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Syntheses, Characterization and Antibacterial Activity Test of Some Organotin(IV) 2-hydroxybenzote

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Abstract: The syntheses of two organotin(IV) derivatives i.e. diphenyltin(IV) 2-hydroxybenzoate (**2**) and triphenyltin(IV) 2-hydroxybenzoate (**4**) have succesfully been performed, tested and compared their antibacterial activities. The compounds syntesiszed were well characterized by means of spectroscopies of UV, IR, ^{1}H and ^{13}C NMR as well as based on microelemental analyzer. The bacteria used in the testing were *Staphylococcus aureus* and *Escherichia coli* by diffusion method. The results showed that all compounds tested were active in the antibacterial test giving the minimun inhibition concentration of 200 ppm (3.66×10^{-4} M and 4.11×10^{-4} M for **2** and **4**, respectively for both bacteria), while chloramphenicol was also giving inhibition concentration at the same concentration (6.19×10^{-4} M).

Keywords: antibacterial activity; *E. coli*; minimum inhibition concentration; organotin(IV); *S. aureus*

1. INTRODUCTION

Infectious disease has become very serious problem in the world as it has caused many deaths in developing countries[1,2]. Giving antibiotics in the right dosage is needed to overcome this problem. However, in the last decade, the use of antibiotics is no longer effective[1] as well as the finding of antibiotics which is less behind compare to the bacterial resistance[3]. Thus, the finding of new antibiotics to overcome the infectious disease and antibiotics resistance are needed[3-5].

One of the ways in an attempt to find the new antibiotics and antibacterial drugs can be done by developing the metal based drug of organotin(IV) compounds[6-8]. The organotin(IV) compounds are very interesting not only because their structure[6-9], but most important due to their strong biological activities[6-18]. The organotin(IV) with carboxylate ligands have been found to be active as antifungi[6,9,10], anticancer and antitumour[6,11-15], antimalaria[16,17], anticorrosion activity[18-22], and also as antibacterial[2,8,23].

The biological activity of organotin(IV) is influenced and depended on the type and number of organic ligands bound to Sn atom, although the organic attached is only secunder determinant[6]. Based on the fact that organotin(IV) compounds have been found to be active as antibacterial, in this paper we reported antibacterial activity of two organotin(IV) 2-hydroxybenzoate againts *S. aureus* and *E.coli*.

2. MATERIALS AND METHOD

2.1 Materials

All reagents used were AR grade. Diphenyltin(IV) oxide ($[(C_6H_5)_2SnO]$), triphenyltin(IV) hydroxide ($[(C_6H_5)_3SnOH$), 2-hydroxybenzoic 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.

2.2 Instrumentation

^{1}H and ^{13}C NMR spectra were recorded on a Bruker AV 600 MHz NMR (600 MHz for ^{1}H and 150 MHz for ^{13}C). All experiments were run in DMSO-D_6 at 298K. The number of runs used for ^{1}H experiments were 32 with reference at DMSO signal at 2.5 ppm, while the ^{13}C were 1000-4000 scans with the reference DMSO signal at 39.5 ppm. Elemental analyses (CHNS) were conducted on Fision EA 1108 series elemental analyser. IR spectra were recorded on a Bruker VERTEX 70 FT-IR spectrophotometer with KBr discs in the range of 4000-400cm^{-1}. 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.

2.3 Synthesis of organotin(IV) 2-hydroxybenzoate

The organotin(IV) 2-hydroxybenzoate compounds used in this work were prepared based on the procedures previously reported[9,10,14,17,19-21,24]. These procedures were obtained as adaptation from the work available in the literature[8]. For example the procedure in the preparation of diphenyltin(IV) di-2-hydroxybenzoate was as follows:

0.866 g (3 mmol) compound **2** in 20 mL of methanol was added with 2 mole equivalents of 2-hydroxybenzoic acid (0.40.834 g) and was refluxed for 4 hours at 60 – 61°C. After removal of the solvent by rotary evaporator, the compound $[(C_6H_5)_2Sn(2\text{-}OOCC_6H_4(OH))_2]$ 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, $[(C_6H_5)_3Sn(OOCC_6H_4(OH))]$, one mole equivalent of 2-hydroxybenzoic acid was added.

2.4 Antibacterial Activity Test

Antibacterial activity test by diffusion and dilution methods were performed based on the procedures used previously in our group[2, 24]. In this work the bacteria used were *S. aureus* and *E. coli*. The control positive used was chloramphenicol.

3. RESULTS AND DISCUSSION

Two organotin(IV) compound derivative namely diphenylitun(IV) di-2-hydroxybenzoate (**2**) and triphenylitun(IV) 2-hydroxybenzoate (**4**) have succefully been prepared by reacting the diphenyltin(IV) dihydroxide and triphenyltin(IV) hydroxide with 2-hydroxybenzoic acid based on the procedure available in the literature[9,10,14,17,19-21,24]. The compounds synthesized then were tested and compared their antibacterial activities against *S. aureus* and *E. coli*. The microanalytical data of the compounds synthesized are tabulated in Table 1, the results in general are very good and close to the theoretical yield.

Table 1. Microanalytical data of the compounds synthesized

Compounds	Elemental Analysis found (Calculated)	
	C	H
2	56.64 (57.04)	3.62 (3.66)
4	60.78 (61.60)	4.04 (4.11)

Table 2. The λ_{max} of the UV spectra of the organotin(IV) compounds

Compound	λ_{max} (nm)	
	π→π*	**n→π***
1	203	263
2	210	296
3	220	258
4	234	288

The analysis of UV spectroscopy gave $\lambda_{max.}$ Values from all compounds. The results are shown in Table 2. From these data, there are some important shiftings of for each compound. The two compounds gave two main characteristic bands from π→π* and n→π* transition. As example, in compound **1** the transition π→π* was observed at 204 nm, in compound **2**, there were changes of λ_{max} for π→π* transition to longer λ_{max} to 235 and 288 nm. The batochromic shift is an indication that the substitution of ligand has occured, i.e. oxygen atom in hydroxyl group has been replaced by oxygen atom in 2-hydroxybenzoate[9,10,19-21,25]. The n→π* transition in **3** was due to the presence of free electron pair of oxygen in carboxylic acid[25]. Similar observations were also occurred for compound **4**.

Some important vibrations of IR spectra for the compound synthesized are presented 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 stretchs at 1243.1 and 1242.6 cm^{-1} appeared and they were from Sn-O-C bond. This means the Sn-O bond in **1** has broken and new bond between Sn and oxygen atom in carboxyl group from 2-hydroxybenzoate has been formed. Other characteristic stretchs were the present of C=O stretch at 1601.1 and 1688.4 cm^{-1} indicating the present of carbonyl in **2**[25].

^{1}H and ^{13}C NMR data of the compounds synthesized are tabulated in Table 4. The careful analysis compared to the previous data has been done. In ^{1}H NMR, the chemical shift (δ) of phenyl proton bound to Sn atom as expected appeared in the range of 7.41-7.43 ppm, while the chemical shift of proton benzote were at 7.75-8.85 ppm. The ^{13}C NMR of the phenyl bound to Sn atom gave δ at 134.84-136 ppm and the carbon benzoate at 128-136. The chemical shift (δ) of carbon carbonyl as exptected appeared ad 166-167 ppm[9,10,14,17,19-21,24-27].

Table 3. Some selected and important IR band of the compounds synthesized

Compound	**2**	**4**	References (cm^{-1})
Sn-Cl	-	-	410-320
Sn-O	598.45	755.42	800-400
Sn-O-C	1289.2	1290.1	1250-1000
Sn-ph	1076.8	1074.6	1100-1000
C=O	1597.2	1624.7	1760-1600
CO_2 sym	1690.1	1632.9	1500-1400
C=C	1479.3	1551.8	1650-1400
C-H Aromatic	3061.3	3069.2	3100-3000
OH	3437.4	3438.7	3100-3500

Table 4. ^{1}H and ^{13}C spectra of the organotin(IV) compounds

Compound	H in phenyl (ppm)	H in benzoate (ppm)	C in phenyl and benzoate (ppm)
2	H2 & H6 7.52 (d,4H); H3 &H5 7.56 (t, 4H); H4 7.52 (t,2H)	7.70-7.90 (m)	C1-6 (phenyl): 129.3 – 128.6; C7 165.7; C8 131.4; C9 130.2; C10 134.0; C11 133.8 ; C12 130.0; C13 128.4
4	H2&H6 7.5 (d,6H); H3&H5 7.49 (t 6); H4 7.47	7.73-7.93 (d)	C1-6 (phenyl): 129.1 - 128.5; C7: 165.4; C8: 131.3; C9: 130.3; C10: 134.0; C11: 134.0; C12: 130.0; C13: 128.2

The result of antibacterial activities by diffusion method of the compounds (**2** and **4**) are shown in Table 5. This method has been used to find the most effective concentration 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 againts the two bacteria, *S. aureus* dan *E.coli* produced various inhibition zone. The two compounds were active at concentration of 200 ppm or equal with 3.66 x 10^{-4} M for **2** and 4.11x10^{-4} M for **4**, the

starting materials giving much higher inhibition concentration.

Table 5. MIC values of all compunds tested compared with chloramphenicol

Compounds	Minimum inhibitory concentration (MIC) (x 10^{-4} M)	
	S. aureus	*E.coli*
Chlormaphenicol	6.19	6.19
2	3.66	3.66
4	4.11	4.11

The control positive drug, chloramphenical was also giving inhibition concentration at 200 ppm (6.19 x 10^{-4} M) where its halozone was bit bigger compared to the compounds tested. The results reported here were quite similar to the previous results[2,24]. These indicated that the compounds tested have been shown a promising result as new antibacterial drug[28].

4. CONCULSIONS

We have succefully prepared two organotin(IV) compound with ligands of 2-hydroxybenzoic acid and tested their antibacterial activities against *S. aureus* and *E. coli*. The inhibition zone obtained was comparable to chloramphenicol as the control positive. Thus this finding opens the chance for these compound for future applications as antibacterial drug. However attempts to find stronger antibacterial drug is still on going in our laboratory in order to get the better new antibacterial drug.

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