

4-AMINOANTIPYRINE-NEW ORGANOTIN COMPLEXES, SYNTHESIS, STRUCTURE AND ANTIOXIDANT ACTIVITY

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ABSTRACT. 4-Aminoantipyrine was used as ligand to prepare new complexes of triphenyltin, di-butyl and dimethyl-tin complexes by condensation reaction with the corresponding organotin chloride salts. The complexes were identified by different techniques, such as infrared spectra, (tin and proton) magnetic resonance and elemental analyses. The antioxidant activity of 4-aminoantipyrine and prepared complexes were studied by two different methods; Free radical scavenging activity DPPH and CUPRRAC methods. Tri and di-tin complexes gave high percentage inhibition than ligand with both methods due to tin moiety, also triphenyltin carboxylate complex was the best compared with the others.

KEY WORDS: 4-Aminoantipyrine, Condensation, Triphenyl tin chloride, DPPH and CUPRRAC methods

INTRODUCTION

Organotin(IV) complexes have an active synthetic chemistry. Extensive range of industrial and antimicrobial applications have made this a research subject. These substances can be utilized as biocides, catalysts [1-3], and effective thermal stabilizers in polymers. There are available multifunctional organotin(IV) carboxylates examples include esterification catalysts [4], silicone cures [5], polyurethane structures [6], antifouling paints [7], PVC stabilizers [8-10], and vegetable transfer esterification from biodiesel to petroleum [11]. It can also be applied to versatile synthesis. Medicines that have the potential to function as effective antifungal and antibacterial agent's effects against tumors and cancer [12, 13], also demonstrated a substantial response due to their capacity to bind to DNA phosphates in malignancies, drug, this is harmful [14]. Their antibacterial activity is generally tied to bound ligands and organotin(IV) units [15,16], and natural ligands help the complex cross-cell membranes. Due to their capacity to bind to proteins, triorganotin compounds are often recognized to have higher activity than their di- and mono-organotin analogs [17, 18]. Organotin compounds were discovered to have differential behavior toward various mammalian cell lines [19] and to be highly cytotoxic to lymphoma cell lines with less toxicity toward the HeLa cervical cancer cell line. A positive reaction and increased therapeutic characteristics were seen when Gómez-Ruiz and Kaluerovi explored innovative nanostructured mesoporous silica SBA-15 as a carrier system for organotin chemicals against various cancer cells and in vivo [20, 21]. Organotin chemicals have significant toxicity, biological activity, and non-specific behavior. These substances are hazardous because of a variety of mechanisms, including the binding of the Sn atom to the SH groups of proteins, damage to the biomembrane, creation of oxidative stress in the body [22], etc. The capacity of organotin compounds to accumulate in cells and their toxicity, however, offer the possibility to think of them as potential pharmaceuticals with a particular action, such as cytotoxic antitumor drugs in

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cancer chemotherapy [23-25]. Tin compounds contain an organic fragment that is crucial to the physiological activity of those chemicals. The addition of a vitamin E mimetic, 2,6-dialkylphenol fragment that is bound to an Sn atom and exhibits antioxidant activity may lessen the general toxicity of metal compounds [26, 27].

One can avoid the unfavorable side effects associated with currently employed platinum derivatives by combining the cytotoxic capability of tin compounds with an antioxidant functional group in the ligand structure to build viable anticancer medicines.

The goal of this research is to examine the impact of novel tin(IV) complexes. We used the 1,1-diphenyl-2-picrylhydrazine (DPPH) and cupric reducing antioxidant capacity CUPRAC methods to report the antioxidant activity of various organotin(IV) 4-aminoantipyridines.

EXPERIMENTAL

Preparation of triphenyl tin(IV) complex 1

4-Aminoantipyridine in methanolic solution (1 mmol, 0.203 g) was stirred with (1 mmol, 0.4 g) NaOH for 30 min at room temperature. A (1 mmol, 0.385 g) from triphenyl tin chloride (Ph_3SnCl) was dissolved in 30ml hot methanol then added to 4-aminoantipyridine mixture, left to reflux about 4 hours with continuously stirred [28-30]. The precipitate was left to evaporate under vacuum, washed with diethyl ether.

Preparation of di- organotin(IV) complexes 2-3

20 mL methanolic solution of 4-aminoantipyridine (2 mmol, 0.406 g) was stirred with (2 mmol, 0.8 g) NaOH for 30 min at room temperature. (1 mmol, 0.25 g or 0.219 g) from dibutyl or dimethyltin dichloride (Bu_2SnCl_2 or Me_2SnCl_2) was dissolved in 20 mL of hot methanol then added to 4-aminoantipyridine mixture, left to reflux about 4 hours with continuously stirred [31-34]. The precipitate was left to evaporate under vacuum, washed with diethyl ether.

Antioxidant activity tests

DPPH technique

Antioxidant activity was measured using the 1,1-diphenyl-2-picrylhydrazine (DPPH) technique, as described by others [35, 36]. The compounds were dissolved in methanol at different concentrations of 2; 4; 8; 16, and 32 M, respectively. DPPH (0.1 mM in methanol) was added to each test solution and carefully mixed. After 30 min, the solution was discarded. A UV-Vis spectrophotometer was used to test the mixture's absorbance at a wavelength of 517 nm. The proportion of inhibition against DPPH was used to calculate antioxidant activity. The percentage inhibition was calculated using equation (1);

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

CUPRAC method

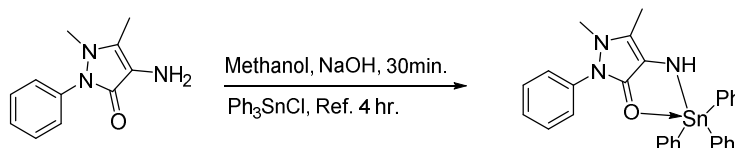
Antioxidant activity test by CUPRAC method was performed according to method used by others [37].

$$\text{Total antioxidants level} = \left[\frac{A_{\text{test}}}{A_{\text{STD}}} \right] \times \text{Conce. of STD} \left(\frac{\text{mmol}}{\text{L}} \right) \quad (2)$$

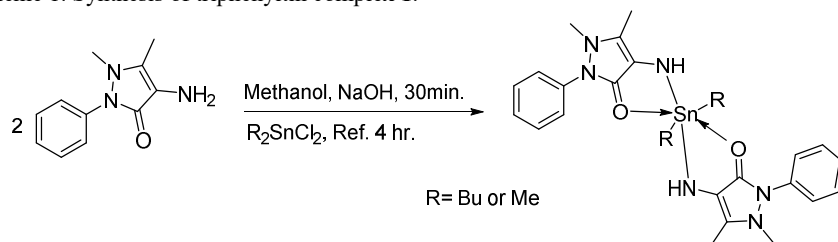
RESULTS AND DISCUSSION

Synthesis of organotin(IV) complexes 1–3

The new complexes were obtained by refluxing methanolic solutions of tri and di-organotin chloride with 4-aminoantipyrene, respectively, with a high yield percentage (90-95%), (Scheme 1 and 2).



Scheme 1. Synthesis of triphenyltin complex 1.



Scheme 2. Synthesis of dibutyl and dimethyl-tin complexes 2 and 3.

The resulting compounds were identified using FTIR, NMR (^1H and Sn^{119}) spectroscopy techniques, as well as elemental analyses. Tables 1-3 summarize the findings of each study. The complexes showed different color with high yield, also the elemental analysis gave a good agreement between calculated and experimental values.

Table 1. Physical analysis data of 4-aminoantipyrene and its complexes.

Compound	Color	Yield %	m.p. (°C)	Elemental analysis % calculated (found)		
				C	H	N
4-Aminoantipyrene	Yellow	-	109-111	65.019(65.96)	6.45(6.78)	20.68(19.03)
Ph_3SnL	White	90.5	220-222	63.52(63.95)	5.33(6.21)	7.41(7.43)
Bu_2SnL_2	Pale orange	94.6	219-221	57.67(58.12)	7.11(7.82)	12.61(13.07)
Me_2SnL_2	Black	95.3	202-204	53.63(54.04)	6.06(6.89)	14.43(14.61)

IR spectral data of 4-aminoantipyrene distinguish by the strong band at 1653 cm^{-1} related to C=O stretching. At $3433\text{-}3329\text{ cm}^{-1}$ absorption of NH_2 group. The CH stretching frequency absorbs at 3000 cm^{-1} , and NH_2 bending at 1683 cm^{-1} . All these bands shifted due to complexation. New bands appeared at $500\text{-}450\text{ cm}^{-1}$ related to Sn-O and Sn-N bonds, respectively.

Table 2. IR spectral data of 4-aminoantipyrene and its complexes.

Compound	NH_2	C-H aromatic	C=O	C=C	M-O	M-N
4-Aminoantipyrene	3433-3329	2989	1653	1591	-	-
Ph-4-aminoantipyrene	3404-3326	2978	1647	1577	522	454
Bu-4-aminoantipyrene	3408-3327	2958	1647	1591	516	459
Me-4-aminoantipyrene	3406-3327	2967	1646	1589	516	450

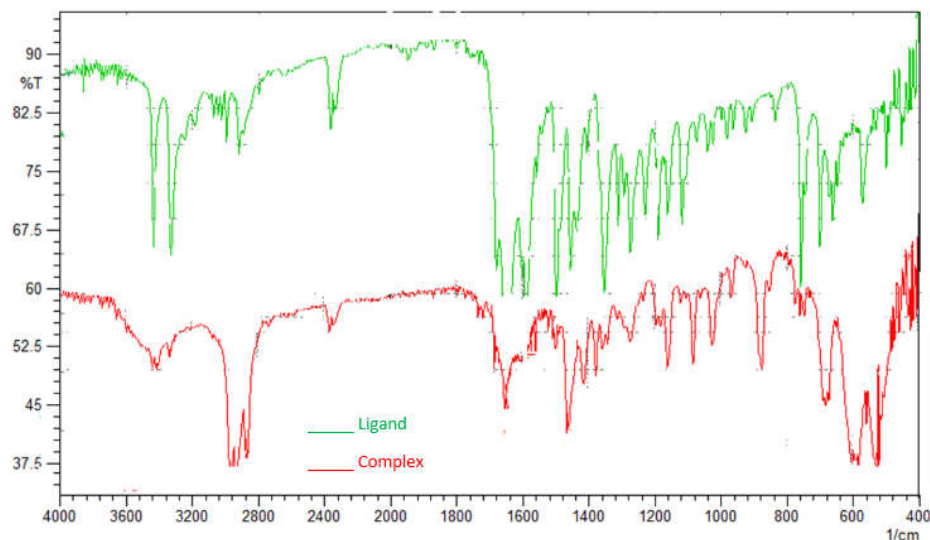
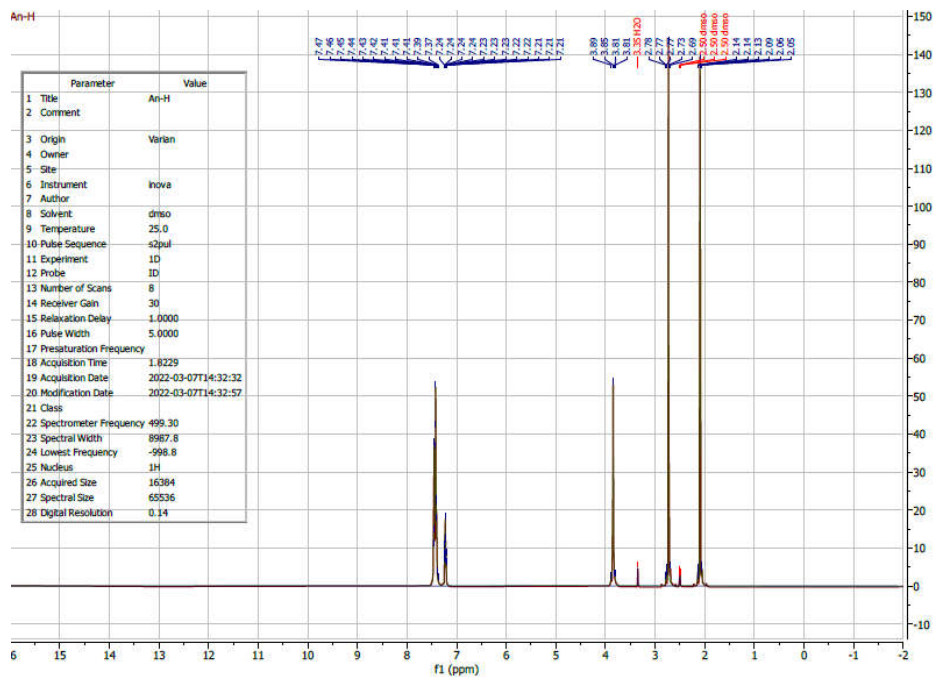
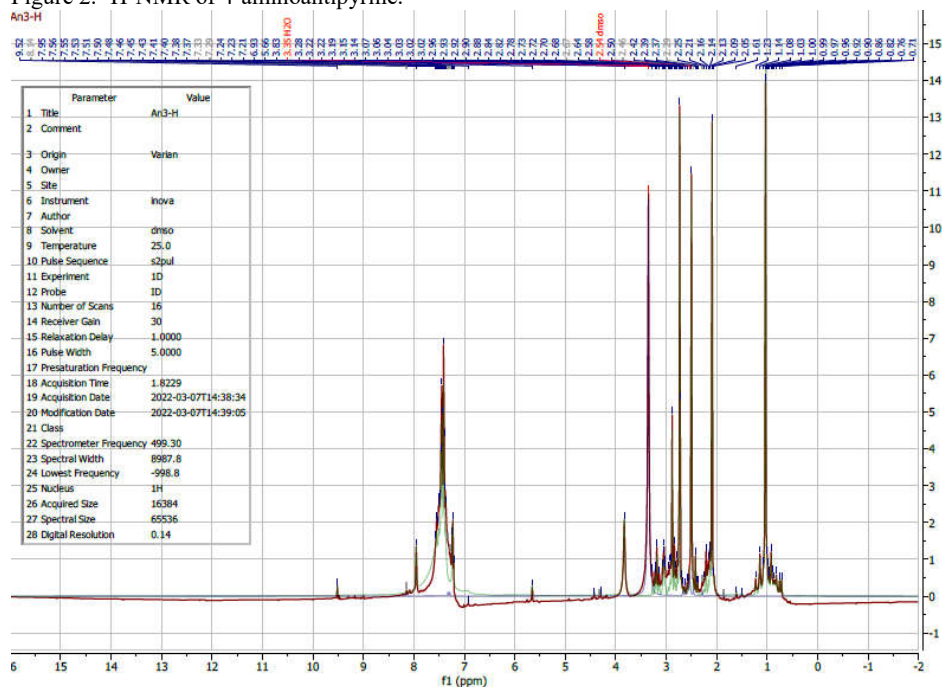


Figure 1. FTIR spectra of 4-aminoantipyrene and complex.

$^1\text{H-NMR}$ spectrum of 4-aminoantipyrene shows three different signals for the benzene ring at 7.21-7.47. Also C-CH₃ at 2.05-2.12, N-CH₃ at 2.69-2.78 and -NH₂ group at 3.81-3.89. All these signals were shifted due to complexation as in Table 3. The $^{119}\text{Sn-NMR}$ were studied to find out the geometrical shape of the prepared complexes, where the value less than 200 means five coordination complexes, when it increases to more than 200, so the complex was expected to be six coordination with octahedral shape [38].

Table 3. $^1\text{H-NMR}$ spectra of 4-aminoantipyrene and complexes.

Compound	$^1\text{H-NMR}$	$^{119}\text{Sn-NMR}$
4-Aminoantipyrene	7.21-7.47(m, 5H, Aromatic H), 3.81-3.89(NH ₂), 2.69-2.78(s, 3H, N-CH ₃), 2.05-2.12(s, 3H, C-CH ₃)	---
Ph-4-aminoantipyrene	7.26-7.50 (m, 5H, Aromatic H), 7.55-7.78(m, 5H, phenyl gr), 2.82(s, 3H, N-CH ₃), 2.1(s, 3H, C-CH ₃)	-181
Bu-4-aminoantipyrene	8.08(s, H, NH), 7.23-7.45(m, 5H, Aromatic H), 2.69-2.78(s, 3H, N-CH ₃), 2.09-2.74(s, 3H, C-CH ₃), 0.83-1.59 (Bu-group)	257-
Me-4-aminoantipyrene	9.5(s, H, NH), 6.21-7.95(m, 5H, Aromatic H), 2.37-2.96(s, 3H, N-CH ₃), 2.05-2.25(s, 3H, C-CH ₃), 0.71-1.23(s, 6H, 2Me)	-226

Figure 2. ¹H-NMR of 4-aminoantipyrine.Figure 3. ¹H-NMR of Me₂Sn-4-aminoantipyrine.

Antioxidant activity

The two techniques (DPPH and CUPPRAC) described above were used to analyze the three synthesized complexes. Various amounts of each complex were used to examine its antioxidant activity following the assays described in the literature [33]. The percentage of inhibition was calculated once the absorbance for each measurement had been obtained. Figures 4 and 5 display antioxidant activity using the two techniques.

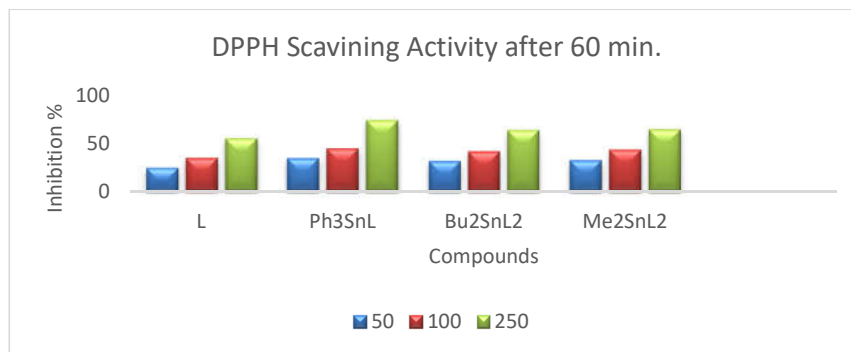


Figure 4. DPPH scavenging activity of 4-aminoantipyrene and complexes.

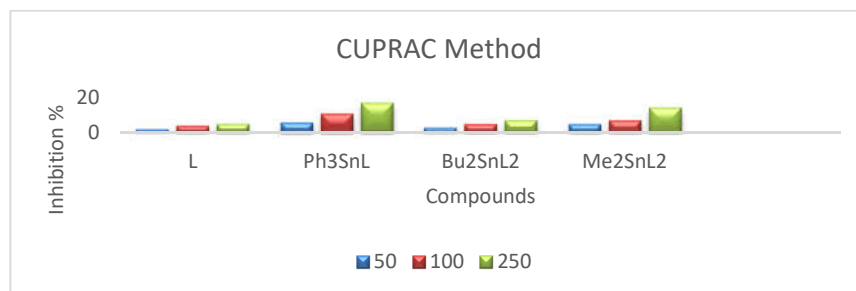


Figure 5. CUPRAC method activity of 4-aminoantipyrene and complexes.

Complex **1** (triphenyltin-antipyridin) demonstrated more significant activity than the other produced compounds; this may be because the complex contains three phenolic groups and has a more substantial aromatic content than the other complexes.

CONCLUSION

The three new tin(IV) complexes were prepared and characterized, and their antioxidant activities were evaluated viz. two known techniques: DPPH and CUPPRAC. The antioxidant activity of the organotin(IV) complexes was higher than that of the 4-aminoantipyridine.

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