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ANTIOXIDANT PROPERTIES OF TRIPHENYLTIN(IV) COMPLEXES DERIVED FROM A NOVEL IBUPROFEN-5-AMINOSALICYLIC ACID LIGAND: SYNTHESIS AND CHARACTERIZATION

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ABSTRACT. In this study, new ligand was prepared by condensation reaction between Ibuprofen and 5-amino salicylic acid (IAS), this prepared ligand was used to prepare three complexes of triorgnotin(IV) salts to obtain the corresponding complexes. The ligand (IAS) and complexes were characterized by several techniques such as infrared spectroscopy, (tin, proton and carbon) magnetic resonance (^{1}H, ^{13}C, ^{119}Sn NMR), elemental analyses. The antioxidant activity of the complexes was also studied. It was produced by two methods: DPPH and CUPRAC. The resulting complexes gave a higher rate of inhibition than the ligand due to the presence of the tin element in the complexes. Complex **1** (tri phenyltin-IAS) also shown greater antioxidant activity than the other compounds.

KEY WORDS: Ligand, Antioxidant activity, Triorganotin(IV), DPPH method, CUPRAC method

INTRODUCTION

Organotins are compounds that have one or more organic substituents bonded to the atom of tin directly through the organic substituent's carbon atom. The British chemist Edward Frankland produced the first organotin compounds in the middle of the 1800s., who synthesized crystals of diethyl tin(IV) di iodide ($(C_2H_5)_2SnI_2$) by heating ethyl iodide with Sn. Tin has two stable oxidation states: +2 and +4, which is why organotin(II) and organotin(IV) compounds are known. In general, organotin compounds(II) tend to polymerize because they are not very stable [1, 2]. Therefore, compounds of organotin(II) readily oxidize to the more stable organotin(IV) [3].

Organotin compounds can be classified as mono, di, (Ar), or alkyl (R) depending on how many organic groups are attached to them. Additionally, there are two types of organotin compounds: aliphatic and aromatic [4, 5] Organotin composites were first noticed in the industrial field in 1940. And in the field of coordination and organometallic chemistry, large-scale synthesis started in 1950. These compounds are now produced at rates between 40000 and 51000 tons annually, making them significant industrial components [6].

The integration of organometallic fragments into biomolecules is the focus of bioorganometallic chemistry in particular, where the chemistry of the metal-carbon bond is a key feature. Research in bio organometallic chemistry includes a range of studies regarding the study of the role of organometallic substances in biology [7, 8] It was discovered that stability of the ligand-metal bond, which prevents hydrolysis characterizes the composition of tin-based anti-tumor drugs. when the connections between Sn and N and Sn and S are the shortest and the tin atom's coordination environment is fully filled (CN = 6), higher cytotoxicity is seen [9, 10].

Besides the theoretical and structural interests, organotin complexes are important and could be taken advantage of them to develop novel metal-based medications [11]. Many investigations have been used metal complexes with drugs as therapeutic agents[12-14]. Current research on elemental complexes has demonstrated that the drug's interaction with the elements enhances its activity; additionally, The complex was shown to have this activity, but the original molecule did not [15].

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Antioxidants are substances that can resist or reduce the negative effects of oxidants. In order to prevent an oxidant component from being active, antioxidants work by giving it one electron [16]. Antioxidant substances may help reduce the oxidative damage linked to aging, cancer, heart disease, inflammation, and skin conditions, and malaria, leading to the extension of some searches for metal antioxidant medicinal molecules, particularly organotin(IV) [17, 18]. Many researches have attempted to use organotin compounds, because of their reactivity, in various biological processes; one such biological function is as an antioxidant [19].

The purpose of this work is to examine the tri organotin(IV) complexes' antioxidant activities and determine the amount of improvement or decrease in antioxidant activity compared to the new ligand (IAS).

EXPERIMENTAL

Materials

All solvents and chemicals used in this field were of the highest purity without any additional purification. Methanol, ibuprofen, 5-amino salicylic acid, tributyltin chloride, and tri phenyl tin chloride, trimethyltin chloride, were all obtained from Sigma-Aldrich in Schlecht, Germany.

Ligand synthesis

The ligand was prepared by reacting an appropriate amount of ibuprofen (4.1g, 20 mol) with 5-amino salicylic acid (3.06 g, 20 mol). Each substance was dissolved in 30 mL of methanol, and then the two substances were mixed together in a condensation flask for 4 hours. The resulting solution was filtered, dried and recrystallized to form pure precipitate of the ligand.

Synthesis of tri-organotin(IV) complexes

To create the complexes, the metal to ligand molar ratios are (1:1), (since a suitable amount of Ph_3SnCl (1.2g, 3 mol), Bu_3SnCl (0.97 g, 3 mol) and Me_3SnCl (0.59 g, 3 mol) were dissolved in 30 mL of methanol and then added to the IAS solution that had been agitated. (1 g, 3 mol), in 30 mL methanol. This mixture was refluxed for 5 hours. The resulting solution was filtered, dried and recrystallized to form pure complex.

Antioxidant activity tests

DPPH free radical scavenging activity

The DPPH technique was employed to assess antioxidant activity, as previously mentioned by others [20-23]. Different quantities of all the synthesized compounds (2, 4, 8, 16, and 32 M) were dissolved in methanol. Each test solution received 0.1 mM of DPPH in methanol, which was included and well combined. After half an hour, the solution was removed.

A UV-Vis pectrophotometer was used to measure the mixture's absorbance at 517 nm in wavelength. The antioxidant activity was determined by calculating the fraction of inhibition against DPPH. Equation (1) was utilized to obtain the % inhibition:

$$I\% = \left[\frac{Control\ Absorbance - Sample\ Absorbance}{Control\ Absorbance}\right] \times 100 \quad (1)$$

CUPRAC method

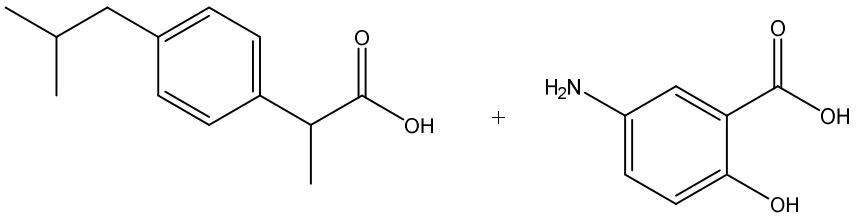
The CUPRAC method was followed to conduct an antioxidant activity test in accordance with other people's procedures [24]:

$$Total\ antioxidants\ \ levels = \left[\frac{Atest}{A\ STD}\right] \times Conc\ of\ STD\ \left(\frac{mmol}{L}\right) \quad (2)$$

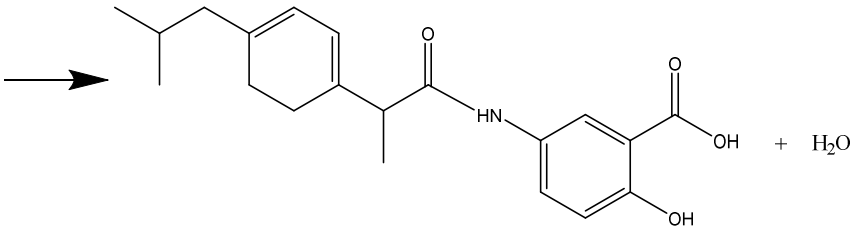
RESULTS AND DISCUSSION

(IAS) ligand synthesis and its tin(IV) complexes

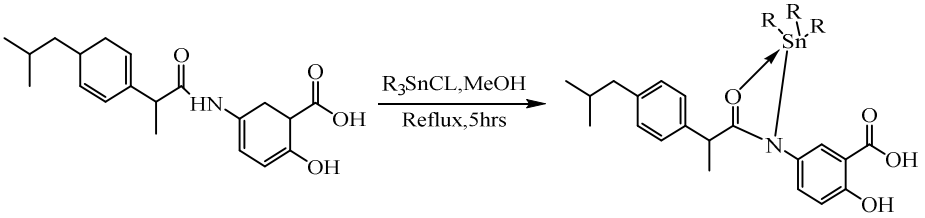
Ligand (IAS) was prepared by reacting an appropriate amount of ibuprofen with 5-amino salicylic acid as in Scheme 1.



Ibuprofen **5 amino salicylic acid**



Scheme 1. Synthesis of iuprofen-5-amino salicylic acid (IAS).



Scheme 2. Synthesis of triorganotin(IV) complexes, R = Ph, Me, Bu.

The synthesis of tin (IV) complexes was carried out by mixing IAS ligand with Bu_3SnCl, Ph_3SnCl and Me_3SnCl in 1:1 molar ratio in (methanol solvent) with reflux about 5 hours produced the conforming (IAS-tri organotin(IV) complexes) with yield of 76%, 91% and 84.3%, respectively, Scheme 2 shows tin(IV) synthesis, while Table 1 gives the physical properties of ligand and its tri organotin(IV) complexes

Table 1. Physical properties of ligand and its triorganotin(IV) complexes.

Sn(IV) complex	R	Color	Yield	M.p./ °C	Elemental analysis % calculated (found)		
					C%	H%	N%
Ligand	--	Gray	--	245-247	67.36 (66.79)	6.79 (6.66)	4.10 (3.99)
Complex 1	Ph_3	Pale gray	91%	256-258	62.11 (61.28)	5.40 (5.15)	2.03 (1.87)
Complex 2	Me_3	Pale black	84%	232-234	50.79 (49.42)	6.20 (5.74)	2.78 (2.52)
Complex 3	Bu_3	Black	76%	214-216	57.36 (56.25)	7.83 (7.35)	2.22 (2.15)

FTIR spectra

Studies of organotin complexes using infrared spectroscopy also revealed novel bands of absorption. These bands are associated with the 438-482 cm^{-1} and 419-430 cm^{-1} for (Sn-O) and (Sn-N) resonance regions respectively .These bands' presence suggests that the coordination between Sn(IV) and ligand is stable. It is coordinated by the carboxyl, aryl, or alkyl groups attached to the tin center [25-27]. The IR statistics are displayed for some of the complexes' distinct groups in Table 2.

Table 2. FTIR spectroscopy data of prepared ligand and its tri organotin complexes.

Sn(IV) Complex	C=O	C-N	Sn-O	Sn-N
Ligand	1719	1233		
Ph_3SnL	1649	1260	438	419
Me_3SnL	1719	1233	482	424
Bu_3SnL	1717	1233	482	430

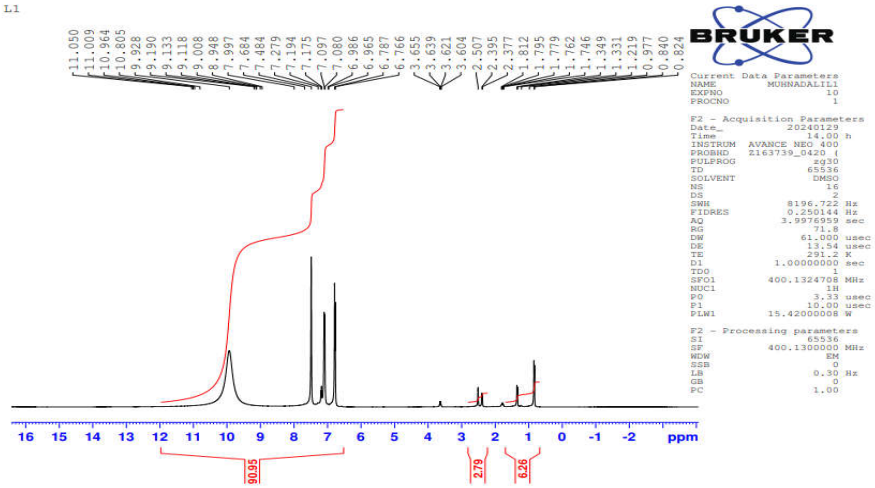


Figure 1. The ^{1}H-NMR spectra of ligand (IAS).

^{1}H-NMR spectroscopy of organotin(IV) complexes

Spectrophotometric analysis (^{1}H-NMR) was employed to validate the ligand and its tri organotin(IV) structures. For every anticipated chemical shift, the NMR displays all of the expected signals. The ^{119}Sn-NMR were studied to determine the produced compounds'

geometrical shape [28, 29], with a value less than -200 indicating five coordination complexes. Table 3 shows ^{1}H NMR signals of the ligand and its complexes

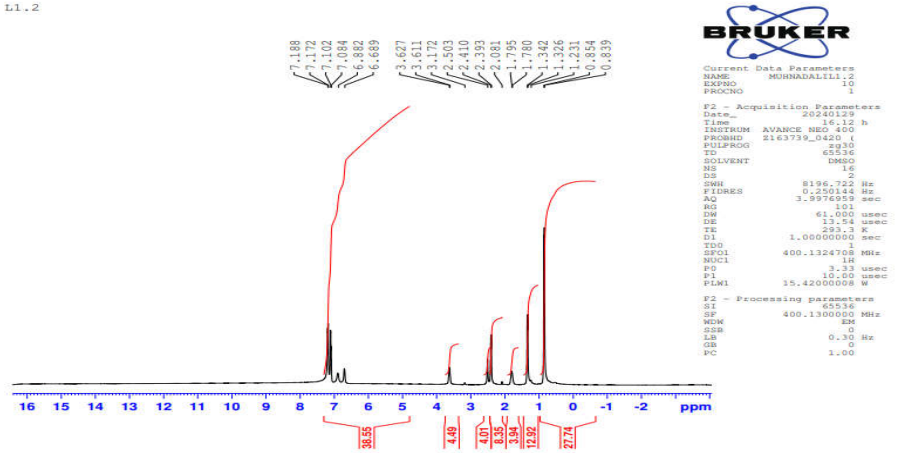


Figure 2. The ^{1}H-NMR spectra of complex (Me_3SnL1).

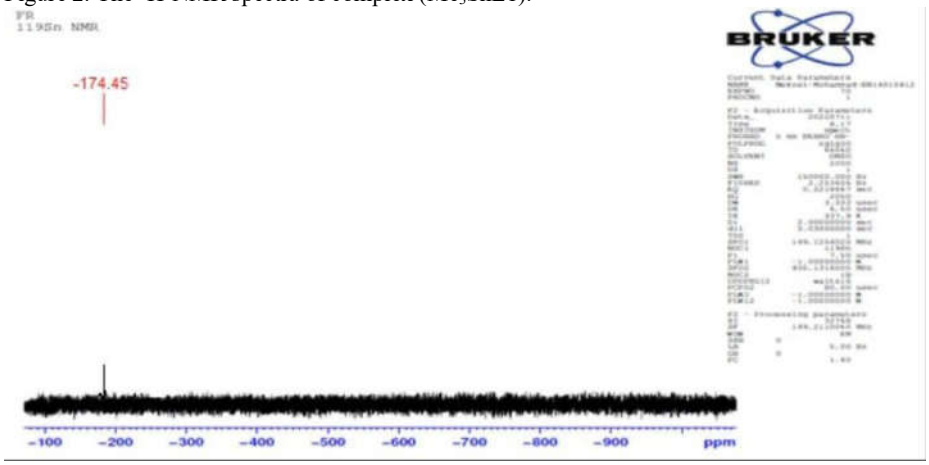


Figure 3. ^{119}Sn-NMR spectrum of complex (Me_3SnI).

Table 3. The ^{1}H-NMR spectra (DMSO-d6; ppm) of ligand (IAS) and its complexes.

Sn(IV) complex	^{1}H–NMR
Ligand	10.8 (s, 1H, NH), 7.68–6.78 (m, 7H, Ar), 3.66 (s, 1H, CH), 2.39 (d, 2H, CH_2), 1.81 (s, 1H, CH), s1.34 (s.3H, Me), 0.84 (s, 6H, 2Me).
Ph_3SnL	7.37-7.92 (m, 5H, Ar), 7.11-7.28 (d, 4H, Ar), 6.72 (d, 2H, 2CH), 3.76 (s, 1H, CH), 2.41 (d, 2H, CH_2), 1.83 (s, 1H, CH), 1.3 (s, 1H, CH), 1.3 (s, 3H, Me), 0.87 (s, 9H, 3Me).
Me_3SnL	7.17 (d, 4H, Ar), 6.88 (d, 2H, 2CH), 3.61 (s, H, CH), 2.39 (d, 2H, CH_2), 1.78 (s, 1H, CH), 1.23 (s, 3H, Me), 0.85 (s, 15H, 5Me).
Bu_3SnL	7.08 (d, 4H, Ar), 6.83 (s, 2H, CH, 6.83 (s, 2H, 2CH), 3.36 (s, 1H, CH), 2.14 (d, 2H, CH_2), 1.53 (s, 1H, CH), 1.07 (d, 18H, $3CH_2CH_2CH_2$), 0.8 (s, 15H, 5Me).

Antioxidant activity

The two techniques (DPPH and CUPPRAC) described above were used to analyze the antioxidant activity of ligand and its three synthesized complexes. The antioxidant activity of each compound was investigated at different concentrations using the tests outlined in the literature [26]. For every measurement, the absorbance was determined before calculating the percentage of inhibition. Antioxidant activity is shown using the two approaches in Figures 4 and 5 [29] .

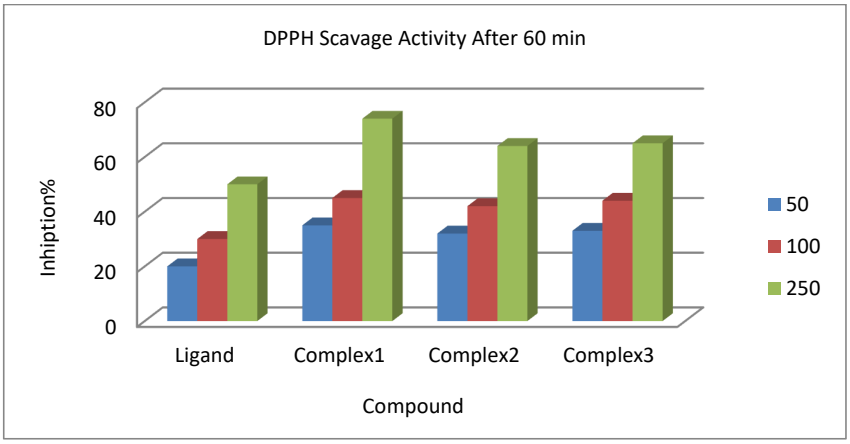


Figure 4. DPPH scavenging activity of (IAS) and complexes.

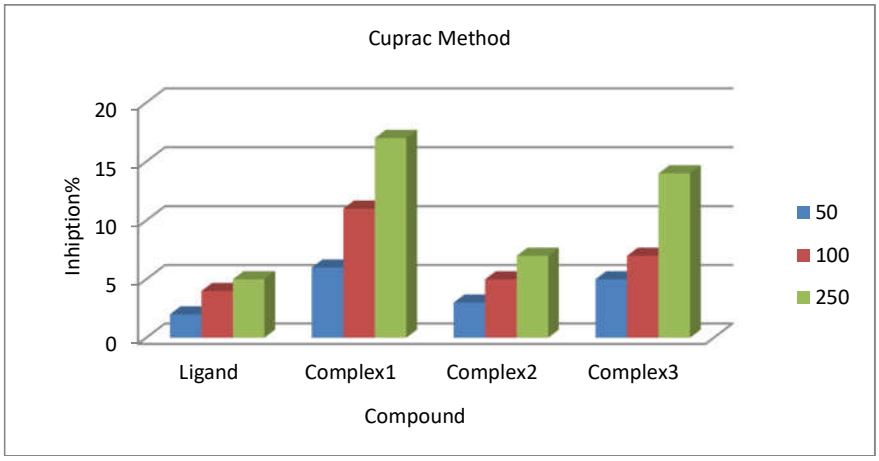


Figure 5. CUPRAC method activity of ligand (IAS) and complexes.

Figures 4 and 5 showed that the all the prepared complexes have higher antioxidant activity than ligand, first complex (triphenyltin-IAS) has a higher antioxidant activity than the other resulting complexes. This could be as a result of the complex having three phenyl groups and having more aromatic material than the other compounds. This study is consistent with other similar studies [30, 31]

CONCLUSION

Suitable complexes for tin were prepared through the condensation reaction of the ligand (IAS) with tri phenyl, methyl and butyl-tin chloride salts, then characterized with different techniques. By determining the antioxidant activity of the ligand and organotin(IV) complexes using the DPPH and CUPRAC procedures, it was found that the antioxidant activity of the complexes is higher than the activity of the ligand.

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