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Optically active polymers prepared from haloacetaldehydes.

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OPTICALLY ACTIVE POLYMERS PREPARED FROM HALOACETALDEHYDES

A Dissertation Presented

By

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In memory of Katherine Lee McCormick who,
ten years ago, as my mentor,
made chemistry wonderful and exciting.

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ABSTRACT

Optically Active Polymers Prepared

From Haloacetaldehydes

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Optically active polychloral was prepared where the optical activity arose exclusively from molecular asymmetry (i.e., helical conformation). Molecular asymmetry requires isotacticity, a high conformational energy barrier for the polymer backbone, and an asymmetric initiator to induce a predominance of one helical screw-sense. Polychloral meets the first two criteria. Asymmetric initiators used to obtain optically active polychloral include tetramethylammonium (+)- or (-)-O-acetylmandelate (TMAAc), tetramethylammonium (+)- or (-)-α-methoxymandelate (TMAαM), lithium methyl (+)- or (-)-hydroxidemandelate (LiMM), and lithium cholesteroxide(LiC). Using the above initiators at 0.5 mole % the following maximum specific rotations were obtained for polychloral: TMA(+)Ac initiated $[\alpha]_D^{25}$ = -1860, TMA(-)αM initiated $[\alpha]_D^{25}$ = +210, and Li(-)MM initi-

ated $[\alpha]_D^{25} = -4760$. Optical activity measurements were made in the solid-state due to polychloral's insolubility. Errors in specific rotation were typically 7%. Polychloral initiated by LiC was used as a chromatographic support to obtain 17% resolution of racemic poly(α-methylbenzyl methacrylate).

These initiators were mixed with chloral at a temperature greater than pure chloral's ceiling temperature ($T_c = 58°C$). It was generally observed that with either increasing holding times or with higher holding temperatures, prior to cryotachensic polymerization, that polychloral's specific rotation increased. This increase was attributed to the formation of oligomers above T_c which help prevent errors in the conformational dyad sequences required for helicity (i.e., g^+t or g^-t). Between TMAAc and TMAαM initiated polychloral there was a nine-fold difference in maximum specific rotation. TMAAc polymer's higher optical activity was attributed to the greater size and polarity of the acetyl group versus the methoxy group in TMAαM. This resulted in stronger, second order nonbonded interactions between the acetyl group and the polymer's trichloromethyl group, resulting in a greater probability for one helical screw-sense. LiMM initiated polychloral had a specific rotation two times greater than TMAAc initiated polychloral. This increase was

attributed to LiMM's asymmetric center being closer to the first trichloromethyl group in the polymer than the TMAAc's asymmetric center resulting in even stronger second order non-bonded interactions to induce molecular asymmetry.

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INTRODUCTION

This dissertation describes the synthesis of optically active polychloral in which the optical activity arises from the molecular asymmetry of the polychloral's helical conformation. A predominance of one helical conformation is induced by asymmetric initiators. This work is a part of the general effort in this laboratory to prepare and to study polyhaloacetaldehydes.

Section A discusses, in general terms, the phenomenon of optical activity, the structures that lead to optical activity, and the mathematical relationships that describe optical activity.

Section B surveys the kinds and the techniques used to prepare optically active, synthetic polymers. This section is divided into three subsections: (1) Polymers with asymmetric centers, (2) Polymers with both asymmetric centers and molecular asymmetry, and finally (3) Polymers with molecular asymmetry. The subsections are arranged in this fashion to show the transition from polymers with only asymmetric centers contributing to the optical activity, to polymers in which many asymmetric centers induce molecular asymmetry, and finally to polymers in which only one

asymmetric center preferentially induces molecular asymmetry in the polymer. The work described in this dissertation deals with optically active polymers where molecular asymmetry is induced by one asymmetric center.

Section C surveys the family of haloacetaldehyde monomers and their polymerization. The emphasis of this section is on the monomer trichloroacetaldehyde (chloral) and the thermodynamics that govern its polymerization.

A. Optical Activity

Optical activity arises from the electronic interaction of plane-polarized light and a molecule that lacks symmetry. This asymmetry can be based on either the primary structure of the molecule (i.e., a tetrahedral carbon with four different substituents) or it can be based on the secondary structure of the molecule (i.e., a helix). Optical activity arising from the primary structure depends on the molecule's configuration (an asymmetric center) while optical activity originating from the secondary structure depends on the molecule's conformation (molecular asymmetry). In much of the literature the terms configuration and conformation are, unfortunately, often used interchangeably. Both configurational and conformational optical activity require that an optically active molecule does not possess any kind of mirror symmetry. Specifically, the molecule cannot possess either a center of

inversion, plane of symmetry, or an alternating rotation-reflection axis of symmetry. From the discussions so far, one should realize that for each optically active molecule there exists another molecule that is an exact mirror image of it and this 'mirror' molecule is nonsuperimposable. This 'mirror' molecule is called either an enantiomer or an antipode.

When light is plane-polarized, its electric field moves sinsoidally in a plane, in a single direction. This electric field can be described by a vector which is composed of two components. One component is left-circularly polarized light and the other component is right-circularly polarized light. When plane-polarized light interacts with an optically inactive (i.e., symmetric) molecule, both electrical components are retarded equally. The sum of these two vectors results in a vector which lies in the same plane of incidence. (The retardation of light in a media is gauged by the refractive index, η.) When plane-polarized light interacts with an optically active (i.e., asymmetric) molecule, the velocities of the left- and right-circularly polarized components are different. This means that the sum of the two components results in a vector that lies in a plane that is not the same as the plane of incidence. The angle of rotation between the incident plane of light and the new plane of light is designated as α. It should be emphasized that an equimolar

mixture of an enantiomeric pair (i.e., both antipodes) cannot rotate plane-polarized light and is therefore optically inactive. They are optically inactive because one antipode causes $+\alpha$ (in a clockwise direction, dextrorotary) and the other antipode causes $-\alpha$ (in a counterclockwise direction, levorotary) with the sum of the two rotations being zero. This equimolar mixture of antipodes is said to be racemic.

The rotation, α, will be proportional to the number of asymmetric molecules that the light interacts with. This implies that the path length and the concentration of the optically active species will affect the magnitude of α. To take into account the variations in path length and concentration, an expression that normalizes their effects has been developed. The expression is called the specific rotation, $[\alpha]_\lambda$, and is defined as:

$$[\alpha]_\lambda = \alpha/\ell c \qquad (1)$$

where α is the plane rotation in degrees, ℓ is the path length in decimeters, and c is the concentration of the optically active species in g/ml.

A more useful expression for optical activity which allows a comparison of optically active molecules of different molecular weights has been developed. The expression is called molar rotation, $[\phi]_\lambda$, and is defined as:

$$[\phi]_\lambda = [\alpha]_\lambda \, M/100 \qquad (2)$$

where M is the molecular weight of the optically active species. Since polymers have a molecular weight distribution, the above M is defined as the molecular weight of the polymer repeat unit.

Since optical activity arises from the interaction of light and an asymmetric molecule, the optical rotation, α, is dependent on the wavelength of measurement, λ. This is much like the dependence of the refractive index on wavelength. The change of specific rotation as a function of wavelength gives rise to an optical rotary dispersion curve (ORD). Generally, an ORD curve is simple (i.e., has no inflections or extrema) provided that the specific rotation is measured far from the wavelength at which a chromophore in the optically active molecule undergoes an electronic transition (i.e., it absorbs light). All optically active chromophores are either inherently dissymetric or perturbed by an asymmetric environment. In the region where the optically active chromophore undergoes an electronic transition, the extinction coefficients of left- and right-circularly polarized light are different and this gives rise to the phenomenon of circular dichroism which is described extensively elsewhere (1,2).

The specific rotation will increase monotonically as wavelength decreases provided that the wavelength of

observation is far from the electronic transition. A relationship that mathematically fits the above qualitative description is the Drude Equation and is shown below:

$$[\alpha]_\lambda = \sum_i a_i \lambda_i^2/(\lambda^2-\lambda_i^2) \qquad (3)$$

where λ_i is the wavelength of the i^{th} optically active electronic transition and a_i is a parameter proportional to the rotary strength of the electronic transition.

Experiments have shown that if there is a simple ORD curve, Equation (3) can be simplified to the following form:

$$[\alpha]_\lambda = k/(\lambda^2-\lambda_c^2) \qquad (4)$$

where k is a characteristic constant and λ_c is a mathematical approximation for λ_i. k and λ_c generally have no physical significance for protein-type polymers.

With manipulation, Equation (4) can be rearranged to a form that can be plotted in a linear fashion. This modified form of a single term Drude Equation is:

$$[\alpha]_\lambda \lambda^2 = [\alpha]_\lambda \lambda_c^2 + k \qquad (5)$$

Plotting $[\alpha]\lambda^2$ versus $[\alpha]_\lambda$ is called a Yang-Doty plot.

Unfortunately, a single term Drude expression works only when the optical activity is measured far from an electronic transition. A single term Drude expression also has difficulties in fitting ORD data for helices. Moffitt

developed a phenomenological equation to predict the molar rotation for α-helical polymers. The graphical form of the Moffitt Equation is:

$$[\phi](\lambda^2/\lambda_o{}^2-1) = a_o + b_o/(\lambda^2/\lambda_o{}^2-1) \qquad (6)$$

where a_o, b_o, and λ_o are adjustable parameters. The graphical solution is obtained by selecting values for λ_o (∿200 nm) and plotting $[\phi](\lambda^2/\lambda_o{}^2-1)$ versus $(\lambda^2/\lambda_o{}^2-1)^{-1}$ until a straight line is obtained. The term b_o reflects the helical content of the polymer, while a_o is influenced by both the inherent optical activity of the protein repeat units and background effects like solvation. The Moffitt approach has limitations. For example it assumes that only two electronic transitions contribute to the protein's optical activity which under favorable circumstances is only a first order approximation. It should be emphasized though that both the single term Drude and the Moffitt equations are very useful provided that their limitations are considered. These equations are extremely useful when the alternative is to use quantum mechanics (3) to describe optical activity.

For the purposes of this dissertation, the more important aspects of optical activity are: (1) the secondary structure of a molecule (i.e., a helix) leads to optical activity; (2) specific rotation is wavelength dependent; and (3) there are empirical relationships

describing specific rotation as a function of wavelength.

The classical work of Huygens, Biot, Fresnel, and Pasteur has not been reviewed here, but can be found detailed elsewhere (4). The sources (1,2,5,6) from which this discussion of optical activity has been drawn provide a more detailed treatment of optical activity.

B. Optically Active Synthetic Polymers

Optically active, synthetic polymers can be divided into three major groupings: (1) polymers with optical activity arising from side or main asymmetric centers; (2) polymers with optical activity arising from both asymmetric centers and molecular symmetry; and (3) polymers with optical activity arising from molecular asymmetry. It is the objective of this section to survey these three groupings of optically active synthetic polymers, but more emphasis will be placed on polymers which have molecular asymmetry contributing to the optical activity. Excellent and extensive reviews of optically active, synthetic polymers are available (7-10).

1. Polymers with optical activity arising from side or main chain asymmetric centers. Optically active polymers in which the asymmetric center is the source of the optical activity are typically based on a tetrahedral carbon which has four different substituents. It was once thought that

isotactic polymers could be optically active since the substituted carbon atom is surrounded by four different substituents where two of the substituents are varying lengths of the polymer chain. Using either optically active initiators or monomers with hydrolyzable, optically active side groups, attempts were made to prepare this kind of optically active polymer with the polymer backbone having only one configuration (11-14). All polymers prepared by this approach were optically inactive. The reason for this was explained in a paper by Frisch, Schuerch, and Szwarc as being due to the pseudoasymmetry of the substituted carbons (i.e., the two different lengths of chain about the substituted carbon are identical close to the substituted carbon, therefore there is no optically active transition) (15). An article by Farina and Bressan (10) distinguished between optically active and optically inactive polymers by using Fisher projections. They also showed why the above polymer was optically inactive.

However, there are two approaches by which optically active polymers with asymmetric centers can be prepared: (a) generate an asymmetric center during the polymerization of the monomer; or (b) polymerize a monomer which already contains an asymmetric center. The former of the two approaches is called asymmetric induction, while the latter process of polymerizing a monomer with an asymmetric center is called asymmetric selection. It is into

these two categories that this section on synthetic, optically active polymers with asymmetric centers is divided.

a. Asymmetric induction. One method that has been used to induce the formation of an asymmetric center in the polymer backbone was to copolymerize, alternatingly, a vinyl monomer with an α,β substituted olefin. One of these two comonomers must contain a large, hydrolyzable, optically active, side group. The resulting copolymer should possess a truly asymmetric center in the polymer backbone since the local environment about the asymmetric center was different along the two directions of the polymer chain. The hydrolyzable, optically active, side group was responsible for inducing a specific configuration in the polymer backbone. The first successful copolymerization that led to asymmetric induction was performed by Schuerch (12,16). He radically copolymerized ℓ(-)-α-methylbenzyl methacrylate and maleic anhydride. The optically active copolymer was initially levrorotary. After complete hydrolysis of the optically actide side group, the copolymer was still optically active, but was now dextrorotary. This demonstrated that asymmetric induction had occurred. The synthesis of other optically active copolymers prepared by asymmetric induction has been described elsewhere (17-21).

Another asymmetric induction process used to create asymmetric centers in the polymer backbone involved the polymerization of either a substituted diene or a cyclic

monomer in the presence of an optically active ionic or coordination initiator. It was the function of the optically active initiator to preferentially induce the formation of an asymmetric center having only one configuration in the polymer backbone. An example of an optically active polydiene in which the asymmetric center had been induced involved the coordination (Ziegler-Natta) polymerization of 1,3-pentadiene using triethyl aluminum/titanium (-)tetramenthoxide catalyst. The resulting polymer had a $[\phi]_D$ = (-)23 (22). Other optically active diene polymers with induced asymmetric centers have been prepared (23-26). A cyclic monomer in which the asymmetric center had been induced during polymerization is benzofuran. The optically active polymer from benzofuran was prepared by the cationic initiator aluminum trichloride/(+)-β-phenylalanine. The resulting optically active polymer had a $[\phi]_D$ = (+)90 (27). Similar cyclic monomers and initiators used in asymmetric induction polymerizations can be found described elsewhere (28-30).

b. Asymmetric selection. There are three methods used in asymmetric selection polymerizations: (1) polymerize an optically active monomer to obtain optically active polymer; (2) polymerize a racemic monomer with the growing end of the polymer chain preferentially or exclusively polymerizing monomer of the same configuration (this is called stereoselection); or (3) polymerize a racemic

monomer in the presence of an optically active ionic or coordination initiator. It was the function of the optically active initiator to preferentially induce the formation of an asymmetric center having only one configuration in the polymer backbone. An example of an optically active polydiene in which the asymmetric center had been induced involved the coordination (Ziegler-Natta) polymerization of 1,3-pentadiene using triethyl aluminum/titanium (-)tetramenthoxide catalyst. The resulting polymer had a $[\phi]_D$ = (-)23 (22). Other optically active diene polymers with induced asymmetric centers have been prepared (23-26). A cyclic monomer in which the asymmetric center had been induced during polymerization is benzofuran. The optically active polymer from benzofuran was prepared by the cationic initiator aluminum trichloride/(+)-β-phenylalanine. The resulting optically active polymer had a $[\phi]_D$ = (+)90 (27). Similar cyclic monomers and initiators used in asymmetric induction polymerizations can be found described elsewhere (28-30).

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polysulfonamides (95-98), phenol-formaldehyde polymers (99-101), and polyesters (102).

The second asymmetric selection process is stereoselection where the configuration of the growing polymer chain-end exclusively selects monomer having the same configuration. This is the ideal case where 100% stereoselection occurs. The polymer from such a process consists of a mixture of two homopolymers--one of d configuration and one of ℓ configuration. This mixture has no measurable optical activity. But if resolution is performed, the resolved polymers will be optically active and have different signs of rotation. One example of a stereoselection process involved the stereospecific polymerization of racemic propylene oxide. The resulting racemic poly(propylene oxide) was partially resolved on a sucrose substrate (103). Other examples of stereoselective polymerizations involved the polymerization of racemic 4-methyl-1-hexene, 3-methyl-1-pentene, and 3,7-dimethyl-1-octene. All three of these racemic polymers were resolved on poly-(s)-3-methyl-1-pentene (104).

The third method used in asymmetric selection processes is stereoelection. This is where an optically active initiator polymerizes only one antipode of a racemic mixture. One such stereoelection process involved a Ziegler-Natta catalyst which contained an asymmetric center. This asymmetric center in the catalyst remained at

the growing end of the polymer chain and selected the configuration of the incoming monomer. Pragmatically though, stereoelection under some circumstances can be a special case of stereoselection. This arises when an optically active initiator attacks only one antipode of the monomer, then the configuration of the growing polymer chain-end selects the configuration of the incoming monomer--a stereoselection process.

One of the first stereoelection polymerizations was performed by Furukawa using d,ℓ-propyleneoxide initiated by dialkylzinc/(+)menthol (105,106). The resulting mixture consisted of levorotary polymer and unreacted dextrorotary monomer. Similar claims of preparing optically active polymer due to a stereoelection process have been reported for: polyalkylenesulfides (107), poly-α-olefins with the asymmetric center α to the polymer backbone (108-110), polyaminoacids prepared from N-carboxyanhydrides (111-115), and polyvinylethers (116).

2. Polymers with optical activity arising from both asymmetric centers and molecular asymmetry. There are a significant number of polymers which have both molecular asymmetry and asymmetric centers contributing to the polymer's optical activity. In these kinds of polymers, the asymmetric center induces the formation of the molecular asymmetry.

Probably the most thoroughly studied classes of polymers which have both asymmetric centers and molecular asymmetry are proteins and polypeptides. For these polymers, the helical conformation (molecular asymmetry) is based on the intramolecular hydrogen bonding of the amino acid moieties (the site of the asymmetric centers). Generally, optically active, synthetic polymers do not have hydrogen bonding, so the component of optical activity originating from their molecular asymmetry has a somewhat different basis than that found in proteins. In light of this difference, optically active proteins and polypeptides are not reviewed here, but have been discussed elsewhere (6,117,118).

Stereoregular, synthetic polymers can exist in a helical conformation. This has been demonstrated for some stereoregular polymers in the solid state (119). It is recognized that the preferred conformation of an isotactic polymer in the solid state is helical (tg^+, tg^-), while for a syndiotactic polymer it was generally a planar zig-zag (120,121). Consequently, a synthetic polymer must be isotactic if it is to have molecular asymmetry making a contribution to the polymer's optical activity. However, more than isotacticity is required for a polymer to have optical activity due to molecular asymmetry. For example, isotactic polypropylene is helical in the solid state, but there is no optical activity because a left-handed helix is just

as probable as a right-handed helix (i.e., they have the same conformational energy, therefore a 50/50 mixture). In order for an isotactic polymer to have optical activity originating from molecular asymmetry, it is necessary to introduce into the polymer some group which makes one screw-sense of the helix more favored (i.e., having a lower conformational energy). Typically, this group is an asymmetric center in the side chain. This asymmetric center can lead to a predominance of one helical form which means the polymer is also optically active due to helicity.

To illustrate how an asymmetric center induces molecular asymmetry in synthetic polymers, the remainder of this section will concentrate on two examples: (1) poly-α-olefins with asymmetric centers in the side chain; and (2) the transesterification of poly(methyl acrylate) with optically active alcohols. Poly-α-olefins with asymmetric centers in the side group are being used as one example because of the meticulous and comprehensive studies performed. The example of the transesterification of poly(methyl acrylate) was chosen because the results convincingly demonstrate that asymmetric centers in the side chain can induce molecular asymmetry in isotactic polymers.

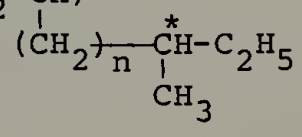
Numerous studies have been performed on poly-α-olefins with asymmetric centers in the side chain (70,71, 122) with the majority of these studies performed by Pino and his associates (8,123,124). One of his studies focused

on determining how the proximity of the asymmetric center to the polymer backbone affected the formation of helical segments. In this study, a series of poly-α-olefins were prepared with the asymmetric center at various distances from the polymer backbone (8,74). The optical activity of the polymer and a model compound were compared, as shown in Table 1.

TABLE 1

MOLAR ROTATIONS OF POLY-α-OLEFINS WITH ASYMMETRIC CENTERS IN THE SIDE CHAIN

n	$[\phi]_D$ polymer[a]	$[\phi]_D$ model compound
0	+161	-11
1	+288	+21
2	+68	+12
3	+20	+13

[a] 

n = 0, 1, 2, 3

As shown in the table, when the asymmetric center was either α or β to the polymer backbone, a large difference between the molar rotation of the polymer and the model compound was observed (10-20 fold difference). But as the asymmetric center was placed further away from the backbone, the molar rotation of the polymer and the model compound eventually became essentially the same. The 'excess' optical activity, when the asymmetric center was

close to the polymer backbone, was taken as one piece of evidence supporting the concept that an asymmetric center in the side chain could preferentially induce a particular helical conformation.

A different study by Pino on these poly-α-olefins focused on how the polymer's stereoregularity (i.e., isotacticity in this case) affected its optical activity (8, 23). One example from this study is shown in Table 2 for poly-(S)-4-methyl-1-hexene.

TABLE 2

ISOTACTICITY AND MOLAR ROTATION OF POLY-(S)-4-METHYL-1-HEXENE

I.R. stereoregularity index	$[\phi]_D$
0.60	+174
0.68	+239
0.83	+261
0.95	+286
0.98	+288

As can be seen in Table 2, the molar rotation increased with increasing stereoregularity (isotacticity). This result was consistent with asymmetric centers inducing molecular asymmetry, since as isotacticity increased more and longer helical sequences could exist in the polymer, creating greater molar rotation.

In still another study, Pino followed the change of molar rotation as a function of temperature for either solutions or melts of these poly-α-olefins with asymmetric centers in the side chain (8,23,125). These results were compared to low molecular weight paraffin model compounds with the results shown in Table 3.

TABLE 3

TEMPERATURE COEFFICIENT FOR THE MOLAR ROTATION OF SOME POLY-α-OLEFINS AND PARAFFINS

Polymer	$\Delta[\phi]/\Delta T$	Paraffin	$\Delta[\phi]/\Delta T$
poly-(S)-3-methyl -1-pentene	-0.36	(S)-3-methylhexane	-0.01
poly-(S)-4-methyl -1-hexene	-0.68	(S)-3-ethyl-5-methyl heptane	-0.07
poly-(S)-5-methyl -1-heptene	-0.34	(R)-5-ethyl-2,3-dimethyl heptane	-0.06

As can be seen in Table 3, the molar rotation of the polymers was 5-10 times more sensitive to temperature changes than the paraffin model compounds. This temperature sensitivity of the polymer's optical activity was consistent with the concept of asymmetric centers inducing molecular asymmetry. This behavior was consistent because the polymer had a variety of conformations with different conformational energies and probabilities. As the temperature of the polymer was increased, the probability of the conformations that led to either the other helical form or a random coil increased. This was why the optical activity for

these polymers decreased with increasing temperature. However, it should be noted that for these same polymers in the solid state, $\Delta[\phi]/\Delta T$ was very small (0.03-0.09). This arose because of the reduced mobility of the polymer in the solid state (i.e., the helical conformation was 'locked in').

One other piece of work by Pino that supports the concept of asymmetric centers inducing molecular asymmetry in synthetic polymers involved the copolymerization of an optically active monomer and an achiral monomer (123,124). This was done to see if the achiral monomer participated in the formation of helical segments, acquiring optical activity. An isotactic, random copolymer of (S)-4-methyl-1-hexene and 4-methyl-1-pentene was prepared and its specific rotation measured. At the same time, the specific rotation was calculated for a physical mixture of the two homopolymers having the same composition as the copolymer. The difference between the specific rotations of the copolymer and the mixture indicated whether the achiral monomer was participating in a helical segment. 4-methyl-1-pentene was chosen as the achiral monomer since it was a good chemical/structural approximation of the optically active monomer, (S)-4-methyl-1-hexene. This similarity between the two monomers was essential to insure that no measurable asymmetric induction occurred in the polymer backbone. The results of this study are shown in Table 4.

TABLE 4

COPOLYMERIZATION OF (S)-4-METHYL-1-HEXENE WITH 4-METHYL-1-PENTENE

Mole % of (S)-4-methyl -1-hexene	$[\alpha]_D$ copolymer	$[\alpha]_D$ homopolymer mixture	$[\phi]_D$ calculated for 4-methyl-1-pentene
100	+292	+292	--
70	+260	+204	+157
40	+233	+117	+162
23	+161	+67	+105
13	+100	+38	+60

From Table 4, it was clear that the achiral monomer in the copolymer was involved in creating some kind of asymmetry, as indicated by the 'excess' specific rotation for the copolymer versus the homopolymer mixture. As argued above, it was improbable that an induced asymmetric center in the backbone could contribute to the 'excess' molar rotation listed in the fourth column in Table 4. Another observation that can be made from Table 4 was that for the copolymer having between 70 and 40 mole % of optically active comonomer, the achiral component made the same optical activity contribution. This implied that a relatively small quantity of asymmetric centers could generate a great deal of molecular asymmetry.

In synopsis, the variety of experiments using poly-α-olefins with asymmetric centers in the side chain tended to support the concept that asymmetric centers could induce

molecular asymmetry in synthetic polymers. The results of these experiments can be summarized as follows: (1) the closer the asymmetric center was to the polymer backbone, the greater the optical activity due to more and/or longer helical segments; (2) higher isotacticity of the polymer led to more and/or longer helical segments; (3) in solution or the melt, the polymer's optical activity decreased with increasing temperature due to the loss of conformations that led to optical activity; and finally (4) in copolymers with an optically active comonomer and an achiral comonomer, the achiral component participated in the formation of helical segments.

The other study that adds considerable credence to asymmetric centers inducing molecular asymmetry was performed by Minoura (126). In this work, atactic and isotactic poly(methyl acrylate) were transesterified with (S)-2-methyl-1-butanol. If the asymmetric center in the side chain ((S)-2-methylbutyl group) did not induce molecular asymmetry, the transesterified atactic and isotactic poly(methyl acrylate) would have the same optical activity. The optical activity would also increase linearly with the degree of transesterification provided that there was no induction of molecular asymmetry. The results of the experiment are shown in Table 5. For the atactic polymer, there was a linear increase in the specific rotation as the mole fraction of 2-methylbutyl groups increased. However,

TABLE 5

TRANSESTERIFICATION OF POLY(METHYL ACRYLATE) WITH 2-METHYL-1-BUTANOL

poly(methyl acrylate)	mole fraction of 2-methylbutyl group in polymer	$[\alpha]_{350}$
atactic	0.377	+7.8
	0.352	+7.4
	0.279	+6.3
	0.251	+6.0
isotactic (99%)	0.444	+17.1
	0.364	+16.8
	0.276	+16.5
	0.140	+9.2
	0.058	+2.1

for the isotactic polymer the specific rotation did not increase as a linear function with the degree of transesterification. Specifically, the transesterified, isotactic polymer had a greater optical activity than a comparable atactic polymer. The implication of this was that the isotactic polymer was being induced into a helix of one screw-sense. This interpretation was reasonable since it was stipulated earlier that isotacticity was required for a helical conformation.

The work outlined here by Pino and Minoura convincingly shows that an asymmetric center in the side chain induces helical conformations of the polymer backbone. Abe and Goodman (9) conceptualized the induced molecular asymmetry in these polymers as being of a varying number and length of helices. Also, the summation of the product of helical length and the number of molecules having that length should be equal to a constant. One implication of this was that the polymer chains are constantly moving in and out of helical conformations (i.e., the polymer does not have a 'fixed' or permanent helical segment).

A variety of other optically active, synthetic polymers have been prepared in which the 'excess' optical activity was due to asymmetric centers inducing molecular asymmetry. Much of the work on these polymers considered some aspect already discussed for the poly-α-olefins. These polymers include polyvinylethers (75-77),

polyaldehydes (34), polyalkylvinylketones (80), polyacrylates (127-131), polyisocyanates (83), polyisocyanides (68, 132), and polyurethanes (91,94).

3. Polymers with optical activity arising from molecular asymmetry. Optically active, synthetic polymers in which the optical activity arises principally from the secondary structure of the polymer (i.e., a helix) are a recent development in polymer synthesis. One of the first syntheses which resulted in a 'pure' helical structure was the preparation of hexahelicene (133). Hexahelicene could be resolved into a right- and a left-handed helix having opposite signs of rotation and has a large specific rotation, $[\alpha]_D^{25}$ = (+)3700. This high optical rotation coming from a helix was one of the driving forces encouraging researchers to synthesize optically active polymers with only molecular asymmetry. In the past few years, three kinds of polymers have been prepared in which the optical activity arises solely from molecular asymmetry. They are polyisocyanides, poly(triphenylmethyl methacrylate), and polychloral. Since the basis of this dissertation deals with the synthesis of optically active polymers having only molecular asymmetry, the literature on these three polymers will be discussed in some detail.

a. Polyisocyanides. Polyisocyanides (also called poly(iminomethylenes)) are prepared by the cationic

polymerization of isocyanides by Lewis acids. The unique chemistry of isocyanides (also called isonitriles) has been discussed in detail by Ugi (134). Millich performed most of the pioneering work on the polymerization of isocyanides and the characterization of these polymers (135). He determined that polyisocyanides had the conformation of a tightly-wound helix with a 4_1 spiral. The polyisocyanide was in a helical conformation because each carbon atom in the polymer backbone was substituted which caused a great deal of steric hindrance. Since polyisocyanides were helical with a high conformational energy barrier, it was highly probable that any sample of polyisocyanides was really a racemic mixture of left and right-handed helices since helix inversion was very unlikely. Realizing that a polyisocyanide with a bulky substituent like a tertiary butyl group should consist of a 1:1 mixture of the two helices, Drenth and Nolte went about trying to resolve them. Using a column packing of insoluble poly((+)-sec-butyl isocyanide) which had only one screw-sense, they were able to resolve poly(tert-butyl isocyanide) into a (+) and a (-) antipode (68,136). This was apparently the first time anyone was able to resolve a polymer which had only molecular asymmetry and no asymmetric centers. This resolution was possible in solution only because polyisocyanides have such a high conformational energy barrier that even in solution helix inversions did not occur.

Drenth and Nolte tried to apply the concept that the screw-sense of a helix should be determined by the initiator in helical polymers prepared from achiral monomers. For a symmetrical initiator, both screw-senses should be equally probable provided the isocyanide does not contain an asymmetric center. However, an asymmetric initiator should lead to a polymer having a predominance of one screw-sense since the interaction of the asymmetric center and the first monomer unit should favor one screw-sense on a conformational energy basis. They attempted using the optically active initiator nickel(II) ℓ-alaninate to promote the formation of helices having one screw-sense (68). However, only a slight predominance of one helical form occurred (i.e., nominal optical rotation). The low optical activity was due to excess isocyanide displacing the alaninate, the asymmetric center, from the initiator. Drenth and Nolte also discussed the chances of helix inversions in polyisocyanide and the difficulties of determining the screw-sense of a helix in these same papers (136,137).

b. Poly(triphenylmethyl methacrylate). One of the first experiments with triphenylmethyl methacrylate that led to optically active polymer was its anionic copolymerization with a small amount of ℓ(-)-α-methylbenzyl methacrylate (130,131). Yuki and Hatada observed for the copolymer a large optical rotation opposite in sign from

the ℓ(-)-α-methylbenzyl methacrylate. They attributed this anomalous optical activity to the ℓ(-)-α-methylbenzyl methacrylate inducing the triphenylmethyl methacrylate segments into a preferred helical conformation. They also observed that copolymer with only short triphenylmethyl methacrylate segments would irreversibly lose its optical activity in solution. This loss of optical activity was attributed to helix reversals starting at the more flexible ℓ(-)-α-methylbenzyl methacrylate component. It became apparent that the homopolymer of triphenylmethyl methacrylate would be loss prone to helix inversion, since earlier work (138,139) indicated that the bulky substituent should lead to a high conformational energy barrier for this highly isotactic polymer.

The researchers at Osaka University went about trying to prepare the optically active homopolymer of triphenylmethyl methacrylate where the optical activity came from the helix. It was realized that an optically active initiator or counterion would be required to prepare a polymer having predominantly one screw-sense. Using the optically active initiator, lithium (R)-N-(1-phenylethyl)-anilide, poly(triphenylmethyl methacrylate) was prepared having a specific rotation of (-)104 at λ = 589 nm in toluene. Using a lithium/(-)-sparteine counterion in polymerizing triphenylmethyl methacrylate, Yuki and coworkers obtained poly(triphenylmethyl methacrylate) with a specific

rotation of (+)363 at λ = 589 nm in toluene (140, 141).

When the first triphenylmethyl methacrylate adds to any initiator, there will be two types of helical precursors--one that leads to a left-handed helix and the other leads to a right-handed helix. If the initiator contains an asymmetric center, one helical precursor will be favored because it has a lower conformational energy. This implies that the polymer will be optically active due to a predominance of one helical form and most likely will not have an optical purity of 100%.

With the asymmetric center residing in the initiator, the specific rotation of the polymer cannot increase during polymerization. This result is inevitable since after the initiation step, the asymmetric center can no longer correct a possible helix inversion in the growing chain. After initiation, only the bulky triphenylmethyl group at the end of the growing polymer chain has any control over the hand of the helix. The other approach of having the asymmetric center in the counterion allows the asymmetric center to stay close to the propagating end of the polymer chain. This permits it to constantly, sterically control the placement of incoming monomer. This should lead to a polymer having primarily one screw-sense. Consequently, by using an optically active counterion, it is possible for the polymer's specific rotation to increase with conversion.

Yuki also reported (142,143) that with the above optically active poly(triphenylmethyl methacrylate) as either a column packing or a coating on silica gel, that resolution or partial resolution of the following compounds was possible: hexa helicene, Tröger base, 1-phenylethyl alcohol, menthol, styrene oxide, 1,2- and 1,3-disubstituted cyclic compounds, and various atropoisomeric 2,2'-disubstituted-1,1'-binaphthyls.

c. Polychloral. One of the first successful experiments that resulted in polychloral having a measurable optical activity originating from the secondary structure (i.e., the helix) was performed by Corley and Vogl (144,145). Earlier attempts were made by Vogl in 1963 and by Hatada and Vogl in 1973 to prepare optically active polychloral initiated by lithium cholesteroxide (186,187). They realized that polychloral was isotactic and helical and it was very improbable that it could undergo helix inversions because of the bulky trichloromethyl group. In one case, Corley and Vogl used the optically active initiator tetramethylammonium (+)-ketopinate to induce molecular asymmetry, obtaining a polymer with a specific rotation of (+)2400 ± 800 at λ = 589 nm. In another case, they used the optically active counterion (+)-methyl-*n*-propyl benzylphenyl phosphonium to induce molecular asymmetry and obtained optically active polychloral with a specific rotation of (-)2700 ± 200 at λ = 589 nm. The

errors in these specific rotations were due to the optical activity measurements being performed in the solid state (polychloral is insoluble). Bonsignori and Lorenzi have discussed the considerable problems of measuring optical activity in the solid state (146).

Because of Corley's encouraging results, this author pursued the preparation of optically active polychloral with the goal of trying to better understand what influences the induction of molecular asymmetry. Preliminary work in which this author was involved included the partial resolution of racemic poly(α-methylbenzyl methacrylate) on polychloral initiated by lithium cholesteroxide (147). Preliminary results have also been reported on the polymerization of chloral by two optically active carboxylate initiators (148). A detailed discussion of the above results will appear later in this dissertation.

d. Requirements for molecular asymmetry polymers. From the prior three examples of optically active, helical polymers, it is apparent that there are several fundamental requirements that must be met if one is to prepare an optically active polymer where the optical activity is derived exclusively from its secondary structure: (1) the polymer must be isotactic so that it can assume a helical conformation; (2) a high conformational energy barrier is required to prevent helix inversion; (3) some asymmetric center in either the initiator or its counterion is

required to induce a prevalence of a particular screw-sense in the polymer; and (4) optical activity measurements in the solid state may be required since helical polymers can have a rod-like structure which often results in poor solubility.

C. Haloacetaldehydes

Haloacetaldehyde monomers are subject to polymerization through their carbonyl group. This carbonyl is highly polarized, with the oxygen atom being nucleophilic and the carbon atom being electrophilic. This polarization of the carbonyl group renders haloacetaldehydes susceptible to both kinds of ionic polymerization--cationic and anionic. In cationic polymerization, the electrophile (i.e., H^+) attacks the oxygen atom of the carbonyl group, while in anionic polymerization the nucleophile (i.e., alkoxide) attacks the carbon atom of the carbonyl group. Of the two ionic polymerization mechanisms, haloacetaldehydes are most readily polymerized anionically. This high susceptibility to anionic polymerization is caused by the electron withdrawal of the halogen atoms α to the carbonyl group. The electron withdrawal makes the carbon atom much more electrophilic and very prone to attack by even very weak nucleophiles (i.e., all types of Lewis bases). These nucleophiles function as polymerization initiators. Various compounds that lead to initiation include tertiary

amines, tertiary phosphines, and tertiary arsines which are all tertiary organic compounds of Group VIA elements. Other initiators used include onium compounds such as the ammonium, phosphonium, or sulfonium salts of fluoride, chloride, bromide, iodide, hydroxide, alkoxide, thioalkoxide, or carboxylate. One final group of initiators were based on IA, IIA, or IIIA metal salts of hydroxides, hydrides, alkoxides, or carboxylates (149). It should be emphasized that ionic polymerizations of haloacetaldehydes are susceptible to the same termination and transfer reactions by protics like any ionic polymerization.

An interesting feature of haloacetaldehydes, and in fact all aldehydes, is that they are incapable of polymerizing at elevated temperatures. This arises strictly from thermodynamic considerations. For a polymerization reaction to proceed, the change in Gibbs free energy (ΔG^{o}) must be negative. Gibbs free energy is related to the change of enthalpy (ΔH^{o}) and the change of entropy (ΔS^{o}) as shown in the following equation:

$$\Delta G^{o} = \Delta H^{o} - T\Delta S^{o} \qquad (7)$$

where T is the temperature (°K). When alkenes are polymerized, the enthalpy change highly favors polymerization (i.e., it is relatively large and negative, $\sim$-20 kcal/mole), while the entropy change works against polymerization (i.e., it is small and negative, $\sim$20-30 cal/°K mole).

Consequently, for the polymerization of most alkenes, ΔG° is negative within any temperature range that a polymerization reaction would be performed. When aldehydes are ionically polymerized, the enthalpy change barely favors polymerization (i.e., it is relatively small and negative, $\sim$-5 kcal/mole), while the entropy change is similar to that mentioned for alkenes. The small, negative enthalpy change for aldehyde polymerization means that at relatively low temperatures the product of $|T\Delta S^{\circ}|$ can be equal to or larger than $|\Delta H^{\circ}|$, forcing ΔG° to be zero or positive and preventing polymerization. This requires for most aldehyde polymerizations that the monomer be cooled so that ΔG° becomes negative, permitting polymerization. The temperature at which $\Delta G^{\circ} = 0$ ($\Delta H^{\circ} = T\Delta S^{\circ}$) is called the threshold polymerization or ceiling temperature. Obviously, at any temperature greater than this, polymerization cannot occur. The threshold polymerization temperature is dependent on the monomer concentration and the following relationship expresses this dependency (derived elsewhere (150,151)):

$$\ln [M]_c = \frac{\Delta H^{\circ}}{RT_c} - \frac{\Delta S^{\circ}}{R} \qquad (8)$$

where $[M]_c$ is the molar concentration of monomer, R is the gas constant, and T_c is the ceiling temperature (i.e., temperature at which $\Delta G^{\circ} = 0$). The standard value reported in literature for the ceiling temperature of a given

monomer is defined as the temperature at which $\Delta G^{\circ} = 0$ for a one molar solution of monomer (151).

As reviewed by Corley (144), attempts to polymerize the haloacetaldehyde, chloral, at ambient temperature resulted in incoherent polymer. The polymer was incoherent because the initiator could not be evenly dispersed in the monomer prior to its 'instantaneous' polymerization. It was recognized by Vogl (149,152), considering the aforementioned thermodynamics, that the initiator could be evenly dispersed in the monomer if the monomer was at a temperature greater than the threshold polymerization temperature (i.e., 58°C for pure chloral monomer). This technique of introducing initiator into monomer at a temperature above its threshold polymerization temperature and then cooling the mixture so that polymerization occurs was called cryotachensic polymerization (152). It was by this technique that coherent pieces of polychloral could be made.

Polychloral, whether it was prepared by cryotachensic polymerization or not, was insoluble in all solvents (153). It was also crystalline (153,154) and isotactic (155) according to X-ray diffraction. It was shown to have the conformation of a 4_1 helix and a tetragonal crystal structure (155). From Equation 8, it is implied that if the polymer is exposed to a temperature greater than T_c, the polymer can depolymerize to monomer. The onset of

depolymerization can be delayed by eliminating all alkoxide endgroups in the polymer (alkoxide endgroups are very susceptible to depolymerization and result from occlusion of growing chain ends). They could be eliminated by post-treating the polymer with dilute acid to obtain hydroxyl endgroups, but other post-treatment reactions gave rise to endgroups that were more thermally stable (156,157).

Numerous studies have been performed on polychloral and have focused on a variety of issues. Some of these studies include copolymerization with isocyanates and ketenes (158,159), cationic polymerization (160), interpenetrating networks (161,162), preparation of different kinds of endgroups (156,163,164), stabilization by post-treatment (157,165), stabilization by copolymerization (158,159), and kinetics (166,167).

Other members of the polyhaloacetaldehyde family that have been prepared include polyfluoral (168), polybromal (169), polydichlorofluoroacetaldehyde (170), polydifluorochloroacetaldehyde (171), polydibromofluoroacetaldehyde (172), polydifluorobromoacetaldehyde (173), polydibromochloroacetaldehyde (174), and polydichlorobromoacetaldehyde (175).

The one polyhaloacetaldehyde (based on Cl, Br, and F) that has not been prepared to date is polybromochlorofluoroacetaldehyde. The synthesis of bromochlorofluoroacetaldehyde (BCFA) monomer was attempted in this

dissertation so that the above polymer with an asymmetric center α to the polymer backbone could be prepared. The synthesis of such an optically active aldehyde requires either an asymmetric reaction or resolution to obtain the optically active compound. The synthetic route designed for BCFA envisions the use of a resolution process.

C H A P T E R I I

EXPERIMENTAL SECTION

A. Materials

acetone (F, MCB)

acetyl chloride (E)

BF_3·etherate (A)

bromine (F)

n-butyl lithium, 2.1 M in n-hexane (AV)

t-butyl lithium, 1.5 M in n-pentane (A)

calcium sulfate, anhydrous (F)

chloral, trichloroacetaldehyde (M)

cholesterol (A)

cyclohexane (F, MCB)

deuterium oxide (A)

deuterochloroform (A, N)

Diazald ® (A)

diethyl ether (F, MCB)

diethyl ether, anhydrous (MCB)

diphenyl ether (F)

1,4-dioxane (F)

d(+)-ephedrine (A)

ℓ(-)-ephedrine (A)

ethanol, 95% (F)

ethanol, absolute (F)

2-(2-ethoxyethoxy)-ethanol (A)

n-hexane (F)

hydrochloric acid (F, MCB)

lithium aluminum hydride (AV)

magnesium sulfate, anhydrous (F)

d(+)-mandelic acid (A)

ℓ(-)-mandelic acid (A)

dℓ-mandelic acid (A)

methanol (F, MCB)

mercuric fluoride (PB)

molecular sieves, 3Å (FAG)

phenolphthalein (F)

phosphorous pentoxide (F, MCB)

potassium hydroxide (MCB)

sodium (F)

sodium bicarbonate (F)

sodium chloride (F)

sodium ethoxide (F)

sodium hydroxide (F, MCB)

sodium sulfate, anhydrous (MCB)

sulfuric acid, concentrated (F, MCB)

tetramethylammonium hydroxide, 20% in methanol (A)

trichloroacetyl chloride (A)

trichloroethylene (A)

trimethyl orthoformate (A)

12-crown-4 (A)

p-toluenesulfonic acid (E)

Sources: A - Aldrich Chemical Co., AV - Alfa-Ventron Co., E - Eastman Kodak Co., F - Fisher Scientific Co., FAG - Fluka Chemical Corp., M - Montrose Chemical Co., MCB - Matheson, Coleman, and Bell, Inc., N - Norell Chemical Co., PB - Pfaltz and Bauer, Inc.

B. Purification of Solvents and Reagents

Chloral (4L) was placed in a dry, one-neck, 5L roundbottom flask. To the chloral was added phosphorous pentoxide (200 g) which converted any residual chloral hydrate to chloral. The heterogeneous mixture was refluxed overnight in a nitrogen atmosphere. The crude chloral was removed from the phosphorous pentoxide char by simple distillation and was further purified by fractional distillation using a 3 ft column packed with glass helices. This polymerization grade chloral had a purity greater than 99.5% as judged by gas chromatography. The monomer was freshly distilled prior to any polymerization (176).

Cholesterol was recrystallized from hot 95% ethanol. The product was dried overnight in an Abderhalden apparatus at 40°C and 0.2 mm Hg.

n-Hexane was washed with concentrated sulfuric acid in a separatory funnel until a yellow color no longer persisted. The n-hexane was neutralized with a 5% sodium bicarbonate aqueous solution and washed with deionized

water. It was then pre-dried by washing with saturated aqueous sodium chloride and by storing over anhydrous magnesium sulfate. The n-hexane was then refluxed overnight over freshly cut sodium metal in a nitrogen atmosphere. The n-hexane was finally fractionally distilled at atmospheric pressure with the forecut discarded. The middle fraction was collected in a Schlenk tube containing activated 3Å molecular sieves.

'Anhydrous' diethyl ether was placed in a fractional distillation apparatus which had been flammed-out and cooled under a nitrogen stream. Diethyl ether was refluxed overnight under nitrogen over freshly cut sodium metal. The diethyl ether was fractionally distilled at atmospheric pressure under nitrogen with a forecut discarded. The middle fraction was collected in a Schlenk tube which contained activated 3Å molecular sieves.

Cyclohexane was washed with concentrated sulfuric acid, neutralized with 5% aqueous sodium bicarbonate, and washed with water. It was then pre-dried by washing with saturated, aqueous sodium chloride and storing over anhydrous magnesium sulfate. The cyclohexane was placed in a fractional distillation apparatus which had been flammed-out under a nitrogen stream. It was refluxed under a nitrogen atmosphere over freshly cut sodium metal. A distillation forecut was discarded with the middle fraction collected in a Schlenk tube which contained activated 3Å

molecular sieves.

2-Octanol was placed in a fractional distillation apparatus which had been flammed-out under a nitrogen stream. A small amount of sodium metal was added, generating some alkoxide from which the 2-octanol was distilled. The vacuum distillation was performed with a forecut discarded. The middle fraction (b.p. 74-76°C, 0.5 mm Hg) was collected in a Schlenk tube containing activated 3Å molecular sieves.

C. Preparation of Initiators

1. Lithium cholesteroxide. In an oven-dried, 25 mm x 150 mm test tube, in a nitrogen-filled glove bag was placed recrystallized cholesterol (3.46 g, 8.95 mmole). A serum cap was used to seal the test tube before removal from the glove bag. The test tube's contents were placed under a nitrogen purge with dry n-hexane then injected (15.4 mL). n-Butyl lithium (2.1 M in n-hexane, 4.3 mL, 9.0 mmole) was added to the heterogeneous contents of the test tube with butane gas evolved. Most of the insoluble cholesterol reacted and formed a solution.

2. Tetramethylammonium d(+)-, ℓ(-)-, or dℓ-0-acetylmandelate.

a. Acetylation of d(+)-, ℓ(-)-, or dℓ-mandelic acid. d(+)-, ℓ(-)-, or dℓ-Mandelic acid (5.0 g, 33 mmole)

was reacted with acetyl chloride (7.0 ml, 98 mmole) as described by Organic Syntheses (177). Yield = 5.5 g (86%), m.p. 97.5-99°C (lit. 96.5-98°C, (178)). For ℓ(-)-O-acetyl mandelic acid, $[\alpha]_D^{25}$ = (-)153, $[\alpha]_D^{25}$ lit. (179) = (-)154 (methanol, c = 0.1 g/mL), optical purity = 99%. For d(+)-O-acetylmandelic acid, $[\alpha]_D^{25}$ = (+)151, $[\alpha]_D^{25}$ lit. (179) = (+)154 (acetone, 2.5 g/100 mL), optical purity = 98%.

b. Titration of d(+)-, ℓ(-)-, or dℓ-O-acetylmandelic acid with tetramethylammonium hydroxide. Dissolve d(+)-, ℓ(-)-, or dℓ-O-acetylmandelic acid (5.0 g, 26 mmole) in methanol (50 mL). A drop of 1% phenolphtalein in methanol was added and the O-acetylmandelic acid solution was titrated to a pink endpoint with 20% tetramethylammonium hydroxide in methanol. The solution was then back-titrated prior to the pink endpoint with a solution O-acetylmandelic acid. The solution volume was reduced in half by boiling off methanol. To this solution was added 1,4-dioxane (60 mL). The solution volume was reduced an additional quarter by boiling. The solution was allowed to cool with white platelet crystals forming. The crystals were collected and dried in an Abderhalden apparatus at 40°C and 0.05 mm Hg. m.p. = 184-187°C (dec.). ^{13}C NMR in D_2O: δ C-$\underline{C}$O-$O^{\ominus}$ 176.1, O-$\underline{C}$O-CH_3 174.2, aromatic 136.9, 129.8, 128.5, Ar-$\underline{C}$H-CO 78.7, $\overset{+}{N}(CH_3)_4$ 56.2, 56.0, 55.8, and CO-$\underline{C}H_3$ 21.4 ppm. Tetramethylammonium d(+)-O-acetylmandelate, $[\alpha]_D^{25}$ = (+)88 (methanol, 0.3 g/100 mL). Tetramethyl-

ammonium ℓ(-)-O-acetylmandelate, $[\alpha]_D^{25}$ = (-)86 (methanol, 1.3 g/100 mL).

3. Tetramethylammonium d(+)-, ℓ(-)-, or dℓ-α-methoxy-mandelate.

a. Esterification of dℓ-mandelic acid. Into a dry, 500 mL roundbottom flask was placed dℓ-mandelic acid (112 g, 736 mmole), p-toluenesulfonic acid (14 g, 74 mmole, 10 mole %), and methanol (300 mL, 3700 mmole--a five-fold excess relative to mandelic acid). The reaction was blanketed with nitrogen and refluxed overnight. The methyl mandelate was isolated by extraction into diethyl ether (300 mL). Unreacted acids were removed from the product by washing with 5% aqueous sodium bicarbonate in a separatory funnel. The ether layer was washed with deionized water and pre-dried by extraction with saturated aqueous sodium chloride and storing over anhydrous magnesium sulfate. The diethyl ether was removed by rotary evaporation at 20 mm Hg. The crystalline methyl mandelate was dried at room temperature and 0.1 mm Hg. m.p. = 54-56°C (lit. m.p. = 57-58°C (180)). Yield = 102 g (83%). ^{13}C NMR: δ $\underline{C}O$ 174.0, aromatic carbons 138.4, 128.6, 128.5, and 126.7, Ar-$\underline{C}$H-CO 72.9, and COO$\underline{C}H_3$ 52.8 ppm.

b. O-methylation of methyl mandelate. In a 1 L, single-neck, roundbottom flask was placed methyl mandelate (70 g, 420 mmole), trimethyl orthoformate (700 mL, 6400

mmole), and BF_3·etherate (7.0 ml, 57 mmole). The trans-etherification reaction (181) was blanketed under nitrogen and refluxed overnight. The crude product was isolated by first destroying BF_3·etherate and trimethylorthoformate with acidified methanol. The product was extracted into diethyl ether in a separatory funnel with the ether layer washed by 5% aqueous sodium bicarbonate and water. The ether layer was subsequently dried by washing with saturated aqueous sodium chloride and storing over anhydrous magnesium sulfate. The ether was removed via rotary evaporation at 20 mm Hg. The crude product was subjected to the same methylation reaction as described above two more times to insure complete methylation. The product was fractionally distilled at 0.15 mm Hg with the middle fraction having a b.p. 63-67°C. Yield = 51.5 g (68.1%). ^{13}C NMR in $CDCl_3$: δ -$\underline{C}$O- 171.1, aromatic carbons 136.3, 128.8, 128.7, 127.2, Ar-$\underline{C}$H-CO- 82.6, -O-$\underline{C}H_3$ 57.3 and -CO-O$\underline{C}H_3$ 52.2 ppm.

c. Hydrolysis of methyl α-methoxymandelate. In a 500 mL roundbottom flask was placed methyl α-methoxymandelate (51.5 g, 285 mmole), methanol (50 mL), and sodium hydroxide (40 g, 1000 mmole) dissolved in water (250 ml). A white salt precipitated shortly and the heterogeneous mixture was heated to a gentle reflux overnight. To isolate the product, concentrated hydrochloric acid was added slowly until the white salt dissolved. This

solution was extracted with diethyl ether in a separatory funnel. The ether layer was washed with 5% aqueous sodium bicarbonate and water. It was then pre-dried by washing with saturated aqueous sodium chloride and by storing over anhydrous calcium sulfate. The ether was removed by a rotary evaporator at 20 mm Hg leaving a viscous oil which slowly crystallized. Yield = 36.0 g (76%). ^{13}C NMR in $CDCl_3$: δ -CO- 174.3, aromatic carbons 135.9, 128.9, 128.7, and 127.3, Ar-CH-CO- 82.3, and $-OCH_3$ 57.2 ppm.

d. Resolution of r-α-methoxymandelic acid. In a 50 mL Erlenmeyer flask was dissolved r-α-methoxymandelic acid (10 g, 60 mmoles) and ℓ(-)-ephedrine (10 g, 55 mmoles) in methanol (27 mL) by gentle heating for one hour. The Erlenmeyer flask was cooled to room temperature and held at room temperature overnight with white crystals forming. The crystals were collected, washed with methanol (6 mL), boiled in methanol (12 mL) for 5 minutes, and chilled to 0°C. White crystals remaining were collected and were designated batch A.

All prior methanol fractions were collected and used to dissolve an additional portion of α-methoxymandelic acid (9.0 g, 54 mmoles) and ℓ(-)-ephedrine (9.0 g, 49 mmole) with gentle heating for one hour. The same isolation and purification processes were repeated as described in the prior paragraph. The resulting crystals were designated batch B.

Again all methanol fractions were collected and an additional portion of α-methoxymandelic acid (11.4 g, 68.6 mmole) and ℓ(-)-ephedrine (11.4 g, 62.2 mmoles) were dissolved in the combined methanol fractions by gentle heating for one hour. The same isolation and purification processes were repeated as already described in this section. The resulting crystals were designated batch C.

All methanol fractions were collected with the methanol removed by rotary evaporation at 20 mm Hg. A gold, crystalline material remained which was designated batch D. Batch D was dissolved in water (120 mL) and concentrated hydrochloric acid (12 mL), giving an opaque, white solution. This solution was extracted with diethyl ether (150 mL) in a 1 L separatory funnel. The ether layer was washed with water, and pre-dried by washing with saturated, aqueous sodium chloride and by storing over anhydrous magnesium sulfate. The ether was removed by rotary evaporation at 20 mm Hg leaving an oil. Crude yield of partially resolved d(+)-α-methoxymandelic acid = 17.9 g. $[\alpha]_D^{25}$ = (+)96.3, $[\alpha]_D^{25}$ lit. (179) = (+)150 (methanol, c = 6.7 g/100 mL), optical purity = 64.2%. This d(+)-α-methoxymandelic acid was re-resolved with d(+)ephedrine as follows: In a 50 mL Erlenmeyer flask was placed d(+)-α-methoxymandelic acid (17.9 g, 108 mmoles), d(+)-ephedrine (17.9 g, 108 mmoles), and methanol (28 mL). Solution was achieved by gentle heating for one hour. The solution was

allowed to remain at room temperature overnight with white crystals forming. The crystals were collected and washed with methanol (10 mL). They were then dissolved in water (75 mL) and concentrated hydrochloric acid (7.5 mL), giving an opaque, white solution which was extracted with diethyl ether (100 mL) in a separatory funnel. The ether layer was washed with water and pre-dried by washing with saturated, aqueous sodium chloride and storing over anhydrous sodium sulfate. The ether was removed by rotary evaporation at 20 mm Hg, leaving an oil which slowly crystallized. Yield of d(+)-α-methoxymandelic acid = 11.3 g (74.2%). $[\alpha]_D^{25}$ = (+)135, $[\alpha]_D^{25}$ lit. (179) = (+)150 (methanol, c = 6.7 g/100 mL), optical purity = 90.0%.

Crystalline batches A, B, and C were combined so that ℓ(-)-α-methoxymandelic acid could be isolated. Batches A, B, and C were dissolved in water (100 mL) and concentrated hydrochloric acid (10 mL), giving a white, opaque solution. This solution was extracted with diethyl ether (150 mL) in a separatory funnel. The ether layer was washed with water and pre-dried by washing with saturated aqueous sodium chloride and storing over anhydrous sodium sulfate. The ether was removed by rotary evaporation at 20 mm Hg, which left a slowly crystallizing oil. Yield of ℓ(-)-α-methoxymandelic acid = 10.2 g (67.0%). $[\alpha]_D^{25}$ = (-)144, $[\alpha]_D^{25}$ lit. (179) = (-)150 (methanol, c = 6.7 g/100 mL), optical purity = 96%.

e. Titration of d(+)-, ℓ(-)-, or dℓ-α-methoxymandelic acid. The appropriate α-methoxymandelic acid (6.0 g, 36 mmoles) was dissolved in methanol (15 mL) in a 125 mL Erlenmeyer flask. (Approximately 0.5 mL of this solution was set aside for back-titration.) A drop 1% phenolphthalein in methanol was added to the α-methoxymandelic acid. This solution was titrated with 10% tetramethylammonium hydroxide in methanol to a pink phenolphthalein endpoint. The solution was then back-titrated just prior to a pink endpoint. 1,4-dioxane (50 mL) was added to the flask and methanol was removed by boiling until the solution became slightly turbid. The mixture was chilled and a white, crystalline product was collected under a nitrogen atmosphere. The tetramethylammonium α-methoxymandelate was dried overnight at 40°C and 0.2 mm Hg in an Abderhalden drying apparatus. ^{13}C NMR in D_2O: δ $\underline{C}O$ 178.8, aromatic carbons 139.1, 129.6, 129.4, 128.2, $\underline{C}H$ 85.7, $-O\underline{C}H_3$ 57.4 and $\overset{+}{N}(\underline{C}H_3)_4$ 56.2, 56.0, and 55.8 ppm. $[\alpha]_D^{RT}$ = (+)52.1 (methanol, C = 0.1 g/2 mL) for tetramethylammonium d(+)-α-methoxymandelate. $[\alpha]_D^{RT}$ = (-)56.4 (methanol, C = 0.026 g/2 mL) for tetramethylammonium ℓ(-)-α-methoxymandelate.

4. Lithium methyl d(+)-, ℓ(-)-, or dℓ-hydroxidemandelate.

a. Esterification of dℓ-mandelic acid. See Chapter II, Section C.3.a., p. 44.

b. Esterification of d(+)- or ℓ(-)-mandelic acid. In a distillation flask was placed potassium hydroxide (6 g, 107 mmoles), water (10 mL), 2-(2-ethoxyethoxy)-ethanol (35 mL), and diethyl ether (20 mL). In a dropping funnel, attached to the distillation flask, was N-methyl-N-nitroso-p-toluenesulfonamide (Diazald®, 21.5 g, 100 mmoles) dissolved in diethyl ether (200 mL). The distillation flask was placed in a 70°C water bath and the Diazald solution was added dropwise to the 70°C potassium hydroxide solution over a 30 minute period. Immediately a yellow solution of diazomethane (CH_2N_2) in diethyl ether distilled and was collected in a chilled Erlenmeyer flask. (The distillation apparatus contains no ground glass joints and was in a ventilation hood due to the high toxicity of diazomethane.)

The diazomethane solution was added slowly to a chilled solution of the appropriate mandelic acid (10.7 g, 70.4 mmoles) dissolved in diethyl ether (75 mL). The rapid evolution of nitrogen gas was observed with the complete dissipation of the yellow diazomethane color. Unreacted mandelic acid was removed by washing the ether solution in a separatory funnel with 5% aqueous sodium bicarbonate and water. The ether solution was pre-dried by washing with saturated, aqueous sodium chloride and by storing over anhydrous sodium sulfate. The diethyl ether was removed on a rotary evaporator at 20 mm Hg, leaving a light-yellow oil

which subsequently crystallized. The crude product was sublimed overnight in a vacuum sublimator at 0.5 mm Hg and 40°C. Yield of methyl d(+)- or ℓ(-)-mandelate = 6.1 g (59%), m.p. 55-56.5°C (lit. 55.5°C (178)). Methyl d(+)-mandelate, $[\alpha]_D^{RT}$ = (+)142.2, $[\alpha]_D^{RT}$ lit. (179) = (+)143 (methanol, C = 0.15 g/2 mL), optical purity = 99.4%. Methyl ℓ(-)-mandelate, $[\alpha]_D^{RT}$ = (-)140.5, $[\alpha]_D^{RT}$ lit. (179) = (-)143 (methanol, C = 0.15 g/2 mL), optical purity = 98.3%.

c. Reaction of methyl d(+)-, ℓ(-)-, or dℓ-mandelate with t-butyl lithium. The appropriate methyl mandelate was resublimed through phosphorous pentoxide at 0.2 mm Hg and room temperature in a vacuum sublimator. The sublimator was placed in a nitrogen-filled glove bag. The methyl mandelate (0.51 g, 3.07 mmoles) was then placed in a dry 25 mm x 200 mm test tube and was covered with a serum cap prior to removal from the glove bag. The methyl mandelate was dissolved by injecting distilled diethyl ether (4.5 mL) and distilled cyclohexane (2.0 mL). The solution was cooled to -22°C with a dry ice/carbon tetrachloride bath. t-Butyl lithium (1.95 mL, 2.93 mmoles, 1.5 M in pentane) was slowly injected into the methyl mandelate solution. Gas evolved and a fine, white suspension formed. After three additional minutes at -22°C, initiator and diluent were allowed to warm to room temperature for five minutes. The initiator was used immediately to polymerize trichloroacetaldehyde.

5. Lithium d(+)-, ℓ(-)-, or dℓ-2-octanoxide. In an oven-dried, serum capped 25 mm x 150 mm test tube was placed distilled cyclohexane (2.25 mL) and the appropriate 2-octanol (0.50 mL, 3.1 mmoles). The hazy solution was cooled to 0°C under a nitrogen atmosphere. By slowly injecting 1.5 M t-butyl lithium (1.90 mL, 2.85 mmoles) into the 2-octanol solution, the initiator solution of lithium 2-octanoxide was prepared. The initiator mixture was allowed to age five minutes at 0°C before injection into chloral for polymerization.

D. Polymerization of Trichloroacetaldehyde

1. Lithium cholesteroxide as initiator. In a dry, serum-capped, 500 mL Erlenmeyer flask was injected trichloroacetaldehyde (150 mL, 1530 mmoles) and dry n-hexane (190 mL). The contents of the Erlenmeyer flask were kept under a nitrogen atmosphere at all times. The Erlenmeyer flask was placed in a 40°C oil bath and allowed 10 minutes to come to temperature. The initiator, lithium cholesteroxide (6.6 mL, 3.1 mmoles, 0.2 mole %), was injected into the trichloroacetaldehyde solution. The initiated monomer was placed in a -20°C freezer overnight so that polymerization could proceed. The polymer was milled and extracted with acidified methanol (10% HCl vol.) at room temperature for one day. The polymer was rinsed with methanol and dried at 0.1 mm Hg prior to final stabilization with phosphorous

pentachloride, PCl_5 (157). The PCl_5 stabilization involved refluxing a 0.64 M solution of PCl_5 in CCl_4 over the polymer for three days. The polymer was collected by filtration, washed successively with CCl_4 and acetone, and extracted for two days with acetone in a Soxhlet extractor. The polymer was dried at 20 mm Hg for one day. Yield of polychloral = 127 g (56%).

2. Tetramethylammonium d(+)-, ℓ(-)-, or dℓ-O-acetylmandelate as initiator. Glass plates (7" x 7" x 1/4") were washed with a sodium dodecyl sulfate solution, rinsed with deionized water, and swabbed with acetone. The plates were dried for two days in a 125°C oven. A film assembly was prepared by placing a 3500 denier polyurethane elastomer thread between two hot glass plates with the plates held together by Boston clamps. The film assembly was placed in an oven whose temperature was the same as the temperature at which the monomer and initiator were mixed and held.

Tetramethylammonium d(+)-, ℓ(-)-, or dℓ-O-acetylmandelate (0.84 g, 3.2 mmoles), 0.5 mole %) was placed in a dry, 125 mL Erlenmeyer flask while in a nitrogen-filled glove bag. The flask was sealed with a rubber septum and removed from the glove bag. In another dry, serum-capped, 125 mL Erlenmeyer flask was injected approximately 70 mL of distilled trichloroacetaldehyde. The two flasks containing initiator and monomer were immersed in an ethylene glycol

thermostat bath set at one of the following temperatures: 70.0, 75.0, or 85.0°C. The flasks were allowed 10 minutes to come to the bath temperature. With a warm syringe, trichloroacetaldehyde (60 mL, 620 mmoles) was injected into the flask containing the tetramethylammonium O-acetylmandelate initiator. A yellow, opaque solution formed. Ten minutes after the monomer and initiator had been mixed, an aliquot of the mixture was removed via a warm syringe and was injected into two, warm, film assemblies. The film assemblies were plunged into an ice water slurry overnight so that polymerization could proceed. This process of casting films from initiated monomer was repeated 20, 30, and 50 minutes after the initial mixing of monomer and initiator.

The next day the film assemblies were separated and the film was floated off the glass plate in acidified methanol (10% HCl). The films were kept in acidified methanol for one day to stabilize the films (157). The films were rinsed with methanol and soaked in methanol for one day. Typically, a 12 mm disc of film was cut with a #6 cork borer from a 'wet' film. The disc was soaked in diphenyl ether for at least two days prior to optical activity measurements.

3. Tetramethylammonium d(+)-, ℓ(-)-, or dℓ-α-methoxymandelate as initiator. Glass plates (7" x 7" x 1/4") were

washed with a sodium dodecyl sulfate solution, rinsed with deionized water, and swabbed with acetone. The plates were dried for two days in a 125°C oven. A film assembly was prepared by placing two 3500 denier polyurethane elastomer threads between two hot glass plates. The glass plates were held together by Boston clamps. The film assembly was placed in an oven whose temperature was the same as the temperature at which the monomer and initiator were mixed and held.

Tetramethylammonium d(+)-, ℓ(-)-, or dℓ-α-methoxymandelate (0.64 g, 2.8 mmole, 0.5 mole %) was placed in a dry, 125 mL Erlenmeyer flask while in a nitrogen-filled glove bag. The flask was sealed with a rubber septum and removed from the glove bag. In another dry, serum-capped, 125 mL Erlenmeyer flask was injected approximately 60 mL of fractionally distilled trichloroacetaldehyde. The two flasks containing initiator and monomer were immersed in an ethylene glycol thermostat bath set at one of the following temperatures: 65.0, 70.0, 80.0, or 85.0°C. The flasks were allowed 10 minutes to come to the temperature of the thermostat bath. With a warm syringe, trichloroacetaldehyde (50 mL, 510 mmoles) was injected into the flask containing the tetramethylammonium α-methoxymandelate initiator forming a yellow, opaque solution. Ten minutes after the monomer and initiator had been mixed, an aliquot of the mixture was removed via a warm syringe and injected

into two warm film assemblies. The film assemblies were plunged into an ice water slurry overnight so that polymerization could proceed. This process of casting films from initiated monomer was repeated at 20, 30, and 50 minutes after the initial mixing of monomer and initiator while in the constant temperature bath.

The next day the film assemblies were separated and the film was floated off the glass plate in acidified methanol (10% HCl). The films were kept in acidified methanol for one day to stabilize the films (157). The films were rinsed with methanol and soaked in methanol for one day. Typically, a 12 mm disc of film was cut from the bulk sample while it was still 'wet' with methanol. The disc was soaked in diphenyl ether for at least two days prior to optical activity measurements.

4. Lithium methyl d(+)-, ℓ(-)-, or dℓ-hydroxide mandelate as initiator. Glass plates (7" x 7" x 1/4") were washed with a sodium dodecyl sulfate solution, rinsed with deionized water, and swabbed with acetone. The plates were dried for two days in a 125°C oven. A film assembly was prepared by placing two 3500 denier polyurethane elastomer threads between two hot glass plates. The glass plates were held together by Boston clamps. The film assemblies were placed in an oven whose temperature was the same as the temperature at which the monomer and initiator were

mixed and held.

In a dry, serum-capped, 125 mL Erlenmeyer flask was placed fractionally distilled trichloroacetaldehyde (60 mL, 620 mmoles). The flask was immersed in an ethylene glycol thermostat bath set at either 65.0 or 75.0°C. The trichloroacetaldehyde was allowed 10 minutes to come to the temperature of the thermostat bath. The heterogeneous suspension of lithium methyl d(+)-, ℓ(-)-, or dℓ-hydroxide mandelate (3.1 mmole, 0.5 mole %) in cyclohexane/diethyl ether was injected into the warm trichloroacetaldehyde, resulting in a clear, colorless solution. Ten minutes after initiator injection, an aliquot of the initiated monomer was removed via a warm syringe and injected into two warm film assemblies. The film assemblies were plunged into an ice water slurry overnight so that polymerization could occur. The film casting process was repeated at 20, 30, and 50 minute intervals after the mixing of initiator and monomer.

The next day the film assemblies were separated and the films were floated off glass plates in the presence of acidified methanol (10% HCl). The films were kept in acidified methanol for one day to stabilize the films. The films were washed with methanol and then soaked in methanol for one day. Typically, a 12 mm disc of film was cut from the bulk sample while it was still wet with methanol. The disc was soaked in diphenyl ether for at least two days

prior to optical activity measurements.

5. Lithium d(+)-, ℓ(-)-, or dℓ-2-octanoxide as initiator. Glass plates (7" x 7" x 1/4") were washed with sodium dodecyl sulfate solution, rinsed with deionized water, and swabbed with acetone. The plates were dried for two days in a 125°C oven. A film assembly was prepared by placing two 3500 denier polyurethane elastomer threads between two hot glass plates. The film assembly was held together by Boston clamps. The film assemblies were placed in an oven whose temperature was the same as the temperature at which the monomer and initiator were mixed and held.

In a dry, septum-covered, 125 mL Erlenmeyer flask was injected distilled trichloroacetaldehyde (60 mL, 620 mmoles). The flask was immersed in an ethylene glycol thermostat bath set at either 65.0 or 75.0°C. The trichloroacetaldehyde was allowed 10 minutes to come to the temperature of the thermostat bath. The heterogeneous suspension of lithium d(+)-, ℓ(-)-, or dℓ-octanoxide (3.1 mmole, 0.5 mole %) in cyclohexane was injected into the warm trichloroacetaldehyde. A clear, colorless solution resulted. Ten minutes after initiator injection, an aliquot of the initiated monomer was removed via a warm syringe and injected into two warm film assemblies. The film assemblies were plunged into an ice water slurry overnight so that polymerization could occur. This film

casting process was repeated at 20, 30, and 50 minute intervals after the mixing of initiator and monomer.

The next day the film assemblies were separated and the films were floated off glass plates in the presence of acidified methanol (10% HCl). The films were kept in acidified methanol for one day to stabilize the films. The films were washed with methanol and soaked in methanol for one day. Typically, a 12 mm disc of film was cut from the bulk sample while it was still 'wet' with methanol. The disc was soaked in diphenyl ether for at least two days prior to optical activity measurements.

E. Preparation of Compounds as Model Polymer Endgroups

1. Methyl ℓ(-)-trichloroacetylmandelate. In a dry, 10 mL roundbottom flask was placed a stir bar and methyl ℓ(-)-mandelate (1.0 g, 6.1 mmole). A condenser fitted with a rubber septum and a nitrogen inlet and outlet was attached to the roundbottom flask. Trichloroacetyl chloride (3.0 mL, 27 mmole) was injected into the flask with the methyl ℓ(-)-mandelate dissolving to form a clear, colorless solution. The reaction was performed at room temperature and the progress of the reaction was followed by ^{1}H-NMR spectroscopy. Reaction was judged to be complete (∿3 days) when the α-proton of methyl mandelate could no longer be seen at δ 5.20 ppm. Excess trichloroacetyl chloride was

removed by a Kuglrohr distillation at 0.10 mm Hg and T = 80°C. The product spontaneously formed white crystals. The product was dried in an Abderhalden apparatus at 0.10 mm Hg and 40°C overnight. m.p. 73.5-75.5°C. ^{1}H NMR in $CDCl_3$: δ Ar-H 7.50 (s), -CH- 6.08 (s), and $COOCH_3$ 3.83 ppm (s). ^{13}C NMR in $CDCl_3$: δ $-CO-OCH_3$ 167.4, $-CO-CCl_3$ 161.2, aromatic carbons 132.1, 129.8, 129.0, 127.5, -CH- 89.0, $-CCl_3$ 77.8, and $-COOCH_3$ 52.9 ppm. $[\alpha]_D^{20}$ = (-)95.4 (methanol, C = 0.1 g/1 mL) for methyl ℓ(-)-trichloroacetylmandelate.

2. Methyl d(+)-trichloroacetylmandelate. In a dry, 10 mL roundbottom flask was placed a stir bar and methyl d(+)-mandelate (1.0 g, 6.1 mmole). A condensor fitted with a rubber septum and nitrogen inlet/outlet was attached to the roundbottom flask. Trichloroacetyl chloride (3.0 mL, 27 mmole) was injected into the flask with the methyl d(+)-mandelate dissolving to form a clear, colorless solution. The reaction is done at room temperature. Reaction progress was monitored with ^{1}H NMR spectroscopy by following the disappearance of the α-proton in methyl mandelate. Reaction was complete after three days. Excess trichloroacetyl chloride was destroyed by adding water. The product was extracted into diethyl ether in a separatory funnel. The ether layer was washed with 2 x 50 mL 5% aq. sodium bicarbonate and 2 x 50 mL water. The ether layer is pre-

dried by washing with 2 x 50 mL saturated, aqueous sodium chloride and finally storing over anhydrous magnesium sulfate. Magnesium sulfate was removed by gravity filtration and the diethyl ether was evaporated. A white, crystalline product was obtained which was dried in an Abderhalden apparatus at 0.1 mm Hg and 40°C overnight. m.p. 73.5-75.5°C. ^{1}H NMR in $CDCl_3$: δ Ar-H 7.50 (s), -CH- 6.08 (s) and $COOCH_3$ 3.83 ppm (s). ^{13}C NMR in $CDCl_3$: δ $-CO-OCH_3$ 167.4, $-CO-CCl_3$ 161.2, aromatic carbons 132.1, 129.8, 129.0, and 127.5, -CH- 89.0, $-CCl_3$ 77.8, and $-COOCH_3$ 52.9 ppm. $[\alpha]_D^{20}$ = (+)97.7 (methanol, C = 0.1 g/1 mL) for methyl d(+)-trichloroacetylmandelate.

F. Miscellaneous Experiments Involving Polychloral

1. Lithium d(+)-α-methoxymandelate. d(+)-α-methoxymandelic acid (2.0 g, 12 mmole) was dissolved in methanol (25 mL) in a 125 mL Erlenmeyer flask. A drop of 1% phenolphthalein indicator in methanol was added to the solution with 1 mL of this solution removed and saved for back-titration. A saturated, aqueous solution of lithium hydroxide was added dropwise until the pink endpoint persists. The aliquot of solution saved for back-titration was added dropwise until the pink endpoint disappeared. Approximately three-fourths of the methanol was removed by rotary evaporation at 20 mm Hg with the lithium salt

precipitating. The lithium salt was collected and subsequently dried in an Abderhalden apparatus at 40°C and 0.1 mm Hg for one day. $[\alpha]_D^{25}$ = (+)77.3 (methanol, C = 0.03 g/2 mL). Lithium d(+)-α-methoxymandelate was insoluble in chloral monomer as well as the following solvents which do not react with chloral: acetone, chloroform, benzene, diphenyl ether, phenyl methyl ether, sulfolane, and 12-crown-4. Because of lithium d(+)-α-methoxymandelate's insolubility, it could not be used as an initiator.

2. Attempted preparation of optically active polychloral oligomer. Tetramethylammonium ℓ(-)-O-acetylmandelate (0.84 g, 3.2 mmole) was placed in a 25 mL Erlenmeyer flask which was then covered with a serum cap. Chloroform (6.0 mL) was injected to dissolve the initiator. The initiator solution was warmed to 50°C and warm chloral (1.5 mL, 15.4 mmole) was injected into the initiator solution. The initiated chloral was cooled to 0°C overnight with polymerization occurring. The 'polymer' was soaked in acidified methanol (10% HCl), washed with methanol, and then dried. Yield = 1.1 g (48%). The product was insoluble in water, methanol, diphenyl ether, dimethyl sulfoxide, and hexafluoroacetone. Observed % Cl = 72.1%.

G. Attempted Preparation of Asymmetric Aldehydes

1. Bromochloroacetaldehyde.

a. Nucleophilic substitution of trichloroethylene to form 1,1-chloroethoxy-2-chloroethylene (183). In a dry, 5 L, 3-neck roundbottom flask was dissolved sodium ethoxide (400 g, 5900 mmoles) in absolute ethanol (3.3 L). To the reaction flask was attached two condensers and a mechanical stirrer. To the sodium ethoxide solution was added trichloroethylene (350 mL, 3870 mmoles). To start the reaction, the roundbottom flask was heated with a heating mantle until the reflux of ethanol was self-sustaining. The heating mantle was temporarily removed until reaction subsided and was reattached with the reaction kept at reflux for two hours. After cooling, the reaction vessel's contents were poured into three, 4 L beakers containing ice water. The crude product was extracted from the heterogeneous mixture by extraction with diethyl ether in a separatory funnel. The ether layer was dried by washing with saturated, aqueous sodium chloride and storing over anhydrous sodium sulfate. The ether was removed on a rotary evaporator at 20 mm Hg, leaving a red oil. The crude product was distilled at atmospheric pressure through a 300 mm Vigreux column with the middle fraction collected at 121-124°C. Yield of 1,1-chloroethoxy-2-chloroethylene = 299 g (55%). ^{1}H NMR in $CDCl_3$: δ =C<u>H</u>Cl 5.57 (s),

O-$\underline{CH}_2$-CH_3 4.13 (q), and -CH_2-$\underline{CH}_3$ 1.40 (t) ppm; the respective integration 1.02:2.00:2.95. Purity by gas chromatograph = 97.5%.

b. Bromination of 1,1-chloroethoxy-2-chloroethylene and dehydrobromination of 1,1,1-bromochloroethoxy-2,2-bromochloroethane. In a 3-neck, 250 mL roundbottom flask was placed 1,1-chloroethoxy-2-chloroethylene (70 g, 500 mmole). Attached to the flask was a condensor, a dropping funnel, and a mechanical stirrer. The flask was immersed in ice water and bromine (80 g, 500 mmoles) was added dropwise over a two hour period.

The crude 1,1,1-bromochloroethoxy-2,2-bromochloroethane was placed in a dropping funnel and was dehydrobrominated by adding over a one hour period to a stirred solution of potassium hydroxide (44 g, 780 mmoles) in ethanol (150 mL) and water (32 mL). To the heterogeneous mixture was added additional water (600 mL) and the product, 1,1-chloroethoxy-2,2-bromochloroethylene, was extracted into diethyl ether in a separatory funnel. The ether layer was washed with water and pre-dried by washing with saturated aqueous sodium chloride and storing over anhydrous sodium sulfate. The ether was removed on a rotary evaporator at 20 mm Hg. Yield of 1,1-chloroethoxy-2,2-bromochloroethylene = 70 g (64%). ^{1}H NMR in $CDCl_3$: O-$\underline{CH}_2CH_3$ 4.12 (q) and $OCH_2\underline{CH}_3$ 1.38 (t) ppm; the respective integration 2.0:3.1. Purity by gas chromatograph = 96.3%.

c. Preparation of ethyl bromochloroacetate (184). In a 500 mL roundbottom flask immersed in ice water was placed 1,1-chloroethoxy-2,2-bromochloroethylene (48.6 g, 221 mmoles). A condenser with drying tube was attached to the flask and concentrated sulfuric acid (4 mL) was added in 1 mL aliquots over a four hour period. Reaction progress was monitored by observing the disappearance of the alkene peak in infrared spectroscopy at 1620 cm^{-1}. After the reaction was completed, absolute ethanol (10 mL) was added and thirty minutes later the reaction was neutralized by adding 5% aqueous sodium bicarbonate. The product was extracted into diethyl ether in a separatory funnel. The ether layer was washed with water and pre-dried by washing with saturated aqueous sodium chloride and storing over anhydrous sodium sulfate. The ether was removed in a rotary evaporator at 20 mm Hg. The crude product was distilled through a 300 mm Vigreux column at 15 mm Hg with a boiling range of 75-80°C. Yield of ethyl bromochloroacetate = 37 g (83%). ^1H NMR in $CDCl_3$: δ $-C\underline{H}ClBr$ 6.07 (s), $-OC\underline{H}_2CH_3$ 4.38 (q), and $-CH_2C\underline{H}_3$ 1.40 (t) ppm; integration ratio respectively, 1.0:2.0:3.1. Purity by gas chromatography = 97.5%.

d. Attempted reduction of ethyl bromochloroacetate to the hemiacetal (172,173). In a dry 100 mL, roundbottom flask was placed lithium aluminum hydride (0.4 g, 11 mmoles) and anhydrous diethyl ether (28 mL). A condensor with a

nitrogen purge was attached to the flask. After twenty minutes, the ether solution was decanted into a dropping funnel attached to a 3-neck, 100 mL, roundbottom flask which contained ethyl bromochloroacetate (8.0 g, 40 mmoles) and anhydrous diethyl ether (16 mL). This flask had a condensor with a nitrogen purge and was immersed in a -78°C bath of dry ice/isopropanol. The lithium aluminum hydride solution was added dropwise to the ethyl bromochloroacetate over 30 minutes. The lithium aluminum hydride sludge in the other flask was restirred in diethyl ether (15 mL) and was also added to the ethyl bromochloroacetate. The reduction was allowed to proceed for 2.75 hours before termination with ethanol (5 mL). The heterogeneous mixture was poured into a mixture of cracked ice and hydrochloric acid. The product was extracted into diethyl ether in a separatory funnel. The ether layer was washed with aqueous sodium bicarbonate and water and subsequently pre-dried by washing with saturated aqueous sodium chloride and storing over anhydrous sodium sulfate. The ether was removed on a rotary evaporator at 20 mm Hg. The crude product was not amenable to distillation and various spectroscopic techniques indicated that a mixture of products existed. This experiment was repeated varying the stoichiometry, time of reduction, and temperature of reduction with no conclusive results obtained.

2. Bromochlorofluoroacetaldehyde.

a. Nucleophilic substitution of trichloroethylene to form 1,1-chloroethoxy-2-chloroethylene. See Chapter II, Section G.1.a., p. 64.

b. Bromination of 1,1-chloroethoxy-2-chloroethylene and dehydrobromination of 1,1,1-bromochloroethoxy-2,2-bromochloroethane. See Chapter II, Section G.1.b., p. 65.

c. Bromination of 1,1-chloroethoxy-2,2-bromochloroethylene (183). In a 25 mL roundbottom flask was placed 1,1-chloroethoxy-2,2-bromochloroethylene (11.1 g, 50.5 mmoles) and a stir bar. A pressure-equalizing, dropping funnel was attacked to the flask which contained bromine (2.6 mL, 50.5 mmoles). The flask was chilled to 0°C in ice water and the bromine was added over a 15 minute period. The orange solution was stoppered and refrigerated overnight, forming a crystalline plug. Yield was quantitative. No isolation of the product was attempted.

d. Thermal rearrangement of 1,1,1-bromochloroethoxy-2,2,2-dibromochloroethane to dibromochloroacetyl chloride. To the roundbottom flask containing crude 1,1,1-bromochloroethoxy-2,2,2-dibromochloroethane was attached a condensor and a nitrogen inlet and outlet. The flask was warmed for one day at 65°C. Ethyl bromide evolved along with the formation of dibromochloroacetyl chloride. No isolation was attempted.

e. Reaction of dibromochloroacetyl chloride and ethanol forming ethyl dibromochloroacetate. To the crude dibromochloroacetyl chloride was added absolute ethanol (5 mL) which had been stored over molecular sieves. The flask warmed with hydrogen chloride gas evolved which was detected with wet, blue litmus. After the evolution of HCl gas had stopped, 30 minutes later the reaction mixture was poured into a 60 mL separatory funnel containing diethyl ether and water. The product was extracted into diethyl ether. The ether layer was washed with 5% aqueous sodium bicarbonate and water and was pre-dried by washing with saturated, aqueous sodium chloride and storing over anhydrous sodium sulfate. The ether was removed on a rotary evaporator at 20 mm Hg, leaving a gold oil. The oil was distilled at 2-3 mm Hg, b.p. 53-56°C. Yield of ethyl dibromochloroacetate = 4.0 g. ^{1}H NMR in $CDCl_3$: δ $-C\underline{H}_3$ 1.43 (t), $-C\underline{H}_2-$ 4.45 ppm (q). ^{13}C NMR in $CDCl_3$: δ $-\underline{C}O-$ 162.8, $-O\underline{C}H_2CH_3$ 65.6, $\underline{C}Br_2Cl$ 51.1, and $-OCH_2\underline{C}H_3$ 13.7 ppm.

f. Fluorination of ethyl dibromochloroacetate with HgF_2 (183). In a 10 mL, 3-neck roundbottom flask was placed ethyl dibromochloroacetate (1.5 g, 5.3 mmole), mercuric fluoride (0.65 g, 2.7 mmole), and a stir bar. A distillation head, condensor, bent adaptor, and a collection flask were attached to a neck of the roundbottom flask. The roundbottom flask was immersed in a 110°C oil

bath for 30 minutes. The flask was removed from the oil bath, and an additional portion of mercuric fluoride (0.65 g, 2.7 mmole) was added. The flask was re-immersed in the oil bath, a vacuum of 45-50 mm Hg was applied, and the product distilled over at 82°C. By elemental analysis %F = 6.6%, theoretical %F = 8.7%. ^{13}C NMR in $CDCl_3$ showed that the reaction product was impure with the following peaks assigned to the ethyl bromochlorofluoroacetate: δ -CO- 161.3 ppm, $-O\underline{C}H_2CH_3$ 64.9 ppm, -CFBrCl 63.2 ppm, and $-OCH_2\underline{C}H_3$ 13.8 ppm.

3. Trichloroacetaldehyde.

a. Esterification of trichloroacetic acid. Trichloroacetic acid (50 g, 306 mmole) was placed in a 500 mL, 1-neck roundbottom flask along with absolute ethanol (190 mL, 3300 mmole), p-toluenesulfonic acid (5.0 g, 29 mmole), and a stir bar. A condensor was attached and the reaction mixture was heated to a gentle reflux for three days. After cooling, unreacted acids were converted to sodium salts by adding aqueous 5% sodium bicarbonate solution. The product was extracted into 200 mL of diethyl ether in a 1 L separatory funnel. The ether layer was washed with 2 x 50 mL water. The ether layer was pre-dried by washing with saturated, aqueous sodium chloride and then storing over anhydrous sodium sulfate overnight. The sodium sulfate was removed by filtration while the ether was removed

by rotary evaporation at 20 mm Hg. Yield = 32.5 g (55.5%). ^{1}H NMR in $CDCl_3$: δ $-OC\underline{H}_2CH_3$ 4.48 (q), $-OCH_2C\underline{H}_3$ 1.47 ppm (t).

b. Reduction of ethyl trichloroacetate. In a dry, 25 mL roundbottom flask was placed a stir bar, lithium aluminum hydride (LAH) (0.23 g, 6.3 mmole), and anhydrous diethyl ether (15 ml). A condensor was attached to the flask and the contents of the flask were kept in a nitrogen atmosphere. After 2 hours, the LAH slurry was transferred to a dropping funnel which was attached to a 3-neck, 100 mL roundbottom flask to which was also attached a condensor with a nitrogen inlet/outlet. Ethyl trichloroacetate (3.6 mL, 25 mmole) and anhydrous diethyl ether (5 mL) were injected into the 3-neck flask which was then immersed into a dry ice/acetone bath. The LAH slurry was added dropwise over a 45 minute period and the reaction was allowed to proceed an additional hour. Ethanol (2 mL) was added to the reaction vessel to destroy excess LAH. The contents of the reaction vessel were poured into ice water which contained concentrated sulfuric acid (2 mL). The ether layer was isolated in a separatory funnel. The ether layer was washed by 1 x 25 mL 5% aqueous, sodium bicarbonate, 1 x 25 mL water and pre-dried by washing with saturated aqueous sodium chloride solution. The ether layer was stored overnight over anhydrous sodium sulfate. The sodium sulfate was removed by filtration and the ether was removed by

rotary evaporation at 20 mm Hg. The crude product was rapidly distilled at atmospheric pressure with the major fraction collected from 96-100°C. ^{1}H NMR in $CDCl_3$ indicates the presence of a hemiformal: δ -O<u>H</u> 4.90 (s), -OC<u>H</u>$_2$CH$_3$ 3.90 (q), -<u>C</u>H- 3.48 (s), and -OCH$_2$C<u>H</u>$_3$ 1.35 ppm (t).

The hemiformal (∿3 mL) was placed in a 15 mL roundbottom flask along with sulfuric acid (∿3 mL). A distillation head, condensor, bent adaptor, and collection flask were attached to the reaction flask. The reaction vessel was heated rapidly. A clear, colorless liquid distilled at 96°C at atmospheric pressure. By gas chromatography, the above compound had the same retention time as a known sample of chloral. By ^{1}H NMR in $CDCl_3$: δ CO-<u>H</u> 9.85 ppm (s).

H. Measurements

Proton nuclear magnetic resonance spectra, ^{1}H NMR, were obtained on a 60 MHz, Varian T-60 NMR Spectrometer. Spectra were typically taken at 25°C in $CDCl_3$ using tetramethylsilane (TMS) as an internal reference. Chemical shifts are reported in ppm using the δ scale with TMS having δ = 0.00 ppm.

Carbon-13 nuclear magnetic resonance spectra, ^{13}C NMR, were obtained on a Varian CFT-20 NMR spectrometer. Spectra were typically taken with complete proton

decoupling at 25°C in $CDCl_3$ or D_2O using TMS or 1,4-dioxane respectively, as internal references. All chemical shifts are reported in ppm relative to TMS being assigned 0 ppm. Typical instrument parameters are as follows: spectral width 4000 Hz, acquisition time 1.023 seconds, pulse width 19 μseconds, pulse delay 0-20 seconds, sensitivity enhancement -0.800 seconds, and width of plot 4000 Hz.

Melting points were measured on a MEL-TEMP capillary melting point apparatus at a heating rate of 2°C/min. All melting points are uncorrected.

Gas chromatograms were obtained on a programmable Varian Aerograph Model 1400. Typically a 3' x 1/8' column was used containing Porapak Q support. Helium was used as a transport medium.

Optical activity measurements were made in an electronic Perkin-Elmer 141MC Polarimeter. Measurements were made at room temperature and at wavelengths which are available from sodium or mercury lamps. For soluble compounds, measurements were made in appropriate solvents in a 1 dm cell. All optical activities were reported as specific rotation. For polychloral films, specific rotations were obtained from measurements made in the solid state. A cell to hold the films (144) consisted of two circular pieces of aluminum 27 mm in diameter with a 10 mm hole drilled in the middle. Two circular pieces of glass 14 mm in diameter were cemented over the holes. Around the

perimeter of the glass was drilled 6 holes in a hexagonal pattern. Three of the holes were used to bolt the two sides of the cell together, sandwiching a film disc in the middle. The other three holes were used to bolt the film holder in the light beam of the polarimeter. A disc of film, whose thickness was determined by a friction stop micrometer, was placed in the film holder along with a drop of diphenyl ether. The optical rotation, α, was read off the polarimeter. Each disc of film was measured at three orientation of the film holder 120° apart. These three optical rotations were averaged to evaluate the disc's anisotropy. Six different discs of film were measured at each time and temperature at which films were prepared. The specific rotations of the films were averaged with the specific rotations determined from Equation 7 listed below:

$$[\alpha]_{\lambda} = \frac{(\bar{\alpha})}{(\ell)(\rho)} \qquad (7)$$

where $\bar{\alpha}$ = average rotation in degrees, ℓ = film thickness (dm), ρ = density of polychloral (1.9 g/cm^3) (189)). Typical film thickness was 1.5 x 10^{-3} dm.

C H A P T E R I I I

RESULTS

A. Polychloral Initiated by Lithium Cholesteroxide

Chloral was polymerized with lithium cholesteroxide initiator (0.5 mole % <) in the presence of n-hexane diluent. The polymer was milled (30-150 mesh) and then stabilized by converting hydroxyl endgroups to chloride endgroups with the reagent, phosphorous pentachloride. The stabilized polymer powder was packed in a 15 mm x 150 mm column.

This polychloral column (147) was used in attempts to resolve a 1:1 mixture (by weight) of isotactic poly(R-(+)-α-methylbenzyl methacrylate) and isotactic poly(S-(-)-α-methylbenzyl methacrylate). The poly(R-(+)-α-methylbenzyl methacrylate) had a $\bar{M}_n$ = 79,300 and $[\alpha]^{25}_{365}$ = (+)377, while poly(S-(-)-α-methylbenzyl methacrylate) had a $\bar{M}_n$ = 53,800 and $[\alpha]^{25}_{365}$ = (-)351. The poly(α-methylbenzyl methacrylate) mixture was dissolved in tetrahydrofuran and eluted through the polychloral column at room temperature and a flow rate of 0.62 mL/min. Aliquots of eluate were collected every 5.5 minutes (a volume of 3.4 mL). Solvent was removed from each aliquot and the residual poly(α-

methylbenzyl methacrylate) was weighed. The polymer fractions were then re-dissolved and the specific rotations determined so that an evaluation could be made as to whether resolution had occurred. The resolution results are found in Table 6.

TABLE 6

RESOLUTION* OF EQUAL AMOUNTS OF POLY(R-(+)- AND S-(-)-α-METHYLBENZYL METHACRYLATE) ON POLYCHLORAL INITIATED BY LITHIUM CHOLESTEROXIDE

Elution Volume (mL)	$[\alpha]^{25}_{365}$
32.3	(+)66
35.7	(+)27
39.1	0
42.5	(-)18
45.9	(-)44
49.3	(-)53

*Experiment performed at Osaka University by S. Shimizu (147).

The elution volumes in Table 6 were taken as the midpoint volume of a collected aliquot. This resolution experiment was also repeated using either toluene or chloroform as solvent carriers instead of tetrahydrofuran. Essentially the same degree of resolution reported in Table 6 was found when either toluene or chloroform was used as the solvent carrier.

As a reference experiment, another chromatographic

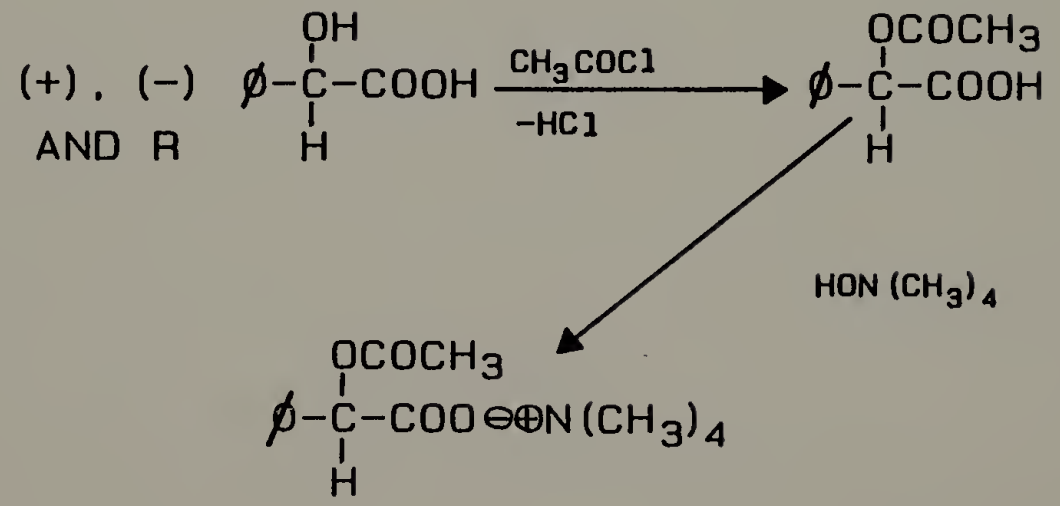
column was packed with polychloral initiated by an achiral initiator, lithium t-butoxide (0.5 mole %). The resolution experiment outlined above was repeated using this new column. A small amount of 'apparent' resolution occurred as evidenced by the first eluate aliquot containing polymer having $[\alpha]^{25}_{365} \doteq (+)7$.

B. Polychloral Initiated by Tetramethylammonium O-acetylmandelate (TMAAc)

The initiators TMArAc, TMA(-)Ac, and TMA(+)Ac were prepared by acetylating the appropriate mandelic acid to obtain O-acetylmandelic acid. This carboxylic acid was titrated with tetramethylammonium hydroxide to obtain the tetramethylammonium O-acetylmandelate initiators (Figure 1). The specific rotation for ℓ(-)-O-acetylmandelic acid was (-)153 and was (+)151 for d(+)-O-acetylmandelic acid. The respective optical purities were 99% and 98%. The specific rotations of the initiators TMArAc, TMA(-)Ac, and TMA(+)Ac were, respectively, 0, (-)86, and (+)88. TMA(-)Ac was re-acidified in methanol to obtain the starting product of ℓ(-)-O-acetylmandelic acid which was then isolated and purified. The specific rotation of ℓ-(-)-O-acetylmandelic acid was (-)144, whereas it was (-)153 prior to conversion to TMA(-)Ac initiator. This indicates that a maximum of 6% racemization could occur during the preparation of TMA(-)Ac. It was also observed that by holding TMA(-)Ac at 75°C for

Fig. 1. Synthesis of the initiator Tetrametyl-ammonium O-acetylmandelate (TMAAc).

TETRAMETHYLAMMONIUM ACETYLMANDELATE (TMAAC)



50 minutes in chloroform resulted in a 2% loss of specific rotation.

TMAAc initiators at 0.5 mole % concentration were added to chloral monomer at one of the following temperatures; 70.0, 75.0, or 85.0°C. From this initiated monomer which was maintained at one of the prior temperatures, polychloral films were cryotachensically cast 10, 20, 30, and 50 minutes after mixing. Translucent films of polychloral were obtained which became transparent upon soaking in diphenyl ether. The specific rotation reported for any polychloral film was averaged from 15-18 measurements. For polychloral initiated by optically inactive TMArAc, $[\alpha]_D^{25}$ = (+)5±10. For polychloral samples initiated by TMA(+)Ac, the specific rotation for various temperatures and holding times are reported in Table 7. For polychloral samples initiated by TMA(-)Ac, the specific rotations are reported in Table 8.

C. Polychloral Initiated by Tetramethylammonium α-methoxymandelate (TMAαM)

Tetramethylammonium α-methoxymandelate initiators were obtained by a five-step reaction sequence (Figure 2). First, dℓ-mandelic acid was esterified with methanol to form the methyl ester. Then the α-hydroxy group was converted to a methoxy group with trimethylorthoformate and boron trifluoride·etherate catalyst. The ester group was

TABLE 7

OPTICALLY ACTIVE POLYCHLORAL INITIATED BY TMA(+)Ac

Time initiated chloral is held at T (°C)	$[\alpha]_D^{25}$, film T = 70.0	T = 75.0	T = 85.0
10 min.	-790±70	-1420±160	-1820±220
20 min.	-1130±80	-1760±70	-1860±70
30 min.	-1290±40	-1650±60	-1570±50
50 min.	-1330±40	-1680±50	-1280±70

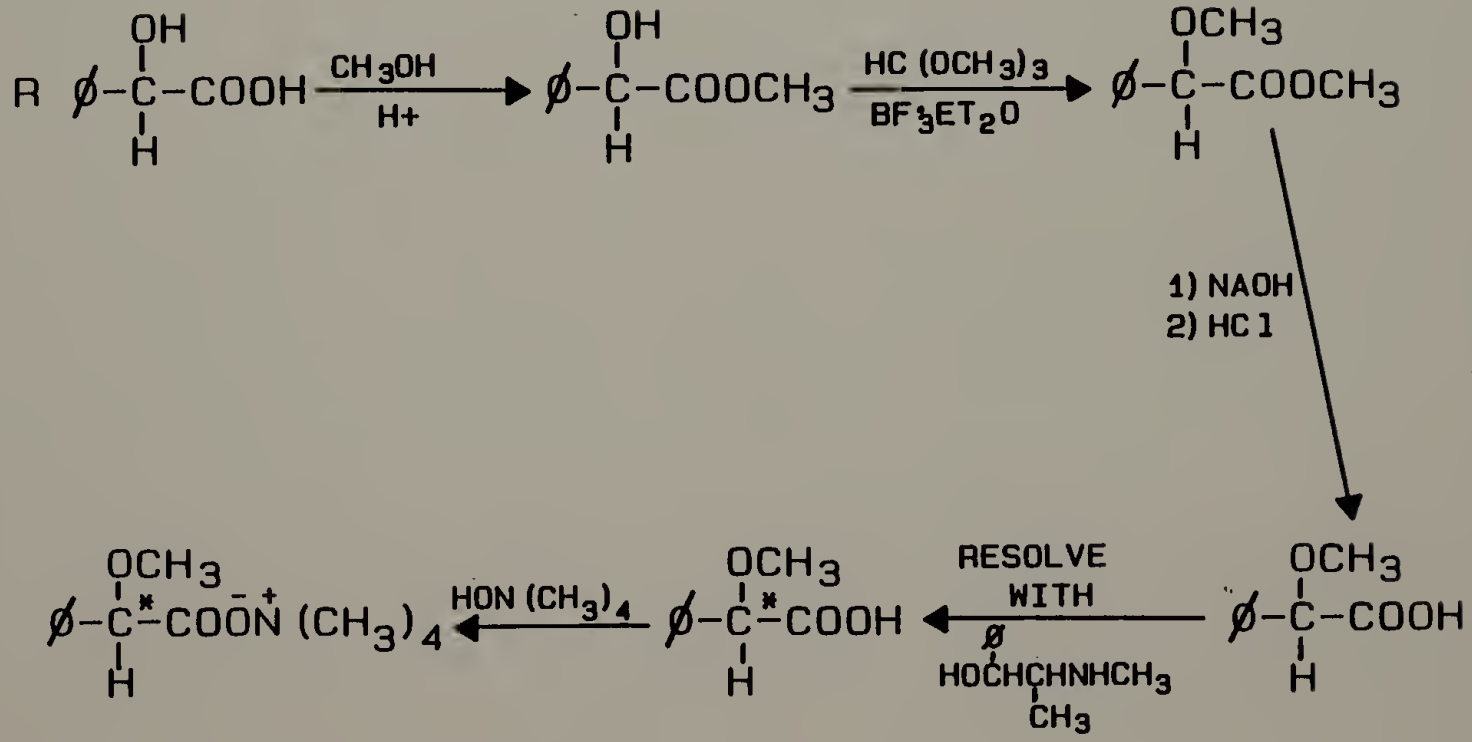
TABLE 8

OPTICALLY ACTIVE POLYCHLORAL INITIATED BY TMA(-)Ac

Time initiated chloral is held at T (°C)	$[\alpha]_D^{25}$, film T = 75.0	T = 85.0
10 min.	+260±70	+1170±40
20 min.	+500±20	+1150±40
30 min.	+580±30	+1020±40
50 min.	+660±30	+1180±90

Fig. 2. Synthesis of the initiator Tetramethylammonium α-methoxymandelate (TMAαM).

TETRAMETHYLAMMONIUM α-METHOXYMANDELATE (TMAαM)



then removed by base hydrolysis and the resulting sodium α-methoxymandelate was acidified to obtain α-methoxymandelic acid. This carboxylic acid was resolved using both d(+)-ephedrine and ℓ(-)-ephedrine. The specific rotation of d(+)-α-methoxymandelic acid was (+)135, while for ℓ(-)-α-methoxymandelic acid it was (-)144. The respective optical purities were 90% and 96%. The α-methoxymandelic acids were titrated with tetramethylammonium hydroxide to finally obtain the tetramethylammonium α-methoxymandelate initiators. TMArαM, TMA(+)αM, and TMA(-)αM had the respective rotations of 0, (+)52.1, and (-)56.4.

Chloral and TMAαM initiators at 0.5 mole % concentration were mixed at either 65.0, 70.0, 80.0, or 85.0°C. From this initiated monomer maintained at one of these temperatures, polychloral films were prepared by cryotachensic casting 10, 20, 30, and 50 minutes after the initial mixing. The polychloral films obtained were initially translucent but became transparent upon soaking in diphenyl ether. The specific rotation reported for any polychloral film was an average of 15-18 measurements. For polychloral initiated by TMArαM, $[\alpha]_D^{25}$ = (+)10±10. For polychloral initiated by TMA(+)αM, the specific rotations for various temperatures and holding times are reported in Table 9. For polychloral initiated by TMA(-)αM, the specific rotations are reported in Table 10.

TABLE 9

OPTICALLY ACTIVE POLYCHLORAL INITIATED BY TMA(+)αM

Time initiated chloral is held at T (°C)	$[\alpha]_D^{25}$, film T = 65.0	T = 70.0	T = 80.0	T = 85.0
10 min.	-105±15	-120±5	-175±20	-160±5
20 min.	-135±10	-160±20	-150±20	-160±20
30 min.	-130±15	-190±15	-160±10	-140±10
50 min.	-140±10	-160±5	-160±10	-160±10

TABLE 10

OPTICALLY ACTIVE POLYCHLORAL INITIATED BY TMA(-)αM

Time initiated chloral is held at T (°C)	$[\alpha]_D^{25}$, film T = 70.0	T = 80.0
10 min.	+210±20	+190±10
20 min.	+180±20	+190±10
30 min.	+190±20	+180±20
50 min.	+180±20	+170±10

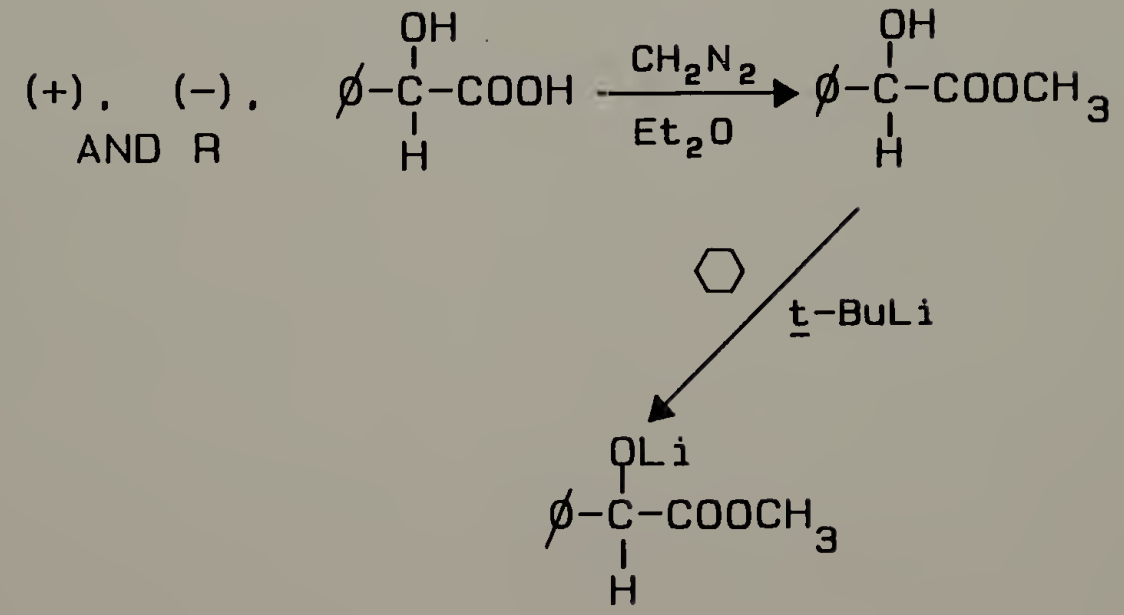
D. Polychloral Initiated by Lithium Methyl Hydroxidemandelate (LiMM)

Lithium methyl hydroxidemandelate was prepared by first esterifying the appropriate mandelic acid and then reacting this α-hydroxy ester with t-butyl lithium to obtain a suspension of alkoxide initiator (Figure 3). The specific rotation of methyl mandelate, methyl d(+)-mandelate, and methyl ℓ(-)-mandelate were 0, (+)142, and (-)141, respectively. The optical purity of methyl d(+)-mandelate was 99%, while for methyl ℓ(-)-mandelate it was 98%. The specific rotation of the lithium methyl hydroxidemandelates initiators could not be determined due to either the initiator's instability in some solvents or its insolubility in other solvents. In initial experiments, cyclohexane and ether diluents were removed from the alkoxide initiator, but substantial initiator racemization occurred as evidenced by the resulting polychloral having a low optical activity and by acidification of the initiator to re-obtain methyl d(+)-mandelate which had undergone 43% racemization during the reaction sequence. However, when the initiator was slurried in ether and cyclohexane and injected into warm chloral, polychloral with much higher optical activity was obtained. There was also no strong evidence indicating that rapid racemization had occurred.

Chloral and LiMM initiators at 0.5 mole % concen-

Fig. 3. Synthesis of the Initiator Lithium methyl hydroxidemandelate (LiMM).

LITHIUM METHYL (HYDROXIDE) MANDELATE
LiMM



tration were mixed together at either 65.0 or 75.0°C. From this initiated monomer maintained at 65.0 or 75.0°C, polychloral films were obtained by cryotachensic casting 10, 20, 30, and 50 minutes after mixing. Films prepared by the LiMM initiators were translucent, but became transparent after soaking in diphenyl ether. Each specific rotation reported for any polychloral film was averaged from 15-18 measurements. For polychloral initiated by LirMM, the specific rotation was (+)5±10. For polychloral initiated by Li(+)MM, the specific rotations for various temperatures and holding times are reported in Table 11. For polychloral initiated by Li(-)MM, the specific rotations are reported in Table 12.

Using a polychloral film with the highest observed specific rotation at the sodium-D line (589 nm) (Li(-)MM initiated polychloral with a holding time of 50 minutes and a bath temperature of 75.0°C), the specific rotations were determined at various light wavelengths available from either a sodium or a mercury lamp. Specific rotations could not be determined at wavelengths shorter than 334 nm due to light sorption by the diphenyl ether. The optical rotary dispersion (ORD) data is found in Table 13.

TABLE 11

OPTICALLY ACTIVE POLYCHLORAL INITIATED BY Li(+)MM

Time initiated chloral is held at T (°C)	$[\alpha]_D^{25}$, film T = 65.0	T = 75.0
10 min.	+940±60	+1420±110
20 min.	+990±140	+3600±110
30 min.	+1100±70	+2890±200
50 min.	+1690±340	---

TABLE 12

OPTICALLY ACTIVE POLYCHLORAL INITIATED BY Li(-)MM

Time initiated chloral is held at T (°C)	$[\alpha]_D^{25}$, film T = 65.0	T = 75.0
10 min.	-900±60[a]	-1310±100
20 min.	-1190±90	-2550±60
30 min.	-1630±180	-4030±480
50 min.	-3580±310	-4670±240[b]

[a] When film assembly was ∿75°C instead of 65°C, $[\alpha]_D^{25}$ = (-)1230±150 -- 37% higher.

[b] Film prepared under this set of conditions was used for optical rotary dispersion measurements.

TABLE 13

OPTICAL ROTARY DISPERSION DATA FOR POLYCHLORAL INITIATED BY Li(-)MM HELD AT 75.0°C FOR 50 MINUTES

λ(nm)	$[\alpha]_{\lambda}^{25}$	λ(nm)	$[\alpha]_{\lambda}^{25}$
589	-4710±110	407.78	-11,300±150
579.07	-4790±140	404.66	-11,100±60
576.96	-4820±150	366.33	-14,700±40
546.07	-5460±160	365.48	-14,700±80
435.83	-9460±210	365.02	-14,400±70
434.75	-9580±140	334.15	-18,400±120

E. Polychloral Initiated by Lithium 2-octanoxide (Li2O)

Either distilled 2-octanol or d(+)-2-octanol, as received, were dissolved in cyclohexane, chilled to 0°C, and reacted with t-butyl lithium to form either the initiator Lir2O or Li(+)2O. Chloral and lithium 2-octanoxide initiator were mixed at either 65.0 or 75.0°C. Using initiated monomer maintained at either 65.0 or 75.0°C, polychloral films were prepared by cryotachensic casting 10, 20, 30, and 50 minutes after the initial mixing. The resulting films were translucent, but became transparent upon soaking in diphenyl ether and were then used for optical activity measurements. For polychloral initiated by Lir2O, the specific rotation was (+)5±15. For polychloral initiated by Li(+)2O, the range of specific rotations obtained is reported in Table 14.

TABLE 14

OPTICALLY ACTIVE POLYCHLORAL INITIATED BY Li(+)2O

Time initiated chloral is held at T (°C)	$-[\alpha]_D^{25}$, film T = 65.0	T = 75.0
10 min.	1970 → 3410	2240 → 3460
20 min.	2620 → 5120	440 → 1860
30 min.	3170 → 4620	1010 → 2760
50 min.	1370 → 2760	220 → 350

As can be seen in Table 14, there were wide variations in the specific rotations for a film cast at a specific time and temperature. This wide variation in specific rotation was also observed in duplicate experiments. This variation is not due to anisotropy in the film discs, since the difference in the optical rotation, α, was almost always less than 15% for the three measurements, 120° apart, made on a disc of film. (This indicates the film disc is optically isotropic.) The wide variations in specific rotations reported in Table 14 originate from discs cut in different regions of a film. This problem of large optical activity variations in a film was not observed for any other optically active polychloral.

Originally, intentions were to use lithium 2-octanoxide as an optically active alkoxide initiator due to its relative ease of preparation. However, the wide variation in specific rotation within a specific film has led to the discontinuation of its use as initiator.

F. Model Endgroups

Methyl d(+)- or ℓ(-)-O-trichloroacetylmandelate was prepared to serve as a model for the initiator endgroup found when chloral was initiated by either Li(+)MM or Li(-)MM. The model compound's specific rotation should be a good approximation for the polymer endgroup due to the electron withdrawal of the trichloroacetyl group.

Methyl d(+)- or ℓ(-)-O-trichloroacetylmandelate was prepared by reacting methyl d(+)- or ℓ(-)-mandelate with an excess of trichloroacetyl chloride at room temperature. Whether the excess trichloroacetyl chloride was removed by vacuum distillation or by aqueous extractions, essentially the same specific rotations were found. The specific rotation for methyl d(+)-O-trichloroacetylmandelate was (+)97.7 and for methyl ℓ(-)-O-trichloroacetylmandelate it was (-)95.4.

To estimate the initiator endgroup's contribution to the polychloral's specific rotation, the model compound's specific rotation of 97.7 was used as an approximation of the initiator endgroup's optical activity. The next assumption made was that all the initiator became a polymer endgroup. A 0.5 mole % concentration of methyl O-trichloroacetylmandelate in chloral monomer would correspond to a concentration of 0.016 g/mL. However upon polymerization, a volume reduction occurred as evidenced by the monomer density, 1.5 g/mL, as compared to the polymer density of 1.9 g/mL. This volume reduction effectively increased the concentration of the model initiator endgroup to 0.021 g/mL. By rearranging Equation 1 to the form in Equation 8,

$$\alpha = [\alpha]\ell c \qquad (8)$$

α for the model endgroup in the polymer can be estimated,

assuming that the average film path length (thickness) was 1.5×10^{-3} dm. The rotation, α, is 0.0031 for the model initiator endgroup. Using Equation 7, the maximum specific rotation the initiator endgroup should contribute to the polymer is 1--much less than the error due to measurement in the solid state.

G. Miscellaneous Experiments

1. Lithium d(+)-α-methoxymandelate. The potential initiator, lithium d(+)-α-methoxymandelate, was prepared by titrating d(+)-α-methoxymandelic acid with lithium hydroxide. It was considered advantageous to have a carboxylate initiator with a lithium counterion instead of an ammonium counterion, since ammonium groups can undergo side reactions. (Specifically, an ammonium group has the capacity to undergo a Hofmann degradation to form tertiary amine, which is capable of leading to achiral initiation--a distinct complication in the analysis of data.)

Unlike the ammonium carboxylate initiators, lithium d(+)-α-methoxymandelate was insoluble in chloral and was incapable of initiating polymerization undissolved. Attempts were made to dissolve lithium d(+)-α-methoxymandelate in a variety of non-protic solvents such as acetone, chloroform, benzene, diphenyl ether, phenylmethyl ether, sulfolane, and dimethyl sulfoxide. Solution was achieved with only dimethyl sulfoxide, but unfortunately

this solvent was reported as being capable of polymerizing chloral (144). Attempts were also made to dissolve the lithium d(+)-α-methoxymandelate using 12-crown-4 which is specific for the lithium counterion. Even with the crown ether, solution could not be achieved. No further attempts were made to use lithium d(+)-α-methoxymandelate as an initiator.

2. Attempted preparation of oligomer. It was considered desirable to prepare optically active oligomers of polychloral so that the critical $\overline{DP}_n$ could be established for the 'locking in' of the helical conformation. TMAAc carboxylate initiators were chosen for the attempted oligomerization since the majority of successful optical activity measurements made on polychloral films were initiated by carboxylates. Using chloral and tetramethylammonium ℓ(-)-O-acetylmandelate initiator in chloroform diluent at a 5:1 mole ratio, the preparation of a chloral pentamer was attempted. The reaction product looked and behaved much like high molecular weight polychloral. It was insoluble and decomposed at elevated temperatures, leaving no residue. Using chlorine elemental analysis, it was possible to estimate the number average degree of polymerization for polychloral initiated by tetramethylammonium ℓ(-)-O-acetylmandelate (assuming the other polymer endgroup is a hydroxyl group). The equation for % Cl as a function

of $\overline{DP}_n$ is shown in Equation 9:

$$\% \text{ Cl} = \frac{106.4\ n}{194.2 + 147.4\ n} \qquad (9)$$

where n is the number of chloral repeat units in the polymer. For a pentamer of chloral, % Cl = 57.1%. However, the product obtained had an experimental % Cl of 72.1%, which corresponds to a $\overline{DP}_n$ of 1120.

H. Attempted Asymmetric Aldehyde Preparation

1. Bromochlorofluoroacetaldehyde (BCFA). The preparation of racemic BCFA requires in our synthetic strategy nine reaction steps as shown in Figures 4 and 5. The reaction steps are: (1) nucleophilic substitution of trichloroethylene by ethoxide to form 1,1-chloroethoxy-2-chloroethylene, (2) bromination of 1,1-chloroethoxy-2-chloroethylene, (3) dehydrobromination of 1,1,1-bromochloroethoxy-2,2-bromochloroethane, (4) bromination of 1,1-chloroethoxy-2,2-bromochloroethylene, (5) thermal rearrangement of 1,1,1-bromochloroethoxy-2,2,2-dibromochloroethane to dibromochloroacetyl chloride, (6) esterification of dibromochloroacetyl chloride by ethanol, (7) fluorination of ethyl dibromochloroacetate with mercuric fluoride, (8) reduction of ethyl bromochlorofluoroacetate to the hemiformal, and (9) acid decomposition of the hemiformal to form BCFA. Of the first six synthetic steps, only the

Fig. 4. Synthetic Scheme for the Attempted Preparation of Bromochlorofluoroacetaldehyde.

ATTEMPTED SYNTHESIS OF BROMOCHLOROFLUOROACETALDEHYDE

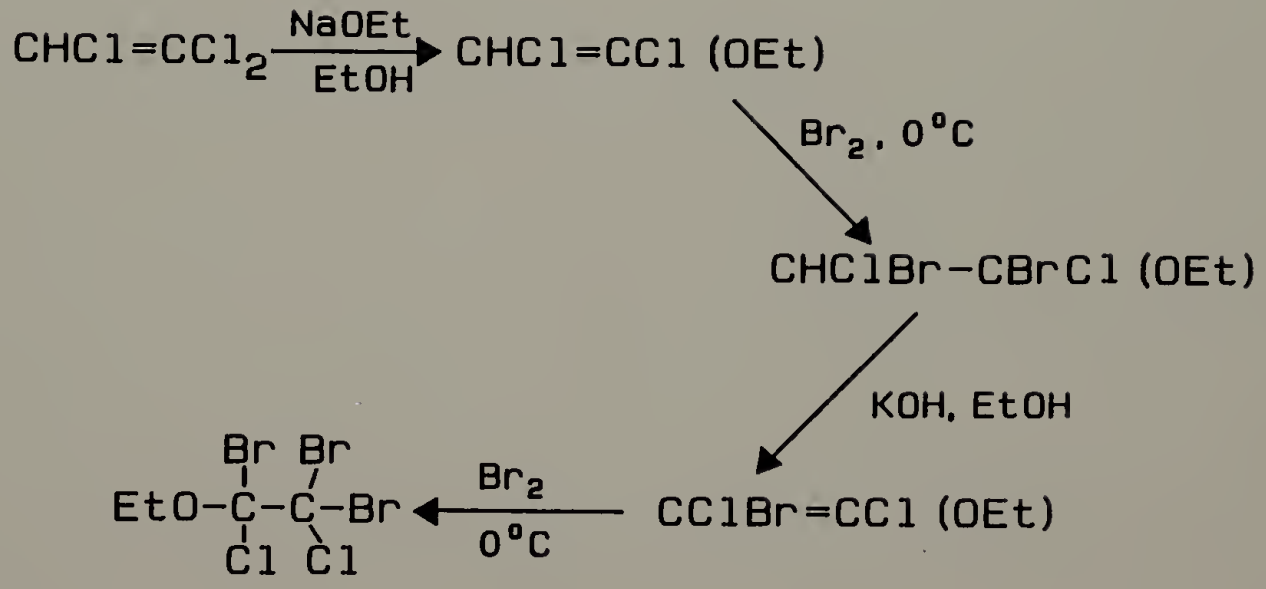
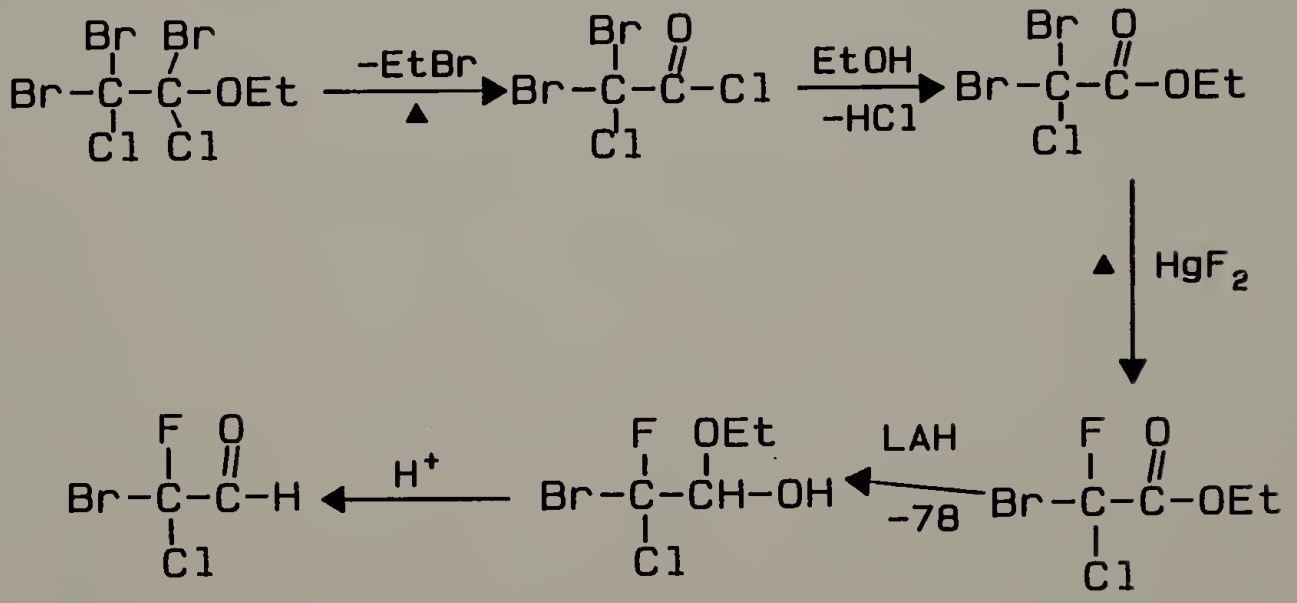


Fig. 5. Synthetic Scheme for the Attempted Preparation of Bromochlorofluoroacetaldehyde, Continued.

ATTEMPTED SYNTHESIS OF BROMOCHLOROFLUOROACETALDEHYDE

continued

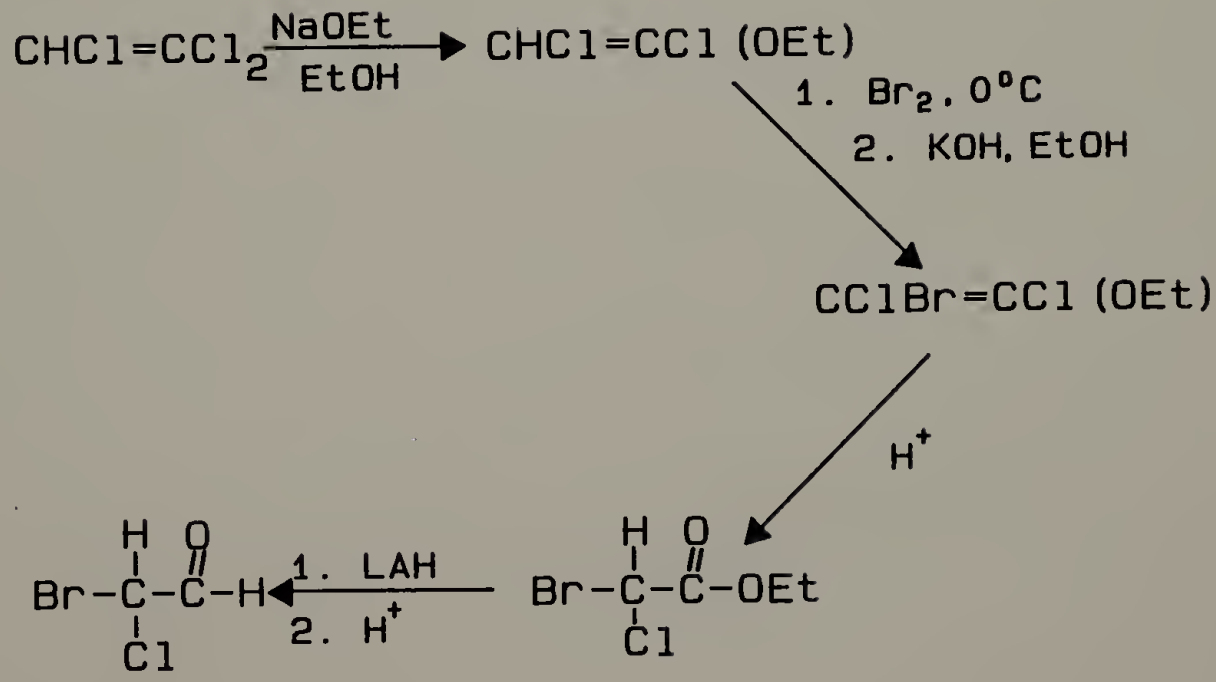


fifth step--the thermal rearrangement to dibromochloroacetate, presented any difficulties. The complication with this step was the incomplete nature of the rearrangement, but this was not prohibitive since the mixture of products could be separated by distillation. The fluorination step, the seventh step, apparently worked as indicated by the fluorine content of the impure product. However, the cost of this step was prohibitive because product yield was only 50% according to literature (183) and the mercuric fluoride fluorinating agent was expensive in light of its molecular weight (MW 238.6). The cost becomes even more prohibitive when one considers that the desired goal of obtaining both antipodes of BCFA would require resolution--an inefficient process. For these reasons, the synthesis of BCFA was discontinued and efforts were concentrated on preparing another asymmetric aldehyde, bromochloroacetaldehyde.

2. Bromochloroacetaldehyde (BCA). The preparation of racemic BCA by our synthesis strategy requires six reaction steps which are shown in Figure 6. The six reaction steps are: (1) nucleophilic substitution of trichloroethylene by ethoxide to form 1,1-chloroethoxy-2-chloroethylene, (2) bromination of 1,1-chloroethoxy-2-chloroethylene, (3) dehydrobromination of 1,1,1-bromochloroethoxy-2,2-bromochloroethane, (4) electrophilic proton attack and an elimination to prepare ethyl bromochloroacetate, (5) reduc-

Fig. 6. Synthetic Scheme for the Attempted Preparation of Bromochloroacetaldehyde.

ATTEMPTED SYNTHESIS OF BROMOCHLOROACETALDEHYDE



tion of ethyl bromochloroacetate to the hemiformal, and (6) acid decomposition of the hemiformal to form BCA. The first four synthetic steps were straightforward and of good yield. However, step 5, the reduction of ethyl bromochloroacetate to the hemiformal was unsuccessful even though the reduction was attempted under a variety of conditions. (The time and temperature of the attempted reduction, as well as reagent stoichiometry were unsuccessfully varied and only an ill-defined product was obtained.) The 'product' could not be readily separated or decomposed by strong acid to give the desired BCA. If this synthesis is to be successfully continued, a more selective or stablier reduction reagent must be used since there is doubt as to whether the hemiformal was ever obtained.

3. Trichloroacetaldehyde. The synthesis of an achiral aldehyde was performed to show that the procedure and technique used to reduce an ethyl ester to the hemiformal and subsequent decomposition by strong acid to the aldehyde was workable. Ethyl trichloroacetate was successfully reduced by 25 mole % lithium aluminum hydride at -78°C to the hemiformal. The hemiformal was successfully decomposed by sulfuric acid to form chloral whose presence was confirmed by ^{1}H NMR and gas chromatography. The success of this experiment showed that the technique used for reducing ethyl bromochloroacetate was adequate. The implication

that must be drawn about the attempted reduction of ethyl bromochloroacetate is that there must be something chemically preventing the selective reduction to the hemiformal. Perhaps, either the acidic α-hydrogen in ethyl bromochloroacetate is deactivating the lithium aluminum hydride or it is difficult to stop the reduction at the hemiformal stage.

C H A P T E R I V

DISCUSSION

A. Objectives and Principles

The primary objectives of this dissertation were to: (1) prove conclusively that optically active polychloral could be prepared where the optical activity arises from an induced molecular asymmetry; (2) to judge how the asymmetric initiators that induce molecular asymmetry influence the polychloral's optical activity; and (3) to evaluate whether optically active polychloral has merit as a chromatographic substrate capable of performing resolution of enantiomers.

For polychloral to be optically active, it must first exist in a helical conformation since the polychloral backbone does not possess any optically active asymmetric centers. A helical conformation typically implies that successive bonds in the polymer backbone are often in an alternating conformational sequence of either plus gauche and trans (g^+t) or a minus gauche and trans conformational sequence (g^-t). These two different conformational sequences result in two different helical screw-senses--either a right-handed screw or a left-handed screw having opposite signs of optical rotation. However,

for a polymer to exist as one of the above helices, it must also be stereoregular. Isotacticity most commonly meets this requirement. In isotactic polymers, a sequence of pseudoasymmetric centers in the polymer backbone must have the same configuration--either d or ℓ (i.e., meso placement, resulting in either dd or ℓℓ dyads). One of these dyad sequences will be predisposed to a left-handed screw while the other is predisposed to a right-handed screw. According to Flory (188), a dd dyad configuration has a preferred dyad conformation of g^+t with a possible helix reversal by a tg^- conformational sequence while a ℓℓ dyad configuration has a preferred dyad conformation of g^-t with a possible helix reversal by a tg^+ conformational sequence. Consequently, it should be apparent that there is an interdependence of conformation and configuration. The essence of this interdependence is that without the proper configurational sequence, a polymer cannot be helical. But in turn, the conformations and their conformational energies (which result from first order interactions and second order non-bonded interactions) nearest to the growing chain-end strongly influences the approach of the incoming monomer and its resulting configuration once the chemical bond is formed. It has been shown (155) that polychloral meets the requirements of being highly isotactic (i.e., meso placement) and that it is helical (g^+t or g^-t conformational sequences). As a result, polychloral is a good

example of this interdependence of configuration and conformation since it polymerizes anionically in an isotactic, helical fashion.

More than isotacticity and helicity are required for the preparation of optically active polychloral since the polymer was always optically inactive as prepared up until the recent past. This optical inactivity arose because with the achiral initiators used, a left-handed helical conformation was just as probable as a right-handed helical conformation (i.e., a racemic mixture of the two helical conformers). This result was due to the achiral initiator's inability to form a polymer mixture having a predominance of one configuration and a helical conformation of one screw-sense. The following quote by Flory (188), clearly implied how a preferred configurational sequence and a predominance of an optically active conformation for a polymer such as polychloral could be obtained:

> The presence of an asymmetric center in a chain molecule introduces a distinction, not otherwise present, between right- and left-handed rotations. The interactions precipitated by rotations ϕ and $-\phi$ about a skeletal bond near the asymmetric center will differ, in general, and the two states thus related will not occur with equal frequency, as is the case for symmetric chains.

This statement once again emphasizes the interdependence of configuration and conformation. This statement also implicitly predicted the preparation of optically active

polymer where optical activity arises from molecular asymmetry induced by an asymmetric center in the initiator. This requirement of having an asymmetric center in the initiator to induce a preferred configurational sequence and an optically active polymer conformation (i.e., a helix) was the approach used in this work to obtain a predominance of one helical screw-sense.

There is one additional requirement for the preparation of optically active polymer due to molecular asymmetry. Once a predominance of one helical screw-sense is obtained, it is highly desirable to maintain this particular conformational predominance. It is possible for the optically active polymer to lose its optical activity either by racemizing to a 50/50 mixture of helices through helical inversions or by changing from a helical conformation to a random coil in solution or the melt (i.e., tt or $g^{\pm}g^{\pm}$ conformational dyad sequences exist). With the absence of hydrogen bonding in most synthetic polymers, the only practical way to prevent or hinder the loss of optical activity by either of the above processes, in helical polymers with no asymmetric centers, is to raise the conformational energy barrier of the polymer backbone through second order non-bonded interactions. This is achieved by having bulky and/or polar substituents close to the polymer backbone. Polychloral meets this requirement since it has a bulky and polar substituent, the trichloromethyl group, α

to the polymer backbone.

In this work, the requirements of helicity, isotacticity, and high conformational energy barriers have been predetermined by the choice of the polymer studied--polychloral. The one requirement over which this dissertation focuses is the interaction of the asymmetric center in the initiator and the trichloromethyl group in the chloral monomer and how it affects the resulting configuration and conformation of the polymer as judged by its optical activity. This interaction is varied by using different asymmetric initiators and variable temperatures. These variations should provide a better understanding of the processes that result in optically active polymers with molecular asymmetry.

At this point, it should be mentioned that the induction of molecular asymmetry which originates in the initiation step can be approached from either a configurational point of view (i.e., does the addition of monomer to the asymmetric initiator result in meso placement (isotactic), therefore determining <u>if</u> the molecule <u>can be</u> helical) or a conformational point of view (i.e., do successive bonds in the product of the asymmetric initiator and monomer (and ultimately the polymer) assume successive gauche/trans conformational sequences due to conformational energies). In this work, the conformational viewpoint is favored since it should be better able to explain the

induction of molecular asymmetry by asymmetric counterions (141,145), but it is favored primarily because the polychloral's optical activity arises from its conformation and it is desired to maintain the emphasis on the polymer's helical conformation.

In this work, the product resulting from the addition of one chloral unit to the initiator will be called a helical precursor. It is implicit that both the configuration (meso versus racemic placement) and the conformational sequence (tg^+, tt, etc.) will ultimately determine the ratio between the two polymer screw-senses and this ratio is reflected by the measurement of specific rotation.

This chapter is broken down into five sections. In this section, the objectives of this dissertation were reiterated and the principles and requirements for preparing optically active polymer due to molecular asymmetry were enunciated.

In section B of this chapter, the use of optically active polychloral initiated by lithium cholesteroxide as a chromatographic support for resolution is discussed.

In section C of this chapter, the use of the following optically active initiators to prepare optically active polychloral is discussed: tetramethylammonium d(+)- and ℓ(-)-O-acetylmandelate, tetramethylammonium d(+)- and ℓ(-)-α-methoxymandelate, and lithium methyl d(+)- and ℓ(-)-hydroxidemandelate.

In section D of this chapter, the key results and conclusions drawn in this dissertation are summarized.

Finally, in section E of this chapter, proposals for future work are made.

B. Resolution Using Polychloral Initiated by Lithium Cholesteroxide

Using the lithium alkoxide of cholesterol as an initiator to induce molecular asymmetry, the first attempt was made to prepare optically active polychloral where the optical activity arose from the polymer's secondary structure (i.e., helical conformation). As suggested in earlier results (186,187), the lithium cholesteroxide was found to be unstable in pure chloral monomer at temperatures greater than 58°C (the ceiling temperature of chloral monomer). It was thought to be impossible to prepare in any quantity this potentially optically active polychloral initiated by lithium cholesteroxide. However, it was soon discovered that polychloral could be readily prepared using lithium cholesteroxide initiator, if the ceiling temperature of the monomer was depressed below 48°C by adding hydrocarbon diluent.

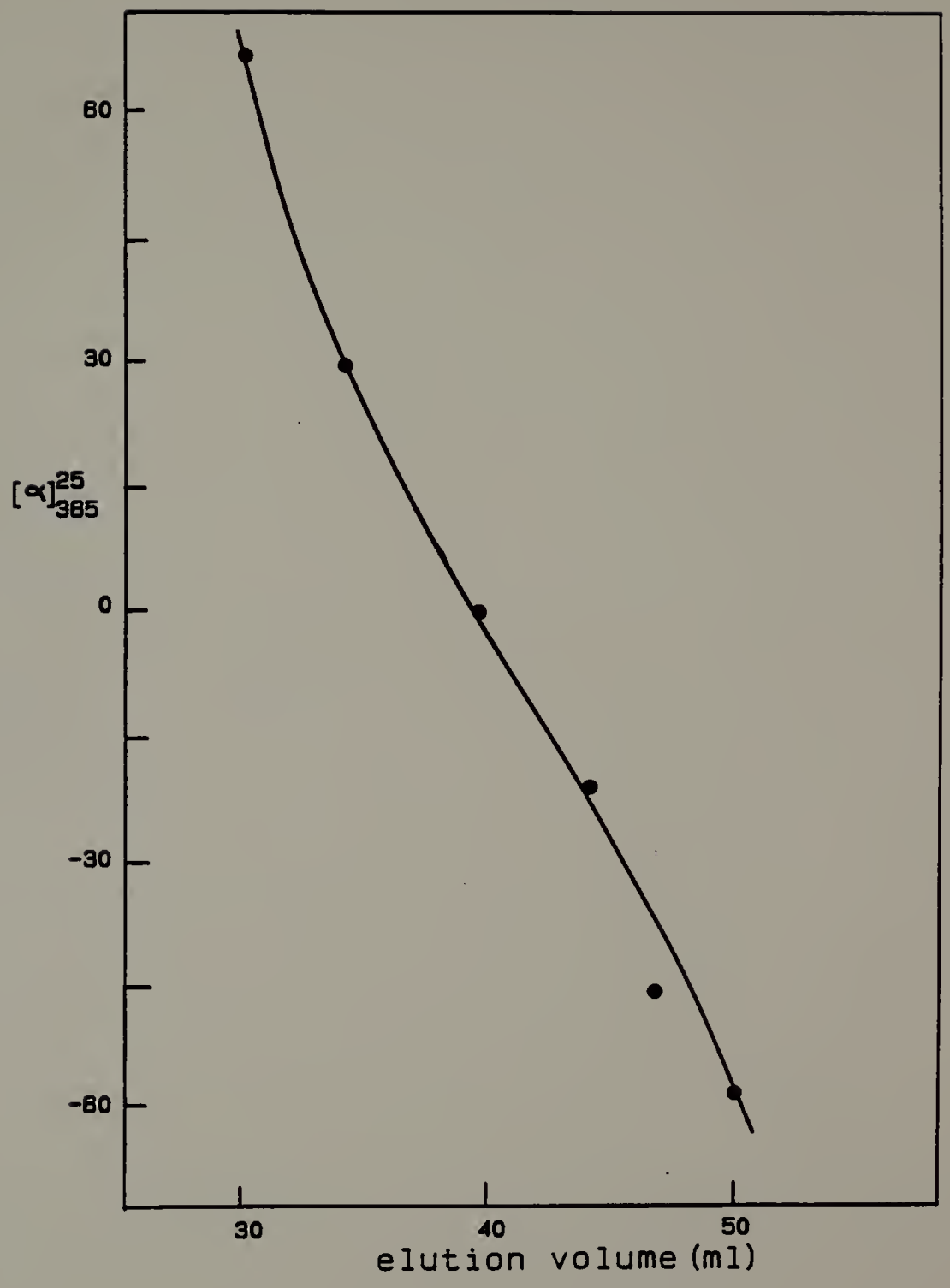
Unfortunately though, the large quantity of hydrocarbon diluent promoted the formation of voids in the polychloral films and made it impossible to cryotachensically cast coherent pieces of film for optical activity

measurements (polychloral is insoluble). Since it was not feasible to directly measure the polychloral's hypothetical optical activity, it was decided to obtain indirect evidence for the existence of polychloral's optical activity. Indirect proof could be obtained if the polychloral was shown to be capable of resolving a racemic mixture of compounds. This test would also indicate whether polychloral might have merit as a chromatographic support for the resolution of enantiomers.

Polychloral initiated by lithium cholesteroxide was provided to Hatada (147) for testing as a chromatographic support. A 50/50 mixture of poly(R-(+)-α-methylbenzyl methacrylate) ($\bar{M}_n$ = 79,300) and poly(S-(-)-α-methylbenzyl methacrylate) ($\bar{M}_n$ = 53,800) were dissolved in tetrahydrofuran and introduced into the chromatographic column with 3.4 mL eluate fractions collected. The mass and the optical activity of polymer was determined for each fraction with the results listed in Table 6, Chapter III. The results in Table 6 are graphically displayed in Figure 7.

As can be seen in Figure 7, the dextrorotary poly(R(+)-α-methylbenzyl methacrylate) was preferentially eluted at short times. The maximum specific rotation that was obtained by resolution for the dextrorotary polymer was (+)66 at an elution volume of 32.3 mL. This corresponded to an optical purity or resolution of 18%. Figure 7 also shows that levorotary poly(S(-)-α-methylbenzyl methacrylate)

Fig. 7. Resolution of Racemic Poly(α-methylbenzyl methacrylate) on Optically Active Polychloral Initiated by Lithium cholesteroxide (Tetrahydrofuran eluant).


60
30
0
-30
-60
$[\alpha]_{365}^{25}$
30
40
50
elution volume (ml)

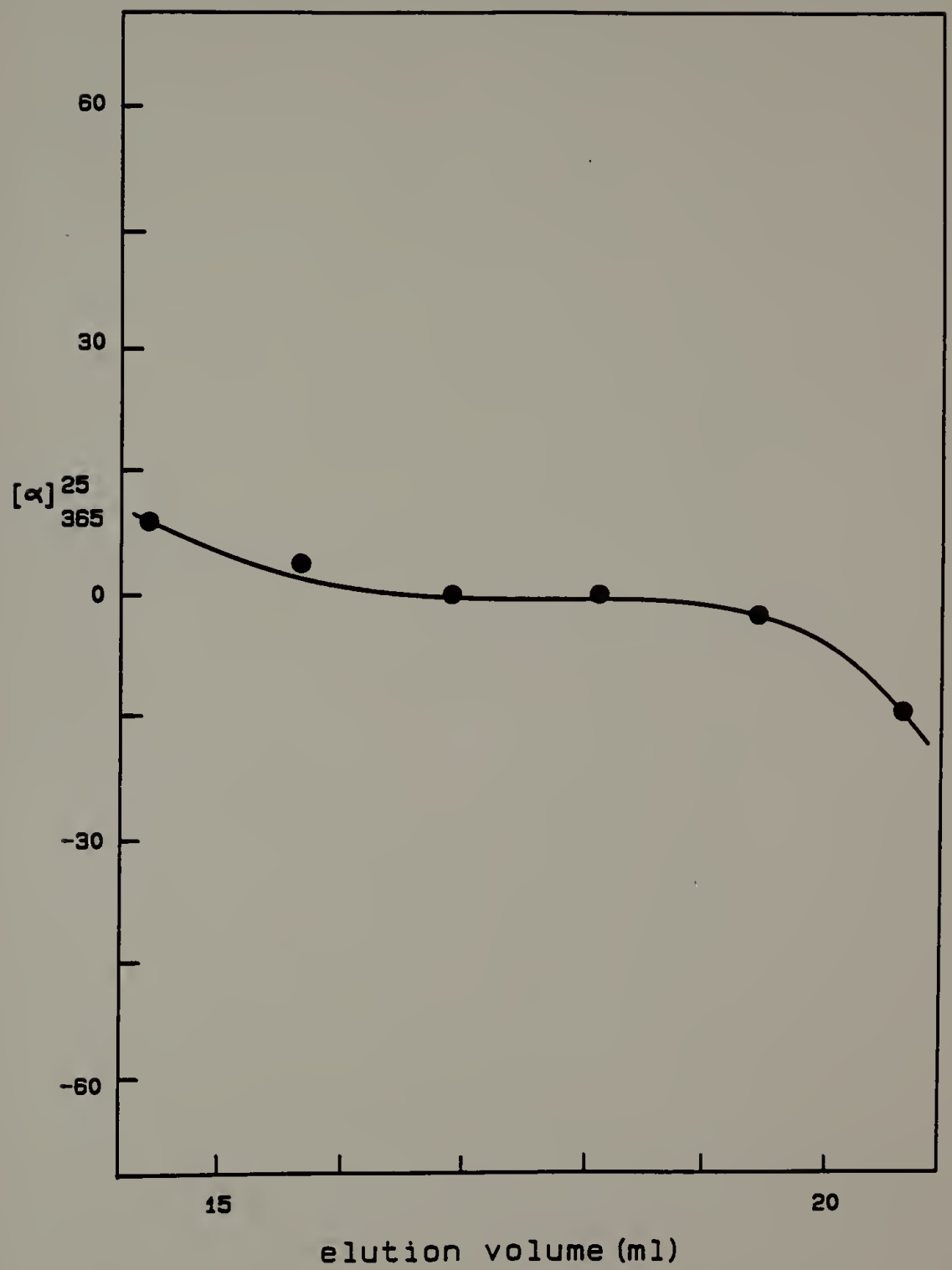
was retained longer on the polychloral substrate. The maximum specific rotation for the levorotary polymer via resolution was (-)53 at an elution volume of 49.3 mL. This corresponded to an optical purity or resolution of 15%.

It was realized that this apparent resolution might be solely due to size exclusion chromatography (i.e., GPC) since the two antipodes of poly(α-methylbenzyl methacrylate) had different number average molecular weights. To see if a GPC effect was responsible for the apparent resolution, another column was packed with polychloral that had been initiated by lithium t-butoxide (an achiral initiator). The racemic mixture of poly(α-methylbenzyl methacrylate) was chromatographed and analyzed as previously described. The results are shown in Figure 8.

As can be seen in Figure 8, a slight fractionation of poly(α-methylbenzyl methacrylate) occurred. As would be expected with gel permeation chromatography, the higher molecular weight poly(R(+)-α-methylbenzyl methacrylate) was eluted first as evidenced by the small positive rotations at short elution times. The lower molecular weight poly(S(-)-α-methylbenzyl methacrylate) was preferentially eluted at longer times as was expected in a size exclusion process.

However, by considering the results from chromatographing racemic poly(α-methylbenzyl methacrylates) on polychloral initiated by either a chiral or an achiral

Fig. 8. Attempted Resolution of Racemic Poly(α-methylbenzyl methacrylate) on Optically Inactive Polychloral Initiated by Lithium t-butoxide (Tetrahydrofuran eluant).


60
30
[α] 25 365
0
-30
-60
15
20
elution volume (ml)

initiator, it is reasonable to say that resolution was achieved by polychloral initiated with lithium cholesteroxide due primarily to the polymer's optical activity. The partial resolution achieved on polychloral initiated by lithium cholesteroxide must be attributed to the interaction of the racemic methacrylate polymer with a predominating helical screw-sense in the polychloral. The results from this experiment are quite good when one considers that this resolution experiment was relatively simple and did not involve such things as longer columns, cycling, variable flow rates, variable temperatures, or polychloral having more surface area. By considering these factors, it should be possible to obtain a much more efficient resolution of the racemic poly(α-methylbenzyl methacrylate).

In order for resolution to be effected on a polychloral substrate, there must be some mechanism to describe the resolution process. A mechanism proposed by Nolte and Drenth for polyisocyanides (137) seemed applicable to the polychloral system. In their mechanism, the polymer substrate was conceptualized as a left-handed screw, while the polymer to be resolved was a mixture of left-handed and right-handed screws. They pointed out that "parallel screws have a smoother mutual fit when they are of opposing [screw] sense than when they are the same [screw] sense." This mechanism implied that of the two screw-senses a right-handed helical polymer would be more

strongly attracted to a left-handed helical substrate. This preferential attraction would result in the left-handed helical polymer being eluted before the right-handed helical polymer. This proposed mechanism seemed appropriate for explaining the results obtained with optically active polychloral since the polychloral substrate was helical and the isotactic poly(α-methylbenzyl methacrylates) apparently possessed helical segments. (This was indicated by 'excess' optical activity observed in isotactic versus atactic poly(α-methylbenzyl methacrylates) (128).) By Drenth and Nolte's mechanism, polychloral initiated by lithium cholesteroxide must be dextrorotary since dextrorotary polymer eluted first. However, Yuki's work using optically active, helical poly(triphenyl methacrylate) substrates to resolve both small molecules with asymmetric centers and helical molecules (142,143) suggested that the Drenth mechanism was too simplistic since it would have difficulty explaining the resolution of the smaller asymmetric molecules having no helical conformation. There is a need to develop a unifying mechanism that explains both the resolution of molecules with asymmetric centers and molecules with molecular asymmetry.

C. Optically Active Polychloral Prepared By Asymmetric Carboxylate and Alkoxide Initiators

1. Measurement of optical activity in the solid state. The determination of the optical activity of polychloral requires that the measurement of optical rotation, α, be performed in the solid state since polychloral is insoluble. Measurement of optical activity in the solid state gives rise to difficulties that are not encountered when optical activity measurements are made on solutions (146). One such difficulty arises from the requirement that the optical activity measurement must be made on an optically isotropic sample. For a solution, this requirement presents no problem since solute is evenly dispersed in the solvent. However, for a polymeric solid it can prove difficult to prepare an optically isotropic sample. For example, if a polymer film is stressed prior to an optical rotation measurement, the molecules in the film will be oriented, creating birefringence. Birefringence can cause the rotation of plane-polarized (depending on the direction of orientation) which means that the film is no longer optically isotropic and is unsuitable for optical activity measurements.

In order to prepare polychloral films for optical activity measurements, it is necessary to avoid stressing the film during its preparation or measurement. It is also

necessary to keep the film in organic media at all times to prevent orientation by shrinkage. To determine if a polychloral film was substantially oriented, the film was placed in a polarimeter at three orientations 120° apart. If the average of the three optical rotations, α, had a standard deviation of 15% or less, the polychloral film was considered to be optically isotropic for the purposes of the optical activity measurements. All films prepared were evaluated by the criteria outlined here.

A second difficulty that can arise in optical activity measurements in the solid state is that a polymeric film, such as polychloral, can possess microvoids, which leads to substantial light scattering (i.e., opacity). To avoid this opacity problem, the voids are simply filled with a liquid possessing the same refractive index as the solid. This void-filling renders the film transparent and allows the transmission of plane-polarized light. For polychloral, the microvoids were filled with diphenyl ether which has a refractive index of 1.576 at the sodium D-line. The difficulties of preparing an isotropic sample and light scattering by voids are manageable provided that care is taken in the handling and manipulation of the film.

As discussed in Chapter I, optical activity is often expressed as the specific rotation (Equation 1) which normalizes optical activity measurements in regards to path length and concentration. Specific rotation was originally

used to describe the optical activity of solutions, not solids. Specific rotation, as defined in Equation 7 (slightly modified form of Equation 1), can be successfully used to describe optical activity of solids. The only difference between Equations 1 and 7 is the concentration term, c--in solutions, c is defined as the mass of solute (in grams) per milliliter of solvent, while for solids, density is used as a substitute for c since density has the proper dimensions. For polychloral, a crystalline density of 2.0 g/cm^3 was calculated from X-ray diffraction for a perfect crystal of isotactic polymer in a 4_1 helix (155). However, an experimentally determined density of 1.9 g/cm^3 (185) has been chosen for use in the determination of specific rotation. It should be noted that the specific rotations reported in Chapter III for polychloral films should be somewhat low. The specific rotations are probably low because the presence of microvoids in the films effectively reduces the film's path length to less than the film thickness (see Equation 7). Film thickness is presently used for the path length, ℓ, since it can be readily evaluated.

As can be discerned from prior discussions, there are larger errors associated with optical activity measurements made on solids than on solutions. The errors in the specific rotations reported in Chapter III are typically 7% of the specific rotations reported. These reported

errors are the standard deviations that arise from averaging optical activity measurements from both different polychloral films and different positions 120° apart in a film disc. For each specific rotation reported for polymer from a given initiator at a given time and temperature, a total of fifteen to eighteen measurements were averaged. This number of measurements was obtained as follows: At each time and temperature, two separate polychloral films were cryotachensically cast simultaneously. From each film, three discs were cut for optical activity measurements leading to a total of six discs being measured. Finally, each disc was measured at three positions 120° apart, leading to a total of eighteen measurements. Any time that the optical rotation's standard deviation was greater than 15% (i.e., the disc was anisotropic) for a specific film disc, those three values were discarded.

As proof that the approach outlined here to determine optical activity in the solid state was reasonable and reliable, optical activity measurements were first made on polychloral films polymerized by racemic initiators. (The racemic initiators should lead to polychloral which has a specific rotation of zero.) Using the racemic initiators of tetramethylammonium α-methoxymandelate, tetramethylammonium O-acetylmandelate, lithium methyl hydroxidemandelate, and lithium 2-octanoxide, polychloral films with the following specific rotations of (+)10±10, (+)5±10,

(+)5±10, and (+)5±15 were, respectively, obtained. As would be predicted, the specific rotations were all effectively zero (especially when the magnitude of the specific rotations available from optically active polychloral are considered (80 → 4700)). The small standard deviations from the optically inactive polychloral indicates that the method used to prepare films for optical activity measurements minimizes the chances of accidentally orienting polychloral films. By repeatedly obtaining optically inactive polychloral having effectively zero rotation proves that the specific rotations reported in this investigation must arise solely from optical activity.

2. Preliminary results. The first experiments that resulted in optically active polychloral film, in this work, involved the initiator tetramethylammonium ℓ(-)-O-acetylmandelate (TMA(-)Ac). TMA(-)Ac initiator was used in a variety of experiments without carefully controlling either the temperature at which chloral monomer and initiator were mixed or the time monomer and initiator were mixed prior to cryotachensic polymerization (i.e., cooling initiated monomer below the ceiling temperature so that polymerization occurs). In these experiments a wide variation in the specific rotation from (+)240 to (+)670 was observed. Because TMA(-)Ac had an acidic α-hydrogen which is prone to racemization by abstraction and TMA(-)Ac was also observed

to undergo 2% racemization in chloroform at 75°C after 50 minutes, it was suspected that initiator racemization was responsible for the variation in the polychloral's optical activity. This was viewed as a reasonable proposition since racemization is a time/temperature dependent process and the importance of time/temperature control in the initial experiments had not been fully recognized. If racemization was responsible for the specific rotation's variation, by mixing initiator and chloral monomer at a fixed temperature ($>T_c$) and cryotachensically casting films at longer times, polymer with decreasing specific rotation should be obtained. Performing this type of experiment with TMA(-)Ac gave rise to the observation that the polychloral's specific rotation was <u>increasing</u> with the length of holding time, not decreasing as expected. The implication of this experiment was that racemization could not be the principal process responsible for polychloral's varying optical activity. Explanation of this increasing optical activity with increasing time initially was elusive since most processes envisioned would lead to a decrease in the polymer's specific rotation. For example, a Hofmann degradation of the tetramethylammonium group to trimethylamine or nucleophilic impurities in the initiator should decrease the polychloral's optical activity.

A preliminary proposal which could possibly explain the increase of specific rotation was that the TMA(-)Ac was

slowly deacetylating. If deacetylation was occurring, the initiating species could be an alkoxide instead of a carboxylate. In this alkoxide initiator, the asymmetric center would be closer to the first trichloromethyl group in the polymer and should lead to a further enhancement of one screw-sense of the polychloral. This would explain the increase in optical activity as a function of increasing time or temperature. (An analogy of this proximity explanation was the work by Pino using poly-α-olefins with the asymmetric centers in the side chain (8).) Efforts were made to evaluate the acetyl group's stability, but results were inconclusive. The decision was made to temporarily curtail the use of tetramethylammonium O-acetylmandelate initiators in favor of tetramethylammonium α-methoxymandelate initiators (TMAαM) so that concern over deacetylation could be avoided.

3. Optically active polychloral initiated by tetramethylammonium d(+)-α-methoxymandelate (TMA(+)αM) and tetramethylammonium ℓ(-)-α-methoxymandelate (TMA(-)αM). With the start of studies using the tetramethylammonium α-methoxymandelate initiators, careful attention was placed upon controlling both the temperature at which initiator and monomer were mixed and the time at which they were held before cryotachensic polymerization. Temperature was controlled by using a 20 L thermostatic bath to heat and hold

the initiator and monomer mixture at the desired temperature above the ceiling temperature (58°C for pure monomer). The temperature of the film assemblies was controlled by placing the assemblies in an oven whose temperature was generally within two degrees of the thermostatic bath. Film assemblies were allowed at least 1.5 hours to equilibrate to oven temperature. All subsequent references to temperature in this chapter refer to the temperature of the bath and the film assemblies.

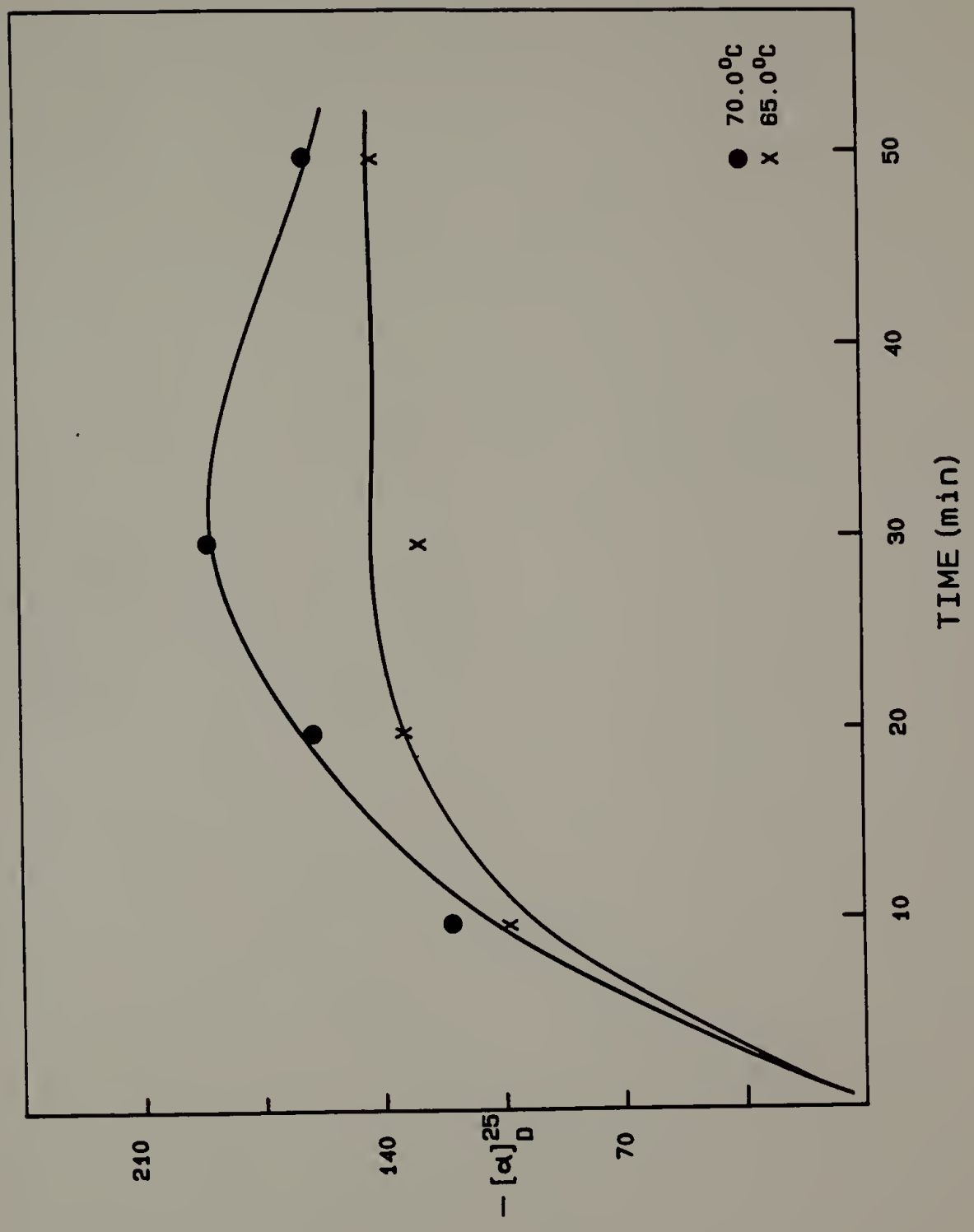
When the chloral monomer and initiator had come to bath temperature, they were mixed (t = 0 minutes) and the mixture was kept sealed in the temperature bath. At timed intervals (monitored by stopwatch) aliquots of initiated monomer were placed in film assemblies which were then plunged into ice water so that polymerization could occur. The time at which the film assembly was plunged into ice water is the time value reported for all cryotachensic polymerizations (i.e., the holding time). Errors reported in the times at which polymerization was started for a film were typically ± 0.5 minutes. All subsequent references to 'time' explicitly refer to the time interval at which cryotachensic polymerization was started after initiator and monomer were mixed (t = 0 minutes).

As mentioned previously, it was decided that the TMAαM initiators were better than the tetramethylammonium O-acetylmandelate (TMAAc) initiators in gaining an initial

understanding as to why the optical activity of the resulting polychloral was so sensitive to the time and temperature to which the initiated monomer was exposed. The results from TMAαM initiators should be easier to interpret than TMAAc initiated polychloral since it is improbable that the TMAαM's methoxy group would undergo a side-reaction under polymerization conditions (this cannot be said of the acetyl group in TMAAc).

Using the optically active initiator tetramethylammonium d(+)-α-methoxymandelate at 0.5 mole %, polychloral films were cast from monomer/initiator mixtures held at either 65.0, 70.0, 80.0, or 85.0°C every 10, 20, 30, and 50 minutes. The specific rotations and errors for these polychloral films are found in Table 9, Chapter III. The results reported in Table 9 are presented in Figures 9, 10, and 11 where the specific rotation is plotted against the holding time at a constant temperature. For the 65.0°C isotherm in Figure 9, the specific rotation increases for polychloral films cryotachensically cast at longer holding times. This increase in optical activity at longer holding times is similar to the increase of specific rotation at longer holding times when TMA(-)Ac was the initiator in the prior section. It now seems highly probable that the increase of specific rotation for both TMA(+)αM and TMA(-)Ac initiated polymer must have the same origins. Consequently, deacetylation could not be responsible for the increasing

Fig. 9. The specific Rotation of Polychloral Initiated by TMA(+)αM as a Function of Holding Time at 65.0°C (x) or 70.0°C (●).


210
140
70
$-[\alpha]_D^{25}$
10
20
30
40
50
TIME (min)
● 70.0°C
X 85.0°C

optical activity observed for polychloral initiated by TMA(-)Ac. (A later experiment with lithium methyl ℓ(-)-hydroxidemandelate initiator proves that deacetylation is not responsible for increasing specific rotation, because the alkoxide initiated polymer has the same sign of rotation as the initiator.)

Also shown in Figure 9 is the 70.0°C isotherm. At 70.0°C, the specific rotation increased from (-)120 to a maximum of (-)190 at the respective times of 10 and 30 minutes, but it subsequently decreased to (-)160 at 50 minutes, so there must be two competing processes occurring at different rates. From Figure 9 it can also be observed that at every holding time, the specific rotation is greater for the higher bath temperature, 70.0°C. These two curves at 65.0 and 70.0°C show that the specific rotation can increase with either increasing time or increasing temperature. This increase in optical activity as a function of time or temperature resembles a relatively slow reaction. This slow reaction is thought to be the formation of chloral oligomers above the ceiling temperature whose rate of formation increases as a function of increasing temperature. These alleged oligomers should play an important role in determining the screw-sense of the polymer through both the interaction of the first trichloromethyl group with the asymmetric center in the initiator and the increasing second order non-bonded interactions

between successive trichloromethyl groups. In these oligomers there should be fewer errors in meso placement and g^+t conformational sequences due to the second order nonbonded interactions. This is reasonable since it has been observed in other systems (91-94) that there is a critical oligomer length at which the helical screw-sense is fixed. Attempts were made to isolate the alleged polychloral oligomers without success; only high polymer was obtained when high initiator concentrations were used.

In Figure 10, the 70.0°C isotherm is plotted once again, but attention should now be focused on the decrease in optical activity to (-)160 at 50 minutes. For the 80.0°C isotherm, shown in the same figure, there also occurs a decrease in specific rotation at longer times (i.e., 20 and 30 minutes) which seems to be approaching an asymptotic value at (-)160. This approach to an asymptote is again noted in Figure 11 where for the 85.0°C isotherm all specific rotations at various times are centered about (-)160. This decrease in specific rotation from (-)190 to an asymptotic value of (-)160 cannot be attributed principally to racemization of the initiator or a Hofmann degradation of the tetramethylammonium counterion to trimethylamine. Both of these processes should lead to a linear decrease in optical activity with increasing holding time at a fixed temperature.

The phenomenon that is thought to be responsible

Fig. 10. The Specific Rotation of Polychloral Initiated by TMA(+)αM as a Function of Holding Time at 70°C (●) or 80.0°C (▲).

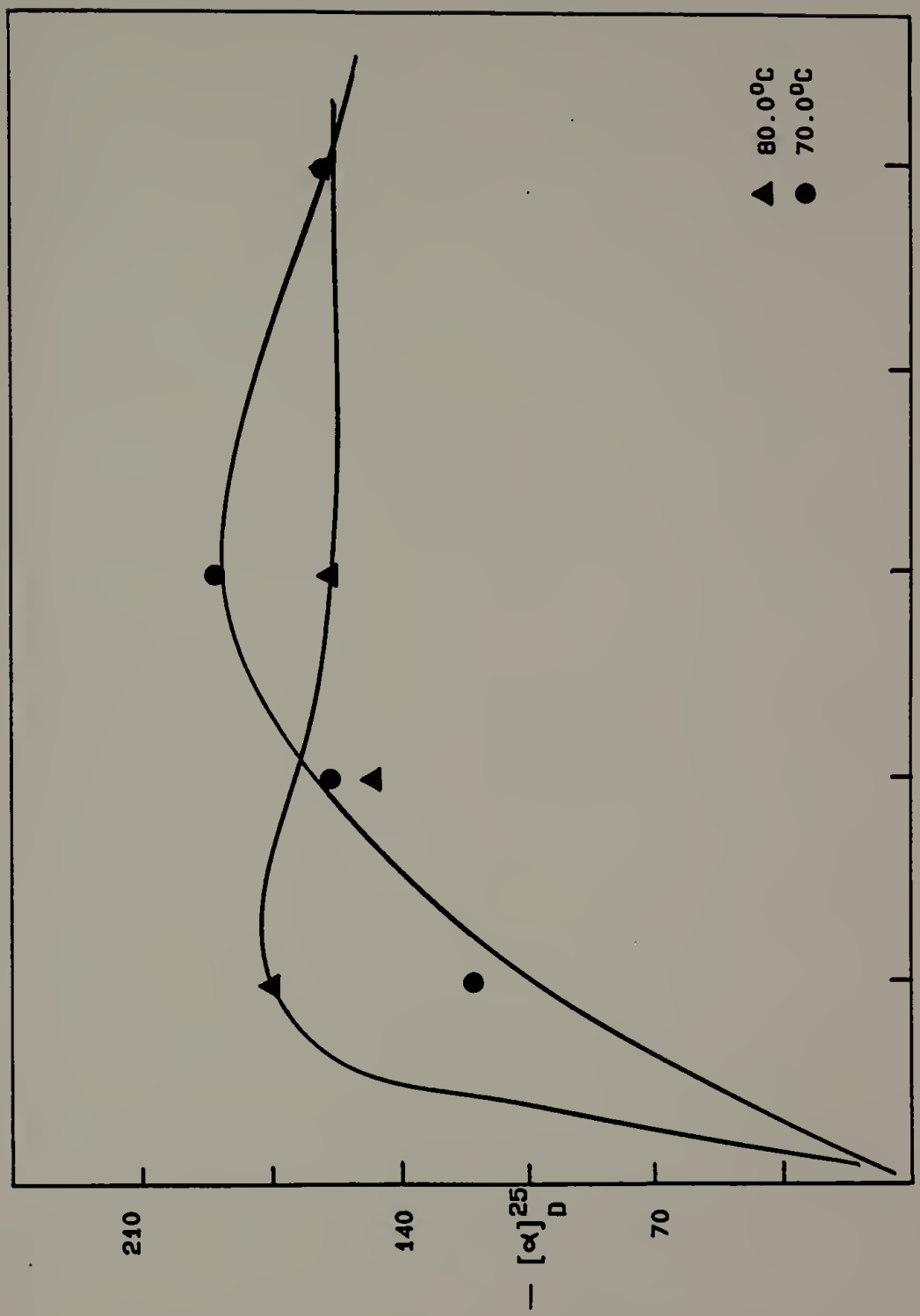
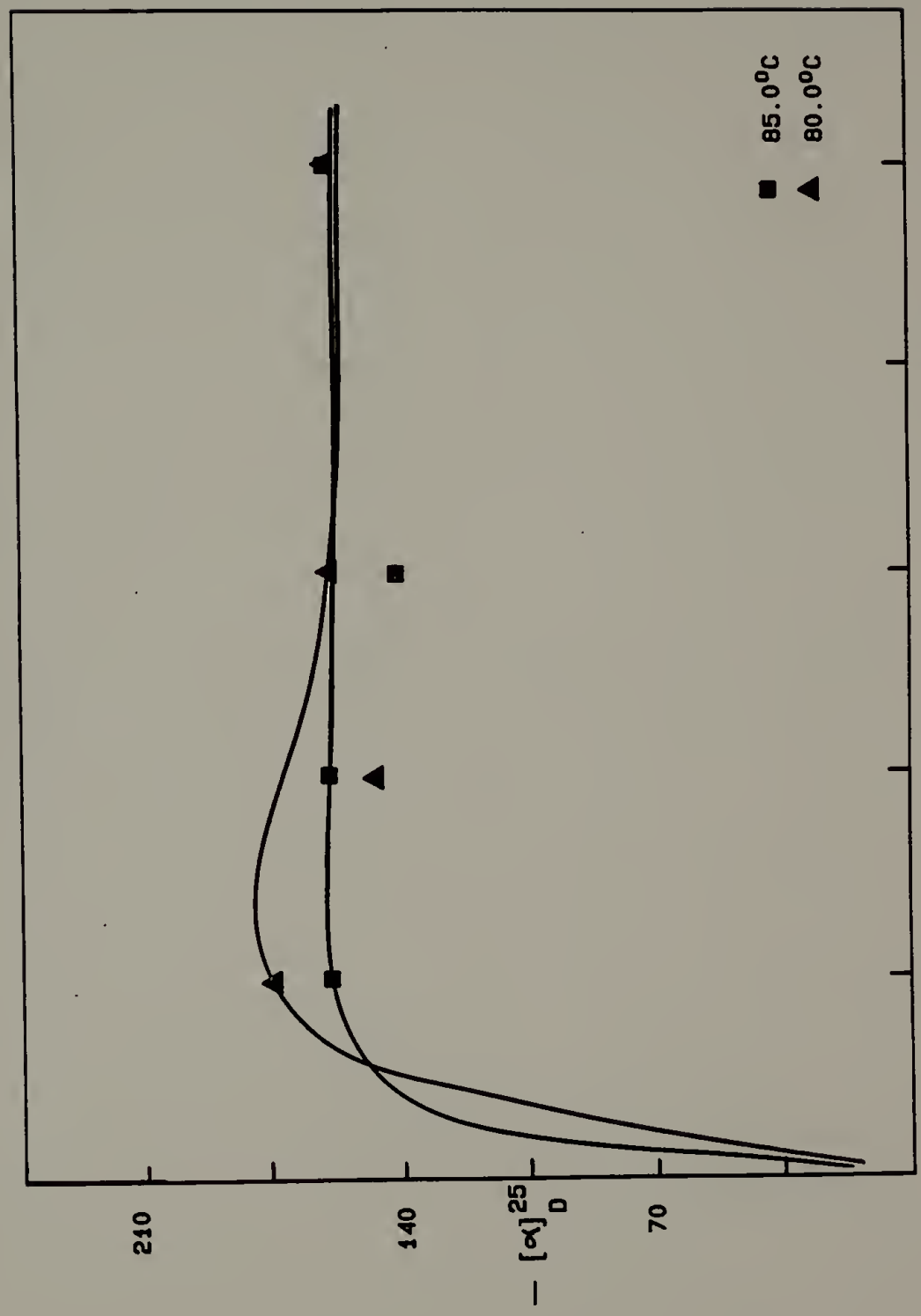

80.0°C
70.0°C
TIME (min)
10
20
30
40
50
210
140
70
— [α]$_D^{25}$

Fig. 11. The Specific Rotation of Polychloral Initiated by TMA(+)αM as a Function of Holding Time at 80.0°C (▲) or 85.0°C (■).


85.0°C
80.0°C
210
140
70
$-[\alpha]_D^{25}$
10
20
30
40
50
TIME (min)

for the decrease in optical activity is explained as follows: as discussed earlier, when an asymmetric initiator adds to a bulky monomer there are basically two types of helical precursors--ones that lead to levorotary helices and ones that lead to dextrorotary helices. One of these two helical types will predominate (i.e., optically active sample) because of the combined effect of the precursors configuration(meso) and the steric interaction of the asymmetric center with the trichloromethyl group leading to a g^+t conformational dyad sequence. The predominance of one helical precursor is due to it having a lower conformational energy. However, as the temperature increases, the probability of a g^+t conformation should decrease as conformational dyad sequences other than g^+t become more probable. (This argument is just as applicable for the other helical conformation having a g^-t conformational sequence.) This would result in less optical activity in polychloral and would help explain why the polymer's specific rotation decreases to an asymptotic value at higher temperature. However, a decreasing probability for a g^+t conformational sequence could arise from racemic placement in the helical precursor and its oligomers. At present it is not possible to distinguish whether it is the change in configuration (meso versus racemic placement) or the change in conformational sequence probability (assuming no change in meso placement as a function of temperature)

that is responsible for the decrease of polymer optical activity. If oligomers could be isolated, NMR should be able to distinguish whether configuration or conformation is more important to the observed decrease in optical activity.

Other than the optical activity of polychloral depending on time and temperature, one additional problem must be addressed--the polychloral's sign of rotation. The optical rotation sign of the TMA(+)αM initiator and its resulting polychloral are opposite and should not be regarded as unusual. This result simply means that when dextrorotary TMAαM adds to chloral monomer, the levorotary helical precursor is favored because it has a lower conformational energy than the dextrorotary type. There are several examples in polymer science where one configuration induces the formation of an asymmetric center having the opposite sign of rotation (12,16) or where an asymmetric initiator preferentially polymerizes the antipode of racemic monomer having the other sign of rotation (107).

So far nothing has been said about the contribution of the asymmetric initiator endgroup to the polymer's optical activity. To allay concern about the endgroup's contribution to the polymer optical activity, it should be noted that the sign of optical rotation for the initiator and the polymer are opposite. It seems unlikely that when the initiator became a polymer endgroup that its sign of

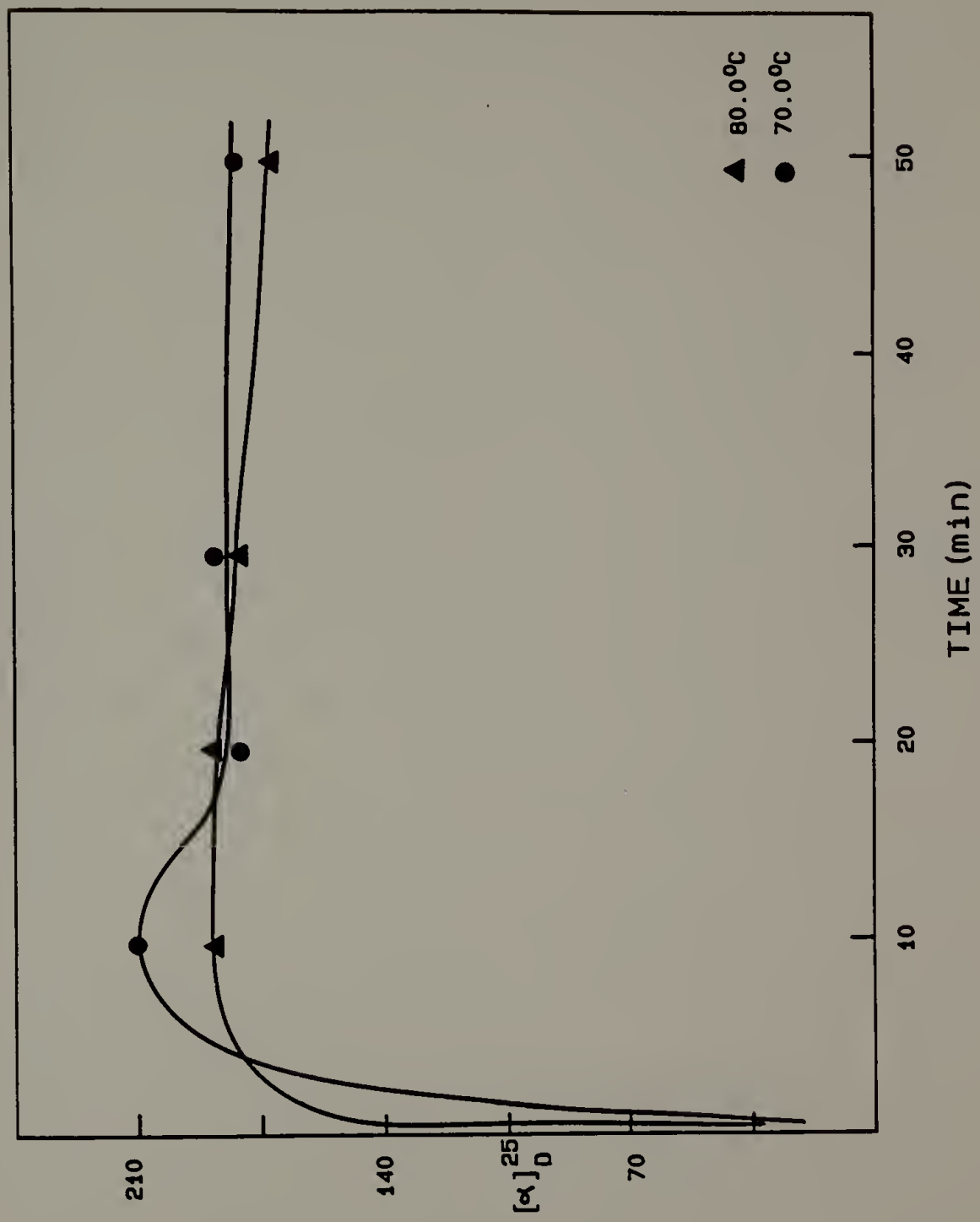
optical rotation would change since the basic polarizability of the configurational bonds does not substantially change. Even if the asymmetric center did undergo a change of rotation sign, at its present concentration in the polymer and assuming that its specific rotation is of the same magnitude as the initiator, the maximum contribution it could make to the polymer's specific rotation would be 1. If one were to assume that the asymmetric endgroup was completely responsible for the observed specific rotation of (-)190 for TMA(+)αM initiated polychloral, it would require that the endgroup have a specific rotation of (-)16,500 at the sodium D-line. Early work by Marvel shows that an asymmetric center in a polymer endgroup leads to a negligible specific rotation (14).

A useful way to corroborate the trends observed when TMA(+)αM initiator was used to prepare optically active polychloral would be to use the other antipode of the initiator, tetramethylammonium ℓ(-)-α-methoxymandelate (TMA(-)αM), to polymerize chloral. TMA(-)αM initiated polychloral should show the same optical activity trends and behavior as observed for TMA(+)αM initiated polychloral except that the results would be of opposite rotation sign. Using TMA(-)αM initiator, polychloral films were cast from 70.0 and 80.0°C initiator/monomer mixtures every 10, 20, 30, and 50 minutes. The specific rotations and errors for all these films are found in Table 10, Chapter III. This

data is presented in Figure 12 with specific rotation plotted against holding time. As can be seen in Figure 12, polychloral initiated by TMA(-)αM exhibits similar trends and has specific rotations comparable to that of polychloral initiated by TMA(+)αM (see Figure 11). For the TMA(-)αM initiated polychloral there is the same trend of the polymer's specific rotation increasing to ∿200 and then at longer times decreasing to an asymptotic value. The absolute specific rotation for the asymptotic values are also approximately the same for both TMA(+)αM and TMA(-)αM initiated polychloral. The final similarity observed is that the sign of optical rotation for TMA(-)αM initiator and its resulting polymer are opposite as was observed for TMA(+)αM and its polychloral. Overall, it can be said that the two antipodes of tetramethylammonium α-methoxymandelate give rise to self-consistent results.

In synopsis, the following conclusions have been drawn about the experiments that led to optically active polychloral initiated by TMA(+)αM and TMA(-)αM: (1) optically active TMAαM initiators preferentially induce molecular asymmetry in polychloral; (2) the contribution of the asymmetric endgroups to polymer optical activity is negligible; (3) the induced optical activity of polychloral shows a dependency on the time and temperature at which initiator and monomer are mixed and held prior to cryotachensic polymerization; (4) the increase in polychloral's

Fig. 12. The Specific Rotation of Polychloral Initiated by TMA(-)αM as a Function of Holding Time at 70.0°C (●) or 80.0°C (▲).


210
140
70
$[\alpha]_D^{25}$
10
20
30
40
50
TIME (min)
80.0°C
70.0°C

optical activity at relatively low mixing temperatures (i.e., 65°C) with increasing holding times (i.e., 10→50 minutes) is attributed to an increasing concentration of oligomer above the ceiling temperature (the helical precursor and its oligomers should determine the screw-sense of the helix); and (5) the decrease in optical activity to an asymptotic value at elevated temperatures (i.e., 85°C) is attributed to the probability change of either the conformational dyad sequence (g^+t or g^-t) or the meso placement in the helical precursor's oligomer at higher holding temperature. From these five conclusions it can be inferred that there are competing processes that influence the development of optical activity in polychloral and these processes are slow relative to the time scale of these experiments.

4. Optically active polychloral initiated by tetramethylammonium d(+)-O-acetylmandelate (TMA(+)Ac) and tetramethylammonium ℓ(-)-O-acetylmandelate (TMA(-)Ac). In the section on preliminary results, it was reported that polychloral's optical activity increased as a function of lengthening holding times when TMA(-)Ac was the initiator. It was initially thought that deacetylation of the TMA(-)Ac might have led to the increase in specific rotation of the polymer. However, results from the prior section on polychloral initiated by TMAαM implied that the increase in

specific rotation had origins other than deacetylation. The use of optically active tetramethylammonium O-acetylmandelate initiators was once again pursued since polychloral initiated by it had higher specific rotations ((+)670) in preliminary experiments than polychloral initiated by TMA(-)αM ((+)210).

Further understanding as to why TMAAc initiator should lead to a greater predominance of one helical conformation (i.e., higher optical activity) was desired. This was the major impetus to study the initiation and polymerization of chloral with TMAAc. As an additional benefit, it was anticipated that the general optical activity trends observed with TMAαM initiated polychloral would be corroborated by the TMAAc--another carboxylate initiator.

TMA(+)Ac and TMA(-)Ac initiators were used at 0.5 mole % concentration relative to monomer. Once again, the same careful control of the temperature at which initiator and monomer were mixed along with careful monitoring of holding times, was used when polychloral films were cryotachensically cast.

Using tetramethylammonium d(+)-O-acetylmandelate and chloral mixtures at temperatures of 70.0, 75.0, or 85.0°C, polychloral films were cryotachensically cast every 10, 20, 30, and 50 minutes. The specific rotations of these films were reported in Table 7, Chapter III. These

values are also plotted as specific rotation versus holding time in Figures 13 and 14. For the 70.0°C isotherm in Figure 13, there is a steady increase in the polychloral's specific rotation from (-)790 to (-)1330 as the holding time increased from 10 to 50 minutes. The same type of trend was also observed for the 75.0°C isotherm where the specific rotation increased from (-)1420 to (-)1680 for the same time period. For the 85.0°C isotherm in Figure 14, the maximum specific rotation for TMAAc initiated polychloral was found to be (-)1860 at 20 minutes. However, the optical activity soon fell off on the 85.0°C isotherm to (-)1280 at 50 minutes. This decrease may indicate an approach to an asymptotic value, but there is not sufficient data to draw this conclusion unequivocally.

Optical activity was observed to increase for polychloral initiated by TMA(+)Ac with either increasing time (10→50 minutes) at relatively low temperatures (70.0°C) or increasing temperature (70.0→85.0°C) at a relatively short time (10 minutes). The origin of this optical activity increase is thought to be the same as that proposed for TMA(+)αM initiated polychloral--that there is the slow formation of oligomers (above the ceiling temperature) which determine the screw-sense of a helix. This once again implies that polychloral initiated by TMA(+)Ac is a mixture of left-handed and right-handed helices with the levorotary form being predominant. The decrease in

Fig. 13. The Specific Rotation of Polychloral Initiated by TMA(+)Ac as a Function of Holding Time at 70°C (●) or 75.0°C (⬤).

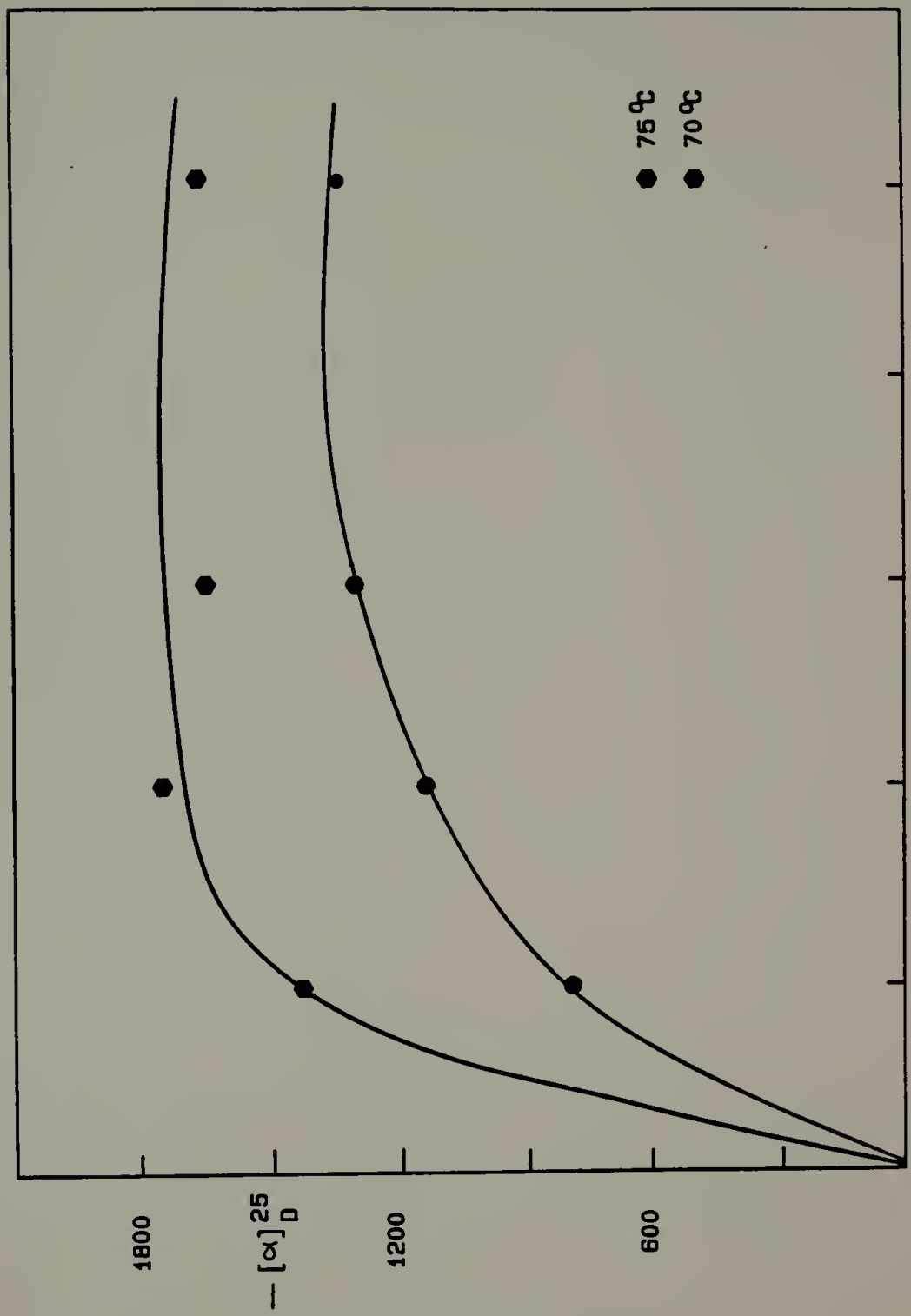
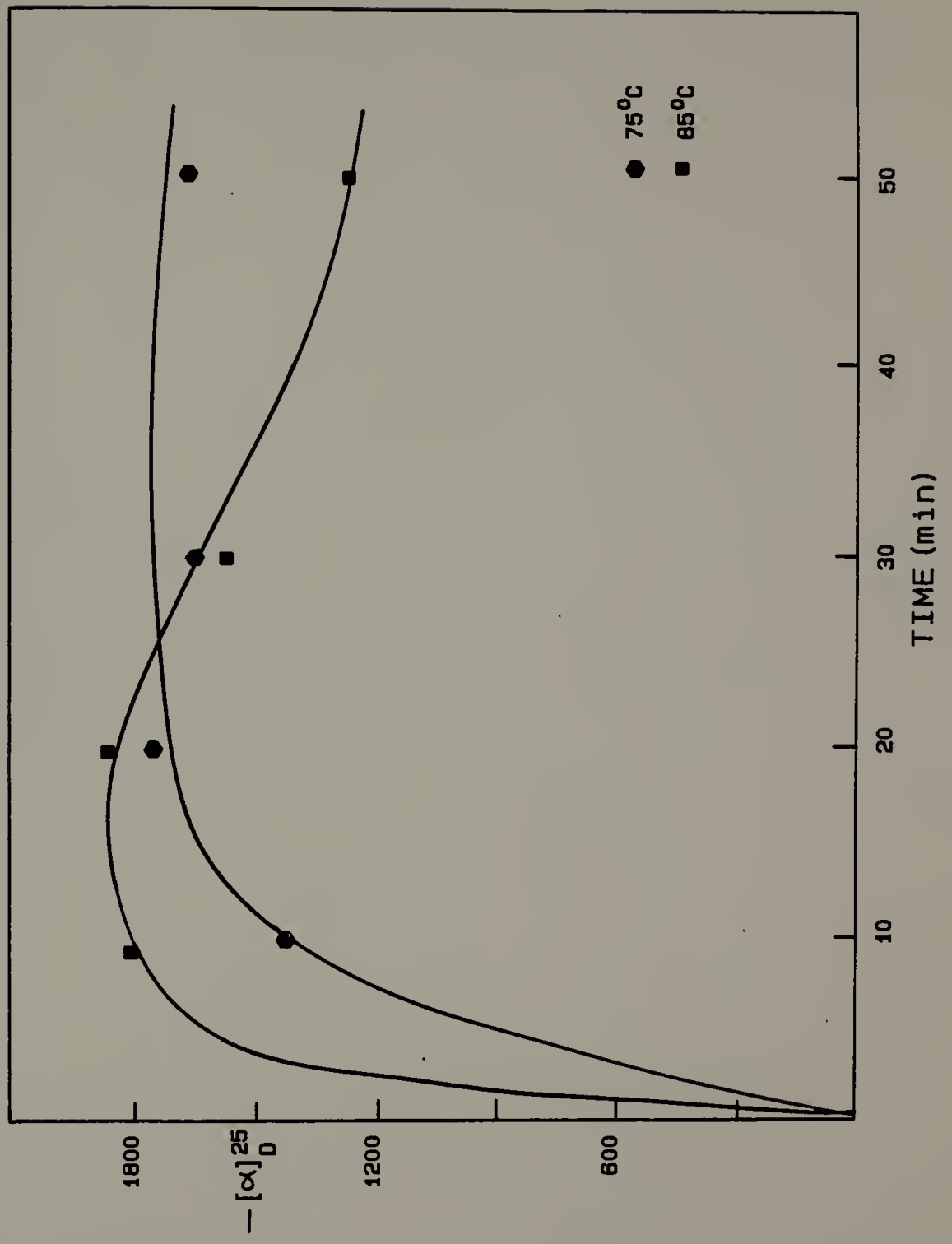

1800
1200
600
$-[\alpha]_D^{25}$
10
20
30
40
50
TIME (min)
75°C
70°C

Fig. 14. The Specific Rotation of Polychloral Initiated by TMA(+)Ac as a Function of Holding Time at 75.0°C (⬢) or 85.0°C (■).


75°C
85°C
TIME (min)
10
20
30
40
50
600
1200
1800
$-[\alpha]_D^{25}$

specific rotation that is observed at relatively high temperature (85.0°C) with increasing time (20→50 minutes) is attributed to the probability of the conformational sequence (g^+t or g^-t) of the helical precursor's oligomer being temperature sensitive or errors in meso placement, as was previously proposed for TMAαM initiated polychloral.

Another similarity found between polychloral initiated by TMA(+)αM and initiated by TMA(+)Ac was that both initiators yielded polymer having the opposite sign of rotation. This result was not surprising since in both initiators the asymmetric centers and the trichloromethyl group have the same basic spatial relationship. Overall, it was reassuring and corroborative that two different asymmetric carboxylate initiators exhibit similar optical activity trends as a function of time and temperature as well as a function of rotation sign.

However, there is one important difference between polychloral initiated by optically active TMAαM and TMAAc. There is a nine-fold difference in the absolute, maximum, specific rotation for polychloral initiated by TMA(-)αM ((+)210) and that of polychloral initiated by TMA(+)Ac ((-)1860). This large difference cannot be attributed to the small difference between the initiators' optical purity (2%). The one significant difference between these two initiators is the chemical group used to block the asymmetric center's hydroxyl group in the mandelic acid

precursor. For TMAαM the blocking group is a methoxy group while for TMAAc it is an acetyl group. There are two major differences between a methoxy and an acetyl group--their sizes and their polarities. Specifically, the acetyl group is both larger and more polar than the methoxy group. These two factors should lead to the acetyl group (versus the methoxy group) interacting much more strongly with the polar trichloromethyl group in the helical precursor and its oligomers. The stronger interaction with the acetyl group should increase the probability of both the conformational sequence of either g^+t or g^-t and meso placement in the helical precursor and its oligomers. This leads to a greater predominance of one of the two helical conformations in the polymer (i.e., more optical activity) than when the initiator has the smaller and less polar methoxy group of TMAαM. The large difference in specific rotation between polychloral initiated by TMAαM and TMAAc emphasizes how important meso placement and conformational sequence probabilities of the initiator and the first repeat units in the polymer are to the induction of molecular asymmetry.

A final observation on polychloral initiated by tetramethylammonium d(+)-O-acetylmandelate is that once again the asymmetric endgroup should make a nominal contribution to the polymer's optical activity. If 100% initiation had occurred and the initiator endgroup retained the same magnitude of rotation, its maximum contribution to

the specific rotation would be 1. However, it was shown in Chapter III of this dissertation that a 1:5 ratio of TMAAc initiator to chloral monomer resulted in a product having a $\overline{DP}_n$ of 1100 instead of a $\overline{DP}_n$ of 5, which would be expected for living anionic. This proves that the assumption of 100% initiation is incorrect and that the contribution of the asymmetric endgroup to the polymer's specific rotation is much less than 1.

To corroborate the high optical activity observed for polychloral initiated by TMA(+)Ac and to also see if the same trends persisted, the other antipode, tetramethylammonium ℓ(-)-O-acetylmandelate (TMA(-)Ac) was used to polymerize chloral. Using TMA(-)Ac as the initiator, polychloral films were cryotachensically cast from 70.0, 75.0, and 85.0°C holding temperatures every 10, 20, 30, and 50 minutes. The specific rotations for these films are reported in Table 8, Chapter III. This data is presented in Figures 15 and 16, with the specific rotation plotted against holding time. As can be seen in these Figures, there is an increase in polychloral's optical activity as a function of increasing holding temperature. These types of trends were previously observed for the other initiator antipode, but with TMA(-)Ac initiated polymer (versus TMA(+)Ac initiated polymer) the specific rotation increase was slower as a function of either time or temperature. This problem can be illustrated by comparing the maximum

Fig. 15. The Specific Rotation of Polychloral Initiated by TMA(-)Ac as a Function of Holding Time at 70.0°C (●) or 75.0°C (⬢).

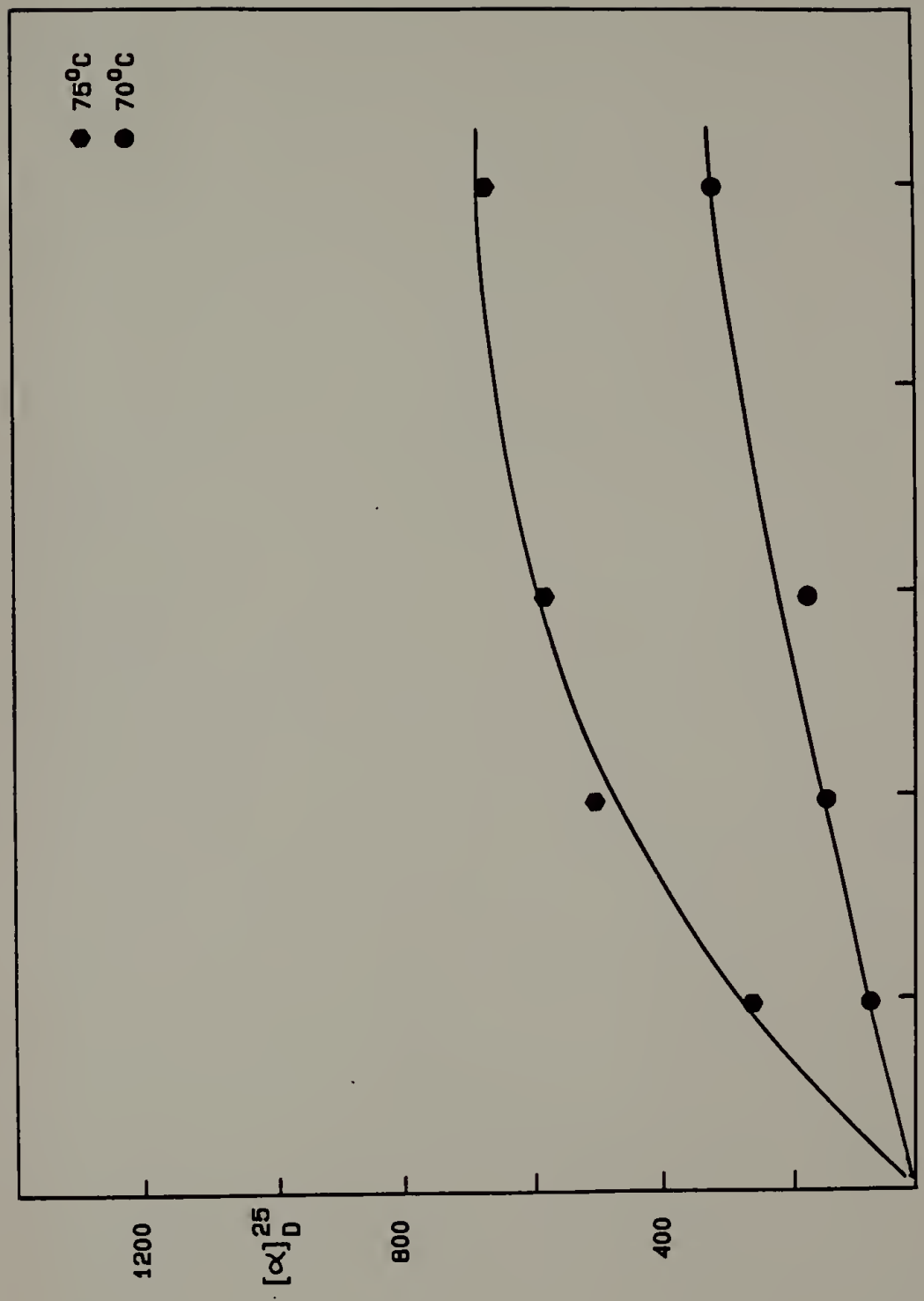
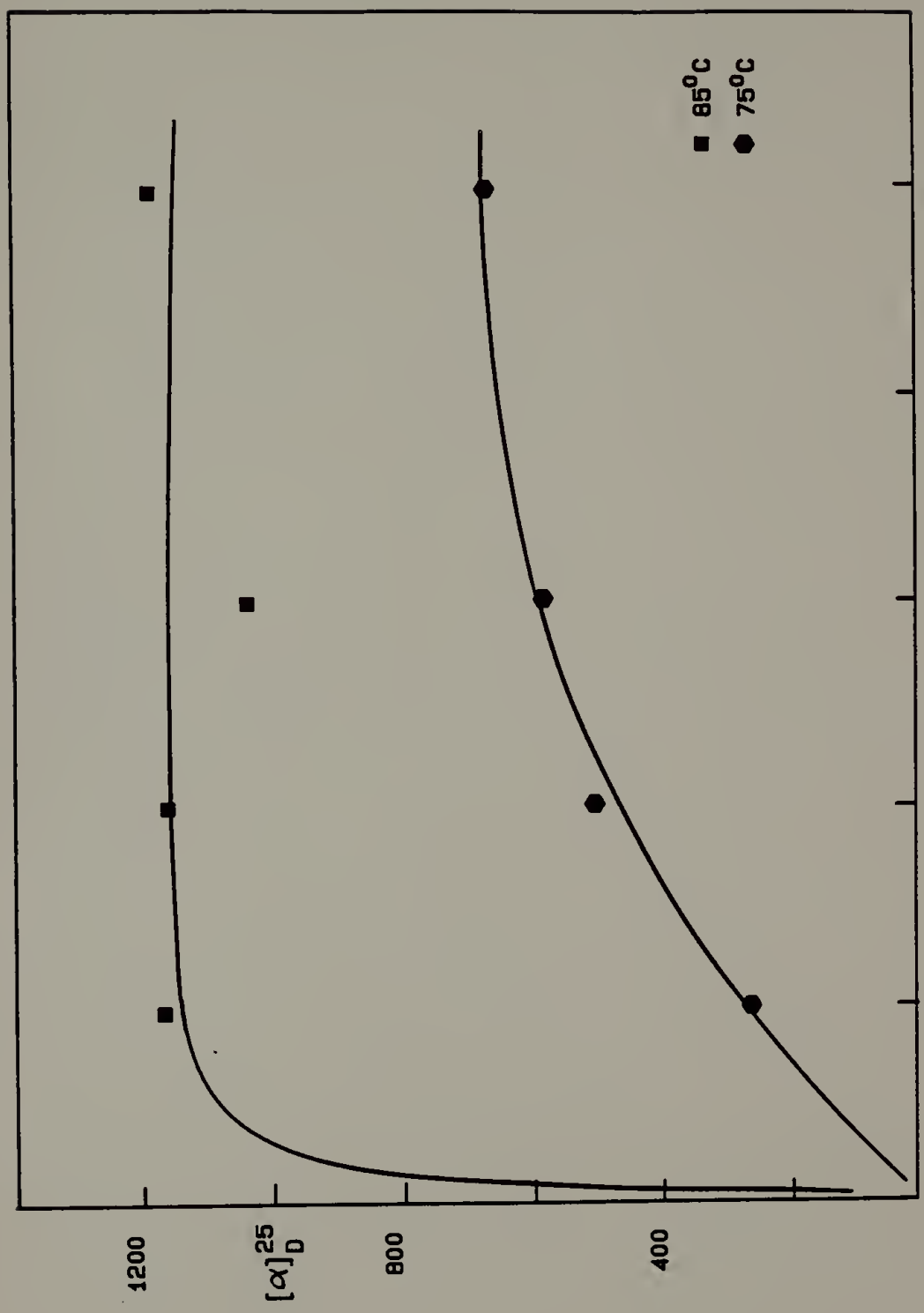

75°C
70°C
1200
800
400
$[\alpha]_D^{25}$
10
20
30
40
50
TIME (min)

Fig. 16. The Specific Rotation of Polychloral Initiated by TMA(-)Ac as a Function of Holding Time at 75.0°C (⬢) or 85.0°C (■).


1200
800
400
$[\alpha]_D^{25}$
10
20
30
40
50
TIME (min)
85°C
75°C

specific rotation of TMA(-)Ac initiated polymer ((+)1180) against TMA(+)Ac initiated polymer ((-)1860). In addition to this, the typical decrease in specific rotation at high temperature, long time was not observed for TMA(-)Ac initiated polychloral. It is strongly suspected that this 'retardation' observed for TMA(-)Ac initiator in the induction of molecular asymmetry is related to the temperature of the film assembly. In the next section, evidence will be presented that shows that a 10 degree differential in the temperature of a film assembly and the thermostatic bath can lead to a 37% difference in polychloral's specific rotation.

In synopsis, many of the conclusions drawn concerning TMAαM initiated polychloral are considered to be equally applicable to TMAAc initiated polychloral. Specifically, that a preferential molecular asymmetry has been induced, endgroup contributions to optical activity are negligible, and the resulting polychloral's optical activity is time/temperature sensitive due principally to a slow oligomerization process and to either varying meso placement or changes in the probability of the conformational sequence $g^{+}t$ or $g^{-}t$ when initiated monomer is held above the ceiling temperature. However, one new conclusion can be drawn from the use of optically active tetramethylammonium O-acetylmandelate initiators--that the size and polarity of groups about an asymmetric center can dramatically change the

distribution between the two polymer conformations of left- and right-handed helices. This was evidenced by the nine-fold increase in specific rotation of polychloral initiated by TMAAc versus TMAαM.

5. Optically active polychloral initiated by lithium methyl d-(+)-hydroxidemandelate (Li(+)MM) and lithium methyl ℓ(-)-hydroxidemandelate (Li(-)MM). In the previous section there were strong indications that by increasing the size and polarity of groups about an asymmetric center in the initiator, it was possible to increase the predominance of one screw-sense in the resulting polychloral (i.e., higher optical activity). If size and polarity lead to increased optical activity, then by placing the asymmetric center closer to the first trichloromethyl group in the polymer should also lead to an even greater predominance of one of the two helical conformations of the polymer. (It is this interaction of the asymmetric center and the trichloro-methyl group that strongly influences the polychloral's optical activity.) With the carboxylate initiators that have been used to date, the asymmetric center was δ to the trichloromethyl group. However, by using the optically active alkoxide initiators of lithium methyl hydroxide-mandelate, the asymmetric center is then γ to the tri-chloromethyl group. This should lead to polychloral with optical activity greater than that obtained with the

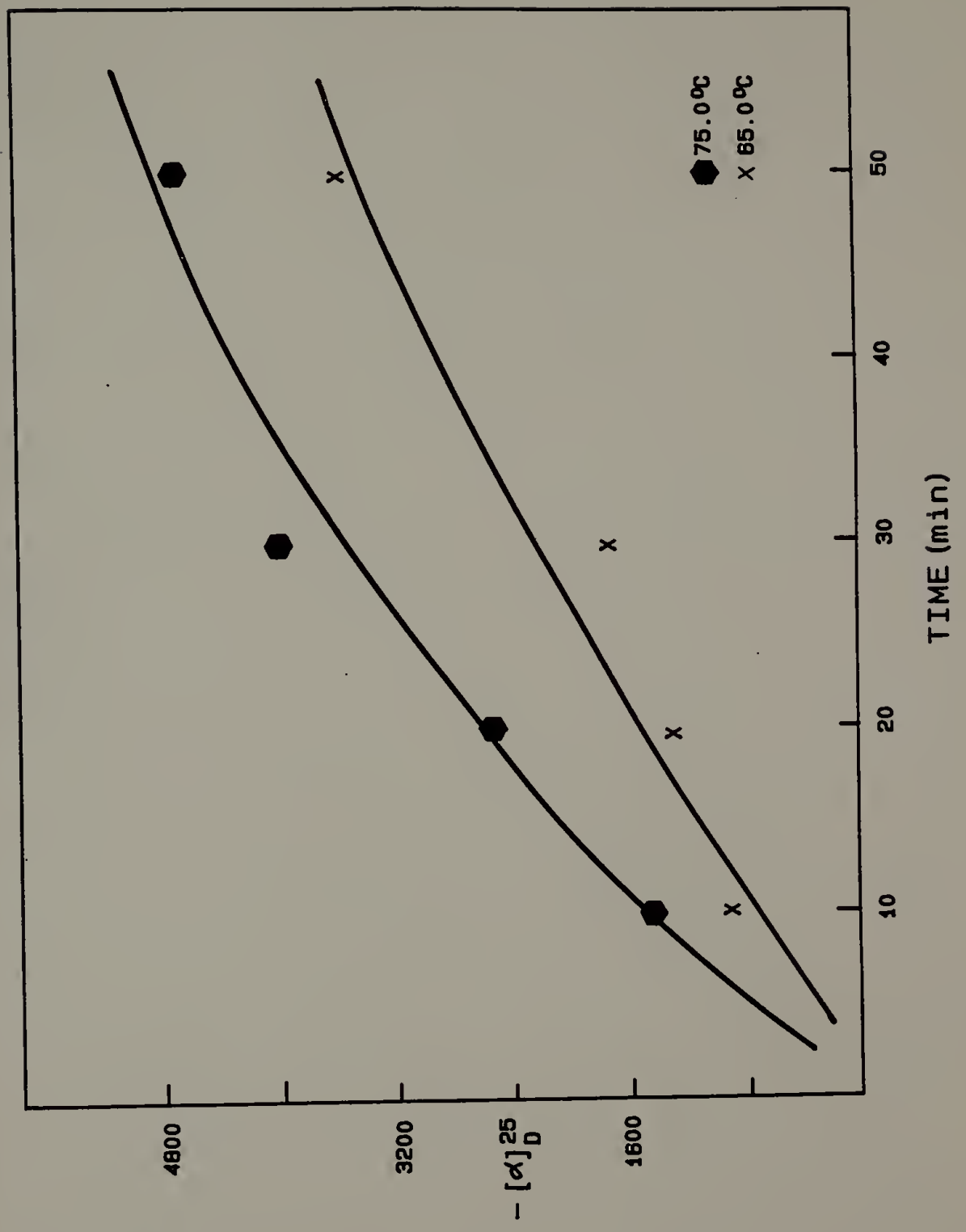
carboxylate initiators.

A prime objective in using optically active LiMM initiators was to see if higher optical activity was possible for polychloral due to the asymmetric center's closer proximity. Another objective was to see if the initiated monomer (LiMM + chloral) exhibited the same sensitivity to temperature and holding time (as judged by the polymer's specific rotation) that was observed when carboxylates were the initiators. If the same specific rotation trends of the carboxylate initiated polychloral are found for polychloral initiated by the more nucleophilic alkoxides, then the propositions of oligomerization and conformational sequence probabilities in conjunction with meso placement will be corroborated further.

Li(+)MM and Li(-)MM initiators were used at 0.5 mole % concentration to polymerize chloral. For these initiators, careful attention was paid to controlling the temperature at which initiator and monomer were mixed and the time at which they were held prior to cryotachensic polymerization.

Using lithium methyl ℓ(-)-hydroxidemandelate initiator at holding temperatures of 65.0 and 75.0°C, polychloral films were cryotachensically cast every 10, 20, 30, and 50 minutes. The specific rotations for these films can be found in Table 12, Chapter III. This data is also presented in Figure 17 as a plot of the specific rotation

Fig. 17. The Specific Rotation of Polychloral Initiated by Li(-)MM as a Function of Holding Time at 65.0°C (X) or 75.0°C (●).


4800
3200
1600
$-[\alpha]_D^{25}$
10
20
30
40
50
TIME (min)
75.0°C
85.0°C

versus holding time. For the 65.0°C isotherm in Figure 17, a steady increase was observed in the specific rotation from (-)900 to (-)3580 as the holding time increased from 10 to 50 minutes. The same general trend was observed in Figure 17 for the 75.0°C isotherm, but the specific rotation increased at a faster rate (from (-)1310 to (-)4670 over the same time period) than observed for the 65.0°C isotherm. These trends of increasing optical activity as a function of increasing holding times or temperature were similar to the results obtained for the carboxylate initiated polychloral at relatively low temperatures. The steady increase in optical activity as a function of increasing time or temperature is once again believed to be due to some slow process of forming oligomers which determine the screw-sense of the helix. Attempts were made to cast polychloral films from 85.0°C monomer, but polymerization could not be reproducibly achieved (much like the type of problem of the lithium cholesteroxide initiator being unstable at higher temperatures). Because of this inability to work at higher temperatures, there was no opportunity to determine if the polychloral's specific rotation decreased at higher temperatures as observed when carboxylate initiators were used.

The maximum specific rotation observed for Li(-)MM initiated polychloral was (-)4670 at a temperature of 75.0°C and a holding time of 50 minutes. This is

approximately a two-fold increase over the maximum specific rotation observed for TMA(+)Ac initiated polychloral ((-)1860). This substantial increase in optical activity supports the concept that by placing the asymmetric center closer to the first repeat unit of the polymer chain, a greater predominance of one helical screw-sense can be obtained.

When polychloral is initiated by Li(-)MM, the rotation sign of both the polymer and initiator are levorotary. This is in contrast to the carboxylate initiated polychloral, where the polymer and initiator have opposite signs of rotation. The fact that these alkoxide initiators and their polymers have the same sign of rotation should not be viewed as peculiar because there is no justification in assuming that all levorotary initiators should yield dextrorotary polymer. It is the spatial relationship of the asymmetric center and the trichloromethyl group in the first repeat unit that leads to a predisposition of the polychloral's screw-sense. Since the asymmetric center of the LiMM initiator and the carboxylate initiators have different spatial relationships with the trichloromethyl group, it is not unreasonable that polychloral initiated by Li(-)MM is levorotary while polychloral initiated by TMA(-)Ac is dextrorotary.

For LiMM initiated polychloral, it was possible to more accurately estimate the contribution of the asymmetric

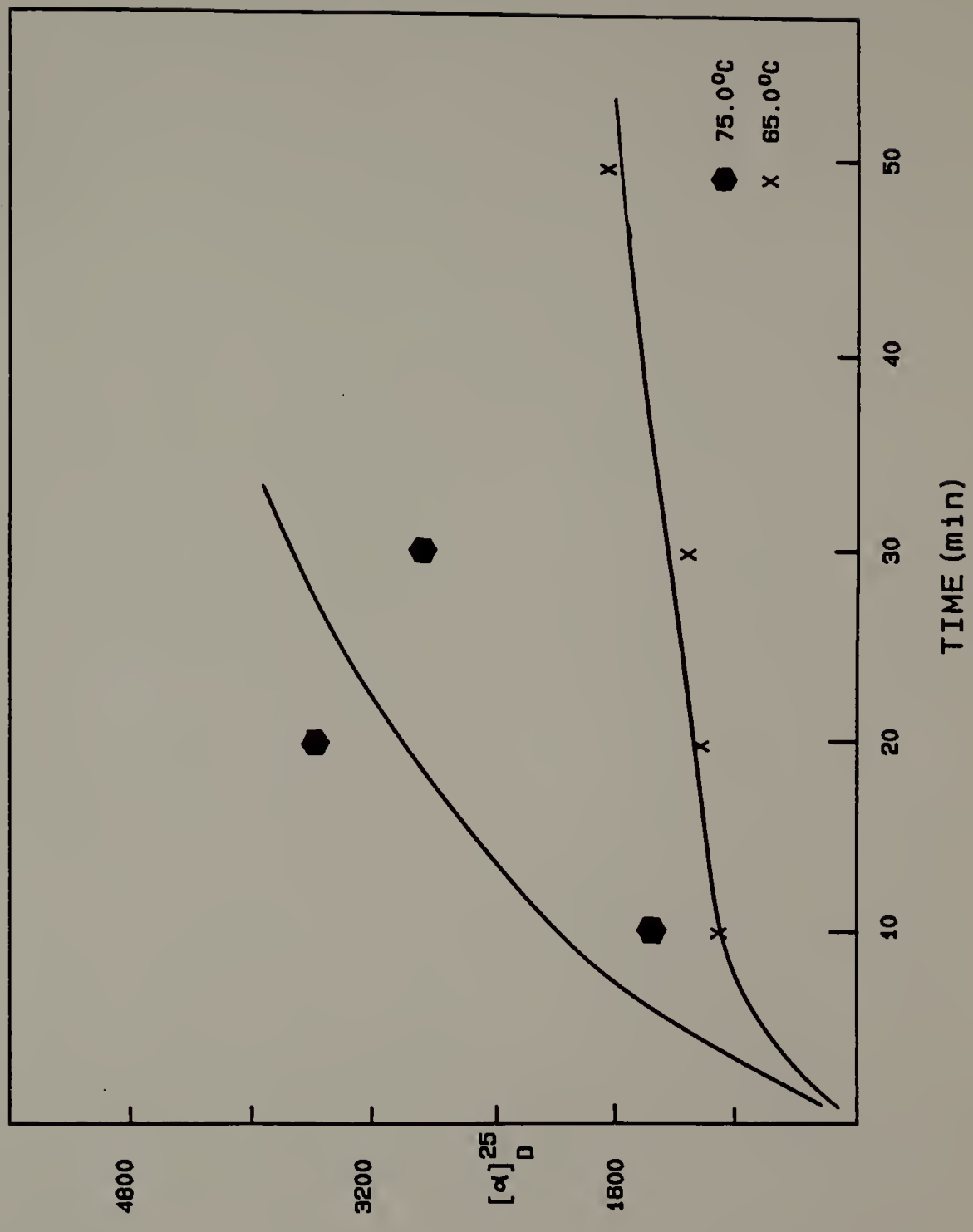
endgroup to the polymer's optical activity than it had been with the carboxylate initiators. This was achieved by preparing a compound that served as a model endgroup. The model compound was methyl ℓ(-)-O-trichloroacetylmandelate which was prepared by reacting trichloroacetyl chloride with methyl ℓ(-)-mandelate. Methyl ℓ(-)-O-trichloroacetylmandelate, $[\alpha]_D^{25}$ = (-)95.4, was regarded as a good model for the polymer endgroup since in the model compound the polar trichloromethyl group is also γ to the asymmetric center like in the polymer.

The specific rotation of methyl ℓ(-)-O-trichloroacetylmandelate indicates that no excessive changes are likely to occur in the specific rotation of the asymmetric initiator when it becomes a polymer endgroup. This result helps to justify some of the assumptions made in estimating the endgroup contribution for TMAαM and TMAAc initiated polychloral. The maximum contribution of the asymmetric Li(-)MM endgroup in polychloral, using the specific rotation of the model endgroup, was shown to be (-)1 in Section H, Chapter III. Once again the endgroup contribution is negligible especially when compared to the magnitude of specific rotation and also to the error arising by performing optical activity measurements in the solid state. It seems safe to say that the optical activity reported for Li(-)MM initiated polychloral is due solely to molecular asymmetry.

To corroborate the results obtained for polychloral initiated by Li(-)MM, the other antipode, Li(+)MM, was used to polymerize chloral to see if the same trends of specific rotations were observed as a function of time and temperature. Using Li(+)MM initiator, polychloral films were cryotachensically cast from temperatures of 65.0 and 75.0°C every 10, 20, 30, and 50 minutes. The specific rotations of these films are reported in Table 11, Chapter III. These specific rotations are plotted against holding time in Figure 18. As can be seen in the Figure, dextrorotary initiator gives rise to dextrorotary polymer--a confirmation that LiMM and its resulting polymer have the same sign of optical rotation. As can also be seen in Figure 18, Li(+)MM initiated polychloral exhibits the same trend of increasing optical activity with either increasing holding time or temperatures as observed for the other antipode. But, the problem that arose with the two TMAAc antipodes exhibiting different rates of molecular asymmetry induction and different maximum optical activities was also observed for LiMM initiated polychloral. The maximum specific rotation for Li(-)MM initiated polychloral was (-)4670, while it was (+)3600 for Li(+)MM initiated polychloral.

This difference in specific rotation can be attributed to the difficulties in precisely controlling the temperature of the film assemblies. This sensitivity of

Fig. 18. The Specific Rotation of Polychloral Initiated by Li(+)MM as a Function of Holding Time at 65.0°C (X) or 75.0°C (●).


4800
3200
1800
$[\alpha]_D^{25}$
10
20
30
40
50
TIME (min)
75.0°C
65.0°C

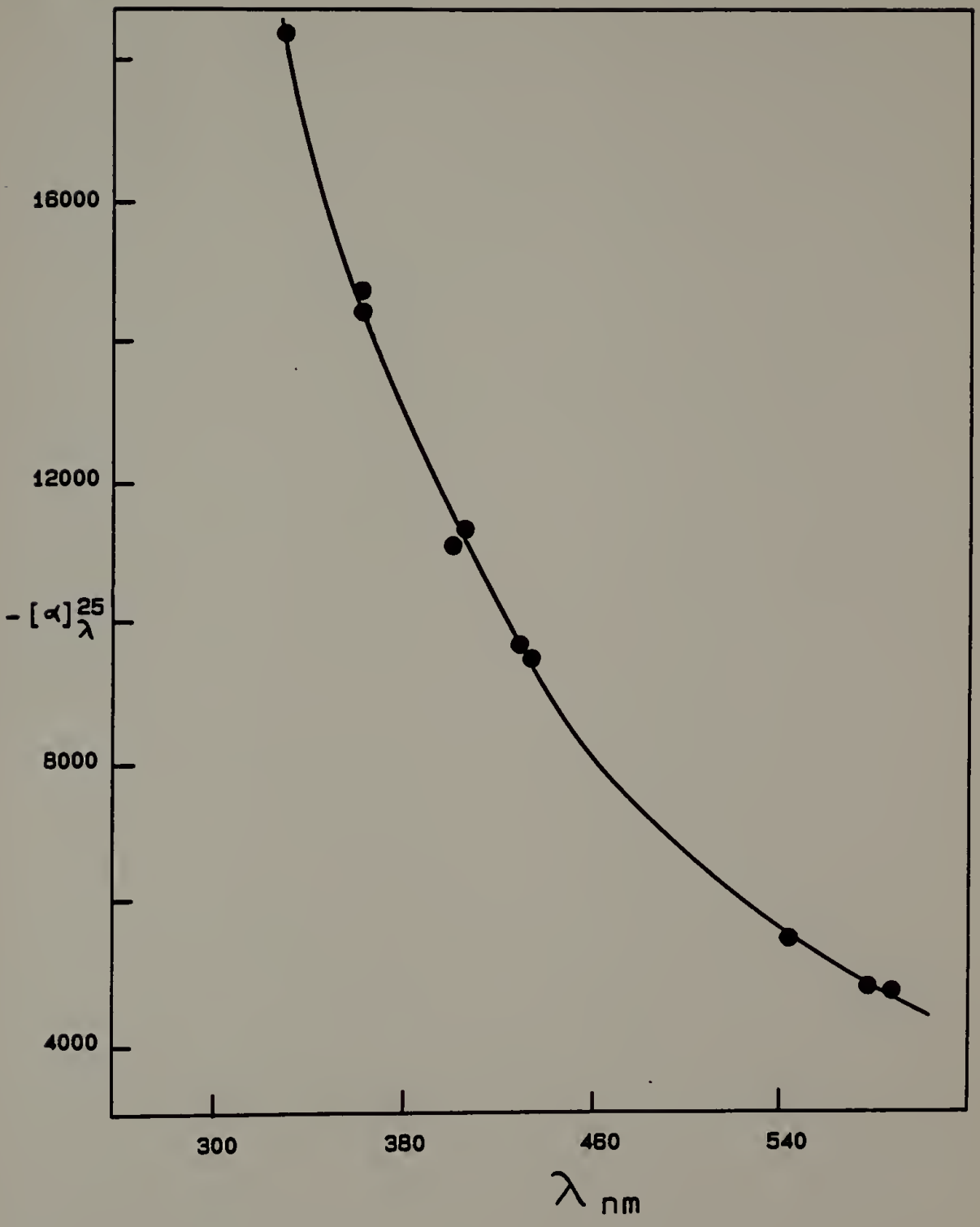
the polychloral's optical activity to the film assembly's temperature was illustrated by the following simple experiment: chloral was initiated by Li(-)MM and held at 65.0°C with films cryotachensically cast at 10 minutes. Using a syringe at 65°C, the initiated monomer was injected into two film assemblies, one at ∿65°C, the other at ∿75°C. The whole process of removing the film assemblies from the ovens, injecting the initiated monomer, and plunging the film assemblies into ice water takes typically 1.5 minutes. The specific rotation of polychloral prepared from the 65°C film assembly was (-)900 while from the 75°C film assembly its specific rotation was (-)1230. This 37% difference can be attributed to only one thing, the temperature of the film assembly. Unfortunately, it now seems inevitable that there will be variations in polychloral's optical activity due in part to the difficulty in regulating the film assembly's temperature and slight variations in casting times. With the requirements for cryotachensic casting, it should prove difficult to control film assembly temperatures and casting times more precisely than performed to date.

With polychloral initiated by optically active lithium methyl hydroxidemandelates, polychloral with the highest optical activity to date was obtained. With such a polymer, the specific rotation of polychloral was studied as a function of wavelength. By studying any compound's

specific rotation as a function of wavelength (giving rise to an optical rotary dispersion curve--ORD), additional information can sometimes be obtained about the nature of the asymmetry leading to optical activity. Using the spectral lines available from a mercury lamp, the ORD curve of polychloral initiated by Li(-)MM at 75.0°C and 50 minutes ($[\alpha]_D$ = (-)4670, highest optical activity) was obtained. The specific rotations as a function of wavelength are listed in Table 13, Chapter III. This data with specific rotation plotted against wavelength is shown in Figure 19. The measurement of specific rotations at wavelengths shorter than 334 nm was impossible due to the light sorption by diphenyl ether. (The function of the diphenyl ether was to make the films transparent.)

As shown in Figure 19, there is a monotonic increase in the specific rotation from (-)4710 to (-)18,400 as the wavelength of measurement decreased from 589 nm to 334.2 nm. This increasing specific rotation with decreasing wavelength is a common phenomenon and is predicted by theory. When the ORD curve is monotonic, the curve is said to be plain since there are no inflections. A plain ORD curve usually implies that ORD measurements are being made far from where an optically active transition is located. If the wavelengths of the optical activity measurements are far from the electronic transition, the specific rotation and its wavelength of measurement can be incorporated into

Fig. 19. Optical Rotary Dispersion Curve of Polychloral Initiated by Li(-)MM with T = 75.0°C and t = 50 minutes.

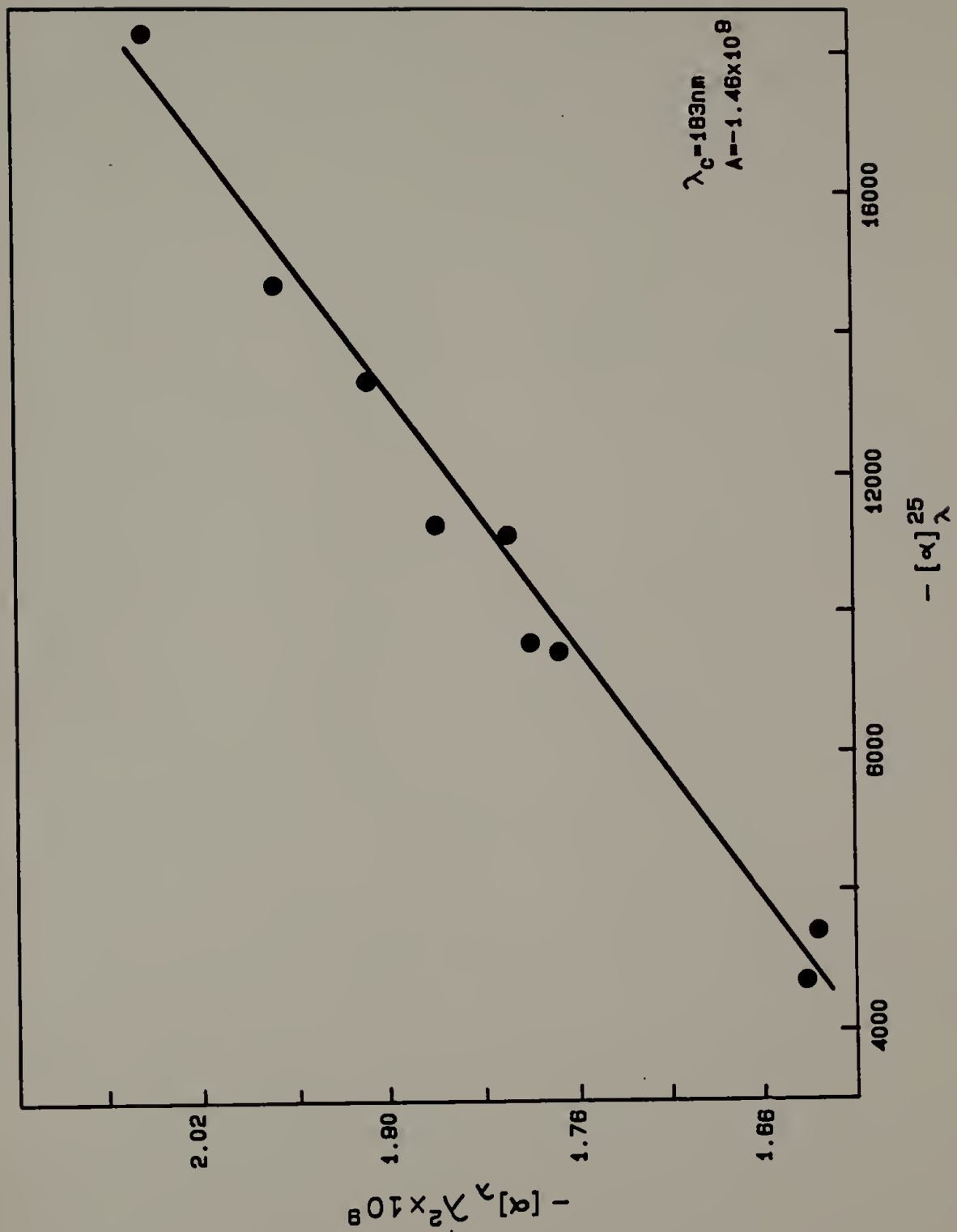

16000
12000
$-[\alpha]_{\lambda}^{25}$
8000
4000
300
380
460
540
λ nm

a linear relationship. The equation most often used for this is the Yang-Doty Equation (Equation 5, Chapter I), which often assumes that there is only one optically active transition. The result of using the ORD data in Table 13 to fit the Yang-Doty Equation is shown in Figure 20. As shown in this Figure, the ORD data fits a straight line having a correlation function of 0.99. The value λ_c, obtained from the line's slope, is 183 nm. The plot's linearity confirms that the optical activity measurements are being made far from the optically active transition. As a first order approximation, one might be able to say that there is only one major optically active transition and it is located at 183 nm, but the only way to confirm this is to perform ORD measurements at shorter wavelengths which is presently impossible.

It should be mentioned while discussing ORD and phenomenological equations that there is no value in trying to fit polychloral's ORD data to the Moffitt Equation (Equation 6, Chapter I), since the Moffitt derivation was made for polypeptides. It assumed that there are two specific electronic transitions associated with polypeptides. These assumptions are inappropriate for polychloral even though it is helical.

In synopsis, the use of optically active lithium methyl hydroxidemandelate initiators yields optically active polychloral having a specific rotation at least twice

Fig. 20. Yang-Doty Plot of ORD Data for Polychloral Initiated by Li(-)MM with T = 75.0°C and t = 50 minutes.


λ_c=183nm
A=-1.46x10^8
$-[\alpha]_\lambda^{25}$
$-[\alpha]_\lambda\lambda^2\times10^8$
2.02
1.80
1.78
1.68
4000
8000
12000
16000

that of polychloral initiated by optically active carboxylates. This doubling is attributed to placing the asymmetric center closer to the trichloromethyl group of chloral. It has also been shown that polychloral ORD data fits the Yang-Doty Equation. Conclusions drawn with the carboxylate initiated polychloral that are applicable to the LiMM initiated polymer include: optical activity results from the induction of molecular asymmetry, the induction process is time/temperature sensitive, the increasing specific rotation with either increasing time or temperature is due to an oligomerization process, and finally, the asymmetric endgroup contributions are negligible.

D. Summary and Conclusions

The synthesis of optically active polychloral where the optical activity arises from molecular asymmetry has been clearly demonstrated in the work described in this dissertation. It has been shown that this preferential molecular asymmetry can be induced by carboxylate or alkoxide initiators that contain asymmetric centers. Using these two types of initiators, polychloral samples with a range of optical activities were prepared. This author feels that a 100% optically pure sample (all one screw-sense) has not been prepared, but the specific rotation at the sodium D-line of (-)4670 is probably one of the largest

specific rotations reported for any polymer.

In this dissertation it has also been shown that the process of inducing a preferential molecular asymmetry in polychloral was very sensitive to the time and temperature that the initiated monomer is exposed to prior to cryotachensic polymerization. The time/temperature influence on the resulting polychloral's optical activity indicates that there are at least two processes involved in the induction of molecular asymmetry. The process that leads to an increase in polychloral's optical activity when time or temperature is increased is attributed to the formation of oligomers that determine the screw-sense of a helix. The other process that is involved in the decrease of polychloral's optical activity at higher temperatures with increasing time is attributed primarily to the decreasing probability of either the preferred conformational sequence (g^+t or g^-t) or possibly the meso placement in the helical precursor and its oligomer prior to cryotachensic polymerization. But, it is possible for processes such as racemization, Hofmann degradation products, and chain transfers to play a role in the decreases of optical activity.

Another conclusion drawn from the work in this dissertation was that the size and polarity of groups about the asymmetric center in the initiator greatly influences the amount of molecular asymmetry that is induced in the polymer. It was demonstrated, using TMAAc initiator versus

TMAαM initiator, that by increasing both the size and the polarity of a group about the asymmetric center that it was possible to induce higher values of optical activity in the polymer due to the interaction of the asymmetric center and the trichloromethyl group. It is this interaction that leads to a predominance of one screw-sense in the polymer.

Another observation made during this work was that by placing the initiator's asymmetric center closer to the first trichloromethyl group (LiMM versus TMAAc), it was possible to enhance the value of the polychloral's optical activity. This enhancement is thought to be due to the closer proximity of the asymmetric center in the initiator to the trichloromethyl group making the existence of one helical precursor (which has both conformational and configurational aspects) more probable and therefore more polymer of one helical screw-sense (i.e., more optical activity).

Finally, research done in cooperation with Osaka University indicates that optically active polychloral may have use as a chromatographic support to perform resolution of racemic mixtures as indicated by the partial resolution of poly(α-methylbenzyl methacrylate).

E. Future Work

There is a need to try to perform conformational energy calculations for the polychloral backbone and for

the conformers of the initiator and one chloral unit. There is also a need to try to determine the probabilities of the initiator/monomer conformers as a function of temperature. By having the conformational energies and probabilities, it should be possible to predict polychloral's sign of rotation, to correlate how the size and polarity of groups about the asymmetric center influences the polymer's optical activity, and finally to correlate how the proximity of the asymmetric center to the trichloromethyl group affects the polymer's optical activity. The ability to calculate conformational energies and probabilities should make it possible to design an asymmetric initiator that maximizes polymer optical activity.

A second area which should be the subject of future work is to pursue the study of optically active polychloral as a chromatographic support to perform resolution. The results presented in this dissertation are encouraging and it should be possible to obtain resolution greater than 17%.

A third area of future study, which should provide further insight into the induction of optical activity by molecular asymmetry, would involve the synthesis and polymerization of an asymmetric haloacetaldehyde--specifically bromochlorofluoroacetaldehyde or bromochloroacetaldehyde. The synthesis of these two compounds were started as part of the work for this dissertation.

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