

Comparative Antibacterial Activity Study of Organotin(IV) 2-Nitrobenzoate

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Abstract-The synthesis of two organotin(IV) 2-nitrobenzoate compounds, diphenyltin(IV) di-2-nitrobenzoate (2) and triphenyltin(IV) 2-nitrobenzoate (4) have successfully been achieved by reacting the diphenyltin(IV) oxide and triphenyltin(IV) hydroxide with 2-nitrobenzoic acid. The success of synthesis was proven by spectroscopies of UV, IR and NMR, while the purity of the compounds was determined by microelemental analyzer. The antibacterial activities were carried out on positive gram bacteria *S. aureus* and negative gram bacteria *E. coli*. The result showed that compound 4 was more active than 2 giving minimum inhibition concentration of 200 ppm (3.87×10^{-4} M), while compound 2 was not active at concentration of 200 ppm. The chloramphenicol the control drug also gave inhibition at the same concentration i.e. 200 ppm, the only different is its halozone was bit bigger than the compounds tested.

Keywords- Antibacterial, *E. Coli*, Organotin(IV) di-2-Nitrobenzoate, *S. Aureus*

I. INTRODUCTION

Bacteria infection is health problem that happens a lot and need serious treatment [1]. The bacteria infection treatment is usually performed by the use of antibiotic [2]. However in the last decade there are many reports indicating that the bacteria resistance toward antibiotics has sharply increased and has caused lost in medical treatment [3].

The bacteria resistances is caused by few factors, one of them is gene mutagenic [4]. Gene mutagenic causing bacteria produces enzyme that inactivate the antibiotic work and protect the antibiotic diffuse to intracellular of bacteria [5]. The bacteria resistance towards antibiotic occur at certain dosage and indicated by no inhibition on bacterial growth observed[6]. The use of antibiotic in high dosage is not a good solution in the treatment of bacteria resistance [7].

The other alternative to get compound that is effective as antibiotic is by synthesizing new compounds [8, 9]. The derivative of organotin(IV) compounds is one of the compound that has attracted much attention, this is due their strong biological activities as they can be applied as antifungi, antitumor, antiviral, anticorrosion, antimalarial as well as antibacteria [8-20].

The activity strength of organotin(IV) towards bacteria is not only influenced by the number of organic groups bound to Sn atom, but the type of organic groups also play important role in the reactivity [10]. The phenyl group that is attached to Sn tom has been known to have better biological activity than aliphatic group [11, 13-19] and the more phenyl group bound will directly correlate to the increase of antibacterial activity [11].

Futhermore, the type of anions attached also play important role as they will be secondary factor for the reactivity. Thus the synthesis of organotin(IV) by varying the organic ligands other than phenyl or aliphatic groups are important to be done. Therefor, in this work we report the synthesis of 2 organotin(IV) compound with 2-nitrobenzoic acid and test their activity against positive gram bacteria *S. aureus* and negative gram of *E. coli*.

II. EXPERIMENTAL

A. Materials

All reagents used were AR grade. Diphenyltin(IV) dihydroxide ($[(C_6H_5)_2Sn(OH)_2]$), triphenyltin(IV) hydroxide ($[(C_6H_5)_3SnOH]$), 2-nitrobenzoic acid were obtained from Sigma, sodium hydroxide (NaOH) and methanol (CH_3OH) were JT Baker products, and the control drug, chloramphenicol were used as received without further purification. Positive gram bacteria *S. Aureus* was obtained from laboratory of PGI Cikini hospital, Jakarta, *E. coli* was obtained from Integrated laboratory and inovation technology center, Universitas Lampung.

B. Instrumentation

Elemental analyses (CHNS) were conducted on Fision EA 1108 series elemental analyser. The UV spectra were recorded in the UV region and were measured using a UV- Shimadzu UV-245 Spectrophotometer. Measurements were performed in 1 mL quartz-cells. Solutions were prepared using methanol as the solvent with concentration of 1.0×10^{-5} M. IR spectra were recorded on a Bruker VERTEX 70 FT-IR spectrophotometer with KBr discs in the range of 4000-400 cm^{-1} . ¹H and ¹³C NMR spectra were recorded on a Bruker AV 600 MHz NMR (600 MHz for ¹H and 150 MHz for ¹³C). All experiments

were run in DMSO-D6 at 298K. The number of runs used for ¹H experiments were 32 with reference at DMSO signal at 2.5 ppm, while the ¹³C were 1000-4000 scans with the reference DMSO signal at 39.5 ppm.

C. Preparation of Organotin(IV) 2-nitrobenzoate

The preparation of the organotin(IV) 2-nitrobenzoate compounds used in this work were performed following the procedures we reported previously [8, 13-19]. These procedures were adapted from the published literature [11]. As an example the procedure in the preparation of diphenyltin(IV) di-2-nitrobenzoate was as follows:

0.867 g (3 mmol) compound 2 in 20 mL of methanol was added with 2 mole equivalents of 2-nitrobenzoic acid (1.002 g) and was refluxed for 4 hours at 60 – 61°C. After removal of the solvent by rotary evaporator, the compound [(C₆H₅)₂Sn(2-OOCC₆H₄(NO₂))₂] which was obtained was dried in vacuo until they are ready for analysis and further use for antibacterial activity test. The average yields were more than 90 %. The same procedure was also adapted in the preparation triphenyltin(IV) derivatives, [(C₆H₅)₃Sn(OOCC₆H₄(NO₂))], one mole equivalent of 2-nitrobenzoic acid was added.

D. Antibacterial Activity Test

Antibacterial activity test by diffusion and dilution methods were performed based on the procedures used previously in our group [8, 22]. In this work the bacteria used were *S. aureus* and *E. coli*. The control positive used was chloramphenicol.

III. RESULTS AND DISCUSSION

The synthesis of organotin(IV) compound derivatives, i.e. diphenyltin(IV) di-2-nitrobenzoate (2) and triphenyltin(IV) 2-nitrobenzoate (4) have been conducted by the reaction of the diphenyltin(IV) dihydroxide (1) and triphenyltin(IV) hydroxide (3) with 2-nitrobenzoic acid based on the procedure previously utilized [9,10,14,17,19-21,24]. The two compounds prepared were well characterized by means of some spectroscopy techniques as well as based on the microanalytical data. The antibacterial activities were then taken against *S. aureus* and *E. coli*. The results of microanalytical data of all compounds are presented in Table 1. The results obtained are very close to the theoretical yield.

TABLE I. MICROANALYTICAL DATA OF THE COMPOUNDS SYNTHESIZED

Compounds	Elemental Analysis found (Calculated)		
	C	H	N
2	51.57 (51.24)	2.98 (2.86)	4.63 (4.59)
4	58.14 (57.97)	3.68 (3.62)	2.71 (2.66)

The most important vibrations of IR spectra for the compound synthesized are shown in Table 3. The characteristic of compound 1 appeared at 729.3 cm⁻¹ which is stretch for Sn-O bond. When 1 was converted to 2, the new stretches at 1079.61 appeared and it was from vibration of Sn-O-C bond. This indicated that the Sn-O bond in 1 has broken and new

bond between Sn and oxygen atom in carboxyl group from 2-nitrobenzoate has been formed. Other characteristic stretches were the present of C=O stretch at 1403.27 and 1536.27 cm⁻¹ indicating the present of carbonyl in 2⁵. Similar patterns were also observed for compound 4.

TABLE II. THE MOST IMPORTANT IR BANDS OF THE COMPOUNDS SYNTHESIZED

Compound	2	4	References (cm ⁻¹)
Sn-Cl	-	-	410-320
Sn-O	719.86	725.39	800-400
Sn-O-C	1079.61	1071.75	1250-1000
Sn-ph	1076.2	1074.9	1100-1000
C=O	1403.27	1425.77	1760-1600
CO ₂ sym	1536.27	1639.85	1500-1400
C-H Aromatic	3061.3	3069.8	3100-3000
N-O	1536.27, 1347.33	1526.85, 1336.49	1585-1345

The analysis of UV spectroscopy produced λ_{max} values from the compounds prepared. The results are presented in Table 3. From these data, there are some important shiftings of for each compound. The two compounds gave two main characteristic bands from $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transition. As example, in compound 1 the transition $\pi \rightarrow \pi^*$ was observed at 204 nm, in compound 2, there were changes of λ_{max} for $\pi \rightarrow \pi^*$ transition to longer λ_{max} to 204 and 303 nm. The bathochromic shift is an indication that the substitution of ligand has occurred, i.e. oxygen atom in oxide group has been replaced by oxygen atom in 2-nitrobenzoate [8-19, 23]. The $n \rightarrow \pi^*$ transition in 3 was due to the presence of free electron pair of oxygen in carboxylic acid [23]. Similar observations were also observed for compound 4.

TABLE III. THE λ_{max} OF THE UV SPECTRA OF THE ORGANOTIN(IV) COMPOUNDS

Compound	λ_{max} (nm)	
	$\pi \rightarrow \pi^*$	$n \rightarrow \pi^*$
1	204	-
2	204	303
3	206	-
4	215	290

¹H and ¹³C NMR data of the compounds synthesized are shown in Table 4. By careful analysis, the data for compounds prepared have been compared with the previous available [8-19, 24-26]. In ¹H NMR, the chemical shift (δ) of phenyl proton bound to Sn atom as expected appeared in the range of 7.45-7.47 ppm, while the chemical shift of proton benzoate were at 7.79-7.89 ppm. The ¹³C NMR of the phenyl bound to Sn atom gave δ at 127-129 ppm and the carbon benzoate at 137. The chemical shift (δ) of carbon carbonyl as expected appeared at 166-167 ppm [8-19, 24-26].

TABLE IV. ¹H AND ¹³C SPECTRA OF THE ORGANOTIN(IV) COMPOUNDS

Compound	H in phenyl (ppm)	H in benzoate (ppm)	C in phenyl and benzoate (ppm)
2	H2 & H6 7.45 (d,4H); H3 & H5 7.47 (t, 4H); H4 7.57 (t,2H)	7.79-7.81 (m)	C1-6 (phenyl): 126.8 ; C7 167.06; C8 130.2; C9 130.4; C10 131.1; C11- C13 132.15
4	H2&H6 7.47 (d,6H); H3&H5 7.52 (t 6); H4 7.50	7.88-7.89 (d)	C1-6 (phenyl): 128.4 – 128.7; C7: 166.64; C8: 131.45; C9: 130.3; C10: 136.76; C11: 137.4; C12-C13: 129.2

TABLE V. MIC VALUES OF ALL COMPOUNDS TESTED COMPARED WITH CHLORAMPHENICOL

Compounds	Minimum inhibitory concentration (MIC) (in x 10 ⁻⁴ M)	
	<i>S. aureus</i>	<i>E.coli</i>
Chloramphenicol	6.19	6.19
2	4.96	4.96
4	3.87	3.87

The antibacterial activities have been determined by diffusion method to the compounds (2 and 4), and the results obtained are shown in Table 5. This method has been used to find the most effective concentration of the compound tested as antibacterial agent. The ratio of inhibition zone against concentration of compound tested were evaluated to know their effectivity. The data revealed that the two compounds tested against the two bacteria, *S. aureus* and *E. coli* produced various inhibition zones. Compound 2 was active at concentration of 200 ppm or equal 3.87x10⁻⁴ M for 4, while compound 2 was not active at concentration 200 ppm, and it started to show activity at concentration of 300 ppm (equal to 4.96 x 10⁻⁴ M). The control positive drug, chloramphenicol was also having inhibition concentration at 200 ppm (6.19 x 10⁻⁴ M) although its halozone was little bit bigger compared to the compound 4. The results reported here were strengthened our previous results [8,22]. These indicated that the organotin(IV) compounds showed a promising result as new antibacterial drug [8, 22].

IV. CONCLUSIONS

The preparation of two organotin(IV) compounds with ligands of 2-nitrobenzoic acid has successfully been carried out and has also been tested as antibacterial activities against *S. aureus* and *E. coli*. The halozone of each compound tested was measured and compared with chloramphenicol as the control positive. Compound 4 gave results that were quite similar to the control drug. From this work, we believe that these compounds will be available for future applications as antibacterial drug. However, we still aim to have better and stronger antibacterial drug.

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