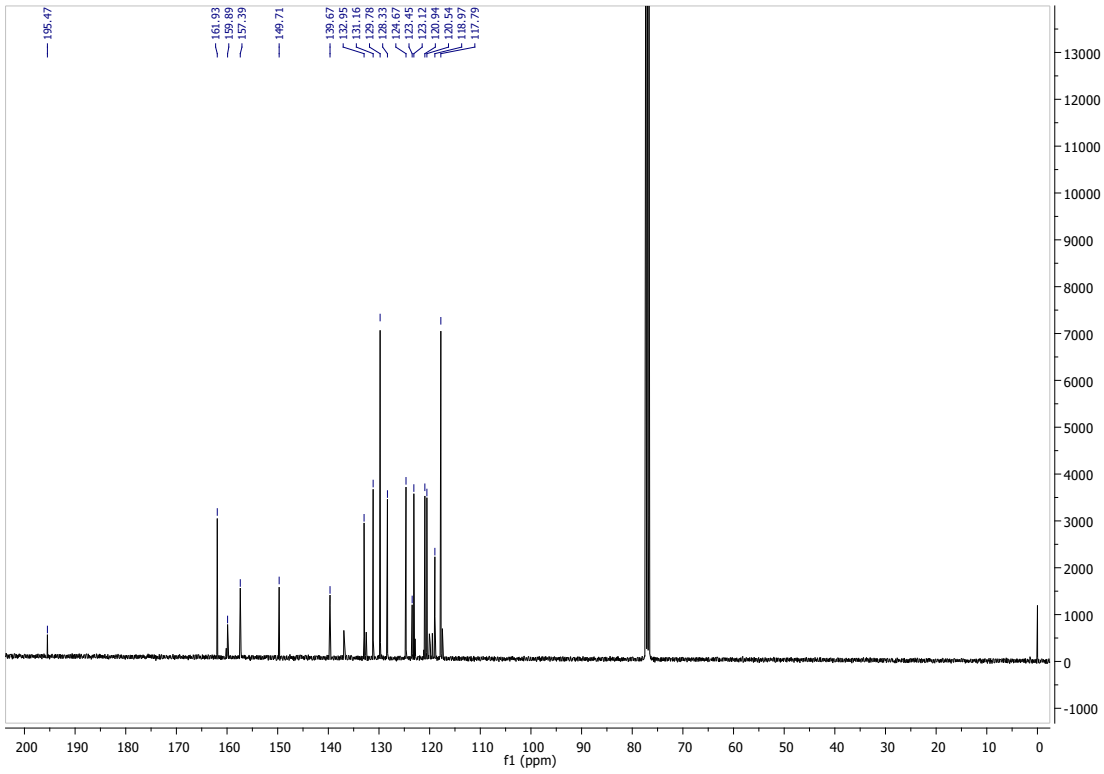

Fig. S09. ^{13}C NMR spectrum of complex [Me_2SnL^1] (3)

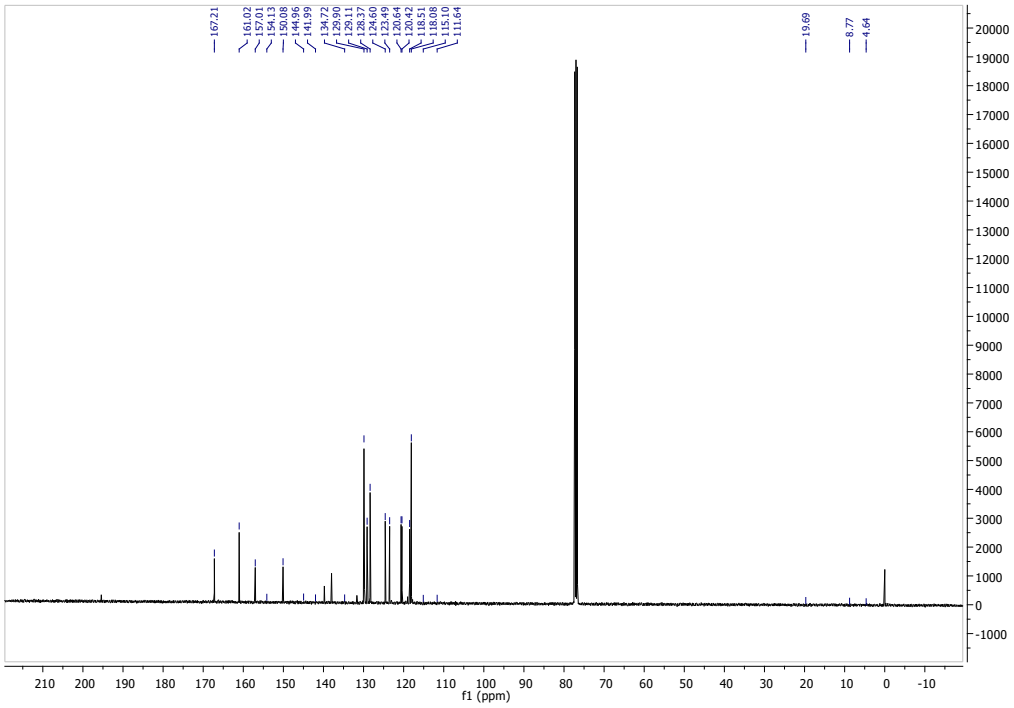

Fig. S10. ^{13}C NMR spectrum of complex $[Et_2SnL^1]$ (4)

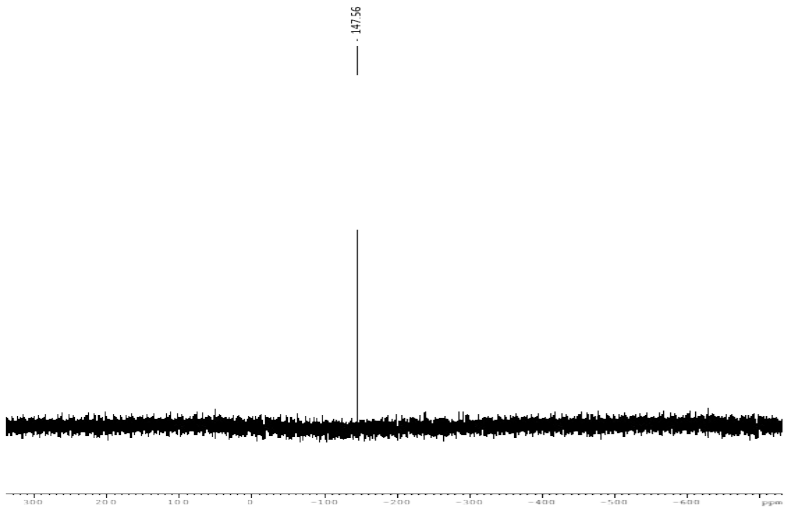

Fig. S11. ^{119}Sn NMR spectrum of metal complex $[Me_2SnL^2]$ (7)

Fig. S12. ^{119}Sn NMR spectrum of metal complex [Et_2SnL^2] (8)

Fig. S13. ^{119}Sn NMR spectrum of metal complex [Bu_2SnL^2] (9)

Fig. S14. ^{119}Sn NMR spectrum of metal complex [Ph_2SnL^2] (10)

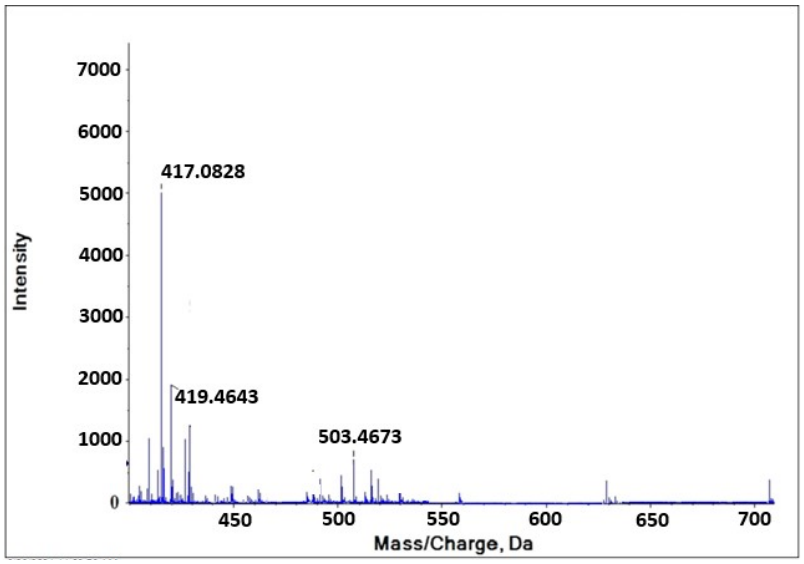

Fig. S15. Mass spectrum of ligand [H_2L^1] (1)

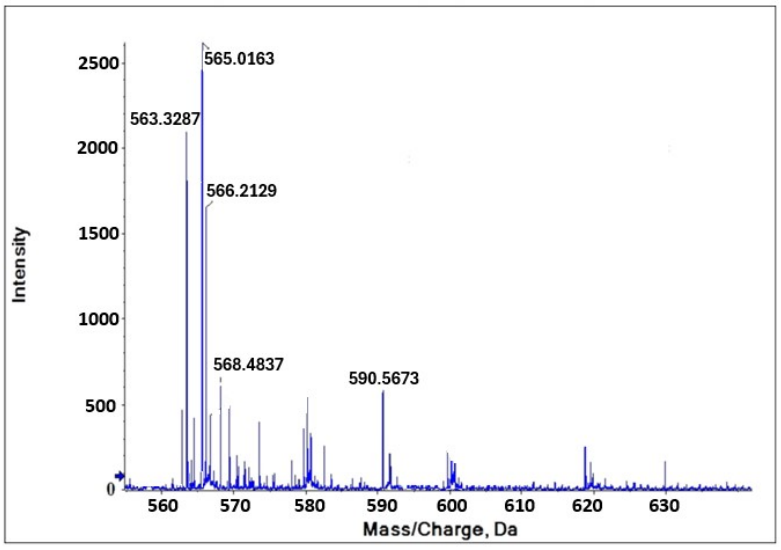

Fig. S16. Mass spectrum of metal complex [Me_2SnL^1] (4)

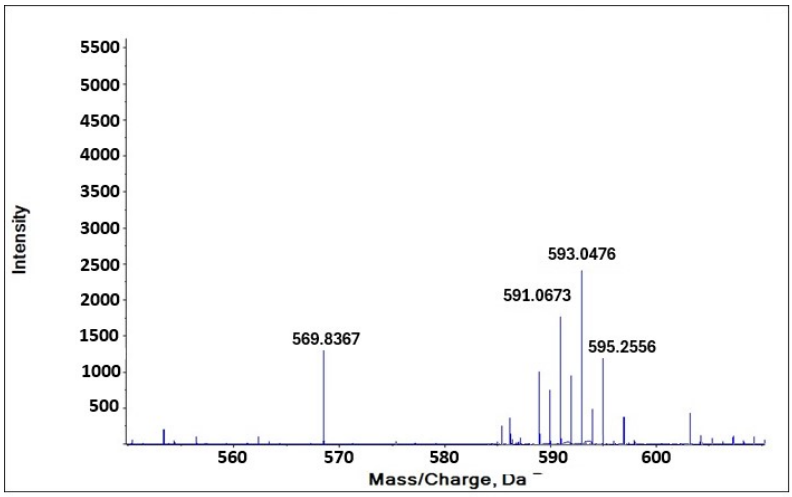

Fig. S17. Mass spectrum of metal complex [Et_2SnL^1] (4)

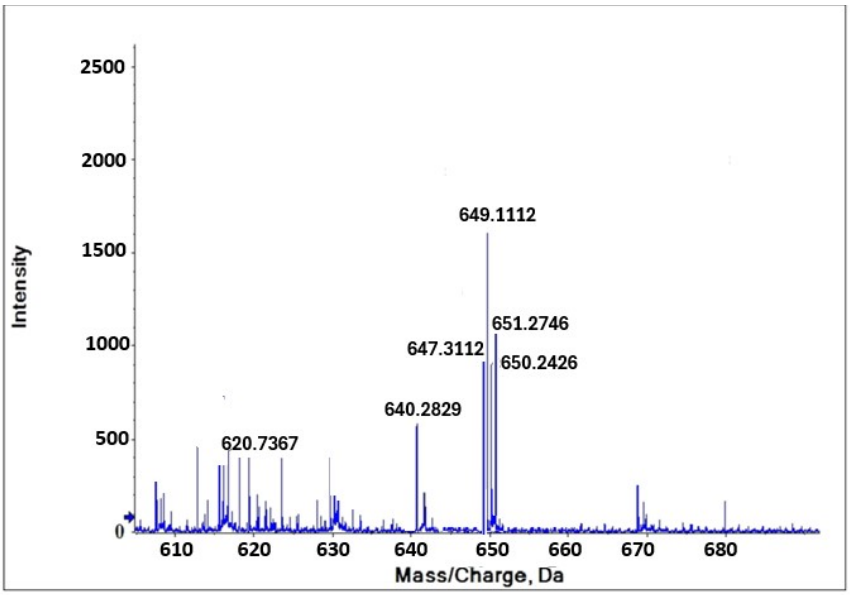

Fig. S18. Mass spectrum of metal complex [Bu_2SnL^1] (5)

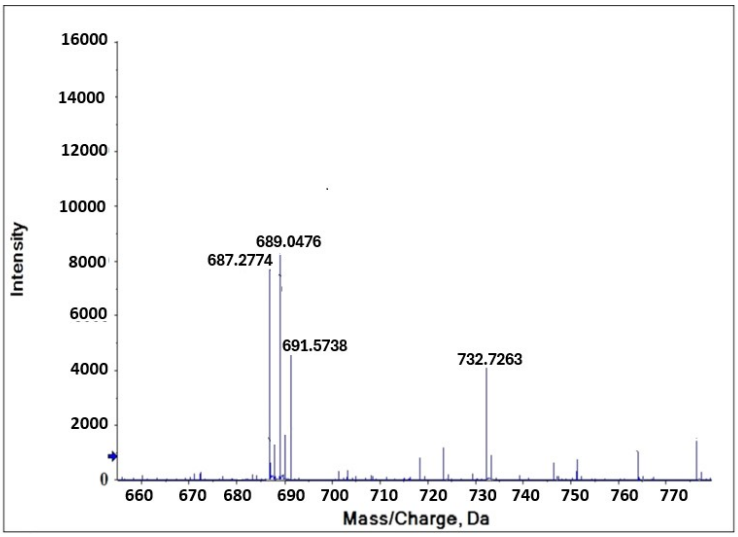

Fig. S19. Mass spectrum of metal complex [Ph_2SnL^1] (6)

Table. S01: Physical data of synthesized Schiff base ligands and their respective diorganotin(IV) complexes.

C. No.	Molecular formulae	Yield (%)	Color	*m/z* / $M+H^+$ Calculated/ Found	(Ω_M) x 10^{-3} $\Omega^1cm^2mol^{-1}$	M.P. (°C)
1	$C_{24}H_{17}ClN_2OS$	76	White	416.0750/417.0828	11.39	194-196
2	$C_{24}H_{18}N_2OS$	81	White	382.1140/383.1218	12.31	195-197
3	$C_{26}H_{21}ClN_2OSSn$	73	yellow	564.0085/565.0163	13.72	223-225
4	$C_{28}H_{25}ClN_2OSSn$	68	yellow	592.0398/593.0476	11.99	227-229
5	$C_{32}H_{33}ClN_2OSSn$	65	yellow	648.1034/649.1112	13.43	231-233

6	$C_{36}H_{25}ClN_2OSSn$	66	yellow	688.0398/689.0476	12.41	233-235
7	$C_{26}H_{22}N_2OSSn$	70	yellow	530.0475/531.0553	11.33	225-227
8	$C_{28}H_{26}N_2OSSn$	68	yellow	558.0788/559.0866	13.82	227-229
9	$C_{32}H_{34}N_2OSSn$	65	yellow	614.1414/615.1492	12.88	231-233
10	$C_{36}H_{26}N_2OSSn$	61	yellow	654.0788/655.0866	11.44	234-236

Table. S02. Characteristic FT-IR frequencies (cm^{-1}) of synthesized Schiff base ligands and their respective diorganotin(IV) complexes.

C. No.	Compounds	υ(O–H)	υ(N–H)	υ(HC=N)	υ(C-O)	υ(M-O)	υ(M-N)	υ(M-S)
1.	H_2L^1	3404		1615	-	-	-	-
2.	H_2L^2	3417		1617	-	-	-	-
3.	$[Me_2SnL^1]$	-		1605	1215	740	526	495
4.	$[Et_2SnL^1]$	-		1611	1219	732	540	492
5.	$[Bu_2SnL^1]$	-		1604	1217	742	542	487
6.	$[Ph_2SnL^1]$	-		1605	1220	733	544	488
7.	$[Me_2SnL^2]$	-		1613	1219	731	538	491
8.	$[Et_2SnL^2]$	-		1607	1212	737	537	493
9.	$[Bu_2SnL^2]$	-		1604	1214	739	543	486
10.	$[Ph_2SnL^2]$	-		1606	1218	738	548	485

Table. S03. ^1H, ^{13}C and ^{119}Sn NMR data of the synthesized Schiff base ligands and their diorganotin(IV) complexes

C. no.	Compounds	^1H NMR (DMSO-d_6/$CDCl_3$) δ in ppm	^{13}C NMR (DMSO- d_6/$CDCl_3$) δ in ppm	^{119}Sn NMR
1	H_2L^1	11.84 (s, 1H), 10.27 (s, 1H), 8.08 (d, *J* = 2.1 Hz, 1H), 8.03 (d, *J* = 2.7 Hz, 1H), 7.71 (d, *J* = 1.2 Hz, 2H), 7.60 (d, *J* = 1.2 Hz, 1H), 7.53 (d, *J* = 2.1 Hz, 1H), 7.48 (dd, *J* = 3.0, 1.2 Hz, 3H), 7.45 (dd, *J* = 4.7, 0.9 Hz, 3H), 7.40(s, 1H), 7.20 (d, *J* = 1.2 Hz, 1H), 7.04 (d, *J* = 1.6 Hz, 1H).	214.0, 184.3, 167.1, 162.3 140.1, 133.7, 132.2, 131.6, 129.6, 129.2, 128.8, 128.1, 127.2, 126.6, 125.6, 124.1, 124.3, 121.9, 121.3, 120.1, 119.4, 119.3, 118.1, 117.6, 116.2, 105.3.	-----
2	H_2L^2	11.84 (s, 1H), 10.27 (s, 1H), 8.10 (d, *J* = 2.1 Hz, 1H), 8.05 (d, *J* = 2.7 Hz, 1H), 7.73 (d, *J* = 1.2 Hz, 2H), 7.63 (d, *J* = 1.2 Hz, 1H), 7.56 (d, *J* = 2.1 Hz, 1H), 7.52 (dd, *J* = 3.0, 1.2 Hz, 3H), 7.48 (dd, *J* = 4.7, 0.9 Hz, 3H), 7.42(s, 1H), 7.20 (d, *J* = 1.2 Hz, 1H), 7.04 (d, *J* = 1.6 Hz, 2H).	214.0, 185.3, 167.6, 163.3 140.7, 133.9, 132.2, 131.2, 129.9, 129.2, 128.8, 128.3, 127.2, 126.2, 125.6, 124.7, 124.3, 121.6, 121.3, 120.0, 119.6, 119.1, 118.5, 117.4, 116.2, 105.3.	----
3	$[Me_2SnL^1]$	8.04 (d, *J* = 2.1 Hz, 1H), 8.01 (d, *J* = 2.7 Hz, 1H), 7.71 (d, *J* = 1.2 Hz,	188, 184.3, 167.1, 162.3 140.1, 133.7, 132.2, 131.6,	-149.43

		2H), 7.60 (d, *J* = 1.2 Hz, 1H), 7.53 (d, *J* = 2.1 Hz, 1H), 7.48 (dd, *J* = 3.0, 1.2 Hz, 3H), 7.45 (dd, *J* = 4.7, 0.9 Hz, 3H), 7.40(s, 1H), 7.20 (d, *J* = 1.2 Hz, 1H), 7.04 (d, *J* = 1.6 Hz, 1H), 0.67 (s, 6H).	129.6, 129.2, 128.8, 128.1, 127.2, 126.6, 125.6, 124.1, 124.3, 121.9, 121.3, 120.1, 119.4, 119.3, 118.1, 117.6, 116.2, 105.3, 19.7, 3.2	
4	[Et_2SnL^1]	8.05 (d, *J* = 2.1 Hz, 1H), 8.02 (d, *J* = 2.7 Hz, 1H), 7.72 (d, *J* = 1.2 Hz, 2H), 7.62 (d, *J* = 1.2 Hz, 1H), 7.55 (d, *J* = 2.1 Hz, 1H), 7.49 (dd, *J* = 3.0, 1.2 Hz, 3H), 7.46 (dd, *J* = 4.7, 0.9 Hz, 3H), 7.42(s, 1H), 7.22 (d, *J* = 1.2 Hz, 1H), 7.05 (d, *J* = 1.6 Hz, 1H) 1.60 (q, 4H), 0.89 (t, 6H)	188, 184.3, 167.1, 162.3 140.1, 133.7, 132.2, 131.6, 129.6, 129.2, 128.8, 128.1, 127.2, 126.6, 125.6, 124.1, 124.3, 121.9, 121.3, 120.1, 119.4, 119.3, 118.1, 117.6, 116.2, 105.3, 19.7, 8.7, 4.9	-169.52
5	[Bu_2SnL^1]	8.04 (d, *J* = 2.1 Hz, 1H), 8.01 (d, *J* = 2.7 Hz, 1H), 7.71 (d, *J* = 1.2 Hz, 2H), 7.60 (d, *J* = 1.2 Hz, 1H), 7.53 (d, *J* = 2.1 Hz, 1H), 7.48 (dd, *J* = 3.0, 1.2 Hz, 3H), 7.45 (dd, *J* = 4.7, 0.9 Hz, 3H), 7.40(s, 1H), 7.20 (d, *J* = 1.2 Hz, 1H), 7.04 (d, *J* = 1.6 Hz, 1H), 1.63 (m, *J* = 9.8, 6.5, 3.2 Hz, 12H), 0.87 (t, 6H).	188, 184.3, 167.1, 162.3 140.1, 133.7, 132.2, 131.6, 129.6, 129.2, 128.8, 128.1, 127.2, 126.6, 125.6, 124.1, 124.3, 121.9, 121.3, 120.1, 119.4, 119.3, 118.1, 117.6, 116.2, 105.3, 28.6, 27.2, 26.1, 19.3, 13.6	-241.34
6	[Ph_2SnL^1]	8.04 (d, *J* = 2.1 Hz, 1H), 8.01 (d, *J* = 2.7 Hz, 1H), 7.71 (d, *J* = 1.2 Hz, 2H), 7.60 (d, *J* = 1.2 Hz, 1H), 7.53 (d, *J* = 2.1 Hz, 1H), 7.48 (dd, *J* = 3.0, 1.2 Hz, 3H), 7.45 (dd, *J* = 4.7, 0.9 Hz, 3H), 7.40(s, 1H), 7.20 (d, *J* = 1.2 Hz, 1H), 7.04 (d, *J* = 1.6 Hz, 1H)	188, 184.3, 167.1, 162.3 140.1, 133.7, 132.2, 131.6, 129.6, 129.2, 128.8, 128.1, 127.2, 126.6, 125.6, 124.1, 124.3, 121.9, 121.3, 120.1, 119.4, 119.3, 118.1, 117.6, 116.2, 105.3.	-342.56
7	[Me_2SnL^2]	8.04 (d, *J* = 2.1 Hz, 1H), 8.01 (d, *J* = 2.7 Hz, 1H), 7.71 (d, *J* = 1.2 Hz, 2H), 7.60 (d, *J* = 1.2 Hz, 1H), 7.53 (d, *J* = 2.1 Hz, 1H), 7.48 (dd, *J* = 3.0, 1.2 Hz, 3H), 7.45 (dd, *J* = 4.7, 0.9 Hz, 3H), 7.40(s, 1H), 7.20 (d, *J* = 1.2 Hz, 1H), 7.04 (d, *J* = 1.6 Hz, 2H), 0.65 (s, 6H).	188, 185.3, 167.6, 163.3 140.7, 133.9, 132.2, 131.2, 129.9, 129.2, 128.8, 128.3, 127.2, 126.2, 125.6, 124.7, 124.3, 121.6, 121.3, 120.0, 119.6, 119.1, 118.5, 117.4, 116.2, 105.3, 19.7, 3.2	-147.56
8	[Et_2SnL^2]	8.04 (d, *J* = 2.1 Hz, 1H), 8.01 (d, *J* = 2.7 Hz, 1H), 7.71 (d, *J* = 1.2 Hz, 2H), 7.60 (d, *J* = 1.2 Hz, 1H), 7.53 (d, *J* = 2.1 Hz, 1H), 7.48 (dd, *J* = 3.0, 1.2 Hz, 3H), 7.45 (dd, *J* = 4.7, 0.9 Hz, 3H), 7.40(s, 1H), 7.20 (d, *J* = 1.2 Hz, 1H), 7.04 (d, *J* = 1.6 Hz, 2H) 1.67 (q, 4H), 0.98 (t, 6H)	188, 185.3, 167.6, 163.3 140.7, 133.9, 132.2, 131.2, 129.9, 129.2, 128.8, 128.3, 127.2, 126.2, 125.6, 124.7, 124.3, 121.6, 121.3, 120.0, 119.6, 119.1, 118.5, 117.4, 116.2, 105.3, 18.7, 9.7, 4.6	-165.39
9	[Bu_2SnL^2]	8.04 (d, *J* = 2.1 Hz, 1H), 8.01 (d, *J* = 2.7 Hz, 1H), 7.71 (d, *J* = 1.2 Hz, 2H), 7.60 (d, *J* = 1.2 Hz, 1H), 7.53	188, 185.3, 167.6, 163.3 140.7, 133.9, 132.2, 131.2, 129.9, 129.2, 128.8, 128.3,	-237.34

		(d, *J* = 2.1 Hz, 1H), 7.48 (dd, *J* = 3.0, 1.2 Hz, 3H), 7.45 (dd, *J* = 4.7, 0.9 Hz, 3H), 7.40(s, 1H), 7.20 (d, *J* = 1.2 Hz, 1H), 7.04 (d, *J* = 1.6 Hz, 2H), 1.40-1.35 (m, *J* = 4.8, 3.5 Hz, 4H), 0.85 (t, 6H).	127.2, 126.2, 125.6, 124.7, 124.3, 121.6, 121.3, 120.0, 119.6, 119.1, 118.5, 117.4, 116.2, 105.3, 27.6, 26.2, 25.1, 18.7, 11.6	
10	[Ph_2SnL^2]	8.04 (d, *J* = 2.1 Hz, 1H), 8.01 (d, *J* = 2.7 Hz, 1H), 7.71 (d, *J* = 1.2 Hz, 2H), 7.60 (d, *J* = 1.2 Hz, 1H), 7.53 (d, *J* = 2.1 Hz, 1H), 7.48 (dd, *J* = 3.0, 1.2 Hz, 3H), 7.45 (dd, *J* = 4.7, 0.9 Hz, 3H), 7.40(s, 1H), 7.20 (d, *J* = 1.2 Hz, 1H), 7.04 (d, *J* = 1.6 Hz, 2H)	188, 185.3, 167.6, 163.3 140.7, 133.9, 132.2, 131.2, 129.9, 129.2, 128.8, 128.3, 127.2, 126.2, 125.6, 124.7, 124.3, 121.6, 121.3, 120.0, 119.6, 119.1, 118.5, 117.4, 116.2, 105.3	-339.43

Table. S04. Docking results, including binding energy and interactions of the compounds (1, 6).

Protein-Ligand Complex	**Binding Energy (Kcal/Mol) (Delta G)**	**Interacting amino acid**	**Hydrogen bonds**	**π-Cation interaction**	**π-Stacking**
H_2L^1 (1)	-7.4	Val-200, Leu-201, Phe-229, Val-233 and Lys-314	Lys-314	-	-
Ph_2SnL^1 (6)	-9.7	Lys-173, Tyr-174, Pro-180, Arg-185, Ile-239, Val-248 and Ala-249	Ser-170	-	-

Table S05. ADMET properties of the synthesized Schiff base ligands (1-2) and their diorganotin(IV) complexes (3-10).

C. No.	Molecular Weight	Density	nHA	nHD	nRot	nRing	TPSA	LogS	LogP	LogD
1.	382.110	0.945	3	2	5	4	44.62	-6.456	5.842	4.69
2.	416.08	0.991	3	2	5	4	44.62	-6.881	6.329	4.826
3.	530.05	0.0	3	0	2	5	33.95	-6.813	5.695	4.754
4.	558.08	0.0	3	0	4	5	33.95	-6.248	5.987	4.805
5.	614.14	0.0	3	0	8	5	33.95	-7.081	7.164	5.277
6.	654.08	0.0	3	0	4	7	33.95	-7.162	7.300	4.777
7.	564.01	0.0	3	0	2	5	33.95	-7.203	6.312	4.713
8.	592.04	0.0	3	0	4	5	33.95	-6.798	6.569	4.732

9.	648.10	0.0	3	0	8	5	33.95	-7.337	7.632	5.242
10.	688.04	0.0	3	0	4	7	33.95	-7.385	7.788	4.663
nHA-number of hydrogen acceptors, nHD- number of hydrogen donors, nRot- number of rotational bonds										

Table S06. Medicinal chemistry properties of the synthesized Schiff base ligands (1-2) and their diorganotin(IV) complexes (3-10).

Property	1	2	3	4	5	6	7	8	9	10
QED	0.349	0.298	0.258	0.239	0.186	0.183	0.233	0.223	0.178	0.175
SAscore	2.262	2.36	3.106	3.247	3.272	3.394	3.184	3.321	3.344	3.462
Fsp3	0.0	0.0	0.077	0.143	0.25	0.00	0.077	0.143	0.250	0.0
MCE-18	20.0	21.0	52.0	52.0	52.0	68.0	54.0	54.0	54.0	70.0
NPscore	-0.734	-0.906	-0.442	-0.424	-0.358	-0.335	-0.606	-0.579	-0.499	-0.463
Lipinski Rule	Accepted	Accepted	Rejected	Rejected	Rejected	Rejected	Rejected	Rejected	Rejected	Rejected
Pfizer Rule	Rejected	Rejected	Rejected	Rejected	Rejected	Rejected	Rejected	Rejected	Rejected	Rejected
GSK Rule	Rejected	Rejected	Rejected	Rejected	Rejected	Rejected	Rejected	Rejected	Rejected	Rejected
Golden Triangle	Accepted	Accepted	Accepted	Rejected	Rejected	Rejected	Rejected	Rejected	Rejected	Rejected
PAINS	0	0	0	0	0	0	0	0	0	0
ALARM NMR	4	4	2	2	2	2	2	2	2	2
BMS	0	0	1	1	1	1	1	1	1	1
Chelator Rule	0	0	0	0	0	0	0	0	0	0

QED: Quantitative Estimate of Drug-likeness, **SAscore**: Synthetic Accessibility Score , **Fsp3**: Fraction of sp^3-Hybridized Carbon Atoms, **MCE-18**: Medicinal Chemistry Evolution 2018, **NPscore**: Natural Product-likeness Score, **PAINS**: Pan-Assay Interference Compounds, **ALARM NMR**: Nuclear Magnetic Resonance Alert for Reactive Compounds, **BMS**: Bristol-Myers Squibb Filter, **Lipinski Rule**: A guideline (Rule of Five) for determining drug-likeness based on molecular weight, hydrogen bonding, and lipophilicity. **Pfizer Rule**: A rule indicating the likelihood of a compound being toxic based on specific physicochemical properties, **GSK Rule**: A guideline from GlaxoSmithKline related to properties that may affect drug development success, **Golden Triangle**: A concept balancing potency, lipophilicity, and molecular weight to enhance the success of drug candidates, **Chelator Rule**: Identifies compounds with potential metal-chelating properties, which could affect bioavailability or toxicity.

Table S07. Absorption properties of the synthesized Schiff base ligands (1-2) and their diorganotin(IV) complexes (3-10).

C. No.	Caco-2 Permeability	MDCK Permeability	Pgp-inhibitor	Pgp-substrate	HIA	F 20%	F 30%
1.	-4.919	1.4e-05	0.149	0.003	0.074	0.869	0.028
2.	-5.054	9e-06	0.039	0.002	0.016	0.219	0.069

3.	-4.838	1.8e-05	0.199	0.0	0.004	0.006	0.003
4.	-5.454	1.5e-05	0.78	0.001	0.004	0.017	0.032
5.	-5.313	1.1e-05	0.999	0.105	0.003	0.022	0.025
6.	-5.009	2.1e-05	0.327	0.001	0.097	0.939	0.008
7.	-4.86	1.2e-05	0.167	0.00	0.004	0.002	0.002
8.	-5.391	1.2e-05	0.826	0.002	0.003	0.005	0.008
9.	-5.259	9e-06	1.0	0.121	0.002	0.005	0.007
10.	-5.022	1.4e-05	0.308	0.002	0.019	0.419	0.005
human colorectal adenocarcinoma (Caco-2), Madin-Darby Canine Kidney (MDCK), P-glycoprotein (Pgp), Human Intestinal Absorption (HIA)							

Table S08. Distribution properties of the synthesized Schiff base ligands (1-2) and their diorganotin(IV) complexes (3-10).

C. No.	PPB (%)	VD	BBB Penetration	Fu (%)
1.	100.50	0.842	0.232	0.646
2.	100.8	0.936	0.092	0.429
3.	98.08	0.666	0.898	1.326
4.	99.60	3.118	0.212	0.468
5.	101.4	4.054	0.165	0.266
6.	101.5	1.431	0.081	0.626
7.	98.91	0.74	0.908	1.301
8.	100.2	3.503	0.101	0.416
9.	102.2	4.627	0.074	0.264
10.	102.3	1.664	0.043	0.481
Plasma Protein Binding (PPB), Volume of Distribution (VD), and Blood-Brain Barrier (BBB) penetration				

Table S09. Metabolism properties of the synthesized Schiff base ligands (1-2) and their diorganotin(IV) complexes (3-10).

C. No.	CYP 1A2 inhibitor	CYP1A2 substrate	CYP2C19 inhibitor	CYP2C19 substrate	CYP2C9 inhibitor	CYP2C9 substrate	CYP2D6 inhibitor	CYP2D6 substrate	CYP3A4 inhibitor	CYP3A4 substrate
1.	0.939	0.396	0.951	0.091	0.772	0.93	0.322	0.116	0.647	0.665
2.	0.922	0.404	0.94	0.072	0.804	0.915	0.421	0.126	0.552	0.695
3.	0.820	0.898	0.945	0.408	0.906	0.923	0.002	0.044	0.349	0.94
4.	0.741	0.852	0.968	0.382	0.819	0.893	0.0	0.019	0.323	0.926
5.	0.431	0.489	0.917	0.313	0.517	0.927	0.00	0.017	0.199	0.899
6.	0.641	0.575	0.919	0.168	0.736	0.909	0.00	0.015	0.246	0.935
7.	0.760	0.881	0.941	0.269	0.899	0.915	0.005	0.045	0.26	0.941
8.	0.682	0.821	0.963	0.251	0.829	0.872	0.000	0.020	0.239	0.927
9.	0.477	0.409	0.909	0.199	0.506	0.915	0.000	0.017	0.165	0.900

10.	0.580	0.500	0.917	0.127	0.785	0.901	0.000	0.014	0.214	0.936
Cytochrome P450 enzymes (CYPs) such as CYP1A2, CYP2C19, CYP2C9, CYP2D6, CYP3A4										

Table S10. Excretion properties of the synthesized Schiff base ligands (1-2) and their diorganotin(IV) complexes (3-10).

C. No.	Clearance	Half life (T ½)
1.	3.264	0.292
2.	3.129	0.157
3.	1.827	0.026
4.	4.666	0.016
5.	4.359	0.006
6.	1.753	0.008
7.	1.9	0.018
8	4.375	0.010
9.	4.125	0.004
10.	1.773	0.006

Table S11. Toxicity properties of the synthesized Schiff base ligands (1-2) and their diorganotin(IV) complexes (3-10).

C. No.	hERG Blockers	H-HT	DILI	AMES Toxicity	Rat Oral Acute Toxicity	FDAMDD	Skin Sensitization	Carcinogenicity	Eye Corrosion	Eye Irritation	Respiratory Toxicity
1.	0.002	0.55	0.985	0.688	0.329	0.754	0.631	0.744	0.003	0.902	0.494
2.	0.005	0.625	0.984	0.69	0.331	0.876	0.315	0.717	0.003	0.757	0.101
3	0.015	0.245	0.979	0.097	0.053	0.99	0.908	0.151	0.003	0.906	0.695
4.	0.025	0.092	0.986	0.049	0.341	0.996	0.919	0.073	0.003	0.755	0.675
5.	0.029	0.013	0.98	0.037	0.165	0.994	0.935	0.119	0.003	0.584	0.571
6.	0.054	0.154	0.99	0.248	0.177	0.99	0.881	0.298	0.003	0.922	0.040
7.	0.04	0.205	0.98	0.059	0.059	0.99	0.768	0.131	0.003	0.851	0.629
8.	0.056	0.095	0.987	0.032	0.354	0.996	0.881	0.064	0.003	0.641	0.589
9.	0.043	0.135	0.983	0.034	0.197	0.993	0.913	0.079	0.003	0.501	0.547
10.	0.070	0.139	0.99	0.182	0.210	0.992	0.703	0.220	0.003	0.898	0.028

hERG (human Ether-à-go-go-Related Gene) channel inhibition, **Drug-Induced Liver Injury (DILI)**, **Ames toxicity (mutagenicity test)**

Table S12. Environmental toxicity properties of the synthesized Schiff base ligands (1-2) and their diorganotin(IV) complexes (3-10).

C. No.	Bioconcentration Factors	IGC50	LC50FM	LC50DM
1.	2.565	4.969	5.323	5.073
2.	2.688	5.143	5.576	5.349
3.	2.713	5.509	7.157	6.117
4.	2.423	5.526	7.328	6.573
5.	1.946	5.86	6.938	6.402
6.	2.518	5.91	7.459	6.452
7.	2.973	5.677	7.433	6.384
8.	2.474	5.69	7.621	6.658
9.	1.986	6.0	7.175	6.484
10.	2.564	6.055	7.736	6.534
Bioconcentration Factor (BCF), **IGC50 (growth inhibition concentration for Tetrahymena pyriformis)**, **LC50FM (lethal concentration for fathead minnow)**, and **LC50DM (lethal concentration for Daphnia magna)**				

Table S13. Tox21 pathway properties of the synthesized Schiff base ligands (1-2) and their diorganotin(IV) complexes (3-10).

C. No.	NR-AR	NR-AR-LBD	NR-AhR	NR-Aromatase	NR-ER	NR-ER-LBD	NR-PPAR-gamma	SR-ARE	SR-ATAD5	SR-HSE	SR-MMP	SR-p53
1.	0.038	0.17	0.925	0.915	0.744	0.724	0.754	0.947	0.339	0.946	0.973	0.764
2.	0.044	0.053	0.932	0.915	0.663	0.366	0.615	0.953	0.243	0.953	0.98	0.855
3.	0.026	0.967	0.733	0.958	0.629	0.895	0.993	0.987	0.955	0.99	0.957	0.952
4.	0.002	0.978	0.696	0.956	0.954	0.95	0.998	0.993	0.99	0.996	0.988	0.993
5.	0.001	0.964	0.502	0.98	0.694	0.883	0.998	0.995	0.94	0.997	0.993	0.991
6.	0.003	0.984	0.765	0.942	0.928	0.903	0.995	0.995	0.99	0.995	0.987	0.979
7.	0.024	0.956	0.79	0.96	0.662	0.792	0.992	0.988	0.939	0.991	0.964	0.967
8.	0.002	0.969	0.754	0.957	0.959	0.892	0.997	0.994	0.982	0.997	0.990	0.995

9.	0.001	0.949	0.579	0.980	0.730	0.777	0.997	0.995	0.894	0.998	0.994	0.994
10.	0.003	0.978	0.810	0.944	0.934	0.809	0.995	0.996	0.982	0.995	0.989	0.986

NR-AR: Nuclear Receptor - Androgen Receptor, NR-AR-LBD: Nuclear Receptor - Androgen Receptor Ligand Binding Domain, NR-AhR: Nuclear Receptor - Aryl Hydrocarbon Receptor, NR-Aromatase: Nuclear Receptor - Aromatase Enzyme (CYP19A1), NR-ER: Nuclear Receptor - Estrogen Receptor, NR-ER-LBD: Nuclear Receptor - Estrogen Receptor Ligand Binding Domain, NR-PPAR-gamma: Nuclear Receptor - Peroxisome Proliferator-Activated Receptor Gamma, SR-ARE: Stress Response - Antioxidant Response Element, SR-ATAD5: Stress Response - ATPase Family AAA Domain-Containing Protein 5, SR-HSE: Stress Response - Heat Shock Element, SR-MMP: Stress Response - Mitochondrial Membrane Potential, SR-p53: Stress Response - Tumor Suppressor Protein p53

Table S14. Toxicophore Rules of the synthesized Schiff base ligands (1-2) and their diorganotin(IV) complexes (3-10).

C. No.	Acute Toxicity Rule	Genotoxic Carcinogenicity Rule	NonGenotoxic Carcinogenicity Rule	Skin Sensitization Rule	Aquatic Toxicity Rule	Non-Biodegradable Rule	SureChEMBL Rule
1.	0	2	1	3	0	0	3
2.	0	2	2	3	1	1	3
3.	0	1	0	0	2	0	0
4.	0	1	0	0	2	0	0
5.	0	1	0	0	2	2	0
6.	0	1	0	0	2	0	0
7.	0	1	1	0	3	1	0
8.	0	1	1	0	3	1	0
9.	0	1	1	0	3	1	0
10	0	1	1	0	3	1	0