Polymer 65 (2015) 124–133

Contents lists available at ScienceDirect

Polymer

journal homepage: www.elsevier.com/locate/polymer

Acrylamide monomers and polymers that contain phosphonate ions

N. Hu, A. Peralta, S. Roy Choudhury, R. Zhang, R.M. Davis, J.S. Riffle*

Macromolecules and Interfaces Institute, Virginia Tech, Blacksburg, VA 24061, USA

ARTICLE INFO

Article history:
Received 8 January 2015
Received in revised form
23 March 2015
Accepted 24 March 2015
Available online 31 March 2015

Keywords:
Phosphonic acid
Graft copolymer
Hydroxyapatite

ABSTRACT

Alkylacrylamide phosphonate monomers were synthesized by aza-Michael addition of an alkylamine onto the double bond of diethyl vinylphosphonate, then reaction with acryloyl chloride. Free radical copolymerization of *n*-butylacrylamide phosphonate with an acrylate-functional PEO macromonomer, then removal of the ethyl groups from the phosphonates led to poly(*n*-butylacrylamide phosphonic acid)-*g*-PEO copolymers. The copolymer comprising 56 wt% of the backbone and 44 wt% of PEO grafts was soluble in DMF, DMSO, methanol and water at pH 7.4. This copolymer formed aggregates in DMF and DMSO with only a few aggregates in methanol or water. Interaction of the phosphonic acid derivative (0.11 mmol) of *n*-butylacrylamide phosphonate with hydroxyapatite (0.15 or 0.30 mmol calcium ions) showed 80 and 95% extent of binding of the phosphonic acid whereas those values for acrylic acid were 47 and 64%. The hydrolytically stable polyacrylamide phosphonates with their excellent binding properties to hydroxyapatite make them potential candidates for adhesives.

1. Introduction

Phosphonic acid-containing compounds have elicited great interest in the biomedical field. Geminal bis(phosphonic acid)s, especially those containing ammonium ions, are well-known to be effective inhibitors of bone resorption due to their capacity to bind calcium cations to target bone minerals and inhibit the actions of enzymes that are responsible for bone resorption [1,2]. Polymers that contain phosphonic acids have been investigated as self-etching enamel-dentin adhesives [3,4]. Phosphonic acid bearing polymers have also been reported to be potential substrates for applications in drug delivery [5–8] and tissue engineering [9,10]. Recently, there has been growing interest in (meth)acrylamide phosphonate monomers and polymers since amides are more stable against hydrolysis than the corresponding esters [11]. Klee et al. [12] prepared *N*-alkyl-*N*-(phosphonoethyl) substituted mono-, bis- and tris-(meth)acrylamides by two different three-step reaction sequencies. The polyacrylamides with the phosphonic acids exhibited better hydrolytic stability than their polyacrylate and polymethacrylamide analogues. Le Pluart and coworkers synthesized a series of acrylamide phosphonic acid monomers that had ether or alkyl spacers. These monomers were homo- or copolymerized with *N,N′*-diethyl-1,3-bis(acrylamide)propane by photoinitiation [13,14]. This group also investigated the polymerization kinetics of acrylamide containing phosphonic acids and esters [15,16]. Rates of copolymerization of the acrylamide phosphonic acid monomers with *N,N′*-diethyl-1,3-bis(acrylamide) propane were significantly faster than homopolymerization of *N,N′*-diethyl-1,3-bis(acrylamide)propane, while no significant rate increase was found for the phosphonate ester derivative. Reversible addition–fragmentation transfer (RAFT) polymerization of a diethyl-2-(acrylamide)ethyl phosphonate monomer was carried out by Monge et al. [17]. Block copolymers consisting of this monomer and *N*-*n*-propylacrylamide maintained approximately the same lower critical solution temperature (LCST) as the poly(*N*-*n*-propylacrylamide) homopolymer. However, the LCST of the deprotected diblock copolymer containing the phosphonic acid and *N*-*n*-propylacrylamide was higher than for the homopolymer, and this was attributed to an increase in hydrophilicity.

Only a few investigations have been reported on the self-assembly behavior of monomers and polymers bearing phosphonic acids. Etemad-Moghadam and coworkers [18,19] synthesized and studied the self-organization and phase behavior of a series of (α-hydroxyalkyl)phosphonic acids with long hydrocarbon substituents (C_8–C_{18}). The cetyltrimethylammonium salts of these compounds aggregated at low concentrations in water with different morphologies (vesicles, ribbons, tubules). Francová and Kickelbick [20,21] prepared phosphonate- and phosphate-bearing methacrylates with alkyl spacers. These monomers formed micelles in water with the hydrophobic alkyl spacer in the core and

* Corresponding author.
E-mail address: judyriffle@aol.com (J.S. Riffle).

http://dx.doi.org/10.1016/j.polymer.2015.03.065
0032-3861/

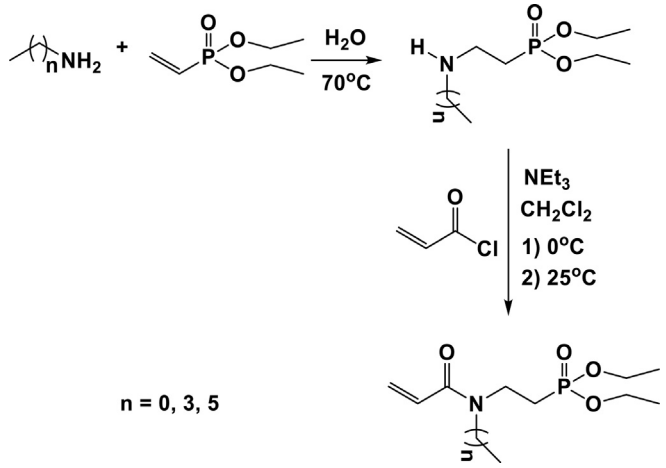

Fig. 1. Synthesis of acrylamide phosphonate monomers.

the phosphonates or the phosphates as the shell. Subsequent crosslinking of the micelles by UV- or thermally-initiated free radical polymerizations led to formation of spheres ranging from 30 to 400 nm in diameter as measured by dynamic light scattering (DLS). Robin et al. described the synthesis of amphiphilic phosphonic acid methacrylamide homopolymers, poly((-methacrylamido)decylphosphonic acid) by RAFT polymerization [22]. These homopolymers self-aggregated in water and acetonitrile. The hydrodynamic diameters were determined to be 2550 and 480 nm as measured by DLS in water and acetonitrile, respectively. This was attributed to their hydrophobic nature (74% hydrophobic groups). Tew and Eren [23] prepared diblock copolymers by ring-opening metathesis polymerization with one block containing phosphonic acid pendent groups and the other consisting of relatively hydrophobic polyoxanorbornene. Some of those compositions formed micelles in a THF:water 1:1 v:v mixed solvent with hydrodynamic radii ranging from 123 to 301 nm by DLS. Previously our group [24] investigated the solution properties of (meth)acrylate graft polymers bearing phosphonate and ammonium ions in the backbone and poly(ethylene oxide) (PEO) grafts. These graft copolymers spontaneously formed aggregates in water due to complementary charges.

Herein we describe the synthesis of acrylamide monomers containing phosphonates and their copolymerization with acrylate-functional PEO macromonomers to yield poly(acrylamide

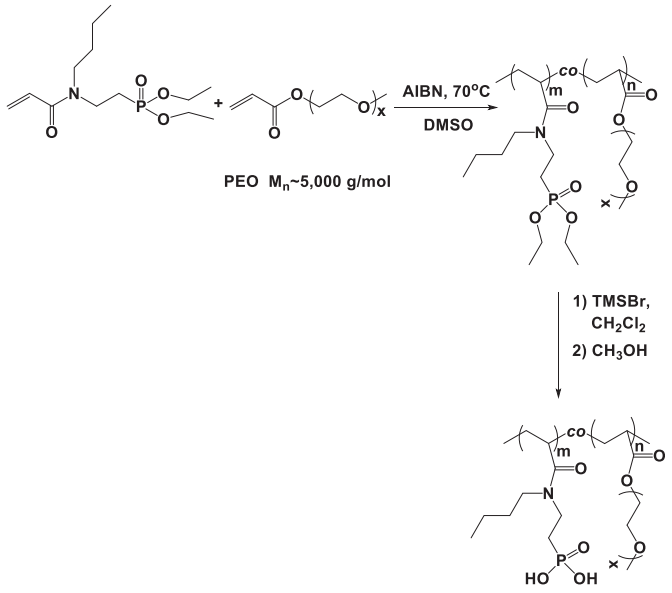

Fig. 3. Synthesis of poly(*n*-butylacrylamide phosphonate)-*g*-PEO and poly(*n*-butylacrylamide phosphonic acid)-*g*-PEO copolymers.

phosphonate)-*g*-PEO copolymers. Subsequent removal of the ethyl groups on the phosphonates produced poly(acrylamide phosphonic acid)-*g*-PEO copolymers. The properties of these copolymers in organic solvents and aqueous media are discussed. Interaction of acrylamide phosphonic acids with hydroxyapatite, the primary mineral of tooth enamel, was also investigated to characterize the binding capacities of the phosphonic acid to calcium cations.

2. Experimental

2.1. Materials

Diethyl vinylphosphonate (Epsilon-Chimie, >98%), dimethyl sulfoxide (DMSO) and dichloromethane (EMD Chemicals, anhydrous, 99.8%) were used as received. Methanol (anhydrous, 99.9%), hexane (99.9%), dichloromethane (99.9%), chloroform (99.9%) and diethyl ether (anhydrous, 99.8%), all from Fisher Scientific, were used as received. *N,N*-Dimethylformamide (DMF, 99.9%), sodium sulfate (anhydrous, 99%), *n*-butylamine (>99%), triethylamine

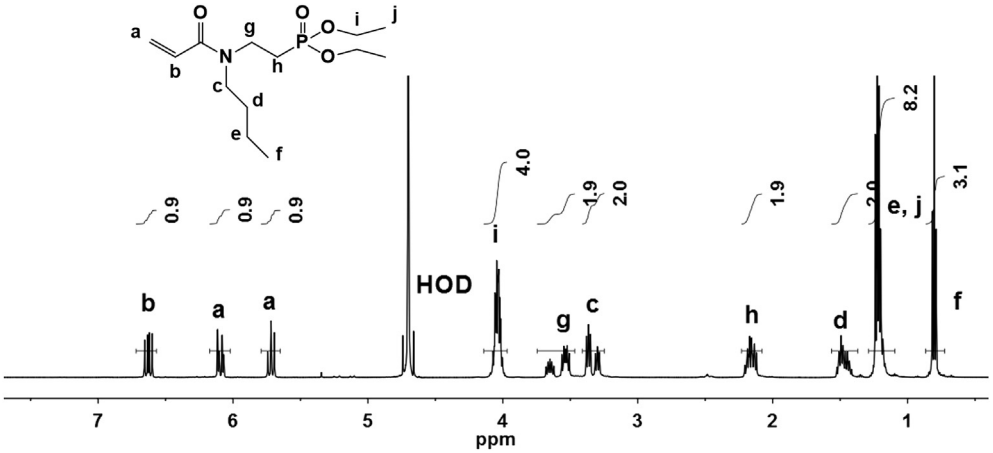

Fig. 2. ^{1}H NMR spectrum of an *n*-butylacrylamide phosphonate monomer.