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REGULAR ARTICLE

Silicon-containing diorganotin complexes with salicylaldehyde thiosemicarbazone and their anticancer activity

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Abstract. Eight novel silicon-containing diorganotin complexes with salicylaldehyde thiosemicarbazone were synthesized. They were characterized by ^{1}H NMR, ^{13}C NMR, IR spectra, elemental analysis and X-ray single-crystal diffraction. Spectroscopic and X-rays studies indicated that the thiosemicarbazone Schiff base and tin atom were coordinated as a parallel five- and six-membered heterocyclic structure. In addition, the bioassay of the synthesized complexes was performed and the results show that the silicon-containing diorganotin complexes with salicylaldehyde thiosemicarbazone have good anticancer activity on human breast cancer cells.

Keywords. Diorganotin; synthesis; structure; anticancer activity.

1. Introduction

Organotin compounds have been widely used in fields like industry, agriculture and others and the research on their bioactivities was getting more attention.[1–5] Schiff base ligands are widely favored in the synthesis of metal compounds due to their mild synthesis condition and good biological activity.[6–8] As a kind of Schiff base, the structure of salicylaldehyde thiosemicarbazone compounds contains the basic unit of activity =N(1)NH(C=S)N(4)H-, and the biological activity changes with the change of the group on N(1), which makes them have rich structural characteristics and antibacterial activity.[9–12] A series of complexes synthesized by zinc(II) with 5-nitro-salicylaldehyde-N-substituted thiosemicarbazones were characterized and showed that these zinc(II) complexes have significant antimicrobial activity against Staphylococcus aureus, Salmonella typhimurium and Candida albicans.[13] Elena Pahontuh combined thirty-two new complexes of Cu(II), Ni(II) and Zn(II) and salicylaldehyde thiosemicarbazone, the results indicated that most ligands and metal complexes showed significant selective and biological activity of Human Leukemia HL-60 Cells in the antimicrobial or antifungal activity tests.[14] Diorganotin compounds also have outstanding anti-tumor properties, but toxicity limits their development in medicine.[15] In agricultural applications, the introduction of silicon can effectively reduce the toxicity of metals, and the presence of Si atoms can often reduce the toxicity and increase the activity of compounds.[16,17] So we tried to investigate the effect of the introduction of silicon atoms on the biological activity of organotin complexes. On this basis, a series of new silicon-containing diorganotin complexes with salicylaldehyde thiosemicarbazone were designed and synthesized, and their biological activities were tested. The target complexes were characterized by ^{1}H NMR, ^{13}C NMR, IR spectra, elemental analysis and X-ray single-crystal diffraction.

2. Experimental

2.1 *Instruments and reagents*

The solvents used in the reaction are all commercially available analytical reagents, in which methanol is treated as an anhydrous solvent, and other solvents are used without further treatment. The intermediate containing silicon dihydrocarbyltin dichloride is synthesized by the reference method.[18] The ligand reference is synthesized by N(4)-phenyl thiosemi-

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carbazide and substituted salicylaldehyde,[17] recrystallized with absolute ethanol.

The instruments are Bruker Avance 400 nuclear magnetic resonance ($CDCl_3$, TMS), Vario EL III organic element analyzer; Guilin Optical instrument Factory X-5 melting Point measuring instrument (temperature uncorrected), Nicolet 460 FT infrared spectrometer) (KBr compression), Bruker APEX-II CCD X-ray single Crystal diffractometer).

2.2 *Synthesis and determination of target products*

2.2a *Synthesis of complexes*: **3aa**: Adding salicylaldehyde N(4)-phenylaminosulfur 0.272 g (1 mmol) into a 100 mL three-neck flask, charging an upper reflux condenser tube and a 25 mL drop liquid funnel, adding 30 mL of anhydrous methanol, and slightly heating to dissolve, adding 15 mL of a methanol solution containing 0.17 g (2 mmol) of sodium ethoxide under stirring, the reaction continues for 2 h, then adding $Ph(Me_3SiCH_2)SnCl_2$ 3.54 g (1 mmol) of anhydrous methanol solution (10 mL), continuing to heat and reflux for 8 h, cooling overnight, and filtering to obtain a dry solvent; filtering the filtrate while hot extracting with 30 mL of anhydrous n-hexane, cooling the filtrate, filtering to obtain a bright yellow powdery substance, 700 mg, and a yield of 63.6%, M.p. 105.6∼107.0 °C. FT-IR (KBr) ν: 3274, 3134, 3046, 1600, 1503, 1435, 1292, 1316, 1251, 1064, 837,755, 589, 519, 451. ^{1}H NMR (400MHz, $CDCl_3$) δ 8.64 (s, 1H, PhNH), 7.86 (d, J = 7.1 Hz, 2H, ArH), 7.54 (d, J = 7.8 Hz, 2H, ArH), 7.30∼7.37 (m, 6H, ArH), 7.13 (d, J = 7.5 Hz, 1H, ArH), 7.06 (t, J = 7.2 Hz, 1H, ArH), 6.92 (d, J = 8.5 Hz, 1H, ArH), 6.72 (t, J = 7.3 Hz, 1H, ArH_r), 6.67 (s, 1H, ArH), 0.78 (d, J = 12.4 Hz, 1H, $SnCH_2$), 0.71 (d, J = 12.5 Hz, 1H, $SnCH_2$), 0.05 (s, 9H, $SiCH_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.59 (C^8), 162.93 (C^7), 162.42 (C^2), 143.31 (C^{15}), 139.29 (C^9), 135.73 ($C^{16,20}$), 135.11 (C^6), 133.93 (C^4), 129.85 ($C^{11,13}$), 128.87 (C^{18}), 128.60 ($C^{17,19}$), 123.30 (C^{12}), 121.72 (C^5), 120.57 ($C^{10,14}$), 117.21 (C^3), 116.76 (C^1), 12.67 ($SnCH_2$), 1.17 ($SiCH_3$). Anal. calcd for $C_{24}H_{27}N_3OSSiSn$: C 52.19, H 4.93, N 7.61; found: C 52.27, H 4.99, N 7.52.

3ab–**3db** obtained by using similar synthetic method.

3ab: 780 mg, bright yellow powder, and a yield of 69.0%, M.p. 100.6∼102.1°C. FT-IR (KBr) ν: 3274, 3131, 3045, 1594, 1504, 1288, 1317, 1250, 1059, 823, 591, 500, 450. ^{1}H NMR (400 MHz, $CDCl_3$)δ 8.63 (s, 1H, PhNH), 7.85∼7.87 (m, 2H, ArH), 7.54 (d, J = 7.9 Hz, 2H, ArH), 7.30∼7.38 (m, 6H, ArH), 7.13 (d, J = 7.6 Hz, 1H, ArH), 7.06 (t, J = 7.4 Hz, 1H, ArH), 6.92 (d, J = 8.4 Hz, 1H, ArH), 6.68∼6.74 (m, 2H, ArH), 0.88 (t, J = 7.9 Hz, 3H, CH_3), 0.73 (d, J = 12.6 Hz, 2H, $SnCH_2$), 0.49 (d, J = 7.8 Hz, 2H, $SiCH_2$), 0.01 (s, 6H, $SiCH_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.65 (C^8), 162.93 (C^7), 162.42 (C^2), 143.43 (C^{15}), 139.38 (C^9), 135.73 ($C^{16,20}$), 135.10 (C^6), 133.93 (C^4), 129.85 ($C^{11,13}$), 128.86 (C^{18}), 128.59 ($C^{17,19}$), 123.29 (C^{12}), 121.71 (C^5), 120.57 ($C^{10,14}$), 117.20 (C^3), 116.87 (C^1), 10.79 ($SnCH_2$), 9.33 ($SiCH_2$), 7.36 (CH_3), −1.17 ($SiCH_3$). Anal. Calcd for $C_{25}H_{29}N_3OSSiSn$: C 53.02, H 5.16, N 7.42; found: C 53.11, H 5.22, N 7.37.

3ba: 430 mg, yellow powder, and a yield of 74.1%, M.p. 129.8∼131.5 °C. FT-IR (KBr) ν: 3287, 1586, 1503, 1429, 1211, 1312, 731, 1246, 1080, 831, 597, 504, 421. ^{1}H NMR (400MHz, $CDCl_3$)δ 8.63 (s, 1H, PhNH), 7.91∼7.93 (m, 2H, ArH), 7.55 (d, J = 7.8 Hz, 2H, ArH), 7.30∼7.39 (m, 5H, ArH), 7.06 (t, J = 7.4 Hz, 1H), 6.91∼6.96 (m, 1H), 6.75∼6.77 (m, 2H, ArH), 6.66 (t, J = 7.8 Hz, 1H), 3.91 (s, 3H, OCH_3), 0.84 (d, J = 12.6 Hz, 1H, $SnCH_2$), 0.77 (d, J = 12.6 Hz, 1H, $SnCH_2$), 0.05 (s, 9H, $SiCH_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.98 (C^8), 162.63 (C^7), 157.42 (C^3), 151.69 (C^2), 143.19 (C^{15}), 139.56 (C^9), 136.01 ($C^{16,20}$), 130.01 ($C^{11,13}$), 128.89 (C^{18}), 128.70∼127.96 ($C^{17,19}$), 125.55 (C^{12}), 123.43 (C^6), 120.74 (C^5), 117.11 ($C^{10,14}$), 116.74 (C^4), 116.19 (C^1), 56.50 (OCH_3), 12.68 ($SnCH_2$), 1.24 ($SiCH_3$). Anal.Calcd for $C_{25}H_{29}N_3O_2SSiSn$: C 51.56, H 5.02, N 7.10; found: C 51.70, H 5.09, N 7.14.

3bb: 480 mg, yellow powder, and a yield of 78.7%, M.p. 105.8∼107.4 °C. FT-IR (KBr) ν: 3316, 1586, 1503, 1429, 1209, 1318, 734, 1247, 1084, 831, 591, 508, 409. ^{1}H NMR (400MHz, $CDCl_3$) δ 8.62 (s, 1H, PhNH), 7.87∼7.95 (m, 2H, ArH), 7.54 (d, J = 7.7 Hz, 2H,ArH), 7.30∼7.38 (m, 5H, ArH), 7.06 (t, J = 7.4 Hz, 1H), 6.90∼6.96 (m, 1H), 6.75 (d, J = 6.7 Hz, 1H), 6.63∼6.69 (m, 2H, ArH), 3.90 (s, 3H, OCH_3), 0.87 (t, J = 7.9 Hz, 3H, CH_3), 0.77 (d, J = 12.6 Hz, 2H, $SnCH_2$), 0.49 (d, J = 8.1 Hz, 2H, $SiCH_2$), -0.01∼0.02 (m, 6H, $SiCH_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.81 (C^8), 162.48 (C^7), 157.22 (C^3), 151.54 (C^2), 143.06 (C^{15}), 139.41 (C^9), 135.82 ($C^{16,20}$), 129.83 ($C^{11,13}$), 128.87 (C^{18}), 128.58 ($C^{17,19}$), 125.37 (C^{12}), 123.27 (C^6), 120.53 (C^5), 116.95 ($C^{10,14}$), 116.58 (C^4), 116.01 (C^1), 56.38 (OCH_3), 10.67 ($SnCH_2$), 9.30 ($SiCH_2$), 7.34 (CH_3), −1.28 ($SiCH_3$). Anal. Calcd for $C_{26}H_{31}N_3O_2SSiSn$: C 52.36, H 5.24, N7.05; found: C 52.58, H 5.33, N 6.98.

3ca: 310 mg, yellow powder and a yield of 51.7%, M.p. 148.5∼151.1 °C. FT-IR (KBr) ν: 3320, 1601, 1499, 1429, 1179, 1318, 752, 1242, 1097, 831, 591, 504, 421. ^{1}H NMR (400MHz, $CDCl_3$) δ 8.68 (s, 1H, PhNH), 8.13∼8.23 (m, 2H, ArH), 7.81∼7.83 (m, 2H,ArH), 7.53 (d, J = 8.0 Hz, 2H, ArH), 7.31∼7.46 (m, 5H, ArH), 7.12 (t, J = 7.4 Hz, 1H, ArH), 6.92 (d, J = 9.2 Hz, 1H,ArH), 6.84 (s, 1H, ArH), 0.87 (d, J = 12.5 Hz, 1H, $SnCH_2$), 0.77 (d, J = 12.5 Hz, 1H, $SnCH_2$), 0.07 (s, 9H, $SiCH_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.48 (C^2), 164.22 (C^8), 160.32 (C^7), 142.21 (C^{15}), 138.83 (C^5), 138.17 (C^9), 135.83 ($C^{16,20}$), 135.54 ($C^{11,13}$), 130.68 (C^4), 130.36 (C^{18}), 129.56 ($C^{17,19}$), 128.94 (C^6), 124.02 (C^{12}), 122.20 ($C^{10,14}$), 121.07 (C^3), 116.03 (C^1), 13.25 ($SnCH_2$), 1.17 ($SiCH_3$). Anal.Calcd for $C_{24}H_{26}N_4O_3SSiSn$: C 48.26, H 4.39, N 9.38; found: C 48.26, H 4.51, 9.20.

3cb: 350 mg, yellow powder, a yield of 57.4%, M.p. 146.5∼151.5 °C. FT-IR (KBr) ν: 3327, 1603, 1506, 1434, 1188, 1321, 752, 1246, 1097, 826, 591, 504, 421. ^{1}H NMR (400MHz, $CDCl_3$) δ 8.68 (s, 1H, PhNH), 8.11∼8.24 (m, 2H, ArH), 7.72∼7.92 (m, 2H, ArH), 7.52 (d, J = 7.8 Hz, 2H, ArH), 7.33∼7.45 (m, 5H, ArH), 7.12 (t, J = 7.3 Hz, 1H, ArH), 6.92 (d, J = 9.2 Hz, 1H, ArH), 6.84 (s, 1H, ArH), 0.84∼0.92 (m, 4H, CH_3, $SnCH_2$), 0.75 (d, J = 12.5 Hz, 1H,

$SnCH_2$), 0.51 (d, J = 8.1 Hz, 2H, $SiCH_2$), 0.02 (d, J = 4.7 Hz, 6H, $SiCH_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.48 (C^2), 164.22 (C^8), 160.31 (C^7), 142.27 (C^{15}), 138.85 (C^5), 138.17 (C^9), 135.54 ($C^{16,20}$), 130.68 ($C^{11,13}$), 130.36 (C^4), 129.55 (C^{18}), 128.98 ($C^{17,19}$), 128.90 (C^6), 124.02 (C^{12}), 122.20 ($C^{10,14}$), 121.07 (C^3), 116.03 (C^1), 11.39 ($SnCH_2$), 9.30 ($SiCH_2$), 7.33 (CH_3), −1.14 ($SiCH_3$). Anal. Calcd for $C_{24}H_{32}N_4O_3SSiSn$: C 49.11, H 4.62, N 9.16; found: C 48.99, H 4.73, N 9.01.

3da: 370 mg, bright yellow powder, and a yield of 63.8%, M.p. 119.9∼122.1 °C. FT-IR (KBr) ν: 3360 ν(NH); 1609, 1515, 1435, 1216, 1314, 746, 1251, 1074, 833, 588, 516, 445. ^1H NMR (400MHz, $CDCl_3$) δ 8.56 (s, 1H, PhNH), 7.88 (d, J = 6.6 Hz, 2H, ArH), 7.53 (d, J = 8.3 Hz, 2H, ArH), 7.37∼7.41 (m, 3H, ArH), 7.30 (t, J = 7.5 Hz, 2H, ArH), 7.01∼7.06 (m, 2H, ArH), 6.59 (d, 1H, J = 4.0 Hz, ArH), 6.33∼6.38 (m, 2H, ArH), 3.85 (s, 3H, OCH_3), 0.79 (d, J = 12.5 Hz, 1H, $SnCH_2$), 0.70 (d, J = 12.5 Hz, 1H, $SnCH_2$), 0.06 (d, J = 2.2 Hz, 9H, $SiCH_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 169.23 (C^8), 166.13 (C^4), 162.08 (C^2), 161.28 (C^7), 143.59 (C^{15}), 139.65 (C^9), 135.74 ($C^{16,20}$), 135.50 (C^6), 129.80 ($C^{11,13}$), 128.84 (C^{18}), 128.59 ($C^{17,19}$), 122.97 (C^{12}), 120.28 ($C^{10,14}$), 110.88 (C^1), 107.20 (C^5), 103.74 (C^3), 55.44 (OCH_3), 12.66 ($SnCH_2$), 1.21 ($SiCH_3$). Anal. Calcd for $C_{25}H_{29}N_3O_2SSi_2Sn$: C 51.56, H 5.02, N 7.22; found: C 51.09, H 5.07, N 6.93.

3db: 430 mg, bright yellow powder, and a yield of 70.3%, M.p. 71.2∼73.3 °C. FT-IR (KBr) ν: 3379, 1609, 1511, 1433, 1216, 1311, 737, 1251, 1072, 824, 588, 501, 442. ^1H NMR (400MHz, $CDCl_3$) δ 8.56 (s, 1H, PhNH), 7.86∼7.88 (m, 2H, ArH), 7.53 (d, J = 8.3 Hz, 2H, ArH), 7.36∼7.41 (m, 3H, ArH), 7.31 (t, J = 7.7 Hz, 2H, ArH), 6.97∼7.08 (m, 2H, ArH), 6.58 (s, 1H, ArH), 6.28∼6.41 (m, 2H, ArH), 3.85 (s, 3H, OCH_3), 0.89 (t, J = 7.9 Hz, 3H, CH_3), 0.76 (d, J = 12.5 Hz, 1H, $SnCH_2$), 0.68 (d, J = 12.6 Hz, 1H, $SnCH_2$), 0.50 (d, J = 7.7 Hz, 2H, $SiCH_2$), 0.02 (d, J = 2.9 Hz, 6H, $SiCH_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.22 (C^8), 166.12 (C^4), 162.07 (C^2), 161.27 (C^7), 143.64 (C^{15}), 139.65 (C^9), 135.73 ($C^{16,20}$), 135.49 (C^6), 129.78 ($C^{11,13}$), 128.83 (C^{18}), 128.57 ($C^{17,19}$), 122.96 (C^{12}), 120.26 ($C^{10,14}$), 110.88 (C^1), 107.17 (C^5), 103.74 (C^3), 55.43 (OCH_3), 10.77 ($SnCH_2$), 9.36 ($SiCH_2$), 7.39 (CH_3), −1.15 ($SiCH_3$). Anal. Calcd for $C_{26}H_{31}N_3O_2SSi_2Sn$: C 52.36, H 5.24, N 7.05; found: C 51.72, H 5.29, N 6.83.

2.2b *Determination of crystal structure*: The crystal suitable for single crystal diffraction was obtained by solvent volatilization method. The single crystal of complex **3ab** and **3da** of suitable size were selected and placed on the SMART-APEX II CCD diffractometer of Bruker Company. The scanning mode was $\omega/2\theta$ and the Mo-Kα ray (λ = 0.71073Å) of graphite Monochromator was used as light source. At the temperature of 296(2)K, the diffraction data of complex **3ab** and **3da** were collected, in the range of $2.50 \leq \theta \leq 25.50$ and $3.08 \leq \theta \leq 26.48$, all the diffraction points 19917 and 92228 are collected, and all the data are calculated on the computer by Bruker SHELXL-97 program, the crystal structure is solved by direct method. All the data were corrected by Lp factor and experiential absorption. All the non-hydrogen atom coordinates were determined successively in the subsequent differential Fourier synthesis, and the anisotropic parameters were modified by the full matrix two-multiplication method. The CCDC numbers of the complexes **3ab** and **3da** are 1022840 and 1040959.

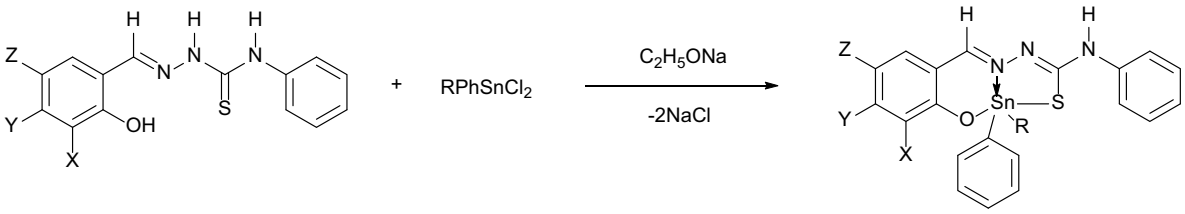
2.2c *Anticancer activity test*: The antitumor activity of human MDA-MB-231 and MCF-7 breast cancer cell lines in vitro was tested by cell Counting K it-8 (CCK-8) assay. The inhibition rate of the sample on tumor cells was calculated indirectly by measuring the absorbance value (OD value) of the cell fluid in the culture medium. The test set up six concentration gradients of 500 mg/L, 100 mg/L, 50 mg/L, 25 mg/L, 12.5 mg/L, 6.25 mg/L, and the steps were as follows: after inoculating 1.5×10^4 tumor cells in each hole of the 96 hole plastic culture plate, they were placed in an incubator (37 °C, concentration of carbon dioxide was 5%). The tumor cells were attached to the wall. After 24 h, the original culture medium was taken out, and the culture medium containing different concentration of DMSO solution was added. At the same time, the control group with various concentrations of DMSO solvent and the blank group with only medium were placed. After the plate was laid, the culture was continued in the incubator for 48 h, and the first 4 h after incubation, 10 μL of CCK-8 was added to each hole for 4 h after incubating in the incubator. The culture plate was quickly removed, the OD value of the medium was measured at the 450 nm wavelength by an enzyme marker, and the average value was calculated by the method of choice. The inhibition rate was calculated by the following formula:

$$\text{Inhibition rate (\%)} = (\text{OD value of control group} - \text{OD value of experimental group})/\text{OD value of control group} \times 100\%$$

3. Results and Discussion

3.1 *Synthesis*

N(4)-phenylthiosemicarbazide was synthesized by literature,[18] and reacted with four silicon-containing dialkyltins to obtain eight target diorganotin complexes separately. Intermediate $(Me_3SiCH_2)PhSnCl_2$ and $(Me_3SiEtCH_2)PhSnCl_2$ were synthesized by literature.[19] The synthetic method of organotin Schiff base chelates has been reported in the literature.[20] In this paper, triethylamine was used as deprotonation agent to synthesize organotin Schiff base chelates, but the by-product triethylamine hydrochloride was difficult to remove, which made the obtained products impure. When sodium ethoxide was used as a base instead of triethylamine, satisfactory results were obtained. The reaction equation is as follows:



1

1a: X=Y=Z=H

1b: X=OCH_3, Y=Z=H

1c: X=Y=H, Z=NO_2

1d: X=Z=H, Y=OCH_3

2

2a: R=Me_3SiCH_2

2b: R=$Me_2EtSiCH_2$

3

3aa: X=Y=Z=H, R=Me_3SiCH_2

3ab: X=Y=Z=H, R=$Me_2EtSiCH_2$

3ba: X=OCH_3, Y=Z=H, R=Me_3SiCH_2

3bb: X=OCH_3, Y=Z=H, R=$Me_2EtSiCH_2$

3ca: X=Y=H, Z=NO_2, R=Me_3SiCH_2

3cb: X=Y=H, Z=NO_2, R=$Me_2EtSiCH_2$

3da: X=Z=H, Y=OCH_3, R=Me_3SiCH_2

3db: X=Z=H, Y=OCH_3, R=$Me_2EtSiCH_2$

3.2 *Structural analysis*

The structure of the target product was preliminarily determined by IR, ^{1}H NMR and ^{13}C NMR spectra.

The IR spectra showed that no sharp bands of S-H bond were found in 2700∼2550 cm^{-1}, indicating that the complexes may exist in the form of thioketom tautomers in the solid state. According to the related literatures,[21,22] the absorption peaks at 1250∼1247 cm^{-1} and 836∼823 cm^{-1} belong to δ(SiCH$_3$) and v(Si-C), respectively. Comparing with the spectra of ligands, the spectra of target compounds showed that the v(O-H) absorption peak at 3200∼3000 cm^{-1} in the ligands disappeared, and the v(C-O) absorption peak at 1290∼1250 cm^{-1} shifted to the low wavenumber direction after the formation of the complexes; v(Sn-O) absorption peak appeared at 510∼485 cm^{-1} in the complexes, which proved the formation of Sn-O in the complexes. In addition, the absorption peaks of v(C-S) at 1348∼1320 cm^{-1} and 887∼826 cm^{-1} in the ligands moved towards low wavenumber, which may be due to the formation of C-S single bond and tin atom by the ligands through tautomerism. The absorption peaks of v(N-N) at 1075∼1026 cm^{-1} in ligands were shifted to 1100∼1033 cm^{-1}, and the absorption peaks of v(Sn-N) at 450∼410 cm^{-1} indicated the formation of Sn-N bonds. Combined with the above data, the complexes were formed by the binding of the ligands with phenolic hydroxyl oxygen, imine nitrogen and sulfur of mercaptan with the central tin atom.

From the ^{1}H NMR data of the complexes, it was observed that the signal of phenolic hydroxy hydrogen (δ9.28∼10.16) and hydrazine hydrogen (δ11.62∼11.67) disappeared after the formation of the complexes. It is shown that the ligands are coordinated with the central tin atom by two groups of phenolic hydroxyl oxygen and hydrazine group. The PhN-H (δ10.1∼11.6) signal in the ligands moved to the high field (δ8.54∼9.49), which may be due to the disappearance of the hydrogen bond in the ligands after the formation of the complexes. The hydrogen signal of CH=N in the ligands was transferred from (δ8.37∼9.15) to (δ7.53∼8.24) because the N atom of CH=N coordinated with the central tin atom when the target compound was formed. Two hydrogen atoms in SnCH$_2$ directly connected to a tin atom are coupled to form a quadruplex (0.76∼0.79 and 0.69∼0.72, J = 12.5Hz) because of the central tin atoms combined with four different groups causing the two hydrogens to be located in a different environment.

In the ^{13}C NMR of ligands, the corollaries in IR and ^{1}H NMR were further verified. After the formation of the complex, the resonance signal of NH-C=S in the spectra of the ligands shifted from 175.68∼176.14 ppm to 162.04∼168.79 ppm in the complexes spectra, which can be considered as an N=C-S group and coordinated with the central tin atom. The resonance signal of CH=N moves from 139.60∼143.95 ppm to low field to 160.31∼162.93 ppm. This may be due to the coordination of N atom in CH=N with the central tin atom, which reduces the electron cloud density of double bond in CH=N and increases the chemical shift.

Figure 1. Complex **3ab**.

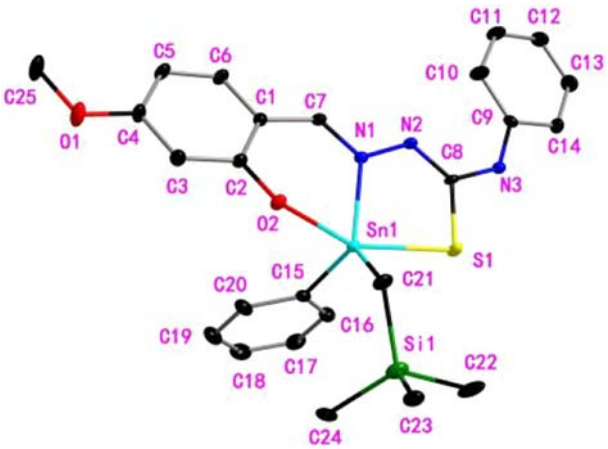


Figure 2. Complex **3da**.

3.3 *Crystal structure*

The molecular structures of the complexes **3ab** and **3da** were determined by X-ray single-crystal diffraction. The crystal data and related materials are listed in the supporting materials Table S1 and S2 (Supplementary Information). The CCDC numbers are 1022840 and 1040959. The molecular structures of the complexes are shown in Figures 1 and 2.

From the X-ray diffraction analysis, it is found that the methyl carbon atom in a silicon hydrocarbyl group in the complex **3da** has a disordered structure, which is due to the crystallographic parameters collected at room temperature.

By observing the molecular structure of **3ab** and **3da**, it was found that both of them were obtained by the reaction of salicylaldehyde acetal, thiourea and mixed dialkyltin dichloride containing silicon to form a pentagonal tin mononuclear center molecule, thus forming a distorted triangular bipyramidal geometry. While thiosemicarbazone Schiff base is used as a ligand to form five-member and six-member heterocyclic parallel structures through the coordination of oxygen, nitrogen, sulfur and tin atoms. In this paper, the structure of the complex **3ab** is discussed as an example, in which two hydrocarbon groups in imine nitrogen and dialkyltin form the equatorial plane. However, the degree of the angle between phenol O and mercaptan S occupies its axial position. The axial angle of O(1)-Sn(1)-S(1) is 154.10 (7)°, which indicates that the structure deviates from the ideal triangular bipyramidal geometry and is a twisted triangular bipyramidal geometry. Sn(1) and N(1), C(15), C(21) in the equatorial position is: C(15)-Sn-(1)-C(21) 124.19 (14)°, respectively, C(15)-Sn(1)-N(1) 102.00 (11)°, C(21)-Sn(1)-N(1) 133.70 (13)°, the sum of the triangles is 359.89°. Therefore, the axial angle of Sn (1) and N (1), C (15), C (21) are coplanar.

In the molecule of **3ab**, the distance of Sn-S is 2.5229(11)Å, which is close to the sum of covalent radius between Sn and S atoms, but is much smaller than that of van der wals radius (4.0Å) between two atoms. This indicated that the complex formed a strong Sn-S bond. The distance between Sn(1)-N(1) is 2.219(3), Sn(1)-O(1) is 2.103(2), which is very close to the sum of the covalent radius of Sn-N (2.15Å) and Sn-O (2.10Å). It is shown that the central tin atom has a strong interaction with phenolic O and imine. The bond length of C(8)-S(1) bond increases from 1.680(2)Å of the ligand to 1.741(3)Å. The distance between C(8)-N(2) was reduced from 1.353(3)Å to 1.291(4)Å, which indicated that the ligand formed a complex with tautomerism and electron delocalization of mercaptan and ketone. The C-S bond is changed from double bond to a single bond, while C(8)-N(2) becomes a double bond, which is consistent with the results of IR and NMR analysis.

Combined with infrared and nuclear magnetic resonance data, it can be inferred that other compounds also have similar structures.

3.4 *In vitro anticancer activity*

The antitumor activity against human MDA-MB-231 and MCF-7 breast cancer cell lines were tested by Cell Counting K it-8(CCK-8) method *in vitro*. The results are shown in Tables 1 and 2.

According to the above test data, *in vitro* activity test of human breast cancer cell MDA-MB-231, most of the complexes showed good biological activity, except for **3da** in the range of 100–50 mg/L. The inhibition rates of the other complexes were above 96%, and the activities of **3aa**, **3ca** and **3da** decreased significantly when the concentration was reduced to 25 mg/L. The inhibition rate of other complexes remained more than 93%. When the concentration decreased to 12.5 mg/L, the inhibition rate of **3bb** remained more than 90%. The inhibition rate of cisplatin was reduced to 29.93%. *In vitro* activity test

Table 1. *In vitro* antitumor activity of title complexes against MDA-MB-231.

Complex	Inhibition rate%				
	100 mg · L^{-1}	50 mg · L^{-1}	25 mg · L^{-1}	12.5 mg · L^{-1}	6.25 mg · L^{-1}
3aa	97.41	96.32	54.43	52.92	43.29
3ab	96.99	97.28	94.47	36.60	30.36
3ba	98.28	97.19	96.73	93.14	–
3bb	99.82	98.13	97.21	86.93	12.73
3ca	98.72	97.55	64.63	22.61	4.33
3cb	98.32	96.97	96.77	69.25	18.93
3da	97.06	78.76	47.98	19.93	14.46
3db	99.74	97.44	93.15	31.34	11.12
Cisplatin	98.84	98.31	65.49	29.93	13.40

Table 2. *In vitro* antitumor activity of title complexes against MCF-7.

Complex	Inhibition rate%				
	100 mg · L^{-1}	50 mg · L^{-1}	25 mg · L^{-1}	12.5 mg · L^{-1}	6.25 mg · L^{-1}
3aa	–	20.83	12.32	54.62	45.75
3ab	85.41	87.75	80.97	28.25	–
3ba	96.64	92.72	45.33	13.68	–
3bb	97.54	95.19	87.68	32.19	17.58
3ca	98.33	90.31	65.19	21.01	22.19
3cb	95.14	92.97	78.11	33.02	30.76
3da	73.49	41.02	33.67	24.22	18.63
3db	93.49	58.94	48.74	28.62	26.17
Cisplatin	0.13	0.16	5.93	3.03	–

of MCF-7, **3aa** showed good activity at low concentration. When the concentration was 100–50 mg/L, the inhibition rate of other complexes was more than 90% except for **3aa**, **3ab** and **3da**, and the inhibition rate was more than 90% in all concentration ranges. The inhibition rate of the complexes was higher than that of cisplatin.

The thiourea complexes of salicylaldehyde-condensed amino acids showed good inhibitory activity in vitro on both cell lines, and many of the complexes showed higher bioactivity than cisplatin, especially **3bb** and **3db**. In general, the activity of MDA-MB-231 in human breast cancer cells is stronger than that of MCF-7.

Combining the inhibition rates of Tables 1 and 2, the IC_{50} values obtained according to the corresponding formula are shown in Tables 3 and 4.

Comparing the IC_{50} values of 1aa and **3ab**, **3ba** and **3bb**, **3ca** and **3cb**, **3da** and **3db**, it can be found that the latter is smaller than the former, that is, the latter has stronger activity against human breast cancer cells (MDA-MB-231 and MCF-7) than the former. This result indicates that small changes in hydrocarbon groups affect the anticancer activity of the complex, and the longer hydrocarbon chain gets better activity of

Table 3. IC_{50} value of title complexes against MDA-MB-231(mg/L).

Complex	IC_{50} value
3aa	8.05
3ab	6.73
3ba	9.75
3bb	7.26
3ca	18.57
3cb	5.70
3da	22.18
3db	11.90
Cisplatin	14.52

the complex. Among them, the best anti-human breast cancer cell MDA-MB-231 activity is **3cb**, and its IC_{50} value is 5.70 mg/L, and the IC_{50} value of cisplatin is 14.52 mg/L, the best anti-human breast cancer cell MCF-7 activity is **3ab**, and its IC_{50} value is 7 mg/L. At this time, the IC_{50} value of cisplatin is more than 100 mg/L. These results provide more possibilities for the research and development of metal anticancer drugs and provide some experimental data and theoretical guidance for the development and application of organotin

Table 4. IC_{50} value of title complexes against MCF-7(mg/L).

Complex	IC_{50} value
3aa	16.89
3ab	7.00
3ba	21.26
3bb	10.88
3ca	15.81
3cb	10.37
3da	35.66
3db	21.23
Cisplatin	>100

anticancer drugs. But their performance should be further studied.

4. Conclusions

Schiff base of salicylaldehyde amino acid thiourea was used as a ligand to react with dialkyltin dichloride. Thirteen complexes were obtained and characterized by IR and ^{1}HNMR, ^{13}C NMR, elemental analysis. The structure of the complex is further illustrated by X-ray single-crystal diffraction. The structure of the complex is a five-coordinate twisting triangular bipyramidal structure with the tin atom as the center. The anticancer activity of all the complexes was tested *in vitro*. The results showed that all the complexes exhibited better anticancer activity against MDA-MB-231 and MCF-7, overall, the biological activity of MDA-MB-231 is superior to that of MCF-7, and some of the complexes showed stronger activity than cisplatin. It provides good experimental data and theoretical guidance for the development and application of organotin complexes as anticancer drugs in the future, but its anticancer mechanism and other characteristics need to be further studied.

Supplementary Information (SI)

Tables S1.1-S2.1 is available at www.ias.ac.in/chemsci.

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