Research paper

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A potential "green" organotin: Bis-(methylthiopropyl)tin dichloride, $[MeS(CH_2)_3]_2SnCl_2$.

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Abstract.

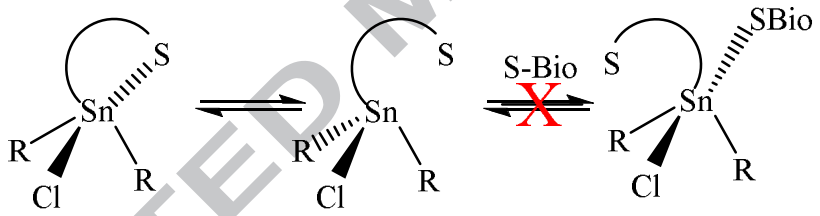
The tetravalent organotin compound $[MeS(CH_2)_3]_2SnCl_2$, **1**, has been synthesized in high yield and structurally characterized as being hexa-coordinate at tin with two intramolecular Sn-S bonds. The specific structure has been shown by theoretical calculations to be the low energy geometric structure available, and the differences associated with the experimental and calculated Sn-S bond lengths ascribed to crystal packing issues. The intramolecular Sn-S bonding produces a benign organotin compound with respect to its interactions with human natural killer cells; however, this blocking of coordination sites at Sn does not reduce its capacity to act as an efficient esterification catalyst.

Introduction.

Organotin materials are valuable as catalysts for, *inter alia*, trans-esterification, siloxane curing, polymerization, etc.[1] They were widely used as anti-fouling additives in paints, and are part of a large class of anti-fungal agrochemicals; however, their use as anti-fouling agents in marine paints has been restricted since the organotin compounds have been shown to bio accumulate in shellfish and indeed the decline in abundance of both oyster and mussel has been linked to subsequently developed growth abnormalities induced by organotin compounds.[2] Despite these negative attributes their use as catalysts remains an important aspect of tin chemistry. One of us has established that organotin compounds have the capacity to modify and degrade the ability of human natural killer cells (NKCs) to function, and for example, concentrations as low as 10^{-6} M/L can effectively stop such functionality.[3] When this latter finding is coupled to the fact that a random human population exhibited the presence of butyltin chlorides in their blood at levels of nanogram/dL,[4] it is clear that the future of organotin derivatives in the market place may be

restricted. Indeed as early as 1986 it was clear that a new approach to the design of organotin derivatives was needed and research into such a program was needed to produce useful chemical reagents without deleterious side effects.[5]

The precise mechanism whereby the organotin derivatives are adverse to many living systems is still under investigation in disparate systems, but a general concept of the initial activity of the organotin derivatives is their capacity, as Lewis Acids, to bind to S, N, and O atoms is various biochemically important molecules (e.g. S-Bio), thus initiating a cascade of events disrupting normal biological behavior.[6] We have suggested that if the organotin derivatives contain an organic functionality with such a heteroatom remote from the Sn atom, but with a conformational capacity to interact with such an atom, then possible intramolecular bonding could effectively compete with the organotin interaction with the biological molecule, Scheme 1.[7]



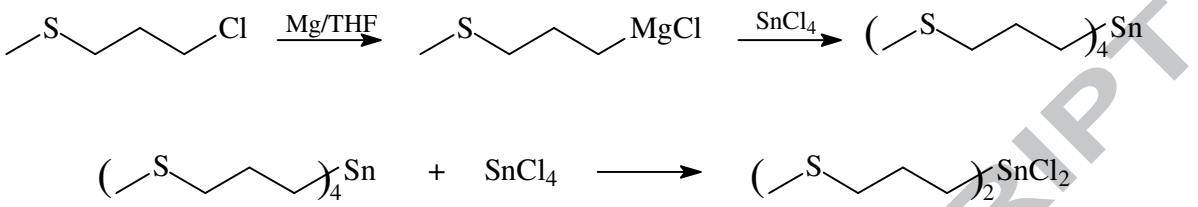
Scheme 1. Possible intramolecular S-Sn bonding modification of organotin bioactivity

To test the validity of this concept, we now report the synthesis, structural analysis, and evaluation of some important biological and catalytic properties of bis(methylthiopropyl)tin dichloride, $(MeSCH_2CH_2CH_2)_2SnCl_2$ (**1**). Such a structural arrangement introduces the potential for the S atom to intramolecularly bind to tin to form a favored 5-membered chelate ring.

Results and Discussion

The synthesis was readily performed as noted in Scheme 2, *via* initial formation of *tetra*-methylthiopropyl tin, followed by a classic *in-situ* redistribution reaction with $SnCl_4$ to form **1** in high yield, >80%. This is similar to the route used by the Pardubice group of Lébl *et al*. for the

corresponding O analog.[8] New material **1** was readily purified *via* recrystallization from a hexane/CH_2Cl_2 solvent mixture.



Scheme 2. Synthesis of $(MeSCH_2CH_2CH_2)_2SnCl_2$ (1).

The use of ^{1}H, ^{13}C and ^{119}Sn NMR spectroscopy, see experimental section, confirmed the product as the desired material. The ^{119}Sn NMR spectrum of **1** exhibited a signal at -93.3 ppm in $CDCl_3$ which is ~ 220 ppm shifted upfield from Bu_2SnCl_2 (126.5 ppm),[9] and is in the same general range observed for $(MeOC(O)CH_2CH_2)_2SnCl_2$ (-66.0 ppm),[10] $(Me_2NCH_2CH_2CH_2)_2SnCl_2$ (-184.7 ppm),[11] $(Ph_2PCH_2CH_2CH_2)_2SnCl_2$ (-130.0 ppm),[12] and $(MeOCH_2CH_2CH_2)_2SnCl_2$ (-108.6 ppm).[8] These data are highly suggestive of a six-coordinate structure maintained in solution formed *via* intramolecular coordination to the central tin atom *via* the O, S, N and P donor atoms. This hexa-coordination is further supported by the large $^{1}J(^{119}Sn\text{-}^{13}C)$ coupling constants for **1** (763 Hz), $(MeOCH_2CH_2CH_2)_2SnCl_2$ (732 Hz)[8], $(Me_2NCH_2CH_2CH_2)_2SnCl_2$ (903 Hz),[11] $(Ph_2PCH_2CH_2CH_2)_2SnCl_2$ (743 Hz),[12] and $(MeOC(O)CH_2CH_2)_2SnCl_2$ (786 Hz).[10]

Structural Analysis of 1.

The single crystal X-ray diffraction structural analysis of **1** resulted in the structure observed in Figure 1.

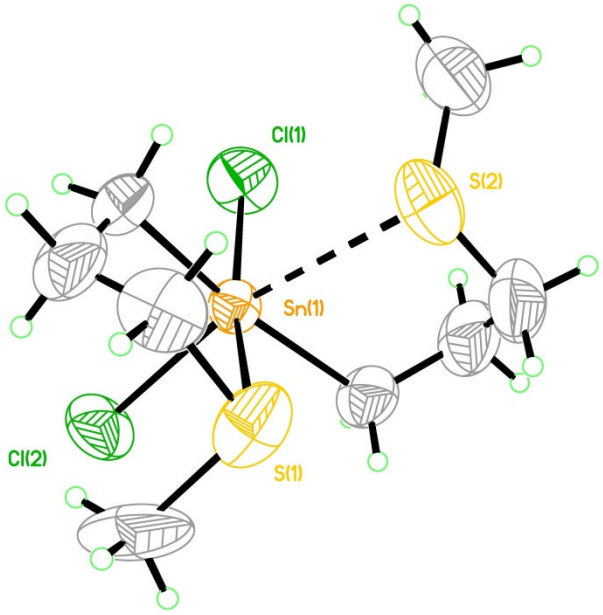


Figure 1. Single crystal X-ray structure of **1,** CCDC = 1530370; Selected bond length in Å; Sn-C5 = 2.139(4); Sn1-C1 = 2.141(4); Sn1-Cl =2.4652(12); Sn1-Cl2 = 2.4433(12); Sn1-S1 = 2.8945(13); Sn1-S2 = 2.9892(12).

In agreement with the NMR data the Sn center is sufficiently Lewis acidic by virtue of the two Sn-Cl bonds to result in two important intramolecular Sn-S bonds resulting in a pseudo-octahedral arrangement at the central Sn, similar to the O analog.[8] The Sn-S interactions are *cis* to each other and *trans* to the two Sn-Cl bonds, the same arrangement as noted for the O analog.

The two Sn-S internuclear distances of 2.8945(13) Å and 2.9892(12) Å are 76% and 78% of the sum of the theoretical van der Waals radii (vdW), respectively. A "regular" single bond is generally in the region of 60-70% of such radii sums, thus these Sn-S interactions are significant, and close to that we have reported for Ph(o-MeS-$C_6H_4CH_2$)$SnCl_2$, 2.2.99Å.[7] However, it has become fashionable to use the Pauling approach to Bond Orders (BO) to assess the relative strength of the intramolecular interaction in hypervalent main group complexes.[13] Using this approach with the "standard" and accepted value for the Sn-S single bond of 2.40 Å, we calculated the Sn-S bond orders of 0.20 and 0.15. These BO values compare to 0.16 for the Sn-O bond in the O analog,

$(MeOCH_2CH_2CH_2)_2SnCl_2$[8]; a Sn-P BO of 0.37 for $(Ph_2PCH_2CH_2CH_2)_2SnCl_2$[12] ; and our recalculated Sn-N BO of 0.40 for $(Me_2NCH_2CH_2CH_2)_2SnCl_2$.[11] By way of comparison, the single Sn-Cl bonds in **1** represent BO values of 0.71 and 0.78. Whilst the authors are unclear concerning the validity of using a BO relationship based upon carbon chemistry for assessing the donor strengths of a heteroatom toward tin in hypervalent systems, it's common usage provides a basis for comparison.[13] Clearly the intramolecular S-Sn interactions reported herein are at the low end of the strength scale for such bonding.

We have performed (MN12SX/3Z level) relative free energies calculations on the five possible geometric isomers of **1**, $(MeSCH_2CH_2CH_2)_2SnCl_2$, shown in Figure 2.

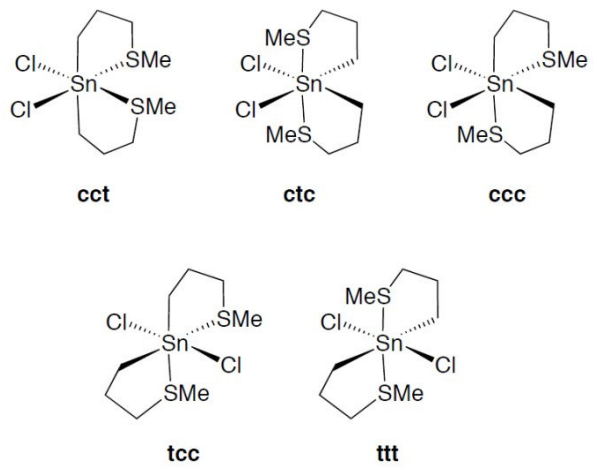


Figure 2. Geometric isomers of $(MeSCH_2CH_2CH_2)_2SnCl_2$, **1**, and their abbreviations

The isomers are labeled in terms of *cis* vs *trans* positioning for identical atoms, and in molecular mass order. So isomer **cct** refers to the case where the heaviest Cl ligand atoms are *cis* to each other, the next heaviest S atoms are also *cis* with respect to each other, and the lowest mass C atoms are *trans* to each other. In the process of examining relative energies of the isomers, it was discovered that the position of the sulfur-bound methyl with respect to the ligand Cl atoms had a sizable energetic impact. Placing the methyl substituent such that it eclipses a Cl ligand lowers the relative energy by 5–25 kJ

mol^{-1} (for example, see Figure 3). Given this, optimized structures, relative electronic energies (ΔE_{0K}), and relative free energies (ΔG_{298K}) of a total of 10 six-coordinate isomers were computationally estimated (Table 1).

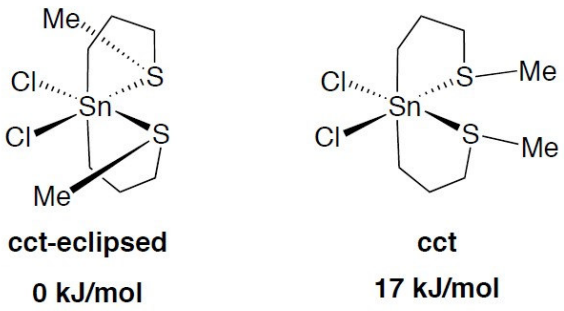


Figure 3. Conformational options for the S-bound methyl groups, associated abbreviations, and relative energies (kJ mol^{-1} ,MN12SX/3Z) of the **cct** isomer of **1**, $(MeSCH_2CH_2CH_2)_2SnCl_2$.

Table 1. Relative computed (MN12SX/3Z level) electronic energies ΔE_{0K} and free energies ΔG_{298K} (kJ mol^{-1}), and Sn–S distances (Å) of geometric isomers of six-coordinate **1**.

		ΔE_{0K}		ΔG_{298K}		Sn–S
cct eclipsed		0.0		0.0		3.1, 3.1
cct		17.1		15.1		3.1, 3.2
ctc eclipsed		54.3		58.1		2.8, 2.8
ctc		71.5		75.7		2.8, 2.8
ccc eclipsed		33.6		35.6		3.0, 3.0
ccc		43.3		40.4		**3.3, 4.1**
tcc eclipsed		22.3		26.0		2.9, 2.9
tcc		21.9		23.0		2.9, 2.9
ttt eclipsed		18.8		18.0		2.8, 2.8
ttt		24.9		26.5		2.8, 2.8

The data recorded in Table 1 shows that the relative electronic and free energies differ only slightly, so discussion below will involve only ΔG_{298K} values. The crystallographically observed structure (**cct eclipsed**) is predicted to be the most stable structure in the gas phase, 15 kJ mol^{-1} more stable than the non-eclipsed conformer and 18–26 kJ mol^{-1} more stable than the next closest geometric isomers (**tcc** and **ttt** pairs). It is notable that the isomers where both the chlorines and carbons are *cis* (**ctc** and **ccc** pairs) are significantly destabilized compared to the **cct eclipsed** isomer. The overall ordering **cct < ttt < tcc < ccc < ctc** does not provide an obvious interpretation of ligand impact, however, orienting carbons *cis* is destabilizing. One also sees that the computational model predicts longer Sn–S distances than those observed in the crystal structure. This is common, as crystal packing forces often shrink distances between weakly interacting atoms. This issue was probed for the **cct eclipsed** isomer in two ways. First, the potential energy surface (PES) for the Sn–S interaction was examined using a relaxed scan over the Sn–S distance range 2.7–3.7 Å. The electronic energy varied from 15 kJ mol^{-1} at 2.7 Å (the crystallographic value) to 0 kJ mol^{-1} at 3.1 Å (the gas phase optimized value) to 9 kJ mol^{-1} at 3.7 Å. The 15 kJ mol^{-1} difference between the first two is small enough to be countered by packing forces. Second, we optimized the **cct eclipsed** isomer using polarized continuum solvent models (PCM) for CH_2Cl_2 and water, as models for a solid state environment. In the former case, the optimized Sn–S distance was 3.0 Å, while in the latter it was 2.9 Å, both smaller than the 3.1 Å gas phase value. Again this suggests that the Sn–S distance discrepancy between experiment and theory arises mostly from packing forces in the former.

Interaction of 1 with Human Natural Killer Cells.

Previous studies have shown that di-butyltin dichloride (DBT), $(CH_3CH_2CH_2CH_2)_2SnCl_2$ is able to significantly decrease the ability of human natural killer (NK) cells to destroy tumor target cells.[3] It is hypothesized that DBT may, in part, exert its inhibitory effects on NK cells by interacting with molecules essential to their function. Specifically the Sn atom of DBT can potentially complex with sulfhydryl groups in proteins or other cellular molecules. As noted above compound **1** possesses significant intramolecular Sn-S interactions that might preclude its interaction with sulfhydryl containing molecules in the NK cells. If interaction with any such group(s) is responsible for the inhibitory effects of DBT on NK function, then compound **1** might be expected to have a less detrimental effect on NK-cell ability to kill tumor target cells. NK cells exposed to control, DBT, bis-pentyltin dichloride and compound **1** were examined for their ability to kill K562 (myelogenous leukemia cells) using a ^{51}Cr- release assay.[3]

Figure 4 shows that NK cells exposed to compound **1** at 500 nM for 24 h were able to kill tumor cells at essentially the same level as control NK cells (70 - 80% of tumor cells were destroyed). This result was in stark contrast to the tumor-killing capacity of NK cells exposed to 500 nM DBT for 24 h. Those NK cells were only able to destroy 18% of tumor targets. This is an approximately 75% loss in NK tumor-lysing function. Since compound **1** may be somewhat more hydrophobic than DBT, we also investigated the activity of bis-pentyltin dichloride, which is a more similar to compound **1** in terms of hydrophobicity. NK cells exposed to bis-pentyltin dichloride for 24 h lysed 33% of tumor cells. This was a 45% decrease in lytic function as compared to NK cells treated with control or compound **1**. These results are consistent with the hypothesis that the Sn atom of organotin derivatives may be complexing with sulfhydryl groups in essential molecules within the NK cell leading to loss of NK lytic function.

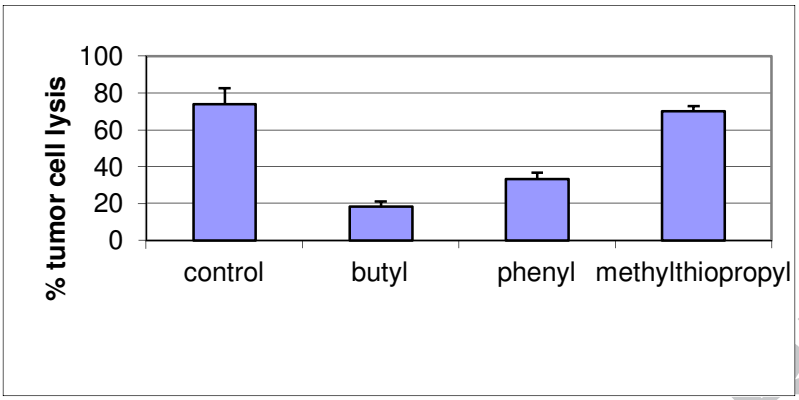


Figure 4. Impact of R_2SnCl_2 (R = butyl, pentyl, 3-methylthiopropyl (**1**) on HNKC function

Catalytic properties of 1 for acetylation of alcohols.

Organotins are well-established, and utilized, as catalysts for numerous reactions including, *inter alia, trans*-esterifications.[1,14] Given the results above, we wished to see if the benign biological activity against NKCs, obtained by virtue of potential hexa-coordinated structure, would impact the capacity of **1** to be a useful catalyst. Is it possible that the intramolecular Sn…S interactions could block sites needed for certain aspects of catalysis? We evaluated **1** as a catalyst for a typical esterification reaction (Table 2) between different alcohols and excess of acetic anhydride to yield esters, eq 1.

$$ROH + (CH_3CO)_2O \longrightarrow ROC(O)CH_3 \qquad (1)$$

The same reaction was performed using the "traditional" dibutyltin dichloride, **2**, as catalyst at the same molar concentrations. The transformation with low loadings of the catalyst results in 100% yield of the ester and indicates that **1** is equally as good a catalyst as **2**, Table 2. A typical product ^{13}C NMR is illustrated Figure 5.

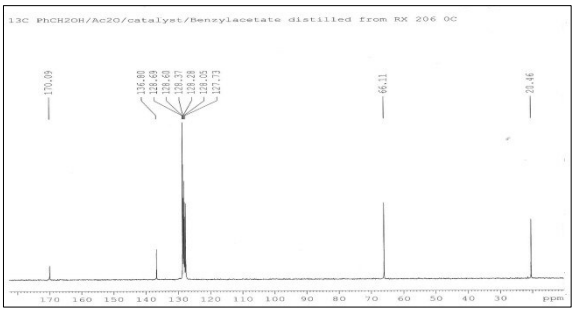


Figure 5: ^{13}C NMR of benzyl acetate (purified) from the reaction of benzyl alcohol and acetic anhydride catalyzed by **1**.

Investigation of a typical *trans*-esterification reaction between benzyl alcohol, BzOH, and ethylacetate, EtOAc, resulted in an equilibrium between the two esters, BzOAc and EtOAC, a result equivalent to that using **2** as a catalyst.

Table 2. Acetylation of alcohols catalyzed by $(MeSCH_2CH_2CH_2)_2SnCl_2$ catalyst

alcohol	(mol %) catalyst	Conditions	Yield (%)[a]
$PhCH_2OH$	0.02	RT, 2d	100 (82)
CH_3CH_2OH	0.02	RT, 2d	100 (88)
$(CH_3)_2CHOH$	0.02	RT, 2d	100 (79)
PhOH	0.02	RT, 3d	80 (65)
$ClCH_2CH_2OH$	0.02	RT, 1d	100 (85)

[a] in the parenthesis, isolated yields

Overall we have demonstrated a high yield synthetic route to produce an organotin compound that by judicious choice of alkyl substituents to include a potentially tin-bonding hetero atom, results in biologically inert materials with excellent catalytic functionality. However, it is well-established that biological systems are very disparate in terms of their

interactions with chemical reagents and lack of bioactivity in one area does not automatically convey to another region. We are expanding these initial studies to garner an in depth analysis of the compound and the potential of the hypothesis behind its use. However, the prospect of a "green" organotin reagent is enticing.

Experimental.

Isolation of NK cells

Peripheral blood from healthy adult (male and female) volunteer donors was used for this study. Buffy coats (source leukocytes) obtained from the American Red Cross (Portland, OR) or Key Biologics (Memphis, TN) were used to prepare NK cells. Highly purified NK cells were obtained using a rosetting procedure. Buffy coats were mixed with 0.6 mL of RosetteSep human NK cell enrichment antibody cocktail (StemCell Technologies, Vancouver, British Columbia, Canada) per 45 mL of buffy coat. The mixture was incubated for 25 min at room temperature (~ 25º C). Following the incubation, 7-8 mL of the mixture was layered onto 4 mL of Ficoll-Hypaque (1.077 g/mL) (MP Biomedicals, Irvine, CA) and centrifuged at 1200 g for 30-50 min. The cell layer was collected and washed twice with phosphate buffered saline (PBS) pH 7.2 and stored in complete media (RPMI-1640 supplemented with 10% heat-inactivated BCS, 2 m*M* *L*-glutamine and 50 U penicillin G with 50 µg streptomycin/ml) at 1 million cells/mL. The resulting cell preparation was >95% CD16+, and CD56+, 0% CD3+ by fluorescence microscopy and flow cytometry.

Cell Viability

Cell viability was determined by trypan blue exclusion. Cell numbers and viability were assessed at the beginning and end of each exposure period. Viability was determined at each concentration for each of the exposure periods. The viability of treated cells was

compared to that of control cells at each length of exposure.[15] Only those concentrations where viability was unaffected were used at a given length of exposure.

Cytotoxicity assay

The ability of NK cells to lyse tumor cells was measured using a ^{51}Cr release assay.[4] The target cell in all cytotoxicity assays was the NK-susceptible K562 (human chronic myelogenous leukemia) cell line. K562 cells were incubated with ^{51}Cr (Perkin-Elmer Life Sciences, Boston,

MA) in 0.2- 0.5 ml of BCS for 1-1.5 h at 37 °C in air/CO_2 (19:1). Following this incubation the target cells were washed twice with cell culture media. NK (effector) cells ($1.2x10^5$/100 µL for 12:1 ratio with target cells) were added to the wells of round-bottom microwell plates. The

effectors were diluted to 6:1 ratio ($0.6x10^5$/100 µL) and 3:1 ratio ($0.3x10^5$/100 µL); each ratio was tested in triplicate. Target cells were added ($1x10^4$/100µL) to each well of the microwell plate and the plate was centrifuged at 300 g for 3.5 min and incubated for 2 h at 37 °C (air/CO_2 ,19:1). After

incubation a 0.1 ml aliquot of the supernatant was collected and counted for radioactivity for 60 sec in a Packard COBRA gamma radiation counter (Packard Instrument Co., Meriden, CT). Target lysis was calculated as follows: 100 x[(test c.p.m - spontaneous c.p.m.)/maximum c.p.m.- spontaneous c.p.m.)]. Maximum release was produced by adding 100 µL of 10% Triton X-100.

Computational Methods

Optimizations and frequency analyses were performed using the Gaussian (G09) suite.[16] All molecules/isomers examined were initially optimized without constraints at the M06-

2X/BS1 level,[17] where BS1 refers to a basis set comprised of the LANL08 basis set on Sn,[18] and the 6- 31+G(d,p) basis set on all other atoms. Examination of the optimized structures by analytical frequency analyses at this level demonstrated that they were minima (no imaginary frequencies). The analyses also provided zero point energies (ZPEs) and thermal correction energies that were used to calculate energies reported in Table 1. All structures were then reoptimized at the MN12SX/3Z level,[19] where 3Z refers to a basis set comprised of the SDB-aug-cc-pVTZ basis seton Sn,[20] and the 6-311+G(d,p) basis set on all other atoms. A sizable integration grid (Gaussian keyword INT(UltraFineGrid)) was used in all cases. Solvent models employed the standard PCM model in G09 (keyword SCRF).

Synthesis of $[MeS(CH_2)_3]_2SnCl_2$ (1). Approximately 10% of a solution of 3-chloropropyl methyl sulfide[21] (6.0 g, 48.4 mmol) in 15 mL of THF was added to Mg turnings (1.16g, 48.4 mmol), along with 2 drops of bromobenzene as an initiator. The remaining 3-chloropropyl methyl sulfide

solution was then added dropwise in such a manner as to maintain the reaction mixture at reflux. The reaction mixture was then heated under reflux for 30 min. After the mixture had cooled to -50

°C, 1 M solution of $SnCl_4$ in CH_2Cl_2 (10.7mL, 12.1 mmol) was added dropwise with vigorous stirring. The reaction mixture was left to warm to room temperature and then heated under reflux

for 5 h. Water (10 mL) was added and the resulting precipitate was filtered off and washed with benzene. The THF and benzene solutions were combined and dried with Na_2SO_4, and the solvents were removed by rotary evaporation giving 5.45g (95%) of the tetrakis compound

$[MeS(CH_2)_2]_4Sn$**,** which was used for the next step without purification. A mixture of

$[MeS(CH_2)_2]_4Sn$ (5.45g, 11.5 mmol) and 1.0 M $SnCl_4$ solution in CH_2Cl_2 (5.74 mL, 5.74 mmol) was heated at 200°C for 3 h. The solvent was then removed by distillation and the crude material was

recrystallized from hot hexanes and cooled to -20°C to yield **1** as a white solid: Yield 1.90 g (90%), mp 138-140°C.

^{1}H NMR ($CDCl_3$) δ 1.11 (4H, t, $-CH_2Sn-$, J = 7.4 Hz), 1.83 (4H, q, $-CH_2$, J = 7.4 Hz), 1.96 (6H,

s, $-CH_3$), 2.54 (4H, t, $-CH_2S-$, J = 7.4 Hz); **^{13}C NMR** ($CDCl_3$) δ 15.68 ($-CH_3$), 21.93 ($-CH_2$, $^2J(^{13}C-^{119}Sn)$ = 54 Hz), 34.70 ($-CH_2Sn$, $^1J(^{13}C-^{119/117}Sn)$ = 763/730 Hz), 37.16 ($-CH_2S$, $^3J(^{13}C-$

$^{119}Sn)$ = 43 Hz); **^{119}Sn NMR** ($CDCl_3$) δ -93.3; Anal. Calcd for $C_8H_{18}Cl_2S_2Sn$: C, 26.11; H, 493. Found: C, 26.29; H, 5.08.

Acetylation of alcohols catalyzed by 1.

In a typical reaction, a 50-mL Schlenk flask was charged with 5.2 g (0.048 mol) of benzylalcohol in 10 mL of acetic anhydride and 0.02 mole % of catalyst **1**.The reaction mixture was stirred for 2

d at room temperature. The progress of the reaction was periodically monitored by NMR spectroscopy. The reaction was quenched with 10 mL with water. The organic layer was washed with 5% $NaHCO_3$ solution and dried over $MgSO_4$ and distilled at 200-206 °C to yield 5.8 g (82%) of benzyl acetate.

Trans-esterification reaction catalyzed by 1.

A 25-mL round-bottom flask was charged with 1.0 g (0.0114 mol) of ethylacetate and 5.0 g (0.0462 mol) of benzylalcohol and 0.3 mole % of catalyst **1**.The reaction mixture was refluxed for 40 h. The progress of the reaction was periodically monitored by NMR

spectroscopy. After 40 h of refluxing an equilibrium mixture of ethyl acetate and benzyl acetate was obtained.

Structural analysis.

A specimen of $C_8H_{18}Cl_2S_2Sn$ was used for the X-ray crystallographic analysis. The X-ray intensity data were measured on a Bruker SMART APEX CCD system equipped with a graphite monochromator and a MoKα fine-focus tube (λ = 0.71073 Å).

The total exposure time was 10.00 hours. The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using an orthorhombic unit cell yielded a total of 15907 reflections to a maximum θ angle of 27.62° (0.77 Å resolution), of which 3330 were independent (average redundancy 4.777, completeness = 99.6%, R_{int} = 1.93%, R_{sig} = 1.49%) and 3232 (97.06%) were greater than $2\sigma(F^2)$. The final cell constants of a = 9.2719(11) Å, b = 11.7256(13) Å, c = 13.2408(15) Å, volume = 1439.5(3) $Å^3$, are based upon the refinement of the XYZ-centroids of 9908 reflections above 20 σ(I) with 4.640° < 2θ < 55.12°. Data were corrected for absorption effects using the multi-scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.903. The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group P 21 21 21, with Z = 4 for the formula unit, $C_8H_{18}Cl_2S_2Sn$. The final anisotropic full-matrix least-squares refinement on F^2 with 122 variables converged at R1 = 2.01%, for the observed data and wR2 = 5.52% for all data. The goodness-of-fit was 1.021. The largest peak in the final difference electron density synthesis was 0.457 $e^-/Å^3$ and the largest hole was -0.518 $e^-/Å^3$ with an RMS deviation of 0.052 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.698 g/cm^3 and F(000), 728 e^-.

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	ΔE_{0K}	ΔG_{298K}	Sn-S
cct eclipsed	0.0	0.0	3.1, 3.1
cct	17.1	15.1	3.1, 3.2
ctc eclipsed	54.3	58.1	2.8, 2.8
ctc	71.5	75.7	2.8, 2.8
ccc eclipsed	33.6	35.6	3.0, 3.0
ccc	43.3	40.4	**3.3, 4.1**
tcc eclipsed	22.3	26.0	2.9, 2.9
tcc	21.9	23.0	2.9, 2.9
ttt eclipsed	18.8	18.0	2.8, 2.8
ttt	24.9	26.5	2.8, 2.8

Synthesis and structural characterization of organotin containing intramolecular secondary Sn-S bonds. Theoretical calculations confirming structure as the low energy conformation. No biocidal impact upon human natural killer cells whilst retaining catalytic activity.