REGIOSELECTIVE RING-OPENING ANIONIC POLYMERIZATION OF β-LACTONES

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Abstract: New aspects of anionic polymerization of 4-membered lactones are presented, attention being paid to regioselectivity of β-lactones ring-opening reactions. It has been demonstrated that supramolecular complexes of alkali metal alkoxides used as initiators enable control of lactones polymerization, and due to anion activation yield polymers with specific molecular architecture. Synthesis of the analogue of natural polymer poly(3-hydroxybutyrate) *via* anionic polymerization of β-butyrolactone is discussed.

INTRODUCTION

Lactones are playing an important role in chemistry as substrates and intermediates in syntheses of bioactive materials, as well as monomers for polyester syntheses *via* ring-opening polymerization.

Many specific polyesters are produced also in the nature *via* enzymatic processes. The most important in this group of polyesters is poly[(R)-3-hydroxybutyrate] (PHB) produced by enzymes in bacteria cells and in eukaryotic organisms (Ref. 1). This stereoregular polymer, complexed with poly(calcium phosphate) forms building blocks of membrane channels, which transport metal ions to the living cells (Ref. 2). Many attempts have been made to synthesize similar man-made polymers.

Along with extensive research on enzymatic processes and new fermentation technologies aimed at the synthesis of analogue of natural microbial polymer (PHB), a great deal of research has been performed on chemical synthesis of PHB mediated by various catalysts and initiators. As far as polycondensation procedure with hydroxyacids as monomers is concerned, low molecular weight polymers showing unsaturated end groups and rather broad molecular weight distribution were obtained. However, Seebach and his group developed (Ref. 3) an elegant multistep condensation strategy starting from (R)-3-hydroxy-butyric acid using protecting groups at each individual condensation step. This procedure yielded linear polymers containing (R) enantiomeric units (up to molecular weight 12.000), and cyclic (R)-3-hydroxybutyric acid oligomers, but was very laborious and time-consuming.

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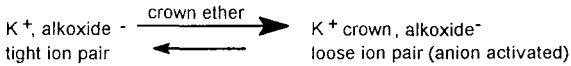
Alternatively to the polycondensation procedure, PHB oligomers and polymers have been synthesized *via* ring-opening polymerization of β-butyrolactone (β-BL) initiated by various coordinative catalysts like aluminoxanes (Pajerski, Lenz, Gross), diethyl zinc/water (Kemnitzer), triethylaluminium/water (Doi, Marchessault, Hocking) and many others. Using these initiators and racemic or optically active β-BL monomer, various type of poly-BL could be obtained with properties depending on a catalyst composition and polymerization conditions. However obtained polymers exhibited polymodal molecular weight distribution, their molecular architecture, as well as end groups being different from those present in the natural poly[(R)-3-hydroxybutyrate] (Ref. 4).

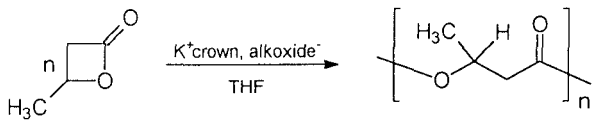
RESULTS AND DISCUSSION

Ring-opening polymerization of α and β substituted β-lactones - Addition-elimination mechanism

In our previous papers we reported that (R,S)-butyrolactone (β-BL) can be polymerized by anionic initiators to yield atactic poly[(R,S)-3-hydroxybutyrate] (Refs. 5-7). It is known that β-butyrolactone is a dormant monomer and does not polymerize by strong nucleophiles like sodium or potassium hydroxides and alkoxides. It is known that the anion activation can be achieved by addition of a cryptand or a crown ether able to complex the counterion. Due to complexation of the cation inside the cavity of a crown ether or a cryptand, its electrostatic interaction with an anion is reduced. This phenomenon described by Lehn and Maia in nucleophilic substitution, alkylation, elimination and other reactions (Ref. 8), has been utilized by us for activation of alkoxide anions in β-butyrolactone polymerization.
In THF solution of alkali metal alcoholates containing a crown ether (18C6) the equilibrium:



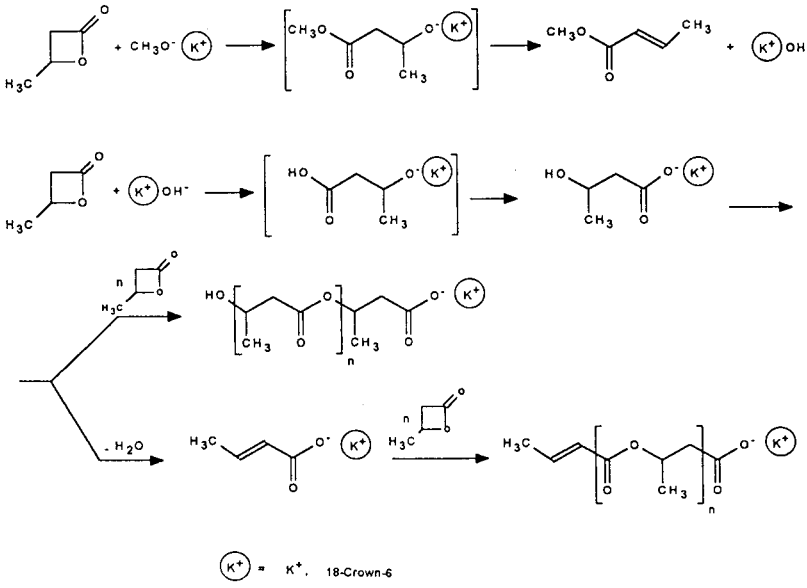
is shifted to the right and the activity of an alkoxide anion is increased. The activated alkoxide anion is able to induce polymerization (Scheme 1) of the dormant (R,S)-β-butyrolactone monomer (Ref. 9)



Scheme 1

Atactic poly(R,S)-3-hydroxybutyrate (M_n ca 20 000) could be obtained using initiator activated by addition of a crown ether. Also copolymers of (R,S) β-butyrolactone and pivalolactone containing amorphous and crystalline blocks with very interesting properties (Refs. 10,11) have been synthesized.

Detailed studies (Refs. 12,13) on the mechanism of racemic β-butyrolactone polymerization with activated potassium methoxide initiator in aprotic solvents (THF, DMF, CH_2Cl_2) revealed that the mechanism of such polymerization is different from that previously reported by some authors. According to the experimental evidence, provided by ^1H NMR measurements and ESI-MS analyses of intermediate products, the polymerization involves addition of an alkoxide anion followed by elimination reaction. In the second step activated potassium hydroxide opens the ring of a monomer inducing immediate rearrangement of active alcoholate centers into carboxylates anions, the latter being responsible for propagation (Scheme 2). Consequently, at the propagation step activated carboxylate anions, induce exclusively alkyl-oxygen bond cleavage without any simultaneous acyl-oxygen bond scission at the propagation step of β-propiolactone and β-butyrolactone polymerization, which was previously suggested by some authors. Thus, the polymerization proceeds regioselectively:



Scheme 2

Growing polymer chains have no end groups from the initiator but hydroxyl and crotonate end groups as revealed by ^1H NMR and ESI-MS (Fig. 1) analyses (Refs. 12,14).

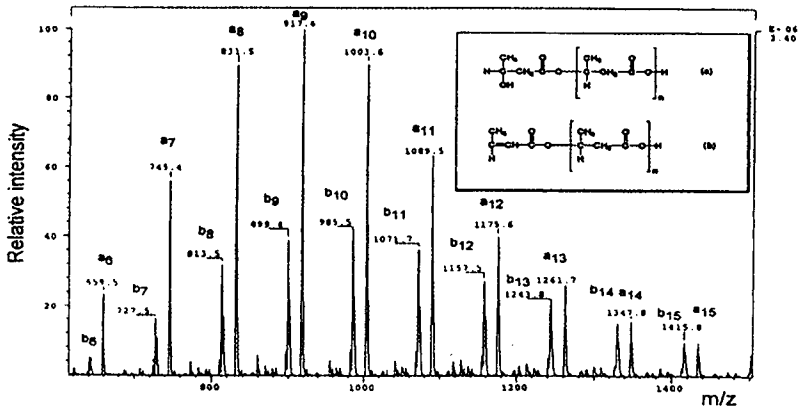
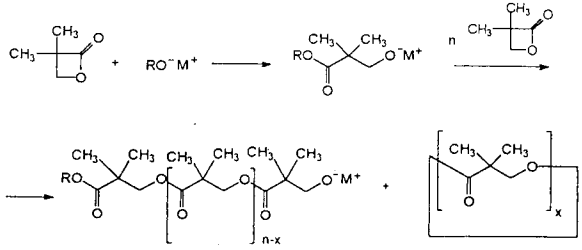


Fig. 1. The ESI-MS spectrum (SSQ-700) of poly(3-hydroxybutyric acid) obtained by polymerization of β-butyrolactone initiated with potassium methoxide/18-crown-6 complex. Two types of polymer chains, (**a**) and (**b**), are visible, showing different either hydroxy or crotonate end groups.

The presented here corrected polymerization mechanism of β-lactones by alkali metal alkoxides (Scheme 2) is valid for the polymerization of all β-lactones with alkali metal alkoxides as initiator except for α,α-disubstituted β-lactones, e.g. pivalolactone. For the latter monomer the elimination reactions do not take place and the attack of an initiator proceeds on the carbonyl carbon atom of the monomer involving acyl-oxygen bond cleavage with formation of alcoholate anions as propagating species (Scheme 3). Thus mechanisms of α,α'-disubstituted β-lactones is different from that of other β-lactones because due to the absence of hydrogens at C-3 (α,α' position) the elimination reactions do not occur (Ref. 13).



where:

R = CH_3 or $C(CH_3)_3$

M = Li or K

$x \geqslant 3$

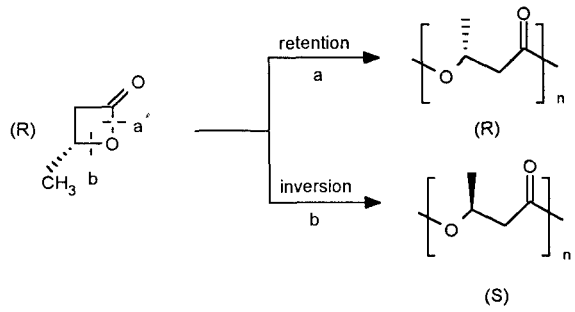
Scheme 3

The regiospecificity of the ring-opening of α,α' disubstituted β-lactones and polymerization mechanism are different from those of other β-lactones having no substituents at α-carbon atom of the ring. Thus the polymer chain architecture formed by β-lactones anionic polymerization strongly depends on the structure of a monomer and the mechanism of the ring-opening.

Thus it is unquestionable that polymerization of β-lactones (except α,α-disubstituted β-lactones) proceeds regioselectively with alkyl-oxygen bond scission via carboxylate anions as propagating species.

Synthesis of Isotactic Polymers from (R)-β-butyrolactone

Isotactic polymers may be formed from optically active β-butyrolactone in which either alkyl-oxygen or acyl-oxygen bond cleavages can occur exclusively to give either retention or inversion of the configuration at the chiral carbon atom, as shown in Scheme 4.



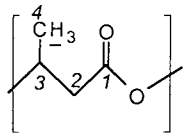
Scheme 4

The recently obtained results have shown that the potassium methoxide/18-crown-6 complex induces polymerization of (R)-β-butyrolactone with inversion of configuration, and an isotactic polyester was produced (Ref. 15). The precipitated polymer was highly crystalline with a melt transition, T_m, of 126°C, as revealed by DSC measurements.

The spectroscopically proven inversion of configuration provides also an unambiguos evidence that polymerization of (R)-β-butyrolactone occurs via alkyl-oxygen bond cleavage according to addition-elimination mechanism as shwon in Scheme 2.

Table 1 shows results of the NMR measurements and diads and triads distribution for two polymers: obtained using either potassium methoxide/18-crown-6 complex or potassium acetate/crown ether complex as initiators.

Table 1. Distribution of diads and triads in poly[(S)-hydroxybutyrate] obtained from [R]-β-butyrolactone.



		diads distribution, %						C^2 triads distribution, [a] %			
		i_d			s_d						
entry	catalyst	CH_3	C^1	C^4	CH_3	C^1	C^4	I	H_i	S	H_S
1.	MeOK/18-C-6[b]	83	83	83	17	17	17	72(73)	9(9)	10(9)	9(9)
2.	AcOK/18-C-6[c]	83	82	84	17	18	16	74(73)	8(9)	8(9)	10(9)

a) The values given in parentheses were calculated according to the following formulas: $I=[R]^3 + [S]^3$; $S=H_S=H_i=[R]^2*[S] + [S]^2*[R]$ where [R] and [S] are the stereochemical contents of R and S enantiomeric units in polymers investigated, assuming total inversion of monomer containing [R]/[S]=90/10. (Ref. 15)
b) Potassium methoxide, 18-Crown-6 complex
c) Potassium acetate, 18-Crown-6 complex

It is well known that activated carboxylate anions cleave alkyl-oxygen bonds in β substituted β-lactones polymerization with inversion of configuration (Ref. 16). The present results indicate that regardless the type of initiator used (alkoxide or carboxylate anions) the polymerization of β-butyrolactone proceeds regioselectively *via* alkyl-oxygen bond cleavage with inversion of configuration at the chiral carbon atom.

CONCLUSIONS

The results presented here demonstrate the enormous versatility of the anionic polymerization of β-lactones performed with activated alkali metal alkoxides as initiators.

Playing with structural parameters of β-lactone monomer, which influence the chemistry of ring-opening by an anionic initiator, the modification of the structure and properties of produced polymers is possible. Thus tailored aliphatic polyesters exhibiting biodegradability and interesting mechanical and thermal properties can be synthesized.

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