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2'3'-ISOPROPYLIDENE 6-MERCAPTOPURINE RIBOSIDE(*S*-,*N*-)TRI-n-BUTYLTIN

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Summary

The synthesis and characterization of 2'3'-isopropylidene 6-mercaptopurine riboside(*S*-,*N*-)tri-n-butyltin is presented. Spectroscopic data indicate that the complex is five-coordinate with an Sn—S bond and N(7) coordination to tin. IR and ^{1}H NMR spectra indicate association via CH_2OH --- N(1) intermolecular H-bonding.

Heterocyclic ligands such as 2-mercaptobenzothiazole and 2-mercapto-4,6-hydroxy-pyrimidine have been shown to react readily with triorganotins under mild conditions and the ligands may bind as either the thiol or the thione form [1]. No identifiable products however, were obtained when thiouracil or 2-amino-6-mercaptopurine were allowed to react under similar conditions. Impure products could be obtained in boiling ethanol or by refluxing in toluene [2].

Our interest in heterocyclic ligands stems from (i) a need to evaluate the influence of tautomerism on the reactivity of -SH and -NH groups towards organotins, and (ii) the likelihood that organotins may bind to S,N groups in biological systems. The ligand 2'3'-isopropylidene-6-mercaptopurine riboside is useful for studies relating to these aspects. A triorganotin may form either a four-coordinate complex through bonding to sulfur or a five-coordinate complex through additional N or O coordination. Sulfur and N-7 coordination by 6-mercaptopurines has been observed in a number of complexes [4,5]. We report here the synthesis and characterization of the first trioganotin derivative of 2'3'-isopropylidene-6-mercaptoriboside, and propose a structure based on NMR, IR and UV spectra.

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Experimental

The complex was prepared by adding 0.67 g (2.06 mmol) of 2'3'-isopropylidene 6-mercaptopurine riboside (Aldrich) to 30 cm^3 $CHCl_3$ followed by 0.62 g (1.03 mmol) bis(tributyltin) oxide (Alfa). The mixture was stirred for 1—3 h. The solvent was evaporated off in an air stream, the product dissolved in 50 cm^3 methanol and stirred for ca. 1 h after which the methanol was air evaporated. The thick, clear oil was dried in a vacuum desiccator for a week. Analysis Found: C, 48. 67; H, 7.11; N, 8.2; S, 5.1; Sn 20.1, $C_{25}H_{42}O_4H_4SSn$ Calcd.: C, 48.96; H, 6.89; N, 9.14; S, 5.23; Sn, 19.36%. The yield was essentially quantitative. The product appears to be thermally stable at room temperature and is soluble in all common organic solvents.

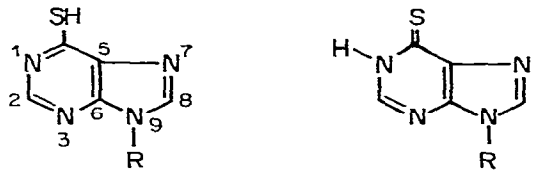
Infrared spectra were obtained using a Perkin-Elmer 457 instrument calibrated with polystyrene film and UV spectra were obtained from $CHCl_3$ solutions with a Varian 634 instrument.

The ^1H spectra were recorded at ambient temperature using a 90 MHz Perkin-Elmer R32 instrument. For ^{13}C NMR spectra, the ligand was dissolved in DMSO-d_6 and the complex in $CDCl_3$ and the spectra were obtained using a JEOL-PFT-100FT spectrometer as described previously [3].

Results and discussion

The compound has been characterized by chemical analyses, ^{13}C and ^1H NMR, IR and UV spectroscopy. A n-Bu_3Sn-S complex with nitrogen coordination is indicated by the ^{13}C NMR spectrum. The αC chemical shift may be compared to that in other compounds containing similar bonding, and the ^1J value is also similar (See Table 1).

In the IR spectrum of the complex, the broad peaks observed in the 3000—2600 cm^{-1} region for the ligand are no longer present. This shows loss of the SH or the NH proton from the tautomers:



Thiol Thione

(R = Riboside)

Bands at 590 cm^{-1} and 515 cm^{-1} are predominantly ν(Sn—C) with some overlapping from ligand peaks. The bands which have shifted relative to those of the free ligand are shown in Table 2 (not all bands listed).

The vibrational modes associated with the purine ring (and the ribose portion) are shifted on compound formation. The shift in ν(O—H) is indicative of strong H-bonding. No evidence for Sn ← O coordination can be obtained from IR or NMR data. The changes in the purine ring vibrational modes are likely to be the result of mass effects from Sn ← N coordination. The changes

TABLE 1

^{13}C NMR RESULTS

Compound	αC Shift [a]	$^1J(^{119}Sn—^{13}C)$	^2J	^3J
Title complex	16.1	343	21	—
n-Bu_3Sn(2-mercaptobenzothiazole)	16.4	336	22	62
n-Bu_3Sn(2-thiol 5-nitropyridine)	16.3	356	22	78
n-Bu_3Sn(2-thiol pyridine oxide)	19.0	361	—	63
Other shift values	(i) Organotin group:			
βC = 28.8, γC = 27.0, δC = 13.7				
	(ii) Ligand:			
166.6, 150.0, 146.9, 142.0 (134.8?), 113.9, 93.8, 86.3, 83.5				
81.7, 63.2, (28.3?), 27.5, 25.2				

[a] Shift values are in ppm relative to internal TMS.

associated with the ribose portion may result from stronger H-bonding involving the -CH_2OH group. A band at 638 cm^{-1} is assigned (tentatively) to ν(Sn ← N) [8].

The ^1H NMR spectra of the complex and ligand (Fig. 1) differ significantly. The shifts to higher field of the C-2 and C-8 protons indicate nitrogen coordination. Changes in the riboside proton chemical shifts, and the concentration dependence of all proton chemical shifts, suggests intermolecular association via H-bonding. The UV spectra of ligand and complex are consistent with Si ← N coordination. The ligand band centred at 340 nm (broad) shifts on compound formation and is present as a narrow strong band at 310 nm with a shoulder at 303 nm. These changes are similar to those observed between the UV spectra of 2-thiol-5-nitro pyridine and its di-n-butyltin complex which contains Sn—S and Sn ← N bonding [9].

The figure below shows the changes in the C-2 and C-8 protons both on compound formation and on dilution. The shift to higher field is probably due to

TABLE 2

INFRARED SPECTRA

Ligand (cm^{-1})	Complex (cm^{-1})	Assignment	Reference
3400m(br)	3290m(br)	ν(O—H)	
1612s, 1593s	1568vs	vibr. of purine	6, 7
1583s			
1417s	1425s		
1430w			
1209s	1220(sh), 1203s		
1155m	1142m		
1100(sh), 1089s 1072s, 1055s	1100s }	degenerate vibr. of C—C(—O)—C in ribose	6
880m, 868m	875(sh)		
663w, 652m	670m, 650m	ribose system degenerate vib.	6
	638m	ν(Sn—N) (?)	8

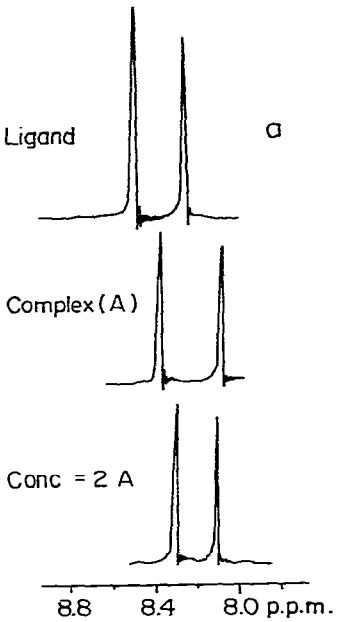


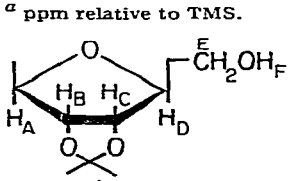
Fig. 1. ^{1}H NMR of the complex and the ligand.

TABLE 3

^{1}H NMR SPECTRA OF COMPLEX AND LIGAND

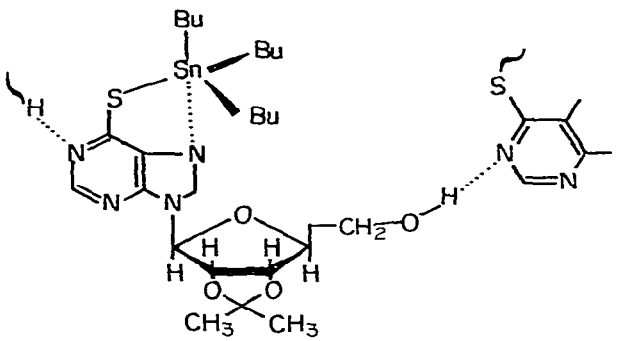
Chem. shift [a]	Peak pattern	Signal sep. (Hz)	No. of protons	Assignment
Complex				
5.91	doublet	^1J = 3.2	1	A
5.81—5.91	quartet	3.2, ca. 9	1	B + C + D
5.11	4-peaks	—	2	
4.49	broad, single	—	1	E
3.89	broad, 4 peaks	—	2	F
1.63	single	—	3	CH_3
8.35	single	—	1	C-2
8.03	single	—	1	C-8
Ligand				
6.14	doublet	^2J = 2.8	1	A
5.34, 5.27	two doublets	2.8, ca. 6	1	B (?)
5.09	broad triplet	ca. 4	1	F
5.00, 4.93	two doublets	2.8, ca. 6	1	C (?)
4.28	six peaks	—	1	D (?)
3.57	broad triplet	ca. 4	2	E
3.32	broad single	—	3	(N—H, S—H?)
1.55	single	—	3	CH_3
1.34	single	—	3	CH_3
8.49	single	—	1	C-2
8.24	single	—	1	C-8

[a] ppm relative to TMS.



coordination by N-7 to tin, while the change on dilution (downfield for C-2 proton) may result from a disruption of H-bonding involving N-1.

The spectra of the riboside portion has changed on compound formation; the values are compared in Table 3. Vicinal coupling constants are sensitive to changes in the dihedral angle [10], while changes in the apparent chemical shifts may arise from a change in the relative orientation of the purine ring. An analysis of the four-spin system, and a study of the solvent-concentration effects is necessary before quantitative deductions may be drawn. The data



presented is consistent with the structure shown: a five-membered chelate ring involving N-7 to tin coordination, and H-bonding between N-1 and the hydroxyl group.

Acknowledgement

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