APPLIED ORGANOMETALLIC CHEMISTRY, VOL. 7, 365–368 (1993)

Fungicidal activity of tributyltin alkylsulfate esters

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Tributyltin alkyl sulfate esters, e.g. tributyltin dodecyl sulfate, tributyltin hexadecyl sulfate and tributyltin octadecyl sulfate, were synthesized from the reaction of bis(tributyltin) oxide and appropriate alkyl hydrogen sulfates. The resulting tributyltin alkyl sulfate esters were found to exhibit fungicidal activity on *Penicillium*, *Aspergillus* and *Syncephalustrum* species.

Keywords: Tributyltin alkyl fulfate, fungicide

INTRODUCTION

The industrial use of organotin compounds has increased over the last three decades, from 5000 tons in 1955 to over 50 000 tons in 1982, as a result of their wide range of application and their effectiveness.[1,2] The amount of organotin compounds used in industry compares with the world tin consumption of about 150 000 tons annually (Ref. 3, p. 1). The toxicological properties of organotin compounds have been attributed to the function of the organic group attached to the tin atom as well as to the number of groups involved.[4,5] For example, triphenyltin compounds are widely used as agricultural fungicides,[6,7] tricyclohexyltin compounds are well accepted as acaricides,[8] while tributyltin compounds are employed as the active agents in antifoulant paints. The biocidal behavior of triorganotin compounds is due to their ability to inhibit mitochondrial oxidative phosphorylation although the exact mechanism is not well understood.[10] At present the industrial use of the nontoxic organotin compounds of the type R_2SnX_2 and $RSnX_3$ account for almost two-thirds of the world consumption, although the other major uses for these derivatives, of the type R_3SnX, as selective biocides and pesticides have also increased rapidly in recent years.[1,2] In the present work we report the synthesis of organotin sulfate ester compounds and their fungicidal activity.

EXPERIMENTAL

Materials and instrumentation

1-Dodecanol, 1-hexadecanol and 1-octadecanol were obtained from Fluka, AG, Switzerland. Bis(tributyltin) oxide was purchased from Acima AG, Buchs, Switzerland. The compounds were used without further purification.

Fungi

The test organisms (*Penicillium* sp., *Syncephalustrum* sp., *Trichoderma* sp. and *Aspergillus* sp.) used for the present study were stock cultures from the Department of Microbiology, Faculty of Science, Chulalongkorn University. These test organisms were maintained on potato dextrose agar (PDA) and subcultured periodically.

Carbon and hydrogen analyses were performed at the Instrument Centre, Chulalongkorn University. Tin was determined with a JEOL JDX-8030 X-ray fluorescent spectrophotometer and a Shimadzu AA670 atomic absorption spectrophotometer. Molecular weights were determined by mass spectrometry on a JEOL JMSPX-300/JMA2000 instrument. Infrared spectra were recorded on a Perkin–Elmer 1430 grating spectrophotometer in KBr pellets. H^1 NMR and C^{13} NMR spectra were recorded on a Bruker ACF 200 MHz.

Synthesis of dodecyl hydrogen sulfate

1-Dodecanol (27.95 g; 0.15 mol) was placed in a 250-ml three-necked flask which was equipped with a mechanical stirrer, reflux condenser, dry-

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0268–2605/93/060365–04 $07.00

Received 17 August 1992
Accepted 24 March 1993

ing tube and dropping funnel. The contents were saturated with hydrogen chloride gas and then chlorosulfuric acid (13.65 g; 0.15 mol) was added dropwise to the reaction flask while maintaining the temperature of the reaction mixture at 5 °C. After the addition of chlorosulfonic acid was completed, the reaction mixture was further stirred for a period of 30 min then the hydrogen chloride gas was displaced by passing nitrogen gas into the reaction mixture. The crude product was purified by recrystallization from methanol to obtain colorless needles of the title compound with a melting point of 48 °C (18.65 g; 70.14% yield).

Synthesis of hexadecyl hydrogen sulfate

The synthetic procedure was similar to that used for the synthesis of dodecyl hydrogen sulfate, except that 1-hexadecanol (19.36 g; 0.08 mol) and chlorosulfuric acid (10.6 g, 0.08 mol) were used. Hexadecyl hydrogen sulfate was obtained as colorless needle-shaped crystals (17.32 g; 76.44%) with a melting point of 65 °C (from methanol).

Synthesis of octadecyl hydrogen sulfate

The synthetic procedure was similar to that used for the synthesis of dodecyl hydrogen sulfate, except that 1-octadecanol (21.6 g; 0.08 mol) and chlorosulfuric acid (10.6 g; 0.08 mol) were used. After the reaction was completed, the reaction mixture was purified by recrystallization from methanol to give 18.1 g of colorless needle-shaped crystals of the title compound (73.9% yield) with a melting point of 72 °C. The spectral data (IR and NMR) confirmed the compound as octadecyl hydrogen sulfate.

Synthesis of Tributyltin dodecyl sulfate

Dodecyl hydrogen sulfate (5.00 g; 0.019 mol), bis-(tributyltin) oxide (5.62 g, 0.009 mol) and anhydrous toluene (50 ml) were placed in a 100-ml round-bottomed flask equipped with a magnetic stirrer, Dean–Stark equipment for water trapping and a condenser with a drying tube. The reaction mixture was stirred at reflux temperature (150–155 °C) for three hours until the water was separated completely by formation of an azeotropic mixture with toluene. The toluene was then removed by distillation under reduced pressure. The residual pale yellow oil was purified by recrystallization from methanol to give colorless crystals (9.96 g; 95.5% yield) with a melting point of 42 °C. Found: C, 52.13; H, 9.47; Sn, 21.06. Calcd for $C_{24}H_{52}SO_4Sn$: C, 51.98; H, 9.38; Sn, 21.3.

Synthesis of tributyltin hexadecyl sulfate

The synthesis was carried out by a procedure similar to that used for the synthesis of tributyltin dodecyl sulfate, but using 5.00 g (0.015 mol) of hexadecyl hydrogen sulfate and 4.63 g (0.008 mol) of bis(tributyltin) oxide to obtain 9.24 g (97.5% yield) of the title compound as colorless crystals with a melting point of 60 °C after recrystallization from ethanol. Found: C, 55.24; H, 9.97; Sn, 19.15. Calcd for $C_{28}H_{60}SO_4Sn$: C, 55.08; H, 9.83; Sn, 19.39.

Synthesis of tributyltin octadecyl sulfate

A similar procedure to that for the synthesis of tributyltin dodecyl sulfate was used for this synthesis but using 6 g (0.017 mol) of octadecyl hydrogen sulfate and 5.11 g (0.008 mol) of bis(tributyl tin) oxide to obtain 10.54 g (96.3% yield) of the title compound as colorless crystals with a melting point of 68 °C (after recrystallization from methanol). Found: C, 56.61; H, 10.13; Sn, 18.32. Calcd for $C_{30}H_{64}SO_4Sn$: C, 56.43; H, 10.03; Sn, 18.49.

Fungicidal assay

Fungicidal activities of the organotin compounds were determined by incorporating tributyltin alkyl sulfate at the specified concentration into PDA agar, which was sterilized and subsequently used for the cultivation of the test organisms; control groups were those of PDA without tributyltin alkyl sulfate. Cultures (in triplicate for each system) were kept at room temperature and observed for mycelial growth daily. Culture(s) that showed no mycelial growth after 30 days of incubation were assigned as no growth and regarded as demonstrating fungicidal effect.

Table 1. Fungicidal effects of tributyltin alkyl sulfate esters

	Tributyltin dodecyl sulfate			Tributyltin hexadecyl sulfate			Tributyltin octadecyl sulfate		
Organism	30 ppm	50 ppm	100 ppm	30 ppm	50 ppm	100 ppm	30 ppm	50 ppm	100 ppm
Trichoderma	—	—	—	—	—	—	—	—	—
Penicillium	—	—	—	—	—	—	—	—	—
Syncephalustrums	+(6)	—	—	—	—	—	+(6)	+(6)	—
Aspergillus	—	—	—	—	—	—	—	—	—

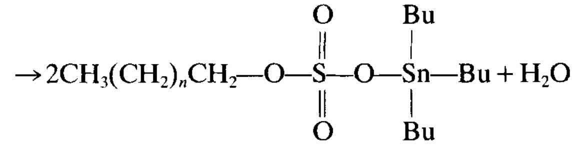
Abbreviations: +(*n*) indicates the day at which mycelium was first observed; — means that no mycelial growth was observed after 30 days of incubation whereas in the control group mycelial growth was observed at day 1 after inoculation.

RESULTS AND DISCUSSION

The organotin sulfate esters tributyltin dodecyl sulfate, tributyltin hexadecyl sulfate and tributyltin octadecyl sulfate were synthesized from the reaction of the alkyl hydrogen sulfates (dodecyl hydrogen sulfate, hexadecyl hydrogen sulfate and octadecyl hydrogen sulfate, respectively) with bis-(tributyltin) oxide in toluene. These alkyl hydrogen sulfates were obtained from the reaction of the alkanols (1-dodecanol, 1-hexadecanol and 1-octadecanol) with chlorosulfonic acid. The reactions were performed as illustrated in Eqns [1] and [2].

$$CH_3(CH_2)_nCH_2OH + ClSO_3H \rightarrow CH_3(CH_2)_nCH_2OSO_3H + HCl \qquad [1]$$

$$2CH_3(CH_2)_nCH_2OSO_3H + Bu_3Sn)_2O$$



$$\rightarrow 2CH_3(CH_2)_nCH_2{-}O{-}\overset{\overset{\displaystyle O}{\|}}{\underset{\underset{\displaystyle O}{\|}}{S}}{-}O{-}\overset{\overset{\displaystyle Bu}{|}}{\underset{\underset{\displaystyle Bu}{|}}{Sn}}{-}Bu + H_2O \qquad [2]$$

$n = 10, 14, 16$

In addition to elemental analysis, the presence of tin in this tributyltin alkyl sulfate was shown by atomic absorption spectrophotometry. The presence of sulfur and tin in these organotin sulfate esters was confirmed by X-ray fluorescent spectrophotometry. The IR peaks at 1505 cm^{-1} and 1460 cm^{-1} could be assigned to S=O bonds and the S—O bond showed an absorption peak at 945 cm^{-1}. The peak observed at 1170 cm^{-1} was due to C–O bonds. The alkyl group in this molecule showed the absorption peaks of the C–H bonds at 2835–2935 cm^{-1}, 1450 cm^{-1}, 1370 cm^{-1} and 710 cm^{-1}. Proton magnetic resonance spectra of these compounds have been recorded in $CDCl_3$ using TMS as internal standard. The chemical shift values (δ, ppm) of the two protons that are attached to carbon bonded to the sulfate group showed triplet signals at 4.2 ppm. The triplet at 0.9 ppm indicating protons of a methylene group showed multiplet signals between 1.1 and 1.8 ppm. The C^{13} NMR spectra showed the chemical shift of carbon in the methylene group attached to sulfate to be at 72.5 ppm and the peaks between 22.5 and 32.5 ppm are indications of alkyl and methylene carbon atoms of these molecules.

It was further found that all the tributyltin alkyl sulfates (at 30, 50 and 100 ppm) exhibited fungicidal effects toward *Penicillium* sp., *Trichoderma* sp., *Aspergillus* sp. and *Syncephalustrum* sp. (Table 1). At lower concentration (30 ppm), tributyltin hexadecyl sulfate and tributyltin octadecyl sulfate gave a fungistatic effect by delaying the mycelial growth from day 1 (as of the control group) to day 6. The results obtained are in agreement with reports that various salts of organotin compounds are potential candidates as wood preservatives against fungi[11–13] as well as other systems such as insects crustaceans.[2,3,13,14] Moreover, by changing the organic moiety of the compound, its spectrum of effectiveness could also be changed; for example the substitution of a methyl by a propionyl group could change from effectiveness against insects to effectiveness against Gram-negative bacteria. Thus, our preliminary result has suggested novel organotin compounds that may also be applied for various other purposes.

Acknowledgement Financial support from the Science and Technology Development Board (STDB), Thailand, is gratefully acknowledged. The authors are also thankful to The Metallurgy and Materials Science Institute, and the Chemistry Department, Chulalongkorn University, for partial support.

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