Journal of the Serbian Chemical Society
JSCS-info@shd.org.rs • www.shd.org.rs/JSCS
J. Serb. Chem. Soc. 78 (9) 1323–1333 (2013) UDC 546.814+547.563+543.422.25:615.28
JSCS–4500 *Original scientific paper*

Reactions of tin and triorganotin(IV) isopropoxides with thymol derivative: synthesis, characterization and *in vitro* antimicrobial screening

GARIMA MATELA[1]*, ROBINA AMAN[1], CHETAN SHARMA[2] and SMITA CHAUDHARY[3]

[1]*Department of Chemistry, Kumaun University, S. S. J. Campus Almora-263 601, India,* [2]*Department of Microbiology, Kurukshetra University, Kurukshetra, Haryana-136 119, India and* [3]*Institute of Environmental Studies, Kurukshetra University, Kurukshetra, Haryana-136 119 India*

(Received 17 September 2012, revised 6 March 2013)

Abstract: New series of diisopropoxytin and triorganotin(IV) complexes of H_2hbgl (**1**) of the general formula $Sn(OPr^i)_2$(hbgl) (**2**), $Sn(OPr^i)_2$(Hhbgl)$_2$ (**3**), Ph_3Sn(Hhbgl) (**4**), Bu_3Sn(Hhbgl) (**5**) and Me_3Sn(Hhbgl) (**6**), where H_2hbgl is a ligand of a thymol derivative, namely, *N*-(2-hydroxy-3-isopropyl-6-methyl-benzyl)glycine, were synthesized by reacting tin and triorganotin(IV) chloride with the ligand, with the aid of sodium isopropoxide in appropriate stiochiometric ratios (1:1 and 1:2). These complexes were characterized by elemental analysis, IR and ^{1}H-NMR. The spectral data suggest that the carboxylate group, in complexes **2**–**5**, was bonded in a bidentate manner, while a unidentate bonding was observed in complex **6**. All five complexes were tested *in vitro* for their antibacterial activity against Gram-positive bacteria, namely, *Staphylococcus aureus* MTCC 96, *Bacillus subtilis* MTCC 121, and two Gram-negative bacteria, namely, *Escherichia coli* MTCC 1652 and *Pseudomonas aeruginosa* MTCC 741. All five complexes were also tested against three pathogenic fungal strains, namely, *Aspergillus niger*, *Aspergillus flavus* and *Penicillium* sp.

Keywords: tri-organotin(IV) complexes; IR, NMR spectral studies; antifungal activity; antibacterial activity.

INTRODUCTION

Organotin(IV) complexes show a spectrum of biological effects and have been extensively studied in various biological fields as anticancer, antiviral, antibacterial and antifungal agents, wood preservatives, pesticides, *etc*.[1–12] It is noteworthy that, for a long time, organotin(IV) complexes have been widely used in a variety of industrial and agricultural applications.[13–15] A unique fluorescent pro-

* Corresponding author. E-mail: matelagarima28@yahoo.in
doi: 10.2298/JSC120917030M

perty of organotin carboxylates has also been investigated in the last few years.[16,17] Thymol, a *p*-cymene-derived compound, is widely used in medicine for its antimicrobial, antiseptic, disinfectant and wound-healing properties.[18–23] As derivatives of *p*-cymene have leishmanicidal activity and are considered important basic structures for the development of novel antiparasitic drugs, in the present study, a new ligand of a thymol derivative derived from glycine was synthesized and investigated for its ligating properties. The interaction of tin metal with the organic groups *via* O–Sn and N–Sn bonds has attracted considerable interest in several research fields.[24] Regarding this, some tin compounds with a thymol derivative were synthesized as potential antibacterial and antifungal agents.

EXPERIMENTAL

Materials and methods

All the reagents, *viz*., tin (Merck), triphenyltin(IV) chloride (Merck), tributyltin(IV) chloride (Merck), trimethyltin(IV) chloride (Merck) and thymol (Sigma–Aldrich) were used as received. All the chemicals and solvents used were dried and purified by standard methods, and moisture was excluded from the glass apparatus using $CaCl_2$ drying tubes. The melting points were determined in open capillaries with an electronic melting point apparatus. C, H and N analyses of the ligand and complexes were performed on a Vario-EL, CHNS elemental analyzer. The tin contents in the synthesized complexes were determined gravimetrically as SnO_2. Infrared spectra of the solid compounds were recorded on a Perkin-Elmer 1600 series FT-IR spectrophotometer over the range 4000–500 cm^{-1} in KBr discs and over 500–200 cm^{-1} in CsI discs. The ^{1}H-NMR spectra were recorded on a Bruker DRX 300 (300 MHz FT-NMR) spectrometer at the Central Drug Research Institute, Lucknow, India, using DMSO or MeOD as solvents with TMS as the internal standard. The conductivity measurements were performed using an Ecotestr EC Low conductometer in 10^{-3} M DMSO solutions at room temperature. The antibacterial and antifungal activities of the synthesized complexes were evaluated by the agar well diffusion method and the poison food technique, respectively.

*Synthesis of H_2hbgl (**1**)*

An equimolar mixture of thymol (11.86 g, 0.05 mol), glycine (3.75 g, 0.05 mol), sodium acetate crystals (6.8 g, 0.05 mol) was dissolved in glacial acetic acid (25 mL). Formalin solution (37 % (w/v), 4.05 mL) was added to it dropwise under stirring and the contents were heated at 60–80 °C, until a viscous mass was obtained. The viscous mass was then added dropwise with brisk stirring into an excess of water. The thus obtained crude product was purified by dissolving it in a requisite quantity of *ca*. 7 M sodium hydroxide solution followed by its reprecipitation by 6 M hydrochloric acid. It was further purified by recrystallisation from ethanol.

Synthesis of the complexes

*[Sn(OPr^i)$_2$(hbgl)] (**2**).* A solution of tin(IV) tetrachloride (1.300 g, 0.005 mol) in benzene (10 mL) was treated with sodium isopropoxide (1.64 g, 0.020 mol) to produce tin(IV) tetraisopropoxide and sodium chloride. The sodium chloride precipitate was removed by filtration and the solvent by distillation. The solution of tin(IV) tetraisopropoxide (1.770 g, 0.005 mol) and H_2hbgl (1.067 g, 0.0045 mol) was refluxed in benzene (20 mL) for 8–10 h at 95–100 °C. The liberated 2-propanol was fractionated out azeotropically with benzene. The complex,

[$Sn(OPr^i)_2$(hbgl)], isolated as a yellow brown solid, was purified by recrystallisation from ethanol at room temperature and dried under reduced pressure.

*[$Sn(OPr^i)_2(Hhbgl)_2$] (**3**).* Complex **3** was prepared in the similar way as complex **2**. Tin(IV) tetraisopropoxide (1.770 g, 0.005 mol) and H_2hbgl (2.135 g, 0.009 mol).

*[$Ph_3Sn(Hhbgl)$] (**4**).* A solution of triphenyltin(IV) isopropoxide (2.045 g, 0.005 mol) and H_2hbgl (1.067 g, 0.0045 mol) was refluxed in benzene (20 mL) for 8–10 h at 95–100 °C. The complex, [Ph_3Sn(Hhbgl)], isolated as a brown solid, was purified by recrystallisation from ethanol at room temperature and dried under reduced pressure.

*[$Bu_3Sn(Hhbgl)$] (**5**).* Complex **5** was prepared in the similar way as complex **4**. Tributyltin(IV) isopropoxide (1.745 g, 0.005 mol) and H_2hbgl (1.067 g, 0.0045 mol).

*[$Me_3Sn(Hhbgl)$] (**6**).* A solution of trimethyltin(IV) isopropoxide (1.115 g, 0.005 mol) and H_2hbgl (1.067 g, 0.0045 mol) was refluxed in toluene (20 mL) for 16–18 h at 95–100 °C. The complex, [Me_3Sn(Hhbgl)], isolated as a yellow solid, was purified by recrystallisation from ethanol at room temperature and dried under reduced pressure.

Antimicrobial assays

Antibacterial activity. The antibacterial activities of the synthesized complexes were evaluated by the agar well diffusion method. All the bacterial cultures were adjusted to 0.5 McFarland standards, which is visually comparable to a bacterial suspension of approximately 1.5×10^8 cfu mL^{-1}. 20 mL of Mueller Hinton agar medium was poured into each Petri plate and plates were swabbed with 100 µL inocula of the test micro-organisms and kept for 15 min for adsorption. Using a sterile cork borer of 8 mm diameter, wells were bored into the seeded agar plates and these were loaded with a 100 µL of each complex reconstituted in dimethyl sulphoxide (DMSO) at a concentration of 2.0 mg mL^{-1}. All the plates were incubated at 37 °C for 24 h. The antibacterial activity of each organotin complex was evaluated by measuring the zone of growth inhibition against the test organisms with a zone reader (HiAntibiotic zone scale). DMSO was used as a negative control whereas ciprofloxacin was used as positive control. This procedure was performed in three replicate plates for each organism.[24-27]

Determination of the minimum inhibitory concentration (MIC) of the synthesized complexes. The *MIC* value is the lowest concentration of an antimicrobial complex that will inhibit the visible growth of a micro-organism after overnight incubation. The *MIC* of the various complexes against the bacterial strains was evaluated through a modified agar well diffusion method.[28] In this method, a twofold serial dilution of each complex was prepared by first reconstituting the complex in DMSO followed by dilution in sterile distilled water to achieve a decreasing concentration range of 256 to 0.5 µg mL^{-1}. A 100 µL volume of each dilution was introduced into the wells (in triplicate) in the agar plates already seeded with 100 µL of standardized inoculum (10^6 cfu mL^{-1}) of the test bacterial strains. All the test plates were incubated aerobically at 37 °C for 24 h and observed for an inhibition zone. The *MIC* of an organotin(IV) complex, taken as the lowest concentration that completely inhibited the growth of the bacteria, showed by a clear zone of inhibition, was recorded for each test organism. Ciprofloxacin was used as the positive control while DMSO was the negative control.

Antifungal activity. The antifungal activities of the five organotin complexes were evaluated by the poisoned food technique.[27,29] The moulds were grown on Sabouraud dextrose agar (SDA) at 25 °C for 7 days and used as inoculates. The 15 mL of molten SDA (45 °C) was poisoned by the addition of 100 µL of each organotin complex reconstituted in the DMSO at a concentration of 2.0 mg mL^{-1}, poured into a sterile Petri plate and allowed it to solidify at room temperature. The solidified poisoned agar plates were inoculated at the centre

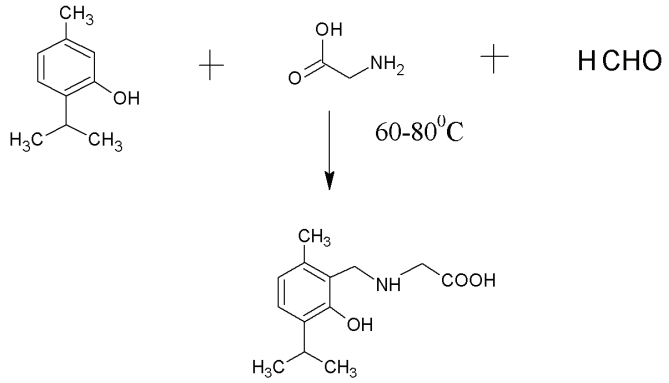
with fungal plugs (8 mm diameter) obtained from the colony margins and incubated at 25 °C for 7 days. DMSO was used as the negative control whereas fluconazole was used as the positive control. The experiments were performed in triplicates. The diameter of fungal colonies was measured and expressed as percent mycelial inhibition by applying the formula:

$$\text{Inhibition} = \frac{(d_c - d_t)}{d_c} \times 100$$

where d_c is the average diameter of fungal colony in the negative control sets and d_t is the average diameter of the fungal colony in the experimental sets.

RESULTS AND DISCUSSION

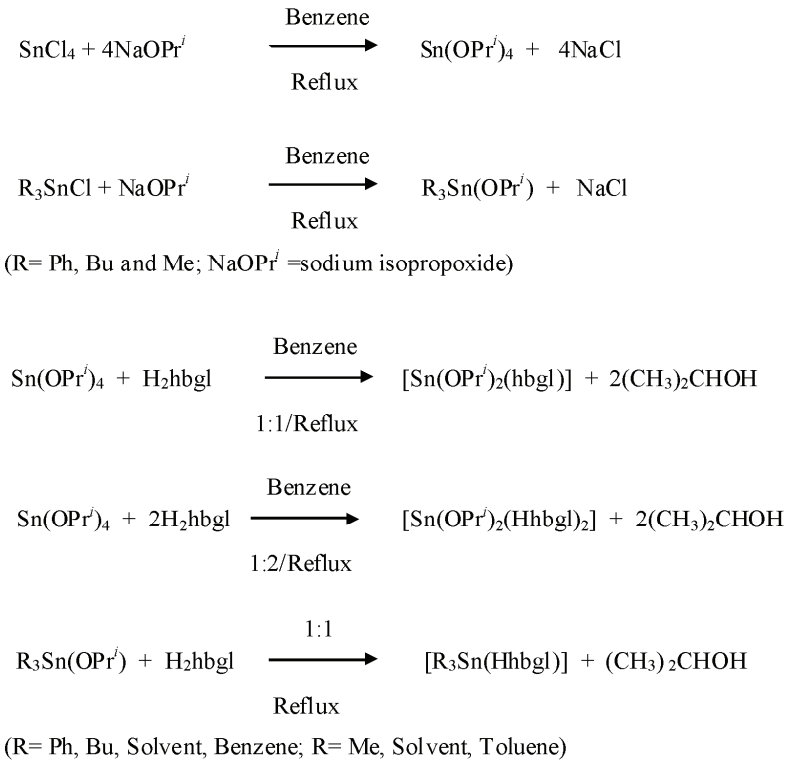
The ligand of the thymol derivative was prepared adopting a procedure almost identical to that described by Mehrotra *et al.*[30] The synthetic route used to synthesise the ligand and its complexes is outlined in Schemes 1 and 2, respectively. A new methodology was used to synthesise the tin and triorganotin(IV) complexes. Organotin complexes are usually prepared by reacting organotin hydroxide or organotin oxide with the corresponding ligand and by reacting organotin halide with the sodium or potassium salt of the ligand. In present study, the halogen of tin or organotin was replaced with the isopropoxide group by reacting them with sodium isopropoxide (Scheme 2). The tin and triorganotin isopropoxides were isolated and reacted with the ligand. These reactions proceeded with the liberation of 2-propanol, which was fractionated out azeotropically and estimated to monitor the completion of reaction. The obtained values are given in Table S-I of the Supplementary material to this paper. Owing to highly hydroscopic nature of tin and tri-organotin(IV) alkoxides, all the reactions were performed under strictly anhydrous conditions.



Scheme 1. Synthesis of the ligand **1**.

Characterisation of the ligand and its complexes

The physical, analytical and spectral data for the ligand and the synthesised complexes are given in the Supplementary material to this paper.



Scheme 2. Synthesis of the complexes.

Elemental analysis. The analytical data were in good agreement with the proposed stoichiometry of the complexes.

Molar conductance. The molar conductance values of the synthesized complexes showed very low values indicating their non-electrolytic nature.[31]

Infrared spectra. The IR spectra of the complexes displayed a broad vibrational band at 3000–3500 cm^{-1}, which is assignable to the unbonded –OH stretching of the phenolic group.[32,33]

These complexes gave a strong asymmetric stretching frequency ν_{as}(COO) near 1588–1626 cm^{-1} and a medium symmetrical stretching frequency ν_{s}(COO) near 1406–1417 cm^{-1}. The magnitude of $\nu_{as}-\nu_{s}$ ($\Delta\nu$) was used to explain the type of boding of the carboxylate group to tin metal.[34,35] For complex **2**, Fig. 1, the $\Delta\nu$ value of 201 cm^{-1} was attributed to a bidentate carboxyl group.[36] The magnitude of $\Delta\nu$ for **3**–**5** (Fig. 1) were smaller than 200 cm^{-1}, indicating bridged tin and triorganotin(IV) carboxylates. While, for the complex **6** (Fig. 1), the values of $\Delta\nu$ exceeded 210 cm^{-1}, which clearly demonstrated that these complexes adopt a monodentate carboxylate structure.

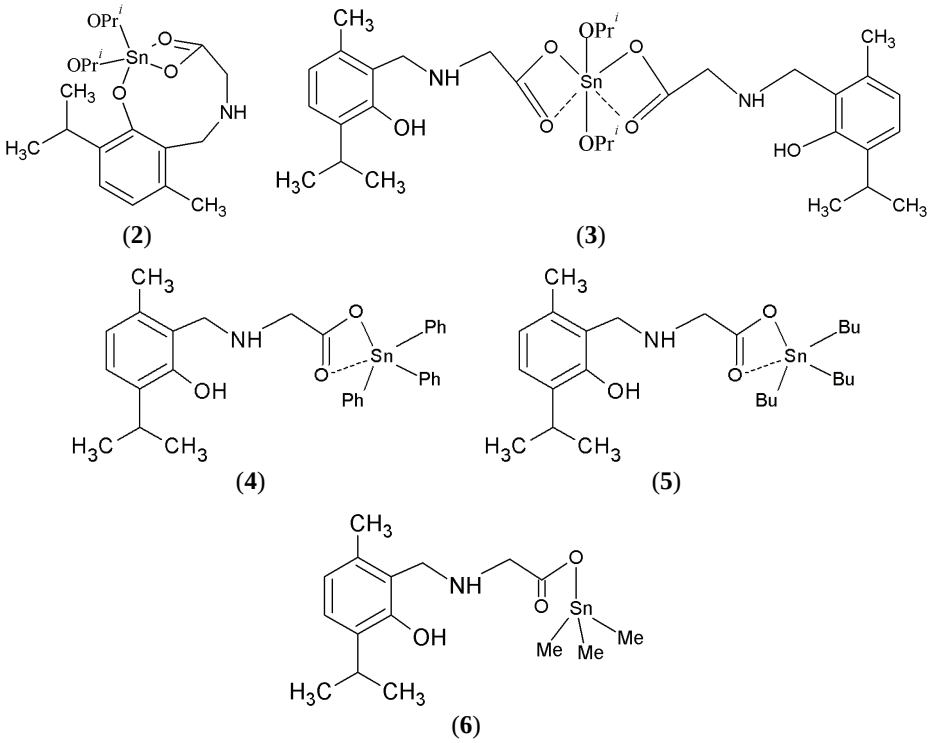


Fig. 1. Proposed structures of the metal complexes of *N*-(2-hydroxy-3-isopropyl-6-methyl-benzyl)glycine.

The bonding of the carboxylate group to the tin metal was further confirmed by the appearance of a band at 500–558 cm^{-1}, assignable to the Sn–O stretching frequency.[37] The far IR spectrum of triphenyltin(IV) complex showed bands at 279 and 207 cm^{-1}, which may be assigned to the ν_{as}(Sn–C) and ν_s(Sn–C), respectively, whereas the corresponding peaks at 528 and at 469 cm^{-1} were found in the spectrum of tributyltin(IV) complex.[38] In the case of trimethyltin(IV) complex the appearance of ν(Sn–C) bands were not certain due to overlapping with the Sn–O stretching vibration.

^{1}H-NMR spectra. The absence of a signal due to the –OH proton at δ 12.00––13.00 ppm suggested deprotonation of the carboxylic oxygen atom of the ligand on complexation.[39] The ^{1}H-NMR spectra of the complexes displayed signals in the region δ 6.45–7.58 ppm due to the aromatic protons of the ligand. A signal at δ 7.80–8.54 ppm may be attributed to the unbonded phenolic group proton.[40] In the complexes, the $–NH_2$ resonances were observed either as a broad weak signal at δ 4.90–6.88 ppm or in conjugation with the phenyl protons.[41,42] The values of coupling constants $^2J(^{117/119}Sn–C–^1H)$ provides important information regarding the coordination number.[38,43] The two-band coupling $^2J(^{117/119}Sn–C–H)$ of tri-

methyltin(IV) complex in DMSO was 68.0 Hz. Using the Lockhart equation,[44] the estimated value of C–Sn–C bond angle for complex **6** was 116.62°, implying a four-coordinated tetrahedral geometry. The $^{2}J(^{117/119}\text{Sn–C–}^{1}\text{H})$ value for **5** was not visible since the protons of butyl group were multiplets in the range of 0.90––1.21 ppm, however a triplet was observed at δ 0.78 ppm.[45,46] In the spectrum of complex **4**, the signals for the phenyl group attached to tin were observed in the δ range 7.22–7.58 ppm, in conjugation with phenyl protons of the ligand.

Antimicrobial evaluation

Antibacterial activity. All the newly synthesized complexes were evaluated for their antibacterial activity against two Gram-positive bacteria (*Staphylococcus aureus* and *Bacillus subtilis*) and two Gram-negative bacteria (*Escherichia coli* and *Pseudomonas aeruginosa*). The results revealed that all the tested organotin(IV) complexes possessed variable antibacterial activity against both Gram-positive and Gram-negative bacteria.

Based on the maximum inhibitory activity shown against Gram-positive bacteria, the complexes **4** and **6** were found to be most effective against *S. aureus*, with inhibition zones of 27 and 25.6 mm, respectively, whereas complex **4** was found to be most effective against *B. subtilis*, with an inhibition zone of 25 mm. However, in case of Gram-negative bacteria, two complexes, **4** and **3**, were found to be most effective against *E. coli* with the zone of inhibition ranging between 21 and 24 mm and one complex, **4**, against *P. aeruginosa* with zone of inhibition of 22 mm (Table I). The synthesized complexes showed comparatively better activity against Gram-positive bacteria.

TABLE I. Antibacterial activity of the metal complexes of *N*-(2-hydroxy-3-isopropyl-6--methylbenzyl)glycine; values of the zone of inhibition include the diameter of the well (8 mm)

Complex	Diameter of the growth of inhibition zone, mm			
	S. aureus	*B. subtilis*	*E. coli*	*P. aeruginosa*
2	22	22	19	16
3	24	22	21	17
4	27	25	24	22
5	22	22	19	15
6	26	22	20	17
Ciprofloxacin	28	26	25	25

In the whole series, the *MIC* values of organotin complexes ranged between 8 and 32 μg mL^{-1} against the Gram-positive bacteria. Complex **4** was found to be best as it exhibited the lowest MIC of 8 μg mL^{-1} against *S. aureus*. In case of the Gram-negative bacteria, the *MIC* values of complexes ranged from 32 to 128 μg mL^{-1}. Complex **4** showed lowest *MIC* of 32 μg mL^{-1} against *E. coli* and *P. aeruginosa* (Table II). Ciprofloxacin was used as the standard antibiotic. The

positive controls produced significantly sized inhibition zones against the tested bacteria; however, the negative control produced no observable inhibitory effect against any of the tested bacteria.

TABLE II. Minimum inhibitory concentration (*MIC* / μg mL^{-1}) of the metal complexes of *N*-(2-hydroxy-3-isopropyl-6-methyl benzyl)glycine

Complex	Bacterium			
	S. aureus	*B. subtilis*	*E. coli*	*P. aeruginosa*
2	32	32	64	128
3	32	32	64	128
4	8	16	32	32
5	32	32	64	128
6	16	16	64	128
Ciprofloxacin	5	5	5	5

Antifungal activity. All the newly synthesized complexes were evaluated for their antifungal activity against three fungal pathogens, *Aspergillus niger*, *A. flavus* and *Penicillium* sp., isolated from ear patients of Kurukshetra.[47] The complexes **3** and **4** showed a more than 60 % inhibition level of mycelial growth against *A. niger* and *Penicillium* sp., whereas complex **4** showed highest inhibition level of 69 %, of fungal mycelium against *A. flavus*. Fluconazole was used as the standard antibiotic (Table III).

TABLE III. Antifungal activity of the metal complexes of *N*-(2-hydroxy-3-isopropyl-6-methyl-benzyl)glycine; all the values are the means of three replicates

Complex	Mycelial growth inhibition, %		
	A. niger	*A. flavus*	*Penicillium* sp.
2	57	56	59
3	63	58	61
4	61	69	66
5	51	44	50
6	56	53	59
Fluconazole	81	78	83

CONCLUSIONS

Based on various studies, such as elemental analysis, IR and ^{1}H-NMR spectroscopy, five- and six-coordinate geometry are proposed for complexes **2**–**5**, while four-coordinate geometry is proposed for complex **6**. The synthesized complexes were screened against various fungi and bacteria to assess their potential as antimicrobial agents. The antimicrobial data revealed that the triphenyltin(IV) complex (**4**) was superior to the other complexes. The synthesized complexes showed remarkable antimicrobial activity.

SUPPLEMENTARY MATERIAL

Table S-I, as well as physical, analytical and spectral data of the ligand and complexes are available electronically from http://www.shd.org.rs/JSCS/, or from the corresponding author on request.

Acknowledgements. One of the authors (R. A.) thanks the U-COST, Dehradun, India, for financial support in the form of a Research Project and another of the authors (G. M.) for the award of Project Fellowship under the same project.

И З В О Д

РЕАКЦИЈЕ КАЛАЈ(IV)- И ТРИОРГАНОКАЛАЈ(IV)-ИЗОПРОПОКСИДА СА ДЕРИВАТОМ ТИМОЛА: СИНТЕЗА, КАРАКТЕРИЗАЦИЈА И *IN VITRO* АНТИМИКРОБНО ИСПИТИВАЊЕ

GARIMA MATELA[1], ROBINA AMAN[1], CHETAN SHARMA[2] и SMITA CHAUDHARY[3]

[1]Department of Chemistry, Kumaun University, S. S. J. Campus Almora-263 601, India, [2]Department of Microbiology, Kurukshetra University, Kurukshetra, Haryana-136 119 India и [3]Institute of Environmental Studies, Kurukshetra University, Kurukshetra, Haryana-136 119 India

У реакцијама калај(IV)- и триорганокалај(IV)-хлорида са H_2hbgl лигандом (**1**; H_2hbgl је дериват тимола, *N*-(2-хидрокси-3-изопропил-6-метилбензил)глицин), уз додатак натријум-изопропоксида у одговарајућим стехиометријским односима (1:1 и 1:2), синтетизовани су нови комплекси опште формуле $Sn(OPr^i)_2$(hbgl) (**2**), $Sn(OPr^i)_2(Hhbgl)_2$ (**3**), Ph_3Sn(Hhbgl) (**4**), Bu_3Sn(Hhbgl) (**5**) и Me_3Sn(Hhbgl) (**6**). Добијени комплекси су окарактерисани применом елементалне анализе, као и IR и ^{1}H-NMR спектроскопије. На основу спектроскопских података, претпостављено је да је у комплексима **2**–**5** карбоксилна група бидентатно координована, док је у комплексу **6** монодентатно координована за јон метала. Испитивана је *in vitro* антибактеријска активност на две грам-позитивне бактерије, *Staphylococcus aureus* MTCC 96 и *Bacillus subtilis* MTCC 121, и на две грам-негативне бактерије, *Escherichia coli* MTCC 1652 и *Pseudomonas aeruginosa* MTCC 741. Поред тога, испитивана је антифунгална активност на три врсте гљива, *Aspergillus niger, Aspergillus flavus* и *Penicillium* sp.

(Примљено 17. септембра 2012, ревидирано 6. марта 2013)

REFERENCES

1. M. Nath, P. K. Saini, *Dalton Trans.* **40** (2011) 7077
2. G. Matela, R. Aman, *Cent. Eur. J. Chem.* **10** (2012) 1
3. K. C. Molloy, in *The Chemistry of Metal Carbon Bond*, Vol. 5, F. Hartley, Ed., Wiley, New York, 1989, Ch. 11
4. E. L. Torres, F. Zani, M. A. Mendiola, *J. Inorg. Biochem.* **105** (2011) 600
5. M.-L. Sun, B.-F. Ruan, Q. Zhang, Z.-D. Liu, S.-L. Li, J.-Y. Wu, B.-K. Jin, J.-X. Yang, S.-Y. Zhang, Y.-P. Tian, *J. Organomet. Chem.* **696** (2011) 3180
6. C. K. Yap, L. T. Hong, R. Hill, K. M. Lo, S. W. Nig, V. G. Kumar-das, *J. Trop. Forest Sci.* **1** (1989) 390
7. J. S. Casas, M. D. Couce, A. Sanchez, J. Sordo, E. M. V. Lopez, *J. Organomet. Chem.* **696** (2012) 4236
8. S. G. Ruiz, J. C. Torres, S. Prashar, M. Fajardo, Z. Zizak, Z. D. Juranic, G. N. Kaluderovic, *J. Organomet. Chem.* **696** (2011) 3023

9. K. S. Prasad, L. S. Kumar, M. Prasad, H. D. Revanasiddappa, *Bioinorg. Chem. Appl.* 2010 (2010) ID 854514; doi: 10.1155/2010/854514
10. A. Alama, B. Tasso, F. Novelli, F. Sparatore, *Drug Discov. Today* **14** (2009) 500
11. A. Alama, M. Viale, M. Cilli, C. Bruzzo, F. Novelli, B. Tasso, F. Sparatore, *Invest. New Drugs* **27** (2009) 124
12. N. Kobakhidze, N. Farfan, M. Romero, J. M. Mendez-Stivalet, M. G. Ballinas-Lopez, H. Garcia-Ortega, O. Dominguez, R. Santillan, F. Sanchez-Bartez, I. Gracia-Mora, *J. Organomet. Chem.* **695** (2010) 1189
13. A. G. Davies, P. J. Smith, in *Comprehensive Organometallic Chemistry*, Vol. 2, G. Wilkinson, F. G. A. Stone, E. W. Abel, Eds., Pergamon Press, Oxford, 1982, p. 519
14. P. J. Smith, *Chemistry of tin*, 2nd ed., Blackie Academic and Professional, London, 1997
15. M. X. Li, D. Zhang, L. Z. Zhang, J. Y. Niu, B. S. Ji, *J. Organomet. Chem.* **696** (2011) 852
16. S. L. Cai, Y. Chen, W. X. Sun, H. Li, Y. Chen, S. S. Yuan, *Bioorg. Med. Chem. Lett.* **20** (2010) 5649
17. E. L. Torres, A. L. Medina-Castillo, J. F. Fernandez-Sanchez, M. A. Mendiola, *J. Organomet. Chem.* **695** (2010) 2305
18. R. Aeschbach, J. Loliger, B. C. Scott, A. Murcia, J. Butler, B. Halliwell, O. I. Aruoma, *Food Chem. Toxicol.* **32** (1994) 31
19. N. Cenas, A. Nemeikaite, E. Sergediene, H. Nivinskas, Z. Anusevicius, J. Sarlauskas, *Biochim. Biophys. Acta* **1528** (2001) 31
20. N. Didry, L. Dubreuil, M. Pinkas, *Pharm. Acta Helv.* **69** (1994) 25
21. S. Kulevanova, A. Kaftandzieva, A. Dimitrovska, G. Stefkov, T. Grdanoska, N. Panovski, *Boll. Chim. Farm.* **139** (2000) 276
22. B. Ogaard, E. Larsson, R. Glans, T. Henriksson, D. Birkhed, *J. Orofac. Orthop.* **58** (1997) 206
23. S. Shapiro, B. Guggenheim, *Oral Microbiol. Immunol.* **10** (1995) 241
24. E. L. Torres, F. Zani, M. A. Mendiola, *J. Inorg. Biochem.* **105** (2011) 600
25. J. M. Andrews, *J. Antimicrob. Chemother.* **48** (2001) 5
26. D. P. Singh, K. Kumar, C. Sharma, K. R. Aneja, *J. Enz. Inhib. Med. Chem.* **25** (2010) 544
27. O. Prakash, D. K. Aneja, K. Hussain, P. Lohan, P. Ranjan, S. Arora, C. Sharma, K. R. Aneja, *Eur. J. Med. Chem.* **46** (2011) 5065
28. M. I. Okeke, C. U. Iroegbu, E. N. Eze, A. S. Okoli, C. O. Esimone, *J. Ethnopharmacol.* **78** (2001) 119
29. S. K. S. Al-Burtamani, M. O. Fatope, R. G. Marwah, A. K. Onifade, S. H. Al-Saidi, *J. Ethnopharmocol.* **96** (2005) 107
30. K. Kumar, N. D. Pandey, J. K. Mehrotra, *J. Indian Chem.* Soc. **51** (1974) 944
31. K. Jamil, R. Wajid, M. Bakhtiar, M. Danish, *J. Iran. Chem. Soc.* **7** (2010) 495
32. M. Singh, *Synth. React. Inorg. Met.–Org. Chem.* **15** (1985) 235
33. M. A. Abdellah, S. K. Hadjikakou, N. Hadjiliadis, M. Kubicki, T. Bakas, N. Kourkoumelis, Y. V. Simos, S. Karkabounas, M. M. Barsan, I. S. Butler, *Bioinorg. Chem. Appl.* 2009 (2009) ID 542979; doi:10.1155/2009/542979
34. G. K. Sandu, S. P. Verma, L. S. Moore, R. V. Parish, *J. Organomet. Chem.* **321** (1987) 15
35. G. Eng, X. Song, A. Zapata, A. C. de Dios, L. Casabianca, R. D. Pike, *J. Organomet. Chem.* **692** (2007) 1398
36. M. Gielen, A. E. Khloufi, M. Biesemans, F. Kayser, R. Willem, B. Mahieu, D. Maes, J. N. Lisgarten, L. Wyns, *Organometallics* **13** (1994) 2849
37. M. Nath, R. Yadav, *Bull. Chem. Soc. Jpn.* **70** (1997) 1331
38. M. Nath, S. Pokharia, R. Yadav, *Coord. Chem. Rev.* **215** (2001) 99

39. M. Nath, C. L. Sharma, N. Sharma, *Synth. React. Inorg. Met.–Org. Chem.* **21** (1991) 807
40. D. H. Williams, I. Fleming, *Spectroscopic methods in organic chemistry*, 5th ed., Tata McGraw Hill, India, 2004, p. 161
41. M. Nath, R. Yadav, *Bull. Chem. Soc. Jpn.* **71** (1998) 1355
42. R. M. Silverstein, F. X. Webster, D. J. Kiemle, *Spectrometric Identification of Organic Compounds*, 7th ed., Wiley, New York, 2005
43. M. M. Amini, A. Azadmeher, H. R. Khavasi, S.W. Ng, *J. Organomet. Chem.* **692** (2007) 3922
44. T. P. Lockhart, W. F. Manders, *Inorg. Chem.* **25** (1986) 892
45. M. Nath, R. Yadav, M. Gielen, H. Dalil, D. de Vos, G. Eng, *Appl. Organomet. Chem.* **11** (1997) 727
46. S. Shahzadi, K. Shahid, S. Ali, M. Bakhtiar, *Turk. J. Chem.* **32** (2008) 333
47. K. R. Aneja, C. Sharma, R. Joshi, *Int. J. Otorhinolaryngol.* **74** (2010) 604.