Synthesis and Characterization of Novel Organotin Monomers and Copolymers and Their Antibacterial Activity

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ABSTRACT: Two novel organotin monomers, (*N*-tri-*n*-butyltin) maleimide and *m*-acryloylamino-(tri-*n*-butyltin benzoate), were synthesized. Copolymerization of these two monomers with styrene was carried out in the bulk at 65°C using asobisisobutyronitrile as the free radical initiator. The monomers and copolymers were characterized by elemental analysis; the molecular weights of the copolymers were determined by GPC, solubility, IR, and ^{1}H-NMR spectral studies. The antibacterial activities of the synthesized organotin monomers and copolymers toward various types of bacteria were also reported. © 2000 John Wiley & Sons, Inc. J Appl Polym Sci 77: 740–745, 2000

Key words: organotin monomers; organotin copolymers; antibacterial activity

INTRODUCTION

Organotin derivatives of a compound containing the bioactive alkyltin groups have considerable interest as biocides.[1] The organotin moiety is attached to the monomers and copolymers via O—Sn and N—Sn bonds.[2–4] In recent years there has been a rise in the popularity of the idea of attaching chemically reactive species to insoluble supports. Applications have been found in organic chemistry, inorganic chemistry, biochemistry, and biology.[5] Activated amides of acrylic and methacrylic acids may be considered valuable tools for the synthesis of multifunctional polymers. Acrylic copolymers with pendant organotin moieties find widespread applications as antifouling agents,[6] wood preservatives,[7] fungicides, pesticides, mosquito larvacides,[8] and heat and light stabilizers in the manufacture of poly(vinyl chloride).[9,10] In addition, various investigators have shown that several classes of organotins possess antitumor activity against p-338 lymphocytic leukemia in mouse cells and biological activities against various species.[11,12]

Copolymerization techniques have a number of advantages in controlling the degree of functional groups in the product, controlling its structure, and predicting the distribution of groups within the copolymer.[5] The aim of the present investigation is to study the antibacterial activity of *N*-(tri-*n*-butyltin) maleimide (N-TBTM) and *m*-acryloylamino(tri-*n*-butyltin benzoate) (*m*-AATBTB) monomers and their styrene (St) copolymers against different species of Gram positive and Gram negative bacteria.

EXPERIMENTAL

Materials

Our sources were tri-*n*-butyltin oxide (TBTO, E. Merck), maleimide (MI, E. Merck), acryloyl chlo-

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Table I Bacterial Strains, Code, and Source

Organism	Code	Source
Gram positive		
Staphylococcus aureus	CBSC 15-5554 A	Carolina Biological Supply Company (USA)
S. aureus	ATCC 29213	American Type Culture Collection (USA)
S. epidermidis	CBSC 15-5556 A	
Streptococcus faecalis	NCTC 370	National Collection of Type Cultures (U.K.)
Bacillus megaterium	CBSC 15-4900 A	
B. cereus	CBSC 15-4870 A	
Gram negative		
Shigella dysenteriae	NCTC 5110	
Shigella sonnei	KKUH 934	King Khalid University Hospital (Saudi Arabia)
Salmonella typhimurium	NCTC 73	
Salmonella typhi	KKUH 1012	
Escherichia coli	ATCC 25922	
Yersinia enterocolitica	ATCC 23715	
Y. pseudotuberculosis	NCTC 10275	

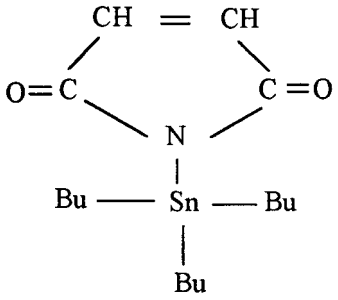
ride (AC, E. Merck), and *m*-amino benzoic acid (*m*-ABA, BDH). The St (Riedel de Hean) was purified by distillation under reduced pressure, and 2,2-azobisisobutyronitrile (AIBN) was recrystallized from methanol. Other reagents were purified by conventional methods.

Bacterial Strains and Growth Conditions

The bacterial strains and their sources are given in Table I. These strains were selected as test organisms because they cover a range of structures, which are usually the target of antibacterial agents. The strains were grown on blood agar base (Difco) slants and maintained at 4°C with monthly transfer.

Monomer Synthesis

The N-TBTM was synthesized as described in our previous article.[13] Reacting MI with TBTO in the presence of acetone at 60°C resulted in monomer **I**.



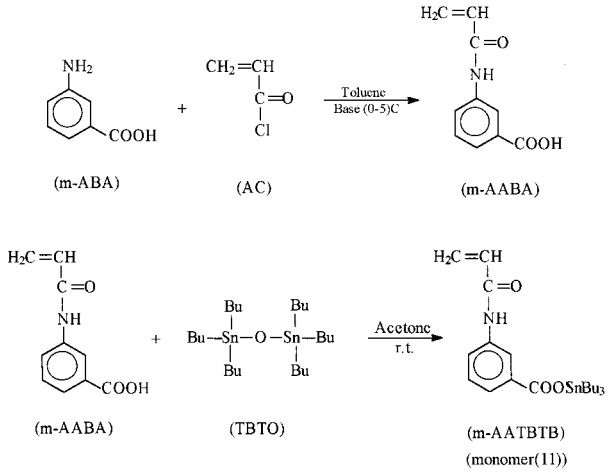
Monomer

The *m*-AATBTB was synthesized as shown in Scheme 1.

Reacting *m*-ABA with AC was done in the presence of an alkaline medium in toluene as the solvent.[14] The crude product of *m*-acryloyl aminobenzoic acid (*m*-AABA) was crystallized from ethanol to yield 15.09 g (79%). Its melting temperature was 229–231°C. IR (KBr): 3272 (NH), 3098, 2992 (arom), 1671 (C═O), 1630 cm^{-1} (C═C). ^{1}H-NMR ($CDCl_3$ + DMSO-$_{d6}$): δ = 9.81 (S, 1H, NH), 8.10–7.50 (d, d, 4H, arom), 6.69 (d, 2H), 5.71 (t, 1H).

ANAL. Calcd for $C_{10}H_9NO_3$ (191.17): C, 62.82%; H, 4.75%; N, 7.32%. Found: C, 62.43%; H, 4.67%; N, 7.14%.

The *m*-AABA was then reacted with TBTO in the presence of acetone at room temperature ac-



Scheme 1 The synthesis of monomer **II**.

Table II Results of Elemental Analysis and Physical Properties of Copolymers I and II

Copolymer Code	Analysis (%) C Calcd	C Found	H Calcd	H Found	N Calcd	N Found	Sn Calcd	Sn Found	Yield[a] (%)	MW[b]	M_n[b]	M_w/M_n[b]	Appearance of Copolymer
I	58.80	59.01	7.61	7.41	2.86	2.69	24.21	24.29	53	761,400	258,200	2.95	Glassy,white
II	61.66	61.29	7.42	2.19	2.40	2.19	20.31	20.93	77	89,000	351,000	2.53	Powder,white

[a] After 5 h of polymerization.
[b] By GPC.

cording to the method of Cummins and Dunn.[15] The crude product was crystallized from petroleum ether (bp 40–60°C) to yield 18.98 g (79%) of *m*-AATBTB monomer (**II**); its melting temperature was 68–70°C, and its tin content as determined by the Gilman and Rosenberg method[16] was 24.22% (calcd: 24.73%). IR (KBr): 3235 (NH), 2951, 2918 (arom), 1673 (C═O), 1610 cm^{-1} (C═O). ^{1}H-NMR ($CDCl_3$ + DMSO-$_{d6}$): δ = 9.48 (d, 2H), 5.69 (t, 1H), 1.32–0.91 (m, 27H).

ANAL. Calcd for $C_{22}H_{35}O_3Sn$ (480.20): C, 55.02%; H, 7.35%; N, 2.92%. Found: C, 55.18%; H, 7.13%; N, 2.49%.

Antibacterial Activity

The antibacterial activity of the chemical compounds was tested as described previously.[17] The bacterial strains were grown in brain heart infusion broth (Difco) for 8 h at 37°C. Each culture was then spread on Mueller–Hinton agar (Merck) plates [0.1 mL (10^6 cfu/mL)/plate]. Ten microliters of 1/mg/mL of each chemical compound (monomers and St copolymers) was absorbed onto the sample application piece (LKB) for 5 min. The sample application pieces were dried under sterilization and then placed on the surface of Mueller–Hinton agar plates immediately after their inoculation with the test bacterium. The plates were incubated at 37°C for 24 h, and the diameter (mm) of the inhibition zone was recorded.

Copolymerization Procedure

Copolymerization of N-TBTM) and *m*-AATBTB monomers with St (in an equimolar ratio) were carried out in bulk at 65°C in sealed tubes under a nitrogen atmosphere and in the presence of a catalytic amount of AIBN (1 mol % based on the total number of moles of the monomer). After polymerization for a given time the content of the tubes was poured into a large amount of methanol to isolate the copolymers. The copolymers obtained were then washed 3 times from methanol and dried under reduced pressure at 40°C for 24 h to constant weight.

The analytical and physical data for the copolymers are listed in Table II.

Copolymer (1) Copolymer (2)

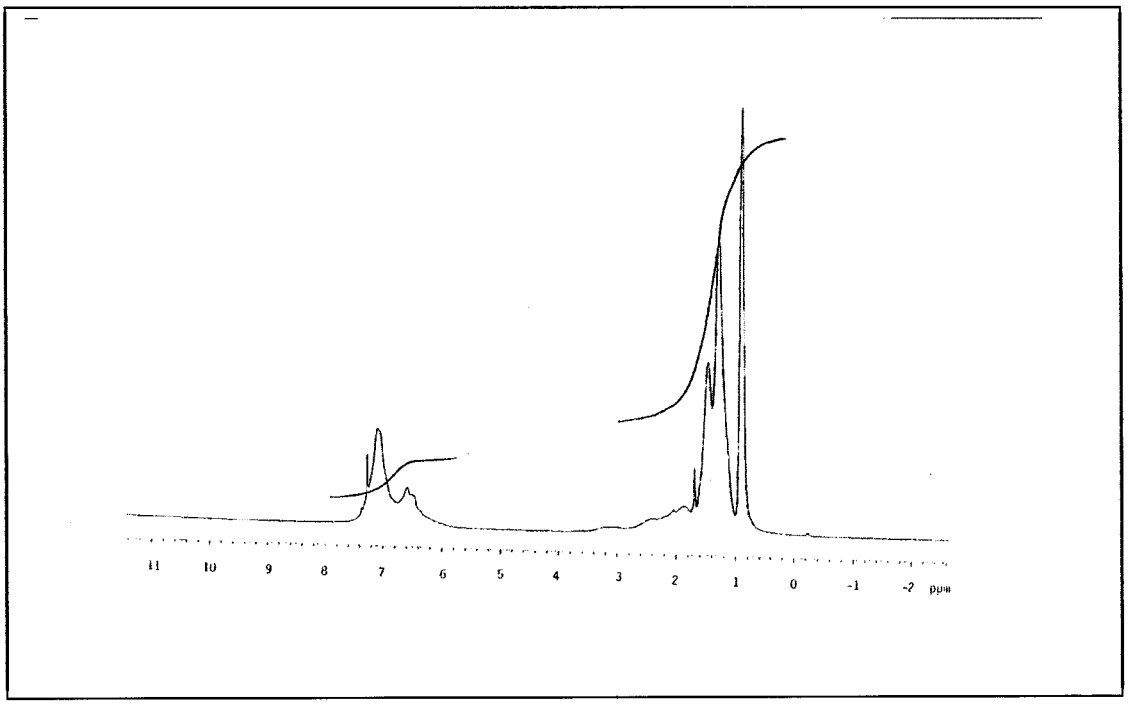


Figure 1 The ^{1}H-NMR spectrum of N-TBTM/St copolymer.

Measurements

The elemental analyses were done on a Perkin–Elmer 2400 CHN elemental analyzer. The IR spectra were recorded on a Perkin–Elmer 883 spectrophotometer. The ^{1}H-NMR spectra were recorded on a Jeol FX (100 MHz) using TMS as an internal standard in $CDCl_3$ as a solvent reported δ (ppm) value. The molecular weights of the copolymers were measured by GPC on a Walters 150-C instrument using THF as an eluent at a flow rate of 1 mL min^{-1}.

RESULTS AND DISCUSSION

Monomer **1** was a liquid while monomer **II** was a solid and soluble in most organic solvents like acetone, DMF, THF, and DMSO. Copolymers **I** and **II** were solid. They were not soluble in water, but they were soluble in some polar solvents such as monomers. The average yield of copolymer **I** was 53% and for copolymer **II** was 77%. The two copolymers were white. Gravimetric determination of tin as tin oxide of the copolymers gave 24.29 and 20.93% (calcd: 24.21 and 20.31%), respectively. The structures of the monomers and copolymers were investigated by IR and NMR spectroscopy. The IR spectra of the two copolymers indicated the presence of carbonyl groups at around 1720 and 1680 cm^{-1}. The N—H stretching vibration was observed at around 3250 cm^{-1} for copolymer **II**. There were bands at around 1600–1345 cm^{-1}, which were possibly due to aromatic and alkyl bending vibrations. The characteristic bands at around 780 cm^{-1} were due to the meta-substitution in copolymer **II**. The ^{1}H-NMR spectra for the two copolymers in Figures 1 and 2 indicate the disappearance of vinylic protons at 6.6 δ for copolymer **I** and between 6.39 and 5.69 δ for copolymer **II**. This indicates that addition polymerization by cleavage of a double bond took place.[18] Copolymer **I** had a much higher M_n and MW than copolymer **II**.

The previous investigations showed that organotin compounds have several applications (industrial, commercial, and agricultural). The use of organotin is dependent on both the nature and the number of organic groups associated with the tin atoms. Triorganotins have biological activities against various species of bacteria, insects, and fungi.[11,12] The antibacterial activities of organotin monomers and their copolymers need further study.

The antibacterial activity of *m*-AATBTB and N-(TBT)MI monomers and their copolymers of St on some Gram positive and Gram negative bacte-

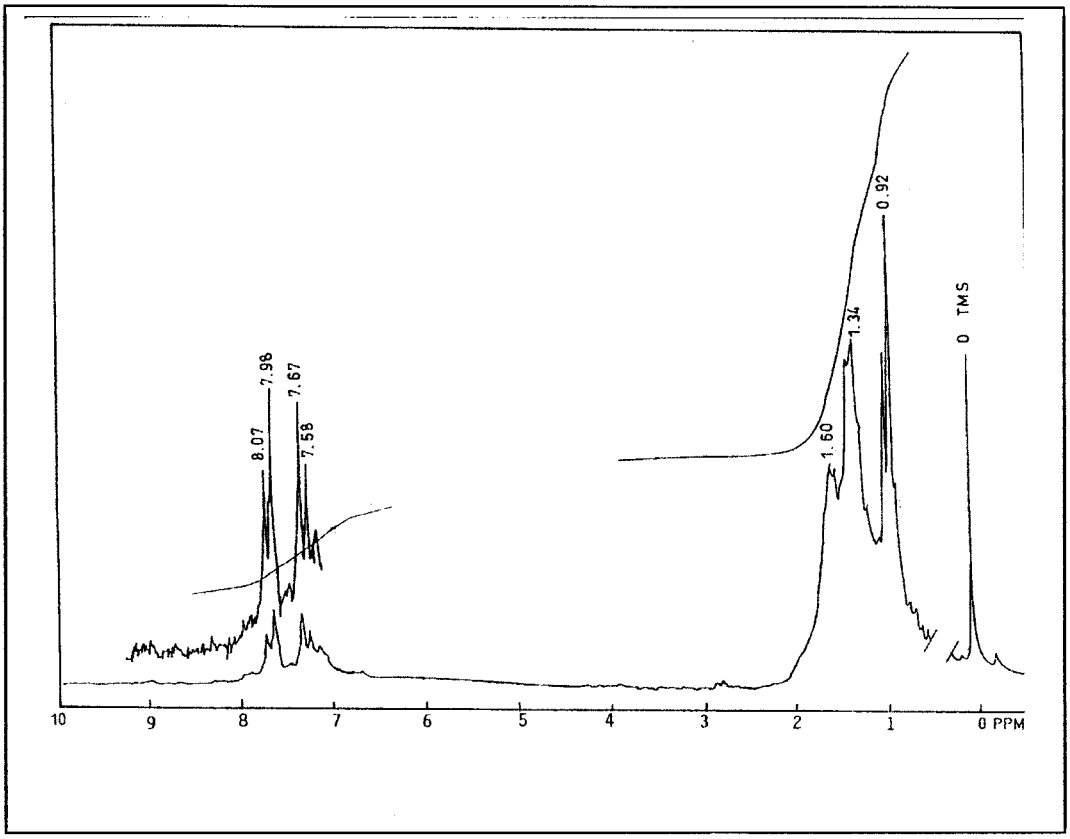


Figure 2 The ^{1}H-NMR spectrum of *m*-AATBTB/St copolymer.

Table III Antibacterial Activity of *m*-AATBTB and N-TBTM and Their Styrene Copolymers

Organism	Actual Inhibition Zone Diameter (mm)			
	m-AATBTB Monomer	*m*-AATBT/ST Copolymer	N-TBTM Monomer	N-TBTM/ST Copolymer
Gram positive				
Staphylococcus aureus (CBSC 15-5554 A)	34	31	34	31
S. aureus (ATCC 29213)	40	35	31	29
S. epidermidis (CBSC 15-5556 A)	35	30	42	36
Streptococcus faecalis (NCTC 370)	26	24	34	26
Bacillus megaterium (CBSC 15-4900 A)	29	24	26	20
B. cereus (CBSC 15-4870 A)	27	22	23	21
Gram negative				
Shigella dysenteriae (NCTC 5110)	Trace	—	16	Trace
Shigella sonnei (KKUH 934)	9	—	13	—
Salmonella typhimurium (NCTC 73)	—	—	9	—
Salmonella typhi (KKUH 1012)	Trace	—	12	Trace
Escherichia coli (ATCC 25922)	8	—	12	9
Yersinia enterocolitica (ATCC 23715)	12	10	23	11
Y. pseudotuberculosis (NCTC 10275)	9	—	19	10

Trace the inhibition zone is less than 8 mm in diameter.

ria are given in Table III. Thirteen isolates of Gram positive and Gram negative bacteria were used in this investigation. These isolates include six isolates of Gram positive bacteria and seven isolates of Gram negative bacteria (Table I).

The results in Table III show that Gram positive bacteria are more sensitive to the two monomers (*m*-AATBTB and N-TBTM) and their St copolymers than Gram negative bacteria. *Staphylococcus aureus* (Gram positive) is the most sensitive bacteria toward the two chemical compounds and their St copolymers, where the inhibition zones were equal to 40, 35, 31, and 29 mm for the compounds *m*-AATBTB, Co(*m*-AATBTB)/St, N-TBTM, and Co(N-TBTM)/St, respectively. *Salmonella typhimurium* (Gram negative) is the most resistant bacteria toward the tested chemical compounds. Generally, the results indicate that St copolymerization decreased the potency of the two monomers (*m*-AATBTB and N-TBTM) against both Gram positive and Gram negative bacteria.

CONCLUSION

Two organotin monomers (N-TBTM and *m*-AATBTB) were copolymerized by free radical polymerization in the bulk at 65°C with St using AIBN as the free radical initiator. Copolymer yields were 53–77% for N-TBTM and *m*-AATBTB, respectively. All monomers and copolymers showed good activity toward 13 types of bacteria.

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