

Radical Polymerization of Vinyl Monomers to Poly(vinyl)s having ${}^n\text{Bu}_3\text{Sn}$ end Groups with Biological Activity

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Abstract

Bu_3Sn -ended poly(vinyl)s with biological activity were obtained by the radical polymerization of vinyl monomers using thianthrene cation radical ${}^n\text{Bu}_3\text{H}$. Thianthrene cation and stannyl radicals promoted the homopolymerization and copolymerization of styrene and ethyl vinyl ether having number average molecular weights of 2000-3100. Tributyltin hydride functions as a chain transfer agent. Such polymerization by cationic thianthrene and stannyl radicals could provide some clues for the biological reaction in living animals. Plausible polymerization mechanisms were suggested.

Key words: Thianthrene, Cation Radical, Tributyltin Hydride, Polymerization

1. Introduction

Radical chemistry has received great attention due to its main role in various important organic reactions^[1]. Nevertheless, little is known for the reactions with unsaturated alkenes and alkynes although cationic radicals are known to react with various nucleophiles^[1]. The addition of cationic radicals such as R_2NH^+ and $t\text{-BuOH}^+$ to alkenes is reported several decade ago^[2]. However, the radical polymerization of alkenes promoted by the addition of a cationic radical is not common^[1], although the radical polymerization of vinyl monomers with a radical initiator is well documented^[3].

The cationic polymerization of vinyls and heterocyclics, which is usually occurred via cationic chain carrying species, can be mediated using various acidic agents (including Lewis and Bronsted acids, oxonium salts) and using ionizing radiation^[4]. The use of carbocation radicals as an initiator of polymerization was reported^[5]. By comparison, polymerization of vinyl

derivatives initiated by the cationic thianthrene radical, a heteroaromatic cycle containing two sulfur atoms in the *para* position, has not been reported. Although carbocation radical crystals are synthesized by anodic electrocrystallization with difficulty or *in situ* generated^[5], the reasonably stable crystals of thianthrene cationic radical perchlorate can be easily prepared^[6,7]. Hence, the reactivity study of thianthrene cation radical toward various nucleophiles including amines, aromatics, ketones, alkenes, alkynes, organometallic complexes, oximes, etc. has been much performed^[6]. Thianthrene cationic radical is reported to just form an adduct with alkenes and alkynes without polymerizing these unsaturated species (Scheme 1)^[6]. The thianthrene cationic radical with two sulfur atoms may display different modes of reaction from the heteroatom free carbocation radicals. Thianthrene is easily oxidized *in vivo* and *in vitro* to monosulfoxide or disulfoxide without cleavage of the ring structure^[6]. Furthermore, thianthrene cationic radical could react with stannyl hydride or tin hydride, an endocrine disruptor. Therefore, stannyl hydride (or tin hydride) could induce some unidentified side reactions in living animals in order to bestow biological activity. Here we report our results on the radical polymerization of vinyl monomers to biologically active poly(vinyl)s having tributyltin end groups, promoted by thianthrene cation radical as an initiator and tributyltin hydride as a chain transfer agent.

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2. Experimental Section

2.1. Materials

All the chemicals used in this study were purchased from Aldrich Chemical Company. Methyl methacrylate and styrene were purified as follows: they were washed with aqueous 5% sodium hydroxide (to remove phenol type inhibitor), washed well with distilled water, dried over anhydrous MgSO_4 , and finally distilled at reduced pressure before use. Acrylonitrile was washed with dilute sulfuric acid, washed with aqueous sodium carbonate, dried over anhydrous MgSO_4 , and then distilled prior to use. Phenyl acetylene, 4-vinylpyridine, and tributyl tin hydride were distilled at reduced pressure before use. Ethyl vinyl ether was distilled at ambient pressure prior to use. Adduct of thianthrene cation radical to phenylacetylene^[6f] and thianthrene cation radical perchlorate^[8] were prepared according to the literature procedure. The thianthrene cationic radical and tributyltin hydride were saved at low temperature in the dark to hold unwanted decomposition.

2.2. Instrumentation

All reactions and manipulations were performed under prepurified nitrogen or argon atmosphere using Schlenk techniques. Dry, oxygen-free solvents were employed throughout. All glasswares were flame-dried or oven-dried before use. Infrared spectra were obtained using a Perkin-Elmer 1600 Series FT-IR FT-IR spectrometer. Proton NMR spectra were recorded on a Varian Gemini 300 spectrophotometer, operating at 300 MHz, using $\text{CDCl}_3/\text{CHCl}_3$ as a reference at 7.24 ppm downfield from TMS. Number average molecular weights (M_n) were determined by vapor pressure osmometry (VPO) in HPLC-grade chloroform using a Wescan Model 233100 osmometer and/or ^1H NMR spectroscopy.

2.3. Polymerization of Styrene with Thianthrene Cation Radical Perchlorate and Tributyl Tin Hydride

To a purple solution of thianthrene cation radical perchlorate (56.8 mg, 0.18 mmol) and tributyl tin hydride (67.3 mg, 0.25 mmol) in methylene chloride (5 mL) cooled to 0°C was added styrene (2.06 mL, 18.0 mmol) under a stream of nitrogen. The reaction mixture turned dark brown within 3 min, and the reaction medium became then rapidly viscous with some exothermicity.

After stirring at room temperature for 24 h, the polymer was precipitated in methanol, filtered off, and dried to yield 1.54 g (85%) of off-white powder. IR (KBr pellet, cm^{-1}): 3050 m, 2900 s(vC-H), 1600 m, 1495 m, 1450 s, 1020 w, 730 s, 670 s. ^1H NMR (δ , CDCl_3 , 300 MHz): 0.8-2.1 (br, 3H, CHCH_2), 6.2-7.4 (br, 5H, ArH). M_n = 2960 (measured by VPO).

2.4. Polymerization of Ethyl Vinyl Ether with Thianthrene Cation Radical Perchlorate and Tributyl Tin Hydride

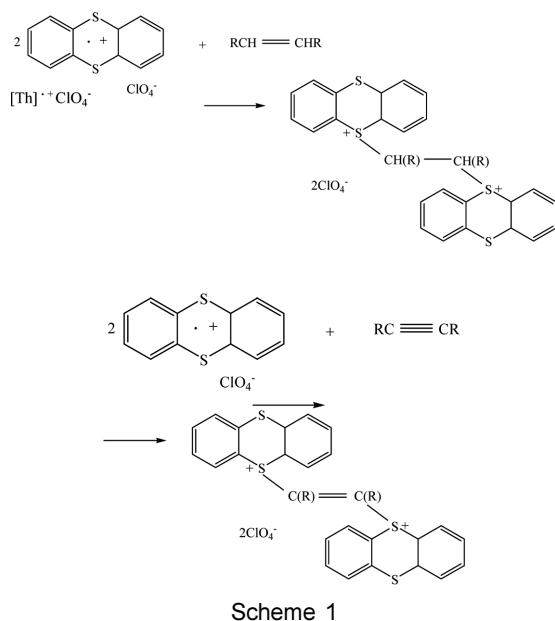
To a solution of thianthrene cation radical perchlorate (56.8 mg, 0.18 mmol) and tributyl tin hydride (67.3 mg, 0.25 mmol) in methylene chloride (5 mL) at 0°C was charged ethyl vinyl ether (1.72 mL, 18.0 mmol) under a stream of nitrogen. The reaction mixture immediately turned dark brown, and the reaction medium became very rapidly viscous with exothermicity. The same workups yielded 1.11 g (86%) of pale yellow powder. IR (KBr pellet, cm^{-1}): 2950 s(vC-H), 1375 m (vC-H), 1100 s (vC-O). ^1H NMR (δ , CDCl_3 , 300 MHz): 1.19 (br, 3H, OCH_2CH_3), 1.60 (br, 2H, backbone CH_2), 1.82 (br, 1H, backbone CH), 3.47 (br, 2H, OCH_2CH_3). M_n = 2210 (measured by VPO).

2.5. Copolymerization of Styrene and Ethyl Vinyl Ether with Thianthrene Cation Radical Perchlorate and Tributyl Tin Hydride

To a purple solution of thianthrene cation radical perchlorate (56.8 mg, 0.18 mmol) and tributyl tin hydride (67.3 mg, 0.25 mmol) in methylene chloride (5 mL) at 0°C was added ethyl vinyl ether (0.86 mL, 9.0 mmol) and styrene (1.03 mL, 9.0 mmol) under a stream of nitrogen. The same workups gave 1.34 g (87%) of pale yellow powder. IR (KBr pellet, cm^{-1}): 3050 s, 2960 s(vC-H), 1807 m, 1716 m, 1600 m, 1445 m, 1450 s, 1375 m (vC-H), 1100 s (vC-O), 700 s, 500 s. ^1H NMR (δ , CDCl_3 , 300 MHz): 0.8-3.8 (br, all aliphatic CHn), 6.5-7.7 (br, ArH). M_n = 3100 (measured by VPO).

3. Results and Discussion

Thianthrene cationic radical perchlorate, a little shock-sensitive, is a very reactive species yet having a moderate storage life and can react with various chemicals in many ways^[6]. Thianthrene cationic radical is known to add to alkenes and alkynes without polym-



erizing them (shown in Scheme 1)^[6f]. The polymerization yields decrease with increasing molar ratio, [phenyl acetylene] over [thianthrene cationic radical perchlorate]: 87% for 0, 55% for 0.01, and 2% for 0.1 because of the possible adduct formation as depicted in Scheme 1.^[9] The adduct of thianthrene cation radical to phenyl acetylene did not polymerize styrene and ethyl vinyl ether appreciably. Thianthrene cation radical was reported to promoted the ring-opening polymerization of THF with heating for 5 days at 50°C to produce oligo(THF) with $M_n = 793$ (obtained by ¹H NMR spectroscopy) in 14% yield^[9].

The molecular weight data of the polymerization reactions were summarized in Table 1.

The polymerization yield and molecular weight gradually decrease with increasing tributyltin hydride concentration because of polymer chain transfer by tin hydride.

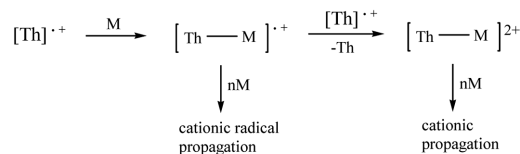
Three mechanisms are plausible for the initiation step: (A) bond-formation, (B) electron-transfer, and (C) HX-generation (Scheme 2). Among them the bond-formation mechanism can be first ruled out for the following reasons. The thianthrene cation radical initiated less effectively in the presence of phenylacetylene. The adduct of thianthrene cation radical to phenylacetylene did not polymerize styrene and ethyl vinyl ether in the presence of tributyltin hydride. Furthermore, the thian-

Table 1. Number average molecular weight data of polymerization of vinyl monomers promoted by thianthrene cationic radical and tributyl tin hydride^a

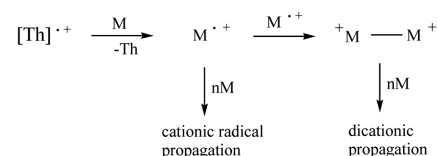
Monomer	Yield (%)	Mol wt ^b
Styrene	85	2960
Styrene ^c	82	2120
Styrene ^d	79	2030
Styrene ^e	84	2920
Styrene ^f	57	2720
Ethyl vinyl ether	86	2210
Styrene + Ethyl vinyl ether ^g	87	3100

^aMonomer, 18 mmol; initiator, thianthrene 0.18 mmol, tin hydride 0.25 mmol; methylene chloride, 5 mL for 24 hrs. ^bMeasure with VPO in chloroform. ^cMonomer, 18 mmol; initiator, thianthrene 0.18 mmol, tin hydride 0.50 mmol; methylene chloride, 5 mL for 24 hrs. ^dMonomer, 18 mmol; initiator, thianthrene 0.18 mmol, tin hydride 0.75 mmol; methylene chloride, 5 mL for 24 hrs. ^ePerformed in the dark. ^fPhenyl acetylene (0.18 mmol) added. ^g1:1molar ratio.

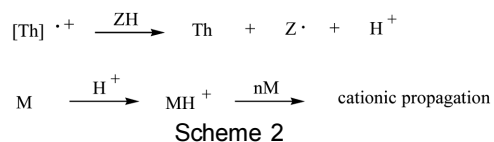
(A) Bond-formation initiation (hardly possible)



(B) Electron-transfer initiation (most possible)



(C) HX-generation initiation (less possible)



threne moiety was found not to be bound to the polystyrene and poly(ethyl vinyl ether)^[9]. The two remaining mechanisms would equally operate for the polymerization of styrene and ethyl vinyl ether to corresponding polymers with tributyltin end groups in the presence of thianthrene cationic radical and tributyl

tin hydride. Thus, the monomer cation radicals, generated by the direct electron-transfer from thianthrene cation radical or via tributyl tin radical to monomers, would initiate the polymerization reaction.

The monomer dication generated by combining monomer cation radicals would also initiate the polymerization reaction. Generally, it will react with a nucleophilic species (ZH) with hydrogen to generate a Bronsted acid, HX, which can initiate the polymerization reactions^[10]. The propagation may proceed via cation radicals, cations, or dications, but simple propagation through free radicals seems unlikely due to facile oxidation by cation radicals^[11]. More than a single mechanism could perhaps be operating simultaneously, giving rise to a very complex situation. The polymers with low molecular weights may be produced by some unidentified side reactions, which could be related to the cationic nature of the initiator, in the complex situation. Sn-H bond is quite weak enough to be used as a radical source^[12]. Therefore, at this time, we prefer the mechanism **B** based on the experimental results. It is well documented that organic tin compounds, used as a stabilizer for polymer formulation, are an environmental hormone^[13]. Study on the biological activity of the polymers possessing tributyltin are currently in progress and will be published as a separate paper^[14].

4. Conclusions

Polymerization of vinyl monomers is initiated by thianthrene cation radical in the presence of Bu₃SnH to elucidate the biological activity. Thianthrene cation/stannyl radical initiated the polymerization of styrene and ethyl vinyl ether to produce the corresponding polymers having tributyltin end groups while thianthrene end group was not observed appreciably. The number average molecular weights of the polymers were in the range of 2000-3100. Such polymereization using cationic thianthrene/stannyl radicals could provide essential clues for the reaction in living animals. Comments on possible polymerization mechanisms were provided.

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