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Conference paper

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Synthesis and *in vitro* activity investigation of some dibutyl-, diphenyl- and triphenyltin(IV) carboxylates against leukemia cancer cell, L-1210

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Abstract: Successful synthesis of several dibutyl-, diphenyl- and triphenyltin(IV) carboxylate compounds and evaluation of their activity as anticancer against leukemia cancer cell, L-1210 was reported. The compounds were synthesized by reacting dibutyltin(IV) oxide (DBTO) (**1**), diphenyltin(IV) oxide (DPTO) (**4**) and triphenyltin(IV) hydroxide (TPTOH) (**7**) with respective carboxylic acids, and subsequently characterized using NMR, FTIR, and UV–Vis spectroscopies, microelemental analyzer, and melting point apparatus. The compounds were then tested as anticancer, revealing that derivatives of triphenyltin(IV) (compounds **8** dan **9**) exhibit the IC_{50} value of 3.7 and 2.9 μg/mL, respectively, which are much higher activity than those of dibutyltin(IV) and diphenyltin(IV) derivatives.

Keywords: Anticancer; IC_{50}; leukemia cancer cell L-1210; organotin(IV) carboxylates; VCCA-2022.

Introduction

Organotin(IV) is a class of compounds with interesting structural features [1–3] which make them as promising biological agents for various applications such as antifungal [3], antibacterial [2, 4–9], antimalarial [10–12], corrosion inhibitor [13–16] and has been shown anticancer [1, 17–19].

The most distinct feature of the organotin(IV) compounds is the presence of at least one covalent Sn–C bond. The tetravalent Sn metal functions as a central atom, and depend on the number of alkyl (R) or aryl (Ar) moieties attached to the metal, the compounds are classified as mono-, di-, tri-, and tetraorganotin(IV). The compounds also contain counter anions, with the most common are chloride, oxide, fluoride, hydroxide, and thiolate [20]. Recently, carboxylates have successfully been utilized as ligands/counter anion since they have been shown to strengthen the biological activity in the organotin(IV) compounds [4, 18, 21–23].

The organotin(IV) compounds are recognized biological agents with strong activity, since normally they exhibit high toxicity even at very low concentration. The biological activities of the compounds are highly

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associated with the number and the characteristics of organic groups attached to the Sn central atom [20], with less significant contribution by the anionic groups as secondary factor. Several workers investigating the characteristics of coordination between carboxylates and organotin compounds reported that some organotin(IV) carboxylates and carboxylate derivatives displayed some encouraging activities such as antimicrobial [2, 4–9], antimalarial [10–12]. Other potentials of organotin(IV) compounds under intensive studies are as antitumor and anticancer [1, 17–19, 22, 23].

This present work was conducted to compare the *in vitro* activities of several dibutyl-, diphenyl- and triphenyltin(IV) carboxylates against leukemia cancer cell, L-1210, in order to gain more insight on promising properties of these compounds.

Experimental

Materials

The AR grade chemicals were used in the study: dibutyltin(IV) oxide ([$(n$-$C_4H_9)_2O$]) (DBTO), diphenyltin(IV) oxide ([$(C_6H_5)_2O$]) (DPTO), triphenyltin(IV) hydroxide ([$(C_6H_5)_3OH$]) (TPTOH), 4-hydroxybenzoic acid, (C_6H_4(4-OH)COOH) (4-HHBz), acetylsalicylic acid (C_6H_4(2-$OCOCH_3$)COOH) (HAcSal), sodium hydroxide (NaOH), and methanol (CH_3OH) were purchased from Sigma-Aldrich (Germany) or JT Baker (United Kingdom). All chemicals were used as received. The L-1210 leukemia cancer cells, were obtained from Center for Application of Isotopes and Radiation Technology, National Agency of Atomic Energy, Pasar Jumat, Jakarta, Indonesia.

Synthesis of organotin(IV) carboxylates

In this study, the organotin(IV) carboxylates was synthesized with the same procedure applied to prepare the similar compounds with different carboxylate ligands as has been reported in previous studies [5, 6, 9, 11, 12, 14, 17, 18]. A typical experiment to synthesize dibutyltin(IV) dicarboxylates was conducted by preparing a reaction mixture consisted of 0.37338 g (1.5 mmol) of compound **2**, an aliquot of 50 mL of methanol, and 2 mol equivalents of specified carboxylic acid. The mixture was refluxed for 4 h at 60–61 °C. The water produced was collected using Dean-Stark apparatus. The solvent was removed by rotary evaporator and the produced compounds [$(n$-$C_4H_9)_2Sn(OOCR)_2$] were dried in vacuo, for analysis and biological test experiments. The average yields obtained are higher than 90 %.

Preparation of diphenyltin(IV) carboxylates, [$(C_6H_5)_2Sn(OOCR)_2$] and triphenyltin(IV) carboxylates, [$(C_6H_5)_3Sn(OOCR)$], were carried out with similar procedure, except for the last compounds the carboxylic acids used was one mole equivalent.

Characterization techniques

A Bruker AV 600 MHz NMR spectrometer (Bruker, Germany) was used to produce ^1H and ^{13}C NMR spectra, with frequency of 600 MHz and 150 MHz for ^{13}C respectively. The measurements were run at 298 K in DMSO-D_6. The ^1H spectrum was produced by 32 runs with reference tetramethylsilane (TMS) signal at 0 ppm, while the spectrum for ^{13}C was produced by 3000–4000 scans with the reference DMSO signal at 39.5 ppm. A Fision EA 1108 series [Carlo Erba (Fisons), Italy] elemental analyser was used to determine the elemental composition (CHNS) of the samples. The FTIR spectrum was recorded on a Bruker VERTEX 70 FT-IR (Germany) spectrophotometer by scanning the KBr disc sample in the wavenumber range of 4000–400 cm^{-1}. The UV spectra were recorded using a UV- Shimadzu UV-245 Spectrophotometer (Japan). The sample with concentration of 1.0×10^{-4} M was prepared using methanol as a solvent, and measurements were performed in 1 mL quartz-cells.

Bioassay experiments

The *in vitro* experiments to investigate the anticancer activity against leukemia cancer cell, L-1210 was run with the procedure previously reported [17, 18]. An aliquot of 1 mL of the cells was placed in each of the holes of a multiwell plate tissue culture containing 2×10^6 cell/mL, and then 10 µL of solution of the compounds tested in methanol was added (if the sample was not completely dissolved in the solvent used, the sample was homogenized by ultrasonic mixing prior to use). The experiments were conducted with varied sample concentrations of 1, 2, 4, 6, 8, 16, 32 µg/mL. A sample of the cell in 10 µL of solvent was used to represent the experiment without the tested compounds as a comparison (negative control). The samples were incubated at 37 °C in a 5 % CO_2 incubator for 48 h, and after the completion of the incubation time, the sum of cell was counted using *haemecytometer Fuch Rosental* (0.200 mm × 0.0625 mm^2).

The performance of the sample was defined in term percentage of inhibition and calculated using Eq. 1:

$$\% \text{ inhibition} = \left(1 - \frac{A}{B}\right) x\,100 \tag{1}$$

where A and B represents the number of living cell in medium tested and in control/blank, respectively.

The IC_{50} was calculated using arithmetic method, which is an adoption of Reed and Muench method [24]. In this method, percentages of inhibition were plotted into probity table to obtain the corresponding probity value. The graph between log of concentration (x) and probity value (y) was then constructed to obtain a regression equation of y = a + bx, from which line equation was obtained. By introducing the value of y = 5 (which represents the probity value of 50 %), then the value of x (which represents log of concentration) was obtained. The anti log of x is the IC_{50} value of the sample.

The compounds synthesized obtained were as follows:

[$Bu_2Sn(4\text{-}HBz)_2$] (**2**): white-light yellowish solid; UV λ_{max}. (MeOH) nm (log ε): 240 and 307.8; IR ν_{max}. (KBr) cm^{-1}: 2955.1, 2862.3 (Bu), 1558.7 (C=O), 1419.6 (CO_2 asym), 1029.9 (Sn–O–C), 674.8 (Sn–Bu), 434.5 (Sn–O); ^{1}H NMR (in DMSO-d_6, 600 MHz) δ (ppm): Hα: 1.6 (t), Hβ:1.4 (m); Hγ: 1.29 (t); Hδ: 0.93 (t), H in benzoate = 7.35–7.85 (m); ^{13}C NMR (in DMSO-d_6, 150 MHz): δ (ppm): Cα: 26.8, Cβ: 25.5, Cγ: 21.4, Cδ: 13.5, C1: 164.3; C2: 131.5, C3: 132.2, C4: 138.4, C5: 125.1, C6: 128.6, C7: 129.7; microelemental analysis: found (calculated): C 52.29 (52.07), H 5.48 (5.52) [23].

[$Bu_2Sn(AcSal)_2$] (**3**): white-yellowish solid; UV λ_{max}. (MeOH) nm (log ε): 239 and 305.7; IR ν_{max}. (KBr) cm^{-1}: 2955.3, 2862.1 (Bu), 1560.7 (C=O), 1418.2 (CO_2 asym), 1028.1 (Sn–O–C), 678.8 (Sn–Bu), 435.7 (Sn–O); ^{1}H NMR (in DMSO-d_6, 600 MHz) δ (ppm): Hα: 1.67 (t), Hβ:1.63 (m); Hγ: 1.33 (t); Hδ: 0.851 (t), H (Acetyl): 2.13, H in benzoate = 7.36–7.76; ^{13}C NMR (in DMSO-d_6, 150 MHz): δ (ppm): Cα: 26.7, Cβ: 25.5, Cγ: 21.3, Cδ: 1351, C1: 164.13; C2: 132.5, C3: 131.3, C4: 131.2, C5: 129.9, C6: 128.3, C7: 127.9, C (CH_3 in Acetyl): 32.3, C (CO in acetyl): 160.0; microelemental analysis: found (calculated): C 52.46 (52.79), H 5.48 (5.41).

[$Ph_2Sn(4\text{-}HBz)_2$] (**5**): white solid; UV $\lambda_{max.}$ (MeOH) nm (log ε): 236 and 287.7; IR $\nu_{max.}$ (KBr) cm^{-1}: 1532.9 (C=O), 1660.8 (CO_2 sym), 1467.6; 751.3 (phen), 1243.1 (Sn–O–C), 591.6 (Sn–O); ^{1}H NMR (in DMSO-d_6, 600 MHz) δ (ppm): H2&H6: 7.60 (d, 6H); H3&H5: 7.48 (t, 6H); H4: 7.36 (t, 3H), H in benzoate: H9&H13: 7.82 (d); H10&H12: 7.76 (d); ^{13}C NMR (in DMSO-d_6, 150 MHz): δ (ppm): C(phen) C2&C6: 131.9, C3&C5: 129.4, C4: 12[illegible], C7: 165.2; C8: 137.3; C9&C13: 133.2; C10&C12: 129.8; C11 = 137.2.; microelemental analysis: found (calculated): C 56.65 (57.04), H 3.61 (3.66) [23].

[$Ph_2Sn(AcSal)_2$] (**6**): white solid; UV $\lambda_{max.}$ (MeOH) nm (log ε): 236 and 308.9; IR $\nu_{max.}$ (KBr) cm^{-1}: 1596.8 (C=O), 1690.2 (CO_2 sym), 1490.8; 725.2 (phen), 1290.1 (Sn–O–C), 591.6 (Sn–O); ^{1}H NMR (in DMSO-d_6, 600 MHz) δ (ppm): H2&H6: 7.61 (d, 6H); H3&H5: 7.48 (t, 6H); H4: 7.35 (t, 3H), H in acetyl: 2.25; H in benzoate: H10: 7.84 (d); H11: 7.66 (t); H12: 7.61 (t); H13: 7.62 (d); ^{13}C NMR (in DMSO-d_6, 150 MHz): δ (ppm): C(phen) C2&C6: 131.9, C3&C5: 129.7, C4: 127.6; C7: 165.1; C8 = 137.5; C9 = 138.1; C10 = 129.9; C11 = 128.7; C12 = 128.6; C13 = 130.3; C14 (CO in acetyl): 161.3; C15 (CH_3 in acetyl): 33.1; microelemental analysis: found (calculated): C 56.84 (57.05), H 3.74 (3.80).

[$Ph_3Sn(4\text{-}HBz)$] (**8**): white solid; UV $\lambda_{max.}$ (MeOH) nm (log ε): 234 and 302.3; IR $\nu_{max.}$ (KBr) cm^{-1}: 1558.8 (C=O), 1631.36 (CO_2 asym), 1428.7; 729.6 (phen), 1243.4 (Sn–O–C), 765.6 (Sn–O); ^{1}H NMR (in DMSO-d_6, 600 MHz) δ (ppm): H2&H6: 7.59 (d, 6H); H3&H5: 7.46 (t, 6H); H4: 7.33 (t, 3H), H in benzoate: H9&H13: 7.80 (d); H10&H12: 7.75 (d); ^{13}C NMR

(in DMSO-d_6, 150 MHz): δ (ppm): C(phen) C2&C6: 131.7, C3&C5: 129.2, C4: 126.9; C7: 164.8; C8: 137.2; C9&C13: 132.9; C10&C12: 129.5; C11 = 137.0.; microelemental analysis: found (calculated): C 61.79 (61.60), H 4.16 (4.11) [23].

[Ph_3Sn(AcSal)] (**9**): white solid, UV $\lambda_{max.}$ (MeOH) nm (log ε): 232 and 282.4; IR $\nu_{max.}$ (KBr) cm^{-1}: 1562.3 (C=O), 1698/7 (CO_2 asym), 1430.2; 729.5 (phen), 1298.7 (Sn–O–C), 755.4 (Sn–O); ^{1}H NMR (in DMSO-d_6, 600 MHz) δ (ppm): H2&H6: 7.59 (d, 6H); H3&H5: 7.46 (t, 6H); H4: 7.33 (t, 3H), H in acetyl: 2.24; H in benzoate: H10: 7.83 (d); H11: 7.64 (t); H12: 7.60 (t); H13: 7.60 (d); ^{13}C NMR (in DMSO-d_6, 150 MHz): δ (ppm): C(phen) C2&C6: 131.7, C3&C5: 129.2, C4: 126.9; C7: 164.9; C8: 137.2; C9: 137.9; C10: 129.5; C11: 128.4; C12: 128.2; C13: 130.0; C14 (CO in acetyl): 160.9; C15 (CH_3 in acetyl): 33.1; microelemental analysis: found (calculated): C 60.95 (61.25), H 4.26 (4.16).

Results and discussion

Successful synthesis for dibutyltin(IV) dicarboxylates, [(*n*-$C_4H_9)_2Sn(OOCR)_2$] (**2, 3**), diphenyltin(IV) dicarboxylates [$(C_6H_5)_2Sn(OOCR)_2$] (**5, 6**), and triphenyltin(IV) carboxylates, [$(C_6H_5)_3Sn(OOCR)$] (**8, 9**), was achieved by reacting DBTO (**1**), DPTO (**4**) and TPTOH (**7**), following the method applied in previous studies [5, 6, 9, 11, 12, 14, 17, 18]. Elemental compositions of all samples were determined using microanalytical method and show that the data obtained are in agreement with the theoretical values. The structure of the compounds studied is shown in Fig. 1.

The ^{1}H and ^{13}C spectra of the synthesized compounds display quite significant of change to the chemical shifts (δ) as a result of complexation.

As an example, in the ^{1}H spectrum, the chemical shift of DBTO (**1**) was only derived due to the presence of protons from butyl with chemical shifts in the region of 0.8–1.6 ppm (Fig. 2a). The significant change was observed after the binding of the ligand (HAcSal) to form compound **3**. The most significant change is the existence of new peaks in the region of 2.1 ppm which corresponds to CH_3 in acetyl and the protons of benzoate at 7.4–7.8 ppm as a result of the formation of bonding between ligand and the Sn atom as shown in Fig. 2b.

Practically similar pattern of chemical shift change due to ligand bonding to the Sn atom was also observed for the ^{13}C spectra as displayed in Fig. 3. In Fig. 3, it can be seen that the spectrum of compound **1** which is before the ligand (HAcSal) bound the Sn atom is characterized by the presence of only carbons belong to butyl ligand (Fig. 3a) in the region of 13–26 ppm, and after the bonding of the ligand (HAcSal) to form compound **3**, the spectrum is characterized by the emergence of extra peaks as demonstrated by chemical shift in the region of δ of 127–132 ppm were observed for carbons in benzoate and two carbons in the carboxyl group at 160 and 165 ppm, confirming successful attachment of the ligand HAcSal on to the Sn central atom. Similar trends were also observed for the rest of the compounds investigated.

Figure 4 presents of example of the FTIR spectra for compound **1** and **3**. In the starting material (compound **1**) is characterized by the appearance of sharp band in the region of 417.4 cm^{-1} which is assigned to stretching of Sn–O bond. Other distinct absorption bands observed are those associated with stretching vibration of butyl ligands at 1069 cm^{-1}, bending vibration of C–H aliphatic, and stretch of the butyl at wavenumber in the range of 2956–2865 cm^{-1}. The FTIR spectra also confirm the formation of dibutyltin (IV) dicarboxylate compounds, [(*n*-$C_4H_9)_2Sn(RCOO)_2$] (**2, 3**), by the existence of absorption bands associated with stretching of the carboxylates at around 1400 cm^{-1} and the symmetric stretch at around 1600 cm^{-1}, confirming successful substitution reaction [3–6]. Other characteristic features of the FTIR spectra of these compounds are the emergence of absorption bands assigned to stretching vibration of butyl ligands at 1069 cm^{-1} and associated with bending vibration of C–H aliphatic of butyl at 2956–2865 cm^{-1}.

The λ_{max} data of UV–Vis spectroscopy of the compounds investigated showing the presence of some important shifting in the position of λ_{max}. For example, in compounds **3**, two peaks are observed, with λ_{max} at 241 nm and 302 nm, suggesting the occurrence of large shift in π→π* and n–л* transitions respectively, as a result of substitution of oxygen in compound **1** by acetylsalicylate in compound **3** (Fig. 5). The presence of C=O– and –C=C– bonds make AcSal ligand as a strong chromophore group. The relatively large shifts of λ_{max} of compound **3**

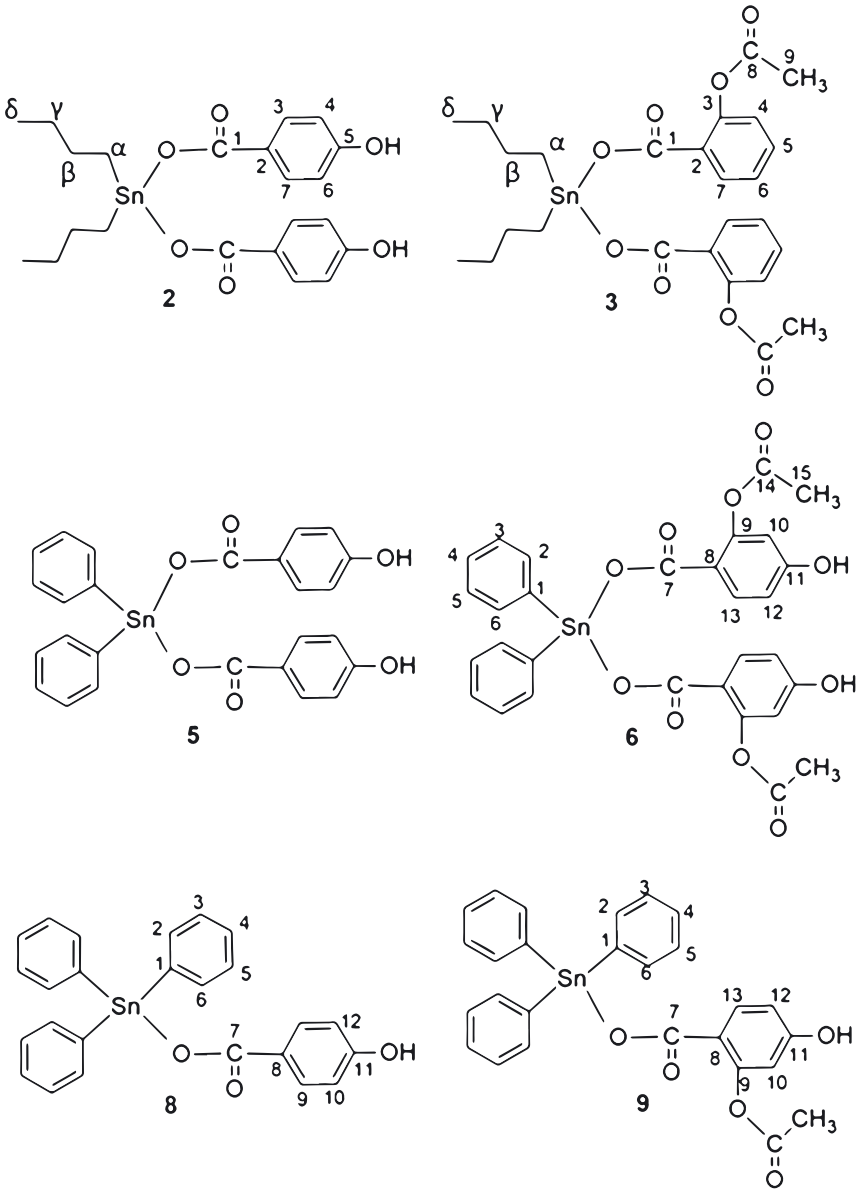

Fig. 1: The structure of the compounds studied.

to higher value as a result of conjugate bond is the result of decreased energy difference between HOMO and LUMO orbitals [2–4]. The same UV–Vis patterns are also observed for the rest of compounds investigated.

It has been well recognized that diorganotin(IV) and triorganotin(IV) compounds exhibit high antifungal and antimicrobial activities, and for these reasons many compounds belong to these groups have been synthesized [1–4, 22, 25, 26]. Appreciable antitumor activity of several organotin(IV) compounds have also been reported [17, 18, 27].

The findings of the previous studies on the antifungal and antimicrobial activity of organotin(IV) compounds [3, 4, 28], indicate that the optimal antifungal activity is associated with the number of carbon atoms. It was also found that the derivative of triphenyltin(IV) carboxylate with 18 carbon atoms exhibit the smallest minimum inhibition concentration in the series [11, 12, 25, 28]. The same trend for the compounds investigated in this study was observed.

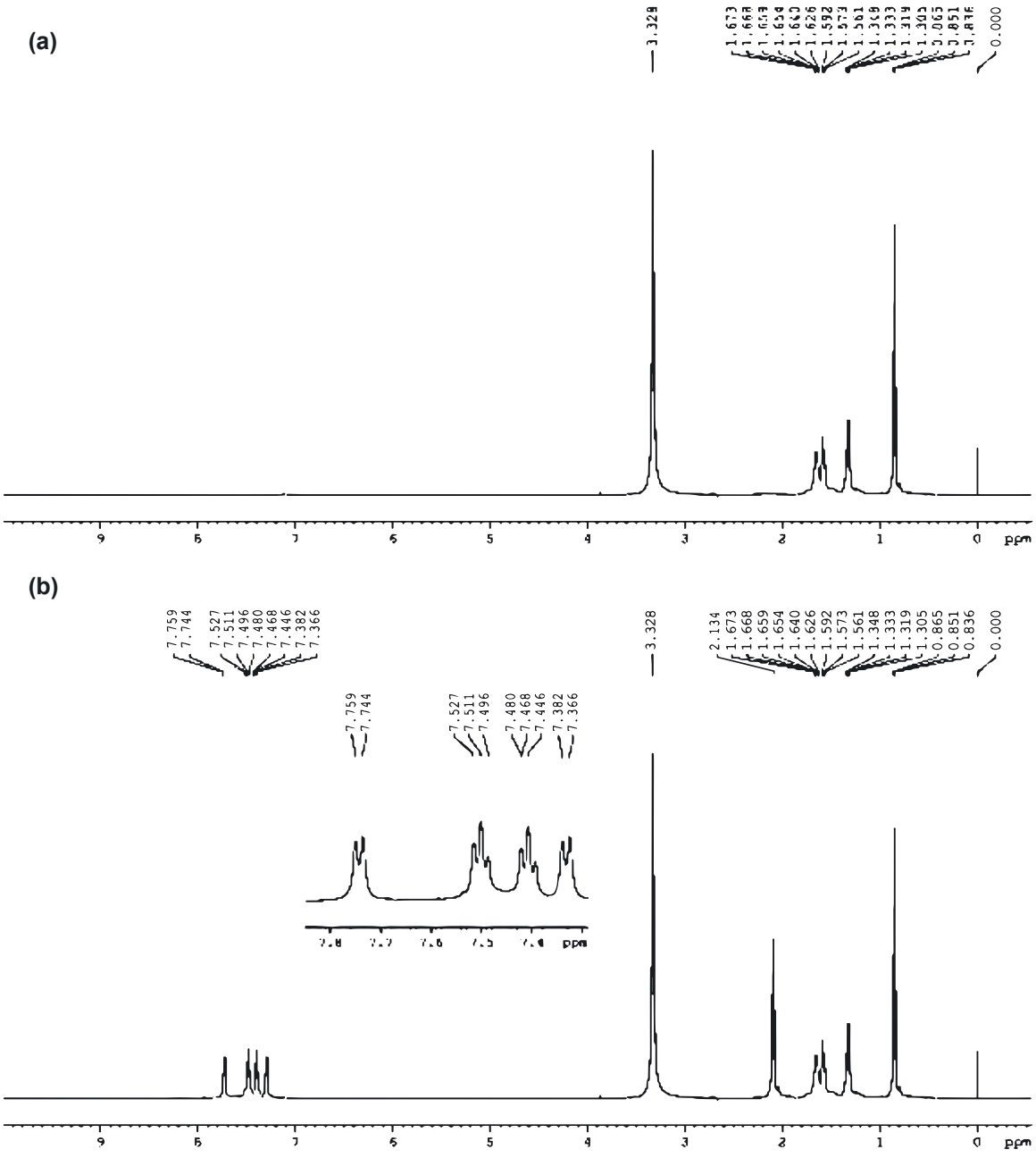

Fig. 2: ^{1}H NMR spectra of compound: (a) DBTO (**1**); (b) compound DBT(AcSal) (**3**).

As can be seen in Table 1, the derivatives of triphenyltin(IV) exhibit smaller IC_{50} value in the series, and the diphenyltin(IV) derivatives exhibit smaller IC_{50} values than those of dibutyltin(IV) derivatives. These results signify the effect of the number of carbon atoms present has effect on the anticancer activity of the organotin(IV) compounds investigated. In addition, the organotin(IV) carboxylate compounds synthesized were found to have smaller IC_{50} values than those found for starting materials and intermediate products. However, it should be noted that the IC_{50} values of all compounds synthesized were higher than the positive control drug doxorubicin with IC_{50} value of 1.5 µg/mL (Table 1). The results reported in this work are similar to the IC_{50} values for other

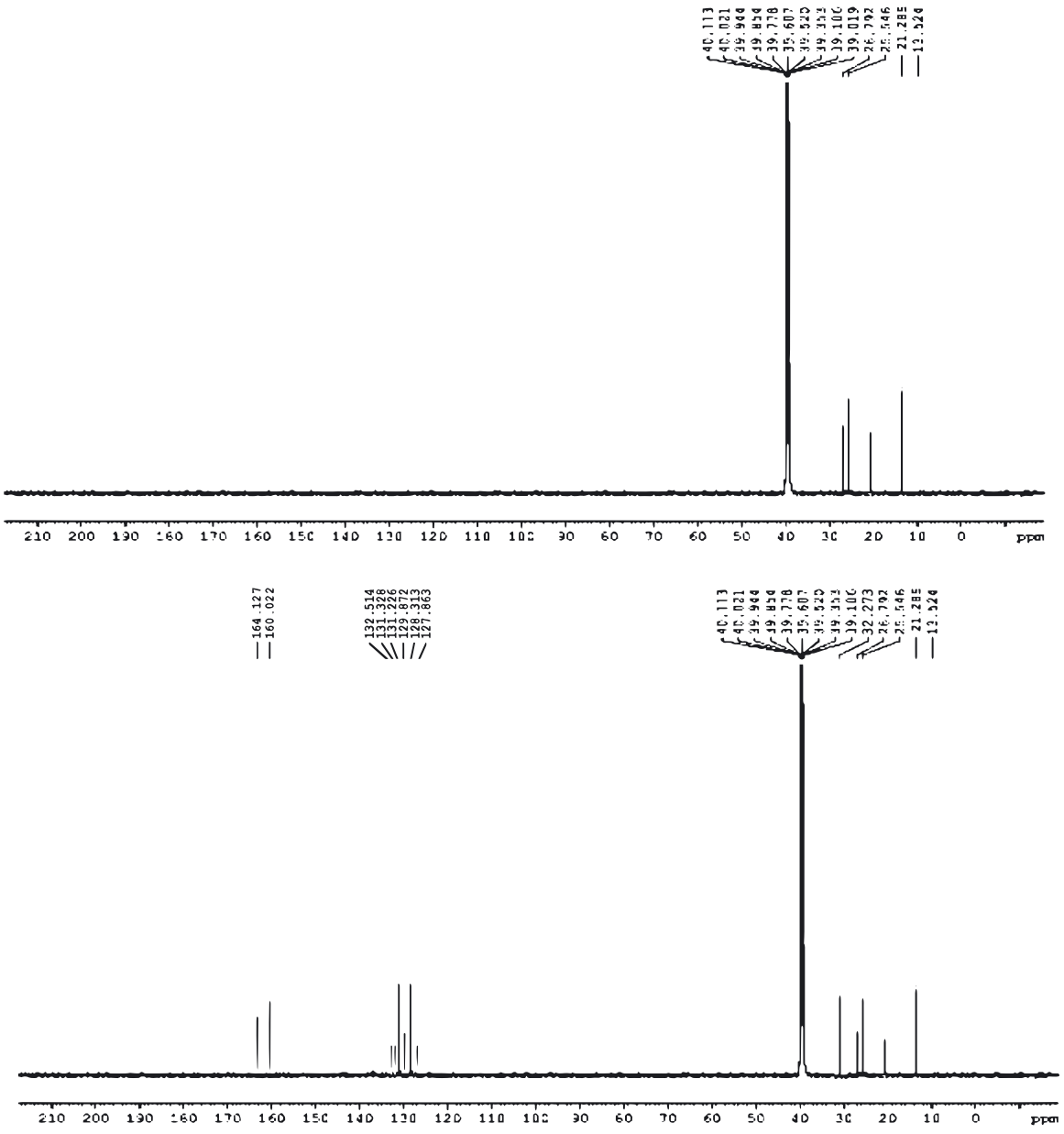

Fig. 3: ^{13}C NMR spectra of compound: (a) DBTO (**1**); (b) compound DBT(AcSal) (**3**).

organotin(IV) carboxylates reported previously [27]. These findings are in agreement with an established fact that the biological activity of many compounds is enhanced by complexation, leading to higher values compared to those of uncomplexed forms [29]. In previous study, it was reported that the biological activity of diorganotin compounds of the type RR'SnXY (R and R' = alkyl or aryl, X and Y = anions) is solely governed by the $RR'Sn^{2+}$ moiety, and the X and Y group influences the delivery of the active $RR'Sn^{2+}$ ion to the cell, although the their mechanism of action have not been fully understood [30].

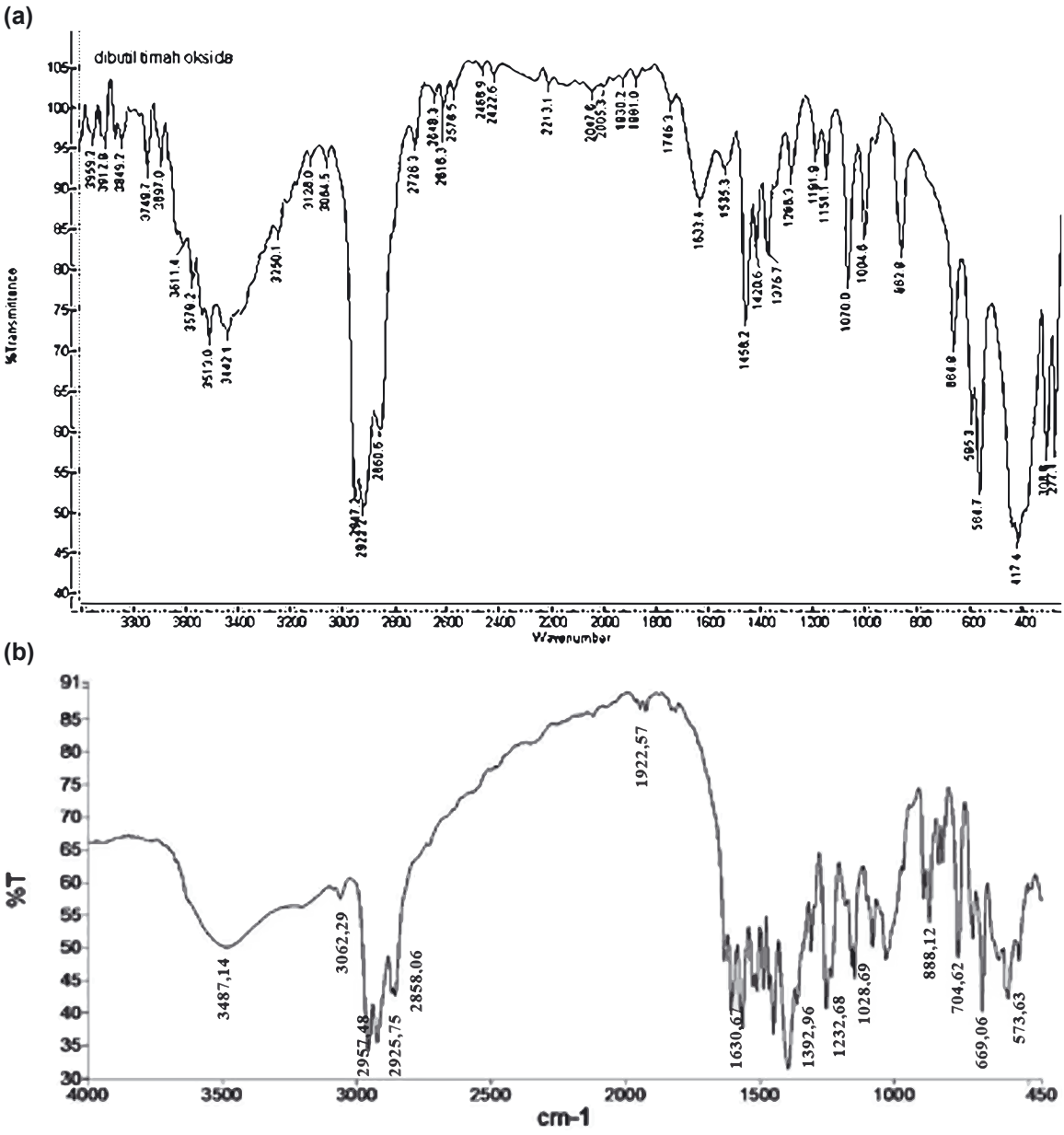

Fig. 4: FT-IR spectra of (a) compound **1**; (b) compound **3**.

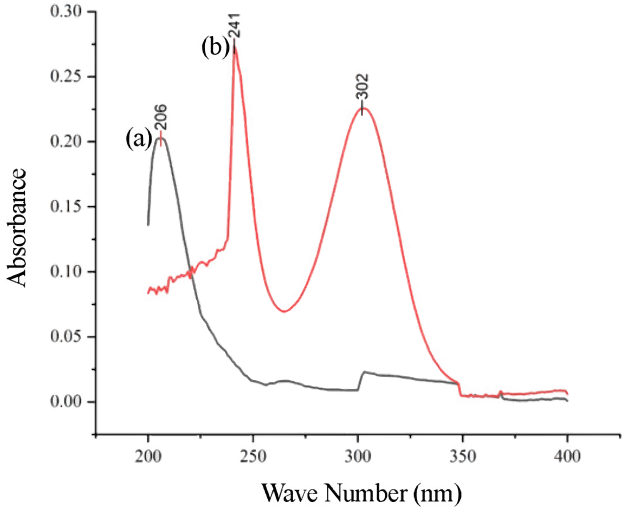

Fig. 5: UV spectra of (a) compound **1**; (b) compound **3**.

Table 1: IC_{50} values of all compounds tested.

Compound	IC_{50} (μg/mL)
$[(n\text{-}C_4H_9)_2Sn(p\text{-}C_6H_4(OH)COO)_2]$ (**2**)	24.4
$[(n\text{-}C_4H_9)_2Sn(C_6H_4(O_2CCH_3)COO)_2]$ (**3**)	21.6
$[(C_6H_5)_2Sn(p\text{-}C_6H_4(OH)COO)_2]$ (**5**)	10.3
$[(C_6H_5)_2Sn(C_6H_4(O_2CCH_3)COO)_2]$ (**6**)	9.1
$[(C_6H_5)_3Sn(p\text{-}C_6H_4(OH)COO)]$ (**8**)	3.7
$[(C_6H_5)_3Sn(OOCC_6H_4(O_2CCH_3))]$ (**9**)	2.9
Doxorubicin	1.5

Conclusions

Based on the discussion above, we have reported successful preparation of several some promising organotin(IV) carboxylate compounds with promising *in vitro* anticancer activity. The results indicated that the derivative of triphenyltin(IV) carboxylate is the most active candidate as anticancer drug. In this respect, the future study to carry out in vivo testing of the compounds is required to evaluate their possible future application as metal base anticancer.

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References

[1] J. Devi, B. Kumar, B. Taxak. *Inorg. Chem. Commun.* **139**, 109208 (2022), https://doi.org/10.1016/j.inoche.2022.109208.
[2] M. A. Salam, M. A. Affan, F. B. Ahmad, M. A. Arafath. *J. Coord. Chem.* **65**, 1999 (2012), https://doi.org/10.1080/00958972.2012.687104.
[3] C. S. Rocha, B. P. de Morais, B. L. Rodrigues, C. L. Donnici, G. M. de Lima, J. D. Ardisson, J. A. Takahashi, R. S. Bitzer. *Polyhedron* **117**, 35 (2016), https://doi.org/10.1016/j.poly.2016.05.031.
[4] S. Samsuar, W. Simanjuntak, H. I. Qudus, Y. Yandri, H. Herasari, S. Hadi. *J. Adv. Pharm. Edu. Res.* **11**(2), 17 (2021), https://doi.org/10.51847/kaijzkafco.
[5] S. Hadi, E. Hermawati, Noviany, T. Suhartati, Yandri. *Asian J. Microbiol. Biotechnol. Environ. Sci.* **20**, 113 (2018).
[6] S. Hadi, S. Samsuar, W. Simanjuntak, H. I. Qudus. *ARPN J. Eng. Appl. Sci.* **15**, 1623 (2021).
[7] A. L. Susangka, S. Hadi, N. Noviany, A. A. Kiswandono, N. Nurhasanah, K. D. Pandiangan. *J. Turk. Chem. Soc. A Chem.* **9**, 1047 (2022).
[8] S. Hadi, S. Lestari, T. Suhartati, H. I. Qudus, M. Rilyanti, D. Herasari, Y. Yandri. *Pure Appl. Chem.* **93**, 623 (2021), https://doi.org/10.1515/pac-2020-1103.
[9] S. Hadi, T. Suhartati, N. Noviany, K. D. Pandiangan, Y. Yandri, W. Simanjuntak, J. Junaidi. *Pure Appl. Chem.* **94**, 799 (2022), https://doi.org/10.1515/pac-2021-1106.
[10] C. Hansch, R. P. Verma. *Eur. J. Med. Chem.* **44**, 260 (2009), https://doi.org/10.1016/j.ejmech.2008.02.040.
[11] S. Hadi, Noviany, M. Rilyanti. *Macedon. J. Chem. Chem. Eng.* **37**, 185 (2018).
[12] S. Hadi, M. D. Fenska, N. Noviany, H. Satria, W. Simanjuntak, M. M. Naseer. *Main Group Met. Chem.* **44**, 256 (2021), https://doi.org/10.1515/mgmc-2021-0028.
[13] R. Singh, P. Chaudary, N. K. Khausik. *Rev. Inorg. Chem.* **30**, 275 (2010).
[14] S. Hadi, H. Afriyani, W. D. Anggraini, H. I. Qudus, T. Suhartati. *Asian J. Chem.* **27**, 1509 (2015), https://doi.org/10.14233/ajchem.2015.18590.
[15] H. Kurniasih, M. Nurissalam, B. Iswantoro, H. Afriyani, H. I. Qudus, S. Hadi. *Orient. J. Chem.* **31**, 2377 (2015), https://doi.org/10.13005/ojc/310467.
[16] N. N. Hazani, Y. Mohd, S. A. I. S. M. Ghazali, Y. Farina, N. N. Dzulkifli. *J. Electrochem. Sci. Technol.* **10**, 29 (2019).
[17] S. Hadi, M. Rilyanti. *Orient. J. Chem.* **26**, 775 (2010).
[18] S. Hadi, M. Rilyanti, Suharso. *Indones. J. Chem.* **12**, 172 (2012), https://doi.org/10.22146/ijc.21359.

[19] C. E. Carraher, Jr., M. R. Roner. *J. Organomet. Chem.* **751**, 67 (2014), https://doi.org/10.1016/j.jorganchem.2013.05.033.
[20] L. Pellerito, L. Nagy. *Coord. Chem. Rev.* **224**, 111 (2002), https://doi.org/10.1016/s0010-8545(01)00399-x.
[21] A. Szorcsik, L. Nagy, K. Gadja-Schrantz, L. Pellerito, E. Nagy, E. T. Edelmann. *J. Radioanal. Nucl. Chem.* **252**, 523 (2002).
[22] M. Gielen. *J. Braz. Chem. Soc.* **14**, 870 (2003).
[23] M. A. Abdellah, S. K. Hadjikakou, N. Hadjiliadis, M. Kubicki, T. Bakas, N. Kourkoumelis, Y. V. Simos, S. Karkabounas, M. M. Barsan, I. S. Butler. *Bioinorg. Chem. Appl.* **2009**, 542979 (2009).
[24] R. A. Turner. *Screening Methods in Pharmacology*, p. 255, Academic Press, New York (1972).
[25] Annissa, T. Suhartati, Yandri, S. Hadi. *Orient. J. Chem.* **33**, 1133 (2017), https://doi.org/10.13005/ojc/330310.
[26] I. J. Mahdi, N. S. Saddam, A. G. Hadi, S. J. Baqir, Y. F. Al-Khafaji, A. S. Abbas. *Egypt. J. Chem.* **66**, 213 (2023).
[27] S. Hadi, E. K. Winarno, H. Winarno, K. N. Berawi, T. Suhartati, Y. Yandri, W. Simanuntak. *Phys. Sci. Rev.* (2023), https://doi.org/10.1515/psr-2022-0303.
[28] Z. H. Chohan, A. Rauf. *Synth. React. Inorg. Met. Org. Chem.* **26**, 591 (1996), https://doi.org/10.1080/00945719608004764.
[29] H. Gershon. *J. Med. Chem.* **17**, 824 (1974), https://doi.org/10.1021/jm00254a009.
[30] A. J. Crowe. The antitumour activity of tin compounds. In *Metal-Based Drugs*, M. Gielen (Ed.), Vol. **1**, p. 103, Freund Publishing House, Freund (1989).

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