Studies of Heterocyclic Compounds. X*. The Synthesis and Properties of some Organotin(IV)–Oxygen and –Nitrogen Heterocycles

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(Received May 20, 1987)

Abstract

Some representative six-membered heterocyclic organotin(IV)–nitrogen and –oxygen compounds were prepared by the condensation of dialkyltin oxides with hydroxycarboxylic acids, substituted aminocarboxylic acids and diols and characterized by infrared and mass spectra. The compounds were screened against nine species of bacteria and five species of fungi.

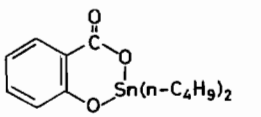
Introduction

The synthesis of organotin heterocycles started receiving attention in the 1960s; these studies were mainly concerned with their characterization through spectral studies (mainly infrared). Typical examples are heterocycles prepared from ortho dihydroxy compounds [2, 3], dicarboxylic acids and Schiff bases [4–6].

There is a lack of information about the antimicrobial properties of organotin heterocycles. A study was undertaken in order to synthesize, characterize and determine the biological activity of a number of organotin(IV)–oxygen and –nitrogen heterocycles. The compounds were characterized using infrared and mass spectra. Biological activity was studied by using bacteriostatic and fungistatic tests.

Experimental

All the chemicals used in this work were of reagent grade. Benzene was dried over sodium wire. Dibenzyltin dichloride was prepared according to a literature procedure [7]. Dibenzyltin oxide was prepared by aqueous potassium hydroxide hydrolysis of an ethanolic solution of dibenzyltin dichloride. The (2-oxybenzoyloxy)dialkyltin(IV) compounds (**1–3**) were prepared by the reaction of the appropriate dialkyltin oxide with the benzene solution of the 2-hydroxybenzoic acid in equimolar proportions. The other compounds (**4–8**) were prepared, in a similar manner, by the reaction of dialkyltin oxide with either 2-acetamidobenzoic acid, 2-benzenesulfonamidobenzoic acid, 2-(4-toluenesulfonamido)-benzoic acid or bis(salicylaldehyde)ethylenedimine



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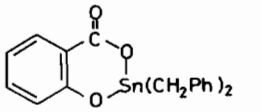

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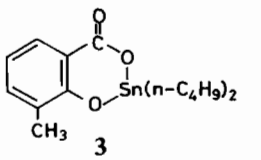

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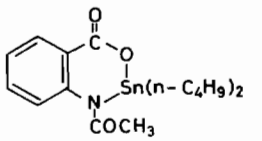

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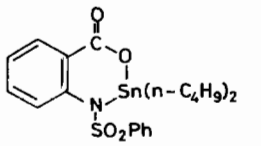

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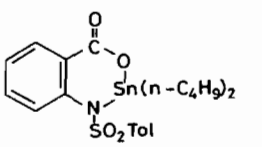

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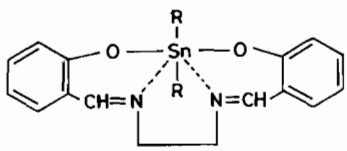

7 R = n-C_4H_9

8 R = n-CH_2Ph

*For Part IX, see ref. 1.

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TABLE I. Physical and Analytical Data of the Tin(IV)–Nitrogen and –Oxygen Heterocycles

Compound no.	Empirical formula of heterocycle	Yield (%)	Melting (°C)	Analysis (%)[a]			
				Sn	C	H	N
1	$C_{15}H_{22}O_3Sn$	95	224–226	31.84 (32.16)	49.01 (48.82)	6.05 (6.01)	
2	$C_{21}H_{18}O_3Sn$	72	216–218	27.67 (27.16)	57.71 (57.71)	4.15 (4.15)	
3	$C_{16}H_{24}O_3Sn$	58	256–259	31.48 (30.98)	50.01 (50.17)	6.48 (6.31)	
4	$C_{17}H_{25}NO_3Sn$	87	130–132	28.41 (28.94)	49.40 (49.79)	6.40 (6.14)	3.55 (3.42)
5	$C_{21}H_{27}NO_4SSn$	88	238–341	22.98 (23.35)	49.23 (49.63)	5.54 (5.35)	2.90 (2.76)
6	$C_{22}H_{29}NO_4SSn$	90	256–257	22.99 (22.73)	50.50 (50.60)	5.40 (5.60)	2.55 (2.68)
7	$C_{24}H_{32}N_2O_2Sn$	90	153–154	23.49 (23.77)	57.48 (57.74)	6.39 (6.46)	5.29 (5.61)
8	$C_{30}H_{28}N_2O_2Sn$	85	172–174	20.40 (20.92)	63.50 (63.52)	4.99 (4.97)	4.89 (4.94)

[a]Figures in parentheses are theoretical yields.

in equimolar proportions. The reagents were refluxed in benzene for about 7 h and the water liberated by the reactions was removed by azeotropic distillation using the Dean and Stark separator. In each case, the resulting solution was concentrated with a rotatory evaporator and left to stand while the solid product formed. In some cases, addition of n-hexane or petroleum ether is necessary for quick precipitation.

Elemental analysis (carbon, hydrogen and nitrogen) was carried out at the Department of Chemistry and Chemical Engineering, University of Saskatchewan, Canada. Tin was estimated gravimetrically as SnO_2.

The infrared spectra (IR) from 4000 to 250 cm^{-1} were obtained using a Perkin-Elmer 457 spectrophotometer. Samples were prepared as KBr pellets. The mass spectra were determined on an AE1 MS12 and Finnigan Model 3300 System coupled to an Incos data system at 70 eV.

Antimicrobial Tests

The antimicrobial activity test was carried out adapting the cup-plate agar diffusion method of Cruickshank *et al.* [8] and Mutreja *et al.* [9]. The test compounds were dissolved in dimethylsulfoxide, then added to a nutrient agar for either bacteria or fungi giving a final concentration of 1000 μg per ml. The extent of inhibition was measured in millimeters using the zone of inhibition produced after 24 h.

Results and Discussion

The two dialkyltin(IV) bis(salicylaldehyde)ethylenediimines are yellow crystalline products. The (2-oxybenzoyloxy)dialkyltin(IV) compounds are white colored while the (2-oxybenzoyloxy)dialkyltin(IV) compounds **4–8** are beige in color. The synthesized compounds with their yields, melting points and elemental analysis are given in Table I.

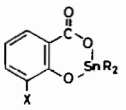
Infrared Spectra

When the spectra of the heterocyclic organotin carboxylates **1–6** are compared with those of the 2-hydroxy- or 2-amido-benzoic acid derivatives, the characteristic, broad carboxylic acid stretching vibration around 3300–2500 cm^{-1} and the C=O stretching vibration at around 1655 cm^{-1} have disappeared. This indicates that the O–H of the carboxylic acid functional group has reacted with the dialkyltin oxide to form a Sn–O bond [6, 10]. Also, the infrared spectra of compounds **1–6** do not show any absorption owing to either ν(OH) or ν(N–H), thus establishing formation of a Sn–O or Sn–N bonds.

It is known that the C=O stretching vibrations of ordinary organic esters occur in the range 1750–1730 cm^{-1} [11]. However, in the infrared spectra of the compounds, there is no absorption in the region 1750–1610 cm^{-1}. Strong absorptions are observed around 1580–1505 cm^{-1} which are assigned to $\nu_{asym}(CO_2)$ [6, 12]. This shift to lower frequency may be due to intermolecular coordination between the oxygen of C=O and the tin atom [6].

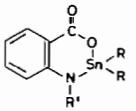
The vibrations due to the azomethine group in the bis(salicylaldehyde)ethylenediimines (**7** and **8**) are shifted to a higher region (1620–1618 cm^{-1}) substantiating coordination through the azomethine nitrogen [13].

TABLE II. Infrared Data and Assignments for (2-)Xybenzoyloxy)dialkyltin(IV) Compounds:



R = Bu; X = H	R = $PhCH_2$; X = H	R = Bu; X = CH_3	Assignments
2940m			ν(C–H)
2900m			
2840w			
1600s	1608s	1610s	ν(C=C)
1555s	1560s	1566s	$\nu_{asym}(CO_2)$
1505s	1510s	1508s	
1510sh	1502sh	1	
1444s	1452s	1447s	
1395w	1380s	1400s	$\nu_{sym}(CO_2)$
1240m	1300w	1330m	
1228s	1224s	1235s	
1138m	1140s	1160m	
1030w	1040s	1106m	
885m	890m	1035m	
870m	874m	875m	
660m	765s	825s	
586m	670m	760m	
	560m	660m	
		585s	
		460m	

TABLE III. Infrared Data and Assignments for (2-Acetamidobenzoyloxy)- and (2-Sulfonamidobenzoyloxy)dibutyltin-(IV) Compounds:



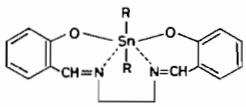
R = Bu; R′ = $COCH_3$	R = Bu; R′ = SO_2Ph	R = Bu; R′ = SO_2Tol	Assignments
2940m	2940m	2940m	ν(C–H)
2900m	2905m	2910m	
2840w	2840w	2840w	
1675s			ν(N–C=O)
	1605s	1610s	ν(C=C)
1580s	1580s	1570s	$\nu_{asym}(CO_2)$
1505b,s	1480s	1515s	
1442s	1440m	1500sh	
1360s	1360s	1380b,s	$\nu_{sym}(CO_2)$
	1320s	1330m	$\nu_{asym}(SO_2)$
		1300m	
1295s	1270s	1250s	
1150m	1165s	1190m	$\nu_{sym}(SO_2)$
		1155s	
1070w	1085m	1040m	
1030b,w	935m	1010	
800m	835m	870m	

(continued)

TABLE III. *(continued)*

R = Bu; R′ = $COCH_3$	R = Bu; R′ = SO_2Ph	R = Bu; R′ = SO_2Tol	Assignments
		810m	
750s	750s	750s	
630b,m	665w	685b,s	
550m	625w	600m	
	585s	570w	
	545m	525m	
		400w	

TABLE IV. Infrared Data and Assignments for Dialkyltin-(IV) Bis(Salicylaldehyde)ethylenediimine:



R = Bu	R = CH_2Ph	Assignments
2940m		ν(C–H)
2900m		
2840w		
1625sh		
1620s	1618s	ν(C=N)
1570w	1588m	
1525m	1542m	
1490w	1480w	
1458sh	1450m	
1440s	1439s	
1390m	1394m	
1338m	1338m	
1312m	1305m	
1280m	1235w	
	1205m	
1180m	1182m	
1140s	1140m	
1120w	1122w	
	1084w	
1040m	1044w	
1017m	10242	
975w		
900w	900m	
850m		
746s	754s	
	695m	
600m	448m	
565m	395m	
395w	370w	

The sulfonyl group in compounds **5** and **6** showed two characteristic bands (asymmetric and symmetric) in the range 1380–1360 cm^{-1} and 1165–1155 cm^{-1} according to the literature data [14]. In the region 900–300 cm^{-1}, the Sn–N and the Sn–O stretching vibrations could not be assigned with certainty. The infrared spectra of the compounds are listed in Tables II, III and IV.

Mass Spectra

The compounds underwent mass spectral analysis. Tin consists of a number of isotopes. The most abundant isotope, ^{120}Sn (32.9%), will be used in calculating the masses of molecular ions and fragment ions in this discussion.

In general, the mass spectra of the compounds did not display the molecular ions, except compound **1** with a weak intensity at *m/e* 370 (<2.0%). The (2-oxybenzoyloxy)dialkyltin(IV) compounds **1–3**, presumably fragmented by simultaneous expulsion of C_2H_3 and CO, give ions at *m/e* 291 and *m/e* 359, for compounds **1** and **2**, respectively. Simultaneous loss of the CH_3 group accounts for the ion at *m/e* 291 in compound **3**. However, the main fragmentation route is the simultaneous loss of CO_2 and the alkyl radical (n-Bu or CH_2Ph) to give a prominent ion at *m/e* 269 (plus the loss of the CH_3 group in compound **3**) in compounds **1** and **3** and at *m/e* 303 for compound **2**. The suggested pathways for the formation of these ions and the ions at *m/e* 121 and *m/e* 120 are noted in Scheme 1.

The mass spectra of the 2-amido compounds **4–6** are characterized mainly either by loss of SO_2R (R = Ph, or $COCH_3$, or P–CH_3Ph), followed by loss of CO giving rise to the ion at *m/e* 339 (3.1–3.2%) or loss of SO_2R (R = Ph, or P–CH_3Ph, or $COCH_3$) followed by loss of C_4H_8 (butylene) to give the ion at *m/e* 313 (3.0–14.0%). The base peaks, at *m/e*

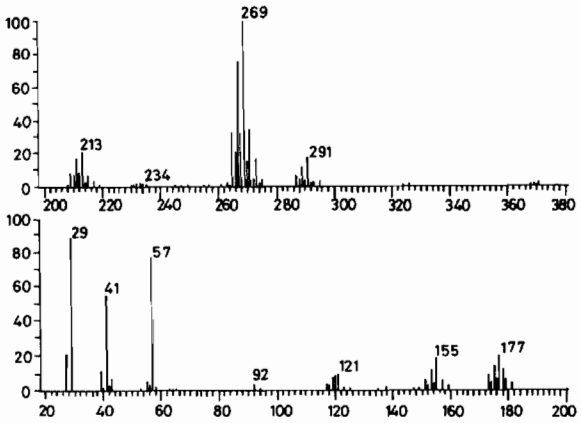
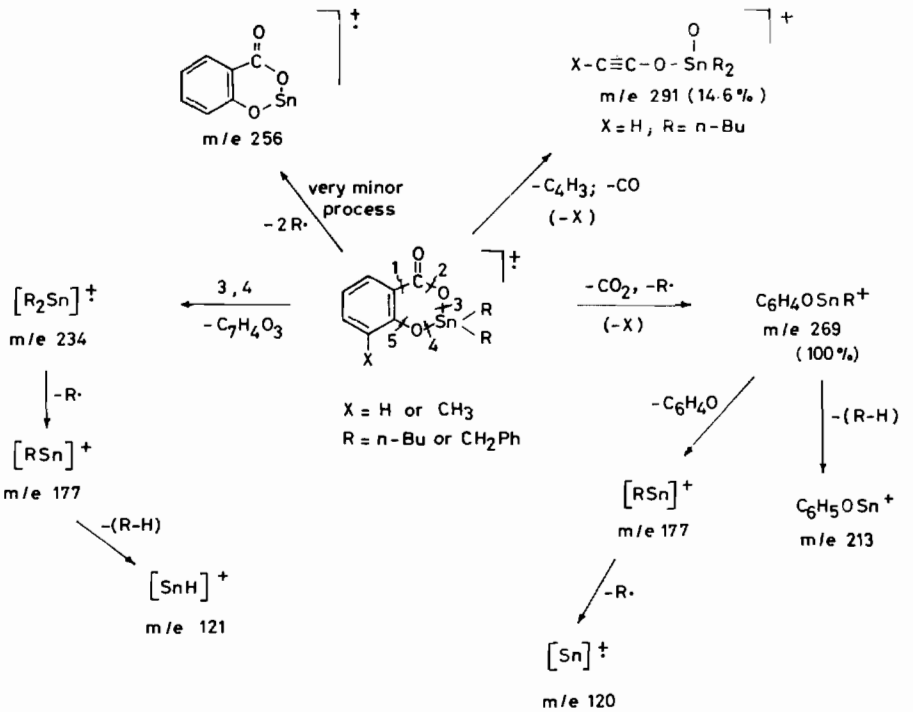


Fig. 1. Mass spectrum of compound **1**.

91, could result from an ion rearrangement (C_6H_5N). The spectra of the bis(salicylaldehyde)ethylenediimines **7** and **8** did not display their molecular ions. The compounds fragmented by loss of the alkyl radical (n-butyl or CH_2Ph) to give an ion at *m/e* 443 (24.2%) for compound **7** and an ion at *m/e* 477 (31.7%) for compound **8**. This was followed by the loss of the second alkyl radical (n-butyl or CH_2Ph) to give the ion noted at *m/e* 386 (1.9–5.5). Other informative fragmentations and rearrangements, from the ion at *m/e* 386, giving rise to ions at *m/e* 293, *m/e* 266, *m/e* 253, *m/e* 238, *m/e* 225,



Scheme 1. Probable fragmentation pathways of (2-oxybenzoyloxy)dialkyltin(IV) compounds.

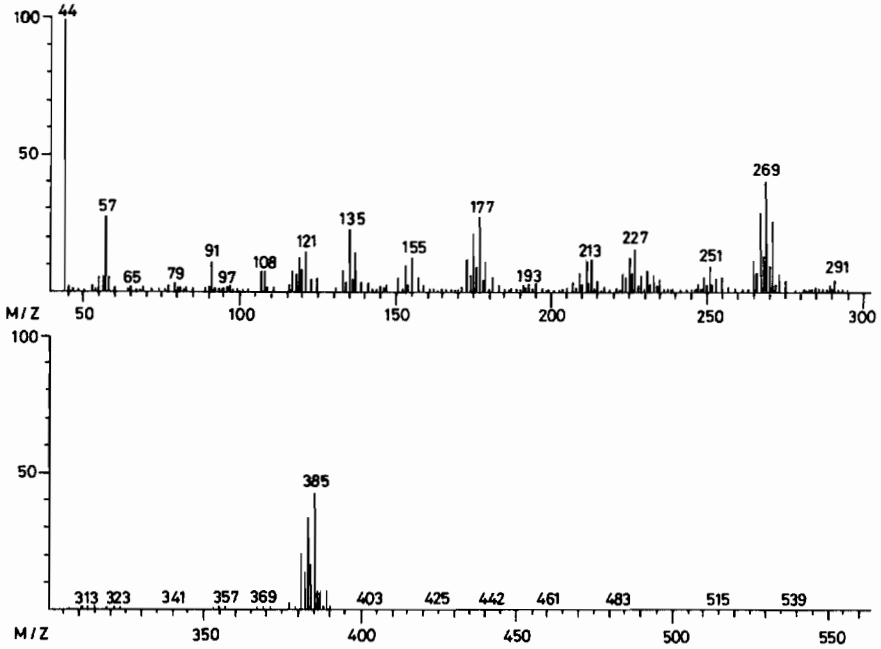


Fig. 2. Mass spectrum of compound **3**.

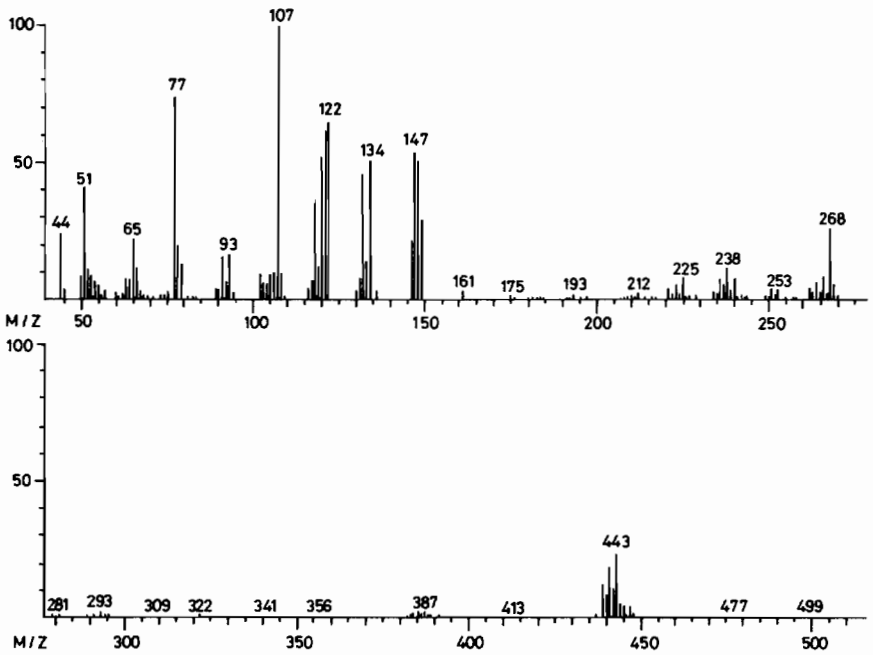
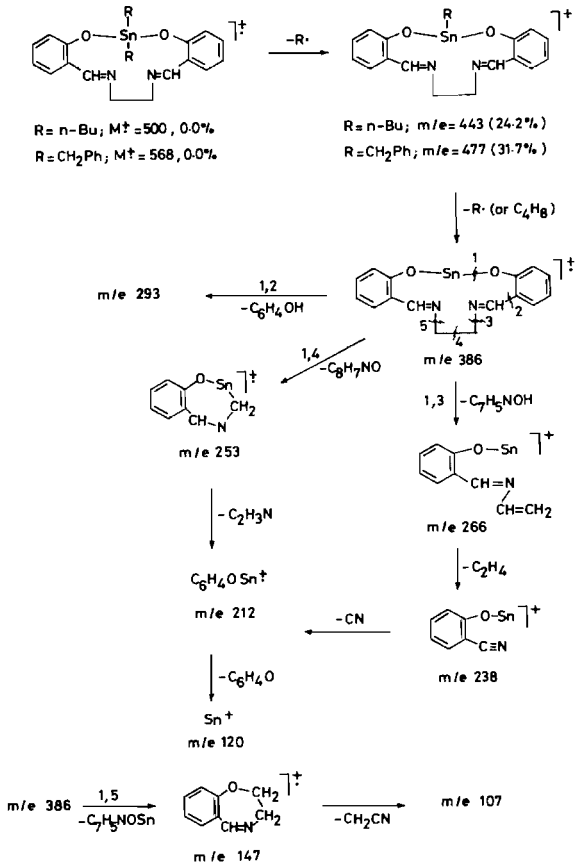


Fig. 3. Mass spectrum of compound **7**.

m/e 1212, *m/e* 147, *m/e* 134 and *m/e* 120 were noted. The suggested fragmentation routes giving rise to these ions are shown in Scheme 2 while the mass spectra of compounds **1**, **3**, 7 and **8** are shown in Figs. 1–4.

Antimicrobial Tests

The antibacterial and antifungial activities of the dialkyltin(IV) heterocycles are summarized in Table V. The compounds were screened for their antibacterial activity using nine microorganisms; namely, *E. coli, P. vulgaris, P. aeruginosa, Y. enterocolitica, K. pneumonia, S. marcescens* and *P. fluorescens* (gram negative), *B. subtilis* and *S. aureus* (gram positive). As for antifungal activity, five microorganisms were used; namely *C. albicans, A. niger, A. flavus, Botryodiplodia theobromae* and *T. mentagrophytes*. These microorganisms were chosen



Scheme 2. Possible fragmentation pathways of the dialkyltin-(IV)–bis(salicylaldehyde)ethylenediimines, 7 and 8.

since they are known commensals and pathogens of human beings. The results show that the compounds exhibit mainly antibacterial activity with little or no antifungal activity, with the concentration used (1000 μg/ml). Furthermore, with the bacteria strains, the compounds were mainly active against two strains; namely, *P. vulgaris* and *P. aeruginosa.*

Acknowledgements

We would like to thank the University of Ife Research Committee for financial assistance and Professor C. C. Lee of the University of Saskatchewan, Saskatoon for helping in the elemental analysis and the recording of the mass spectra.

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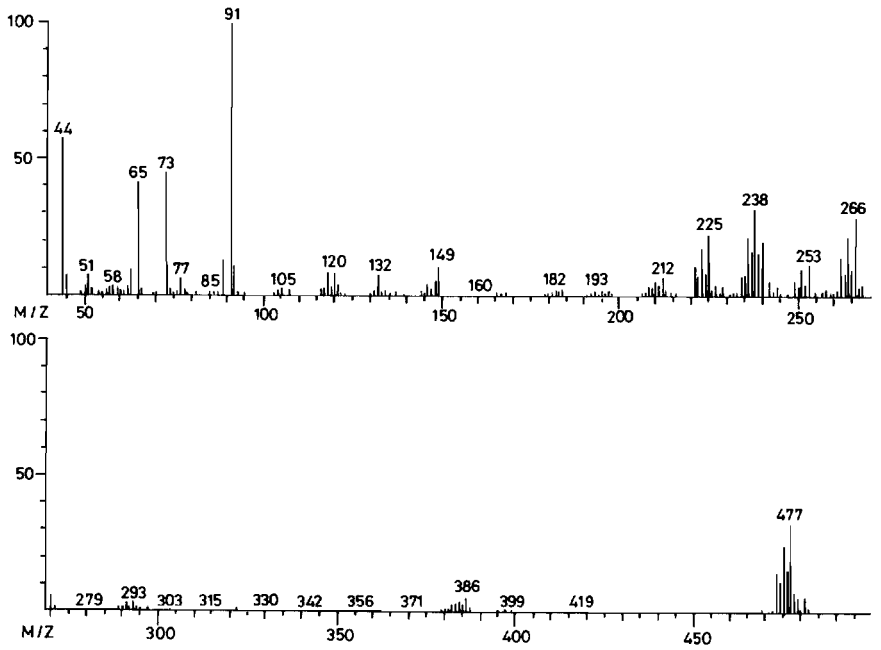

Fig. 4. Mass spectrum of compound 8.

TABLE V. Antimicrobial Activity of some Dibutyltin(IV)– and Dibenzyltin(IV)–Heterocycles[a]

Compound No.	Bacteria								
	E. coli (86)	*B. subtilis* (3610)	*S. aureus* (8588)	*P. vulgaris* (67)	*P. aeniginosa* (950)	*Y. entero-colitica*	*K. pneumonia* (3756)	*S. marcescens* (1377)	*P. fluorescens* (418)
1	N		N	25	22	13	18	13	13
2	10		N	22	20	15	10	15	
3		N		23	21	12	24	N	N
4		N		9	15	N	10	9	12
5	17	10	N	12	18	13	10	10	16
6	17	13	N	15	19	13	12	13	16
7		N	18	25	25	11			14
8			N	20	20	13	N		12
	Fungi								
	C. albicans		*A. niger*		*A. flavus*		*Botryodiplodia* sp.		*I. mentagrophytes*
1									
2									
3									12
4					N				N
5									15
6									18
7	12						13		N
8	13						10		N

[a]The zones of inhibition are in mm; N = narrow zone of inhibition.

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