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Mixed aryl–alkyl organotin compounds, $Ar_nMeSnCl_{3-n}$ (Ar = RC_6H_4, R = H, ethyl, i-propyl, t-butyl; *n*-hexyl, *n*-octyl) and the effect of R upon antibiotic activity†

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The synthesis of a new series of arylmethyltin chlorides is reported, $Ar_nMeSnCl_{3-n}$ (Ar = RC_6H_4, R = H, ethyl, i-propyl, t-butyl; hexyl, octyl). The synthesis involves initial formation of triarylmethyltin compounds, Ar_3MeSn, via Grignard techniques followed by HCl–Et_2O aryl group cleavage, preferably in a stepwise manner. Preliminary biological activity against *Staphylococcus aureus* illustrates the importance of the para-alkyl substituents and reinforces that an optimal hydrophobic character is needed for maximum efficacy. Copyright © 2005 John Wiley & Sons, Ltd.

KEYWORDS: arylmethyltin chlorides; synthesis; biocide; MIC; organotin; hydrophobicity

INTRODUCTION

The ability of organotin compounds to be effective biocidal and stabilizer materials is well established.[1–3] In particular, the use of tributyltin preparations in antifouling paints has been a particularly important societal use. However, the discovery of organotins in marine species of the food chain, and even in beer!, has resulted in their imminent removal from paint formulations.[4,5] Furthermore, a very recent finding that a significant percentage of random human blood samples contain tributyltin suggests that a serious effort must be made to replace these materials.[6]

One approach is to seek other types of formulation, e.g. silicone additives to paints, copper biocides, etc., that will presumably pose a lesser threat to the health and environment of the human species. However, an alternative suggestion has been promulgated whereby, rather than simply ceasing the use of organotins, it seems prudent to continue and expand the range of such compounds to understand better their structure–reactivity relationships against a range of biological systems.[8] We are engaged in such a programme, initially involving synthesis and evaluation of simple heteroleptic aryl–alkyl organotins, since the vast majority of organotins previously used were of the homoleptic R_3SnX variety. Furthermore, changing the organic radicals in the homoleptic species [R_3Sn] results in altering the target species in terms of biocidal activity, e.g. Et_3Sn with mammals, *n*-Bu_3Sn with bacteria and marine organisms, Ph_3Sn with fungi, etc.[9] Only a limited number of heteroleptic mixed alkyl systems are known.[10] We recently reported a series of $ArMe_2SnCl$ compounds,[11] and a brief note concerning the formation of $PhMe_2SnCl$ appears in the patent literature.[12] We now report the synthesis, characterization and preliminary biocidal evaluation of a previously unreported series of simple aryl(methyl)tin chlorides, $Ar_nMeSnCl_{3-n}$ (Ar = RC_6H_4, R = H, ethyl, i-propyl, t-butyl; *n*-hexyl, *n*-octyl).

EXPERIMENTAL

All manipulations were carried out under an argon atmosphere or under high vacuum. Tetrahydrofuran (THF) was distilled under a nitrogen atmosphere from sodium benzophenone ketyl before use and the following reagents were used as received from the suppliers named: methyltin trichloride (Strem Chemicals, Inc.); 1-bromo-4-ethylbenzene, 1-bromo-4-isopropylbenzene (Lancaster Inc.); 1-bromo-4-hexylbenzene and 1-bromo-4-octylbenzene (Alfa Aesar); 1 M

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HCl in diethyl ether and triphenyltin chloride (Aldrich). NMR spectra were recorded on a Bruker 300 MHz spectrometer in $CDCl_3$ solvent. Elemental analyses were performed by Galbraith Laboratories.

Triarylation of methyltin trichloride by the Grignard method

All Ar_3SnMe (Ar = Ph (**1**), *p*-Et–C_6H_4 (**2**), *p*-*i*-Pr–C_6H_4 (**3**), *p*-*t*-Bu–C_6H_4 (**4**); *p*-hexyl–C_6H_4 (**5**), *p*-octyl–C_6H_4) compounds were synthesized using the same procedure and the specific synthesis of $(EtC_6H_4)_3SnMe$ (**2**) is provided below as illustrative of these reactions. Experimental yields and the spectroscopic and analytical data are presented in Tables 1 and 2 respectively.

Table 1. Experimental data for Ar_3SnMe

R	Product		B.p. (m.p.)[a]	Yield (%)
H	**1**	Ph_3SnMe[13]	(47–48)	78
Et	**2**	$(p\text{-}EtC_6H_4)_3SnMe$	200	80
i-Pr	**3**	$(p\text{-i-}PrC_6H_4)_3SnMe$	(92–93)	75
t-Bu	**4**	$(p\text{-t-}BuC_6H_4)_3SnMe$	(242–244)	70
n-Hex	**5**	$(p\text{-}n\text{-}HexC_6H_4)_3SnMe$	250	60
n-Oct	**6**	$(p\text{-}n\text{-}OctyC_6H_4)_3SnMe$	300	70

[a] Molecular distillation at 0.5 mmHg.

Synthesis of $(p\text{-Et–}C_6H_4)_3SnMe$ (2)

In a 250 ml three-necked flask, equipped with a condenser and a dropping funnel, was placed 1.40 g (57 mmol) of magnesium turnings with 30 ml of THF. To this was added dropwise a solution of 1-bromo-4-ethylbenzene (10 g, 54 mmol) in 30 ml of THF. A few crystals of iodine were sufficient to initiate the reaction. The reaction mixture was then refluxed for 1 h. After completion of the reaction, the mixture was allowed to cool to room temperature and the solution was added dropwise to a solution of methyltin trichloride (4.32 g, 18.0 mmol) in 30 ml of THF at 0 °C. The mixture was stirred for 15 h. The solvent was removed under reduced pressure and the residue was extracted with hexane. The resulting solution was filtered and the solvent was removed to give a clear viscous liquid material, which upon fractional distillation at 200 °C/0.5 mmHg yielded **2** (6.5 g, 14.5 mmol, 80%).

Chlorination of Ar_3SnMe to form $Ar_2SnMeCl$

The preparation of $(p\text{-Et–}C_6H_4)_2MeSnCl$ (**8**) is outlined below as typical of the general method used for the preparation. Experimental results and the spectroscopic and analytical data are presented in Tables 3 and 2 respectively.

Synthesis of $(p\text{-Et–}C_6H_4)_2MeSnCl$ (8)

A solution of hydrogen chloride (1.0 M in diethyl ether, 7.8 ml, 7.8 mmol) was added dropwise to a stirred solution of $(p\text{-Et–}C_6H_4)_3SnMe$ (3.5 g, 7.8 mmol) in 20 ml of dry

Table 2. Spectral and analytical data for new compounds[a]

2[b]	^1H	0.84 (3H, s, $SnCH_3$), 1.36 (9H, t, J = 6.0 Hz, CH_2CH_3), 2.78 (6H, q, J = 6.0 Hz, CH_2CH_3), 7.36, 7.58 (12H, d, d, J = 6.0 Hz, Ph)
	^{13}C	−9.9 ($SnCH_3$), 16.02 (CH_2CH_3), 29.39 (CH_2CH_3), 128.57, 136.40, 137.04, 145.3 (Ph)
	^{119}Sn	−90.09
		Found: C, 66.71; H, 6.69. Calc.: C, 66.84; H, 6.73%
3[b]	^1H	0.64 (3H, s, $SnCH_3$), 1.23 (18H, d, J = 6.0 Hz, $CH(CH_3)_2$), 2.87 (3H, sep, J = 6.0 Hz, $CH(CH_3)_2$), 7.21, 7.48 (12H, d, d, J = 9.0 Hz, Ph)
	^{13}C	−10.06 ($SnCH_3$), 24.26 ($CH(CH_3)_2$), 34.42 ($CH(CH_3)_2$), 126.90, 136.48, 137.11, 149.71 (Ph)
	^{119}Sn	−92.27
		Found: C, 68.24; H, 7.57. Calc.: C, 68.45; H, 7.39%
4[b]	^1H	0.63 (3H, s, $SnCH_3$), 1.33 (27H, s, $C(CH_3)_3$), 7.37, 7.49 (12H, d, d, J = 9.0 Hz, Ph)
	^{13}C	−10.10 ($SnCH_3$), 31.60 ($CH(CH_3)_3$), 34.95 ($CH(CH_3)_3$), 125.68, 136.09, 136.90, 151.90 (Ph)
	^{119}Sn	−93.46
		Found: C, 69.52; H, 8.19. Calc.: C, 69.80; H, 7.94%
5[b]	^1H	0.77 (3H, s, $SnCH_3$), 0.97 (9H, t, J = 6.6 Hz, CH_3hexyl), 1.40 (18H, m, CH_2hexyl), 1.64 (6H, m, CH_2hexyl), 2.67 (6H, t, J = 7.5 Hz, CH_2hexyl), 7.29, 7.51 (12H, d, d, J = 9.0 Hz, Ph)
	^{13}C	−9.99 ($SnCH_3$), 14.56, 23.08, 29.53, 31.88, 32.21, 36.47 (*n*-hexyl), 129.01, 136.31, 137.13, 143.95 (Ph)
	^{119}Sn	−90.49
		Found: C, 71.94; H, 9.19. Calc.: C, 71.96; H, 8.81%
6[b]	^1H	0.69 (3H, s, $SnCH_3$), 0.92 (9H, t, J = 6.6 Hz, CH_3octyl), 1.31–1.34 (30H, m, CH_2octyl), 1.65 (6H, m, CH_2octyl), 2.68 (6H, t, J = 9.0 Hz, CH_2octyl), 7.26, 7.50 (12H, d, d, J = 8.0 Hz, Ph)
	^{13}C	−10.0 ($SnCH_3$), 14.57, 23.15, 29.74, 29.88, 29.98, 31.93, 32.38, 36.49 (*n*-octyl), 128.80, 136.31, 137.13, 143.93 (Ph)
	^{119}Sn	−90.60

Table 2. (*Continued*).

8[c]	^{1}H	1.06 (3H, s, $SnCH_3$), 1.33 (6H, t, $J = 7.8$ Hz, CH_2CH_3), 2.74 (4H, q, $J = 7.8$ Hz, CH_2CH_3), 7.36, 7.65 (8H, d, d, $J = 9.0$ Hz, Ph)
	^{13}C	−2.84 ($SnCH_3$), 15.97 (CH_2CH_3), 29.41 (CH_2CH_3), 129.07, 136.02, 136.13, 146.99 (Ph)
	^{119}Sn	30.82
		Found: C, 53.72; H, 5.58. Calc.: C, 53.80; H, 5.58%
9[c]	^{1}H	0.93 (3H, s, $SnCH_3$), 1.22 (12H, d, $J = 6.0$ Hz, $CH(CH_3)_2$), 2.87 (2H, sep, $J = 6.0$ Hz, $CH(CH_3)_2$), 7.28, 7.52 (8H, d, d, $J = 9.0$ Hz, Ph)
	^{13}C	−3.01 ($SnCH_3$), 24.17 ($CH(CH_3)_2$), 34.52 ($CH(CH_3)_2$), 127.50, 135.5, 136.0, 151.47 (Ph)
	^{119}Sn	30.36
		Found: C, 55.13; H, 6.10. Calc.: C, 55.99; H, 6.18%
10[c]	^{1}H	0.92 (3H, s, $SnCH_3$), 1.37 (18H, s, $C(CH_3)_3$), 7.40, 7.45 (8H, d, d, $J = 9.0$ Hz, Ph)
	^{13}C	−3.06 ($SnCH_3$), 31.48 ($CH(CH_3)_3$), 35.11 ($CH(CH_3)_3$), 126.27, 135.69, 135.75, 153.67 (Ph)
	^{119}Sn	30.30
		Found: C, 56.64; H, 6.75. Calc.: C, 57.90; H, 6.71%
11[c]	^{1}H	0.89 (3H, s, $SnCH_3$), 0.96 (6H, t, CH_3hexyl), 1.31 (12H, m, CH_2hexyl), 1.62 (4H, m, CH_2hexyl), 2.61 (4H, t, CH_2hexyl), 7.28, 7.52 (8H, d, d, $J = 9.0$ Hz, Ph).
	^{13}C	−2.98 ($SnCH_3$), 14.48, 22.99, 29.36, 31.71, 32.09, 36.39 (*n*-hexyl), 130.01, 135.06, 135.91, 145.63 (Ph)
	^{119}Sn	31.09
		Found: C, 60.38; H, 7.82. Calc.: C, 60.16; H, 7.58%
12[c]	^{1}H	0.71 (3H, s, $SnCH_3$), 0.86 (6H, t, $J = 6.0$ Hz, CH_3octyl), 1.26–1.29 (20H, m, CH_2octyl), 1.59 (4H, m, CH_2octyl), 2.61 (4H, t, $J = 8.0$ Hz, CH_2octyl), 7.29, 7.47 (8H, d, d, $J = 7.5$ Hz, Ph)
	^{13}C	−1.79 ($SnCH_3$), 14.50, 23.04, 29.61, 29.67, 29.83, 31.62, 32.25, 36.40 (*n*-octyl), 129.34, 134.7, 135.40, 145.44 (Ph)
	^{119}Sn	27.58
13[d]	^{1}H	1.28 (3H, s, $SnCH_3$), 7.45–7.59 (5H, m, Ph)
	^{13}C	5.17 ($SnCH_3$), 129.93, 132.03, 134.87, 139.09 (Ph)
	^{119}Sn	55.53
		Found: C, 29.49; H, 2.85. Calc.: C, 29.84; H, 2.86%
14[d]	^{1}H	1.22 (3H, s, $SnCH_3$), 1.27 (3H, t, $J = 7.5$ Hz, CH_2CH_3), 2.68 (2H, q, $J = 7.5$ Hz, CH_2CH_3), 7.34, 7.56 (4H, d, d, $J = 6.6$ Hz, Ph)
	^{13}C	5.35 ($SnCH_3$), 15.83 (CH_2CH_3), 29.38 (CH_2CH_3), 128.77, 129.57, 134.73, 148.63 (Ph)
	^{119}Sn	57.89
		Found: C, 35.18; H, 3.95. Calc.: C, 34.90; H, 3.91%
15[d]	^{1}H	1.19 (3H, s, $SnCH_3$), 1.23 (6H, d, $J = 6.0$ Hz, $CH(CH_3)_2$), 2.88 (1H, sep, $J = 6.0$ Hz, $CH(CH_3)_2$), 7.32, 7.51 (4H, d, d, $J = 9.0$ Hz, Ph)
	^{13}C	4.80 ($SnCH_3$), 24.05 ($CH(CH_3)_2$), 34.58 ($CH(CH_3)_2$), 128.07, 134.82, 135.88, 153.87 (Ph)
	^{119}Sn	59.16
		Found: C, 37.06; H, 4.33. Calc.: C, 37.09; H, 4.35%
16[d]	^{1}H	1.25 (3H, s, $SnCH_3$), 1.27 (9H, s, $C(CH_3)_3$), 7.46, 7.52 (4H, d, d, $J = 9.0$ Hz, Ph)
	^{13}C	4.78 ($SnCH_3$), 31.39 ($CH(CH_3)_3$), 35.30 ($CH(CH_3)_3$), 126.88, 134.58, 135.57, 151.41 (Ph)
	^{119}Sn	59.76
		Found: C, 38.90; H, 4.93. Calc.: C, 39.10; H, 4.80%
17[d]	^{1}H	1.14 (3H, s, $SnCH_3$), 1.28 (3H, t, CH_3hexyl), 1.38 (2H, m, CH_2hexyl), 1.58 (2H, m, CH_2hexyl), 2.60 (2H, t, CH_2hexyl), 7.29, 7.51 (4H, d, d, $J = 9.0$ Hz, Ph)
	^{13}C	5.02 ($SnCH_3$), 14.48, 22.95, 29.26, 31.57, 32.02, 36.27 (*n*-hexyl), 130.01, 134.04, 135.72, 145.35 (Ph)
	^{119}Sn	59.20
		Found: C, 42.46; H, 5.43. Calc.: C, 42.67; H, 5.51%

[a] NMR spectra run in $CDCl_3$ solvent, ppm.
[b] Average $^{1}J(^{119/117}Sn-^{13}C(methyl)$ for compounds **2**–**6** = 375(1) Hz; ^{1}J, ^{2}J, ^{3}J and ^{4}J (Hz) for Sn–aryl carbon atoms $^{1}J = 506(2)$, $^{2}J = 38(1)$, $^{3}J = 51(1)$, $^{4}J = 11(1)$; $^{2}J(Sn-H) = 56(1)$. All data in the expected ranges.[14]
[c] Average $^{1}J(^{119/117}Sn-^{13}C(methyl)$ for compounds **7**–**12** = 393(1) Hz; ^{1}J, ^{2}J, ^{3}J and ^{4}J (Hz) for Sn–aryl carbon atoms $^{1}J = 586(2)$, $^{2}J = 63(1)$, $^{3}J = 51(1)$, $^{4}J = 13(1)$; $^{2}J(Sn-H) = 59(1)$. All data in the expected ranges.[14]
[d] Average $^{1}J(^{119/117}Sn-^{13}C(methyl)$ for compounds **13**–**17** = 486(1) Hz; ^{1}J, ^{2}J, ^{3}J and ^{4}J (Hz) for Sn–aryl carbon atoms $^{1}J = 750(3)$, $^{2}J = 66(2)$, $^{3}J = 85(1)$, $^{4}J = 17(1)$; $^{2}J(Sn-H) = 69(1)$. All data in the expected ranges.[14]

benzene. The progress of the reaction was monitored by ^{119}Sn NMR spectroscopy, i.e. disappearance and appearance of the resonances at −90.0 and 30.8 ppm respectively. The reaction was complete after 15 min and the solvent was removed under reduced pressure. The liquid obtained was then distilled at 160 °C/0.2 mmHg to yield **8** (2.49 g, 85%).

Hydrochlorination of $Ar_2MeSnCl$ to form $ArMeSnCl_2$

The preparation of $PhMeSnCl_2$ (**13**) is outlined below as typical of the general method used for this process. Experimental results and the spectroscopic and analytical data are provided in Tables 4 and 2 respectively.

Synthesis of $PhMeSnCl_2$

A solution of hydrogen chloride (1.0 M in diethyl ether, 6.2 ml, 6.2 mmol) was added dropwise to a stirred solution of $Ph_2MeSnCl$ (2.0 g, 6.2 mmol) in 20 ml of dry benzene. The progress of the reaction was monitored by ^{119}Sn NMR spectroscopy. The reaction was complete after 15 min and the solvent was removed under reduced pressure. The liquid product obtained was then distilled at 79 °C/0.5 mmHg to yield **13** (1.23 g, 70%).

Table 3. Experimental data for $Ar_2MeSnCl$

R	Product		B.p. (m.p.)[a]	Yield (%)
H	**7**	$Ph_2MeSnCl$	125–118	70
Et	**8**	$(p\text{-}EtC_6H_4)_2MeSnCl$	160	85
i-Pr	**9**	$(p\text{-i-}PrC_6H_4)_2MeSnCl$	(66–67)	70
t-Bu	**10**	$(p\text{-t-}BuC_6H_4)_2MeSnCl$	(138–140)	70
n-Hex	**11**	$(p\text{-}n\text{-HexylC}_6H_4)_2MeSnCl$	200	90
n-Oct	**12**	$(p\text{-}n\text{-OctylC}_6H_4)_2MeSnCl$	210	80

[a] Molecular distillation at 0.5 mmHg.

Table 4. Experimental data for $ArMeSnCl_2$

R	Product		B.p. (m.p.)[a]	Yield (%)
H	**13**	$PhMeSnCl_2$	79–81	70
Et	**14**	$(p\text{-}EtC_6H_4)MeSnCl_2$	80	80
i-Pr	**15**	$(p\text{-i-}PrC_6H_4)MeSnCl_2$	(74–75)	75
t-Bu	**16**	$(p\text{-i-}BuC_6H_4)MeSnCl_2$	(108–109)	66
n-Hex	**17**	$(p\text{-}n\text{-HexylC}_6H_4)MeSnCl_2$	130	86

[a] Molecular distillation at 0.5 mmHg.

Minimum inhibitory concentration determinations (NCCLS, M7-A4, 1997)[15]

Stock solutions of organotin compounds were made 10^{-2} M in dimethylsulfoxide (DMSO; Aldrich). A tenfold dilution in DMSO of each stock compound was made, providing 10^{-3} M solutions. Twofold serial dilutions of each compound were obtained by using Mueller Hinton broth (Difco Laboratories, Detroit, MI). The resulting concentrations ranged from 10^{-3} to 3.1×10^{-7} M. A 96-well polypropylene microdilution plate was used for each compound. 100 µl of each twofold dilution concentration were placed in triplicate in each well. *Staphylococcus aureus* (ATCC 25923) was obtained from American Type Collection, Manassas, VA, and was revived using trypticase soy medium (Beckton Dickinson and Company, Cockeysville, MD). Colonies of *S. aureus* were further transferred weekly to tryptic soy agar plates (Beckton Dickinson and Company, Cockeysville, MD). Three to five, isolated, morphologically similar colonies were transferred to a tube of 3 ml tryptic soy broth medium (Beckton Dickinson and Company, Cockeysville, MD) and incubated at 37 °C for 1–2 h. A bacterial suspension was made by adding sterile saline solution (0.9%) to the culture. It was further diluted in saline by a factor of 1 : 10, providing a final population density of (1–2) $\times 10^7$ CFUs (colony forming units). The 96-well plate was inoculated with 5 µl of the final bacterial suspension. Incubation of the plate proceeded at 35 °C for 16–20 h. Positive and negative growth controls containing 100 µl of Mueller Hinton broth were present in each plate. The minimum inhibitory concentration (MIC) resulted from recording the lower concentration that inhibited growth.

RESULTS AND DISCUSSION

Synthesis and characterization

The synthetic procedures and reagents used in this study are similar to those reported earlier for the synthesis of the mono-aryl(dimethyl)tin chlorides, a combination of Grignard chemistry and acid cleavage of Sn–C(sp^2) bonds. Thus, the preferred starting organotin reagent was $MeSnCl_3$ for direct transformation to the triaryl(methyl)tin:

$$Cl_3SnMe + 3ArylMgBr \longrightarrow Ar_3SnMe + MgClBr \quad (1)$$

When $Ar = RC_6H_4$ (R = H (**1**), i-Pr (**3**) and t-Bu (**4**)) the resulting compounds are crystalline materials, whereas for R = Et (**2**), *n*-hexyl (**5**) and *n*-octyl (**6**) high boiling-point liquids were obtained. All spectroscopic and analytical data confirm their composition.

The second step in the synthetic strategy was the removal of the aryl groups using the useful and commercially available HCl–diethyl ether reagent. With a single equivalent of the reagent high yields of the tin monochloride derivatives are obtained in high yield:

$$Ar_3SnMe + HCl\text{–}Et_2O \longrightarrow Ar_2MeSnCl + ArH \quad (2)$$

Subsequent to purification of the monochloro compounds a second treatment with one equivalent of HCl–Et_2O resulted in similarly high yields of the dichloro derivatives:

$$Ar_2MeSnCl + HCl{-}Et_2O \longrightarrow ArMeSnCl_2 + ArH \quad (3)$$

No evidence for any Sn–Me bond cleavage was observed in the chemistry described in either Equation (1) or (2). The spectroscopic data are as expected, with no unusual features: the ^{119}Sn chemical shift data for the Ar_3SnMe, $Ar_2SnMeCl$ and $ArMeSnCl_2$ compounds change progressively from *ca* −90 ppm to *ca* 30 ppm and *ca* 58 ppm respectively, as expected for the attachment of the electronegative chlorine atoms.

Biological activity

We have initiated a biological assay of the $ArMe_2SnCl$ and $Ar_2MeSnCl$ compounds involving a screening against a variety of bacterial suites and their capacity to modify the efficacy of human natural killer cells. We present here a single set of data involving the capacity of the new mixed arylalkyltin chlorides, $Aryl_nMe_{3-n}SnCl$ to inhibit the growth of *S. aureus*. The results are illustrated in Figures 1 and 2 and show an interesting pattern for the properties of the $ArMe_2SnCl$ and $Ar_2MeSnCl$ systems as a function of changing the para-substituent on the aryl groups in the order H, Et, i-Pr, t-Bu, *n*-hexyl, *n*-octyl. It is clear that for the monoaryl system an increase in the hydrophobicity of the substituent R favours the antibiotic character of the organotins up to a 3–4 carbon substituent; beyond that the efficacy begins to decrease. On the other hand, for the diaryl compounds there is a decrease in biocidal activity as the carbon content of the substituent increases. These data suggest clearly that there appears to be an optimum hydrophobicity needed for the activity investigated. These results are similar to the biocidal pattern noted for the homoleptic organotins R_3SnCl, against, for example, *B. subtilis*, $R_3 = Me_3 < Et_3 < n\text{-}Pr_3 \approx n\text{-}Bu_3 > n\text{-hexyl}_3 > n\text{-heptyl}_3$.[16] Our preliminary data indicate that the location of the hydrophobic groups is not site specific for the related changes in activity, the first such demonstration in the literature. It has been pointed out that exchanging phenyl groups for butyl groups does not have a profound effect upon certain types of biological activity, for example Na^+ regulation in fish when transferred to tin-enriched aqueous environments.[17] However, in other systems, including those reported herein, this is not the case.

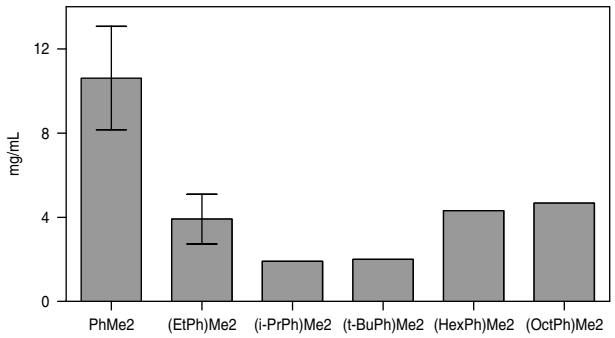

Figure 1. MIC for aryldimethyltin chlorides, $ArMe_2SnCl$, against *S. aureus*.

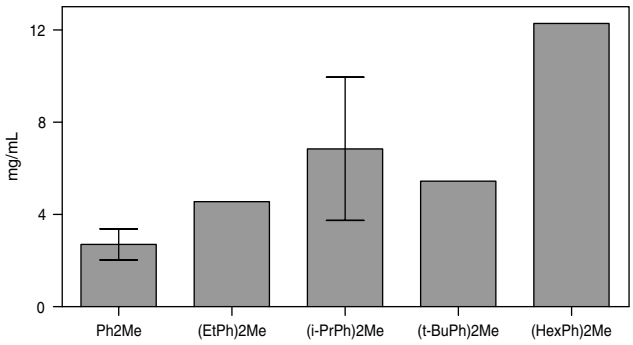

Figure 2. MIC for diarylmethyltin chlorides, $Ar_2MeSnCl$ against *S. aureus*.

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