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ORIENTAL JOURNAL OF CHEMISTRY
An International Open Access, Peer Reviewed Research Journal

www.orientjchem.org

ISSN: 0970-020 X
CODEN: OJCHEG
2023, Vol. 39, No.(4):
Pg. 835-844

Synthesis of New Organotin(IV) *N*-methyl-*N*-benzyl Dithiocarbamate Compounds and Cytotoxicity assessment on Human Lung Carcinoma Cell Line (A549)

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http://dx.doi.org/10.13005/ojc/390403

(Received: April 07, 2023; Accepted: July 14, 2023)

ABSTRACT

Using the *in situ* method, the successful synthesis of dibutyltin(IV) *N*-methyl-*N*-benzyl dithiocarbamate (Compound 1) and tricyclohexyltin(IV) *N*-methyl-*N*-benzyl dithiocarbamate (Compound 2) was achieved. Both compounds were characterized by the CHNS elemental analysis, FTIR, NMR spectroscopies and X-ray crystallography study. The experimental CHNS values demonstrated good congruence with the CHNS's theoretical values of the suggested formula structures. The key infrared absorbance peaks, v(C–N) and v(C–S), which were found between 1475–1481 cm^{-1} and 971–975 cm^{-1}, respectively. The ^{13}C chemical shift of carbon in the NCS_2 group was observed in the range of 200.66–202.32 ppm. The crystal structure of Compound 1 shows the anisobidentate's coordination mode between the central metal of the Sn atom and the dithiocarbamate ligands. Compound 1 and Compound 2 have shown great toxicity effects against carcinoma cells in the human lung (A549) with lower IC_{50} values of 0.80 µM and 2.77 µM, respectively.

Keywords: Organotin, Dithiocarbamate, A549 cells, Cytotoxicity, Anticancer.

INTRODUCTION

In developing and developed nations, a major cause of death is cancer. Cancer was responsible for nearly 10 million deaths in 2020. Worldwide, in statistical terms, most of these occurred due to lung cancer, after which came colorectal cancer, cancers of the liver and stomach, and breast cancer in females[1]. Meanwhile, in Malaysia, patients with lung cancer have a low survival rate in comparison to those with different forms of cancer since nearly one in ten generally obtain a diagnosis when their situation is critical, at stages III or IV[2]. This leads to an urgent study to discover useful anticancer drugs for lung cancer patients.

Chemotherapy, surgery, radiotherapy, and targeted therapy are commonly used for lung cancer treatment[3]. Nevertheless, when treating patients with lung cancer, particularly if they have NSCLC, the typical form of care remains platinum-based chemotherapy[4], with the standard drug utilized generally being cisplatin[5,6]. The action of cisplatin is to bind to the N7 reactive center on purine residues, resulting in damage to the deoxyribonucleic acid of the cancer cells and apoptotic cell death[7]. Although cisplatin is an effective anticancer agent, its side effects and resistance limit its clinical use in cancer treatment[8]. Certain patients can experience side effects such as nephrotoxicity, nausea, hepatotoxicity, cardiotoxicity and neurotoxicity from cisplatin. Meanwhile, damage to DNA can be repaired to a greater extent and the cisplatin's accumulation intracellular and cytosolic inactivation can be reduced, which are the principal causes of the development of resistance to cisplatin[9].

As a result, scientists have conducted several studies to replace existing treatments, including using non-platinum metals, such as organotin(IV). The anti-tumor properties of the first organotin(IV) compounds have been studied, and they have shown properties almost identical to cisplatin[10]. Recent studies have highlighted the therapeutic potential of the organotin(IV) dithiocarbamate compounds[11–13]. At even a low concentration, an organotin(IV) compound has high toxicity and, in cancer cells, they display anticancer activity through gene-mediated pathways[14]. The coordination number as well as the characteristics of groups bonded to the centre of tin atom are responsible for the ability to bind to this type of compound's DNA[14]. The complexes formed from the binding of organotin (IV) compounds with stable ligands like dithiocarbamate might cause them to have greater lipophilic properties, thus creating reactions with the components of the cells, which might result in the cells dying[15–17]. Therefore, the synthesizing, characterizing, and evaluating the cytotoxic effects of novel organotin(IV) dithiocarbamate compounds against carcinoma cells in the human lung (A549) will be conducted in the study.

MATERIALS AND METHODS

Reagents

The following suppliers sold all the chemicals and reagents involved, which were utilized precisely as received: *N*-methylbenzylamine, dibutyltin(IV) dichloride, tricyclohexyltin(IV) chloride, and cisplatin (Sigma-Aldrich, Germany); ethanol and chloroform (Systerm, Malaysia); carbon disulfide and ammonia solution 25% were supplied by Merck; DMSO (Sigma-Aldrich, USA).

Synthesis of organotin(IV) *N*-methyl-*N*-benzyl dithiocarbamate

Two compounds were synthesized via the *in situ* method by the reaction between organotin(IV) salt and secondary amines. According to the molar ratio of 1:1 and 2:1 for triorganotin(IV) and diorganotin(IV), respectively, dibutyltin(IV) dichloride and tricyclohexyltin(IV) chloride was allowed to react with the secondary amines; *N*-methylbenzylamine and carbon disulfide in ethanolic solution. For 120 min at a temperature under 4°C, stirring of the reaction mixture was performed. After filtering, cold ethanol was used to wash the mixture. Upon the formation of white precipitate, it was left to dry in a desiccator over several days.

Physical Measurement

Both of synthesized compounds were characterized by using analytical techniques and basic spectroscopies, including CHNS elemental analysis, FTIR spectroscopy, NMR spectroscopy, and an X-ray single crystallography study. MPA120 EZ-Melt automated melting point apparatus was used to measure the melting points of each compound. The melting point of a pure compound should be in the range of 1–3°C. Next, the CHNS Elemental Analyzer model Perkin Elmer 2400 was used to elementally analyze the carbon, hydrogen, nitrogen, and sulfur, whereby a comparison was made between the analytical value and theoretical percentage. Next, the infrared spectra of each compound were determined by using a Bruker (Vertex 70v) FTIR Spectrometer in the spectral range of 4000–80 cm^{-1}. Functional groups presence in each compound could be detected through FT-IR analysis. The chemical shifts of ^{1}H, ^{13}C, and ^{119}Sn NMR spectra were obtained by using an NMR spectrophotometer model Bruker AVANCE 400 III HD in $CdCl_3$, with tetramethylsilane as an internal standard.

A Rigaku single-crystal X-ray diffractometer was used to determine compound's crystal structure. Both FTIR and X-ray single crystallography study was

conducted at Sunway University. The measurements of CHNS analysis were conducted at the Organic Synthesis Research Laboratory, Institute of Science, Universiti Teknologi MARA (UiTM) Puncak Alam, whereby the NMR spectroscopies were conducted in Centre for Research and Instrumentation Management (CRIM), UKM.

Recrystallization and Crystallographic study

To perform the stages of crystallization, the compound was dissolved at room temperature in a solution of ethanol and chloroform at a 1:2 ν/ν ratio. Then, the mixture was slowly evaporated for three to four days until colorless crystals formed. The formed crystals were harvested and then examined using X-ray crystallography in a cold liquid nitrogen stream.

Cell and Cell Culture

Human lung carcinoma cells (A549) were purchased from the American Type Culture Collection (ATCC). A549 cells were cultured in Dulbecco's Modified Eagle Medium (DMEM) (Sigma USA). The L-glutamine-enriched media were supplemented with 1% penicillin/streptomycin and 10% fetal bovine serum (FBS).

MTT Cytotoxicity Assay

By using the 3-(4,5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide (MTT) assay[18], the synthesized compounds were screened against the A549 cell line. Six concentrations of the serial dilution of each compound were formulated, including 0.16 µM, 0.31 µM, 0.63 µM, 1.25 µM and 2.5 µM, with the highest being 5.00 µM. In the MTT assay, the positive control utilized was cisplatin; meanwhile, a negative control was provided by the untreated cells. The A549 cells were seeded in a 96-well plate at a density of 5×10^4 mL^{-1} and incubated overnight at 37°C in 5% CO_2. Following incubation for 24 h the removal of the media from each well occurred, with each compound used to replace them. After the cells had been treated for 24 h, 20 µL of MTT was added to each well in a dark environment because MTT is light-sensitive. Following this, a four-hour incubation of the cells took place, after which the removal from each well of 180 µL of supernatant occurred. Then, the newly formed formazan crystals were dissolved with the addition of 180 µL DMSO. Once DMSO had been introduced, a 15 min incubation of the 96-well plate was performed again. At 570 nm, a Multiskan GO microplate reader (Thermo Fisher Scientific) was used to detect the compounds' cytotoxicity effects. To plot the cytotoxicity graphs, the viable-cell percentages and compound concentrations were set against each other. Once the graphs had been plotted, the IC_{50} values could be ascertained, indicating that in comparison to the cells that had not been treated, the cell population in the treated cells had been halved.

Statistical analysis

The data obtained from this study was analyzed using one-way ANOVA by using IBM Statistical Package for Social Sciences (SPSS). The data is statistically significant when $p<0.05$.

RESULTS AND DISCUSSION

Synthesis of Compounds 1 and 2

Two new organotin(IV) dithiocarbamate compounds were synthesized by using the *in situ* method in this study. Both compounds were synthesized through the reactions of organotin(IV) salt [dibutyltin(IV) dichloride or tricyclohexyltin(IV) chloride] and secondary amines [*N*-methylbenzylamine] in the presence of carbon disulphide in ethanol. The compounds were synthesized in an ice bath at temperatures below 4°C to prevent the dithiocarbamate ligand from decomposing. Two hours later, after filtration, cold ethanol was used to wash the mixture three times. The mixture was left to dry in a desiccator up to the point at which a white powder of the compounds had been produced.

Table 1 shows the compounds' physical characteristics and the data related to the analysis. Based on Table 1, the percentage yields of both compounds were in the range of 57.6–75.3%, which is higher than 50% of the theoretical yield. Both compounds can be assumed to be pure compounds because their melting points were less than 3°C. Found to be white solids, at room temperature, each compound (1 and 2) was stable in the atmosphere. Using the recommended formula, the values from the experiment and the theory demonstrated good agreement with the data from the C, H, N, and S elemental analysis.

The results of two newly synthesized organotin(IV) *N*-methyl-*N*-benzyldithiocarbamate compounds are confirmed to be similar to the suggested structural formula. The structural formulas for these compounds are dibutyltin (IV) *N*-methyl-*N*-benzyldithiocarbamate $(C_4H_9)_2Sn[S_2CN(CH_3(C_6H_5)(CH_2)]_2$ (Compound 1) (Fig. 1) and tricyclohexyltin(IV) *N*-methyl-*N*-benzyldithiocarbamate $(C_6H_{11})_3Sn[S_2CN(CH_3(C_6H_5)(CH_2)]$ (Compound 2) (Figure 2).

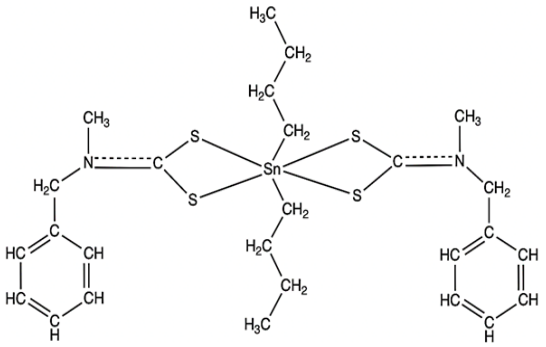

Fig. 1. The chemical structure of Compound 1

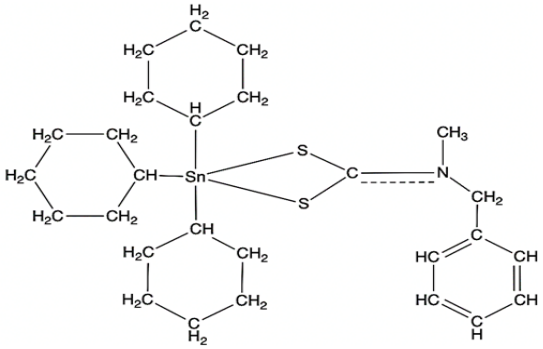

Fig. 2. The chemical structure of Compound 2

Table 1: The Physical Properties and Elemental Analytical Data of Compounds 1 and 2

Molecular formula	Color	Yield(%)	Melting Point (°C)	C	H	N	S
Compound 1 $(C_4H_9)_2Sn[S_2CN(CH_3(C_6H_5)(CH_2)]_2$	White	75.3	92.4–94.4	48.66	5.98	4.31	20.08
Compound 2 $(C_6H_{11})_3Sn[S_2CN(CH_3(C_6H_5)(CH_2)]$	White	57.6	72.6–74.6	57.35	8.12	1.55	8.79
				57.45	**7.68**	**2.48**	**11.36**

*Bold: Theoretical value

Infrared Spectroscopy Analysis

The key vibrational bands obtained using Fourier-transform infrared (FTIR) spectroscopy for compounds 1 and 2 are shown in Table 2. The important absorbance peaks that identify the presence of dithiocarbamate ligands were based on the presence of ν(C---N) and ν(C---S). The ν(C---N) band, also known as the thiouride band, was discovered in the 1475–1481 cm^{-1} range. The thiouride band is usually observed in the range of wavelengths between 1450 and 1550 cm^{-1} [19,20]. Adeyemi *et al.,* (2019) reported the existence of the thiouride band at wavelengths ranging from 1443 to 1488 cm^{-1} [21].

Meanwhile, the ν(C---S) band was discovered at 971–975 cm^{-1}. The presence of the ν(C---S) absorption band in the infrared spectrum indicates the mode of coordination of the ligand with the central metal, either monodentate or bidentate[22]. The bonding between the Sn atom and the organotin(IV) compound can be determined by the presence of ν(Sn-C). The ν(Sn-C) band was found in the spectral range of 496–552 cm^{-1} [11,23]. Therefore, as revealed in the analysis, dithiocarbamate groups and organotin(IV) compounds were present, which were comprised of the recommended formulae for each compound and fulfilled the criteria proposals of prior researchers.

Table 2: Infrared Absorption Bands of Compounds 1 and 2

Compound	Wavelength (cm^{-1})					
	νν(C-H)	νν(C---N)	νν(N-C)	νν(C---S)	νν(Sn-C)	νν(Sn-S)
1	3057	1481	1239	975	552	382
2	2915	1475	1246	971	496	379

Nucleus Magnetic Resonance Spectroscopy Analysis

Apart from FTIR analysis, NMR analysis has also been carried out to identify the molecular structure, ^{1}H, ^{13}C, and ^{119}Sn atoms in each of the synthesized compounds. Based on Table 3, the ^{1}H proton NMR of Compounds 1 and 2 shows the presence of a single signal for the methyl proton directly bound to the N atoms in dithiocarbamate at 3.328 ppm and 3.388 ppm[24], respectively. Besides, the methylene proton of methylene group attached directly to the N atom of dithiocarbamate ligands were observed in the range of 5.148–5.255 ppm[25]. A broad signal for the butyl group attached to the Sn atom was found in the range of 0.972–2.127 ppm[11,26], confirming that it's attached to the Sn atom, which is electropositive, through the

nuclei of carbon. This causes shielding, which occurs through the carbon chain[27].

Meanwhile, in Compound 2, proton signals in a range of 1.374–2.047 ppm were assigned for the tricyclohexyl group on the tin(IV) atom[28]. The aromatic multiplet signal of the proton of the phenyl group bound to Compounds 1 and 2 was observed in the chemical shift range of 7.249–7.374 ppm and 7.270–7.385 ppm, respectively. Consistently, the chemical shifts of 7.27 to 8.07 ppm were reported for the proton of the phenyl group (C_6H_5-N)[17,29]. Furthermore, for bis(p-substituted-*N*-methyl benzyl dithiocarbamate) compound that was synthesized by Khan *et al.,* (2015), the chemical shift of the aromatic proton of the phenyl group were observed in a range of 7.14–7.94 ppm[27].

Table 3: ^{1}H NMR Spectra Data of Compound 1 and Compound 2

Compound	Chemical shifts, δ (ppm)			
	N-R"(R"=C$\underline{H}_3$)	-NR'(R'=C$\underline{H}_2$)	-NR'R aromatic	Sn-R(R=C$_4\underline{H}_9$, C$_6\underline{H}_{11}$)
1	3.328	5.148	7.249–7.374	C$\underline{H}_2$:2.127 C$\underline{H}_2$: 1.986 C$\underline{H}_2$: 1.512 C$\underline{H}_3$: 0.972
2	3.388	5.255	7.270–7.385	1.374–2.047

Next, the presence of each carbon signal in the synthesized compound can be identified through the ^{13}C NMR spectra. Table 4 shows the data spectra of ^{13}C NMR. An important chemical shift in characterizing organotin(IV) dithiocarbamate compounds is the CS_2 carbon signal. The carbon atom signal in N-CS_2 of Compounds 1 and 2, appears in the chemical shift range between 200.66 and 202.32 ppm. The signal is usually observed in the chemical shift range of 185–220 ppm[30]. Through the CS_2 signal, it shows that the sulfur atom has formed a bond with the central metal of the Sn atom in the compound[13].

Furthermore, carbon signals for other carbon-containing substances were also observed in the ^{13}C NMR spectroscopy. Signals derived from the methylene carbon near the electronegative atom of nitrogen appeared to range from 59.95 to 60.70 ppm[11,31]. The resonation between 13.89 ppm and 34.46 ppm was observed for the dibutyltin(IV) compound[32], where the chemical shift in the range of 26.20–34.76 ppm was assigned for the tricyclohexyltin(IV) compound[28]. The diphenyl complex was obtained within the 127.45 to 135.83 ppm region, which corresponded to the information provided by Haezam *et al.,*[13] that showed resonation in the range of 119.0–136.75 ppm.

Table 5 shows the data spectra of the ^{119}Sn NMR of Compounds 1 and 2. The coordination number of the synthesized compound's Sn atom was determined through analysis using ^{119}Sn NMR spectroscopy. The result shows the ^{119}Sn spectra for Compounds 1 and 2 are in the range of –338.75 to –22.55 ppm. It explains that Compounds 1 and 2 have the expected coordination geometry of hepta[33] and tetra[34] around the tin center, respectively. The signal of the complex can have the same coordination and various chemical shifts in ^{119}Sn due to its dependence on the R group's number and characteristics, as well as the characteristics of the dithiocarbamate ligand to which the Sn atom is bound[35]. This may be due to the sensitivity of the chemical environment of tin[36,37].

Table 4: ^{13}C NMR Spectra Data of Compounds 1 and 2

Compound	Chemical shifts, δ (ppm)				
	N–C$\underline{S}_2$	Sn–R(R=C$_4\underline{H}_9$,C$_6\underline{H}_{11}$)	N-C$\underline{H}_2$C$_6$H$_5$	N-C$\underline{H}_3$	N–C$\underline{H}_2$C$_6$H$_5$
1	202.32	13.89(C$\underline{H}_2$), 26.48(C$\underline{H}_2$), 28.70(C$\underline{H}_2$), 34.46 (C$\underline{H}_3$)	59.95	41.77	127.55, 127.92, 128.83, 135.36
2	200.66	26.20–34.76	60.70	42.52	127.45,127.71,128.74, 135.83

Table 5: ^{119}Sn NMR Spectra Data of Compounds 1 and 2

Compound	Chemical shifts ^{119}Sn,δ(ppm)
1	–338.75
2	–22.55

X-ray single crystallography study

The data related to crystallography and refinement are shown in Table 6 , while compound 1's chosen bond lengths and angles are shown in Table 7. The recrystallization process was

carried out for both synthesized compounds through an evaporation process at room temperature using a mixture of two solvents: ethanol and chloroform at a certain ratio (1:2 v/v). Once evaporation at room temperature over a number of days had taken place, colorless crystals had been formed by only compound 1. Compound 1 (dibutyltin(IV) *N*-methyl-*N*-benzyldithiocarbamate) has a colorless crystal structure with dimensions of 0.27x0.20x0.11 mm and a molecular mass of 625.57 g. Compound 1's single crystal is in the triclinic system and the P1 space, where α = 9.6272(1) Å, *b* = 12.1043(2) Å, *c* = 13.3584(2) Å,α = 82.296(1)° *A*, and β = 86.611(1)°[38].

A significant difference can be detected in the bond distance of the four sulfur atoms that coordinate with the Sn atom, which is Sn–S1= 2.5334(4) and Sn–S3 = 2.5497(4). The central metal, Sn (IV) is covalently bonded to S1 and S3 within a normal Sn–S bond distance of 2.48–2.57 Å[23]. The asymmetric coordination of the dithiocarbamate ligands results in a large disparity of C–S bond lengths, with C1–S1 bonds being shorter than S2-bonds [C1–S1, S2 = 1.7477(19) & 1.6910(19) Å and 1.7528(19) & 1.6944(19) Å]. The crystal structure of Compound 1 shows the coordination mode by anisobidentate between the central metal of the Sn atom and the dithiocarbamate ligands. The C19–Sn–C23 for this compound is 137.83(7)° which is larger than the ideal angle for a tetrahedron (109.5°)[17,34], resulting in a distorted tetrahedron geometry. However, the S1–Sn–S3 bond angle which falls at 80.289(14)° was parallel to the S_{short}-Sn-S_{short} bond angles reported in previous studies (78°–88°)[23].

Figure 3 portrays the plotted ORTEP of Compound 1. The coordinate geometry depicted in the X-ray single crystal crystallographic analysis results is described as a skewed trapezoidal-bipyramidal geometry with a short trapezoidal edge formed through strong bonds between S1 and S3, while S2 and S4 bonds affect the length of the sides of the geometry.

Table 6: Crystallographic Data and Refinement Parameters for Compound 1[38]

Chemical formula	$C_{26}H_{38}N_2S_4Sn$
Molar mass (g)	625.57
α(Å)	9.6272(1)
b(Å)	12.1043(2)
c(Å)	13.3584(2)
α(°)	82.296(1)
β(°)	86.611(1)
y(°)	66.912(1)
V(Å^3)	1419.02(4)
Z	2
$R_{gt}(F)$	0.0235
$wR_{ref}(F^2)$	0.0612
SuhuT(K)	100
μ(mm^{-1})	10.0
Wavelength	Cu Kα radiation (1.54184Å)
Diffractometer, scan mode	XtaLAB Synergy, ω ν
θ_{max}, completeness	75.3°,>99%
$N(hkl)_{measured}$,	
$N(hkl)_{unique,}$ R_{int}	37, 119, 5854, 0.033
Criterion for I_{obs},$N(hkl)_{gt}$	I_{obs}>2σ (I_{obs}), 5841
$N(param)_{refined}$	302
Programs	CrysAlis^{PRO}, SHELX, W_{IN}GX/ORTEP

Table 7: Selected bond length (Å) and angles (°) for Compound 1

Bond lengths (Å)		Bond angles (°)	
Sn-C19	2.1479(18)	C19-Sn-C23	137.83(7)
Sn-C23	2.1530(18)	C19-Sn-S1	109.80(5)
Sn-S1	2.5334(4)	C23-Sn-S1	103.99(5)
Sn-S3	2.5497(4)	C19-Sn-S3	104.60(5)
S1-C1	1.7477(19)	C23-Sn-S3	105.32(5)
S2-C1	1.6910(19)	S1-Sn-S3	80.29(14)
S3-C10	1.7528(19)	C1-S1-Sn	94.16(6)
S4-C10	1.6944(19)	C10-S3-Sn	95.34(6)
N1-C1	1.337(2)	C1-N1-C2	122.40(16)
N1-C2	1.463(2)	C1-N1-C9	119.73(16)
N1-C9	1.465(2)	C2-N1-C9	117.72(15)
N2-C10	1.335(2)	C10-N2-C18	120.59(16)
N2-C18	1.467(2)	C10-N2-C11	124.05(15)
N2-C11	1.475(2)	C18-N2-C11	115.35(15)
C2-C3	1.519(3)	N1-C1-S2	122.35(14)
C3-C8	1.391(3)	N1-C1-S1	118.35(14)
C3-C4	1.391(3)	S2-C1-S1	119.30(11)
C4-C5	1.388(3)	N1-C2-C3	114.04(15)
C5-C6	1.391(3)	N2-C10-S4	122.09(14)
C6-C7	1.384(3)	N2-C10-S3	118.89(14)
C7-C8	1.392(3)	S4-C10-S3	119.01(10)
C11-C12	1.514(3)	N2-C11-C12	112.93(15)
C12-C13	1.388(3)	C20-C19-Sn	112.43(13)

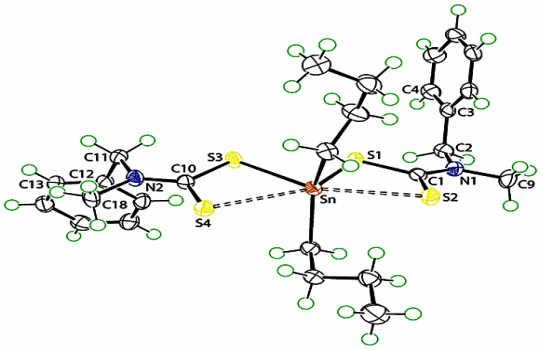

Fig. 3. ORTEP plot of Compound 1

Cytotoxicity of organotin(IV) *N*-methyl-*N*-benzyl dithiocarbamate compounds in A549 cells

Table 8 shows the IC_{50} values for Compound 1 (dibutyltin(IV) *N*-methyl-*N*-benzyl dithiocarbamate) and Compound 2 (tricyclohexyltin(IV) *N*-methyl-*N*-benzyl dithiocarbamate). As shown by the the MTT assay findings, each compound had a major cytotoxic effect on carcinoma cell lines in the human lung (A549). However, based on the inhibitory IC_{50} values of Compounds 1 and 2 at 0.80 µM (0.50 g/cm^3) and 2.77 µM (1.56 g/cm^3), it is observed that Compound 1 is highly toxic. Moreover, when compared with a standard drug, cisplatin, both compounds exhibit higher cytotoxicity activity toward A549 cell lines. As shown in Fig. 4, after being treated for 24 h the cytotoxic effects against A549 cells of organotin(IV) *N*-methyl-*N*-benzyl dithiocarbamate compounds could be identified.

Compound 1, which is dibutyltin(IV) *N*-methyl-*N*-benzyl dithiocarbamate, has a stronger cytotoxic effect than tricyclohexyltin(IV) *N*-methyl-*N*-benzyl dithiocarbamate because the toxicity is dependent on the structure of the compound. Study by Pellerito *et al.,* (2006) stated that certain elements or functional groups in a compound provide different proliferative effects to treated cells[39]. Furthermore, the cytotoxic effect can be influenced by the length and count of the alkyl groups connected to the metal tin atom in the center[40]. Greater toxicity is evident in organotin compounds that are highly substituted; meanwhile, compounds' cytotoxic effects are enhanced by shorter alkyl substituents[41–43]. Thus, the conclusion was that these published data demonstrated the generally greater anticancer activity of the diorganotin compound, compared to the triorganotin (IV) compound.

Table 8: IC_{50} values of Compound 1 and Compound 2 against A549 cells

Compound	IC_{50}(µM)±S.E.M
1	0.80 ± 0.09
2	2.77 ± 0.34
Cisplatin	32.00 ± 0.29

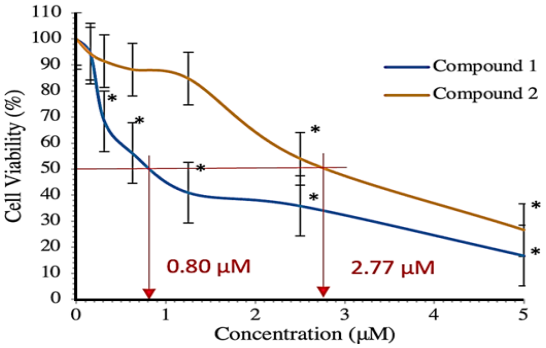

Fig. 4. The cytotoxicity of organotin(IV) *N*-methyl-*N*-benzyl dithiocarbamate compounds against A549 cells upon a 24-h treatment. The data show cell viability (%) ±S.E.M obtained from three separate experiments

CONCLUSION

Utilizing the *in situ* method enabled the successful synthesis of two novel organotin(IV) obtained via *N*-methyl-*N*-benzyldithiocarbamate. Elemental and spectroscopies analysis, namely CHNS analysis, FT-IR and NMR spectroscopies were then employed to characterize these compounds. In general, the theoretical CHNS values were exhibited by the experimental CHNS values of each compound. Moreover, each compound displayed the presence of crucial absorbance peaks: v(C---N), v(C---S), v(Sn-S) and v(Sn-C) which indicates that the organotin(IV) dithiocarbamate compounds have formed. Furthermore, the presence of significant nuclear magnetic resonance (NMR) signals confirms the structure of compounds obtained. An X-ray single crystallography study was also used to determine the crystal structure of dibutyltin(IV) *N*-methyl-*N*-benzyldithiocarbamate (Compound 1). The result showed that the geometry of Compound 1 is a skewed trapezoidal bipyramidal with a short trapezoidal edge. Both compounds showed strong toxicity against A549 cells compared to cisplatin, with Compound 1 being more potent than Compound 2.

ACKNOWLEDGEMENT

We would like to thank the Ministry of

Higher Education (FRGS/1/2021/STG04/UKM/02/5) for the financial support given to this study. We would also like to acknowledge the Faculty of Health Sciences of Universiti Kebangsaan Malaysia and Sunway University for the technical support provided in this study. Additionally, we would like to thank the Center for Research and Instrumentation Management (CRIM), UKM and Organic Synthesis Research Laboratory, Institute of Science (UiTM) for the laboratory services given.

Conflicts of interest

The authors declare that they have no conflict of interest.

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