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Review Article

Synthesis and Biological Activities of Organotin (IV) Carboxylates: A Review

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ABSTRACT
Organotin(IV) compounds have gained significant interest in both the chemical and pharmaceutical industry. Tin (IV) form stable complexes with a unique structure and physicochemical properties that are used in organic synthesis as heat stabilizers and catalysts, in drug development as biologically active agents and in other areas. This review concentrates on recent progress in the classical and convenient synthesis procedure and biological activities as antitumoral and antimicrobial agents.
Key words: Organotin(IV), Carboxylates, Stabilizers, Antitumor, Triorganotin(IV), Diorganotin(IV).

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INTRODUCTION

Organotin carboxylates comprise one of the most important classes of compounds. Besides the theoretical and structural interests, organotin carboxylates are finding great importance in industry and agriculture. New applications are likely to emerge in the near future. The compounds containing – OCOR' groups bonded to tin are defined as organotin-esters which may be either monomeric or polymeric and of three general types, viz. $R_3SnOCOR'$, $R_2Sn(OCOR')_2$ and $RSn(OCOR')_3$, where R and R' may be same or different groups.

SYNTHESIS OF ORGANOTIN CARBOXYLATES

Because of the hydrolysable nature of organotin halides, which are employed as starting material, their complexes have been prepared by carrying out the reactions in anhydrous organic solvent such as; n-hexane, benzene, acetone, methanol, ethanol. Hameed A. *et al*. prepared triorganotin (IV) complexes of the type Ph_3SnL, Bu_3SnL and Me_3SnL of the ligand benzamidomethionine (HL). The general chemical reaction for the synthesis of the triorganotin (IV) complexes are given in equation below.

$$R_3SnCl + LH \rightarrow Et_3N\ R_3SnL + Et_3NHCl$$

From Infra-Red Spectroscopy and Nuclear Magnetic Resonance Tetrahedral geometry was proposed for the prepared complexes,[1] Figure 1.

Yousif E. studied the synthesis of triorganotin with benzamidoglycin. Ligand formed by reaction of benzoyl chloride with glycin presence of sodium hydroxide. The prepared complexes were characterized by elemental analysis, infrared, conductance measurements and nuclear magnetic resonance (^1H, ^{13}C and ^{119}Sn NMR) spectral data. From the spectral measurements, monomer structures, monodentate and tetrahedral geometry Figure 2 were proposed for the complexes prepared.[2]

Also Yousif E. *et al*. studied the preparation of triorganotin complexes with benzamidoalanine, which was formed by reaction of benzoyl chloride with alanine in the presence of sodium hydroxide. The complexes were characterized by elemental analysis, conductance measurements and infrared, ultraviolet visible and ^1H, ^{13}C and ^{119}Sn nuclear magnetic resonance spectroscopy. Monomer structures were proposed from the spectral measurements Figure 3, with a bidentate form.[3]

Diorganotin carboxylate were prepared by reflexing of organotin derivatives and carboxylic acid. Farina *et al*. prepared complexes of the type R_2SnL_2, where R = phenyl, butyl and methyl and L = N-methyl-m-nitrobenzohydroxamic acid.[4] Bidentate and Octahedral geometry was proposed for the complexes prepared Figure 4.

It may conclude that the ligand coordinated through oxygen to the Tin atom leading to the formation of five member ring chelate.[4] Also new diorganotin(IV) complexes of the type $Ph_2\ SnL_2$, $Bu_2\ SnL_2$ and $Me_2\ SnL_2$ of the ligand H benzamidoleucine(L). Ligand formed by reaction of benzoyl chloride with leucine in presence of sodium hydroxide. Octahedral geometry was proposed for the prepared complexes.[5] Graisa *et al*. new diorganotin(IV) complexes of the type Ph_2SnL_2, Bu_2SnL_2 and Me_2SnL_2 of the ligand N-tolyl m-Nitrobenzohydroxamic acid. Ligand formed by condensation reaction of 3-Nitrobenzoyl chloride with N-tolyl hydroxylamine in presence of sodium hydrogen carbonate as a catalyst. The prepared complexes were characterized by FTIR Spectroscopy, electronic spectroscopy, ^{1H}NMR and ^{13C}NMR. From the spectral measurements, monomer structures for the complexes were proposed. Octahedral geometry Figure 5 was proposed for the complex prepared.[6]

Anew diorganotin(IV) complexes of the type $Ph_2\ SnL_2$, $Bu_2\ SnL_2$ and $Me_2\ SnL_2$ of the ligand H benzamidoacetic acid (L). Ligand formed by reaction of benzoyl chloride with glycin in presence of sodium hydroxide. The ligand coordinated through carboxylate to the Tin atom leading to the formation of four member ring chelate. Tetrahedral geometry Figure 6 was proposed for the prepared complexes.[7]

On 2010 the ligand 2-[(phenylcarbonyl)amino]propanoic acid (HL) formed by reaction of benzoyl chloride with alanine in presence of sodium hydroxide and a new diorganotin(IV) complexes were investigated.[8] The ligand coordinated through carboxylate to the Tin atom leading to the formation of a four membered ring chelate. Octahedral geometry was proposed for the prepared complexes Figure 7.

Yousif E. *et al*. were studied the synthesis, characterization and fungicidal activity of some diorganotin(IV) with 2-thioacetic-5-phenyl-1,3,4-oxadiazole.[9] Octahedral geometry was proposed for the prepared complexes Figure 8.

Graisa A. *et al*. have showed bidentate and Octahedral geometry was proposed for the complexes prepared from the ligand N-methyl-m-methoxybenzohydroxamic acid and different diorganotin(IV) oxide

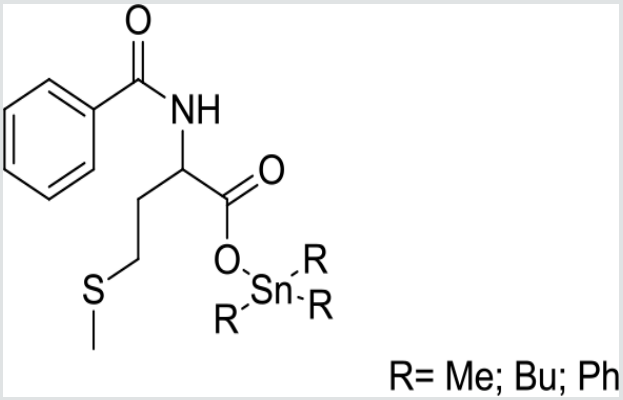

Figure 1: Triorganotin(IV)- Benzamidomethionine complex.

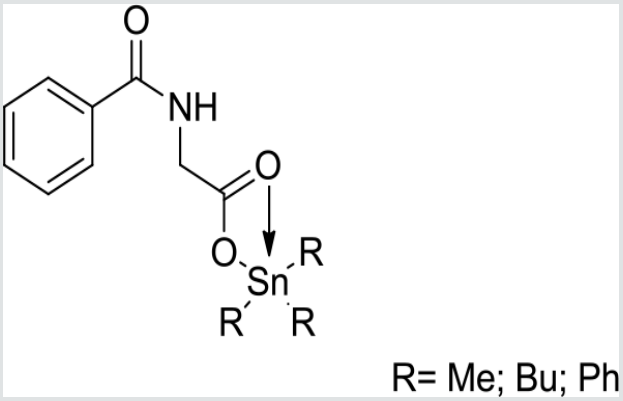

Figure 2: Triorganotin(IV)- Benzamidoglycin complex.

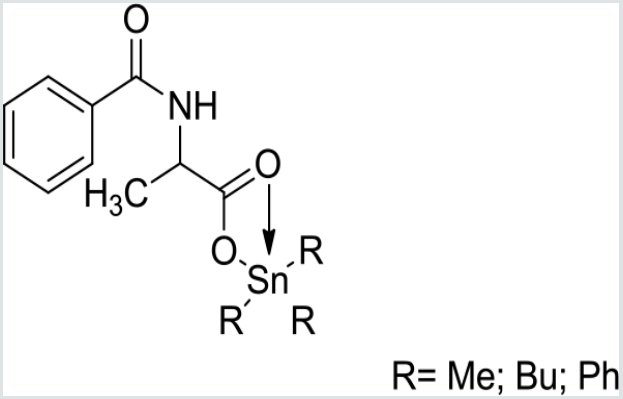

Figure 3: Triorganotin(IV)- Benzamidoalanine complex.

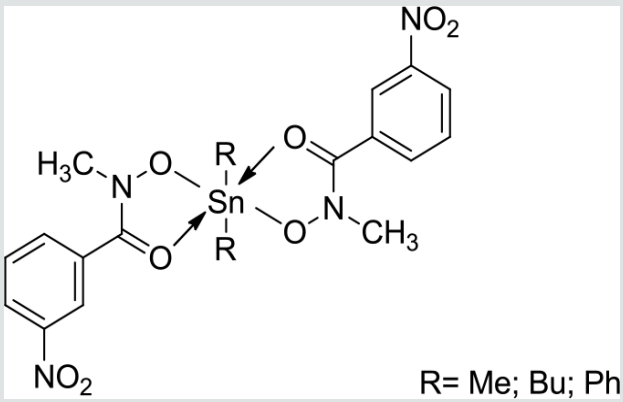

Figure 4: Diorganotin(IV)- N-methyl-m-nitrobenzohydroxamic acid complex.

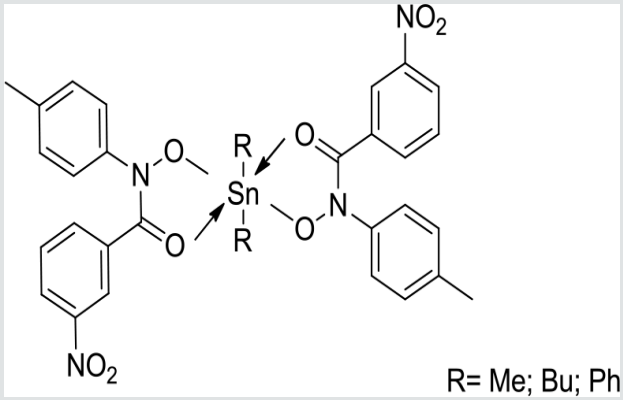

Figure 5: Diorganotin(IV)- N-tolyl m-Nitrobenzohydroxamic acid complex.

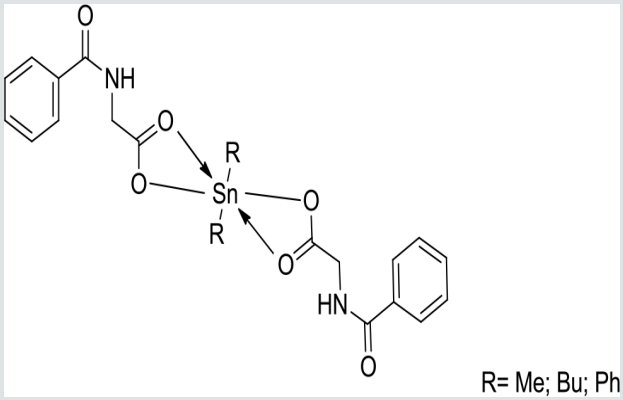

Figure 6: Diorganotin(IV)- benzamidoacetic acid complex.

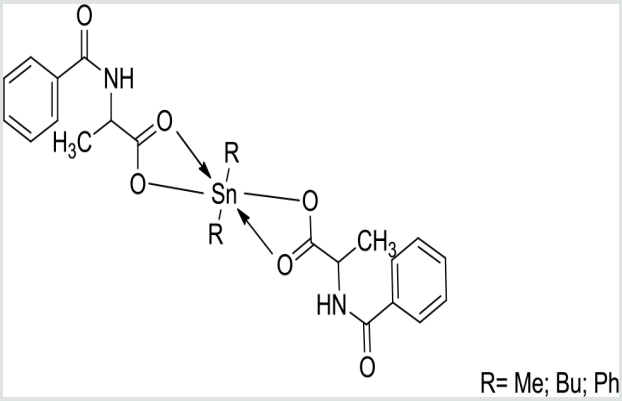

Figure 7: Diorganotin(IV)- 2-[(phenylcarbonyl)amino]propanoic acid complex.

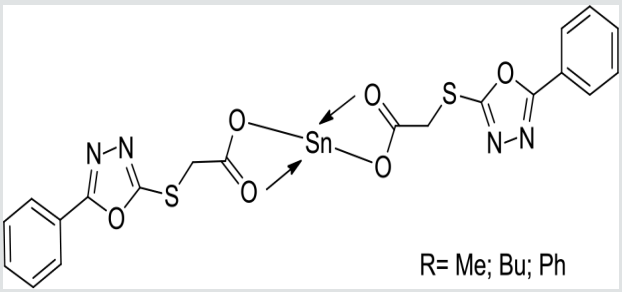

Figure 8: Diorganotin(IV)- 2-thioacetic-5-phenyl-1,3,4-oxadiazole complex.

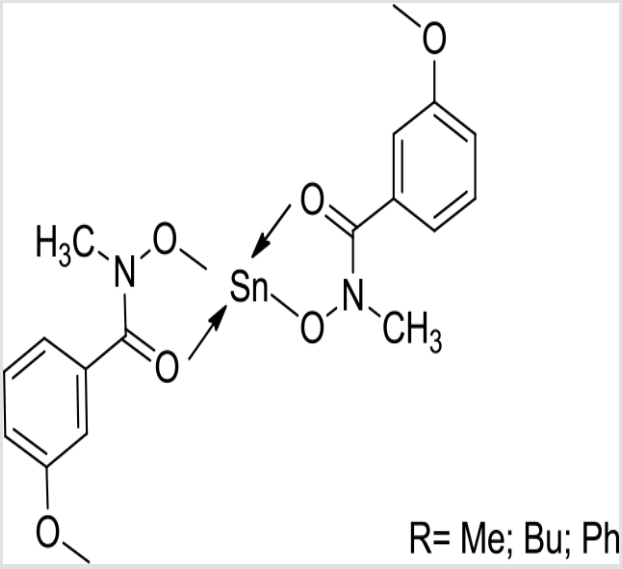

Figure 9: Diorganotin(IV)- N-methyl-m-methoxybenzohydroxamic acid complex.

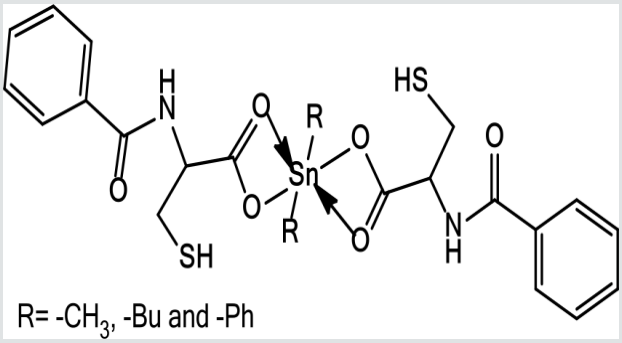

Figure 10: Diorganotin(IV)- Benzamidocysteine complex.

metal to afford the corresponding complexes Figure 9.[10]

Najeeb D. *et al*. reported a new structural class of organotin compounds by synthesis of new diorganotin (IV) complexes of the ligand benzamidocysteine. The Ligand formed by reaction of benzoyl chloride with cysteine in presence of sodium hydroxide. Octahedral geometry was proposed for the prepared complexes. Biological activity data have shown that these complexes have a significant biological activity against *Gibberela, Cercospora arachidicola, Physolospora piricola* and *Fusarium oxysporum* in DMF by the serial plate dilution method Figure 10.[11]

BIOLOGICAL ACTIVITIES

The inorganictin(IV) compounds are non-toxic or only slightly toxic towards mammals, insects, bacteria and fungi, whereas tin(IV) compounds, having an organic moiety, show varying biological activities. For alkyl organotin(IV), the longer the alkyl chain, the less toxic it is.[12,13] The particular pattern for methyl, ethyl, propyl and butyl varies according to the test organism. Activity also depends on the structure of the organotin(IV) compounds. Triorganotin(IV) compounds, which are compounds that have three Sn-C bonds, have the highest cytotoxicity[14-16] and compounds that contain aryl groups are less toxic than those with alkyl groups.[17,18] The X group can increase activity if it is biologically active or can assist in the transportation of the compound to the site of activity and the X group can also decrease activity, if it is chelated to the tin(IV) atom.[14,15,19] Compounds with a Sn-O linkage have been shown to have better activity than compounds that have tin(IV) connected to sulfur.[20,21] For tri-n-alkyltin(IV) acetates, the methyl organotin(IV) compounds are the most active in insects and mammals while the propyl and butyl compounds are the most active in fungi and certain bacteria. Activity decreases as the number of alkyl groups decreases as follows $R_4Sn > R_3Sn > R_2Sn > RSn > Sn$ all for tin(IV) compounds with the anionic X group exerting little influence on activity.[22,23] The compounds most used commercially are tributyltin(IV) chloride, dibutyltin(IV) dichloride, tributyltin(IV) oxide and dibutyltin(IV)oxide as in Figure 11 since they are among the least toxic alkyltin(IV) derivatives in humans.[12,23]

Microorganisms have existed on the earth for more than 3.8 billion years and exhibit the greatest genetic and metabolic diversity. They are an essential component of the biosphere and serve an important role in the maintenance and sustainability of ecosystems, comprising about 50% of the living biomass. In order to survive, they have evolved mechanisms that enable them to respond to selective pressure exerted by various environments and competitive challenges. The disease-causing microorganisms are particularly vulnerable to man's selfishness for survival, who has sought to deprive them of their habitat by using antimicrobial agents. These microorganisms[3]

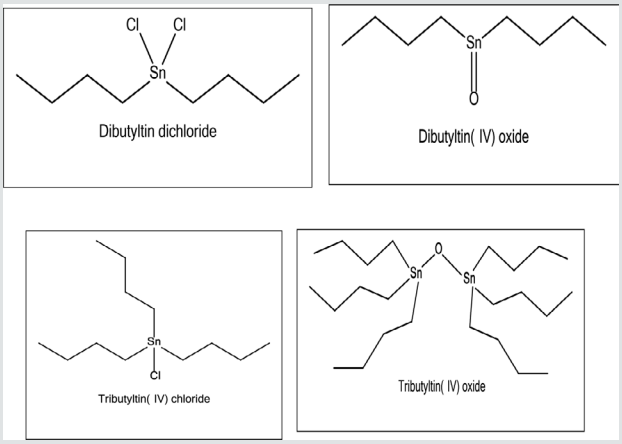

Figure 11: Organotin compounds with biological activity.

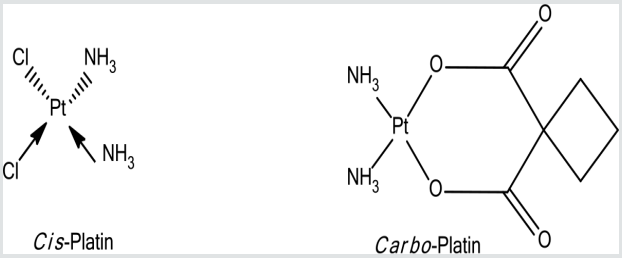

Figure 12: Structure of antitumoral drugs.

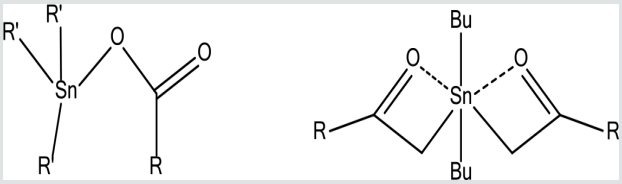

Figure 13: Structures of diorganotin carboxylates with antitumor activity.

BIOLOGICAL PROPERTIES OF ORGANOTIN CARBOXYLATES

Organotin compounds have received more attention for their biological effects than organic compounds of any other metal. The inorganic tin compounds hardly have any biological activity whereas organotin compounds exhibit high biocidal activity, probably due to their lipid solubility, which facilitates better transport to the reaction sites than the corresponding inorganic tin compounds. The systematic studies of biological activities of organotins were initiated in 1950.[24] Van der Kerk and Luijten[25] in 1954 published that many organotin derivatives having the general formula of R_3SnX are powerful fungicides. Within any R_3SnX series, the activity is markedly dependent upon the nature of the organic group (R) but relatively independent of the anionic radial.[26,27]

Numerous studies on organotin(IV) complexes have been carried out in order to study its biological properties against bacterial strains and cancer cell lines to explore its structural activity relationship.[26] It was believed that the coordinated methanol molecule aided the transportation of active triphenyltin(IV) to the cell or active sites (receptor sites) which enhanced its biological activity.[26]

For a high anti-fungal activity the total number of carbon atoms in the alkyl groups of a tri alkyltin compound should be about 9-12.[28] Organotin(IV) carboxylates have been used in silicone curing,[29] formation of polyurethane,[30] antifouling paints[31] and PVC stabilization.[32-34] Organotin(IV) carboxylates possess significant properties as antibacterial and antifungal agents and also as antitumor and anticancer drugs.[35] The antifungal, antibacterial and antitumor activities of organotin(IV) carboxylates are essentially related to the number and nature of the organic groups attached to the central Sn atom.[36] In general, triorganotin(IV) compounds display better biological activity than their diorganotin and mono organotin analogs. This has been attributed to their ability to bind proteins.[37] Research on the structure of organotin(IV) carboxylates continues and, at the same time, some new applications of high importance are being discovered which are relevant to ecological medicinal applications. The increasing interest in the chemistry of organotin(IV) compounds has led to the extended studies on their reactions with different biomolecules.[38] Antitumor activities of some organotin(IV) carboxylates are showed promising cytotoxic activities against various cancer cells like, sarcoma cancer cells, lungs, liver, breast and colon carcinoma etc. Antitumor activities of some of the complexes are also found to be competing with cis-platin.[39-42]

ANTITUMORAL ACTIVITY

Cisplatin and carboplatin Figure 12 have a wide range of applications in cancer chemotherapy. The serious negative side effects of platinum-pharmaceuticals diverted the attention of researchers to non-platinum chemotherapeutics with positive, low or no side effects.[43,44]

Among these organotins (IV) have received the greatest attention on account of their potential apoptotic inducing characteristics and high therapeutic index.[45,46] Some complexes of organotin(IV) Figure 13 are already known to possess antitumor activity.[47-49] There have been a large number of reports highlighting the use of diorganotin(IV) complexes as antitumor agents.[44,45,48-51]

Organotin(IV) compounds have been tested for antitumor activities as early as 1929.[52] First (1963) found that chelation plays a role in both the cause and cure of malignancy.[53] Since this discovery, molecules containing metal sites as chelating agents have been employed in the fight against cancer. According to Mutter *et al.* the structures of all organotin(IV) antitumor active compounds are characterized by (i) the availability of coordination positions at Sn and (ii) the occurrence of relatively stable ligand-Sn bonds; e.g., Sn-N, Sn-S, Sn-O and their slow hydrolytic decomposition.[43,54] Thioamide-organotin(IV) complexes, on the other hand, have shown high antitumor activity, which is rather related to the ligand type and not to the geometry of the compounds.[55] Therefore, five coordinated tri-organotin(IV) complexes should exhibit higher activity.[56] The anticancer activity of organotin(IV) carboxylates is reviewed recently.[57] It is found that organotin(IV) geometry has role in their biological activity. It has been found that five-coordinated organotin(IV) carboxylates display strong enzyme inhibition activity as compared to six coordinated compounds. It is also found that nature and size of alkyl or aryl group attached to Sn^{IV} also play a decisive role in biological activities of organotin(IV) carboxylates.[56]

CONCLUSION

Organotin(IV) derivatives were synthesized in quantitative yield by refluxing the synthesized carboxylic acids and respective organotin(IV) compounds in suitable solvent. The FT-IR spectral data that the organotin(IV) moieties react with the [O,O] atoms of the ligand, which behaves as bidentate. NMR data showed that the bidentate nature of carboxylate group is probably lost in solution and that the tri-organotin(IV) derivatives contained four-coordinated tin with a tetrahedral arrangement, while the diorganotin(IV) derivatives exhibit penta- or hexa-coordinated geometry due to fluxional behavior. Triorganotin(IV) compounds display better biological activity than their diorganotin and mono organotin analogs. Structure-activity relationship also showed some important information such as that the organic moiety attached to Sn plays an important role and that the coordination of Sn with the ligand and that the geometry of the complex is more important in determining the cytotoxity of the compound. Therefore, in a short time, organotin compounds can play a vital role in drug development.

ACKNOWLEDGEMENT

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

Me: Methyl group; **Bu:** Butyl group; **Ph:** Phenyl group; **NMR:** Nuclear magnetic resonance; **R:** Organic group; **Sn:** Tin; **L:** Ligand; **FTIR:** Fourier Transformed Infra-Red.

REFERENCES

1. Hameed A, Mohamad T, Elbay SE, Farina Y, Graisa A, Yousif E. Synthesis and Characterization and Fungicidal Activity of Triorganotin (IV) with Benzamidomethionine. Eur J Sci Res. 2009;34(2):212-7.
2. Yousif E. Triorganotin(IV) complexes photo-stabilizers for rigid PVC against Photodegradation. J Taibah Univ Sci. 2013;7(2):79-87.
3. Yousif E, Mehdi B, Yusop R, Salimon J, Salih N, Bashar M. Synthesis, structure and antibacterial activity of some triorganotin(IV) complexes with a benzamidoalanine ligand. J Taibah Univ Sci. 2014;8(3):276-81.
4. Farina Y, Graisa A, Yousif E, Kassim M. Synthesis and Structure of Some Diorganotin(IV) with N-methyl-mnitrobenzohydroxamic Acid. Aust J Basic Appl Sci. 2009;3(1):291-4.
5. Farina Y, Adil H, Ahmed A, Graisa A, Yousif E. Synthesis, Structural and Fungicidal Studies of Some Diorganotin(IV) with Benzamidoleucine. Aust J Basic Appl Sci. 2009;3(3):1670-3.
6. Graisa A, Farina Y, Yousif E, Kassem M. Synthesis And Characterization Of Some Diorganotin(IV) Complexes Of N-Tolyl- M-Nitrobenzohydroxamic Acid. ARPN J Eng App Sci. 2008;3(6):47-50.
7. Yousif E, Farina Y, Graisa A. Synthesis and Characterization of Some Diorganotin (IV) Complexes of Benzamidoacetic Acid. Aust J Basic Appl Sci. 2008;2(4):900-3.
8. Yousif E. Synthesis, spectroscopic studies and fungicidal activity of some diorganotin(IV) with 2-[(phenylcarbonyl)amino]propanoato. J King Saud Univ Sci. 2012;24(2):167-70.
9. Yousif E, Adil H, Majeed A, Farina Y. Synthesis, characterization and fungicidal activity of some diorganotin(IV) with 2-thioacetic-5-phenyl-1,3,4-oxadiazole. J Fundam Sci. 2009;5(2):94-8.
10. Graisa A, Farina Y, Yousif E, Kassim M. Preparation And Spectroscopic Studies Of Diorganotin(Iv) Complexes Of N-Methyl-M-Methoxybenzohydroxamic Acid. Prosiding Seminar Kimia Bersama UKM-ITB. 2009;8:9-11.
11. Najeeb D, Shalan N, Ibraheem H, Farina Y, Yousif E. Synthesis and fungicidal activity of some diorganotin(IV) with benzamidocysteine. J Al-Nahrain Univ. 2009;12(1):24-8.
12. Van der K, Luijten JGA. Investigations on organo-tin compounds. III. The biocidal properties of organo-tin compounds. J App Chem. 1954;4(6):314-9.
13. Van der KGJM, Luitjten JGA. Investigations on organo-tin compounds. V The preparation and antifungal properties of unsymmetrical tri-n-alkyltin acetates. J App Chem. 1956;6(2):56-60.
14. Song X, Zapata A, Eng G. Organotins and quantitative-structure activity/property relationships. J Organomet Chem. 2006;691(8):1756-60.
15. Blunden SJ. Chapman APJ. Craig (Ed.), Organotin Compounds. Organometallic Compounds in the Environment, Wiley, New York. 1986.
16. Pollar RC. The Chemistry of Organotin Compounds, Academic Press, New York, NY. 1970.
17. Doctor SV, Fox DA. Effects of organotin compounds on maximal electroshock seizure (MES) responsiveness in mice TRI(n-alkyl)tin compounds. J Toxicol Environ Health. 1982;10(1):43-52.
18. Mushak P, Krigman MR, Mailman RB. Comparative organotin toxicity in the developing rat: somatic and morphological changes and relationship to accumulation of total tin. Neuro Toxicol Teratology. 1982;4(2):209-15.
19. Kuthubutheen AJ, Wickneswari R, Kumar DVG. Efficacy of selected triorganotin(IV) compounds on leaves against Phytophthora palmivora (Butler) Butler isolated from black pepper and cocoa. Appl Organomet Chem. 1989;3(3):243-8.
20. Boualam M, Meunier-Piret J, Biesemans M, Willem R, Gielen M. Organotin(IV) compounds of 2-thiopyridine. Crystal and molecular structure of dicyclohexyltin(IV) bis(2-pyridylthiolate). Inorg Chim Acta. 1992;198:249-55.
21. Cardarelli NF, Caradarelli BM, Libby EP, Dobbins E. Organotin implications in anticarcinogenesis. Effects of several organotins on tumour growth rate in mice. Aust J Exp Biol Med Sci. 1984;62(2):209-14.
22. Carraher C, Scherubel G. Synthesis of poly [alkylene(arylene) oxystannanes] using a new modified system. Makromol Chem. 1972;152(1):61-6.
23. Carraher C, Scherubel G. Synthesis of poly oxystannyloxy alkylenes. J Poly Sci. 1971;9:983-9.
24. Hussain S, Ali S, Shahzadi S, Tahir MN, Shahid M. Synthesis, characterization, biological activities, crystal structure and DNA binding of organotin(IV) 5-chlorosalicylates. J Coord Chem. 2015;86(14):2369-87.
25. Evans CJ, Karpel S. Organotin Compounds in Modern Technology, Elsevier Science. Amsterdam, the Netherlands. 1985.
26. Choong CS, Win YF, Ha ST, Yousif E. Synthesis, Characterization and Antibacterial Activity of Organotin(IV) Complexes Derivatives of 2-Chloro-4-nitrobenzoic Acid. Asian J Org Chem. 2014;26(10):2949-53.
27. Win YF, Teoh SG, Ha ST, Muhammad TST, Yousif E. Preliminary in vitro Cytotoxic Assay on HepG2 and Antibacterial Screening Activity: Synthesis and Characterization of Organotin(IV) Complexes Derivatives of 2-Methyl-3-nitrobenzoic Acid. Asian J Org Chem. 2013;25(6):3376-80.
28. Van der W. The action of tin compounds in condensation-type RTV silicone rubbers. Macromol Chem Phys. 1980;181(12):2541-48.
29. Iftikhar SH, Gilani SR, Taj MB, Raheel A, Ud-Din I, Termizi SA, *et al*. Design, synthesis and biological evaluation of organotin(IV) complexes of flumequine and cetirizine. J Serb Chem Soc. 2018;83(4):425-37.
30. Tan C, Luona V, Tirri T, Wilen CE. The Synthesis of Low-iscosity Organotin-Free Moisture-Curable Silane-Terminated Poly(Urethane-Urea)s. Polymers. 2018;10(7):781.
31. Mahmoud A, Shaaban A, Azab M, Messiha N. Organotin polymers-XVI. Synthesis of p-acryloyloxybenzoic acid and n-methacryloyloxytetrabromophthalimide and copolymerizations with tri-n-butyltin acrylate and methacrylate. Eur Polym J. 1992;28(5):555-9.
32. Gachter R, Muller H. Plastics Additives Handbook. Hanser, Munich, Germany. 1990.
33. Yousif E, Ahmed A, Abood R, Jaber N, Noaman R, Yusop R. Poly(vinyl chloride) derivatives as stabilizers against photodegradation. J Taibah Univ Sci. 2015;9(2):203-12.
34. Yousif E, Salimon J, Salih N, Jawad A, Win YF. New stabilizers for PVC based on some diorganotin(IV) complexes with benzamidoleucine. Arabian J Chem.

2016;9:S1394-S1401.

35. Pellerito L, Nagy L. Organotin(IV)$^{n+}$ complexes formed with biologically active ligands: equilibrium and structural studies and some biological aspects. Coord Chem Rev. 2002;224(1-2):111-50.
36. Rehman K, Shahid S, Ali M, Bhatti H, Parvez M. Organotin esterification of (E)-3-(3-fluoro-phenyl)-2-(4-chlorophenyl)-2- propenoic acid: synthesis, spectroscopic characterization and in vitro biological activities. Crystal structure of [$Ph_3Sn(OC(O)C(4\text{-}ClC_6H_4) = CH(3\text{-}FC_6H_4))$]. J Organomet Chem. 2005;690(5):1396-408.
37. Arena G, Cal`R, Contino A, Musumeci A, Purrello R. Coordination properties of dialkyltin (IV) in aqueous solution. Thermodynamic study of dimethyltin (IV) complexes with l-amino acids. Inorganica Chimica Acta. 1995;237(1-2):187-91.
38. Aldridge WN, Zuckerman JJ. Organotin Compounds: New Chemistry and Applications. Advanced Chemistry, American Chemical Society, Washington, DC, USA. 1976.
39. Gielen M. Tin-based antitumor drugs: New developments. Met Based Drugs 2. 1995;2(2):99-103.
40. Li W, Zhang ZW, Ren SM, Sibiril Y, Massin DP, *et al*. Synthesis and antitumor activity of novel dibutyltin carboxylates of aminoglucosyl derivatives. Chem Biol Drug Des. 2009;73(6):682-6.
41. Kang W, Wub X, Huang J. Synthesis, crystal structure and biological activities of four novel tetranuclear diorganotin(IV) carboxylates. J Organomet Chem. 2009;694(15):2402-8.
42. Danish M, Ali S, Shahid K, Mazhar M. Synthesis and in vitro antitumour studies of trimethyltin(IV) trans-mmethylcinnamate. J Chem Soc Pak. 2004;26:140-2.
43. Mutter S, Margiotta N, Papadia P, Platts J. Computational evidence for structural consequences of kiteplatin damage on DNA. J Biol Inorg Chem. 2015;20(1):35-48.
44. Gielen M. Review: Organotin compounds and their therapeutic potential: a report from the Organometallic Chemistry Department of the Free University of Brussels. Appl. Organomet. Chem. 2002;16(9):481-94.
45. Tabassum S, Pettinari C. Chemical and biotechnological developments in organotin cancer chemotherapy. J Organomet Chem. 2006;691(8):1761-6.
46. Pellerito C, D'Agati P, Fiore T, Mansueto C, Mansueto V, Stocco G, *et al*. Synthesis, structural investigations on organotin(IV) chlorin-e6 complexes, their effect on sea urchin embryonic development and induced apoptosis. J Inorg Biochem. 2005;99(6):1294-305.
47. Gielen M, Tiekink ERT. Tin compounds and their therapeutic potential. in: M. Gielen, E.R.T. Tiekink (Eds.), Metallotherapeutic Drugs and Metal-Based Diagnostic Agents: The Uses of Metals in Medicine. John Wiley and Sony Ltd. 2005;421-39.
48. Gielen M, Tiekink E.R.T. (Eds.). Metallotherapeutic Drug and Metal-Based Diagnostic Agents: 50Sn Tin Complexes and Their Therapeutic Potential, Wiley, New York. 2005.
49. Tiekink ER, Gielen M. Metallotherapeutic Drugs and Metal-Based Diagnostic Agents: The Use of Metals in Medicine, John Wiley and Sons Ltd, The Atrium, Southern gate, Chichester, West Sussex PO19 8SQ, England. 2005;421-35.
50. Pellerito C, Nagy L, Pellerito L, Szorcsik A. Biological activity studies on organotin(IV)$^{n+}$ complexes and parent compounds. J Organomet Chem. 2006;691(8):1733-47.
51. Shang X, Meng X, Alegria ECBA, Li Q, Guedes da SMFC, Uznetsov ML, Pombeiro AJL. Syntheses, molecular structures, electrochemical behavior, theoretical study and antitumor activities of organotin(IV) complexes containing 1-(4-chlorophenyl)-1-cyclopentanecarboxylato ligands. Inorg Chem. 2011;50(17):8158-67.
52. Saxena AK, Huber F. Organotin compounds and cancer chemotherapy. Coord. Chem. Revs. 1989;95(1):109-23.
53. Furst A. Chemistry of Chelation in Cancer, Thomas Springfield, New York. 1963.
54. Iqbal M, Ali S, Haider A, Khalid N. Therapeutic properties of organotin complexes with reference to their structural and environmental features. Rev Inorg Chem. 2017;37(2):51-70.
55. Balas VI, Hadjikakou SK, Hadjiliadis N, Kourkoumelis N, Light ME, Hursthouse M, *et al*. Crystal structure and antitumor activity of the novel zwitterionic complex of tri-n-butyltin(IV) with 2-thiobarbituric acid. Bioinorg Chem Appl. 2008:654137.
56. Rehman S, Aziz M, Ahmad Z, Mirza A, Ali S. Synthesis, structural elucidation and biological activity to organotin(IV) derivatives of (E)-2,3-bis(4-chlorophenyl)-2-propenoicacid. Heteroatom chemistry. 2017;28(5):e21393.
57. Qurrat-ul-Ain H, Nadhman A, Sirajuddin M, Shahnaz G, Ali Shah A, Masoom M. Organotin(IV) complexes of carboxylate derivative as potential chemotherapeutic agents against Leishmania. Inorganica Chimica Acta. 2014;423:220-8.