Molecular assemblies of organooxotin compounds

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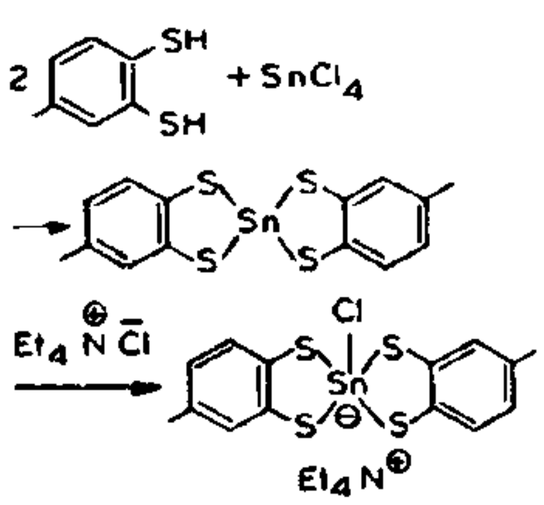
Several new structural forms of tin have been discovered recently. Most of these contain a distannoxane unit as the fundamental building block. In this account we review the reactions of mono-, di- and triorganotin precursors with carboxylic and phosphorus-based acids, and discuss the reaction pathways followed and the structures of the tin clusters.

TRADITIONALLY research in organotin chemistry has been centred around the utility of tin derivatives in organic synthesis[1]. Trialkyltin hydrides, for example, have been studied extensively and are finding a wide range of application in a number of organic reactions. With the advent and ready availability of powerful structural techniques, such as multinuclear NMR and single-crystal X-ray methods, a number of other aspects of tin chemistry are also being investigated in recent years. In the past few years many hypervalent tin compounds have been synthesized. A typical synthesis is as follows:



Structure solution of several such derivatives has shown conclusively that, depending upon the substituents on the tin atom, the pentacoordinated geometry varies from trigonal bipyramidal through intermediate structures to square pyramidal[2,3]. This variation follows the traditional low-energy 'Berry coordinate' analogous to isoelectronic species derived from phosphorus[4] and silicon[5].

Another facet of tin chemistry that is becoming increasingly important is its cluster chemistry. It is being shown that organotin units can be linked in a number of ways affording a variety of structures. Most of these are based on a stannoxane [Sn–O] or a distannoxane $\left[\begin{smallmatrix} Sn-O \\ | \quad | \\ O \quad Sn \end{smallmatrix}\right]$ framework. In the following account some recent findings in this burgeoning area are presented. Emphasis is laid on illustrating representative examples.

Triorganotin derivatives

Triorganotin compounds are important biochemically[6]. Many of them possess antifungal activity. Some of them are toxic to mammals. Studies have shown that the R_3Sn unit has a site-specific action on the oxidative phosphorylation process. While the nature of the active site has not been elucidated in detail, research carried out on rat liver mitochondria suggests the presence of a low-affinity and a high-affinity sites[7,8]. From Mössbauer studies it has been inferred that a five-coordinate tin atom is found at the high-affinity binding site[9–11]. With a view to elucidating the active site, a number of triorganotin derivatives have been studied. The synthesis involves the use of R_3SnCl, $R_3Sn–O–SnR_3$ or R_3SnOH and an organic carboxylic acid R′COOH or its silver salt R′COOAg as reagents:

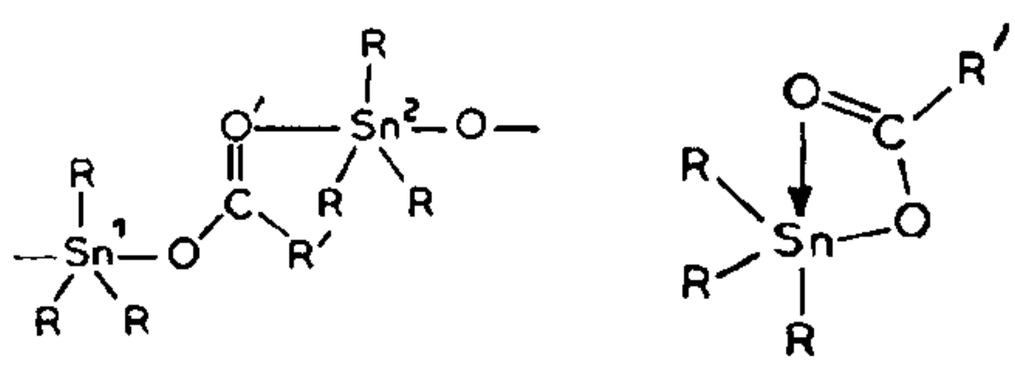
$$R_3SnOH + R'COOH \rightarrow R_3SnOCR' + H_2O$$

$$R_3Sn–OSnR_3 + 2R'COOH \rightarrow 2R_3SnOCR' + H_2O$$

$$R_3SnCl + R'COOAg \rightarrow R_3SnOCR' + AgCl$$

(R and R′ are alkyl or aryl).

Detailed structural studies for over 30 derivatives are now available. From these it is possible to classify the structures as belonging to two types:

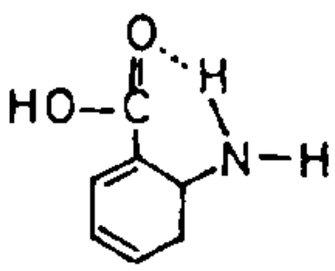


Chain structure (A) Discrete structure (B)

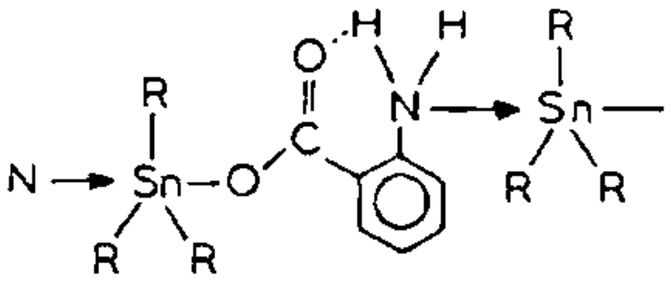
The discrete structure is a monomeric form[12] with tin being five-coordinate and in a distorted trigonal bipyramidal geometry. In contrast, the chain structure is a polymeric aggregate[13]. Here also the tin is

essentially pentacoordinate and the local environment around tin is trigonal bipyramidal, with the axial positions being occupied by oxygen atoms (labelled O′ and O). There is a weak bonding interaction between O′ and Sn′ resulting in some distortion of the structure. The Sn–O and Sn–O′ distances do not differ very much (Table 1). A recent crystallographic analysis has revealed that there is a constant repeat distance of 5.19 ± 0.21 Å in these polymers, which is insensitive to the types of substituents on tin or the carboxylic acid[14].

A variation in the chain structure is found for derivatives where the carboxylic acid acyl group is tied up in intramolecular hydrogen bonding; for example in glycine[15] and anthranilic acid[16] (see below). This situation renders the nitrogen atom more basic and leads to chains as follows (C):



Anthranilic acid

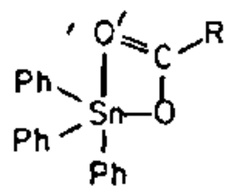
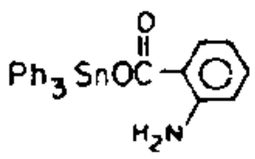
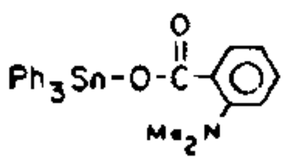
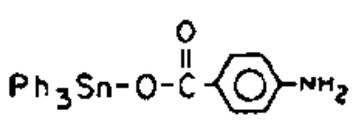
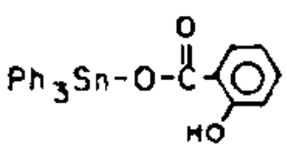
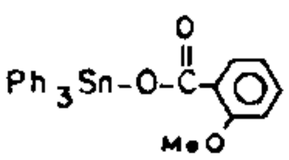
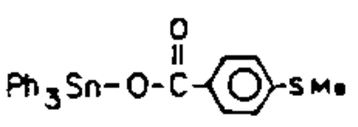
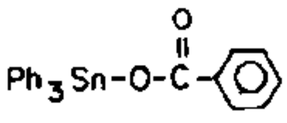
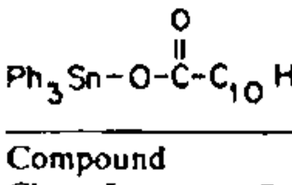
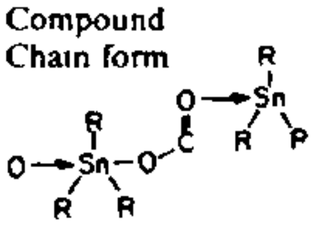
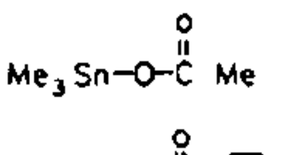
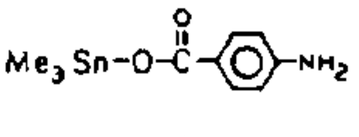
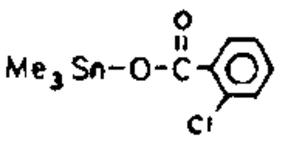
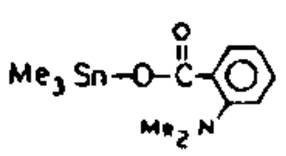
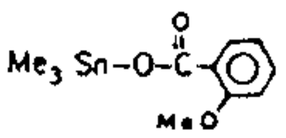
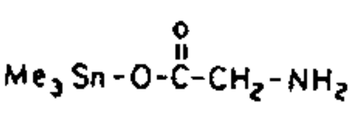
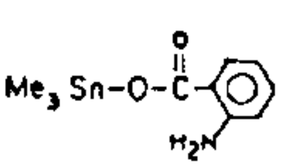
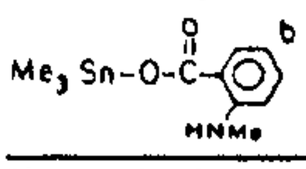


Chain structure (C)

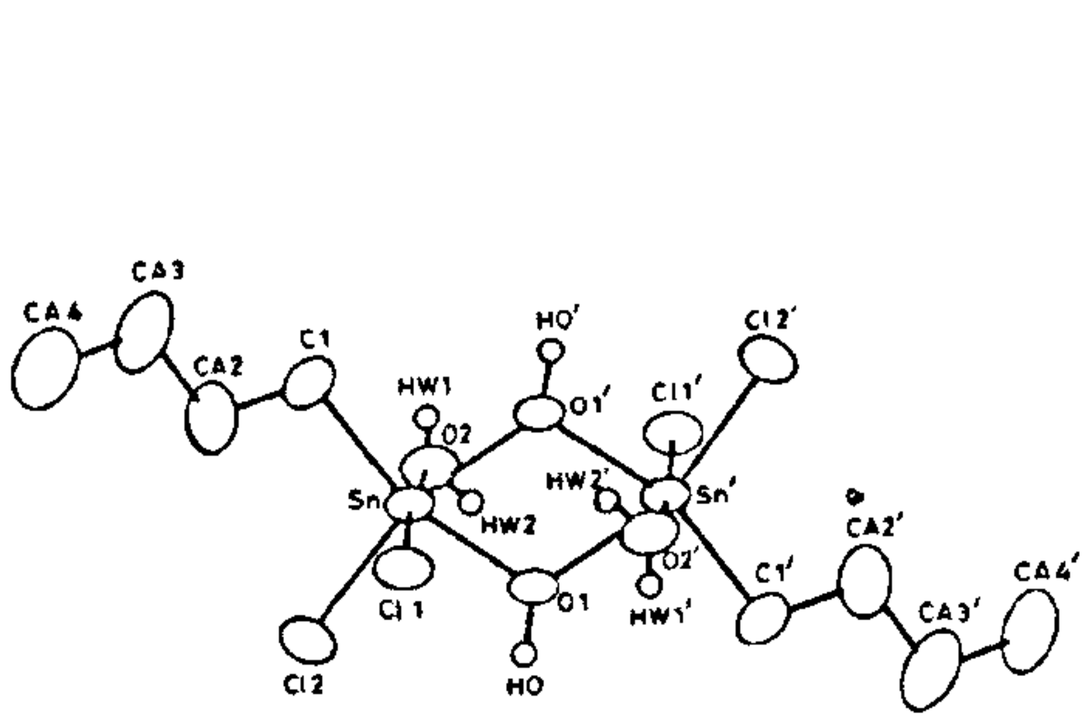
Although polymeric structures exist in the solid state, in dilute solutions they fall back to monomeric structures possibly containing weak intramolecular interaction between the acyl C=O and Sn leading to a situation similar to that found in 'discrete structures'. Whereas the Sn–O bond lengths do not differ much in the chain form, in the discrete form containing one oxygen in equatorial and the other in the axial position, there is considerable difference in the bond lengths (Table 1). Mössbauer data are also useful in distinguishing between the two structural forms: the quadrupole splitting parameter falls in the range 2.30–2.55 mm s^{-1} for discrete forms, whereas it is 3.59–3.74 mm s^{-1} for normal chain forms[13a].

The discrete structures are formed only when the substituents on tin and the carboxylic acid are aromatic. In all other situations 'chains' prevail. This has been rationalized keeping in view the principles of pentacoordination. Thus, in the trigonal bipyramidal geometry of the discrete form, the carboxylate group spans the axial-equatorial position because of geometric constraints. This leads to placing an alkyl or aryl group in the other axial position. While the aryl group has an electronegativity comparable to that of chlorine and therefore can occupy an axial position, the alkyls being less electronegative favour equatorial geometry, leading to predominantly chain forms[12b]. However, the available data clearly suggest that there probably are other factors that tip the delicate balance between the two structural forms.

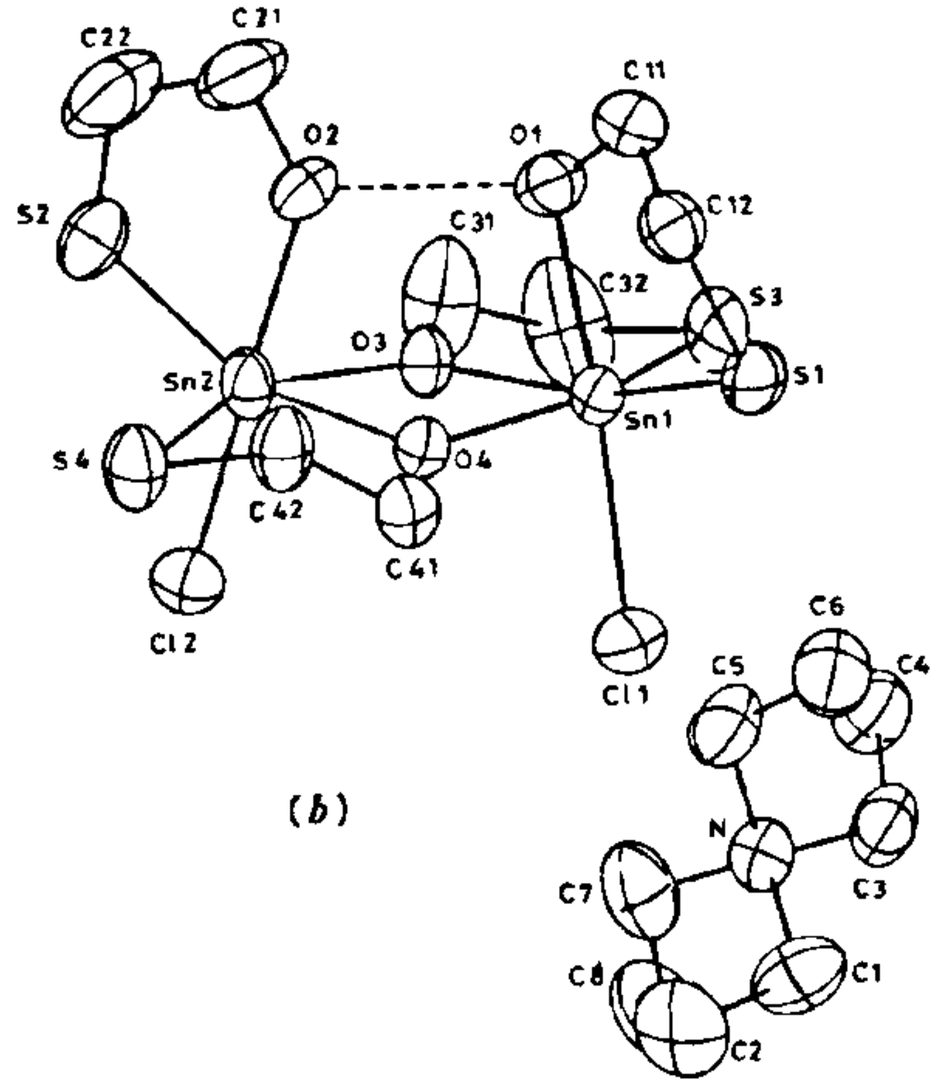
Table 1. Structural parameters for triorganotin carboxylates.

Compound	Bond lengths (Å) Sn–O	Sn O′	Δ	Ref.
Discrete form 				
	2 043	2 823	0.780	12a
	2.115	2 564	0 449	12a
	2 072	2.629	0 557	12a
	2.083	3.071	0 988	12b
	2 054	2.781	0 727	12b
	2 060	2 783	0.723	12b
	2.074	2.695	0.621	16
	2 068	2.711	0.643	16
Chain form 				
	2 140	2.530	0 390	13b
	2 169(5) 2 168(5)	2 477(5) 2 416(6)	0 208 0 248	16 16
	2 200	2 414	0 214	16
	2 201	2 426	0 225	16
	2 208	2.381	0 173	16
	2 140	2 530	0 390	15
	2 146	2 781	0 635	16
	2 128	3 162	1 034	16

[a] Two molecules are present in the asymmetric unit
[b] Here the chain is propagated through 'O' and 'N'. The (Sn O') bond length given refers to Sn N bond length



(*a*)



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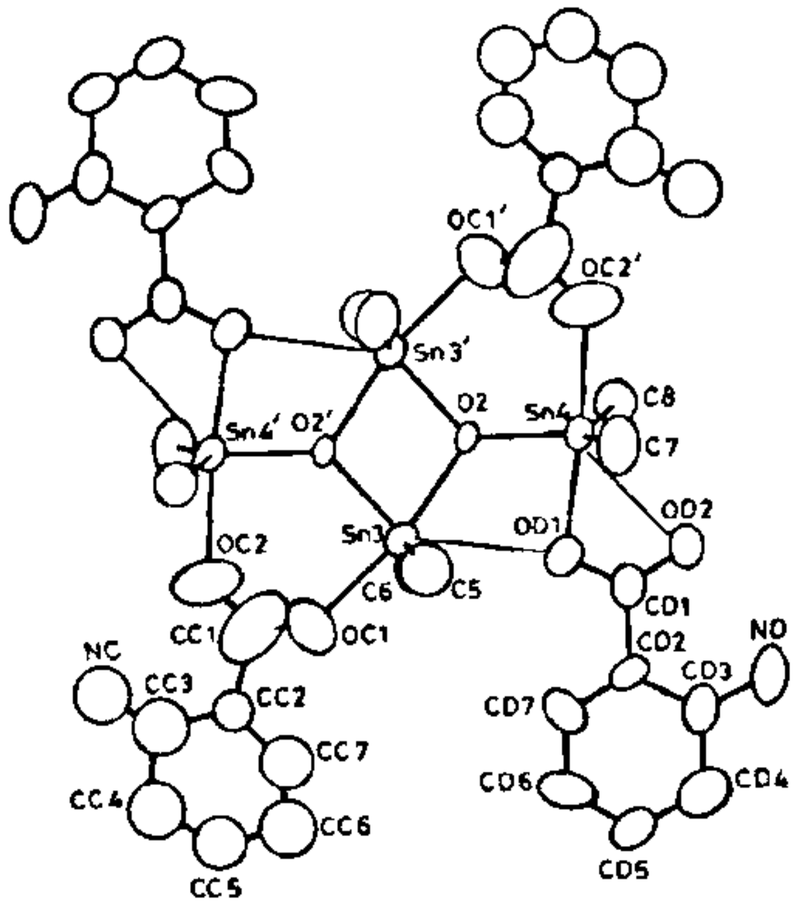
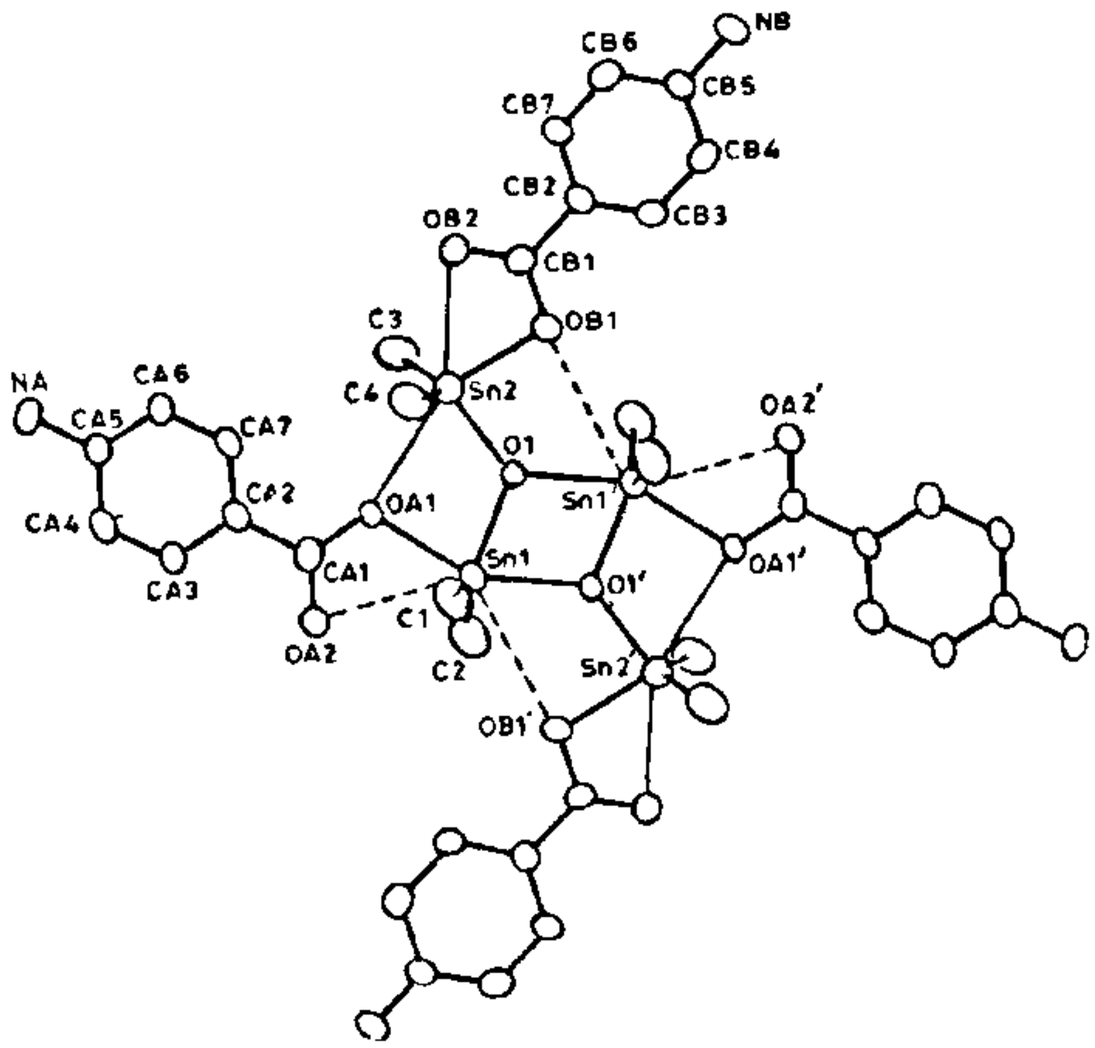


(*c*)



(*d*)

Figure 1. Distannoxane structures of (*a*) $[BuSnCl_2(OH)\ H_2O]_2$ ('D') and (*b*) $[(C_2H_4OS)_2SnCl]_2[H^+][Et_4N]^+$, and ladder structures of (*c*) $[(Me_2SnO_2C_6H_4\text{-}O\text{-}NH_2)_2O]_2$ ('G') and (*d*) $[(Me_2SnO_2C_6H_4\text{-}p\text{-}NH_2)_2O]_2$ ('G') [Reprinted with permission from refs. 18 and 20 (Copyright 1988, American Chemical Society)].

Clusters based on diorgano- and monoorganotin groups

Organooxotin clusters formed from monoorganotin and diorganotin groups are based on the 4-membered distannoxane ring unit $\left[\begin{smallmatrix} Sn-O \\ | \quad | \\ O-Sn \end{smallmatrix}\right]$. These are the structural units of products formed from hydrolysis reactions of a number of mono-[17,18] and diorganotin halides[19]:

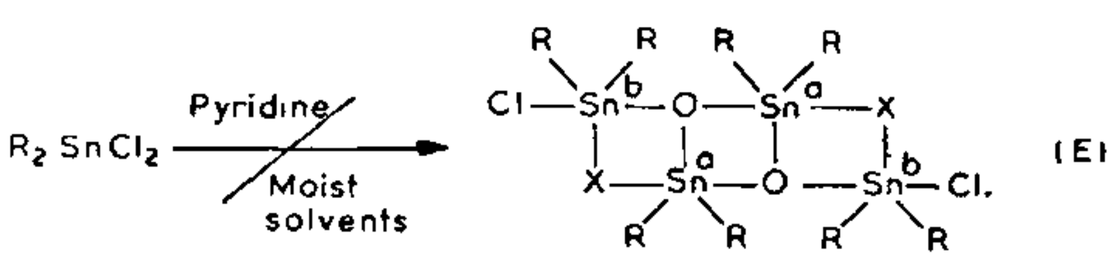
$$R\,SnCl_3 \xrightarrow[\text{Solvents}]{\text{Moist}} \left[\begin{smallmatrix} Cl & R & Cl & & H \\ & | & & & | \\ & Sn & & & O \\ H_2O & & & & \\ & O & & & OH_2 \\ & | & & & | \\ H & & Sn & & \\ & Cl & | & Cl & \\ & & R & & \end{smallmatrix}\right] \qquad (D)$$

This simple distannoxane ring is also formed from reactions of inorganic tin halides[18]:

$$2SnCl_4 \cdot 5H_2O + 4Na_2[S\,CH_2CH_2O] + Et_4N^+Cl^- \rightarrow [(C_2H_4OS)_2SnCl]_2\,H^+\,Et_4N^+ + 7NaCl + NaOH + 4H_2O$$

The product formed is dimeric, and has the distannoxane ring Sn_2O_2 with an octahedral arrangement of ligand atoms about tin (IV) (Figure 1).

Similarly diorganotin dihalides also are easily hydrolysable, affording products containing 'ladder' or 'staircase' structures[19]:



(E)

(R = alkyl or aryl, X = OH or Cl

In these structures (E) tin is present in a pentacoordinate state in a pseudotrigonal bipyramidal geometry. The central tins (a) are distinguishable from terminal tins (b) by ^{119}Sn NMR.

Ladders are also formed in the reactions of diorganotin oxides with carboxylic acids. Reaction of R_2SnO with two equivalents of carboxylic acid affords simple monomeric diesters with tin in an octahedral geometry[20]:

$$R_2SnO + 2R'COOH \rightarrow R_2Sn(O_2CR')_2. \qquad (F)$$

However, these diesters are prone to ready hydrolysis affording organooxy carboxylates that possess ladder structures[20-23]:

$$4R_2Sn(O_2CR')_2 + 2H_2O \rightarrow [(R_2SnO_2CR')_2O]_2 + 4R'COOH. \qquad (G)$$

The oxy carboxylates (G) are also synthesized by a direct 1:1 reaction between R_2SnO and the carboxylic acid[20]:

$$4R_2SnO + 4R'COOH \rightarrow [(R_2SnO_2CR')_2O]_2 + H_2O. \qquad (G)$$

This reaction has been shown to be very general[24]. The resulting oxycarboxylate (G) has a 'ladder' structure with two types of 'tin'. One type forms the central $(Sn-O)_2$ ring and the other type is coordinated to the oxygen atom of the distannoxane ring. The carboxylic acid group is anisobidentate and/or forms a symmetrical bridge between the two types of tins (Figure 1). Table 2 summarizes some of the structural details.

Clusters from stannonic acid/carboxylic acid or phosphinic acid reactions

A wide range of clusters are found to form from relatively simple reactions between stannonic acids, RSn(O)OH, and R'COOH or $R'_2P(=O)OH$. This aspect has been reviewed. recently[25].

It was discovered a long time ago that organotin tricarboxylates, $RSn(OCR')_3$, hydrolyse rapidly to give

Table 2. Structural details for tin clusters based on distannoxane unit.

Compound	Structure[a]	Frame work Sn–O distance (Å)	Bridge Sn–O distance (Å)	Ref.
$[BuSn(OH)(OH)_2Cl_2]_2$	Distannoxane	2.108	—	18
$[EtSn(OH)(OH)_2Cl_2]_2$	Distannoxane	2.110	—	16
$[(C_2H_4OS)_2SnCl]_2[H]Et_4N$	Distannoxane	2.114	—	18
$[((CN)_2C_2S_2)SnOH]_2[Et_4N]_2$	Distannoxane	2.128	—	18
$[(Me_2SnO_2CC_6H_4\text{-}O\text{-}NH_2)_2O]_2$	Ladder	2.096	2.257	20
$[(n\text{-}BuSn(O)O_2CR)_2\text{-}(nBuSnO_2CR_3)]_2$, R = Ph	Ladder	2.067	2.2085	32
R = Me	Ladder	2.060	2.210	32
$[(n\text{-}BuSn(O)O_2CPh)_2\text{-}n\text{-}BuSn(Cl)(O_2CPh)_2]_2$	Ladder	2.063	2.166	30
$[PhSn(O)OCC_6H_{11}]_6$	Drum	2.079	2.153	29
$[BuSn(O)O_2CC_5H_9]_6$	Drum	2.086	2.166	30
$[BuSn(O)O_2CC_6H_4NO_2]_6 \cdot 3C_6H_6$	Drum	2.087	2.195	32
$[(n\text{-}BuSn(OH)O_2PPh_2)_3O]\text{-}[Ph_2PO_2]$	Oxygen-capped cluster	2.128 2.075	2.122	33
$[(n\text{-}BuSn(O)O_2P(C_6H_{11})_2]_4$	Cube	2.108	2.142	35
$[(n\text{-}BuSn(O)O_2P(t\text{-}Bu)_2)\text{-}(n\text{-}BuSn(OH)_2O_2P(Bu^t)_2)]_2[H][O_2P(Bu^t)_2]$	Crown	2.086	2.123	36

[a]The ^{119}Sn chemical shift ranges for the different structural types: distannoxane (−408.0); pentacoordinate ladder (−210.0, −220.0); hexacoordinate ladders (−523.0, −549.0, −622.0); drum (−488.0); cube (−466.0), O-capped cluster (−510.0), crown (−525.4); butterfly (−547.0).

compositions of the type $[RSn(O)O_2CR']_n$ (refs. 26–28). Recently it has been shown that RSn(O)OH reacts with a wide range of carboxylic acids to afford $[RSn(O)O_2CR']_6$ (ref. 25):

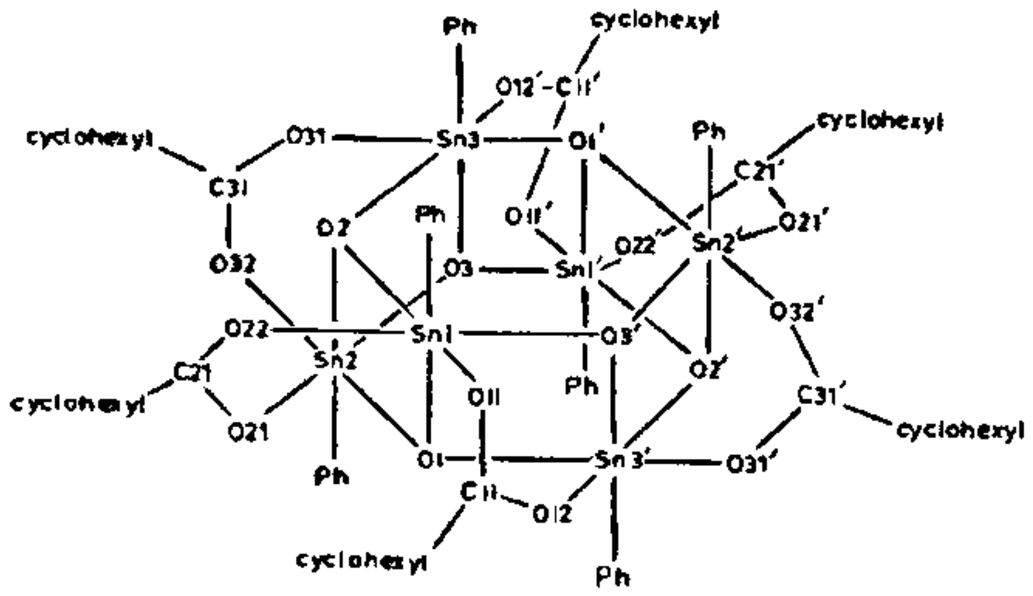
$$6RSn(O)OH + 6R'COOH \rightarrow [RSn(O)\overset{O}{\overset{\|}{O}}CR']_6 + 6H_2O. \quad (H)$$

The hexameric organooxytin carboxylate (H) has a novel drum structure (Figure 2) (ref. 29–31). The structure comprises two hexameric $(Sn–O)_3$ rings linked to each other. The faces of the drum comprise six distannoxane units. Each of the four-membered rings of the core is spanned by a carboxylate group that forms a symmetrical bridge between two tin atoms. The tin atoms, which are all chemically equivalent, are hexacoordinate, with the coordination sphere being completed by one alkyl group and two oxygen atoms from different carboxylate groups (Figure 2).

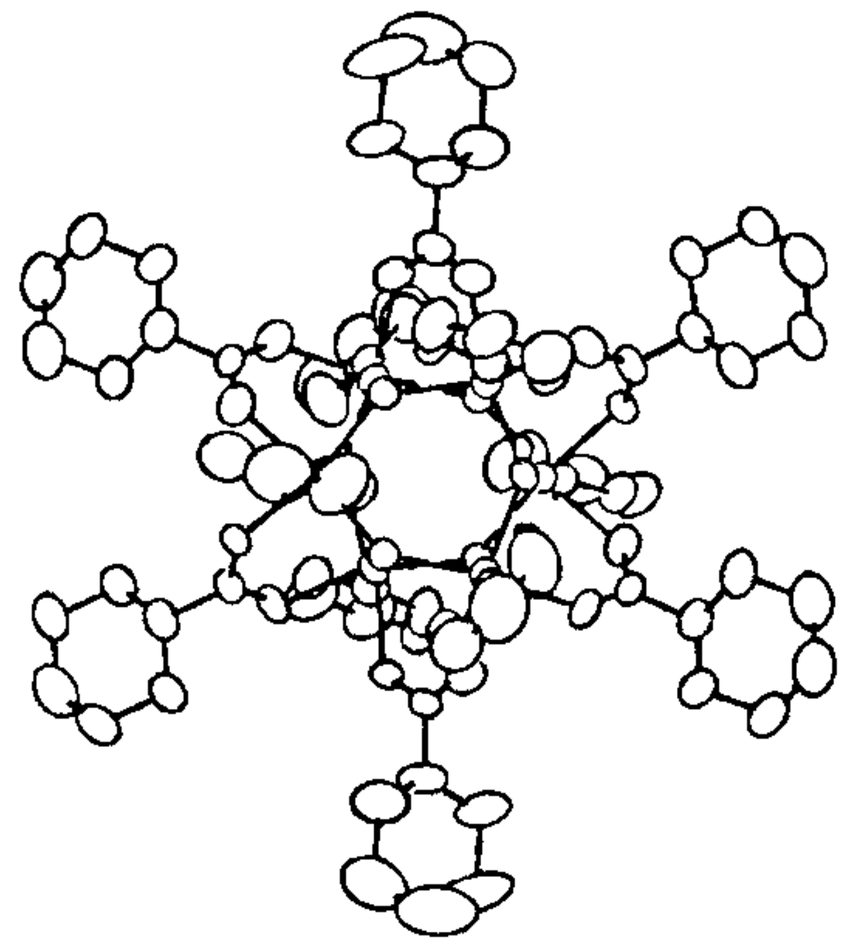
Reaction of $RSnCl_3$ with the silver salt of a carboxylic acid in a wet solvent or reaction of RSn(O)OH with an excess of carboxylic acid followed by controlled hydrolysis affords a 'ladder' product[30,32].

$$6RSnCl_3 + 10\,Ag^+R'CO_2^- + 4H_2O \rightarrow [(RSn(O)O_2CR')_2RSn(\overset{O}{\overset{\|}{O}}CR')_3]_2 + 10AgCl + 8HCl. \quad (I)$$

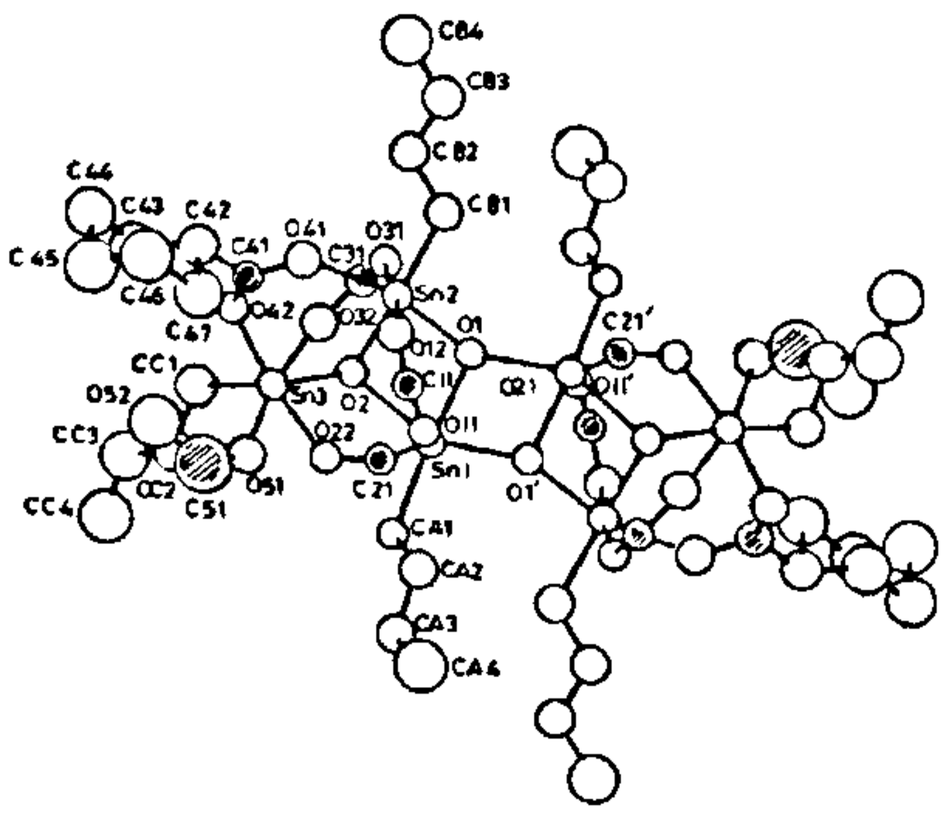
X-ray structures of several ladder forms reveal that the structure is essentially a 'drum' that is 'unfolded'. There are three chemically nonequivalent types of tin atoms, with the central tins being always hexacoordinate and the terminal tins being hexa- or heptacoordinate. Once again the carboxylic acids aid in forming a



(a)



(b)



(c)

Figure 2. *a* and *b*, Drum structures of $[PhSn(O)O_2CC_6H_{11}]_6$ ('H'); *c*, ladder structure of $[(n\text{-}BuSn(O)O_2CC_6H_{11})_2\text{-}nBuSn(O_2CC_6H_{11})_3]_2$ ('J'). Carbon atoms of only two of the cyclohexyl groups are shown. [Reprinted with permission from ref. 29 (Copyright 1985, American Chemical Society) and ref. 30 (Copyright 1987, American Chemical Society)].

symmetric bridge between alternate tin atoms[30,32] (Figure 2).

The 'drum' and 'ladder' forms are interconvertible in solution. Thus hydrolysis of the 'ladder' form leads to a 'drum' while addition of excess acid opens up the 'drum' and leads to the 'ladder'[30].

$$[(RSn(O)O_2CR')_2(RSn(O_2CR')_3)]_2 + 2H_2O \downarrow [RSn(O)O_2CR']_6 + 4R'COOH.$$

This interconversion can be readily studied by ^{119}Sn NMR, because, while the drum form shows only one signal (~480.0 ppm: all tins equivalent), the ladder form shows three signals (−523.0, −549.0, −622.0).

Clusters from phosphinic acids

Reactions of stannonic acids with phosphinic acids $R_2P(=O)OH$ lead to, apart from drums[31], clusters such as 'O'-capped[31,33,34], butterfly[34], cube[34,35], crown[36], and 'extended clusters'[36]. These are summarized in Scheme 1. Surprisingly the ladder form has not been isolated by this route. Most structures are formed by small, nevertheless significant variations in stoichiometries of the reactants. Thus, the 'O'-capped cluster is formed as follows[33]:

$$3n\text{-}BuSn(O)OH + 4\,Ph_2P(=O)OH \rightarrow [(n-BuSn(OH)O_2PPh_2)_3O][Ph_2PO_2] + 2H_2O. \quad (J)$$

It is noted (Figure 3) that the three distannoxane ring units in (J) are formed as a consequence of the presence of the unique capping oxygen atom. These three four-membered Sn_2O_2 rings contain the capping oxygen atoms and form a portion of the cube.

Whereas, upon heating, the 'O'-capped cluster leads to other structural forms, it appears that 'O'-capped cluster is the most stable hydrolysis product from other forms[33,34] (Scheme 1).

Finally, when bulky phosphinic acids such as dicyclohexyl phosphinic acid are allowed to react with stannonic acid in a 1:1 stoichiometry, only tetrameric forms containing cubic structures are formed instead of the usual hexameric form. It appears that this is primarily a result of steric factors[35] (Figure 3).

Conclusions and outlook

A number of structural forms based on either stannoxane or distannoxane units have been discovered recently. It is certain that several more would be delineated by subtle alterations in the reaction schemes. Efforts are under way in various research laboratories

$6RSn(O)OH + 6R'COOH \longrightarrow [RSn(O)OCR']_6$ (drum)

$6RSn(O)OH + X'SS\ R'COOH \xrightarrow{H_2O} [(RSn(O)OCR')_2RSn(OCR')_3]_2$ (ladder)

$3RSn(O)OH + 4Ph_2PO_2H \rightarrow [(n-BuSn(OH)O_2PPh_2)_3][Ph_2PO_2]$ (O-capped)

$4RSn(O)OH + 4C_6H_{11}PO_2H \rightarrow [RSn(O)OP(C_6H_{11})_2]_4$ (cube)

$4RSn(O)OH + 5Bu^tPO_2H \rightarrow [RSn(O)O_2P(Bu^t)_2(RSn(OH)_2O_2P(Bu^t)_2)]_2\ [H]\ [O_2P(Bu^t)_2]$ (crown)

$2RSn(O)OH + 4(C_6H_{11})_2PO_2H \rightarrow [RSn(OH)(O_2P(C_6H_{11})_2O_2]_2$ (butterfly)

Interconversions

$[RSn(O)OCR']_6 \underset{H_2O}{\overset{R'COOH}{\rightleftharpoons}} [(RSn(O)OCR')_2RSn(OCR')_3]_2$

Drum — Ladder

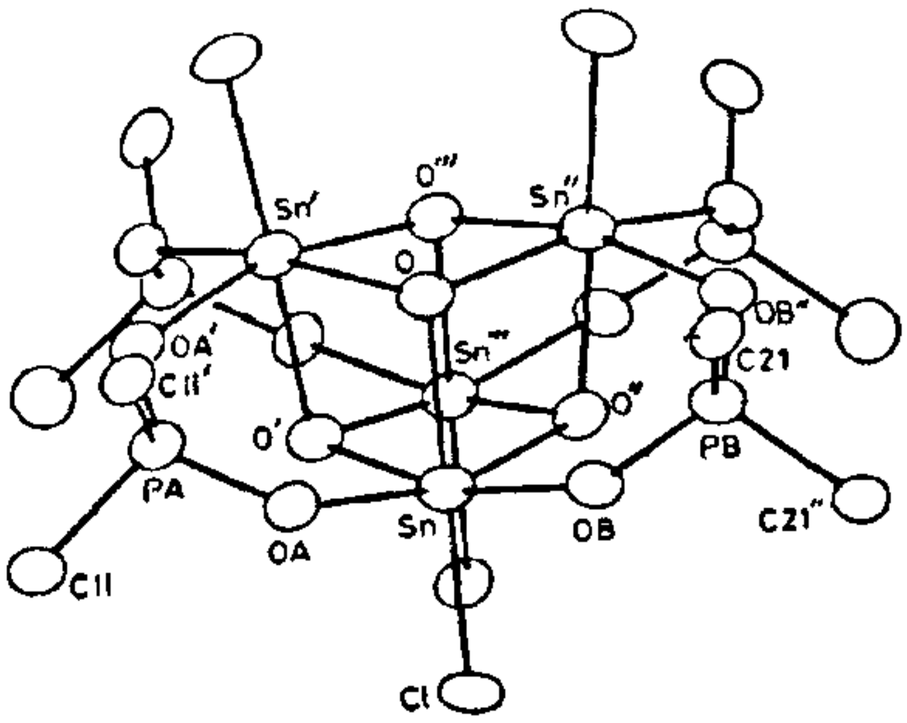
$[RSn(O)OPR_2]_4 \xrightarrow{H_2O} [(RSn(OH)O_2PR_2)_3O][R_2PO_2]$

Cube — 'O'-capped cluster

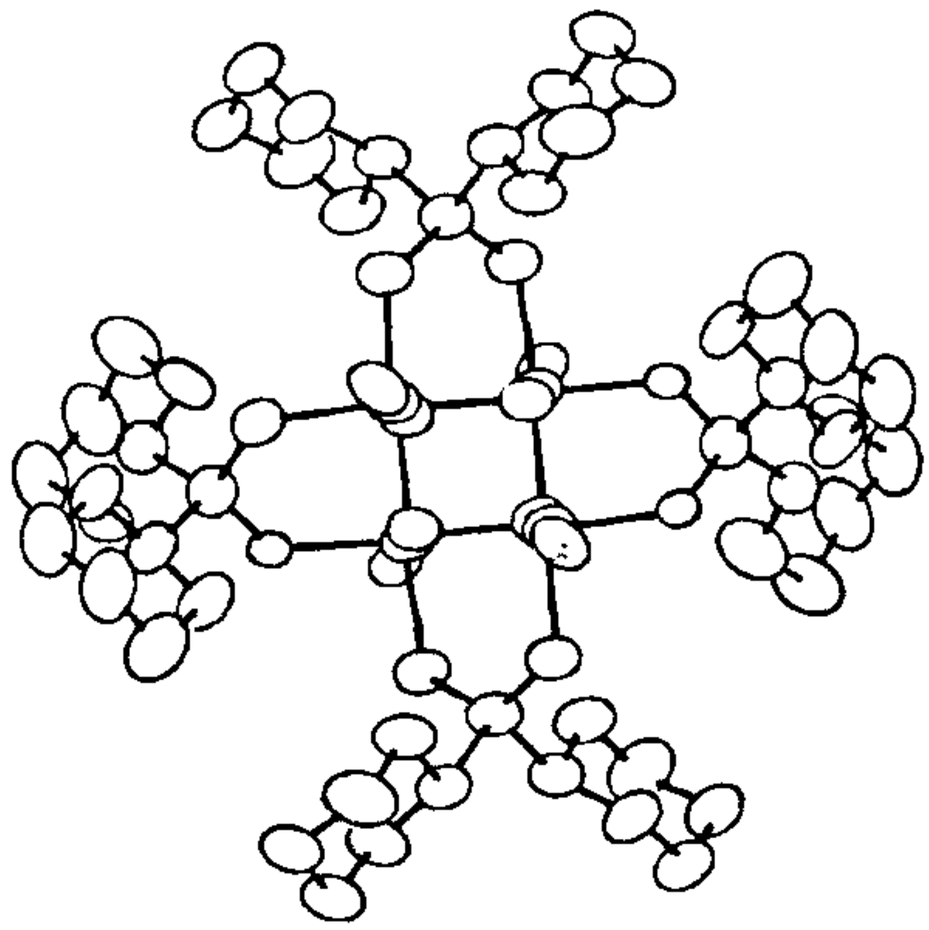
$2[(RSn(OH)O_2PR_2)_3O][R_2PO_2] \rightarrow [RSn(OH)(O_2PPh_2)_2]_2 + [RSn(O)O_2PR_2]_4$

'O'-capped cluster — butterfly — Cube.

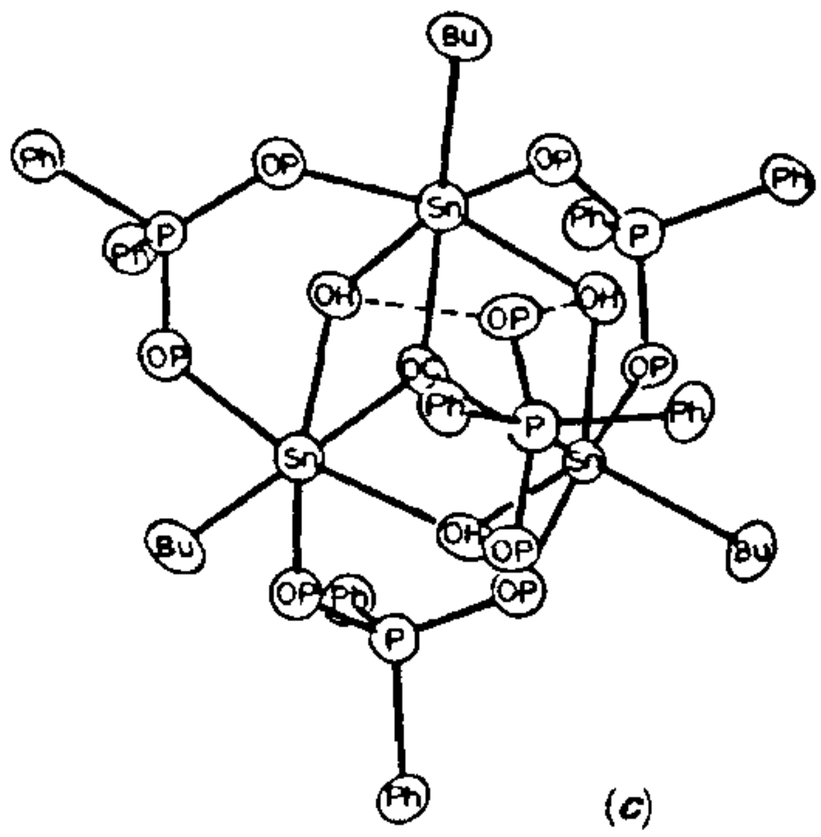
Scheme 1. Synthesis and interconversions of some distannoxane clusters.



(a)



(b)



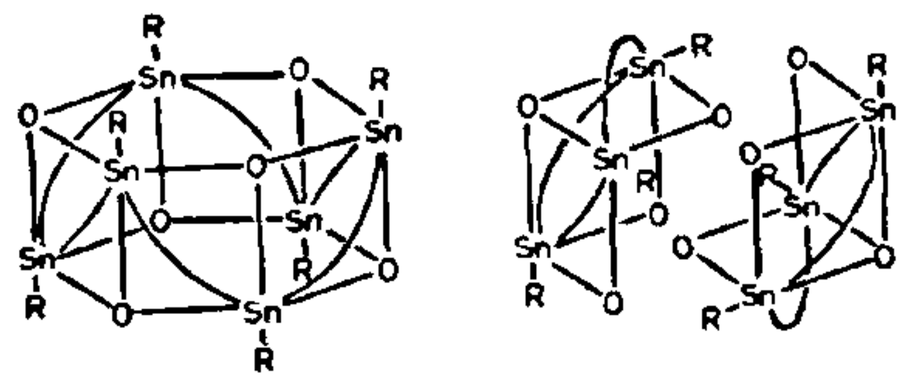


Figure 3. *a*, and *b*, Cube structure of $[BuSn(O)O_2P(C_6H_{11})]_4$; *c*, 'O'-capped structure of $[(BuSn(OH)O_2PPh_3)_3O][Ph_2PO_2]$ ('J'), *d*, Schematic of a drum indicating its relation to two 'O'-capped molecules. [Reprinted with permission from refs. 35 and 33 (Copyright 1987, American Chemical Society)].

to develop new synthetic routes, as well as to explore some of the possible catalytic applications of the tin clusters.

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ACKNOWLEDGEMENTS. We thank CSIR, New Delhi, for financial support. VC is especially thankful to Prof. R. R. Holmes in whose laboratory a major portion of the work has been carried out, in collaboration with Prof. R. O. Day and Mrs J. M. Holmes.

9 April 1990

RESEARCH ARTICLE

Rigid and flexible regions in lysozyme and the invariant features in its hydration shell

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Water-mediated transformations provide a useful handle for exploring the flexibility in protein molecules and the invariant features in their hydration shells. Low-humidity monoclinic hen egg white lysozyme, resulting from such a transformation, has perhaps the lowest solvent content observed in any protein crystal so far and has a well-ordered structure. A detailed comparison involving this structure, low-humidity tetragonal lysozyme, and the other available refined crystal structures of the enzyme permits the delineation of the relatively rigid, moderately flexible and highly flexible regions of the molecule. The relatively rigid region forms a contiguous structural unit close to the molecular centroid and encompasses parts of of the main β-structure and three α-helices. The hydration shell of the protein contains 30 invariant water molecules. Many of them are involved in holding different parts of the molecule together or in stabilizing local structure. Five of the six invariant water molecules attached to the substrate-binding region form part of a water cluster contiguous with the side-chains of the catalytic residues Glu-35 and Asp-52.

FLEXIBILITY of protein molecules[1-7] and the invariant features in their hydration shell[8-12] are problems of considerable current interest. Water-mediated transformations, first described in haemoglobin in the early days of protein crystallography[13,14] and recently shown by us to occur in many protein crystals[8,15,16], provide a useful handle for exploring these two related problems. In these transformations, the unit cell dimensions, the diffraction pattern and the solvent content of protein crystals change abruptly, typically in the relative humidity range 90–93%, when the environmental humidity is systematically varied[16]. In terms of composition, the difference between the native and the low-humidity forms is only in the amount of bulk water in the crystals. The change in the amount of bulk water, however, leads to significant changes in the hydration shell, which in turn cause structural perturbations in the protein molecule[8]. Withdrawal of a small amount of water from the solvent regions in the crystal, as in the water-mediated transformations outlined above, is perhaps the gentlest way to cause a structural transformation. The changes that accompany the transformation are therefore likely to correspond to the