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Synthesis, spectroscopic characterization and *in vitro* antitumour activity of di-n-butyltin and diethyltin trimethoxybenzoates: X-ray structure analysis of bis[di-n-butyl(3,4,5-trimethoxybenzoato)tin] oxide

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Di-n-butyltin(IV) and diethyltin(IV) 2,3,4-, 2,4,5- and 3,4,5-trimethoxybenzoates $[(CH_3O)_3C_6H_2COO]_2SnR$ [Type a] and $\{[(CH_3O)_3C_6H_2COO]R_2Sn\}_2O$ [Type b] have been synthesized and characterized spectroscopically.

The crystal structure of bis[di-n-butyl(3,4,5-trimethoxybenzoato)tin] oxide has been determined. The triclinic unit cell contains one centrosymmetric dimer; $a = 15.919(2)$ Å, $b = 11.711(3)$ Å, $c = 13.475(1)$ Å, and $\alpha = 63.63(2)°$, $\beta = 67.49(1)°$, $\gamma = 76.61(2)°$. The geometry of the dimer is very similar to that of bis[di-n-butyl(5-methoxysalicylatotin] oxide, with two different types of five-coordinate tin atoms and one central planar Sn_2O_2 ring.

Keywords: Organotin, benzoate, antitumour, X-ray, NMR, Mössbauer, mass spectrometry

INTRODUCTION

Diorganotin methoxysalicylates have showed promising antitumour activity.[1] We have prepared some di-n-butyltin and diethyltin trimethoxybenzoates in order to compare their activities with those of the methoxysalicylates. They are characterized by X-ray diffraction analysis as well as by ^1H, ^{13}C and ^{119}Sn NMR, and by Mössbauer and mass spectrometry. The compounds prepared are either diorganotin bistrimethoxybenzoates, which

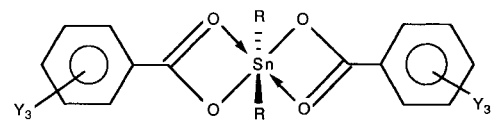

Figure 1 Structure of diorganotin dibenzoates (Type **a**).

are compounds of Type **a** (Fig. 1)[2] or bis(diorgano-[trimethoxybenzoato]tin) oxides, which are compounds of Type **b** (Fig. 2).[3]

In compounds of Type **a**, the structure is that of a strongly distorted square bipyramid, with equatorial bidentate carboxylate groups and apical organic groups bound to tin, as found for instance for di-n-butyltinbis(*o*-aminobenzoate).[2] For compounds of type **b**, the expected structure is a dimeric one, as for bis(5-methoxysalicylato-di-n-butyltin) oxide.[3]

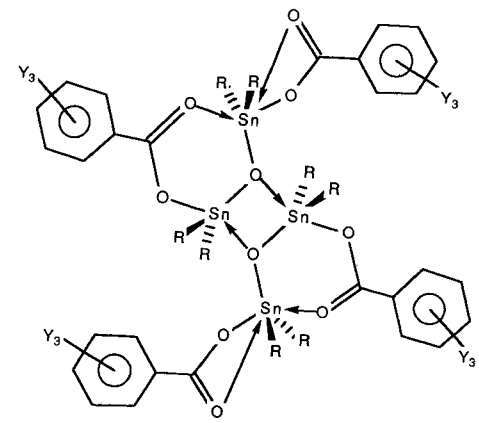

Figure 2 Structure of bis[diorgano(benzoato)tin] oxides (Type **b**).

Atomic coordinates and further X-ray data are available from the author.

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RESULTS AND DISCUSSION

Syntheses

The compounds prepared are of the type $(XYZC_6H_2COO)_2Sn(n\text{-}C_4H_9)_2$ (Type **a**) and $[(XYZC_6H_2COO)(n\text{-}C_4H_9)_2Sn]_2O$ (Type **b**), with:

X, Y, Z = 2-OCH_3, 3-OCH_3, 4-OCH_3 (compounds **1a** and **1b**),

X, Y, Z = 2-OCH_3, 4-OCH_3, 5-OCH_3 (compounds **2a** and **2b**),

X, Y, Z = 3-OCH_3, 4-OCH_3, 5-OCH_3 (compounds **3a** and **3b**),

and

$(XYZC_6H_2COO)_2Sn(C_2H_5)_2$ (Type **a**) and $[(XYZC_6H_2COO)(C_2H_5)_2Sn]_2O$ (Type **b**), with

X, Y, Z = 2-OCH_3, 3-OCH_3, 4-OCH_3 (compounds **4a** and **4b**),

X, Y, Z = 2-OCH_3, 4-OCH_3, 5-OCH_3 (compounds **5a** and **5b**),

X, Y, Z = 3-OCH_3, 4-OCH_3, 5-OCH_3 (compounds **6a** and **6b**).

They are obtained from the condensation of the appropriate diorganotin oxide and trimethoxybenzoic acid, in the molar ratio 1:2 for type **a** compounds, and 1:1 for type **b** ones.

X-ray diffraction data

The final atomic coordinates obtained for compound **3b** are given in Table 1 and its structure is shown in Fig. 3. Selected bond lengths and angles are described in Table 2.

The triclinic unit cell contains one centrosymmetric dimer, the geometry of which is very similar to that of bis[di-n-butyl(5-methoxysalicylatotin] oxide (see Fig. 2). The structure is built around a four-membered ring Sn_2O_2; it contains two different types of tin atoms and two distinct carboxylate moieties. One carboxylate group is bidentate and bridges a tin atom of the Sn_2O_2 unit to the exocyclic Sn(2) atom; the other carboxylate [with O(11) and O(12)] is monodentate and coordinates Sn(2).

Both tin atoms in the asymmetric moiety of the compound form five short bonds in a distorted trigonal bipyramidal geometry. In addition, each tin atom forms a weaker intramolecular coordination with one oxygen of the non-bridging carboxylate group [Sn(1) · · · O(12) and Sn(2) · · · O(11)]. In a recent review,[4] Tiekink classifies organotin carboxylate compounds according to their structural patterns. There is a great similarity between the present compound and the structural Type **1** described in Section 3.3.1. The structural para-

Table 1 Final atomic coordinates of $[3,4,5\text{-}(CH_3O)_3C_6H_2COO)(n\text{-}C_4H_9)_2O$, compound **3b** ($\times 10^4$, except $\times 10^5$ for Sn) with e.s.d. values in parentheses

	x/a	*y/b*	*z/c*
Sn(1)	47442(4)	7359(7)	37701(5)
Sn(2)	28646(4)	6774(7)	64706(5)
O(1)	7013(4)	872(7)	1774(5)
O(2)	5580(5)	716(9)	1999(6)
O(3)	5391(5)	2571(8)	−2079(6)
O(4)	7089(6)	3132(8)	−3516(6)
O(5)	8469(5)	2723(9)	−2701(6)
O(6)	4200(4)	289(6)	5630(5)
O(11)	1487(5)	2322(8)	5728(6)
O(12)	2904(4)	1991(7)	4687(5)
O(13)	−122(6)	4829(10)	2651(8)
O(14)	1202(7)	5594(9)	612(8)
O(15)	2968(6)	4912(9)	482(7)
C(1)	6578(6)	1609(9)	65(7)
C(2)	5862(6)	1796(10)	−350(8)
C(3)	6039(7)	2337(10)	−1561(9)
C(4)	6920(7)	2650(10)	−2327(8)
C(5)	7629(7)	2420(10)	−1874(8)
C(6)	7472(7)	1894(10)	−668(8)
C(7)	6381(7)	1033(10)	1378(8)
C(8)	4498(9)	2171(12)	−1325(11)
C(9)	6999(10)	4484(15)	−4069(13)
C(10)	9241(9)	2308(12)	−2296(11)
C(11)	1857(7)	3345(10)	3667(9)
C(12)	949(7)	3690(10)	3742(10)
C(13)	734(7)	4420(11)	2711(11)
C(14)	1439(9)	4807(12)	1621(10)
C(15)	2334(7)	4452(11)	1585(9)
C(16)	2570(7)	3708(10)	2607(3)
C(17)	2078(7)	2525(10)	4771(9)
C(18)	−853(11)	4587(15)	3745(14)
C(19)	1228(14)	4925(20)	−72(19)
C(20)	3895(10)	4858(14)	401(12)
C(21)	4967(8)	2704(12)	3121(11)
C(22)	5524(14)	2958(19)	3637(19)
C(23)	5748(13)	4334(17)	3126(18)
C(24)	6596(17)	4472(25)	3260(26)
C(25)	3842(7)	−366(10)	3735(9)
C(26)	3546(11)	484(17)	2595(14)
C(27)	2641(13)	228(22)	2759(18)
C(28)	2453(10)	1062(15)	1559(14)
C(29)	2078(7)	−660(11)	6564(10)
C(30)	1174(10)	−912(15)	7488(13)
C(31)	640(11)	−1764(15)	7328(14)
C(32)	280(14)	−978(20)	6323(17)
C(33)	2887(7)	2128(11)	7035(9)
C(34)	2277(8)	2004(13)	8263(10)
C(35)	1320(8)	1712(14)	8544(11)
C(36)	694(9)	1710(15)	9733(12)

meters in compound **3b** are quite similar to those reported by Tiekink for 11 compounds of the type $\{[R_2(R'COO)Sn]_2O\}_2$. The only noticeable difference is observed in the rather weak contacts Sn(1)···O(12) (3.020 Å) and Sn(2)···O(11) (2.744 Å), the corresponding values reported by Tiekink being in the ranges 2.746–3.164 and 2.632–2.886 Å. Steric factors might be responsible for the lengthening of Sn(1)···O(12).

Spectroscopic data

The ^{1}H NMR spectra of compounds of Type **a** and of Type **b** (see Experimental section) confirm the expected structures.

Indeed, for compounds of Type **a**, a single triplet is observed for the methyl group of the ethyltin or butyltin substituent, as expected for the monomeric structure shown in Fig. 1. In contrast, for compounds of Type **b**, two triplets are observed for the methyl groups, one for the alkyl groups linked to the tin atoms involved in the dioxadistannetane ring and another one for the alkyl groups bound to the other tin atoms. This shows that the dimeric structure of the solid state is maintained in $CDCl_3$ solution.

The ^{13}C NMR spectra also basically exhibit pairs of signals for the butyl or ethyl carbons for compounds of Type **b**, and single signals for those of compounds of Type **a**. The ^{13}C assignments in the aromatic parts are easily achieved on the basis of DEPT spectra and incremental chemical shift rules on substituted benzene compounds.[5] The calculated values are given between parentheses and in italics in the Experimental section.

From the $J(^{13}C-^{119}Sn)$ coupling constants observed experimentally (see Experimental section), C–Sn–C angles as small as 130° and as large as 170° can be estimated using the equations proposed by Lockhart[6,7] and Howard[8] for compounds **2a** and **6a**, respectively, whereas these two compounds are characterized by quite similar Mössbauer parameters (Q.S. = 4.12 and 3.97 and I.S. = 1.44 and 1.56 mm s^{-1}, respectively), which underlines the low sensitivity of these Mössbauer parameters to structural changes, in contrast with the $J(^{13}C-^{119}Sn)$ coupling constant. The angles estimated for the other compounds lie between these two values.

The ^{119}Sn NMR spectra also show the same dichotomy: a single resonance is observed for the monomeric dibenzoates. Two signals with identical intensities exhibiting the unresolved $^2J(^{119}Sn-O-^{117/119}Sn)$ coupling satellites are observed for the dimeric distannoxanes, as previously reported.[3,6–9]

Generally, Mössbauer spectrometry does not reveal two different types of tin atoms in compounds of Type **b**.[1,3] However, for compound **4b**, two doublets of equal intensities have been obtained. For the other compounds, only a single doublet is seen.

All the mass spectrometric fragment-ions observed are compatible with the fragmentation rules described in the literature.[10–12]

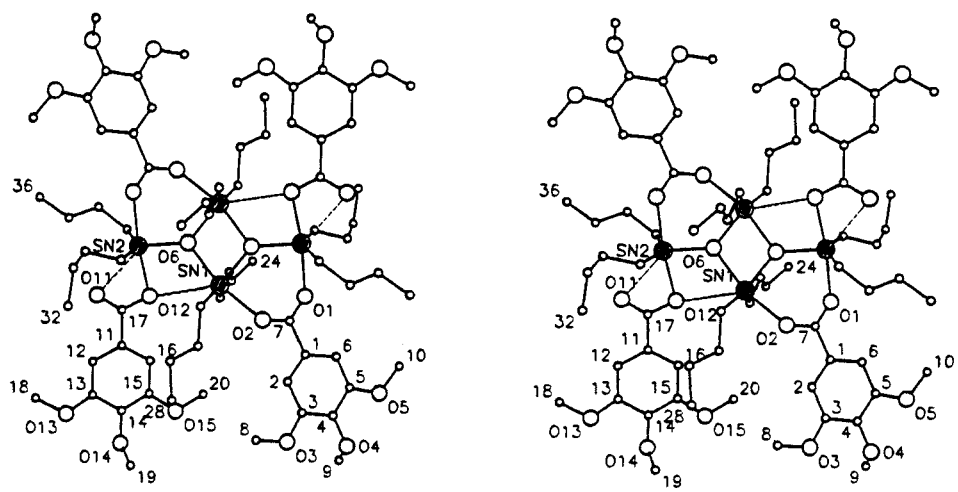

Figure 3 Stereoview of the molecular structure and numbering scheme for compound **3b**

Table 2 Selected bond distances (Å) and angles (deg) of $[3,4,5\text{-}(CH_3O)_3C_6H_2COO)(n\text{-}C_4H_9)_2Sn]_2O$, compound **3b**, with e.s.d. values in parentheses

O(2)–Sn(1)	2.251(7)	O(6)–Sn(1)–O(2)	163.8(3)
O(6)–Sn(1)	2.166(6)	C(21)–Sn(1)–O(2)	89.9(4)
O(6*)–Sn(1)	2.040(6)	C(21)–Sn(1)–O(6)	100.1(4)
O(12)–Sn(1)	3.020(6)	C(25)–Sn(1)–O(2)	84.2(3)
C(25)–Sn(1)	2.167(11)	C(25)–Sn(1)–O(6)	96.8(3)
C(21)–Sn(1)	2.134(12)	C(25)–Sn(1)–C(21)	137.1(4)
O(1*)–Sn(2)	2.303(6)	O(12)–Sn(2)–O(6)	81.9(2)
O(6)–Sn(2)	2.044(5)	C(29)–Sn(2)–O(6)	107.5(3)
O(12)–Sn(2)	2.189(6)	C(29)–Sn(2)–O(12)	94.2(3)
C(29)–Sn(2)	2.156(11)	C(33)–Sn(2)–O(6)	104.8(3)
C(33)–Sn(2)	2.159(11)	C(33)–Sn(2)–O(12)	95.9(3)
O(11)–Sn(2)	2.744(7)	C(33)–Sn(2)–C(29)	147.2(4)
C(17)–O(11)	1.227(11)	C(7)–O(2)–Sn(1)	129.8(7)
C(17)–O(12)	1.304(11)	Sn(2)–O(6)–Sn(1)	123.4(3)
C(7)–O(1)	1.252(11)	C(17)–O(12)–Sn(2)	105.7(6)
C(7)–O(2)	1.260(11)	O(2)–Sn(1)–O(6*)	88.8(4)
O(6)–Sn(1)–O(6*)	76.2(4)	O(11)–C(17)–O(12)	121.1(9)
O(6*)–Sn(1)–C(21)	106.5(4)	O(6*)–Sn(1)–C(25)	115.7(4)
O(12)–Sn(1)–O(2)	133.5(4)	O(12)–Sn(1)–O(6)	62.2(4)
O(12)–Sn(1)–O(6*)	137.6(4)	O(12)–Sn(1)–C(21)	75.0(4)
O(12)–Sn(1)–C(25)	78.8(4)	O(6)–Sn(2)–O(1*)	90.9(4)
O(12)–Sn(2)–O(1*)	171.9(4)	C(33)–Sn(2)–O(1*)	89.5(4)
C(29)–Sn(2)–O(1*)	84.5(4)	O(11)–Sn(2)–O(1*)	135.6(4)
O(11)–Sn(2)–O(6)	133.4(4)	O(11)–Sn(2)–O(12)	51.6(4)
O(11)–Sn(2)–C(29)	80.1(4)	O(11)–Sn(2)–C(33)	82.0(4)
Sn(1)–O(6)–Sn(1*)	103.8(3)	Sn(2)–O(6)–Sn(1*)	132.3(3)
Sn(2)–O(1*)–C(7*)	125.9(7)	O(1)–C(7)–O(2)	124.4(9)

In vitro antitumour activity

The results of the *in vitro* tests performed[13] on selected compounds are given as ID_{50} values in Table 3 and compared with data on some compounds that are currently used clinically as antitumour agents.

From Table 3, it is clear that all compounds tested are more active *in vitro* than cisplatin and etoposide against the two tumour cell lines; they are however less active than doxorubicin and mitomycin C; their activity is also lower than that of several substituted di-n-butyltin salicylates previously tested.[1,3]

Table 3 ID_{50} values (ng cm^{-3}) of organotin derivatives tested against two human tumour cell lines, MCF-7 and WiDr

Compound no.	MCF-7	WiDr
1a	93	398
2a	132	368
3a	84	356
1b	82	323
3b	87	364
Cisplatin[13]	850	624
Doxorubicin[13]	63	31
Etoposide[13]	187	624
Mitomycin C[13]	3	17

EXPERIMENTAL

Instruments

The Mössbauer spectra were recorded with constant acceleration mode on an Elscint MVT4 Promeda counting instrument, with a $Ca^{119m}SnO_3$ source from Amersham. The probe was maintained at a temperature between 90 and 100 K, whereas the source was kept at room temperature. The digital data, treated by least squares with an iterative program, were deconvoluted as a sum of lorentzians. The ^1H NMR spectra were recorded on a Bruker AM 270 instrument working in the FT mode, equipped with an Aspect 2000 computer; the ^{13}C NMR spectra were obtained from a Bruker SF 250 instrument

equipped with an Aspect 3000 computer. The ^{119}Sn NMR spectra were obtained from a Bruker WM 500 instrument at 186.5 MHz.

The mass spectra were recorded on a V.G. Micromas 7070 F instrument (source temperature: 200 °C).

X-ray diffraction analysis of compound 3b

A crystal with dimensions 0.15 mm × 0.20 mm × 0.33 mm was used for the X-ray study. Crystal data of $[C_{36}H_{58}O_{11}Sn_2]_2$: $M = 1808.47$; $D_{calc}(g\,cm^{-3}) = 1.45$; $\mu_{MoK} = 11.45\,cm^{-1}$; triclinic space group $P\bar{1}$; $a = 15.919(2)$, $b = 11.711(3)$, $c = 13.475(1)$ Å, $\alpha = 63.63(2)$, $\beta = 67.49(1)$, $\gamma = 76.61(2)°$, $V = 2073.5(7)$ Å^3, $Z = 1$; $F(000) = 924$. Lattice parameters were obtained from least-squares fits with 21 reflections of 2Θ between 4 and 27. Data collection was done with a HUBER-diffractometer using graphite-monochromated molybdenum radiation ($\lambda = 0.71069$ Å) at ambient temperature. Data were collected with ω–2Θ scan mode (scan width = 1.20°) to 2Θ = 49°. A total of 6908 independent reflections was measured of which 5003 [$I > 2.5\sigma(I)$] were used in the calculations ($h - 16/18$, $k - 11/13$, l 0/14). No absorption correction was made. The structure was solved by interpretation of the Patterson function and refined by Fourier synthesis and full-matrix least-squares procedure (SHELX76),[14] using anisotropic thermal parameters (except for the atoms of methyl and butyl groups). No attempt was made to locate hydrogen atoms. The largest peak in the final ΔF map has a height of 1.8 eÅ^3. Final Δ/σ_{max} is 0.06. The final agreement factor R is 0.055 for 5003 observed reflections, $S = 2.731$.

Syntheses

Compounds of Type **a** were typically prepared as follows. To 1.36 g (6.4 mmol) of trimethoxybenzoic acid dissolved in 150 cm^3 of toluene and 50 cm^3 of ethanol were added 0.8 g (3.2 mmol) di-n-butyltin oxide or 0.93 g (3.2 mmol) diethyltin oxide. The mixture was refluxed for 6 h and the ternary azeotrope water/ethanol/toluene was distilled off with a Dean–Stark funnel. Half of the remaining solution was evaporated under vacuum. The oily compound obtained was crystallized (*vide infra*). The synthesis of compounds of Type **b** was similar but typically only one-half of the quantity, i.e. 0.68 g (3.2 mmol) of trimethoxybenzoic acid was used.

Spectroscopic characterization

Abbreviations: d, doublet; q, quartet; s, singlet; t, triplet; m, complex pattern; nv, non-visible; u, unresolved because of overlappings (Fig. 4).

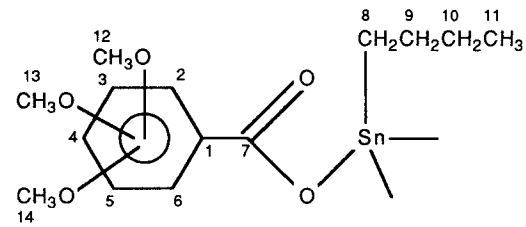

Figure 4

Compound 1a

[2,3,4-(CH$_3$O)$_3$C$_6$H$_2$COO]$_2$Sn(n-Bu)$_2$

Yield: 97%; recrystallized from ethanol, m.p. 57–58 °C.

Mössbauer: QS, 3.61; IS, 1.44; Γ_1 0.92, Γ_2 0.88 mm s^{-1}.

^{1}H NMR ($CDCl_3$): H(5), 6.73 (d, 9); H(6), 7.82 (d, 9); H-8 and 9, 1.71–1.80 (m); H (10), 1.42 (tq, 7,7); H(11), 0.89 (t, 7); H(12), H(13) and (14), 3.90 (s), 3.92 (s), and 3.95 (s).

^{13}C NMR (DMSO-d_6): C(1), 119.2 (*calcd, 109.1*); C(2), 153.4 (*148.4*); C(3), 142.0 (*130.8*); C(4), 155.8 (*151.0*); C(5), 107.1 (*107.1*); C(6), 126.1 (*124.7*); C(7), 172.5; C(8) 29.3 [$^1J(^{119/117}Sn–^{13}C) = 862/822$]; C(9), 26.4 [$^2J(Sn–C) = 40$]; C(10), 25.2 [$^3J(Sn–C) = 134$]; C(11), 13.1; C(12), C(13) and C(14): 55.6, 60.0 and 61.0.

^{119}Sn NMR ($CDCl_3$): −152.7.

Mass spectrometry: $[(CH_3O)_3C_6H_2COO]_2SnBu^+$, 100; $[(CH_3O)_3C_6H_2COO]$ $[(CH_3O)_3C_6H_2]SnBu^+$, 34; $[(CH_3O)_3C_6H_2]_2SnBu^+$, 37; $[(CH_3O)_3C_6H_2COO]SnBu_2^+$, 14; $[(CH_3O)_3C_6H_2]SnBuH^+$, 3; $[(CH_3O)_3C_6H_2COO]Sn^+$, 10; $[(CH_3O)_3C_6H_2]Sn^+$, 71; $[(CH_3O)_2C_6H_3]Sn^+$: 14%.

Compound 2a

[2,4,5-(CH$_3$O)$_3$C$_6$H$_2$COO]$_2$Sn(n-Bu)$_2$

Yield: 94%; recrystallized from ethanol, m.p. 143–144 °C.

Mössbauer: QS, 4.12; IS, 1.44; Γ_1, 0.98, Γ_2, 0.97 mm s^{-1}.

^{1}H NMR ($CDCl_3$): H(3), 6.49 (s); H(6), 7.54 (s); H(8), H(9), 1.69–1.74 (m); H (10), 1.35 (tq, 7,7); H(11), 0.83 (t, 7); H(12), H(13) and H(14): 3.85 (s), 3.88 (s) and 3.90 (s).

^{13}C NMR ($CDCl_3$): C(1), 110.1 (*calcd, 109.1*); C(2), 156.0 (*155.1*); C(3), 97.3 (*100.4*); C(4), 153.9 (*151.0*); C(5), 142.5 (*137.5*); C(6), 115.5 (*118.0*); C(7), 174.1; C(8), 25.2 [$^1J(^{119/117}Sn-^{13}C) = 603/576$]; C(9), 26.6 [$^2J(Sn-C) = 41$]; C(10), 26.2 [$^3J(Sn-C) = 109$]; C(11), 13.4; C(12), C(13) and C(14), 55.9, 56.4 and 56.9.

^{119}Sn NMR ($CDCl_3$): −161.0.

Mass spectrometry: $[(CH_3O)_3C_6H_2COO]_2SnBu^+$, 100; $[(CH_3O)_3C_6H_2COO][(CH_3O)_3C_6H_2]SnBu^+$, 53; $[(CH_3O)_3C_6H_2COO]_2Sn^+$, 11; $[(CH_3O)_3C_6H_2]_2SnBu^+$, 67; $[(CH_3O)_3C_6H_2COO]SnBu_2^+$, 14; $[(CH_3O)_2C_6H_2COO]SnBu_2^+$, 8; $[(CH_3O)_2C_6H_2COO]SnBuH^+$, 4; $[(CH_3O)_3C_6H_2]SnBuH^+$, 6; $[(CH_3O(_3C_6H_2COO]Sn^+$, 14; $[(CH_3O)_2C_6H_3COO]Sn^+$, 9; $[(CH_3O)_3C_6H_2]Sn^+$, 94; $[(CH_3O)_2C_6H_3]Sn^+$, 37 %.

Compound 3a
$[3,4,5\text{-}(CH_3O)_3C_6H_2COO]_2Sn(n\text{-}Bu)_2$

Yield: 91%; recrystallized from ethanol, m.p. 112–113 °C

Mössbauer: QS, 3.98; IS, 1.53; Γ_1: 0.84, Γ_2: 0.88 mm s^{-1}.

^{1}H NMR ($CDCl_3$): H(2) and H(6), 7.41 (s), H (8) and H(9): 1.70–1.85 (m); H(10): 1.43 (tq, 7,7); H(11), 0.91 (t, 7); H(12) and H(14), 3.95 (s); H(13), 3.93 (s).

^{13}C NMR (DMSO-d_6): C(1), 126.7 (*calcd, 124.5*); C(2) and C(6), 106.5 (*109.3*); C(3) and C(5), 152.3 (*146.2*); C(4), 141.0 (*135.6*); C(7), 172.9; C(8), 30.1 [$^1J(^{119/117}Sn-^{13}C) = 893/863$]; C(9), 26.5 [$^2J(Sn-C) = 40$]; C(10), 25.3 [$^3J(Sn-C) = 141$]; C(11), 13.2; C(12) and C(14), 55.6; C(13), 59.7.

^{119}Sn NMR ($CDCl_3$) −157.5.

Mass spectrometry: $[(CH_3O)_3C_6H_2COO]_2SnBu^+$, 100; $[(CH_3O)_3C_6H_2COO][(CH_3O)_2C_6H_3COO]SnBu^+$, 4; $[(CH_3O)_3C_6H_2COO][(CH_3O)_3C_6H_2]SnBu^+$, 7; $[(CH_3O)_3C_6H_2COO]_2Sn^+$, 11; $[(CH_3O)_3C_6H_2COO]SnBu_2^+$, 12; $[(CH_3O)_3C_6H_2COO]Sn^+$, 59; $[(CH_3O)_2C_6H_3]SnBuH^+$, 5; $[(CH_3O)_3C_6H_2]Sn^+$, 26 %.

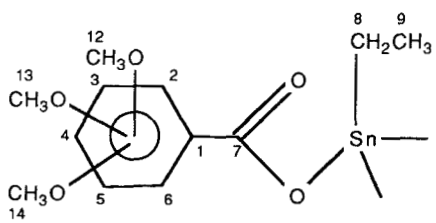

Figure 5

Compound 1b, dimer of
$\{[2,3,4\text{-}(CH_3O)_3C_6H_2COO]n\text{-}Bu_2Sn\}_2O$

Yield: 79%; recrystallized from ethanol, m.p. 87–88 °C.

Mössbauer: QS, 3.47; IS, 1.33; Γ_1, 0.95, Γ_2, 0.94 mm s^{-1};

^{1}H NMR ($CDCl_3$): H(5), 6.66 (d, 9); H(6), 7.41 (d, 9); H(8), 1.62–1.79 (m); H(9), 1.52–1.58 (m); H(10), 1.28 (tq, 7, 7) and 1.33 (tq, 7, 7); H(11), 0.79 (t, 7) and 0.84 (t, 7); H(12), H(13) and H(14), 3.85 (s), 3.87 (s) and 3.88 (s).

^{13}C NMR ($CDCl_3$): C(1), 122.0 (*calcd, 109.1*); C(2), 153.4 (*148.4*); C(3), 142.4 (*130.8*); C(4), 155.4 (*151.0*); C(5), 106.2 (*107.1*); C(6), 125.4 (*124.7*); C(7), 171.8; C(8), 24.7 and 25.9 [$^1J(Sn-C) = u$]; C(9), 26.9 and 27.1 [$^2J(Sn-C) = u$]; C(10), 26.4 and 26.5 [$^3J(Sn-C) = u$]; C(11), 13.1; C(12), C(13) and C(14): 55.6, 60.5 and 61.2

^{119}Sn NMR ($CDCl_3$): −212.2 and −212.6 ($^2J(SnOSn) = 101$].

Mass spectrometry: $[(CH_3O)_3C_6H_2COO]_2SnBu^+$, 3%; $[(CH_3O)_3C_6H_2COO][(CH_3O)_3C_6H_2]SnBu^+$, 6; $[(CH_3O)_3C_6H_2]_2SnBu^+$, 4; $[(CH_3O)_3C_6H_2COO]SnBu_2^+$, 100; $[(CH_3O)_2C_6H_3COO]SnBu_2^+$, 2; $[(CH_3O)_3C_6H_2]SnBu_2^+$, 23; $[(CH_3O)_2C_6H_3COO]SnBuH^+$, 6; $[(CH_3O)_3C_6H_2]SnBuH^+$, 23; $[(CH_3O)_3C_6H_2COO]Sn^+$, 24; $[(CH_3O)_2C_6H_3]Sn^+$, 88; $BuSn^+$, 19.

Compound 2b (main signals; decomposes partly in solution), dimer of $\{[2,4,5\text{-}(CH_3O)_3C_6H_2COO]n\text{-}Bu_2Sn\}_2O$

Yield: 87%; recrystallized from ethanol, m.p. 123–124 °C.

Mössbauer: QS, 3.20; IS, 1.30; Γ_1, 0.94, Γ_2, 0.90 mm s^{-1}.

^{1}H NMR ($CDCl_3$): H(3), 6.51 (s); H(6), 7.33 (s); H(8) and H(9), 1.51–1.78 (m); H(10); 1.33 (m, 7); H(11), 0.82 (t, 7) and 0.84 (t, 7); H(12), H(13) and H(14), 3.85 (s), 3.86 (s) and 3.93 (s).

^{13}C NMR ($CDCl_3$): C(1), 115.2 (*calcd, 109.1*); C(2), 152.1 (*155.1*); C(3), 97.6 (*100.4*); C(4), 154.2 (*151.0*); C(5), 142.2 (*137.5*); C(6), 114.6 (*118.0*); C(7), 172.2; C(8), 28.1 [$^1J(Sn-C) = ca$ 695, noisy and badly resolved] and 28.9 [$^1J(Sn-C) = ca$ 679, noisy and badly resolved]; C(9), 27.3 and 27.6 [$^2J(Sn-C) = u$]; C(10), 26.8 and 27.0 [$^3J(Sn-C) = u$]; C(11), 13.6; C(12), C(13) and C(14), 56.0, 56.3 and 56.5.

^{119}Sn NMR ($CDCl_3$): −210.0 and −221.6 [$^2J(SnOSn) = 123$].

Mass spectrometry: $[(CH_3O)_3C_6H_2COO]_2SnBu^+$, 100%; $[(CH_3O)_3C_6H_2COO][(CH_3O)_3$

C_6H_2]SnBu$^+$, 68; [$(CH_3O)_3C_6H_2]_2$SnBu$^+$, 67; [$(CH_3O)_3C_6H_2]_2$Sn$^+$, 7; [$(CH_3O)_3C_6H_2$COO]SnBu$_2^+$, 56; [$(CH_3O)_3C_6H_2$]SnBu$_2^+$, 28; [$(CH_3O)_3C_6H_2$]SnBuH$^+$, 14; [$(CH_3O)_3C_6H_2$COO]Sn$^+$, 15; [$(CH_3O)_3C_6H_2$]Sn$^+$, 52; [$(CH_3O)_2C_6H_3$]Sn$^+$, 12; BuSn$^+$, 17 %.

Compound 3b, dimer of {[3,4,5-$(CH_3O)_3C_6H_2$COO]n-Bu_2Sn}$_2$O

Yield: 84%; recrystallized from ethanol, m.p. 123–124 °C.

Mössbauer: QS, 3.77; IS, 1.31; Γ_1, 0.99, Γ_2 0.98 mm s^{-1}.

^{1}H NMR ($CDCl_3$): H(2) and H(6), 7.27 (s); H(8), 1.73–1.80(m); H(9), 1.56–1.62 (m); H(10), 1.28–1.43 (m); H(11), 0.82 (t, 7) and 0.87 (t, 7); H(12) and H(14), 3.93 (s); H(13), 3.92 (s).

^{13}C NMR ($CDCl_3$): C(1), 128.2 (*calcd, 124.5*); C(2) and C(6), 107.1 (*109.3*); C(3) and C(5), 152.6 (*146.2*); C(4), 141.7 (*135.6*); C(7), 172.4; C(8), 29.6 [$^1J(^{119/117}Sn-^{13}C) = 732/704$] and 28.6 ($^1J(^{119/117}Sn-^{13}C) = 728/694$]; C(9), 27.6 [$^2J$(Sn–C) = 37] and 27.3 [$^2J$(Sn–C) = 37]; C(10), 26.6 and 26.5 [^3J(Sn–C) = 136]; C(11), 13.34 and 13.27; C(12) and C(14), 56.0; C(13), 60.6

^{119}Sn NMR ($CDCl_3$): −206.9 and −220.8 [^2J(Sn–O–Sn) = 141].

Mass spectrometry: [$(CH_3O)_3C_6H_2$COO]$_2$SnBu$^+$, 58; [$(CH_3O)_3C_6H_2$COO][$(CH_3O)_3C_6H_2$]SnBu$^+$, 4; [$(CH_3O)_3C_6H_2$COO]$_2$Sn$^+$, 5; [$(CH_3O)_3C_6H_2$COO]SnBu$_2^+$, 100; [$(CH_3O)_3C_6H_2$COO]Sn$^+$, 44; [$(CH_3O)_3C_6H_2$]Sn$^+$, 28; BuSn$^+$: 5 %.

Compound 4a, [2,3,4-$(CH_3O)_3C_6H_2$COO]$_2$SnEt$_2$ (Fig. 5)

Yield: 71%; recrystallized from ethanol, m.p. 109–111 °C.

Mössbauer: QS, 4.32; IS, 1.545; Γ_1, 0.94, Γ_2, 0.94 mm s^{-1}.

^{1}H NMR ($CDCl_3$): H(5), 6.69 (d, 9); H(6), 7.79 (d, 9); H(8), 1.77 [q, 8; ^2J(Sn–H) = 68]; H(9), 1.36 (t, 8; $^3J(^{119/117}Sn-^1H) = 142/135$]; H(12), H(13) and H(14), 3.84 (s), 3.86 (s) and 3.94 (s).

^{13}C NMR ($CDCl_3$): C(1), 116.6 (*calcd, 109.1*); C(2), 154.8 (*148.4*); C(3), 142.4 (*130.8*); C(4), 157.1 (*151.0*); C(5), 106.4 (*107.1*); C(6), 127.8 (*124.7*); C(7). 173.9; C(8), 17.1 [$^1J(^{119/117}Sn-^{13}C] = 615/588$]; C(9), 8.6 [$^2J$(Sn–C) = 43]; C(12), C(13) and C(14), 55.6, 60.6 and 61.4.

^{119}Sn NMR ($CDCl_3$): −156.9.

Mass spectrometry: [$(CH_3O)_3C_6H_2$COO]$_2$SnEt$^+$, 100; [$(CH_3O)_3C_6H_2$COO][$(CH_3O)_3C_6H_2$]SnEt$^+$, 39; [$(CH_3O)_3C_6H_2]_2$SnEt$^+$, 78; [$(CH_3O)_3C_6H_2$COO]SnEt$_2^+$, 17; [$(CH_3O)_3C_6H_2$]SnEt$_2^+$, 15; [$(CH_3O)_3C_6H_2$COO]Sn$^+$, 10; [$(CH_3O)_2C_6H_3$COO]Sn$^+$, 6; [$(CH_3O)_3C_6H_2$]Sn$^+$, 48; [$(CH_3O)_2C_6H_3$]Sn$^+$, 12; C_6H_5Sn$^+$, 18%.

Compound 5a, [2,4,5-$(CH_3O)_3C_6H_2$COO]$_2$SnEt$_2$

Yield: 90%; recrystallized from petroleum ether, m.p. 135–139 °C.

Mössbauer: QS, 3.89; IS, 1.52; Γ_1, 0.86; Γ_2, 0.90 mm s^{-1}.

^{1}H NMR ($CDCl_3$): H(3), 6.52 (s); H(6), 7.58 (s); H(8), 1.77 [q, 8; $^2J(^{119/117}Sn-^1H) = 71/69$]; H(9), 1.34 [t, 8; $^3J(^{119/117}Sn-^1H) = 148/140$]; H(12), H(13) and H(14), 3.88 (s), 3.93 (s) and 3.94 (s).

^{13}C NMR ($CDCl_3$): C(1), 109.3 (*calcd, 109.1*); C(2), 155.6 (*155.1*); C(3), 96.8 (*100.4*); C(4), 153.7 (*151.0*); C(5), 142.3 (*137.5*); C(6), 115.1 (*118.0*); C(7), 173.1; C(8), 17.4 [$^1J(^{119/117}Sn-^{13}C) = 624/597$]; C(9), 8.6 [$^2J$(Sn–C) = 43]; C(12), C(13) and C(14), 55.5, 56.1 and 56.5.

^{119}Sn NMR ($CDCl_3$): −164.9.

Mass spectrometry: [$(CH_3O)_3C_6H_2$COO]$_2$SnEt$^+$, 93; [$(CH_3O)_3C_6H_2$COO][$(CH_3O)_3C_6H_2$]SnEt$^+$, 46; [$(CH_3O)_3C_6H_2]_2$SnEt$^+$, 100; [$(CH_3O)_3C_6H_2$COO]SnEt$_2^+$, 28; [$(CH_3O)_3C_6H_2$]SnEt$_2^+$, 25; [$(CH_3O)_3C_6H_2$COO]Sn$^+$, 18; [$(CH_3O)_2C_6H_3$COO]Sn$^+$, 6; [$(CH_3O)_3C_6H_2$]Sn$^+$, 49; [$(CH_3O)_2C_6H_3$]Sn$^+$, 19 %.

Compound 6a, [3,4,5-$(CH_3O)_3C_6H_2$COO]$_2$SnEt$_2$

Yield: 84%; recrystallized from petroleum ether, m.p. 167–169 °C.

Mössbauer: QS, 3.97; IS, 1.56; Γ_1, 0.89, Γ_2, 0.94 mm s^{-1}.

^{1}H NMR ($CDCl_3$): H(2) and H(6), 7.39 (s); H(8), 1.79 [q, 8; ^2J(Sn–H) = 71]; H(9), 1.36 [t, 8; $^3J(^{119/117}Sn-^1H) = 149/141$]; H(12) and H(14), 3.92 (s); H(13), 3.90 (s).

^{13}C NMR (DMSO-d_6): C(1), 126.6 (*calcd, 124.5*); C(2) and C(6); 106.5 (*109.3*); C(3) and C(5), 152.2 (*146.2*); C(4), 141.0 (*135.6*); C(7), 173.4; C(8), 23.7 [$^1J(^{119/117}Sn-^{13}C)$] = 974/922); C(9), 9.27 [^2J(Sn–C) = 50]; C(12) and C(14), 55.6; C(13) 59.7.

^{119}Sn NMR ($CDCl_3$): −161.4.

Mass spectrometry: [$(CH_3O)_3C_6H_2$COO]$_2$SnEt$^+$, 100%; [$(CH_3O)_3C_6H_2$COO]$_2$Sn$^{+\bullet}$, 11; [$(CH_3O)_3C_6H_2$COO] [$(CH_3O)_3C_6H_2$]SnEt$^+$, 12; [$(CH_3O)_3C_6H_2]_2$SnEt$^+$, 4; [$(CH_3O)_3C_6H_2$COO]SnEt$_2^+$, 9; [$(CH_3O)_3C_6H_2$]SnEt$_2^+$, 1; [$(CH_3O)_3C_6H_2$COO]Sn$^+$, 21; [$(CH_3O)_3C_6H_2$]Sn$^+$, 16; [$CH_3OC_6H_4$COO]Sn$^+$, 17 %.

Compound 4b dimer of
$\{[2,3,4\text{-}(CH_3O)_3C_6H_2COO]Et_2Sn\}_2O$
Yield: 72%; recrystallized from ethanol, m.p. 145–146 °C.

Mössbauer: QS_1, 3.03; IS_1, 1.30 (53%); QS_2, 3.75, IS_2, 1.34 (47%); Γ, 0.90 mm s^{-1}.

^1H NMR ($CDCl_3$): H(5), 6.69 (d, 9); H(6), 7.49 (d, 9); H(8), 1.53–1.63 (m); H(9), 1.35 (t, 8) and 1.38 (t, 8); H(12), H(13) and H(14), 3.88 (s) and 3.90 (s, twice as intense)

^{13}C NMR ($CDCl_3$): C(1), 121.9 (*calcd, 109.1*); C(2), 154.0 (*148.4*); C(3), 142.7 (*130.8*); C(4), 155.9 (*151.0*); C(5), 106.5 (*107.1*); C(6), 125.9 (*124.7*); C(7), 172.2; C(8), 21.8 [^1J(Sn–C) = *ca* 750] and 20.2 [^1J(Sn–C) = *ca* 730]; C(9), 9.6 [^2J(Sn–C) = *ca* 48] and 9.4 [^2J(Sn–C) = *ca* 46; satellites noisy and badly resolved]; C(12), C(13) and C(14), 55.9, 60.8 and 61.5.

^{119}Sn NMR ($CDCl_3$): −212.9 and −214.7 [^2J(Sn–O–Sn) = 134].

Mass spectrometry: $[(CH_3O)_3C_6H_2COO]_2SnEt^+$, 100; $[(CH_3O)_3C_6H_2COO][CH_3O)_3C_6H_2]SnEt^+$, 41; $[(CH_3O)_3C_6H_2]_2SnEt^+$, 76; $[(CH_3O)_3C_6H_2COO]SnEt_2^+$, 23; $[(CH_3O)_2C_6H_3COO]SnEt_2^+$, 3; $[(CH_3O)_3C_6H_2]SnEt_2^+$, 20; $[(CH_3O)_3C_6H_2COO]Sn^+$, 14; $[(CH_3O(_2C_6H_3]$-$SnEt_2^+$, 5; $[(CH_3O)_2C_6H_3COO]Sn^+$, 8; $[(CH_3O)_3C_6H_2]Sn^+$, 56; $[(CH_3O)_2C_6H_3]Sn^+$, 15; $C_6H_5COOSnH^+$, 6; $CH_3OC_6H_4Sn^+$, 7; $C_6H_5Sn^+$, 18 %.

Compound 5b, dimer of
$\{[2,4,5\text{-}(CH_3O)_3C_6H_2COO]n\text{-}Bu_2Sn\}_2O$
Yield: 97%; recrystallized from ethanol, m.p. 209–211°C.

Mössbauer: QS, 3.36; IS, 1.32; Γ_1, 0.89, Γ_2, 0.91 mm s^{-1}.

^1H NMR ($CDCl_3$): H(3), 6.52 (s); H(6), 7.41 (s); H(8), 1.56 (q, 8) and 1.69 (q, 8); H(9), 1.37 (t, 8) and 1.39 (t, 8); H(12), H(13) and H(14), 3.87 (s), 3.88 (s) and 3.93 (s).

^{13}C NMR ($CDCl_3$): C(1), 114.0 (*calcd, 109.1*); C(2), 154.3 (*155.1*); C(3), 97.3 (*100.4*); C(4), 152.1 (*151.0*); C(5), 141.9 (*137.5*); C(6), 114.7 (*118.0*); C(7), 171.9; C(8), 20.4 [$^1J(^{119/117}Sn–^{13}C) = 747/720$] and 21.3 [$^1J(^{119/117}Sn–^{13}C) = 734/707$]; C(9), 9.2 [$^2J$(Sn–C) = 38 ± 3, badly resolved, because of overlappings] and 9.4 [^2J(Sn–C) = 38 ± 3, badly resolved, because of overlappings]; C(12), C(13) and C(14), 55.6, 56.1 and 56.2.

^{119}Sn NMR ($CDCl_3$): −206.6 and −223.2 [^2J(SnOSn) = 127].

Mass spectrometry: $[(CH_3O)_3C_6H_2COO]_2SnEt^+$, 27; $[(CH_3O)_3C_6H_2COO][CH_3O)_3C_6H_2]SnEt^+$, 16; $[(CH_3O)_3C_6H_2]_2SnEt^+$, 35; $[(CH_3O)_3C_6H_2COO]SnEt_2^+$, 93; $[(CH_3O)_3C_6H_2]SnEt_2^+$, 100; $[(CH_3O)_3C_6H_2COO]Sn^+$, 18; $[(CH_3O)_2C_6H_3]SnEt_2^+$, 16; $[(CH_3O)_3C_6H_2]Sn^+$, 80; $[(CH_3O)_2C_6H_3]Sn^+$, 25; $CH_3CO_2Sn^+$, 12; $C_2H_5Sn^+$: 20 %.

Compound 6b, dimer of
$\{[3,4,5\text{-}(CH_3O)_3C_6H_2COO]n\text{-}Bu_2Sn\}_2O$
Yield: 84%; recrystallized from petroleum ether, m.p. 220–221 °C.

Mössbauer: QS. 344; IS, 1.33; Γ_1, 0.82, Γ_2, 0.92 mm s^{-1}.

^1H NMR ($CDCl_3$): H(2) and H(6), 7.29 (s); H(8), 1.59 (q, 8) and 1.75 (q, 8); H(9), 1.41 (t, 8) and 1.43 (t, 8); H(12) and H(14), 3.94 (s); H(13), 3.92 (s).

^{13}C NMR ($CDCl_3$): C(1), 127.7 (*calcd, 124.5*); C(2) and C(6), 106.9 (*109.3*); C(3) and C(5), 152.4 (*146.2*); C(4), 141.5 (*135.6*); C(7), 172.3; C(8), 22.0 [$^1J(^{119/117}Sn–^{13}C) = 734/707$] and 20.6 [$^1J(^{119/117}Sn–^{13}C) = 747/720$]; C(9), 9.2 [$^2J$(Sn–C) = 40 ± 3, badly resolved because of overlappings] and 9.4 [^2J(Sn–C) = 40 ± 3, badly resolved because of overlappings]; C(12) and C(14): 55.9; C(13): 60. 4.

^{119}Sn NMR ($CDCl_3$): −204.4 and −219.0 [^2J(Sn–O–Sn) = 126].

Mass spectrometry: $[(CH_3O)_3C_6H_2COO]_2SnEt^+$, 100; $[(CH_3O)_3C_6H_2COO]_2Sn^{+\bullet}$, 13; $[(CH_3O)_3C_6H_2COO][(CH_3O)_3C_6H_2]SnEt^+$, 17; $[(CH_3O)_3C_6H_2]_2SnEt^+$, 12; $[(CH_3O)_3C_6H_2COO]SnEt_2^+$, 29; $[(CH_3O)_3C_6H_2]SnEt_2^+$, 9; $[(CH_3O)_3C_6H_2COO]Sn^+$, 32; $[(CH_3O)_3C_6H_2]Sn^+$, 26; $[(CH_3OC_6H_4COO]Sn^+$, 28; $CH_3CO_2Sn^+$, 3; $EtSn^+$, 7; $SnOH^+$: 8 %.

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REFERENCES

1. Bouâlam, M, Willem, R, Gelan, J, Sebald, A, Lelieveld, P, de Vos, D and Gielen, M *Appl. Organomet. Chem.*, 1990, 4: 335

2. Meriem, A, Willem, R, Meunier-Piret, J, Biesemans, M, Mahieu, M and Gielen, M *Main Group Met. Chem.*, 1990, 13: 167
3. Bouâlam, M, Willem, R, Biesemans, M, Mahieu, B, Meunier-Piret, J and Gielen, M *Main Group Met. Chem.*, 1991, 14: 41
4. Tiekink, E R T *Appl. Organomet. Chem.*, 1991, 5: 1
5. Kalinowski, H O, Berger, S and Braun, S *Carbon-13 NMR Spectroscopy*, John Wiley, Chichester, 1988
6. Lockhart, T P, Calabrese, J C and Davidson, F *Organometallics*, 1987, 6: 2479
7. Lockhart, T P and Manders, W F *Inorg. Chem.*, 1986, 25: 892
8. Howard, W F, Crecely, R W and Nelson, W H *Inorg. Chem.*, 1985, 24: 892
9. Yano, T, Nakashina, K, Otera, J and Okawara, R *Organometallics*, 1985, 4: 1501
10. Gielen, M, Simon, S and Van de Steen, M *Org. Mass Spectrom.*, 1983, 18: 451
11. Gielen, M., *Org. Mass Spectrom.*, 1983, 18: 453.
12. Gielen, M *Bull. Soc. Chim. Belg.*, 1985, 94: 1075
13. van Lambalgen, R and Lelieveld, P *Invest. New Drugs*, 1987, 5: 161
14. Sheldrick, G M, SHELX76 (1976), Program for Crystal Structure Determination, University of Cambridge, UK, 1976