APPLIED ORGANOMETALLIC CHEMISTRY
Appl. Organometal. Chem. **13**, 637–641 (1999)

Organotin(IV) Complexes of Biologically Active Schiff Bases Derived from Heterocyclic Ketones and Sulpha Drugs

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Some new hexa-coordinated organotin complexes [$Bu_2Sn(NN)_2$] (where NN is the anion of various Schiff bases) have been synthesized and characterized on the basis of elemental analysis, conductivity measurements, molecular weight determination, and ultraviolet, infrared and multinuclear magnetic resonance (^1H, ^{13}C and 119Sn) spectral studies. A few representative complexes have also been screened for their antibacterial and antifungal activity and found to be quite active in this respect. Copyright © 1999 John Wiley & Sons, Ltd.

Keywords: heterocyclic ketones; dibutyltin oxide; sulpha drugs; microorganisms; spectral studies.

Received 21 September 1998; accepted 29 January 1999

INTRODUCTION

Schiff bases continue to occupy an important position as ligands in metal coordination chemistry, even almost a century since their discovery. Sulpha drugs have also been reported to be active against different type of bacteria and viruses[1] and have been used as drugs for diseases such as cancer[2] and tuberculosis.[3] The condensation products of sulpha drugs with aldehydes and ketones are active biologically and they also have good complexing ability.[4,5] It was, therefore, considered worthwhile to synthesize and characterize some dibutyltin(IV) complexes of Schiff bases derived from heterocyclic ketones and various sulpha drugs (Fig. 1), viz. sulphaguanidine (a), sulphathiazole (b), sulphisoxazole (c) and sulphadiazine (d).

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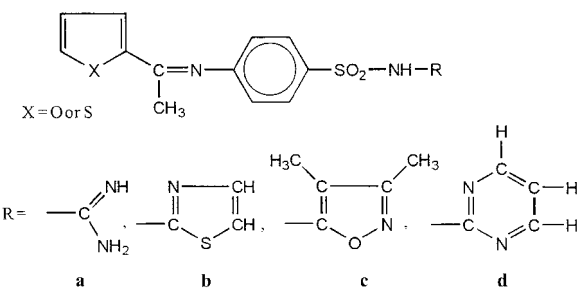


Figure 1 The Schiff bases used in this study.

EXPERIMENTAL

Chemicals and solvents were dried and purified by standard methods and moisture was excluded from the glass apparatus using $CaCl_2$ drying tubes.

Synthesis of the ligands

The Schiff bases were synthesized by the condensation of 2-acetylfuran (2-AcF) and 2-acetylthiophene (2-AcT) with sulphaguanidine, sulphathiazole, sulphisoxazole and sulphadiazine in a 1:1 molar ratio using ethanol as the reaction medium. The solutions were refluxed on a water bath for 4–5 h and then allowed to cool at room temperature. The products so obtained were recrystallized from acetone (Table 1).

Synthesis of organotin(IV) complexes

Dibutyltin(IV) oxide and the ligand in 1:2 molar ratio were refluxed in dry benzene and the water liberated in the reaction was removed azeotropically on completion of the reaction; the resulting products were rendered free from the solvent and then washed repeatedly with dry cyclohexane. The

 CCC 0268–2605/99/090637–05 $17.50

Table 1 Physical properties and characteristics of monofunctional bidentate Schiff bases

	Ligand	Colour	M.p. (°C)	Elemental analysis (%) C Found (Calcd)	H Found (Calcd)	N Found (Calcd)	S Found (Calcd)	Mol.wt Found (Calcd)
A	2-AcF-sulphaguanidine $C_{13}H_{14}N_4O_3S$	Cream	132–134	50.67 (50.97)	4.56 (4.61)	18.00 (18.29)	10.28 (10.47)	313.08 (306.34)
B	2-AcF-sulphathiazole $C_{15}H_{13}N_3O_3S_2$	Light yellow	129–130	51.39 (51.86)	3.70 (3.77)	11.90 (12.10)	18.25 (18.46)	360.12 (347.42)
C	2-AcF-sulphisoxazole $C_{17}H_{17}N_3O_4S$	Brown	158–160	56.70 (56.81)	4.69 (4.77)	11.28 (11.69)	8.72 (8.92)	366.22 (359.41)
D	2-AcF-sulphadiazine $C_{16}H_{14}N_4O_3S$	Light brown	158 (d)[a]	56.00 (56.13)	4.00 (4.12)	16.07 (16.37)	9.13 (9.36)	355.44 (342.37)
E	2-AcT-sulphaguanidine $C_{13}H_{14}N_4O_2S_2$	Creamish white	108	48.11 (48.43)	4.30 (4.38)	17.03 (17.40)	19.62 (19.89)	330.26 (322.40)
F	2-AcT-sulphathiazole $C_{15}H_{13}N_3O_2S_3$	Light brown	132	49.20 (49.57)	3.53 (3.60)	11.29 (11.56)	26.20 (26.46)	371.45 (363.48)
G	2-AcT-sulphisoxazole $C_{17}H_{17}N_3O_3S_2$	Brown	160(d)	54.18 (54.52)	4.47 (4.57)	11.00 (11.22)	17.00 (17.12)	365.52 (374.50)
H	2-AcT-sulphadiazine $C_{16}H_{14}N_4O_2S_2$	Light brown	165(d)	53.34 (53.62)	3.90 (3.94)	15.50 (15.63)	17.72 (17.89)	362.89 (358.43)

[a] d, decomposed.

products so formed were finally dried *in vacuo* at 50 °C for 5 h.

Tin was estimated gravimetrically as SnO_2; nitrogen and sulphur were estimated by Kjeldahl's and Messenger's methods respectively.[6–9]

Infrared spectra were recorded on a Perkin-Elmer 577 instrument in the region 4000–200 cm^{-1}. A Perkin-Elmer model RB-12 spectrometer was used for proton magnetic resonance spectra in deuterated dimethyl sulphoxide or deuterated chloroform dimethylformcmide and tetramethylsilane as internal standard. Molar conductance measurements were made in anhydrous (DMF) at 36 ± 1 °C using a Systronics conductivity bridge model 305. Molecular weight determinations were carried out by the Rast camphor method. The electronic spectra were recorded in methanol on a Toshniwal spectrophotometer. ^{13}C and ^{119}Sn NMR spectra were recorded on a 90 MHz JEOL spectrometer in dry dimethyl sulphoxide (DMSO) with tetramethylsilane (TMS) and tetramethyltin (TMT) as internal and external standareds at 22.59 MHz and 22.7 MHz, respectively.

RESULTS AND DISCUSSION

The reactions of Bu_2SnO with the Schiff bases in benzene in a 1:2 molar ratio take place according to Eqn [1]. All these newly synthesized complexes are off-white solids and are soluble in DMSO, DMF and common organic solvents (Table 2).

$$Bu_2SnO + 2\,\overbrace{NN}H \rightarrow Bu_2Sn(\overbrace{NN})_2 + H_2O \quad [1]$$

The molecular weights of the complexes determined by the Rast camphor method correspond to the formula weight, indicating a monomeric nature. The stoichiometry of the complexes were confirmed by the elemental analyses. The low values of their molar conductances in DMF indicate their non-electrolytic nature.

Electronic spectra

Electronic spectra of the Schiff bases exhibit three bands around 240, 280 and 360 nm. Bands at 240 and 280 nm are possibly due to π–π^* transitions within the benzene ring and the (>C=N) band of the azomethine group, respectively. The band around 360 nm may be due to n–π^* transitions of the non-bonding electrons present on the nitrogen of the azomethine group. The first two bands remain unchanged in the corresponding complexes, whereas the third one undergoes a hypsochromic shift due to coordination of nitrogen to the central metal atom.

Table 2 Synthesis and characteristics of diorganotin(IV) complexes

Reactants						Elemental analysis (%)			Mol.wt
Tin	Ligand	Molar ratio	Product	Yield (%)	M.p. (°C)	Sn Found (calcd)	N Found (calcd)	S Found (calcd)	Found (calcd)
Bu_2SnO	$C_{13}H_{14}N_4O_3S$	1:2	$Bu_2Sn(C_{13}H_{13}N_4O_3S)_2$	78	172	13.91 (14.07)	13.00 (13.28)	7.44 (7.59)	828.89 (843.50)
Bu_2SnO	$C_{15}H_{13}N_3O_3S_2$	1:2	$Bu_2Sn(C_{15}H_{12}N_3O_3S_2)_2$	81	241(d)[a]	12.66 (12.82)	8.86 (9.07)	13.72 (13.85)	910.92 (925.66)
Bu_2SnO	$C_{17}H_{17}N_3O_4S$	1:2	$Bu_2Sn(C_{17}H_{16}N_3O_4S)_2$	79	158	12.40 (12.50)	8.58 (8.85)	6.66 (6.75)	938.08 (949.64)
Bu_2SnO	$C_{16}H_{14}N_4O_3S$	1:2	$Bu_2Sn(C_{16}H_{13}N_4O_3S)_2$	75	155	12.83 (12.96)	12.01 (12.23)	6.87 (7.00)	901.79 (915.56)
Bu_2SnO	$C_{13}H_{14}N_4O_2S_2$	1:2	$Bu_2Sn(C_{13}H_{13}N_4O_2S_2)_2$	76	161	13.42 (13.55)	12.60 (12.79)	14.51 (14.64)	867.50 (875.62)
Bu_2SnO	$C_{15}H_{13}N_3O_2S_3$	1:2	$Bu_2Sn(C_{15}H_{12}N_3O_2S_3)_2$	76	128	12.11 (12.39)	8.69 (8.77)	19.98 (20.08)	945.26 (957.78)
Bu_2SnO	$C_{17}H_{17}N_3O_3S_2$	1:2	$Bu_2Sn(C_{17}H_{16}N_3O_3S_2)_2$	82	153	11.90 (12.11)	8.40 (8.57)	12.89 (13.09)	960.70 (979.82)
Bu_2SnO	$C_{16}H_{14}N_4O_2S_2$	1:2	$Bu_2Sn(C_{16}H_{13}N_4O_2S_2)_2$	80	210(d)	12.41 (12.52)	11.68 (11.82)	13.38 (13.53)	932.01 (947.68)

[a] d, decomposed.

Infrared spectra

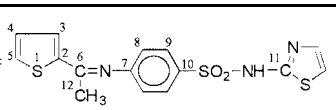
The IR spectra of these derivatives do not show bands in the region 3400–3150 cm^{-1} which could be assigned to ν(NH) vibrations. This indicates deprotonation of the functional groups of the ligands as a result of complexation with the tin atom.

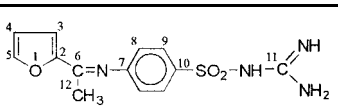
A sharp and strong band at *ca* 1635 cm^{-1} in all these complexes, compared with one at *ca* 1620 cm^{-1} in the ligands, may be attributed to ν (C=N).[10,11] The upfield shift of this band is probably caused by an increase in the >C=N bond order due to coordination of nitrogen to the metal atom.

Medium to sharp intensity bands are observed at 595 and 525 cm^{-1} which may be assigned to the asymmetric and symmetric modes of Sn–C stretching vibrations. Also, two bands observed at *ca* 420 cm^{-1} and *ca* 420 cm^{-1} are probably due to ν(Sn—N) and ν(Sn←—N) bonds, respectively, which are not observed in the spectra of the Schiff bases.[12]

Table 3 ^{13}C NMR data of ligands and their organotin(IV) complexes

	Chemical shift δ(ppm)											
Compound	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-11	C-12	Sn–Bu
2-AcT-STH[a]	141.2	126.4	126.68	127.8	170.4	121.6	121.2	115.25	115.35	168.4	12.6	
Bu_2Sn(2-AcT-ST)$_2$	138.9	126.6	126.2	127.3	163.0	120.6	121.3	115.3	115.3	160.7	14.10	25.9, 27.6, 27.1, 13.8
2-AcF-SGH[b]	144.3	124.2	121.1	135.4	172.3	122.5	121.6	116.1	116.2	168.2	12.8	
Bu_2Sn(2-AcF-SG)$_2$	142.2	123.9	121.4	135.2	162.8	121.8	121.8	116.2	116.4	155.6	15.2	28.2, 27.1, 26.00, 13.0

[a] 2-AcT-STH = 

[b] 2-AcF-SGH = 

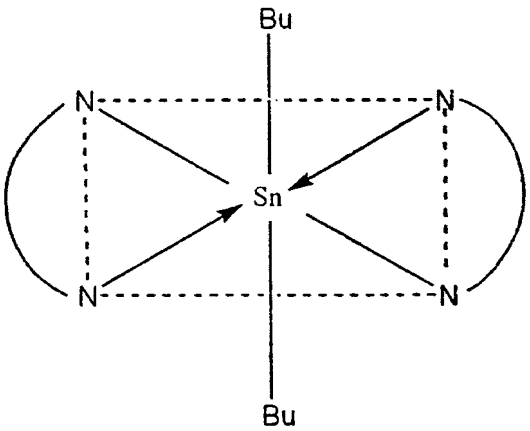


Figure 2 Structure assigned to the dibutyltin(IV)- Schiff base complexes.

^{1}H NMR spectra

The ^{1}H NMR spectra of the ligands also exhibit NH proton signals at $\delta = 10.00 \pm 0.05$ ppm which disappear in the complexes, showing the involvement of adjacent nitrogen in bonding with the tin atom. A proton signal at $\delta = 1.85$ ppm is observed due to —C(CH_3)=N—; this moves downfield ($\delta = 1.95$ ppm) in the complexes from its original position in the ligands, due to coordination of >C=N to the metal atom. The ligands show complex multiplets in the region $\delta = 7.90$–6.80 ppm for the aromatic protons and it remains at almost the same position in the spectra of the organotin(IV) complexes. The complexes, however, show additional signals at $\delta = 0.65$–2.00 ppm (m) owing to the proton of the butyl group.

^{13}C NMR spectra

^{13}C NMR data for a few representative samples have been recorded and are given in Table 3. The shifts in the position of carbon atoms attached to nitrogen are indicative of their coordination to the metal atoms. The carbon atoms of butyl groups are observed at positions ($\delta = 26.7$–13.6 ppm) comparable with other similar compounds.

^{119}Sn NMR spectra

^{119}Sn NMR spectra of the organotin complexes show signals between $\delta = -275$ and -290 ppm which are in good agreement with values for hexacoordination around tin atoms. Values for similar six-coordinated Bu_2Sn(IV) complexes have been reported[13,14] in the range of $\delta = -210$ to -365 ppm.

Thus, on the basis of the above evidence, the structure in Fig.2 can be assigned to these complexes.

Table 4 Antimicrobial activities of ligands and their metal complexes

Organism		Compound[c]									
		A	**I_A**	**B**	**I_B**	**C**	**I_C**	**E**	**I_E**	**F**	**I_F**
S. aureus	IZ[a]	7.1	12	8	14	8	12.8	5	11	8.2	15
	(AI)[b]	(0.78)	(1.33)	(0.88)	(1.55)	(0.88)	(1.42)	(0.55)	(1.22)	(0.91)	(1.66)
B. thuringiesis	IZ	7.8	14	8.2	18	8	16	7	16	9	25
	(AI)	(0.6)	(1.07)	(0.63)	(1.38)	(0.62)	(1.23)	(0.54)	(1.23)	(0.69)	(1.92)
E. coli	IZ	5.6	8.8	6.4	10	6.8	13	4.2	10	6.1	10.6
	(AI)	(0.62)	(0.98)	(0.71)	(1.11)	(0.75)	(1.44)	(0.46)	(1.11)	(0.67)	(1.77)
P. mirabilis	IZ	4.2	8	7.2	10	5.8	11	4.6	10	4.8	15
	(AI)	(0.52)	(1.0)	(0.9)	(1.25)	(0.72)	(1.37)	(0.57)	(1.25)	(0.60)	(1.87)
P. syringae	IZ	4.4	8.9	4.7	11	4.4	12	4.2	9	4.6	11
	(AI)	(0.44)	(0.89)	(0.47)	(1.10)	(0.44)	(1.20)	(0.42)	(0.90)	(0.46)	(1.10)
A. flavus	IZ	6.9	15.6	7	16	5.6	16	6.8	15	6.7	17.5
	(AI)	(0.86)	(1.95)	(0.87)	(2.0)	(0.70)	(2.0)	(0.85)	(1.87)	(0.84)	(2.18)
A. niger	IZ	8	12	6.2	14	6.7	13	6.9	16	7.0	12
	(AI)	(0.80)	(1.20)	(0.62)	(1.40)	(0.67)	(1.30)	(0.69)	(1.60)	(0.70)	(1.20)
R. phaseoli	IZ	7.8	12	8.2	15	6.6	13	7.6	15	7.8	10
	(AI)	(0.78)	(1.20)	(0.82)	(1.50)	0.66	1.30	0.76	1.50	(0.78)	(1.0)

[a] IZ = inhibition zone (mm)
[b] AI = activity index = inhibition zone of test compounds/inhibition zone of standard.
[c] See Table 1 for identities of ligands **A**–**F**. **I_A**–**I_F** are the corresponding dibutyltin(IV) complexes.

Antimicrobial activity results

The Antibacterial and antifungal tests were carried out using the disc-diffusion method[15–17] for their activities at a concentration of 100 ppm. Streptomycin and mycostatin were used as reference compounds for antibacterial and antifungal activities, respectively. *Staphylococcus aureus, Escherichia coli, Proteus mirabilis, Bacillus thuringiesis* and *Pseudomonas syringae* (bacteria) or *Aspergillus flavus, Aspergillus niger* and *Rhizoctonia phaseoli* (fungi) were used as the test organisms. Results have been recorded in the form of inhibition zones (diameter, mm) and activity indices in Table 4.

Further, the tin complexes are more active than the ligands, which indicates that metallation increases activity. The above studies indicate that the tin complexes synthesized in the present studies are highly active against all these microorganisms.

Acknowledgements One of the anothors (H.L. Singh) is thankful to the CSIR, New Delhi, for the award of a senior research fellowship.

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