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Dinuclear heptacoordinate dibutyltin (IV) complexes derived from Schiff bases and dicarboxylates: Synthesis, cytotoxicity, and antioxidant activity

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The synthesis of dinuclear dibutyltin (IV) complexes **1a**–**4d**, prepared in one pot by the reaction of 2-amino-4-R-phenol (R = H, Me, Cl, NO_2), 2-pyridinecarboxaldehyde, dicarboxylic (2,5-pyridine-dicarboxylic, terephthalic, isophthalic, and oxalic) acids and dibutyltin oxides, is described. The complexes were characterized using IR, MS and ^{1}H, ^{13}C and ^{119}Sn NMR techniques. The molecular structures of complexes **1a**, **1c** and **4c** were established using X-Ray diffraction, and these complexes exhibited a distorted pentagonal-bipyramidal (BPT) geometry in which the equatorial plane consisted of three oxygen atoms and two nitrogen atoms, and the butyl groups occupied the axial positions. The cytotoxicity of the terephthalic acid derivatives **1a**–**d** in HCT-15 colon cancer, MCF7 breast cancer and PC3 prostate cancer cell lines was investigated *in vitro*. The antioxidant activity of these complexes was also measured using the DPPH (1,1-diphenyl-2-picrylhydrazyl) assay.

1. Introduction

Organotin(IV) complexes have been widely investigated because of their structural diversity and possible applications as cytotoxic, anti-inflammatory, antimicrobial, cardiovascular, insecticidal, and antifungal agents [1–5]. Several ligands have been reported to lead to a variety of complexes, including monomeric, dimeric, trimeric, tetrameric and polymeric complexes with different geometries and coordination modes [6–10]. Special attention has been devoted to Schiff Base ligands, which form organotin complexes with different structural arrangements and interesting biological activities [11-12]. Carboxylates are also important from the biochemical point of view due to their antiproliferative properties [13–17]. Additionally, numerous studies have been undertaken concerning the types of coordination geometries assumed by these complexes. Some examples of dinuclear organotin complexes are the molecular adducts of diorganotin dichloride with *N*-(2-oxidearylideneaminoacidato) [18] and the dinuclear diorganotin(IV) derivatives of pyruvic acid picolinoacylhydrazone, which exhibit supramolecular structures with 1D chains or 2D networks [19]. The Schiff base ligands containing an ONO donor system also afford dinuclear tin(IV) complexes with five- or six-coordinative geometries depending on the type of substituent bonded to the metal center [20], whereas bifunctional tridentate ligands form three classes of organotin(IV) complexes: diorganotin, triorganotin and dinuclear organotin derivatives [21]. Although a number of reports of this class of compounds have been described, few examples of dinuclear organotin complexes containing mixed ligands have been described. Thus, we recently reported the synthesis of a series of mononuclear organotin(IV) complexes with mixed ligand. In that study, we demonstrated that penta- or heptacoordinated complexes can be obtained depending on the reaction conditions and the stoichiometry [22]. As part of our interest in this type of complexes, in this report, we describe the synthesis of dinuclear heptacoordinated dibutyltin(IV) complexes containing mixed ligands and dicarboxylates. In an *in vitro* study, complexes **1a**–**d** exhibited varied antiproliferative activities against three cell lines. These complexes also exhibited antioxidant activity in the DPPH (1,1-diphenyl-2-picrylhydrazyl) assay; specifically, complexes **1b** (IC_{50} = 9.24 μM) and **1c** (IC_{50} = 9.24 μM) were more active than α-tocopherol (IC_{50} = 31.74 μM), which was used as a positive control.

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2. Results and discussion

The complexes were obtained in a one-step reaction from 2-pyridinecarboxaldehyde, 2-amino-4-R-phenol (R = H, CH_3, Cl, NO_2), di-*n*-butyltin(IV) oxide and the corresponding dicarboxylic acid in a 2:2:2:1 M ratio (Scheme 1). The compounds were isolated in yields ranging from 53 to 93%.

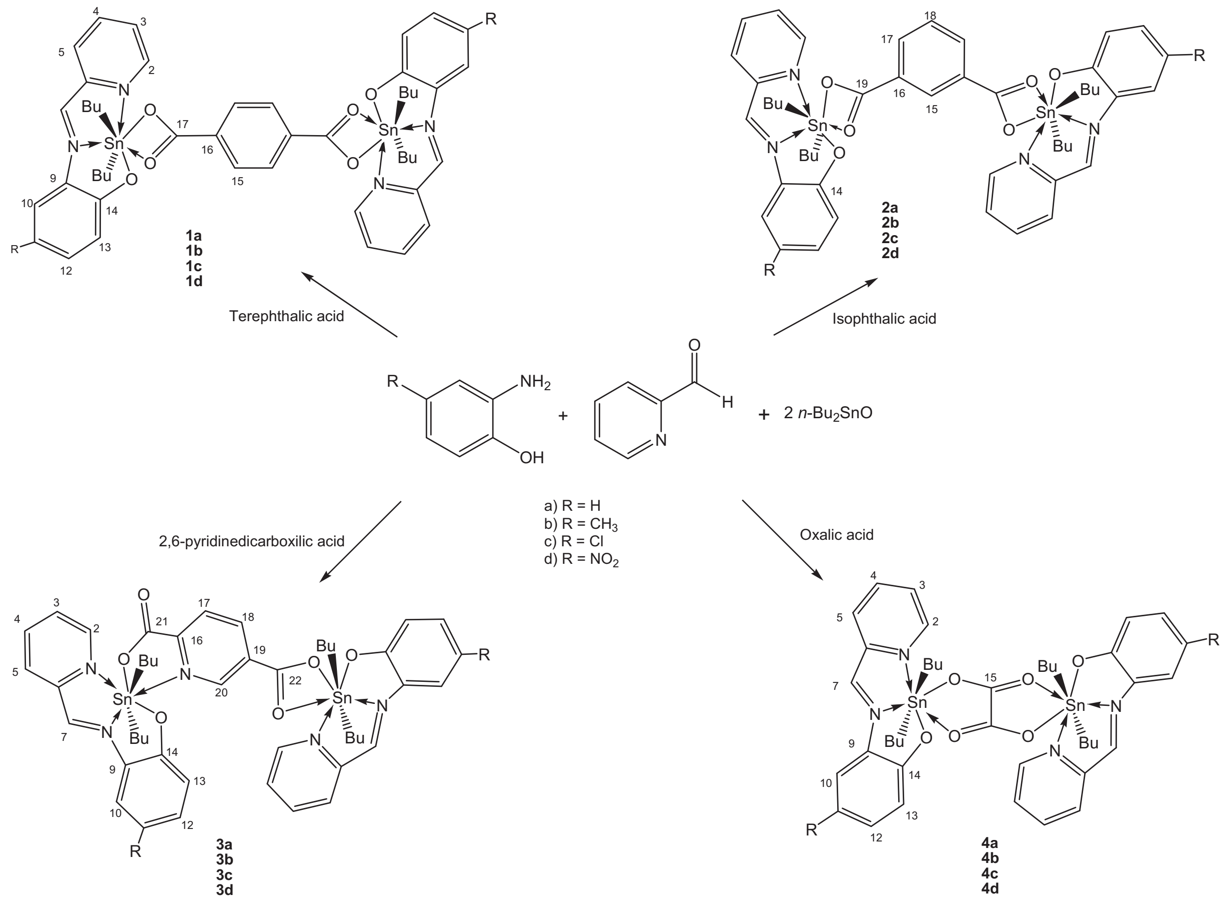
2.1. FTIR analysis

The infrared spectra (FTIR) of complexes **1a**–**4d** exhibited bands in the region of 1588–1612 cm^{-1} that were assigned to the C=N stretching vibrations of the different complexes. These bands are shifted to lower energies compared with the ν(N=C) stretch of the Schiff base ligand [12,22]. This shift has been attributed to the donation of the lone pair of the azomethine nitrogen to the tin atom [11]. The absence of the carboxylic acid and phenol OH groups resulted in the deprotonation of the ligand and the formation of a Sn–O bond. The spectra of complexes **1a**–**d** and **2a**–**d** exhibited two different absorption bands in the range of 1371 cm^{-1} to 1560 cm^{-1}, which correspond to the $\nu_{sym}(COO^-)$ and $\nu_{asym}(COO^-)$ vibrational modes of the carboxyl groups, respectively. The energy difference between the asymmetric and symmetric carboxylate stretching vibrations is in the range of 160–195 cm^{-1}, which is attributed to the formation of a chelating carboxylate with anisobidentate coordination (see Table 1) [23]. However, the spectra for the 2,5-pyridinedicarboxylic acid derivatives **3a**–**d** exhibited two different bands in the ranges of 1648 to 1607 and 1371–1345 cm^{-1} that were assigned to the $\nu_{asym}(COO^-)$ and $\nu_{sym}(COO^-)$ vibrations. The energy difference between the asymmetric and symmetric carboxylate stretching vibrations indicated that the carboxylates are coordinated to metal center in both the monodentate and anisobidentate coordination modes. These $\Delta\nu$ values are similar to those of the monomeric complex and the 2,5-pyridine tin carboxylates previously described, which verifies the presence of the two

Table 1
Assignment of characteristic FT-IR vibrations (cm^{-1}).

Compound	ν_{asym}	ν_{sym}	$\delta\nu$
1a	1567	1372	195[a]
1b	1556	1387	169[a]
1c	1548	1369	179[a]
1d	1561	1400	161[a]
2a	1564	1379	185[a]
2b	1545	1381	164[a]
2c	1545	1379	166[a]
2d	1560	1387	173[a]
3a	1639	1345	294[b]
	1607	1373	234[a]
3b	1637	1346	291[b]
	1612	1371	241[a]
3c	1639	1347	291[b]
	1616	1373	243[a]
3d	1648	1355	293[b]
		1381	–
4a	1639	1459	180[c]
4b	1640	1467	173[c]
4c	1641	1460	181[c]
4d	1640	1489	151[c]

Carboxylate coordination mode (a) anisobidentate, (b) monodentate (c) bidentate.



Scheme 1.