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Synthesis and Spectroscopic Studies of Organotin(IV) Complexes of Biologically Active Schiff Bases Derived from Sulpha Drugs

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The reaction of dibutyltin oxide with Schiff bases derived from sulpha drugs in 1:1 molar ratio leads to the formation of a new series of organotin(IV) complexes. An attempt has been made to probe their structure on the basis of UV, IR, NMR (^{1}H,^{13}C and ^{119}Sn) and Mössbauer spectral studies. A few representative compounds have also been screened for bactericidal activity and found to be quite active in this respect. Copyright © 2000 John Wiley & Sons, Ltd.

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INTRODUCTION

Heterocyclic compounds containing both nitrogen and sulphur in the ring system have been utilised in the synthesis of biologically active metal complexes. The biocidal activity of sulpha drugs as well as the ligands derived from them has been known for a long time.[1] Some of these drugs have now been observed to have increased biological activity when administered in the form of metal complexes.[2, 3] The condensation products of sulpha drugs with aldehydes, ketones or their derivatives are very active biologically, besides having good complexing ability.[4–7] Their activity, too, increases on complexation with metal ions.

We have therefore synthesized and characterized organotin(IV) complexes of the Schiff bases derived from the condensation of 2-hydroxy-1-naphthaldehyde (**I**) and benzoylacetone (**II**) with various sulpha drugs (Fig. 1), namely sulphathiazole (a), sulphadiazine (b), sulphisoxazole (c) and sulphaguanidine (d).

EXPERIMENTAL

All the reactions were carried out under strictly anhydrous conditions and analytical-grade chemicals were used for all the experiments.

Preparation of ligands

The Schiff bases were synthesized by the condensation of 2-hydoxy-1-naphthaldehyde and benzoylacetone with sulphathiazole, sulphadiazine, sulphisoxazole and sulphaguanidine in 1:1 molar ratios using ethanol (75 ml) as the reaction medium. The solution was refluxed on a water bath for 3–4 h and then allowed to cool at room temperature. The crystalline solids were seperated out and purified by recrystallization from the acetone.

Synthesis of organotin(IV)–Schiff base complexes

(Bu_2SnO (0.45 g, 1.807 mmol) was dissolved in dry benzene (70 ml), and the requisite amount of ligand (0.647–0.761 g, 1.807 mmol) was added. The contents were refluxed on a fractionating column for about 20 h. The water liberated in the reaction was removed azeotropically with benzene. On completion of the reaction, the resulting products were rendered free of solvent and then washed repeatedly with dry cyclohexane. The products so formed were finally dried *in vacuo* at 50−60 °C for 2–3 h. Their properties and analysis are recorded in Table 1.

Analytical methods and physical measurements

Tin was estimated gravimetrically as SnO_2. Nitro-

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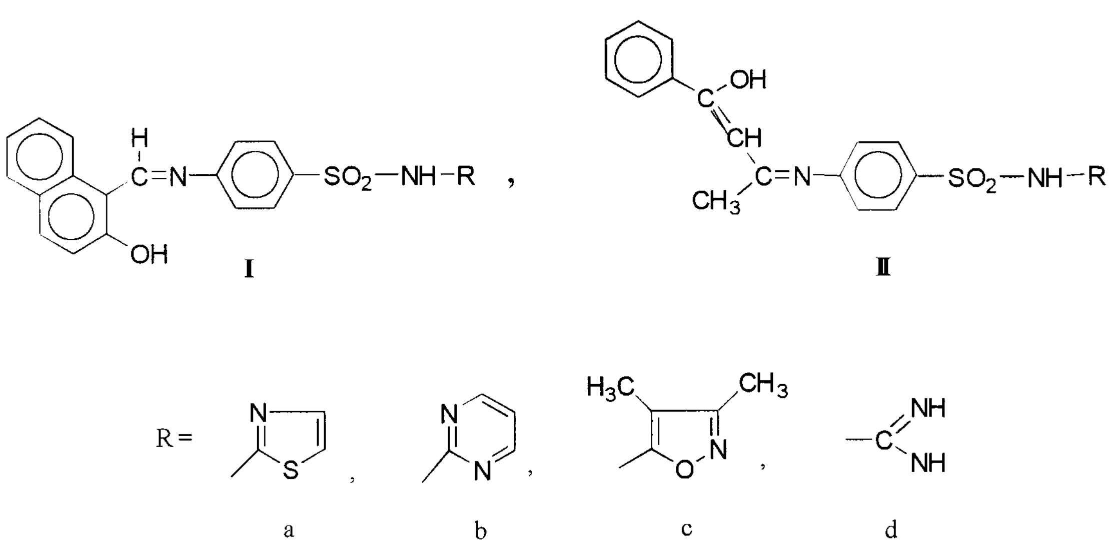


Figure 1 Schuff bases (**I** and **II**) used as ligands in this work.

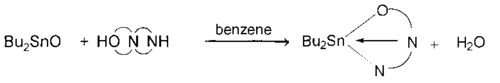
gen and sulphur were estimated by Kjeldahl's and Messenger's methods, respectively.[8–10]

IR spectra were recorded on a Perkin-Elmer 577 spectrophotometer in the region 4000–200 cm^{-1} using KBr optics. The electronic spectra (in methanol) were taken on a Toshniwal spectrophotometer. A Perkin-Elmer (model R-12B) spectrometer was used for obtaining the ^1H NMR-spectra recorded at 90 MHz, employing [D_6]-dimethyl sulphoxide (DMSO-d_6) as the solvent and tetramethylsilane (TMS) as the internal standard. ^{119}Sn NMR spectra was recorded on a 90 MHz JEOL spectrometer in dry DMSO with tetramethyltin (TMT) as external standard at 22.7 MHz. Molar conductance measurements were made in anhydrous dimethylformamide (DMF) at 36 ± 1 °C using a Systronics conductivity bridge, model 305. Molecular weight determinations were carried out by the Rast camphor method.

^{119}Sn Mössbauer spectra were obtained using a constant accelerating microprocessor (Cryophysics Ltd, Oxford, UK) with a 512-channel data store. A 15-mCi $Ba^{119m}SnO_3$ source was used at room temperature and the values were recorded relative to SnO_2. Samples were packed in Perspex discs and cooled to 80 K by means of a liquid-nitrogen cryostat. The experimental error in the measured values of isomers-shift δ) and quadrupole splitting (ΔE_o) parameters was ± 0.05 mm s^{-1}.

RESULTS AND DISCUSSION

Bu_2SnO reacts with the above-mentioned Schiff bases in a 1:1 molar ratio in a benzene medium according to Eqn [1].



[1]

All these newly synthesized complexes are coloured solids and are soluble in DMSO, DMF and $CDCl_3$. The low molar conductance values (8–15 Ω^{-1} cm^2 mol^{-1}) reveal the nonelectrolytic nature of all the complexes. The molecular weights of the complexes determined by the Rast camphor method correspond with the formula weight, indicating their monomeric nature.

Electronic spectra

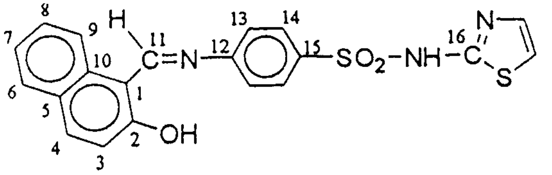
The electronic spectra of the ligands show a maximum at *ca* 246 nm due to π–π^* (benzenoid) transitions. The auxochromic (OH) group attached to the ring is responsible for the shift of this band to the lower-energy region. This band shifts to *ca* 266 nm in complexes;[11] the shift may be attributed to the increase in the degree of availability of the lone electron pair on the auxochromic oxygen in the absence of hydrogen bonding, which is present

Table 1 Synthesis and characteristics of organotin(IV) complexes

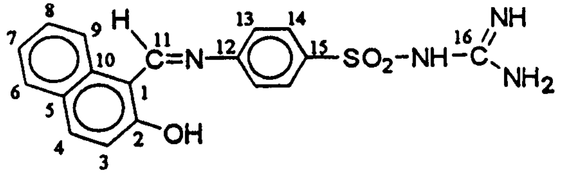
No.	Reactants		Yield (%)	Compound, colour and state	M.p. (°C)	Elemental analysis (%): Found (Calcd)					Mol.wt: Found (Calcd)
	Tin	Ligand				Sn	C	H	N	S	
Ia	$(C_4H_9)_2SnO$	$C_{20}H_{15}N_3S_2O_3$	68	$C_{28}H_{31}N_3S_2O_3Sn$ Yellow solid	142	18.19 (18.54)	52.41 (52.49)	4.85 (4.88)	6.38 (6.56)	9.89 (10.02)	645.11 (640.06)
Ib	$(C_4H_9)_2SnO$	$C_{21}H_{16}N_4SO_3$	73	$C_{29}H_{32}N_4SO_3Sn$ Light green solid	140	18.61 (18.69)	54.76 (54.80)	5.01 (5.08)	8.80 (8.82)	5.02 (5.05)	621.42 (635.01)
Ic	$(C_4H_9)_2SnO$	$C_{22}H_{19}N_3SO_4$	78	$C_{30}H_{35}N_3SO_4Sn$ Yellow solid	172	18.03 (18.20)	55.00 (55.21)	5.37 (5.41)	6.28 (6.44)	4.90 (4.92)	640.89 (652.03)
Id	$(C_4H_9)_2SnO$	$C_{18}H_{16}N_4SO_3$	80	$C_{26}H_{32}N_4SO_3Sn$ Brown solid	192	19.72 (19.81)	52.00 (52.08)	5.25 (5.38)	9.24 (9.35)	5.10 (5.35)	588.69 (599.01)
IIa	$(C_4H_9)_2SnO$	$C_{19}H_{17}N_3S_2O_3$	70	$C_{27}H_{33}N_3S_2O_3Sn$ Cream solid	158	18.68 (18.84)	51.31 (51.42)	5.20 (5.28)	6.50 (6.66)	10.01 (10.18)	645.80 (630.07)
IIb	$(C_4H_9)_2SnO$	$C_{20}H_{18}N_4SO_3$	72	$C_{28}H_{34}N_4SO_4Sn$ Cream solid	138	18.78 (18.99)	53.60 (53.76)	5.42 (5.48)	8.79 (8.96)	5.00 (5.13)	630.48 (625.02)
IIc	$(C_4H_9)_2SnO$	$C_{21}H_{21}N_3SO_4$	75	$C_{29}H_{37}N_3SO_4Sn$ Grenish yellow solid	124	18.20 (18.49)	54.05 (54.20)	5.78 (5.81)	6.50 (6.54)	4.80 (4.99)	670.38 (642.05)
IId	$(C_4H_9)_2SnO$	$C_{17}H_{18}N_4SO_3$	79	$C_{25}H_{34}N_4SO_4Sn$ Light yelow solid	133	20.01 (20.15)	50.84 (50.93)	5.70 (5.82)	9.47 (9.51)	5.38 (5.44)	592.11 (589.02)

Table 2 ^{13}C NMR data for the ligands **Ia** and **Id** and the corresponding metal complexes

No.	Ligand or complex	Chemical shifts, δ (ppm)																
		C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-11	C-12	C-13	C-14	C-15	C-16	Sn-Bu
Ia	$C_{20}H_{15}N_3S_2O_3$	118.1	152.6	121.2	128.5	128.1	123.0	132.8	123.3	127.7	123.6	162.4	126.4	121.3	117.0	116.6	165.1	
	$Bu_2SnC_{20}H_{13}N_3S_2O_3$	115.2	164.3	121.0	128.9	128.0	123.1	133.0	123.2	127.6	123.7	168.9	126.1	121.3	116.8	116.5	155.5	28.1, 27.9, 27.1, 14.6
Id	$C_{18}H_{16}N_4SO_3$	117.2	155.5	120.1	129.5	128.2	122.2	133.4	122.5	122.8	128.3	165.17	125.81	121.31	115.2	115.15	163.3	
	$Bu_2SnC_{18}H_{14}N_3SO_3$	114.9	162.5	120.0	129.8	128.0	122.0	133.4	122.2	122.7	128.4	167.3	125.6	121.1	115.1	115.0	158.1	26.8, 27.3, 26.1, 13.5



Ia



Id

Table 3 Mössbauer spectral data of tin complexes

No.	Compound	IS, δ(mm s^{-1})	QS, ΔE_Q (mm s^{-1})
Ic	$Bu_2SnC_{22}H_{17}N_3SO_4$	1.22	2.89
IIc	$Bu_2SnC_{21}H_{19}N_3SO_4$	1.21	2.91

initially in the ligand molecule and is removed after coordination by the metal atom. The spectrum also shows two bands at *ca* 312 and *ca* 390 nm due to π–π^* and n–π^* transitions of the $\rangle C=N$ chromophore[11] An appreciable blue shift in these bands that is observed in the spectra of the tin complexes may be attributed to coordination of the azomethine nitrogen to the tin atom. It has been reported[12] that a metal is capable of forming, $d\pi$–$p\pi$ bond, with a ligand containing nitrogen as the donor atom.

Infared spectra

In the IR spectra of ligands a broad band is observed in the region, 3450–3150 cm^{-1}. This band, attributable to ν(OH) or ν(NH), does not appear in the complexes.[13] A medium-to-strong band appearing at *ca* 1285 cm^{-1} may be assigned to the phenolic C–O stretching mode. This slightly shifts towards the higher-frequency side (*ca* 1300 cm^{-1}), showing the coordination of phenolic oxygen to the metal atom.

A sharp and strong band at 1635 ± 10 cm^{-1} in all these complexes, compared with one at 1620 ± 10 cm^{-1} in the ligands, may be assigned to $\nu(C=N)$.[14] The shift of this band towards the higher side is probably due to an increase in the C=N bond order due to coordination of nitrogen with the metal ion. Two medium-to-strong intensity bands which are observed at 590 ± 5 and 520 ± 7 cm^{-1} may be assigned to asymmetric and symmetric

Sn–C stretching modes. Several new bands in the complexes at 522 ± 8 and 410 ± 10 cm^{-1} are probably due to ν(Sn-O) and $\nu(Sn\longrightarrow N)$ respectively.[8–10]

^{1}H NMR spectra

The ^{1}H NMR spectra of the ligands contain broad signals in the region δ 10.25–13.00 ppm, assignable to hydrogen-bonded NH or OH protons. These signals completely disappear in all the diorganotin complexes and demonstrate deprotonation of the functional group due to coordination of the central tin atom to oxygen as well as to the nitrogen atom of the ligand moiety.

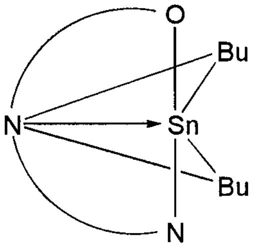


Figure 2 Geometry of the dibutyltin(IV) complexes.

In the case of the ligands, the proton signal for the azomethine proton CH=N in the δ region of 8.30–8.80 ppm shifts downfield in the spectra of the corresponding tin complexes on account of deshielding which is attributed to the donation of the lone pair of electrons by the azomethine nitrogen to the tin atom. The complexes, however, show additional signals at δ 0.75–1.95 ppm owing to the the butyl protons.

^{13}C NMR spectra

^{13}C NMR spectra of 2-hydroxy-l-naphthaldehyde sulphaguanidine and its corresponding tin complexes have also been recorded. A considerable shift (Table 2) in the positions of carbon atoms attached to the different participating groups clearly indicate the bonding of azomethine nitrogen and phenolic oxygen to the tin atom. The $^1J(^{119}Sn$–$^{13}C)$ value of 465.5 Hz indicates five-coordination[15] around tin in such complexes. Since in the IR spectra both symmetric and asymmetric Sn–C bonds are present, the C–Sn–C moiety is bent in trigonal-bipyramidal geometry.[18]

^{119}Sn NMR spectra

The compounds $Bu_2SnC_{22}H_{17}N_3SO_4$ and $Bu_2SnC_{21}H_{19}N_3SO_4$ give sharp signals at δ -138.3 or -146 ppm in the ^{119}Sn NMR spectra, which strongly supports five-coordination around tin in a trigonal-bipyramidal geometry. Values[16,17] for similar five-coordinated Bu_2Sn(IV) complexes have been reported in the δ range of -128 to -165 ppm.

^{119}Sn Mössbauer spectra

The Mössbauer spectra of the tin complexes have also been recorded (Table 3) and the observed

Table 4 Antibacterical activity of ligands and their complexes

		E. coli		*S. aureus*		*P. syringae*		*P. mirabilis*	
No.	Ligand or complex	IZ[a] (mm)	AI[b]	IZ (mm)	AI	IZ (mm)	AI	IZ (mm)	AI
	$C_{20}H_{15}N_3S_2O_3$	7	0.87	9	1.20	5	1.31	4	1.00
Ia	$Bu_2Sn(C_{20}H_{13}N_3S_2O_3)$	12	1.50	15	2.00	9	2.36	8	2.00
	$C_{21}H_{16}N_4SO_3$	8	1.00	9.2	1.22	4	1.05	4	1.00
Ib	$Bu_2Sn(C_{21}H_{14}N_4SO_3)$	14	1.75	17	2.27	10	2.63	8	2.00
	$C_{18}H_{16}N_4SO_3$	6	0.75	8	1.06	5	1.31	4	1.00
Id	$Bu_2Sn(C_{18}H_{14}N_4SO_3)$	10	1.25	14.5	1.94	9	2.36	9	2.25
	$C_{19}H_{17}N_3S_2O_3$	9	1.12	9.8	1.30	3	0.78	3	0.75
IIa	$Bu_2Sn(C_{19}H_{15}N_3S_2O_3)$	14	1.75	16	2.14	8	2.10	7	1.75
	$C_{20}H_{18}N_4SO_3$	9	1.12	9	1.20	6	1.58	5	1.25
IIb	$Bu_2(C_{20}H_{16}N_4SO_3)$	14.2	1.77	17.2	2.30	10	2.63	10	2.50

IZ = Inhibition zone.
AI = Inhibition zone of test compounds / inhibition zone of standard.

isomer shifts indicate the presence of tin in its +4 oxidation state; the presence of quadrupole splitting shows that the EFG (electric field gradient) around the tin nucleus is produced by inequalities in the tin–ligand σ-bonds.[12] These compounds give a ρ value of >2.1, which indicates a coordination number greater than four. Comparison of the isomer shift of these complexes with those already reported indicates the coordination number to be more than four, as these isomer shifts are much lower than those Retetrahedral tin.[23] The lowering of isomer shifts in these complexes is due to the interaction of tin(IV) with nitrogen donors having ($Sn\longrightarrow N$) bonds.[18] On the basis of quadrupole splitting data, the configuration of these complexes has been assumed to be of the trigonal-bipyramidal type, with the azomethine nitrogen atom and both carbon atoms (attached to tin) occupying equatorial sites; the opical sites being occupied by other two ligand atoms (O, N).[19, 20]

On the basis of the above spectral evidence, dibutyltin(IV) complexes with the tin atom in trigonal-bipyramidal geometry are shown in Fig. 2. Geometry of the dibutyltin(IV) complexes.

Antibacterial test results

The bactericidal activity of a few representative ligands and corresponding tin(IV) complexes has been tested against *Escherichia coli* (−), *Pseudomonas syringae* (−), *Proteus mirabilis* (−) and *Staphylococcus aureus* (+) by the paper disc plate method[21] at 100 $\mu g\,ml^{-1}$ concentration in DMF. The discs, diameter 5 mm, were soaked in the test solutions, then placed on the appropriate medium previously seeded with organisms in Petri dishes and stored in an incubator at $36 \pm 1\,°C$. The inhibition zone around each disc was measured after 24 h (Table 4).

The results suggest that although the ligands have toxic properties, their tin complexes inhibit the growth of bacteria to an even greater extent. It can be inferred that the higher activity is due to chelate formation and the presence of the butyl group with the tin atom.[23] Further, the greater activity of the complexes can also be explained on the basis of their higher solubility, particle size and the size of the metal ion. From the results achieved, it can also be inferred that complexes are more active than free ligands against all micro-organisms tested.

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REFERENCES

1. Tiwari GD, Mishra MN, *Curr. Sci.* 1980; **49**: 8.
2. Jain P, Chaturvedi KK, *J. Inorg. Nucl. Chem.* 1977; **39**: 901.
3. Williams DR, *Chem. Rev.* 1972; **72**: 203.
4. Roy P, Mukherjee AK, *J. Ind. Chem. Soc.* 1955; **32**: 604.
5. Jain P, Chaturvedi KK, *J. Ind. Chem. Soc.* 1975; **52**: 805.
6. Jain P, Chaturvedi KK, *J. Ind. Chem. Soc.* 1975; **52**: 1220.
7. Jain P, Chaturvedi KK, *J. Inorg. Nucl. Chem.* 1976; **38**: 799.
8. Varshney AK, Tandon JP, Crowe AJ, *Polyhedron* 1986; **5**: 739.

9. Varshney AK, Varshney S, Sharma M, Singh HL, *Main Group Metal Chem.* 1998; **21**: 495.
10. Varshney AK, Varshney S, Singh HL, *Bull. Pol. Acad. Sci. Chem.* 1997; **45**: 373.
11. Varshney AK, Varshney S, Tandon JP, *J. Prakt. Chem.* 1989; **331**: 511.
12. Saxena A, Tandon JP, Molloy KC, Zuckerman JJ, *Inorg. Chim. Acta* 1982; **63**: 71.
13. Sandhu GK, Gupta R, Sandhu SS, *J. Organomet. Chem.* 1985; **279**: 373.
14. Kumari A, Singh I, Tandon JP, *Main Group Met. Chem.* 1994; **17**: 347.
15. Mitchell TN, *J. Organomet Chem.* 1974; **71**: 39.
16. Antonin L, Holecek J, Angelika S, Ivan T, *J. Organomet. Chem.* 1991; **409**: 331.
17. Molloy KC, Waterfield PC, *J. Organomet. Chem.* 1992; **424**: 281.
18. Saxena A, Tandon JP, Crowe AJ, *Polyhedron* 1985; **4**: 1085.
19. Barbieri R, Pellerito L, Huber F, *Inorg. Chim. Acta* 1978; **30**: 339.
20. Casas JS, Sanchez A, Sordo J, Vazquez-Lopez A, Casterllano EE, Zukerman-Schpector J, Rodriguez-Argueelles MC, Russo U, *Inorg. Chim. Acta* 1994; **216**: 169.
21. Saxena A, Sinha SK, Tandon JP, *Antifung. Antibact. Agents* 1981; **9**: 435.
22. Nath M, Goyal S, *Bull. Chem. Soc. Jpn.* 1996; **69**: 605.
23. Saxena A, Tandon JP, *Polyhedron* 1984; **3**: 681.