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Editor-in-Chief,
*Journal of Molecular Structure*

September 27th, 2019

Dear Sir/Madam,

We have just now uploaded files in support of a paper entitled "**Homoleptic tin(IV) compounds containing tridentate ONS dithiocarbazate Schiff bases: Synthesis, X-ray crystallography, DFT and cytotoxicity studies**" by Enis Nadia Md Yusof, Muhammad A. M. Latif, Mohamed I. M. Tahir, Jennette A. Sakoff, Abhi Veerakumarasivam, Alister J. Page, Edward R. T. Tiekink, and Thahira B. S. A. Ravoof that we wish to have considered for publication in *Journal of Molecular Structure*. This research article discusses the structural and spectroscopic characterization, as well as the cytotoxicity of the compounds via different assays and mechanistic studies and *in-silico* analyses comprehensively.

We hope the submission meets with your Editorial requirements.

Yours sincerely,

Thahira B. S.A. Ravoof
(for the authors)

Reviewer #4: I recommend the publication of this manuscript in its current form, since the authors have addressed all the issues which were brought up during the last peer-review round.

***Thank you for the review.***

Reviewer #5: The authors successfully addressed most of my concerns. There are however still a couple of issues that should be better clarified. 1. The DNA binding experiments should be provided in vitro, such as UV-vis spectral method.

***Thank you for the review.***

**As was outlined in the comments addressing the previous review round, normally we would only carry out DNA binding interaction studies when the cytotoxicity of the compounds are interesting, meaning high $IC_{50}$ values and/or significant cytotoxicity difference between the Schiff bases and their Sn compounds. However, in this work, the compounds only displayed moderate/weak cytotoxicity against the panel of cancer cell lines tested.**

**We do not have access to the samples to run UV-visible spectroscopic DNA binding experiments as the samples are in another country where the student carried out some of her research.**

**In light of the moderate/weak cytotoxicities of the compounds and unavailability of samples, we have removed the discussion on DNA binding in the manuscript.**

# Homoleptic tin(IV) compounds containing tridentate ONS dithiocarbazate Schiff bases: Synthesis, X-ray crystallography, DFT and cytotoxicity studies

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**Abstract** Six new tin(IV) compounds derived from tridentate dinegatively charged ONS dithiocarbazate Schiff bases derived from 2-hydroxy-3-methoxybenzaldehyde ($H_2L1$, $H_2L2$ and $H_2L3$) and 2,3-dihydroxybenzaldehyde ($H_2L4$, $H_2L5$ and $H_2L6$) (where $H_2Ln$ = di-acids of Schiff base) are reported. The compounds were characterised by elemental analysis, FT-IR and multinuclear NMR ($^1H$, $^{13}C$ and $^{119}Sn$) spectroscopy. The crystal structures of tin(IV) [*S*-4-methybenzyl-*β*-*N*-(2-hydroxy-3-methoxybenzylmethylene)dithiocarbazate] (**2**) and tin(IV) [*S*-benzyl-*β*-*N*-(2-hydroxy-3-methoxy benzylmethylene)dithiocarbazate] (**3**) were determined by X-ray single crystal diffraction analysis. X-ray crystallography showed the molecular geometries in homoleptic **2** and **3** to be quite similar in which the dinegative tridentate ligand coordinated the tin atoms via thiolate-S, phenoxide-O and imine-N atoms. The coordination geometries are based on an octahedron with like-atoms mutually trans. The

experimental findings were validated by density functional theory (DFT) calculations at the B3LYP/LanL2DZ/6-311G(d,p) level of theory. All the tin(IV) compounds, except the insoluble compound **2** were screened for their in vitro cytotoxicity against a panel ten of cancer cell lines and one normal breast cell line (MCF-10A) by MTT assay. Interestingly, the cytotoxicity of five tin(IV) compounds against HT29, MCF7 and MIA was higher than the reference drug, cisplatin.

**Keywords** tin complex; X-ray crystallography; cytotoxicity

## 1. Introduction

Metal ions play an important role in biological systems and are involved in various applications, such as cancer therapy and diagnosis of diseases [1]. Metal-based drugs including compounds of mercury, copper, gold and arsenic have been used since ancient Egyptian, Greek and Chinese societies to treat a broad spectrum of diseases including cancer [2–4]. For example, mercury sulphide (cinnabar) was used in the treatment of ailments and arsenic trioxide (ATO) for the treatment of rheumatoid diseases, syphilis and psoriasis. In the $18^{th}$ century until early $20^{th}$ century, ATO was among the first group of compounds used in the treatment of leukemia, before it was replaced by radiation and chemotherapeutic agents [4]. Targeting cancer with chemotherapy after the failure of other therapeutic treatments was a valid option due to the effectiveness and action of the chemotherapeutic drugs throughout the entire body [5]. In the 1960s, a platinum-based drug, cisplatin was discovered for cancer treatments [6] and following its success, the development of platinum drugs flourished, with some of them approved as chemotherapeutic drugs. However, platinum-based drugs suffer from ineffectiveness in the treatment of platinum-resistant cancers and also have severe side effects. Despite the wide use of platinum-based drugs, their biggest challenges - unclear therapeutic mechanisms and high toxicity - remain. Hence, the development of improved non-platinum-based anticancer drugs became one of the fundamental goals in medicinal chemistry.

There are many possible advantages in using non-platinum-based compounds, such as: (i) a variety of coordination sites, (ii) diversity of oxidation states and (iii) affinity and kinetics of the bound organic ligands [7–9]. Keeping this in view, tin(IV) compounds have shown a wide range of applications and were one of the most in-demand class of organometallic

compounds due to their biomedical effectiveness as antifouling, antimicrobial and antiviral agents. Saxena and Huber (1989) reported that tin-based compounds were known to localise in tumour tissues, hence explaining their effectiveness [10–12]. Since then, tin-based compounds have been in the pipeline as potential chemotherapeutic drugs to modulate toxicity effects. On top of reduced side effects, tin(IV) compounds exhibited no gametogenesis, as cisplatin did, and had increased solubility in water. Tin(IV) compounds also did not develop tumour drug resistance which was reported to be the major problem in chemotherapy for cisplatin and its analogues towards certain cancer cells [13–15]. Further, tin(IV) compounds had potential industrial applications, such as bactericides, fungicides and pesticides [16–20].

Ligand selectivity can be introduced into a system in order to determine their effectiveness in bioactivity, particularly in anticancer activity. Ligands not only modify the solubility in lipid permeable membranes, but also play a role in transporting and addressing the compound to their specific target site [21]. On this note, Schiff bases have long been studied as potential target ligands to enhance the bioactivity of chemotherapeutic drugs. Schiff bases can coordinate to the tin centre and form stable ligand-tin bonds. Therefore, any modification of the structure could modulate the structural diversity and activity of the entire compound [22]. A number of reports [23–31] on the complexation of dithiocarbazate Schiff bases have received much attention because of their special abilities, including (i) formation of an interesting series of ligands where the properties can be greatly modified by introducing different types of aldehyde or ketones and (ii) the interaction of donor atoms to the centre metal ions creating different geometries and properties, as well as their potential biological activities [32]. The number and diversity of applications of tin(IV) compounds, and the synthesis and characterisation of tin(IV) compounds containing O-, N-, S- donor Schiff bases have been a subject of interest for researchers in the inorganic field, where sulphur is of paramount importance in the metal-ligand linkage. The well elucidated structures of the Schiff base containing compounds showed interesting biological activities depending on their substituents and geometries [33–35].

In view of all these findings and in continuation of our previously reported research work [36] on the chemistry, therapeutic potential and structure-activity relationship of tin(IV) compounds coordinated with two dithiocarbazate Schiff bases, we report here the synthesis of six new octahedral tin(IV) compounds derived from 2-hydroxy-3-methoxybenzaldehyde and

2,3-dihydroxybenzaldehyde dithiocarbazate. The compounds were characterised by FT-IR, multinuclear NMR ($^{1}$H, $^{13}$C and $^{119}$Sn), mass spectroscopy, UV-vis and density functional theory (DFT) calculations. The *in vitro* cytotoxicity studies were explored and the compounds were found to have good activity against the tested cell lines.

## 2. Experimental Section

### *2.1. Materials and Instruments*

All solvents and reagents were of analytical reagent grade and used without further purification. Chemicals: hydrazine hydrate, 80% (Fluka), benzylchloride, ≥ 99% (Merck), 2-methybenzyl chloride, 99% (ACROS), 4-methylbenzyl chloride (ACROS), potassium hydroxide (HmbG), carbon disulphide (Merck), 2-hydroxy-3-methoxybenzaldehyde (Merck), tin(II) dichloride, 97% (Merck), trimethylamine and > 99% (Sigma Aldrich). Solvents: acetonitrile (Baker), absolute ethanol, 99.8% (Scharlau), ethanol, 95% (J. Kollin Chemical), methanol (Fisher Scientific) and dimethylsulfoxide (Scharlau). Melting points were determined using an Electrothermal digital melting point apparatus. C, H and N elemental analyses were carried out using a LECO CHNS-932 instrument and Thermo Flash EA110 elemental analyser. FT-IR spectra were recorded using PerkinElmer Spectrum 100 with Universal ATR Polarization in the range of 4000–280 $cm^{-1}$ at room temperature. Molar conductivities of $10^{-3}$ M solutions of the metal complexes in DMSO were measured at 27 °C using a Jenway 4310 conductivity meter and a dip-type cell with a platinized electrode. Electronic spectra were recorded on a Shimadzu UV-2501 PC recording spectrophotometer (1000–200 nm). Multinuclear ($^{1}$H and $^{13}$C) Nuclear Magnetic Resonance (NMR) spectroscopic analyses were recorded using NMR JNM ECA400 spectrometer. $^{119}$Sn NMR were measured using a Bruker BioSpin Avance III (600 MHz) spectrometer.

### *2.2. Synthesis*

#### *2.2.1. Synthesis of Schiff bases*

Schiff bases were synthesised following references [37,36]. Dithiocarbazate (S-2-methylbenzyldithiocarbazate, S-4-methylbenzyldithiocarbazate or S-benzyldithiocarbazate) (10 mmol) was dissolved in hot acetonitrile or ethanol (100 $cm^{3}$) and added to an equimolar

amount of 2-hydroxy-3-methoxybenzaldehyde (1.52 g) or 2,3-dihydroxybenzaldehyde (1.38 g) in absolute ethanol (20 $cm^3$). The mixture was heated (80 °C) with continuous stirring for about 30 min and then allowed to stand overnight at room temperature. The resultant product was recrystallised from $CH_3CN$/EtOH (1:1) to give a light-yellow crystalline solid that was filtered and washed with cold absolute ethanol.

### *2.2.2. Synthesis of tin(IV) compounds (**1-3**)*

The Schiff base (0.35 g ($H_2L1$, $H_2L2$); 0.33 g ($H_2L3$, $H_2L4$, $H_2L5$); 0.32g ($H_2L6$), 1 mmol) was dissolved in absolute ethanol (50 $cm^3$) and dichloromethane (20 $cm^3$) and was mixed with an ethanolic solution (2 mmol) of triethylamine. With continuous stirring, an ethanolic solution of $SnCl_2$ (0.20 g, 1 mmol) was added to the mixture. A cloudy solution formed which was filtered. The yellow filtrate was then heated under reflux for *ca* 6 h. The mixture was left overnight and the reduction of the volume of the reaction mixture resulted in an orange precipitate, which was filtered off. The precipitate was recrystallised in dry ether to remove the remaining triethylamine hydrochloride salt from the mixture.

#### *2.2.2.1. Tin(IV) [S-2-methylbenzyl-β-N-(2-hydroxy-3-methoxybenzylmethylene) dithiocarbazate] (**1**)*

Orange solid. Yield: 82%. Melting point: >300°C. Analysis calculated for $C_{34}H_{32}N_4O_4S_4Sn$: C, 50.56; H, 3.99; N, 6.94%. Found: C, 50.87; H, 3.58; N, 5.27%. FT-IR (ATR, $cm^{-1}$): 1587, *ν*(C=N); 1088, *ν*(N-N); 955, *ν*(C-S). $^1$H NMR ($CDCl_3$) δ (ppm.): 8.81, 8.45 (s, 2H, CH), 6.77-7.32 (multiplet, 14H, Ar-H), 4.35, 4.47 (s, 4H, $CH_2$), 3.57, 3.85 (s, 6H, O-$CH_3$), 2.40, 2.36 (s, 6H, $CH_3$); $^{13}$C NMR ($CDCl_3$) δ (ppm.): 177.2, 171.0 (C-S), 165.4, 161.7 (C=N); 115.2, 117.2, 118.4, 119.0, 120.2, 121.9, 126.1, 126.2, 126.4, 126.7, 127.6, 128.0, 130.4, 130.4, 130.5, 130.6, 133.5, 134.5, 137.2, 137.3, 147.6, 150.4, 152.0, 156.7 (aromatic-C), 55.3, 56.9 (O-$CH_3$), 36.2, 34.0 ($CH_2$), 19.4 ($CH_3$),.$^{119}$Sn NMR ($CDCl_3$) δ (ppm.): -446.

#### *2.2.2.2. Tin(IV) [S-4-methybenzyl-β-N-(2-hydroxy-3-methoxybenzylmethylene) dithiocarbazate] (**2**)*

Orange crystals. Yield: 87%. Melting point: 211-214°C. Analysis calculated for $C_{34}H_{32}N_4O_4S_4Sn$: C, 51.56; H, 3.99; N, 6.94%. Found: C, 51.89; H, 4.22; N, 6.53%. FT-IR

(ATR, $cm^{-1}$): 1593, *v*(C=N); 1083, *v*(N-N); 958, *v*(C=S). $^{1}H$ NMR ($CDCl_3$) δ (ppm.): 8.77, (s, 2H, CH), 6.76-7.24 (multiplet, 14H, Ar-H), 4.36 (s, 4H, $CH_2$), 3.56 (s, 6H, O-$CH_3$), 2.33 (s, 6H, $CH_3$); $^{13}C$ NMR ($CDCl_3$) δ (ppm.): 170.8 (C-S), 165.4 (C=N); 117.2, 118.4, 119.0, 126.7, 129.2, 129.4, 133.1, 137.3, 152.0, 156.7 (aromatic-C), 56.9 (O-$CH_3$), 35.5 ($CH_2$), 21.2 ($CH_3$). $^{119}Sn$ NMR ($CDCl_3$) δ (ppm.): -446.

*2.2.2.3. Tin(IV) [S-benzyl-β-N-(2-hydroxy-3-methoxybenzylmethylene)dithiocarbazate] (**3**)*

Orange crystals. Yield: 53%. Melting point: >300°C. Analysis calculated for $C_{32}H_{28}N_4O_4S_4Sn$: C, 49.30; H, 3.62; N, 7.19%. Found: C, 49.26; H, 3.26; N, 6.02 %. FT-IR (ATR, $cm^{-1}$): 1582, *v*(C=N); 1031, *v*(N-N); 958, *v*(C-S). $^{1}H$ NMR ($CDCl_3$) δ (ppm.): 8.78 (s, 2H, CH), 6.76-7.36 (multiplet, 16H, Ar-H), 4.44 (s, 4H, $CH_2$), 3.55 (s, 6H, O-$CH_3$); $^{13}C$ NMR ($CDCl_3$) δ (ppm.): 170.7 (C-S), 165.5 (C=N); 117.2, 118.4, 119.0, 126.7, 127.6, 128.7, 129.3, 136.3, 152.0, 156.9 (aromatic-C), 56.9 ($CH_3$), 35.7 ($CH_2$).$^{119}Sn$ NMR ($CDCl_3$) δ (ppm.): -447.

*2.2.2.4. Tin(IV)[S-2-methylbenzyl-β-N-(2,3-dihydroxybenzylmethylene) dithiocarbazate] (**4**)*

Orange powder. Yield: 40%. Melting point: 188-192 °C. Analysis calculated for $C_{32}H_{28}N_4O_4S_4Sn$: C, 49.30; H, 3.62; N, 7.19%. Found: C, 49.14; H, 3.43; N, 7.50%. FT-IR (ATR, $cm^{-1}$): 1610, *v*(C=N); 1035, *v*(N-N); 964, *v*(C-S). $^{1}H$ NMR ($CDCl_3$) δ (ppm.) : 8.90 (s, 2H, CH), 6.02-7.34 (multiplet, 14H, Ar-H), 4.48 (s, 4H, $CH_2$), 2.42 (s, 6H, $CH_3$); $^{13}C$ NMR ($CDCl_3$) δ (ppm.): 171.3 (C-S), 165.6 (C=N), 115.1, 119.0, 119.6, 125.4, 126.5, 128.3, 130.5, 130.8, 133.2, 137.4, 148.2, 152.1 (aromatic-C), 34.3 ($CH_2$), 19.5 ($CH_3$).$^{119}Sn$ NMR (DMSO-$d_6$) δ (ppm.): -441.

*2.2.2.5. Tin(IV) [S-4-methybenzyl-β-N-(2,3-dihydroxybenzylmethylene) dithiocarbazate] (**5**)*

Orange powder. Yield: 83%. Melting point: 206-209 °C. Analysis calculated for $C_{32}H_{28}N_4O_4S_4Sn$: C, 49.30; H, 3.62; N, 7.19%. Found: C, 49.02; H, 3.16; N, 7.85%. FT-IR (ATR, $cm^{-1}$): 1620, *v*(C=N); 1006, *v*(N-N); 965, *v*(C-S). $^{1}H$ NMR (DMSO-$d_6$) δ (ppm.): 8.65, (s, 2H, CH), 6.50-7.35 (multiplet, 14H, Ar-H), 4.41 (s, 4H, $CH_2$), 2.29 (s, 6H, $CH_3$); $^{13}C$ NMR (DMSO-$d_6$) δ (ppm.): 150.8 (C-S), 145.2 (C=N); 118.4, 129.5, 129.6, 134.2, 136.8 (aromatic-C), 21.2 ($CH_3$), 37.8 ($CH_2$).$^{119}Sn$ NMR (DMSO-$d_6$) δ (ppm.): -443.

*2.2.2.6. Tin(IV) [S-benzyl-β-N-(2,3-dihydroxy-benzylmethylene)dithiocarbazate] (**6**)*

Orange powder. Yield: 67%. Melting point: 206-208 °C. Analysis calculated for $C_{30}H_{24}N_4O_4S_4Sn$: C, 47.95; H, 3.22; N, 6.46%. Found: C, 47.72; H, 2.93; N, 6.25%. FT-IR (ATR, $cm^{-1}$): 1612, *ν*(C=N); 1016, *ν*(N-N); 960, *ν*(C-S). $^1$H NMR (DMSO-$d_6$) δ (ppm.): 8.60, (s, 2H, CH), 6.27-7.41 (multiplet, 16H, Ar-H), 4.44 (s, 4H, $CH_2$); $^{13}$C NMR (DMSO-$d_6$) δ (ppm.): 155.9 (C-S), 153.4 (C=N); 111.6, 114.3, 115.9, 116.9, 127.5, 128.9, 129.7, 137.6, 146.9 (aromatic-C), 38.1 ($CH_2$).$^{119}$Sn NMR (DMSO-$d_6$) δ (ppm.): -462.

## *2.3 Single crystal X-ray structure determination*

An Oxford Diffraction Gemini Eos CCD diffractometer fitted with Mo Kα radiation (λ = 0.71073 Å) was employed to measure intensity data for the orange crystals of **2** and **3** at T = 150 K. The data reduction and analytical absorption corrections were accomplished with CrysAlisPro [38]. The structures were solved by direct-methods [39] and refined (anisotropic displacement parameters, C-bound H atoms in the riding model approximation) on $F^2$ [40]. A weighting scheme $w = 1/[\sigma^2(F_o^2) + (aP)^2 + bP]$ where $P = (F_o^2 + 2F_c^2)/3$) was introduced in each case. In the final cycles of the refinement of **2**, a reflection, i.e. (-6 -4 8), was omitted owing to poor agreement. The molecular structure diagrams was generated with ORTEP for Windows [41] with 50% displacement ellipsoids and the packing diagrams were drawn with DIAMOND [42]. Additional data analysis was made with PLATON [43]. Crystal data and refinement details are given in Table 1.

## *2.4 Computational calculations*

DFT calculations were performed as reported previously from our group [36].

## *2.5 In vitro cytotoxic activity*

The cytotoxicity of tin(IV) compounds against HT29 (colon), U87 and SJ-G2 (glioblastoma), MCF-7 (breast), A2780 (ovarian), H460 (lung), A431 (skin), Du145 (prostate), BE2-C (neuroblastoma), MIA (pancreas) cell lines and one normal breast cell line, MCF-10A

(normal breast) were performed by MTT assay using the same method reported by Yusof *et al* [36].

**Table 1**

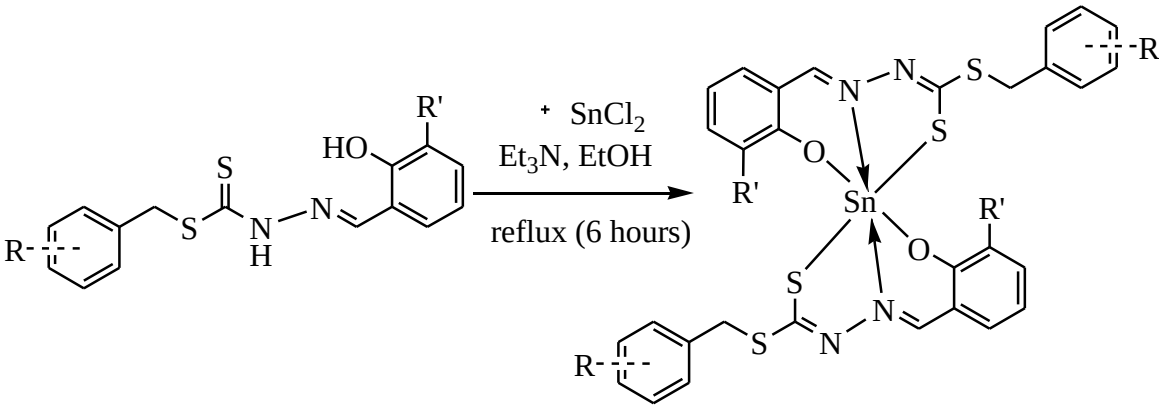
Crystal data and refinement details for complexes **2** and **3**.

| Complex | **2** | **3** |
|---|---|---|
| Formula | $C_{34}H_{32}N_4O_4S_4Sn$ | $C_{32}H_{28}N_4O_4S_4Sn$ |
| Formula weight | 807.56 | 779.51 |
| Crystal system | Monoclinic | Monoclinic |
| Space group | $P2_1/n$ | $P2_1/c$ |
| $a$/Å | 12.8540(2) | 12.8656(3) |
| $b$/Å | 19.4686(5) | 8.4693(2) |
| $c$/Å | 27.2466(6) | 29.8639(7) |
| $\beta$/° | 101.109(2) | 96.634(2) |
| $V$/Å$^3$ | 6690.7(3) | 3232.26(13) |
| $Z$ | 8 | 4 |
| $D_c$/g cm$^{-3}$ | 1.603 | 1.602 |
| $F$(000) | 3280 | 1576 |
| μ(Mo$K\alpha$)/mm$^{-1}$ | 1.059 | 1.093 |
| Measured data | 44247 | 36728 |
| θ range/° | 3.3 – 25.2 | 3.4 – 25.2 |
| Unique data | 15972 | 7934 |
| Observed data ($I \geq 2.0\sigma(I)$) | 10737 | 6324 |
| No. parameters | 855 | 408 |
| $R$, obs. data; all data | 0.041; 0.079 | 0.035; 0.072 |
| $a$; $b$ in weighting scheme | 0.036; 1.389 | 0.032; 2.061 |
| $R_w$, obs. data; all data | 0.076; 0.093 | 0.052; 0.080 |
| GoF | 1.05 | 1.02 |
| Range of residual electron density peaks/eÅ$^{-3}$ | -0.75 – 0.91 | -0.57 – 0.50 |

## 3. Results and discussion

### *3.1 Synthesis*

Six new homoleptic tin(IV) compounds were synthesised by the condensation reaction of S-substituted dithiocarbazate Schiff bases of 2-hydroxy-3-methoxybenzaldehyde or 2,3-dihydroxybenzaldehyde with tin(II) chloride (Scheme 1), whereby the tin(II) precursor underwent oxidation to tin(IV) after reflux for 6 hours [44]. The tin(IV) compounds were stable at room temperature and soluble in most organic solvents, especially dimethylsulfoxide (DMSO) and dimethylformamide (DMF), except **2** which was not soluble in DMSO. Due to the insolubility of **2**, cytotoxic activity was not determined. The molar conductance of $10^{-3}$ M solutions of synthesised compounds in DMSO were in the range 1.12-6.07 $\Omega^{-1}$ $cm^2$ $mol^{-1}$, indicating their non-electrolytic nature [45].




Where: R = *o*-$CH_3$, R' = O-$CH_3$ (**1**)
R = *p*-$CH_3$, R' = O-$CH_3$ (**2**)
R = H, R' = O-$CH_3$ (**3**)
R = *o*-$CH_3$, R' = OH (**4**)
R = *p*-$CH_3$, R' = OH (**5**)
R = H, R' = O-H (**6**)

**Scheme 1**: Synthetic pathway for the synthesis of **1**-**6**.

### *3.2 Infrared spectra analysis*

The infrared spectra of **1**-**6** were measured in the range of 4000 to 280 $cm^{-1}$ and verified using frequencies predicted using DFT. Complete experimental and calculated IR data are provided in Supplementary Information, Table S1. In the experimental IR spectra of Schiff bases ($H_2$L1-6), the vibration bands of *ν*(*o*-O-H), *ν*(NH), *ν*(C=N), *ν*(N-N) and *ν*(C-S) were observed in the range of 3488-3501, 3084-3106, 1598-1608, 1114-1125 and 1012-1030 $cm^{-1}$, respectively. However, the *ν*(O-H) of $H_2$L1, $H_2$L2 and $H_2$L3 were not observed in the IR spectra due to the intra- and inter-molecular interactions between the molecules, which was similar to that reported in our previous work [36]. The disappearance of the *ν*(N-H) band for all Schiff bases and the *ν*(O-H) band for $H_2$L4, $H_2$L5 and $H_2$L6 indicate the deprotonation of N-H and O-H groups and its subsequent coordination to the central tin atom. The shifting of *ν*(C=N) band observed in the spectra of tin(IV) compounds proves that the complexation occurred through the azomethine nitrogen. The IR group assignments for the experimental and theoretical calculation in gas phase appeared in good agreement with experimental data, shown in Fig. S1.

### *3.3 Multinuclear ($^1$H, $^{13}$C and $^{119}$Sn) NMR spectral analysis*

The important signals observed in the range of 9.51-9.61 ppm and 13.32-13.41 ppm were assigned to the proton of -OH and -NH in the Schiff base, respectively, which were reported in our previous publications [36]. Both of the signals disappeared in the $^1$H NMR of the tin(IV) compounds indicating the deprotonation of the -OH and -NH groups upon complexation. This confirmed the coordination of the oxygen and nitrogen donor atom of Schiff bases to the tin ion. Moreover, the signal of the HC=N proton in the spectra of tin(IV) compounds shifted to the downfield region due to the coordination of –NH to tin atom, which was a result of the formation of the C=N-N=C conjugated systems [46]. The downfield shift of the HC=N signal in the $^{13}$C NMR spectra, due to electron density transfer from the Schiff bases to the acceptor (Sn atom), was consistent with that observed in earlier reports [47,48]. Furthermore, the signal attributable to the C–S moiety in the $^{13}$C NMR spectra of the tin(IV) compounds was shifted upfield compared to their Schiff bases, suggesting coordination of the sulphur atom to the tin centre. These observations supported the FTIR analysis noted above.

All the data obtained in the $^{1}$H NMR and $^{13}$C NMR spectra are listed in Tables S2 and S3, respectively.

The geometry of compounds **1**-**6** was verified further *via* $^{119}$Sn NMR spectroscopy. A sharp signal was observed in the range δ -441 to -462 in the $^{119}$Sn NMR spectra of compounds **1**-**6**, which strongly supported a six-coordinated, distorted octahedral geometry around tin, comparable to reported literature [49].

### *3.4 UV-vis absorption spectral analysis*

The experimental UV-vis spectra of tin(IV) compounds in DMSO showed a prominent absorption peak in the range of 343-355 nm, which is attributed to the n→π* and π→π* transitions, and showed excellent correlation with the TD-DFT electronic excitations between 348-353 nm (gas phase). The other experimental absorption peak to take into account ranged from 415-427 nm, which indicated the presence of the S→$Sn^{IV}$ LMCT band; TD-DFT predicted equivalent transitions between 428-438 nm. The HOMO in **1**-**6** was primarily located on the dithiocarbazate backbone, the phenyl ring of the aldehyde moiety, and the oxygen atom coordinated to central tin. The LUMO centred on the dithiocarbazate backbone and phenyl ring of aldehyde. Analysis of these frontier MO's (Fig. 1) supported the hypothesis that the n→π* transition occurred due to the presence of the electron lone-pairs in the azomethine nitrogen, thiolate sulphur and phenoxide oxygen atoms. The π→π* transition observed in all tin(IV) compounds corresponded to the electron delocalisation around the aromatic rings. Complete transitions are tabulated in Table S4.

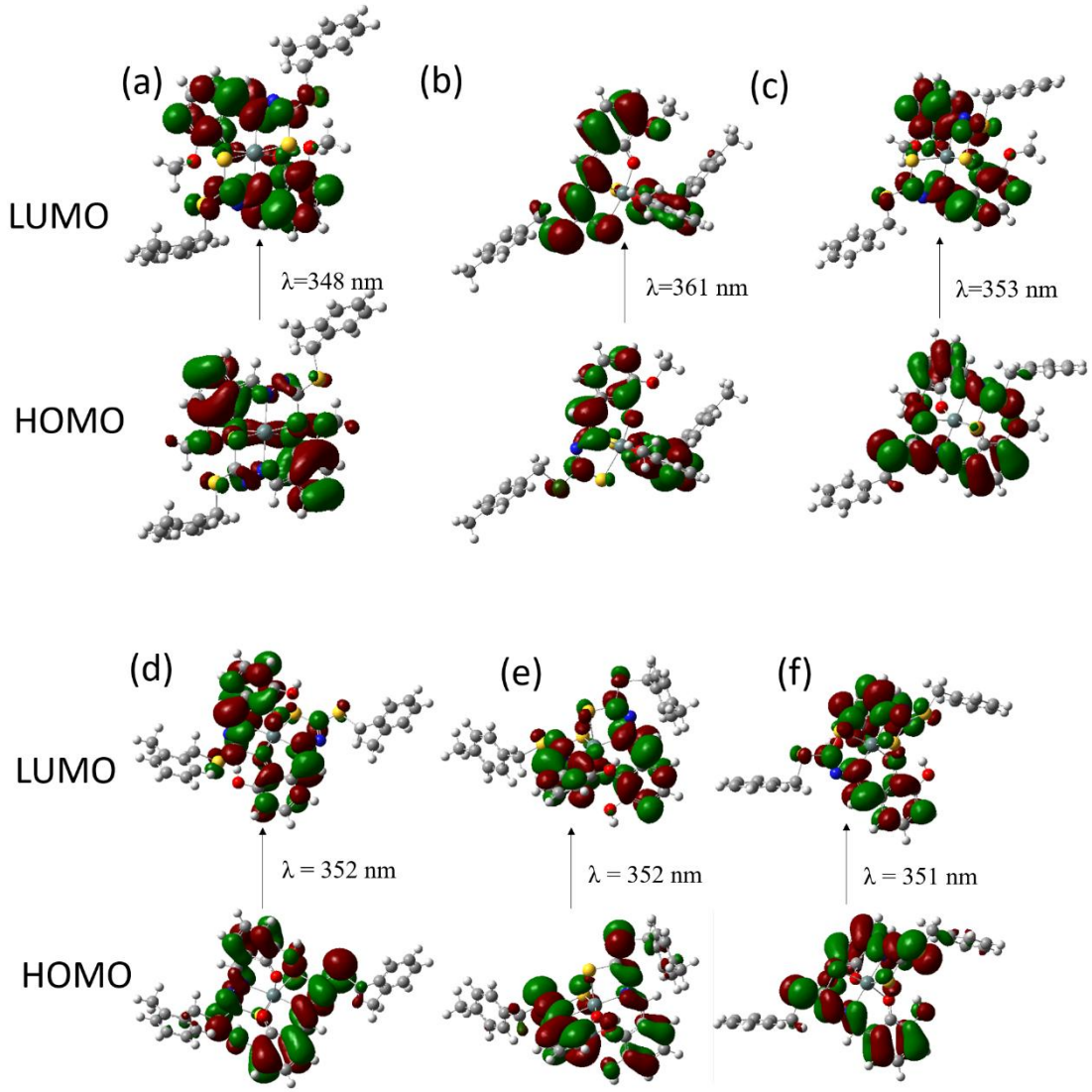



**Fig. 1.** Frontier MOs of (a) **1**, (b) **2**, (c) **3**, (d) **4**, (e) **5** and (f) **6**.

### *3.5 X-ray crystallography*

Crystal structure determinations were achieved for each of the homoleptic compounds **2** and **3**; selected geometric parameters are collected in Table S5. The crystallographic asymmetric unit of **2** comprises two independent molecules with the first shown in Fig. 2(a) and the second molecule shown in Fig. S2. For **3**, one molecule comprises the asymmetric unit, Fig. 2(b). For the first independent molecule of **2**, the dinegative tridentate ligand coordinates the tin atom *via* thiolate-S, phenoxide-O and imine-N atoms to establish five-membered Sn,S,C,$N_2$ and six-membered Sn,O,$C_3$,N rings. Evidence for the presence of thiolate-sulphur

atoms is found in the elongation of the C1−S1 and C18−S3 bond lengths (Table S5) from 1.670(2) Å, which is found in the most closely related acid molecule for which a crystallographic analysis has been reported, i.e. the benzyl ester rather than the 4-tolyl$CH_2$ ester [37]. Concomitantly, the C1−N1 and C18−N3 bond lengths (Table S5) have decreased considerably from 1.338(2) Å in the acid [37]. The conformation of the two tridentate ligands is such that all like atoms are mutually trans in a distorted octahedral environment. The major distortions from the ideal octahedral geometries are due to the acute chelate angles in the five-membered rings, i.e. 78.88(7)° for S1−Sn−N2 and 78.94(7)° for the S3−Sn−N4 angle.

The S1-five-membered chelate ring formed by the tridentate ligand is strictly planar with the RMSD of the fitted atoms being 0.0036 Å. However, the S3-ring is less planar with the RMSD being 0.0629 Å. A better description for the latter is an envelope in which the tin atom lies 0.308(4) Å out of the least-squares plane defined by the remaining four atoms (RMSD = 0.0060 Å). Envelope conformations also apply for the six-membered chelate rings. For the O1-ring, the tin atom lies 0.579(4) Å out the plane through the five remaining atoms. For the O3-ring the envelope is somewhat flattened with the tin atom 0.135(4) Å out of the plane (RMSD = 0.0234 Å), see Table S6. The dihedral angle between the five-membered chelate rings is 81.56(8)°.

As seen from the overlay diagram in Fig. 2(c), there are conformational differences between the independent molecules of **2**, at least with respect to the terminal thioester residues. The data in Table S5 and Table S6 confirm the close similarity between the independent molecules in terms of the tin-atom geometries.

The trends in the structure of **3** follow those established for **2**, with the most obvious difference relating to the coordination of the imine-N2 and N4 atoms. The angle they subtend at the tin atom is wider by *ca* 6-7°, and there is evidence to suggest the Sn–N2, N4 bond lengths are marginally shorter than the equivalent bonds in the molecules of **2**. Each of the chelate rings adopts an envelope conformation with data presented in Table S6. The dihedral angle between the five-membered chelate rings in **3** is 81.77(5)°, *i.e.* within experimental error of the value computed for **2**.

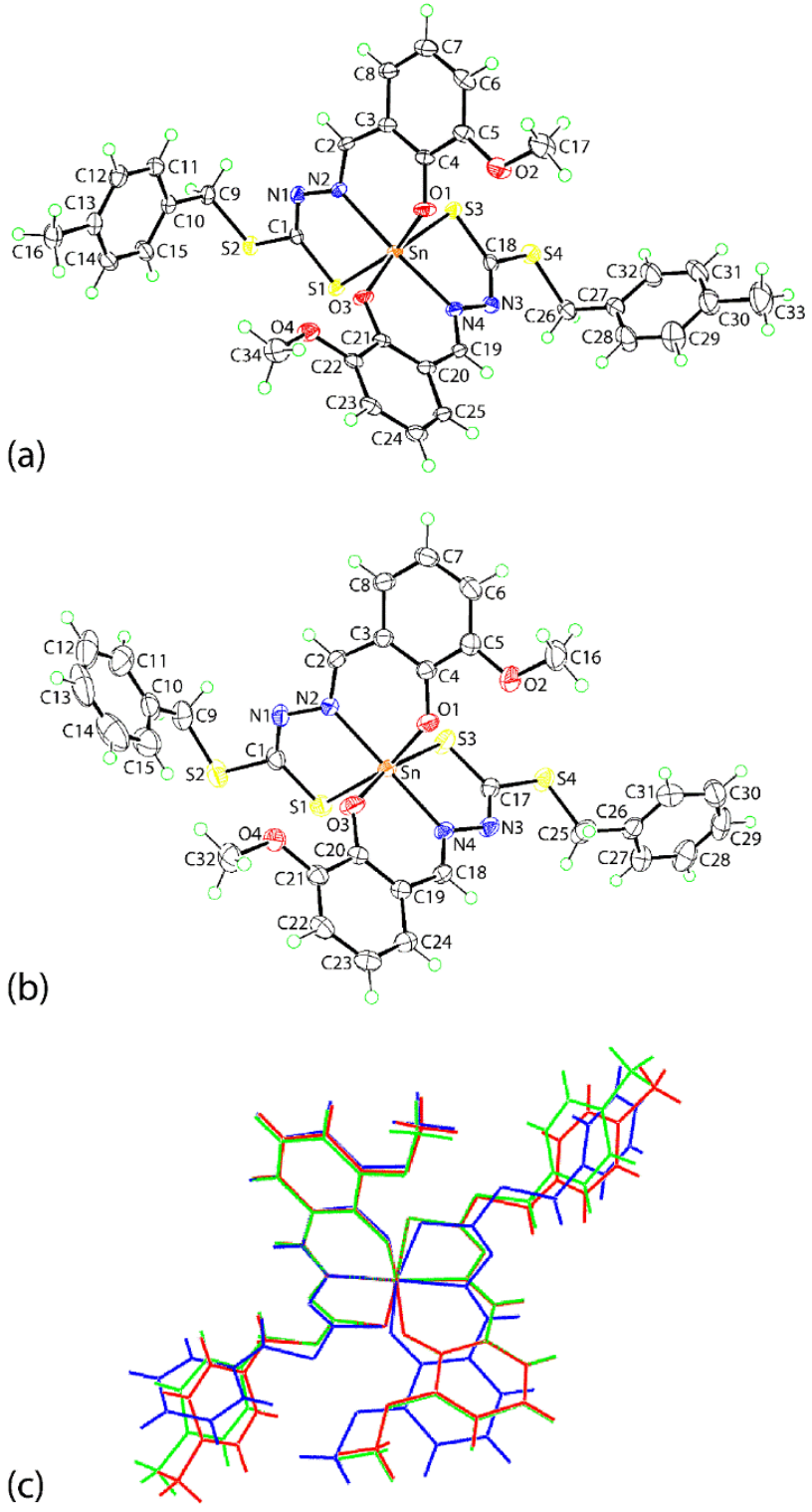



**Fig. 2.** Molecular structures of the molecules in (a) **2** (first independent molecule; the structure for the second independent molecule is shown in Fig. S2) and (b) **3**, showing atom labelling schemes and 50% displacement ellipsoids. (c) Overlay diagram of the molecules in

**2** (red image for the first independent molecule), **2a** (green, inverted second molecule) and **3** (blue). Molecules have been overlapped so the Sn,S1,N2 chelate rings are coincident.

There are three related homoleptic tin(IV) compounds that have been structurally characterised in the literature, namely the ethyl thioester and unsubstituted phenoxide residue [50], benzyl thioester, unsubstituted phenoxide residue and methyl bound to the imine-carbon [51] and benzyl thioester with a ferrocenyl substituent adjacent to the alkoxide-oxygen atom [44]. The contrasting and curious feature of the literature structures is that the thiolate-sulphur atoms are mutually cis, as are the alkoxide-oxygen atoms. The reasons for the different conformations observed in **2** and **3**, and those in the literature remain unclear.

In the absence of conventional hydrogen bonding, the crystals of **2** and **3** are sustained by a variety of other non-covalent interactions; the geometric parameters characterising these are included in the captions to the respective figures in the Tables 2 and 3. In the molecular packing of **2**, each of the independent molecules form equivalent intermolecular contacts with the other independent molecule to sustain a supramolecular layer in the *ab*-plane. These are imine-C2-H···S3(thiolate), imine-C19-H···S1(thiolate), methoxybenzene-C7-H···O2(methoxy), methoxybenzene-C24-H···O4(methoxy) and π(C3-C8)···π(C20-C25). The connections between layers along the *c*-axis direction are of the type methyl-C16a-H···O2a, methyl-C16-H···π(C10-C15) and methoxy-C34-H···π(C10-C15). These occur between like-molecules and hence, differentiate the independent molecules comprising the asymmetric unit in terms of their supramolecular association. Images of the supramolecular association operating in the crystal of **2** are shown in Fig. S3.

As seen in Fig. S4, supramolecular layers in the *ab*-plane are also formed in the crystal of **3** *via* a combination of methoxybenzene-C7–H···O4(methoxy), methoxybenzene-C23–H···O2(methoxy), methylene-C25–H···S1(thiolate), methoxy-C16–H···π(C10-C15) and π(C3-C8)···π(C3…C8) interactions. Layers inter-digitate along the c-axis direction but, without directional interactions between them. Geometric parameters characterising intermolecular interactions in the crystal of **3** are given in Table 3.

**Table 2**

Geometric parameters (Å, °) characterising intermolecular interactions in the crystal of **2**.

| A | H | B | H···B | A···B | A–H···B | Symmetry operation |
|---|---|---|---|---|---|---|
| C2 | H2 | S3a | 2.81 | 3.721(3) | 162 | -1+x, y, z |
| C2A | H2a | S3 | 2.81 | 3.628(3) | 145 | 1+x, y, z |
| C7 | H7 | O2a | 2.49 | 3.421(4) | 166 | ½-x, -½+y, ½-z |
| C7a | H7a | O2 | 2.49 | 3.267(4) | 139 | 1½-x, ½+y, ½-z |
| C16a | H16f | O2a | 2.56 | 3.425(4) | 147 | -1+x, y, z |
| C19 | H19 | S1a | 2.72 | 3.564(3) | 148 | x, y, z |
| C19a | H19a | S1 | 2.77 | 3.699(3) | 166 | x, y, z |
| C24 | H24 | O4a | 2.45 | 3.267(4) | 144 | 1½-x, -½+y, ½-z |
| C24a | H24a | O4 | 2.53 | 3.464(3) | 169 | ½-x, ½+y, ½-z |
| C16 | H16b | Cg(C10-C15) | 2.85 | 3.533(4) | 127 | -x, -y, -z |
| C34 | H34b | Cg(C10-C15) | 2.84 | 3.609(4) | 136 | -x, -y, -z |
| Cg(C3-C8) | | Cg(C20a-C25a) | | 3.4564(19) | | ½-x, -½+y, ½-z |
| Cg(C20-C25) | | Cg(C3a-C8a) | | 3.5716(19) | | 1½-x, -½+y, ½-z |

**Table 3**

Geometric parameters (Å, °) characterising intermolecular interactions in the crystal of **3**.

| A | H | B | H···B | A···B | A–H···B | Symmetry operation |
|---|---|---|---|---|---|---|
| C7 | H7 | O4 | 2.60 | 3.487(3) | 156 | 1-x, -y, 2-z |
| C23 | H23 | O2 | 2.37 | 3.140(3) | 138 | 2-x, -y, 2-z |
| C25 | H25b | S1 | 2.79 | 3.645(3) | 145 | 2-x, 1-y, 2-z |
| C16 | H16a | Cg(C10-C15) | 2.95 | 3.354(4) | 106 | 1-x, -y, 2-z |
| Cg(C3-C8) | | Cg(C3-C8) | | 3.5623(15) | | 1-x, -y, 2-z |

### *3.6 In vitro cytotoxic activity*

The cytotoxic assay of **1**, **3**, **4**, **5** and **6** were carried out against a panel ten of cancer cell lines and one normal cancer cell line. All the compounds, except compound **2** used in this work were insoluble in water. However, they were very soluble in DMSO, and the presence of 1% DMSO proved sufficient for their dissolution in aqueous media for cytotoxicity test. The stability of the compounds was analysed by monitoring the electronic spectra of the compounds in DMSO as well as DMSO-$H_2O$ (1:99) over 72 h at room temperature, and an unchanged pattern in the spectra was indicative that the compounds were stable in both the solvent systems tested. We were unable to determine the cytotoxicity of **2** due to its insolubility in 100% DMSO at 1 mM. Cisplatin (standard drug) was used as a positive control and DMSO was used as the negative control. Table 4 shows that the cytotoxicity of the tin(IV) compounds and their respective Schiff bases. **1**, **3**, **4**, **5** and **6** exhibited moderate activity against all the tested cancer cell lines. The cytotoxicities of these compounds against HT29, MCF7 and MIA were higher than cisplatin. With respect to the cytotoxicity of the precursor Schiff bases, **1**, **2**, **5** and **6** were equipotent to their corresponding Schiff bases, with the exception of **4**. Compound **4** demonstrated higher potency than their corresponding Schiff bases against HT29, U87, MCF-7, A431 and Du145 cells. The mechanism of action of **4** is worthy of further in-depth investigation. In general, for compounds **1**, **2**, **5** and **6**, it can be inferred that the presence of tin does not influence cytotoxicity. This is possibly due to the bulkiness of the compound and only the coordinated Schiff bases playing a role in binding to macromolecules [52].

**Table 4**

Summary of the *in vitro* cytotoxicity of tin(IV) compounds in several cell lines, determined by the MTT assay and expressed as a $GI_{50}$ value with standard error. $GI_{50}$ is the concentration of tin(IV) compounds at which cell growth is inhibited at 50% over 72 hours.

| Compounds | Growth inhibition concentration, $GI_{50}$ (μM) | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | HT29 | U87 | MCF-7 | A2780 | H460 | A431 | Du145 | BE2-C | SJ-G2 | MIA | MCF10A |
| $H_2L1$ | 3.9 ± 0.71 | 4.3 ± 0.30 | 2.7 ± 0.21 | 3.2 ± 0.15 | 4.3 ± 0.12 | 3.8 ± 0.033 | 4.1 ± 0.09 | 3.1 ± 0.00 | 3.0 ± 0.09 | 4.9 ± 0.37 | 3.1 ± 0.07 |
| **1** | 3.9 ± 0.53 | 4.2 ± 0.03 | 2.9 ± 0.07 | 3.3 ± 0.10 | 4.0 ± 0.09 | 3.8 ± 0.15 | 4.6 ± 0.17 | 3.0 ± 0.13 | 2.9 ± 0.12 | 4.2 ± 0.27 | 3.2 ± 0.21 |
| $H_2L2$ | 8.0 ± 3.5 | 3.9 ± 0.00 | 3.5 ± 0.00 | 3.1 ± 0.40 | 5.5 ± 0.73 | 4.2 ± 0.74 | 5.4 ± 0.23 | 3.6 ± 0.27 | 3.3 ± 0.87 | 11 ± 2.3 | 3.5 ± 0.23 |
| **2** | nd | nd | nd | nd | nd | nd | nd | nd | nd | nd | nd |
| $H_2L3$ | 2.2 ± 0.033 | 3.1 ± 0.26 | 2.5 ± 0.12 | 3.0 ± 0.06 | 3.3 ± 0.21 | 3.0 ± 0.15 | 3.4 ± 0.30 | 2.8 ± 0.20 | 2.4 ± 0.26 | 4.5 ± 0.25 | 3.0 ± 0.067 |
| **3** | 2.5 ± 0.30 | 3.1 ± 0.13 | 2.5 ± 0.23 | 2.6 ± 0.12 | 3.0 ± 0.12 | 2.5 ± 0.32 | 3.5 ± 0.26 | 2.1 ± 0.00 | 1.4 ± 0.36 | 2.7 ± 0.21 | 2.8 ± 0.19 |
| $H_2L4$ | 10 ± 3.5 | 20 ± 5.2 | 10 ± 3.1 | 1.8 ± 1.2 | 8.7 ± 1.9 | 14 ± 1.5 | 23 ± 3.6 | 0.38 ± 0.07 | 6.4 ± 2.2 | 5.5 ± 1.1 | 3.7 ± 0.50 |
| **4** | 4.4 ± 0.83 | 9.3 ± 1.8 | 4.4 ± 1.9 | 2.7 ± 0.20 | 4.7 ± 0.23 | 3.7 ± 0.25 | 6.4 ± 1.4 | 1.7 ± 0.33 | 1.9 ± 0.36 | 4.6 ± 0.97 | 3.3 ± 0.19 |
| $H_2L5$ | 2.8 ± 0.033 | 4.0 ± 0.43 | 2.8 ± 0.067 | 2.8 ± 0.20 | 3.7 ± 0.10 | 3.7 ± 0.20 | 4.2 ± 0.59 | 3.2 ± 0.30 | 3.3 ± 0.30 | 6.6 ± 1.7 | 2.9 ± 0.033 |
| **5** | 3.3 ± 0.26 | 4.8 ± 0.52 | 3.0 ± 0.15 | 3.3 ± 0.26 | 4.2 ± 0.12 | 3.7 ± 0.32 | 6.0 ± 0.58 | 2.7 ± 0.43 | 3.0 ± 0.27 | 11 ± 0.88 | 2.8 ± 0.33 |
| $H_2L6$ | 2.1 ± 0.35 | 2.7 ± 0.47 | 2.3 ± 0.32 | 2.2 ± 0.25 | 2.6 ± 0.27 | 2.4 ± 0.26 | 2.8 ± 0.15 | 2.0 ± 0.23 | 2.2 ± 0.47 | 2.2 ± 0.64 | 2.9 ± 0.21 |
| **6** | 2.1 ± 0.44 | 3.3 ± 0.23 | 2.2 ± 0.20 | 2.4 ± 0.38 | 2.1 ± 0.28 | 2.8 ± 0.23 | 3.8 ± 0.52 | 2.1 ± 0.17 | 1.4 ± 0.23 | 2.5 ± 0.64 | 2.8 ± 0.088 |
| $SnCl_2$ | > 25 | > 25 | > 25 | > 25 | > 25 | > 25 | > 25 | > 25 | > 25 | > 25 | > 25 |
| Cisplatin | 11.0 ± 2.0 | 4.0 ± 1.0 | 6.5 ± 0.8 | 1.0 ± 0.1 | 0.9 ± 0.2 | 2.4 ± 0.3 | 1.2 ± 0.1 | 1.9 ± 0.2 | 0.4 ± 0.1 | 8.0 ± 1.0 | nd |

$GI_{50}$ (μM): (the colors indicate) = 0.1 – 0.99; = 1.0 – 9.9; = 10 - 100; = nd (not determined)

(The compounds $H_2L1$, $H_2L2$ and $H_2L3$ published as S2MoVaH, S4MoVaH, SBoVaH, respectively in ref [36])

## 4. Conclusions

Six octahedral tin(IV) compounds were synthesised by the condensation reaction of tin(II) chloride with dithiocarbazate Schiff bases. The oxidation of tin(II) to tin(IV) occurred in this work as two binegatively charged Schiff bases ONS-bonded to the tin centre with general formulae $[Sn(Ln)_2]$. X-ray crystallography indicated that the dinegative tridentate ligands of **2** and **3** coordinated to the tin atoms via thiolate-S, phenoxide-O and imine-N atoms, leading to octahedral geometries in which the like-atoms were mutually trans. The *in vitro* cytotoxicity against a panel of cancer cell lines viz., HT29, U87, SJ-G2, MCF-7, A2780, H460, A431, Du145, BE2-C and MIA cancer cell lines revealed that compounds **1**, **3**, **5** and **6** showed moderate cytotoxicity; similar to that of their respective Schiff bases. However, compound **4** exhibited a higher potency against HT29, U87, MCF-7, A431 and Du145 cells as compared to the precursor Schiff base.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## Supplementary data

Crystallographic data for **2** and **3** reported in this paper have been deposited with the Cambridge Crystallographic Data Centre (CCDC) as supplementary publication nos 1916354 (**2**) and 1916354 (**3**). These data can be obtained free of charge via

www.ccdc.cam.ac.uk/getstructures. Crystallographic diagrams and details of intermolecular interactions are given in Figures S2-S4, Tables S5-S6.

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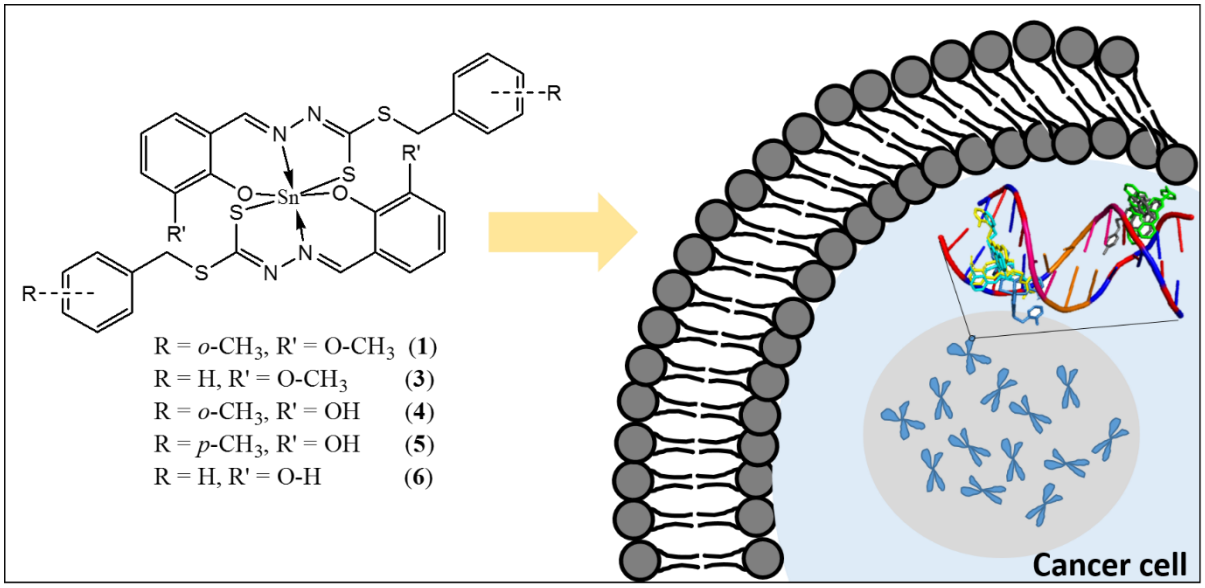
## Graphical Abstract




## Highlight

A series of octahedral homoleptic tin(IV) compounds were designed, synthesised and evaluated for their *in vitro* cytotoxicity against ten cancer cells.

**Figure 1**

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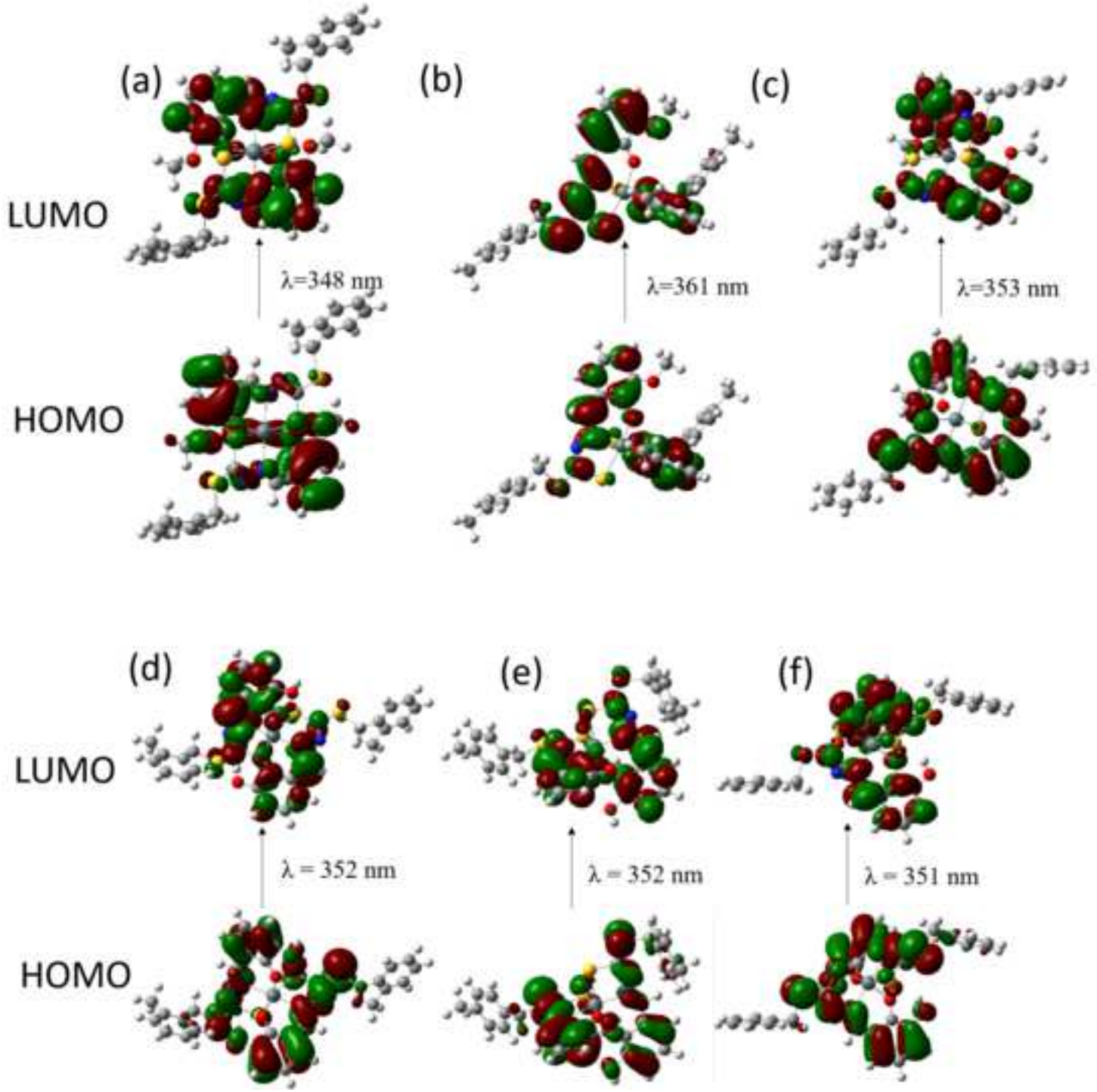

**Figure 2**

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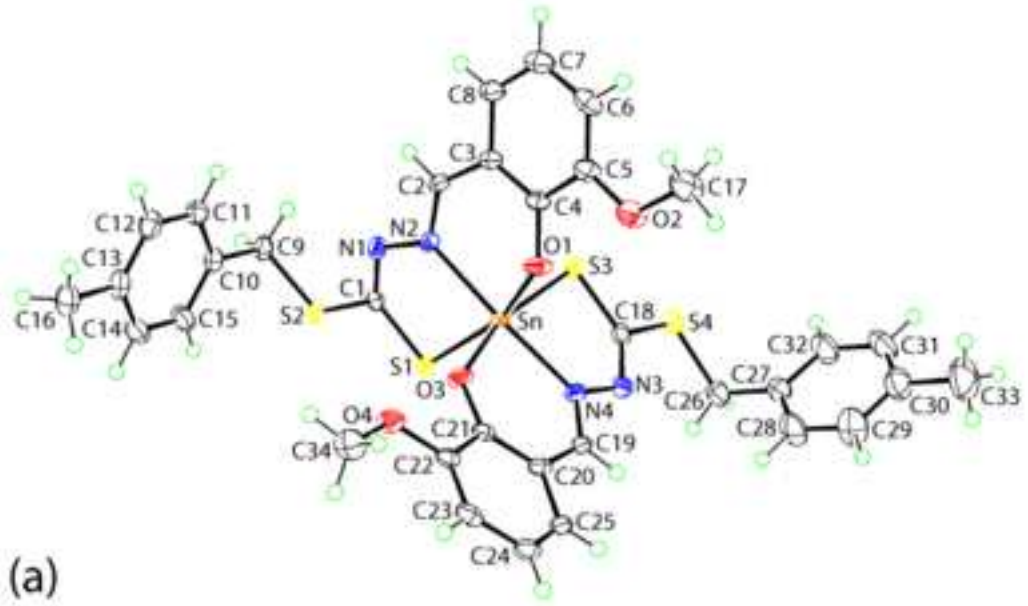
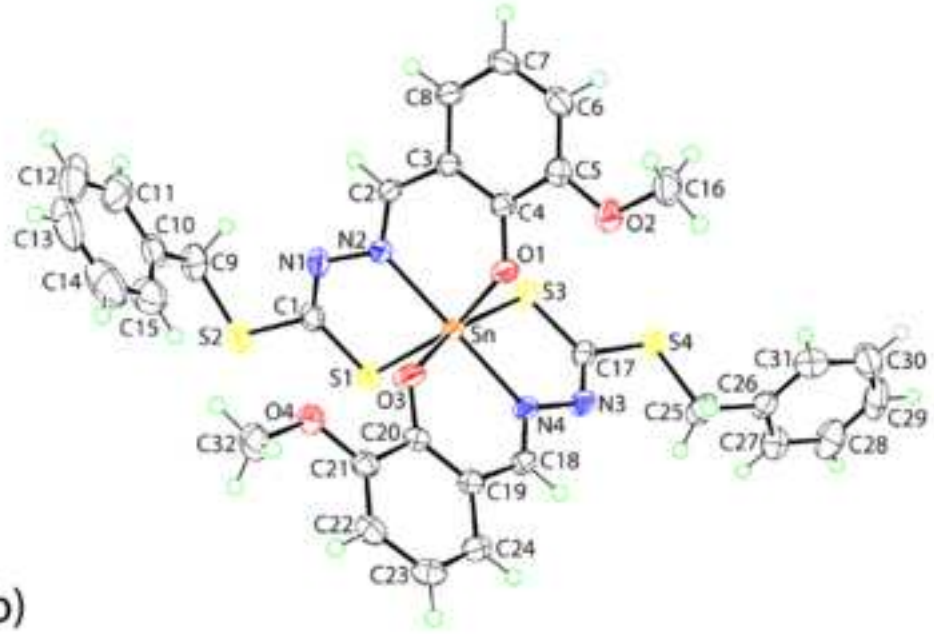



(a)

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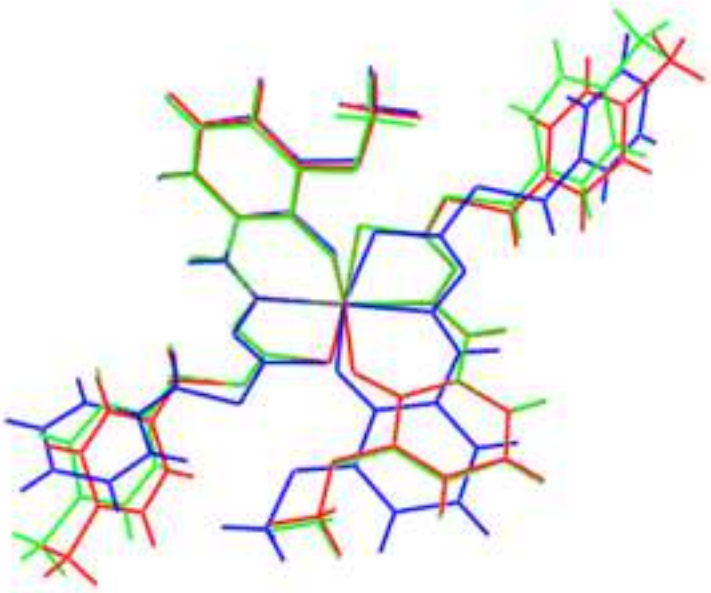

(c)

**Figure 3**

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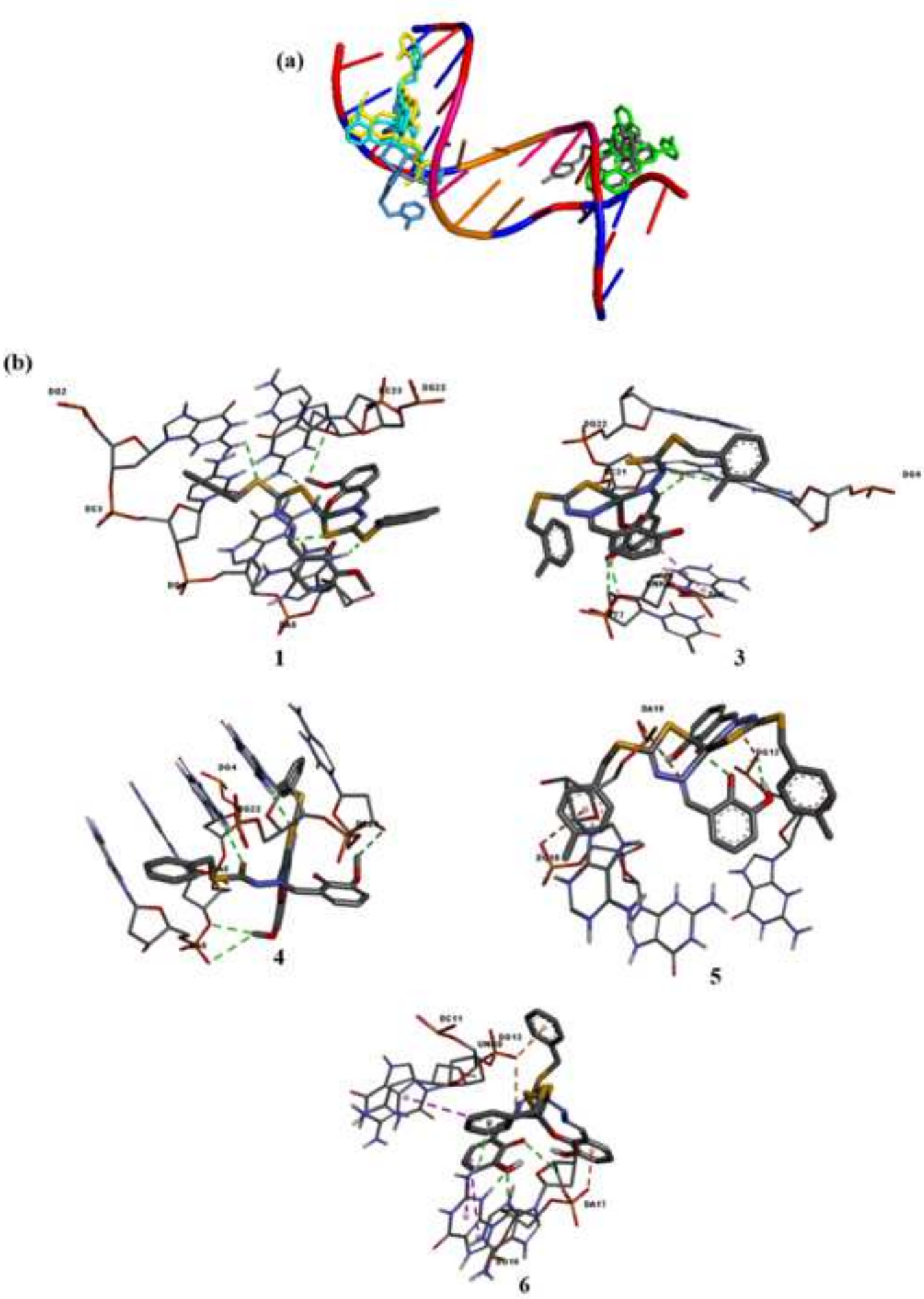

# Homoleptic tin(IV) compounds containing tridentate ONS dithiocarbazate Schiff bases: Synthesis, X-ray crystallography, DFT and cytotoxicity studies

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## SUPPLEMENTARY INFORMATION

**Table S1.** Experimental and calculated vibrations ($cm^{-1}$) of tin(IV) compounds

| Compound | Method | IR bands ($cm^{-1}$) | | | | | |
|---|---|---|---|---|---|---|---|
| | | *ν*(*m*-OH) | *ν*(*o*-OH) | *ν*(NH) | *ν*(C=N) | *ν*(N-N) | *ν*(C-S) |
| $H_2L1$ | Experimental | - | - | 3084 | 1600 | 1117 | 1026 |
| | B3LYP/ 6-311G(d,p) | - | 3419 | 3377 | 1596 | 1112 | 1024 |
| $H_2L2$ | Experimental | - | - | 3092 | 1598 | 1118 | 1030 |
| | B3LYP/ 6-311G(d,p) | - | 3415 | 3378 | 1596 | 1112 | 1024 |
| $H_2L3$ | Experimental | - | - | 3090 | 1598 | 1125 | 1030 |
| | B3LYP/ 6-311G(d,p) | - | 3419 | 3377 | 1596 | 1112 | 1025 |
| $H_2L4$ | Experimental | - | 3496 | 3097 | 1608 | 1119 | 1013 |
| | B3LYP/ 6-311G(d,p) | 3712 | 3368 | 3359 | 1597 | 1112 | 1025 |
| $H_2L5$ | Experimental | | 3501 | 3106 | 1607 | 1114 | 1012 |
| | B3LYP/ 6-311G(d,p) | 3711 | 3365 | 3358 | 1597 | 1113 | 1027 |
| $H_2L6$ | Experimental | | 3488 | 3097 | 1608 | 1119 | 1018 |
| | B3LYP/ 6-311G(d,p) | 3712 | 3363 | 3358 | 1614 | 1113 | 1026 |
| **1** | Experimental | - | - | - | 1587 | 1088 | 955 |
| | B3LYP/LanL2DZ/6-311G(d,p) | - | - | - | 1578 | 1024 | 929 |
| **2** | Experimental | - | - | - | 1593 | 1083 | 958 |
| | B3LYP/LanL2DZ/6-311G(d,p) | - | - | - | 1623 | 1058 | 967 |
| **3** | Experimental | - | - | - | 1582 | 1031 | 958 |
| | B3LYP/LanL2DZ/6-311G(d,p) | - | - | - | 1619 | 1056 | 949 |
| **4** | Experimental | 3384 | - | - | 1610 | 1035 | 964 |
| | B3LYP/LanL2DZ/6-311G(d,p) | 3706 | - | - | 1623 | 1073 | 966 |
| **5** | Experimental | 3452 | - | - | 1620 | 1006 | 965 |
| | B3LYP/LanL2DZ/6-311G(d,p) | 3708 | - | - | 1622 | 1074 | 962 |
| **6** | Experimental | 3033 | - | - | 1612 | 1016 | 960 |
| | B3LYP/LanL2DZ/6-311G(d,p) | 3707 | - | - | 1628 | 1074 | 962 |

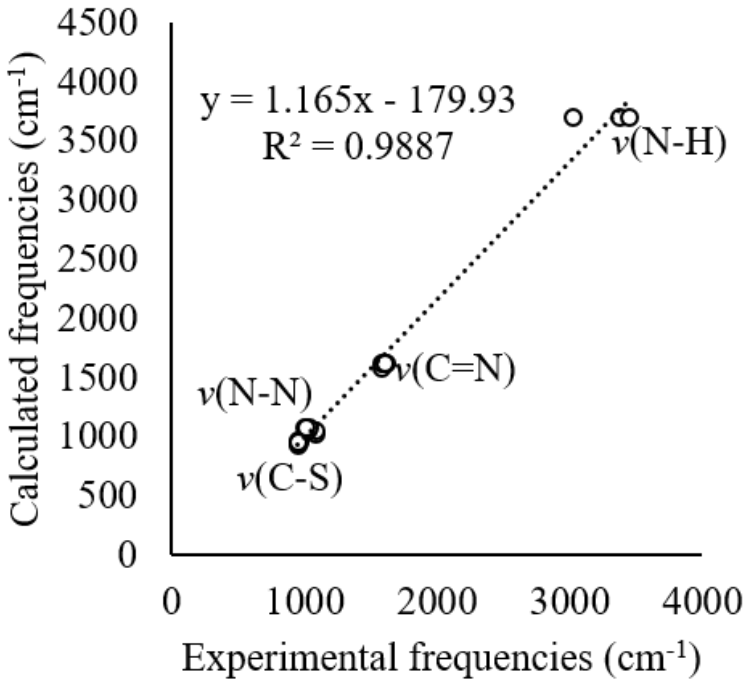



**Fig. S1.** The linear regression between the experimental and theoretical frequencies of compounds **1-6**.

**Table S2**

$^{1}$H NMR spectral data for the tin(IV) compounds

| Compound | $^{1}$H NMR Assignment, δ (ppm) | | | | | | |
|---|---|---|---|---|---|---|---|
| | NH | OH | CH | $CH_2$ | O-$CH_3$ | Bz- $CH_3$ | Aromatic Protons |
| $H_2$L1 | 13.34 (s, 1H) | 9.57 (s, 1H) | 8.51 (s, 1H) | 4.40 (s, 2H) | 3.76 (s, 3H) | 2.30 (s, 3H) | 6.75-7.34 (m,7H) |
| $H_2$L2 | 13.32 (s, 1H) | 9.61 (s, 1H) | 8.51 (s, 1H) | 4.39 (s, 2H) | 3.76 (s, 3H) | 2.23 (s, 3H) | 6.97-9.79 (m,7H) |
| $H_2$L3 | 13.34 (s, 1H) | 9.58 (s, 1H) | 8.52 (s, 1H) | 4.45 (s, 2H) | 3.77 (s, 3H) | - | 6.77-7.37 (m,8H) |
| $H_2$L4 | 13.41 (s, 1H) | 9.55 (s, 1H); 9.51 (s, 1H) | 8.51 (s, 1H) | 4.45 (s, 2H) | 2.34 (s, 3H) | - | 6.69-7.39 (m, 7H) |
| $H_2$L5 | 13.39 (s, 1H) | 9.54 (s, 1H); 9.53 (s, 1H) | 8.51 (s, 1H) | 4.44 (s, 2H) | 2.29 (s, 3H) | - | 6.69-7.30 (m, 7H) |
| $H_2$L6 | 13.39 (s, 1H) | 9.56 (s, 1H); 9.53 (s, 1H) | 8.50 (s, 1H) | 4.47 (s, 2H) | - | - | 6.67-7.39 (m, 8H) |
| **1** | - | - | 8.81, 8.45 (s, 2H) | 4.47, 4.35 (s, 4H) | 3.85, 3.57 (s, 6H) | 2.40, 2.36 (s, 6H) | 6.77-7.33 (m,14H) |
| **2** | - | - | 8.77 (s, 2H) | 4.36 (s, 4H) | 3.56 (s, 6H) | 2.33 (s, 6H) | 6.76-7.24 (m,14H) |
| **3** | - | - | 8.78 (s, 2H) | 4.44 (s, 4H) | 3.55 (s, 6H) | - | 6.76-7.36 (m, 16H) |
| **4** | - | - | 8.90 (s, 2H) | 4.48 (s, 4H) | - | 2.42 (s, 6H) | 6.02-7.34 (m, 14H) |
| **5** | - | - | 8.65 (s, 2H) | 4.41 (s, 4H) | - | 2.29 (s, 6H) | 6.51-7.31 (m, 14H) |
| **6** | - | - | 8.60 (s, 2H) | 4.44 (s, 4H) | - | - | 6.27-7.41 (m, 16H |

**Table S3**

$^{13}C\{^{1}H\}$ NMR spectral data for the tin(IV) compounds

| Compound | $^{13}C\{^{1}H\}$ NMR Assignment, δ (ppm) | | | | | |
|---|---|---|---|---|---|---|
| | -C=S/ -C-S | C=N | O-$CH_3$ | -$CH_2$ | Bz-$CH_3$ | Aromatic carbons |
| $H_2$L1 | 196.1 | 148.6 | 56.4 | 36.9 | 19.4 | 114.4, 118.8, 120.0, 126.7, 128.2, 130.7, 130.8, 134.4, 137.4, 144.9, 147.4, 148.6 |
| $H_2$L2 | 196.2 | 148.6 | 56.4 | 38.0 | 21.2 | 114.4, 118.8, 120.0, 129.6, 129.7, 134.0, 137.0, 145.0, 147.4, 148.6 |
| $H_2$L3 | 196.1 | 148.6 | 56.4 | 38.1 | - | 114.4, 118.8, 120.0, 127.8, 129.0, 129.8, 137.3, 144.9, 147.4, 148.6 |
| $H_2$L4 | 195.6 | 146.5 | - | 36.9 | 19.3 | 118.1, 118.5, 119.7, 120.0, 126.6, 128.2, 130.7, 130.8, 134.3, 137.3, 146.2, 146.2 |
| $H_2$L5 | 195.8 | 146.5 | - | 38.0 | 21.2 | 118.1, 118.4, 119.8, 119.9, 129.6, 129.7, 133.8, 137.0, 146.1, 146.2 |
| $H_2$L6 | 195.6 | 146.5 | - | 38.1 | - | 118.1, 118.4, 119.7, 119.9, 127.7, 129.0, 129.7, 137.1, 146.1 |
| **1** | 177.2, 171.0 | 165.4, 161.7 | 55.3, 56.9 | 34.2, 36.2 | 19.4 | 115.2, 117.2, 118.4, 119.0, 120.2, 121.9, 126.1, 126.2, 126.4, 126.7, 127.6, 128.0, 130.4, 130.4, 130.5, 130.6, 133.5, 134.5, 137.2, 137.3, 147.6, 150.4, 152.0, 156.7 |
| **2** | 170.8 | 165.4 | 56.9 | 35.5 | 21.2 | 117.2, 118.4, 119.0, 126.7, 129.2, 129.4, 133.1, 137.3, 152.0, 156.7 |
| **3** | 170.7 | 165.5 | 56.9 | 35.7 | - | 117.2, 118.4, 119.0, 126.7, 127.6, 128.7, 129.3, 136.3, 152.0, 156.7 |
| **4** | 171.3 | 165.6 | - | 34.3 | 19.5 | 115.1, 119.0, 119.6, 125.4, 126.5, 128.3, 130.5, 130.8, 133.2, 137.4, 148.2, 152.1 |
| **5** | 152.2 | 150.8 | - | 37.8 | 21.2 | 115.7, 118.4, 129.5, 129.6, 134.2, 136.8, 145.2 |
| **6** | 155.9 | 153.4 | - | 38.1 | - | 111.6, 114.3, 115.9, 116.9, 127.5, 128.9, 129.7, 137.6, 146.9 |

**Table S4**

Experimental and calculated UV-vis absorption data of tin(IV) compounds

| Compound | Wavelength (nm) | |
|---|---|---|
| | Experimental | B3LYP/LanLD2Z/6-311G(d,p) |
| **1** | 415 | 436 |
| | 345 | 348 |
| **2** | 419 | 437 |
| | 355 | 361 |
| **3** | 419 | 438 |
| | 348 | 353 |
| **4** | 417 | 428 |
| | 345 | 352 |
| **5** | 427 | 432 |
| | 345 | 352 |
| **6** | 424 | 432 |
| | 343 | 351 |

**Table S5**

Selected geometric parameters (Å, °) for **2** and **3**.

| Compound | **2** (x = 18, y = 19) | **2a** (x = 18, y = 19) | **3** (x = 17, y = 18) |
|---|---|---|---|
| Parameter | | | |
| Sn–S1 | 2.4828(8) | 2.4871(9) | 2.4932(7) |
| Sn–S3 | 2.4961(9) | 2.4898(8) | 2.4873(7) |
| Sn–O1 | 2.025(2) | 2.026(2) | 2.0304(18) |
| Sn–O3 | 2.032(2) | 2.032(2) | 2.0242(18) |
| Sn–N2 | 2.198(2) | 2.189(2) | 2.169(2) |
| Sn–N4 | 2.189(2) | 2.196(2) | 2.173(2) |
| N1–N2 | 1.398(3) | 1.399(3) | 1.395(3) |
| C1–S1 | 1.753(3) | 1.749(3) | 1.744(3) |
| C1–S2 | 1.744(3) | 1.743(3) | 1.741(3) |
| C1–N1 | 1.288(4) | 1.286(4) | 1.289(3) |
| C2–N2 | 1.299(4) | 1.309(4) | 1.302(3) |
| N3–N4 | 1.393(3) | 1.396(3) | 1.397(3) |
| C(x)–S3 | 1.744(3) | 1.754(3) | 1.745(3) |
| C(x)–S4 | 1.743(3) | 1.745(3) | 1.751(2) |
| C(x)–N3 | 1.295(4) | 1.289(4) | 1.288(3) |
| C(y)–N4 | 1.307(4) | 1.303(4) | 1.304(3) |
| S1–Sn–O1 | 162.46(6) | 165.07(6) | 164.51(5) |
| S3–Sn–O3 | 164.42(6) | 162.30(6) | 165.46(5) |
| N2–Sn–N4 | 170.18(10) | 170.45(9) | 177.76(8) |

**Table S6**

Least-squares plane data for **2a** and **3**.

**2a**

S1a-chelate ring: envelope with Sn1a lying 0.307(4) Å above the remaining atoms (RMSD = 0.0060 Å)

S3a-chelate ring: planar with RMSD = 0.0057 Å

O1a-chelate ring: envelope with Sn1a lying 0.579(4) Å above the remaining atoms (RMSD = 0.0279 Å)

O3a-chelate ring: envelope with Sn1a lying 0.135(4) Å above the remaining atoms (RMSD = 0.0234 Å)

**3**

S1-chelate ring: envelope with Sn1a lying 0.392(4) Å above the remaining atoms (RMSD = 0.0066 Å)

S3-chelate ring: envelope with Sn1a lying 0.309(4) Å above the remaining atoms (RMSD = 0.0124 Å)

O1-chelate ring: envelope with Sn1a lying 0.463(4) Å above the remaining atoms (RMSD = 0.0392 Å)

O3-chelate ring: envelope with Sn1a lying 0.271(4) Å above the remaining atoms (RMSD = 0.0343 Å)

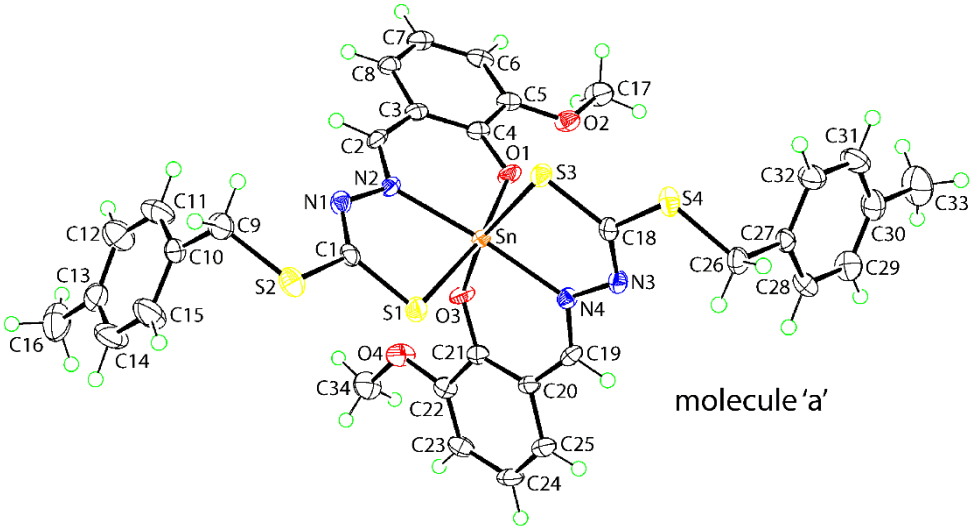



**Fig. S2.** The molecular structure of the second independent molecule of **2**, i.e. **2a**, showing atom labelling scheme and 50% displacement ellipsoids.

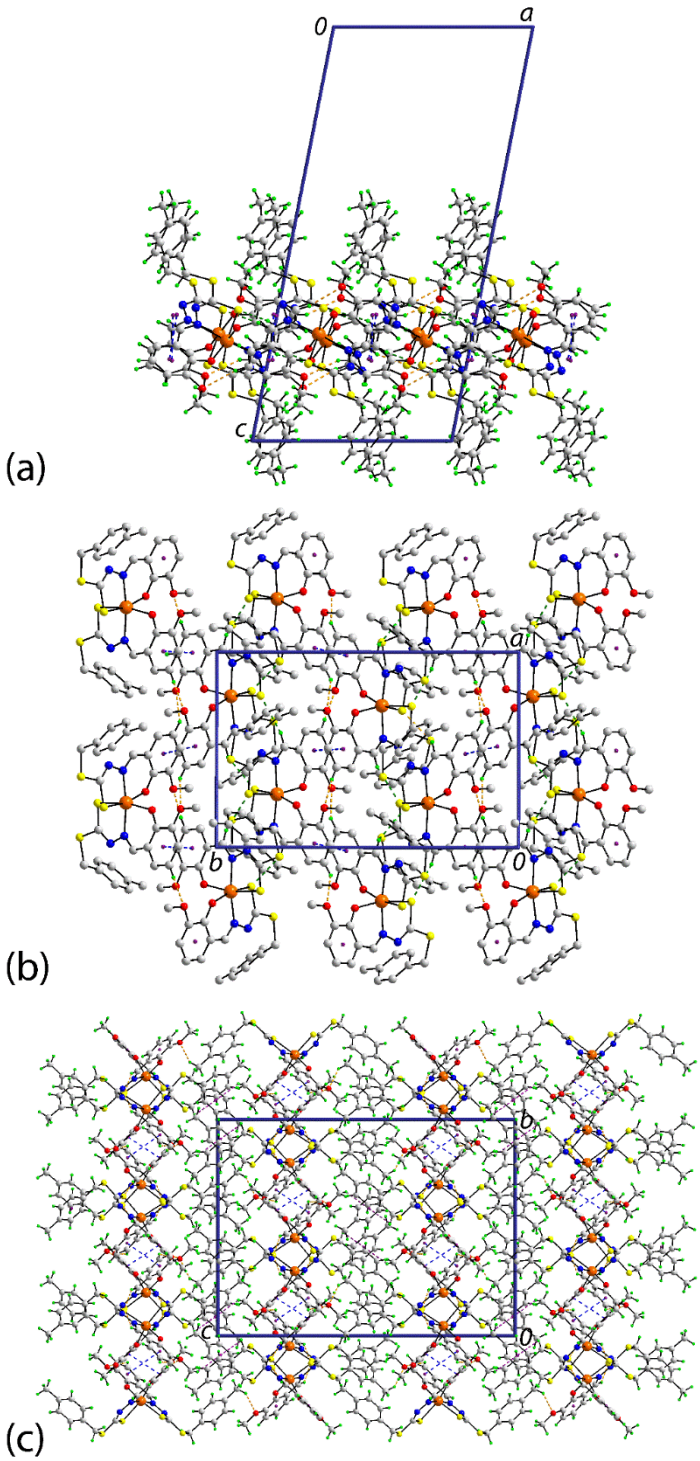



**Fig. S3.** Molecular packing in **2**: (a) a side-on view of the supramolecular layer in the *ab*-plane, (b) plane view of the supramolecular layer (non-participating hydrogen atoms have been removed for clarity) and (c) unit cell contents in projection down the *a*-axis. The C–H···O, C–H···S, C–H···π and π···π interactions are shown as orange, green, purple and blue dashed lines, respectively.

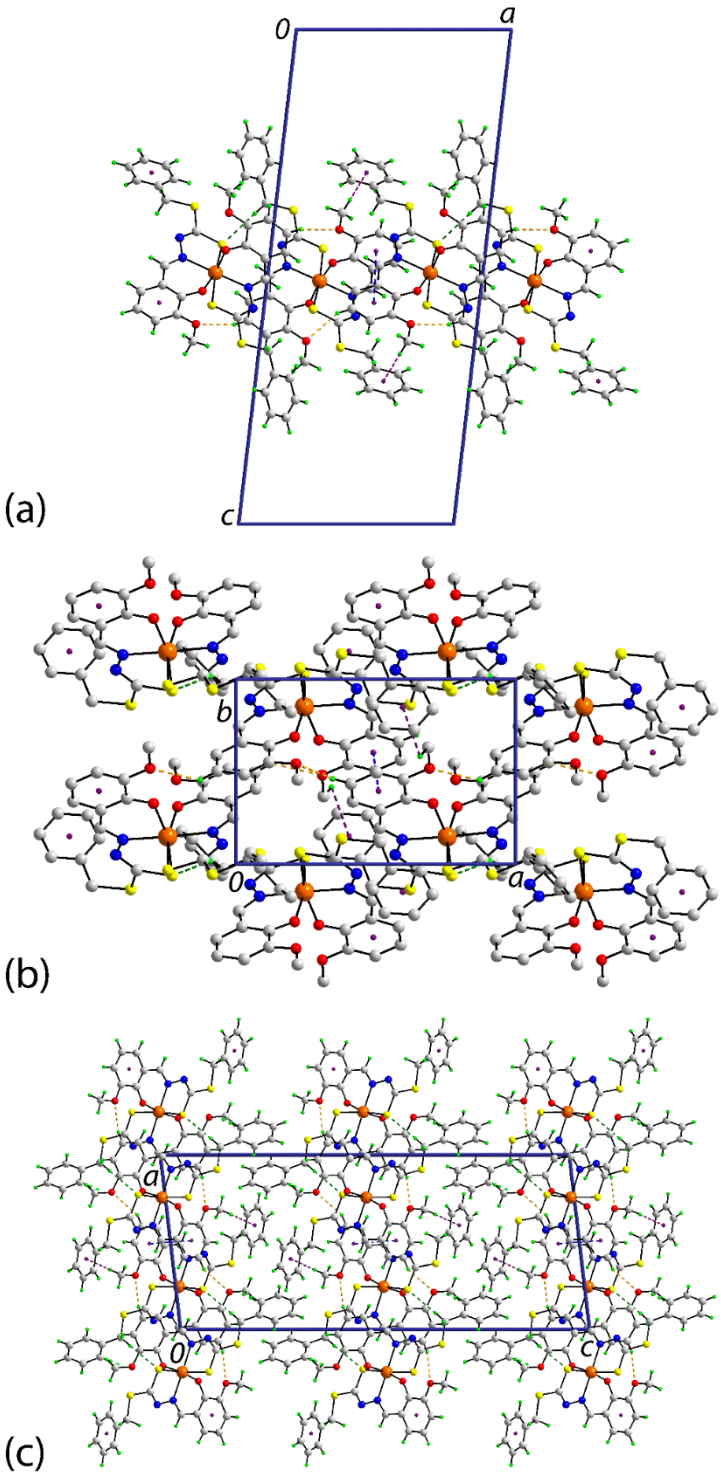
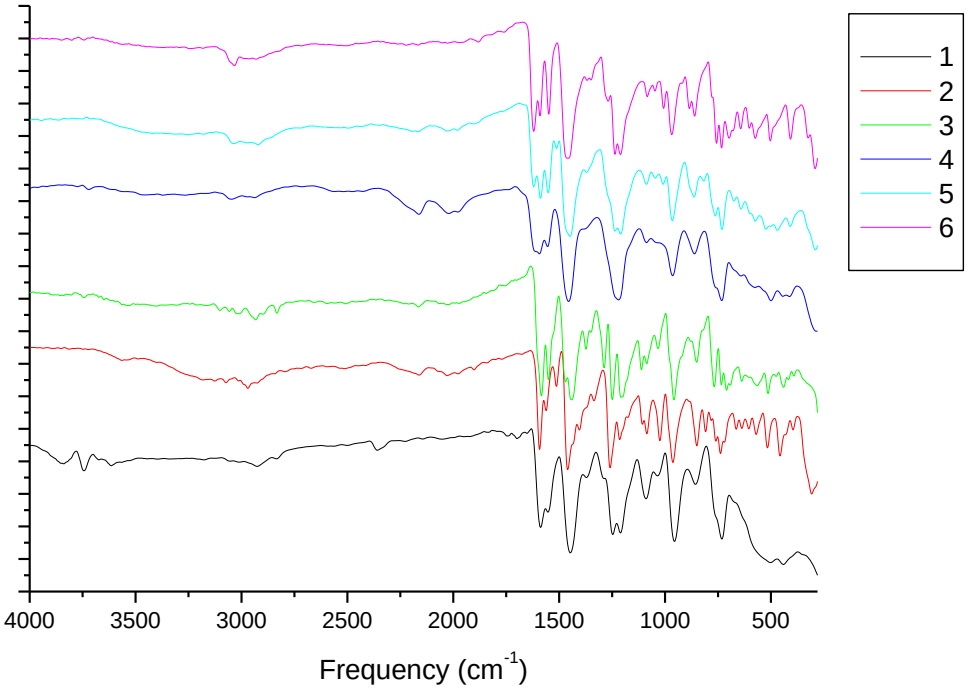
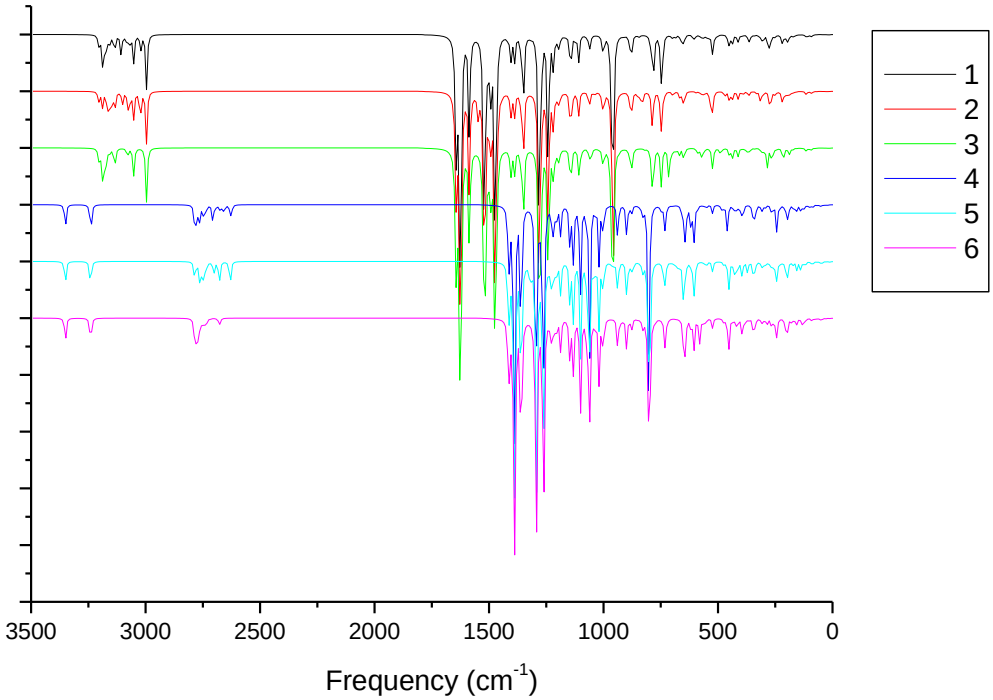


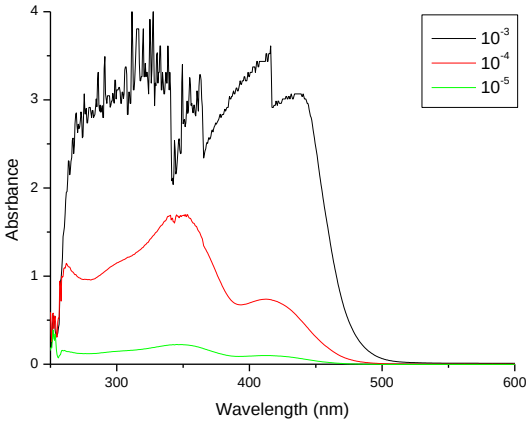

**Fig. S4.** Molecular packing in **3**: (a) a side-on view of the supramolecular layer in the *ab*-plane, (b) plane view of the supramolecular layer (non-participating hydrogen atoms have been removed for clarity) and (c) unit cell contents in projection down the *b*-axis. The C–H···O, C–H···S, C–H···π and π···π interactions are shown as orange, green, purple and blue dashed lines, respectively.



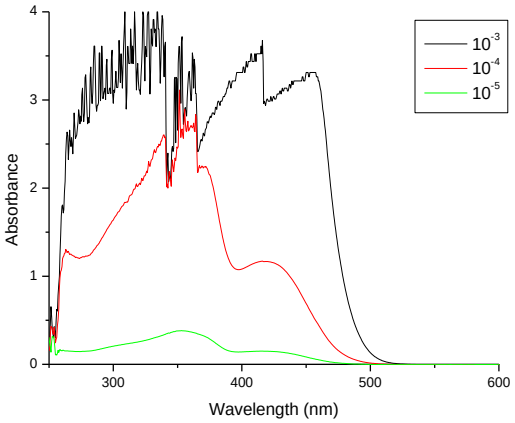

Experimental FTIR spectra of tin(IV) compounds



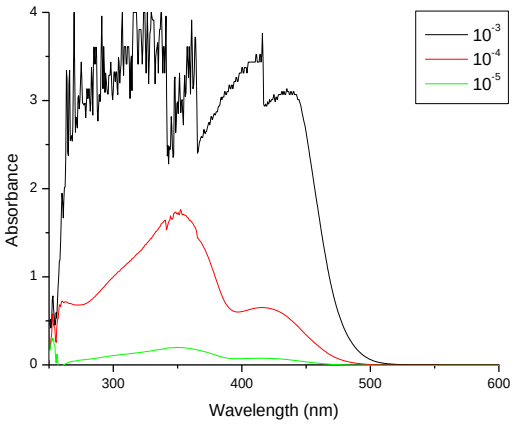

Simulated FTIR spectra of tin(IV) compounds



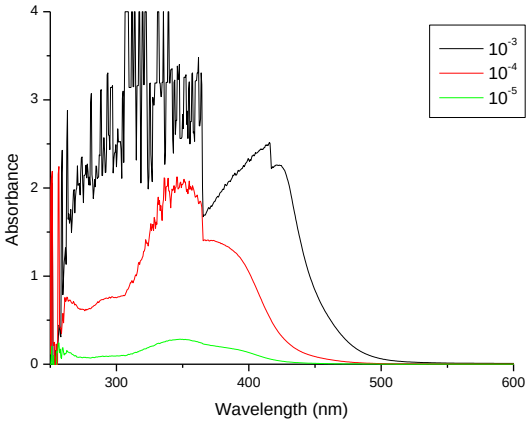

Experimental UV-vis spectra of 1.



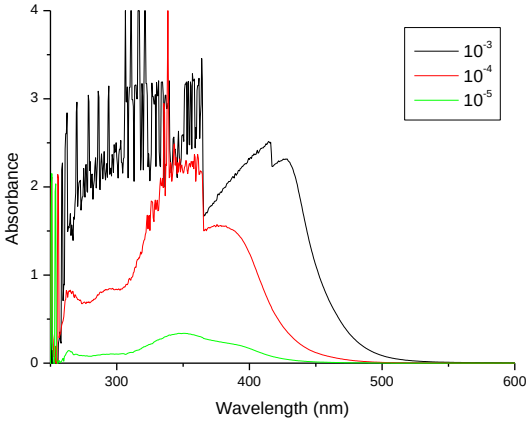

Experimental UV-vis spectra of 2.



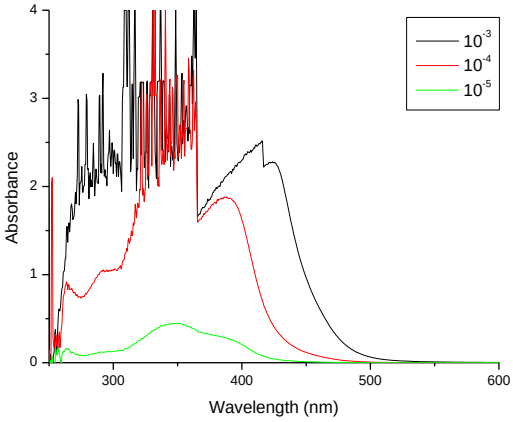

Experimental UV-vis spectra of 3.



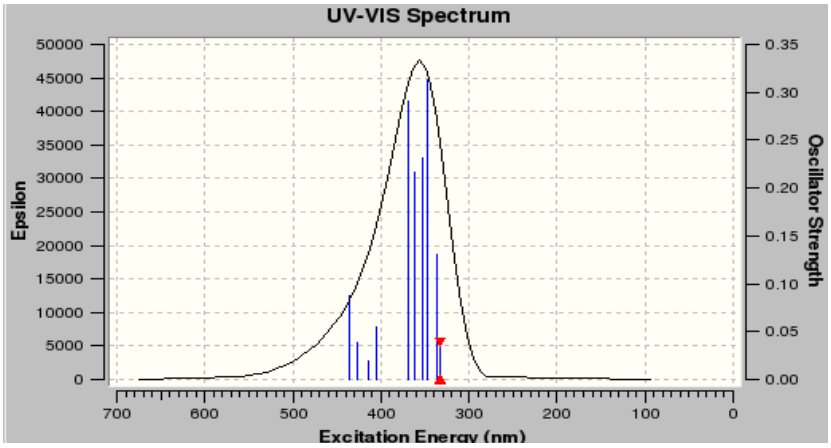

Experimental UV-vis spectra of 4.



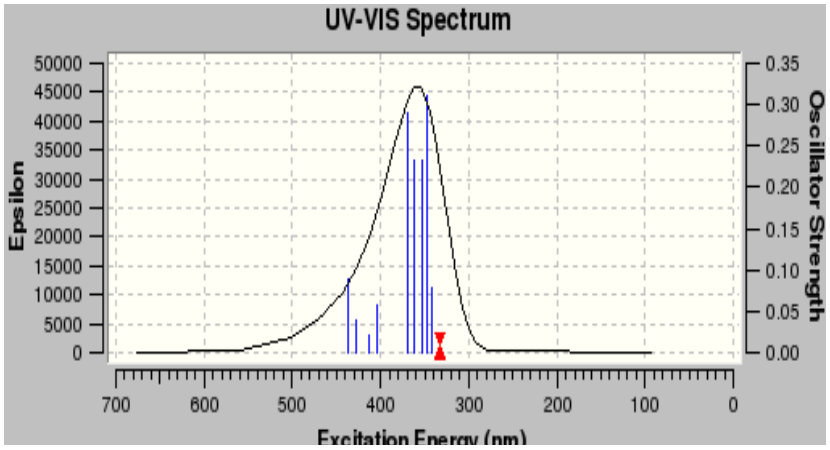

Experimental UV-vis spectra of 5.



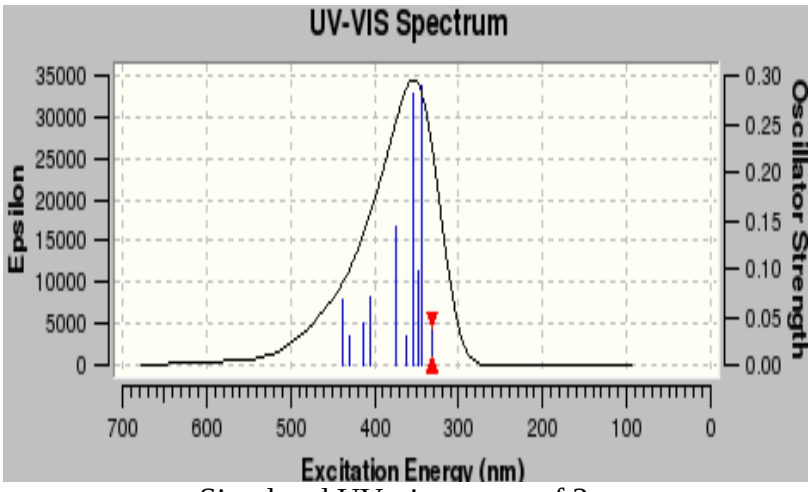

Experimental UV-vis spectra of 6.



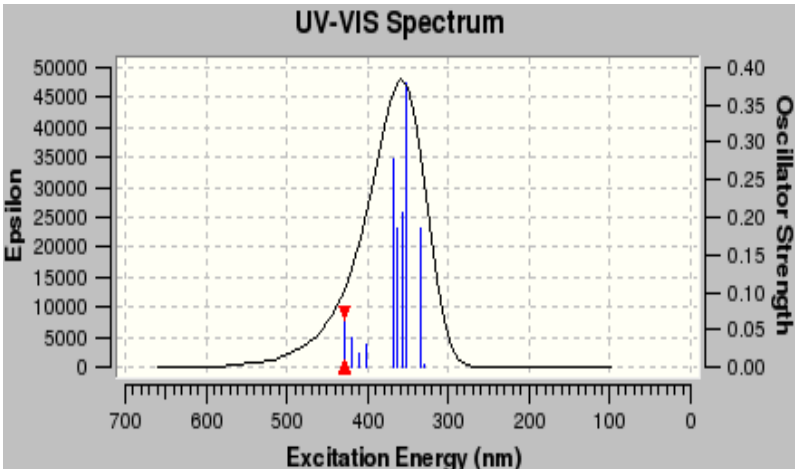
Simulated UV-vis spectra of 1.



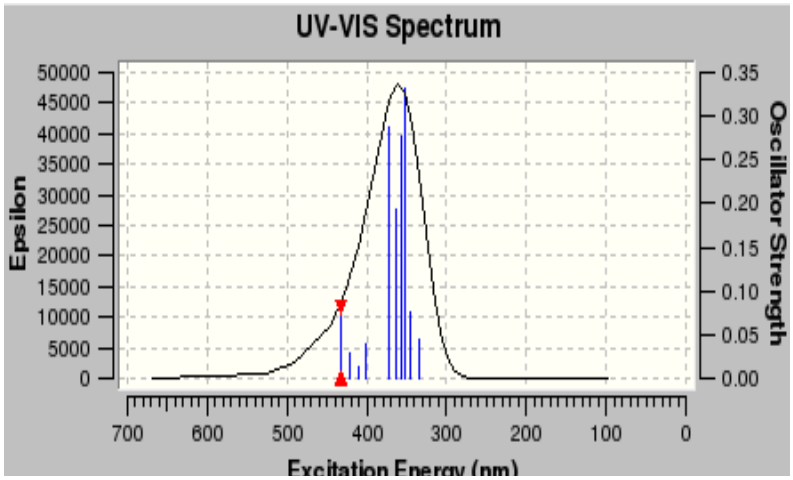
Simulated UV-vis spectra of 2.



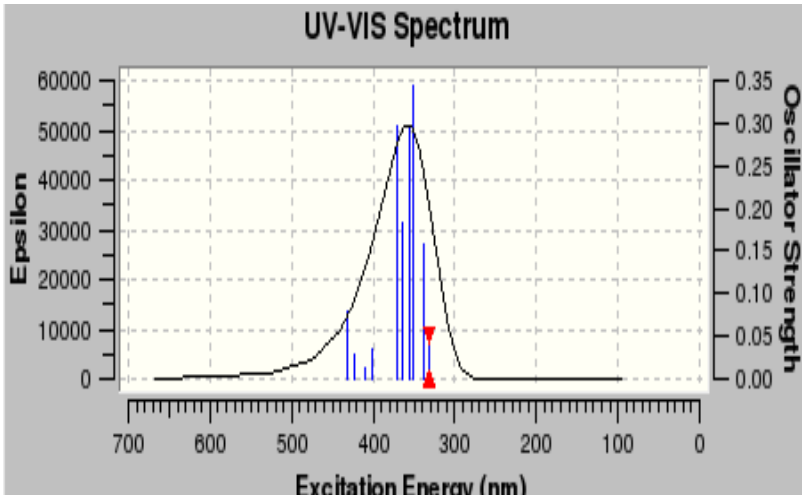
Simulated UV-vis spectra of 3.



Simulated UV-vis spectra of 4.



Simulated UV-vis spectra of 5.



Simulated UV-vis spectra of 6.

Click here to download Supplementary Material: 2_checkcif.pdf

# checkCIF/PLATON report

Structure factors have been supplied for datablock(s) shelx

THIS REPORT IS FOR GUIDANCE ONLY. IF USED AS PART OF A REVIEW PROCEDURE FOR PUBLICATION, IT SHOULD NOT REPLACE THE EXPERTISE OF AN EXPERIENCED CRYSTALLOGRAPHIC REFEREE.

No syntax errors found. CIF dictionary Interpreting this report

## Datablock: shelx

---

```
Bond precision:  C-C = 0.0047 A          Wavelength=0.71073

Cell:            a=12.8540(2)    b=19.4686(5)        c=27.2466(6)
                 alpha=90        beta=101.109(2)     gamma=90
Temperature:     150 K

                 Calculated                Reported
Volume           6690.7(3)                 6690.7(3)
Space group      P 21/n                    P 21/n
Hall group       -P 2yn                    -P 2yn
Moiety formula   C34 H32 N4 O4 S4 Sn       C34 H32 N4 O4 S4 Sn
Sum formula      C34 H32 N4 O4 S4 Sn       C34 H32 N4 O4 S4 Sn
Mr               807.59                    807.56
Dx,g cm-3        1.604                     1.603
Z                8                         8
Mu (mm-1)        1.059                     1.059
F000             3280.0                    3280.0
F000'            3279.77
h,k,lmax         17,26,37                  17,26,35
Nref             18644                     15972
Tmin,Tmax        0.898,0.948               0.830,1.000
Tmin'            0.881

Correction method= # Reported T Limits: Tmin=0.830 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 0.857          Theta(max)= 29.506

R(reflections)= 0.0406( 10737)    wR2(reflections)= 0.0932( 15972)

S = 1.005                 Npar= 855
```

---

The following ALERTS were generated. Each ALERT has the format
**test-name_ALERT_alert-type_alert-level**.
Click on the hyperlinks for more details of the test.

---

### Alert level B

PLAT910_ALERT_3_B Missing # of FCF Reflection(s) Below Theta(Min). 31 Note

**Author Response: he theta range for the data collection was 3.3 to 29.5 deg., presumably established by CrysAlis PRO. While theta(min) is a little high, the exclusion of these data is unlikely to be detrimental to the model.**

---

### Alert level C

PLAT220_ALERT_2_C Non-Solvent Resd 1 C Ueq(max)/Ueq(min) Range 4.2 Ratio
PLAT220_ALERT_2_C Non-Solvent Resd 2 C Ueq(max)/Ueq(min) Range 3.2 Ratio
PLAT222_ALERT_3_C Non-Solv. Resd 1 H Uiso(max)/Uiso(min) Range 4.4 Ratio
PLAT906_ALERT_3_C Large K Value in the Analysis of Variance ..... 4.485 Check

---

### Alert level G

PLAT720_ALERT_4_G Number of Unusual/Non-Standard Labels ..... 2 Note
PLAT794_ALERT_5_G Tentative Bond Valency for Sn1 (IV) . 4.25 Info
PLAT794_ALERT_5_G Tentative Bond Valency for Sn1A (IV) . 4.26 Info
PLAT912_ALERT_4_G Missing # of FCF Reflections Above STh/L= 0.600 2547 Note
PLAT952_ALERT_5_G Calculated (ThMax) and CIF-Reported Lmax Differ 2 Units
PLAT958_ALERT_1_G Calculated (ThMax) and Actual (FCF) Lmax Differ 2 Units
PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density. 3 Info

---

0 **ALERT level A** = Most likely a serious problem - resolve or explain
1 **ALERT level B** = A potentially serious problem, consider carefully
4 **ALERT level C** = Check. Ensure it is not caused by an omission or oversight
7 **ALERT level G** = General information/check it is not something unexpected

1 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
3 ALERT type 2 Indicator that the structure model may be wrong or deficient
3 ALERT type 3 Indicator that the structure quality may be low
2 ALERT type 4 Improvement, methodology, query or suggestion
3 ALERT type 5 Informative message, check

---

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

**Publication of your CIF in IUCr journals**

A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (*Acta Crystallographica, Journal of Applied Crystallography, Journal of Synchrotron Radiation*); however, if you intend to submit to *Acta Crystallographica Section C* or *E* or *IUCrData*, you should make sure that full publication checks are run on the final version of your CIF prior to submission.

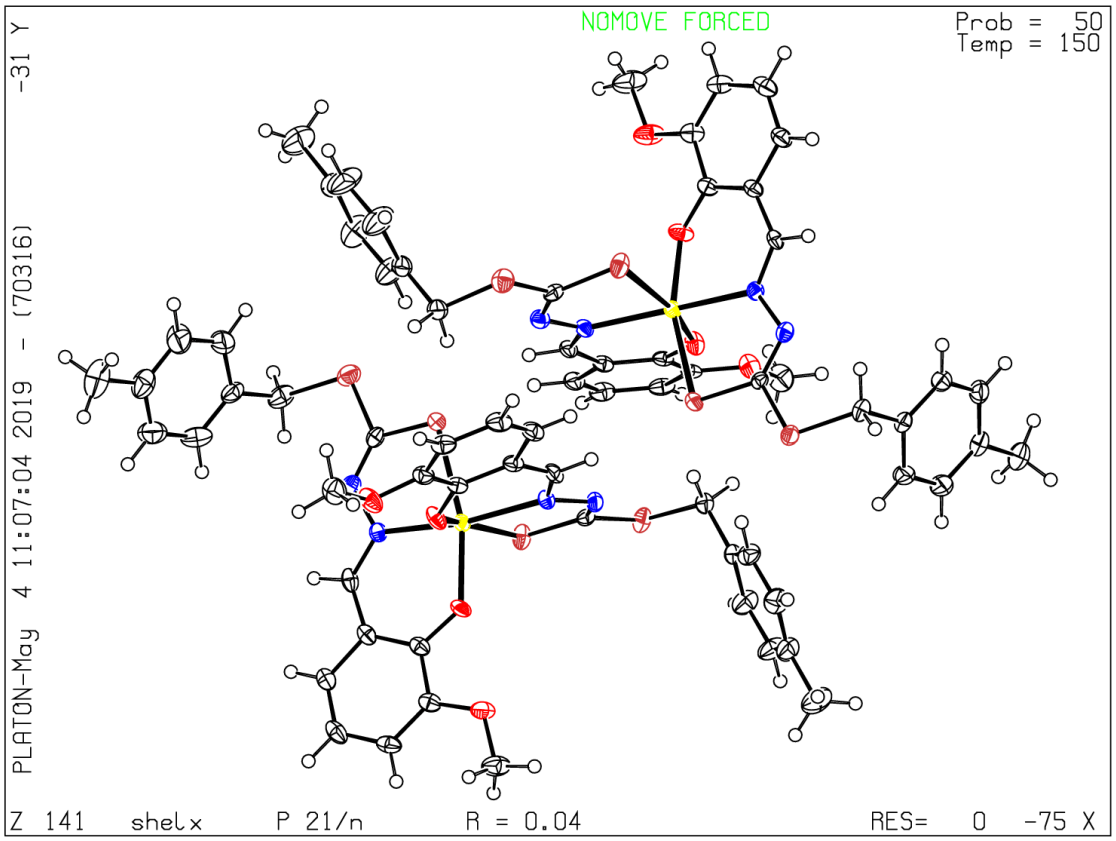
**Publication of your CIF in other journals**

Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIF submission.

---

**PLATON version of 03/05/2019; check.def file version of 29/04/2019**

**Datablock shelx** - ellipsoid plot



Click here to download Supplementary Material: 3_checkcif.pdf

# checkCIF/PLATON report

Structure factors have been supplied for datablock(s) shelx

THIS REPORT IS FOR GUIDANCE ONLY. IF USED AS PART OF A REVIEW PROCEDURE FOR PUBLICATION, IT SHOULD NOT REPLACE THE EXPERTISE OF AN EXPERIENCED CRYSTALLOGRAPHIC REFEREE.

No syntax errors found. CIF dictionary Interpreting this report

## Datablock: shelx

---

```
Bond precision:  C-C = 0.0043 A          Wavelength=0.71073

Cell:            a=12.8656(3)    b=8.4693(2)        c=29.8639(7)
                 alpha=90        beta=96.634(2)     gamma=90
Temperature:     150 K

                 Calculated                Reported
Volume           3232.26(13)               3232.26(13)
Space group      P 21/c                    P 21/c
Hall group       -P 2ybc                   -P 2ybc
Moiety formula   C32 H28 N4 O4 S4 Sn       C32 H28 N4 O4 S4 Sn
Sum formula      C32 H28 N4 O4 S4 Sn       C32 H28 N4 O4 S4 Sn
Mr               779.53                    779.51
Dx,g cm-3        1.602                     1.602
Z                4                         4
Mu (mm-1)        1.093                     1.093
F000             1576.0                    1576.0
F000'            1575.87
h,k,lmax         17,11,41                  17,11,39
Nref             8947                      7934
Tmin,Tmax        0.827,0.926               0.833,1.000
Tmin'            0.786

Correction method= # Reported T Limits: Tmin=0.833 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 0.887          Theta(max)= 29.421

R(reflections)= 0.0348( 6324)     wR2(reflections)= 0.0795( 7934)

S = 1.024                 Npar= 408
```

---

The following ALERTS were generated. Each ALERT has the format
**test-name_ALERT_alert-type_alert-level**.
Click on the hyperlinks for more details of the test.

---

## Alert level B

PLAT910_ALERT_3_B Missing # of FCF Reflection(s) Below Theta(Min). 17 Note

**Author Response: he theta range for the data collection was 3.4 to 29.4 deg., presumably established by CrysAlis PRO. While theta(min) is a little high, the exclusion of these data is unlikely to be detrimental to the model.**

---

## Alert level C

PLAT220_ALERT_2_C Non-Solvent Resd 1 C Ueq(max)/Ueq(min) Range 3.4 Ratio
PLAT906_ALERT_3_C Large K Value in the Analysis of Variance ..... 2.240 Check

---

## Alert level G

PLAT232_ALERT_2_G Hirshfeld Test Diff (M-X) Sn --S1 . 5.8 s.u.
PLAT794_ALERT_5_G Tentative Bond Valency for Sn (IV) . 4.34 Info
PLAT912_ALERT_4_G Missing # of FCF Reflections Above STh/L= 0.600 969 Note
PLAT952_ALERT_5_G Calculated (ThMax) and CIF-Reported Lmax Differ 2 Units
PLAT958_ALERT_1_G Calculated (ThMax) and Actual (FCF) Lmax Differ 2 Units
PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density. 5 Info

---

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2 **ALERT level C** = Check. Ensure it is not caused by an omission or oversight
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2 ALERT type 3 Indicator that the structure quality may be low
1 ALERT type 4 Improvement, methodology, query or suggestion
2 ALERT type 5 Informative message, check

---

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A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (*Acta Crystallographica, Journal of Applied Crystallography, Journal of Synchrotron Radiation*); however, if you intend to submit to *Acta Crystallographica Section C* or *E* or *IUCrData*, you should make sure that full publication checks are run on the final version of your CIF prior to submission.

**Publication of your CIF in other journals**

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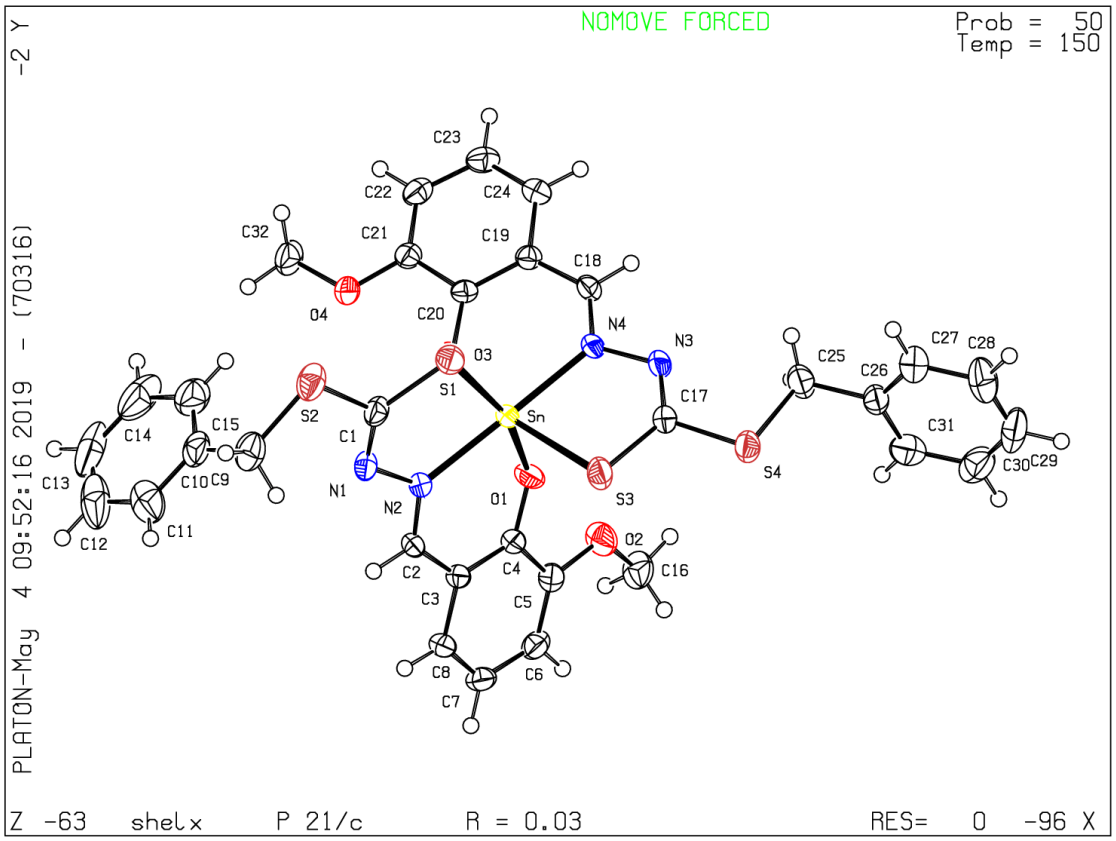
---

**PLATON version of 03/05/2019; check.def file version of 29/04/2019**

**Datablock shelx** - ellipsoid plot



CCDC Depository Request
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Gmail

**Edward Tiekink <edward.tiekink@gmail.com>**

# CCDC Depository Request

1 message

**CCDC Deposit** <deposit_reply@ccdc.cam.ac.uk> 16 May 2019 at 07:52
To: Edward Tiekink <edward.tiekink@gmail.com>

Dear Depositor,

Thank you for depositing your crystal structure(s) via the joint CCDC/FIZ Karlsruhe deposition service.

The data have been assigned the following deposition numbers which can either be quoted as CCDC Numbers or CSD Numbers. A CCDC Number is usually quoted for an organic or metal-organic structure, whereas a CSD Number is usually quoted for an inorganic structure.

CCDC XXXXXXX-YYYYYYY (generally used for organic and metal-organic structures)

CSD XXXXXXX-YYYYYYY (generally used for inorganic structures)

CCDC 1916354-1916355

---
Summary of Data CCDC 1916354
---
Compound Name:
Formula: C34 H32 N4 O4 S4 Sn1
Unit Cell Parameters: a 12.8540(2) b 19.4686(5) c 27.2466(6) P21/n
---
---
Summary of Data CCDC 1916355
---
Compound Name:
Formula: C32 H28 N4 O4 S4 Sn1
Unit Cell Parameters: a 12.8656(3) b 8.4693(2) c 29.8639(7) P21/c
---

After publication your data will be made available through our joint Access Structures service. In addition, organic and metal-organic experimental structures will be curated into the Cambridge Structural Database and inorganic experimental structures will be curated into the Inorganic Crystal Structure Database.

If you selected “Publish in a Database” your data will be immediately published through our joint Access Structures service.

Please note, if any of these structures are not published within one year from today and we cannot contact you to discuss the matter, then we may publish the data directly through the CSD as a *CSD Communication* or the ICSD as an *ICSD Communication*.

If we have any queries relating to the data then we may contact you later.

Kind Regards,

The CCDC and FIZ Karlsruhe Deposition Teams

Email: deposit@ccdc.cam.ac.uk
The Cambridge Crystallographic Data Centre
https://www.ccdc.cam.ac.uk

For more information about CSD Communications see:
https://www.ccdc.cam.ac.uk/Community/Depositastructure/CSDCommunications/
FIZ Karlsruhe
www.fiz-karlsruhe.de

The CCDC and FIZ Karlsruhe are delighted to be working together on shared deposition and access services for crystallographic data across all domains of chemistry

More details can be found in our press release: https://www.ccdc.cam.ac.uk/News/List/2018-07-new-joint-services/

**cif 2**

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**cif 3**

**Click here to download Mol Files: 3.cif**

**Scheme 1**

**Click here to download Mol Files: Scheme1.cdx**

# Author contributions

Use this form to specify the contribution of each author of your manuscript. A distinction is made between five types of contributions: Conceived and designed the analysis; Collected the data; Contributed data or analysis tools; Performed the analysis; Wrote the paper.

For each author of your manuscript, please indicate the types of contributions the author has made. An author may have made more than one type of contribution. Optionally, for each contribution type, you may specify the contribution of an author in more detail by providing a one-sentence statement in which the contribution is summarized. In the case of an author who contributed to performing the analysis, the author's contribution for instance could be specified in more detail as 'Performed the computer simulations', 'Performed the statistical analysis', or 'Performed the text mining analysis'.

If an author has made a contribution that is not covered by the five pre-defined contribution types, then please choose 'Other contribution' and provide a one-sentence statement summarizing the author's contribution.

**Manuscript title: Homoleptic tin(IV) compounds containing tridentate ONS dithiocarbazate Schiff bases: Synthesis, X-ray crystallography, DFT and cytotoxicity studies**

**Author 1:** Enis Nadia Md Yusof

☒ Conceived and designed the analysis
Specify contribution in more detail (optional; no more than one sentence)

☒ Collected the data
Specify contribution in more detail (optional; no more than one sentence)

☒ Contributed data or analysis tools
Specify contribution in more detail (optional; no more than one sentence)

☒ Performed the analysis
Specify contribution in more detail (optional; no more than one sentence)

☒ Wrote the paper
Specify contribution in more detail (optional; no more than one sentence)

☐ Other contribution
Specify contribution in more detail (required; no more than one sentence)

**Author 2:** Muhammad A. M. Latif

☒ Conceived and designed the analysis
Specify contribution in more detail (optional; no more than one sentence)

☐ Collected the data
Specify contribution in more detail (optional; no more than one sentence)

☒ Contributed data or analysis tools
Specify contribution in more detail (optional; no more than one sentence)

☐ Performed the analysis
Specify contribution in more detail (optional; no more than one sentence)

☒ Wrote the paper
Specify contribution in more detail (optional; no more than one sentence)

☐ Other contribution
Specify contribution in more detail (required; no more than one sentence)

**Author 3:** Mohamed I. M. Tahir

☐ Conceived and designed the analysis
Specify contribution in more detail (optional; no more than one sentence)

☒ Collected the data
Specify contribution in more detail (optional; no more than one sentence)

☒ Contributed data or analysis tools
Specify contribution in more detail (optional; no more than one sentence)

☐ Performed the analysis
Specify contribution in more detail (optional; no more than one sentence)

☒ Wrote the paper
Specify contribution in more detail (optional; no more than one sentence)

☐ Other contribution
Specify contribution in more detail (required; no more than one sentence)

**Author 4:** Jennette A. Sakoff

☒ Conceived and designed the analysis
Specify contribution in more detail (optional; no more than one sentence)

☒ Collected the data
Specify contribution in more detail (optional; no more than one sentence)

☒ Contributed data or analysis tools
Specify contribution in more detail (optional; no more than one sentence)

☒ Performed the analysis
Specify contribution in more detail (optional; no more than one sentence)

☐ Wrote the paper
Specify contribution in more detail (optional; no more than one sentence)

☐ Other contribution
Specify contribution in more detail (required; no more than one sentence)

**Author 5:** Abhi Veerakumarasivam

☒ Conceived and designed the analysis
Specify contribution in more detail (optional; no more than one sentence)

☐ Collected the data
Specify contribution in more detail (optional; no more than one sentence)

☒ Contributed data or analysis tools
Specify contribution in more detail (optional; no more than one sentence)

☐ Performed the analysis
Specify contribution in more detail (optional; no more than one sentence)

☒ Wrote the paper
Specify contribution in more detail (optional; no more than one sentence)

☐ Other contribution
Specify contribution in more detail (required; no more than one sentence)

**Author 6:** Alister J. Page

☒ Conceived and designed the analysis
Specify contribution in more detail (optional; no more than one sentence)

☒ Collected the data
Specify contribution in more detail (optional; no more than one sentence)

☒ Contributed data or analysis tools
Specify contribution in more detail (optional; no more than one sentence)

☒ Performed the analysis
Specify contribution in more detail (optional; no more than one sentence)

☒ Wrote the paper
Specify contribution in more detail (optional; no more than one sentence)

☐ Other contribution
Specify contribution in more detail (required; no more than one sentence)

**Author 7:** Edward R. T. Tiekink

☒ Conceived and designed the analysis
Specify contribution in more detail (optional; no more than one sentence)

☒ Collected the data
Specify contribution in more detail (optional; no more than one sentence)

☒ Contributed data or analysis tools
Specify contribution in more detail (optional; no more than one sentence)

☒ Performed the analysis
Specify contribution in more detail (optional; no more than one sentence)

☒ Wrote the paper
Specify contribution in more detail (optional; no more than one sentence)

☐ Other contribution
Specify contribution in more detail (required; no more than one sentence)

**Author 8:** Thahira B. S. A. Ravoof

☒ Conceived and designed the analysis
Specify contribution in more detail (optional; no more than one sentence)

☒ Collected the data
Specify contribution in more detail (optional; no more than one sentence)

☒ Contributed data or analysis tools
Specify contribution in more detail (optional; no more than one sentence)

☒ Performed the analysis
Specify contribution in more detail (optional; no more than one sentence)

☒ Wrote the paper
Specify contribution in more detail (optional; no more than one sentence)

☐ Other contribution
Specify contribution in more detail (required; no more than one sentence)

**Author 9:** Enter author name

☐ Conceived and designed the analysis
Specify contribution in more detail (optional; no more than one sentence)

☐ Collected the data
Specify contribution in more detail (optional; no more than one sentence)

☐ Contributed data or analysis tools
Specify contribution in more detail (optional; no more than one sentence)

☐ Performed the analysis
Specify contribution in more detail (optional; no more than one sentence)

☐ Wrote the paper
Specify contribution in more detail (optional; no more than one sentence)

☐ Other contribution
Specify contribution in more detail (required; no more than one sentence)

**Author 10:** Enter author name

☐ Conceived and designed the analysis
Specify contribution in more detail (optional; no more than one sentence)

☐ Collected the data
Specify contribution in more detail (optional; no more than one sentence)

☐ Contributed data or analysis tools
Specify contribution in more detail (optional; no more than one sentence)

☐ Performed the analysis
Specify contribution in more detail (optional; no more than one sentence)

☐ Wrote the paper
Specify contribution in more detail (optional; no more than one sentence)

☐ Other contribution
Specify contribution in more detail (required; no more than one sentence)

***Declaration of Interest Statement**

**Declaration of interests**

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: