To the Graduate Council:

I am submitting herewith a dissertation written by Ronald Curtis Marks entitled "New Tetraarylborate and Ethyldibutylstannane Reagents." I have examined the final copy of this dissertation for form and content and recommend that it be accepted in partial fulfillment of the requirements for the degree of Doctor of Philosophy, with a major in Chemistry.

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NEW TETRAARYLBORATE AND ETHYLDIBUTYLSTANNANE REAGENTS

A Dissertation

Presented for the

Doctor of Philosophy

Degree

The University of Tennessee, Knoxville

Ronald Curtis Marks
Major, United States Air Force

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"Doth that man love his Lord who would be willing to see Jesus wearing a crown of thorns, while for himself he craves a chaplet of laurel? Shall Jesus ascend to his throne by the cross, and do we expect to be carried there on the shoulders of applauding crowds? Be not so vain in your imagination. Count you the cost, and if you are not willing to bear Christ's cross, go away to your farm and to your merchandise, and make the most of them; only let me whisper this in your ear, 'What shall it profit a man if he gain the whole world and lose his own soul?'"

Charles Haddon Spurgeon[1]

DEDICATION

This dissertation is humbly dedicated to my wife;

Joann Paula Marks

and to my parents;

LtCol Glenn M. Marks (USAF, retired) and Jo E. Marks

and to my wife's parents;

MSgt Hugh C. Williams (USAF, retired) and Kathleen Ball Williams

I join my wife in thanking our parents for a tremendous heritage and faith.

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PART I

INTRODUCTION

CHAPTER 1

POLYMERS

A. Approach to the Study

This research was divided into two studies. The primary goal of both was to investigate the preparation and reactivity of new organometallic reagents attached to polymer backbones. Secondary goals corresponding to each part of the investigation were established to clarify the separate issues of research. The first goal was construction of boronate esters covalently attached to a polystyrene backbone. This part of the study is presented in Part II, Tetraarylborate Anchor Groups Supported on Commercial Polystyrene. The second was a study of the stereochemical aspects of the hydrostannation reaction of alkynes with a stannyl reagent supported on polystyrene, and is presented in Part III, Stereochemical Aspects of Hydrostannation Using Poly{dibutyl[2-(3- and 4-ethenylphenyl)ethyl]tin. Prior to discussion of the research accomplished, it is appropriate to present a short background on the use of polymers in organic synthesis.

B. Overview of Polymers and Polymer-Supported Reagents

Throughout the relatively short history of polymer chemistry, polymer researchers have studied the synthesis, characterization, and practicable applications of the product of

their craft. Berzelius is attributed with the first use of the word "polymer" in 1833.[3] Plastics, rubber, and other polymers (synthetic and natural) began to flow from the laboratory through the factories and eventually into the home. This flow into the home lead to increased familiarization and dependence on both the technologies associated with polymers and the polymers themselves.

Mankind has used natural polymers since prehistoric times. These uses of natural resins and gums continue today, though their use has diminished due to progression in modern technology and the introduction of synthetic counterparts. The Greeks knew of amber, the Romans made use of gum mastic, and asphalt used in "prebiblical times".[4] Christopher Columbus is attributed with the Western World's discovery of rubber while watching natives of Haiti use it to make playballs.[5] It was not until 1820 that England's first rubber factory was built by Thomas Hancock. About that time Charles MacIntosh's method of waterproofing cloth opened the demand for natural rubber, and drier clothes. Research continued, and in 1826 Michael Faraday discovered that isoprene was the building block of natural rubber. Robert Thomson's invention of the pneumatic tire in 1845 (reinvented in 1888 by John Dunlap) firmly entrenched the demand for rubber in Western civilization.[3]

As with other human endeavors, the polymer sciences began to collect their own history, father figures, and legends. A favorite legend associated with rubber must be the

story, perhaps as much truth, of Charles Goodyear leaving a block of tacky natural rubber near his stove too long only to discover it had hardened. Vulcanization, as this process came to be known, was the transformation that opened the technological door for many elastomers. Vulcanization was found to be the process of tying together separate polymer chains by sulfur "crosslinks" which changed the gross physical properties of the substance. Crosslinked elastomers increased the application of polymers, and eventually lead to the technological breakthroughs which would give us rubber tires and a multitude of crosslinked elastomers found throughout society. The impact of Goodyear's observation is probably impossible to measure. With similar instances of serendipity or detailed scientific investigation, the polymer field blossomed.

Synthetic plastic first became available in 1856 when Alexander Parkes synthesized celluloid from cellulose nitrate and camphor. This new synthetic polymer was used as a substitute for ivory in billiard balls, combs, and piano keys. In 1909 Leo Bakeland developed bakelite, a phenol–formaldehyde resin. Nylon, casein, polyester, polyethylene, polystyrene, and polyvinyl chloride were all developed prior to World War II.[3]

As polymer chemistry began to emerge, organic chemists continued their study of organic chemistry. One way of extending organic research was to utilize the unique properties associated with polymers. It was the marriage of these two branches of

chemistry that led to the field of polymer-supported organic reactions. Polymer-supported reagents capitalized on the wealth of knowledge already developed by polymer chemists and organic chemists to create polymer-supported reagents, and hence, to study the utility of polymer-supported reactions.

Polymer-supported reagents have a short but rich history. The best, though dated, work on the subject is by Hodge and Sherrington; *Polymer-Supported Reactions in Organic Synthesis.*[6] A recent survey, by Keith Smith, *Solid Supports and Catalysts in Organic Synthesis,*[7] though not a comprehensive review, updates the field to work through 1991.

C. General Aspects of Polymerizations

Polymers are traditionally classified based on the mechanism of the polymerization reaction used to form the polymer. Step-growth polymers are distinguished from chain-growth polymers primarily by the kinetics of the polymerization. For step-growth polymers, the rate of initiation and propagation are essentially the same, with no termination reaction. In contrast, chain-growth polymers grow via an "active site" on each chain, and the kinetics of each step are unequal.[8] The two polymer types are further contrasted in Table 1.

Table 1. Definition and Comparison of Step-Growth and Chain-Growth Polymers.[8]

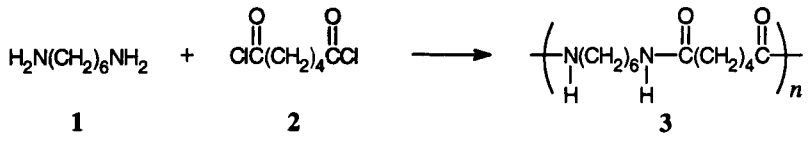
Step-Growth	Chain-Growth
Growth occurs throughout matrix by reaction between monomers, oligomers, and polymers.	Growth occurs by successive addition of monomer units to limited number of growing chains.
Low average degree of polymerization.	Degree of polymerization can be very high.
Monomer consumed rapidly while molecular weight increases slowly.	Monomer consumed relatively slowly, but molecular weight increases rapidly.
Reaction mechanism the same throughout.	Initiation and propagation mechanisms different.
No termination step; end groups remain reactive.	Usually chain-terminating step involved.
Polymerization rate decreases steadily as functional groups consumed.	Polymerization rate increases initially as initiator units generated; remains relatively constant until monomer depleted.

Other important factors are used to define a polymer and describe its physical and chemical properties. By selecting specific polymerization conditions, a polymer of desired physical characteristics and properties is obtained. These characteristics include forming polymer blocks versus beads, gels versus crosslinked polymers, and the incorporation of channels within the polymer.

Step-Growth and Chain-Growth Polymerization

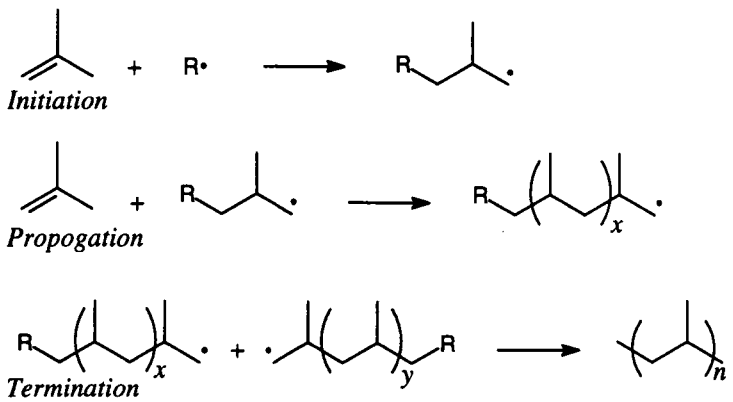
Step-growth polymers are formed from difunctional monomers in one of two ways. The first method utilizes a monomer possessing two identical functional groups in

a reaction with a second monomer also possessing two identical functional groups, though different but complementary to the first monomer. The second method places both of the functional groups necessary for the reaction on a single monomer. The Schotten-Baumann reaction in the polymerization of hexamethyldiamine (**1**) with adipoyl chloride (**2**) to form Nylon–66 (**3**) is an example of a step-growth polymerization after the first method (Equation I-1).



1 **2** **3** I-1

Vinyl polymerization is a chain-growth, free-radical process, and encompasses the leading method for formation of polymers used in the commercial market.[9] Chain-growth polymerizations occur by way of three steps (Scheme 1); initiation, propagation,



Scheme 1. Chain-Growth Polymerization of Isobutylene. R• is a free-radical source. Termination is represented by a recombination step, although disproportionation may also occur.

and termination, which may occur by way of a recombination or a disproportionation reaction.

Bulk and Solution Polymerization

Bulk polymerization is the simplest method of polymer formation. A system containing only monomer and initiator in the absence of solvent characterizes the bulk polymerization. However, they are also characterized as the most difficult to control, especially when a reaction exotherm occurs.[10] The addition of solvents, diluents, and stabilizers increases the complexity of the system. These methods are known as solution, suspension, emulsion, or precipitation polymerizations.

Suspension polymerization uses a multiphase system consisting of an organic phase and an aqueous phase. The phase present in excess is designated as the continuous phase and is generally referred to as the solvent. For most organic polymers, this means the aqueous phase is the solvent and is present in excess. Suspension polymerizations utilize an aqueous solvent, producing polymer beads by formation of stabilized monomer droplets in stirred solution. Initiation and polymerization occur within these monomer droplets. A stabilizer is added to increase the interfacial tension between the phases, reducing the tendency of the droplets to coalesce.

A highly complex relationship between reaction components, and the reaction vessel influences particle size in suspension polymerizations. No complete theory has been established for predicting or controlling particle size. Guyot[11] noted that suspension polymerization is more art than science. He attributes the difficulty in controlling bead size to reactor and stirrer design which influence shear distribution within the reactor. These shear forces differ throughout the reactor. Shear forces also change during the course of polymerization due to increases in viscosity of the organic phase. Droplet size is the result of a process described as a "quasi-equilibrium between the thermodynamically favored droplet coalescence and the division of the coalesced droplets under the shear field of stirring."[11] Scully[12] has formulated this association by relating the particle size, $\bar{d}$, to the shape factor of the reaction vessel, K; the interfacial tension between the liquid phases, s,; the volume fraction of the dispersed phase, f; the droplet density, P; the stirrer blade diameter, L; and the stirrer speed, N (Equation I-2).

$$\bar{d} \propto \left\{ \frac{(K)(\sigma)(\phi)}{(L)(N)(P)} \right\} \qquad \text{I-2}$$

As an example, a suspension polymerization in a 500 mL round bottomed flask will give 0.24 mm diameter beads at 200 revolutions per minute (rpm), and 0.12 mm beads at 280 rpm A cylindrical flask at the same stirring speeds will give 0.35 mm beads and 0.24 mm beads, respectively.[13]

Linear and Crosslinked Polymers

Linear polymers may be soluble depending on solvent, chain length, and polarity of the polymer chain. In solution, these polymers would provide a homogeneous system of polymer-supported reagent or catalyst. Placing the polymeric reagent in a solvent with other reactants minimizes diffusion effects since all reactants have ready access to the ligands on the polymer backbone. For kinetic studies, this provides freedom from diffusion effects on the rate caused by an insoluble polymer matrix.[13] A primary disadvantage of reactions involving soluble polymers is the difficulty associated with separation of the polymer following reaction.

Crosslinking results in extreme changes to a polymer system. Crosslinked resins are insoluble in all solvents and provide a heterogeneous system. With a separate matrix containing the reagent or catalyst, reactants must now diffuse into the matrix, and the products must diffuse out. The reaction system is complicated by these diffusion requirements. Formation of macrochannels (discussed in the next section) in the polymer matrix moderates diffusion effects. Swelling the beads in a compatible solvent also moderates these effects. Even though swelling moderates the diffusion effects, its ability to assist is limited. In addition, a covalently crosslinked polymer loses its ability to flow, resulting in a solid with physical properties characteristic of those in elastics or plastics. A principal advantage of crosslinked polymers is ease of separation from a reaction

system due to their insolubility. Simple filtration is generally sufficient to separate the reaction products from the polymer.

Crosslinking may be introduced during the polymerization by incorporation of a crosslinking agent. Generally, this occurs by formation of chemical bonds that connect two separate chains. These bonds may be covalent or ionic. A commonly used crosslinking agent that produces covalent crosslinks in free-radical polymerizations is divinylbenzene.

Macroporous and Gel Polymers

When a crosslinked polymer is formed without any other macrostructural features, it is termed a gel. Stevens[14] notes that the term gel is correctly applied to any solvent-swollen, but not dissolved, polymer system, whether crosslinked or not. In common use, crosslinked polymers are known as gels. Gel beads are characterized by their low crosslinking (generally 1–5%), transparency, ability to swell in compatible solvents, and their microporosity. The microporosity is a function of interchain distances (on the order of 50 Angstroms) and is inversely proportional to the level of crosslinking.

Three main types of diluents are used to form the pores: solvents for the polymer, non-solvents for the polymer, and linear polymers.[15] Solvating diluents used with large amounts of crosslinking agents result in permanent porosity with pore sizes averaging

0.3 mL per gram. For non-solvating diluents, a more complex system of microspheres, mesospheres, and agglomerates form pore sizes of up to 3 mL per gram.

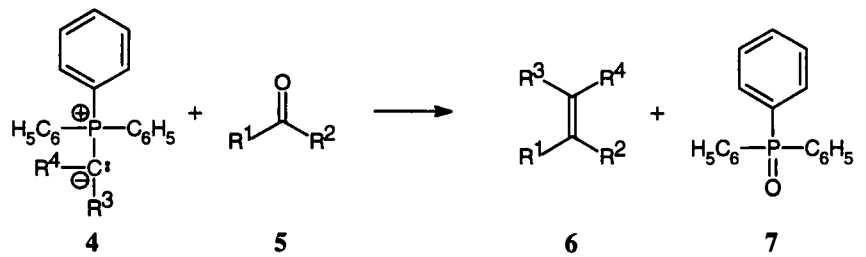
Crosslinked beads may be affected by diffusion limitations. Incorporation of "macrochannels" into the beads reduces diffusion effects. A bead with macrochannels is termed macroreticular or macroporous. These beads are characterized by higher levels of crosslinking (generally 5–60%), and are opaque or translucent.

Macroporosity is introduced into the bead by utilizing a diluent during the polymerization. This diluent is chemically inert to the polymerization reaction, yet provides a solvent envelope to the growing polymer chains, introducing pores into the polymer network. Removal of the diluent following polymerization leaves permanent channels or pores. These pores remain in the absence of solvent, though solvent swelling may decrease the size of the pores. A principal advantage of pores is the decrease in diffusion effects due to the increase in interior surface area and the presence of open channels into the interior, as well as adding the capability to react reagents in solvents incompatible with the polymer matrix.

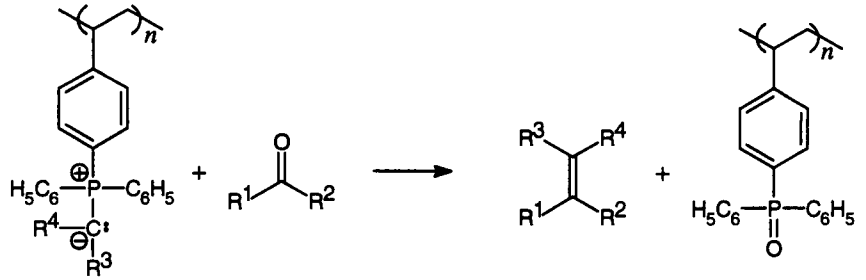
CHAPTER 2

BACKGROUND OF POLYMER-SUPPORTED REAGENTS

Polymer-supported reagents are fabricated by attaching either organic or inorganic ligands to a polymer matrix. Organic substrates, catalysts, and other reagents have all been successfully attached to polymeric backbones and used in subsequent reactions. The ligands are attached to the polymer backbone by either ionic or covalent bonds, and provide stationary reagents that react similarly to their unsupported analogues. The non-polymer-supported systems are referred to as the small-molecule analogues. The concept is outlined in Equations I-3 and I-4. Equation I-3 presents a small molecule analogue of the Wittig reaction of a triphenylphosphonium ylide **4** with a ketone.. This small molecule analogue can be compared to a system in which the phosphonium ylide **8** is covalently attached to a polymer backbone (Equation I-4).



4 **5** **6** **7** I-3



8 **5** **6** **9** I-4

A. Advantages of Polymer-Supported Reagents in Organic Synthesis

Very few organic reactions yield products in a straightforward manner. The experimental technique of the researcher can have a great influence on yield and purity of the product in a given reaction. Impurities, in the form of side products and other contaminants, such as unreacted starting material, must be considered in the overall reaction and removed from the target product. Indeed, as new reactions are discovered, those which yield the purest products directly will always be chosen over reactions that involve complicated workup or separation schemes. Only when an increase in yield outweighs the desire for simplicity will the researcher choose a technique entailing complex experimental requirements.

Polymer-supported reagents often provide simplicity to the laboratory environment. This simplicity allows the researcher to focus on the details of the reaction or the details of the science instead of concentrating on requirements of technique. In fact, polymer supports have many advantages. Perhaps the single most important advantage is the straightforward separation of the reaction products from the reagents. Other advantages include:

1. Simplified workup.
2. Ability to use an excess of either the polymeric reagent or reactant

3. Simplified recovery of polymer and regeneration of the polymeric reagent for use in subsequent reactions.

4. Insolubility of the polymer matrix, leading to immobilization of the reagent, or reagents on the polymer backbone.

5. Heterogeneous catalysis using catalyst bound to the polymer matrix.

6. Nonvolatility of the polymer, and therefore, the reagent bound to the polymer. This reduces the toxicity of reagents. For reagents that are noxious or characterized by offensive odors, binding to the polymer matrix eliminates this problem.

7. Possibility of specificity and kinetic effects due to the microenvironment within the vicinity of each polymer chain.

8. The capacity to place two chemically incompatible reagents together in a reaction vessel (e.g., a reducing agent and oxidizing agent bound to separate polymeric supports or the same support).

Polymer-supported reagents tremendously expand the potential of organic chemistry. Each of these advantages provides for the more efficient use of the researcher's time.

B. Important Considerations of Polymer-Supported Reagents

Polymer-supported reagents are not the panacea of synthetic chemistry. Although their use often enhances synthetic procedures, there are important factors to be considered. For example, even though immobilization of the reagent simplifies handling, the presence of the polymer backbone may complicate the reaction environment by changing the microenvironment of the functional group. These microenvironmental changes are associated with the relationship between functional group and polymeric matrix and are dependent on the chemical characteristics and properties of the polymer backbone as well as the chemical characteristics of parts of the polymer matrix that are close to the reaction sphere of the functional group. J. M. Maud[16] notes that although these changes are of fundamental importance, study of the microenvironment is difficult. Only a few studies have been published to date. Several of the factors that influence the reaction by introducing differences in local concentration, adsorption requirements, diffusion phenomena, and specific neighboring-group effects are summarized below.[17]

Local Concentration Effects

Local reaction rates (rates of reactions occurring within the microenvironment surrounding the reagent) of polymer-bound reagents are generally enhanced when compared to their homogeneous analogues. These increased reaction rates result from higher reagent "density" within a polymer-supported matrix. However, measurement of

reaction rates is accomplished by quantifying the disappearance or appearance of a specific species, which is a bulk characteristic of the reaction. Sherrington[6] discusses this effect in detail, relating the local rate, R_L, to a first approximation of a second-order rate equation (Equation I-5); where k_H is the bimolecular, or homogeneous, rate constant, N_A

$$R_L = k_H\left(\frac{N_A}{v}\right)\left(\frac{N_B}{V}\right) \qquad \text{I-5}$$

and N_B are the numbers of molecules A and B in the reaction volume V, while v is the interior volume of the polymer support. This equation is based on three assumptions: (1) the interior volume of the support is only a small portion of the total volume V which is constant, (2) the rate constant for the homogenous system does not change, and (3) the normal motion of reagent B through the polymeric matrix will not be impeded by the matrix or matrix material. For crosslinked polymers, the last assumption may be invalid.

Diffusion Effects

The unusual microenvironment of the polymer-supported reagent introduces the need to address the accessibility of other reactants into the polymer matrix. Accessibility may be influenced by the polarity of reagents and polymer, swelling of the polymer, gel versus macroreticular structure of the polymer, and steric factors.

Porosity and pore size may affect the ability of a reagent or substrate to diffuse into or out of a polymer matrix, though as a general rule this does not seem to be a

problem. Beads have been characterized with pore volumes of 0.3–4 mL g^{-1} with pore diameters of 20–2000 Angstroms.[18] It has been theorized that, for a gel bead, the rate of reaction R is inversely proportional to the particle size r, Equation I-6.[19] With macroporous resins, this relationship does not provide an adequate picture of the reaction environment. The presence of large pores has been shown to greatly enhance the

$$R \propto \frac{1}{r} \qquad \text{I-6}$$

reactivity.[20] However, diffusion limitations are still a variable that may influence the reaction system. Grubbs *et al.*,[21] reported reactivity changes in a system employing a polymer-supported Wilkinson's catalyst in the hydrogenation of terminal alkenes. A dependence on the molecular size of the alkene and changes in polymer matrix associated with solvation of the polymer were observed, as well as changes on going from cyclic alkenes to linear alkenes.

Theory suggests that placing a ligand on a polymer support will increase the steric bulk of the ligand, and this increase may be used to advantage in the synthetic process. However, theory also indicates that when a good solvent for the polymer and ligand are used, that is, if the ligand and polymer are both well solvated, then no difference in polymer-supported reactions versus a small molecule analogue of the reaction should be observed.[13]

Functional Group Site Differentiation

The primary distinguishing feature of a polymer-supported reagent compared to the small molecule analogue of the reagent is the immobilization of the reagent on a polymer backbone. This immobilization creates a microenvironment that is very different from the environment around a reagent in the small molecule or solution chemistry analogue. Instead of solvation spheres, the polymeric reagent may encounter an environment of solvent, additional polymer, or crosslinking site.

Lightly crosslinked polymers swell more readily in a compatible solvent, providing larger channels into the polymer matrix. The converse occurs for increasingly crosslinked polymers which swell less with increasing crosslinking.

Copolymers provide a multitude of microenvironments to the supported reagents. Crosslinking agents are an important component of many copolymers. Theory suggests that a functional site located at a crosslink junction may react differently than a functional site far removed along the polymer chain. McKenzie and Sherrington[22] observed the reaction of carbon tetrachloride with alcohol on a polymeric phosphine reagent. They prepared two triphenylphosphine-modified polystyrenes (Figure 1). In the first, triphenylphosphine was copolymerized with styrene and divinylbenzene as the crosslinking agent to give copolymer **10**, while the second was copolymerized with styrene and crosslinked with a functionalized monomer, bis(*p*-styryl)phenylphosphine, to

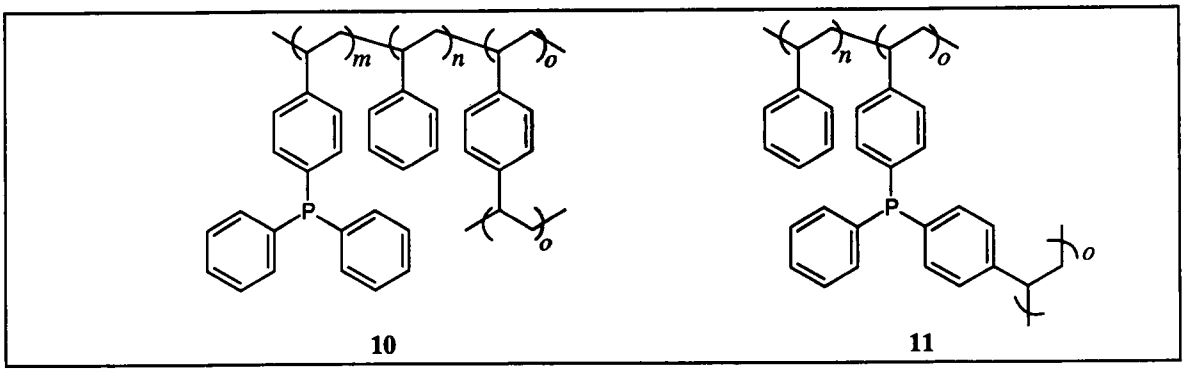


Figure 1. Polymeric Phosphine at Site Removed from Crosslinking Junction Compared to Phosphine at Crosslinking Site.

yield crosslink sites as in **11**. Their work showed no discernible difference in reactivity between the two types of polymer.

Distribution of Functional Sites

Formation of copolymers does not always result in random mixtures of the monomer repeat units due to the different reactivities of each monomer toward other monomers and crosslinking agents in the mixture. For copolymers with one of the monomers acting as a crosslinking agent, this results in regions within the copolymer of higher density of crosslink sites, and regions of "open" non-crosslinked areas. This phenomenon is explained using the copolymer composition equation[23] (Equation I-7).

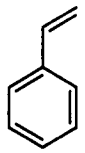
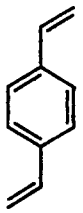
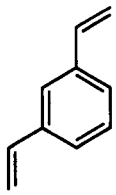
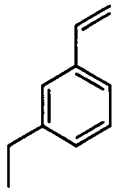
$$\frac{d[M_1]}{d[M_2]} = \frac{[M_1]}{[M_2]}\left(\frac{r_1[M_1]+[M_2]}{[M_1]+r_2[M_2]}\right) \qquad \text{I-7}$$

The copolymer equation relates the monomer molar ratio in the copolymer, $d[M_1]/d[M_2]$, to the initial concentrations of the monomers, $[M_1]$ and $[M_2]$, and the

reactivity ratios, r_1 and r_2, of each monomer. Reactivity ratios are used to define the relative tendency of a monomer to react with another identical monomer (self-propagation) or a monomer of a different species (cross-propagation). Five scenarios may be envisioned for the reactivity ratios, and predictions about the copolymers based on these scenarios. For $r_1 \simeq r_2 \simeq 1.0$, neither cross- nor self-propagation predominates, and a random copolymer results. An alternating copolymer may be expected when r_1 and $r_2 < 1$. The other extreme case results in formation of either block copolymers or homopolymer when r_1 and $r_2 > 1$. The fourth scenario occurs for $r_1 \gg 1$ and $r_2 \ll 1$, the monomer tends to self-propagate forming a homopolymer. Finally, perfectly alternating copolymers may be expected for $r_1 \sim r_2 \sim 0$.

For a styrene-divinylbenzene copolymer, the crosslinking agent generally used is a technical mixture of *p*-divinylbenzene, *m*-divinylbenzene, and *m*- and *p*-ethylvinylbenzenes. The reactivity ratios of these compounds with styrene are shown in Table 2. Polymers with reactivity ratios greatly different from the divinylbenzene–ethylvinylbenzene mixture will be a heterogeneous network with "pockets" of crosslinking agent and pockets of monomer(s).

Table 2. Comparison of Reactivity Ratios of Technical Divinylbenzene Mixture with Styrene.[24]

	Reference	Component of Technical Divinylbenzene			
Chemical Structure of Compound					
Reactivity Ratio of First Vinyl Group Reacting With Styrene	1	7	4	1	1.4

C. Classes of Polymer-Supported Reagents

Classification of polymer-supported reagents may be made based on physical or chemical characteristics of the polymer, chemical characteristics of the supported reagent, type of reaction associated with the reagent, or method of polymer functionalization. There are also classifications that describe physical attributes of the polymers: soluble, crosslinked beads (or network polymers), plastics, and rubbers are several examples.

Classification by Polymer Physical and Chemical Characteristics

For polymer-supported reactions, the most common reagents are crosslinked beads and soluble polymers. The crosslinking may be accomplished using chemical crosslinking agents such as divinylbenzene, to form covalent links between polymer chains, or a reagent which leads to an ionic link. Crosslinking produces extreme changes

in the polymer's physical properties that include making the polymer insoluble, severely restricting chain rotation and chain movement, and a loss of elasticity. The degree of crosslinking is described as a weight percent (the weight of crosslinking agent as a percent of the total polymer weight) or as crosslink density as defined by Equation I-8,

$$\Gamma = \frac{\left(\overline{M}_n\right)_o}{\left(\overline{M}_n\right)_c} \qquad \text{I-8}$$

where Γ is the crosslink density, $\left(\overline{M}_n\right)_o$ is the number average molecular weight of uncrosslinked polymer and $\left(\overline{M}_n\right)_c$ is the number average molecular weight between crosslinks.

Crosslinked beads may be further classified as macroporous or as gels. Gels are formed from the suspension copolymerization of a monomer and crosslinking agent. They are generally transparent or translucent and lightly crosslinked (from 1–5%). The light crosslinking allows for swelling of the beads in compatible solvents, which results in nonpermanent micropores containing the solvent, polymer segments, and crosslinking units. These micropores can be contrasted with the permanent pores of the macroporous resins that are an artifact of polymerization in the presence of diluents or porogens. To create macropores, polymerization is accomplished with monomer, crosslinking agent, and diluent, which results in large areas of the bead being occupied by the nonpolymerizing porogen. Removal of the porogen leaves large permanent pores in the

beads. The beads may still swell in compatible solvents, but the pores remain in both the swollen and collapsed bead state. This effectively increases the surface area of the polymer support and makes the beads appear opaque due to scattering of light from the pores.

Classification by Chemical Characteristics of Supported Reagent

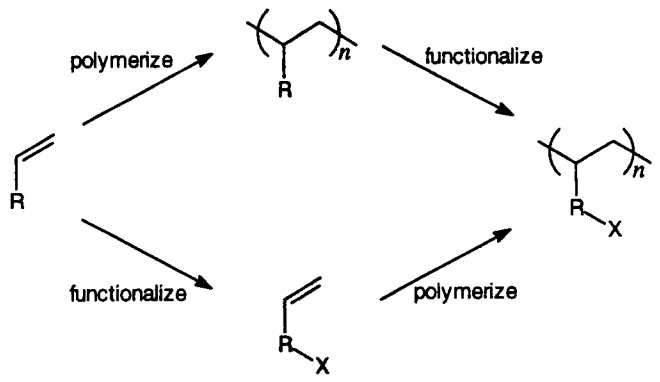
Polymers may be classified by the manner in which the ligand is bound to the support to give two major categories: ionic reagents or covalent reagents.

Classification by Ligand Chemistry

Polymer-supported reagents may be categorized by the type of reaction the ligands accomplish: reagents used in oxidations, reductions, substitutions, condensations, dehydrations, acylations, ylides, and organometallic reactions.

Classification by Method of Functionalization

Another method involves classifying the polymer-supported reagents by the method of synthesis. Two types of classifications are apparent. The first category of functionalized polymers encompasses those in which the polymer network is formed first and then functionalized, while the second utilizes an already functionalized monomer in the polymerization process as shown in Equation I-9. These two types may provide polymers containing the same functional groups and crosslinking ratio, but with very



I-9

different chemical characteristics. These differences arise from the distribution of crosslinks and ligands within the polymer matrix, resulting in different microenvironment for the ligands.

Functionalization of preformed polymer beads has several advantages and disadvantages.[13] Of the advantages, the most important one is the ability to estimate the macroproperties of the preformed polymer. Much of the polymerization process for beads has been well defined, including the methods of suspension polymerization and the knowledge of reactivity ratios. This allows the researcher to accurately estimate the properties of the beads. Once functionalized, the macroproperties of the beads would not be expected to differ significantly from the original matrix. Two important disadvantages are the difficulty of ensuring uniform distribution of ligands within the polymer matrix and the possibility that functionalization may produce side reactions.

PART II

TETRAARYLBORATE ANCHOR GROUPS SUPPORTED ON COMMERCIAL POLYSTYRENE

CHAPTER 1

INTRODUCTION

A. Approach to the Investigation

The goal of this part of the research was to synthesize new cation exchange resins from tetraarylboronates supported on commercial polystyrene. Following functionalization of the resin, we intended to submit samples of the polymer-supported tetraarylborates for analysis of their selectivity and affinity for alkali metal ions. A brief background of boron and polymer-supported boron reagents will be presented, followed by the results of this research.

B. Chemical Background of Boron

The element boron has a long and fascinating history. In its naturally occurring forms, boron has been used in ancient times for tinting glass and, by the Romans, to soak up blood in coliseums. These historical applications made use of the naturally occurring forms of boron, the borate oxides: $Na_2B_4O_7 \cdot X\ H_2O$, the most common of which is borax, $Na_2B_4O_7 \cdot 10H_2O$. More recent uses of this element include the formation of boron fibers, which have very high melting points (2300 °C), and the development of boron alloys. Because of the glass-like properties of boric oxides, they have been used in conjunction with silicon oxide to form borosilicate glasses such as Pyrex. Boron possesses an outer

shell electron configuration of $2s^2\ 2p^1$ and is found in approximately 0.0003% abundance in the earth's crust.[25] Gay-Lussac was the first to isolate the elemental form of boron.[26]

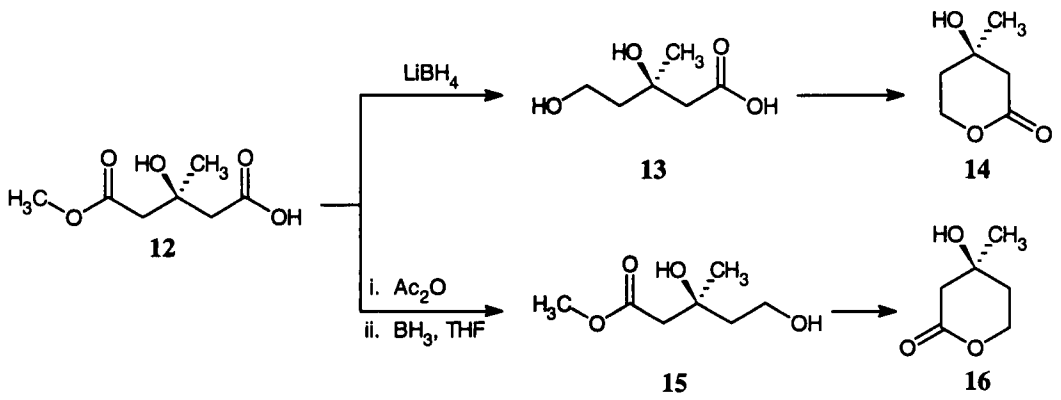
The first organoboranes were discovered by Frankland in 1859, just ten years after he reported the first organostannanes. This discovery was a result of research into the reaction of alkylzinc with triethoxyborane to yield triethylborane and diethoxyzinc.[27] Stock later isolated the simple boron hydride compounds including B_2H_6, B_4H_{10}, B_5H_{11}, and $B_{10}H_{14}$.[28] A lineage of boron investigators, researchers, and academicians was established from H. I. Schlesinger to H. C. Brown and then to G. W. Kabalka, with each scientist contributing volumes to the scholarship of organoborane chemistry.[29]

C. Brief Chemical Survey of Organoboranes

For a complete treatment of the full range of reactions of borane and organoboranes, the following sources are noted: Pelter, Smith, and Brown, *Borane Reagents*[30]; Brown, *Organic Synthesis via Boranes*[31] and *Boranes in Organic Chemistry*.[32]

Reductions Using Borane

Boranes possess the ability to selectively reduce a specific functional group in a molecule while leaving other functional groups unaffected. An example of a selective reduction is shown in Equation II-1. Borane in tetrahydrofuran reduces the carboxylic



II-1

acid group in **12** faster than it does the ester, leading to (*R*)-mevalonolactone (**16**). Conversely, lithium borohydride reacts quicker with the ester functionality to give the (*S*)-lactone (**14**).[33]

Hydroboration

Anti-Markownikov hydration of alkenes is the hallmark of the hydroboration reaction. Diborane, and the multitude of other hydroborating agents—thexylborane, diisoamylborane, diisopinocampheylborane, 9-borabicyclo[3.3.1]nonane, catecholborane (Figure 2)—has allowed the synthesis of many compounds. Some researchers have labeled organoboranes "the most versatile intermediates now available to the organic chemist."[34] Regioselectivity in the hydroboration reaction is controlled primarily by

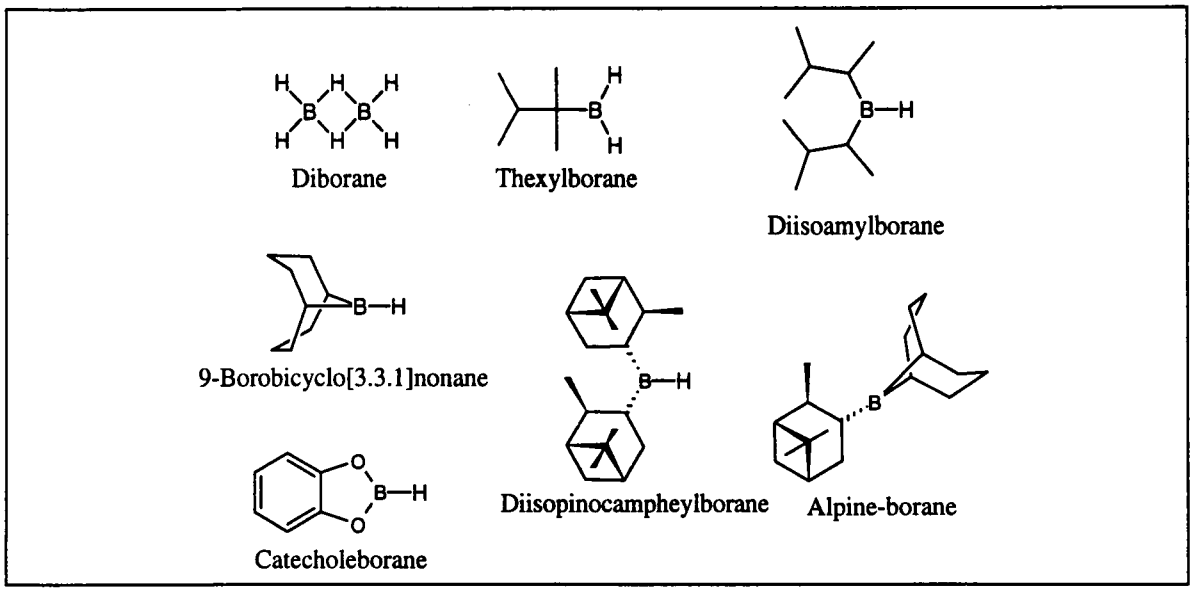
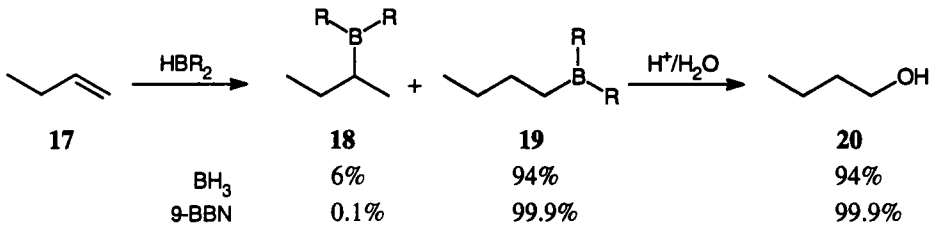


Figure 2. Several Boranes Used in Hydroboration Reactions.

steric interactions between the borane and alkene. For example, in the hydroboration of terminal alkenes (Equation II-2), borane produces the primary product **19** in 94% yield as



	17		18	19	20
		BH_3	6%	94%	94%
		9-BBN	0.1%	99.9%	99.9%

II-2

well as 6% of the secondary product **18**. Increasing the "bulkiness", or steric size, of the hydroborating reagent by using 9-borabicyclo[3.3.1]nonane (9-BBN) increases the yield of the primary product to 99.9%.

The reactivity of metal borohydrides changes with modification of the metal counter-ion. Changing of the counter-ion increases the reducing power of the

borohydrides according to the series $NaBH_4 < LiBH_4 < Mg(BH_4)_2 < Al(BH_4)_3$, with the aluminum borohydride the strongest reagent. Borohydride reducing strength is also influenced by changes to substituents on the boron atom. Attaching an oxygen directly to the boron decreases the strength of the reagent.

Although the handling of organoboranes requires some expertise and careful laboratory practices to protect them and their intermediates from reaction with atmospheric water, polymeric boranes are attractive enough to pursue due to other advantages associated with polymer-supported reagents.

Boron "Anchor Groups"

Chelating agents are a particular class of chemical ligands which form complexes with metal ions. In a classical sense, they possess one or more electrons available for donation to another species, thus "chelating" or binding that chemical species. Monodentate chelates posses a single donor group, while bidentate and tridentate possess two and three donor groups, respectively. This classical definition assumes the formation of chelate rings in the sorbent phase during metal complexation. When placed on polymeric supports, these chelates find use in the separation (or concentration) of ions from solution by binding the ions onto an insoluble matrix. Polymer-supported chelates are classified as chelating sorbents, chelate resins, ion-exchange resins, or chelating ion-exchangers. A generalized function of a chelating resin is shown in Figure 3.

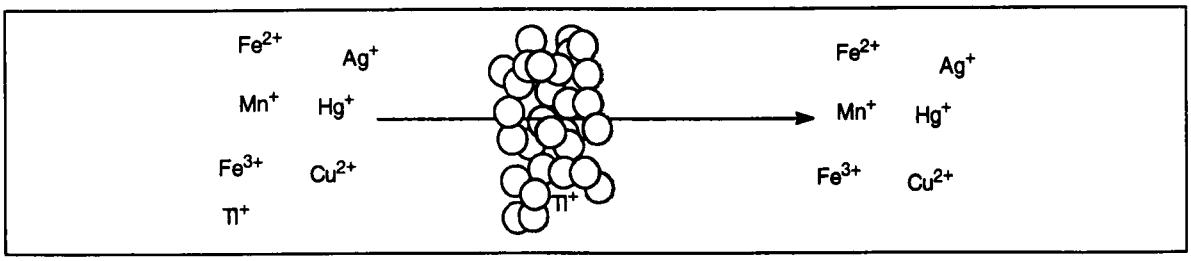


Figure 3. Schematic Representation of a Chelating Resin. This representation shows the selective chelation of thallium(I) ion from a solution of metal ions.

Myasoedova and Savvin have published two reviews on use of chelating sorbents.[35] By design, these agents selectively bind or interact with specific ions in solution, thereby removing them from the solvent. Synthesis of a resin that selectively distinguishes one ion from a multitude of ions may be accomplished by selectively building the appropriate ligand on a polymer support.

Myasoedova and Savvin[8b] note that the most widely known chelating sorbents are based on polymeric matrices. Lieser[36] notes the advantages associated with polymer-bound chelating agents along with two disadvantages, low selectivity and long equilibration times. Equation II-3 describes the selectivity of a resin, S, by differences in

$$S = \log K_d(1) - \log K_d(2) \qquad \text{II-3}$$

affinity, or distribution coefficient, $K_d(1)$, of the resin for an ion, element, or compound, compared to the affinity of a standard species present, $K_d(2)$. The low affinity of a polymer bound complexing agent for a specific ion compared to its homogeneous analogue is most likely a function of incompatible microenvironment of the polymer

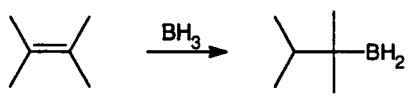
matrix with the ion. This change in microenvironment may also result in longer reaction times. Careful selection of a polymer matrix to include compatible backbone polarity and formation of macrochannels would reduce or eliminate these problems.

The polymer bound borate salts in the polymeric anchor groups may be exploited in several ways. Like their non-polymer counterparts, polymeric tetraorganoborate compounds possess a negatively charged, four-coordinate boron and positively charged counterion. These borate salts are known to react with electrophiles in a mechanistically similar manner to the reactions of organoboranes with ylides.[37] Additionally, the anions formed may be used for cation exchange, providing a cation exchange resin of interesting properties.

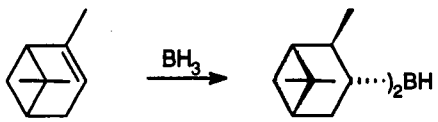
D. Synthesis of Organoboranes

Hydroboration of Alkenes

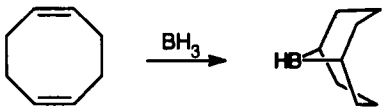
Trialkylboranes are formed from the reaction of borane with simple alkenes. Careful control of the reaction conditions may lead to synthesis of monoboranes such as thexylborane (Equation II-4), dialkylboranes such as diisopinocampheylborane (Equation II-5), or cyclic boranes like 9-borabicyclo[3.3.1]nonane (Equation II-6).



II-4



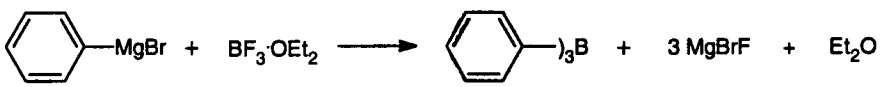
II-5



II-6

Transmetallation

Transmetallation incorporates a broad spectrum of reactions, with the best known being the Grignard reaction. As a route to organoboranes, a typical reaction is shown in Equation II-7 which was reported by Koster *et al.*,[38] who reacted the phenyl Grignard



II-7

21 **22**

reagent **21** with boron triflouride etherate to yield triphenylborane (**22**). This reaction may be modified either by changing groups attached to the boron or modifying the Grignard reagent. These changes provide a wide range of reactive combinations, with the most reactive combination involving the reaction of a boron halide with an alkali metal alkyl derivative.[39]

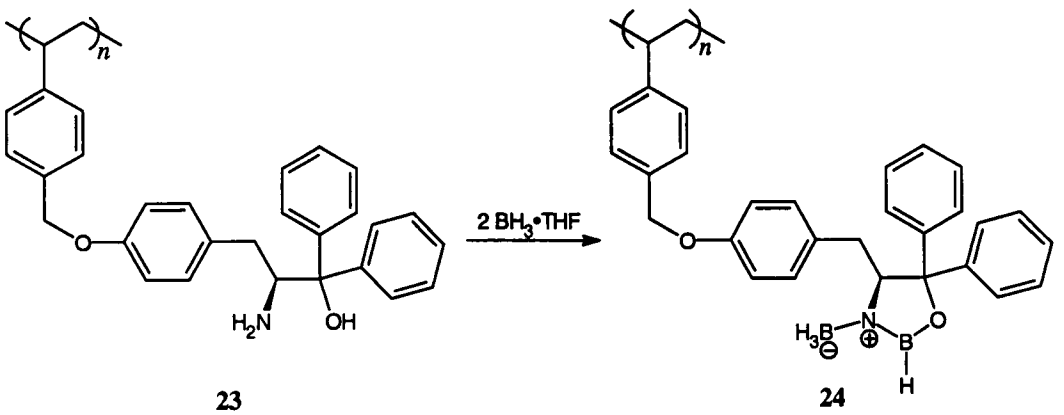
E. Review of Previous Work: Polymer-Supported Organometallic Reagents

Polymeric Boranes

The demonstrated versatility of organoboranes in organic synthesis has been extended to polymer supports. The applications in polymer-supported asymmetric synthesis will be surveyed first. This will be followed by a review of boron-containing polymeric reducing agents, protecting groups, and chelating compounds.

Asymmetric Syntheses

An outstanding example of the application of an asymmetric synthesis using an organoborane attached to a polymer-supported reagent was reported by Itsuno and coworkers.[40,41,42] Itsuno first reported the synthesis of a new reducing agent prepared from (*S*)-(-)-2-amino-3-methyl-1,1-diphenylbutan-1-ol and two equivalents of borane. This amine–borane complex reduced aromatic ketones to alcohols in 94–100% optical yield. Two years after the initial report, a polymer-supported (*S*)-(-)-2-amino-3-(*p*-hydroxyphenyl)-1,1-diphenylpropan-1-ol (**23**) was reported, which upon addition of two equivalents of borane, gave the polymer-supported analogue to the Itsuno reagent **24** (Equation II-8).[43]



23 24 II-8

Biomimetic applications of a polymeric organoborane were studied by Wulff *et al.*,[44] who used an organoborane monomer to build analogues of biopolymers by introducing optical activity into the polymer backbone in contrast to functionalization of a polymer with optically active ligands. They accomplished this by building a polymer containing asymmetric triads, in a specified conformation, from 3,4-*O*-cyclohexylidene-D-mannitol-1,2,5,6-bis-*O*-(4-vinylphenyl boronate) and selected co-monomers, yielding polymers similar to that shown in Figure 4. Polymers with negative optical rotation $[\alpha]_{365}^{20}$, were obtained in contrast to positive rotations for the monomers.

The second phase of Wulff's work focused on the formation of stereogenic cavities within a polymer matrix. Again, vinylboronic acids were prepared and then reacted with phenyl-α-D-mannopyranoside to build the sterically defined monomer **25**, followed by polymerization with very high levels of crosslinking, to give polymer **26** (Scheme 2). Removal of the template molecules using alcohol or water led to the formation of stereogenic cavities in the polymer **27**. The ability of the polymer to resolve

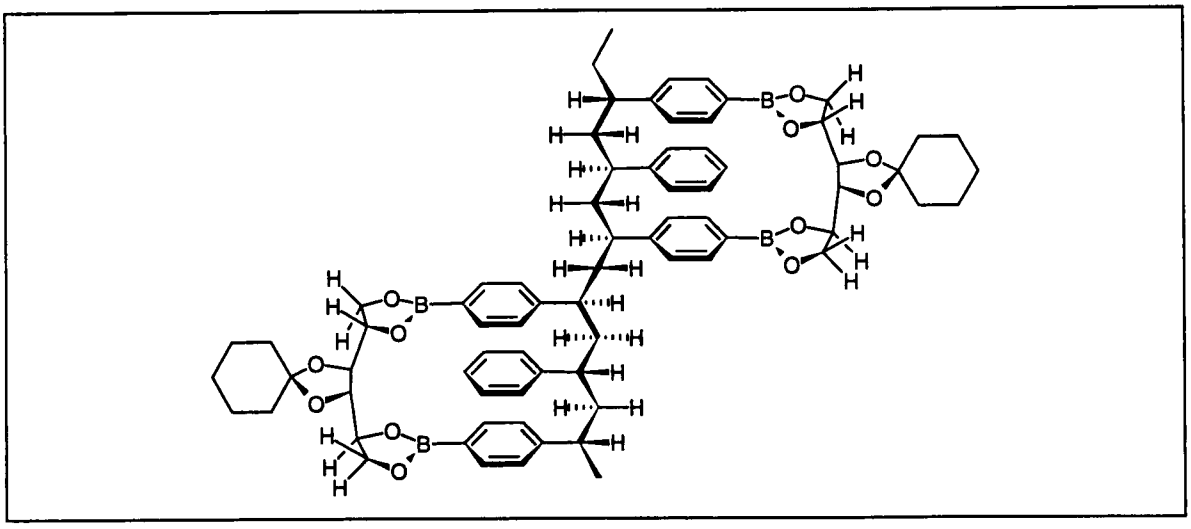
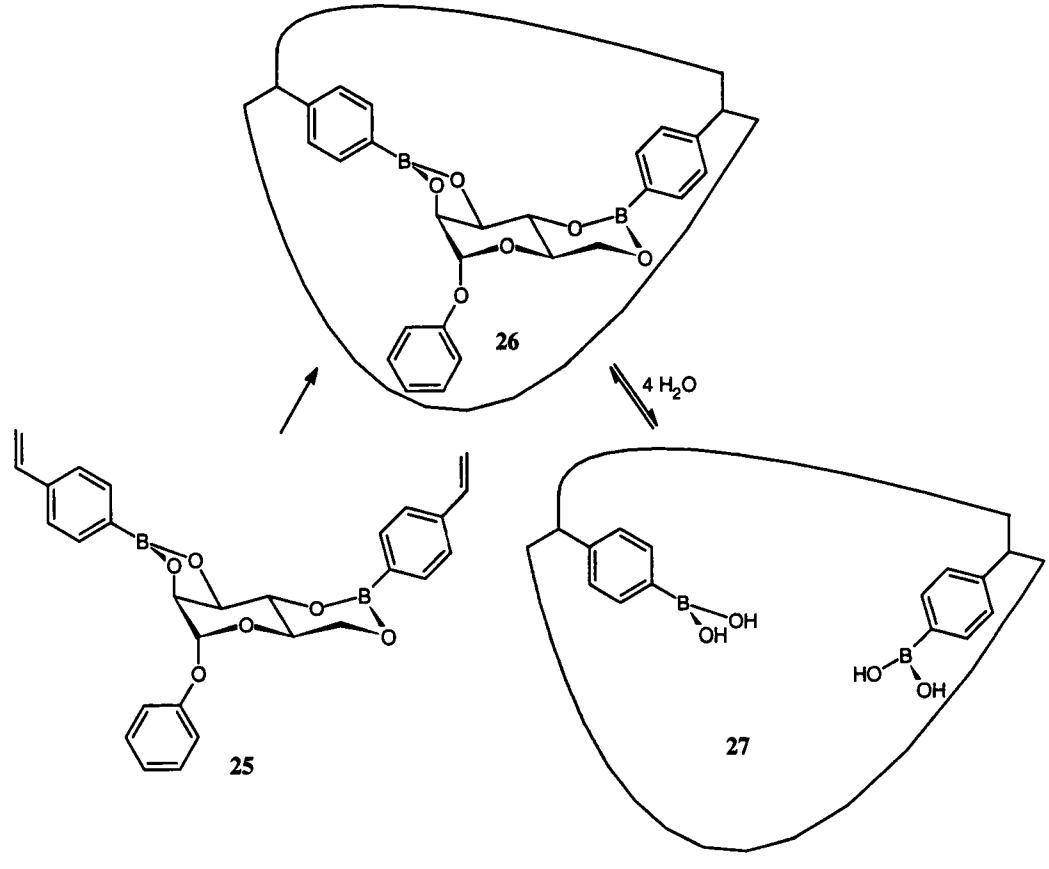


Figure 4. Biomimetic Polymer Possessing Chiral Atoms in the Polymer Backbone Formed from Borane Monomer.



Scheme 2. Formation of Stereogenic Cavity via Borane Template Molecule in Highly Crosslinked Polymer.

a racemic mixture of template molecules was tested and the specificity expressed by the separation factor, α, which the authors define as the ratio of the distribution coefficients between solution and polymer of the L- and D-form. Using ethyleneglycol dimethacrylate as the co-monomer, a separation factor of 3.66 was reported.

Reducing Agents

Complexes of boranes with amines, ethers, and sulfides are well known in solution chemistry.[45] Borane, or BH_3, exists in the pure form as a dimeric complex which is a gas at room temperature. It is very difficult to handle, reacting with atmospheric water. To facilitate handling of this reagent, it is generally complexed with Lewis bases. A partial list of commercially available boranes includes complexes with tetrahydrofuran, methyl sulfide, *tert*-butylamine, pyridine, triphenylphosphine, 1,4-oxathiane, dimethylamine, and diethyl ether.

Gibson and Bailey[46] reported the first polymer-supported borohydride in 1977, although a patent for borohydride anion exchange resins was awarded to Perrier, Benerito and Steele[47] that same year. Gibson and Bailey reported the development of a borohydride anion-complexed resin **28** based on anion-exchange resins treated with 2 to 3 equivalents of sodium borohydride (Figure 5). This polymer-supported borohydride was shown to readily reduce aldehydes.

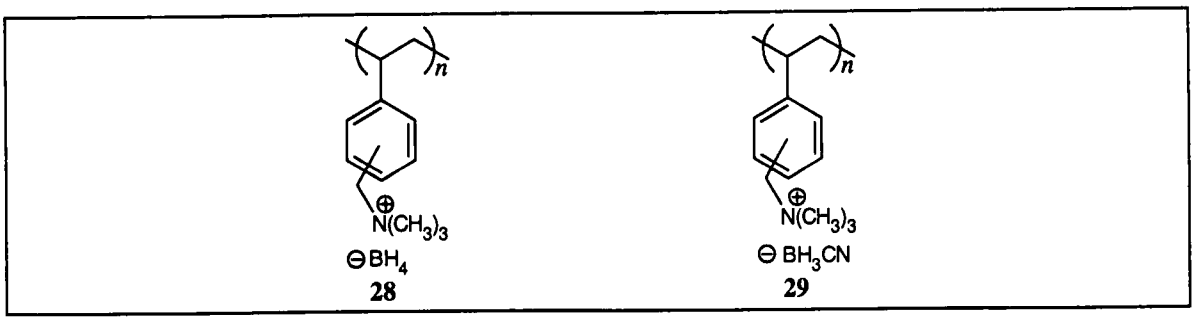
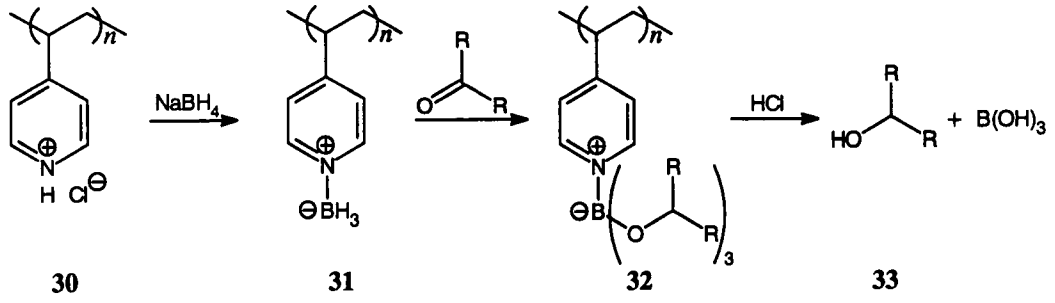


Figure 5. Borohydride and Cyanoborohydride Supported on Anion Exchange Resins.

The next year, Hutchins, Natale, and Taffer[48] reported synthesis of the polymer-supported cyanoborohydride reagent **29** (Figure 5). Cyanoborohydride was complexed to a quarternary ammonium cation exchange resin, Amberlyst A-26. The resin was reported to contain 3.3 milliequivalents cyanoborohydride anion per gram of polymer, and has been used in reductive aminations, amine dimethylations, reduction of conjugated enones to the allylic alcohols, dehalogenations, and conversion of pyridinium ions into tetrahydro derivatives. Important advantages of the polymeric resin include ease of handling of the toxic cyanide residues which remain bound to the polymer matrix, plus regeneration and reuse of the resin.

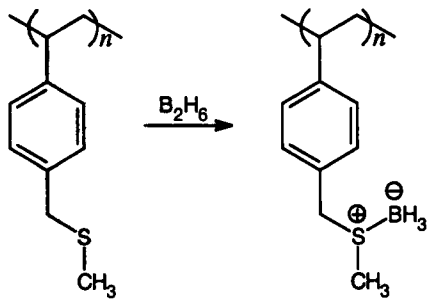
Boranes have also been complexed with polymeric supports. The hydrochloride salt of both linear and crosslinked 4-vinylpyridine **30** (Equation II-9) was reacted with borohydride to yield the polymer amine-borane **31** which has been shown to reduce a wide range of aromatic aldehydes and ketones to the corresponding alcohols.[49]



30 31 32 33

II-9

An alkyl sulfide complex was reported and patented by Crosby.[50] Crosby reacted borane with polymer-supported methyl sulfide **34** to yield the borane alkyl sulfide **35** (Equation II-10).

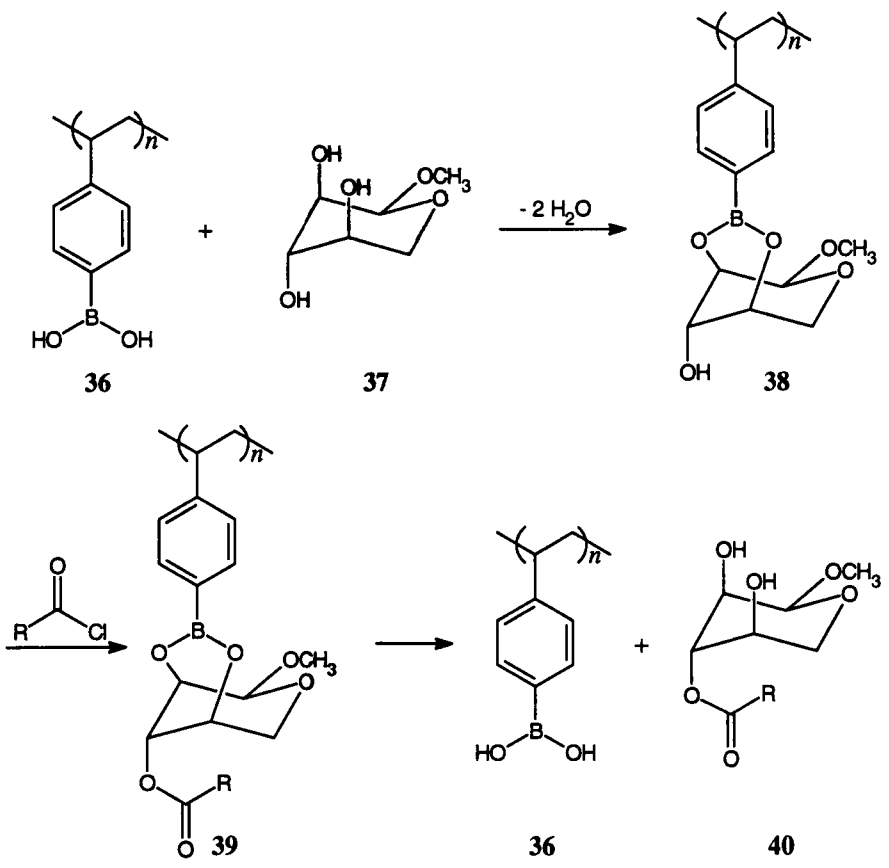


34 35

II-10

Protecting Groups

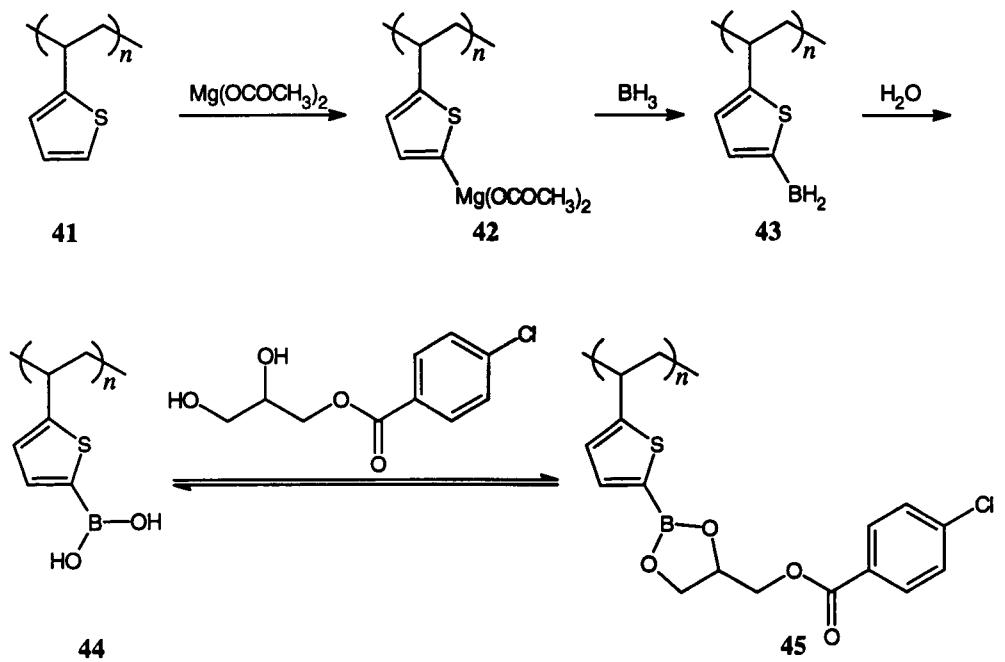
Polymeric boronic acids have also been synthesized and used in the chromatographic separation of diols[51] and the acylation of acyclic polyols.[52] Fréchet and coworkers[53] developed a polystyrene boronic acid **36** (Scheme 2) from the lithiated polystyrene and trialkylborate and used the resulting polymeric boronic acid as a protecting group for glycosidic diols. The selective acylation of methyl α D-xylopyranoside (**37**) is shown in Scheme 2. The protection of the two equatorial alcohols



Scheme 3. Polymer-Supported Boronic Acid as a Protecting Group in Glycosidic Diol Functionalization.

by the polymeric boronic acid **36** left the remaining alcohol in **38** free for acylation. Removal of the polymeric protecting group produced the acylated glycoside **40** in 87% yield with recovery of polymer reagent.

Al-Kadumi, Hodge, and Thorpe[54] utilized the enhanced reactivity of thiophene to compare the functionalization of poly(2-vinylthiophene) to polystyrene. They prepared linear and crosslinked polymers and compared its ease of functionalization to polystyrene using mercury(II) acetate, mercury(II) trifluoroacetate, and thallium(III) trifluoroacetate (Scheme 4). They observed an increase in the degree of substitution for the poly(2-vinylthiophene), and for a crosslinked copolymer of 2-vinylthiophene, styrene, and divinylbenzene. The new copolymer showed exceptional functionalization that indicated



Scheme 4. Functionalization of Poly(2-Vinylthiophene) with Boronic Acid and Use as Protecting Group for Diols.

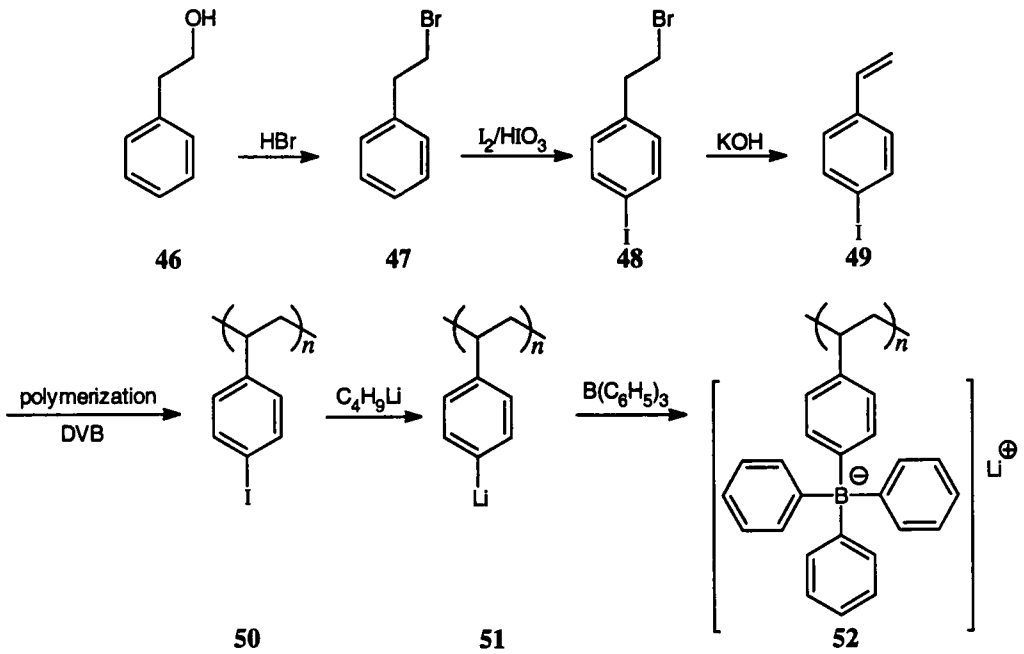
that the phenyl rings of the styrene were also being functionalized. They attributed this to enhanced swelling properties of the polymer under their reaction conditions due to the presence of thiophenyl residues

The metallated polymer **42** was then reacted with borane in THF to yield the thiophenyl borane ligand **43** which was not isolated but immediately subjected to hydrolysis, giving the polythiophenyl boronic acid **44**. The crosslinked polyvinylthiophenyl boronic acid beads **44** were used as protecting groups for diols as illustrated by the reaction of 2,3-dihydroxypropyl-*p*-chlorobenzoate with **44** in pyridine to yield the protected diol **45**.

Chelating Compounds

Boron ligands have also been used as chelating agents, or ion anchor groups, in analytical chemistry. These borates provide a charged binding site without acting as Lewis bases. A reagent in which the tetraphenylborate anion was attached to a polystyrene backbone was developed and tested by Lieser in 1979 for use in ion separation.[55] The synthesis is shown in Scheme 5, resulting in resin **52** which contains up to 2 millimoles lithium tetraphenylborate per gram of polymer, and shows a high selectivity for alkali ions (including Tl^+). Lieser noted the ability of the resin to separate alkali ions from one another, and to separate the alkali ions as a group from other ions.

However, two disadvantages were noted: the lengthy synthesis and instability below pH 4 and above pH 9.



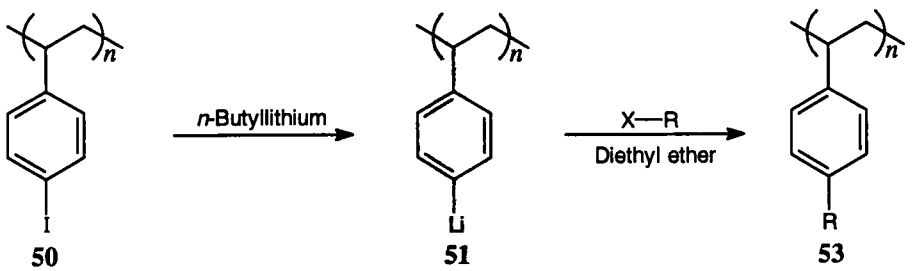
Scheme 5. Synthesis of Polymer-Supported Chelating Agent, Lithium Tetraphenylborate.

CHAPTER 2

RESULTS AND DISCUSSION

A. Polymer-Supported Ligands

The earliest work in polymer bound organometallic reagents was by Braun[56] and later by Braun and Seelig.[57] They treated iodinated polystyrene (**50**) with excess *n*-butyllithium in benzene to give the lithiated polymer **51** (Equation II-11). This analog



50 **51** **53** II-11

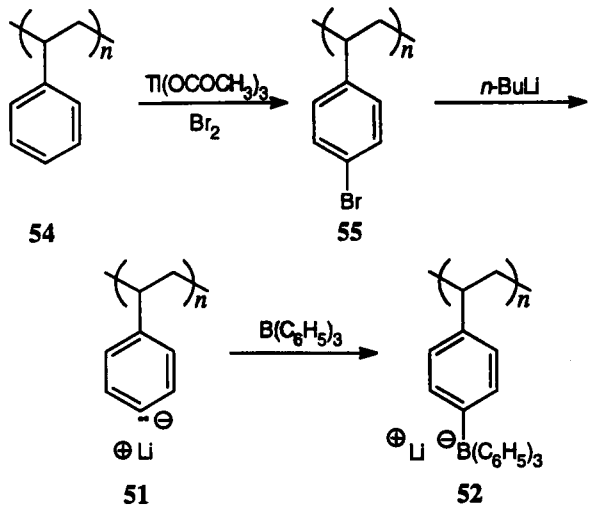
of phenyllithium was further reacted with either an aromatic organic or haloorganic compound to yield the corresponding functionalized polystyrene **53**. This method produced polymers which were limited in functional group loading of 1–2 millimoles per gram. Loadings of up to 6 millimoles per gram have been achieved using thallium triacetate to incorporate the halogen, with the additional advantage of obtaining *para*-specific substitution. The halogenated polymer was then subjected to halogen lithium exchange to yield the desired polymer-supported reagent.

One of the disadvantages of polymer-supported reagents, when compared to their solution counterparts, is manifested in low functional group loading. Inert, bulky polymer supports require large volumes in the reacting vessel which reduces the total reagent available for the reaction. This effect may be diminished by increasing the functional group loading of the polymer. Increased functional group loading may be achieved by enhancing the reactivity of the polymer backbone to receive functionalization. Two approaches to provide this increased susceptibility of polystyrene to functionalization have been utilized. The first approach emphasized modification to the existing polymer with a functional group that increased the reactivity of the polymer to further functionalization. The second approach substituted a more reactive ring system for benzene. The five-membered heteroaromatic rings (furan, tellurophene, selenophene, and thiophene) are each more reactive than benzene, with thiophene exhibiting the least reactivity toward electrophilic aromatic substitution.[58] Utilizing the increased reactivity of thiophene versus benzene,[59] researchers studied the replacement of thiophene for benzene in solution chemistry, including the synthesis and evaluation of biologically active compounds.[60] Extending this substitution to polymers, Al-Kadhumi, Hodge, and Thorpe[61] investigated 2-vinylthiophene as an attractive replacement for vinylbenzene in the polystyrene backbone. They concluded that poly(vinylthiophene) could be directly lithiated without use of catalysts or excess of organolithium reagent to achieve a high degree of metallation, unlike polystyrene.

In addition to increased reactivity, the heteroaromatic ring of thiophene possesses unique properties. Thiophene has a dipole in the direction of the heteroatom, in contrast to the benzene ring in polystyrene which possess almost none.[62] The dipole associated with the heteroaromatic ring could increase accessibility of polar reagents to the polymer matrix. In addition, the 2-position of thiophene is much more reactive than any position in the benzene ring.[59] By taking advantage of this increased reactivity, direct lithiation of the heteroaromatic ring may be accomplished with increased functional loading.

B. Preparation of Polymer-Supported Lithium Tetraphenylborate

Polymer-supported tetraarylborates as selective complexing agents or "anchor groups" were first prepared by Lieser.[63] He prepared a polymer-supported lithium tetraphenylborate **52** through an arduous scheme that consisted of monomer preparation followed by functionalization to yield iodostyrene, which was then polymerized and further functionalized to yield the borate (Scheme 5). This tedious synthetic scheme was required to avoid the difficulties inherent in the direct iodination of the phenyl ring in styrene. Lieser first prepared 2-iodophenylbromoethane followed by dehydrohalogenation to give the iodophenyl monomer. After copolymerization with divinylbenzene, the polymer was subjected to a transmetallation with butyllithium and finally treated with triphenylborane to yield the lithium tetraphenylborate copolymer. J. F. Green[64] suggested an alternative method of preparation that utilized preformed



Scheme 6. Functionalization of XE-305 via Transmetallation Reaction to Give Lithium Tetraphenylborate.

polymer beads **54** (Scheme 6) and provided the dual advantages of fewer synthetic steps and use of a polymer whose bulk properties were well established. Like the work of Leiser, this method requires an additional pre-functionalization step.

Green proposed a prefunctionalization step that utilized a transmetallation reaction to direct functionalization of the phenyl ring. Functionalization of the preformed polymer beads on the phenyl ring can occur at the *ortho*, *meta*, or *para* positions. Steric constraints inhibit functionalization at the *ortho* sites. Selective functionalization of the *para* site has been utilized by bromination of the phenyl rings in the presence of a Lewis acid. Weinshenker *et al.*,[65] reported the bromination of preformed polystyrene-divinylbenzene beads yielding a copolymer containing 4.02 millimoles bromine per gram polymer using iron(III) chloride as the Lewis acid and 3.62 millimoles per gram with thallium(III) acetate sesquihydrate. Use of thallium(III) acetate was reported to produce, exclusively, the *para*-substituted bromo isomer on the phenyl rings of polystyrene.[66]

Following the method suggested by Green, commercial crosslinked polystyrene beads **54** (Amberlite XE-305) were functionalized with trithiophenylboron. Amberlite XE-305 was chosen as a macroreticular polymer-support since its physical properties are well known. Amberlite XE-305 is copolymer of styrene and four percent divinylbenzene as the crosslinking agent, with an average pore diameter of 900 Angstroms, and size of 20–50 mesh.

The beads were first washed to remove any contaminants using a method designed to alternately swell the beads in a compatible solvent followed by collapsing the beads in a non-solvent. This swell-collapse cycle allowed for removal of contaminants from the swollen or open beads and then collapse of the macropores to further remove contaminants. The procedure used toluene (or benzene) as the compatible solvent, followed by washing with carbon tetrachloride, and then acetone to collapse the polymer matrix. Hexanes were then added, followed by toluene, and then acetone to collapse the matrix a second time. Following filtration, drying at 60 ^{o}C under reduced pressure was used to remove residual solvents.

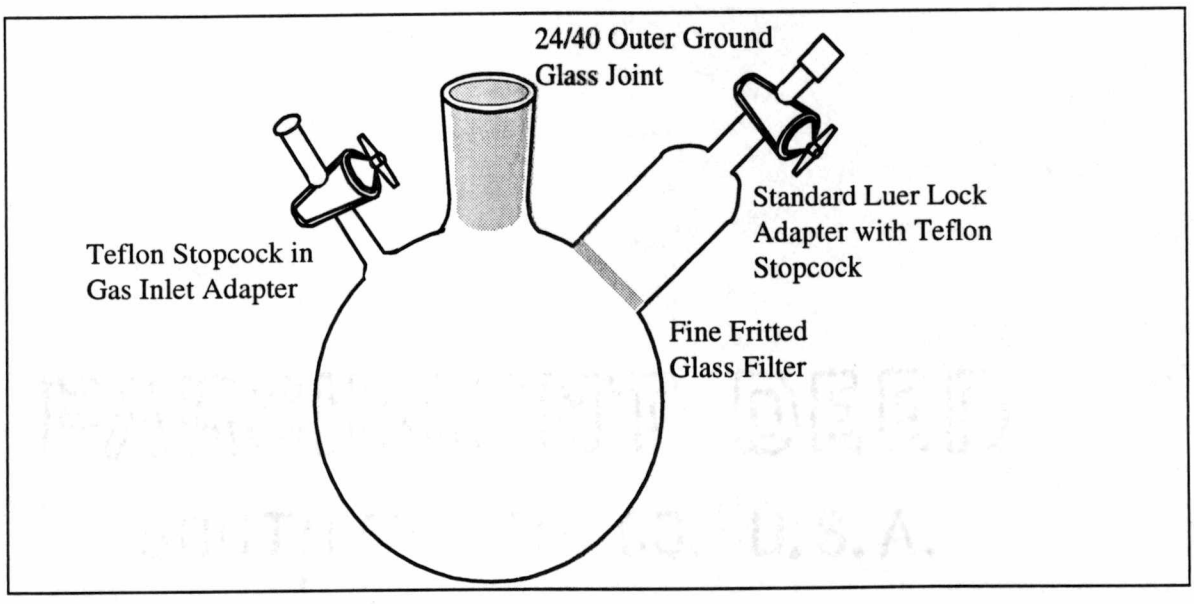


Figure 6. Kabalka-Green Reactor Designed at the University of Tennessee, Knoxville. Used for synthesis and filtration of oxygen or water sensitive compounds.

The washed and dried beads were brominated using thallium(III) acetate in carbon tetrachloride to give beads with 3.1 mmol bromine per gram of polymer. The brominated polystyrene was then lithiated in anhydrous tetrahydrofuran using a Kabalka–Green Reactor (Figure 6) under argon to give the lithiated polymer **51**. The reactor permits isolation of the functionalized polymer beads from the reaction solution under inert atmosphere by use of a "built in" filter frit. Following lithiation, the beads were separated from the solvent and unreacted butyllithium, and then washed with anhydrous tetrahydrofuran. Following lithiation, the beads were again swollen in anhydrous tetrahydrofuran and reacted with triphenylborane over four hours. Filtration to remove the solvent and washing with tetrahydrofuran yielded the polymer-supported lithium tetraphenylborate.

Solid state nuclear magnetic resonance (NMR) of the beads using Cross-Polarization of Solids, Magic Angle Spinning (CP-MAS) technique resulted in a single broad peak in the boron-11 spectra at δ 0.00 (externally referenced to sodium tetraphenylborate, δ 0.00) (Figure 7). This indicates the presence of only one boron species that absorbs in the tetraphenylborate region. Thus, the functionalization to yield polymer-supported tetraphenylborate was successful.

C. Preparation of Polymer-Supported Lithium Trithiophenyl-phenylborate

As an alternative to the tetraphenylborate reagent, a polymer-supported lithium trithiophenylphenylborate analogue would provide a reagent whose reactivity would complement that of the polymer-supported tetraphenylborate and non-supported tetraphenylborate reagents. Substitution of thiophene for benzene is well known. By utilizing thiophene as an analogue of benzene, researchers have taken advantage of the increased reactivity of the 2-position of the thiophene ring over benzene. Other important differences include the different binding affinities for metal ions due to the differences between the two ring systems. Thiophene possesses a permanent dipole compared to benzene's lack of polarity; the sulfur atom on thiophene posses two pairs of electrons, one pair contributes to the aromatic system, while the other remains in an non-bonding orbital.

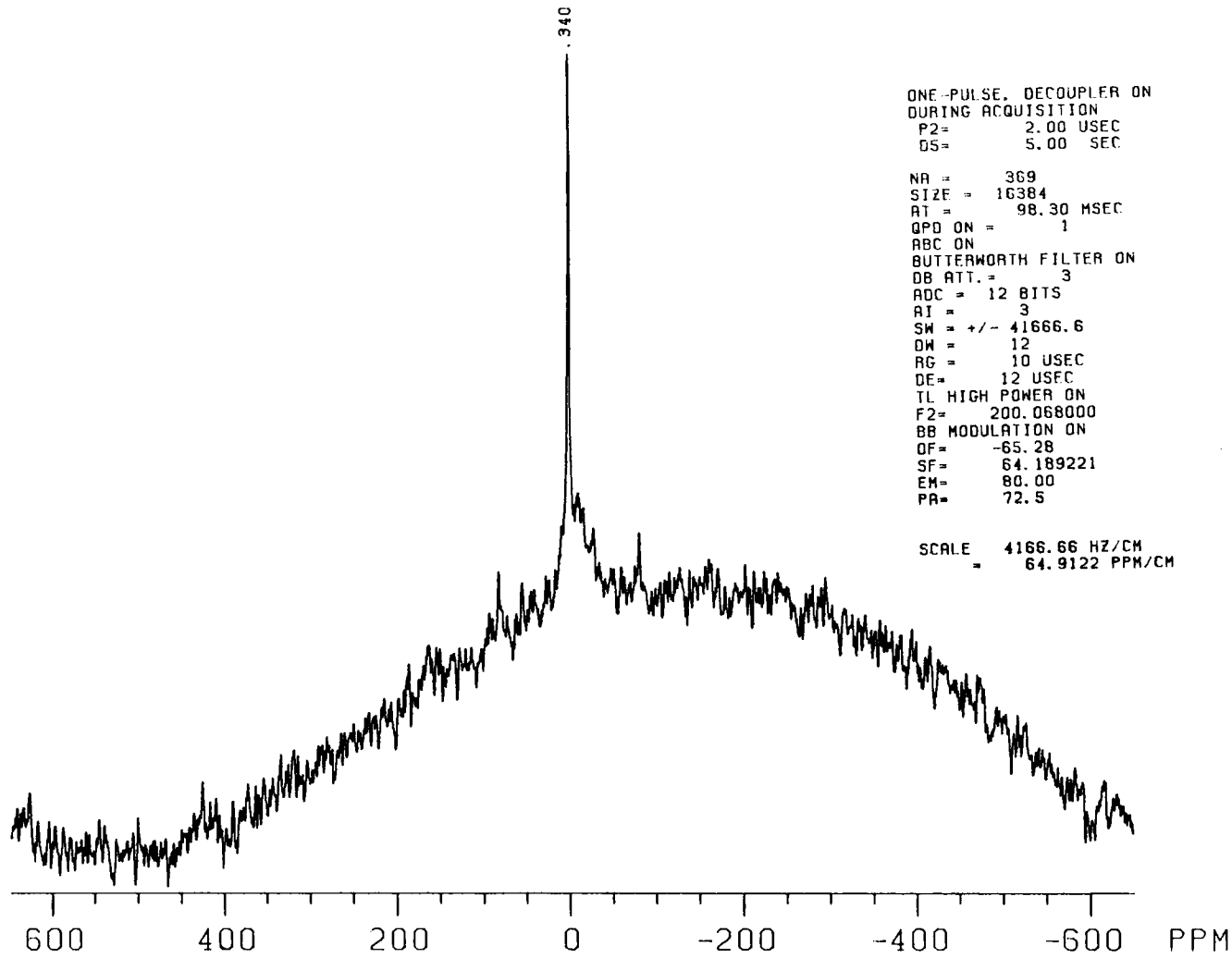
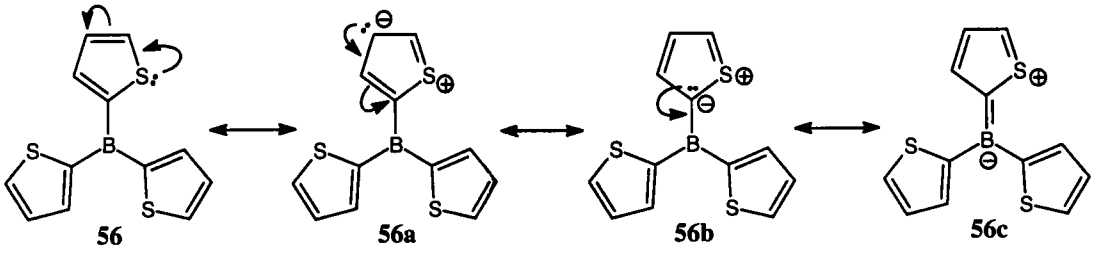


Figure 7. Solid State, Cross-Polarization Magic Angle Spinning Boron-11 Nuclear Magnetic Resonance Spectra of Lithium Tetraphenylborate Beads. Externally referenced to sodium tetraphenylborate (δ 0.00).

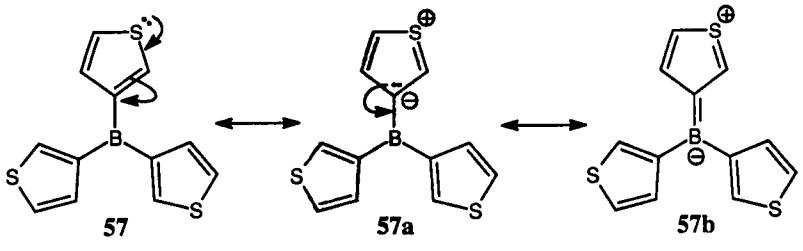
Preparation of Trithiophenylborane

Commercial sources of trithiophenylborane were not available. Therefore, it was necessary to develop a synthesis for the reagent. Pelter, Smith, and Brown[67] reported the synthesis of triphenylborane using a transmetallation reaction. They reacted three equivalents of phenylmagnesiumbromide with boron trifluoride etherate to produce the triphenylborane.

Two possible isomers of trithiophenylborane are possible: the 2-isomer, tri(2-thiophenyl)borane (**56**) (Equation II-12) and the 3-isomer, tri(3-thiophenyl)borane (**57**) (Equation II-13). Although a mixture of 2- and 3-substituted trithiophenylborane could also be prepared, the synthetic difficulty and scope of this study preclude its consideration. Tri(2-thiophenyl)borane was chosen to simplify the study and



II-12



II-13

characterization of the final product due to the enhanced reactivity of the 2-position of thiophene compared to the 3-position. This enhanced reactivity at the 2-position is supported by resonance arguments.

Resonance contributors of both isomers of trithiophenylborane indicate an ability to donate electron density from the *pi*-system to the borane atom. This resonance distribution of electron density may be compared to back donation of electron density of oxyboranes which results in a shorter bond length and increased bond strength of the oxygen-boron bond as shown in Equations II-12 and II-13. The effects of shorter bond length and increased bond strength contribute to molecule stability, and indicate a thermodynamic contribution formation of both **56** and **57**.

2-Bromothiophene (**58**) was reacted with magnesium turnings in anhydrous diethyl ether to form the Grignard reagent **59** (Equation II-14). Reagent concentration of

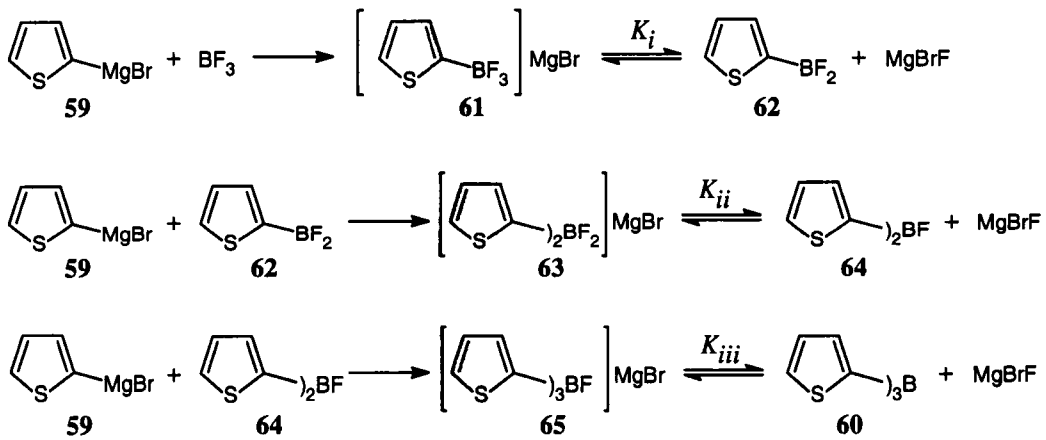


58 **59** **60** II-14

the thiophenylmagnesiumbromide was determined by titration[68] with *iso*-butylalcohol in toluene using 1,10-phenanthroline as an indicator. After establishing the molarity of the reagent solution, three equivalents of **59** were reacted with one equivalent of boron trifluoride etherate to yield trithiophenylborane (**60**).

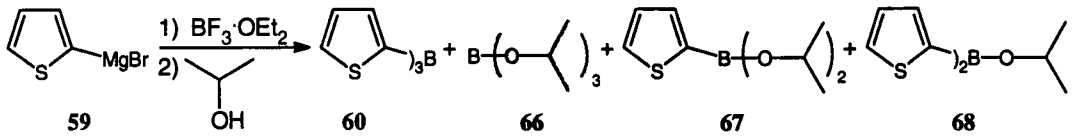
A study of the effect of reaction temperature on product yield was undertaken. Generally, formation of triarylboranes is accompanied by formation of diarylfluoroboranes and aryldifluoroboranes as byproducts. These byproducts are the result of the dissociation of the various borate salt intermediates to give the thiophenyldifluoroborane (**62**), dithiophenylfluoroborane (**64**), and trithiophenylborane (**60**), as shown in Scheme 7. Temperature dependence of these equilibria allows for control of product distribution by manipulation of reaction temperature.

Varying temperatures and two solvents were studied and the product distribution estimated from boron-11 solution NMR. At each temperature (shown in Table 3) thiophenylmagnesiumbromide in the specified solvent was added to boron trifluoride etherate in the same solvent and the reaction allowed to proceed for one hour. After quenching with isopropanol, each reaction was analyzed by boron-11 NMR. The results



Scheme 7. Equilibrium in the Formation of Trithiophenylborane Showing Dissociation of Borate Salt Intermediates.

presented in Table 3 support the product distribution shown in Equation II-15. The maximum yield of trithiophenylborane was achieved in ether at 35 °C. In THF, no trithiophenylboron was isolated at any temperature.



II-15

Table 3. Temperature Effect of Equilibrium Distribution of Thiophenyl Grignard with Boron Trifluoride Etherate in Ether and Tetrahydrofuran.

	Temperature		Product Distribution (%)				Reaction
Entry	(°C)	Solvent	60	66	67	68	Time
1	-78	Et_2O	0.0	90.3	9.7	0.0	1.0 hr
2	20	Et_2O	15.8	28.6	8.7	46.9	1.0 hr
3	35	Et_2O	84.9	8.6	4.3	2.2	1.0 hr
4	-78	THF	0.0	100.0	0.0	0.0	1.0 hr
5	18	THF	0.0	56.6	12.1	31.3	1.0 hr
6	66	THF	0.0	81.9	0.0	18.1	1.0 hr

Preparation of Trithiophenylborane Supported on Amberlite XE-305

Trithiophenylborane was reacted with lithiated Amberlite XE-305 without further purification. Boron-11 and carbon-13 solid-state NMR (CP-MAS) indicated the presence of the desired product. The carbon-13 NMR is presented in Figure 8, and the boron-11 NMR in Figure 9.

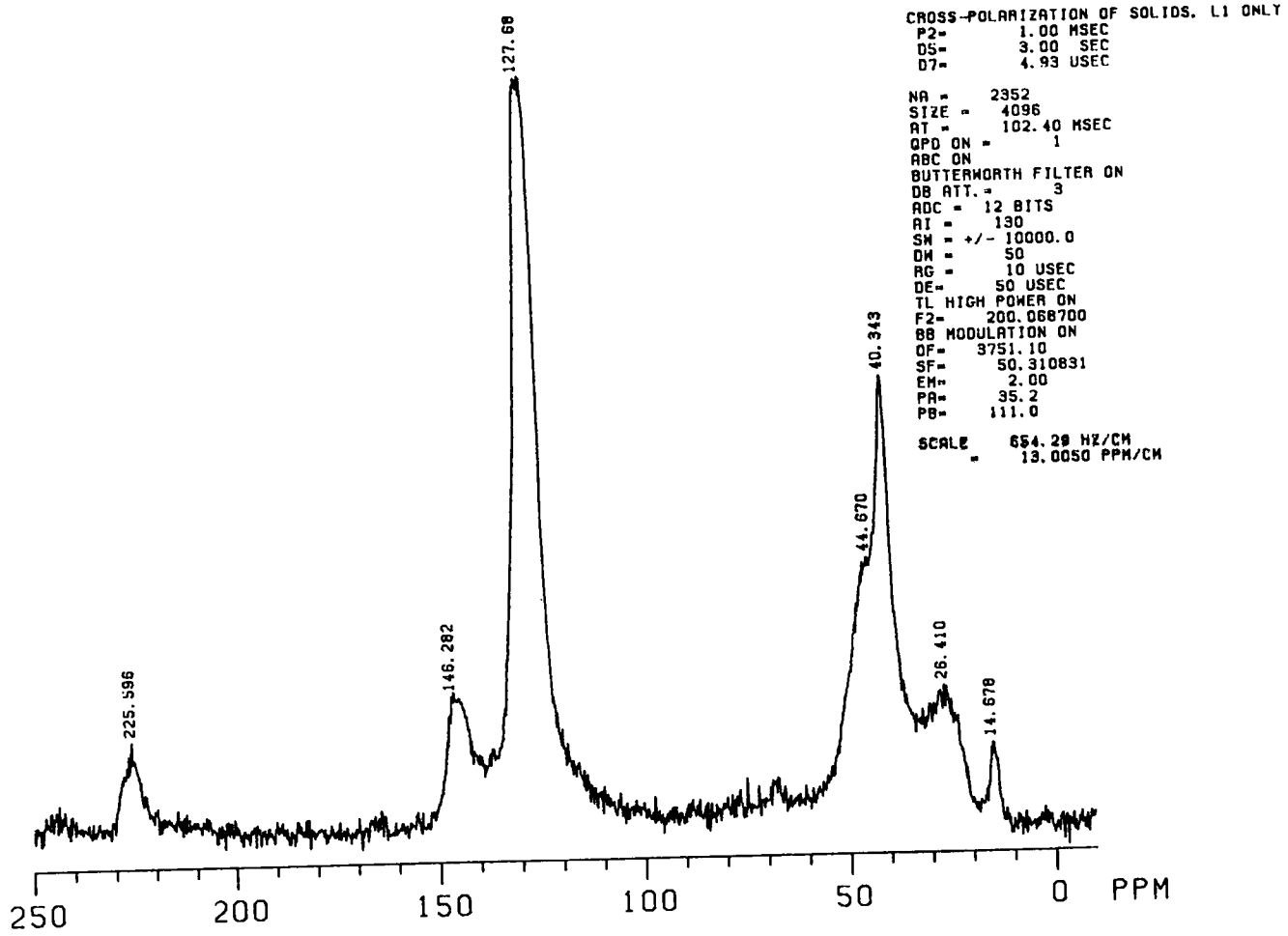


Figure 8. Carbon-13 Solid-state Nuclear Magnetic Resonance Spectra of Trithiophenylphenylborate on Amberlite XE-305. Externally referenced to hexamethylbenzene, δ 17.36.

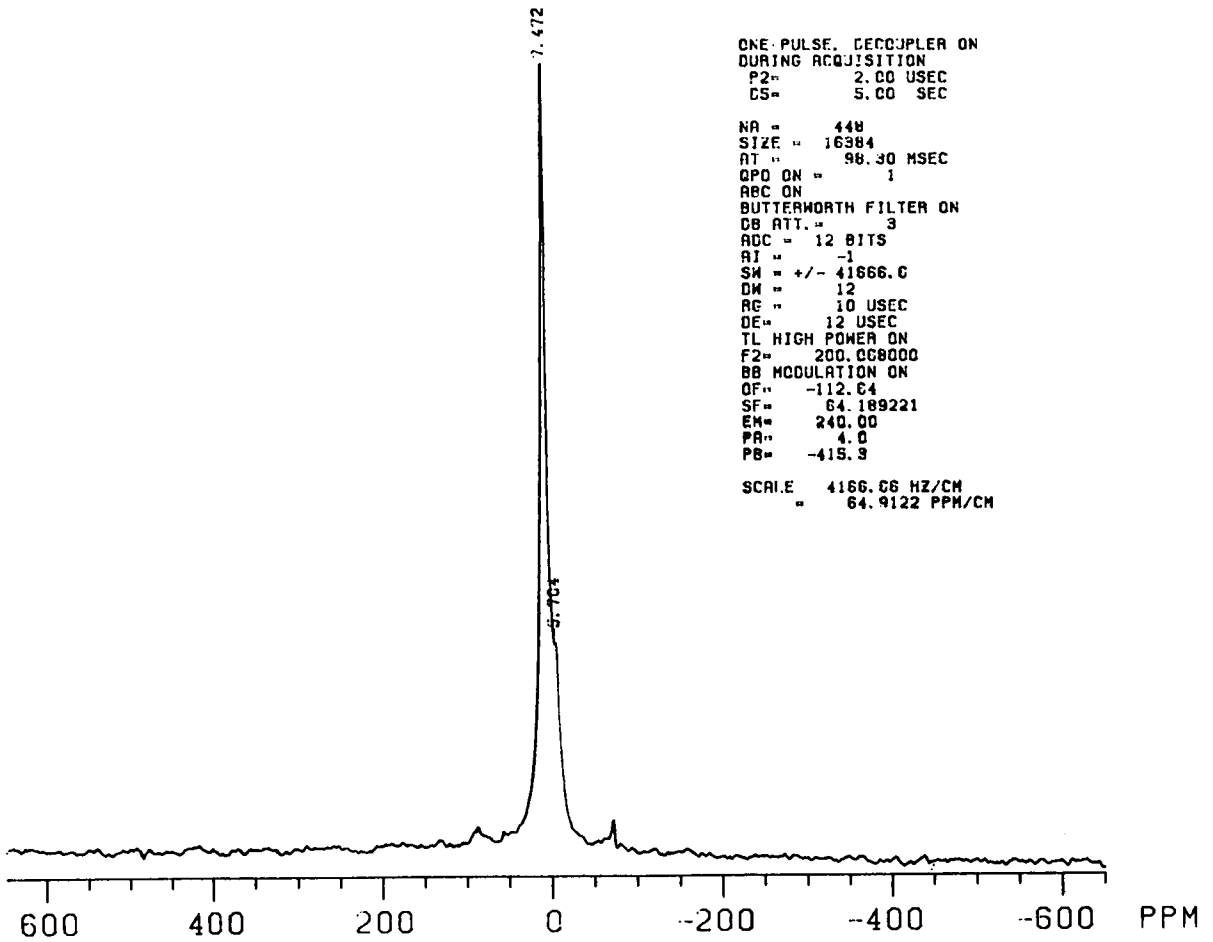


Figure 9. Boron-11 Solid-state Nuclear Magnetic Resonance Spectra of Trithiophenylphenylborate on Amberlite XE-305. Externally referenced to tetraphenylborate, δ 0.00.

CHAPTER 3

EXPERIMENTAL

A. General

Solution nuclear magnetic resonance (NMR) spectroscopy was performed on the Joel FX-90Q and Varian 250 spectrometers. Boron trifluoride etherate (set to δ 0.00) was used as a reference for boron-11 NMR spectroscopy, while tetramethyltin (set to δ 0.00) or dibutyltin dichloride (set to δ 124.8) was used for tin-119 NMR. Carbon-13 NMR was referenced to deuterochloroform (set to δ 77.0), and proton NMR referenced to tetramethylsilane (set to δ 0.00).

Solid-state NMR spectra were obtained using a Nicolet NT-200 spectrometer fitted with a solid-state probe by Doty Scientific, Inc. Cross-Polarization Magic Angle Spinning (CP-MAS) techniques were used for both the carbon-13 and boron-11 spectra. Carbon-13 solid-state NMR spectrometer frequencies were set at: observation frequency, 50.310831 MHz; decoupler frequency, 200.068700 MHz; spinning frequency, 4 kHz; Hartmann-Hahn setting 1.2 dB. Carbon-13 solid-state chemical shifts were externally referenced to hexamethylbenzene (set to 17.36 ppm). Boron-11 solid-state NMR spectrometer frequencies were 64.189221 MHz for the observation channel and

200.068700 MHz for the decoupler; spinning frequency 4 kHz, Hartmann-Hahn setting 1.2 dB. The boron-11 solid-state reference was sodium tetraphenylborate externally referenced (set to δ 0.00).

Dry tetrahydrofuran and dry diethyl ether were obtained from commercial sources and distilled from sodium–benzophenone ketal under argon atmosphere. Other solvents were used without further purification.

B. Preparation of Polymer-Supported Borate Reagents

Preparation of Polystyrene-Triphenylborate

Bromination and lithiation of polystyrene beads were accomplished via a modification of the method of Farrall and Fréchet.[69]

Bromination of Commercial Crosslinked Polystyrene Beads

Amberlite XE-305 was washed sequentially with toluene, acetone, and methanol and then dried under vacuum at 60 °C for 24 hours. Each washing consisted of sufficient solvent to swell and cover the beads with solvent, allowing fifteen to thirty minutes for swelling to occur.

The washed and dried resin [200 grams] was placed in a 3000 mL, three-necked, round-bottomed flask equipped with a 250 mL pressure equalizing dropping funnel and Fischer condenser. The system was flushed with argon and then shielded from direct light by wrapping the flask, dropping funnel, and condenser with aluminum foil. Carbon tetrachloride [1 L] was added and the beads allowed to swell. Thallium triacetate [4.74 mmol, 1.81 g] was added under an argon flush. Bromine [2.40 mol, 192 g] dissolved in 200 mL carbon tetrachloride was placed in the dropping funnel and then added dropwise to the polystyrene-thallium triacetate slurry. Slow, careful stirring was necessary to mix the solution while not fracturing or crushing the polymer beads.

After stirring at room temperature for one hour, the reaction was brought to reflux and allowed to stir at reflux for 5 hours, and then allowed to cool to room temperature. During the reaction, the solvent color changed from dark brown to a light yellow. The dark brown beads were then collected on a fritted glass filter and washed sequentially with 1 L each of carbon tetrachloride, acetone, acetone:water (2:1), benzene, and then methanol. The beads were then dried under vacuum for 24 hours at 60 °C to yield 265 g brominated beads (3.10 mmol bromine per gram polymer).

Lithiation of Brominated Polystyrene Beads

A reflux condenser and a specially constructed 1000 mL round-bottomed reaction vessel fitted with a 24/40 ground glass joint, a fritted glass filter segment with a Luer

Lock fitting, and a gas inlet with Teflon stopcock (the Kabalka-Green reactor) were oven dried and assembled hot under argon. A magnetic follower was placed in the flask prior to closing the system. After cooling to room temperature, brominated polystyrene beads [31.50 mmol, 10.16 g] were added to the flask under an argon purge, minimizing atmospheric contamination to the vessel interior. Dry benzene [100 mL] was added and the beads allowed to swell for thirty minutes while stirring. An ice-water bath was placed around the reaction vessel and *n*-butyllithium [88.0 mmol, 55.0 mL of 1.60 M] was added slowly using a syringe to the stirred slurry. After the addition was complete, the mixture was allowed to come to room temperature. A heating mantle was placed under the flask and the solution heated to reflux for 5 hours. After cooling to room temperature, the solution was filtered using the Kabalka–Green reactor via the frit to leave the lithiated beads. The beads were washed with dry tetrahydrofuran and flushed with argon to "dry" the beads.

Triphenylboronation of Lithiated Resin; Formation of the Polymer-Supported Tetraphenylborate

The lithiated beads were used without further purification. Dry tetrahydrofuran [50 mL] was added to the Kabalka-Green reactor and the beads allowed to swell for thirty minutes. Triphenylboron [42.90 mmol, 10.38 g] was placed in a second 250 mL round bottomed flask and dissolved in dry tetrahydrofuran [50 mL]. The triphenylboron

solution was then added to the polymer by way of double-ended needle and the polymer stirred for four hours.

Excess triphenylboron was filtered from the beads and the beads washed with THF. Boron-11 solid-state NMR using cross polarization-magic angle spinning (CP-MAS): single absorbance, δ 0.00 (contact time, 2.50 μsec; delay, 5.00 sec; acquisitions, 800; externally referenced to tetraphenylborate δ 0.00).

Synthesis of Polymer-Supported Trithiophenylphenylborate

Preparation of 2-Thiophenylmagnesium Bromide

Magnesium turnings were washed with 1 M hydrochloric acid and then anhydrous ether and dried at 250 °C. An oven-dried, 500 mL, three-necked, round-bottomed flask fitted with a magnetic stirring bar, 150 mL pressure equalizing dropping funnel, and Fisher condenser were assembled hot and allowed to cool under an argon flush. All open joints were sealed with rubber septa. Freshly prepared magnesium turnings [320 mmol, 7.78 g] were added to the flask while maintaining an argon flush. The flask was sealed with a septum and a static pressure of argon maintained by way of a mercury bubbler. Dry ether [100 mL] was added to the magnesium turnings and stirring begun. 2-Bromothiophene [300 mmol, 48.9 g] was added to the dropping funnel. Several drops of 2-bromothiophene were added to the magnesium turnings to initiate the reaction, followed by addition of dry ether [100 mL] to the dropping funnel, dissolving the

remaining 2-bromothiophene. Addition of the bromothiophene solution was continued at a rate sufficient to maintain reflux of the ether. Following completion of addition, the reaction was refluxed for 8 hours, or until the majority of the magnesium turnings were dissolved.

The solution was standardized under argon using 1 M isobutanol in toluene with 1,10-phenanthroline as an indicator to give 1.66 M solution of 2-thiophenylmagnesium bromide. This solution was used without further purification.

Preparation of Trithiophenylboron

An oven dried, 250 mL, three-necked, round-bottomed flask was fitted with magnetic stirring bar, pressure equalizing dropping funnel, and reflux condenser and allowed to cool under an argon flush. After cooling, the reaction vessel was maintained under a static pressure of argon by way of mercury bubbler. Dry ether [100 mL] was added to the flask followed by boron trifluoride etherate [26.1 mmol, 3.71 g]. The freshly prepared Grignard, 2-thiophenylmagnesium bromide, in ether [47.2 mL, 1.66 M] was syringed into the dropping funnel and then added dropwise to the stirred boron trifluoride etherate solution. The rate of addition was adjusted to maintain moderate reflux of the solvent. After completion of the addition, the ether was distilled leaving a yellow solid containing the trithiophenylborane and magnesium salts. The borane was dissolved in heptane [500 mL] and used without further purification.

Trithiophenylboronation of Polystyrene Support

Lithiated Amberlite XE-305 beads, prepared in the Kabalka-Green reactor, were swollen in dry tetrahydrofuran [50 mL]. Trithiophenylboron [26.1 mmol] was dissolved in dry tetrahydrofuran [50 mL] and the added to the lithiated beads by way of double-ended needle to yield the trithiophenylboronated resin.

Boron-11 solid-state NMR of the washed and dried beads using CP-MAS showed an absorbance at δ 7.5. Carbon-13 solid-state NMR using CP-MAS; δ 150–140 (quaternary aromatic), δ 130–120 (tertiary aromatic), δ 45 (tertiary alkyl), δ 40 (secondary alkyl).

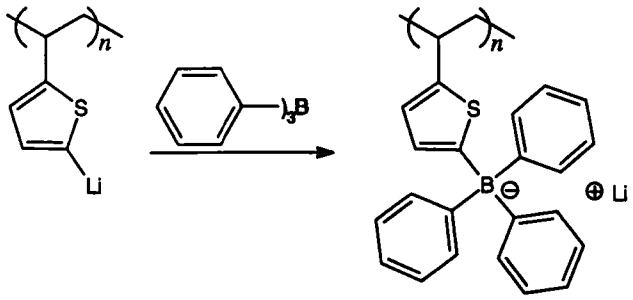
CHAPTER 4

CONCLUSIONS AND FUTURE RESEARCH OBJECTIVES

A study of the polymer-supported thiophenyl and phenyl borate chelating agents was initiated and tetraphenylborate supported on commercial polystyrene and trithiophenylphenylborate supported on commercial polystyrene were prepared. Boron-11 NMR of the borates was obtained and indicated the presence of the tetraphenylborate by an absorbance at δ 0.0, and the trithiophenylphenylborate with an absorbance of δ 7.5. Evaluation of the polymer-supported borate's affinity and selectivity was not accomplished. These studies are pending the synthesis of tetrathiophenylborate and dithiophenyldiphenylborate resins.

Additional areas of investigation into polymer-supported boron chelates became apparent as the study matured. Changes in the nature of the boron in tetraphenylborate versus trithiophenylphenylborate, indicated by boron-11 NMR, leave an interest in further explorations. Expanding the present study to include a polymer-supported thiophenyltriphenylborate, tetrathiophenylborate, and other heteroatom borates would allow for a broader comparison of properties and synthetic methods. In addition, analytical data on the selectivity and affinity of each reagent could be used to make comparisons concerning the nature of the chelates. The following areas of research are presented as a continuation of research of these resins.

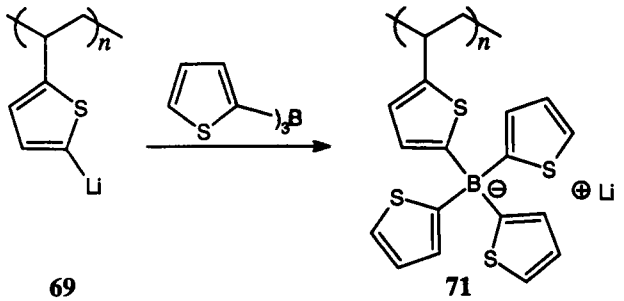
Lithiated macroporous beads of poly(2-vinylthiophene) (**69**) crosslinked with 4% DVB (analogous of XE-305), could be functionalized with commercial triphenylborane as shown in Equation II-16 to yield the polymer-supported thiophenyltriphenylborate **70**.



II-16

69 **70**

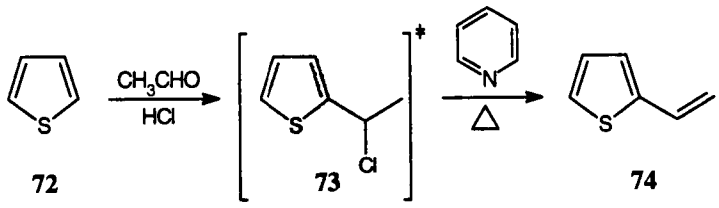
The tetrathiophenyl system **71** could be similarly synthesized from poly(2-vinylthiophene) and trithiophenylborane (Equation II-17). The trithiophenylborane could be produced by the methods described in Chapter 3 of Part II.



II-17

69 **71**

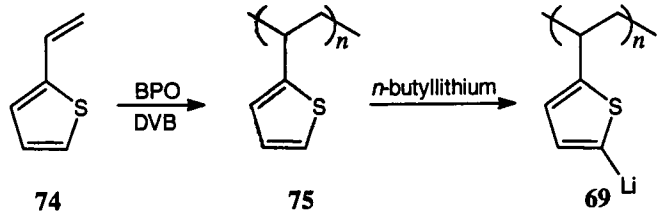
2-Vinylthiophene is a known compound, and could also be synthesized using the method published by Emerson and Patrick.[70] This synthetic method was successfully employed to produce 2-vinylthiophene (**72**) from thiophene and acetaldehyde (Equation II-18). The unstable intermediate, 2-(1-chloroethyl)thiophene (**73**) was not isolated, but subjected to dehydrohalogenation to yield monomer **74**. Proton NMR of the product



II-18

showed aromatic protons at δ 7.3–7.1, a vinylic multiplet at δ 6.8 with corresponding doublet at δ 5.2. Mass spectrum gave the expected molecular ion peak of m/z = 110. Bulk polymerization was attempted using benzoyl peroxide without achieving satisfactory results. The project was halted as investigations of the dibutyltin functionalized polymers were initiated.

Polymerization of 2-vinylthiophene occurs via free-radical initiation similar to styrene. Macroporous beads of **75** could be formed from the monomer **74**, using a diluent such as 1-octanol and crosslinked with divinylbenzene (Equation I-19). Lithiation could



II-19

then be accomplished via addition of n-butyllithium without any prefunctionalization of the ring. Functionalization would occur preferentially at the 5-position. Al-Kadhumi, Hodge, and Thorpe[71] synthesized both linear and crosslinked poly(2-vinylthiophene), functionalizing the polymer with dimethyl sulfate, methyl sulfide, quinoline, *N,N*-dimethylformamide, phenylisocyanate, benzophenone, diphenylphosphine, and trimethylsilane.

Following synthesis of the polymer-supported tetraarylborates, each would be tested for selectivity and binding affinity of alkali metal ions.

PART III

STEREOCHEMICAL ASPECTS OF HYDROSTANNATION USING POLY{DIBUTYL[2-(3- AND 4-ETHENYLPHENYL)ETHYL]TIN HYDRIDE

CHAPTER 1

CHEMICAL BACKGROUND: TIN AND ORGANOSTANNANES

A. Approach to the Investigation

In this second research topic, we studied the stereochemical aspects associated with the hydrostannation of alkynes using a polymer bound tin-hydride reagent, poly(dibutyl[2-(3- and 4-ethenylphenyl)ethyl]tin hydride), crosslinked with divinylbenzene.

B. Chemical Background of Tin

Elemental tin has an outer shell electronic configuration of $5s^2 5p^2$. Two allotropes are known, designated as gray tin and white tin. Gray tin is stable only to 18°C. White tin has a melting point of 232 °C and a boiling point of 2270 °C.[72] Organotins are usually found in the organotin(IV) state (organotin(II) is known) and generally exist as oligomers of the form $(R_2Sn)_n$. Tin exhibits tetrahedral sp^3 hybridization for the tetraorganotins, hexaorganotins, organotin hydrides and most thiotin derivatives.[73] Complexes with Lewis bases may result in sp^3d^2 hybridization leading to dimers or polymers.

Tin's covalent radius of 0.14 nm is twice that of carbon (0.07 nm), but less than twice boron's (0.086 nm). This large radius results in long covalent bonds: Sn-H 0.17

nm, Sn-C 0.22 nm, Sn-Cl 0.24 nm, and Sn-Sn 0.28 nm.[74] These long bonds are associated with lower bond dissociation energies, higher kinetic activities, and lower thermodynamic stability.

Of the ten naturally occurring isotopes of tin (Table 4), only three posses a nuclear spin of one-half: ^{115}Sn, ^{117}Sn, and ^{119}Sn. The most abundant isotope with nuclear susceptible spin is ^{119}Sn.

Table 4. Naturally Occurring Isotopes of Tin, Their Abundance, and Nuclear Spin.

Isotope	**^{112}Sn**	**^{114}Sn**	**^{115}Sn**	**^{116}Sn**	**^{117}Sn**	**^{118}Sn**	**^{119}Sn**	**^{120}Sn**	**^{122}Sn**	**^{124}Sn**
Abundance %	0.95	0.65	0.34	14.24	7.57	24.01	8.58	32.97	4.71	5.98
Nuclear Spin	0	0	½	0	½	0	½	0	0	0

C. Tin Toxicity

Organotin compounds show considerable toxicity. As a general trend, decreasing the number of organic groups on the central tetravalent tin atom, as well as increasing the size of the organic substituents, decreases the toxicity of the compound (Table 5). When possible from chemical and physical requirements, the butyltins are preferred over the ethyl and methyl compounds to decrease toxic exposure.

Table 5. Organotin Compound Toxicity (LD_{50} oral administration to rats).[75]

Compound	LD_{50}/mg kg^{-1}	Compound	LD_{50}/mg kg^{-1}	Compound	LD_{50}/mg kg^{-1}
Me_3SnCl	9-20	Me_2SnCl_2	74-237	$MeSnCl_3$	575-1370
Et_3SnCl	10	Et_2Cl_2	66-94		
Bu_3SnCl	122-349	Bu_2SnCl_2	112-219	$BuSnCl_3$	2200-2300
Ph_3SnCl	118-135				
Oct_3SnCl	>4000	Oct_2SnCl_2	>4000	$OctSnCl_3$	>4000

D. History of Tin and Organotins

The are many excellent, concise histories of organotin chemistry. Wilhelm P. Neumann's short history[76] or a parallel work by G. J. M. van der Kerk and J. G. A. Luijten[77] provide an introduction to the very rich history of tin chemistry. Although tin was known from ancient times, by both the Egyptians and Babylonians, the first chemist to report an organotin compound was E. Frankland in 1849.[78] This work focused on the reaction of tin and ethyl iodide to produce an organotin compound which Frankland characterized as diethyltin diiodide in 1853. About the same time, C. Löwig reported the synthesis of organotin compounds, triethyltin iodide and hexaethylditin, from the reaction between ethyl iodide and a tin-sodium alloy.[79] Kekulé, known for his work in the theory of organic structures, studied tin alkyls, remarking on the analogy between tin and carbon compounds.[80] Other researchers have, of course, further defined and refined the understanding of this analogy. Neumann notes that organotin research faded in

comparison to the numerous advances in organic chemistry during the remainder of the century. Although "individual important results appeared at intervals, . . . intensive work is evident again only from about 1917."[81]

The second major step in tin chemistry is attributed to Kocheshkov who reported the reaction between tetraalkyltin and tetrahalotin compounds in 1929.[82]

As with many advances in science, accelerated studies in organotin chemistry are closely tied to the discovery and development of industrial applications. A striking increase in the number of publications focusing on organotin compounds was seen in the year 1949.[83] This increase followed the discovery by Yngve in 1936 of the stabilizing effect of organotin on poly(vinylchloride) and other chlorinated polymers.[84] By 1957, the world's production of organotin was reported at 1000-2000 tons, but quickly grew to 10,000 tons by the mid-1960's.[85] Table 6 contains examples of the principal industrial uses of organotin compounds today.

E. Chemistry of Organostannanes

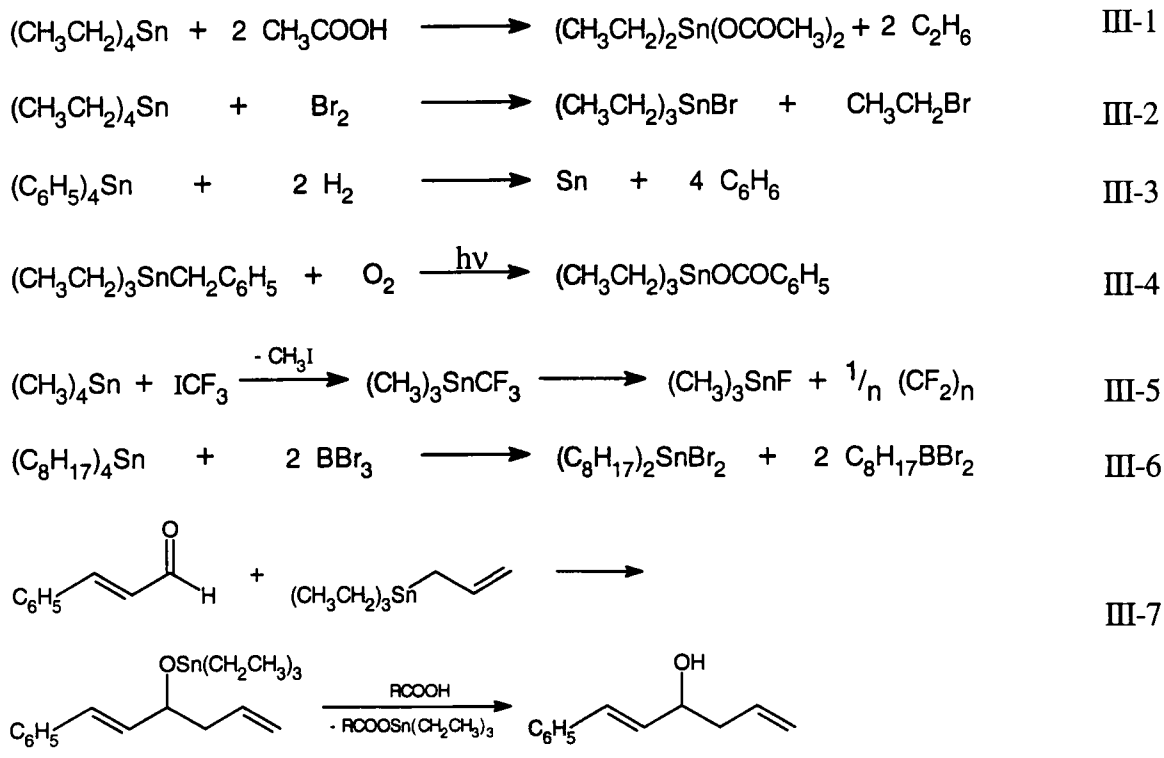
Chemistry of the Carbon-Tin Bond

The carbon-tin bond is known to react with many substrates. It will hydrolyze in the presence of acids or bases (Equation III-1), it is cleaved by halogens (Equation III-2), hydrogen (Equation III-3), free radicals (Equation III-4), and strongly polar alkyl halides

Table 6. Principal Industrial Uses of Organotin Compounds.[86]

Application	Function	Principal Compounds Used
Polyvinylchloride Stabilization	Stabilization against the effects of heat and light	Dialkyltin diisooctyl-thioglycolate Dialkyltin maleate
Polyurethane Foams	Homogeneous catalysis	Dibutyltin diacetate Dibutyltin dioctoate Dibutyltin dilaurate
Esterification	Homogeneous catalysis	Butanestannoic acid Dibutyltin diacetate Methyltin trichloride
Glass Treatment	Precursor for Tin(IV) oxide films on glass	Dimethyltin dichloride Butyltin trichloride Methyltin trichloride
Poultry Management	Anthelminthic	Dibutyltin dilaurate
Wood Preservation	Fungicide	Bis(tributyltin) oxide Tributyltin naphthenate Tributyltin phosphate
Disinfectant	Bacteriostat	Tributyltin benzoate
Materials Protection	Fungicide Algaecide Bactericide	Bis(tributyltin) oxide Tributyltin benzoate
Agricultural Chemicals	Fungicide Insecticide Miticide Antifeedant	Triphenyltin acetate Triphenyltin hydroxide Tricyclohexyltin hydroxide 1-Tricyclohexystannyl-1,2,4-triazole
Antifouling Paints	Biocide	Triphenyltin chloride Bis(tributyltin) oxide Tributyltin acrylate polymers

(Equation III-5). Organotin reagents are alkylated by other metal-carbon bonds (transmetallation) (Equation III-6) and undergo Grignard-like chemistry (Equation III-7).



III-1

III-2

III-3

III-4

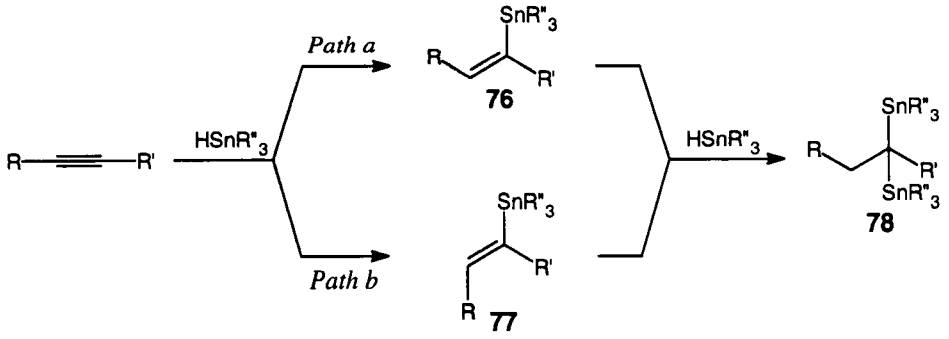
III-5

III-6

III-7

Hydrostannation of Alkynes

Terminal and internal alkynes react with tin hydrides to yield the hydrostannylated isomeric alkenes **76** and **77** (Equation III-8). Addition of a single tin hydride yields the

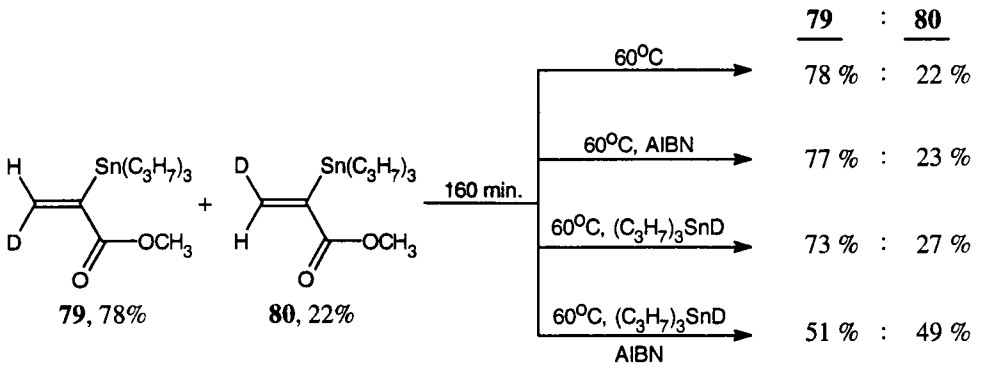


III-8

corresponding alkene, which may add a second tin hydride to give the distannylated alkane **78**.

Two mechanistic pathways have been suggested for the reaction of one equivalent of tin hydride with alkynes, leading to either the (*Z*)-alkene **76** or (*E*)-alkene **77**. Originally, the reaction was thought to proceed through a four-centered transition state.[87] The reaction of phenylacetylene with tin hydride results in the (*Z*)-hydrostannylated vinyl styrene followed by rearrangement to the (*E*)-isomer. Further investigations indicated the uncatalyzed reaction follows two concurrent pathways.[88] Pathway "a" proceeds by way of a polar transition state, leading to the (*Z*)-product, while the second pathway "b" follows a radical transition state to give the (*E*)-product as shown in Equation III-8. Each pathway may be selected by careful control of solvent polarity, by addition of radical catalysts or radical sponges, by changing polar substituents on the alkynyl carbons, and by modifying the reactivity of the tin hydride. Triorganotin hydrides exhibit increased reactivity in the series $Ph_3SnH \ll (CH_3)_3SnH < (C_2H_5)_3SnH \approx (C_4H_9)_3SnH$.[89]

In 1968, Leusink *et al.*,[90] investigated the catalyzed hydrostannation of alkynes and showed that the (*Z*)-products rearrange to the (*E*)-product through a stannyl radical catalyzed mechanism. They studied a mixture of activated (*E*)- and (*Z*)-ethenyltriethyltins **79** and **80** (Equation III-9) at 60°C with varying proportions of free-radical sources and triethyltin deuteride. No significant rearrangement was observed until both the triethyltin



III-9

deuteride and free-radical source were added. After the addition, an isomerization occurred which resulted in an equimolar mixture of the (*E*)- and (*Z*)-isomers. Similar results were observed for non-activated alkenes.[91]

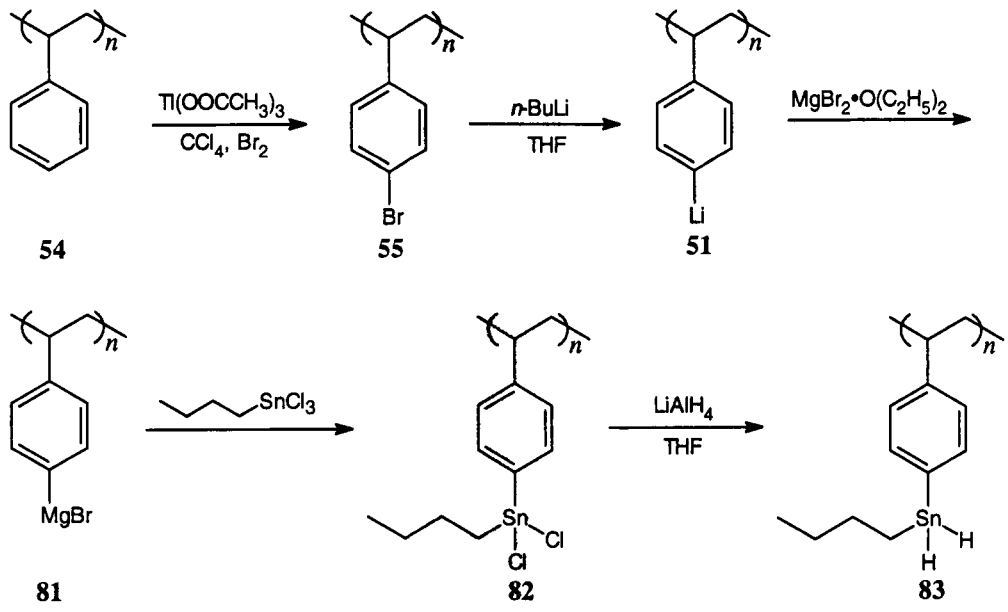
CHAPTER 2

REVIEW OF POLYMER-SUPPORTED ORGANOSTANNANE REACTIONS

A. Polymeric Stannanes

Organotin reduction reactions proceed through either a free-radical or polar mechanism (dependent on reaction conditions) which makes organotin reagents ideal candidates for attachment to polymer supports. Organotin ligands bound to polymer supports have focused on tin halides and corresponding tin hydrides. Both soluble polymers and insoluble polymers have been functionalized with tin and utilized as reagents and catalysts. Functionalization of polystyrene beads as well as polymerization of a preformed tin monomer have been investigated in the preparation of polymer-supported tin compounds.

Functionalization of macroreticular polystyrene–divinylbenzene copolymer **54** (Amberlite XE-305) (Scheme 8) with butyltin trichloride was accomplished by Weinshenker, Crosby and Wong.[92] They chose the macroreticular resin over the gel to take advantage of the increased number of accessible reactive sites and to control the swelling and shrinking associated with solvent changes. The resulting butylphenyltin dichloride polymer **82** was further reduced to the butylphenyltin dihydride **83** using lithium aluminum hydride in tetrahydrofuran to give the first reported styrene-bound tin



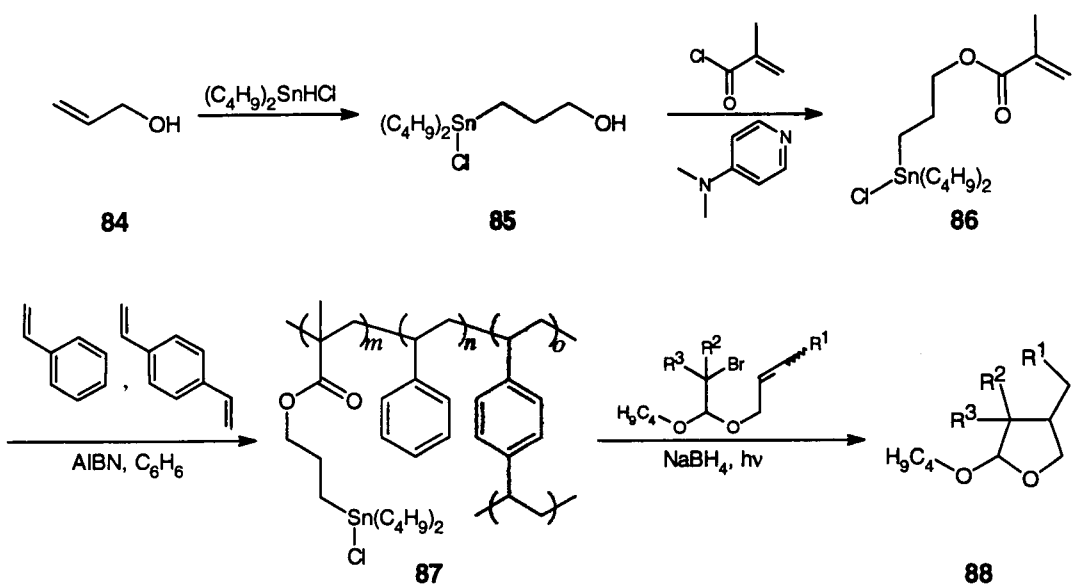
Scheme 8. Functionalization of Polystyrene with Butyltin Dichloride Ligand and Subsequent Reduction to the Butyltin Dihydride.

dihydride reagent. The polymeric tin dihydride reagent was used to prepare alkanes from haloalkanes, and in the reduction of aldehydes and ketones to the corresponding alcohol. A maximum loading of 2.0 mmol hydride/gram of resin was realized.

Important considerations of polymer-supported reagents were introduced in Part I, Chapter 2, Section B. Accessibility of reagents into the polymer matrix during resin functionalization is a consideration seen in the functionalization of polymer-supported reagents such as **81** whose synthesis is summarized in Scheme 8. Formation of the polymeric Grignard reagent **81** would appear to be straightforward starting from the brominated matrix **55**. The small molecule analogue of the Grignard reagent is readily formed from solid magnesium and the haloorganic compound, with the magnesium inserting into the halogen-carbon bond. Addition of a polymer matrix prohibits any but

the externally located halogen ligands from ready access to the metal. Weinshenker's method is then necessary for functionalization of internal sites of the polymer as well as the sites on the bead surface.

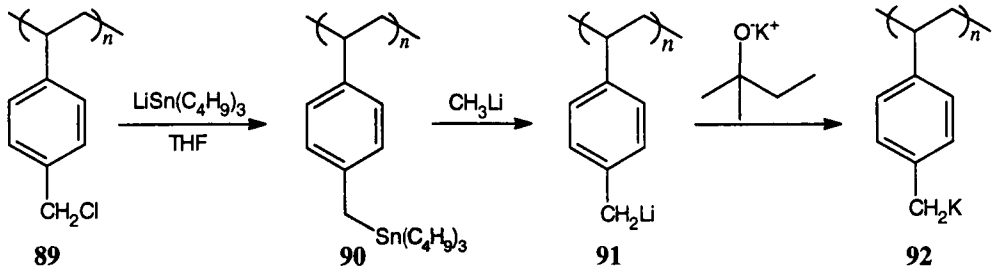
While exploring radical catalyzed homolytic carbocyclization reactions as a route to furans and lactones, Ueno *et al.*,[93] reported difficulty in separating the homogeneous tin catalyst from products. To overcome this, they prepared a crosslinked copolymer from dibutyl[3-(2-methyl-2-propenoate)propyl]tin chloride monomer **86**, styrene, and 5% divinylbenzene (Scheme 9). Use of the polymer-supported dibutylpropyltin chloride **87** with sodium borohydride as a catalyst resulted in yields of 73–96% compared to 50–78%



Scheme 9. Polymeric Dibutyl[3-(2-methyl-2-propenoate)propyl]tin Chloride in a Homolytic Carbocyclization Reaction.

using the homogeneous catalyst tributyltin hydride. Ueno *et al.*, attributed this difference in yields to the additional purification steps required when using the homogeneous tin catalyst. Comparisons of yields may be tenuous since the researchers used different methods to generate the radical. In the small molecule system, α,α'-azobisisobutyronitrile and heat were utilized with a tin-hydride, while in the polymer, addition of ultraviolet irradiation provided the radical from a tin-chloride/sodium borohydride system. The ability to recycle the polymer was noted with the comment that site isolation of the tin groups increased the life of the polymer by reducing the formation of distannane crosslinking.

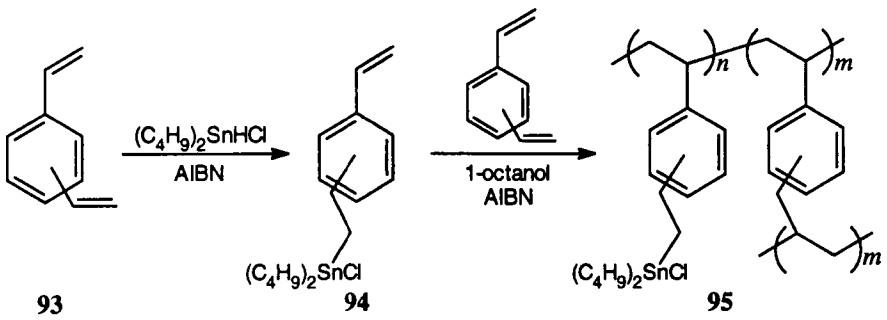
Brix and Clark[94] reacted Merrifield resin **89** with lithium tributyltin to yield the benzyltriethyltin polymer **90** (Equation III-10). Reaction with methyllithium yielded the



III-10

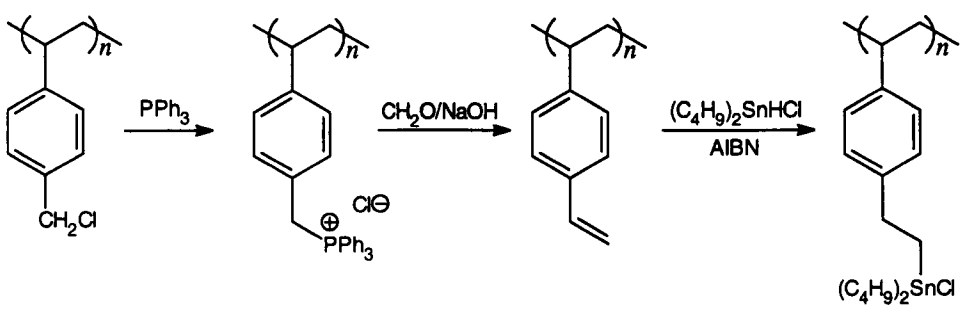
lithiated polymer **91**, which they used as an intermediate to the methylpotassium polymer **92**. They note that the tributyltin polymer **90** "is not only a valuable intermediate for organometallic-substituted polymers but may also have considerable potential as a precursor for radical centers on the polymer."[95]

Gerigk and coworkers[96] chose to investigate two synthetic strategies to prepare tin polymers: stannylation of divinylbenzene followed by polymerization, and functionalization of commercial polystyrene beads. The first method, (Equation III-11), began with hydrostannylation of purified technical divinylbenzene (**93**) using



93 **94** **95** III-11

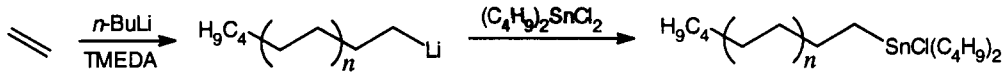
dibutylchlorotin hydride under free-radical conditions at room temperature. The resulting mono-hydrostannylated vinyl monomer **94** was then copolymerized with divinylbenzene in a suspension polymerization to yield macroreticular beads **95** with 1.9 millimoles tin per gram of polymer (0.76 degree of functionalization reported). The procedure to functionalize commercially available beads (Amberlite XE-305 and Lewatit OC 1018) utilized a Wittig reaction (Equation III-12). The functionalized commercial beads gave



89 **96** **97** **98** III-12

the stannylated polymer **98** with a degree of functionalization of 0.33 from the Amberlite XE-305 and 0.67 from the Lewatit OC 1018.

Bergbrieter and Walker[97] synthesized and studied linear polymers with terminal tin halides as homogeneous catalysts for reductions using sodium borohydride. Their method focused on the formation of a linear polymer prepared for functionalization in a single step by reacting ethylene with *n*-butyllithium to yield lithium terminated polyethylene **99** (Equation III-13). Addition of the organotin halide resulted in a



99 **100** III-13

transmetallation reaction which gave the tin chloride polymer **100**. This polymer was used as a solid catalyst, along with benzo-15-crown-5 and sodium borohydride, to reduce bromododecane to dodecane at 110 °C. Bergbrieter and Walker also formed the polyethylene terminated butyltin dichloride, tin trichloride, diphenyltin chloride; the polystyrene terminated dibutyltin chloride and butyltin dichloride; and the *bis*-polyethylene tin dichloride.

Research into alkyl halide catalyzed reductions lead to an ingenious approach to polymeric supports. Since both crown ethers and tin halides show catalytic activity in this reaction, it seemed reasonable that they could both be attached to a polymeric support. Beads containing the tin halide and beads containing the crown ether were

synthesized and placed together in a single reaction vessel along with the sodium borohydride and the alkyl halide. Although the reaction showed an enhanced rate when compared to the uncatalyzed solution reduction, it was slower than the homogeneous reaction with both catalysts present. This lead Glanton and Salley[98] to synthesize a co-catalyst containing both incompatible reagents on a single polymeric backbone (Figure 10). The polymer that contained both species in a single bead demonstrated a 40–48% rate increase for the alkyl halide reduction when compared to the same reaction utilizing catalysts in separate beads.

Tin hydrides have also been immobilized on alumina and silica to provide a heterogeneous reagent.[99]

An intriguing technical application of polymer-supported organotins is their use as marine antifouling agents. Tributyltin formate attached to a polyethylene backbone was

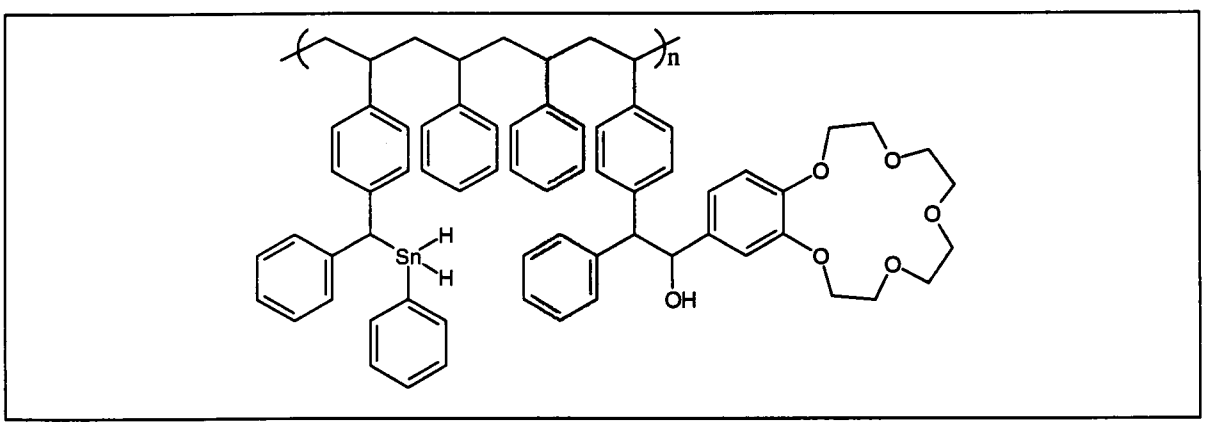
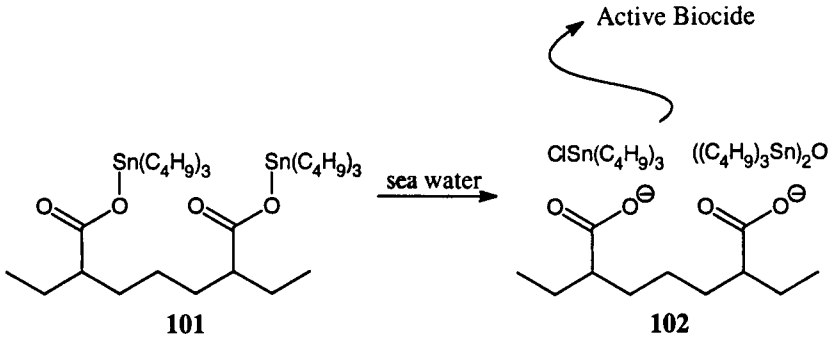


Figure 10. Catalytic Polymer Containing 15-Crown-5-ether and Tin Hydride Within a Single Bead for Reduction of Alkyl Halides.

proposed for use as an antifouling agent, **101**, increasing the effectiveness of the toxic metal compound through controlled release as the tin compound slowly hydrolyzed in contact with the sea water (Equation III-14). Many other marine anti-fouling agents have

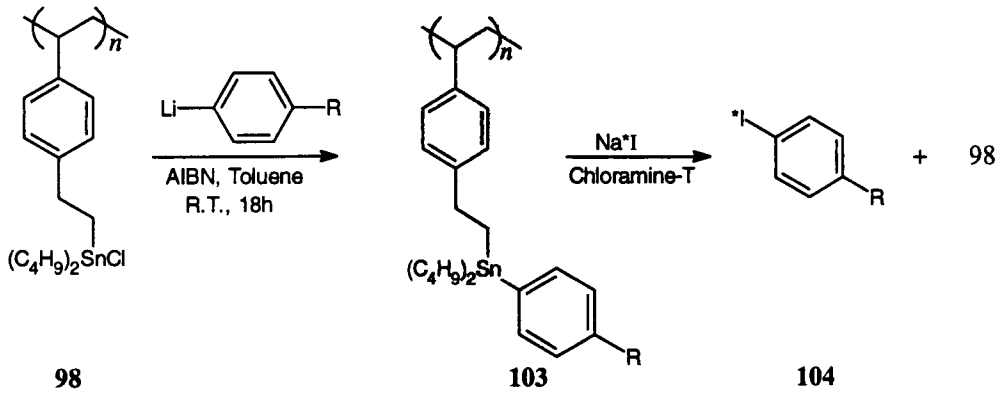


101 **102** III-14

been synthesized and tested, including linear and crosslinked polymers containing triorganotin esters.[100] This artificial introduction of toxic organotin into coastal waters has lead to increased interest into their effects on both vertebrate and invertebrate marine life. These studies have been summarized by Evans and Karpel,[101] and confirm the high toxicity of organotins, though the toxic effect is mediated by the rapidly decreasing organotin concentration as distance from the coated surface increases. In addition, several mechanisms have been suggested which convert the organotin to nontoxic inorganic tin over short periods of time.

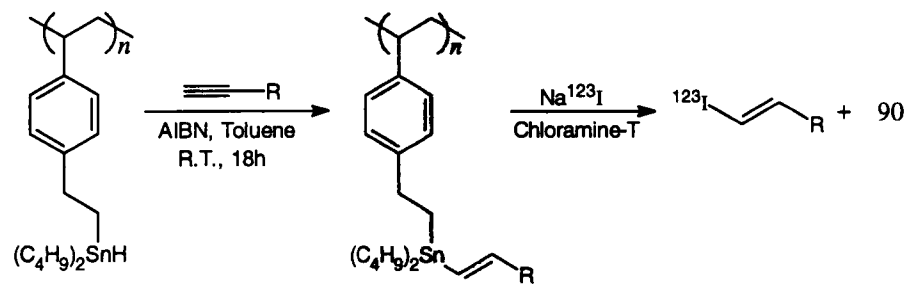
Recently, organotin polymers have been synthesized in which the tin atom is bound to an ethyl linkage to enhance the stability of the functional group.[102] Culbert and Hunter prepared the tin polymer **98** from divinylbenzene and dibutyl[2-(3- and 4-ethenyl-phenyl)ethyl]tin chloride. Reaction with a phenyllithium compound yielded the polymer

bound reagent **103**. This polymer was then used in the synthesis of radiolabelled aryl iodides by addition of oxidant and radiolabelled sodium iodide to give the radiolabelled aryl compound **104** (Equation III-15).



98 **103** **104** III-15

Kabalka *et al.*,[103] utilized **poly{dibutyl[2-(3- and 4-ethenylphenyl)ethyl]tin hydride}** (**105**) to prepare radioiodoalkenes **106** for use as radiopharmaceuticals. Reduction to the tin hydride was accomplished with diisobutylaluminum hydride in tetrahydrofuran, followed by alkenylation under free-radical conditions with selected alkynes. Addition of sodium iodide in the presence of an oxidizing agent released the iodoalkenes (Equation III-16).



105 **106** **107** III-16

CHAPTER 3

RESULTS AND DISCUSSION

A. Preparation Tin Chloride Monomer

Preparation of the dibutyltin reagent required polymerization of a prefunctionalized monomer copolymerized with a crosslinking agent in a suspension polymerization. The crosslinking agent used was divinylbenzene (DVB) because of its established use in other polymerization and ready availability and ease of handling. Although not particularly toxic, divinylbenzene possesses a strong odor, mandating the use of adequate ventilation. Additionally, the tin compounds used in synthesis of the monomer possess slight, though significant toxicity, which requires the use of appropriate protective clothing, gloves, eye-wear, and ventilation.

Preparation of Dibutyl[2-(3- and 4-ethenylphenyl)ethyl]tin Chloride

Purification of Divinylbenzene

Divinylbenzene is available commercially as a technical mixture of 55 % (by weight) *para*- and *meta*-divinylbenzene and 45% *para*- and *meta*-ethylvinylbenzene. Analysis of technical mixture by capillary Gas Chromatography revealed a mixture of 56.5% divinylbenzene (39.9% *para*- and 16.5% *meta*-isomer), and 43.5%

ethylvinylbenzene (33.5% *para*- and 10% *meta*-isomer). The boiling point of the divinylbenzene isomers is 195 °C, while *meta*-ethylvinylbenzene boils at 190 °C and *para*-ethylvinylbenzene at 192 °C[104]. Separation by distillation would be a formidable task. Leikin, Davankov, and Krivova[105] investigated methods of concentrating the divinylbenzene by taking advantage of differing chemical properties of the compounds. They reported tests of recrystallization, zone refining, and chemisorption using copper(I) chloride. Recrystallization provided an increase of only 12% of divinylbenzene, while zone refining, though tedious, resulted in a maximum purification of 80% by weight. Noting that chemisorption had been used in purification of butadiene, isoprene and vinyltoluene, they examined purification by utilizing the differences in the ability of ethylvinylbenzene and divinylbenzene to form coordination compounds with copper(I) chloride. Purification was accomplished by forming the coordination compound of copper(I)-divinylbenzene, washing with cold heptane (-10 °C) to remove the ethylvinylbenzene, decomposing the copper(I)-divinylbenzene complex by forming a more stable ammonium-copper complex, and then isolation of the divinylbenzene. Leikin *et al.*, reported purified divinylbenzene of 98–100% purity.

Purification of divinylbenzene from the technical mixture, though feasible, demanded large volume of chemicals and excessive laboratory time. It was suggested that the unpurified reagent could be utilized without sufficient degradation of final results.[106] Functionalization of technical divinylbenzene with the tin reagent would yield

a combination of dibutyl[2-(3- and 4-ethenylphenyl)ethyl]tin chloride monomer and dibutyl[2-(3- and 4-ethylphenyl)ethyl]tin chloride. Following polymerization, careful washing of the crosslinked resin would remove the dibutyl[2-(3- and 4-ethylphenyl)ethyl]tin chloride contaminants. Dibutyl[2-(3- and 4-ethenylphenyl)ethyl]tin chloride monomer was prepared from the unpurified divinylbenzene and dibutylchlorotin hydride and then polymerized. A separate preparation of the monomer from purified divinylbenzene was also accomplished.

Preparation of the dibutyl[2-(3- and 4-ethenylphenyl)ethyltin chloride from technical divinylbenzene provided a mixture of the desired product with dibutyl[2-(3- and 4-ethylphenyl)ethyl]tin chloride contaminant. This presented the opportunity to utilize the dibutyl[2-(3- and 4-ethylphenyl)ethyl]tin chloride as a solvating diluent during subsequent polymerization. The two different diluents, 1-octanol and dibutyl[2-(3- and 4-ethylphenyl)ethyl]tin chloride, would theoretically provide polymer beads containing macrochannels of different characteristics.

Preparation of Dibutyltin Dihydride

Tin hydrides are prepared by reaction of tin halides with any of several reducing agents. The reaction of dibutyltin dichloride (**108**) with lithium aluminum hydride in diethyl ether to give dibutyltin dihydride (**109**) was the system chosen for hydride preparation in this study (Equation III-17).

$$(C_4H_9)_2SnCl_2 \quad + \quad LiAlH_4 \longrightarrow (C_4H_9)_2SnH_2 \qquad \text{III-17}$$

108 **109**

Tin-119 nuclear magnetic resonance spectra was used to follow the progress of tin functionalization for both the solution segment of the synthesis and the solid-state work. Solution tin-119 NMR was referenced to tetramethyltin which resonates as a multiplet due to coupling with protons (Figure 11). The absorbance is set at δ 0.00 An expanded spectra shows the fine nature of the multiplet of nine peaks from the coupling, with a coupling constant of $^2J^{119}$Sn,^{1}H/Hz = 54.32 (Figure 12). Dibutyltin dichloride in ether (referenced to tetramethyltin) absorbs at δ 123, as compared to the literature value[107] of δ 123.4 (Figure 13). A distinct change in chemical shift in the tin NMR is observed upon reduction to the dibutyltin dihydride which resonates at δ -206.05 (Figure 14). The proton decoupled spectra shows a single broad absorbance.

Separation of the dibutyltin dihydride from the solvents and lithium chloride salts was difficult and time consuming, but had to be accomplished as quickly as possible to preserve the reagent. Although not very reactive with water, the tin hydrides decompose quickly on contact with oxygen. To minimize this decomposition during workup, a free-radical inhibitor, benzophenone, was added to the reaction mixture. After addition of the benzophenone, the excess lithium aluminum hydride was quenched with distilled water, and a twenty percent solution of potassium sodium tartrate (Rochelle's Salt) added to complex and solvate the aluminum salts.

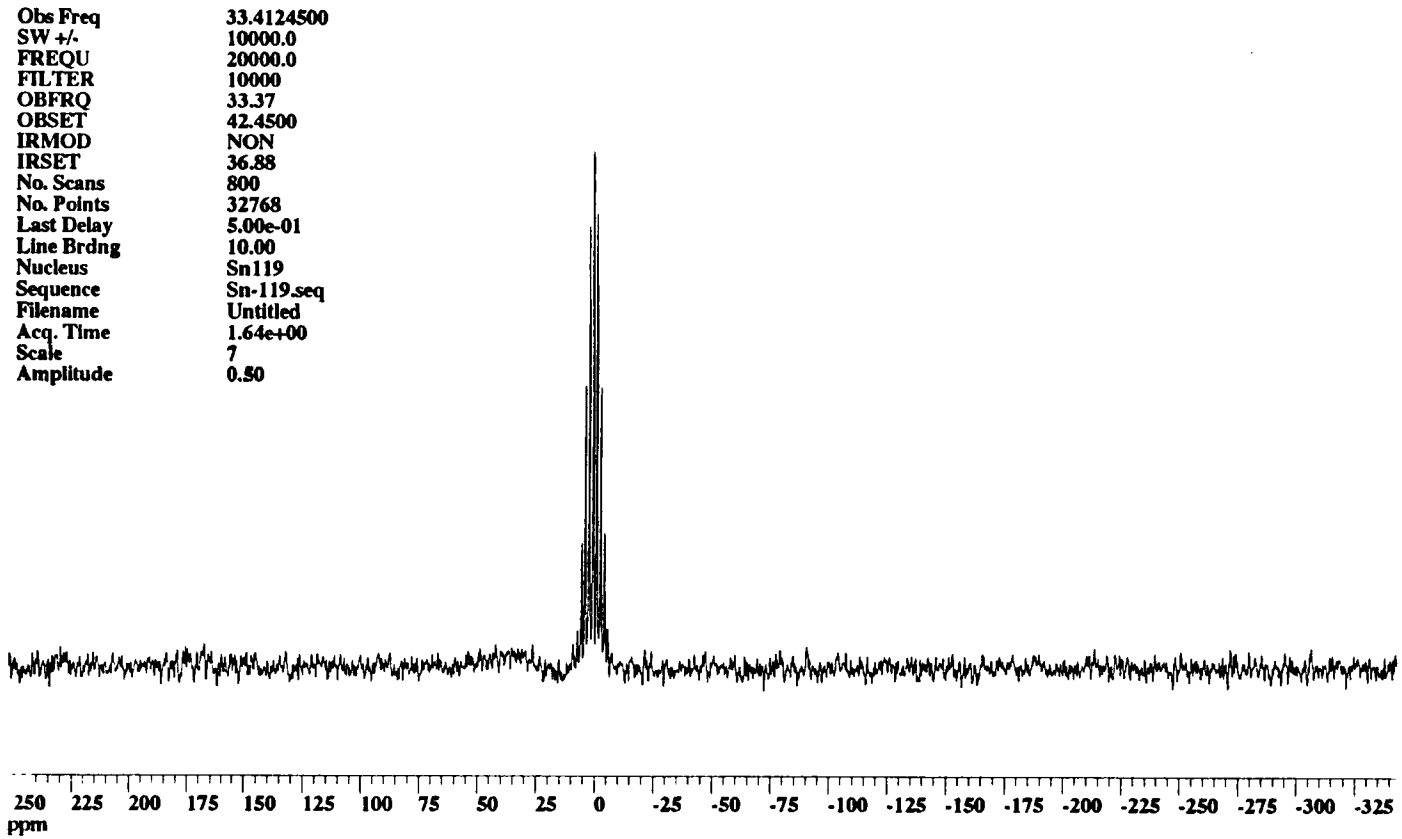


Figure 11. Tin-119 Solution Nuclear Magnetic Resonance Spectra of the Reference Compound Tetramethyltin. Decoupler power off showing multiplicity due to tin-proton coupling ($^{2}J^{119}$Sn,^{1}H/Hz = 54.32).

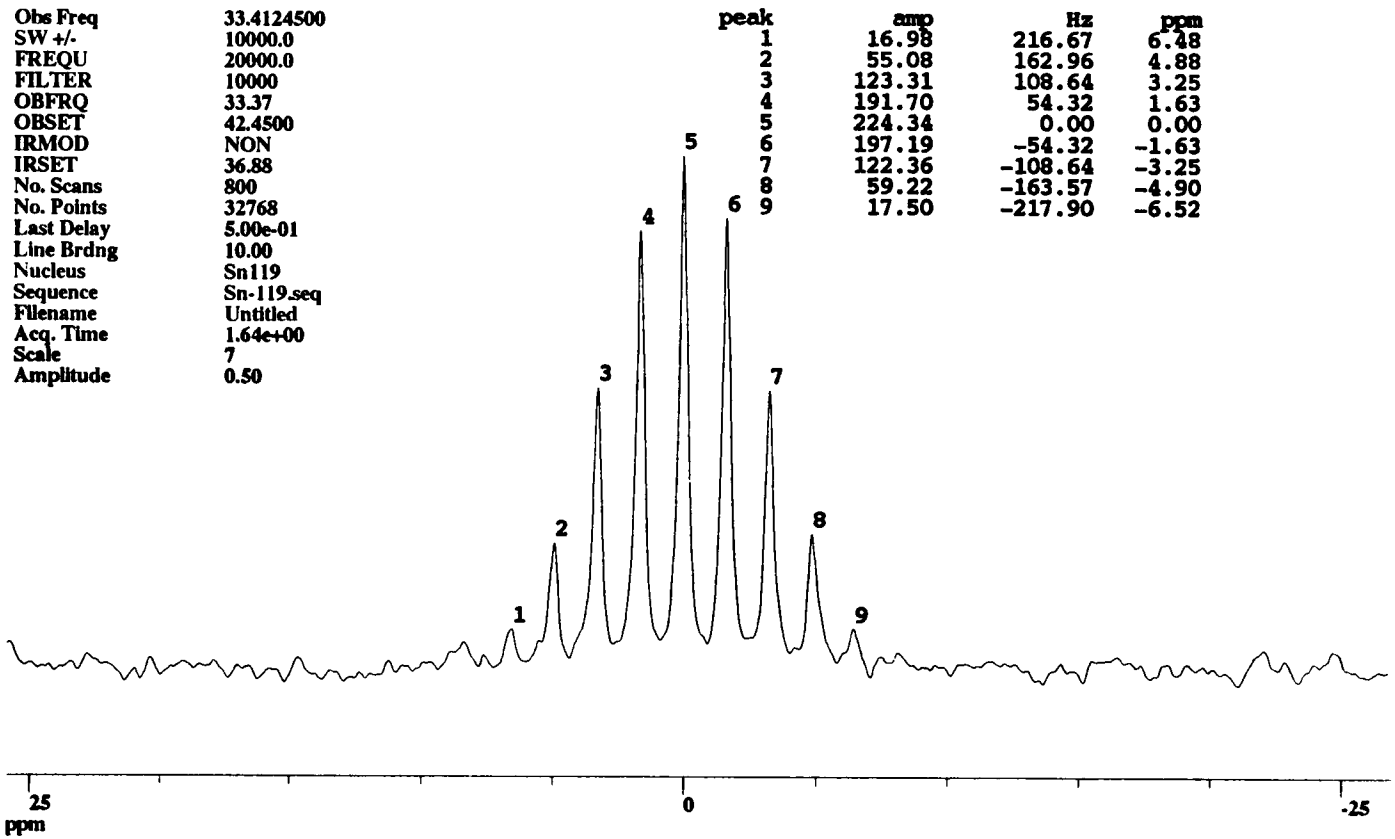


Figure 12. Expansion of Tin-119 Solution Nuclear Magnetic Resonance Spectra of Tetramethyl Tin. Pattern of coupled peaks and central peak with coupling constant shown.

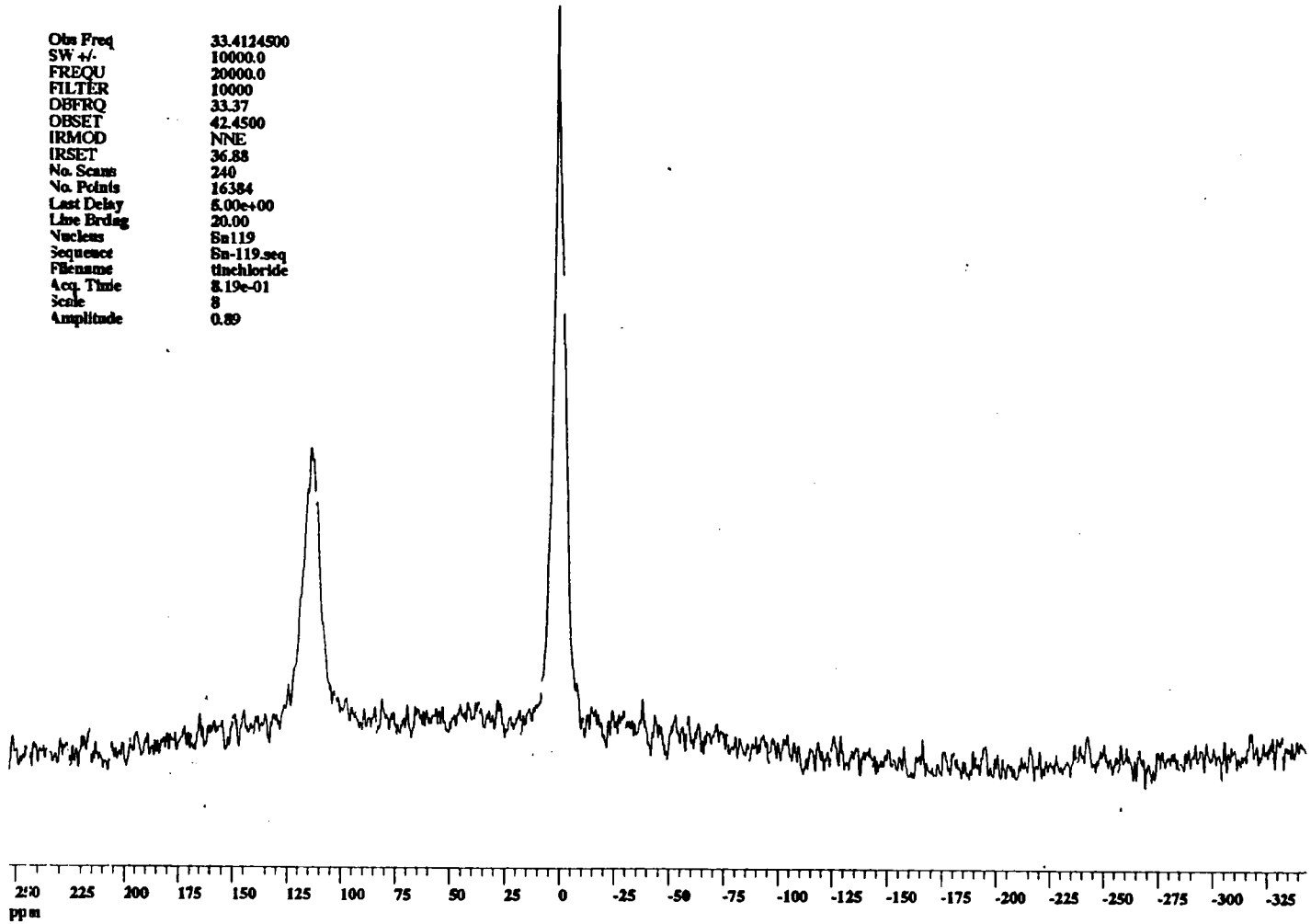


Figure 13. Tin-119 Solution Nuclear Magnetic Resonance Spectra of Dibutyltin Dichloride. Reference: Tetramethyltin set at δ 0.00, solvent: diethyl ether.

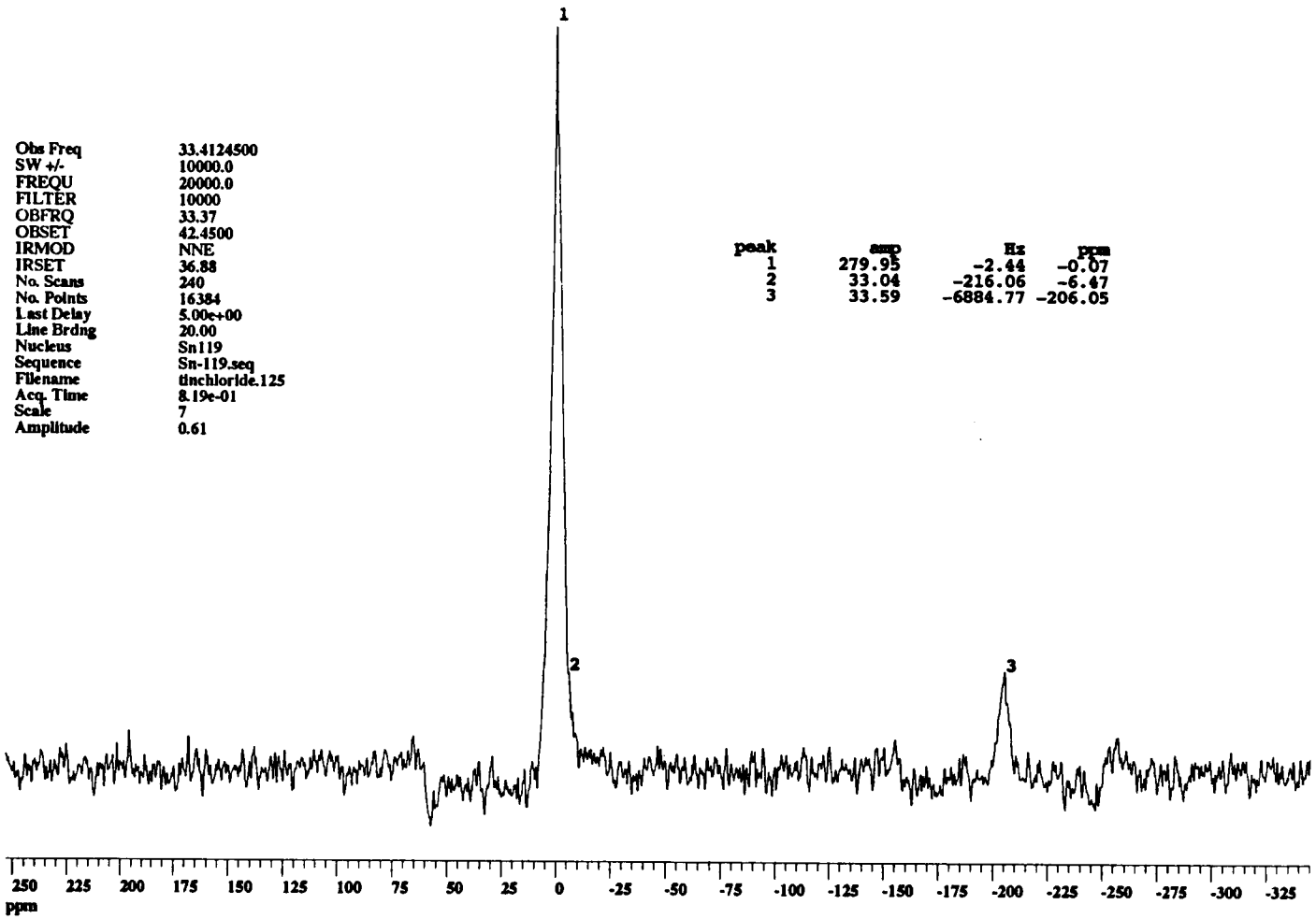


Figure 14. Tin-119 Solution Nuclear Magnetic Resonance Spectra of Dibutyltin Dihydride. Reference: Tetramethyltin set at δ 0.00, solvent: diethyl ether.

Following separation of the layers and drying of the organic phase, the solvent was partially removed under reduced pressure until ten percent of the original volume remained. The remaining solvent was removed by vacuum distillation while maintaining an inert atmosphere. Even though excess $LiAlH_4$ was employed to increase yield of the dibutyltin dihydride, dibutyltin dichloride and butylchlorotin hydride could still constitute portion of the reaction mixture. Neumann[108] noted that upon heating a mixture of dibutyltin dichloride (**108**) and dibutyltin dihydride (**109**) *in vacuo,* the dihydride distills first and shifts the equilibrium of the reaction between the dichloride and dihydride toward the reactants as shown in Equation III-18, which maximizes the yield of dibutyltin

$$\underset{\textbf{108}}{(C_4H_9)_2SnCl_2} + \underset{\textbf{109}}{(C_4H_9)_2SnH_2} \rightleftharpoons \underset{\textbf{110}}{(C_4H_9)_2SnHCl} \qquad \text{III-18}$$

dihydride. It was found that vacuum distillation of the dibutyltin dihydride yielded a clear liquid, which showed no loss of activity over a three week period when stored under argon at 0 °C. This was consistent with other reports of storage of up to two months with no discernible loss of activity.[109]

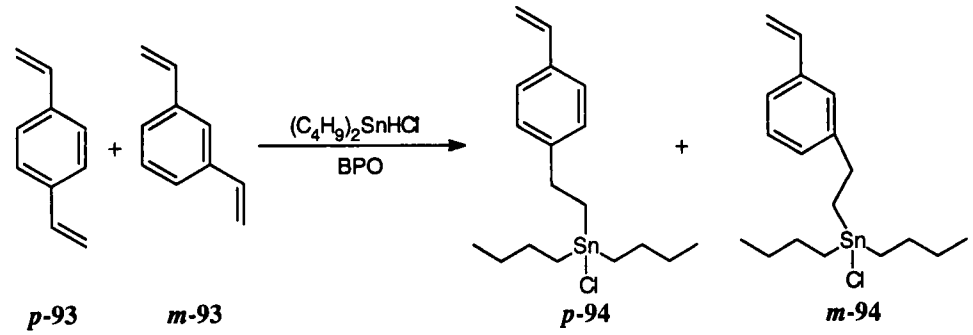
Synthesis of Dibutyl[2-(3- and 4-ethenylphenyl)ethyl]tin Chloride

Dibutyl[2-(3- and 4-ethenylphenyl)ethyl tin chloride was prepared using a modification of the method of Gerigk *et al.*[109]

Due to the tendency toward polymerization, storage of the dibutyl[2-(3- and 4-ethenylphenyl)ethyl]tin chloride was not possible. Without separation from remaining free-radical sources or stabilization by a free-radical sponge and storage at 0 ^{o}C, we observed bulk polymerization occurring within twenty-four hours. No storage even with radical sponges was obtained in excess of forty-eight hours.

The dibutyl[2-(3- and 4-ethenylphenyl)ethyl]tin chloride was prepared by the free-radical addition of dibutylchlorotin hydride to one of the vinyl groups of divinylbenzene. Dibutylchlorotin hydride was formed *in situ* by the equimolar addition of dibutyltin dichloride and dibutyltin dihydride. The monochlorotin hydride was reported to be more reactive than either the dibutyltin hydride or tributyltin hydride,[109] making it the more attractive reagent for hydrostannation of carbon-carbon multiple bonds. Gerigk *et al.*,[109] noted that careful attention to stoichiometric proportions and reaction temperature provided the mono-hydrostannation exclusively of the divinylbenzene. At reaction temperatures less than 30 ^{o}C, the dissociation of the initiator and subsequent hydrostannation occurs via a photolitic process.

Functionalization of divinylbenzene (*m*-**93** and *p*-**93**), purified to remove ethylvinylbenzene, yielded a monomer mixture of dibutyl[2-(4-ethenylphenyl)ethyl]tin chloride *p*-**94** and dibutyl[2-(3-ethenylphenyl)ethyl]tin chloride *m*-**94** (Equation III-19) which was polymerized without further purification. In the case of the unpurified



p-93 *m*-93 *p*-94 *m*-94

III-19

technical mixture of divinylbenzene, the by-product dibutyl[2-(3- and 4-ethylphenyl)ethyl]tin chloride was utilized as the diluent during polymerization.

A solution proton-NMR of the monomer is presented in Figure 15. Resonances from the vinyl protons at δ 5.5 and δ 5.7 indicate that the benzylic ethylene group is present in the monomer, and the absorbance at δ 3.0 indicates the presence of an ethyl linkage between the dibutyltin moiety and aromatic ring of polymer backbone. This ethyl resonance indicates functionalization of the second vinyl group to yield the dibutylethyltin chloride ligand. An additional resonance at δ 2.6 results from remaining ethylvinylbenzene impurities not completely removed during purification of the technical divinylbenzene. The resonances between δ 08–1.6 are those due to the butyl groups on the tin ligand. The Fourier Transform Infrared spectrum of the monomer is presented in Figure 16.

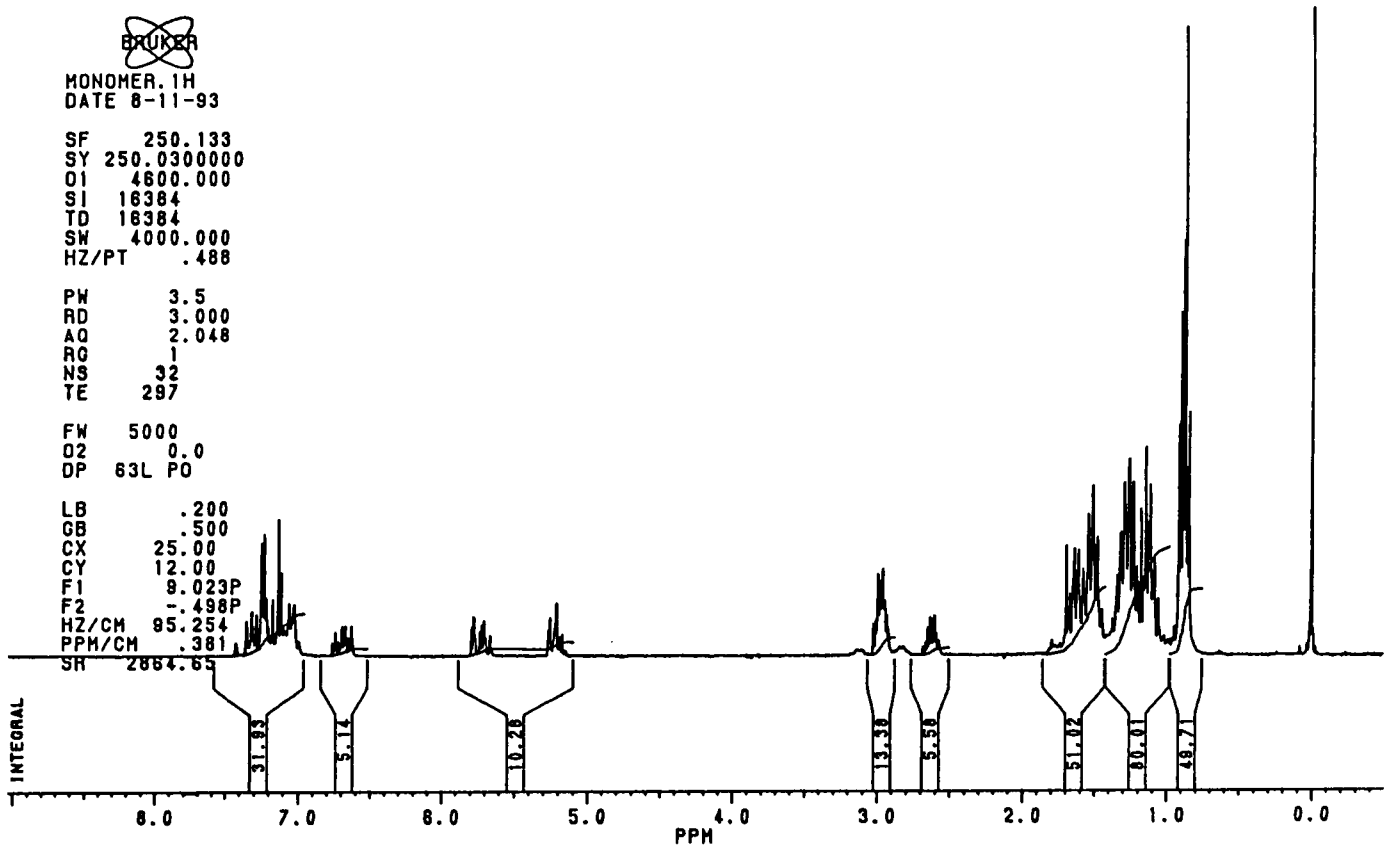


Figure 15. Nuclear Magnetic Resonance Spectrum of Dibutyl[2-(3- and 4-ethenylphenyl)ethyl]tin Chloride. Reference: tetramethylsilane δ 0.00, solvent carbon tetrachloride.

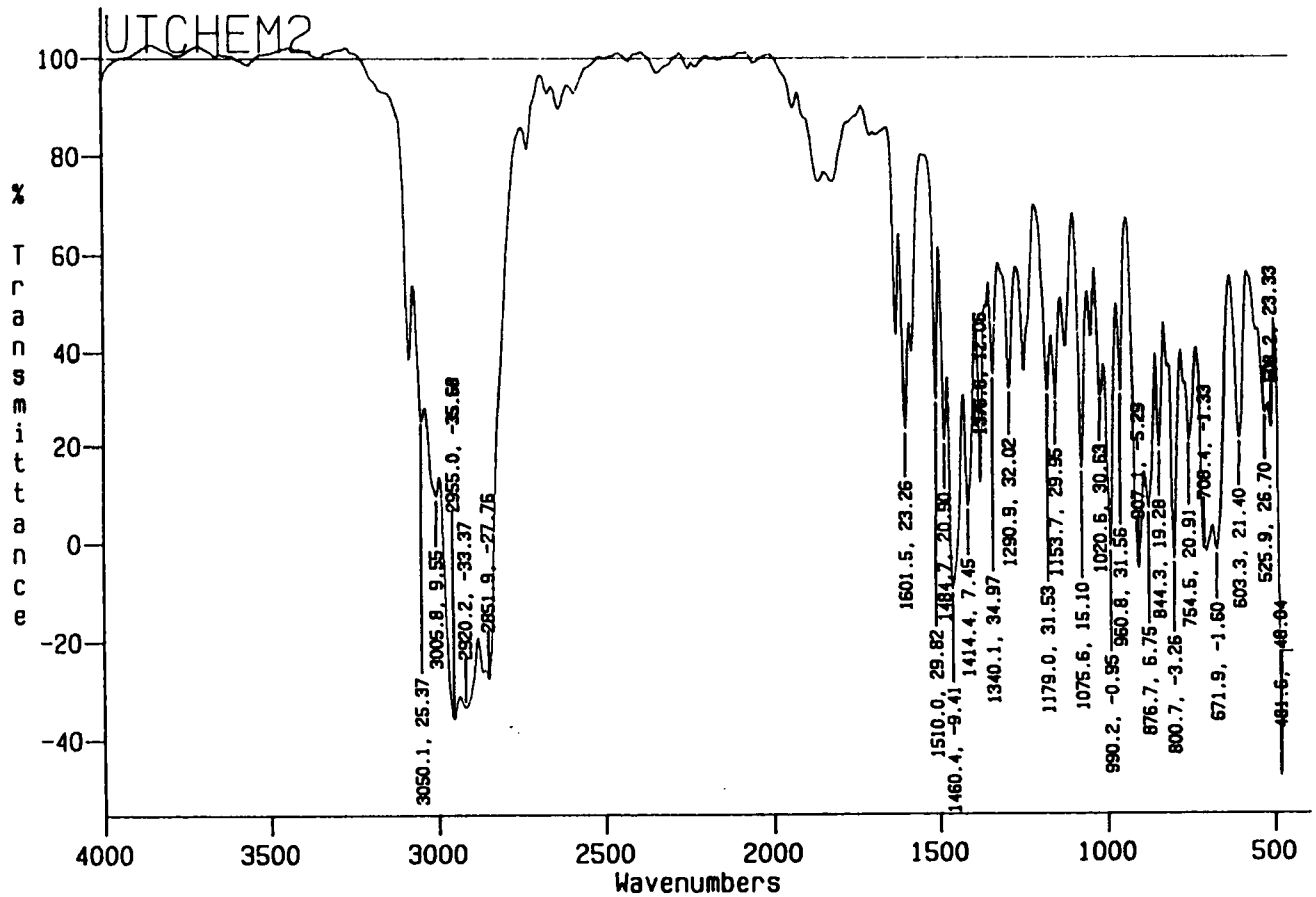
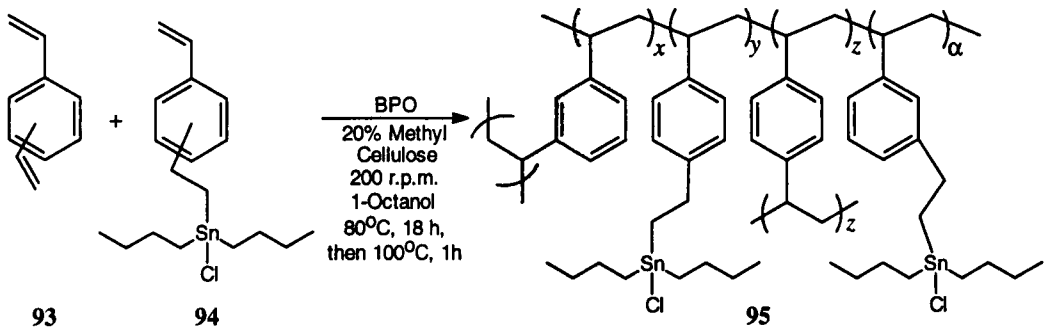


Figure 16. Fourier Transform Infrared Spectra of Dibutyl[2-(3- and 4-ethenylphenyl)ethyl]tin Chloride (neat).

B. Preparation of Poly{dibutyl[2-(3- and 4-ethenylphenyl)ethyl]tin Chloride} Reagent

Polymerization of Dibutyl[2-(3- and 4-ethenylphenyl)ethyl]tin Chloride with Divinylbenzene

Preparation of poly{dibutyl[2-(3- and 4-ethenylphenyl)ethyl]tin chloride} reagent was accomplished by copolymerization of the tin reagent with divinylbenzene. Macroporous copolymer beads were prepared via a suspension polymerization which utilized 1-octanol as diluent and methyl cellulose as the stabilizer. The resulting dibutyltin reagent is schematically presented in Equation III-20.



III-20

Polymerization conditions were carefully monitored and controlled to provide a tin reagent of consistent size and shape. The equipment used for polymerization is shown Figure 17. A 100 or 50 mL, two-piece, cylindrically-shaped reaction vessel was used as volume requirements dictated. The volume of the stirred suspension and the ratio

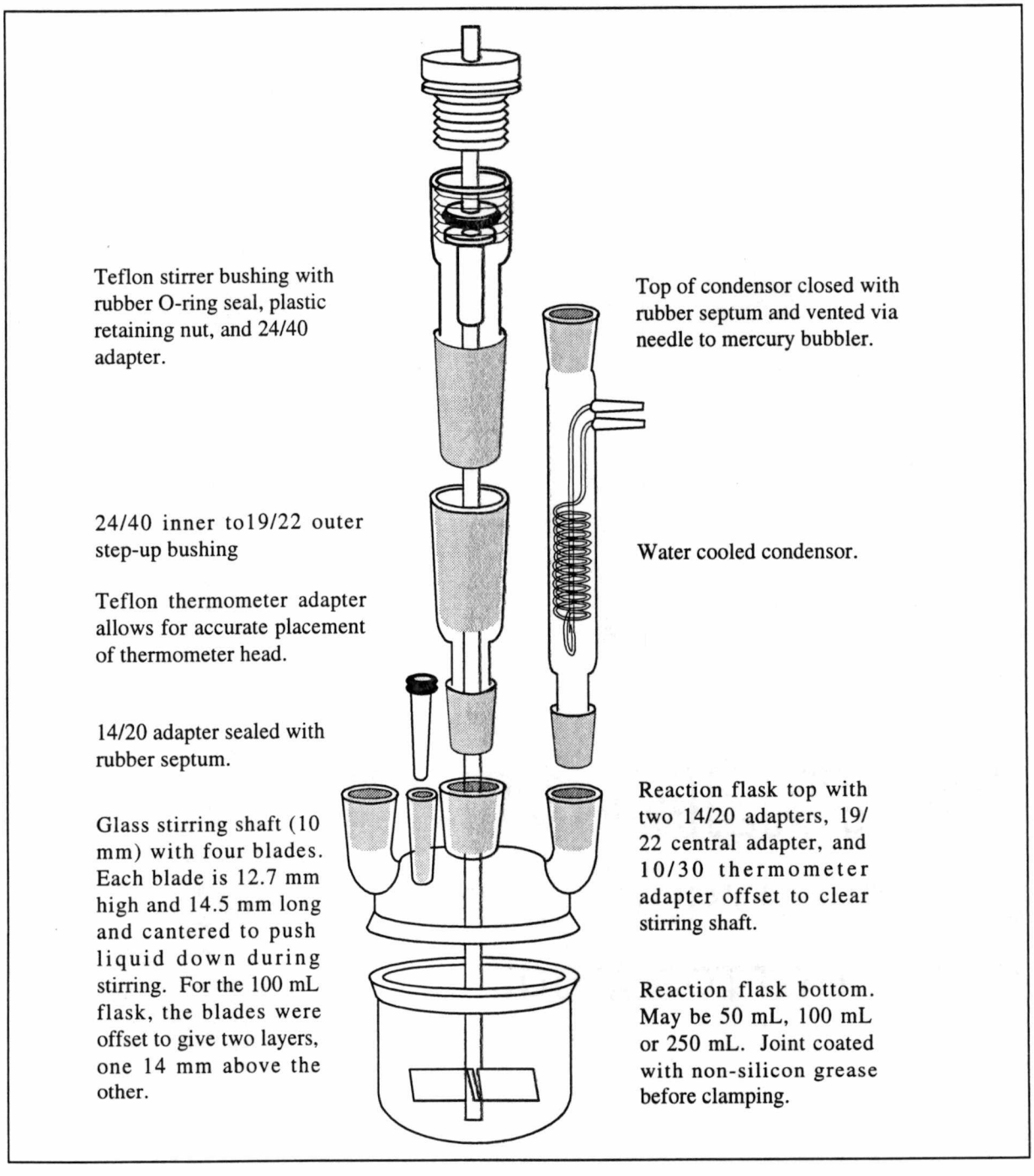


Figure 17. Polymerization Vessel for Suspension Polymerization With Stirring Shaft, Stirring Bearing, Water-Cooled Condenser, Thermometer Inlet, and Two-Piece Flask.

of the organic to aqueous phases were carefully monitored. Beads of consistent and reproducible size were obtained. For each solid reagent preparation, a ratio of organic to aqueous phases of approximately 1:1.1 was used. An overhead glass stirring paddle was used with a rod diameter of 10 mm and blade size of 12.7 mm by 14.5 mm of 4 mm thickness and angled at 30–45° so that stirring pushed the liquid down. The stirring rate was 200 revolutions per minute (rpm), and the formation of monomer droplets was monitored by reflection of light prior to initiation of polymerization.

Macroporous polymer-supported reagents of 2, 5, 10, 15, and 20 percent crosslinking agent were formed utilizing technical divinylbenzene. The dibutyl[2-(3- and 4-ethenylphenyl)ethyl]tin chloride, divinylbenzene, diluent, and benzoyl peroxide were mixed and poured into a stirred solution of 20% methyl cellulose which had been previously sparged with argon to remove dissolved oxygen.

After addition of the monomer solution, the suspension was stirred at room temperature under an argon flush for one hour. After that time, the reaction vessel was heated at a rate of approximately 0.5 ^{o}C per minute. Heating was accomplished using a 150 watt heat lamp connected via a temperature control unit attached to a potentiometer for variable control of power to the heat lamp. Several increases in power were necessary to maintain the heating rate. The temperature was then maintained at 80 ^{o}C for 18 hours, followed by one additional hour at 100 ^{o}C.

Reagent beads of spherical shape and 20–80 mesh size were obtained by this method. Beads produced using the 1-octanol diluent were opaque, a result of light scattering from the surface irregularities which are a characteristic of macroporous beads. In contrast, beads formed in the presence of the dibutyl[2-(3- and 4-ethylphenyl)ethyl]tin chloride diluent presented a translucent appearance. This difference in appearance is an indication of different pore characteristics of the two polymers as a result of the different diluents used.

The poly{dibutyl[2-(3- and 4-ethenylphenyl)ethyl]tin chloride} tin-119 solid-state NMR reveals a resonance at δ 144 (Figure 18) (externally referenced to dibutyltin dichloride). Dibutyltin dichloride shows a complex spectra due to spinning side bands, but central peak absorbance of δ 84.00[107] (Figure 19) was assigned by altering the spinning rate and locating the stationary peak. The carbon-13 solid-state NMR spectrum of dibutyltin dichloride reveals four resonances, with the tin-carbon coupling easily discerned, is shown in Figure 20. The solid-state NMR spectrum of the poly{dibutyl[2-(3- and 4-ethenylphenyl)ethyl]tin chloride} (Figure 21) may be compared to the spectrum of a standard sample of 4% divinylbenzene-styrene copolymer (Amberlite XE-305) (Figure 22). Resonances from the butyl groups attached to the tin are apparent at δ 14-28, the polymer chain carbons at δ 40–50, and the aromatic ring carbon resonances at δ 120–150. Broad peaks and spinning side bands at ~δ 65, ~δ 207, and ~δ 225 are characteristic of solid-state NMR of rigid polymers with constrained molecular motion.

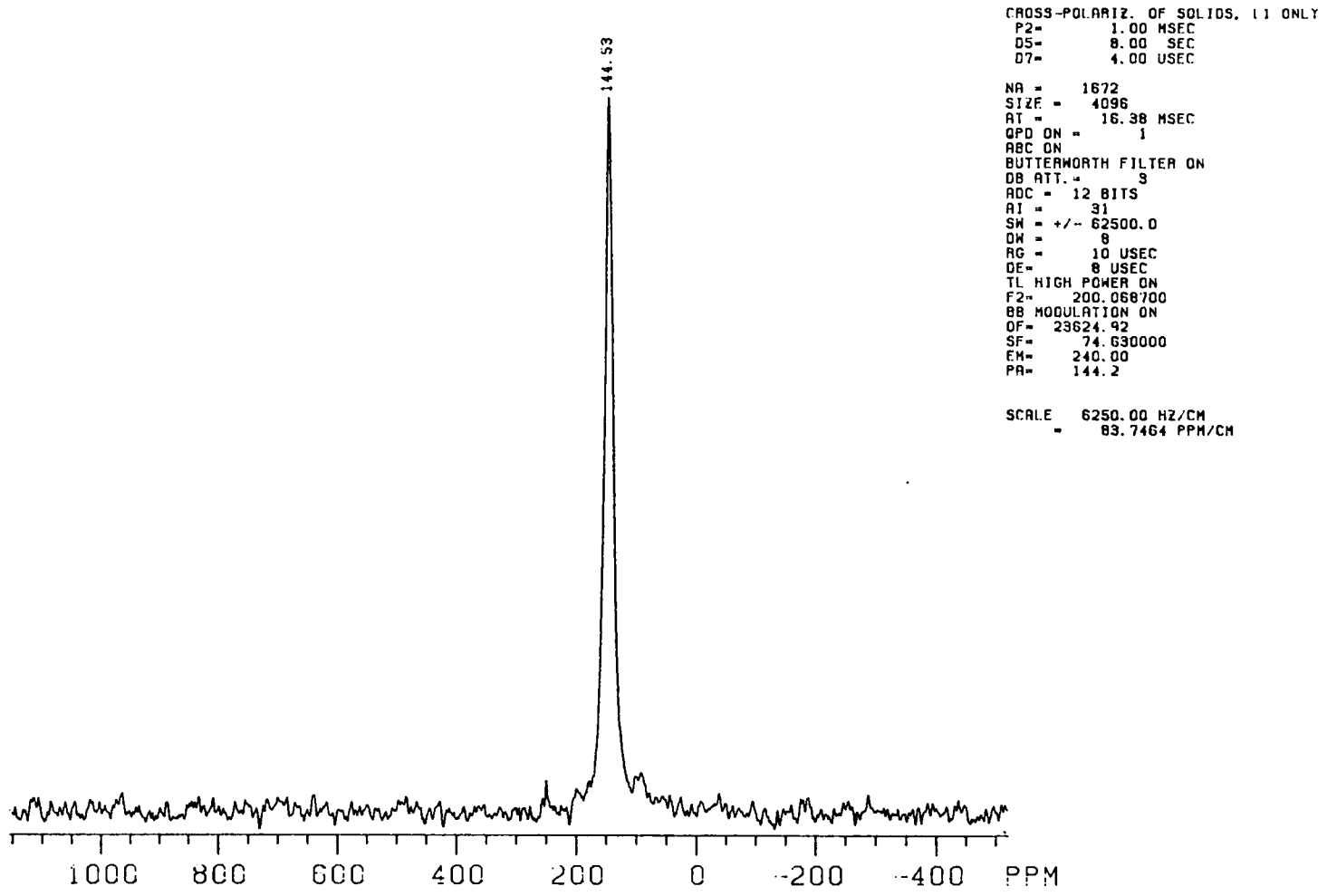


Figure 18. Tin-119 Solid-state Nuclear Magnetic Resonance Spectrum of Poly{Dibutyl[2-(3- and 4-ethenylphenyl)ethyl]tin Chloride}. Cross-Polarization of Solids - Magic Angle Spinning techniques used. Externally referenced to dibutyltin dichloride set at δ 84.000.

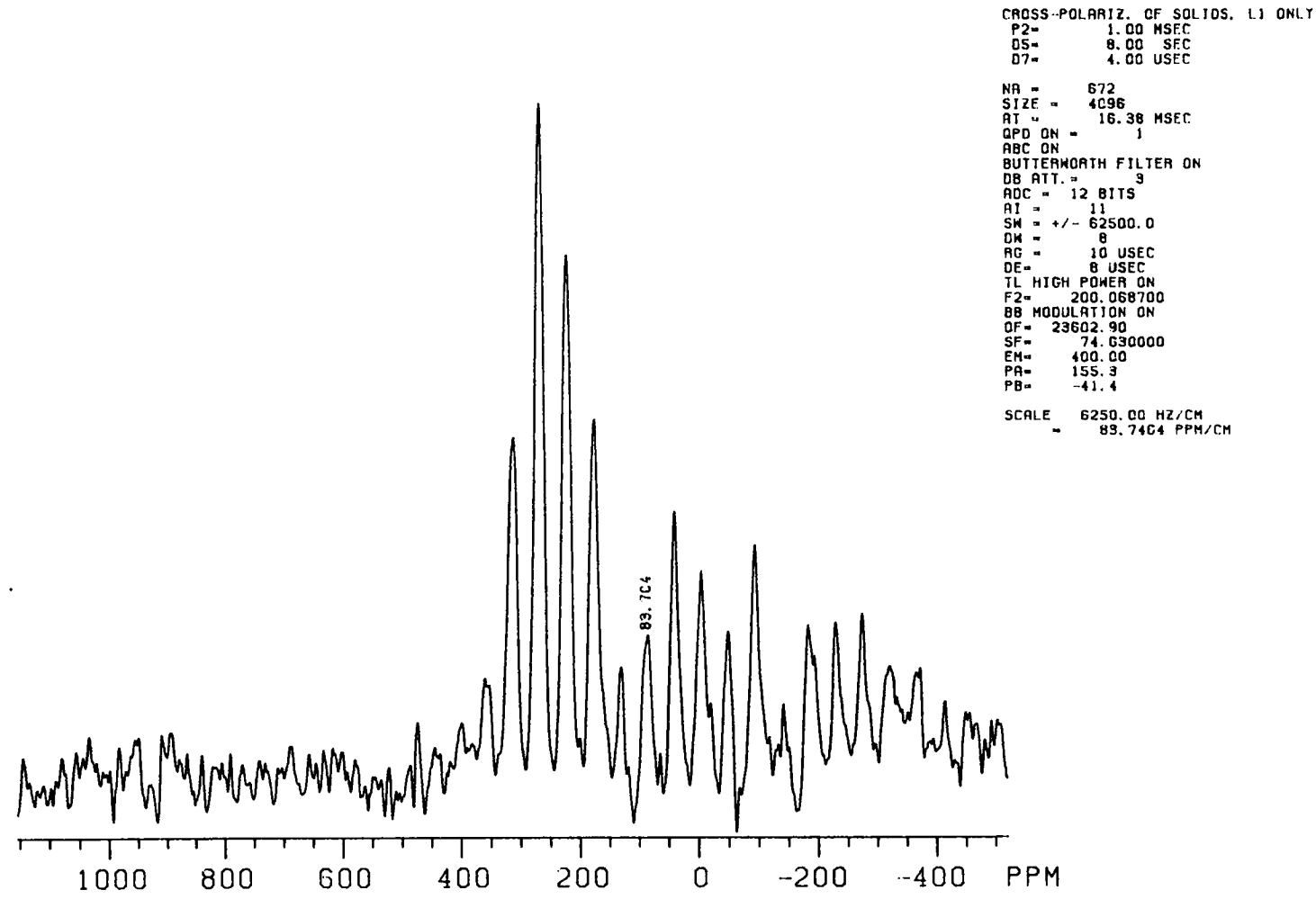


Figure 19. Tin-119 Solid-state Nuclear Magnetic Resonance Spectrum of Dibutyltin Dichloride. Cross-Polarization of Solids - Magic Angle Spinning techniques used. Central peak established by variation of spinning rate and location of stationary peak.

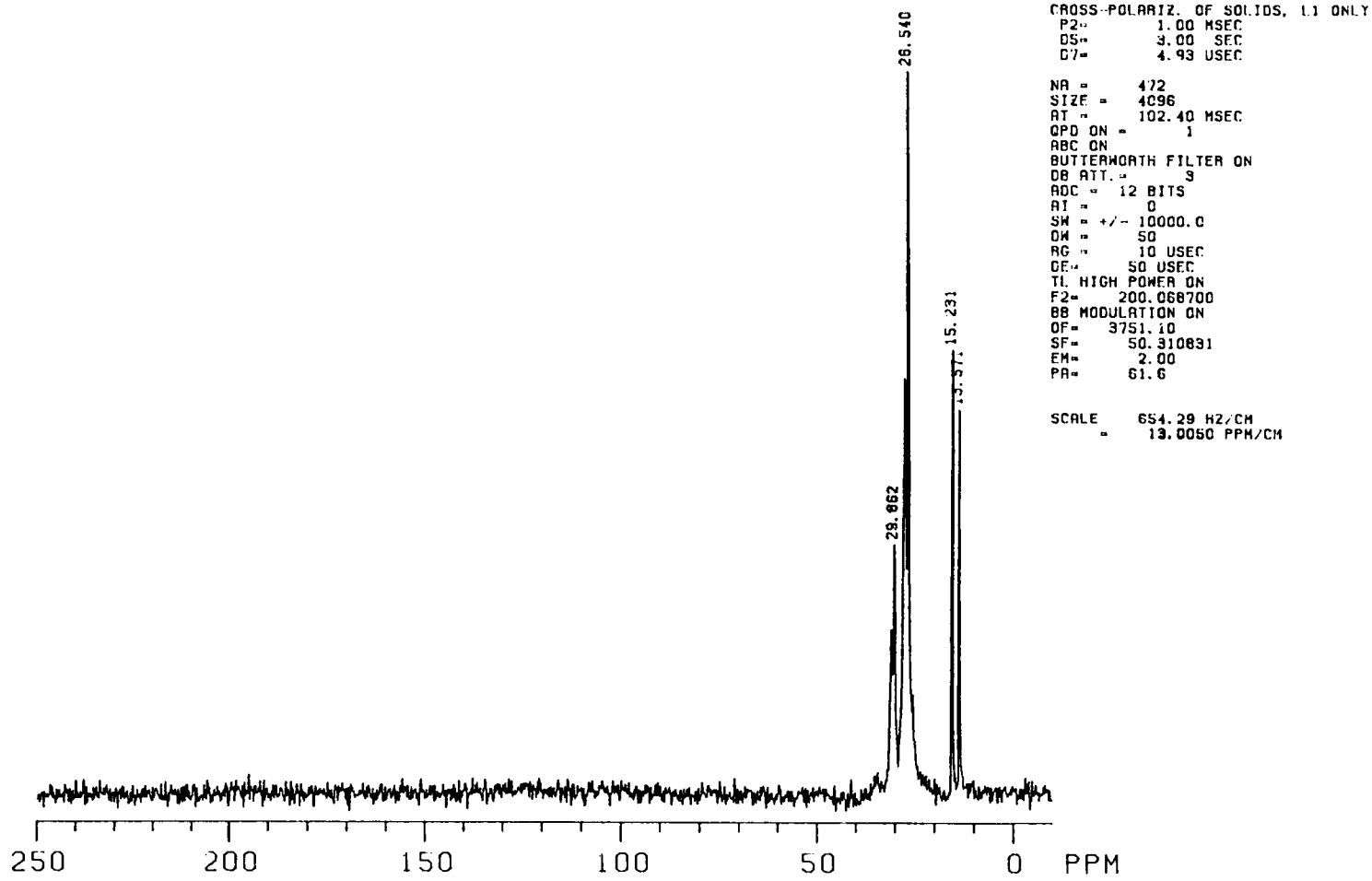


Figure 20. Carbon-13 Solid-State Nuclear Magnetic Resonance Spectrum of Dibutyltin Dichloride. Cross-Polarization of Solids - Magic Angle Spinning techniques used. Externally referenced to hexamethylbenzene set at δ 17.36.

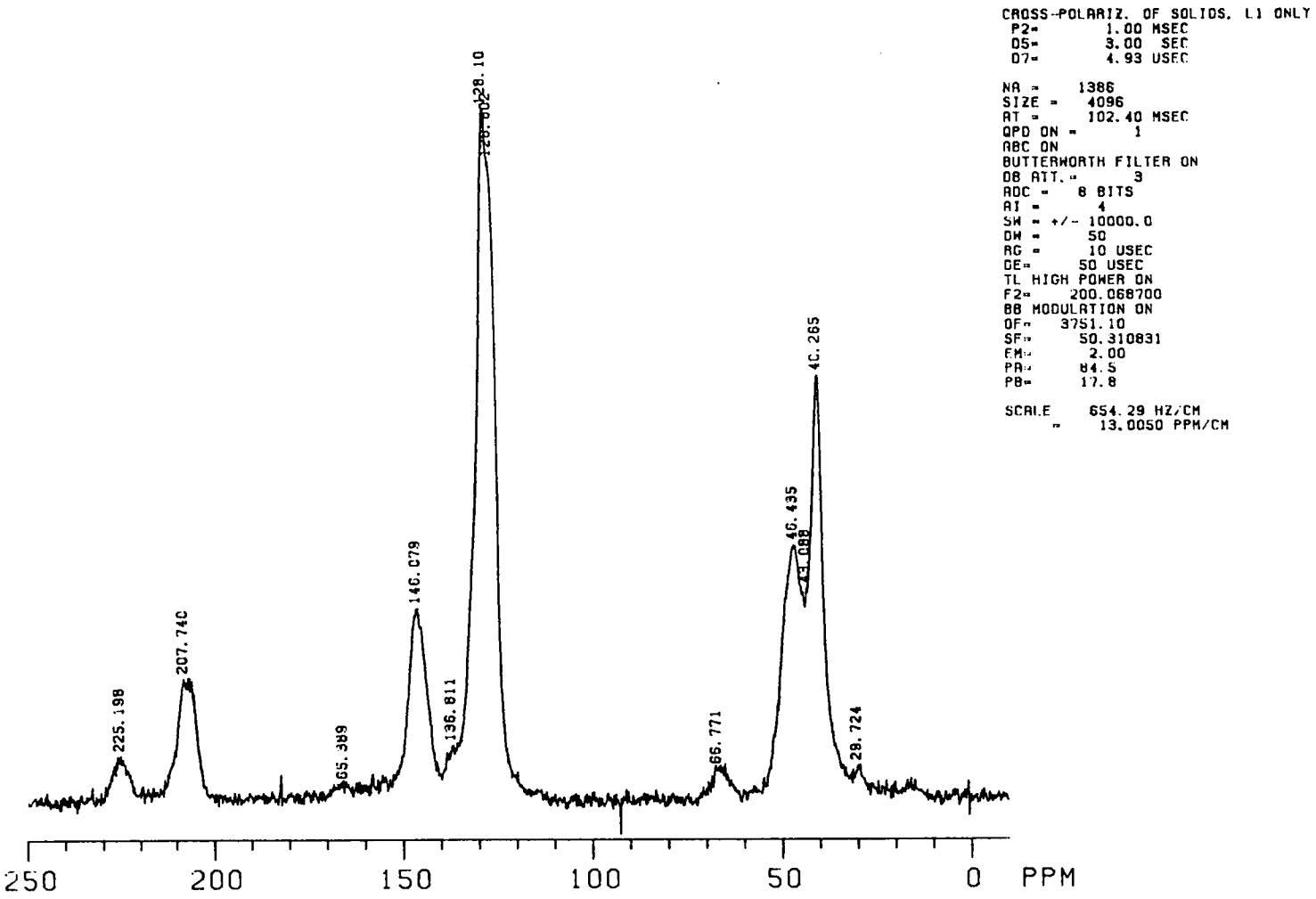


Figure 21. Carbon-13 Solid-State Nuclear Magnetic Resonance Spectrum of Amberlite XE-305. Cross-Polarization of Solids - Magic Angle Spinning techniques used. Externally referenced to hexamethylbenzene set at δ 17.36.

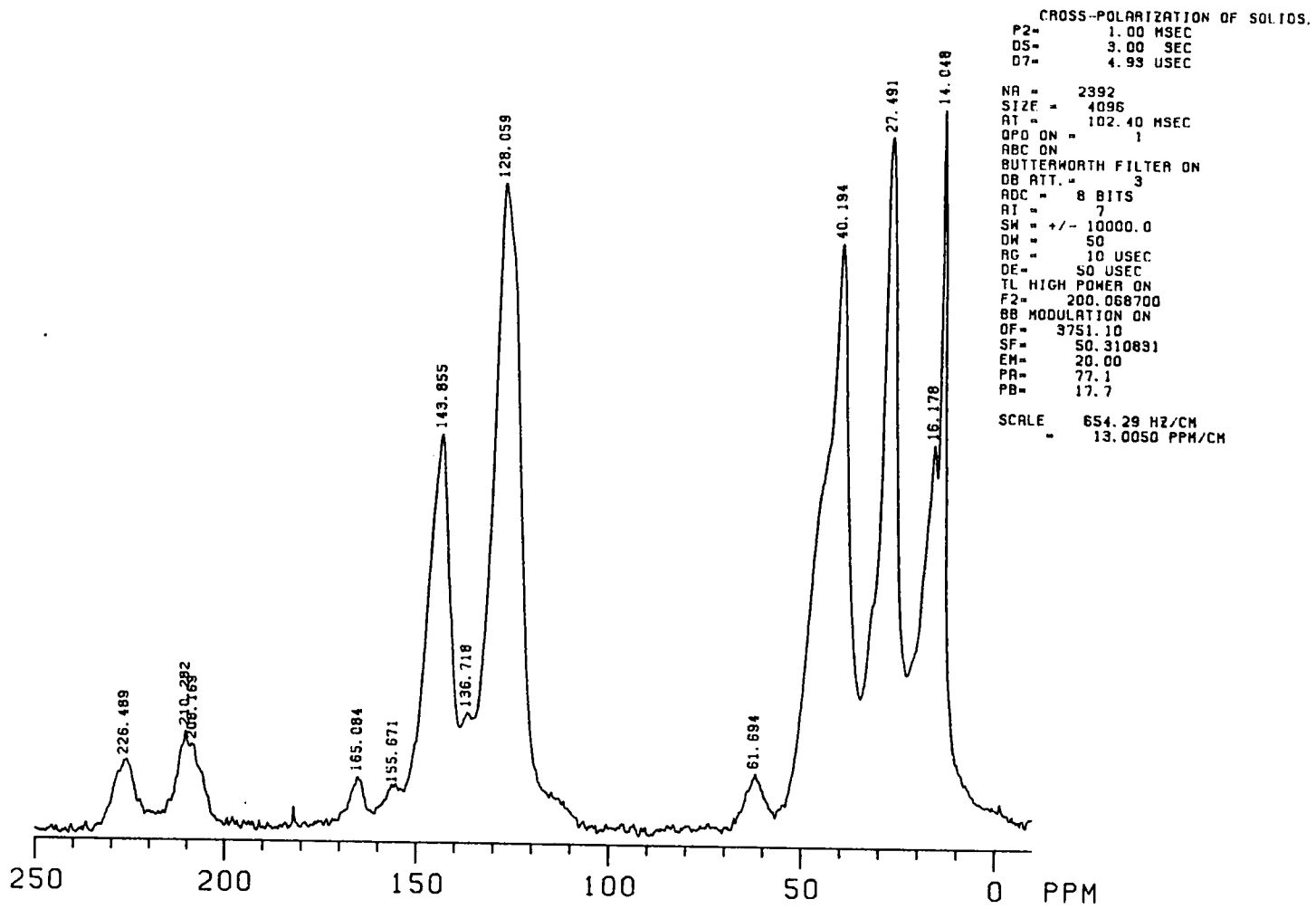


Figure 22. Carbon-13 Solid-State Nuclear Magnetic Resonance Spectrum of Poly{Dibuty[2-(3- and 4-ethenylphenyl)ethyl]tin Chloride. Cross-Polarization of Solids - Magic Angle Spinning techniques used. Externally referenced to hexamethylbenzene set at δ 17.36.

Carbon-13 of each polymer species was obtained and shows no discernible difference from that provided at Figure 22.

The absence of vinyl carbon absorbances, which resonate at δ 130 and δ 115, in any of the polymer species, 2%, 5%, 10%, 15%, and 20% DVB, indicate a high degree of conversion of the DVB vinyl groups in the polymerization. This was confirmed by probing the crosslinked nature of the beads by measuring the swelling ratio. A volume of each polymer was placed in toluene and the swollen volume measured. The results are presented in Table 7. Comparison of these results with the elemental analysis of chlorine content of the polymers presents some difficulties. The chlorine content does not reflect a linear trend as would be expected with changes of tin-chloride ligand content associated with changes to the polymer DVB content.

Table 7. Swelling Study of DVB-Dibutyltin Ligand Polymer Beads Compared to Chlorine Content.

DVB Content	**2**	**5**	**10**	**15**	**20**
Beginning Volume	1.00 mL	1.00 mL	n/a	1.00 mL	1.00 mL
Ending Volume	2.87 mL	2.25 mL	n/a	2.09 mL	1.98 mL
Ratio % (End/ Beginning)	287	225	n/a	209	198
Chlorine Content (by elemental analysis)	1.735	1.630	0.883	0.934	1.061

Chlorine content by elemental analysis is consistent for increasing DVB content for the 2%, 5%, and 15% beads. This linear trend of chlorine content changes between beads of 15% and 20% DVB content. Analysis of experimental data shows that DVB added to the reaction mixtures did not always maintain the targets, although these are still representative of the DVB content. However, for the 15% DVB target, actual content was 16.2%, and for the 20% target, actual content was only 18%. Therefore, the difference in chlorine content between the 16.2% DVB bead of 0.934 and the 18% DVB bead of 1.061 may represent other factors than changes in crosslink ratios.

The reflectance Fourier Transform Infrared spectrum is reproduced in Figure 23 and shows the characteristic C-H alkyl stretch at 2800 cm^{-1}, 1603–1490 cm^{-1}, phenyl pair, Sn-C asymmetric stretch 599 cm^{-1}, Sn-C symmetric stretch 500 cm^{-1}.[110]

Preparation of Poly{dibutyl[2-(3- and 4-ethenylphenyl)ethyl]tin Chloride Reagent Using Dibutyl[2-(3- and 4-ethylphenyl)ethyl]tin Chloride Diluent

To distinguish between the two types of polymer-supported reagents prepared, different terms will be used to designate the type of diluent used in the polymerization. The first macroporous type utilized a non-solvating diluent for the polymer and resulted in the formation of macroporous polymer beads. The second type utilized a solvating diluent, dibutyl[2-(3- and 4-ethylphenyl)ethyl]tin chloride, and will be referred to as pseudo-macroporous. The pseudo-macroporous polymer-supported reagent was formed

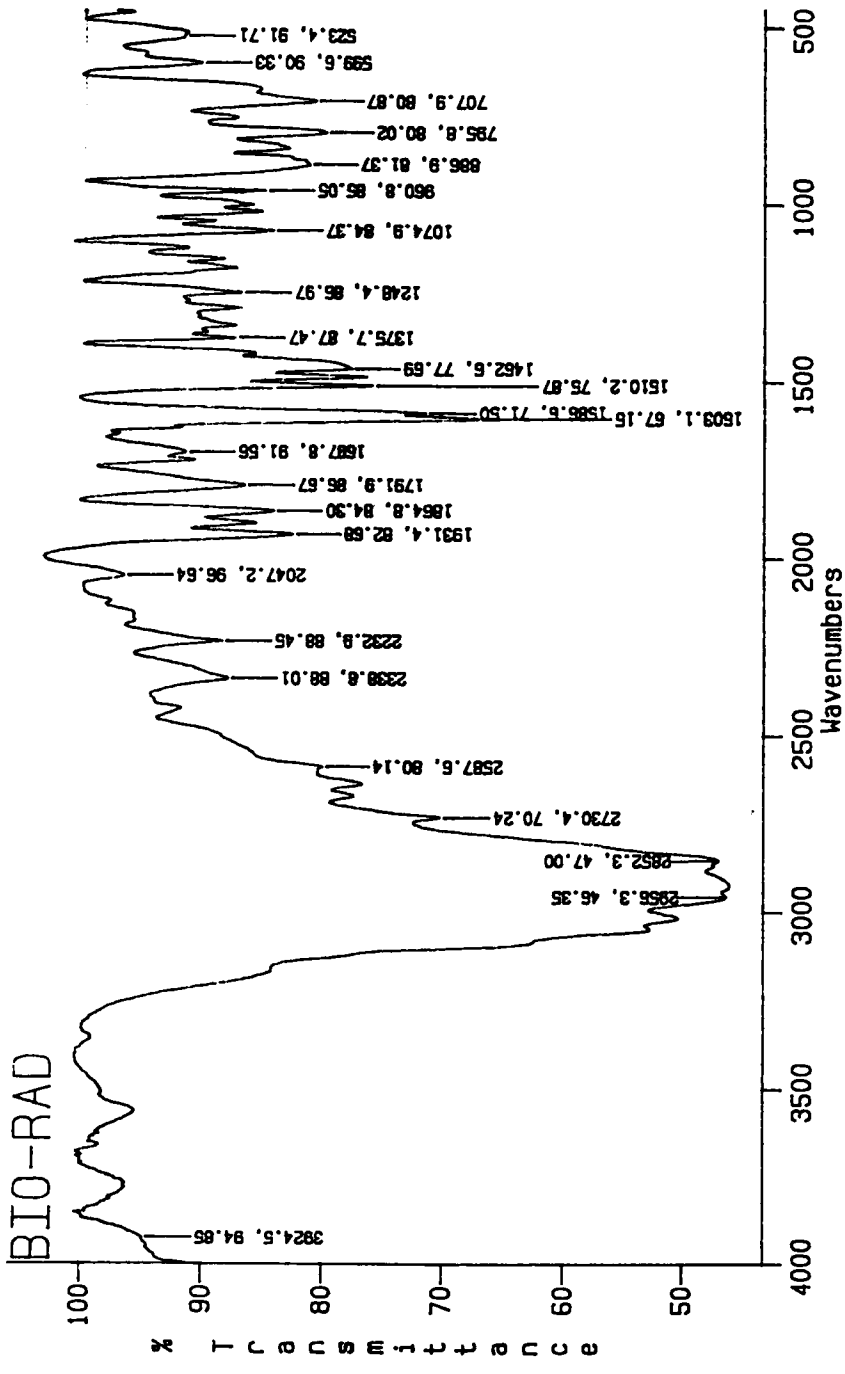
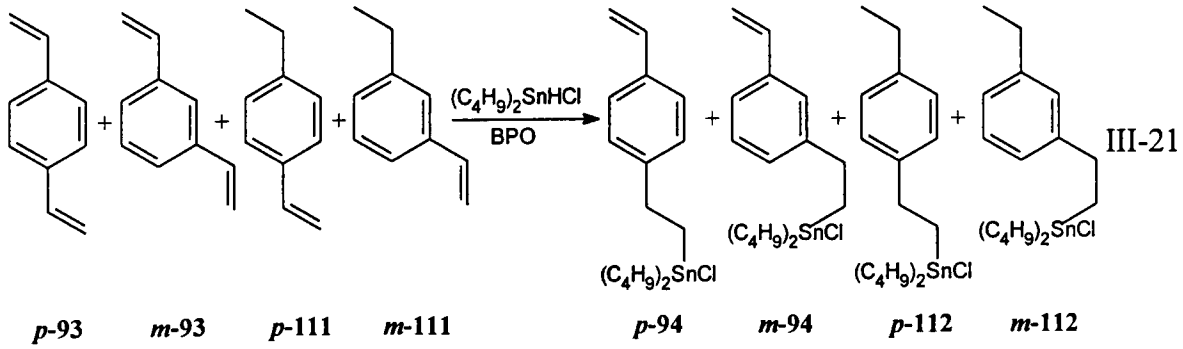


Figure 23. Reflectance Fourier Transform Infrared Spectra of Poly{Dibutyl[2-(3- and 4-ethylphenyl)ethyl]tin Chloride}.

from monomer synthesized from the unpurified technical divinylbenzene-ethylvinylbenzene mixture containing *m*-**93** and *p*-**93**, and *m*-**111** and *p*-**111** which forms the monomer/diluent mixture of *m*-**94** and *p*-**94**, and *m*-**112** and *p*-**112** (Equation III-21).



III-21

p-93 *m*-93 *p*-111 *m*-111 *p*-94 *m*-94 *p*-112 *m*-112

The formation of the macroporous and pseudo-macroporous polymer-supported reagent were identical with the exception of the diluent used. The diluents were removed following polymerization by solvent extraction of the beads in a Soxhlet extractor using, sequentially, toluene, acetone, and finally methanol. Microphotographs of the pseudo-macroporous beads were obtained and are presented in Figure 24. The translucent nature of the beads indicates the presence of pores, but of a different characteristic than those which are formed using the 1-octanol.

The proton NMR spectrum of dibutyl[2(3- and 4-ethylphenyl)ethyl]tin chloride diluent is presented in Figure 25. The resonances from aromatic protons at δ 7.2, methylene protons on carbon attached to aromatic ring at δ 3.0 and δ 2.6, and remaining

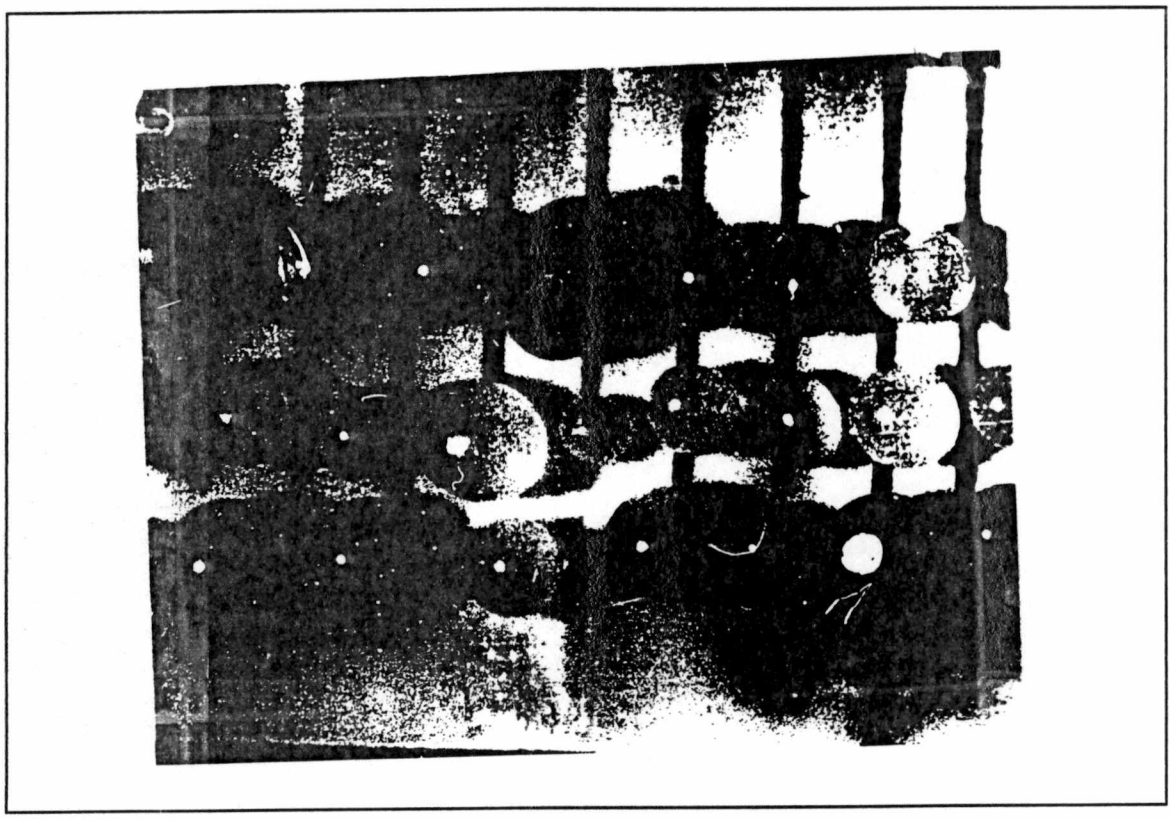


Figure 24. Microphotographs of Macroporous-2 Dibutyl[2-(3- and 4-ethenyl-phenyl)ethyl]tin Chloride–Divinylbenzene Copolymer.

alkyl absorbances are evident. Figure 26 is the tin-119 solution NMR spectrum of dibutyl[2(3- and 4-ethylphenyl)ethyl]tin chloride diluent with the dibutyltin chloride absorbance at δ 106 referenced to tetramethyltin. The solution carbon-13 NMR spectrum of the compound is presented in Figure 27.

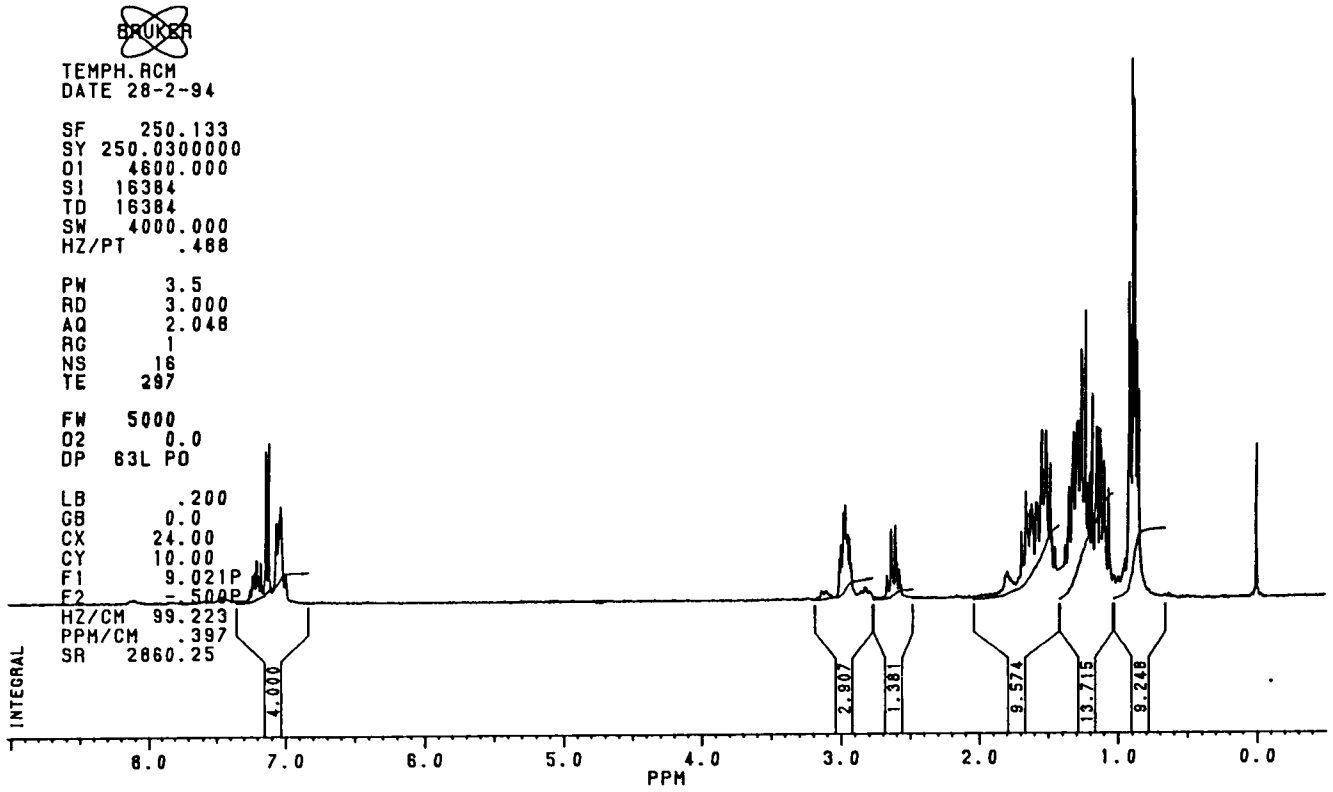


Figure 25. Proton Nuclear Magnetic Resonance Spectrum of Dibutyl[2-(3- and 4-ethylphenyl)ethyl]tin Chloride. Solvent: Deuterochloroform. Reference: Tetramethylsilane, δ 0.00.

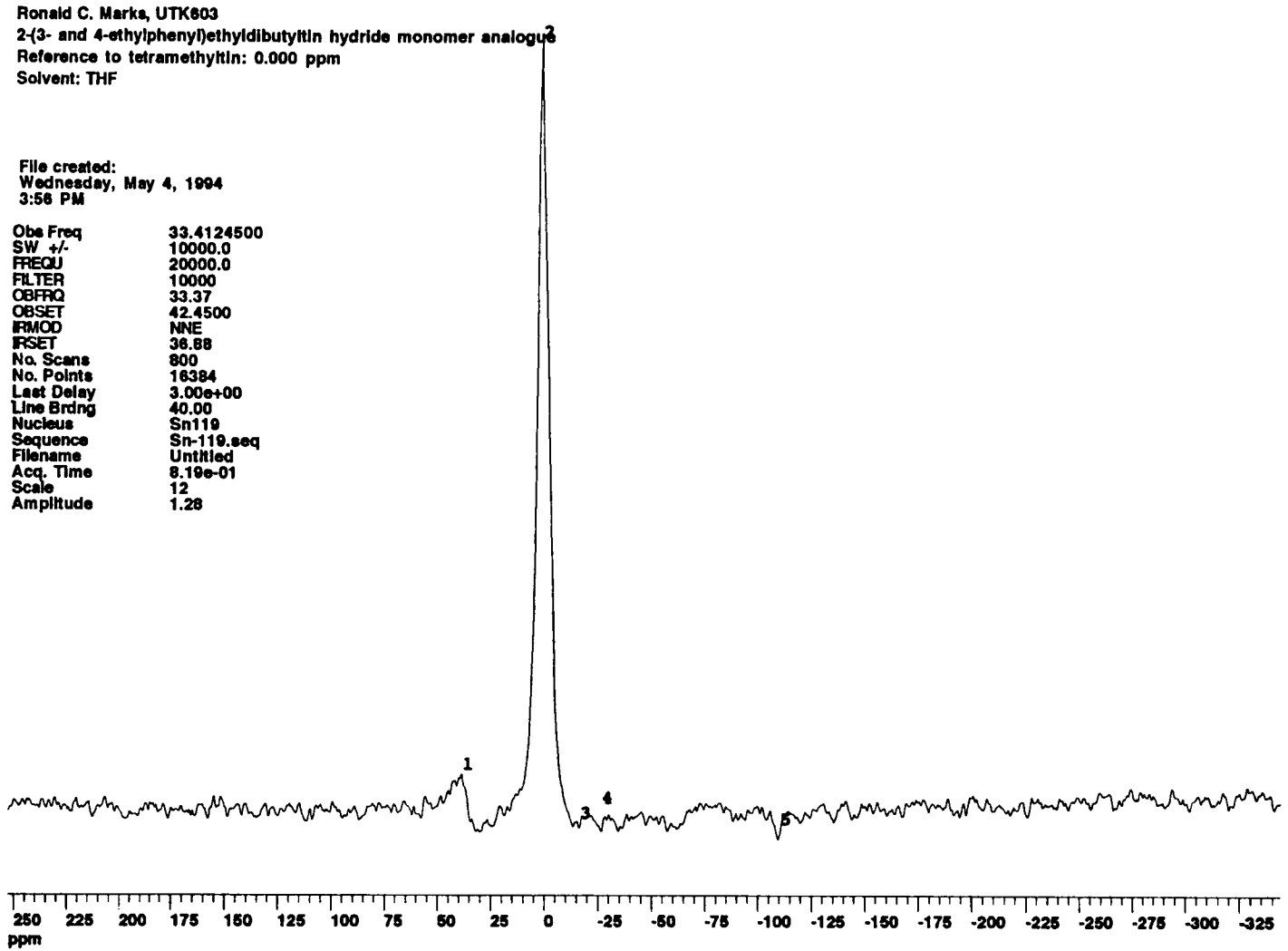


Figure 26. Solution Tin-119 Nuclear Magnetic Resonance Spectrum of Dibutyl[2-(3- and 4-ethylphenyl)ethyl]tin Chloride. Solvent: Tetrahydrofuran. Reference: Tetramethyltin, δ 0.00.

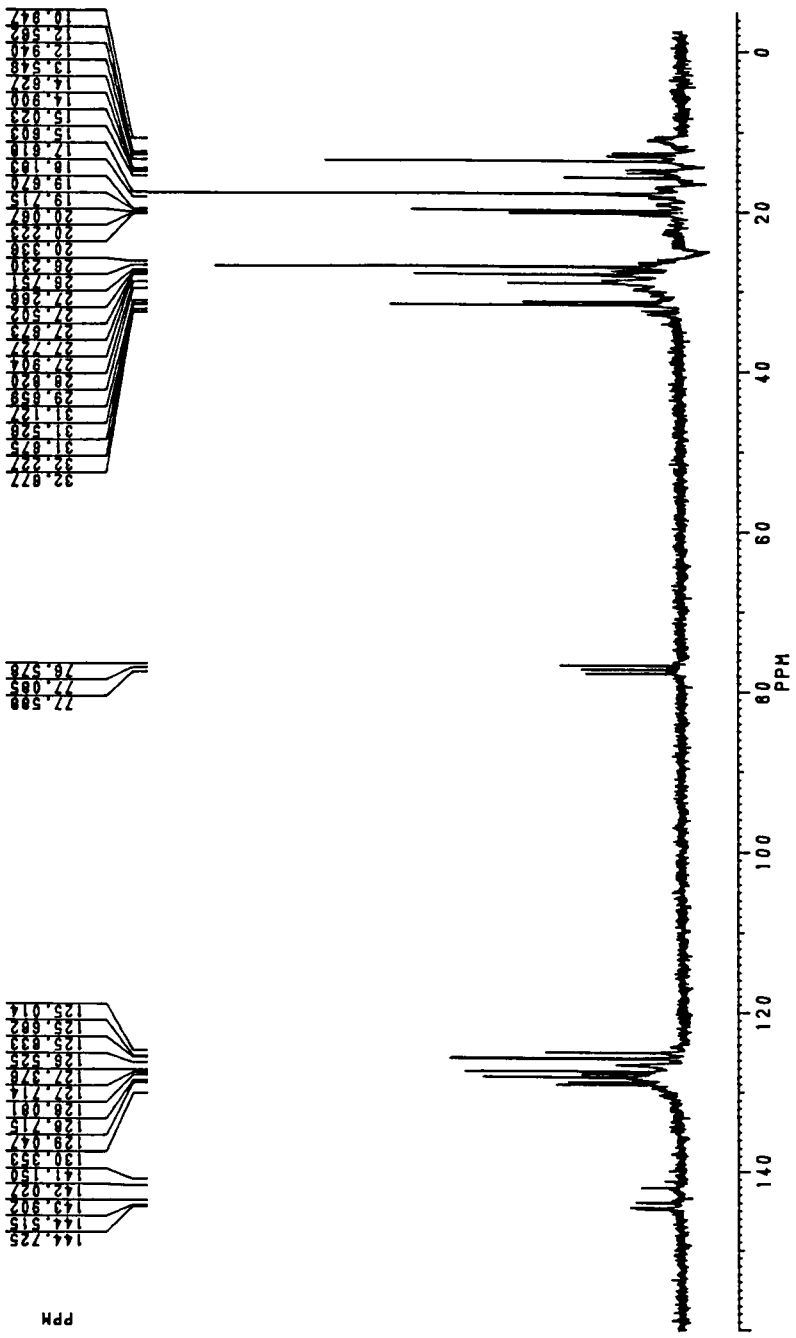


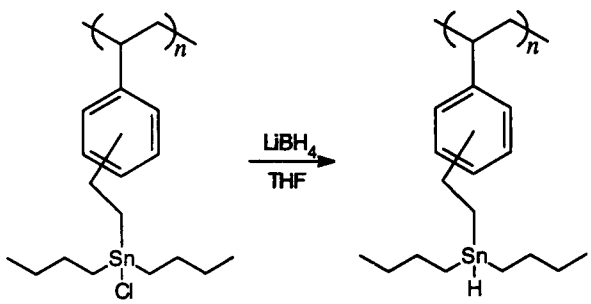
Figure 27. Solution Carbon-13 Nuclear Magnetic Resonance Spectrum of Dibutyl[2-(3- and 4-ethylphenyl)ethyl]tin Chloride. Solvent: Deuterochloroform. Reference: Deuterochlorform, δ 77.0.

C. Hydrostannation of Alkynes Using the Polymer-Supported Dibutyl[2-(3- and 4-ethenylphenyl)ethyl]tin Hydride Reagent

Reagent Preparation

Reduction to the Dibutyltin Hydride

Reduction of the dibutyltin chloride ligand **98** was investigated using lithium borohydride in tetrahydrofuran and diisobutylaluminum hydride in toluene. The reduction using $LiBH_4$ as the reducing agent is shown in Equation III-22.



98 **105**

III-22

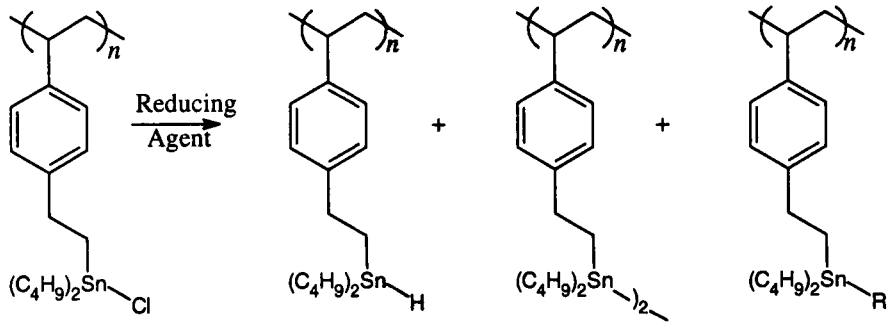
Gerigk *et al.*,[109] investigated six systems for the reduction of dibutyltin chloride moiety: lithium aluminum hydride ($LiAlH_4$) in tetrahydrofuran, sodium borohydride ($NaBH_4$) in diglyme, diisobutylaluminum hydride (DIBALH) in benzene/toluene and in tetrahydrofuran, and dibutylaluminum hydride (Bu_2AlH) in benzene/toluene and in tetrahydrofuran. Gerigk *et al.*, tested each of these reagents on a model compound, dibutyl[2-(4-isopropylphenyl)ethyl]tin chloride, and determined the product distributions

using high-performance liquid chromatography (HPLC). The results were extended to poly{dibutyl[2-(4-ethenylphenyl)ethyl]tin chloride} and are reproduced in Table 8. They concluded the strength of the reducing agent greatly influenced the yield of tin hydride due to formation of distannane; furthermore, complexing solvents reduced formation of the alkylation product during the reaction (Equation III-23). Although $LiAlH_4$ in THF gave initial good results, they reported that the dibutyltin hydride **105** was rapidly reduced to the distannyl product **113**. Their research on the model compound lead them to select Bu_2AlH in THF for their remaining work to give highest overall yield of the tin hydride **105**.

Table 8. Distribution of Reduction Products Using Various Reducing Systems on Dibutyl[2-(4-isopropylphenyl)ethyl]tin Chloride, a Small Molecule Analogue of the Polymer-Supported Reagent.

Reduction Product	**$LiAlH_4$ in THF**	**$NaBH_4$ in diglyme**	**DIBALH in benzene/ toluene**	**DIBALH in THF**	**Bu_2AlH in benzene/ toluene**	**Bu_2AlH in THF**
Tin-hydride **105**	1.40	1.40	0.50	1.10	0.60	1.50
Di-tin **113**	-	0.18	0.20	0.30	0.18	0.15
Alkylation Product **114**	-	-	1.00	0.20	0.90	0.10

All data is in mmol/g resin and is related to a tin-Cl content of the polymer of 1.9 mmol/g (degree of functionalization = 0.76)



98 **105** **113** **114**

III-23

The researchers limited their report by excluding $LiBH_4$ and ignoring THF and diethyl ether as a complexing solvent for the borohydrides. It is known that borohydrides show an increase in reducing power as the metal ion changes along the series $NaBH_4$ < $LiBH_4$ < $Mg(BH_4)_2$ < $Al(BH_4)_3$.[111] Additionally, they could have reduced the strength of the aluminum hydrides by introducing alkoxy substituents, which are reported to have increasing strength along the series $Li(t\text{-BuO})_3AlH$ < $Li(CH_3O)_3AlH$ < $LiAlH_4$.[111] The results reported in this dissertation using DIBALH in toluene and $LiBH_4$ in THF agree with the conclusions of Gerigk. The non-complexing solvent toluene, in conjunction with the strong reducing agent DIBALH, lead to the predominant formation of distannyl links and alkylation of the functional site, while complexing solvents such as THF combined with moderate reducing agents, in this case $LiBH_4$, provided higher yields of the tin hydride functionality. The reduction was monitored using tin-119 NMR.

The tin-119 solid-state NMR spectrum of the polymer beads, after reduction, reveal that the tin alkylation product, resonating at δ -14, is the major product from

DIBALH in toluene (Figure 28), while use of $LiBH_4$ in THF leads to the formation of the tin hydride, which resonates at δ -85 (Figure 29). Attempts to hydrostannate the polymer formed from DIBALH in toluene showed no change in the tin-alkyl resonance even though the tin-hydride resonance indicates hydrostannation of those sites had occurred (Figure 30).

The reduction was accomplished using the apparatus shown in Figure 31. Beads containing the dibutyltin chloride ligand were swollen in dry THF, and then the $LiBH_4$ in ether was added slowly over approximately one hour. The reaction was allowed to proceed for 12 hours to insure access to all active sites, and then the beads separated. Additional washings with dry THF were followed by passing argon over the beads to dry them. The beads were used without further purification.

Hydrostannation of Alkynes Using Poly{Dibutyl[2-(3- and 4-ethenylphenyl)ethyl]tin Hydride Reagent

The tin hydride **105** was used in the hydrostannation of 1-decyne (Equation III-24). Leusink *et al.*,[112] reported that hydrostannations of alkynes preferentially form the (*Z*)-isomer as the kinetic product. Rearrangement to the thermodynamically favored (*E*)-isomer proceeds via *anti*-addition and *anti*-elimination of a trialkyltin radical, formed by a free-radical source and the trialkyltin hydride. This rearrangement may be visualized using Neumann projections of the addition product intermediate shown in Scheme 10.

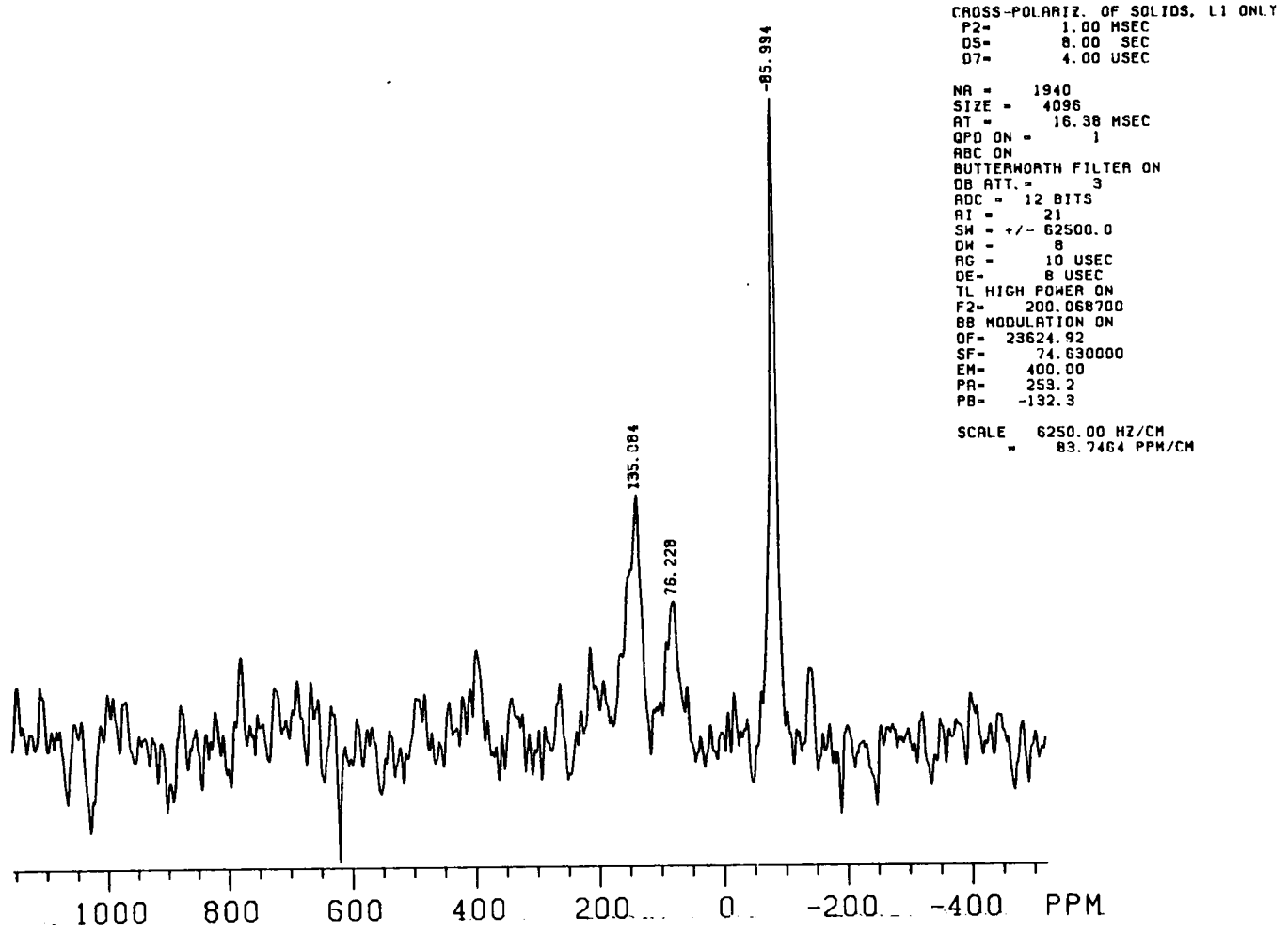


Figure 28. Tin-119 Solid-State Nuclear Magnetic Resonance Spectra Using Cross-Polarization Magic Angle Spinning of Reduction of Tin Chloride Moiety Using $LiAlH_4$ in THF.

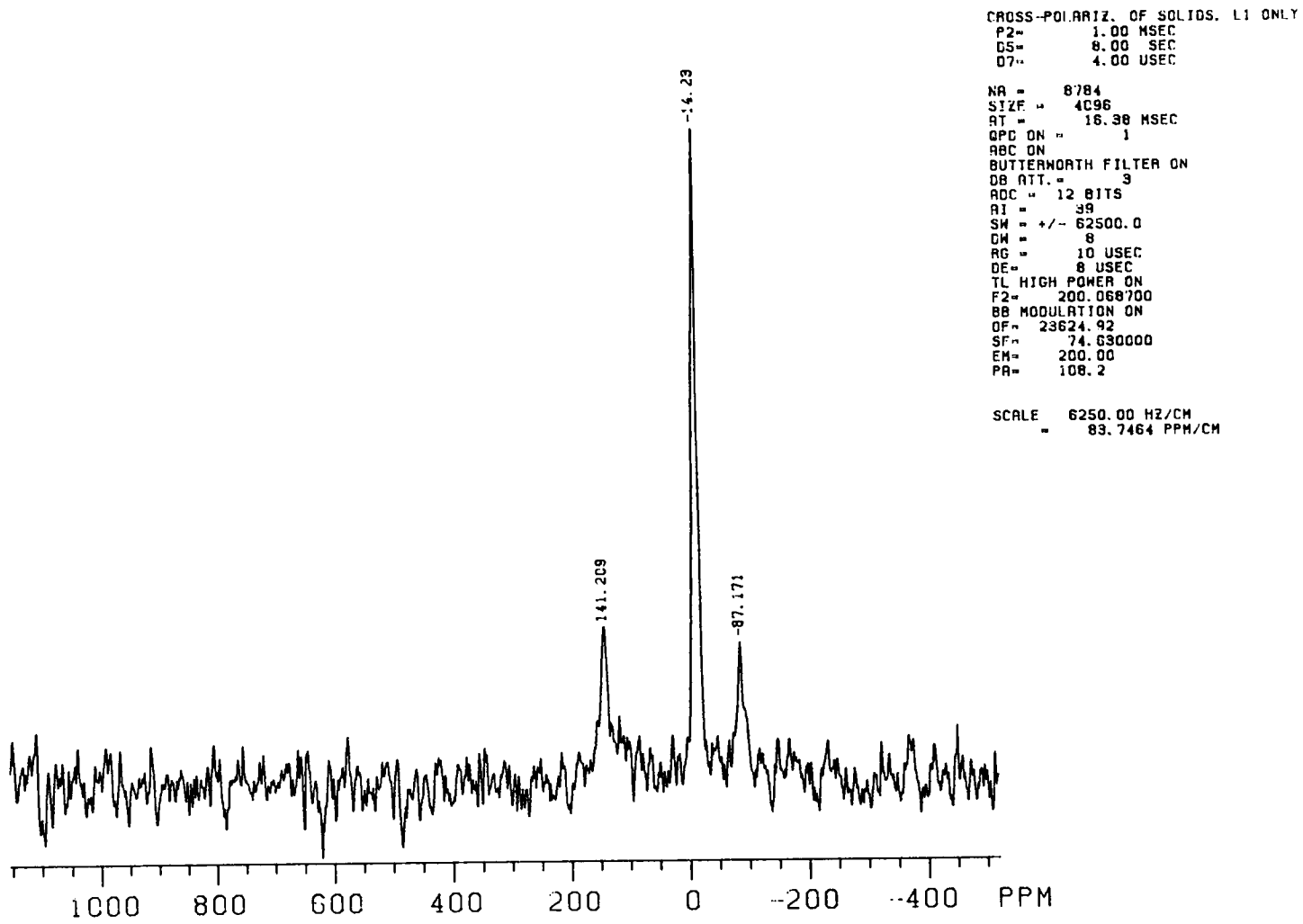


Figure 29. Tin-119 Solid-State Nuclear Magnetic Resonance Spectra Using Cross-Polarization Magic Angle Spinning of Reduction of Tin Chloride Moiety Using Diisobutylaluminum Hydride in Toluene.

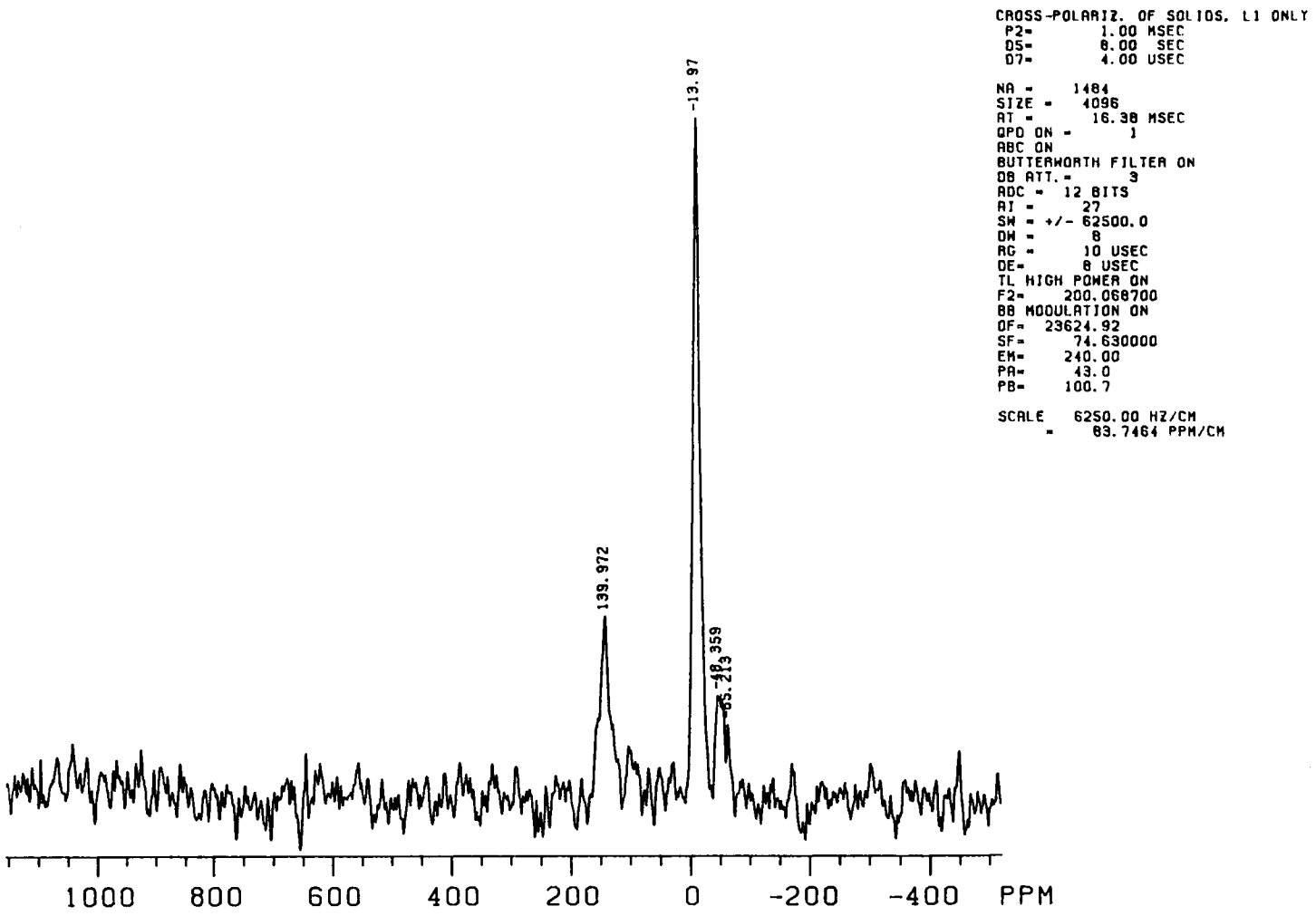


Figure 30. Tin-119 Solid-State Nuclear Magnetic Resonance Spectra Using Cross-Polarization Magic Angle Spinning of Polymer Following Hydrostannation of Tin Hydride from Diisobutylaluminum Hydride Reduction in Toluene.

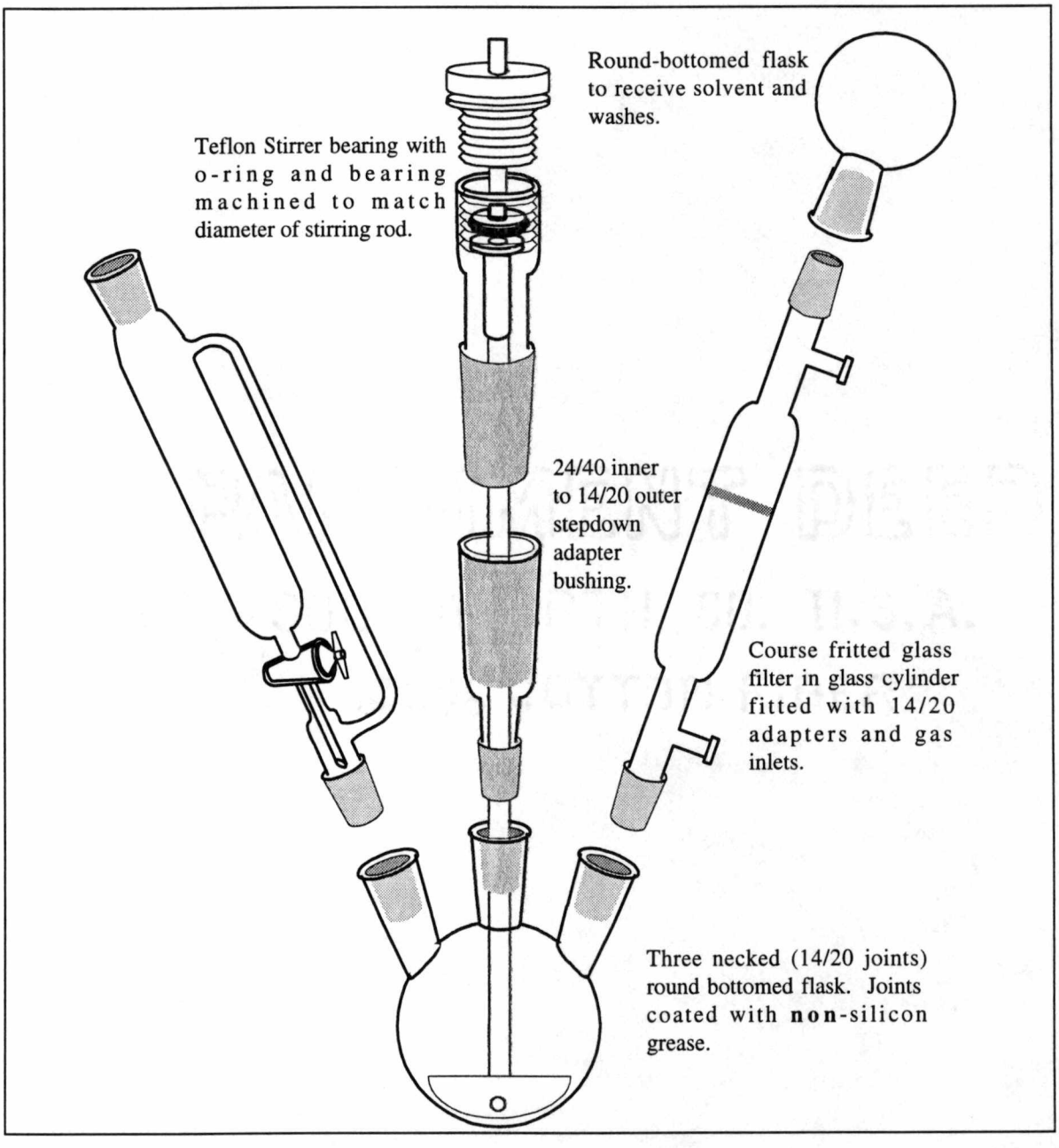
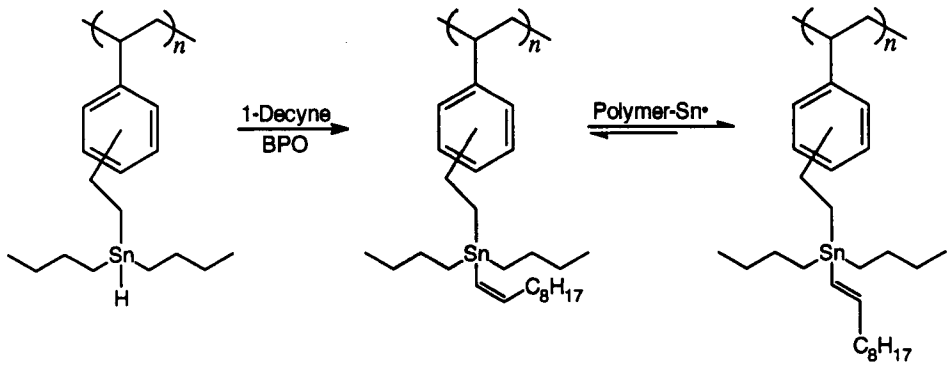


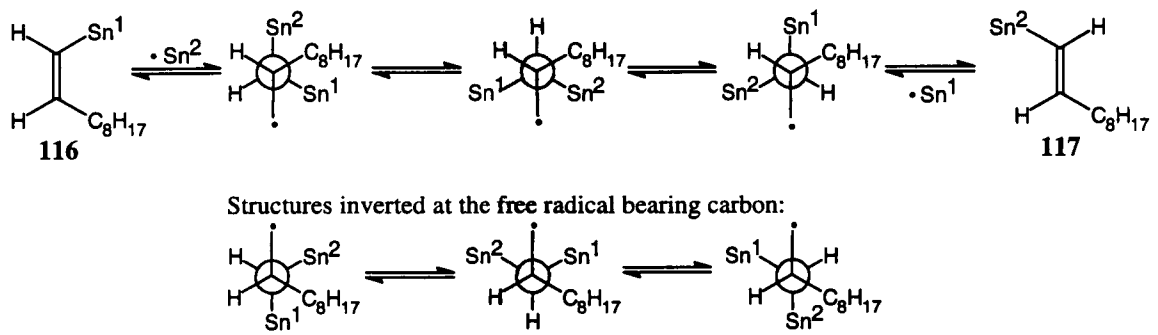
Figure 31. Reaction Flask with Dropping Funnel, Stirring Paddle, and Filtering System for Reduction of Polymeric Dibutylethyltin Chloride.



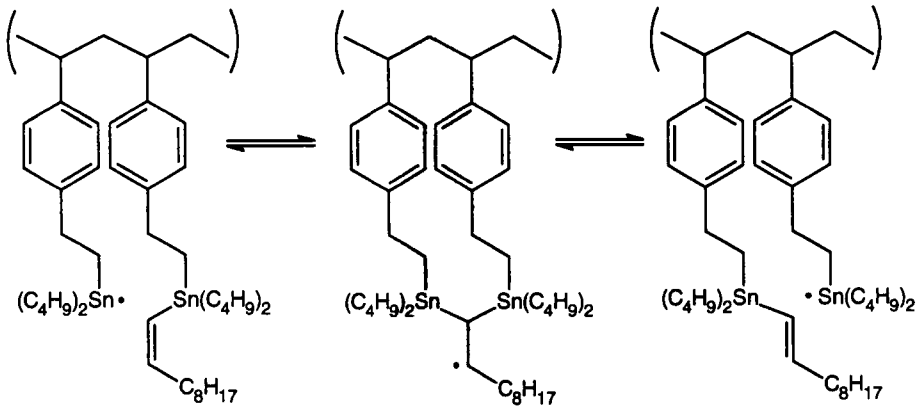
III-24

105 *(Z)*-**115** *(E)*-**115**

Addition of the tin radical to the (*Z*)-isomer **116** yields the *anti*-adduct. Rotomers of this adduct are shown, with the final rotomer in the conformation for *anti*-elimination of Sn^1 to yield the thermodynamically favored (*E*)-isomer **117**. Leusink noted that the addition of a tin radical is assumed to form a tetrahedral radical center which is capable of quick inversion. The inversion isomers of the rotomers are also shown in Scheme 10, with the rotomer leading to *anti*-elimination to give the (*E*)-isomer.



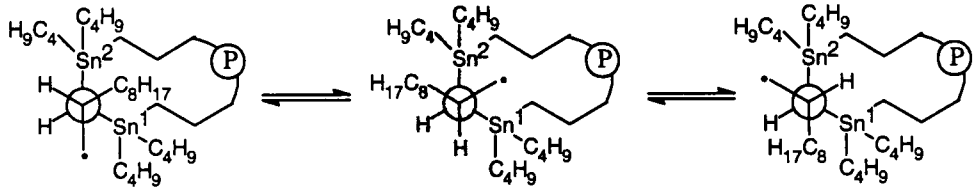
Scheme 10. Tin Radical Catalyzed Rearrangement of Hydrostannylated Alkene to the Thermodynamic Product.



118 119 120

III-25

The extension of this reasoning to the polymer-supported dibutylethyltin reagent is presented in Equation III-25. Addition of a tin radical to the product of the hydrostannation of 1-decyne, (*Z*)-dibutyl[2-(3-ethenylphenyl)ethyl]-1-decenyltin (**118**) gives an intermediate ditin radical **119**. Elimination of a tin radical results in the thermodynamically favored (*E*)-dibutyl[2-(3-ethenylphenyl)ethyl]-1-decenyltin (**120**). Rotomers of the radical addition product are shown in Equation III-26. Rotomer **119c**



119a **119b** **119c**

III-26

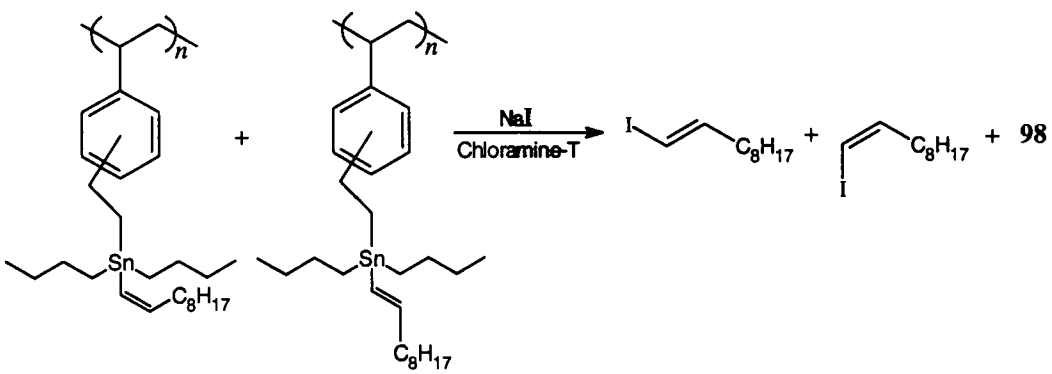
possesses the correct conformation for *anti*-elimination to give **120**, which indicates the polymer matrix, though providing some rigidity to the structure, should not prohibit the rearrangement. Several important differences between the polymer and solution reactions should be noted. Equation III-25 shows only a single possibility of the multitude of microenvironments of the polymer-supported vinyltin reagent. The combination shown

of a proximal tin radical with vinyltin ligand, in the absence of any other tin radical source, reveals the necessity of having two tin atoms near one another. This arrangement may occur by the existence of two reagent ligands next to one another on the same chain segment, or on separate segments but arranged to be close to one another. Only for the case of proximal tin groups can this radical catalyzed rearrangement occur. Leusink *et al.*, indicated rearrangement only proceeds with the assistance of a tin radical, and does not occur with the free-radical initiator or tin hydride alone. Polymer diad **119** corresponds to the initial addition of a second tin radical to the tin containing carbon, forming the radical intermediate necessary for rearrangement.

In each experiment of this study, excess alkyne was utilized to reduce the availability of tin hydride sites which would result in the isomerization process and to maximize functionalization of available sites. By limiting this variable, it was theorized that the processes occurring within the polymer matrix could be clarified. However, diffusion effects may limit the reaction rate such that not all sites would be functionalized simultaneously. In each situation where a hydrostannation occurs adjacent to an unfunctionalized tin hydride, the resulting radical would initiate rearrangement to the (*E*)-isomer.

Iododestannylation: Formation of Iodoalkenes

Iodination of alkynes using the polymer bound alkenyl reagent was straightforward. After swelling the dibutyltin hydride polymer in technical tetrahydrofuran in a flask shielded from direct light, sodium iodide was added and the iodide allowed to diffuse into the bead. The oxidant was added and the reaction allowed to proceed for three hours (Equation III-27). This excessive time was designed to allow diffusion of the hydrophilic reagents into the hydrophobic polymer matrix. The reaction was quenched using a saturated sodium thiosulfate solution, followed by extraction of the products.

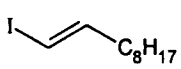
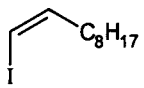


III-27

(Z)-**115** *(E)*-**115** *(E)*-**121** *(Z)*-**121**

The product extracts, in ether, were analyzed by capillary gas chromatography to determine isomer ratios. These ratios and their relationship to the various polymer crosslinkings are shown in Table 9.

Table 9. Isomeric Ratios Related to Divinylbenzene Content.

Isomer	Target DVB Content of Copolymer Beads 2	5	10	15	20
 (*E*)-**121**	74.5 %	46.5 %	56.5 %	62.6 %	74.3 %
 (*Z*)-**121**	25.5 %	53.5 %	43.5 %	37.4 %	25.7 %

Two striking anomalies are apparent from the data in Table 9: the reversal of major isomer ratios between the 2% and 5% DVB beads and the similar distribution of isomers for both 5% and 10% DVB beads.

Iododecene Isomeric Ratio Considerations

Halodemetallation of the vinylic tin to the vinylic iodide is known to proceed with retention of configuration at the vinylic carbon.[113] Therefore, the *E*/*Z* ratios of the iododecenes reflects the original stereochemistry of the vinyltin ligand. Stereochemistry of this ligand is controlled by solvent polarity, application of radical catalysts, effects of polar substituents on alkynyl carbons, and general reactivity of the tin hydride. The system utilized for hydrostannation incorporated a very slightly polar solvent, toluene, with a free-radical source and a relatively reactive tin hydride. Although the tin hydride was not present in excess, containing the reagent within a polymer framework could provide a microenvironment for the reaction in which an excess of tin hydride would be

present due to diffusional effects of reagents in and out of the polymer matrix. The chemical properties of this microenvironment may be influenced by modification of the bulk physical properties of the polymer such as crosslinking, porosity, and polarity of polymer matrix.

Polymer beads used in this study differed by amount of crosslinking agent added during polymerization and by selection of two different diluents. By assuming that the reactants proceeded to high degrees of reaction, then the crosslink ratios achieved will approximate the amount of DVB added, resulting in the five polymer systems reported. This assumption is supported by two experiments. Swelling ratios of four of the polymer systems, 2, 5, 15, and 20% DVB content, presented results consisted with assumed degree of crosslinking. In addition, carbon-13 solid-state NMR showed no evidence of residual vinyl groups in the polymer beads. Conversly, elemental analysis for chlorine content gave inconclusive results concerning polymer content other than for chlorine-tin ligand content. Chlorine content of the polymer may not reflect the tin ligand content due to formation of tin-tin bonds, or other tin-atoms bonds formed during monomer preparation and polymerization.

Comparison of the mole percent of crosslinking agent in each polymer system of the crosslink levels indicates DVB changes, though providing polymers of different bulk physical strength, are of greater composition difference than weight percent indicates.

Table 10. Crosslinking Agent Added Showing Theoretical Polymer Content by Weight Percent and Mole Percent of Divinylbenzene, Ethylvinylbenzene, and Dibutyltin Ligand.

Weight % DVB Added	**2**	**5**	**10**	**15**	**20**
DVB mole %	3%	8%	14%	19%	24%
EVB mole %	3%	6%	11%	16%	19%
Tin ligand mole %	94%	86%	75%	65%	57%

Using the data in Table 10, comparisons can be made concerning the amount of DVB in each polymer by weight percent and mole percent. At 20% crosslinking agent added, the mole percent of DVB has reached 24% of the polymer composition, with EVB providing 19% mole percent, and the tin ligand only 57%. The polymer with 2% crosslinking agent added would theoretically have a mole composition of 94% tin ligand. In the absence of any other considerations, the probability of two tin ligands adjacent are much greater in the 2% DVB polymer, and decreases to the 20% DVB polymer.

The isomeric ratio of the iododecene from 2% and 20% DVB copolymers is nearly identical at 74:25 *E*:*Z*. This may be a result of the distribution of functional sites within the polymer matrix. Diads, triads, and other units of functional ligands will exist within the matrix due to the different reactivity ratios of divinylbenzene, ethylvinylbenzene, and the tin monomer. As summarized in Part I, Chapter 2, Table 2, the reactivity ratios vary from 1 for *p*-EVB to 7 for *p*-DVB and 4 for *m*-DVB. By assuming the dibutyl[2-(3- and 4-ethenylphenyl)ethyl]tin chloride monomer will have a

reactivity ratio similar to EVB, a comparison of reactivity ratios indicates that using this system will result in the monomer, EVB, and DVB wil not form a block-like copolymer, nor an alternating copolymer. However, small units containing adjacent monomer units of DVB, EVB, and the monomer ligand will form during the polymerization. Formation of tin ligand units may be supported by the experimental data which requires the concurrent availability of adjacent tin species for rearrangement of the *Z*-to *E*-isomer to occur. It should be emphasized that the existance of two tin units concurrent on the polymer chain is not required for this reaction to occur, with the possiblity of chain-chain ligand interaction also contributing to the observed rearrangement.

The remaining anomaly of *E:Z* ratio for the 5 and 10% crosslinked copolymers may be understood through changes in diluent. For these polymers, the solvating diluent, dibutyl[2-(3- and 4-ethylphenyl)ethyl]tin chloride, was utilized in contrast to a combination of 1-octanol and dibutyl[2-(3- and 4-ethylphenyl)ethyl]tin chloride for the 2, 15, and 20% copolymers. Polymers with macrochannels of different characteristics would be formed from these two differing diluents, though the characteristics of these macrochannels were not obtained.

Variables which influence the extent of site interactions in a polymer matrix include the degree of crosslinking, degree of functionalization, solvent swell, and physical changes to the polymer which result in bulk physical changes.[114] As crosslinking

increases, the mobility of polymer segments decreases, increasing the opportunity for two sites to be in close enough proximity to interact. Increasing the number of functional sites also increases the availability of two or more adjacent sites for interaction. Chang and Ford[115] studied ester conversions to their enolates using functional loadings up to 0.67 mmol per gram polymer and found the highest yields resulting from a 20% DVB macroporous polymer.

The system utilized in this study employed functional site loadings of 0.883 to 1.735 mmol per gram polymer. These could be effected by formation of tin-tin links formed during reduction of the tin chloride, although steps were taken to reduce this occurrence. Variations of the *E/Z* ratios indicate site-site interactions are occurring. Without the interaction of a tin radical, the rearrangement of (*Z*)- to (*E*)-isomer should not occur. Very little change in the *E/Z* ratio is observed between the 5%, 15%, and 20% crosslinked polymers, indicating that site interaction is unaffected at these crosslinked levels with toluene as solvent. For the 5% and 10% polymers made from solvating porogen, the results indicate site isolation is occurring, though not complete.

CHAPTER 4

EXPERIMENTAL

A. General

Gas chromatography (GC) was performed on a Hewlett-Packard 5890A capillary instrument equipped with a 30 meter x 0.25 mm fused silica column packed with 0.25 μ polymethylsiloxane (SE-30) using helium carrier gas and flame ionization detector. Gas chromatography/mass spectrometry (GC/MS) was performed using a Hewlett-Packard 5970 gas chromatograph/mass spectrometer. Solid-state and solution NMR parameters were summarized in Section II, Chapter 3. Fourier-transform infrared (FTIR) spectra were obtained using a BIORAD FTS-7 spectrometer controlled by a SPC3200 computer.

Dry toluene and dry benzene were distilled under argon over calcium hydride. Diethyl ether and tetrahydrofuran were distilled under argon from sodium/benzophenone ketyl. Other solvents were used without further purification or drying.

Dry glassware, when called for, was oven dried and assembled hot and allowed to cool under argon flush, or the assembled apparatus was flamed under argon flush.

B. Preparation of Dibutyltin Monomer

Purification of Divinylbenzene

Commercial divinylbenzene was purchased as a mixture of 55% 3- and 4-divinylbenzene, and 45% ethylvinylbenzenes. For preparation of the tin monomer, the mixture was purified using the method of Leikin, Davankov, and Krivova.[116]

Technical divinylbenzene [84 g] and carbon tetrachloride [16 g] were mixed and then carefully added to finely ground copper(I) chloride [100 g] at room temperature. A slurry formed which was allowed to stand at room temperature overnight. After standing, the mixture solidified. This solid was powdered and washed in a Büchner funnel with 100 mL of heptane previously cooled to -10 °C with either dry-ice/acetone bath or an ice/salt mixture. The dry-ice/acetone bath allowed for quicker cooling and greater control of the length of time that the bath may be kept at lower temperature.

Following the heptane wash, the solid was transferred to a beaker and treated with 250 mL of 30% ammonium hydroxide. Two layers formed which were separated. The aqueous layer was extracted with 100 mL of ether, and the organic layer and ether extracts were combined. Hydroquinone (0.5 g) was added to the organic layer, and the solvent was removed under reduced pressure. Vacuum distillation under argon (51 °C/2.2 mm Hg) yielded a mixture of 3- and 4-divinylbenzene as a yellow oil.

Preparation of Dibutyltin Dihydride.

Dibutyltin dihydride was prepared from lithium aluminum hydride ($LiAlH_4$) and dibutyltin dichloride ($(C_4H_9)_2SnCl_2$) in a modification of the method described by G. J. M. van der Kerk, J. G. Noltes, and J. G. A. Luijten.[117]

A 1000 mL, three-necked (24/40 joints) round-bottomed flask fitted with a magnetic stirring bar, 100 mL pressure equalizing dropping funnel, Fisher condenser, thermometer and thermometer adapter were oven dried, assembled hot, and allowed to cool under argon flush. All glass joints were lubricated using non-silicon grease. (Silicon stopcock grease is known to react with tin hydrides and was therefore avoided.) The flask was charged with $LiAlH_4$ [160 mmols, 160 mL of 1.0 M solution] in diethyl ether. An additional 100 mL of dry diethyl ether was added to the flask.

In a separate 250 mL, dry, round-bottomed flask was placed $(C_4H_9)_2SnCl_2$ [150 mmols, 45.5 g]. The flask was sealed with a septum and flushed with argon. The $(C_4H_9)_2SnCl_2$ was dissolved by adding 100 mL of dry diethyl ether, and the resulting solution was transferred to the 100 mL pressure equalizing dropping funnel already fitted to the 1000 mL three neck flask noted previously. The 1000 mL flask was then cooled in an ice bath while purging with argon. After temperature stabilization (~10 °C), the dibutyltin dichloride/diethyl ether solution was added slowly with vigorous stirring.

Following the addition, the solution was allowed to come to room temperature and then refluxed for two hours.

Following reflux, the solution was allowed to cool to room temperature and hydroquinone [0.5 g] was added followed by slow addition of 20 mL of distilled water to destroy any unreacted $LiAlH_4$. This was followed by the addition of 300 mL of a 20% aqueous solution of sodium potassium tartrate. The two layers were poured into a 1000 mL separatory funnel (Teflon stopcock, no silicon grease) and the layers separated. The aqueous layer was extracted with a second 200 mL aliquot of ether, the ether layers were then combined and dried over anhydrous sodium sulfate.

Removal of the drying agent was accomplished by filtration through a fine sintered glass filter funnel. The solvent volume was reduced using a rotary evaporator to approximately 50 mL. Distillation through a Vigreux column under reduced argon pressure (54°C/4.1 mm Hg) yielded the dibutyltin dihydride as a clear liquid. This was stored at 0 °C under an argon atmosphere.

Solution tin-119 NMR in diethyl ether referenced to tetramethyltin (δ 0.00): δ -206.5.

Preparation of Dibutyl(2-ethyl-3- and 4-vinylbenzene)tin Chloride Monomer

Dibutyl[2-(3- and 4-ethenylphenyl)ethyl]tin chloride monomer was prepared according to the method of Geigk *et al.*[118]

An oven-dried, 50 mL, three-necked round-bottomed flask, thermometer adapter, 10 mL pressure equalizing dropping funnel, and magnetic follower were oven dried and assembled hot with the open joints sealed with rubber septa and a thermometer placed in an adapter. The system was allowed to cool under argon purge. Silicon grease was avoided and Teflon stopcocks utilized to prevent decomposition of the tin hydride. Dibutyltin dichloride [53.88 mmols, 16.37 g] and 0.3 g α,α'-azobisisobutyronitrile (AIBN) was placed in the flask while maintaining an argon purge. After closing the system, freshly distilled and previously purified 3- and 4-divinylbenzene [107.8 mmols, 14.03 g] was added by way of a syringe. Dibutyltin dihydride [51.97 mmols, 12.21 g] was transferred to the dropping funnel. The dibutyltin dihydride was added with stirring at a rate that was sufficient to keep the internal temperature below 30 °C. The mixture was stirred overnight and used in the polymerization reactions.

Fourier-transform infrared spectra revealed: 2955–2850 cm^{-1}, alkane stretch; 1601 cm^{-1}, 1510 cm^{-1}, aromatic stretching; 990 cm^{-1}, 907 cm^{-1}, alkene bending. Proton NMR: δ 7.4–7.0 (6H, d, aromatic), δ 6.8–6.6 (1H, m, -C<u>H</u>=CH_2), δ 5.7–5.1 (2H, m, -CH=C<u>H</u>$_2$),

δ 2.9 (2H, m, Ar-C$\underline{H}_2$-), δ 1.6 (8H, m, Sn-CH_2-C$\underline{H}_2$-), δ 1.55 (2H, t, Sn-C$\underline{H}_2$-CH_2-Ar), δ 1.3–1.1 (8H, m, Sn-C$\underline{H}_2$-C$\underline{H}_2$-CH_3), δ 0.85 (6H, t, -C$\underline{H}_3$). Carbon-13 NMR: δ 143, δ 144 (*ipso*-carbon to ethyltin); δ 136.5 (vinylic); δ 124.3, δ 125, δ 126, δ 127.4, δ 129 (aromatic); δ 113.2 (terminal vinylic); δ 31.5 (2-ethyl carbon); δ 19.8, δ 26.7, δ 27.6 (butyl carbons); δ 13.6 (terminal butyl); δ 17.7 (1-ethyl carbon).

C. Preparation of Polymer

Preparation of Macroporous Poly{Dibutyl[2-(3- and 4-ethylphenyl)ethyl]tin Chloride–Divinylbenzene} Copolymer

The macroporous copolymer of dibutyl[2-(3- and 4-ethenylphenyl)ethyl]tin chloride and divinylbenzene was prepared using 2%, 5%, 10%, 15%, and 20% divinylbenzene as the crosslinking agent. Preparation of the 2% DVB macroporous copolymer is representative of the procedure. The only modification to this procedure involved changing the weight of commercial divinylbenzene added to the monomer mixture and adjusting the aqueous phase (20% methyl cellulose) to maintain a 1.1:1 aqueous:organic ratio. The amounts of monomer and divinylbenzene used in each polymerization are summarized in Table 11.

Table 11. Dibutyl-2-(3- and 4-(ethenylphenyl)ethyl)tin Chloride and Divinylbenzene Proportions for Crosslinked Polymer Preparation.

Target Crosslinking	2% DVB	5 % DVB	10% DVB	15% DVB	20% DVB
Technical Divinylbenzene (grams)	2.00	2.06	3.495	6.55	21.33
Calculated Weight of Divinylbenzene (grams)	1.10	1.13	1.92	3.6	11.73
Total Monomer Weight (grams)	41.80	21.59	19.74	18.63	53.42
Theoretical Maximum Crosslinking (% by weight)	2.63	4.99	8.86	16.2	18.0

Into a 100 mL, two-piece reaction flask fitted with two 14/20 joints, a central 19/22 joint, one 10/30 thermometer adapter, and a four-bladed glass stirrer with a Teflon stirring bearing was placed 100 mL of aqueous methyl cellulose solution (0.25 g in 100 mL distilled water). A modified Fisher condenser was placed in one of the 14/20 joints, the second sealed with a rubber septum, and a 20–120 °C mercury thermometer was placed in the thermometer adapter. The thermometer was positioned so as to clear the stirring paddle while maintaining sufficient contact with the solution. The flask was sealed and the methyl cellulose solution stirred for one hour while argon was purged through the system.

Freshly prepared monomer, dibutyl[2-(3- and 4-ethenylphenyl)ethyl]tin chloride [102 mmols, 40.7 g], technical divinylbenzene [8.5 mmols, 1.1 g], 1-octanol [10 mL,

volume equal to the monomer plus crosslinking agent], and benzoyl peroxide [0.5 g] were combined and added to the stirred solution of methylcellulose. Monomer droplets formed upon mixing. The two-phased system was stirred at 200 rpm at room temperature with argon purge for one hour.

After one hour at room temperature, the flask was wrapped in foil and heated with a sun lamp at a rate of approximately 0.5 °C/hour to a maximum of 80 °C. Stirring at 80 °C was maintained for 18 hours, followed by 100 °C for one hour. The two-phased system was cooled, and the beads collected on a Büchner funnel. The beads were washed with water, and then washed in a continuous Soxhlet extractor with toluene, acetone, and methanol, each for at least six hours. Following washings, the beads were dried at 60 °C under vacuum for 18 hours. A sample of the beads was submitted for elemental analysis to establish functional loading of the polymer. For each polymer, the following functional loadings of percent chlorine was found: 2% DVB, 6.15; 5% DVB, 5.78; 10% DVB, 3.13; 15% DVB, 3.31; 20% DVB, 3.76.

Solid-state carbon-13 NMR spectroscopy, using CP-MAS, externally referenced to hexamethylbenzene at δ 17.3: contact time, 1.00 msec; delay, 3.00 sec; proton 90° pulse, 4.93 msec; number of acquisitions, 4000; δ 14.3, δ 16.5, δ 27.6, δ 32.2, δ 40.4, δ 45.9, (polymer backbone, dibutyl groups, and ethyl group); δ 126.2; δ 128.2; δ 138; δ 144.6 (aromatic carbons). Solid-state tin-119 NMR spectroscopy, externally referenced

to dibutyltin dichloride at δ 84.00: contact time, 1.00 msec, acquisition delay, 8.00 sec, proton 90° pulse, 4.00 msec; δ 140.9.

Preparation of Macroporous-2 Poly{Dibutyl[2-(3- and 4-ethylphenyl)ethyl]tin Chloride–Divinylbenzene} Copolymer

Preparation of the polymer using dibutyl[2-(3- and 4-ethylphenyl)ethyl]tin chloride as the diluent was accomplished for 5%, 10%, and 15% polymers. The procedure described above was followed except for the removal of 1-octanol as diluent, which allowed only the dibutyl[2-(3- and 4-ethylphenyl)ethyl]tin chloride to act as diluent during polymerization.

D. Preparation of Iodoalkenes Using a Polymer-Supported Tin Reagent

Reduction of the Dibutyltin Chloride Copolymer to the Dibutyltin Hydride Copolymer using Diisobutylaluminum Hydride in Toluene

Reduction of the poly{dibutyl[2-(3- and 4-ethylphenyl)ethyl]tin chloride} to the tin-hydride was accomplished using the method of Gerigk *et al.*[3] The procedure for reduction of 10% crosslinked beads is representative.

A 50 mL, three-necked round-bottomed flask equipped with a stirring paddle connected through a Teflon stirring bearing, pressure equalizing addition funnel with

Teflon stopcock, and sealed fritted glass funnel (fritted glass funnel in 20 cm long by 3 cm diameter tube fitted with inner 14/20 ground glass joints and gas inlet tube at each end) was oven dried and assembled hot under argon flush. All ground-glass joints were coated with non-silicon grease. The tin-chloride polymer [2.0 g, 1.8 mmols chloride] was added to the flask while maintaining the argon flush. The system was sealed, and 20 mL of dry toluene was added by way of a syringe. The polymer was allowed to swell for 15 minutes and stirring was initiated at very slow speeds (25 rpm or slower). Diisobutylaluminum hydride in toluene [19 mmols, 19 mL of a 1.0 M solution] was placed in the dropping funnel and added dropwise to the swollen copolymer over approximately 1 hour. The mixture turned from light gray to a dark gray over the addition period and was allowed to stir overnight.

The beads were isolated from the remaining reagents by filtration through a glass frit, and then washed with 200 mL additional solvent. Following the washing, argon was passed over the beads for 6 hours, or more, to "dry" the beads.

Solid-state carbon-13 NMR spectroscopy using CP-MAS externally referenced to hexamethylbenzene (δ 17.36): contact time, 1.00 msec; delay, 3.00 sec; proton 90^{o} pulse, 4.93 msec; number of acquisitions, 1000: δ 144, δ 137, δ 128 (aromatic carbons); δ 41, δ 33, δ 30, δ 16, δ 14, δ 10 (polymer backbone, butyl, and ethyl). Solid-state tin-119 NMR spectroscopy externally referenced to dibutyltin dichloride (δ 84.00); contact time,

1.00 msec; acquisition delay, 8.00 sec; proton 90° pulse, 4.00 msec; number of acquisitions, 3000: δ - 87.9.

Reduction of the Dibutyltin Chloride Copolymer to the Dibutyltin Hydride Copolymer using Lithium Borohydride in Tetrahydrofuran

A 50 mL, three-necked, round-bottomed flask equipped with a stirring paddle connected through a Teflon stirring bearing, pressure equalizing addition funnel with Teflon stopcock, and sealed fritted glass funnel (fritted glass funnel in 20 cm long by 3 cm diameter tube fitted with inner 14/20 ground glass joints and gas inlet tube at each end) was oven dried and assembled hot under argon flush. All ground-glass joints were coated with non-silicon grease. The tin-chloride polymer [2.0 g, 1.8 mmols chloride] was added to the flask while maintaining argon flush. The system was sealed and 20 mL of dry tetrahydrofuran was added by way of syringe. The polymer was allowed to swell for 15 minutes and stirring initiated at very slow speeds (25 rpm or slower). Lithium borohydride in THF [20 mmols, 20 mL of a 2.0 M solution] was placed in the dropping funnel and subsequently added dropwise to the swollen copolymer over approximately 1 hour. Stirring was continued at room temperature for 18 hours.

The beads were isolated from the remaining reagents by filtration through a glass frit, and then washed with 200 mL of additional dry solvent. Following the washing, argon was passed over the beads for 6 hours, or more, to "dry" the beads.

Solid-state carbon-13 NMR spectroscopy, externally referenced to hexamethylbenzene (δ 17.3); contact time, 1.00 msec; delay, 3.00 sec; proton 90° pulse, 4.93 msec; number of acquisitions, 5744; δ 144, δ 137, δ 127 (aromatic); δ 44, δ 41, δ 28, δ 14, δ 10 (polymer backbone, butyl, ethyl). Solid-state tin-119 NMR spectroscopy, externally referenced to dibutyltin dichloride (δ 84.00); contact time, 1.00 msec; acquisition delay, 8.00 sec; proton 90° pulse, 4.00 msec; number of acquisitions, 8304; δ -87 (Sn-H).

Hydrostannation: Decenylation of the Dibutyltin Copolymer

Using a glove bag with argon as an inert atmosphere, the tin-hydride copolymer [2 g] and free-radical initiator (α,α'-azobisisobutyronitrile or benzoylperoxide) [0.1 mg] were placed in an oven-dried three-necked round-bottomed flask equipped with a single-paddled stirring shaft through a Teflon bearing. The remaining two openings were sealed using rubber septa, and the apparatus was removed from the glove bag. The copolymer was swollen in dry toluene [25 mL] for thirty minutes before addition of the alkyne by way of syringe. The reaction is carefully stirred for 18 hours at room temperature.

The polymer beads were then filtered using a glass frit, washed with methanol and acetone, and oven dried at 60 °C for 18 hours.

Solid-state carbon-13 NMR spectroscopy, externally referenced to hexamethylbenzene (δ 17.3); contact time, 1.00 msec; delay, 3.00 sec; proton 90° pulse, 4.93 msec; number of acquisitions, 4000; δ 144, δ 136, δ 128, δ 126 (aromatic); δ 45, δ 48, δ 39, δ 29, δ 27, δ 23, δ 16, δ 14 (polymer backbone, butyl, ethyl, alkyl). Solid-state tin-119 NMR spectroscopy, externally referenced to central peak of dibutyltin dichloride (δ 84.00); contact time, 1.00 msec; acquisition delay, 8.00 sec; proton 90° pulse, 4.00 msec; number of acquisitions, 8272; δ -47.6 [(*E*)-Sn-decene], δ -57.9 [(*Z*)-Sn-decene].

Iododestannylation: Formation of 1-Iododecene

Iododestannylation was based on the method of Kabalka *et al.*[119] A typical method for 20% DVB tin-decene polymer beads is presented.

A 100 mL round-bottomed flask was charged with 2.09 g of 20% DVB–dibutyl[2-(3- and 4-ethenylphenyl)ethyl]tin chloride macroporous beads. The beads were swollen in 25 mL THF for 30 minutes, and the flask was shielded from direct light.

Preparation of both the sodium iodide and Chloramine-T solutions immediately preceded addition to the beads. Sodium iodide [5.0 mmols, 0.75 g] was dissolved in 5.0

mL of 0.1 M NaOH. This solution was added to the swollen beads and allowed to stand for 15 minutes before addition of the Chloramine-T.

Chloramine-T [5.00 mmols, 1.41 g] was dissolved in 10 mL of a 50% aqueous THF solution and added to the beads. The system was gently agitated by swirling for approximately 15 seconds every 30 minutes for 2 hours, and then allowed to stand for 2 hours. The reaction was quenched with sodium thiosulfate [10 mL, saturated solution] and the beads were removed by filtration. The resulting two-phase system was separated into organic and aqueous layers, and the aqueous layer was extracted twice with 25 mL of diethyl ether. After combining the organic phases and drying over anhydrous magnesium sulfate, the solvent was removed to yield a yellow solid. The solid was powdered and extracted with hexanes to yield 0.74 g of a yellow oil (14% yield).

FTIR spectroscopy revealed: 3044 cm^{-1} (alkene C-H stretch); 1654 cm^{-1}, 1602 cm^{-1} (alkene C=C). Mass spectrometry; *m/z* 266 (molecular ion), 127 (M-CHI). Proton NMR spectroscopy revealed: δ 6.5 (1H, d of triplets, -C<u>H</u>=CHI), δ 5.95 (1H, d, -C=C<u>H</u>I), δ 2.1 (2H, m, -C<u>H</u>$_2$-C=C), δ 2.0 (2H, m, C=C-C<u>H</u>$_2$-) δ 1.3 (12H, m, -C<u>H</u>$_2$-), δ 0.85 (3H, t, -C<u>H</u>$_3$). Carbon-13 NMR solution spectroscopy in $CDCl_3$ referenced to deuterochloroform (δ 77.0): δ 147 (-<u>C</u>=CI); δ 74 (-C=<u>C</u>I); δ 36, δ 31, δ 29.7, δ 29.3, δ 29.2, δ 28.9 (C3-C8); δ 22.6 (CH_3-<u>C</u>H_2-CH_2-); δ 14 (<u>C</u>H_3-).

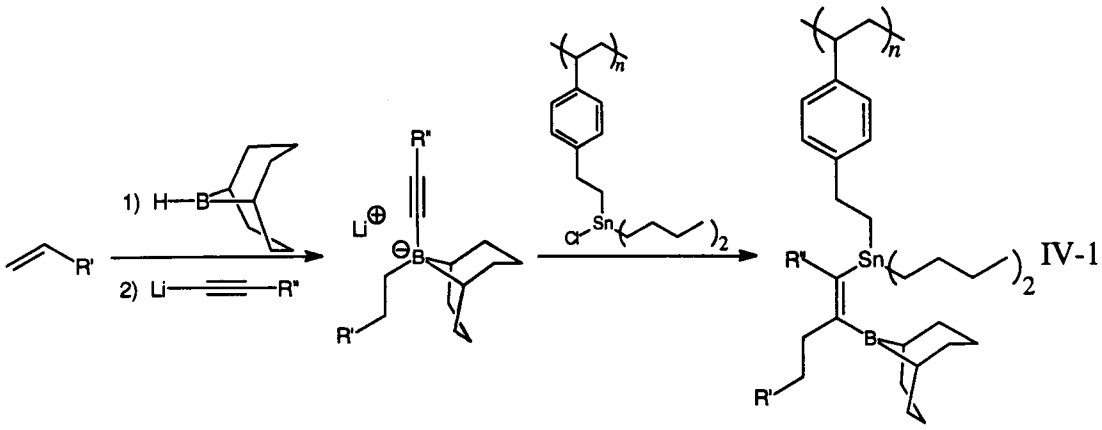
CHAPTER 5

CONCLUSIONS AND FUTURE RESEARCH OBJECTIVES

Hydrostannation of alkynes using a broad range of polymer-supported dibutyl[2-(3- and 4-ethylphenyl)ethyl]tin reagents were completed. The (*E*):(*Z*) ratios of the product alkenes following iododestannylation were obtained and compared to solution chemistry analogues, which show (*E*):(*Z*) ratios in excess of 85:15.[120]

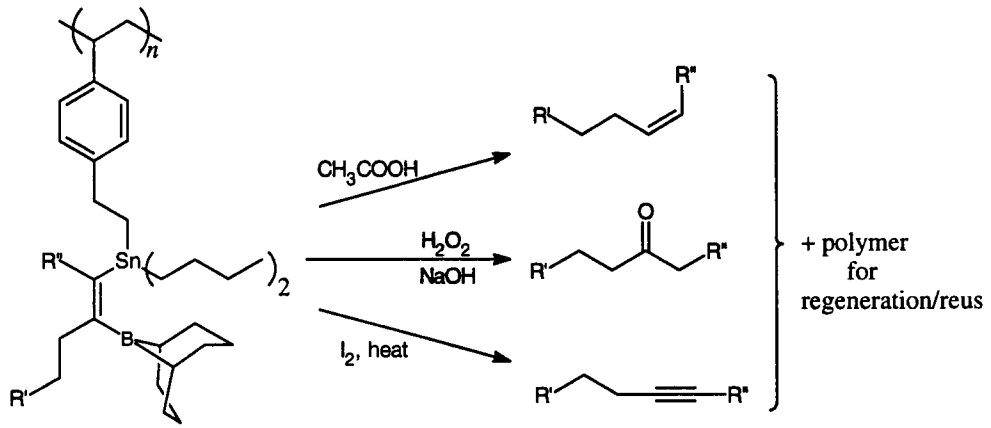
Polymer-supported tin reagents present promising areas for future research. The combination of tin chemistry with the advantages of a polymer support provides an expanse of untapped resources for research. As this study progressed, specific areas of exploration became apparent. A few have been outlined below. A multitude of additional applications are possible due to the broad chemistry associated with organotin reagents. The proposed areas of research are represented by the poly(dibutyl[2-(3- and 4-ethenylphenyl)ethyl]tin chloride), but they still represent only a small fraction of possible research areas.

Vinyltin reagents used in combinations with boron chemistry are known in solution chemistry. One striking example which could be nicely applied to polymeric systems is the use of 9-borabicyclo[3.3.1]nonane in combination with tin chloride (Equation IV-1).



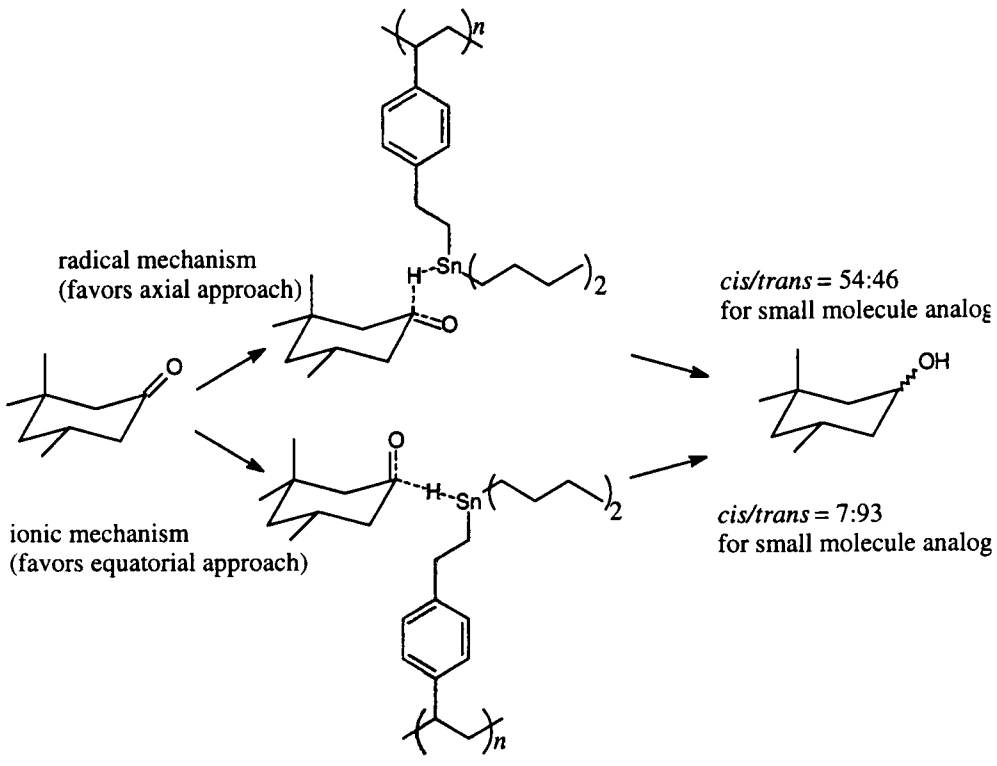
IV-1

Tributyltin chloride has been shown to induce intramolecular transfer reactions of lithium 1-alkynylthrialkylborates, providing a stereoselective method of obtaining substituted alkenes,[121] as well as ketones, and alkynes.[122] The polymer-supported analogue is shown in Equation IV-2.



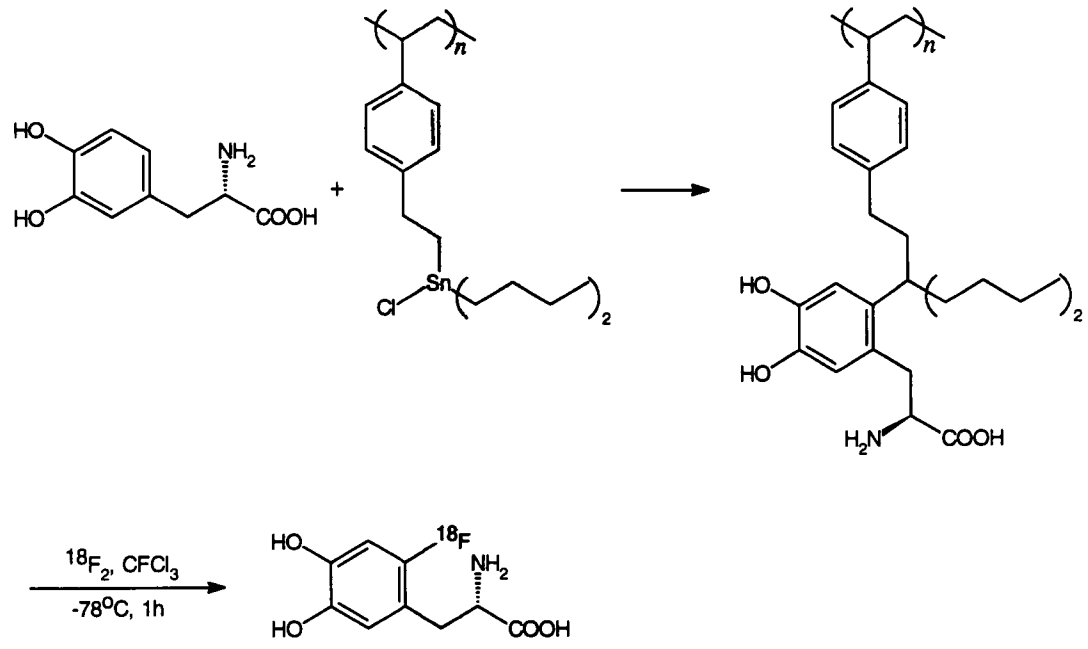
IV-2

Tributyltin hydrides have also been utilized in the stereoselective reduction of cyclic ketones.[123,124] Selection of the *cis*- or *trans*-isomer is greatly influenced by reaction conditions as shown in Scheme 11.



Scheme 11. Experimental Condition Influence on Stereochemical Outcome of Proposed Poly(dibutyl[2-(3- and 4-ethenyl-phenyl)ethyl]tin Hydride) Reaction with Cyclic Ketone.

An application into radiolabeling was recently suggested by N. K. Reddy[125] which utilizes the dibutyltin ligand as an intermediate to radiofluorination of 2-amino-3-(3,4-dihydroxyphenyl)propanoic acid (DOPA) (Scheme 12).



Scheme 12. Proposed Use of Polymer-Supported Dibutyltin Chloride in Radiofluorination of DOPA.

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LIST OF REFERENCES

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APPENDIX

Chemical Genealogy



George Walter Kabalka
Ph. D. 1970 Purdue

Herbert Charles Brown
Ph. D. 1938 Chicago

Morris S. Karasch
Chicago

Henry Irving Schlesinger
Ph. D. 1905 Chicago

Julius Stieglitz
Ph. D. 1889 Berlin

Victor Meyer
Gottingen

John U. Nef
Clark

Johan Carl Wilhelm Ferdinand Tiemann
Ph. D. 1870 Gottingen

August Wilhelm von Hoffmann
1841 Giessen

Justus von Liebig
1822 Erlangen

Wilhelm Gottlob Kastner

Joseph Gay-Lussac
1800 Paris

Claude L. Berthollet
1779 Paris
1768 Turin

Pierre J. Macquer
1742 Paris

Claude L. Bourdelin
Lecturer, 1696-1777, Paris

Guillaume F. Rouelle
Demonstrator 1740 Paris

J. G. Spitzley
German Pharmacist

Nicholas Lemery
1683 Paris

Christopher Glaser
1628-1672 Paris

Nicaise Le Febvre
1610-1669 Paris

William Davisson
1593 -1669 Paris

Guy de la Brousse
1568 -1641 Paris

Jean Herouard
?-1627, Paris

Jacques Gohory
1520 -1576 Paris

Paracelsus
1493-1541

VITA

VITA

Ronald Curtis Marks was born on March 31, 1959, in Greenville, South Carolina. He graduated from Montezuma-Cortez High School, Cortez Colorado, in June of 1977. After attending Grand Canyon College in Phoenix, Arizona, Ron entered The University of Tennessee, Knoxville, in September of 1980. In July 1981, Ron and Joann Williams were married. Ron was awarded a Bachelor of Arts Degree in Chemistry in June of 1982, and graduated with honors. At graduation he was commissioned as a Second Lieutenant in the United States Air Force and designated a Distinguished Graduate of the Reserve Officer Training Corps, Detachment 800.

While stationed at Wright-Patterson Air Force Base, Dayton, Ohio, in 1984, Ron and Joann had a beautiful daughter, Rebekah Ann. Ron was awarded the Air Force Commendation Medal while at the Aeronautical Systems Division at Wright-Patterson. He was assigned in 1984 to the Naval Air Systems Command in Washington, District of Columbia. Promotion to First Lieutenant in 1984 was followed by promotion to Captain in 1986. The Joint Service Commendation Medal was awarded to Ron in 1986, and he was selected for an Air Force sponsored graduate education. Ron entered The University of Tennessee a second time in 1987, completing a research program under Dr. George W. Kabalka and receiving a Masters of Science Degree in Chemistry in August 1988.

Ron's next assignment was at the Department of Chemistry, United States Air Force Academy, were he attained the academic rank of Assistant Professor of Chemistry. He was awarded the Air Force Meritorious Service Medal in 1991, and selected for an Air Force sponsored doctoral education. Ron entered The University of Tennessee in 1991, again under the direction of Dr. Kabalka.