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On the behaviour of organotin compounds with cyclodextrins Part 1. The complex between allyl-di-*n*-butyltin chloride and β-cyclodextrin

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Abstract

A complex between allyl-di-*n*-butyltin chloride and β-cyclodextrin has been obtained in good yield by the coprecipitation method in aqueous solution at room temperature. The stoichiometry, determined by NMR and elemental analysis, was found to be 1:1. The complex was characterised by means of several techniques, such as TGA, DSC, ESIMS, SEM, NMR, and Mössbauer spectroscopy. On the basis of these results, we suggest a structure for this complex where the tin derivative is included in the cyclodextrin, replacing about six of the ca. nine water molecules coordinated to it and where the metal centre displays a pentacoordination, probably due to Sn···O long range contacts with the hydroxyl groups of the rim of the macrocycle.

Keywords: Organotin comlpexes; Allyltin; β-Cyclodextrin

1. Introduction

Organotin compounds are largely used in a variety of practical applications, e.g. as PVC stabilisers [1], pesticides and marine antifouling agents [2], catalysts and reagents in organic synthesis [3].

Recently, for some of them, antitumor activity has also been ascertained [4], which makes this class of compounds also interesting for the pharmaceutical industry.

An important reaction in which organotin derivatives have found wide application is the allylstannation of carbonyl compounds as a direct route to homoallylic alcohols [5]. Interestingly, by using crotyltin derivatives [6a] or metal-mediated allylation protocols [6b] in aqueous media instead of the traditional anhydrous organic solvents, racemic homoallylic alcohols were obtained in good yields, with several practical advantages. However, since homoallylic alcohols are particularly interesting in their chiral form, as useful intermediates for the synthesis of complex chiral substances [7], new approaches are needed, which allow this synthesis to be carried out in an enantioselective manner also in aqueous media. One possibility is to complex the allylating agent and/or the carbonyl substrate with waterproof chiral complexing agents. Such complexes, depending on their solubility, could work as either soluble or insoluble reagents or catalysts for homogeneous or heterogeneous enantioselective allylation reactions, respectively. Cyclodextrins [8], natural cyclic oligosaccharides derived from enzymatic degradation of starch, appear to be matrices suitable for these purposes. In fact they can form inclusion complexes with a variety of molecules, including organometallics and have proved to be valuable chiral auxiliaries in several instances, in particular in the Zn-Barbier allylation reaction of aldehydes in aqueous medium [9]. As far as organotin compounds are con-

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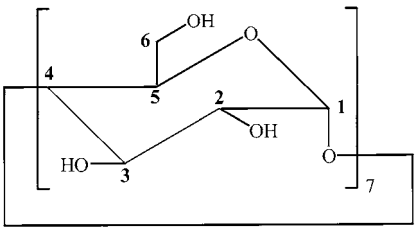

Fig. 1. Schematic drawing of β-cyclodextrin.

cerned, only a few studies have been reported so far on the complexation with cyclodextrins [4] and, therefore, much work needs to be done in this field. We wish to describe here the preparation of a complex between allyl-di-*n*-butyltin chloride, $(n\text{-}C_4H_9)_2(Cl)SnCH_2$–$CH{=}CH_2$, one of the best allylating agents for aldehydes and β-cyclodextrin (see Fig. 1) and its characterisation by means of several techniques including TGA, DSC, ESIMS, SEM and Mössbauer spectroscopy.

2. Experimental

2.1. Materials and methods

Allyl-di-*n*-butyltin chloride was prepared by a redistribution reaction between di-*n*-butyltin dichloride and di-allyl-di-*n*-butyltin, following a known procedure [10], and was purified before use by fractional distillation under reduced pressure (b.p. 65°C at 0.05 mmHg). All the spectral data were in agreement with those reported in the literature [10].

β-Cyclodextrin was commercially available and used without further purification.

^{1}H-NMR spectra were performed on a Bruker AC 250 FT spectrometer operating at 250 MHz in DMSO-d_6 as the solvent; chemical shifts were taken from tetramethylsilane (TMS) as internal standard. ^{13}C- and ^{119}Sn-NMR spectra were recorded with a JEOL FX 90Q FT multinuclear instrument using DMSO-d_6 as the solvent. The chemical shifts were referred to the solvent signal and to TMT (tetramethyltin) as external standard, respectively; ^{13}C-NMR signals were assigned by means of full decoupling and out-of-resonance techniques.

ESIMS was performed with a LCQ (ThermoQuest Italia) instrument on samples dissolved in a 1:1 water–methanol (v/v) matrix under the following working conditions: capillary voltage 10 V, spray voltage 4 kV and capillary temperature 200°C.

Thermogravimetric analyses (TGA) were performed with a Perkin–Elmer TGS-2 Thermogravimetric System (0.2 μg sensitivity), controlled by a System 4 Microprocessor Controller, under the following working conditions: sample weight 1–10 mg; heating rate 40°C min^{-1} in the range 20–200°C, nitrogen flow 40 ml min^{-1}.

Differential scanning calorimetric (DSC) traces were recorded on a Perkin–Elmer DSC-4 calorimeter in the temperature range 50–300°C at a scanning rate of 20°C min^{-1} under nitrogen flow (40 ml min^{-1}). The samples (1.5–2.5 mg) were put in standard aluminium pans with a hole in the cover.

FTIR spectra were recorded on a Perkin–Elmer mod. 580B Spectrophotometer equipped with a 3006 Data Station in Nujol mulls with CsI discs.

FTIR diffuse reflectance spectra were registered with a Bruker IFS-66 Spectrophotometer equipped with a Spectra-Tech Inc. DRIFT® (diffuse reflectance infrared Fourier transform) device fitted with a Spectra-Tech Inc. HTHP chamber in the temperature range 20–160°C.

UV spectra were registered with a Perkin–Elmer LAMBDA 16 spectrophotometer.

Induced circular dichroism (ICD) measurements were performed with a JASCO J-715 instrument, in the range 195–240 nm, in water as a solvent.

Mössbauer measurements were performed in a TBT cryostat at 80.0 K: the $Ca^{119m}SnO_3$ source (NEN, nominal strength 15 mCi) at room temperature (r.t.) was moved at constant acceleration with a triangular waveform. Suitable computer programs were employed in the fitting procedure of the experimental points to Lorentzian line shape. Allyl-di-*n*-butyltin chloride was used neat or dissolved in different solvents, as indicated in Table 1 (volume of sample 2 ml), whereas its complex with β-cyclodextrin (70 mg) was used as a mull in vaseline.

SEM analyses were carried out with a Philips XL 40 LaB6 scanning electron microscope equipped with an energy dispersion spectrometer EDAX PV 99. Samples were prepared by suspending the β-cyclodextrin complex in petroleum ether at 30–40°C, followed by ultrasound treatment for about 10 min; after evaporation of the solvent, the sample was covered by a graphite thin film (about 20 nm) produced by means of a Balteis MED 010 evaporator.

X-ray powder patterns were obtained with a diffractometer Philips PW 1820 equipped with a graphite monochromator utilising Cu–K_α (1.5418 Å) radiation. Diffraction data were collected on a horizontal scan D III/Max Rigaku diffractometer equipped with a parallel (Soller) slit, a secondary beam curved graphite monochromator, a Na(Tl)I scintillation detector and pulse height amplifier discrimination. The generator was operated at 40 kV and 40 mA. Slit used: divergence 1.0°, antiscatter 1.0° and receiving 0.2 mm, step scan $\Delta 2\vartheta$ 0.02°, $t = 1$ s per step.

Molecular models of the inclusion complex between allyl-di-*n*-butyltin chloride and β-cyclodextrin were simulated by means of a MM+ molecular mechanics routine.

Table 1
Mössbauer spectroscopy data collected at 80.0 K

Entry	Compound [a]	δ [b] (mm s^{-1})	ΔE_Q (mm s^{-1})	Γ (mm s^{-1})
1	$(n\text{-}C_4H_9)_2(Cl)SnCH_2\text{–}CH{=}CH_2$	1.68	3.22	1.08
2	$(n\text{-}C_4H_9)_2(Cl)SnCH_2\text{–}CH{=}CH_2$	1.61	3.35	0.87
3	$(n\text{-}C_4H_9)_2(Cl)SnCH_2\text{–}CH{=}CH_2$	1.70	3.28	0.79
4	$(n\text{-}C_4H_9)_2(Cl)SnCH_2\text{–}CH{=}CH_2$	1.67	3.26	0.83
5	$(n\text{-}C_4H_9)_2(Cl)SnCH_2\text{–}CH{=}CH_2$	1.66	3.39	0.83
6	$(n\text{-}C_4H_9)_2(Cl)SnCH_2\text{–}CH{=}CH_2{\cdot}\beta CD$	1.56	2.80	1.05

[a] In entries 1 and 6 neat sample was used; in entry 2 the sample was suspended in vaseline; in entries 3–5 10^{-2} M solutions in benzene, acetonitrile and dimethylsulfoxide were used, respectively.
[b] Relative to room temperature $CaSnO_3$.

2.2. Preparation of the complex

The complex between β-cyclodextrin and $(n\text{-}C_4H_9)_2(Cl)SnCH_2\text{–}CH{=}CH_2$ was prepared by the following method: β-cyclodextrin (1 mmol) was dissolved in distilled water (60 ml) with gentle warming; the solution was allowed to cool to ambient temperature and then a solution of the organotin derivative (1 mmol) in diethyl ether (3 ml) was added. The mixture was stirred at r.t. for at least 8 h and the white precipitate so formed (the precipitation begins within a few minutes of the mixing) was collected on a filter, washed with distilled water, then with a few ml of cold ethanol and dried by a flow of air and finally over P_2O_5 until constant weight. The isolated yield of the complex was 78% based on the 1:1 stoichiometry determined by integration of the ^{1}H-NMR signals in DMSO-d_6 and by elemental analysis (C, H, Cl). The ^{1}H-, ^{13}C- and ^{119}Sn-NMR spectra (in DMSO-d_6) of the complex corresponded practically to the sum of those of the pure reactants [10,11] at the same concentration and under the same experimental conditions. The ratio Sn:Cl in the complex was determined by SEM analysis and was found to be 1:1. In the IR spectrum (Nujol mull, CsI discs) the Sn–Cl stretching was present as a relatively weak band at 357 cm^{-1} and the C=C stretching of the allyl group was also detectable at 1624 cm^{-1}. The complex was further characterised by means of other techniques (see Section 3).

3. Results and discussion

The complex between allyl-di-*n*-butyltin chloride and β-cyclodextrin was obtained in rather good yield (78% isolated yield). The presence of both molecules in the complex was proven by ^{1}H- and ^{13}C-NMR spectroscopy; the stoichiometry was determined by integration of the ^{1}H-NMR signals of the alkyl protons of the organotin compound relative to those of the β-cyclodextrin, which, in DMSO-d_6, are well distinguishable and was found to be 1:1.

ESI mass spectrometry showed a fragmentation in which several clusters of ions were present, the most abundant being those at m/z 1408 ($[M-Cl]^+$), 1367 ($[M-Cl\text{–}CH_2{=}CHCH_2]^+$), 1134 (β-cyclodextrin), 1124, 804, 607 and 541; the molecular ion at m/z 1444 was absent because of loss of the chlorine atom. This is unexpected on the basis of the relative bond energies; a possible explanation could be that the organotin derivative is included in the cavity of the cyclodextrin by means of one of its organic residues (vide infra), coordination of tin (see comment to Mössbauer data in the following) and eventually of the chlorine atom (by hydrogen bonding) to the hydroxyl groups of the rim might favour the breakage of the Sn–Cl bond under the experimental conditions used for the ESI measurement.

The physical nature of the complex was investigated using the scanning electron microscope (SEM). The solid compound appears as a highly homogeneous material, in which chlorine and tin are present in the ratio 1:1. One of the several recorded scans is reported as an example in Fig. 2.

The solid complex was also investigated by means of the X-ray powder diffraction technique (see Fig. 3). Significant differences between the pattern of this sample and that of pure β-cyclodextrin, obtained under the same experimental conditions [12], were found mainly in the region between 5 and 20°, which indicates that the sample is not merely a mixture of β-cyclodextrin and organotin derivative, but that the two substances have strongly interacted together forming a new compound.

In order to ascertain the modes of interaction between the organotin molecule and the cyclodextrin, several analyses with different techniques were attempted. NMR studies in solution (except that for determination of the stoichiometry in DMSO-d_6) were hindered by the poor solubility and/or stability of the complex in all the common solvents, including water. For the same reason we think UV spectroscopy and ICD also failed. Nevertheless, interesting information was obtained by the thermal analysis and Mössbauer spectroscopy.

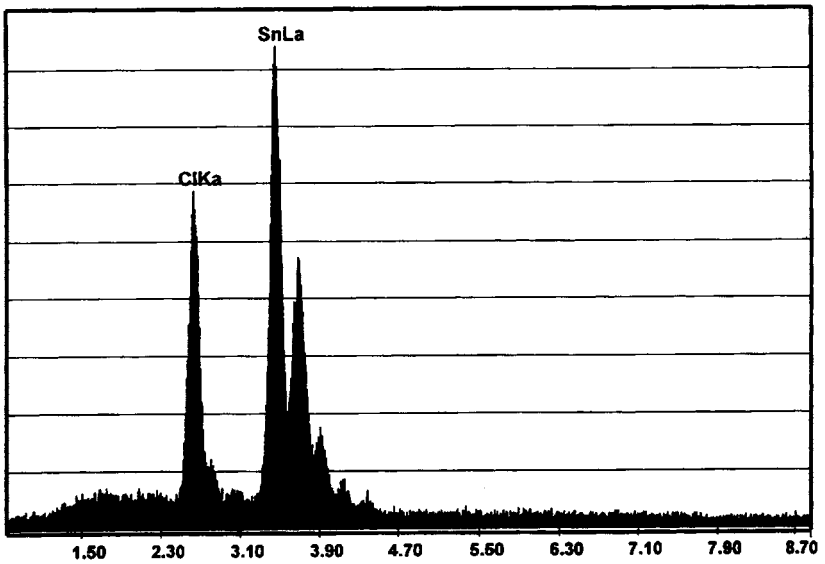

Fig. 2. Scanning electron microscope spectrum of the complex.

The thermogravimetric curves of the native β-cyclodextrin and of its complex with allyl-di-*n*-butyltin chloride in the range 25–150°C are shown in Fig. 4. β-Cyclodextrin (Fig. 4(a)) shows a mass loss corresponding to 12% of the initial weight. Independent IR reflectance measurements made in the same temperature range indicated that this step has to be ascribed essentially to loss of water, that is about 8.7 mol of water per mole of cyclodextrin (the thermal decomposition of the β-cyclodextrin begins over 300°C). Furthermore, the DSC curves recorded in the range 50–300°C showed only one endothermic peak centred at 140 ± 4°C, with an enthalpy of vaporisation of 363 ± 21 J g^{-1} (average of ten experiments). The rather high uncertainty of these measurements ($\pm 6\%$) probably depends on the poor reproducibility of the holes made in the cover of the aluminium caps used for each experiment. The measured average enthalpy of vaporisation actually corresponds to 54 kJ mol^{-1} of water, which is significantly higher than the 38 kJ mol^{-1} enthalpy of vaporisation reported for the pure water at 140°C [13]. This means that the interactions (mainly hydrogen bonding) between the water molecules and the functional groups of the cyclodextrin are stronger than those exhibited by the water molecules themselves in the liquid phase. It is well known that β-cyclodextrin crystallises with several molecules of water of crystallisation and that some of them occupy the inside of its cavity [14].

The thermogravimetric curve of the 1:1 complex (Fig. 4(b)) shows a mass loss corresponding to only three molecules of water per molecule of complex; apparently one molecule of allyl-di-*n*-butyltin chloride takes the place of about 5.7 molecules of water of crystallisation in the formation of the complex in aqueous solution. Furthermore, over 150°C there is a continuous changing of the slope of the curve, which is due to the superposition of the decomposition of the organotin derivative with that of the cyclodextrin.

The results of Mössbauer spectroscopy for the organotin derivative and its complex with β-cyclodextrin are reported in Table 1.

As far as the neat organotin derivative is concerned, both the values of the isomeric shift and of the quadrupole splitting indicate a pentacoordination of the metal. This can be explained with the formation of chlorine bridges between tin atoms of different molecules [15], so that the neat metallorganic compound displays a polymeric structure, which is also maintained in solution (see Table 1, entries 3–5). The interaction with the β-cyclodextrin causes a decrease of both the isomeric shift (-0.12 mm s^{-1}) and the quadrupole splitting (-0.42 mm s^{-1}), indicating a decrease of electronic density and an increase of symmetry around the metal. These data are still compatible with a pentacoordination of tin, but in a different surrounding compared

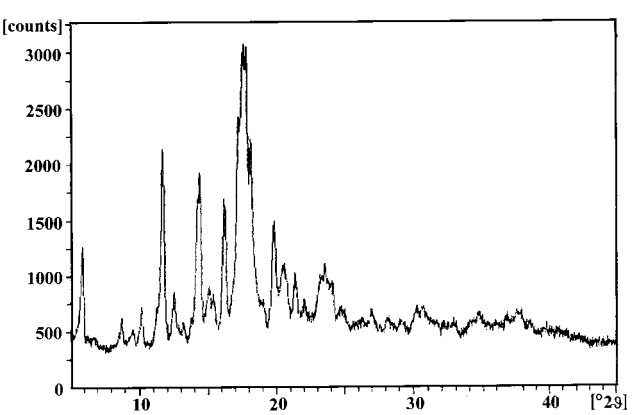

Fig. 3. X-ray powder diffraction pattern of the complex.

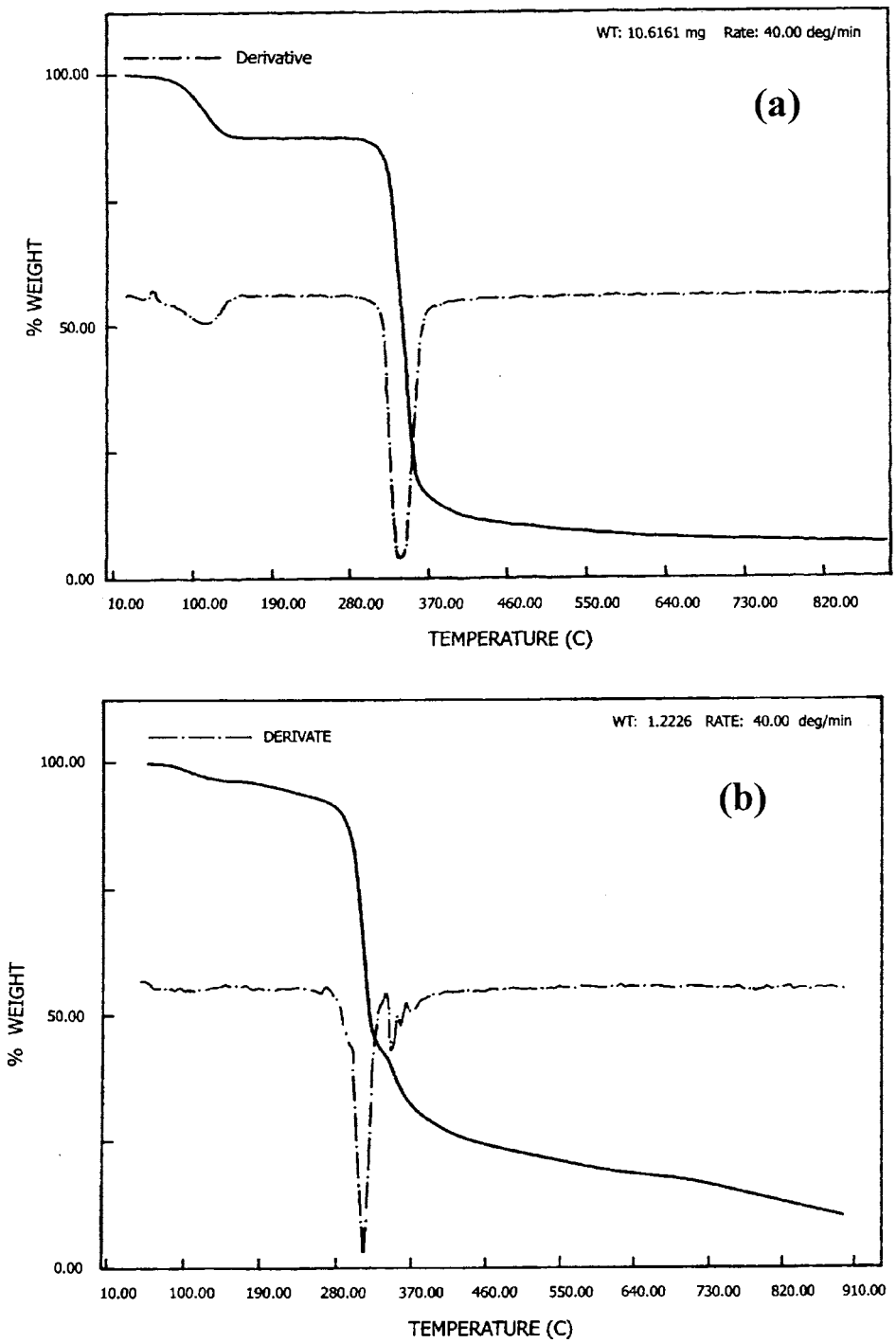

Fig. 4. Thermogravimetric analyses of β-cyclodextrin (a) and of its complex with allyl-di-*n*-butyltin chloride (b).

with that of the pure organotin compound. A reasonable interpretation could be that in case the organotin derivative is included in the cavity of the cyclodextrin by means of one of its organic residues, forming a 1:1 complex, the fifth coordination site of the metal could be occupied by one oxygen atom of the cyclodextrin, probably of one of the hydroxyl groups at the C(2) or C(3) positions of the upper rim, since the glycosidic oxygens are located too deeply into the cavity (see the CPK models below) and the C(6)–OH groups are on the bottom of the macrocycle; water molecules and hydrogen bonding with the chlorine atom could also be involved in such a coordination. Furthermore, the interactions between the organic groups of the organotin derivative and the hydrophobic cavity of the macrocycle could modify the symmetry of the molecule. It must

be pointed out that the effect exerted by the cyclodextrin is definitely more important than a simple solvent effect, as demonstrated by the Mössbauer data of the allyltin derivative taken in three different solvents of increasing coordination power, such as benzene, acetonitrile and dimethylsulfoxide (see Table 1, entries 3–5). Alternatively, the formation of a 2:2 complex between a chlorine bridged dimeric form of the organotin derivative and two molecules of β-cyclodextrin could be invoked, but this seems more unlikely, at least from a steric point of view.

4. Conclusions

In light of the above results, we conclude that a stable 1:1 complex between allyl-di-*n*-butyltin chloride and β-cyclodextrin is formed in aqueous solution. However, it is quite difficult to say whether, besides the Sn···O interactions suggested by the Mössbauer data, which probably play an important role in the formation of the complex (the formation of a covalent Sn–O σ-bond with the cyclodextrin accompanied by loss of HCl can be excluded under our experimental conditions), interactions between the organic groups of the tin derivative and the hydrophobic cavity of the β-cyclodextrin are also active, in other words, if the isolated compound is a true inclusion complex. In our opinion the last hypothesis is quite reasonable on the basis of the following considerations:

1. in the cavity of the β-cyclodextrin there is room enough to host one molecule of tin derivative, in spite of its rigid tetrahedral structure, as also shown by the CPK models (see Fig. 5),
2. the organic groups bonded to tin are hydrophobic and, therefore, they should exhibit much more affinity for the hydrophobic inside than for the hydrophilic outside of the macrocycle and its surroundings,
3. the *n*-butyl or the allyl group could therefore be the 'arm' by which the organotin derivative is inserted into the cavity of the macrocycle. These groups have almost the same chance to be included, the preference for one with respect to the other possibly depending on a subtle balance of enthalpic and entropic factors. The butyl group seems a little more favoured with respect to the allyl because it is longer and more flexible (it has been estimated that for the complexation of an alkyl chain into the cavity of a β-cyclodextrin the standard free energy variation is about -2.8 kJ mol^{-1} for each additional CH_2 unit [7]); on the other hand, the carbon–carbon double bond of the allyl group could have in its favour C–H···π contacts between the π-bond and the C(3)–H and C(5)–H protons of the cyclodextrin oriented towards the inside of the cavity, as found, in some cases, in the solid state [16]. The CPK models of these two possible isomers are represented in Fig. 5,
4. in both the above arrangements, the tin atom seems rather close to the hydroxyl groups C(2)–OH and C(3)–OH of the rim of the macrocycle (see CPK models), thus justifying, eventually with the intervention of a hydrogen bonded intermediary water molecule, the retention of the pentacoordination around the metal centre, as suggested by Mössbauer data,
5. preliminary experiments carried out in allylation reactions of aldehydes have shown that this complex is able to transfer the allyl group to carbonyl compounds, although at a rate much lower than that of the pure organotin compound and that, in some cases, optically active homoallylic alcohols can be obtained. This is also in accord with the hypothesis of a 'tight' complexation between the two reagents.

Further experimental and computational studies are in progress in our laboratories to shed more light on the structure and reactivity of the complexes of organotin compounds with cyclodextrins.

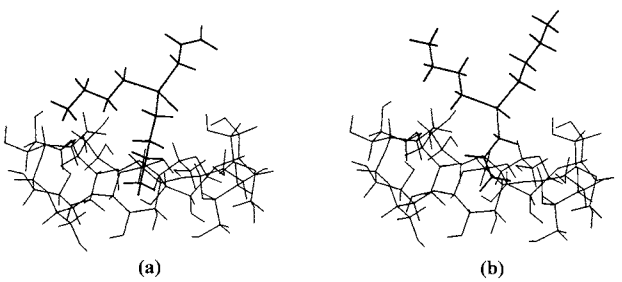

Fig. 5. Simulated limiting configurations of the complex between β-cyclodextrin and allyl-di-*n*-butyltin chloride with the butyl (a) and the allyl (b) group inserted into the cavity.

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