

STEREOCHEMISTRY OF THE POLYMERIZATION OF THREE-MEMBERED AND FOUR-MEMBERED RING MONOMERS USING CHIRAL INITIATORS

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Abstract - Two main stereochemical control steps must be considered in polymerizations of heterocyclic monomers using chiral initiators. The first one, coordination-stereoelection step, concerns the choice of a particular stereoisomeric species by the initiator. A general configurational relationship based on recognition of homochiral asymmetric carbon atoms has been established. The influence on stereoelectivity of chiral factors due to initiator, monomer and microenvironment is examined. The second one, ring-opening step, determines the final configuration of the polymer chain. A mechanism based on these two steps is proposed for stereoelective processes. Applications for resolution of racemic monomeric mixtures and determination of unknown configurations are discussed.

INTRODUCTION

Heterocyclic monomers having an asymmetric carbon atom in the ring are usually found as racemic mixtures.

According to the stereochemistry of the polymerization process they may lead to stereoregular or non-stereoregular polymers.

If the initiator system is chiral, optically active products may be obtained.

The study of the stereochemistry of polymerization of cyclic monomers using chiral initiators started with the work of Inoue, Tsuruta and Furukawa (1) who prepared optically active polypropylene oxide from racemic monomer using diethylzinc-d-borneol system as catalyst. This procedure was then successfully applied to other three-membered ring monomers such as oxiranes and thiiranes. The results obtained were described in several reviews (2-6).

Recently these reactions were extended to four-membered rings, namely β -propiolactones (7).

In such reactions the chiral initiator preferentially polymerizes one of the stereoisomers from the mixture leading to a polymer enriched in this species. At the same time the unreacted monomer is enriched in the opposite stereoisomer. Therefore these processes can be considered as a particular method of kinetic resolution of racemic monomers (8). They are called either "stereoelective", "asymmetric-selective" or "enantioselective" polymerizations. An "anionic-coordinated" mechanism was proposed in which the monomer, in a first step coordinates to the initiator, then in a second step the ring-opening occurs.

We want to report here some of the features substantiating these two steps and showing that they are both stereochemically controlled.

The first stereochemical control deals with the choice of a particular stereoisomer by the initiator and it depends on the respective natures of both of them. This step determines the resolution of the monomeric mixture. The second stereochemical control occurs at the ring-opening reaction, which is immediately followed by incorporation of the monomeric unit in the polymer chain. The stereoisomeric composition of the latter depends on both steps.

We shall examine successively the different chiral factors coming from the initiator, the monomer, the microenvironment, the polymer chain which affect the stereochemical control of both steps.

STEREOELECTION STEP

Chiral factors due to initiator

The initiators used in stereospecific ring-opening polymerizations are generally containing the $-M_t(II)-X-$ bound. $M_t(II)$ is divalent metal (Zn, Cd) and X being a heteroatom: O, S, N(9,10). Their stereospecificity was explained in terms of enantiomorphic sites concept (2). It is assumed that zinc dimethoxide, for example, contains sites of both chiralities which insure the formation of stereoregular polymers (2,9).

An optically active initiator is composed of sites with one predominant chirality.

As classical example, when an organometallic compound (M_tR_2) is reacted with an hydroxylated

asymmetric reagent (R^*OH) mixed chiral alkylalkoxide-dialkoxide species $[R-M_t-OR^*]_x [R^*O-M_t-OR^*]_y$ are produced.

The chiral component $-OR^*$ determines what we shall call the "local asymmetry" of the initiator.

Let us first consider initiators with predominant dialkoxide species i.e. with a chemical composition $x/y < 1$.

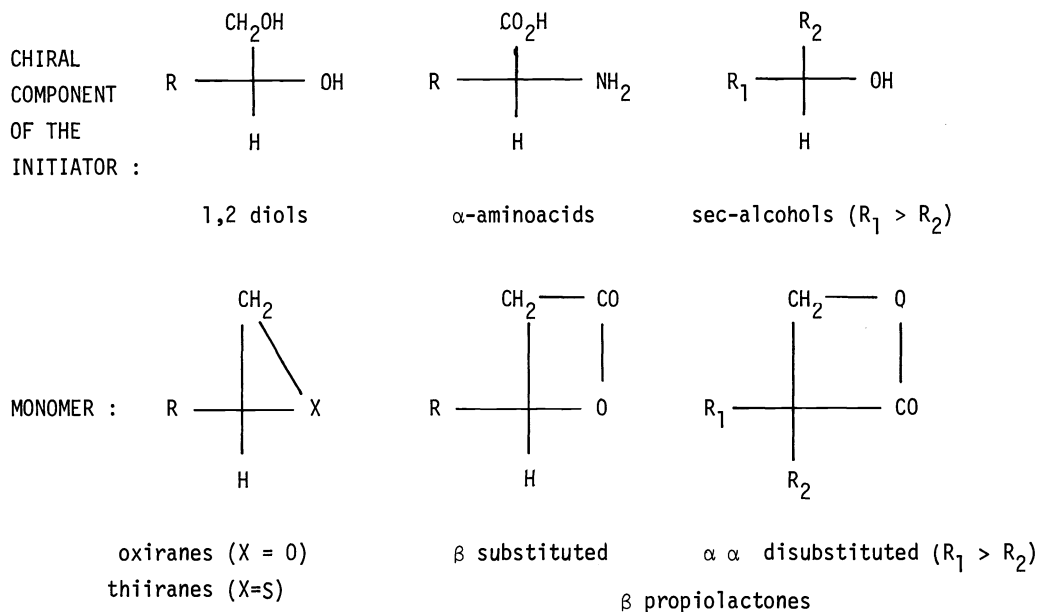
The preferential choice of such chiral initiators for a given stereoisomeric species of the monomer is depending on the configuration of the chiral component (OR^*).

A systematic study carried out on zinc or cadmium initiators with various chiral components (derived from alcohols, diols, aminoacids...) allows us to define a general configurational relationship for the stereoselective choice :

"The spatial configurations of asymmetric carbons in the preferentially chosen stereoisomer and in the chiral component of the initiator must be homochiral".

Such a process is called "homosteric" type choice. Examples of homochiral relationships between monomers and components of initiator are given in Fig. 1 (see Note a).

Fig. 1. Homosteric monomer-initiator relationships



More than fifteen initiators with variously substituted alcohols, glycols, aminoacids tested by us or taken from the literature fitted successfully for methyloxirane or methylthiirane (11).

On the other hand taking as initiator zinc $R(-)$ 3,3-dimethyl-1,2-butane diolate the homosteric choice was observed for more than twenty different oxiranes, thiiranes and β -propiolactones (11) as indicated in Fig. 2.

No exceptions were found up to now, this supporting the general trend of this rule.

A second type of rule applies to initiators with chemical composition $x/y > 3$ i.e. having an excess of alkyl-alkoxide species.

In this case the opposite "heterochiral" configurational choice is observed.

Initially this process was called "antisteric", it seems now more suitable to call it "heterosteric".

It was, at first, observed on few thiiranes with cadmium initiators (12) and recently it was extended to β -propiolactones (7) and seems also to have a general character. (It can not be verified on oxiranes as these monomers are not polymerizable in usual conditions by initiators containing an excess of alkylalkoxide species).

These findings indicate that another type of chirality must be considered in the monomer-initiator stereochemical interaction : it is the "overall asymmetry" of the catalytic species which are more or less aggregated in solution.

Note a. A correct application of this rule necessitates a careful placement of defined analogous substituent groups at the same positions in asymmetric carbon atoms of the monomer and of the initiator components. In some cases the configurational relations fit with R and S rule, but not always. Nevertheless when (R,S) rule is applicable, we shall use it for simplification.

Fig. 2. Examples of homosteric choice for different monomers using an initiator prepared from diethylzinc and R(-)tBu-CHOH-CH₂OH as chiral component.

OXIRANES	Me, secBu, tBu, Ph CH ₂ OH, CH ₂ OCH ₃ , CH ₂ OSiMe ₃ , CH ₂ Cl
THIIRANES	Me, Et, iPr, secBu, tBu CH ₂ OCH ₃ , CH ₂ NEt ₂ , CH ₂ N(Me)(secBu)
β-PROPIOLACTONES	
β subst.	Me
α α disubst.	Me, Et Me, nPr Et, nBu

Depending on the composition of the initiator, i.e. x/y ratio, the catalytic species although bearing the same chiral hand-OR^x, could have two type of arrangements: one giving the "homochiral" choice, the other giving opposite "heterochiral" choice.

Some soluble homosteric and heterosteric species were isolated and studied by NMR, namely, in the diethylzinc-(+) 3,3-dimethyl-2-butanol system (12). One particular composition of hetero(anti)stereic species (x/y = 6) was similar to that obtained by Ishimori et al (13) in the reaction between diethylzinc and methanol [Zn(OMe)₂·(EtZnOMe)₆]. The structure of the latter species was established by X-rays and was shown to be formed of two enantiomeric distorted cubes (14). According to cryoscopic measurements these species exist under monomeric form in benzene (15). They are active for methyloxirane polymerization only at 80°C (15).

Zinc and cadmium diolate initiators, we have mainly used, are heterogeneous systems and their structure is not yet known. No informations on the arrangement of these species in solution are available and they would require some special techniques for investigation.

The previous configurational studies lead to the following conclusions:

General relationships exist between configurations of initiator and monomer in stereoselective type polymerizations.

The type of enantiomeric choice (homosteric or heterosteric) depends first on the local asymmetry, then on the overall chirality of the initiator.

Let us now consider some of the factors dealing with the magnitude of the resolution process, that we shall call "stereoselectivity". It can be defined as the preferential consumption of one of the stereoisomers by the initiator and expressed by the ratio K_R/K_S found in kinetic equations.

The stereoselectivity is generally determined from the optical purity of unreacted monomer, to avoid the problems which can be raised in optical activities of polymers.

For a given monomer it will depend on the nature of the chiral component of the initiator. This problem was examined in detail in previous publications (4,8,12). For a series of analogous components the stereoselectivity increases with the bulkiness of substituents. Among the components represented in Fig. 1, 1,2-diols are the most efficient in stereoselective processes. Zinc R(-) 3,3-diMe-1,2-butanediolate (ZnEt₂-R(-)DMBD system) gave up to now the best stereoselectivities with most of the systems presented in Fig. 2. It will be taken as standard basic initiator for the studies of other parameters examined in next chapters which describe the chiral influence of the monomer and of the environment.

Chiral factors coming from the monomer

For a given initiator the stereoselectivity is depending on the nature of the monomer. In order to establish the kinetic behavior of monomer-initiator system, i.e. to obtain K_R/K_S value, the stereoselective polymerization must be studied on full scale of the conversion. Three types of kinetic equations were found defining three classes of monomers, characterized by different expressions of the relative rates of enantiomer consumption $d[R]/d[S]$, which are respectively equal to :

$$(1st\ class) : r_R \frac{[R]}{[S]} \quad (2nd\ class) : \rho_R \frac{[R]^2}{[S]^2} \quad (3rd\ class) : \gamma_R [R]^2$$

r_R , ρ_R and γ_R being the stereoselectivities of the systems which are constant during the polymerization reaction.

After introduction of experimental data, e.g. the conversion (x) and the optical purity of unreacted monomer (α/α_0), one can integrate these expressions and obtain the three different kinetic equations.

Two monomers (isopropyl and t-butylthiirane) were found to obey to the 2nd class equation (16) and one, transdimethylthiirane to the 3rd class (17). According to recent results re-

reaction one isolates an unreacted monomer with 30 % optical purity. This monomer is reused in a second polymerization and a new monomer of 70 % optical purity is recovered at half reaction. Finally the last step provides a monomer of 98 % of optical purity (8) (Table 2).

TABLE 2. Dependence of the stereoelectivity on enhancement of intracyclic chirality of monomers. ZnEt₂-R(-)DMBD was used as initiator system.

	Starting monomer		r _R	O.p. (%) of unreacted monomer at half reaction
	S _o /R _o	o.p. (%)		
Methylthiirane	1.0	0	2.3	30
	1.53	35	4.4	75
	3.44	55	8.0	98
Methyloxirane	1.0	0	1.8	21
	3.17	53	1.3	61

The stereoelective polymerization appears in this case as a potentially interesting method for preparation of optically active monomers especially when the latter cannot be easily obtained by conventional ways.

The behavior of oxiranes on the example of methyloxirane (Table 2) seems to be different. The stereoelectivity is found to decrease when working with enantiomerically enriched monomers (20). This phenomenon needs more detailed studies for explanation.

The enantiomeric effect was not yet tried on β-propiolactones.

The "extracyclic" chirality assistance is promoted by using monomers bearing asymmetric centers in the substituent. This leads to the formation of diastereoisomers. The efficiency of the chiral assistance is depending on the proximity of the two asymmetric centers, i.e. of the length of the spacer (n). When n=0, the two asymmetric centers being in vicinal positions, a very positive assistance effect was observed as demonstrated on example of (S)secBu (R,S) oxirane for which a stereoelectivity of r_p = 4.0 was found (21). This is much higher than the value found for methyloxirane (r_p = 1.8) for example. It is interesting again to underline, that inspite of the opposite configuration (S) of the assistant asymmetric center the stereoelection works according to homosteric choice with enhancement effect.

The spacer effect was examined with -CH₂ - N - Me₂ substituent on a thiirane cycle. In

this case apparently no enhancement was observed if compared with the achiral component

bearing -CH₂ - N₂Et substituent (r_R=2.0). However the stereoelectivity was somewhat lower to that observed with simple alkyl groups (Me or Et) (r=2.3) (22,23).

Chiral assistance due to microenvironment

The stereoelectivity for a given monomer-initiator system can be changed by modifying the microenvironment of reactive sites.

For example significant differences were observed when the standard initiator ZnEt₂-R(-)DMBD was aged in the presence of different achiral additives such as n-butylether, pyridine or crown-ether (Table 3).

TABLE 3. Dependence of stereoelectivity on the nature of additives in the polymerization of racemic methylthiirane using ZnEt₂-R(-)DMBD initiator system. All polymerizations were carried out in toluene solution at room temperature; (additive)/(initiator) ratio = 1.2 to 1.7.

Additive	r _R
no	2.3
nBu ₂ O	2.9
R(-)tBuCH(OCH ₃)CH ₂ OCH ₃	3.6
dicyclohexyl-18-crown-6	3.9
pyridine	2.7
sparteine	4.0
S(+)-EtCH(Me)CH ₂ SEt	4.5
R(+)-limonene(*)	4.3

(*) polymerization run in pure limonene (no toluene)

By adding some optically active compounds with strong coordinative properties (ethers, amines, thioethers) or even very weak one (limonene, pinene) a substantial enhancement of the stereoselectivity was observed (Table 3).

In the case of methylthiirane polymerization, for example, r value is almost doubled with most of these additives (24). Once again, the intrinsic configurational choice of the initiator remained the same, in agreement with the homosteric rule, even when additives or solvents with heterochiral asymmetric carbon atoms were used. This indicates that such additives increase in some way the overall chirality of the system without changing the configuration. From the results presently obtained it is difficult to estimate the real contribution of asymmetry in these additive effects.

Effects due to the chirality of the polymer chain

In most of the cases studied up to now, no effect of polymer chain was observed in stereoselective polymerizations. Two kinds of experiments were done for this demonstration. The first consists to run a copolymerization of the racemic monomer with an achiral monomer in the presence of optically active initiator. If an end-chain exists, a decrease in stereoselection should be observed due to the incorporation of achiral monomeric units. Methyl-oxirane and methylthiirane were copolymerized respectively with ethylene oxide (25) and ethylene sulfide (26) using zinc alkoxide or glycolate initiators and no effect on stereoselectivity was observed.

The second experiment consists in the polymerization of monomers with unbalanced enantiomeric composition in the presence of achiral initiator and to follow the optical activity of unreacted monomer. If an effect exists, one of the enantiomers will be preferentially consumed and the optical activity of residual monomer will vary with conversion. Enantiomerically enriched methyl-oxirane was polymerized with KOH and $ZnEt_2$ -MeOH but no variation was observed (27). The same behavior was found in the polymerization of enriched methylthiirane (28) and *t*-butylthiirane (29) in the presence of anionic initiators. In all cases the resulting polymer has the same enantiomeric composition as the initial monomer.

The first observation of a stereoselective effect due to the chiral chain-end was reported by Sato et al. (30) in the polymerization of unbalanced mixtures of *t*-butyloxirane enantiomers using potassium *tert*-butoxide as initiator. Using $nBuO(CH_2CH_2O)_6K$ Kazanskij et al. (31) have observed on styrene oxide the same phenomenon: the enantiomer in excess in the initial mixture is preferentially consumed during the polymerization. The results are reported in Table 4.

TABLE 4. Stereoselective effects in the anionic polymerization of enantiomerically enriched *t*-butyl and phenyloxiranes using potassium alkoxides as initiators. In bulk, at 60 and 80°C, respectively.

Oxirane	Initial monomer		Conversion	Unreacted monomer		Ref.
	α/α_0 (%)	S/R		α/α_0 (%)	S/R	
tBu	40	70/30	50	26	63/37	(30)
	50	75/25	60	32	66/34	
Ph	53	76.5/23.5	55	48	74/26	(31)
	80	90/10	46	67	83.5/16.5	
	80*	90/10	74	79	89.5/10.5	

*) additive : dicyclohexyl-18-crown-6 ; $18/6/[C] \approx 1$

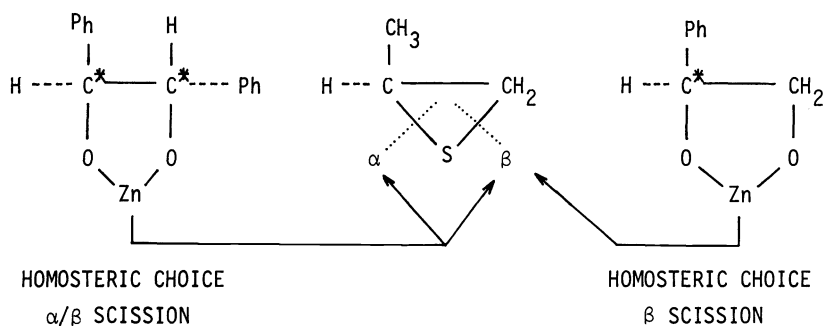
As seen from the data the more unbalanced is the initial mixture, the stronger is the stereoselective effect.

The most reasonable explanation of the observed features seems to be an effect of the growing chiral polymer chain which forms a chiral moiety around the K^+ counterion. This hypothesis is substantiated by the almost complete disappearance of stereoselectivity when using complexing agents, e.g. crown-ethers or cryptands, as seen in data reported in Table 4. In that case the counterion is trapped in the complexing agent and is no more able to be chelated by the polymer chain.

Thus, the polymer chain may play a role in some cases, however in most of stereoselective reactions its influence is not established and these processes are mainly controlled by catalytic chiral sites.

The main chiral factors involved in the stereochemical control of ring-opening polymerizations are summarized in Table 5.

observed for both types of homosteric initiators (with one and two asymmetric carbon atoms) are schematically represented below :



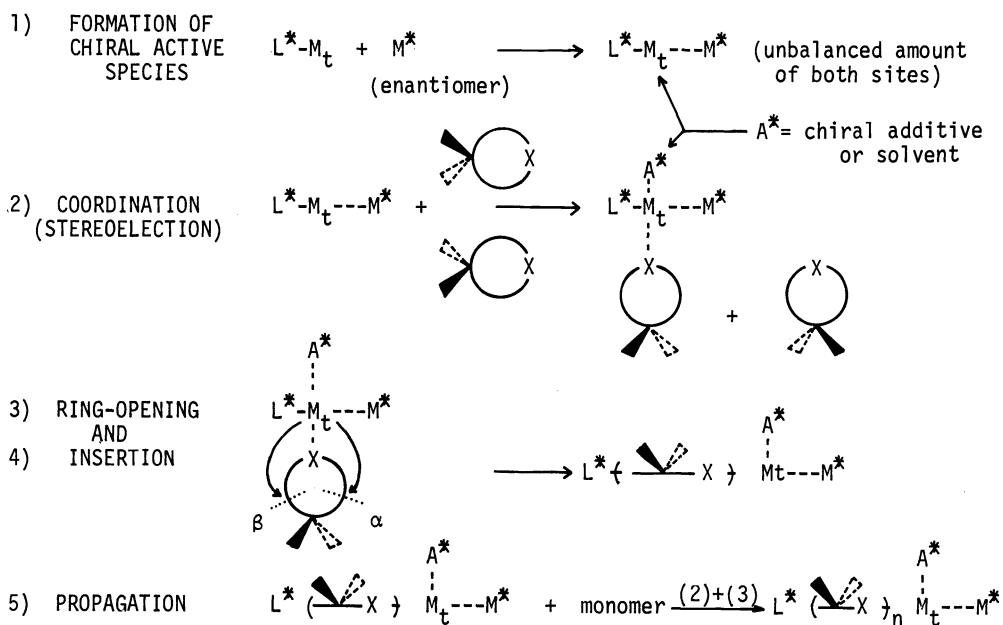
It was already pointed out that the real structure of these initiators is far more complex than that represented. Moreover, it is known from \overline{DP} measurements, that in these heterogeneous systems only a small fraction (sometimes 10^{-3}) of the original catalyst is participating in the initiation. For this reason, it is not possible presently to make any valid assumption on the steric requirements directing the regioselectivity of the ring-opening reaction.

MECHANISM OF THE STEREOCONTROL AND APPLICATIONS

The previous findings on stereochemical control in these reactions can be interpreted as follows: in a first coordination step the stereoelective choice by the initiator occurs according to the homosteric rule.

Then, depending on the nature of the initiator, regioselective ring-opening occurs. On the basis of these features we can now propose the following tentative mechanism of polymerization, which is illustrated in Fig. 3.

Fig. 3 Mechanistic steps in stereoelective polymerization.



1 - In a primary step, chiral active species are formed in an irreversible way by reaction or complexation of the monomer with initiator. This step is substantiated particularly by the fact that when polymerizing enantiomerically enriched monomers, the stereoelectivity i.e. the chirality of the initiator, is increased as compared to the racemic monomer mixture. The activity of the chiral species is thus depending on the composition of the initial mixture. It is possible that chiral additives (A^*) are also involved in this primary reaction of for-

mation of active chiral species.

2 - Then occurs the stereoelection-coordination step in which one of the stereoisomers is preferentially coordinated on the active chiral species according to the chirality rule. The magnitude of the choice can be modified by external chiral agents (A^*) which are either additives, such as optically active ethers, thioethers, amines or solvents like limonene or pinene or all that can modify the microenvironment.

3 - Depending on the nature of the initiator (one asymmetric or two asymmetric centers) a regioselective ring-opening occurs in β or/and α position, followed by the insertion of the monomeric unit in the polymer chain.

4 - The next insertions of monomers necessitate the repetition of steps 2 and 3.

This scheme is certainly oversimplified for many reasons. First, it is believed that a full spectrum of sites of different selectivities is formed which lead to chains of different tacticities (isotactic and heterotactic).

In some of the cases, methyloxirane for example, the contribution of species of different selectivities could be estimated on the basis of fractions of different tacticities isolated from the whole polymer (35). Such fractionation is not always possible.

On the other hand, it is still not known if one or several metal atoms of a site participate in the coordination and the ring-opening steps.

Nevertheless the formation of rigid sites with established asymmetry kept constant during the polymerization is substantiated by all experimental features discussed in this review.

The main applications of stereoelective polymerizations appears to be the following ones :

1- The resolution of racemic enantiomeric mixtures. In some favorable cases using stepwise type reactions or modified initiators it is possible to obtain in small amounts almost optically pure monomers from racemic mixtures. Both enantiomers can be isolated using the same chiral component in the initiators (homosteric-heterosteric processes). This method seems particularly interesting for monomers which could not be easily obtained by classical organic reactions.

2 - The preparation of optically active polymers. The usual method would imply the preparation of optically active monomer and its polymerization. The stereoelective polymerization presents the advantage to prepare at the same time optically active polymers and monomers. It is again possible with the same chiral precursor to tailor polymers of given chirality.

3 - The determination of unknown configurations. The established homochiral relationships allow to use the stereoelective polymerization as a simple method for determination of configurations. According to the rule, the unreacted monomer has a determined configuration.

Extension of stereoelective processes to other heterocyclic monomers is presently under study.

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