Stereoelective polymerization of β-butyrolactone

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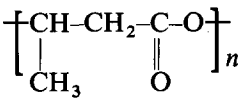
Racemic β-butyrolactone was polymerized using chiral initiators obtained from the reaction of organometallic derivatives ($ZnEt_2$, $CdMe_2$, $AlEt_3$) with R(−) 3,3 dimethyl-1,2 butanediol. With the zinc initiator, R(+) enantiomer is preferentially incorporated in the polymer chain with a stereoelectivity ratio r_R equal to 1.6. Crude polymer was fractionated into a crystalline, predominantly isotactic, part and an amorphous heterotactic part, both optically active. Sites of different stereospecificities, present in the initiator, are all active for the stereoelective polymerization. With the cadmium initiator, S(−) enantiomer is preferentially polymerized ($r_S = 1.01$), extending homosteric–antisteric rules previously established for thiiranes. Aluminium initiator leads to an homosteric process ($r_R = 1.1$). Chiroptical properties (o.r.d. and c.d.) of polymers prepared with zinc initiator show a predominance of R-configurational units, indicating that ring-opening occurs by O–acyl cleavage with retention of configuration.

(Keywords: stereoelective polymerization; β-butyrolactone; chiral initiator systems; chiral recognition; optically active polyester; poly-β-hydroxybutyrate)

INTRODUCTION

R-poly-β-hydroxybutyrate (R-PHB):



is one member of the family of poly-β-hydroxyalkanoates found in a wide variety of bacteria.

This polyester is optically active (monomeric units of R configuration) and thus has an isotactic structure. R-PHB is used by microorganisms as a reserve of energy and is stocked under the form of intracellular granules[1]. Its accumulation occurs when an excess of a carbon source is supplied and when the growth medium contains limited amounts of nitrogen source. The amount of polymer produced varies with the species and can reach up to 80% of the dry content of bacteria (for example in *Alcaligenes eutrophus* H16 (ref. 2)). R-PHB has a high degree of crystallinity (≈80%), high molecular weight (up to 5×10^5) and high melting point (≈175°C) (ref. 3).

It can be considered as a thermoplastic material having properties comparable to those of polypropylene. It is presently produced using bacteria in a pilot plant by the chemical company ICI[3,4] and considered as a potential biodegradable polymer.

Synthesis of PHB can be also achieved by ring-opening polymerization of β-butyrolactone. Although synthetic PHBs have received little attention, it appears, however, interesting to prepare such polymers, for at least two reasons. If they are prepared synthetically it is possible, in principle, to obtain a great variety of stereocopolymers. The following structures can thus be considered:

~RRSRSSSR~	(atactic)	(1)
~RRRRRR~	(isotactic, polyenantiomer)	(2)
~RRRRRR~ + ~SSSSSS~	(isotactic, polyracemate)	(3)

Intermediate structures between (1) and (2) or (2) and (3) can be also prepared.

Physicochemical and biological properties of polymers are often dependent on the composition and on the distribution of enantiomeric units in the polymer chain[5]. The properties of the polymer can be modified by varying the distribution of configurational units and eventually adjusted to that required for a given application.

In addition, PHBs having a predominance of chiral centres with opposite configuration to that found in biopolymer can be prepared. Biological properties of these polymers are unknown.

The first synthesis of PHB having properties (crystallinity, melting point, morphology) similar to that of the natural polymer has been reported by Agostini *et al.*[6,7]. The polymerization of racemic β-butyrolactone using the initiator system $AlEt_3/H_2O$ (1:1) leads to a mixture of crystalline isotactic and amorphous atactic fractions of polymer[6]. Initiators derived from $ZnEt_2$, e.g., ($ZnEt_2/H_2O$) (1:1), ($ZnEt_2$/ROH) (1:2) give only amorphous polymers. The synthesis of optically active PHB, using R(+) β-butyrolactone (enantiomeric excess: 73%) with $AlEt_3/H_2O$ (1:1) was also described by the same authors[7]. It has been proposed that ring opening occurs by acyl–oxygen bond cleavage with retention of configuration.

Racemic isotactic PHB was prepared by Tani *et al.*[8,9] using also $AlEt_3/H_2O$ (1:1) as initiator system. The influence of initiator preparation conditions (effect of an additive compound, effects of ageing or high-vacuum treatment of initiator) on the amount of isotactic fraction was thoroughly examined. Proportion of crystalline fraction as high as 72% has been obtained under suitable conditions.

Under different conditions of preparation of the same initiator, Gross *et al.*[10] obtained only 20% of insoluble crystalline fraction. It was also shown by the group of Tani[9] that the initiator system $ZnEt_2/H_2O$ leads to the

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formation of amorphous atactic PHB. This inability of the zinc initiator system to give stereoregular polymers was ascribed to the absence of coordination of the lactone monomer on the zinc atom. It was also proposed that ring-opening occurs through acyl–oxygen bond cleavage.

Very recently, polymerization of enantiomerically pure S(−) β-butyrolactone (prepared from R-PHB) by organoaluminium derivatives, $AlEt_3/H_2O$ (1:1) or (1:0.6) and zinc-based initiator, $ZnEt_2/H_2O$ (1:0.6) has been reported by Lenz and colleagues[11,12]. According to optical rotation observed, polymers of R-configuration were obtained with $AlEt_3/H_2O$ (1:1) initiator system. It was therefore concluded that the ring-opening reaction involves the cleavage of the alkyl–oxygen bond with inversion of configuration. This result is in contradiction to the mechanism proposed previously by Agostini *et al.*[6,7]. The discrepancy was ascribed to the differences in the experimental procedures used to prepare the corresponding $AlEt_3/H_2O$ (1:1) initiators. The polymerization of β-butyrolactone with $ZnEt_2/H_2O$ (1:0.6) initiator system occurs, on the contrary, by O–acyl cleavage and therefore with retention of configuration.

'Stereoelective' polymerization may be also used for the preparation of optically active polymers. This method has the advantage to start from racemic monomer, generally more easily available. The use of a chiral initiator which consumes preferentially one of the enantiomers leads to an enantiomerically enriched polymer. At the same time, the unreacted monomer is enriched in the opposite enantiomer. This method which can be considered as a particular kinetic resolution reaction was successfully applied in the case of three-membered ring monomers (oxiranes and thiiranes)[13–15] and was extended to α,α-disubstituted β-propiolactones e.g. α-methyl α-n-propyl β-propiolactone[16].

In the present paper, we describe the application of the stereoelective process to the case of β-substituted β-propiolactones using the example of β-butyrolactone. The initiators used are zinc, aluminium and cadmium glycolates derived from R(−) 3,3 dimethyl 1,2 butanediol (R(−) DMBD). Some information about the characterization of polymers is also presented.

EXPERIMENTAL

Reagents

Racemic β-butyrolactone (K and K, or Lonza) was distilled (chemical purity >99.7%, by v.p.c.), dried on CaH_2 and distributed in graduated tubes with break seals under vacuum. Commercial organometallic derivatives (solution of $ZnEt_2$ in heptane (Orgmet), $CdMe_2$ (Orgmet), $AlEt_3$ (Schuchardt)) were introduced in flasks in a dry box, distilled under vacuum and distributed in graduated tubes sealed under vacuum.

Enantiomerically pure R(−) 3,3 dimethyl 1,2 butanediol (DMBD) was prepared by enzymatic reduction of the corresponding ketoalcohol as described previously[17].

Polymerizations

All the polymerizations are carried out in apparatus sealed under high vacuum (10^{-6} mm Hg). Transfers of reagents are performed using break seals and by cold trap distillation. Chiral initiators are prepared by reacting the organometallic derivative in toluene or heptane solution with R(−) DMBD at 20°C over 2 h. Molar ratios: $ZnEt_2$/DMBD = 1:1; $CdMe_2$/DMBD = 1:1; $AlEt_3$/DMBD = 2:3.

Then, the solvent is evaporated and the initiator (white powder in the case of $ZnEt_2$/R(−) DMBD) is dried for two hours under vacuum at 20°C. The monomer is introduced by distillation and the polymerization is carried out in bulk at a given temperature. At the end of the polymerization, the unreacted monomer is recovered in a trap by vacuum distillation and its optical activity measured. Chloroform and few drops of acetic acid are added to the polymer. The catalyst residue is separated by centrifugation. The chloroform solution is poured in a large excess of methanol. The insoluble part of polymer is recovered by centrifugation.

The methanolic solution is evaporated, the residue dissolved in $CHCl_3$. This solution is washed several times with water in order to eliminate all traces of chiral diol. The chloroformic solution is then dried on Na_2SO_4 and after evaporation of solvent, the recovered polymer (soluble fraction) is dried under vacuum.

Characterization of polymers

The prepared polymers were characterized by the following techniques. Molecular weights were measured by g.p.c. in THF using a Waters apparatus (pump model 510) with refractometer R 401 and u.v. (254 nm) 440 detectors and a set of five microstyragel columns: 10^5, 10^4, 10^3, 500 and 100 Å, flow rate 1 ml/min. Optical rotations were measured with a Perkin Elmer 241 polarimeter. Circular dichroism spectra were recorded, in 1,1,1,3,3,3 hexafluoropropanol-2 using a Jobin–Yvon Dichrograph 3. ^{13}C n.m.r. spectra were recorded on Bruker 62.89 MHz apparatus using $CDCl_3$ as solvent. ^1H n.m.r. spectra were recorded on Bruker 360 MHz apparatus using $CDCl_3$ as solvent and with a Bruker 250 MHz apparatus using $CCl_4 + C_6D_6$ (10%) as solvent. D.t.a. analyses were carried out on Dupont 900 thermal analyser (heating rate: 15°C/min).

RESULTS AND DISCUSSION

Polymerization of racemic β-butyrolactone with $ZnEt_2$/R(−) DMBD initiator system

Efficient initiator systems for the stereoelective polymerization of oxiranes and thiiranes are generally prepared by reaction between $ZnEt_2$ and chiral alcohols or glycols. Chiral 1,2 diols give the best resolution results. One of the best stereoelective initiator systems for polymerization of oxiranes and thiiranes resulted from the reaction of $ZnEt_2$ and R(−) 3,3 dimethyl 1,2 butane diol (molar ratio, 1:1)[13–15]. The stereoelectivity is generally higher for thiiranes than for oxiranes.

It must be pointed out that recently, Sepulchre[18] has reported that the initiator system $ZnEt_2$/S-binaphthol leads in the case of methylthiirane to an almost ideal stereoelective polymerization, i.e. to practically exclusive choice of one of the enantiomers. However, this initiator system is very specific for methylthiirane, less for other thiiranes, but has, in the case of β-lactones, an efficiency significantly lower than the $ZnEt_2$/R(−) DMBD initiator system[19].

The results of polymerization of racemic β-butyrolactone by $ZnEt_2$/R(−) DMBD are presented in *Table 1*. The polymerizations have been carried out in bulk at 20°C. The rate of polymerization of β-butyrolactone is

Table 1 Polymerization of racemic β-butyrolactone using $ZnEt_2$/R(−) 3,3 dimethyl 1,2 butanediol (1:1) as initiator system in bulk at 20°C

Experiment number	C/M (mol%)	Polymerization time (h)	Polymer yield (%)	Unreacted monomer		$[\alpha]_D^{25}$, polymer[a]		Stereoelectivity ratio, r_R
				α_D^{25} (neat, dm)	Enantiomer excess (%)	Insoluble fraction in MeOH	Soluble fraction in MeOH	
1[b]	6.4	15	36	−2.29	8.2	−1.2	−6.1	1.45
2	3.05	2.75	53	−4.11	14.8	−1.0	−1.8	1.5
3	5.15	2.5	61.5	−5.25	18.9	−0.5	−2.1	1.5
4	5.05	5.5	84	−12.8	46.0	−0.6	−1.5	1.7
5[c]	4.9	7	56	−3.8	13.7	-	−2.7	1.4

[a] In $CHCl_3$ − c = 0.8 g/100 ml
[b] Experiment carried out at 0°C
[c] Experiment carried out in presence of sparteine as chiral additive

higher than that of α,α-disubstituted β-propiolactones (for example, in the case of α-methyl α-n-propyl β-propiolactone, a yield of 61% is obtained only after 24 h[16]). The unreacted monomer is laevorotatory and the absolute value of the rotatory power increases with conversion as it was observed previously for oxiranes and thiiranes.

The configuration of dextrorotatory β-butyrolactone is known to be R (ref. 7). This means that in the present case R enantiomer is preferentially incorporated in the polymer, while the unreacted monomer is enriched in S enantiomer. This type of choice in which the configurations of asymmetric carbon atoms in the preferentially incorporated enantiomer and in the initiator are 'homochiral' is called 'homosteric'. It has been observed for a great number of oxiranes and thiiranes and seems to have quite a general character[20]. Stereoelective polymerization of β-butyrolactone indicates that homosteric processes are also found in four membered rings such as β-lactones. Another example has been found in the case of α-methyl α-ethyl β-propiolactone[21].

The magnitude of stereoelective choice (the stereoelectivity) can be determined from the enantiomeric excess of recovered monomer. Although Agostini *et al.*[7] have reported the enantiomeric purity of optically active β-butyrolactone (determined after ring opening with aniline, reaction of resulting amide with optically active α-methoxy α-trifluoromethylphenyl acetic acid chloride (MTPA) and analysis of diastereomeric esters by ^{19}F n.m.r.), no information concerning the rotary power of optically pure monomer is reported in their paper. In order to establish the enantiomeric purity of unreacted monomers (obtained by stereoelective polymerization), we have used a more direct method which does not involve any transformation reaction, thus avoiding possible racemization reaction which can occur during ring opening. This method is based on the observation by ^1H n.m.r. spectroscopy of the splitting of proton signals in the presence of a chiral solvating agent: S(+) or R(−) 2,2,2 trifluoro-1 (9-anthryl)-ethanol[22].

In the presence of this agent, at 250 MHz (in $CCl_4 + C_6D_6$ (10%) solutions) using a molar ratio alcohol/β-lactone = 3, a doubling of all groups of protons is observed. The most useful signals for the determination of enantiomeric excess are, due to their simplicity, the methyl protons which appear as a set of two doublets located around 1.5 ppm (*Figure 1*). ($\Delta\delta = 0.0165$ ppm).

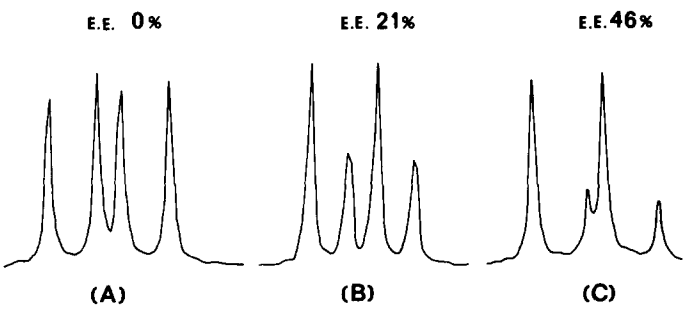


Figure 1 Expanded signals of methyl protons (^1H n.m.r. 250 MHz) of β-butyrolactones of various enantiomeric excesses, in presence of S(+) 2,2,2 trifluoro-1 (9-anthryl)ethanol, solvent: $CCl_4 + C_6D_6$ (10%). Curve a, Racemic monomer; curve b, $\alpha_D^{25} = -5.81°$ (neat, dm); curve c, $\alpha_D^{25} = -12.8°$ (neat, dm)

Enantiomeric excesses are determined from the areas of signals of the two enantiomers. From these results, the rotatory power of optically pure β-lactone (neat, dm) was estimated

$$\alpha_{OD}^{25} = 27.8 \pm 1.6$$

The knowledge of α_{OD}^{25} allows the determination of the stereoelectivity ratio r_R, which is a measure of the preferential consumption of enantiomer R by the initiator (r_R is the ratio of rate constants of polymerization of the two enantiomers, $r_R = K_R/K_S$).

Most of the racemic monomers studied up to now follow a first-order law for enantiomer consumption. In this case the following relationship correlating α/α_0 (optical purity of unreacted monomer), with conversion x has been established[13–15].

$$(1-x)^{r_R-1} = \frac{(1+\alpha/\alpha_0)}{(1-\alpha/\alpha_0)^{r_R}}$$

r_R can be determined from experimental data.

Results presented in *Table 1* show that the average value found for r_R is 1.6 ± 0.1. This value corresponds to (α/α_0) of 16% for 50% of conversion. A slight increase of r_R with conversion is observed. The value of r_R is higher than that found for α-methyl α-n-propyl β-propiolactone ($r_R = 1.25$) (ref. 16). Stereoelectivities of the same order were found for several oxiranes with the same initiator[14,15]. It must be noted that sparteine, used as chiral additive (experiment 5) does not increase the stereoelectivity, in contrast with what was observed for methylthiirane[14,15].

PROPERTIES OF THE POLYMERS

Polymers prepared with $ZnEt_2/R(-)$ DMBD initiator system may be fractionated in two parts according to their solubility in methanol. The insoluble fraction in methanol corresponds approximately to 25% of the whole polymer. No insoluble fraction was obtained in experiment 5 (run in the presence of sparteine). The characterization of polymers is presented in *Table 2*. The soluble fractions have lower molecular weights (less than 5000) than insoluble fractions according to g.p.c. measurements (polystyrene standards). A slight increase in the proportion of insoluble fraction is observed at high conversion.

Thermal properties

The thermal properties of both fractions have been examined by d.t.a.. Soluble fractions are amorphous while insoluble fractions show a peak near 170°C. This value is in the range of that observed for the naturally occurring polymer[23] (PHB with $\bar{M}_n = 85\,500$ ($\overline{DP}_n = 994$) presents a melting point of 180°C while PHB of $\bar{M}_n = 15\,000$ ($\overline{DP}_n = 176$) has a melting point of 168°C) as well as for racemic polymers prepared using stereospecific initiators prepared by treating Et_3Al with H_2O[8,24]. An example of thermogram is shown in *Figure 2*. The existence of a fraction presenting a melting point indicates the formation of a stereoregular polymer. Indeed, isotactic poly β-hydroxybutyrate (optically active or racemic) is crystalline.

Table 2 Fractionation of poly (β-butyrolactone)s prepared by $ZnEt_2/R(-)$ DMBD initiator system

Experiment number	Insoluble fraction in methanol (%)[a]	Molecular weights ($\bar{M}_n \times 10^{-3}$)[b] Insoluble fraction $\bar{M}_n$	I	Soluble fraction $\bar{M}_n$	I
2	18	20	2.5	4.8	1.3
3	21	15	2.1	4	1.3
4	27	[d]	[d]	4.3	1.3
5[c]	–	–	–	2.8	1.4

[a] Relative to the whole polymer
[b] G.p.c. (polystyrene standards)
[c] Experiment carried out in presence of sparteine
[d] Viscosity of insoluble fraction $|\eta| = 0.85$ ($CHCl_3$)

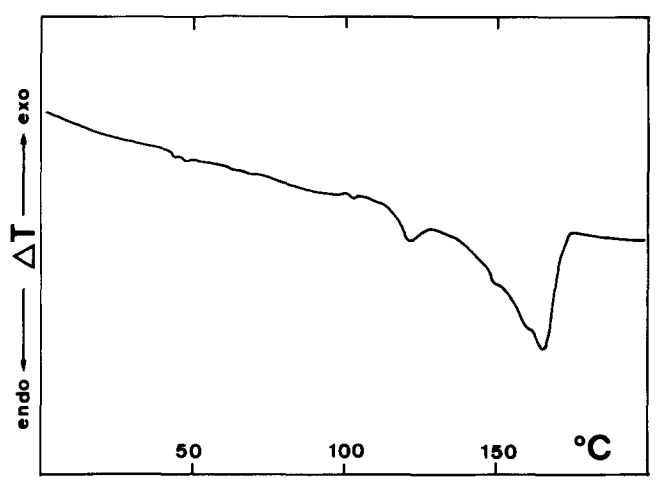


Figure 2 Thermogram (d.t.a.) of insoluble fraction of PHB (run 4)

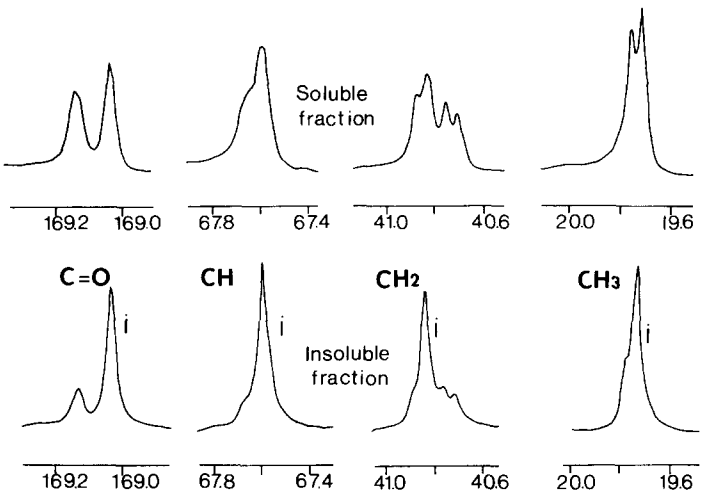
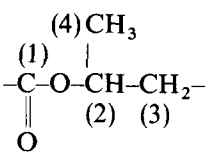


Figure 3 ^{13}C n.m.r. spectra (62.89 MHz) in $CDCl_3$ of both fractions of PHB (run 2, expanded signals)

Microstructure by ^1H and ^{13}C n.m.r.

The microstructure of prepared polymers has been analysed by n.m.r. (^{13}C (62.89 MHz) and ^1H (360 MHz)). In ^{13}C n.m.r. the following chemical shifts have been observed in $CDCl_3$:



C(1): 169.14–169.04
C(2): 67.59
C(3): 40.86–40.82–40.75–40.70
C(4): 19.75–19.71

(in ppm, from t.m.s.).

^{13}C n.m.r. spectra of soluble and insoluble fractions of poly β-hydroxybutyrate are shown in *Figure 3*.

Chemical shifts are in good agreement with those reported by Iida *et al.*[25]. All carbons are stereosensitive. The carbonyl carbon (1) shows a dyad effect: the peak at 169.04 ppm corresponds to isotactic dyad, the other one at 169.14 ppm to syndiotactic enchainment. The signal of carbon (3) is composed of four peaks corresponding to a triad effect (the isotactic triad is located at 40.82 ppm). However, these peaks are not as well resolved, as the signals of carbons (2) and (4) which present a dyad effect. Therefore, analysis was carried out on carbonyl carbon. The proportion of isotactic dyads is lower for soluble fraction (53%) than for insoluble fraction (80%). The average length of isotactic sequences is not actually known. Nevertheless, these sequences are long enough, allowing appearance of crystallinity. Up to now, the minimal length of isotactic blocks required for crystallinity for poly β-hydroxybutyrate has not been determined. It must be mentioned that for related polymers (poly(β-trichloromethyl) β-propriolactone and poly(β-trifluoromethyl β-methyl) β-propiolactone)[26] having random distribution of configurational units R and S, crystallization of polymers is observed for optical purities larger than 70–80%, corresponding to an average length of sequences of 6 to 9 units (proportion of isotactic dyads: 75–80%).

Thermogram of insoluble fraction (*Figure 2*) shows two broad peaks at 122°C and at 166°C, the last being

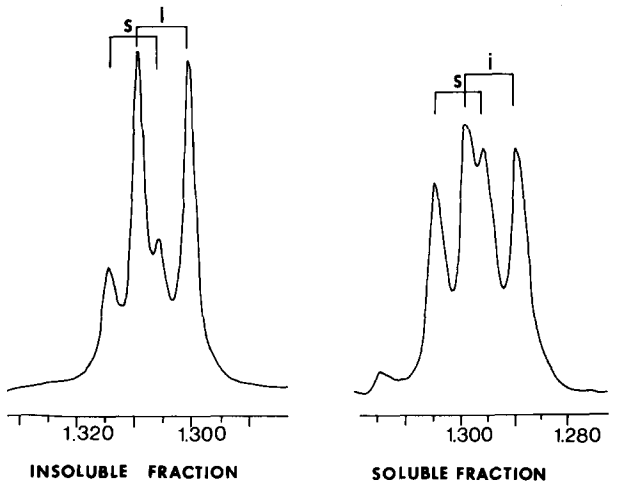


Figure 4 Expanded signals of methyl protons of both fractions of PHB (^{1}H n.m.r. 360 MHz) in $CDCl_3$ (run 4)

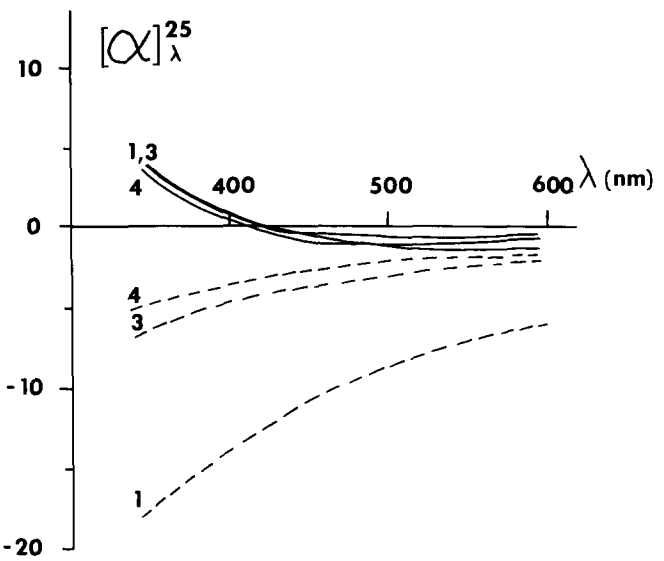


Figure 5 O.r.d. curves (in $CHCl_3$) of PHB's (runs 1, 3, 4). —, Insoluble fraction; ---, soluble fraction

predominant indicating the presence of an extended distribution of isotactic sequences of different lengths.

The microstructure of synthetic poly β-hydroxybutyrates was also examined by ^{1}H n.m.r. (360 MHz). The most useful signals are the methyl protons for which a doubling is observed. Two sets of doublets located around 1.3 ppm ($\Delta\delta = 0.0056$ ppm) correspond to isotactic dyad (lower field). The isotactic doublet is predominant in the case of insoluble fraction (75%) (cf. ^{13}C n.m.r.) (*Figure 4*).

Chiroptical properties

Chiroptical properties (optical rotatory dispersion (o.r.d.) and circular dichroism (c.d.)) of polymers have been also examined.

Optical rotatory dispersion. O.r.d. curves in chloroform are presented on *Figure 5*. The polymers soluble in methanol (molecular weights below 5000) have negative rotatory powers between 600 and 350 nm while insoluble polymers ($\bar{M}_n = 15\,000$–$20\,000$) have weak negative rotation in the visible part which changes to a positive rotation at about 420–430 nm. A similar behaviour has been observed by Marchessault *et al.*[28] for samples of PHB of bacterial origin. A strong effect of molecular weight on rotatory powers has been noticed; polymers with $\bar{M}_n$ values of 569 and 1870 ($\overline{DP}_n$ 7 and 22) have negative rotatory powers while inversion of sign occurs with polymer of $M_n = 31\,400$ ($\overline{DP}_n = 365$) at about 410 nm. A PHB with $\bar{M}_n = 127\,000$ ($\overline{DP}_n = 1476$) presents a positive o.r.d. curve between 600 nm and 350 nm. However, no indication about the polydispersity index of these samples is given.

The origin of this behaviour is not clearly understood. Influence of terminal groups on the rotatory power of optically active low molecular weight polymers (or oligomers) have been noticed in several cases, e.g. for polyterbutyloxiranes[28] or for oligomers derived from propylene oxide[29]. In the case of soluble PHBs, that we have prepared, $\overline{DP}_n$ values seem *a priori* to be high enough (>50) in order to exclude contributions of terminal groups. The examination of n.m.r. spectra (^{13}C and ^{1}H) of polymers reveals the presence of initiator moiety as attested by weak signals at 25.96 ppm $(\underline{CH_3})_3C$, 42.51 ppm $(CH_3)_3\underline{C}$ in ^{13}C spectra and at 1.67 ppm $(\underline{CH_3})_3C$ in ^{1}H spectra. Therefore the influence of these end groups derived from initiator can be indeed considered.

The initiator glycol fragment is of pure R configuration, while the polymer chain is only slightly enriched in one type of configuration. Moreover PHBs of high molecular weights (>30 000) have rather low optical rotation. Thus terminal groups could possibly contribute in some way to optical activity. However, in order to answer this question, a complete study with synthesis of models of PHB with various terminal groups is required.

Circular dichroism. C.d. spectrum of an optically active monomer of S configuration ($\alpha_D^{25} = -5.25°$ (neat,

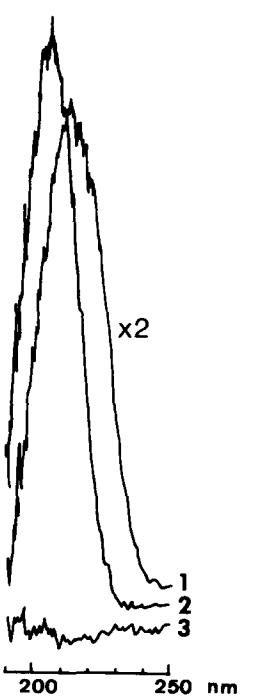


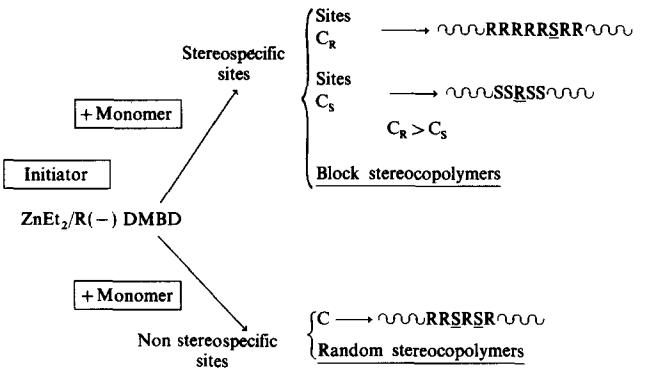
Figure 6 C.d. spectra of an optically active monomer and of an optically active PHB in 1,1,1,3,3,3 hexafluoropropanol-2 solution. Curve 1, R-PHB (c 8.25 g/l, Δε+0.0091) run 3; curve 2, S(−) β-butyrolactone (e.e. 19%, c 7.45 g/l, Δε+0.024); curve 3, solvent alone

dm), optical purity 19%, run in 1,1,1,3,3,3 hexafluoropropanol-2 solution, shows a positive Cotton effect located at 205 nm (dichroic intensity $\Delta\varepsilon_{205} = +0.024$). Similarly, the spectrum of an optically active polymer prepared stereoelectively: $|\alpha_p|_D^{25} = -2.1$ ($c = 0.8$, $CHCl_3$) presents a positive Cotton effect located at 213 nm. ($\Delta\varepsilon_{213} = +0.0091$ in 1,1,1,3,3,3 hexafluoropropanol-2; *Figure 6*). Since natural PHB shows a positive Cotton effect at 213 nm, corresponding to $n \rightarrow \pi^*$ transition[28,31] this indicates a predominance of R configurational units in the PHBs prepared by stereoelective method.

MECHANISM OF POLYMERIZATION

Stereospecificity of the initiator

The existence of a crystalline fraction in poly-β-hydroxybutyrate is an indication of the presence of two kinds of active sites having different stereospecific characters. All these sites have a stereoelective character because they lead to optically active fractions of polymers. Sites producing crystalline fraction are at the same time stereoselective and lead to polymer chains with blocks of R or S units.



If one calls C, C_R and C_S the concentrations of non-stereospecific sites, stereospecific R-type sites and S-type sites, respectively and k'_R, k'_S, k_R and k_S the global rate constants of polymerization on these sites (we do not take in account, here, the reaction of R or S enantiomer with stereospecific sites of opposite chirality C_S or C_R, thus assuming a perfect stereospecificity of these sites), one obtains the following kinetic equations for the consumption of R and S enantiomers:

$$-\frac{d(R)}{dt} = k'_R(C)\,(R) + k_R(C_R)\,(R)$$

$$-\frac{d(S)}{dt} = k'_S(C)\,(S) + k_S(C_S)\,(S)$$

then

$$\frac{d(R)}{d(S)} = \frac{k'_R(C) + k_R(C_R)}{k'_S(C) + k_S(C_S)}\frac{(R)}{(S)} = r_R\frac{(R)}{(S)}$$

The stereoelectivity ratio $r_R = k'_R(C) + k_R(C_R)/k'_S(C) + k_S(C_S) = 1.6 \pm 0.1$ is constant during the polymerization. This value is an average value. The contributions of the different sites to the stereoelective process ('partial' stereoelectivities) are not actually known. Identical behaviour of the $ZnEt_2/R(-)$ DMBD initiator system has been previously observed in the polymerization of propylene oxide[31].

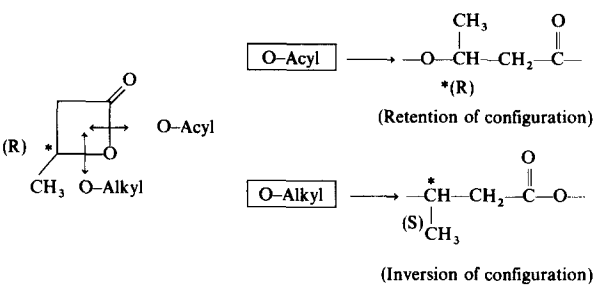
On the contrary, the initiator system prepared by reaction between $ZnEt_2$ and H_2O (molar ratio 1:0.6) does not give crystalline polymer and leads only to amorphous atactic PHB as shown by Iida *et al.*[9]. Crystalline isotactic PHB is obtained with $AlEt_3/H_2O$ initiator system.

The results presented here show that the stereospecific character of an organometallic initiator system does not depend only on the nature of the metal atom, but also on that of the cocatalyst used for its preparation (diol instead of water). The absence of crystalline fraction, when using sparteine, a tetracyclic diamine, as additive in $ZnEt_2/R(-)$ DMBD initiator system, can be explained by coordination of the diamine on zinc atoms leading to a blocking of the stereospecific sites.

Ring-opening reaction

The o.r.d. studies indicate that PHBs prepared by stereoelective polymerization with $ZnEt_2/R(-)$ DMBD initiator system are enriched in R configurational units. Since unreacted monomer is enriched in S enantiomer, this means that the preferentially polymerized R enantiomer is incorporated in the polymer chain without (or with little) racemization.

From these considerations, O-acyl ring-opening seems to be predominant in stereoelective polymerization of β-butyrolactone:



Recently, the ring-opening mechanism in the polymerization of β-butyrolactone by covalent metal alkoxides ($Al(OiPr)_3$, $Ti(OnBu)_4$, Bu_3SnOMe) has been investigated by Kricheldorf *et al.*[32]. On the basis of n.m.r. end-group analysis, it has been established that ring-opening occurs by O-acyl cleavage. A coordination mechanism was proposed. The first step is a complexation of the monomer at the carbonyl oxygen followed by opening of the acyl–oxygen bond (insertion of the β-lactone in the metal–oxygen bond). A similar mechanism can be considered operative in the case of the polymerization of β-butyrolactone by $ZnEt_2/R(-)$ DMBD initiator system.

From c.d. studies, it was concluded that the polymerization occurs with retention of configuration. This is in favour of an O–acyl cleavage which leaves untouched the asymmetric carbon atom.

Polymerization of racemic β-butyrolactone with $AlEt_3/R(-)$ DMBD and $CdMe_2/R(-)$ DMBD

Racemic β-butyrolactone was also polymerized by chiral initiators prepared by reaction between triethyl aluminium or dimethylcadmium and R(−) DMBD. Results are presented in *Table 3*.

Table 3 Polymerization of racemic β-butyrolactone with $AlEt_3$/R(−) DMBD and $CdMe_2$/R(−) DMBD at 20°C in bulk

Initiator system	C/M (mol%)	Polymerization time	Polymer yield (%)	α_D^{25} unreacted monomer (neat, dm)	Insoluble fraction in MeOH (%)	Stereoelectivity ratio r
$AlEt_3$/R(−) DMBD (2/3)	5.25	18 days	13[a]	−0.225	11	1.1
$CdMe_2$/R(−) DMBD (1/1)	3.95	2h	80[b]	+0.20	4.5	1.01

Molecular weights (g.p.c., polystyrene standards)
[a] soluble fraction: 8000
[b] insoluble fraction: 27000–soluble fraction: 16000

Initiator system $AlEt_3$/R(−) DMBD appears to be a stereoelective initiator for the polymerization of β-butyrolactone. Homosteric choice is observed. However, the efficiency (on the basis of polymerization time and stereoelectivity ratio) of this initiator is much lower than that of $ZnEt_2$/R(−) DMBD system. The same behaviour was observed in the case of propylene oxide using as initiator a glycolate of aluminium prepared by reaction between AlH_3 and R(−) DMBD[33]. Polymerization with this system is very sluggish. The combination of this initiator with $ZnCl_2$ leads to a more active initiator which is, however, weakly stereoelective for propylene oxide.

The initiator system $CdMe_2$/R(−) DMBD, on the contrary, is very reactive (a conversion of 80% is obtained after 2h at 20°C). Unreacted monomer has a very low optical activity ($\alpha_D^{25} = +0.2$ (neat, dm); enantiomeric excess < 1%), but is dextrorotatory, weakly enriched in R enantiomer. This means that S antipod, whose configuration is opposite to that of the chiral glycol used in the preparation of initiator, is preferentially incorporated in the polymer chain. Such a choice is called 'antisteric', Such inversion of choice was previously observed in the case of thiiranes[13–15,34] (and also for α-methyl α-ethyl β-propiolactone[21]). It can be correlated with the chemical composition of the initiator (proportions of monoalkylalcoholate (RM_tOR') and dialcoholate species ($R'O–M_t–OR'$)).

The following rule was established. When $I_S = R–Mt–OR/R'O–Mt–OR' < 2$, homosteric choice is observed, but a composition with $I_S > 3$ leads to antisteric choice. The stereoelectivity ratio ($r_S = 1.01$) is very weak in the case of β-butyrolactone. Nevertheless, this result confirms the application to β-lactones (α,α-disubstituted and β-substituted) of homosteric and antisteric rules of choice previously established for thiiranes[20].

CONCLUSION

Different features of the polymerization of racemic β-butyrolactone using chiral initiators have been examined. The standard chiral initiator system $ZnEt_2$/R(−) DMBD used previously in the polymerization of thiiranes and oxiranes shows a valuable stereoelective efficiency. The stereoelectivity observed ($r_R = 1.6$) is the highest found in the series of β-lactones[35]. Recently Japanese workers[35] have reported stereoelective polymerization of β-butyrolactone with N,N'-disalicylidene (1R, 2R) 1,2 cyclohexanediaminato cobalt (1)/$AlEt_3$ initiator system. Efficiency of this complex is very low. Rotatory power of unreacted monomer for a conversion of 34.7% is of −0.143° (neat, e.e. = 0.5%) while with $ZnEt_2$/R(−) DMBD initiator system, for a comparable yield (36%) α_D^{25} is −2.29° (e.e. = 8.2%). This weak asymmetric induction may be due to the remoteness of aluminium atom (where monomer coordinates) with the chiral moiety of the complex.

Homosteric–antisteric processes observed with Zn and Cd initiators have been extended to β-lactones and seem to have quite a general character. Thus, using convenient chiral initiators, it appears now possible to prepare polymers showing properties similar to that of naturally occurring products and to synthesize also polymers having opposite configuration to that of the natural one.

Crystalline and amorphous fractions were isolated from the crude polymer, confirming the presence of sites having different stereospecificities in the active species. Chiroptical properties of PHBs prepared with $ZnEt_2$/R(−) DMBD initiator system indicate that during polymerization the ring-opening reaction occurs predominantly by O–acyl cleavage with retention of configuration.

Further developments include improvements of the efficiency of the initiator system (increase of enantiomeric enrichment and stereoelectivity) and extension of the stereoelective process to other β-substituted β-propiolactones. Application of this process to mixtures of β-lactones should lead to optically active copolyesters which can be compared to natural copolyesters like poly-β-hydroxybutyrate-co-poly-β-hydroxyvalerate recently studied by Bloembergen *et al.*[36], Bluhm *et al.*[37] and Doi *et al.*[38].

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