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Optically active polytrichloroacetaldehyde based on macromolecular asymmetry/

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OPTICALLY ACTIVE POLYTRICHLOROACETALDEHYDE

BASED ON MACROMOLECULAR ASYMMETRY

A Thesis Presented

By

Gary D. Jaycox

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DEDICATION

To my parents, Delmar and Katherine Jaycox,

for their love, guidance, and support

over the past twenty five years.

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I would like to take this opportunity to thank my entire family for the love and support extended to me during my stay in Amherst.

At this time, too, I would like to offer thanks to my research advisor and friend, Professor Otto Vogl, for his patience, understanding, and encouragement. The helpful comments of Professor C. P. Lillya were also greatly appreciated.

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ABSTRACT

Optically Active Polytrichloroacetaldehyde

Based on Macromolecular Asymmetry

(September 1984)

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Trichloroacetaldehyde (chloral) was polymerized with asymmetric secondary alkoxide initiators, affording an optically active polymer in which the observed optical rotation arose from macromolecular asymmetry, i.e. from the predominance of one helical screw sense. Optical activity based on macromolecular asymmetry requires a helical polymer with a high rotational energy barrier along its backbone and the use of asymmetric initiating species which induce the formation of one helical screw over the other.

Optically active polychloral films were cast by cryotachensic polymerization of initiated monomer solutions held isothermally at elevated temperatures for varying amounts of time. Typically, optical rotation values were noted to decrease with increases in holding time or holding temperature. Specific rotations approaching 4,500° at the sodium D-line were obtained, representing some of the highest such values to be reported for any polymer.

Model endgroup studies confirmed that the presence of asymmetric initiator endgroups contributed little to the overall optical rotations exhibited by polychloral.

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CHAPTER I

INTRODUCTION

This thesis describes the synthesis of optically active polytrichloroacetaldehyde (polychloral) from asymmetric, secondary alkoxide initiators. The present three-part chapter will serve to review a number of concepts on which this study is based.

The first section will examine the chiroptical phenomenon.

The second section will survey a number of conformationally asymmetric, optically active macromolecules.

A final section will be devoted to the mechanisms governing trichloroacetaldehyde (chloral) polymerization, to the properties of the polymer, and to the techniques for the measurement of its optical activity in the solid state.

Optical Activity

Asymmetric molecules devoid of a center of inversion, a symmetry plane, and an alternating rotation-reflection axis have a unique property in their ability to rotate transmitted, plane polarized light. Such compounds are said to possess optical rotatory power, or more simply, are optically active. Optical rotation, α, is a function of both the number and spatial arrangement of atoms encountered by the plane polarized wave.

According to the classical theory of Maxwell, electromagnetic radiation travelling through space has associated with it an electric field, E, and a perpendicular magnetic field, H, which vibrate at right angles to the direction of propagation. For a monochromatic, plane polarized wave, E will oscillate sinusoidally in a single direction and is described by a vector which can be decomposed into left and right circularly polarized components, E_L and E_R respectively.

The phenomenon of optical activity arises from the interaction of a monochromatic, plane polarized wave with an asymmetric medium, resulting in the unequal retardation of E_L and E_R such that the magnitude of one component no longer balances the other. If the incident wave is not absorbed, this behavior can be attributed to a difference in the refractive indices possessed by the medium for the two components of E, ultimately giving rise to a polarized wave which resides in a new plane rotated on angle α from the plane of incidence. This concept is quantified in Fresnel's equation below:

$$\alpha = \frac{\pi}{\lambda}(\eta_L - \eta_R) \qquad (1)$$

where α, either positive or negative, is the observed optical rotation of the plane polarized wave expressed in degrees, λ the wavelength of the wave, and n_L, n_R the refractive indices of the asymmetric medium for E_L and E_R, respectively.

The required conditions for molecular asymmetry can be satisfied either through a molecule's primary configurational structure, e.g. a

chiral carbon atom, or through its secondary conformational structure, e.g. a helical macromolecule. Whether configurationally or conformationally asymmetric, all optically active molecules exist as a pair of nonsuperimposable, mirror image stereoisomers. Each isomer, or enantiomer, differs from the other in its behavior toward an asymmetric environment and in its opposite sign of rotation. In all other respects, the enantiomeric pair share similar physical properties. It should be noted that an equimolar mixture of any enantiomeric pair, i.e. a racemic mixture, will be optically inactive since half of its molecules generate a $+\alpha$ (dextrorotatory rotation) while the other half generate a $-\alpha$ (levorotatory rotation) of the same magnitude. The reader is cautioned to differentiate between optical inactivity arising from a racemic mixture of enantiomers and that which is the direct result of the interaction of plane polarized light with symmetrical molecules.

The optical activity of a substance observed at a fixed temperature, T, and fixed wavelength, λ, can be conveniently expressed as specific rotation, $[\alpha]^T_\lambda$, a term normalized to account for the number of active species encountered by the polarized wave. Specific rotation is equated to α below:

$$[\alpha]^T_\lambda = \frac{\alpha}{l\ c} \tag{2}$$

where l is the optical path length expressed in decimeters and c, the concentration of active species expressed as grams of solute per

milliliter of solution. For measurements in the solid or liquid state, (2) can be modified to give:

$$[\alpha]^{T}_{\lambda} = \frac{\alpha}{l\ \rho} \tag{3}$$

where ρ is the density of the substance in grams per cubic centimeter. Alternately, the activity of a medium can be reported as molecular rotation, $[M]^{T}_{\lambda}$, a term which includes M, the molecular weight of the active species or the repeat unit of an optically active macromolecule and allows for the comparison of optical rotation on a molar basis:

$$[M]^{T}_{\lambda} = \frac{[\alpha]^{T}_{\lambda}\ M}{100} \tag{4}$$

Although early investigators were quick to note the marked dependency of rotation on wavelength, it was not until much later that activity measurements were studied over a wide spectral range. The variation in optical activity with wavelength is termed optical rotatory dispersion (ORD). The type of information gained from ORD analyses is dependent upon both the nature of the active compound and the spectral region investigated.

If ORD measurements are conducted within a region having one or more optically active transitions, i.e. absorptions, a plot of specific rotation versus wavelength will give rise to an anomalous ORD curve complete with extrema, i.e. peaks and troughs. An ORD curve having a peak as the first extremum is said to display a positive Cotton effect while a curve exhibiting a trough as a first extremum is

said to display a negative Cotton effect. The particular wavelength where an ORD curve inverts its sign has been found to correspond to the approximate wavelength of the optically active transition. Additional information concerning the nature of molecular asymmetry can be had from inspection of the curve's shape, width, and amplitude.

ORD measurements removed from optically active transition regions give rise to plain or normal curves which are completely free of any inflections or extrema. Such curves are characterized by a monotonic increase in the magnitude of rotation at shorter wavelengths. Drude (1) showed that these data could be mathematically fit into a simplified expression, assuming the presence of only one dominant transition, such that:

$$[\alpha]_\lambda = A/(\lambda^2 - \lambda^2_c) \qquad (5)$$

where $[\alpha]_\lambda$ is the specific rotation observed at wavelength λ, λc the wavelength of the dominant optical transition, and A a constant specific to the system under investigation. For most optically active molecules $\lambda >> \lambda_c$, and the single term Drude equation shown above can be further simplified leading to the approximation:

$$[\alpha]_\lambda \simeq A/\lambda^2 \qquad (6)$$

which clearly shows the inverse relationship between specific rotation and wavelength. Further manipulation by Yang and Doty (2) led to the expression:

$$[\alpha]_\lambda \lambda^2 = [\alpha]_\lambda \lambda^2_c + A \qquad (7)$$

which allows for the determination of the dispersion constant, i.e. wavelength of the dominant transition, λ_c, and the rotatory constant, A, by plotting $[\alpha]_\lambda \lambda^2$ against $[\alpha]_\lambda$. The dispersion constant has found limited use in providing information on the higher ordered structures of some native macromolecules (3).

It should be noted that both plain and anomalous ORD curves are uniquely characteristic of the optically active species under investigation. Over the past several decades, ORD analysis has proven to be a powerful analytical technique for the elucidation of complex molecular structure and has figured prominently in the study of proteins, steroids, and other naturally occurring molecules as well as in the characterization of a host of synthetic compounds.

For a more extensive review of the phenomenon of optical activity, or for a description of other chiroptical techniques not mentioned above, the reader is advised to consult any number of excellent reviews devoted to this subject (4,5,6,7).

Optically Active Macromolecules

Optically active macromolecules can be conveniently classified according to the nature of the asymmetry which they possess. Three major categories are: (1) those possessing configurational asymmetry, i.e. main chain or pendent side chain chiral centers, (2) those having both configurational asymmetry described above and conformational

asymmetry, e.g. helicity inherent in their polymer backbone, and (3) those possessing only conformational asymmetry.

As this thesis will stress the relationship between conformational asymmetry (also termed macromolecular asymmetry) and optical activity, only (2) and (3) are reviewed here. The reader should note that this section is not intended to review all macromolecules known to fit within these two categories. Instead, it is hoped that the information presented below will provide a suitable background against which further concepts can be developed. A number of extensive reviews on optically active polymers are presently available (8, 9, 10, 11).

Optically active macromolecules based on a combination of configurational and conformational asymmetry

Macromolecules within this category derive their optical activity from the presence of chiral centers within or alongside the polymer backbone (configurational asymmetry) and from the existence of a helical conformation in which one helical screw exists exclusively of, or preferentially to, the other (conformational or macromolecular asymmetry). The conformational asymmetry exhibited by these macromolecules is usually a direct result of their configurational asymmetry, i.e. one helical screw sense is energetically favored by the presence of chiral centers which reside within the macromolecule. A number of examples follow.

Proteins. Probably the most extensively studied class of optically active macromolecules are the proteins and their synthetic

analogues, the polyamino acids. Their ubiquitous role in the life processes of all living organisms has made them prime candidates for investigation. Generally, proteins are linear macromolecules of varying molecular weight which yield L-amino acids upon hydrolysis. Many occupy complex three dimensional forms, their geometry highly specific to recognized function.

The structural complexity of proteins is best described on several different levels. Primary structure refers to the sequence of L-amino acids joined covalently along the polypeptide backbone. Secondary and tertiary structures describe the ordered helical twisting and folding of the polymer chain. Optical activity arises both from the presence of the asymmetric L-amino acid moieties and from the conformational asymmetry which they impart to portions of the protein backbone.

The precise nature of higher ordered protein structure has been the subject of intense investigation over the past several decades. The α-helix, a right handed helical coil with 3.6 to 3.7 residues per turn, is one such form recognized to be an integral part of many proteins (12). Other conformational arrangements of the polypeptide backbone have also been found (13). It is now generally realized that these ordered structures are further stabilized by the presence of hydrogen bonds, hydrophobic-hydrophillic interactions, and ionic attractions between charged groups along the chain. These secondary bonding forces allow the protein to maintain its conformational shape in aqueous environments. Only when subjected to strong acids or alkali, detergents, or high temperatures does the protein unfold, i.e.

denature. Denaturation results in a drastic alteration of biological activity and is accompanied by changes in optical activity which arise from the loss of helical structure.

Attempts to determine the overall helical content of proteins by ORD analyses were undertaken by a number of investigators. It was recognized early that the single term Drude equation was inappropriate for analysis of protein molecules. Moffitt and Yang (14) developed the following relationship which resembles a two term Drude equation (assumes two electronic transitions in the molecule):

$$[M]_\lambda = a_o \lambda_o^2/(\lambda^2-\lambda_o^2) + b_o \lambda_o^4/(\lambda^2-\lambda_o^2)^2 \qquad (8)$$

where a_o, b_o, and λ_o are adjustable parameters. The equation lends itself to graphical solution when $1/(\lambda^2 - \lambda_o^2)$ is plotted against $[M]_\lambda(\lambda^2 - \lambda_o^2)$ and the proper λ_o selected to yield a straight line. For many proteins, a suitable λ_o was found to lie near 210 nm (4). The variable parameter a_o, determined from the intercept, was found to reflect the nature of the protein side chains and type of solvent employed. The parameter b_o, which can be obtained from the line's slope, was correlated to helical content.

Although the Moffitt and Yang equation was used extensively for the analysis of many proteins, these analyses were later found to be over-simplified as they failed to consider a number of important factors which contribute to protein structure. Moreover, the equation assumes that only two electronic transitions are present within the protein molecule, an assumption which is valid only under favorable

circumstances (15). More recently, a number of empirical approaches have been proposed for the determination of helical content (16, 17). These include linear interpolation based on ORD measurements of helically and randomly coiled polyamino acid standards.

All of these analyses, whether theoretically or empirically based, have been developed specifically for use with proteins and polyamino acids and are extremely useful when their limitations are considered. Attempts to extend this treatment to helical polymers differing structurally and chemically from proteins should not be made, however.

Stereoregular, synthetic polymers. A large number of stereoregular polymers have been prepared in which there exists both configurational and conformational asymmetry. These include poly-α-olefins (18, 19), polyaldehydes (20), polyvinylethers (21), polyalkylvinylketones (22), polyacrylates (23), and others (24, 25). The optically active poly-α-olefins and polyaldehydes will be briefly discussed below and should serve as an introduction to all polymers found within this category.

Isotactic polymers prepared from chiral α-olefins ($R(R')C^*(H)-(CH_2)_n-CH_2-CH=CH_2$) have been reported by several groups (18, 19). Recognizing that a helical screw is the preferred conformation for isotactic polymers in the solid state, these investigators hoped that the use of chiral α-olefins would result in the preferential formation of one screw sense over the other and that optical activity would arise from both the presence of chiral centers

located in the polymer side chains and from macromolecular asymmetry, i.e. helicity, imparted by them to portions of the polymer backbone.

Studies conducted by Pino and his school (18) indicated that the proximity of the chiral centers to the polymer backbone greatly influenced the formation of helical segments in a preferred direction. Optical activity based on this macromolecular asymmetry rapidly decreased in magnitude as the chiral center was removed from the backbone. Other studies suggested that the observed optical rotation was temperature dependent, that as temperature was increased, the probabilities for other conformations, e.g. opposite helical screw or random coil, also increased, leading to a drop in optical activity (18, 19). Finally, Pino found that decreasing the stereoregularity of the poly-α-olefin, i.e. decreasing isotacticity, lowered the observed optical activity by shortening the helical sequences which exist in the polymer (18, 19).

Optically active polyaldehydes were later investigated by Abe and Goodman (20). The polymerization of S-(+)-2-methylbutanal, R-(+)-Citronellal, and S-(+)-6-methoxy-4-methylhexanal was effected by a number of organometallic initiators. Generally, an enhancement in the observed optical rotation was seen relative to low molecular weight model compounds. Furthermore, the investigators found that the separation between the asymmetric side group and the polymer backbone affected the magnitude of the optical activity enhancement, confirming Pino's earlier observations. The authors attributed the optical activity of their polyaldehydes to the presence of side chain chiral centers and to short range helical order in the polymer's main chain.

Optically active macromolecules based on conformational asymmetry

Macromolecules possessing only conformational asymmetry differ fundamentally from those discussed above. Optical activity arises solely from the predominance of one helical screw sense, i.e. from macromolecular asymmetry.

The absence of main chain or side chain chiral centers requires that left and right helical screws be energetically equivalent, and therefore, equally probable during the course of polymerization with symmetrical initiators. For statistically large numbers of polymer chains, such processes must inevitably yield a racemic mixture of left and right helices, resulting in an optically inactive polymer sample, e.g. isotactic polypropylene in the solid state.

A predominance of one helical screw sense required for optically active macromolecules of this type can be obtained in one of two ways: (1) through the complete or partial resolution of the helical screw pair, usually with the aid of an optically active substrate, or (2) through the use of asymmetric initiator species which preferentially induce the formation of one helical screw sense over the other. While the former method has enjoyed some success, e.g. synthesis of the optically active helical oligomer hexahelicene (26), the use of asymmetric initiators or counterions has received more attention.

Presently, only a limited number of optically active macromolecules have been prepared in which all activity is the result of macromolecular asymmetry. These include optically active polytrichloroacetaldehyde, optically active poly(triphenylmethyl

methacrylate), and optically active polyisocyanides. Each will be discussed below.

Polytrichloroacetaldehyde (Polychloral). Some of the earliest attempts to synthesize an optically active polymer based entirely on macromolecular asymmetry were undertaken by Vogl in 1963 (27) and by Hatada and Vogl in 1973 (28). From X-ray analyses (29), these investigators realized that polychloral was isotactic and helical. It was hoped that the steric interaction between an asymmetric initiating species and the first monomer units to undergo addition would be sufficiently great to allow for the induction of only one helical screw sense and that the presence of bulky trichloromethyl side groups along the polymer chain would effectively act to stabilize the helical screws. Using the asymmetric initiator tetramethylammonium-(+)-ketopinate or the optically active (+)-methyl-n-propylbenzylphenyl phosphonium counterion, Corley and Vogl successfully obtained optically active polychloral films having specific rotations at the sodium D-line of (+)2,400° ± 800° and (-)2,700° ± 200° respectively (30, 31). As will be discussed later, the errors inherent in the optical rotations were due to the technical difficulties of measuring optical activity in the solid state.

This initial success in obtaining optically active polymers based entirely on macromolecular asymmetry prompted Harris and Vogl to extend their investigation for the purposes of better understanding the mechanisms which lead to optical activity in polychloral. The asymmetric anionic initiators tetramethylammonium (+)- or (-)-O-acetylmandelate, tetramethylammonium (+)- or (-)-α-methoxymandelate,

and lithium methyl (+)- or (-)-hydroxidemandelate were used successfully to cryotachensically cast optically active polychloral films from initiated monomer solutions held isothermally for varying amounts of time above their ceiling temperatures (32, 33). The maximum optical rotations obtained for each initiator are shown in Table 1 below.

- TABLE 1 -

MAXIMUM OPTICAL ROTATIONS OBTAINED
BY HARRIS AND VOGL (32, 33)

INITIATOR	$[\alpha]^{RT}_D$, film (+)	$[\alpha]^{RT}_D$, film (-)
tetramethyl ammonium (+)- or (-)-O-acetyl-mandelate	(-)1,860° ± 70°	(+)1,180° ± 90°
tetramethyl ammonium (+)- or (-)-α-methoxy-mandelate	(-)190° ± 15°	(+)210° ± 20°
lithium methyl (+)- or (-)-hydroxide-mandelate	(+)3,600° ± 110°	(-)4,670° ± 240°

As reviewed by Harris (32), the optical activity of the polymer films was highly dependent upon the holding times and holding temperatures of the initiated monomer solutions prior to cryotachensic polymerization. Specifically, an increase in either was seen to bring about an increase in the observed rotations of the films. This behavior was attributed to the formation of oligomers above the ceiling temperature which favored the induction of helices in one screw sense.

The investigators also noted that an increase in the size and/or polarity of the groups located about the chiral center of the initiator effectively enhanced the magnitude of the optical rotations exhibited by the polymer films as did placing the initiator's chiral center closer to the anion, e.g. alkoxide versus carboxylate. In both instances, this was believed to be the result of an increased steric interaction between the asymmetric initiator and incoming monomer units undergoing addition.

Finally, studies undertaken with optically active polychloral in powdered form successfully demonstrated its utility as a chromoatographic support, affording the partial resolution of racemic poly(α-methylbenzyl methacrylate)s (32, 34).

Poly(triphenylmethyl methacrylate). The preparation of optically active, isotactic poly(triphenylmethyl methacrylate) was reported by Yuki, Hatada, and co-workers (35, 36). A preferred helical screw sense was induced by the asymmetric initiator lithium (R)-N-(1-phenylethyl)anilide or by the asymmetric (-)-sparteine-butyllithium complex, yielding specific rotations at the sodium D-line of (-)104° and (+)363° respectively.

The authors attributed the polymer's activity in solution to the predominance of a rigid helical screw stabilized by the presence of bulky triphenylmethyl side groups positioned at regular intervals along the helix. The conversion of this optically active polymer to poly(methyl methacrylate) (acid hydrolysis in methanol followed by methylation with diazomethane) afforded an optically inactive solution. The investigators rationalized that the steric bulk

provided by the newly formed methyl side groups of poly(methyl methacrylate) was not sufficient to prevent inversion or uncoiling of the helix in solution. With the absence of macromolecular asymmetry, all optical activity was lost.

Yuki also reported the partial resolution of hexahelicene, 1-phenylethyl alcohol, menthol, 1,2- and 1,3-disubstituted cyclic compounds, and other low molecular weight compounds with optically active poly(triphenylmethyl methacrylate) as a chromatographic support (37, 38).

Polyisocyanides. Drenth and co-workers attempted to synthesize optically active polyisocyanides based entirely on macromolecular asymmetry (39). Polymers of substituted isocyanides are known to possess a tightly wound 4_1 helical conformation in solution (39, 40). However, the polymerization of α-phenylethyl isocyanide with the chiral catalyst (+)-nickel alaninate failed to yield a polymer with a significant specific rotation.

A predominance of one helical screw sense was obtained indirectly through the partial resolution of optically inactive, i.e. racemic, poly(t-butyl isocyanide) on an optically active chromatography column (39, 41). The resolution afforded an optically active polymer with a specific rotation of (-)16° at the sodium D-line and represents the second route by which polymers possessing only macromolecular asymmetry can be obtained.

Polymerization of Chloral and the Properties of its Polymer

Haloacetaldehydes, including chloral, are endowed with electron withdrawing halogen atoms α to their carbonyl carbon and are readily susceptible to anionic polymerization in the absence of protic impurities. Suitable initiators include tertiary amines, tertiary phosphines, tertiary arsines, ammonium, phosphonium, or sulfonium salts of fluoride, chloride, bromide, iodide, hydroxide, alkoxide, or carboxylate, and group IA, IIA, or IIIA metal salts of hydrides, hydroxides, alkoxides, or carboxylates (42).

Unlike a host of vinyl compounds which are readily polymerized through their carbon-carbon double bonds, aldehydes are incapable of polymerization at elevated temperatures due to the relatively small, favorable changes in enthalpy which occur during the polymerization process, e.g. (-)5 Kcal/mol. Because entropy changes are usually in the range of (-)25 cal/°K mol, low polymerization temperatures are required to maintain a negative change in the Gibbs free energy, a requirement if polymerization is to take place. These thermodynamic considerations give rise to the phenomenon of ceiling temperature, a temperature above which polymerization can not occur, i.e. $\Delta G^0 \geq 0$.

The ceiling or threshold polymerization temperature, T_c, is related to enthalpy change, ΔH^0, to entropy change, ΔS^0, and to the equilibrium monomer concentration, $[M]_c$, by the following expression:

$$T_c = \frac{\Delta H^0}{\Delta S^0 + R\mathrm{Ln}[M]_c} \qquad (9)$$

where R is the gas constant (43). The threshold polymerization temperature for pure chloral monomer is reported to be 58°C (44).

As reviewed by Corley (30), attempts to polymerize chloral at room temperature resulted in incoherent polymer because the initiator could not be uniformly dispersed within the monomer before the onset of polymerization. It was realized that a homogeneous dispersal could be achieved if the monomer and initiator were mixed together above 58°C. Polymerization could then be induced by rapidly cooling the solution below its threshold polymerization temperature. This process, developed in this laboratory, is referred to as cryotachensic polymerization (42, 44) and has been used throughout this investigation. Typically, initiated monomer solutions were held isothermally for varying amounts of time at 65°, 75°, or 85°C. Polymerization was then effected by rapidly quenching the solutions to ice temperature.

The physical and chemical properties of polychloral have been extensively studied and are reviewed elsewhere. X-ray diffraction analyses (45) and 35-Cl NQR data (46) have shown that polychloral is partially crystalline (density approximately 2.0 gm/cm^3) and isotactic, possessing a 4_1 helical conformation and a tetragonal crystalline structure (29). The polymer is insoluble in all known solvents and solvent combinations and does not lend itself to standard solution characterization techniques. A limited amount of information has been provided by endgroup analyses (47).

Much attention has been focused on the thermal and chemical stability of polychloral. The presence of alkoxide endgroups renders

the polymer highly susceptible to depolymerization above 100°C. The thermal stability of polychloral can be enhanced by exposing the polymer's crystalline surfaces to acidic methanol (10% HCl), a process which effectively replaces all alkoxide residues with a more thermally stable hydroxyl functionality (30). Other stabilization methods have been devised which provide polychloral with a greater measure of thermal and chemical stability (48, 49).

The absence of a suitable solvent for polychloral precludes the measurement of its optical activity in solution. Bonsignori and Lorenzi (50) have outlined a number of difficulties which are associated with the determination of optical activity in the solid state. For polychloral, these include sample opacity and optical anisotropy. Each will be discussed briefly below.

Sample opacity encountered in solid state measurements can be minimized by shortening the pathlength through which the plane polarized beam must travel. Polychloral film disks having a thickness on the order of 0.1 mm were typically used in this investigation. Unfortunately, the presence of microvoids in the polymeric films led to a substantial amount of light scattering and the disks appeared translucent, unsuitable for optical rotation measurements. As mentioned by Harris (32), this problem could be corrected by filling the microvoids with diphenyl ether, an optically transparent, inert liquid which was found to have a refractive index similar to that of polychloral at the sodium D-line. All polychloral films were typically observed to become transparent after soaking in dephenyl ether for several days at room temperature.

Probably the greatest obstacle encountered in solid state optical activity measurements is the need for optically isotropic samples. Polymeric films tend to display varying amounts of optical anisotropy, e.g. birefringence, usually the direct result of unwanted orientation within the films. Birefringence can cause the rotation of plane polarized light, the magnitude and sign of the rotation a function of the degree and the direction of orientation (51). As outlined by Corley (30) and Harris (32), it is possible to obtain optically isotropic polychloral films only if great care is exercised during their preparation and measurement. At no time can a film be subjected to mechanical stress. Furthermore, the films must be continuously exposed to organic media in order to prevent orientation by shrinkage. It was largely because of the lack of optical isotropy that early experiments with optically active polychloral were unsuccessful (28).

The experimental techniques used to determine the specific rotation of polychloral films are discussed extensively in the next chapter of this thesis. Briefly, the degree of optical anisotropy present in a given polymer film was evaluated by measuring its optical rotation at three different orientations, 120° apart. If the average of the three rotations had a standard deviation greater than 15%, the film was judged to be anisotropic and not suitable for use. Birefringent samples typically displayed large variations in the magnitude and sign of their optical rotation.

EXPERIMENTAL SECTION

Materials

The following materials were used for this investigation. Letters contained within parentheses refer to source. A complete listing of all sources can be found below.

acetic acid, glacial (F)

acetic anhydride (A)

acetone (F)

benzene (F)

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

carbon tetrachloride (AV)

chloral (trichloroacetaldehyde) (M)

chloroform (MCB)

5(6)-cholesten-3β-ol (cholesterol) (A) (S)

5(6)-cholesten-3β-ol, 99% (CD)

cholestan-3β-ol (PB)

coprostan-3α-ol (PB)

coprostan-3β-ol (PB)

deuterochloroform (A)

diphenyl ether (F)

ethanol, 95% (F)

ethanol, absolute (F)

n-heptane, 99% (A)

n-hexane, 99% (A)

hydrochloric acid (F)

lithium-t-butoxide (AV)

magnesium sulfate (F)

l-menthol (A)

methanol (MCB)

methanol, spectra analyzed (F)

Molecular Sieves, 3A (TF)

(±)-2-octanol, 99% (A)

R-(-)-2-octanol, puriss. (TF)

S-(+)-2-octanol, puriss. (TF)

phosphorous pentachloride (AV)

phosphorous pentoxide (MCB)

potassium hydroxide (MCB)

sodium, metal (F)

sodium bicarbonate (MCB)

sodium hydroxide (MCB)

Sources: A - Aldrich Chemical Co.

AV - Alfa-Ventron Co.

CD - Chemical Dynamics Corp.

F - Fisher Scientific Co.

M - Montrose Chemical Co.

MCB - Matheson, Colman, and Bell, Inc.

PB - Pfaltz and Bauer, Inc.

S - Sigma Chemical Co.

TF - Fluka Chemical Corp.

Purification of Solvents and Reagents

All materials listed in Part A were used as received unless specified below.

Chloral (3.5 L) (52) was placed in a dry 5 L roundbottom flask. To the flask was added phosphorous pentoxide (200 g) to convert any residual chloral hydrate to chloral. The mixture was heated to reflux for 24 hours under a dry nitrogen atmosphere. Simple distillation then afforded crude chloral which was further purified by fractional distillation on a 3 ft. column packed with glass helices. Polymerization grade chloral, 99.9% as determined by gas chromatography, was freshly distilled from the column prior to any polymerization.

5(6)-Cholesten-3β-ol was recrystallized from warm, absolute ethanol and dried for two days in an Abderhalden apparatus at 40°C and 0.2 mm Hg. m.p. 145° - 147°C.

Cholestan-3β-ol was recrystallized from warm, absolute ethanol and dried for two days in an Abderhalden apparatus at 40°C and 0.2 mm Hg. m.p. 140° - 141°C.

Coprostan-3α-ol was recrystallized from warm, absolute ethanol and dried for three days in an Abderhalden apparatus at 40°C and 0.2 mm Hg. m.p. 116° - 117°C.

Coprostan-3β-ol was recrystallized from warm, absolute ethanol and dried for three days in an Abderhalden apparatus at 40°C and 0.2 mm Hg. m.p. 100° - 102°C.

n-Heptane, 99%, was heated to reflux over freshly cut sodium metal for one day under a dry nitrogen atmosphere. It was then fractionally distilled at atmospheric pressure and the middle fraction collected in a dried Schlenk tube containing activated 3A Molecular Sieves.

n-Hexane, 99%, was heated to reflux over freshly cut sodium metal for one day under a nitrogen atmosphere. It was then fractionally distilled at atmospheric pressure and the middle fraction collected in a dried Schlenk tube containing activated 3A Molecular Sieves.

Lithium-t-butoxide was sublimed at 150°C and 0.2 mm Hg. The purified material was then placed into a dry vial under a dry nitrogen atmosphere.

Preparation of Initiators

The secondary alkoxide initiators used for the polymerization of chloral were prepared by reaction of the desired secondary alcohol (optical purity greater than 97%) with 2.1 M n-butyl lithium in n-hexane under a dry nitrogen atmosphere. The initiator solutions so prepared were allowed to stand at room temperature for several minutes before their use. A detailed description of initiator preparation is presented below for each initiator species investigated.

Polymerization of Chloral To Optically Active Polymer Films

R(-)-, S(+)-, or (±)-Lithium-2-octanoxide as initiator.

Borosilicate glass plates were soaked in a concentrated sodium hydroxide solution for one day, then each plate was scrubbed with a soap solution, washed with deionized water, and swabbed dry with acetone. The plates were dried at 150°C for several days. Film casting assemblies were prepared by sandwiching a 3500 denier polyurethane elastomer thread between two hot glass plates; the plates held together with the aid of Boston clamps. A total of eight film assemblies were then placed in an oven thermostated to a temperature at which the initiator and monomer were mixed and held. The assemblies remained in the oven for at least two hours prior to their use.

R(-)-, S(+)-, or (±)-2-octanol (0.131 g, 1.01 mmol, 0.25 mol %) was first placed into a dry, serum capped 50 mL roundbottom flask while under continuous nitrogen flow, followed by the addition of n-hexane (1 mL). With the contents of the flask chilled, a solution of n-butyl lithium (0.48 mL, 1.0 mmol, 2.1 M in n-hexane) was slowly injected into the flask, affording a clear solution and n-butane gas evolution. The contents of the flask were allowed to stand under nitrogen at room temperature for several minutes.

To a dry 125 mL Erlenmeyer flask sealed with a serum cap under nitrogen flow was injected approximately 50 mL of freshly distilled chloral. Both flasks were then immersed in an ethylene glycol constant temperature bath thermostated to 65.0° or 85.0°C and given 10

minutes to equilibrate to bath temperature. During this time, the n-hexane present in the initiator flask was allowed to evaporate under a continuous stream of dry nitrogen.

With a preheated syringe (65° or 85°C), chloral (40 mL, 409 mmol) was injected into the initiator flask containing the alkoxide, resulting in the formation of a slightly opaque, orange solution (darker orange for 85°C) and gas evolution. The contents of the flask were agitated for 15 seconds to insure proper mixing of the monomer and initiator.

Ten minutes after the initial mixing, an aliquot of the monomer/initiator solution was quickly transferred with a preheated syringe (65° or 85°C) to two preheated film casting assemblies (65° or 85°C) which were temporarily stored in a thermally insulated carton. The assemblies were then rapidly plunged into an ice water slurry and agitated until the formation of opaque polymer films was detected. The film assemblies were allowed to remain at ice temperature overnight. The film casting process was repeated 30, 50, and 70 minutes after the initial mixing.

The next day, the eight assemblies were split open and the films gently floated off the glass plate surfaces with acidified methanol (10% HCl). After 24 hours, the stabilized films were first rinsed, then soaked in methanol for an additional 24 hours. While still wet, six - 12 mm disks were cut from each film with the aid of a #6 cork borer, and the disks placed in diphenyl ether for at least 24 hours prior to optical rotation measurements to ensure a desired level of optical transparency.

Lithium-cholesten-3β-oxide as initiator.

Twelve film assemblies prepared as described above were placed in an oven thermostated to a temperature at which the monomer and initiator were mixed and held. The assemblies were stored in the oven for several hours prior to their use.

5(6)-cholesten-3β-ol (0.395 g, 1.02 mmol, 0.25 mol %) was added to a dry 50 mL roundbottom flask. The flask was sealed with a serum cap and then flushed with nitrogen followed by the addition of n-hexane (1 mL) yielding a heterogeneous mixture. With the contents of the flask chilled, a solution of n-butyl lithium (0.48 mL, 1.0 mmol, 2.1 M in n-hexane) was slowly injected into the flask, affording a light yellow solution containing the alkoxide and n-butane gas evolution. The contents of the flask were allowed to remain at room temperature under nitrogen for several minutes.

To a dry 125 mL Erlenmeyer flask sealed with a serum cap under dry nitrogen flow was injected approximately 50 mL of freshly distilled chloral. Both flasks were then immersed in an ethylene glycol constant temperature bath thermostated to 65.0°, 75.0°, or 85.0°C, and given 10 minutes to equilibrate to bath temperature. During this time, the n-hexane present in the initiator flask was allowed to evaporate under a steady stream of dry nitrogen.

With a preheated syringe (65°, 75°, or 85°C), chloral (40 mL, 409 mmol) was injected into the flask containing the alkoxide resulting in the formation of a yellow solution (darkest at 85°C) which was noted to gradually turn orange as the experiment proceeded. The contents of the flask were agitated for 15 seconds to insure proper mixing.

2.5 minutes after the monomer and initiator were mixed, an aliquot of the solution was quickly transferred with a preheated syringe (65°, 75°, or 85°C) into two preheated film casting assemblies (65°, 75°, or 85°C) which were temporarily placed in a thermally insulated carton. The assemblies were then rapidly plunged into an ice water slurry and agitated until the formation of opaque polymer films was detected. The film assemblies were kept at ice temperature overnight. The film casting process was repeated for times of 10, 30, 50, 70, and 180 minutes after the mixing of monomer and initiator.

The next day, the twelve film assemblies were split open and the films gently floated off the glass plate surfaces with acidified methanol (10% HCl). After 24 hours, the stabilized films were first rinsed with methanol and then soaked in methanol for an additional day. While still wet, six - 12 mm disks were cut from each film with a #6 cork borer and placed into diphenyl ether for at least 24 hours prior to optical rotation measurements to ensure a desired level of optical transparency.

Lithium-cholestan-3β-oxide as initiator.

Eight film assemblies prepared as described above were placed in an oven thermostated to a temperature at which the monomer and initiator were mixed and held. The assemblies were stored in the oven for several hours prior to their use.

Cholestan-3β-ol (0.397 g, 1.02 mmol, 0.25 mol %) was added to a dry 50 mL roundbottom flask. The flask was sealed with a serum cap and then flushed with nitrogen followed by the addition of n-hexane

(1 mL), yielding a heterogeneous mixture. While the contents of the flask were chilled, a solution of n-butyl lithium (0.48 mL, 1.0 mmol, 2.1 M in n-hexane) was slowly injected into the flask, affording a light yellow solution containing the alkoxide and the evolution of n-butane gas. The contents of the flask were allowed to remain at room temperature under dry nitrogen for several minutes.

To a dry 125 mL Erlenmeyer flask sealed with a serum cap under nitrogen flow was injected approximately 50 mL of freshly distilled chloral. Both flasks were then immersed in an ethylene glycol constant temperature bath thermostated to 65.0° or 85.0°C, and given 10 minutes to equilibrate to bath temperature. During this time, the hexanes present in the initiator flask were allowed to evaporate under a dry stream of nitrogen gas.

With a preheated syringe (65° or 85°C) chloral (40 mL, 409 mmol) was injected into the initiator flask containing the alkoxide which resulted in the formation of a yellow solution (darker yellow for the 85°C holding temperature). The contents of the flask were agitated for 15 seconds to insure proper mixing.

Ten minutes after the monomer and initiator were mixed, an aliquot of the solution was rapidly transferred with a preheated syringe (65° or 85°C) into two preheated film assemblies (65° or 85°C) which were temporarily placed in a thermally insulated carton. The assemblies were then quickly plunged into an ice water slurry and agitated until the formation of opaque polymer films was detected. The film assemblies were kept at ice temperature overnight. This

process was repeated for times of 30, 50, and 70 minutes after the mixing of the monomer and initiator.

The next day, the eight assemblies were split open and the films gently floated off the glass plate surfaces with acidified methanol (10% HCl). After 24 hours, the stabilized films were first rinsed then soaked in methanol for an additional 24 hours. While still wet, six - 12 mm disks were cut from each film with the aid of a #6 cork borer and then transferred into diphenyl ether. The film disks remained in the diphenyl ether for several days to ensure a desired level of optical transparency.

Lithium-coprostan-3α-oxide as initiator.

Three film assemblies prepared as described above were placed in an oven thermostated to 85°C. The assemblies were stored in the oven for several hours prior to their use.

Coprostan-3α-ol (0.080 g, 0.206 mmol, 0.25 mol %) was added to a dry 50 mL roundbottom flask. The flask was sealed with a serum cap and then flushed with nitrogen, followed by the addition of n-hexane (0.5 mL) yielding a heterogeneous mixture. With the flask's contents chilled, a solution of n-butyl lithium (0.09 mL, 0.19 mmol, 2.1 M in n-hexane) was slowly injected into the flask, affording a light yellow solution containing the alkoxide. The contents of the flask were allowed to remain at room temperature under dry nitrogen for several minutes.

To a dry 125 mL Erlenmeyer flask sealed with a serum cap under nitrogen was injected approximately 35 mL of freshly distilled

chloral. Both flasks were then immersed in an ethylene glycol constant temperature bath thermostated to 85°C and given 10 minutes to equilibrate to bath temperature. During this time, the hexanes present in the flask were allowed to evaporate under a stream of dry nitrogen.

With a preheated syringe (85°C), chloral (8.0 mL, 82 mmol) was injected into the initiator flask which contained the alkoxide, yielding a light yellow solution. The contents of the flask were agitated for 15 seconds to insure proper mixing.

Ten minutes after the monomer and initiator were mixed, an aliquot of the solution was transferred with a preheated syringe (85°C) into a preheated film casting assembly (85°C) temporarily stored in a thermally insulated carton. The assembly was then rapidly plunged into an ice water slurry and agitated until the formation of a polymer film was detected. The film assembly remained at ice temperature overnight. The film casting process was repeated for times of 30 and 50 minutes after the initial mixing of monomer and initiator.

The next day, the three film assemblies were split open and the polymer films gently floated from the glass plate surfaces with acidified methanol (10% HCl). After one day, the stabilized films were first rinsed and then soaked with methanol for an additional 24 hours. While still wet, ten - 12 mm disks were cut from each film with the aid of a #6 cork borer and then transferred into diphenyl ether. The film disks remained in diphenyl ether for several days to ensure a desired level of optical transparency.

Lithium-coprostan-3β-oxide as initiator.

Three film assemblies prepared as described above were placed in an oven thermostated to 85°C. The assemblies were stored in the oven for several hours prior to their use.

Coprostan-3β-ol (0.080 g, 0.206 mmol, 0.25 mol %) was added to a dry 50 mL roundbottom flask. The flask was sealed with a serum cap and then flushed with nitrogen followed by the addition of n-hexane (0.5 mL), yielding a heterogeneous mixture. With the contents of the flask chilled, a solution of n-butyl lithium (0.09 mL, 0.19 mmol; 2.1 M in n-hexane) was slowly injected into the flask affording a yellow alkoxide solution and n-butane gas evolution. The contents of the flask were allowed to remain at room temperature for several minutes under a dry nitrogen atmosphere.

To a dry 125 mL Erlenmeyer flask sealed with a serum cap was added approximately 35 mL of chloral which had been freshly distilled. Both flasks were immersed in an ethylene glycol constant temperature bath thermostated to 85°C and given several minutes to come to bath temperature. During this time, the n-hexane in the initiator flask was allowed to evaporate under a steady flow of dry nitrogen.

With a preheated syringe (85°C), chloral (8.0 mL, 82 mmol) was injected into the initiator flask which contained the alkoxide, resulting in the formation of a yellow solution. The contents of the flask were agitated for 15 seconds to insure proper mixing.

Ten minutes after the monomer and initiator were mixed, an aliquot of the solution was transferred with a preheated syringe

(85°C) into a preheated film assembly stored in a thermally insulated carton. The assembly was then rapidly plunged into an ice water slurry and agitated until the formation of a polymer film was detected. The film assembly remained at ice temperature overnight. The film casting process was repeated for times of 30 and 50 minutes after the initial mixing of the monomer and initiator.

The next day, the three film assemblies were split open and the films gently floated from the glass plate surfaces with acidified methanol (10% HCl). After one day, the stabilized films were first rinsed then soaked in methanol for an additional 24 hours. While still wet, ten - 12 mm disks were cut from each polymer film with the aid of a #6 cork borer and immediately transferred into diphenyl ether. The disks remained in the diphenyl ether for several days to insure optical transparency.

Lithium-l-menthoxide as initiator.

Four film assemblies prepared as described above were placed in an oven thermostated to 75°C. The assemblies were kept in an oven for several hours prior to their use.

l-Menthol (0.082 g, 0.525 mmol, 0.25 mol %) was added to a dry 50 mL roundbottom flask. The flask was sealed with a serum cap and then flushed with dry nitrogen followed by the addition of n-hexane (0.5 mL). With the contents of the flask chilled, a solution of n-butyl lithium (0.24 mL, 0.50 mmol, 2.1 M in n-hexane) was slowly injected into the flask, yielding a clear solution and n-butane gas

evolution. The contents of the flask were allowed to remain at room temperature under a nitrogen atmosphere for several minutes.

To a dry 125 mL Erlenmeyer flask sealed with a serum cap under nitrogen was injected 50 mL of freshly distilled chloral. Both flasks were then immersed into an ethylene glycol constant temperature bath thermostated to 75.0°C and given 10 minutes to equilibrate to bath temperature. During this time, the n-hexane in the initiator flask was allowed to evaporate under a stream of dry nitrogen.

With a preheated syringe (75°C), chloral (20.0 mL, 205 mmol) was injected into the initiator flask containing the alkoxide, affording an opaque, white colored solution. After several minutes, a heterogeneous mixture resulted with fine white precipitate gradually accumulating at the bottom of the flask. An aliquot of precipitate-free solution was carefully removed and injected into a preheated film assembly (75°C) stored in a thermally insulated carton. The assembly was rapidly plunged into an ice water slurry and agitated for approximately five minutes. During this time, the solution remained unchanged inside the chilled film assembly and no evidence of polymerization was detected.

Further attempts to cast polymer films from the solution proved to be unsuccessful, apparently a result of the insolubility of the alkoxide in chloral.

Polymerization of Chloral to Optically Active Polymer Powder

5(6)-Cholesten-3β-ol (2.00 g, 5.16 mmol, 0.25 mol %) was added to a dry 50 mL roundbottom flask. The flask was sealed with a serum cap and flushed with nitrogen followed by the addition of n-hexane (5 mL), yielding a heterogeneous mixture. With the flask's contents chilled, a solution of n-butyl lithium (2.50 mL, 5.2 mmol, 2.1 M in n-hexane) was injected into the flask, affording a yellow solution and n-butane gas. The contents of the flask were allowed to remain at room temperature under a dry nitrogen atmosphere for several minutes.

To a dry 250 mL Erlenmeyer flask sealed with a serum cap under nitrogen was added freshly distilled chloral (200.0 mL, 2050 mmol). Both flasks were then immersed into an ethylene glycol constant temperature bath thermostated to 65.0°C and given 15 minutes to equilibrate to bath temperature.

With a preheated syringe (65°C), the alkoxide initiator solution was injected into the monomer flask, affording a light yellow colored solution which was agitated for 15 seconds to insure proper mixing. Several minutes later, the initiated monomer solution was transferred into rapidly stirred, chilled (0°C) n-hexane (2 L), resulting in the immediate formation of a white slurry of polychloral particles. The mixture was stirred at ice temperature for 12 hours and gradually thickened to a paste-like consistency.

The next day, the polymer was collected by filtration, ground into a fine powder, and acid stabilized by exposure to acidified

methanol (10% HCl) for 12 hours. The material was repeatedly washed with methanol until neutral to pH paper, and air dried for seven days.

When desired, chlorination of the polymer's hydroxyl endgroups was effected by exposing the dried powder to a warmed solution of phosphorous pentoxide and carbon tetrachloride (0.5 M solution) for one day followed by continuous extraction with acetone for five days. Upon air drying, a fine white powder was obtained.

Polymerization of Chloral to Optically Inactive Polymer Powder

Lithium-*t*-butoxide (0.390 g, 5.13 mmol, 0.25 mol %) was added to a dry 250 mL Erlenmeyer flask in a nitrogen filled glove bag. The flask was sealed and flushed with nitrogen. To a second 250 mL Erlenmeyer flask sealed with a serum cap and flushed with nitrogen was added freshly distilled chloral (200.0 mL, 2050 mmol). Both flasks were then immersed in a constant temperature bath thermostated to 75.0°C and given 15 minutes to equilibrate to bath temperature.

With a preheated syringe (75°C), the warmed chloral was injected into the initiator flask containing the alkoxide, affording a slightly opaque solution which was agitated for 15 seconds to insure proper mixing. Several minutes later, the initiated monomer solution was transferred into rapidly stirred, chilled (0°C) *n*-hexane (2 L), resulting in the immediate formation of a white slurry of polymer particles. The mixture was stirred at ice temperature for 12 hours and gradually thickened to a paste-like consistency.

The next day, the polymer was collected by filtration, ground into a fine powder, and acid stabilized by exposure to acidified methanol (10% HCl) for 12 hours. The material was then washed with methanol until neutral to pH paper and air dried for seven days.

When desired, chlorination of the polymer's hydroxyl endgroups was effected by exposing the dried powder to a warm solution of phosphorous pentoxide in carbon tetrachloride (0.5 M solution) for one day, followed by extraction with acetone for five days. Upon drying, a fine white powder was obtained.

Test for Rearrangement of Lithium-Cholesten-3β-Oxide in a Hydrocarbon Environment

Cholesten-3β-ol (1.95 g, 5.04 mmol) was added to a dry 50 mL roundbottom flask. The flask was sealed with a serum cap and flushed with nitrogen, followed by the addition of n-hexane (10 mL) yielding a heterogeneous solution. With the contents of the flask chilled, n-butyl lithium (2.40 mL, 5.0 mmol, 2.1 M in n-hexane) was slowly injected into the flask, affording a yellow solution and n-butane gas evolution.

The flask was then fitted with a condenser and its contents brought to reflux under dry nitrogen. After one hour, the condenser was removed and the n-hexanes allowed to evaporate under a steady stream of nitrogen, leaving a viscous yellow residue in the bottom of the flask. Glacial acetic acid (15 mL) and deionized water (15 mL) were then added, resulting in the gradual formation of a white solid

from the yellow residue. The mixture was stirred at room temperature for one hour.

The contents of the flask were then transferred directly to a separatory funnel and extracted with three, 10 mL portions of benzene. The benzene solution was washed first with three, 20 mL portions of dilute sodium bicarbonate solution, followed by repeated washings with deionized water until neutral to pH paper. The benzene fraction was dried over anhydrous magnesium sulfate, then filtered from the drying agent. The solution was placed in a vacuum distillation apparatus and the benzene removed at room temperature, leaving behind a white residue. The residue was recrystallized three times from warm ethanol, affording a white solid of cholesten-3β-ol at a yield greater than 90%. m.p. 144° - 146°C, $[\alpha]^{20}D$ = (-)18.6° (1.0 g/2.0 mL $CHCl_3$).

Synthesis of Addition Product Between Lithium-Cholesten-3β-Oxide and Chloral

Cholesten-3β-ol (20.0 g, 51.7 mmol) was added to a dry 250mL roundbottom flask. The flask was sealed with a serum cap and then flushed with nitrogen, followed by the addition of n-heptane (80 mL), yielding a heterogeneous mixture. With the contents of the flask chilled, a solution of n-butyl lithium (24 mL, 50.1 mmol, 2.1 M in n-hexane) was slowly injected into the flask, yielding a yellow colored solution. The contents of the flask were allowed to remain at room temperature under nitrogen for five minutes.

To a dry 50 mL roundbottom flask sealed with a serum cap and flushed with nitrogen was added n-heptane (15 mL) and freshly distilled chloral (5 mL, 51.1 mmol). Both flasks were then immersed in an ethylene glycol constant temperature bath thermostated to 65.0°C and given 15 minutes to equilibrate to bath temperature. With a preheated syringe (65°C), the diluted chloral solution was injected into the initiator flask. A vigorous reaction immediately resulted, affording a deep brown mixture which was held under nitrogen at 65°C for 15 minutes.

Endcapping was effected by the addition of acetic anhydride (25 mL, 265 mmol) to the chilled reaction mixture. During this time, the contents of the flask gradually thickened and changed to a tan color. The mixture was stirred at room temperature for several hours.

The reaction product was dissolved in benzene (75 mL) and extracted with three, 50 mL portions of dilute sodium bicarbonate solution, followed by repeated washings with deionized water until neutral to pH paper. The benzene solution was dried over magnesium sulfate, and then filtered. The deep orange colored solution was placed in a vacuum distillation apparatus and the benzene removed at room temperature leaving behind a dark orange, viscous oil.

The oil was dissolved in warm ethanol (50 mL) and this solution chilled to 0°C overnight, affording a tan solid which upon repeated recrystallizations from warm ethanol yielded a white solid in 65% yield. m.p. 104 - 106°C, $[\alpha]^{25}D$ = (-)13.2° (1.0 g/2.0 mL $CHCl_3$), elemental analysis: calc: C - 64.64%, H - 8.51%, O - 8.34%, Cl -

18.51%, found: C - 64.64%, H - 8.65%, O - 8.3%, Cl - 18.33%. See Appendix for spectra.

Measurements

Gas chromatograms were obtained on a Varian Aerograph model 920 equipped with a 100 cm x 0.64 cm silicon - DC200 column. Typical operating temperatures: Column - 65°C, Injector - 130°C, Detector - 140°C. Helium was used as the transport medium with a flow rate of 10 cm/7 seconds.

Melting points were measured on a MEL-TEMP capillary melting point apparatus. Heating rates of 2.5°C/minute were employed. All melting points were obtained in open capillaries and are uncorrected.

Infrared spectra were obtained on a Perkin-Elmer 727 infrared spectrophotometer. Samples were typically measured in solution.

Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were obtained on a Varian CFT-20 NMR spectrometer. Spectra were taken with complete proton decoupling at 25°C in $CDCl_3$ using TMS as an internal reference.

Optical rotation measurements were obtained on a Perkin-Elmer 141 MC polarimeter at wavelengths available with standard sodium and mercury lamps. Soluble compounds were measured in appropriate solvents in a 1 dm cell thermostated to 20.0° or 25.0°C. Polychloral films were measured in the solid state with a redesigned film holding assembly.

The film assembly consisted of two circular aluminum pieces, 26 mm in diameter, each with a 10 mm hole drilled in the middle. Two circular disks of optically transparent glass, 15 mm in diameter, were positioned over the holes. Polychloral films having a thickness as predetermined by a friction stop micrometer were gently sandwiched between the glass plates. The assembly was then bolted together and fitted inside a glass tube having approximate exterior dimensions equal to a polarimetry solution cell. The entire apparatus was placed in the polarimeter cavity, and α determined at three different orientations, 120° apart, for each polymer film disk. The magnitude of the variation in α for each orientation was used to judge the overall anisotropy of the polymer film. Films which displayed anisotropy were discarded. A total of six to eight separate film disks were measured in this way for each holding time and holding temperature studied. The specific rotations of the disks were averaged together and one specific rotation value based on 18 to 24 separate rotation measurements was calculated. All rotation data were obtained at room temperature.

CHAPTER III

RESULTS AND CONCLUSIONS

The primary goal of this investigation was to elucidate further the mechanisms responsible for optical activity in polychloral. Studies undertaken by Hatada and Vogl (28), Corley (30), and Harris (32) suggested that polychloral could be prepared in an optically active form, that its activity could be measured in the solid state, and that the observed optical rotation was the result of macromolecular asymmetry, i.e. preferred helicity within the polymer. Their initial success prompted this investigator to initiate a new generation of studies aimed at better correlating the magnitude and sign of optical rotation to the structure of the asymmetric initiator used to polymerize chloral. Ultimately, it was desired to determine the experimental conditions under which maximum optical activity might be obtained. A detailed account of all experimental results will be provided later in this chapter.

As reviewed earlier, synthetic polymers displaying macromolecular asymmetry are isotactic, their chains arranged in a stable helical conformation. Isotacticity requires that the sequence of pseudo-asymmetric centers along the chain be of the same configuration, yielding dd or ll dyads, i.e. meso placement. Helicity implies that the successive bonds along the chain are arranged in either a +gauche/trans (g^+t) or -gauche/trans (g^-t) conformation, each specifying a particular screw direction, i.e. right or left. As

detailed by Flory (53), a dd dyad configuration has a preferred bonding sequence of g^+t while a ll dyad configuration has a preferred bonding sequence of g^-t. Stated in another way, there exists an interdependence between isotacticity and helical order in the solid state. Without the proper configurational sequence along the chain, many synthetic polymers cannot be helical.

The inherent stability of a polymer helix is also of prime concern for macromolecular asymmetry. Most synthetic, isotactic polymers lack the secondary bonding forces which tend to stabilize conformational order in native macromolecules, e.g. hydrogen bonding, ionic interactions. In the absence of these forces, a helical coil may invert to the opposite screw sense or unwind to a random coil. The incorporation of large or polar side groups adjacent to the polymer backbone can effectively block these rearrangements, however. In such cases, the rotational energy barrier along the chain becomes sufficiently high so as to preserve the conformational sequences required for helicity.

From the discussion presented thus far, it should seem reasonable that polychloral is ideally suited for this investigation. X-ray diffraction analyses have shown the polymer to be completely isotactic, possessing a 4_1 helical conformation in the solid state (29). Furthermore, the presence of bulky trichloromethyl side groups along the polymer backbone effectively act to stabilize each helical screw in place. The final requirement for macromolecular asymmetry, a means to generate a predominance of one helical screw sense, is the topic on which this investigation is focused. It is through the use

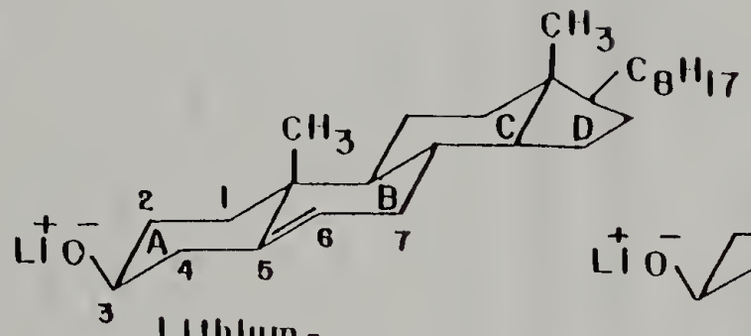
of asymmetric initiator species that optically active polychloral is obtained. Macromolecular asymmetry, i.e. optical activity, arises from the steric interaction between an asymmetric initiator molecule and incoming monomer units undergoing addition. In all cases, it is postulated that one helical screw direction is partially or completely favored relative to the other.

Preliminary results with carboxylate and alkoxide initiators tended to suggest that the degree of steric interaction provided by the asymmetric initiator directly influenced the enhancement of optical activity in polychloral as did the relative "strength" of the initiator. Generally, strong initiators, e.g. alkoxides, which possessed steric bulk in the region of the anion were seen to yield the highest optical activity values. Weak initiators, e.g. carboxylates, or those with little steric bulk near the anion, afforded lower optical rotations (32). For the purposes of this investigation, it was desired to select a series of closely related initiators, each differing only slightly, i.e. sterically, electronically, near the region of their anionic sites. In this way, it was hoped that changes in the sign and magnitude of the optical rotation of polychloral could be correlated to concomitant variations in initiator structure.

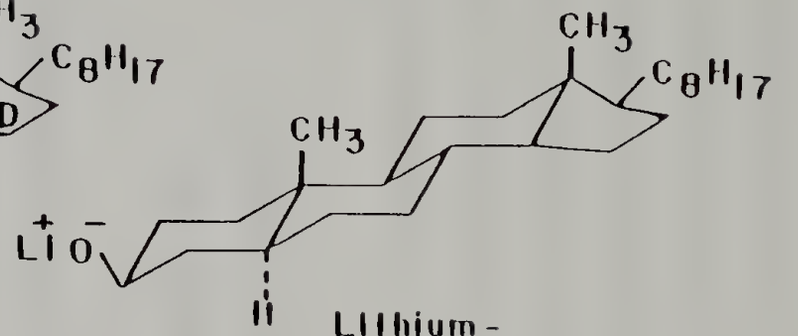
The asymmetric initiators selected for this study were derived from C_{27} monohydroxy, secondary alcohols (sterols) and are shown in Figure 1. Each initiator molecule consists of three fused cyclohexane rings (A,B,C), a terminal cyclopentane ring (D), and an aliphatic chain at C_{17}. The desired steric and electronic modifications near

Figure 1

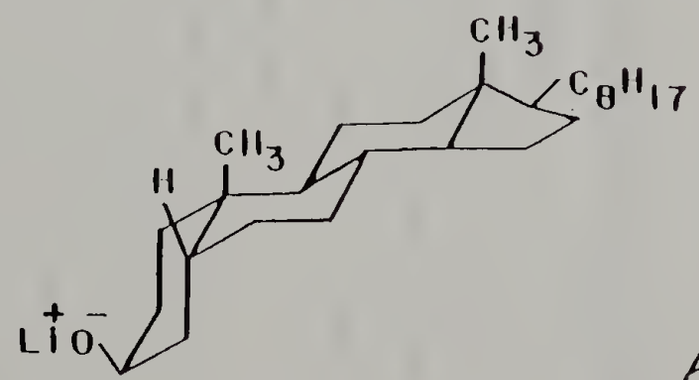
Steroid Initiators Used for the Polymerization of Chloral.



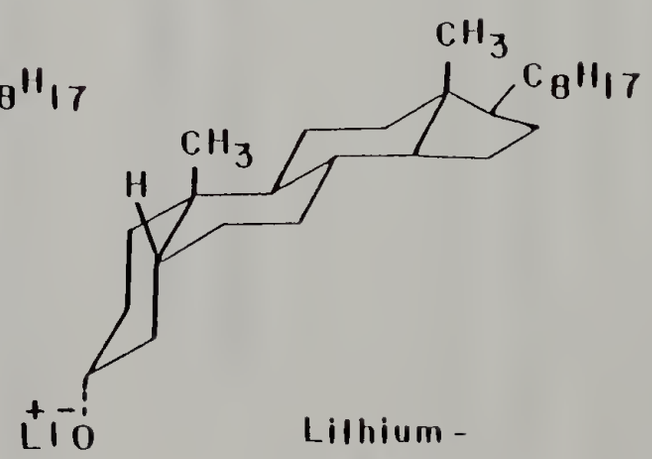
Lithium-
cholesten-3β-oxide



Lithium-
cholestan-3β-oxide



Lithium-
coprostan-3β-oxide



Lithium-
coprostan-3α-oxide

the initiator's reactive site include β versus α orientation of the alkoxide, saturation versus unsaturation at C_5-C_6, and trans versus cis A/B ring juncture. As will be discussed below, these minor structural modifications were often sufficient to alter the observed optical rotations exhibited by polychloral under a given set of experimental conditions. An excellent though slightly dated review of the chemical, physical, and chiroptical properties of steroids is currently available (54).

Synthesis of Optically Active Polychloral With Asymmetric Secondary Alkoxides

Optically active polychloral initiated by lithium R(-)-2-octanoxide, S(+)-2-octanoxide, and (±)-2-octanoxide

The alkoxides of 2-octanol were selected to serve as controls for the more complex steroid initiators. It was also of interest to compare their overall effectiveness in imparting preferred helicity into polychloral relative to the steroids.

The lithium salt of R(-)-2-octanoxide (0.25 mol %, 98% optical purity), S(+)-2-octanoxide (0.25 mol %, 97% optical purity), or (±)-2-octanoxide (0.25 mol %) was mixed with chloral monomer and the solutions held at 65° or 85°C for 10, 30, 50, and 70 minutes before being cryotachensically polymerized in film form. The films were stabilized and their optical rotations measured as described in Chapter II. Specific rotation data are tabulated in Table 2 and graphically displayed in Figure 2.

Optically active polychloral initiated by lithium-cholesten-3β-oxide

The secondary alkoxide of cholesten-3β-ol (cholesterol) was the first steroid initiator studied in this investigation (27). The molecule is characterized by β configuration at C_3, unsaturation at C_5-C_6, and trans A/B ring juncture.

Lithium-cholesten-3β-oxide (0.25 mol %, 98% optical purity) was mixed with chloral monomer and individual solutions held at 65°, 75°, and 85°C for 2.5, 10, 30, 50, 70, and 180 minutes before being cryotachensically polymerized in film form. The resultant films were stabilized and their optical rotations measured as described in Chapter II. Specific rotations are tabulated in Table 3 and graphically displayed in Figure 3.

Optically active polychloral initiated by lithium-cholestan-3β-oxide

The secondary alkoxide of cholestan-3β-ol is characterized by β configuration at C_3, saturation between C_5-C_6, and trans A/B ring juncture.

Lithium-cholestan-3β-oxide (0.25 mol %, 98% optical purity) was mixed with chloral monomer and individual solutions held at 65° or 85°C for 10, 30, 50, and 70 minutes before being cryotachensically polymerized in film form. The resultant films were stabilized and their optical rotations measured as described in Chapter II. The specific rotation data are tabulated in Table 4 and graphically displayed in Figure 4.

Optically active polychloral initiated by lithium-coprostan-3α, 3β-oxides

The secondary alkoxides of coprostan-3α-ol and coprostan-3β-ol are characterized by both α and β configuration at C_3, saturation between C_5-C_6, and cis A/B ring juncture.

Lithium-coprostan-3α-oxide (0.25 mol %, 97% optical purity) and lithium-coprostan-3β-oxide (0.25 mol %, 98% optical purity) were mixed with chloral monomer and the solutions held at 85°C for 10, 30, and 50 minutes before being cryotachensically polymerized in film form. The films were stabilized and their optical rotations measured as described in Chapter II. The specific rotation data are tabulated in Table 5 and graphically displayed in Figure 5.

- TABLE 2 -

$[\alpha]_D^{RT}$ VS HOLDING TIME
OPTICALLY ACTIVE POLYCHLORAL
INITIATED BY 0.25 MOL % R(-)-LITHIUM-2-OCTANOXIDE

HOLDING TIME (min.)	$[\alpha]_D^{RT}$ 65.0°C	$[\alpha]_D^{RT}$ 85.0°C
10	(+)4280° ± 190°	(+)2280° ± 90°
30	(+)2990° ± 200°	(+)1595° ± 70°
50	(+)2070° ± 250°	(+)1130° ± 45°
70	(+)1100° ± 90°	(+)706° ± 40°

INITIATED BY 0.25 MOL % S(+)-LITHIUM-2-OCTANOXIDE

HOLDING TIME (min.)	$[\alpha]_D^{RT}$ 85.0°C
10	(-)1450° ± 100°
30	(-)610° ± 130°
50	(-)470° ± 50°
70	(-)280° ± 50°

INITIATED BY 0.25 MOL % (±)-LITHIUM-2-OCTANOXIDE

HOLDING TIME (min.)	$[\alpha]_D^{RT}$ 85.0°C
10	(+)7° ± 16°
30	(+)4° ± 11°
50	(+)9° ± 6°
70	(+)9° ± 25°

- TABLE 3 -

$[\alpha]_D^{RT}$ VS HOLDING TIME

OPTICALLY ACTIVE POLYCHLORAL
INITIATED BY 0.25 MOL % LITHIUM-CHOLESTEN-3β-OXIDE

HOLDING TIME (min.)	$[\alpha]_D^{RT}$ 65.0°C	75.0°C	85.0°C
2.5	-----	(+)3350° ± 110°	-----
10	(+)3400° ± 130°	(+)2500° ± 115°	(+)1840° ± 88°
30	(+)2250° ± 70°	(+)1457° ± 130°	(+)827° ± 40°
50	(+)1510° ± 60°	(+)990° ± 60°	(+)425° ± 45°
70	(+)830° ± 100°	(+)600° ± 10°	(+)230° ± 20°
180	-----	-----	(+)2° ± 3°

- TABLE 4 -

$[\alpha]_D^{RT}$ VS HOLDING TIME

OPTICALLY ACTIVE POLYCHLORAL
INITIATED BY 0.25 MOL % LITHIUM-CHOLESTAN-3β-OXIDE

HOLDING TIME (min.)	$[\alpha]_D^{RT}$ 65.0°C	85.0°C
10	(+)3000° ± 180°	(+)1995° ± 130°
30	(+)2350° ± 90°	(+)610° ± 80°
50	(+)1860° ± 90°	(+)92° ± 15°
70	(+)1100° ± 130°	(-)26° ± 11°

- TABLE 5 -

$[\alpha]_D^{RT}$ VS HOLDING TIME

OPTICALLY ACTIVE POLYCHLORAL

INITIATED BY 0.25 MOL % LITHIUM-COPROSTAN-3α-OXIDE

HOLDING TIME (min.)	$[\alpha]_D^{RT}$ 85.0°C
10	(+)1690° ± 180°
30	(+)1550° ± 90°
50	(+)1465° ± 50°

INITIATED BY 0.25 MOL % LITHIUM-COPROSTAN-3β-OXIDE

HOLDING TIME (min.)	$[\alpha]_D^{RT}$ 85.0°C
10	(+)2970° ± 300°
30	(+)2607° ± 150°
50	(+)2617° ± 150°

Figure 2

$[\alpha]_D^{RT}$ of Polychloral Initiated by Lithium R(-)-2-Octanoxide, S(+)-2-Octanoxide, and (±)-2-Octanoxide as a Function of Holding Time at 65.0° and 85.0°C.

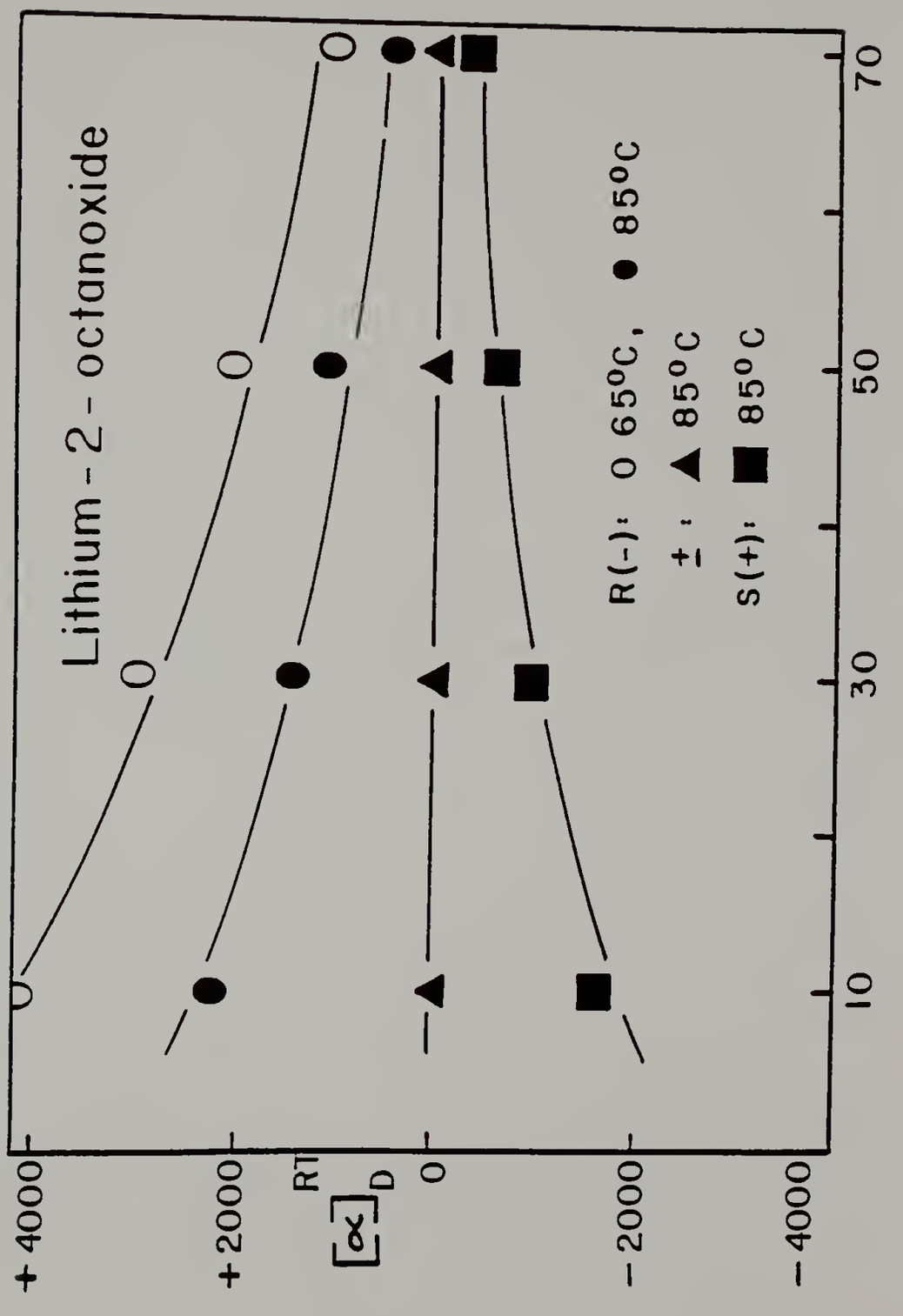

Lithium-2-octanoxide
R(-): ○ 65°C, ● 85°C
±: ▲ 85°C
S(+): ■ 85°C
+4000
+2000
0
−2000
−4000
$[\alpha]_D^{RT}$
10
30
50
70
TIME (min)

Figure 3

$[\alpha]_D^{RT}$ of Polychloral Initiated by Lithium-Cholesten-3β-Oxide as a Function of Holding Time at 65.0°, 75.0°, and 85.0°C.

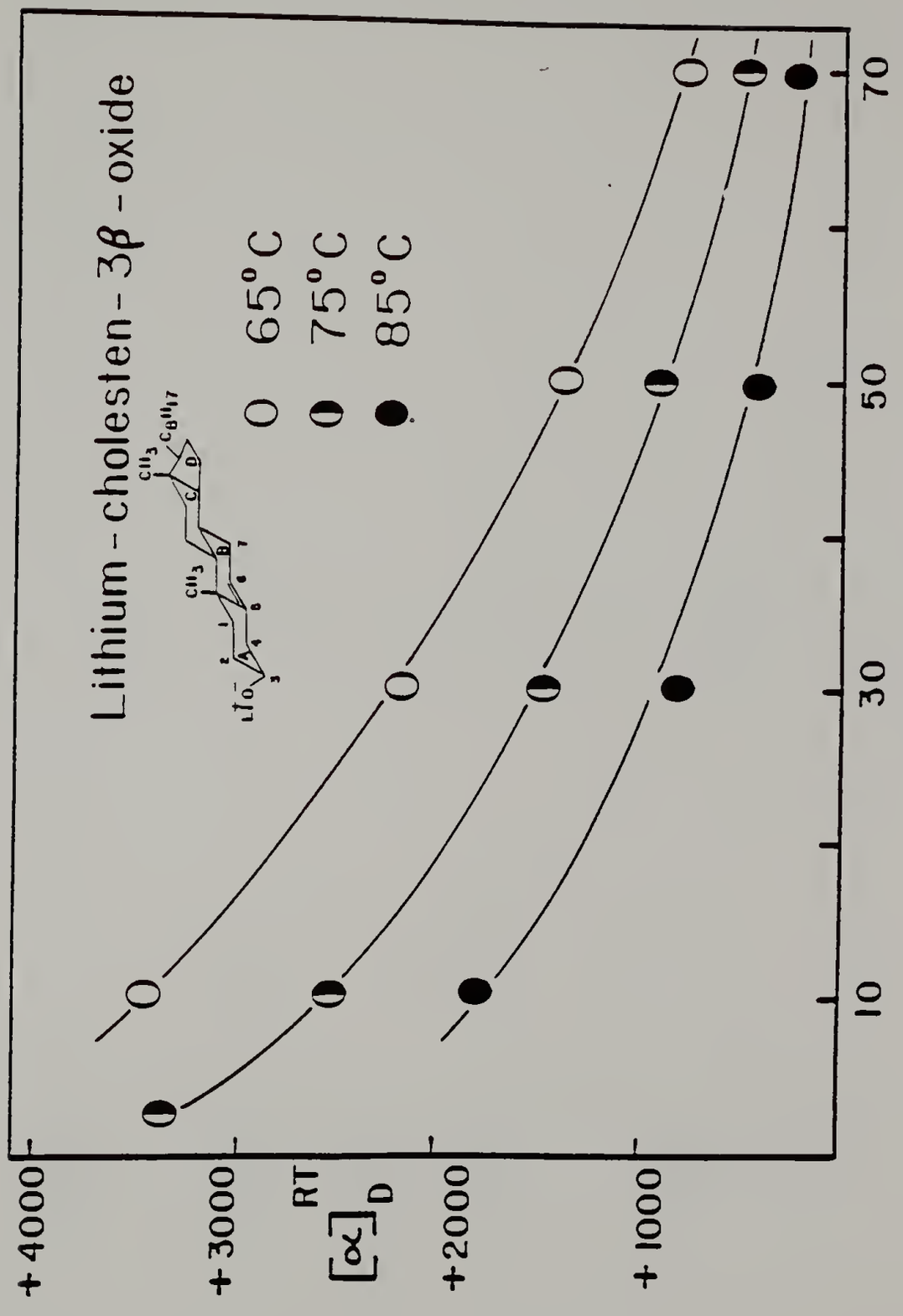

Lithium-cholesten-3β-oxide
0 65°C
0 75°C
● 85°C
+4000
+3000
+2000
+1000
[α]D RT
10
30
50
70
TIME (min)

Figure 4

$[\alpha]_D^{RT}$ of Polychloral Initiated by Lithium-Cholestan-3β-Oxide as a Function of Holding Time at 65.0° and 85.0°C.

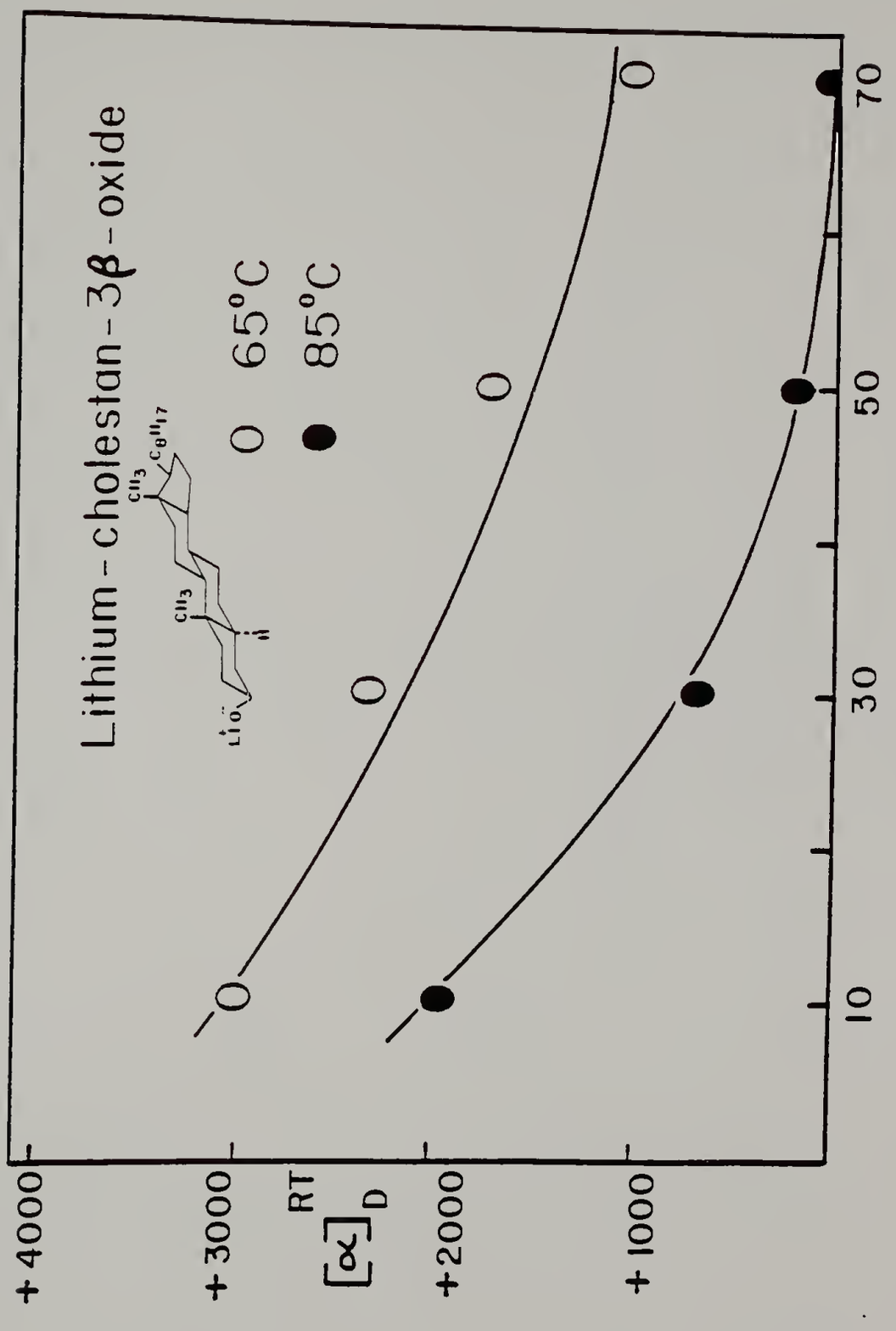
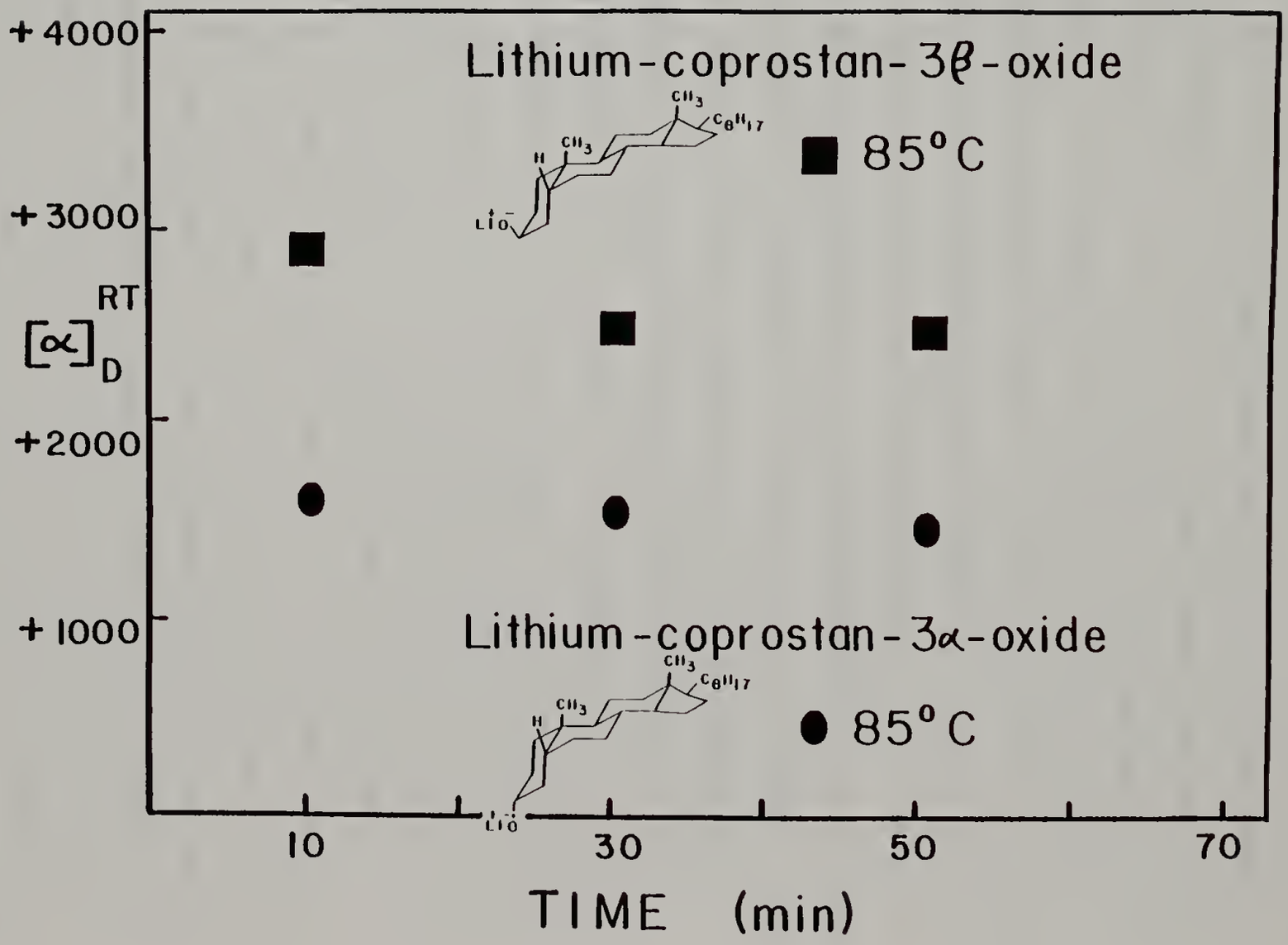

Lithium-cholestan-3β-oxide
0 65°C
● 85°C
+4000
+3000
+2000
+1000
RT
[α]D
10
30
50
70
TIME (min)

Figure 5

$[\alpha]_D^{RT}$ of Polychloral Initiated by Lithium-Coprostan-3α-Oxide and Lithium-Coprostan-3β-Oxide as a Function of Holding Time at 85.0°C.


+4000
+3000
+2000
+1000
$[\alpha]_D^{RT}$
Lithium-coprostan-3β-oxide
85°C
Lithium-coprostan-3α-oxide
85°C
10
30
50
70
TIME (min)

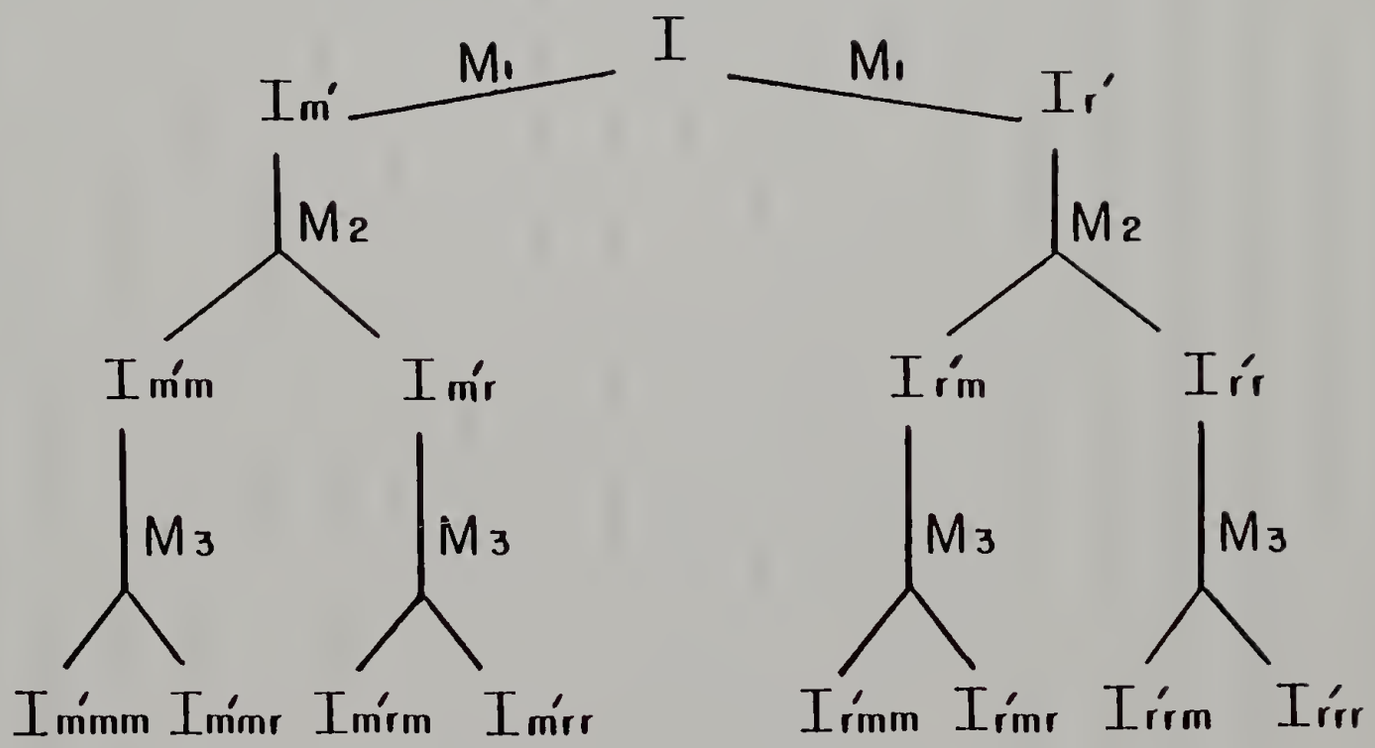
Summary

Before the data presented above can be critically evaluated, it will be necessary to establish, in a general sense, the ways in which optical activity can arise in polychloral. As may be recalled from Chapter I, an initiated monomer mixture held above its threshold polymerization temperature (58°C) is incapable of polymerizing to high molecular weights because any gains in enthalpy are readily offset by the exoentropic nature of the chain forming process, i.e. the Gibbs free energy change associated with the polymerization is greater than zero. However, the formation of chloral n-mer, i.e. oligomer, where n is an inverse function of temperature should be thermodynamically allowable at the holding temperatures routinely employed in this investigation. For the purposes of this discussion, it will be postulated that: (1) the alkoxide present in the monomer/initiator solution is most accurately represented by chloral n-mer, and (2) the structure of the chloral n-mer predetermines the exact nature of the polychloral helices which form upon polymerization below 58°C.

The formation of chloral trimer (n = 3) is depicted schematically in Figure 6 and is shown to consist of three separate steps. Each step is characterized by two possible modes of addition, representing those routes available for nucleophilic attack on the carbonyl carbon of chloral, i.e. attack above or below the plane of the molecule affording either meso (m) or racemic (r) placements. For each step, the approach of the alkoxide (initiator or n-mer) will favor that route which offers the least amount of steric and/or electrostatic interaction between the groups positioned asymmetrically around the

Figure 6

Routes for Chloral Trimer Formation
in the Holding Solution.


I
M1
M1
Im′
Ir′
M2
M2
Im′m
Im′r
Ir′m
Ir′r
M3
M3
M3
M3
Im′mm
Im′mr
Im′rm
Im′rr
Ir′mm
Ir′mr
Ir′rm
Ir′rr

anion and the trichloromethyl group on chloral. Stated in a different way, the more probable mode of attack will be that which is characterized by the lower energy of activation.

The first addition step between the initiator alkoxide, I, and monomer, M_1, should be extremely favorable considering the enhanced reactivity of the unstabilized anion. The predominant route of attack will be dictated by the asymmetric configuration near the anionic site. Highly stereoefficient initiators will code for all m' or r' placements with respect to their secondary hydrogen atom. Asymmetric initiators which lack steric bulk near their anionic sites can be expected to code for a mixture of m' and r' placements where one is predominant over the other. Of course, in the limiting case, symmetrical initiators will code for equal numbers of m' and r' placements as the activation energies associated with both routes of attack are identical. The effect of temperature will be the same in all cases. Raising the temperature of the monomer/initiator solution will lower the stereoselectivity of the alkoxide, enhancing the probability that the less preferential placement will occur. Subsequent additions between the chloral n-mer alkoxide, Im' or Ir', and M_2, M_3 will be less favorable than the first addition step, primarily a result of the inductively stabilized propagating anion. The predominant route of attack will again be dictated by the configuration near the site of the anion. However, unlike the asymmetric initiator species discussed above, the n-mer alkoxide will always favor m placement (polychloral is isotactic, not syndiotactic). In this case, the energy of activation for m placement is

always smaller than that for r placement along the n-mer chain. Again, increases in holding temperature can be expected to raise the probability for an occasional r placement in the n-mer.

For the purposes of simplifying this discussion, the highest ordered chloral n-mer will be arbitrarily defined as a trimer. Table 6 lists eight possible structures for the trimer along with their relative probabilities of formation.

- TABLE 6 -

TRIMER STRUCTURES
POSSIBLE IN THE HOLDING SOLUTION

TRIMER STRUCTURE*	RELATIVE PROBABILITY IN SOLUTION
Im'mm	most probable
Ir'mm	
Im'rm	
Im'mr	
Ir'rm	
Ir'mr	
Im'rr	least probable
Ir'rr	

*See Figure #6

Assuming efficient initiation, i.e. all m' or r' placements, the most probable trimer for a given set of experimental conditions will be Im'mm or Ir'mm. Upon cooling such a mixture below 58°C, polymerization will occur by a rapid succession of m placements (r placements are highly unfavorable as they disrupt the ordered crystalline matrix of polychloral) ultimately yielding perfect helical coils lying completely in the left or right screw direction. In such cases, maximum optical activity can be expected with the sign of rotation dependent upon the helical screw direction of the coils. On the other hand, for initiation which yields only a predominance of m' or r' placements, or for higher holding temperatures where the alkoxides become less selective, a mixture of trimer structures becomes possible. Upon cooling this solution below 58°C, polymerization will yield a mixture of helical coils and maximum optical rotations will not be obtained. Instead, both the magnitude and sign of the rotations will be dependent upon the number of excess helical coils which lie in the predominant direction.

The importance of the chloral n-mer (helical precursor) can not be over emphasized. Asymmetric initiators which are not completely stereo-efficient in specifying a single helical direction and/or the incorporation of an odd number of the less probable r placements into the n-mer (which act to invert the direction of the helical screw) can effectively lower the optical activity exhibited by polychloral. It is with the use of these concepts that the data presented above will be evaluated.

Focusing first on the structurally less complex octanoxide initiators, the rotation data displayed in Figure 2 suggest: (1) the optical activity imparted into the polymer films is directly influenced by the configuration of the 2-octanoxide and (2) the magnitude of the rotations is inversely related to both holding time and holding temperature prior to cryotachensic polymerization. Specifically, opposite initiator configurations did lead to opposite optical rotations, with racemic initiator yielding optically inactive polymer films. Furthermore, higher holding temperatures resulted in smaller rotation values.

These trends can be rationalized by considering the effects of initiator configuration and temperature on the formation of the chloral n-mer in the holding solution. The two mirror forms of the 2-octanoxide should specify, with equal stereoefficiency, m' or r' placements in the chloral n-mer. As holding temperature is raised, the efficiency of both initiator antipodes must drop, reflecting some loss in their selectivity. Furthermore, increases in holding temperature will enhance the probability for random r placements in the n-mer, again a result of the lowered selectivity of the alkoxide species. As the structures of the respective chloral n-mers become more varied, the number of helices which will be directed into the predominant direction, i.e. the magnitude of optical rotation, must decrease. In other words, both the magnitude and sign of the optical activity are predetermined before polymerization begins.

If these processes were solely responsible for the optical rotations exhibited by the films, one might expect optical activity to be independent of holding time. As shown in Figure 2, however, such is not the case. Instead, the activity values asymptotically decrease with increases in holding time, suggesting that the chloral n-mer in the holding solution becomes more stereo-random and, thus, less selective in specifying one screw direction as time continues. While little can be said of the overall stability of the n-mer species in the polar chloral environment, the data would suggest that racemization, i.e. partial inversion of configuration at the alkoxide end (initiator and/or n-mer), is occurring as time continues. Racemization at either site would effectively invert the helical direction coded for by the n-mer and could be expected to lower significantly the number of predominant helical coils which form upon polymerization. While the possibility of racemization in chloral media was not directly explored, it is believed that this process remains a viable explanation for the behavior observed in this experiment. As will be discussed below, similar trends are reported for other initiator species.

Finally, it is with the R(-)-2-octanoxide initiator, 65°C and 10 minute holding time, that the largest specific rotations were achieved; 4,300° ± 200° at the sodium D-line. While these values are among the highest in magnitude yet reported for any macromolecule, they are not the highest attainable rotations for optically active polychloral. As the trends in the rotation data indicate, greater

optical rotations should be possible with the use of lower holding temperatures and shorter holding times.

Armed with an understanding of the 2-octanoxide data, attention can now be focused on the structurally more complex steroid initiators. The secondary alkoxides of cholesten-3β-ol and cholestan-3β-ol were the first such initiators used in this study. As shown in Figure 1, the cholestan-3β-oxide differs from its unsaturated analogue in the presence of an axial hydrogen located at C_5. For 3β alkoxide configurations, this C_5 axial hydrogen atom can offer little in the way of steric interaction with incoming monomer units. Therefore, the two initiator species share similar steric bulk in the regions of their anionic sites. In the absence of any major electronic effects, one might expect little relative difference in the behavior of each initiator toward the formation of the chloral n-mer in the holding solution.

Analysis of Figures 3 and 4 will show that both initiators do behave similarly. Furthermore, a striking feature of the data presented here is its similarity to that generated with the 2-octanoxides discussed earlier. Optical rotation values are dependent upon holding temperature, and for each holding temperature, there exists an asymptotic drop in the rotation magnitudes with longer holding times. After extended holding periods, all optical activity in the polychloral films is lost. These trends can be attributed to the same processes discussed above for the 2-octanoxide initiators. Again, structural changes in the chloral n-mer can be expected to

bring about concomitant variations in the optical rotations exhibited by the polychloral films.

In comparing the relative magnitudes of the rotations induced by the 2-octanoxides and the present steroid initiator species, it would seem that the former are more stereoefficient in generating a predominant helical direction despite their less complex structure. Although this may seem surprising, examination of Figure 1 will show that the bulk of the steroid molecule is actually directed away from its anionic site at C_3 and thus is probably not directly involved in orienting incoming monomer units.

A second point of interest centered on the asymptotic behavior of the rotation data afforded by both steroid initiators also demands some attention. As may be recalled from the analysis of the 2-octanoxide data above, asymptotically decreasing rotation values with holding time were attributed to a "randomization" of the chloral n-mer through racemization of either the initiator alkoxide (while temporarily uncoupled from monomer) or the n-mer alkoxide in the holding solution. For the 2-octanoxide experiment, extensive racemization at either alkoxide site would be expected to yield a racemic mixture of left and right helical coils upon polymerization. Yet, in the present experiment, only racemization centered at the n-mer alkoxide would afford similar behavior. Racemization of the β alkoxide of either steroid initiator, i.e. epimerization, should not contribute to an asymptotic drop in the rotation data toward optical inactivity. Very simply, the products of epimerization, i.e. the 3α and 3β epimers of either steroid initiator, are not mirror

forms of one another and can not be expected to behave accordingly. Extensive epimerization would not necessarily lead to the formation of an equimolar mixture of left and right helical screws in the holding solution. While the magnitude (and perhaps the sign) of the optical rotations ultimately exhibited by polychloral would certainly be altered by an epimerization process, it is believed that racemization of the chloral n-mer alkoxide must also be operative to fully account for the observed behavior.

The second set of steroid initiators used in this study, the coprostan-3α,3β-oxides, provided a direct opportunity to examine the relative behavior of 3α, 3β configurations at the anionic site. As Figure 1 indicates, the coprostanoxides are characterized by cis A/B ring juncture. Furthermore, the presence of the C_5 equitorial hydrogen on the steroid skeleton endows the 3β epimer with a higher degree of steric crowding near its anionic site relative to the 3α species. Thus, the route of approach between the initiator alkoxide and the chloral monomer should be more closely defined or regulated for the coprostan-3β-oxide, affording a higher degree of stereoselectivity for either m' or r' placements in the chloral n-mer. This, in turn, should result in a greater predominance of one helical screw sense upon polymerization of the holding mixture. As is readily apparent in Figure 5, the 3β epimer of the coprostanoxide did yield significantly higher rotation values under a given set of experimental conditions.

Also apparent in Figure 5, however, is a marked deviation in the trend of the rotation values with holding time. The near constant

magnitude of the optical rotations suggests that, in contrast to all previous experiments, the structure of the chloral n-mer does not randomize with time. A suitable explanation can not be offered to fully account for this anomalous behavior. It is possible that the geometry associated with the coprostanoxides (cis A/B ring juncture) might act to stabilize the chloral n-mer through specific steric interactions in the holding solution. This possibility has not been verified, however.

Synthesis of Optically Active Polychloral Powder

An additional point of interest was centered on the continued evaluation of optically active polychloral as a chromatographic support. Earlier studies had successfully demonstrated the utility of this material as a column packing, affording both the partial resolution of isotactic poly((±)-α-methylbenzyl methacrylate) (34) and the separation of aromatic hydrocarbons (55), the latter based on the polymer's high affinity for aromatic compounds (56). Little attention had been directed toward the potential for the resolution of low molecular weight enantiomers, however. Toward that end, a collaborative research effort was initiated with Professor Karl Schlogl of the Institute of Organic Chemistry, University of Vienna, Austria. Unfortunately, at the time of this writing, the preliminary results regarding this investigation were not available.

The synthesis of optically active polychloral powder was modified to gain better control over the magnitude of its optical rotation. The full details of the synthesis are reported in Chapter II.

Test for Rearrangement of Lithium-Cholesten-3β-Oxide in a Hydrocarbon Environment

It was of interest to determine the susceptibility of the lithium-cholesten-3β-oxide to rearrangement reactions in hydrocarbon media. Ffrom Chapter II, it may be recalled that all secondary alkoxides were prepared and stored at elevated temperatures in a hydrocarbon solution prior to their use as initiators. It was feared that any rearrangements during this time might effectively alter the structure of the chloral n-mer which would form upon addition of chloral monomer.

As detailed in Chapter II, a known quantity of cholesten-3β-ol was converted to the desired alkoxide with n-butyl lithium and brought to reflux in n-hexane for one hour under dry nitrogen. The alcohol was then regenerated with acetic acid in a 90% yield and compared to a cholesten-3β-ol standard. The results follow: Regenerated alcohol; m.p. 144° - 146°C, $[\alpha]^{20}D$ = (-)18.6° (C = 1.0 g/2.0 mL, $CHCl_3$). Cholesten-3β-ol standard; m.p. 144° - 146°C, $[\alpha]^{20}D$ = (-)18.4° (C = 1.0 g/2.0 mL, $CHCl_3$). The results of this test strongly suggest that the secondary alkoxide does not undergo structural rearrangements in hydrocarbon media at the temperatures used in this investigation.

Synthesis of an Addition Product Between Lithium-Cholesten-3β-Oxide and Chloral

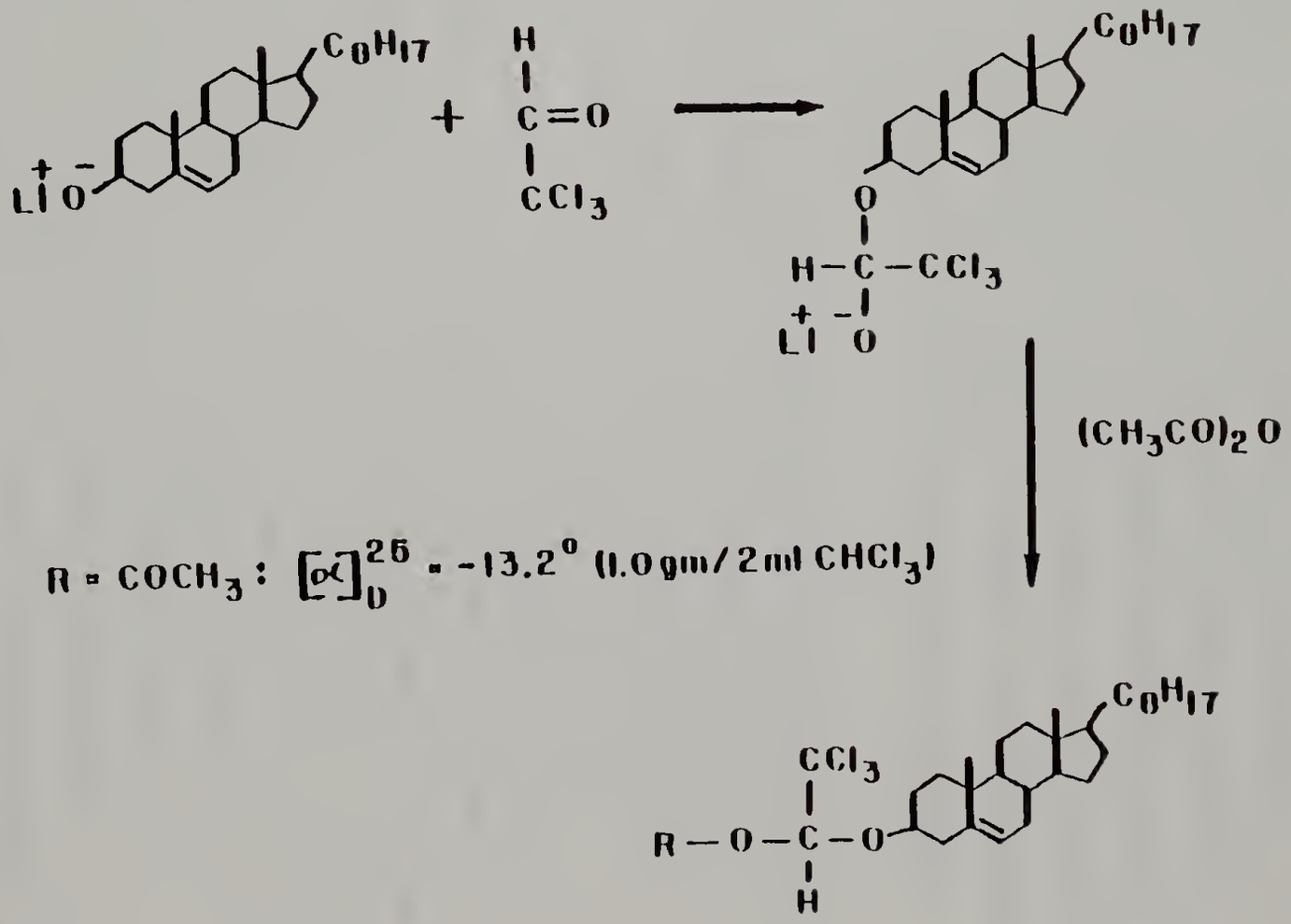
Thus far into the discussion, it has been stated that optically active polychloral derives its activity solely from the predominance of one helical screw sense, i.e. from macromolecular asymmetry, a requirement in the absence of main chain or side chain chiral centers. However, the activity contribution afforded by the presence of asymmetric initiator endgroups in the polymer has not been addressed extensively.

It was desired to synthesize a stable addition product which might serve as a low molecular weight model compound approximating endgroup structure (Figure 7). The full details of the synthesis are reported in Chapter II. Acetic anhydride was used to provide an acetate endcap for the addition product. It should be noted that the corresponding hemi acetal (via H+ endcap) is quite unstable and unsuitable for use as a model compound.

The specific rotation of the model compound at the sodium D-line was found to be (-)13.2° (1.0 g/2.0 mL $CHCl_3$), opposite in sign and several orders in magnitude smaller than the strong dextrorotatory behavior observed for optically active polychloral initiated by lithium-cholesten-3β-oxide. These results are in good agreement with similar endgroup studies undertaken by Harris (32) and earlier work by Marvel (57). In short, the presence of asymmetric initiator endgroups within the polymer contributes little to the observed rotations reported in this investigation.

Figure 7

Synthesis of an Addition Product Between
Lithium-Cholesten-3β-Oxide and Chloral.


C_8H_{17}
H
C=O
CCl_3
Li O
O
H—C—CCl_3
Li O
$(CH_3CO)_2O$
R = $COCH_3$: $[\alpha]_D^{25}$ = -13.2° (1.0 gm/2 ml $CHCl_3$)
CCl_3
R—O—C—O
H
C_8H_{17}

ORD Analysis of Optically Active Polychloral Initiated by Lithium-Cholestan-3β-Oxide

As previously discussed, ORD analyses can provide detailed information concerning the nature of molecular asymmetry. Earlier studies by Abe and Goodman (20, 58) suggested that ORD data typical of optically active polyaldehydes (with chiral centers) could be fitted by single term Drude equations. It was of interest to observe the ORD behavior of optically active polychloral which had been synthesized with steroid initiators.

A minimally birefringent polymer film which had been initiated with lithium-cholestan-3β-oxide (65°C, 10 minute holding time) was selected for this study. Using the spectral lines available on a standard polarimeter, a plain ORD curve shown in Figure 8 was constructed. Treatment of the data according to Yang and Doty (2) afforded a linear relationship between $[\alpha]_\lambda \lambda^2$ and $[\alpha]_\lambda$ (Figure 9) which confirmed that optical rotation measurements made at the sodium D-line were far removed from electronic transition regions. From the line's slope, the dispersion constant, λ_c, was found to be 197 nm, in good agreement with earlier values reported by Harris (32). To a first approximation, it would seem that the major electronic transition within the polymer lies near 200 nm. Unfortunately, optical rotations could not be directly measured below 300 nm due to unwanted absorption by the diphenyl ether used to soak the polymer films.

- TABLE 7 -

$[\alpha]_{\lambda}^{RT}$ and $[\alpha]_{\lambda}\ \lambda^2$

OPTICALLY ACTIVE POLYCHLORAL
INITIATED BY 0.25 MOL % LITHIUM-CHOLESTAN-3β-OXIDE

λ(nm)	$[\alpha]_{\lambda}^{RT}$	$[\alpha]_{\lambda}\ \lambda^2$
589	(+)2650	9.20×10^8
546.1	(+)3140	9.36×10^8
435.8	(+)5435	10.32×10^8
407.8	(+)6410	10.66×10^8
365.5	(+)8755	11.70×10^8
334.1	(+)11035	12.32×10^8

Figure 8

O.R.D. Curve for Optically Active Polychloral.

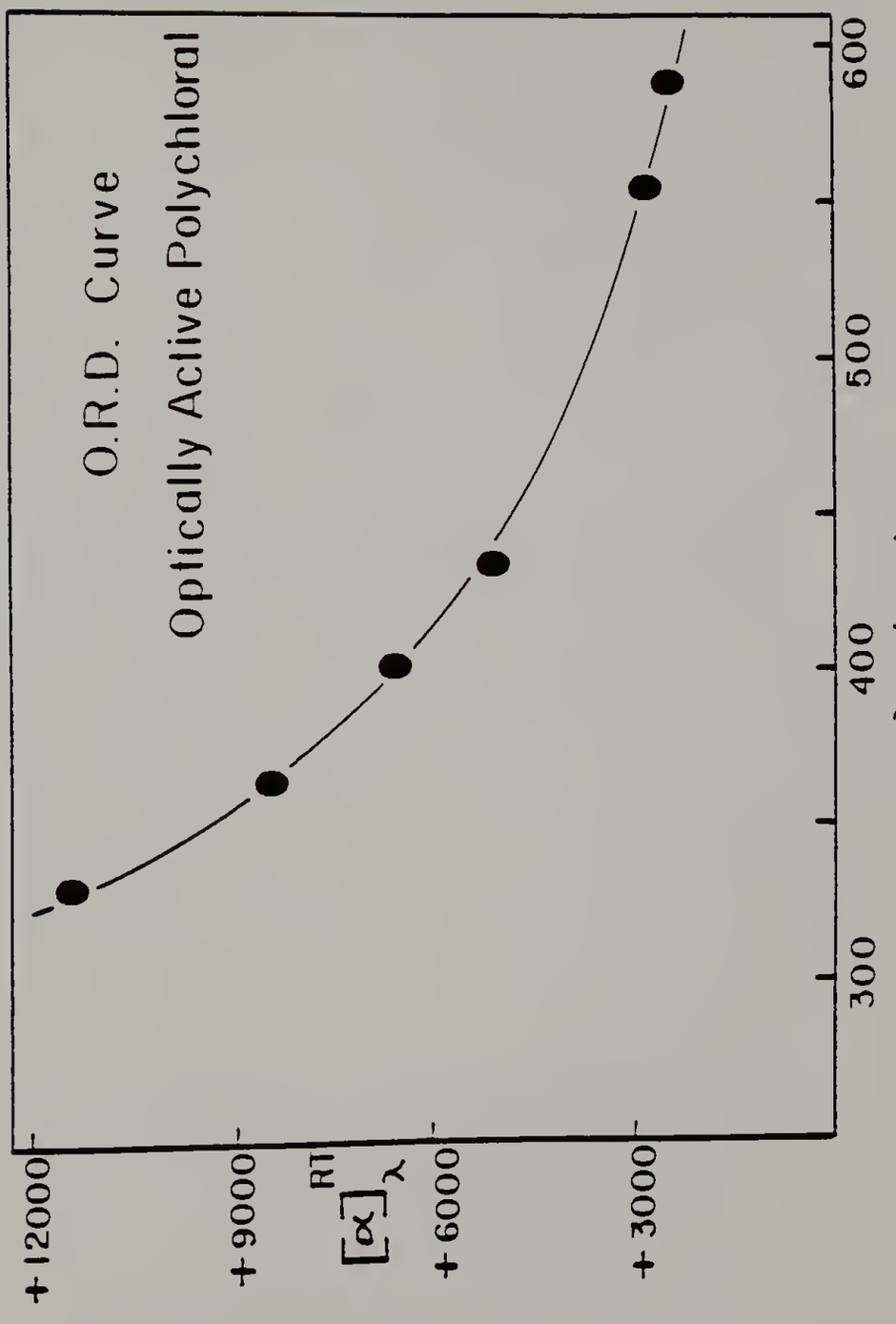
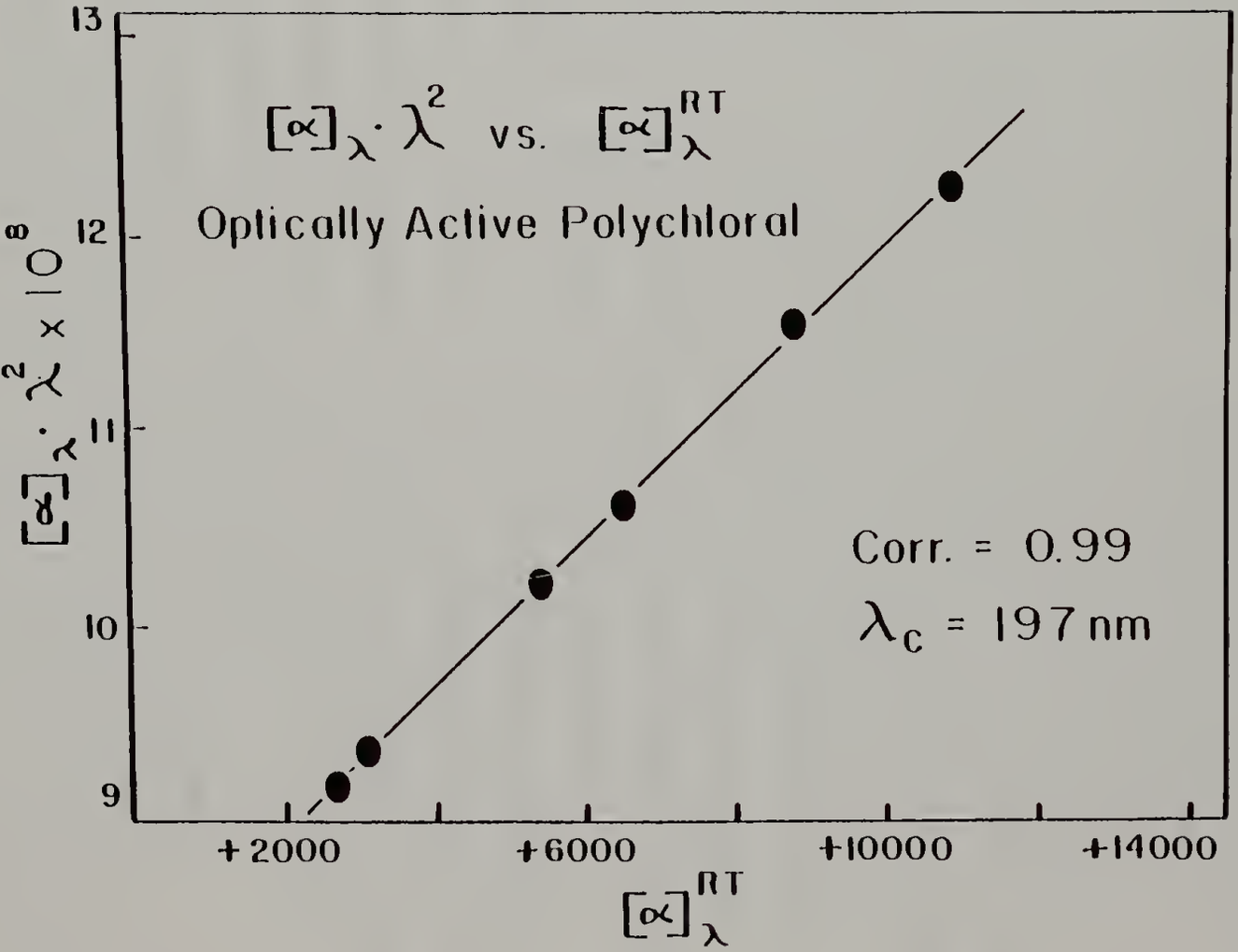

O.R.D. Curve
Optically Active Polychloral
+12000
+9000
+6000
+3000
$[\alpha]^{RT}_{\lambda}$
300
400
500
600
λ (nm)

Figure 9

Single Term Drude Plot (Yang-Doty Plot)
for Optically Active Polychloral.


$[\alpha]_\lambda \cdot \lambda^2$ vs. $[\alpha]_\lambda^{RT}$
Optically Active Polychloral
Corr. = 0.99
λ_c = 197 nm
$[\alpha]_\lambda \cdot \lambda^2 \times 10^8$
13
12
11
10
9
+2000
+6000
+10000
+14000
$[\alpha]_\lambda^{RT}$

Summary and Suggestions for Future Work

The primary goal of this investigation was to elucidate further the mechanisms responsible for optical activity in polychloral. Optically active polymer films were obtained by cryotachensic polymerization of initiated monomer solutions held isothermally at elevated temperatures for varying amounts of time. Variations in the magnitude and sign of the optical rotations were correlated to changes in holding time, holding temperature, and initiator structure, and could best be explained by the presence of a hypothetical chloral n-mer alkoxide in the holding solutions. Maximum optical rotations approached (+)4,500° at the sodium D-line and model endgroup studies confirmed that optical activity arose from the presence of macromolecular asymmetry, i.e. from the predominance of one helical screw sense in the polymer. Finally, a collaborative research effort was initiated with Professor Karl Schlogl at the University of Vienna for the purposes of further evaluating the potential of optically active polychloral as a chromatographic support.

At the present time, this author feels that a complete understanding of the processes responsible for optical activity in polychloral has not been reached. Future studies with chiral tertiary alkoxide initiators and optically active counterions are encouraged as is the polymerization of asymmetric haloacetaldehydes. The partial synthesis of chiral bromochlorofluoroacetaldehyde has recently been achieved in this laboratory (32).

The continued evaluation of optically active polychloral as a chromatographic support is also encouraged. The polymer's high optical activity, insolubility, and affinity for aromatic compounds make it ideally suited for studies of this type.

And finally, there exists a need to approach this entire problem from a theoretical point of view. The calculation of the conformational energies and relative probabilities of formation associated with the conformers of chloral n-mer could provide insight into the exact nature of the helix formation process and allow for the maximization of optical activity in polychloral.

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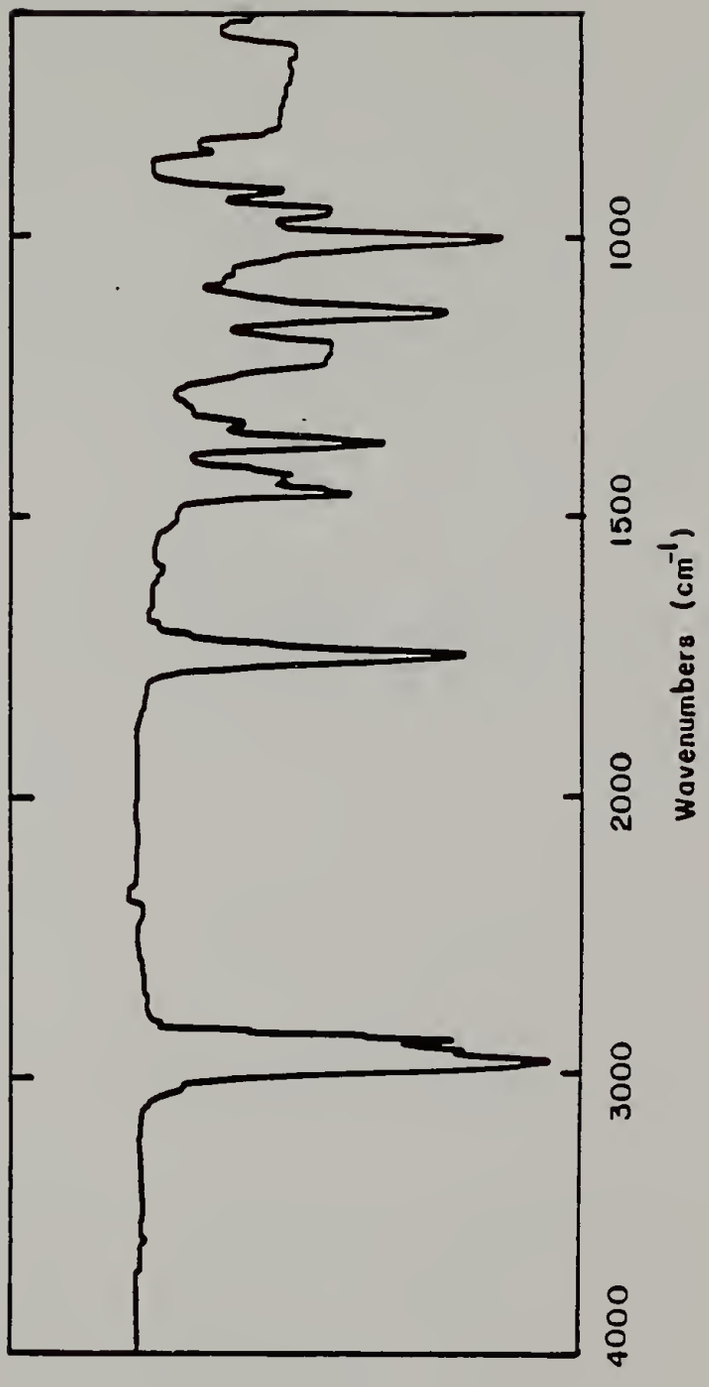
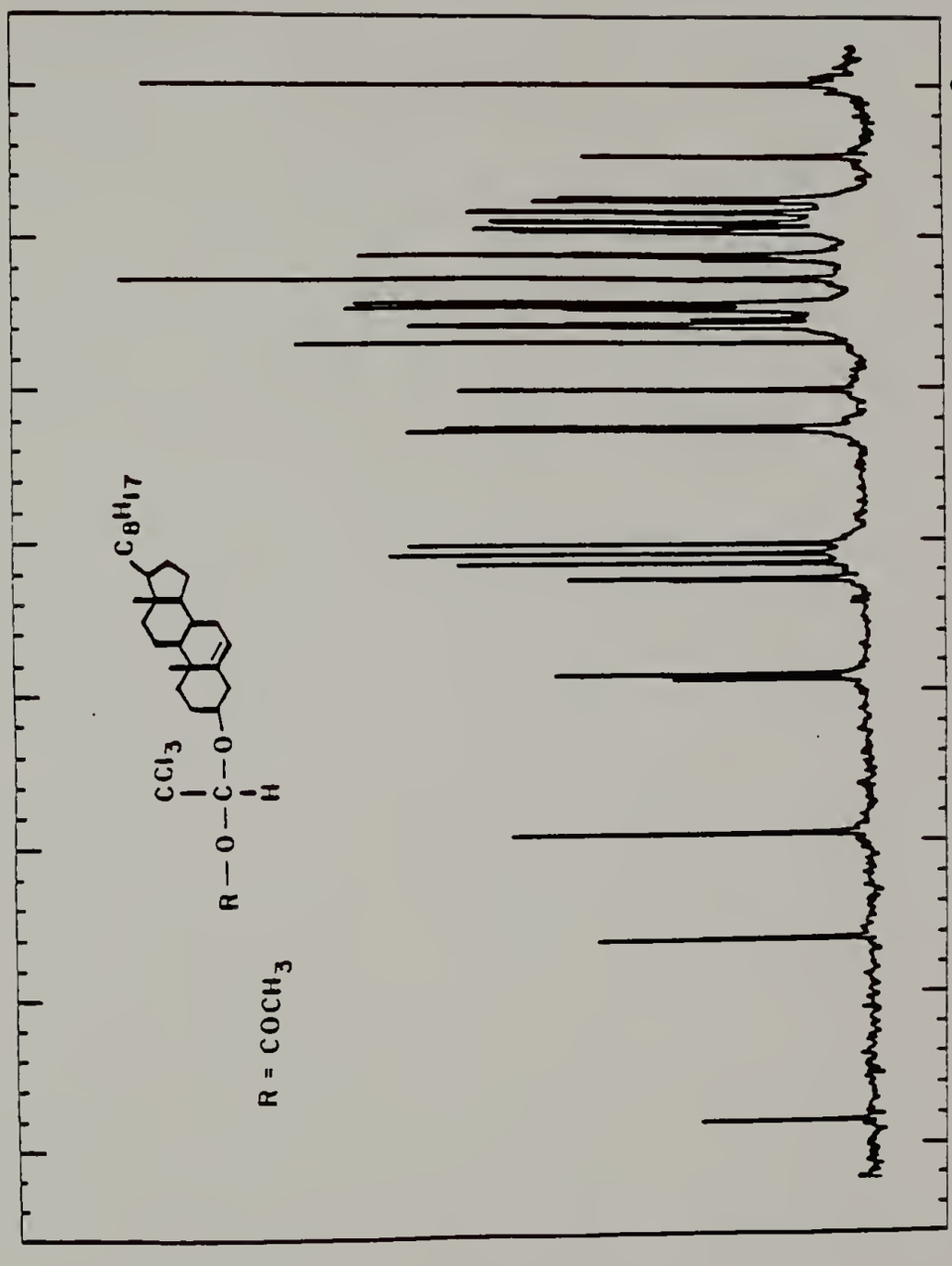
APPENDIX

Infrared Spectrum of Cholesten-3β-Oxide-
Chloral Addition Product.


4000
3000
2000
1500
1000
Wavenumbers (cm⁻¹)

^{13}C-NMR Spectrum of Cholesten-3β-Oxide-Chloral Addition Product.


C_8H_{17}
CCl_3
R — O — C — O
H
R = $COCH_3$
0
25
50
75
100
125
150
175
CHEMICAL SHIFT, ppm