APPLIED ORGANOMETALLIC CHEMISTRY, VOL. 10, 393–404 (1996)

Organometallic Complexes with Biological Molecules, VI. Diorganotin(IV) and Triorganotin(IV) Ampicillin and Methicillin Derivatives: Spectroscopic Investigations in the Solid State

Lorenzo Pellerito,*† Francesco Maggio*, Tiziana Fiore* and Alessandro Pellerito‡
* Dipartimento di Chimica Inorganica and ‡ Dipartimento di Chimica Fisica, Università di Palermo, 26 Via Archirafi, I-90123 Palermo, Italy

Derivatives of D(−)-α-aminobenzylpenicillin (ampicillin) and of 2,6-dimethoxyphenylpenicillin (methicillin) with diorgano- and triorgano-tin(IV) moieties have been synthesized. The stoichiometries of the compounds obtained were of the type $R_2SnClL{\cdot}H_2O$, $R_3SnClLNa{\cdot}H_2O$ [L=ampicillin or methicillin monoanion; R=Me, Bu, Ph] and $R_2Snampic_2 \cdot 2H_2O$ (ampic=ampicillin; R=Me, Bu, Ph). For $R_2SnClL{\cdot}H_2O$ and $R_3SnClLNa{\cdot}H_2O$, infrared (IR) data suggest five-coordination around the tin(IV) atom; in $R_2Snampic_2{\cdot}2H_2O$ six-coordination is most likely to occur. Thermogravimetric (TG) analysis excludes any involvement in the coordination of tin(IV) by water molecules, in any of the compounds. Trigonal bipyramidal configurations in the solid state are proposed for both $R_2SnClL{\cdot}H_2O$ and $R_3SnClLNa{\cdot}H_2O$ (L=ampicillin or methicillin) on the basis of the abovementioned IR and Mössbauer data.

As far as $R_2Snampic_2{\cdot}2H_2O$ compounds are concerned, the coordination geometry at tin could be, as previously reported for analogous $R_2Snamox_2.2H_2O$ derivatives, skew-trapezoidal bipyramidal, the monoanionic bidentate chelating ampicillin residue being in the trapezoidal plane and having bent axial organic groups.

Electronegativity equalization procedures have been applied to idealized trigonal bipyramidal structures for $R_2SnClL{\cdot}H_2O$ and $R_3SnClLNa{\cdot}H_2O$ (L=ampicillin or methicillin) and to octahedral *trans*-R_2 for $R_2Snampic_2{\cdot}2H_2O$, to estimate the partial atomic charges on the tin atoms, Q_{Sn}, which have been correlated with the isomer shift (δ) Mössbauer parameter.

Keywords: organotin; antibiotics; ampicillin; methicillin; infrared; Mössbauer

INTRODUCTION

Complexes of penicillin antibiotics (penicillin= penicillin G and amoxicillin) with organotin(IV) have been reported previously, and structural aspects both in the solid and in solution phase, together with their *in vivo* biological activity, have been discussed.[1–4] On the other hand, to the best of our knowledge, there have been only few other papers published recently dealing with ampicillin–metal interactions,[5,6] with none on methicillin–metal derivatives. The little information available deals with solid-state and solution-phase investigations with pure ampicillin[7–11] and methicillin only.[8,9,12] Different conformations of the five-membered thiazolidine ring, adopted by ampicilin in the solid state, have been demonstrated by X-ray crystallographic studies,[10] while its conformation in aqueous solution has been investigated in detail from analysis of the shifts and relaxation perturbations induced by lanthanide cations via ^1H and ^{13}C NMR data.[11]

EXPERIMENTAL

Materials and methods

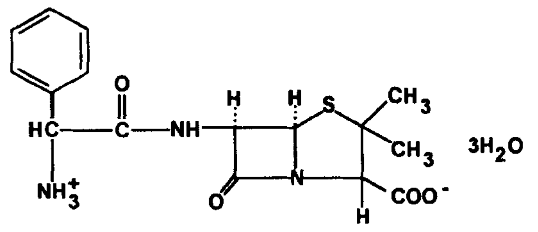
All reactants and solvents were reagent grade. Diorganotin(IV) dichloride, R_2SnCl_2(R=Me, Bu,

---

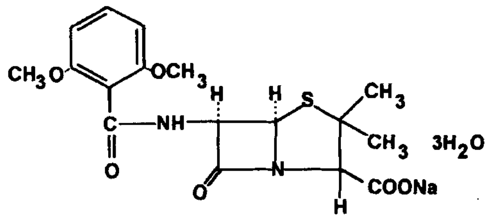
† Author to whom all correspondence should be addressed.

CCC 0268–2605/96/060393–12

Received 9 June 1995
Accepted 28 September 1995



Ampicillin



Methicillin Sodium salt

Figure 1 Ampicillin and methicillin structures.

Ph) and triorganotin(IV) chloride, R_3SnCl (R=Me, Bu, Ph) were a gift from Witco GmbH (Bergkamen, Germany).

D(−)-α-Aminobenzylpencillin trihydrate (ampicillin trihydrate) and 2,6-dimethoxyphenylpenicillin monosodium monohydrate (methicillin monosodium monohydrate), Fig. 1, were US Biochemical Corporation (Cleveland, OH, USA) products.

C, H and N analyses were performed at the Laboratorio di Chimica Organica, Università di Milano. Sn and Cl contents were determined in our laboratory according to standard methods (Table 1).[13, 14]

Thermogravimetric (TG) measurements (Table 1) were carried out with a Mettler TA-3000 system in a pure nitrogen atmosphere. SnO_2 and NaCl contents of the residual products were determined according to standard analytical procedures. In particular, a model 372 Perkin–Elmer atomic absorption spectrophotometer equipped with a graphite furnace has been used to assay sodium and tin contents.

IR spectra were recorded, as Nujol and hexachlorobutadiene mulls, on a Perkin–Elmer grating spectrometer model 983G, between CsI windows.

The spectra were recorded with a Perkin–Elmer 3600 data station with Perkin–Elmer PE983 software.

The ^{119}Sn Mössbauer spectra were measured with a model 639 TAKES (Bergamo) multichannel analyser and the following MWE (Munchen) apparatus: MR250 driving unit, FG2 digital function generator and MA250 velocity transducer, moving at linear velocity, constant acceleration in a triangular waveform.

A DN700 Oxford cryostat with an ITC502 temperature controller was used to maintain the absorber samples (absorber thickness, 0.50–0.60 mg $^{119}Sn/cm^2$) at the temperature under investigation. The temperature control was better than ±0.1 K.

The multichannel calibration was performed with an enriched iron foil (^{57}Fe=99.99%, thickness 0.06 mm, Dupont, MA, USA), at room temperature, by using a ^{57}Co–Pd (10 mCi), source (Dupont, MA, USA), while the zero point of the Doppler velocity scale was determined at room temperature through the absorption spectrum of natural $CaSnO_3$ (^{119}Sn=0.5 mg/cm^2) and $Ba^{119}SnO_3$ (10 mCi, Amersham) as source.

Syntheses

Diorganotin(IV) chloroampicillinate ($R_2SnClampic{\cdot}H_2O$) and triorganotin(IV) chloroampicillinate sodium ($R_3SnClampicNa{\cdot}H_2O$)

The sodium salt of the ampicillin was prepared by stirring 2 mmol of sodium methoxide and 2 mmol of ampicillin trihydrate in 100 cm^3 of methanol at room temperature, until solution was completed. After the addition of 2 mmol of organotin(IV) chloride (R_nSnCl_{4-n}, $n = 2, 3$), the suspension obtained was refluxed until a clear solution was obtained. Several products precipitated by cooling; they were filtered off and recrystallized from methanol. The solutions of several other derivatives were concentrated up to 10 cm^3 and diethyl ether was added if no precipitation occurred. The solids were filtered and recrystallized from ethanol.

Diorganotin(IV) bisampicillinate ($R_2Snampic_2{\cdot}2H_2O$)

The complexes were obtained by refluxing, in methanol, 2 mmol of diorganotin(IV) oxide, freshly prepared from the parent R_2SnCl_2 (R_2SnO, R=Me, Bu, Ph) and 4 mmol of

Table 1 Analytical data (calculated percentages in parentheses)

Compound[a]	H_2O[b]	C	H	N	Sn	Cl	Na
$Me_2SnClampic \cdot H_2O$	2.82	39.62	4.76	7.68	21.12	7.06	
	(3.27)	(39.26)	(4.76)	(7.63)	(21.56)	(6.44)	
$Bu_2SnClampic \cdot H_2O$	2.61	44.28	5.48	7.45	19.11	6.31	
	(2.84)	(45.41)	(6.03)	(6.62)	(18.70)	(5.59)	
$Ph_2SnClampic \cdot H_2O$	2.56	47.93	4.46	7.16	17.36	5.47	
	(2.67)	(49.84)	(4.48)	(6.23)	(17.59)	(5.25)	
$Me_3SnClampicNa \cdot H_2O$	3.07	38.20	5.16	6.97	19.88	5.76	3.80
	(2.92)	(38.77)	(4.97)	(7.14)	(20.16)	(6.02)	(3.91)
$Bu_3SnClampicNa \cdot H_2O$	2.57	47.28	6.74	5.34	16.48	4.65	3.19
	(2.52)	(47.04)	(6.62)	(5.88)	(16.60)	(4.96)	(3.22)
$Ph_3SnClampicNa \cdot H_2O$	2.13	52.28	4.78	5.12	15.36	4.72	2.91
	(2.32)	(52.70)	(4.55)	(5.42)	(15.32)	(4.58)	(2.97)
$Me_2Snampic_2 \cdot 2H_2O$	4.06	45.80	5.33	8.62	13.36		
	(4.08)	(46.32)	(5.26)	(9.53)	(13.46)		
$Bu_2Snampic_2 \cdot 2H_2O$	3.46	50.85	6.39	8.47	11.80		
	(3.73)	(49.75)	(6.05)	(8.07)	(12.29)		
$Ph_2Snampic_2 \cdot 2H_2O$	3.71	51.46	5.13	9.01	10.46		
	(3.58)	(52.55)	(5.01)	(8.36)	(11.81)		
$Me_2SnClmethic \cdot H_2O$	2.98	40.16	4.71	5.48	20.75	6.40	
	(3.09)	(39.24)	(4.68)	(4.82)	(20.41)	(6.10)	
$Bu_2SnClmethic \cdot H_2O$	2.53	45.41	5.65	4.90	18.51	6.02	
	(2.70)	(46.07)	(5.80)	(4.13)	(17.51)	(5.23)	
$Ph_2SnClmethic \cdot H_2O$	2.32	48.11	4.71	4.59	17.74	6.00	
	(2.55)	(49.35)	(4.43)	(3.97)	(16.82)	(5.02)	
$Me_3SnClmethicNa \cdot H_2O$	3.03	39.20	5.42	4.77	19.51	5.96	3.58
	(2.90)	(38.77)	(4.88)	(4.52)	(19.73)	(5.72)	(3.71)
$Bu_3SnClmethicNa \cdot H_2O$	2.53	45.66	6.32	3.73	15.63	5.49	2.95
	(2.41)	(46.70)	(6.49)	(3.76)	(15.91)	(4.75)	(3.08)
$Ph_3SnClmethicNa \cdot H_2O$	2.18	52.25	4.68	3.46	14.96	4.72	2.74
	(2.23)	(52.17)	(4.50)	(3.48)	(14.73)	(4.40)	(2.85)

[a] $Ampic^-$ $=ampicillin^-$ =D(−)-α-aminobenzylpenicillinate; $methic^-$ $=methicillin^-$ =2,6-dimethoxyphenylpenicillinate.

[b] H_2O was determined by TG.

ampicillin trihydrate, until clear solutions were obtained. On cooling, or after concentration to small volume (10 cm^3), the solid derivatives precipitated, and were then filtered and recrystallized from methanol.

Diorganotin(IV) chloromethicillinate ($R_2SnClmethic \cdot H_2O$) and triorganotin(IV) chloromethicillinate sodium ($R_3SnClmethicNa \cdot H_2O$)

Methanolic suspensions of methicillin sodium monohydrate (2 mmol) and of organotin(IV) chloride (2 mmol; R_nSnCl_{4-n}, $n = 2, 3$) were refluxed until clear solutions were obtained. The derivatives were recovered on cooling or by concentration to a small volume (10 cm^3). After filtration, the solids were recrystallized from ethanol.

RESULTS AND DISCUSSION

Infrared data

The infrared spectra of the new antibiotic derivatives have been analysed by comparing the experimental absorptions with those of the free ampicillin and methicillin ligands and with the spectra of the previously reported organotin(IV) penicillin G and amoxicillin compounds.[1,3] As in the case of the previous reported diorganotin(IV) complexes,[1,3] the major variations occurred in peptidic NH and amide I C═O stretches, in the β-lactamic C═O stretches and in the carboxylic COO^- asymmetric and symmetric stretching vibrations while shifts in peptidic NH and amide I C═O stretches and in the β-lactamic C═O stretches have been found in the cases of

Table 2 Assignment of significant absorption bands of ampicillin·$3H_2O$, $R_2Sn(IV)Clampic{\cdot}H_2O$, $R_2Sn(IV)ampic_2{\cdot}2H_2O$ and $R_3SnClampicNa{\cdot}H_2O$ derivatives in the 4000–250 cm^{-1} region[a, b]

Assignment	ampic·$3H_2O$[c]	I	II	III	IV	V	VI	VII	VIII	IX
ν_{OH}	3445 s	3500 s, bd	3450 s, bd	3450 s, bd	3450 s, bd			3450 m, bd	3460 m, bd	3490 s, bd
ν_{NH}	3200 m	3312 s, vbd	3290 s, vbd	3329 s, bd	3307 s, bd	3309 s, bd	3395 s, bd	3324 s, bd	3301 s, bd	3289 s, bd
$\nu_{NH_3^+}$	2700–2500 s, bd									
$\nu_{C{=}O}$ (β-lactam.)	1771 s	1737 s	1741 s	1737 s	1740 s	1752 s	1737 s	1739 s	1743 s	1740 s
$\nu_{C{=}O}$ (amide)	1688 s	1666 s	1670 s	1670 s	1666 s	1658 s	1660 s	1652 s, bd	1660 s, bd	1660 s, bd
ν_{asCOO^-}	1607 s	1612 s	1613 s	1594 s, bd	1607 s	1601 s	1597 s	1629 s, bd	1631 s, bd	1626 s, bd
$\nu_{NH_3^+}$	1572 s									
Amide II	1495 m	1516 m	1513 m	1502 s	1490 m	1510 w	1512 w	1514 m	1514 w	1515 w
ν_{sCOO^-}	1456 s	1366 s	1366 m	1367 s	1434 s	1453 s	1430 m	1366 s	1367 m	1366 m
ν_{CN}	1020 m	1026 m	1015 m	1023 m	1029 m	1020 m	1021 m	1025 m	1026 m	1022 m
ν_{CS}	588 m	600 w	600 m	580 m	600 m	595 m	580 m	580 w	598 m	596 m
ν_{asSnC_2}		560 m	560 m		550 m	530 m		559 m	563 w	
ν_{sSnC_2}		510 w	510 w		505 w	510 w		511 m	507 m	
Y-Ph				450 s			450 s			450 s
ν_{SnCl}		235 w	248 w	219 w	240 w	270 w	240 w			
$\Delta\nu$ (cm^{-1})	151	246	247	227	173	148	167	263	264	235

[a] Nujol and hexachlorobutadiene mulls; s, strong; m, medium; w, weak; bd, broad.

[b] ampic$^-$ =ampicillin$^-$ = *d*(−)-α-aminobenzylpenicillinate. I, $Me_2SnClampic{\cdot}H_2O$; II, $Bu_2SnClampic{\cdot}H_2O$; III, $Ph_2SnClampic{\cdot}H_2O$; IV, $Me_3SnClampicNa{\cdot}H_2O$; V, $Bu_3SnClampicNa{\cdot}H_2O$; VI, $Ph_3SnClampicNa{\cdot}H_2O$; VII, $Me_2Snampic_2{\cdot}2H_2O$; VIII, $Bu_2Snampic_2{\cdot}2H_2O$; IX, $Ph_2Snampic_2{\cdot}2H_2O$.

[c] Assignments according to Ref. 1.

Table 3 Assignment of significant absorption bands of methicillinNa·H_2O, $R_2Sn(IV)Clmethic\cdot H_2O$, and $R_3SnClmethicNa\cdot H_2O$ derivatives in the 4000–250 cm^{-1} region[a, b]

Assignment	methicNa	I	II	III	IV	V	VI
ν_{OH}	3450 s, bd	3450 s, bd	3450 s, bd	3450 s, bd	3450 s, bd	3400 s, bd	3430 s, bd
ν_{NH}	3361 s, bd	3337 s, bd	3296 s, bd	3350 s, bd	3375 s,bd	3312 s, bd	3395 s, bd
$\nu_{C=O}$(β-lactam)	1769 s	1737 s	1736 s	1736 s	1735 s	1731 s	1730 s
$\nu_{C=O}$(amide)	1641 s, bd	1643 s, bd	1643 s	1640 s	1642 s	1642 s	1641 s
ν_{asCOO^-}	1594 s, bd	1596 s	1598 s	1596 s	1597 s	1597 s	1596 s
Amide II(amido)	1510 m	1513 m	1513 m	1513 m	1510 m	1510 m	1510 w
ν_{sCOO^-}	1432 s	1367 m	1371 m	1370 m	1433 m	1430 m	1442 m
ν_{CN}	1028 m	1027 m	1028 m	1023 m	1029 m	1030 m	1022 m
ν_{asSnC_2}		558 m	560 w		549 s		
ν_{sSnC_2}		530 w	517 w		510 w	520 w	
Y-Ph				450 s			450 s
ν_{SnCl}		235 m	250 w	220 s	211 w	250 w	271 s
$\Delta\nu$(cm^{-1})	162	232	227	226	164	167	154

[a] Nujol and hexachlorobutadiene mulls; s, strong; m, medium; w, weak; bd, broad.

[b] $methic^-$ =$methicillin^-$ = 2,6-dimethoxyphenylpenicillinate. I, $Me_2SnClmethic\cdot H_2O$; II, $Bu_2SnClmethic\cdot H_2O$; III, $Ph_2SnClmethic\cdot H_2O$; IV, $Me_3SnClmethicNa\cdot H_2O$; V, $Bu_3SnClmethicNa\cdot H_2O$; VI, $Ph_3SnClmethicNa\cdot H_2O$.

triorganotin(IV) chloro-ampicillin and -methicillin.

As far as the peptidic NH and amide I C=O stretches are concerned, the shifts observed, in all the synthesized derivatives, in respect of the free ampicillin and methicillin ligands (Tables 2, 3) are a consequence of intermolecular hydrogen bondings.[10]

These findings, observed also in the penicillin G and amoxicillin organotin(IV) derivatives reported previously,[1, 3] would support probable hydrogen-bonded polymeric configurations for

Table 4 Experimental Mössbauer parameters,[a] isomer shift, δ (mm s^{-1}) and nuclear quadrupole splittings, $|\Delta E_{exp}|$ (mm s^{-1}), measured at liquid N_2 temperature and calculated nuclear quadrupole splittings, $\Delta E_{calcd.}$, according to the point charge formalism applied to the idealized structures of Fig. 2(a, b)

Compound	δ (mm s^{-1})	$\lvert\Delta E_{exp}\rvert$ (mm s^{-1})	Γ_1	Γ_2	C–Sn–C angle (deg.)	$\Delta E_{calcd.}$ (mm s^{-1})	Figure
$Me_2SnClampic\cdot H_2O$	1.18	3.12	1.03	1.09	123	3.17	2a
$Bu_2SnClampic\cdot H_2O$	1.35	2.98	0.91	1.03	120	3.17	2a
$Ph_2SnClampic\cdot H_2O$	1.07	2.64	1.04	1.10	121	2.78	2a
$Me_3SnClampicNa\cdot H_2O$	1.26	3.24	1.08	0.91	b	−3.77	2b
$Bu_3SnClampicNa\cdot H_2O$	1.40	3.42	1.01	0.99	b	−3.77	2b
$Ph_3SnClampicNa\cdot H_2O$	1.17	2.73	0.86	0.89	b	−3.26	2b
$Me_2SnClmethic\cdot H_2O$	1.27	3.20	1.00	1.09	125	3.17	2a
$Bu_2SnClmethic\cdot H_2O$	1.37	3.19	0.94	0.98	125	3.17	2a
$Ph_2SnClmethic\cdot H_2O$	1.19	2.73	0.96	1.03	124	2.78	2a
$Me_3SnClmethicNa\cdot H_2O$	1.32	3.53	1.00	1.03	b	−3.77	2b
$Bu_3SnClmethicNa\cdot H_2O$	1.44	3.53	0.79	0.84	b	−3.77	2b
$Ph_3SnClmethicNa\cdot H_2O$	1.28	2.82	1.01	1.07	b	−3.26	2b
$Me_2Snampic_2\cdot 2H_2O$	1.29	3.02	1.08	1.10	128	c	
$Bu_2Snampic_2\cdot 2H_2O$	1.37	3.10	1.01	1.03	130	c	
$Ph_2Snampic_2\cdot 2H_2O$	1.16	2.56	1.02	1.05	121	c	

[a] $ampic^-$ =$ampicillin^-$ =D(−)-α-aminobenzylpenicillinate; $methic^-$ =$methicillin^-$ =2,6-dimethoxyphenylpenicillinate; sample thickness ranged between 0.50 and 0.60 mg ^{119}Sn cm^{-2}; isomer shift, $\delta \pm 0.03$ mm s^{-1} with respect to $BaSnO_3$; Γ_1 and Γ_2 values are the full width at half height of the resonant peaks, respectively at greater and lower velocity with respect to the centroid of the Mössbauer spectra; nuclear quadrupole splittings, $\Delta E \pm 0.02$ mm s^{-1}.

[b] Not calculated (see Results and Discussion, Mössbauer data).

[c] Not reported in the Table (see Results nad Discussion, Mössbauer data).

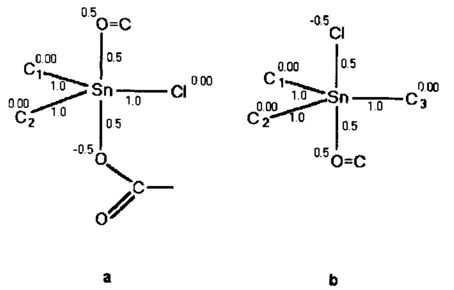


Figure 2 Regular tbp structures of tin assumed to estimate the nuclear quadrupole splittings according to the point charge model, for (a) $R_2SnClL{\cdot}H_2O$ and (b) $R_3SnClLNa{\cdot}H_2O$ derivatives (L=ampicillin and methicillin; Table 4). The partial quadrupole splittings used in the calculations are: $\{Alk\}^{tbe} = -1.13$; $\{Ph\}^{tbe} = -0.98$; $\{Cl\}^{tbe}_{unid} = 0.20$; $\{COO^-\}^{tba} = -0.10$; $\{CO\}^{tba}_{lact} = \{CO\}^{tba}_{DMA} = 0.16$ (see Refs 19). The indicated bond orders and formal charges are assumed as input in the calculation of partial atomic charge on the tin atom, Q_{Sn} (see text, Table 5 and Table 6).

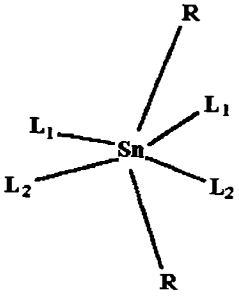


Figure 3 Skew trapezoidal bipyramidal configuration proposed for the $R_2Snampic_2{\cdot}2H_2O$ derivatives. L_1 and L_2 represent the oxygen donor atoms for each ampicillin moiety.

all the organotin(IV) ampicillin and organotin(IV) methicillin complexes.

Furthermore, in $R_2SnClL{\cdot}H_2O$ (L=ampicillin and methicillin; R=Me, Bu, Ph) and $R_2Snampic_2{\cdot}2H_2O$ complexes (Tables 2 and 3), β-lactamic $\nu_{C=O}$, $\nu_{as\,COO^-}$ and $\nu_{s\,COO^-}$ were subject to noticeable displacements, with respect to the free ligands, and $\Delta\nu$ values ($= \nu_{as\,COO^-} - \nu_{s\,COO^-}$) ranged from 235 to 264 cm^{-1} for $R_2Snampic_2{\cdot}2H_2O$, from 227 to 247 cm^{-1} for $R_2SnClampic{\cdot}H_2O$ and from 226 to 232 cm^{-1} for $R_2SnClmethic{\cdot}H_2O$; ($\Delta\nu$ for free ampicillinNa

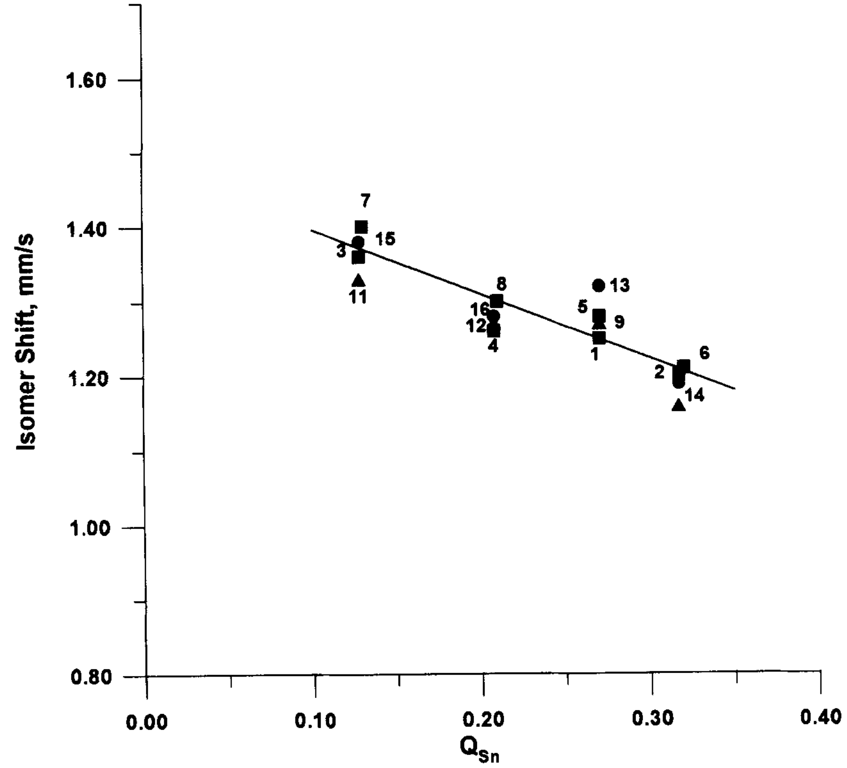


Figure 4 Isomer shifts, δ, versus atomic charge, Q_{Sn}, for $R_2SnClL{\cdot}H_2O$ and $R_3SnClLNa{\cdot}2H_2O$ (L=ampicillin and methicillin), amox and penG derivatives (Table 6). Full lines are the least-squares fits of data points. The related equations are: $\delta = 1.48 - 0.86Q_{Sn}$; $r = 0.938$.

Table 5 Calculated Q (CHELEQ)[22–30] values for the atoms bonded to the tin(IV) atoms, according to structures, bond orders and charges of Fig. 2(a, b) and Fig. 5

Compound[a]	Sn	C_1	C_2	C_3	Cl	$^{-}O{-}C{=}O$	C=O (β-lactamic)
$Me_2SnClL\cdot H_2O$	0.268	−0.025	−0.025		−0.093	−0.516	−0.040
$Bu_2SnClL\cdot H_2O$	0.271	−0.011	−0.011		−0.093	−0.516	−0.040
$Ph_2SnClL\cdot H_2O$	0.317	−0.042	−0.042		−0.091	−0.515	−0.051
$Me_3SnClLNa\cdot H_2O$	0.150	−0.028	−0.028	0.018	−0.507		−0.042
$Bu_3SnClLNa\cdot H_2O$	0.105	−0.017	−0.017	−0.464	−0.509		−0.042
$Ph_3SnClLNa\cdot H_2O$	0.208	−0.009	−0.009	−0.110	−0.506		−0.042
$Me_2Snampic_2\cdot 2H_2O$	0.443	−0.164	−0.164			−0.396	0.011
						−0.396	0.011
$Bu_2Snampic_2\cdot 2H_2O$	0.445	−0.148	−0.148			−0.396	0.011
						−0.396	0.011
$Ph_2Snampic_2\cdot 2H_2O$	0.481	−0.140	0.140			−0.395	0.012
						−0.395	0.012

[a] L=ampicillin$^-$ or methicillin$^-$.

and methicillinNa were 151 and 162 cm^{-1}, respectively (Tables 2 and 3).

Such $\Delta\nu$ values are characteristic, in all these cases, of monodentate ester-type coordination of the carboxylic group.[15, 16].

In $R_3SnClLNa\cdot H_2O$ (L=ampicillin and methicillin; R=Me, Bu, Ph) variations occurred only in β-lactamic $\nu_{C=O}$, while $\Delta\nu$ values ranged from 148 to 173 cm^{-1} for $R_3SnClampicNa\cdot H_2O$ and from 154 to 167 cm^{-1} for $R_3SnClmethicNa\cdot H_2O$. Calculated $\Delta\nu$ values suggest that the carboxylate group maintains, both in $R_3SnClampicNa\cdot H_2O$ and in $R_3SnClmethicNa\cdot H_2O$, the same configuration is possessed in the free ligands, which, consequently are not involved in coordination of the tin atom.

In conclusion, as in the previously reported penicillin G and amoxicillin derivatives,[1, 3] the infrared data suggest coordination of β-lactamic C=O and unidentate ester-type COO$^-$ groups to

Table 6 Experimental Mössbauer parameter, isomer shift δ (mms^{-1} and calculated partial atomic charge on tin atoms. Q_{Sn} (CHELEQ)[22–30] for homologous series of penta-coordinated triorgano- and diorgano-tin(IV) derivatives.

Compound[a]	δ[b]	Q_{Sn}[b]	Point N[c]	Reference
$Alk_2SnClamox\cdot 2H_2O$	1.24	0.270	1	3
$Ph_2SnClamox\cdot 2H_2O$	1.20	0.317	2	3
$Alk_3SnClamoxNa\cdot 2H_2O$	1.36	0.128	3	3
$Ph_3SnClamoxNa\cdot 2H_2O$	1.26	0.208	4	3
$Alk_2SnClpenG$	1.28	0.270	5	1
$Ph_2SnClpenG$	1.21	0.317	6	1
$Alk_3SnClpenGNa$	1.40	0.128	7	1
$Ph_3SnClpenGNa$	1.30	0.208	8	1
$Alk_2SnClampic\cdot H_2O$	1.27	0.270	9	This work
$Ph_2SnClampic\cdot H_2O$	1.07	0.317	10	This work
$Alk_3SnClampicNa\cdot H_2O$	1.33	0.128	11	This work
$Ph_3SnClampicNa\cdot H_2O$	1.17	0.208	12	This work
$Alk_2SnClmethic\cdot H_2O$	1.32	0.270	13	This work
$Ph_2SnClmethic\cdot H_2O$	1.19	0.317	14	This work
$Alk_3SnClmethicNa\cdot H_2O$	1.38	0.128	15	This work
$Ph_3SnClmethicNa\cdot H_2O$	1.28	0.208	16	This work

[a] amox$^-$ =Amoxicillin$^-$; penG$^-$ =penicillinG$^-$; ampic$^-$ =ampicillin$^-$; methic$^-$ =methicillin$^-$.

[b] Average of the δ and Q_{Sn}(CHELEQ) values reported in the cited references.

[c] Identification numbers of the points plotted in Fig. 4.

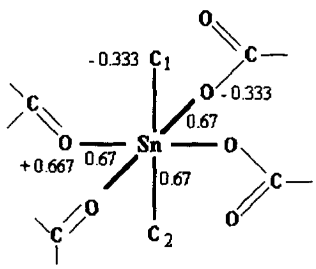


Figure 5 Regular octahedral structure of tin assumed to calculate the partial atomic charge on tin atom, Q_{Sn}, for the derivatives of Table 7. Bond orders and formal charges assumed as input in the calculation are also indicated (see text, Table 5 and Table 7).

the R_2SnCl moiety in $R_2SnClL{\cdot}H_2O$, and coordination through the β-lactamic C=O to the R_3SnCl moiety in $R_3SnClLNa{\cdot}H_2O$, (L= ampicillin and methicillin; R = Me, Bu, Ph). For both $R_2SnClL{\cdot}H_2O$ and $R_3SnClLNa{\cdot}H_2O$ the tin atom would reach five-coordination in a trigonal bipyramidal configuration. Finally, for $R_2Snmpic_2 \cdot 2H_2O$, six-coordination would be attained through the coordination of the β-lactamic C=O and the unidentate ester type COO^- groups of the two ampicillinate ligands.

Thermogravimetric analysis, carried out up to 600 °C, excluded, for all the derivatives, the possible involvement of the water molecules in coordination to the tin atom. Indeed, a single-step water loss, occurring between 60 and 110 °C, is present in all of the compounds synthesized.

The residual products, at 600 °C, for organotin(IV) ampicillin and methicillin derivatives depend, as in the case of the organotin(IV) amoxicillin compounds,[3] on which derivatives are being analysed. $R_2SnClL{\cdot}H_2O$ and $R_2Snampic_2{\cdot}2H_2O$ compounds gave SnO_2 as the final residue, while a mixture of SnO_2 and NaCl was obtained from the $R_3SnClLNa{\cdot}H_2O$ derivatives.

Mössbauer data

The Mössbauer parameters isomer shift (δ, mm s^{-1}) and quadrupole splitting ($|\Delta E|$, mm s^{-1}) are reported for all the newly synthesized organotin(IV) ampicillin and methicillin derivatives in Table 4, together with the full-width-at-half-height of the resonant peaks at greater and lower velocities respectively, respect to the centre of the Mössbauer spectra, Γ_1 and Γ_2. Table 4 summarizes also the C–Sn–C angles calculated for the diorganotin(IV) derivatives according to the Sham and Bancroft model,[17] which states that such C–Sn–C angles in $R_2Sn(IV)$ derivatives can be calculated approximately by ignoring the contribution of atoms other than the carbons of the organic groups bonded to the tin atom as the reference point. If these conditions held, C–Sn–C angles may be calculated as (180°−2θ) (Table 4), where θ may be derived from [Eqn [1]:

$$|\Delta E| = 4\{R\}[1 - 3\cos^2\theta \sin^2\theta]^{1/2} \qquad [1]$$

Table 7 Experimental Mössbauer parameter, isomer shift δ (mms^{-1}) and calculated partial atomic charge on tin atoms. Q_{Sn} (CHELEQ)[22–30] for homologous series of skew trapezoidal bipyramidal diorganotin(IV) derivatives

Compound[a]	δ^b	$Q_{Sn}{}^b$	Point N[c]	References
$Alk_2Snamox_2{\cdot}2H_2O$	1.31	0.443	1	3
$Ph_2Snamox_2{\cdot}2H_2O$	1.14	0.481	2	3
$Bu_2Snhydroxamate_2$	1.28	0.443	3	31
$Alk_2Sn[S_2CNR_2]_2$	1.59	0.227	4	32, 33
$Alk_2Snpdtc$	1.54	0.227	5	34
$Alk_2Snbis(2-SPy)$	1.56	0.178	6	35
$Me_2Sn(2\text{-}SPyO)_2$	1.30	0.330	7	36
$Alk_2Snampic_2{\cdot}2H_2O$	1.33	0.443	8	This work
$Ph_2Snampic_2{\cdot}2H_2O$	1.16	0.481	9	This work

[a] $amox^-$ =amoxicillin$^-$; hydroxamate=(*N*-alkyl-*N*-benzoylhydroxylamino) or (*N*-alkyl-*N*-*p*-bromobenzoylhydroxylamino); $S_2CNR_2^-$ =dialkyl and diphenyl dithiocarbamate; $pdtc^-$ = piperazinebis(dithiocarbamate); $2\text{-}SPy^-$ = 2-pyridinethiolato; $2\text{-}SPyO^-$ =2-pyridinethiolato-*N*-oxide; ampic=ampicillin$^-$.

[b] Average of the δ and Q_{Sn}(CHELEQ) values reported.

[c] Identification numbers of the points plotted in Fig. 6.

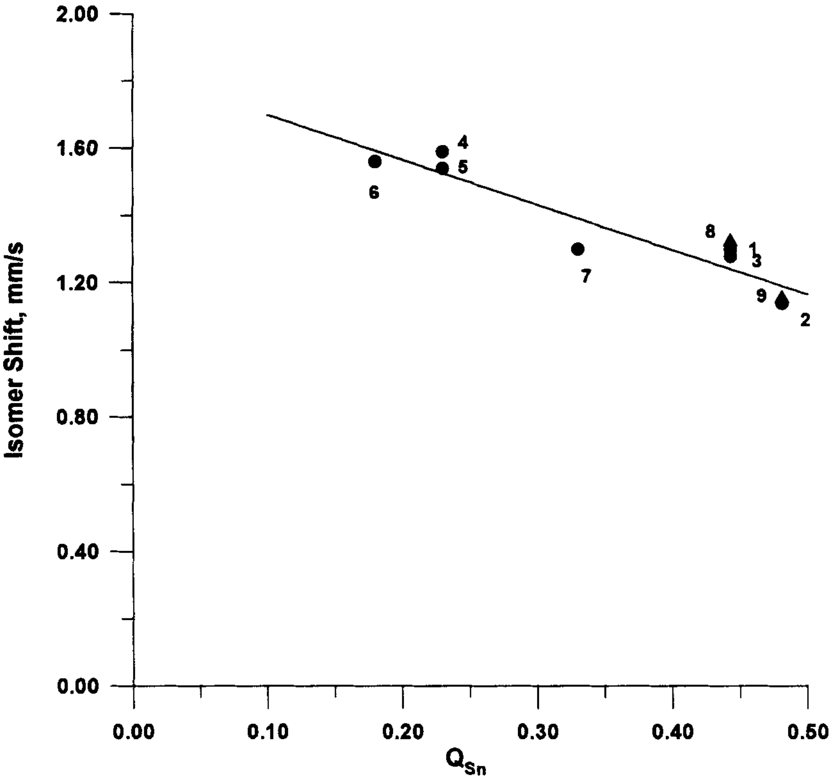


Figure 6 Isomer shifts, δ, versus atomic charge, Q_{Sn}, for $R_2Snampic_2 \cdot 2H_2O$ and related derivatives of Table 7. Full lines are the least-squares fits of data points. The related equations are: $\delta = 1.83 - 1.33Q_{Sn}$; $r = 0.962$.

where $\{R\}$ is the partial quadrupole splitting of the hydrocarbon groups.[18, 19]

Furthermore, rationalization of the nuclear quadrupole splittings according to the point charge model formalism,[18–21] applied to the idealized trigonal bipyramidal of Fig. 2(a, b), has been used for both $R_2SnClL \cdot H_2O$ and $R_3SnClLNa \cdot H_2O$ derivatives (L=ampicillin and methicillin; R=Me, Bu, Ph) to estimate the calculated ΔE values reported in Table 4, which agree with the experimental data to less than ± 0.4 mm s^{-1}, the maximum difference allowed between experimental and calculated ΔE values in order to accept the predicted geometry[21]).

For $R_2Snampic_2 \cdot 2H_2O$, calculations according to the point charge model formalism are not reported in Table 4. Owing to the high distortion from idealized octahedral geometry [as can be inferred on the basis of the calculated C–Sn–C angles in such derivatives (Table 4)], it is unrealistic to report such calculations.[18–21] Differences between experimental and calculated ΔE are, in these cases, much greater than the allowed ± 0.4 mm s^{-1}. As an example, for both $Me_2Snampic_2 \cdot 2H_2O$ and $Bu_2Snampic_2 \cdot 2H_2O$ the calculated ΔE is 4.19 mm s^{-1}, while for $Ph_2Snampic_2 \cdot 2H_2O$ the calculated ΔE is 3.93 mm s^{-1}.

Experimental $|\Delta E|$ values for diorganotin(IV)ampic$_2$ compounds ranged from 2.56 mm s^{-1} for $Ph_2Snampic_2 \cdot 2H_2O$, 3.02 mm s^{-1} for $Me_2Snampic_2$. $2H_2O$, up to 3.10 mm s^{-1} for $Bu_2Snampic_2 \cdot 2H_2O$ (Table 4). These values are normally consistent with a tetrahedral arrangement around the tin(IV) atoms (although highly distorted towards octahedral *trans*-R_2 configuration), but with anisobidentate ampicillinate, whose coordination would occur through ester-type carboxylate and β-lactamic carbonyl oxygens, the C–Sn–C angles range from 121° in $Ph_2Snampic_2 \cdot 2H_2O$ up to 130° in $Bu_2Snampic_2 \cdot 2H_2O$ (Table 4; Fig. 3). Such values are far from the 180° value characteristic of the C–Sn–C angle in the idealized *trans*-R_2Sn octahedral configuration of Fig. 5.

Further structural information can be deduced by correlating the partial atomic charges on the tin(IV) atom, Q_{Sn}, and the isomer shift, δ (mm s^{-1}), of the derivatives under investigation

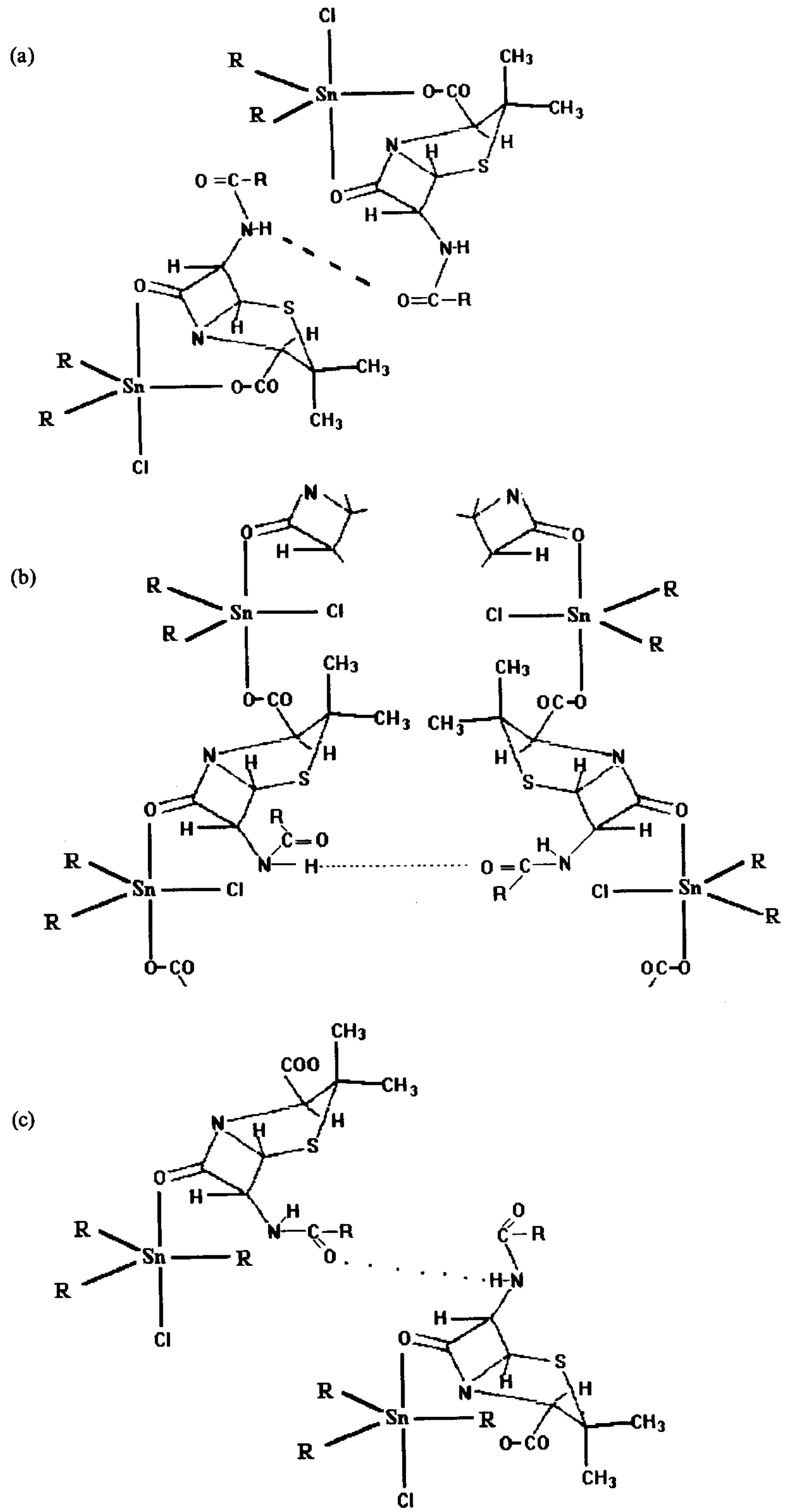


Figure 7 Proposed structures for $R_2SnClL{\cdot}H_2O$ (a, b) and $R_3SnClLNa{\cdot}2H_2O$ (c) derivatives (L=ampicillin and methicillin).

with those of congener and isostructural compounds.[22–30] It is important, therefore, that the structures of the comparison compounds have been determined by X-ray methods and also that the isomer shifts of such compounds have been measured. The partial atomic charges on the tin(IV) atom and on the atoms directly bonded to the tin, Q_{ai}, can be calculated according to the orbital electronegativity equalization procedure, described in detail by Jolly and Perry.[28–30]

Such an equalization procedure can be performed by equating, for any two atoms a_ia_j bonded to each other, the orbital electronegativity of the atom a_i forming a bond with the atom a_j, $\chi\widehat{a_ia_j}$, with the orbital electronegativity of the atom a_j bonded to the atom a_i, $\chi\widehat{a_ja_i}$. In molecules possessing $n+1$ atoms with n bonds, the sum of the negative charges, $\Sigma q\widehat{a_ia_k}$, transferred from the atom a_i to all the other atoms except a_j, may be calculated by resolution of n linear equations (Eqn [2]) with n unknowns.[26, 28–30]

$$\chi\widehat{a_ia_j} = \chi\widehat{a_ja_i} \qquad [2]$$

Finally, the partial atomic charge, Q_{a_i} on each of the n atoms, may be obtained according to Eqn [3].[28, 29]

$$Q_{a_i} = F_{a_i} + \sum q_{a_i a_k} \qquad [3]$$

by the use of software program CHELEQ, which has been developed by Jolly and co-workers.[28–30] Bond orders and formal charges, used as input data in the CHELEQ program, have been attributed by assuming the idealized tbp valence bond structures for $R_2SnClL{\cdot}H_2O$ and $R_3SnClLNa{\cdot}H_2O$ derivatives (L=ampicillin and methicillin; R=Me, Bu, Ph) and the idealized octahedral structure for $R_2Snampic_2{\cdot}2H_2O$ shown in Figs 2(a), 2(b) and 5, respectively. Table 5 summarizes the partial atomic charges on the tin atoms and on the atoms directly bonded to tin, obtained as output of the CHELEQ program for all the diorgano- and triorgano-tin(IV) ampicillin and methicillin derivatives under investigation.

For comparison, partial atomic charges on tin(IV) atoms, Q_{Sn}, for the analogous diorganotin(IV)ClpenG, triorganotin(IV)ClpenGNa, diorganotin(IV))Clamox·2H$_2$O and triorganotin(IV) ClamoxNa·2H$_2$O compounds, whose trigonal bipyramidal configuration has been previously suggested,[1, 3] are reported in Table 6, together with their experimental isomer shifts, δ.

The experimental isomer shifts, δ, for all the derivatives in Table 6 have been subsequently plotted as a function of the partial atomic charges on tin, Q_{Sn} (Fig. 4).

The dependence of δ on Q_{Sn} is linear, in agreement with results obtained for a number of homologous organotin(IV) compounds.[22–27]

An analogous linear trend has been obtained for the isomer shifts, δ, for the diorganotin(IV) bisampicillinates, $R_2Snampic_2{\cdot}2H_2O$, and for the other six-coordinated comparison complexes reported in Table 7, as a function of the partial atomic charge on tin atom, Q_{Sn}, calculated using the CHELEQ program; the bond orders and formal charges for the assumed *trans*-R_2 octahedral configuration of Fig. 5 were input to the program.

Figure 6 shows the reasonably good linear trend of the data within the homologous series represented; this, qualitatively, led us to assume that at least the analyzed six-coordinated derivatives must be congeners and isostructural.[22–27]

In conclusion, Figs. 7(a–c) represent the probable structures of the organotin(IV) chloroampicillin and -methicillin derivatives obtained, as extracted from IR data and from preliminary molecular dynamic investigations of tin nuclei carried out in analogous organotin(IV)chloroamoxicillin complexes by variable-temperature ^{119}Sn Mössbauer spectroscopy.[37]

Acknowledgement Financial support by the Ministero per l'Università e la Ricerca Scientifica e Tecnologica, Roma, is gratefully acknowledged.

REFERENCES

1. F. Maggio, A. Pellerito, L. Pellerito, S. Grimaudo, C. Mansueto and R. Vitturi, *Appl. Organomet. Chem.* **8**, 71 (1994).
2. R. Vitturi, C. Mansueto, A. Gianguzza, F. Maggio and L. Pellerito, *Appl. Organomet. Chem.* **8**, 509 (1994).
3. L. Pellerito, F. Maggio, M. Consiglio, A. Pellerito, G. C. Stocco and S. Grimaudo, *Appl. Organomet. Chem.* **9**, 227 (1995), and references quoted therein.
4. R. Vitturi, B. Zava, M. S. Colomba, A. Pellerito, F. Maggio and L. Pellerito, *Appl. Organomet. Chem.* **9**, 561 (1995).
5. P. G. Navarro, A. M. Garcia and P. M. De Las Parras, *Polyhedron* **11**, 1049 (1992).
6. S. J. Lyle and S S. Yassin, *Anal. Chim. Acta* **274**, 225 (1993).
7. E. Ivashkiv, in *Ampicillin in Analytical Profiles of Drug*

Substances, Vol. 2, Florey, K. (ed.), Academic Press, New York, 1973, pp. 1—61 and references quoted therein.
8. S. K. Branch, A. F. Casy and E. M. A. Ominde, *J. Pharm. Biomed. Anal.* **5**, 73 (1987).
9. S. K. Branch, A. F. Casy, A. Lipczynski and E. M. Ominde, *Magn. Res. Chem.* **24**, 465 (1986).
10. M. N. G. James, D. Hall and D. C. Hodgkin, *Nature (London)* **220**, 168 (1968).
11. C. M. Dobson, L. O. Ford, S. E. Summers and R. J. P. Williams, *J. Chem. Soc., Faraday Trans.* **71**, 1145 (1975).
12. F. Cotta Ramusino and R. Intonti, *Farmaco* **16**, 227 (1961).
13. W. P. Neuman, *Die Organische Chemie des Zinns*, Verlag, Stuttgart, 1967.
14. W. Schöniger, *Microchim. Acta* **9**, 123 (1955).
15. G. B. Deacon and R. J. Phillips, *Coord. Chem. Rev.* **33**, 227 (1980).
16. G. B. Deacon, F. Huber and R. J. Phillips, *Inorg. Chim. Acta* **104**, 41 (1985).
17. T. K. Sham and G. M. Bancroft, *Inorg. Chem.* **14**, 2281 (1975).
18. G. M. Bancroft and R. H. Platt, *Adv. Inorg. Chem. Radiochem.* **15**, 59 (1972).
19. G. M. Bancroft, V. G. Kumar Das, T. K. Sham and M. G. Clarck, *J. Chem. Soc., Dalton Trans.* 643 (1976), and references quoted therein.
20. R. L. Collins and J. C. Travis, The electric field gradient tensor. In: *Mössbauer Effect Methodology*, Vol. 3, Gruverman, I. J. (ed.), Plenum Press, New York, 1967, p. 123.
21. M. G. Clark, A. G. Maddock and R. H. Platt, *J. Chem. Soc., Dalton Trans.* 281 (1972).
22. E. Rivarola, A. Silvestri and R. Barbieri, *Inorg. Chim. Acta* **28**. 223 (1978).
23. R. Barbieri and A. Silvestri, *Inorg. Chim. Acta* **47**, 201 (1981).
24. R. Barbieri and A. Silvestri, *J. Chem. Soc., Dalton Trans.* 1019 (1984).
25. R. Barbieri, A. Silvestri, G. Ruisi and G. Alonzo, *Inorg. Chim. Acta* **97**, 113 (1985).
26. R. Barbieri and F. Huber, *Gazz. Chim. Ital.* **123**, 223 (1993).
27. C.-D. Hager, F. Huber, A. Silvestri, A. Barbieri and R. Barbieri, *Gazz. Chim. Ital.* **123**, 583 (1993).
28. W. L. Jolly and W. B. Perry, *J. Am. Chem. Soc.* **95**, 5442 (1973).
29. W. L. Jolly and W. B. Perry, *Inorg. Chem.* **13**, 2686 (1974).
30. W. B. Perry and W. L. Jolly, The calculation of atomic charge in molecules by an electronegativity equalization procedure: a description of program CHELEQ. US Atomic Energy Comm., Contract W-7405-ENG-48 (Nov. 1974).
31. V. S. Petrosyan, N. S. Yashina, T. V. Sizova, T. V. Leonova, L. A. Aslanov, A. V. Yatsenko and L. Pellerito, *Appl. Orgaomet. Chem.* **8**, 11 (1984).
32. B. W. Fitzsimmons, A. A. Owusu, N. J. Seelev and A. W. Smith, *J. Chem. Soc. (A)* 935 (1970).
33. J. C. May, D. Petridis and C. Curran, *Inorg. Chim. Acta* **5**, 511 (1974).
34. K. C. Molloy and T. G. Purcell, *J. Organomet. Chem.* **303**, 179 (1986).
35. M Bouâlam, J. Meunier-Piret, M. Biesemans, R. Willem and M. Gielen, *Inorg. Chim. Acta* **198**, 249 (1993).
36. W. S. Ng, C. Wei, V. G. Kumar Das and T. C. Mak, *J. Organomet. Chem.* **334**, 295 (1987).
37. A. Pellerito, F. Maggio and L. Pellerito, *Abstracts of 35th Meeting of the Mössbauer Spectroscopy Discussion Group, University of Nottingham*, 1994, p. 21.