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Synthesis of Diorganotin(IV) Complexes with Nucleosides and Their Characterization by Mössbauer and Infrared Spectroscopy

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Abstract

A number of new complexes of R_2Sn^{IV} with adenosine, guanosine, inosine, cytidine and uridine were synthesized by reaction of ribonucleosides with diorganotin oxide in hot methanol. The complexes were characterized by infrared and ^{119}Sn Mössbauer spectroscopy as O(2′), O(3′) (diorganostannylene) nucleosides; the occurrence of dimers with three-co-ordinate oxygen atoms is inferred on the basis of spectroscopic data.

Introduction

The study of the interaction of transition metal ions with nucleosides has recently attracted considerable interest [1–24]. Bonding to the metal center almost invariably occurs through the heterocyclic atoms of the purine and pyrimidine bases in the solid state [1–6], although in rare cases binding to exocyclic base atoms was observed and weak interactions with such atoms have also been described [1]. Analogous results were obtained in the solution phase, mainly by spectroscopic and magnetic studies [7–19]. On the other hand, bonding may also take place through the O(2′) and O(3′) atoms of the ribose residue, such as in the bis-(pyridine)osmate(VI) ester of adenosine [20] and in nucleoside complexes of Co^{III}(dien) [21], Cu^{II} [22–24] and Mn^{II} [25].

The only non-transition metal derivatives of nucleosides previously investigated are, to our knowledge, a series of complexes with diorganotin(IV) moieties [26, 27]. The reaction of $Bu_2{}^nSnO$ with nucleosides affords the synthesis of O(2′), O(3′) (dibutylstannylene) nucleosides, characterized by the occurrence of 2-stanna-1,3-dioxolane rings, as demonstrated by NMR spectroscopy [26]. In the solid state, evidence has been obtained for co-ordination number five of tin in Me_2Sn^{IV} (adenosinate), from the magnitude of its experimental Mössbauer parameter nuclear quadrupole splitting, ΔE; infrared spectra ruled out metal co-ordination by adenine donor atoms, and intermolecular bridging by a ribose oxygen was suggested, with the formation of solid state species where the metal environment, C_2SnO_3, would be of trigonal bipyramidal type [27]. This structure would correspond to that advanced for $Bu_2{}^nSn^{IV}$ stannoxanes, and derivatives of cyclic alkoxides, on the basis of NMR and Mössbauer spectroscopy [28, 29], as well as to that of the $Bu_2{}^nSn^{IV}$ derivative of methyl 4,6-O-benzylidene-α-D-glucopyranoside, recently determined by X-ray diffractometry [30].

With the aim of widening the knowledge in this field, and completing our previous investigation [27], the synthesis of several R_2Sn^{IV} derivatives of adenosine, guanosine, inosine, uridine and cytidine was carried out, and the complexes obtained were characterized in the solid state by Mössbauer and infrared spectroscopy. The results obtained are reported and discussed in this paper. It is worth mentioning that further work is in progress in order to evaluate both the biological activity and the possible structure–activity relationship of the above mentioned derivatives. In fact preliminary results showed that several diorganotin(IV) complexes, among them $Bu_2{}^nSnAdo$, inhibited the ATP-synthesis of rat liver mitochondria up to 50% with concentration of the organotin(IV) compounds ranging between 0.5 and 5 nmol/mg of protein [31].

Experimental

Pure reagents and solvents (C. Erba, Milano) were used, which, whenever necessary, were dried according to standard procedures. Dialkyltin oxides were gifts from Schering A.G. (Bergkamen, B.R.D.); the nucleosides were Fluka A.G. (Switzerland) products. The synthesis of Alk_2Sn^{IV}-nucleosidates, Alk_2SnL, was carried out according to literature reports [26] by the following reaction:

$$Alk_2SnO + H_2L \longrightarrow Alk_2SnL + H_2O \qquad (1)$$

The procedures employed were as follows:

Method (1)

Equimolar amounts of R_2SnO and nucleoside (see Table I for abbreviations) suspended in dry methanol were refluxed for half an hour to two hours. On cooling the resulting clear solution, a white compound precipitated which was recrystal-

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TABLE I. Analytical Data [% Found (Calcd)], and Experimental Mössbauer Parameters.

Compound	Procedure	M.P. (°C)	C	H	N	Sn	δ^{b} (mm s^{-1})	ΔE^{c} (mm s^{-1})	$\Gamma_{av}{}^{d}$ (mm s^{-1})
$Bu_2{}^nSnAdo$	I	156–158	43.11	5.77	13.90	23.80	1.28	3.06	0.99
			(43.40)	(5.87)	(14.06)	(23.83)			
$Oct_2{}^nSnAdo$	I	203–205	51.50	7.70	11.20	19.38	1.29	3.08	0.97
			(51.16)	(7.43)	(11.47)	(19.45)	1.27^{e}	$+3.00\ (\eta = 0.62)^{e}$	
Me_2SnGuo	II	280 dec	32.30	3.75	15.50	27.34	1.15	3.09	0.96
			(33.52)	(3.98)	(16.29)	(27.60)			
$Bu_2{}^nSnGuo$	II	235 dec	41.78	5.58	13.49	22.67	1.27	3.12	0.94
			(42.05)	(5.68)	(13.62)	(23.09)			
$Oct_2{}^nSnGuo$	II	244–247	49.95	7.40	11.17	18.47	1.33	3.24	0.88
			(49.86)	(7.24)	(11.18)	(18.95)			
Me_2SnIno	II	290 dec	33.78	3.89	12.90	28.23	1.14	3.06	0.94
			(34.73)	(3.89)	(13.50)	(28.60)			
$Bu_2{}^nSnIno$	II	202–204	41.00	5.64	10.28	21.85	1.29	3.08	0.98
			(43.31)	(5.65)	(11.22)	(23.76)			
Me_2SnCyd	II	250 dec	33.55	4.50	10.56	30.70	1.17	3.05	1.02
			(33.88)	(4.39)	(10.78)	(30.44)			
$Oct_2{}^nSnCyd$	I	220	51.24	8.00	7.11	20.03	1.26	2.97	1.09
			(51.21)	(7.73)	(7.17)	(20.24)			
Me_2SnUro	II	275 dec	33.56	4.20	6.94	30.26	1.16	3.10	1.02
			(33.79)	(4.12)	(7.17)	(30.36)			
$Bu_2{}^nSnUro$	I	233	43.00	6.21	5.74	24.52	1.29	3.02	0.94
			(42.98)	(5.94)	(5.90)	(24.98)			
$Oct_2{}^nSnUro$	I	226	50.97	7.80	4.70	20.26	1.29	3.08	0.86
			(51.13)	(7.55)	(4.77)	(20.21)			

[a] H_2Ado = adenine-9-D-ribonucleoside (= Adenosine); H_2Uro = 2,6-deoxopyrimidine-3-D-ribonucleoside (= Uridine); H_2Cyd = 6 amino-2-hydroxypyrimidine-3-D-ribonucleoside (= Cytidine); H_2Guo = Guanine-9-D-Ribofuranoside (= Guanosine); H_2Ino = Hypoxanthine-9-D-Ribofuranoside (= Inosine). [b] Isomer shift with respect to R. T. $CaSnO_3$. [c] Nuclear Quadrupole Splitting. [d] Full width at half height of the resonant peaks, average. [b,c,d] Data referred to measurements at liquid N_2 temperature unless otherwise stated. [e] Data obtained at A.E.R.E. Harwell by fitting the 4.2 K Mössbauer–Zeeman spectrum (see Fig. 1); $\eta = (V_{xx} - V_{yy})/V_{zz}$ is the asymmetry parameter.

lized from the appropriate solvent (methanol for $Bu_2{}^nSnUro$; methanol/acetone 1:1 for $Bu_2{}^nSnAdo$; methanol/acetone 2:1 for $Oct_2{}^nSnAdo$; ethanol for $Oct_2{}^nSnCyd$ and $Oct_2{}^nSnUro$).

Method (II)

Equimolar amounts of R_2SnO and nucleoside suspended in dry methanol were refluxed for 3 to 5 hours, then the white solid product was filtered off, washed and dried.

The results of the elemental analyses and the melting points (uncorrected), are reported in Table I. Data for the already known $Bu_2{}^nSnAdo$ and $Bu_2{}^nSnUro$ perfectly correspond to literature reports [35].

The Mössbauer spectra at liquid N_2 temperature were measured by the apparatus, techniques and data reduction procedures already reported [32], using a 10 mCi $Ca^{119}SnO_3$ source (R. C. Amersham) moving at room temperature, with constant acceleration and triangular waveform. Experimental parameters are listed in Table I.

The infrared spectra were determined by a Perkin-Elmer mod. 457 spectrometer, in nujol and hexachlorobutadiene mulls between CsI discs. Relevant absorption bands are reported in Table II.

Discussion

The elemental compositions reported in Table I clearly demonstrate that reaction (1) yields complexes with 1:1 diorganotin:nucleoside stoichiometry, in consonance with previous results [26, 27]. The pathway of the synthetic reaction seems then not to be influenced by the nature of the nitrogen bases of the nucleosides, nor by changing the alkyl groups bound to tin; this suggests common bonding and structure throughout the homologous series, and in particular a general primary involvement of O(2′), O(3′) atoms of ribose residues of nucleosides in bonds to tin [26, 27].

The Mössbauer parameter isomer shift, δ (Table I), is typical of dialkyltin(IV) salts and complexes [35]. The experimental nuclear quadrupole splittings of all compounds, ΔE (Table I), are fully consistent with the occurrence of trigonal bipyramidal C_2SnO_3 units with equatorial C_2 [33, 27].

TABLE II. Relevant Infrared Absorptions[a] (in the 4000–250 cm^{-1} region).

Compound	$\nu(NH_2)$, $\nu(OH)$	ν(ring)	ν(C=O)	ν(CO) in C–O–Sn	ν(Sn–C)	ν(Sn–O)
H_2Ado	3320s,br; 3140s,br[b]	1605s; 1575s[b]				
$Bu_2{}^n$SnAdo	3320s,br; 3140s,br	1605s; 1575s		1105s,sh; 1080s,bd	570m	475m; 450m,sh
$Oct_2{}^n$SnAdo	3220s,br; 3100s,br	1610s; 1575m		1100s,sh; 1085s	560m	475m; 445w
H_2GuO	3440s; 3310s; 3190s[b]	1493s; 1405s[b]	1730s[b]			
Me_2SnGuo	3380s; 3300s; 3250s; 3200s; 3100m	1485s; 1410m	1705s	1110s; 1090s	570m; 545w	440m; 425m
$Bu_2{}^n$SnGuo	3480s; 3310s; 3160s	1485s; 1410m	1695s	1120s; 1095s	590m; 555w	465m; 440m
$Oct_2{}^n$SnGuo	3320m; 3210m	1480s; 1412m	1680s	1108s; 1070s	595m; 560m	455m; 445m
H_2Ino	3540s; 3460m; 3340s,sh; 3300s; 3140s; 3040s	1590s; 1555s	1705s, 1685s[c]			
Me_2SnIno	3265m; 3100s; 3040m	1585s; 1540s	1720s	1105s; 1090s	570m; 550m	445m
$Bu_2{}^n$SnIno	3530m; 3300s; 3120w; 3060w; 3040w	1590s; 1565s	1710s	1115s; 1095s	595s; 530m	460m
H_2Cyd	3450s; 3350s; 3230s,br; 3090s[b]	1605s[b]	1650s[b]			
Me_2SnCyd	3340s; 3200s	1605s	1650s	1085s	570m; 520w	455m
$Oct_2{}^n$SnCyd	3450s; 3350s	1610s	1640s	1085s	575m; 535w	480m; 455m
H_2Uro	3350s; 3110m[b]	1470s; 1425s[b]	1665s,br[b]			
Me_2SnUro	3400s; 3160s; 3060s	1465s; 1430s	1685s,br		570s; 520w	430m; 420m
$Bu_2{}^n$SnUro	3470s	1470s; 1450s	1680s,br		590m; 510w	425m
$Oct_2{}^n$SnUro	3460s	1470s; 1445s	1680s,br		585m; 510w	420w

[a]Measured in nujol and hexachlorobutadiene mulls with a Perkin-Elmer mod. 457 spectrometer; s = strong, m = medium, w = weak, bd = broad, sh = shoulder. Attributions are made according to Refs: [b]47, [c]48. Ligand abbreviations are in Table I.

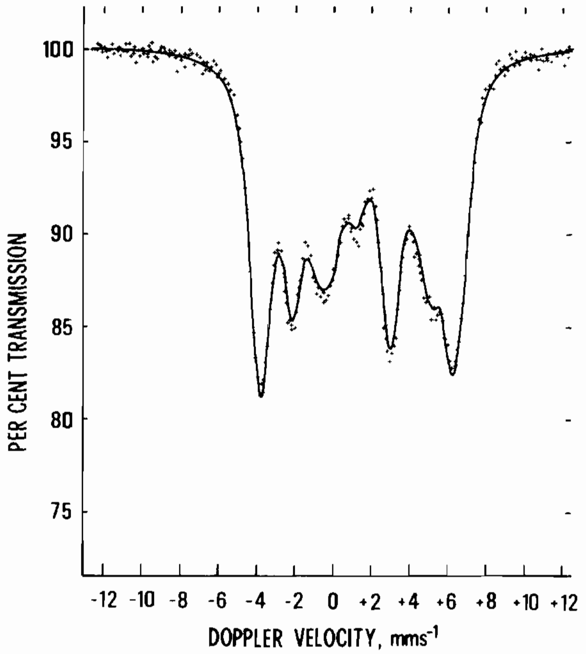

Fig. 1. The Mössbauer-Zeeman spectrum of Di-n-octyltin adenosinate, as measured at A.E.R.E., Harwell, at 4.2 K in a transverse magnetic field of 6 Tesla. Full line is computer fitting of experimental data points. Parameters are in Table I.

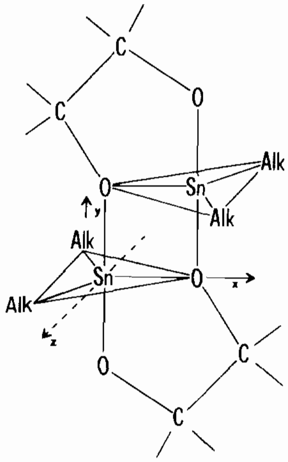

Fig. 2. The dimeric structure [38, 39] and the idealized regular trigonal bipyramidal environment of tin in R_2Sn-nucleosidates, assumed for point-charge model calculations of nuclear quadrupole splittings, ΔE, and asymmetry parameters, η. The directions of the components of the E.F.G. tensor V_{xx}, V_{yy} and V_{zz}, as obtained from computer outputs, are also indicated for one tin site. Calculated parameters are: ΔE_{calcd} = +2.67 mm s^{-1}; η_{calcd} = 0.36 (see text and Table I).

The determination of the Mössbauer–Zeeman spectrum [34] of $Oct_2{}^nSnAdo$ (Fig. 1), taken as a representative term of the series, and the consequent obtainment [34] of the sign (positive) of ΔE and the value of η (Table I), allow the structural rationalization of ΔE_{exp} data, in terms of the metal environment, by the point-charge model approach [33, 35]. The regular trigonal bipyramidal [33] configuration of Fig. 2 was assumed, which idealizes the probable structure (the latter could indeed be severely distorted, as determined in the reported dimeric glucopyranoside derivative [30]). In the calculation of ΔE and η parameters, tabulated partial quadrupole splittings, p.q.s. [35], were used for $\{Alk\}^{tbe}$ [33]. As far as p.q.s. values for oxygen-bearing groups are concerned, the correct choice of data was severely hampered by the fact that three-co-ordinated atoms are at the same time axial and equatorial with respect to the two distinct tin sites (Fig. 2). Anyway, it was here attempted to employ the reported p.q.s.s $\{OAlk\}^{tbe} = -0.13$ and $\{OAlk\}^{tbe} = +0.02$, mm s^{-1} [36] for three-co-ordinated oxygens of our compounds (Fig. 2), further assuming that the p.q.s. of axial bi-co-ordinated oxygen is –0.10 mm s^{-1}, *i.e.*, it practically corresponds to the value $\{OAlk\}^{tba}$ commented above. Despite these drastic assumptions about structure and p.q.s. data, it is observed that the calculated parameters (caption to Fig. 2) are in reasonable agreement with experimental data (Table I). In particular, the positive sign of ΔE of $Oct_2{}^nSnAdo$ obtained from its Mössbauer–Zeeman spectrum is reproduced by the point-charge model estimate. Besides, $\Delta(\Delta E) = \Delta E_{exp} - \Delta E_{calcd}$ is +0.33 for $Oct_2{}^nSnAdo$, *i.e.*, within the maximum accepted deviation of ±0.4 mm s^{-1} [35], while $\Delta E_{av.} = 3.08$ of Alk_2Sn nucleosidates yields a slightly larger value ($\Delta(\Delta E) = 0.41$ mm s^{-1}). It is worth mentioning that our value ΔE_{calcd} = +2.67 mm s^{-1} is in excellent agreement with the average data of $Bu_2{}^nSn$ 1,2-glycoxides, $\Delta E_{exp} = 2.79$ mm s^{-1} [29]. It may be concluded that the point-charge model treatment of ΔE strongly suggests the tin environment of Fig. 2 for all of our compounds.

The infrared spectra essentially support the preceding structural assumptions. In particular, vibrations concerning the purine or pyrimidine rings and C=O groups are fully coincident in nucleosides and their derivatives, the apparent discordance between ν(C=O) in guanosine and its complexes being explainable in terms of a particular situation of hydrogen bonds which shift ν(C=O) at abnormally high values (1730 cm^{-1}) in guanosine [37], while in its derivatives ν(C=O) lies in the expected range, *i.e.* near 1700 cm^{-1}. The differences in $\nu(NH_2)$ bands of ligand and complexes probably also arise from differences in hydrogen bonding. No evidence is found of any ν(Sn–N) mode, which could occur around 600 cm^{-1} [39, 27]. Any co-ordination of tin(IV) by the donor atoms of purine and pyrimidine residues can therefore be ruled out. Moreover, two strong bands have been identified in the spectra of almost all complexes at about 1100 and 1090 cm^{-1} (the presence of numerous and intense ligand bands in this region makes unequivocal assignments impossible in some cases) which can be assigned to ν(C–O) of C–O–Sn moieties [27]. The two observed ν(C–O) vibrations could be interpreted as previously reported for Me_2SnAdo [27], in terms of the presence of two different C–O groups, one of which could contain a three-co-ordinate oxygen atom according to the proposed structure. In the 400–600 cm^{-1} region there are expected vibrations concerning Sn–C and Sn–O bonds [27, 40] and tentative assignments are reported in Table II. In particular, the couple of ν(SnC) bands observed for the Me_2Sn^{IV} complexes (Table II) may be safely attributed to SnC_2, ν_s and ν_{as} modes [27], which again strongly suggests the occurrence of bent CSnC skeletons.

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References

1 L. G. Marzilli, in G. L. Eichhorn and L. G. Marzilli (eds.) 'Advances in Inorganic Biochemistry', Elsevier, North-Holland, Amsterdam, 1981, pp. 47–85 and refs. therein.
2 R. Melanson and F. D. Rochon, *Acta Crystallogr., Sect. B:, 34,* 3594 (1978).
3 S. Neidle, G. L. Taylor and A. B. Robins, *Acta Crystallogr. Sect. B:, 34,* 1838 (1978).
4 F. D. Rochon, P. C. Kong, B. Coulombe and R. Melanson, *Can. J. Chem., 58,* 381 (1980) and refs. therein.
5 R. E. Cramer, P. L. Dahlstrom, M. J. T. Seu, T. Norton and M. Kashivagi, *Inorg. Chem., 19,* 148 (1980).
6 F. Belanger-Gariepy andA. L. Beauchamp, *Cryst. Struct. Commun., 11,* 991 (1982).
7 B. T. Khan, G. N. Goud and S. V. Kumari, *Inorg. Chim. Acta, 80,* 145 (1983).
8 N. Hadjiliadis and G. Pneumatikakis, *J. Chem. Soc., Dalton Trans.,* 1691 (1978).
9 G. Pneumatikakis and N. Hadjiliadis, *J. Chem. Soc., Dalton Trans.,* 596 (1979).
10 P. Peringer, *Z. Naturforsch., Teil B:, 34,* 1459 (1979).
11 T. O'Connor and W. M. Scovell, *Chem. Biol. Interact., 26,* 227 (1979).
12 H. C. Nelson and J. F. Villa, *J. Inorg. Nucl. Chem., 42,* 133 (1980).
13 E. Matczak-Jon, B. Jeżowska-Trzebiatowska and H. Kozłowski, *J. Inorg. Biochem., 12,* 143 (1980).
14 P. C. Kong and F. D. Rochon, *Inorg. Chim. Acta, 46,* L1 (1980).
15 N. Farrel, *J. Inorg. Biochem., 14,* 261 (1981).
16 K. H. Scheller, V. Scheller-Krattiger and R. B. Martin, *J. Am. Chem. Soc., 103,* 6833 (1981).
17 N. Hadjiliadis, G. Pneumatikakis and R. Basosi, *J. Inorg. Biochem., 14,* 115 (1981).
18 B. Jeżowska-Trzebiatowska and S. Wolowiec, *Biochim. Biophys. Acta, 708,* 12 (1982).
19 D. W. Abbot and C. Woods, *Inorg. Chem., 22,* 1918 (1983) and refs. therein.
20 J. F. Conn, J. J. Kim, F. L. Suddath, P. Blattmann and A. Rich, *J. Am. Chem. Soc., 96,* 7152 (1974).
21 S. Suzuki, W. Mori and A. Nakahara, *Bioinorg. Chem., 3,* 281 (1974).
22 Y. H. Chao and D. R. Kearns, *J. Am. Chem. Soc., 99,* 6425 (1977).
23 H. C. Nelson and J. F. Villa, *J. Inorg. Nucl. Chem., 41,* 1643 (1979).
24 I. Sovago and B. Martin, *Inorg. Chim. Acta, 46,* 91 (1980).
25 E. Kupce and I. Sekacis, *Khim. Prir. Soedin,* 565 (1979).
26 D. Wagner, J. P. H. Verheyden and J. G. Moffatt, *J. Org. Chem., 39,* 24 (1974).
27 L. Pellerito, G. Ruisi, R. Barbieri and M. T. Lo Giudice, *Inorg. Chim. Acta, 21,* L33 (1977) and refs. therein.
28 A. G. Davies, L. Smith, P. J. Smith and W. McFarlane, *J. Organomet. Chem., 29,* 245 (1971).
29 P. J. Smith, R. F. M. White and L. Smith, *J. Organomet. Chem., 40,* 341 (1972).
30 S. D. David, C. Pascard and M. Cesario, *Nouveau J. de Chimie, 3,* 63 (1979) and refs. therein.
31 M. Famà, L. Pellerito, E. Bertoli, M. A. Girasolo and G. Spampinato, *XXIX Congr. Naz. Soc. Ital. Biochim.,* Saint Vincent (26–28 September 1983).
32 A. Silvestri, E. Rivarola and R. Barbieri, *Inorg. Chim. Acta, 23,* 149 (1977).
33 G. M. Bancroft, V. G. Kumar Das, T. K. Sham and M. G. Clark, *J. Chem. Soc., Dalton Trans.,* 643 (1976).
34 R. L. Collins andJ . C. Travis, in I.J . Gruverman, (Ed.), 'Mössbauer Effect Methodology, Vol. 3', Plenum, New York, 1967, p. 123.
35 G. M. Bancroft and R. H. Platt, *Adv. Inorg. Chem. Radiochem., 15,* 59 (1972) and refs. therein.
36 C. D. Hager, F. Huber, A. Silvestri and R. Barbieri, *Inorg. Chim. Acta, 49,* 31 (1981) and refs. therein.
37 C. L. Angell, *J. Chem. Soc.,* 504 (1961).
38 W. Beck and N.K ottmair, *Chem. Ber., 109,* 970 (1976).
39 A. Marchand, M. Riviere Baudet, R. Gassend and M. H. Soulard, *J. Organomet. Chem., 118,* 27 (1976).
40 H. Geissler and H. Kriegsmann, *J. Organomet. Chem., 11,* 85 (1968) and refs. therein.