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Crystal structure and *in vitro* antitumor activity of bis(dicyclohexylammonium) bis(2-sulfobenzoato)dibutylstannate

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An X-ray structure determination is presented for bis(dicyclohexylammonium) bis(2-sulfobenzato)dibutylstannate, and its antitumor properties against mammary and colon carcinoma cell lines are reported.

Keywords: Crystal structure, organotin, antitumor

INTRODUCTION

We have recently reported[1] the crystal structure of bis(dicyclohexylammonium) bis(oxalato)dibutylstannate. This ammonium stannate when screened *in vitro* against mammary and colon carcinoma cell lines was found to be as effective as the antineoplastic drug cisplatin. In an extension of the work on diorganostannates, we report the structure and antitumor properties of bis(dicyclohexylammonium) bis(2-sulfobenzato)-dibutylstannate.

EXPERIMENTAL

Synthesis and crystallography

The ammonium stannate was synthesized by reacting 2-sulfobenzoic acid trihydrate, dicyclohexylamine and dibutyltin oxide in a 2:2:1 stoichiometry in a small volume of ethanol. It is poorly soluble in the common NMR solvents, but yielded a satisfactory ^{119}Sn NMR spectrum (JEOL JNM GX 270; 100.55 MHz) in d^6-DMSO: δ −290.37 ppm (relative to tetramethyltin). Single crystals of the compound were obtained from the same solvent medium. Intensity data were collected at room temperature on an Enraf–Nonius CAD4 diffractometer (Mo-K_α, $\lambda = 0.71073$ Å) up to $2\theta_{max} = 45°$ (collection range: h, 0 to 13; k, −14 to 14; l, −17 to 17); 5173 reflections obeyed the $I \geq 3\sigma(I)$ criterion. The structure was solved by the heavy-atom method. Corrections for absorption were applied following isotropic refinement.[2] The non-hydrogen atoms were refined anisotropically; geometrically generated (C–H or N–H, 0.95 Å; B, 5 Å^2) hydrogen atoms were included in the structure factor calculations. The full-matrix least-squares refinements converged to $R = 0.047$, $R_w = 0.055$ $\{w = [\sigma(F)^2 + (0.02F)^2 + 1]^{-1}\}$ $(\Delta/\sigma)_{max}$ 0.09; ρ_{max} 0.69(7)eÅ^{-3}. Computations were performed using the *MolEN* structure determination package[3] on a DEC MicroVAX II minicomputer. Atomic coordinates and isotropic temperature factors are listed in Table 1.

Crystal data

2[(cyclo-$C_6H_{11})_2NH_2]^+$ $[(C_4H_9)_2Sn(O_2CC_6H_4$-2-$SO_3)_2]^{2-}$, $C_{46}H_{74}N_2O_{10}S_2Sn$: M_r 997.93; $F(000)$1052 triclinic, $P\bar{1}$; a, 12.8965(9) Å; b, 13.241(1) Å; c, 16.3264(9) Å; α, 101.93(5)°; β 94.47(5)°; γ, 112.65(7)°; V, 2478.7(3) Å^3; D_x, 1.337 g cm^{-3}; μ, 6.49 cm^{-1} for $Z = 2$.

Antitumor test

The compound was screened against MCF-7 (mammary tumor) and WiDr (colon carcinoma) cell lines by using an automated *in vitro* method.[4] The inhibition dosage (ID_{50}) values were found to be 108 and 530 ng cm^{-3}, respectively, in dimethyl sulfoxide (DMSO), and 312 and 1607 ng cm^{-3}, respectively, in ethanol.

DISCUSSION

The crystal structure of bis(dicyclohexylammonium) bis(2-sulfobenzato)dibutylstannate consists of an ionic network of ammonium cations and six-coordinate, skew-trapezoidal bipyramidal

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Table 1 Atomic coordinates and isotropic temperature factors
Anisotropically refined atoms are given in the form of the isotropic equivalent displacement parameter defined as:

$$4/3[a^2B_{1,1}+b^2B_{2,2}+c^2B_{3,3}+ab(\cos\gamma)B_{1,2}+ac(\cos\beta)B_{1,3}+bc(\cos\alpha)B_{2,3}$$

Atom	x	y	z	B (Å²)	Atom	x	y	z	B (Å²)
Sn	0.08340(4)	0.26424(4)	0.16288(3)	4.41(1)	C(17)	−0.1032(5)	0.1482(6)	0.3477(4)	4.2(2)
S(1)	0.4963(1)	0.4806(1)	0.2802(1)	3.77(4)	C(18)	−0.0852(5)	0.0600(5)	0.3701(5)	4.2(2)
S(2)	−0.0224(2)	−0.0204(2)	0.3075(1)	4.88(5)	C(19)	−0.1173(6)	0.0300(6)	0.4449(5)	5.4(2)
O(1)	0.2402(3)	0.2661(4)	0.2071(3)	4.2(1)	C(20)	−0.1658(7)	0.0905(7)	0.4969(6)	6.3(2)
O(2)	0.2524(4)	0.2828(4)	0.0764(3)	5.5(1)	C(21)	−0.1887(6)	0.1741(7)	0.4719(6)	6.2(2)
O(3)	0.4588(4)	0.4528(4)	0.3571(3)	5.6(1)	C(22)	−0.1590(6)	0.2041(6)	0.3975(5)	5.3(2)
O(4)	0.6130(4)	0.5661(4)	0.2985(3)	4.5(1)	C(23)	0.2610(5)	0.3628(5)	0.4831(4)	3.3(1)
O(5)	0.4199(4)	0.5059(4)	0.2279(4)	5.3(1)	C(24)	0.2280(6)	0.4464(5)	0.4464(4)	4.5(2)
O(6)	0.0516(4)	0.2283(4)	0.2783(3)	4.7(1)	C(25)	0.2004(6)	0.5230(5)	0.5195(5)	5.3(2)
O(7)	−0.1170(5)	0.2092(5)	0.2202(4)	6.9(2)	C(26)	0.1011(6)	0.4496(6)	0.5572(5)	5.4(2)
O(8)	−0.0800(5)	−0.1343(4)	0.3181(4)	6.9(2)	C(27)	0.1320(5)	0.3639(5)	0.5912(5)	4.4(2)
O(9)	−0.0484(5)	−0.0168(5)	0.2206(4)	6.7(2)	C(28)	0.1650(5)	0.2882(5)	0.5222(4)	4.0(2)
O(10)	0.0964(4)	0.0331(4)	0.3438(4)	6.3(2)	C(29)	0.3355(5)	0.2102(5)	0.4303(4)	3.6(1)
N(1)	0.2839(4)	0.2883(4)	0.4086(3)	3.3(1)	C(30)	0.4457(6)	0.2760(6)	0.4951(5)	5.6(2)
N(2)	−0.2794(4)	−0.2879(4)	0.1985(3)	3.4(1)	C(31)	0.4940(7)	0.1902(7)	0.5116(6)	7.2(2)
C(1)	−0.0096(8)	0.1160(9)	0.0638(6)	8.5(3)	C(32)	0.5171(6)	0.1291(7)	0.4290(6)	7.0(2)
C(2)	−0.103(1)	0.108(2)	0.009(1)	23.6(7)	C(33)	0.4064(6)	0.0666(6)	0.3631(5)	5.8(2)
C(3)	−0.131(1)	0.155(1)	−0.032(1)	23.5(6)	C(34)	0.3570(5)	0.1504(5)	0.3465(4)	4.3(2)
C(4)	−0.227(2)	0.132(1)	−0.100(1)	21.5(8)	C(35)	−0.2523(5)	−0.3506(5)	0.1199(4)	3.6(2)
C(5)	0.1201(8)	0.4384(6)	0.1770(6)	7.4(2)	C(36)	−0.3586(6)	−0.4556(6)	0.0734(5)	5.3(2)
C(6)	0.089(1)	0.4961(8)	0.2481(8)	11.8(4)	C(37)	−0.3292(7)	−0.5261(6)	−0.0025(5)	5.9(2)
C(7)	0.123(1)	0.623(1)	0.256(1)	12.8(5)	C(38)	−0.1263(7)	−0.4462(7)	0.0717(6)	7.4(2)
C(8)	0.222(1)	0.689(1)	0.297(1)	16.6(7)	C(39)	−0.1551(6)	−0.3804(6)	0.1501(5)	6.1(2)
C(9)	0.2963(6)	0.2787(5)	0.1444(4)	4.1(2)	C(40)	−0.2322(7)	−0.5551(6)	0.0265(6)	6.5(2)
C(10)	0.4114(5)	0.2756(5)	0.1577(4)	3.7(2)	C(41)	−0.3676(5)	−0.2408(5)	0.1827(4)	3.5(1)
C(11)	0.5032(5)	0.3562(5)	0.2184(4)	3.5(1)	C(42)	−0.3287(6)	−0.1576(5)	0.1275(5)	5.0(2)
C(12)	0.6057(6)	0.3440(5)	0.2305(4)	4.5(2)	C(43)	−0.4159(7)	−0.1048(6)	0.1178(5)	6.4(2)
C(13)	0.6155(6)	0.2489(6)	0.1812(5)	5.6(2)	C(44)	−0.4301(7)	−0.0464(6)	0.2056(5)	6.3(2)
C(14)	0.5246(7)	0.1701(6)	0.1189(5)	5.9(2)	C(45)	−0.4695(6)	−0.1337(6)	0.2594(5)	5.9(2)
C(15)	0.4226(6)	0.1828(5)	0.1070(5)	5.0(2)	C(46)	−0.3810(6)	−0.1830(5)	0.2701(4)	4.7(2)
C(16)	−0.0575(6)	0.1957(6)	0.2758(5)	4.7(2)					

diorganostannate anions. The tin atom is intramolecularly coordinated [2.648(5), 2.700(5) Å] by two carbonyl oxygen atoms which, together with the two covalently bonded oxygen atoms, define the basal trapezoidal plane (Fig. 1). The butyl groups are bent over the long edge (C–Sn–C 133.5(4) °) of the trapezoidal plane. The ammonium cations are hydrogen-bonded to the sulfonato groups [N(1)···O(3), 2.794(6) Å; N(2)···O(8), 2.848(7) Å]; one of them is additionally hydrogen-bonded to an adjacent sulfonato group (N(2)···O(4′), 2.814(6) Å) to form a tight network (Fig. 2).

In the crystal structures of the related dicyclohexylammonium (2-sulfobenzato)triorganostannates, the 2-sulfobenzato anion links planar triorganotin cations into chains through the sulfonyl oxygen ends. The covalent sulfonyl oxygen–tin bond distances in the tributyl- (2.575(5) Å)[5] and triphenyl- (2.449(3) Å)[6] stannates are somewhat longer however, an indication that the sulfonato group is probably not strongly Lewis basic despite the presence of a formal negative charge. The negatively charged sulfonato groups do not coordinate to tin in spite of the greater degree of Lewis acidity of tin in the dibutylstannate; instead, the carboxylato groups raise the coordination number through chelation.

In the *in vitro* antitumor trials on the mammary MCF-7 and WiDr colon carcinoma cell lines, the ID_{50} values for bis(dicyclohexylammonium) bis(oxalato)dibutylstannate in ethanol are 76 (MCF-7) and 323 ng cm^{-3} (WiDr);[1] for cisplatin, the corresponding values are 850 and 624 ng cm^{-3}. The ID_{50} values in tests against MCF-7 (108 ng cm^{-3}) and WiDr (312 ng cm^{-3})

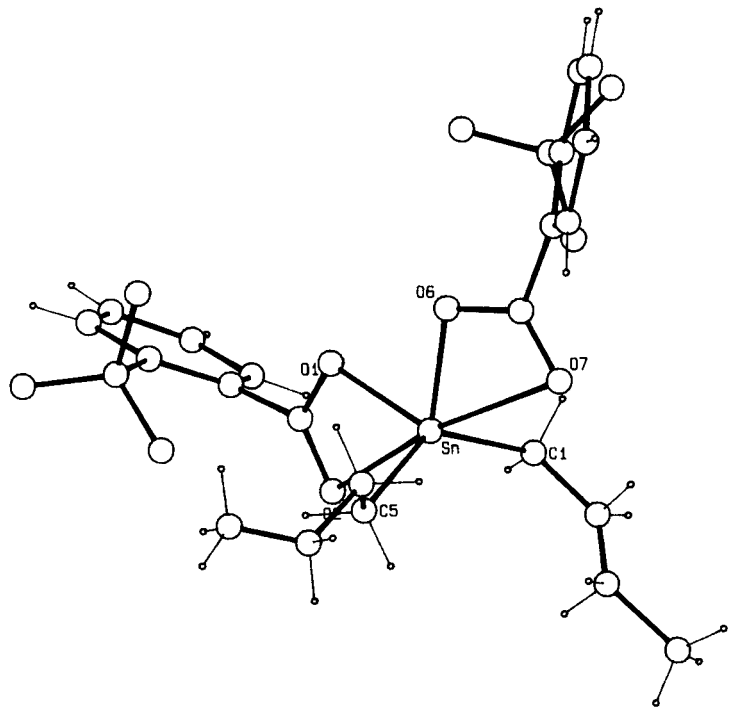

Figure 1 Structure of the $[(C_4H_9)_2Sn(O_2CC_6H_4\text{-}2\text{-}SO_3)_2]^{2-}$ ion. Selected bond distances (Å) and angles (°): Sn–O(1), 2.083(4); Sn–O(2), 2.648(5); Sn–O(6) 2.070(4); Sn–O(7), 2.700(5); Sn–Cl, 2.116(8); Sn–C(5), 2.125(8); O(1)–Sn–O(2), 53.9(1); O(1)–Sn–O(6), 80.9(2); O(1)–Sn–O(7), 133.5(2); O(1)–Sn–C(1), 109.6(3); O(1)–Sn–C(5), 103.4(3); O(2)–Sn–O(6), 134.4(2); O(2)–Sn–O(7), 167.4(2); O(2)–Sn–C(1), 83.8(3); O(2)–Sn–C(5), 90.3(2); O(6)–Sn–O(7), 53.0(2); O(6)–Sn–C(1), 108.9(3); O(6)–Sn–C(5), 107.8(3); O(7)–Sn–C(1), 83.7(3); O(7)–Sn–C(5), 96.6(3); C(1)–Sn–C(5), 133.5(4).

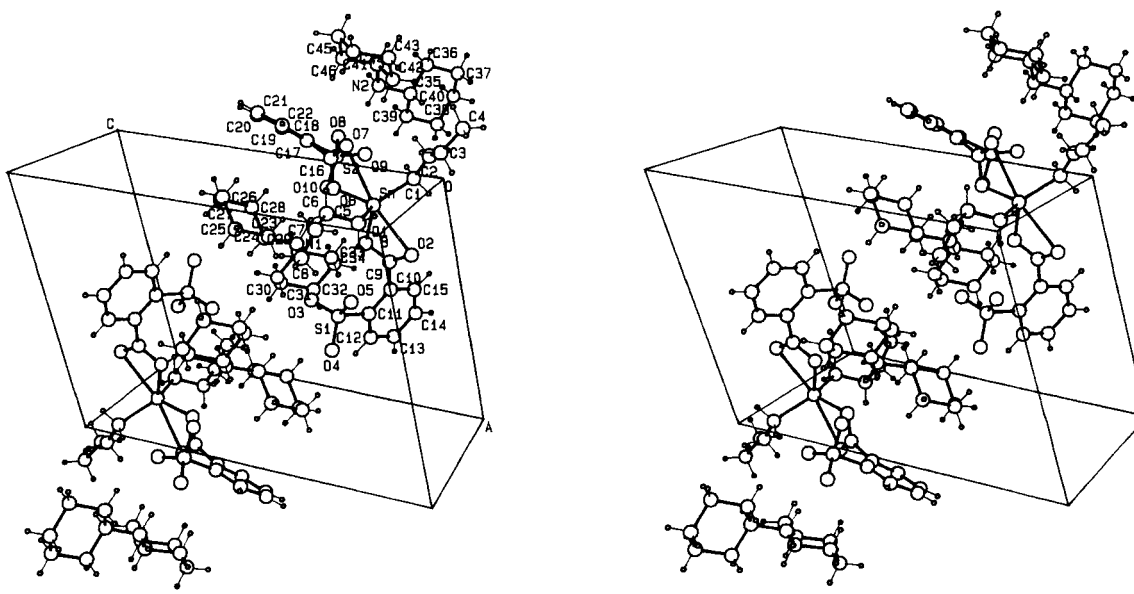

Figure 2 Stereoview of the unit cell. Hydrogen bonds: N(1) · · · O(3), 2.794(6) Å; N(2) · · · O(4^{i}), 2.814(6) Å; N(2) · · · O(8), 2.848(7) Å (^{i}: $-x, -y, -z$).

for the present dicyclohexylammonium bis(2-sulfobenzato)dibutylstannate in DMSO compare well with the values for the oxalatostannate. The compound, however, appears to be less effective in ethanol.

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