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Letter

Synthesis of Poly(Glycolide -CO-2-hydro-2-oxo-1,3,2-Dioxaphosphorinane)

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Abstract A novel polyester containing glycolic acid (GA) and 2-hydro-2-oxo-1,3,2-dioxaphosphorinane (TMP) was prepared by ring-opening polymerization. The composition and the structure of the titled polymer were investigated by ^1H NMR, ^{13}C NMR, FT-IR, EA, and VPO. The influence of time on total conversion and molecular weight was also studied.

Key words glycolide, 2-hydro-2-oxo-1,3,2-dioxaphosphorinane, ring-opening polymerization

0 Introduction

Poly(glycolic acid) [PGA], poly(lactic acid) [PLA] and their copolymers are now used or are being developed for many medical applications, such as drug carriers in controlled drug release systems, as orthopaedic implants, and so on. The great advantage of them is degradation by simple hydrolysis of the ester backbone in aqueous environments such as body fluids. Furthermore, the degradation products are ultimately metabolized to carbon dioxide and water, or are excreted via kidneys[1]. Biodegradable polyphosphates, related to analogues of the natural products, can increase pinocytosis and enhance the penetration of the carriers through the cell membranes. They are aslo showing good targeting ability as drug carriers[2]. We have previously reported the synthesis and derivation of polyphosphates containing lactic acid and alkylenephosphate[3]. In this paper we designed and synthesized a novel copolymer of glycolic acid [GA] and 2-hydro-2-oxo-1, 3, 2-dioxaphosphorinane [TMP] via ring-opening polymerization by method using triisobutylaluminium [TIBA] as a initiator.

The scheme is shown in Figure 1.

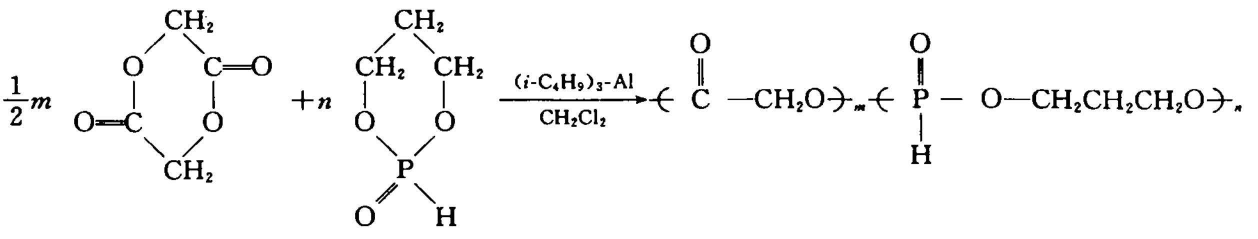

Figure 1

Received July 20, 1996. Fan Changlie: born in 1939, Professer

1 Experimental

1.1 Synthesis of glycolide and TMP

Glycolide and TMP were prepared according to the literature[4,5,6] respectively.

1.2 Synthesis of poly[GA-co-TMP]

Glycolide and TMP were dissolved in anhydrous dichloromethane. A solution of TIBA was added to the above solution and the mixture was stirred for 48 h at 20℃ under argon (Ar) atmosphere. After that, the resulting white crude product was collected by filtration, washed with anhydrous dichloromethane and dried under vacuum.

2 Results and discussion

The structure of the copolymer was affirmed by ^{1}H NMR, ^{13}C NMR, FT-IR spectra and EA (Table 1).

The preliminary date show that there are segment units of GA and TMP in the polymer.

The composition of the copolymer was investigated by ^{1}H NMR (Table 2 and Figure 2).

The data show that if the concentration of monomer of GA is greater than TMP, the segment units of PGA will increase accordingly when the concentration of monomer of GA increases.

Table 1 Spectral and EA data of the copolymer

Segment	^{1}H NMR (in TFA-d, δ)	^{13}C NMR (in TFA-d, δ)	FT-IR (cm^{-1})
GA	4.71 (s, $-CH_2-$)	171.35, 171.54 ($\underline{C}=O$)	1744 ($C=O$)
		66.31, 65.67, 63.56	1172 ($C-O$)
		($CO-\underline{C}H_2-O$)	2962 ($C-H$)
TMP	2.25 (m, $-C-CH_2-C-$)	61.84 ($\underline{C}H_2-O$)	1244 ($P=O$)
	4.52 (t, CH_2-C-CH_2)	30.78 ($CH_2-\underline{C}H_2-CH_2$)	2400 ($P-H$)
			967, 1047 ($P-O-C$)
	*element analysis found (calc)	C 40.92% (40.85%)	H 4.08% (4.04%)

* copolymer Ⅰ

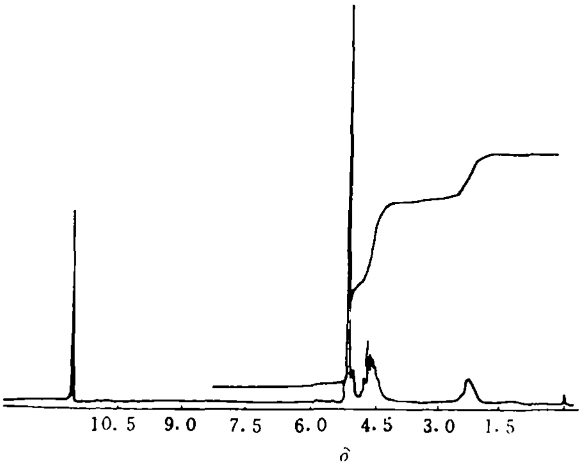

Fig 2 **^{1}H NMR of Copolymer Ⅱ**

Table 2 Effect of the molar ratio of monomers on the composition of the poly(GA-co-TMP)

Molar ratio of GA to TMP	Intergral height in ^{1}H NMR		Molar ratio of GA to TMP in the copolymer
	$-CH_2-$	$C-CH_2-C$	
Copolymer Ⅰ 2 : 1	42	10	2.1
Copolymer Ⅱ 1 : 1	43	19	1.1
Copolymer Ⅲ 1 : 2	22	9.5	1.1

However,If the concentration of monomer of GA is less than TMP,the segment units of PTMP will not increase accordingly when the concentration of monomer of TMP increase. Thus the reactivity of GA is greater than TMP.

A series of copolymerizations were carried out according to the method described in the "Experimental" section for different periods of time ranging from 15 min to 48 hour. The conversion levels of these copolymerizations were shown in Table 3. 30% conversion was obtained within 40 min and an additional 26% occurred after 48 h. Increasing reaction time increased molecular weight of the copolyester.

Table 3 Effect of time on total conversion and moleular weight

Time/h	$\frac{1}{4}$	$\frac{2}{3}$	1	2	4	8	24	48
Conversion/%	22.5	30	39	46	52.5	53.5	56	56
** $\overline{M}_n$			3000	3200			4000	6000

** $\overline{M}_n$ was measured by VPO(DMSO,70℃)

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