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Stability and Microtox response of butenyltin compounds

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Tributenyltin bromides containing double bonds at carbon atoms C-1, C-2 or C-3 were synthesized from symmetrical tetrabutenyltins. Although all three tetrabutenyltin compounds were stable, only the tributenyltin bromides with double bonds at C-1 and C-3 were sufficiently stable for further studies. In aqueous sodium bromide (NaBr) solution containing 1% acetone, tri-1-butenyltin bromide was more stable in sunlight than tri-3-butenyltin bromide, yet neither compound was as stable as tributyltin bromide. Stability in seawater, in the absence of ultraviolet (UV) light, was less for both tri-1-butenyltin bromide and tri-3-butenyltin bromide than for tributyltin bromide. The relative toxicities of the tributenyltin bromides were determined using a bioluminescent bacteria assay. The concentrations of tributenyltin bromides necessary to produce a toxic response were three to six times greater than for tributyltin bromide.

Keywords: Tetrabutenyltin, tributenyltin bromide, stability, toxicity, bioassay, synthesis, infrared, mass spectra, half-life

INTRODUCTION

The use of tributyltin compounds as antifoulants for ships' hulls has become of increasing concern because of their potential toxicity to non-target organisms and because of the potential for bioaccumulation. It is known from the literature that when ethyl and propyl groups are replaced by vinyl and allyl groups in tetraorganotins, the resulting double-bonded compounds show enhanced chemical reactivity.[1–3] In an attempt to create more reactive compounds, we synthesized organotin compounds in which butyl groups were replaced with butenyl groups. Such compounds, used as antifoulants, might be expected to degrade more quickly in the environment while retaining sufficient toxicity to target organisms.

Tetraorganotins are commonly prepared by reaction of the appropriate Grignard reagent with anhydrous tin(IV) chloride ($SnCl_4$) or with organotin halides to obtain symmetrical and unsymmetrical tetraorganotins, respectively.[1,3] Tetra-allyltin[4,5] tetravinyltin[6,7] and but-3-enyltriphenyltin[8] have been prepared by this method. Two routes to the synthesis of triorganotin halides have been generally used on a laboratory scale: the redistribution reaction between tetraorganotin (R_4Sn) and tin(IV) chloride ($SnCl_4$)[9] or selective cleavage of the tetraorganotin with hydrogen halide or halogen.[10–12] The latter reaction is generally used to prepare trialkyltins with mixed alkyl groups.

EXPERIMENTAL

Chemicals

1-Bromo-1-butene, 4-bromo-1-butene and 1-chloro-2-butene were obtained from Pfaltz and Bauer (Waterbury, CT, USA). Resublimed magnesium chips, tetrabutyltin [$(CH_3CH_2CH_2CH_2)_4Sn$], and tributyltin bromide [$(CH_3CH_2CH_2CH_2)_3SnBr$], were obtained from Alfa Products (Danvers, MA, USA). All were used without further purification. *n*-Hexylmagnesium bromide (2.0 mol dm^{-3} in diethyl ether) was obtained from Aldrich Chemical Company, Inc. (Wilwaukee, WI, USA).

Preparation of tetra-n-alkenyltin compounds

For synthesis of tetra-1-butenyltin [$(CH_3CH_2CH=CH)_4Sn$] and tetra-3-butenyltin $CH_2=CHCH_2CH_2)_4Sn$], a Grignard reagent was prepared by the dropwise addition of approximately

10 g of 1-bromo-1-butene or 4-bromo-1-butene in 10 cm^3 anhydrous tetrahydrofuran to an excess of magnesium chips, which were just covered with tetrahydrofuran and kept under dry argon. After adding the alkenyl halide, the mixture was maintained at reflux for 4 h. For preparation of tetra-2-butenyltin, $[(CH_3CH{=}CHCH_2)_4Sn]$, the Grignard reagent was formed from 1-chloro-2-butene. After initiation of the *reaction*, the reagent was immediately cooled to $-10°C$ and stirred at that temperature for 9 h during and after the addition of 1-chloro-2-butene.

To prepare the tetra-alkenyltin compound, the Grignard reagent was first decanted from the excess magnesium chips, then cooled to 0°C. Approximately 2 g of anhydrous $SnCl_4$ in 10 cm^3 of hexane was added dropwise to the stirred solution. The mixture was refluxed for 4 h and then left at room temperature overnight.

The reaction mixture was cooled to 0°C and hydrolyzed with 3% hydrochloric acid (HCl). The separated organic layer was shaken with 5% aqueous potassium fluoride (KF) to precipitate organotin chlorides or bromides as insoluble fluorides. The solvent and low-boiling side-products were then removed under vacuum at room temperature from the separated organic layer, and the residue was washed through a 22 cm × 1 cm Florisil column with hexane. The solvent was again removed under vacuum.

Preparation of the tri-n-alkenyltin bromides

Approximately 1 g of the tetra-alkenyltin was suspended in 10 cm^3 methanol. A stoichiometric amount of bromine in methanol was added dropwise in dim light to the stirred tetrabutenyltin mixture. Monobromination of the tetra-alkenyltin to form tri-1-butenyltin bromide $[(CH_3CH_2CH{=}CH)_3SnBr]$, tri-2-butenyltin bromide, $[(CH_3CH{=}CHCH_2)_3SnBr]$ and tri-3-butenyltin $[(CH_2{=}CHCH_2CH_2)_3SnBr]$ bromide was achieved by conducting the reaction at 0, −50 and 20°C, respectively. Upon completion of the reaction, the solvent and low-boiling side-products were removed under vacuum at room temperature. The crude product was washed through a Florisil column first with hexane to recover unreacted tetra-alkenyltin and then with 1:4 (v/v) ethyl acetate/hexane to elute selectively the trialkenyltin bromide. Solvent was then removed under vacuum.

Degradation experiments

Ethanol solutions of the organotin bromides were prepared at a concentration of approximately ~1 mg cm^{-3}. Aliquots of the ethanol solutions were added to either 3.5% sodium bromide (NaBr) containing 1% acetone or to filtered seawater to obtain approximately 1–5 ppm concentrations in the seawater. The sodium bromide (NaBr) solution was placed in 125 cm^3 quartz tubes and exposed to sunlight over 48 h. The seawater solutions were kept in closed 500 cm^3 polycarbonate jars in the laboratory. Aliquots (10 cm^3) of the solutions were extracted at timed intervals with 1 cm^3 hexane after acidification with 0.1 cm^3 concentrated hydrochloric acid (HCl). Samples were analyzed directly and after derivatization with an excess of hexylmagnesium bromide[13] by GC MS using tetra-n-propyltin as an internal standard in the hexane extractant.

Toxicity testing

Relative toxicity of compounds was determined using the Microtox® Toxicity Analyzer Model 2055, manufactured by Microbics Corporation, Carlsbad, CA, USA.[14–16] This bioassay measures the relative reduction in light output by a luminescent bacterium, *Photobacterium phosphoreum* NRRL B-11177, when exposed to a toxicant. The bacteria are provided in a convenient freeze-dried form by Microbics Corporation and are immediately activated by the addition of 1 cm^3 of distilled water.

For Microtox® testing, stock solutions of the compounds were prepared in 95% ethanol at approximately ~1–2 mg cm^{-3}. Appropriate amounts of the ethanol solutions were added to 2% aqueous sodium chloride (NaCl) to achieve a workable concentration while keeping the ethanol concentration as low as possible. Typically the ethanol concentration was about 0.05%.

Serial dilutions of each compound for measurement were performed in the Microtox® photometer/incubator at 15°C. Controls consist of triplicate 1 cm^3 portions of 2% sodium chloride and candidate toxics were prepared in and subsequently serially diluted in 2% sodium chloride, with a final volume of 1 cm^3 for each dilution. After a 5-min period for temperature equilibration, 10 μl of rehydrated bacteria was added to each of the controls and the serial dilutions of the test compound. Meaurements in the photometer were

made at 5 and 15 min after addition of the reagent. This procedure was repeated at least four separate times for each compound to provide four independent toxicity values.

The toxicity value is expressed as an EC_{50} concentration, which is the concentration of a compound which caused a 50% reduction in light output. The EC_{50} concentrations were determined by graphic interpolation on log–log paper, plotting the gamma-function against concentration. The gamma-function is the ratio of the amount of light lost to the amount of light remaining. A gamma-value of 1 corresponds to a 50% reduction in light, or EC_{50}.

Instrumentation

Retention times and mass spectra of synthesized and purchased compounds were obtained with a Hewlett–Packard Model 5890A Gas Chromatograph directly connected to a Hewlett–Packard Model 5970 Mass Selective Detector (GC–MS). Data collection and reduction was performed with a Hewlett–Packard 9000-300 Computer using Model 59970C ChemStation software. Samples were run using splitless injection onto a 12.5 m × 0.2 mm (i.d.) HP-1 fused silica capillary column with 0.33 μm coating thickness. Helium carrier gas was used at a head pressure of 40 kPa. The oven was programmed, after an initial 2-min hold at 50°C, to 230°C at 30°C min^{-1}. Injector, transfer line and detector were at 250°C. Masses were scanned between 50 and 450 amu. Electron energy is fixed at 70 eV for this instrument.

Infrared (IR) spectra were obtained using a Digilab FTS-60 Fourier Transform IR Spectrometer interfaced with a Hewlett–Packard Model 5890A Gas Chromatograph at the chromatographic conditions detailed above. Spectra were obtained in a 250°C gold-coated gas capillary cell.

RESULTS AND DISCUSSION

Synthesis of the tetrabutenyltins presented no great difficulty as long as the Grignard reagent was present in large excess to assure complete alkylation. The tetrabutenyltins were all stable as neat compounds and in inert solvents. The tributenyltin bromides exhibited considerable variation in stability. Tri-2-butenyltin bromide was so reactive with the synthesis side-products that it could not be isolated although GC retention times and MS could be obtained on compounds present in the reaction mixture for a time. Tri-1-butenyltin bromide, and to a lesser extent, tri-3-butenyltin bromide tended spontaneously to form black precipitates during solvent evaporation of the crude mixture prior to column chromatography clean-up, especially if the distillation flask was warmed. Under these conditions we identified alkenyltin compounds containing various numbers of eight carbon groups in the mixture. Once purified, tri-3-butenyltin bromide and tri-1-butenyltin bromide were stable as neat compounds and in inert solvents.

Progress of the synthesis reactions and purity of the products were monitored using GC MS. Differentiation of the tetrabutenyltins and tributenyltin bromides was achieved by gas chromatographic retention times, mass spectrometry and IR spectrometry. Where *cis–trans* isomers were present in the starting butenyl halides, a mixture of isomeric butenyltins was formed. Although these isomers could be separated by gas chromatography, we did not attempt to separate them chemically and purify them. These isomers are responsible for the multiple retention times listed in Table 1. Mass spectra of stereoisomers were identical.

Table 1 GC retention times

Compound	Retention times (min)
Tetrabutyltin	7.23
Tetra-1-butenyltin	7.06, 7.10
Tetra-2-butenyltin	8.27, 8.45, 8.65, 8.87, 9.07
Tetra-3-butenyltin	7.34
Tributyltin bromide	7.30
Tri-1-butenyltin bromide	7.09
Tri-2-butenyltin bromide	8.12, 8.25, 8.40, 8.56
Tri-3-butenyltin bromide	7.24

Tetra-alkyltins exhibit mass spectra (MS) characterized by the successive loss of alkyl groups from the tin atom.[11,17–19] Typically, the parent ion is weak or non-existent; there is low abundance of ions from fragmentation of the alkyl chain; and the favored ions are tri- and mono-coordinated tin. Trialkyltin halides

Table 2 Fragment ion intensities of R_4Sn

	SnH_i^+		$RSnH_i^+$		$R_2SnH_i^+$		R_3Sn^+	
R group	*m/z*	Rel. int.	*m/z*	Rel. int.	*m/z*	Rel. int.	*m/z*	Rel. int.
Butyl	121	67	179	100	235	66	291	49
1-Butenyl	120	59	175	44	231	41	285	100
2-Butenyl	121	22	175	100	230	7	285	35
3-Butenyl	121	38	175	81	231	20	285	100

i = 0–3.

Table 3 Fragment ion intensities for R_3SnBr

	SnH_i^+		$RSnH_i^+$		$SnBr^+$		$RSnH_i^+$		$R_2SnH_i^+$	
R group	*m/z*	Rel int.	*m/z*	Rel. int.	*m/z*	Rel. int.	*m/z*	Rel. int.	*m/z*	Rel. int.
Butyl	121	21	177	21	199	49	257	45	313	100
1-Butenyl	121	29	175	39	199	98	255	11	309	100
2-Butenyl	121	12	175	36	199	100	254	10	309	28
3-Butenyl	121	19	175	63	199	52	255	4	309	100

i = 0–3.

show a similar MS fragmentation pattern where successive loss of the alkyl groups is favored over loss of the halide ion.[20] Qualitatively, the mass spectra of the tetrabutenyltins and tributenyltin bromides resemble those of the fully saturated analogues in their fragmentation patterns. In general, these spectra are characterized by analogous clusters of tin-containing fragments with two less mass units (H atoms) per attached carbon chain than the tetrabutyltin.

The relative intensities of the major fragment ions, normalized to the largest peak occurring between *m/z* 100 an 350 for tetrabutyltin and the tetrabutenyltins are shown in Table 2. These data for both experimental compounds and purchased reference materials were obtained in our laboratory. The unique ion ratios for each compound show that the precursor tetra-alkenyltin compounds are different from each other and different from the fully saturated tetrabutyltin.

The fragmentation patterns of tributyltin bromide and tributenyltin bromides are dominated by tin–bromine (SnBr)-containing ions and resemble each other to the same extent as the tetraalkyltin (R_4Sn) compounds. Major ion fragments are summarized in Table 3 for tributyltin bromide, tri-1-butenyltin bromide, tri-2-butenyltin bromide and tri-3-butenyltin bromide.

Since double-bond migration is a common occurrence under electron impact, the double-bond position in the parent compound cannot be directly determined by the presence or absence of distinctive ion fragments. We used infrared spectrometry to determine the position of the double bond and to show that this position was retained after bromination of the compound. These data are summarized in Table 4 as the vibration of the carbon–carbon double bond (C=C) in alkenyltin com-

Table 4 IR bands of alkenyltin compounds

Compound	ν(C=C) (cm^{-1})	Reference[b]
$(CH_2{=}CH)_2SnL_2$[a]	1602–1588	8
$(CH_3CH_2CH{=}CH)_4Sn$	1597.1	Data
$(CH_3CH_2CH{=}CH)_3SnBr$	1600	Data
$(CH_2{=}CHCH_2)_4Sn$	1623–1614	8, 21
$(CH_2{=}CHCH_2)_4Sn$	1624.1	Data
$(CH_3CH{=}CHCH_2)_2SnL_2$[a]	1644–1638	8
$(CH_3CH{=}CHCH_2)_4Sn$	1647	Data
$(CH_2{=}CHCH_2CH_2)SnL_3$[a]	1638–1635	8
$(CH_2{=}CHCH_2CH_2)_4Sn$	1639.5	Data
$(CH_2{=}CHCH_2CH_2)_3SnBr$	1639.5	Data

Spectra were calibrated against polyethylene film.
[a] L = counteranion.
[b] 'Data' means measured in our laboratory.

pounds in the literature[8,21] and measured in our laboratory.

The tributenyltins exhibit considerable variation in stability and chemical reactivity. As mentioned above, tri-2-butenyltin bromide, an allylic compound, was highly reactive and therefore transient; the compound readily underwent redistribution reactions with side-products of the synthesis reactions, and so could not be isolated.[22,23] The other two tributenyltin bromides were stable as neat compounds, in inert solvents and in ethanol for a reasonable length of time. Chemical reactivity appeared to follow the order allyl > vinyl > alkyl, as found by other workers.[2,7,10] The tri-3-butenyltin bromide fell between tri-1-butenyltin bromide, containing vinylic carbons, and tributyltin bromide, the alkyl compound.

In a more environmentally realistic experiment, the following results were obtained. Upon exposure to direct sunlight, seawater solutions of tri-1-butenyltin bromide and tri-3-butenyltin bromide in quartz tubes showed about 80% and 100% loss of compound, respectively, after 48 h; tributyltin bromide showed a loss of only about 15% over the same period. Half-lives of 33 days, 17 days and 16 days were estimated for tributyltin bromide, tri-3-butenyltin bromide and tri-1-butenyltin bromide in seawater, protected from UV light and held at a constant room temperature.

Relative toxicities of the new compounds were determined by using the Microtox® Toxicity Analyzer.[24] As mentioned above, the toxicity value is expressed as an EC_{50}, the concentration of the compound which causes a 50% reduction in light output. The results are shown in Table 5 as EC_{50} values at 5 min and 15 min. A low EC_{50} indicating a more toxic compound, tri-1-butenyltin bromide and tri-3-butenyltin bromide were less toxic than tributyltin bromide by factors of about three and six respectively.

Table 5 Toxicity of tributyl- and tributenyl-tin bromides

Compound	5-min EC_{50} (μmol dm^{-3})	15-min EC_{50} (μmol dm^{-3})
$(CH_3CH_2CH_2CH_2)_3SnBr$	0.13 ± 0.01	0.06 ± 0.02
$(CH_3CH_2CH{=}CH)_3SnBr$	0.82 ± 0.16	0.44 ± 0.04
$(CH_2{=}CHCH_2CH_2)_3SnBr$	0.44 ± 0.05	0.27 ± 0.03

CONCLUSIONS

Tributenyltin bromides containing double bonds at C-1 and C-3, synthesized from symmetrical tetrabutenyltins, were sufficiently stable for degradation and toxicity experiments. Tri-2-butenyltin bromide was too reactive for other than structural studies. Both tri-1-butenyltin bromide andd tri-3-butenyltin bromide were less stable in seawater, in the presence and absence of light, than tributyltin bromide. The relative toxicities of the tributenyltin bromides, determined using a bioluminescent bacteria assay, were somewhat lower than that of tributyltin bromide.

On the basis of the above properties the new compounds might satisfy the requirements for a good anti-foulant. The desirable requirements are rapid degradation in the environment to a non-toxic form after acting on target organisms. However, there are several questions that need to be scrutinized. For example, the compounds may exhibit too great a reactivity to be successfully incorporated into coating materials. Further, the toxicity to non-bioassay organisms and especially to mammals and other non-target organisms needs to be addressed.

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