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Studies of effect of molecular structure and alkyl groups bound with tin(IV) on their cytotoxicity of organotin(IV) 2-phenyl-4-selenazole carboxylates

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1. Preparation of the ligand

2-Phenyl-4-selenazole carboxylic acid prepared by the modified methods reported in the literature [S1-S3]. The detailed synthesis procedure was described as bellow:

(1). Synthesis of selenium substituted benzamide

A mixture of 100 mmol selenium and 120 mmol sodium borohydride was added to a 250 mL round bottom flask, which was vacuumized and purged with nitrogen. Then 50 mL anhydrous ethanol was added slowly under the ice condition. The reaction mixture was stirred for 1 h. The excess of sodium borohydride was destroyed by refluxing and the NaHSe solution system was obtained.

To a solution of NaHSe system was added anhydrous pyridine (16 mL) and benzonitrile (100 mmol) dropwise at room temperature. The reaction mixture was refluxed for 5 h. After that, the mixture was acidified with 2 mol/L HCl solution and then refluxed for 0.5 h. The salts were removed by hot filtration, and the filtrate was stirred for 0.5 h under the condition of ice-water. After that, the yellow crude product was obtained by filtration, which was recrystallized from benzene to give selenium substituted benzamide. Yield: 85%.

(2). Synthesis of 2-phenyl-4-chloro-methyl selenazole

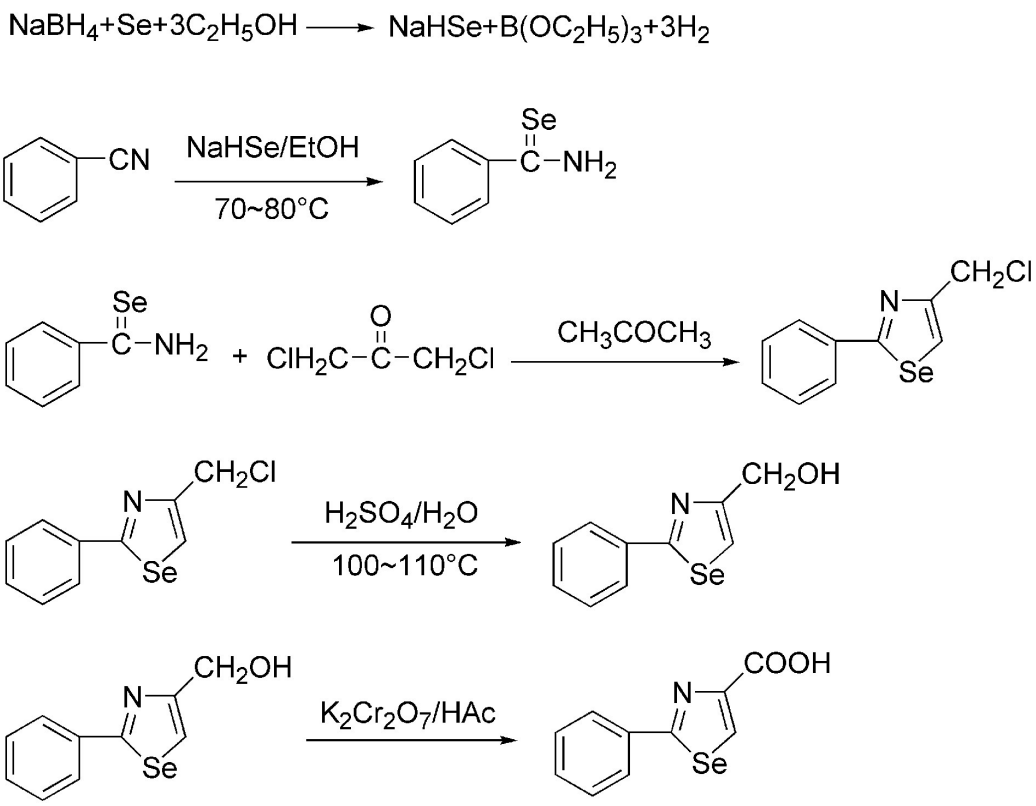
A mixture of selenium substituted benzamide (50 mmol) and 1,3-dichloroacetone (50 mmol) in acetone (50 mL) was stirred for 2 h at room temperature, which allowed to stand overnight at 0 ℃. After that, the mixture was filtered, and the precipitate was acidified with sulfuric acid (10 mL) and stirred for 15 min. Then water (30 mL) was added and the solution was adjusted with NaOH to pH = 8. The salts were removed by filtration and the filtrate was extracted with chloroform. The solvent was removed for the combined extract under the reduced pressure, and the resulting residue was recrystallized from ether to afford 2-phenyl-4-chloro-methyl selenazole. Yield: 79%.

(3). Synthesis of 2-phenyl-4-selenazole methanol

A mixture of 2-phenyl-4-chloro-methyl selenazole (20 mmol), water (60 mL) and concentrated sulfuric acid (15 mL) was heated at reflux for 8 h. Then the solution was adjusted with NaOH to pH = 8 and extracted with chloroform. The solvent was removed for the combined extract under the reduced pressure, and the resulting residue was recrystallized from ether to afford 2-phenyl-4-selenazole methanol. Yield: 86%.

(4). Synthesis of 2-phenyl-4-selenazole carboxylic acid

To a mixture of 2-phenyl-4-selenazole methanol (10 mmol) in HAc (50 mL) was added $K_2Cr_2O_7$ (20 mmol). The reaction mixture was heated at reflux for 2 h. Then, HAc was removed under the reduced pressure. The residue was treated with diluted HCl (50 mL) and stirred for 3 h. The solid which separated was collected by filtration and washed with water (2 × 25 mL). The solid obtained above was dissolved into the solution of NaOH. After that, diluted sulfuric acid was added dropwise into the reaction mixture. After a short time, some white precipitates were formed which were collected by filtration. The crude product was crystallized from methanol-water solution to give 2-phenyl-4-selenazole carboxylic acid. Yield: 41%. M.p: 166-168 ºC. Anal. Calc. for $C_{10}H_7O_2NSe$: C, 47.63; H, 2.79; N, 5.56%. Found: C, 47.27; H, 2.41; N, 5.78%. IR (KBr, cm-1): 3441, 1683(-COOH); ^{1}H NMR (400Hz, $CDCl_3$, ppm): δ = 8.98 (s, 1H, Se-CH); 7.95-7.42 (m, 5H, Ar-H).



Scheme S1. Synthesis procedure of 2-phenyl-4-selenazole carboxylic acid ligand.

Table S1. Crystal data and structure refinement parameters for complexes **1-3**.

Compound	**1**	**2**	**3**
Empirical formula	$C_{28}H_{21}NO_2SeSn$	$C_{144}H_{192}N_8O_{20}Se_6Sn_8$	$C_{114}H_{167}N_5O_{12}Se_5Sn_4$
Formula weight	601.11	3778.34	2669.09
Temperature [K]	298(2)	298(2)	298(2)
Wavelength (Å)	0.71073	0.71073	0.71073
Crystal system	Triclinic	Triclinic	Monoclinic
Space group	P-1	P-1	P2(1)/c
a [Å]	9.9209(9)	12.8180(12)	21.0757(13)
b [Å]	14.2128(13)	14.5201(14)	16.4218(11)
c [Å]	18.9285(17)	23.081(2)	36.968(3)
α [°]	109.323(2)	95.0770(10)	90.00
β [°]	101.2380(10)	92.2830(10)	97.594(8)
γ [°]	94.0190(10)	112.183(2)	90.00
Volume [$Å^3$]	2444.1(4)	3949.7(7)	12682.4(15)
Z	4	1	4
Calculated d [g/cm^3]	1.634	1.588	1.398
Absorption coefficient [mm^{-1}]	2.560	2.687	2.267
F (000)	1184	1876	5408
Crystal size [mm]	0.42 × 0.40 × 0.31	0.24 × 0.19 × 0.11	0.91 × 0.72 × 0.49
Theta range for data collection [°]	2.43-25.02	2.21-25.02	2.54-25.02
Limiting indices	-11 ≤ h ≤11	-15 ≤ h ≤10	-14 ≤ h ≤25
	-15≤ k ≤16	-17 ≤ h ≤17	-19≤ k ≤17
	-22≤ l ≤ 16	-26≤ l ≤ 27	-43≤ l ≤ 42
Reflections collected	12463	20077	45786
Independent reflections	8507	13721	22370
R(int)	0.0301	0.0929	0.1312
Completeness to theta = 25.02°	98.7%	98.5%	99.9 %
Max. and min. transmission	0.6924 and 0.6155	0.7565 and 0.5649	1.0000 and 0.9369
Data / restraints / parameters	8507 / 0 / 595	13721 / 1993 / 807	22370 / 0 / 1270
Goodness-of-fit on F^2	0.942	1.042	1.02014
Final R indices [I>2σ (I)]	R1 = 0.0347, wR2 = 0.0716	R1 = 0.1361, wR2 = 0.3662	R1 = 0.1206, wR2 = 0.2779
R indices (all data)	R1 = 0.0580, wR2 = 0.0787	R1 = 0.2688, wR2 = 0.3255	R1 = 0.2878, wR2 = 0.4023
Largest diff. peak and hole [$e·Å^{-3}$]	0.418 and -0.960	4.326 and -0.867	1.366 and -1.222

Table S2 Crystal data and structure refinement parameters for complexes **4** and **5**.

Compound	**4**	**5**
Empirical formula	$C_{52}H_{84}C_{l2}N_2O_6Se_2Sn_4$	$C_{2853.8}H_{65.40}Cl_4N4O_{12}Se_4Sn_8$
Formula weight	1536.79	2367.26
Temperature [K]	298(2)	293(2)
Wavelength (Å)	0.71073	0.71073
Crystal system	Monoclinic	Triclinic
Space group	P2(1)/n	P-1
a [Å]	11.656(7)	10.9295(5)
b [Å]	22.167(13)	14.0488(6)
c [Å]	25.229(15)	14.6562(7)
α [°]	90	107.5950(10)
β [°]	101.513(8)	92.3480(10)
γ [°]	90	112.045(2)
Volume [$Å^3$]	6387(7)	1957.69(15)
Z	4	1
Calculated d [g/cm^3]	1.598	2.008
Absorption coefficient [mm^{-1}]	2.812	4.554
F (000)	3040	1116
Crystal size [mm]	0.38 × 0.34 × 0.31	0.73 × 0.58 × 0.21
Theta range for data collection [°]	2.36-25.02	2.65-25.02
Limiting indices	-13 ≤ h ≤13	-13 ≤ h ≤12
	-26≤ k ≤26	-16≤ k ≤16
	-27≤ l ≤ 30	-17≤ l ≤ 17
Reflections collected	30843	11966
Independent reflections	11130	6889
R(int)	0.1395	0.0279
Completeness to theta = 25.02°	98.7%	99.9%
Max. and min. transmission	0.4760 and 0.4146	0.5762 and 0.4537
Data / restraints / parameters	11130 / 148 / 597	6889 / 0 / 541
Goodness-of-fit on F^2	1.091	1.134
Final R indices [I>2σ (I)]	R1 = 0.1250, wR2 = 0.2210	R1 = 0.0443, wR2 = 0.1089
R indices (all data)	R1 = 0.2672, wR2 = 0.2925	R1 = 0.0630, wR2 = 0.1207
Largest diff. peak and hole [$e.Å^{-3}$]	1.201 and -1.261	0.985 and -0.647

Table S3 Selected bond lengths (Å) and angles (º) for compound **1**.

Sn1-O1	2.086(3)	Sn2-O4	2.064(3)
Sn1-C11	2.110(4)	Sn2-C39	2.118(4)
Sn1-C17	2.115(4)	Sn2-C51	2.120(4)
Sn1-C23	2.120(4)	Sn2-C45	2.135(4)
O1-Sn1-C11	104.31(13)	O4-Sn2-C39	112.33(14)
O1-Sn1-C17	113.49(13)	O4-Sn2-C51	117.67(17)
C11-Sn1-C17	117.38(15)	C39-Sn2-C45	109.74(16)
O1-Sn1-C23	98.08(12)	O4-Sn2-C45	94.94(14)
C11-Sn1-C23	111.49(15)	C39-Sn2-C51	117.67(17)
C17-Sn1-C23	110.31(15)	C51-Sn2-C45	111.92(16)

Table S4 Selected bond lengths (Å) and angles (º) for compound **2**.

Sn1-C25	2.03(2)	Sn2-O3	1.775(14)
Sn1-C21	2.09(2)	Sn2-C33	2.05(2)
Sn1-O3	2.199(12)	Sn2-C29	2.07(3)
Sn1-O3#1	2.247(14)	Sn2-O2	2.210(17)
Sn1-O4	2.251(18)	Sn2-O4	2.401(17)
C25-Sn1-C21	128.0(10)	O3-Sn2-C33	108.7(9)
C25-Sn1-O3	116.3(8)	O3-Sn2-C29	109.3(9)
C21-Sn1-O3	114.2(7)	C33-Sn2-C29	139.8(11)
C25-Sn1-O3#1	98.9(9)	O3-Sn2-O2	75.9(6)
C21-Sn1-O3#1	97.6(9)	C33-Sn2-O2	100.3(8)
O3-Sn1-O3#1	83.9(5)	C29-Sn2-O2	101.2(8)
C25-Sn1-O4	94.4(9)	O3-Sn2-O4	71.1(6)
C21-Sn1-O4	93.7(9)	C33-Sn2-O4	93.6(8)
O3-Sn1-O4	67.8(6)	C29-Sn2-O4	86.5(8)
O3#1-Sn1-O4	151.6(6)	O2-Sn2-O4	146.8(7)

Symmetry transformations used to generate equivalent atoms: #1 -x+1, -y, -z+1

Table S5 Selected bond lengths (Å) and angles (º) for compound **3**.

Sn1-O4	2.014(13)	Sn3-O3	2.027(14)
Sn1-C9	2.06(2)	Sn3-C41	2.09(3)
Sn1-C1	2.13(2)	Sn3-O8	2.127(15)
Sn1-O9	2.162(14)	Sn3-C33	2.14(2)
Sn1-O5	2.384(15)	Sn3-O2	2.410(16)
Sn2-O4	2.045(13)	Sn4-O3	2.035(14)

Sn2-C49	2.11(2)	Sn4-C25	2.06(3)
Sn2-O3	2.131(14)	Sn4-C17	2.11(2)
Sn2-C57	2.14(3)	Sn4-O4	2.149(13)
Sn2-O5	2.316(14)	Sn4-O2	2.230(15)
O4-Sn1-C9	110.8(8)	O3-Sn3-C41	108.8(9)
O4-Sn1-C1	112.1(7)	O3-Sn3-O8	82.3(6)
C9-Sn1-C1	134.4(9)	C41-Sn3-O8	102.8(9)
O4-Sn1-O9	79.9(6)	O3-Sn3-C33	111.9(8)
C9-Sn1-O9	100.8(8)	C41-Sn3-C33	135.8(10)
C1-Sn1-O9	100.9(7)	O8-Sn3-C33	99.1(8)
O4-Sn1-O5	69.8(5)	O3-Sn3-O2	67.2(5)
C9-Sn1-O5	89.3(8)	C41-Sn3-O2	89.1(8)
C1-Sn1-O5	91.5(7)	O8-Sn3-O2	149.5(6)
O9-Sn1-O5	149.7(5)	C33-Sn3-O2	91.1(8)
O4-Sn2-C49	114.5(8)	O3-Sn4-C25	114.2(9)
O4-Sn2-O3	74.4(5)	O3-Sn4-C17	114.2(8)
C49-Sn2-O3	102.5(8)	C25-Sn4-C17	131.7(11)
O4-Sn2-C57	111.4(9)	O3-Sn4-O4	74.2(5)
C49-Sn2-C57	133.7(10)	C25-Sn4-O4	94.4(8)
O3-Sn2-C57	95.1(9)	C17-Sn4-O4	98.4(8)
O4-Sn2-O5	70.8(5)	O3-Sn4-O2	70.8(6)
C49-Sn2-O5	92.3(7)	C25-Sn4-O2	98.9(9)
O3-Sn2-O5	145.2(5)	C17-Sn4-O2	96.6(8)
C57-Sn2-O5	97.1(9)	O4-Sn4-O2	145.0(5)

Table S6 Selected bond lengths (Å) and angles (º) for compound **4**.

Sn1-O3	1.992(13)	Sn3-O4	2.077(15)
Sn1-C45	2.03(3)	Sn3-C41	2.08(2)
Sn1-C49	2.14(2)	Sn3-C37	2.12(2)
Sn1-O2	2.299(14)	Sn3-O3	2.130(12)
Sn1-Cl1	2.488(7)	Sn3-O5	2.333(18)
Sn2-O3	2.062(15)	Sn4-O4	2.002(15)
Sn2-O4	2.097(15)	Sn4-C23	2.05(3)
Sn2-C11	2.13(2)	Sn4-C19	2.18(4)
Sn2-C15	2.14(3)	Sn4-O5	2.305(16)
Sn2-O2	2.368(14)	Sn4-Cl2	2.493(8)
O3-Sn1-C45	115.8(10)	O3-Sn2-O4	74.9(5)
O3-Sn1-C49	115.7(9)	O3-Sn2-C11	110.3(9)
C45-Sn1-C49	127.8(12)	O4-Sn2-C11	101.7(8)
O3-Sn1-O2	71.4(5)	O3-Sn2-C15	110.0(10)
C45-Sn1-O2	93.8(10)	O4-Sn2-C15	98.8(10)
C49-Sn1-O2	94.2(9)	C11-Sn2-C15	138.2(12)

O3-Sn1-Cl1	84.2(4)	O3-Sn2-O2	68.8(5)
C45-Sn1-Cl1	96.3(9)	O4-Sn2-O2	143.7(5)
C49-Sn1-Cl1	97.0(8)	C11-Sn2-O2	90.1(8)
O2-Sn1-Cl1	155.5(4)	C15-Sn2-O2	94.4(10)
O4-Sn3-C41	109.1(9)	O4-Sn4-C23	114.8(10)
O4-Sn3-C37	109.0(7)	O4-Sn4-C19	115.2(13)
C41-Sn3-C37	140.0(9)	C23-Sn4-C19	128.0(15)
C41-Sn3-O3	103.1(7)	C19-Sn4-Cl2	101.6(12)
C37-Sn3-O3	98.6(7)	O5-Sn4-Cl2	155.6(5)
C41-Sn3-O5	88.1(9)	O4-Sn4-C20	106.8(14)
C37-Sn3-O5	94.0(7)	C23-Sn4-C20	138.3(16)
O3-Sn3-O5	143.6(6)	O5-Sn4-C20	103.4(15)

Table S7 Selected bond lengths (Å) and angles (º) for compound **5**.

Sn1-O3	2.042(5)	Sn2-O3	2.038(5)
Sn1-C12	2.085(9)	Sn2-C14	2.090(9)
Sn1-C11	2.097(9)	Sn2-C13	2.089(10)
Sn1-O3#1	2.109(5)	Sn2-O1	2.368(6)
Sn1-O1	2.312(59)	Sn2-Cl1	2.483(3)
O3-Sn1-C12	110.8(3)	O3-Sn2-C14	102.1(3)
O3-Sn1-C11	108.6(3)	O3-Sn2-C13	105.5(3)
C12-Sn1-C11	139.4(4)	C14-Sn2-C13	149.9(4)
O3-Sn1-O3#1	74.6(2)	O3-Sn2-O1	70.33(19)
C12-Sn1-O3#1	98.0(3)	C14-Sn2-O1	90.6(3)
C11-Sn1-O3#1	101.5(3)	C13-Sn2-O1	87.4(3)
C12-Sn1-O1	90.9(3)	C14-Sn2-Cl1	97.0(3)
C11-Sn1-O1	92.5(3)	C13-Sn2-Cl1	96.2(3)
O3#1-Sn1-O1	145.9(2)	O1-Sn2-Cl1	157.43(14)

Symmetry transformations used to generate equivalent atoms: #1 -x, -y, -z

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