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Novel iniferter-based synthetic approach to hetero-telechelic precursors and multiblock copolymers composed of vinyl polymer blocks and condensation linkages

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Dedicated to Professor Teiji Tsuruta on the occassion of his 88th birthday (Beiju).

Abstract

A novel synthetic approach, leading to the formation of hetero-telechelic precursors and multiblock copolymers composed of vinyl polymer [polystyrene or poly(*N*,*N*-dimethylacryl amide)] blocks and condensation linkages (ester or amide) or its polycondensate blocks, was developed using iniferters containing two different types of functional group (hydroxyl, carboxyl or amine) in their molecules via two different routes, each of which consisted of two-step reactions: photoiniferter living radical polymerization and subsequent polycondensation or *vice versa*. Both reactions proceeded at room temperature. The formation of multiblock copolymers was confirmed by ^{1}H NMR and IR spectroscopic measurements and molecular weight measurements. Irrespective of the type of iniferter, the livingness of the iniferter polymerization step was verified by a linear relationship between the conversion and molecular weight under appropriate reaction conditions, indicating that the vinyl polymers' block lengths were well controlled. The decrease in molecular weight of copolymers subjected to mild alkaline hydrolysis indicated that these multiblock copolymers might be degraded in a living body. This study is preliminary, but synthetic strategy proposed here may enable various choices of macromolecular architecture. Once the optimized reaction condition is achieved, functional macromolecular architectures with sequentially ordered complexity including well-controlled block lengths and multiple condensation linkages are feasible.

Keywords: Telechelic polymer; Iniferter; Multiblock copolymer

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1. Introduction

Poly(glycolide) and poly(lactide) are classified as biodegradable polyester which is hydrolyzed in living body, whereas vinyl polymers, the main chains of which comprise hydrocarbons, cannot be

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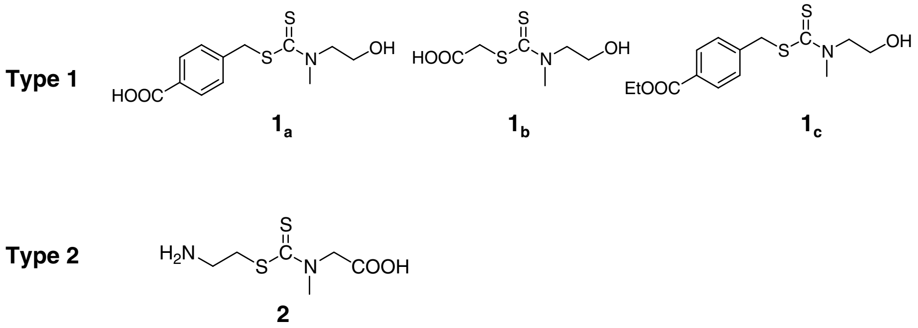
degraded by hydrolytic or enzymatic attacks. Therefore, a long-term implantation of vinyl polymers often induces unfavorable effects on surrounding tissues [1,2]. For example, continuous inflammatory reactions resulting from recruited immunocompetent cells such as macrophages and its fused multinucleolated foreign-body giant cells occur in long-term implantation; these cells slowly induce oxidation and cracking that is limited to surface regions [3]. If vinyl polymers have hydrolyzable condensation linkages such as ester or amide in their main chains, the hydrolysis of such condensation linkages will degrade main chains to form microfragments, which can then be scavenged by immunocompetent cells via pinocytosis for water-soluble polymer fragments and via phagocytosis for water-insoluble polymer fragments, resulting in the complete disappearance of implants in a relatively short period [4], which might provide an "ideal" situation for implants that are not at all needed chronically.

To achieve that end, a new synthetic strategy that enables the formation of vinyl polymers with hydrolyzable groups in their main chains has been anticipated for biomedical applications. The designed-to-degrade hybrid type of condensation linkage and vinyl polymers may find new biomedical applications such as drug delivery carrier and scaffold for engineered tissues.

Our strategy of preparation of new types of copolymer with vinyl polymer blocks that are multiply conjugated with condensation linkages in their main chains is based on sequential two-step reactions of polycondensation and subsequent living polymerization, or *vice versa*. The starting materials used are dithiocarbamate esters (called iniferters [5]) with two hetero-functional groups (e.g., hydroxyl, carboxyl, amine group), each of which is derivatized either at the dithiocarbamyl group or dithiocarbamate ester group as depicted in Scheme 1.

Scheme 2 shows that, in principle, two routes exist for the preparation of copolymers comprising vinyl polymer blocks and multiple condensation linkages. An example of preparation using a hetero-functional iniferter with a hydroxyl group and a carboxyl group (Scheme 1: $\mathbf{1_a}$ or $\mathbf{1_b}$), is described below. The preparation of copolymers via *Route 1* in Scheme 2 proceeds first with iniferter-based *quasi-living* radical polymerization to form a hetero-telechelic vinyl polymer precursor with a carboxyl group at the starting polymer end and a hydroxyl group at the growing chain end. The second reaction is the polycondensation reaction of the precursor using a potent condensation agent at room temperature. *Route 2* is first initiated with polycondensation reaction to form a hetero-telechelic poly(iniferter) precursor, which is a polycondensed dithiocarbomate linkage, followed by iniferter polymerization. In this step, a monomer is inserted stepwisely into the main chain of the poly(iniferter). Irrespective of the route, a multiblock copolymer composed of vinyl polymer blocks and condensation linkages in their main chains should be obtained. To realize such molecular architectures, two chemistries were used as described below.

Iniferter-based polymerization, enabling quasi-living radical polymerization upon ultraviolet (UV) light irradiation in the presence of a radically polymerizable vinyl monomer under appropriate reaction conditions, proceeds with radical pair generation, monomer addition, and rapid recombination [5–7]. That is, dithiocarbamate linkage is photocleaved to generate two different nature of radicals: the generated dithiocarbamyl radical hardly initiates vinyl polymerization, whereas the counterpart alkyl radical can initiate radical polymerization. Rapid spontaneous radical recombination between a generated pair of these



Scheme 1. Structures of hetero-functional group-bearing iniferters.