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Synthesis and chiroptical properties of optically active polymers from [alpha], [alpha]-disubstituted-[beta]-lactones/

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SYNTHESIS AND CHIROPTICAL PROPERTIES OF OPTICALLY ACTIVE POLYMERS FROM α,α-DISUBSTITUTED-β-LACTONES

A Dissertation Presented

By

CHRISTIAN G. D'HONDT

Submitted to the Graduate School of the
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November, 1975

Polymer Science and Engineering

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(November, 1975)

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ABSTRACT

The crystalline properties of poly-α, α-disubstituted-β-propiolactones having different contents of isotactic configuration were studied.

Poly-(-)-α-phenyl-α-ethyl-β-propiolactone was prepared from a starting material having an optical purity of 80%. Its properties were compared to the polymers obtained from racemic and from 50% optically pure starting materials.

Poly-α-methyl-α-isopropyl-β-propiolactone was prepared from racemic monomer. The polymer was fractionated into a methanol soluble and a methanol insoluble fraction. The latter showed a crystalline melting whereas the former exhibited only a softening temperature.

An attempted resolution of the intermediate α-methyl-α-isopropyl-β-aminopropionic acid ethyl ester yielded a material of only 15-20% optical purity.

The chiroptical properties of the optically active poly-(-)-α-phenyl-α-ethyl-β-propiolactone were recorded in solution and in the solid state. No evidence for a secondary structure in solution was found.

X-ray diffraction of optically active and racemic poly-α-phenyl-α-ethyl-β-propiolactone showed that both polymers had a high degree of crystallinity. The differences in the crystalline peaks and in the melting points suggested that the optically active and the racemic polymer crystallize in different structures.

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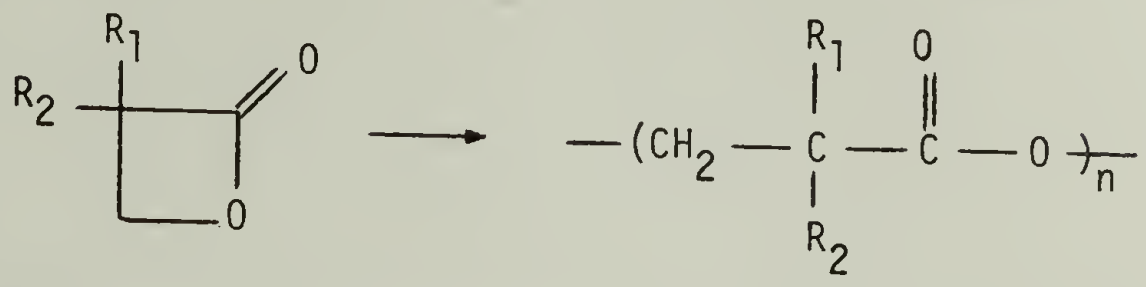
INTRODUCTION

Poly-(α,α-disubstituted-β-lactones) are obtained by the ring-opening polymerization of the corresponding β-lactones:



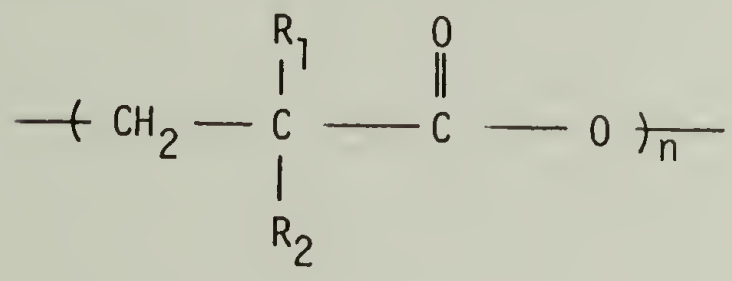
The first to investigate the possibility of obtaining high-molecular weight linear polyesters via this route was Gresham et al.[1] in 1948. Using both cationic and anionic initiators they obtained low molecular weight polymers only. It was around 1960 that Fischer and Etienne[2,3,4] successfully synthesized for the first time high molecular weight aliphatic polyesters from the ring-opening polymerization of α,α-disubstituted-β-lactones.

Subsequently a series of papers and patents appeared which dealt with the polymerization of β-lactones, most of which were concerned with the two simplets members of this family of monomers, β-propiolactone and the symmetrically substituted α,α-dimethyl-β-propiolactone (pivalolactone).

Since then these polymers have become of increasing interest because of their unique properties, although high monomer cost and the difficulty of introducing a new polymer into the market remains a problem. Continuous polymerization processes up to the pilot-plant stage have been carried out for polypivalolactone[5], and eventually polyesters from other α,α-disubstituted-β-lactones could find their

way into the market and compete against other plastics.

Studies of the crystalline and mechanical properties of the polymer of α-methyl-α-n-propyl-β-propiolactone have been made by Allegrezza[6,7]. It has been proven by X-ray analysis[8], that most α,α-disubstituted-β-propiolactone polymers have two crystalline forms: one is a 2_1-helix, the other, a planar zig-zag conformation. The repeating unit of these polymers is the following:



If there are two different substituents at the α-carbon ($R_1 \neq R_2$) such that an asymmetric center is present, one would not expect the polymer to be crystalline, unless it would be either stereoregular to some extent or capable of crystallizing despite the irregularities caused by the asymmetric center in the monomer unit.

The polymers prepared from the D,L monomer mixture, as expected, showed no optical rotation[7], nevertheless they were crystalline. There are several different possibilities which could account for the crystallinity of the polymer, as follows:

1) there is a mixture of chirally homogeneous polymers; or
2) there are randomly formed sequences of sufficient length of either or both D or L units to permit crystallization; or
3) the polymer has a syndiotactic structure, which means alternating D and L monomer units; or

4) there is no need of any stereoregularity in order for these polymers to be crystalline.

In the case of the planar zig-zag conformation the syndiotactic as well as the isotactic structure may not be needed[7], and an atactic structure has been postulated. For the helical form, molecular models have shown that a helix of given handedness can accommodate either a D or an L monomer unit[8].

To resolve this problem one would have to prepare optically active polymers and determine the crystalline properties of the products. This was the aim of the present project.

Synthesis of α,α-disubstituted-β-lactones. The first review article on the synthesis of β-lactones was published by Zaugg[9] in 1954. The article gives a survey of the field up to 1953 and contains numerous references. About ten years later two other review papers on β-lactones appeared, one by Etienne and Fischer[10] the other by Kroper[11]. These articles cover the field up to 1962. Another ten years later the latest review on β-lactones was published by Brash, et al.[12].

In Figure 1 some possible ways of synthesizing α,α-disubstituted--β-lactones are outlined.

The route through the ketene[9,10,11,12] has no particular advantage, except the saving of one step, compared to the route through the β-halogen acid. Because the α,α-disubstituted-malonic acid diethyl esters are not commercially available, there is no difference in the first two steps.

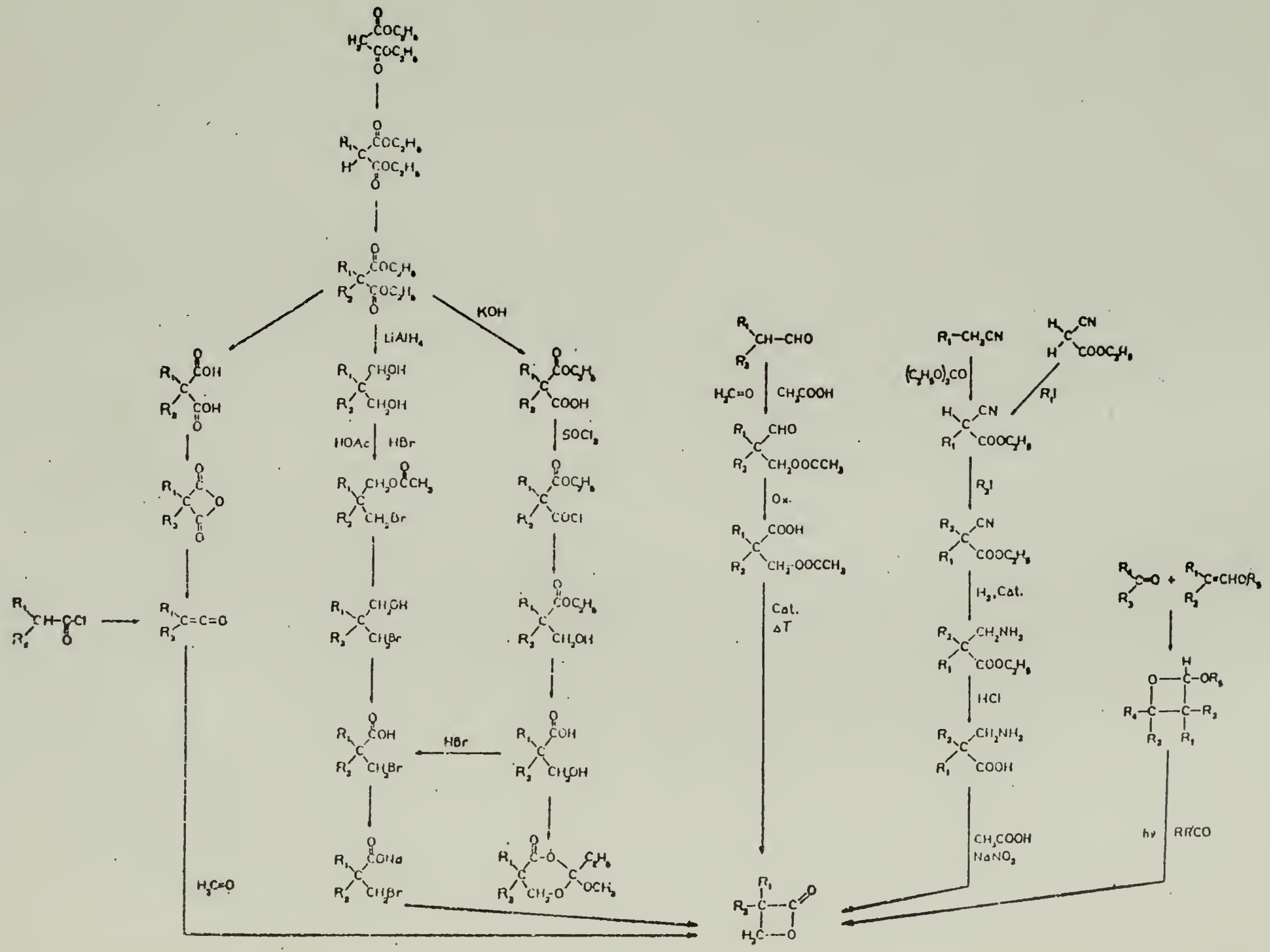


FIGURE 1. SYNTHESIS OF α,α-DISUBSTITUTED-β-LACTONES

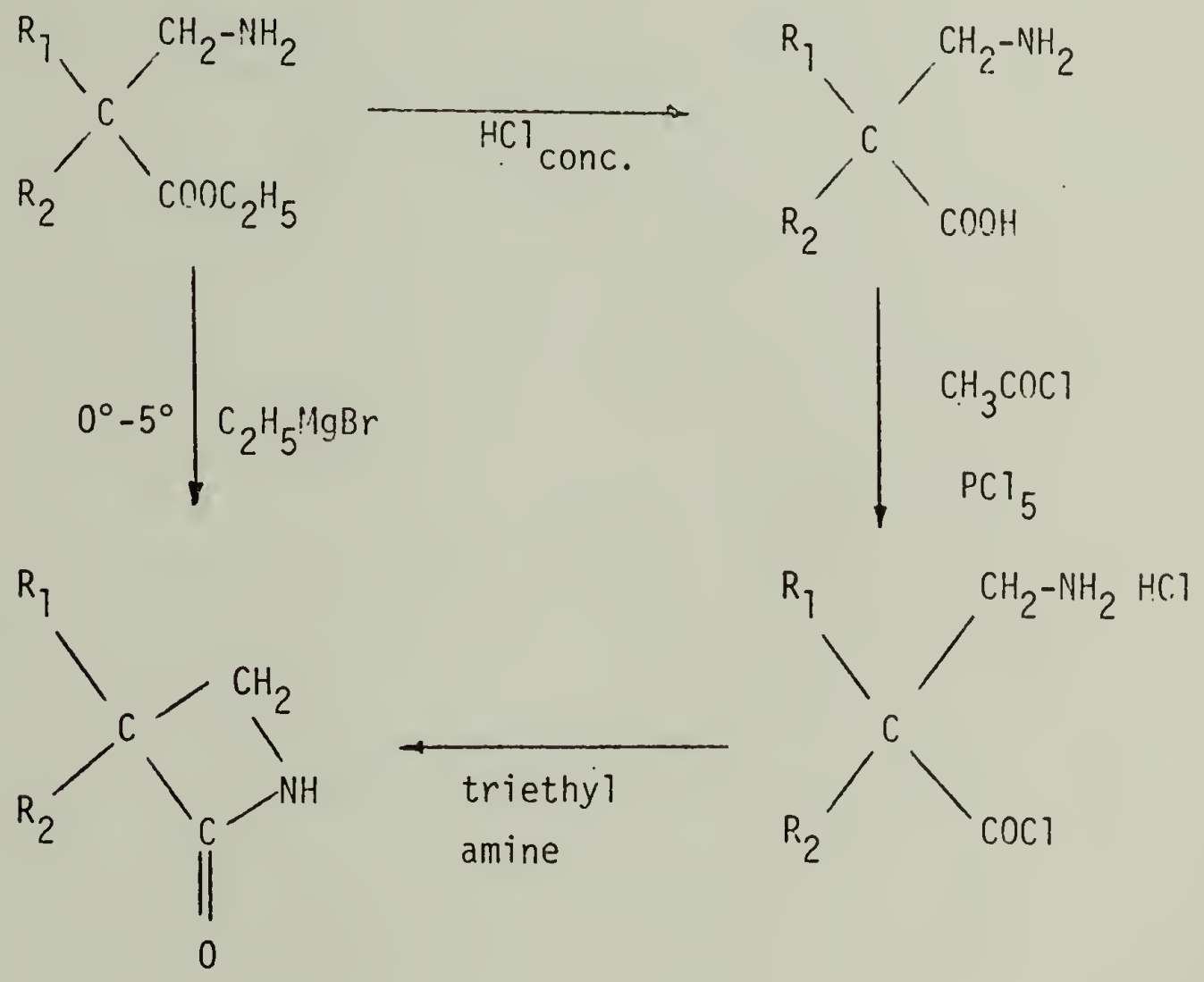
In the ketene-synthesis a low yield is probable, and besides that a dimerization of the product is to be expected. Another point of importance is that the synthesis of the lactone from the ketene goes through symmetric intermediates, and thus a separation of the optical isomers is not possible.

The synthesis of the lactone starting with malonic acid esters via the disubstituted propanediols covers eight steps[2,6]. A variant of this route, as outlined in the scheme, goes from the disubstituted malonic acid diethyl ester through the monoethyl ester to the acid chloride monethyl ester[13]. The latter is reduced selectively to the β-hydroxyester, which is converted to the β-hydroxyacid. The separation of the optical isomers has already been carried out at the stage of the disubstituted malonic acid monoethyl ester[14].

Another possibility[15] to make the lactone is to start with an aldehyde, convert it to a β-acetoxyaldehyde and oxidize the latter to the β-acetoxyacid. The lactone is finally obtained by vapor-phase pyrolysis of the acid. For the pyrolysis, temperatures around 300°C are needed, and this reaction path is thus also excluded for our purpose because racemization has to be expected at such high temperatures.

Two newer methods of β-lactone synthesis should be mentioned also. The first involves ring-contraction of 4-oxo-1,3-dioxanes[16] but is no improvement because it leads over the disubstituted hydroxyacid, which is not commercially available and would have to be synthesized. The second, which goes through 2-alkoxyoxetanes[17], is probably not favorable because the separation of the optical isomers could cause some problems.

The most interesting route appears to be the one starting with the ethyl cyanoacetate which yields finally the α,α-disubstituted-β-aminoacids[18,19,20]. Advantages of this method are that there are only five steps and the last step (diazotization) is carried out at 0°C, which would minimize the racemization, and that it readily leads also to the corresponding lactams[18]:



These α,α-disubstituted-β-propiolactams form a potentially interesting family of monomers and the polyamides of these could be of considerable interest as new materials.

Polymerization of β-lactones. Etienne, Fischer, et al.[2,3,4,21] obtained high molecular weight aliphatic polyesters from β-lactones using betaine initiators. Since then a variety of initiators have

been used for the polymerization of β-lactones and Allegrezza[6] and and Agostini[22] discuss those in their thesis. Table I summarizes the reported initiators of β-lactone polymerization and gives the appropriate references.

TABLE I

Reported Initiators of β-lactone Polymerizations

INITIATOR	REFERENCES
Betaines	23,24,25,26,27,28,29,30,31
Tertiary Phosphines	32,33,34,35,36,37
Phosphorus Amides	38
Lewis Acids	26,39,40,21,42,43,44,45,46
Acids (CF_3COOH)	26,39,46,47,48
Aluminum Alkyls	39,41,49,50,51
Alkali	26,47
Metals (Na)	39,47,49
Quat. Ammonium Salts	29,52,53,54
Metal Alkoxides	55
Potassium Imides	56
Organometallic	57,58,59,60,61
Tert. Sulfonium Salts	62
Org. Heterocyclic Compounds	63
Phenyl Alkyl Silylamines	64
Organo Silanolates	65
p-chlorobenzenediazonium-hexafluorophosphate	66
Cyclic Sulfides	67
Sodium Acetate	68
Pyridine	69

C H A P T E R I I

RESULTS AND DISCUSSION

Introduction. It was clear from the beginning that for the present work very high optical purity materials would be needed in order to be able to make conclusive investigations on the stereochemistry of the α,α-disubstituted-β-lactone polymers. Thus an optical purity of at least 90% was set as goal for the monomer which in turn would give a polymer with at least 90% isotactic configuration.

The resolution of an organic compound is still very much an art in which trial and error is a common approach, and the outcome can never be certain at the beginning of the work. To obtain optically-active compounds, different experimental techniques are used, the more important of which are the following:

1. Spontaneous resolution by crystallization
2. Resolution via diastereomeric salt formation
3. Enzymatic optical activation
4. Kinetic resolution
5. Chromatographic resolution
6. Asymmetric synthesis
7. Stereospecific synthesis from chiral precursors

From these possible methods the best ones had to be evaluated and the less promising ones had to be eliminated. Spontaneous resolution by crystallization could not be expected to occur in

our case and a seeding with optically-active compound had to be excluded because the aminoacids to be resolved were not available as separate isomers. Enzymatic optical activation had to be excluded since no suitable enzymes are known or available in the present case.

In the kinetic resolution optical enrichment is obtained by the difference in the rate of reaction of enantiomers with chiral reagents. One drawback of this method is that high optical purity is rarely attained, which thus makes this method unsuitable for our purposes.

The chromatographic resolution is a very interesting approach which requires stereoselective sorption of enantiomers on, or in, chromatographic columns. This technique can be applied to polymers also, if the optically inactive polymer is actually a mixture of pure D- and L- homopolymer, as is the case for some poly-α-olefins[70]. In the present case this situation is unknown, and to find suitable optically-active polymers for adsorption in a chromatographic column would be a large and a separate research project in itself. Asymmetric synthesis would be a possible approach, however, in this type of synthesis optical purities of 20-30% are more common and purities of higher than 90% are seldom obtained.

The stereospecific synthesis from chiral precursors requires that such a precursor is available and suitable for obtaining the desired compound. This method had been used by Overberger and

Kaye[71] for the synthesis of their optically-active caprolactones. In our case such optically active precursors were not available.

Having excluded six out of the seven possible methods listed above, this leaves one method, the resolution by diastereomeric salt formation. This method has the advantage that usually very high optical purities can be obtained once a good resolving agent has been found. In the present case, were α,α-disubstituted-β-aminoacids had to be separated it had other advantages in that many resolving agents for α-aminoacids are known and could be evaluated on the β-aminoacids. Furthermore, in the case that base resolution would not work, one would still have the acid function for resolution to be tried.

In conclusion, resolution via diastereomeric salt formation was considered to be the best and only way to go in the present work.

Resolution via diastereomer formation. The resolution of a basic racemic compound by diastereomer salt formation using an optically-active acidic resolving agent can be drawn schematically as follows:

$$\left\{\begin{matrix}\text{(+)-Base}\\ \\ \text{(-)-Base}\end{matrix}\right\} + \text{(-)-Acid} \rightleftharpoons \begin{matrix}\text{(+)(-)-Salt}\\ \\ \text{(-)(-)-Salt}\end{matrix}$$

Requirements for a good resolving agent are: a) high optical purity because this determines the maximum optical purity possible for the compound to be resolved; b) availability in both enantiomers;

c) low price if available commercially, otherwise d) relatively easy to synthesize; e) stable under the reaction-conditions and on the shelf; and if possible, f) it should be non-toxic.

The requirements for an optimal separation are: a) complete and fast reaction under mild conditions which do not destroy either substrate or resolving agent; b)easy isolation of product with minimal loss; c) easy and complete separation of the diastereomer product in high yield; d) facile and complete reversal of the equilibrium to the desired optically active compound under conditions minimizing racemization; e) isolation of both enantiomers, each optically pure; f) recovery in high yield and reuse of the resolving agent should be facile; g) choice of right solvent; h) satisfactory crystallization.

The most important of the above features to be met is the easy and complete separation of the diastereomer product. Even if in a resolution a salt is formed and crystallization occurs the differences in solubility between the two diastereomeric salts may not be large enough to allow a separation. The equilibrium between diastereomer in solution and in crystalline form is influenced by the choice of solvent, and the best solvent will always have to be found by trial and error.

Once a racemic compound has been partially or totally resolved in its isomers, the optical purity of the obtained product has to be measured. If the rotation of the pure enantiomer is known, the

optical purity can be calculated according to the following formula:

$$\% \text{ optical purity} = \frac{[\alpha] \text{ mixture}}{[\alpha] \text{ pure enantiomer}} \times 100$$

If, however, the rotation of the optically pure compound is not known, or, if one doesn't know the optical purity of the compound obtained after only partial optical enrichment in the recrystallization of a diastereomer, the above formula cannot be used.

In the present study the optical purity of the α,α-disubstituted-β-aminoacids to be resolved was not known and determination of optical purity had to be carried out.

Once the rotation of the optically pure compound was established, the completeness of resolution could be monitored polarimetrically.

Measurement of optical purity by NMR. Different methods for the determination of optical purity exist, such as: thin-layer chromatography, gas chromatography, NMR-spectroscopy etc., these methods have been reviewed by Raban and Mislow[73].

In the present study the optical purity of the resolved α,α-disubstituted-β-aminoesters was carried out using NMR-spectroscopy and a chiral shift reagent. This method is based on the pseudo-contact-shift differences induced on a compound in the presence of a chiral shift reagent. In most cases a solution having a slight excess in substrate compared to shift reagent is used. The solvent need not be optically active. Typically a molar ratio of shift reagent to substrate of 0.6 - 0.8 is used. A similar method, based

on chemical-shift nonequivalence of enantiomers in chiral solvents has been reported[73,74]. However, the magnitude of the chemical-shift difference between corresponding protons of enantiomers obtained using this technique is normally small[74].

The method of using a chiral shift reagent for the direct determination of enantiomeric compositions had been employed successfully by several investigators. H. L. Goering, et al.[75] applied the method to polar chiral substances such as alcohols, ketones, esters, epoxides and amines. Whitesides and Lewis[76] synthesized a series of europium shift reagents which they used to determine the enantiomeric purity of relatively nonbasic substances.

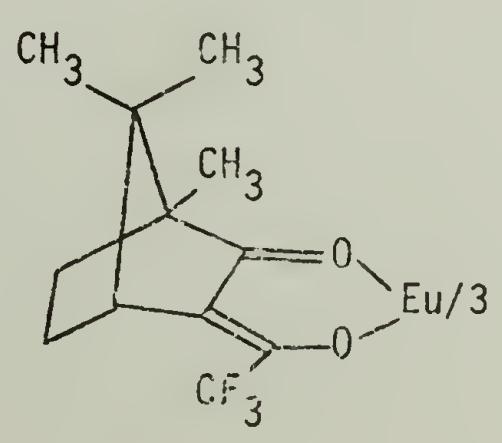
The two α,α-disubstituted-β-aminopropionic acid ethyl esters investigated in this study were:

α-phenyl-α-ethyl-β-aminopropionic acid ethyl ester

α-methyl-α-isopropyl-β-aminopropionic acid ethyl ester

The α-phenyl-α-ethyl-β-aminopropionic acid ethyl ester had been resolved previously by Fontanella and Testa[77]. They had reported a specific rotation of + 27.1° for the (+)-isomer, however, no optical purity was given in their paper.

The shift reagent used was Tris[3-(trifluoromethylhydroxymethylene)-d-camphorato] europium (III):



The NMR spectra for the optically active compounds with different ratios of shift reagents are shown in Figure 2 and Figure 3 for the α-phenyl-α-ethyl-β-aminopropionic acid ethyl ester. Large differences between corresponding resonances of the enantiomers dissolved in carbon tetrachloride containing the shift reagent are observed. The large downfield shift of the resonances of the amino-ester from their positions in the absence of the shift reagent (see Appendix I) can be explained as a result of the pseudocontact interaction between the europium (III) ion and a rapidly exchanging mixture of coordinated and free amine. The pseudocontact shift differences for corresponding protons of (+)-and (-)- form range from 0.25 ppm for the ortho-hydrogen of the aromatic ring to 0.03 ppm for the methylene proton of the ester group (Figure 4). These separations depend strongly on the ratio of the shift reagent to substrate as can be seen from Figure 2, where a series of solutions is shown in which the above ratio varies between 0.75 for curve 1 and 0.37 for curve 5. The assignment for the protons of the α-phenyl-α-ethyl-β-aminoester in presence of the shift reagent in Figure 2, curve 3, is given as follows:

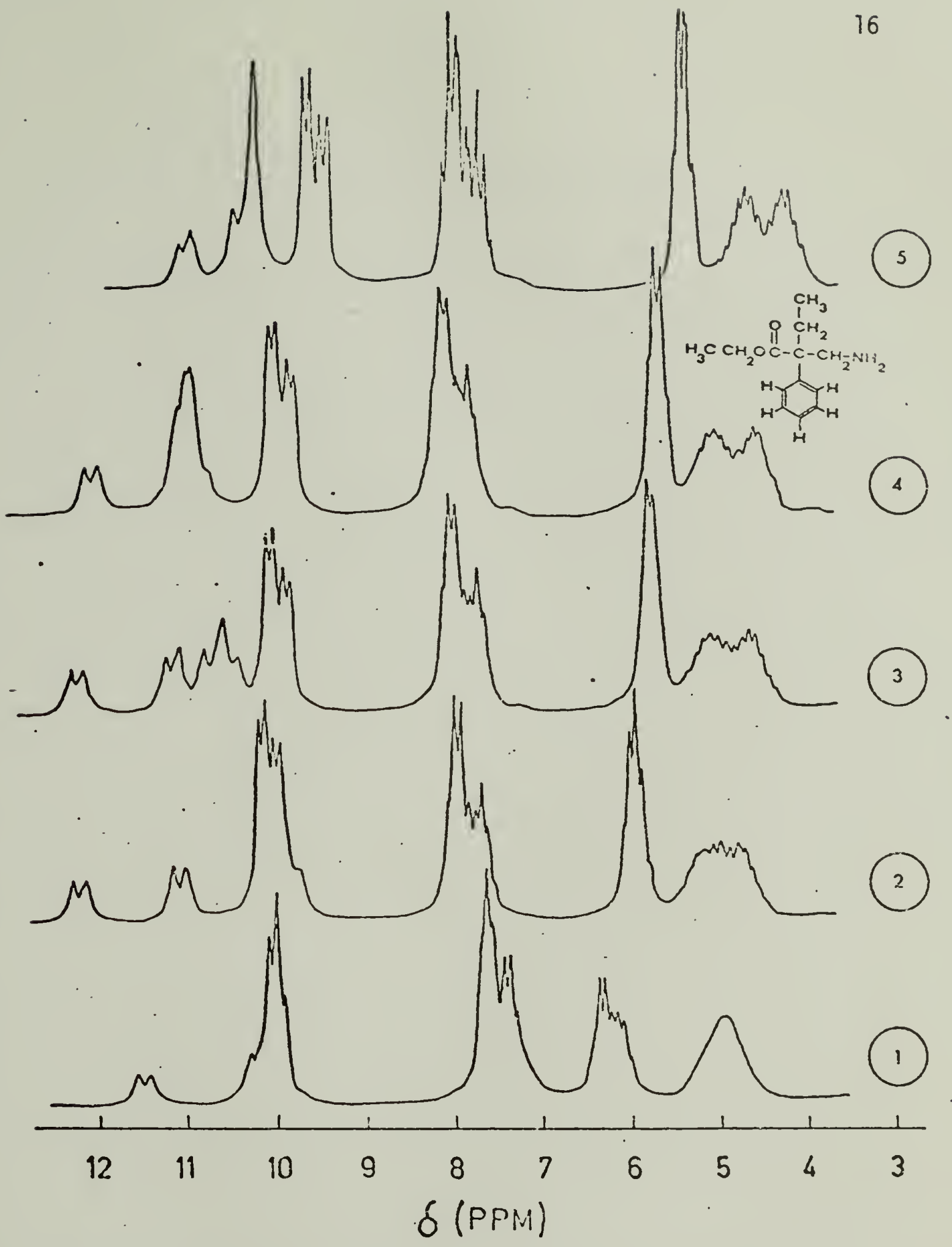
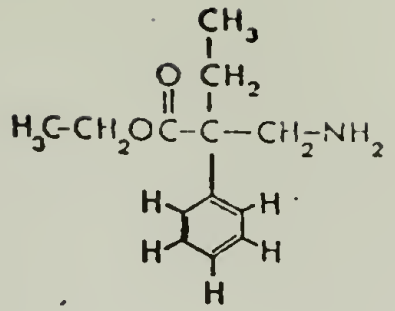


FIGURE 2. NMR SPECTRA OF CCl_4 SOLUTIONS OF α-PHENYL-α-ETHYL -β-AMINOPROPIONIC ACID ETHYL ESTER IN THE PRESENCE OF DIFFERENT AMOUNTS OF EUROPIUM (III) SHIFT REAGENT



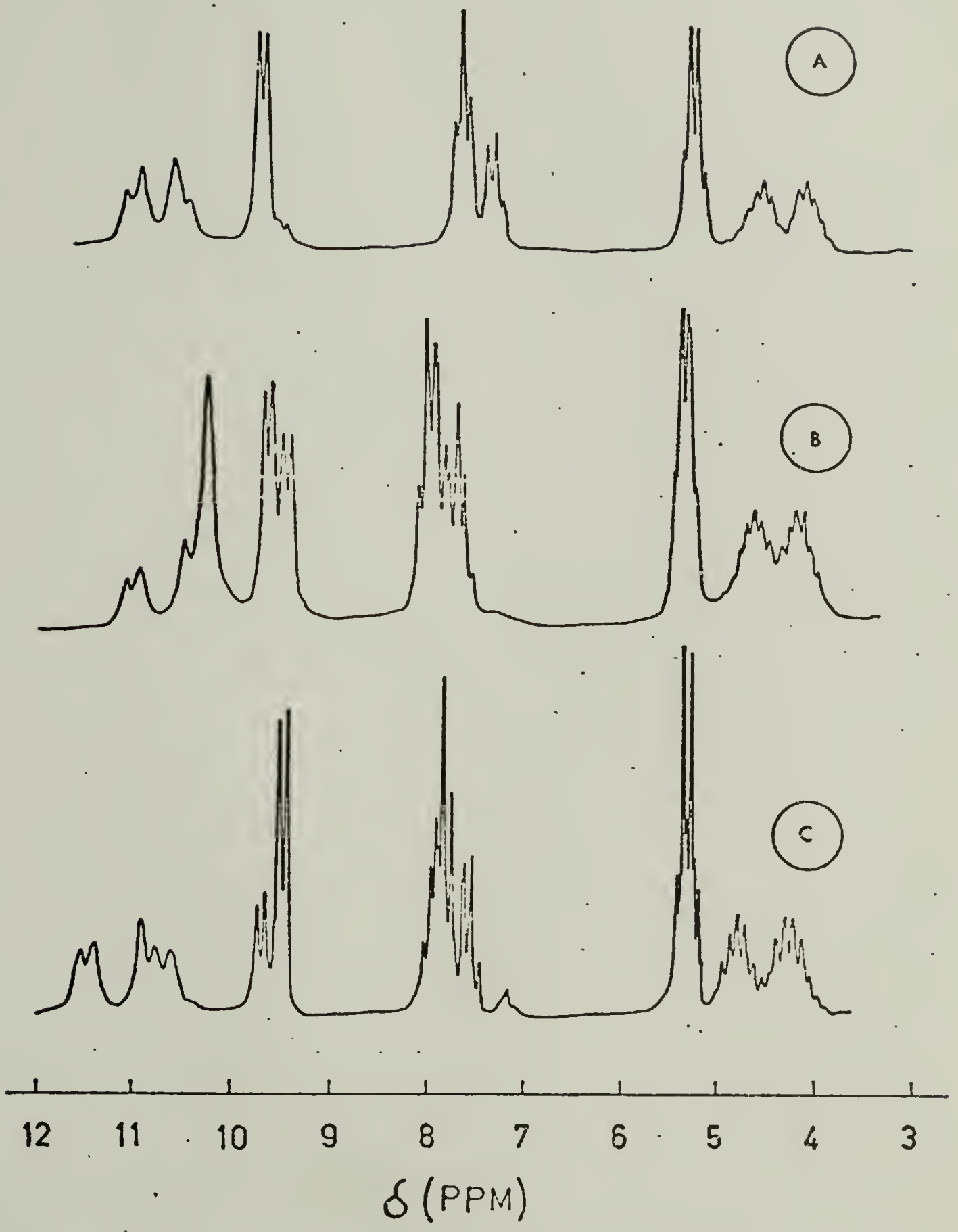


FIGURE 3. NMR SPECTRA OF CCl_4 SOLUTIONS OF α-PHENYL-α-ETHYL -β-AMINOPROPIONIC ACID ETHYL ESTER OF DIFFERENT OPTICAL PURITY IN THE PRESENCE OF EUROPIUM (III) SHIFT REAGENT

OPTICAL PURITY 80% (A); 12.6% (B); 47% (C)

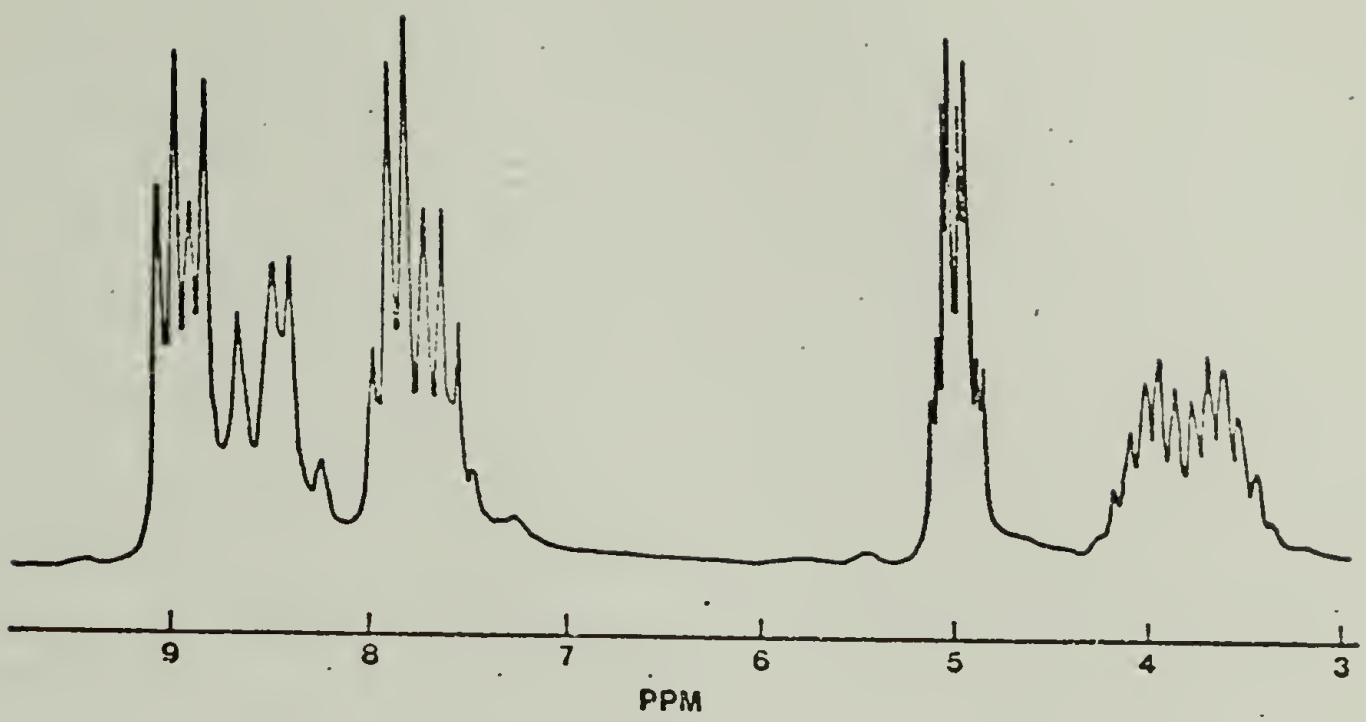
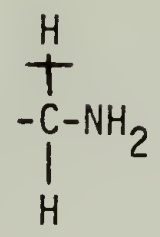
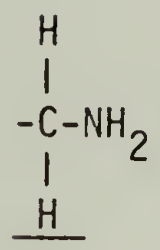


FIGURE 4. NMR SPECTRUM OF A CCl_4 SOLUTION OF α-PHENYL-α-ETHYL-β-AMINOPROPIONIC ACID ETHYL ESTER IN THE PRESENCE OF EUROPIUM (III) SHIFT REAGENT. PSEUDOCONTACT SHIFT DIFFERENCE OF THE METHYLENE PROTONS OF THE ESTER GROUP AT 5PPM.

Going from left to right, i.e. upfield (Figure 5),

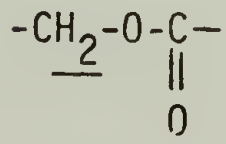


11.8 ppm*

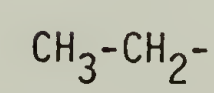


10.8 ppm

<u>ortho</u> hydrogen of aromatic ring	10.0 ppm
<u>meta</u> hydrogen of aromatic ring	8.0 ppm
para hydrogen of aromatic ring	7.8 ppm



5.8 ppm



4.9 ppm

*TMS was used as internal standard.

The methyl protons are not shown in the spectra because below 3 ppm the protons of the shift reagent interfere with the protons of the substrate. From the <u>ortho</u>-protons of the aromatic ring in Figure 3 (curve B), and through comparison with practically optically pure (curve A) and 25% (+)/75% (-) enantiomeric mixture (curve C), it can be seen that a slight enrichment of (+)-isomer was present

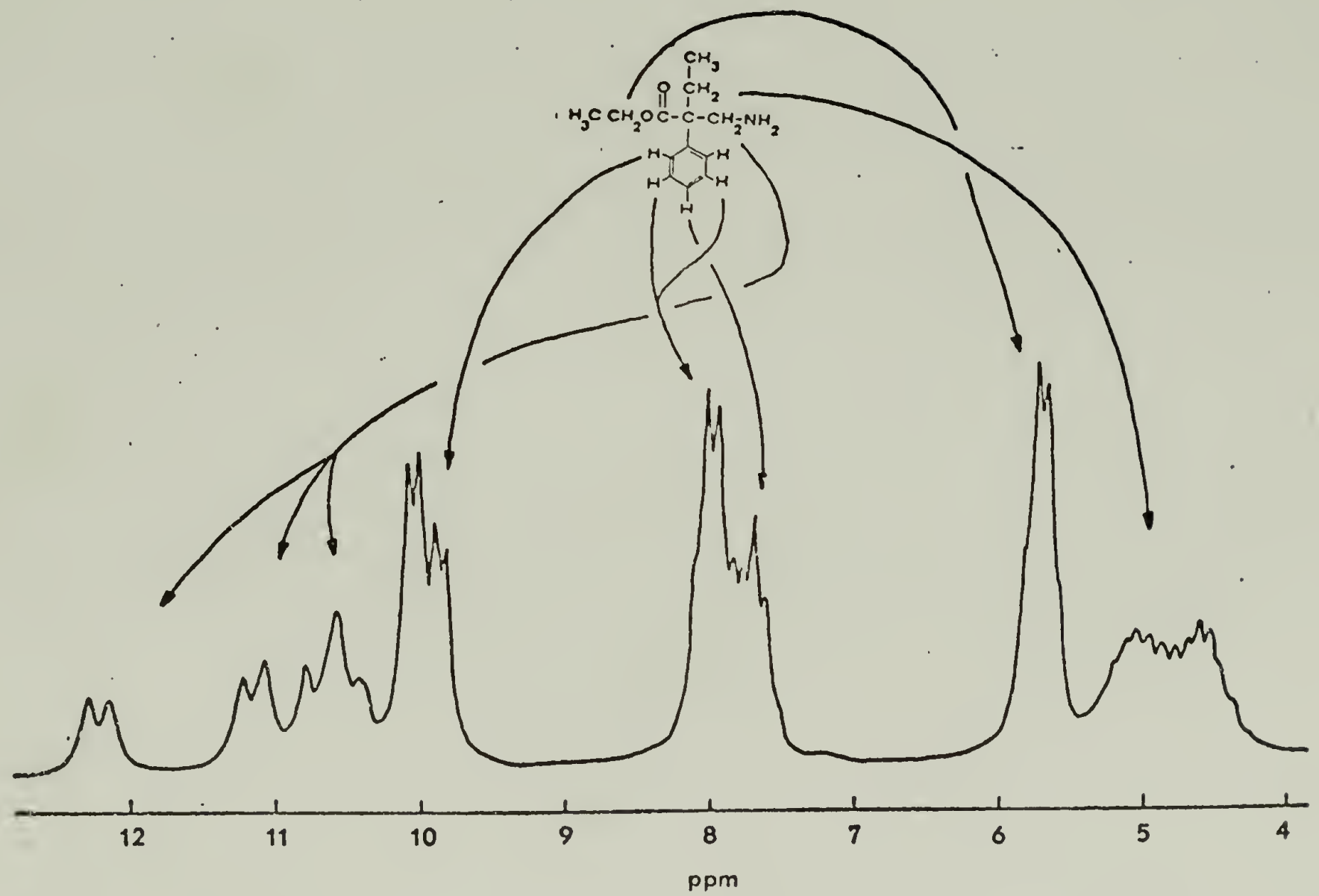


FIGURE 5. NMR SPECTRUM OF A CCl_4 SOLUTION OF α-PHENYL-α-ETHYL-β-AMINOPROPIONIC ACID ETHYL ESTER IN THE PRESENCE OF EUROPIUM (III) SHIFT REAGENT. ASSIGNMENT OF CHEMICAL SHIFTS.

in the substrate used for the concentration studies in Figure 2. Thus in the case of α-phenyl-α-ethyl-β-aminopropionic acid ethyl ester, optical purity could be measured by NMR, using an europium (III) shift reagent and by monitoring the signals for the ortho-proton of the aromatic ring in the spectrum.

It can be seen from Table II that the optical purity measurements by NMR and polarimetry are in reasonable agreement. The former are probably somewhat more accurate because the rotation measurements are subjected to larger errors. Another possibility to account for the difference is, that the value of 27.1° obtained by Fontanella[77] did not correspond to 100% optical purity, which would explain the deviations in Table II.

The result for the second compound to be studied, α-methyl-α-isopropyl-β-aminopropionic acid ethyl ester, is shown in Figure 6. A large pseudocontact shift difference is observed in this case only for the methyl protons in α-position. The difference is between 0.25 and 0.3 ppm, depending on concentration. The signal for the methylene protons next to the amine at 9 ppm is similar in shape to that observed for the α-phenyl-α-ethyl-β-aminopropionic acid ethyl ester.

The methylene protons of the ester group appear at 5.7 ppm, and the methine proton of the isopropyl side group has a chemical shift of 5.1 ppm. The methyl proton in α-position gives a doublett at 4 ppm. Thus, in presence of the europium (III) shift reagent, the corresponding protons of the enantiomers are not equivalent in

TABLE II

Optical Purity of α-Phenyl-α-ethyl-β-aminopropionic Acid Ethyl Ester

Rotation $[\alpha]_D$ (c=2, MeOH)	Optical purity % Polarimetric[c]	by NMR	Composition[a] Isomer (+) %	(-) %	Spectrum
------	-------	12.6	56.3	43.7	Fig. 3 Curve B
-14.5°	53.5	47.0	26.5	73.5	Fig. 3 Curve C
+24.8°[b]	91.0	80.0[b]	90.0	10.0	Fig. 3 Curve A

a) by NMR

b) the measurement was done after the compound had been stored for over 3 months on the shelf during which some racemization might have occurred.

c) using 27.1° as 100% optically pure; value obtained by Fontanella[77]

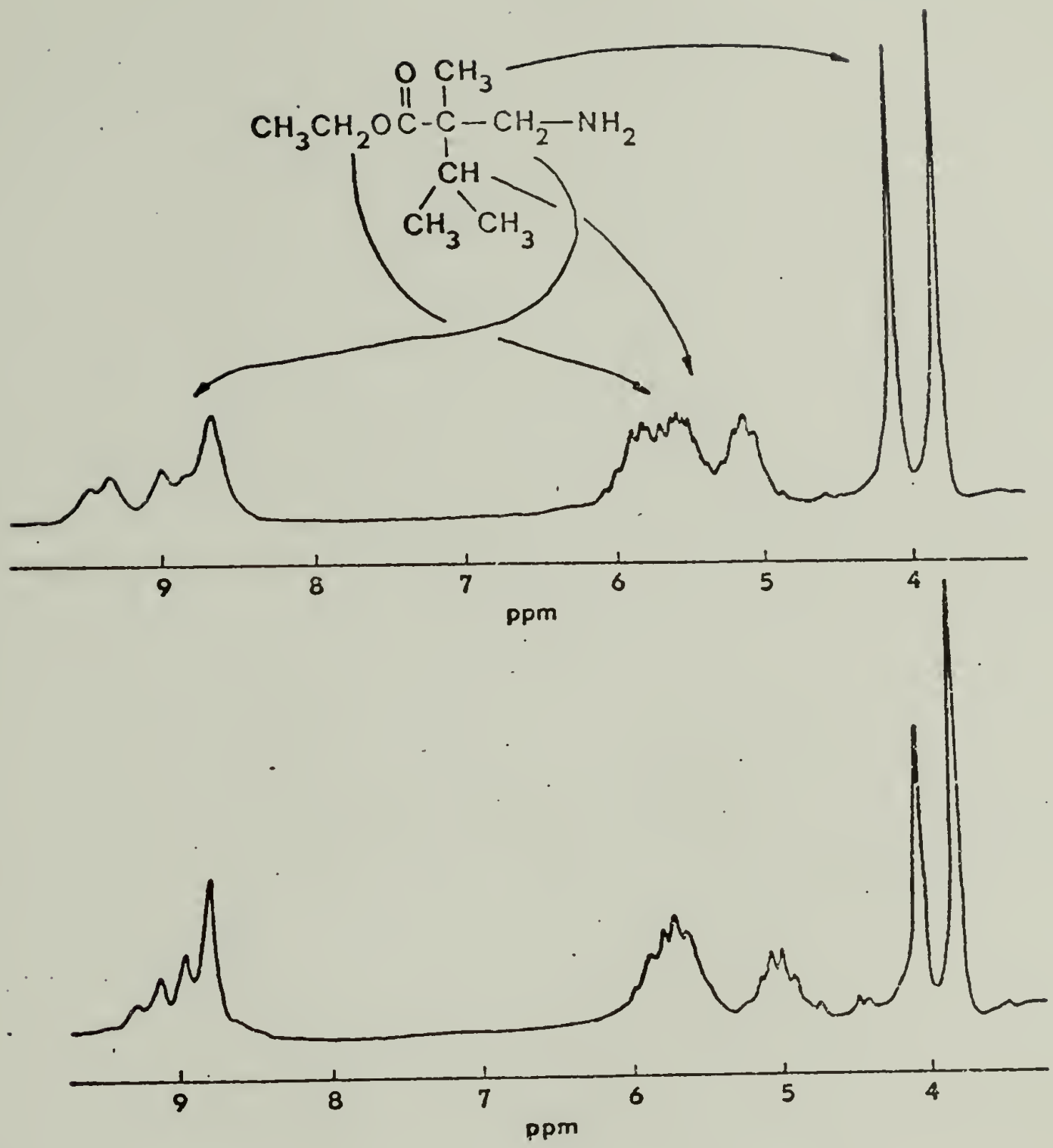


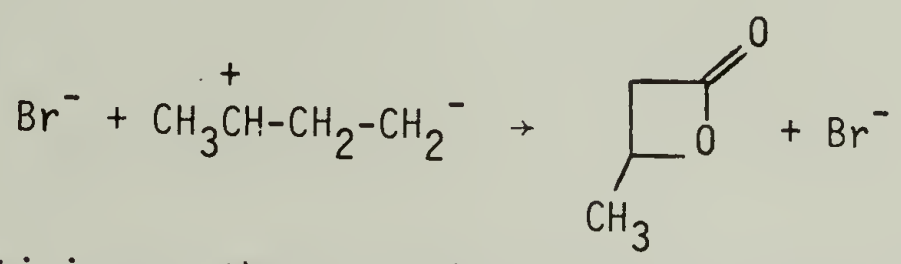
FIGURE 6. NMR SPECTRA OF CCl_4 SOLUTIONS OF α-METHYL-α-ISOPROPYL-β-AMINOPROPIONIC ACID ETHYL ESTER OF DIFFERENT OPTICAL PURITY IN THE PRESENCE OF EUROPIUM (III) SHIFT REAGENT. RACEMIC COMPOUND (UPPER CURVE): APPROXIMATELY 15% OPTICALLY PURE COMPOUND (LOWER CURVE).

this case and can be used to monitor the optical purity of the compound. It can be seen from the spectra that only slight enrichment of one enantiomeric form was possible for this compound and the optical purity was only 15-20%. The problems of the resolution will be discussed later. Nevertheless, optical purity measurement using a shift reagent in NMR-spectroscopy proved to be successful in this case.

Optically active α-phenyl-α-ethyl-β-propiolactone. As mentioned above, the resolution of α-phenyl-α-ethyl-β-aminopropionic acid ethyl ester to its pure (+)-isomer had been reported by Fontanella and Testa[77]. For their product they gave a maximum rotation of $[\alpha]_D$ = + 27.1° (c=2, MeOH), however, no optical purity was given. Their method, using dibenzoyl-d-tartaric acid as resolving agent, was used in the present work and the optical purity was determined by NMR, as outlined above. It could be shown that the value of + 27.1° (c=2, MeOH) corresponded to an optical purity of higher than 90%, thus Testa et. al. had indeed obtained an isomer of high optical purity.

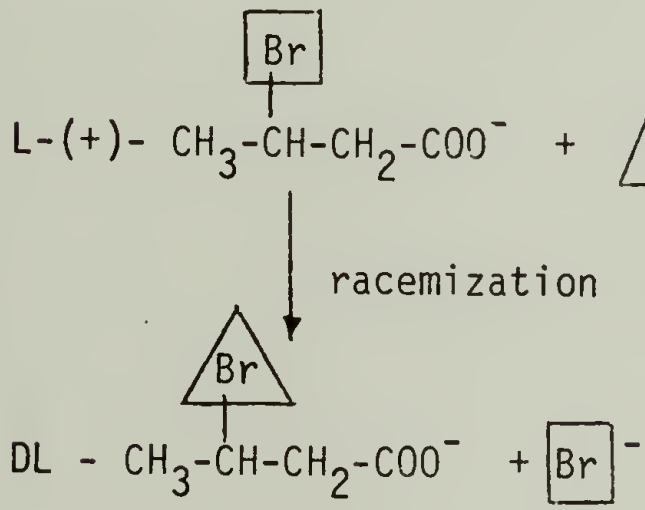
In the present study it was taken as a reasonable assumption that in going from the aminoester to the β-lactone (see Figure 1), no appreciable racemization should occur because none of the reactions would involve the chiral center directly and ring-closure to the lactone was carried out under extremely mild conditions at 0° - 5°C (see Experimental part for details). Agostini[22], in his preparation

of β-butyrolactone, had 18% racemization because in his case the chiral center was the site of the reaction, and a secondary carbonium-ion was probably formed which had to react with the neighboring carboxylate anion:

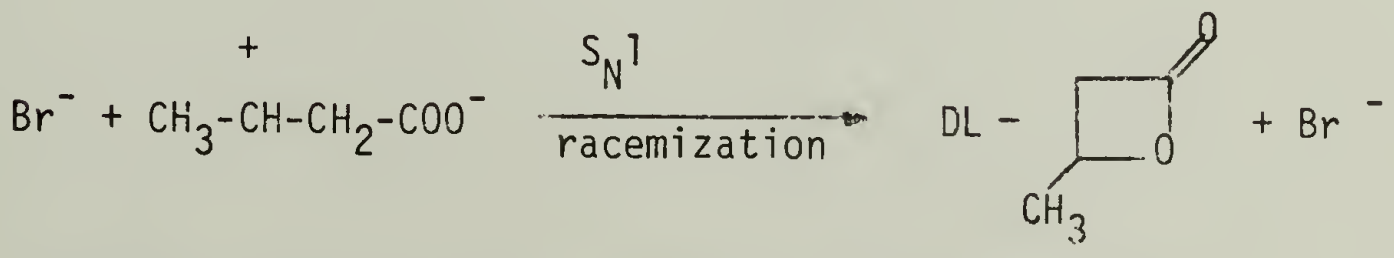


Agostini gave three possible ways by which racemization could have occurred:

-by S_N2 attack of bromide ions produced in the reaction on the β-carbon:

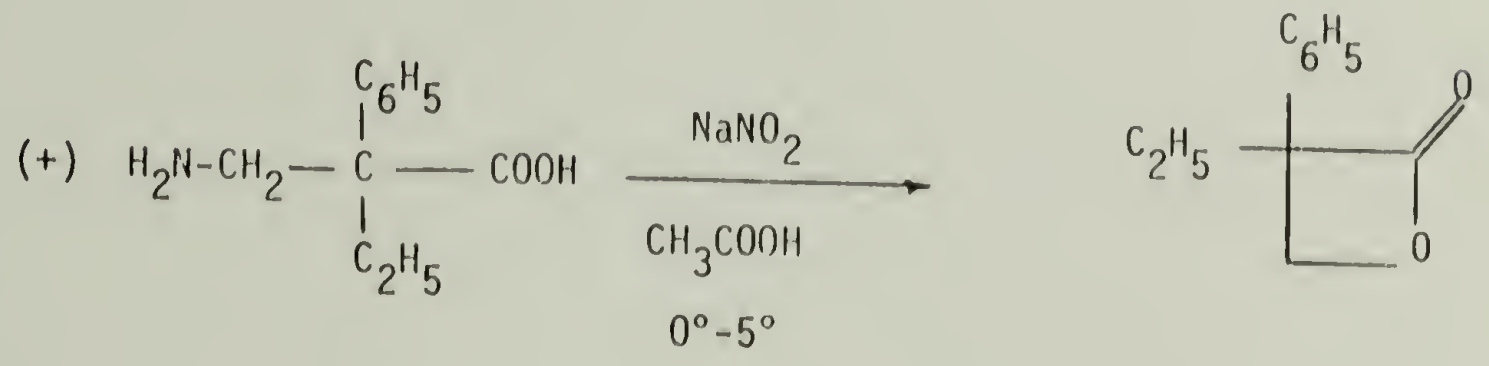


-because of an S_N1 reaction mechanism during the replacement of bromide:



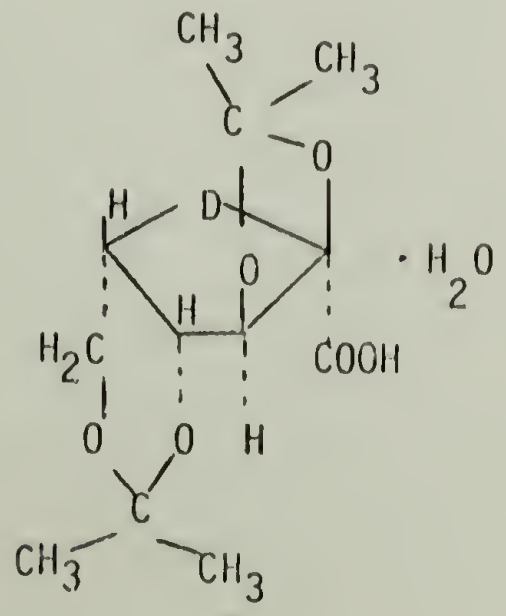
-racemization of the lactone after it has been formed.

He pointed out that the first alternative, racemization of the bromo-acid before attack of the carboxylate anion, was the most likely. This type of racemization was not possible in the present study because one went from an α,α-disubstituted-β-aminoacid to the β-lactone via diazotization:



Hence, it is to be expected that the α,α-disubstituted-β-lactone would have approximately the same optical purity as the α,α-disubstituted-β-aminoester.

Attempted resolution of α-methyl-α-isopropyl-β-aminopropionic acid ethyl ester. The first attempt on the resolution of α-methyl-α-isopropyl-β-aminopropionic acid ethyl ester was made using (-)-2,3:4,6-di-O-isopropylidene-2-keto-L-gluconic acid hydrate; (-)-di-acetone-2-keto-L-gluconic acid hydrate (DAG) as resolving agent.



DAG'

mw. 292.28

mp. 100-101°C

$[\alpha]_D^{25}$ = -21.3° (2%,MeOH)

0.01 mole of the aminoester together with 0.01 mole resolving agent were refluxed for 15 minutes in 10 ml methanol, after which one allowed to cool to room-temperature. The precipitate was filtered off and dried in the vacuum oven at 40°C (Mp: 140-154°C).

The resolving agent was split off in order to obtain the free aminoester. However, no optical rotation of the aminoester could be observed at the α_D-line.

The second attempt on the resolution of α-methyl-α-isopropyl-β-aminopropionic acid ethyl ester was done using dibenzoyl-d-tartaric acid hydrate as resolving agent:

0.05 moles resolving agent were given into 150 ml methanol and the solution was brought to the boiling point, after which 0.05 moles aminoester in 95 ml methanol were added. The solution was refluxed for 15 minutes, then approximately 145 ml methanol were distilled off, after which one allowed to cool to room-temperature. The solution was then put in the refrigerator overnight after which the formed crystals were filtered off. The salt showed a specific rotation of $[\alpha]_D^{r.t.} = -82.5°$ (c=2, MeOH). After recrystallization the same rotation was obtained.

The salt was treated with saturated sodium carbonate solution to obtain the free aminoester. The latter was distilled under high vacuum. A solution of c=2.307 (g/dl) was made up to measure the optical rotation listed below:

λ(nm)	$[\alpha]_{\lambda}^{r.t.}$
576.96	-0.35°
407.78	-1.04°
280.35	-2.25

The optical purity of this material was determined by NMR using an europium shift reagent (see p. 13). It could be shown that the optical purity was only ca. 20%.

All further attempts of recrystallization of the diastereomer salt, in order to obtain higher optical purity, yielded salts of approximately the same rotation ($[\alpha]_{D}^{r.t}$ = -85° to -79°, c=2, MeOH) and it had to be concluded that further enrichment of one isomer using dibenzoyl-d-tartaric acid hydrate as resolving agent and methanol as solvent, could not be obtained.

Thermal Studies of the Polymers

Thermal analysis was carried out on a Perkin-Elmer Model 1B Differential Scanning Calorimeter under nitrogen atmosphere using sealed DSC caps.

Multiple melting endotherms were observed during analysis by differential scanning calorimetry (DSC) of the highly crystalline, optically-active poly-α-phenyl-α-ethyl-β-propiolactone. This phenomenon has also been reported by Allegrezza[6] in the case of poly-α-methyl-α-n-propyl-β-propiolactone and is known to occur as well in a series of other polymers[78-86]. In his study Allegrezza concluded that the lower melting endotherm is caused by melting of folded

chain lamellae, whereas the higher temperature peak is caused by a broad distribution of crystallite sizes and perfection. Based on his results he felt that the multiple endotherms do not represent different crystalline forms.

The results of the present study show similarity to the behavior of poly-α-methyl-α-n-propyl-β-propiolactone[6] in that two melting endotherms were observed. The higher temperature peak was large and broad, the lower temperature peak was narrower and, in the present case, smaller (Figure 7).

In the first melting cycle of optically-active poly-α-phenyl-α-ethyl-β-propiolactone, obtained by precipitation out of the reaction mixture and unannealed, the lower endotherm peak was not observed rather a very broad peak was observed (Figure 7). This behavior can be explained by the distribution of crystallite sizes present in the sample. The sample was heated to 272°C, about 20° above the melting point, then cooled down to 180°C at a rate of 10°/minute, after which the temperature was raised again to obtain the melting endotherm of the second cycle. The third and fourth cycle were run in the same manner. It can be seen that the lower temperature peak appeared in the second cycle and that the peak positions and sizes of cycles 2-4 were about the same.

Upon cooling of the sample, crystallization from the melt was observed (Figure 8). The exotherm peak, indicating crystallization, started at about 212°C, corresponding to a supercooling of 40°C. Rapid crystallization was obtained, giving a single exo-

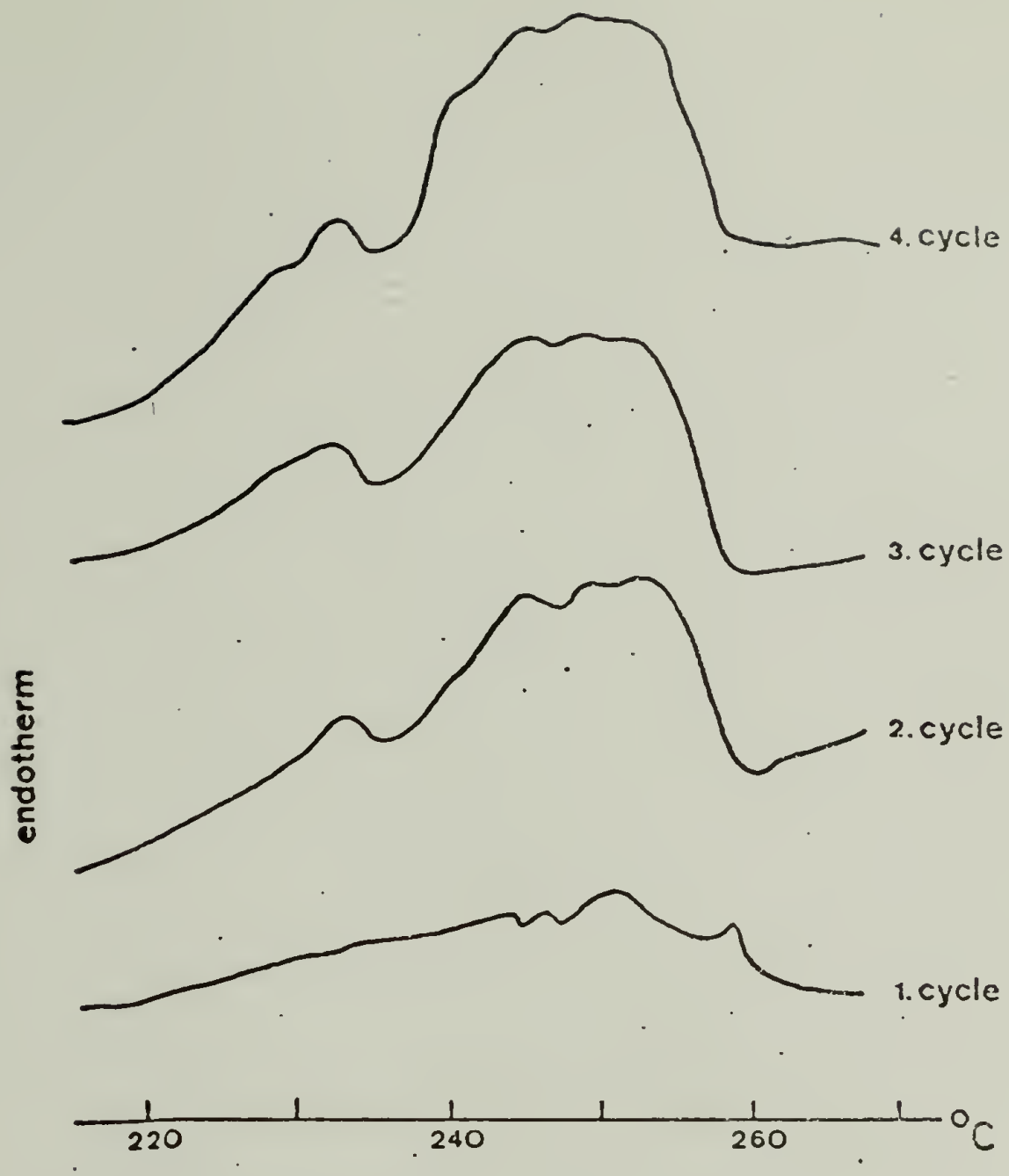


FIGURE 7. DSC-CURVE (MELTING) OF OPTICALLY ACTIVE POLY-(-)-α-PHENYL-α-ETHYL-β-PROPIOLACTONE (1. CYCLE ON RANGE 8, OTHERS ON RANGE 2).

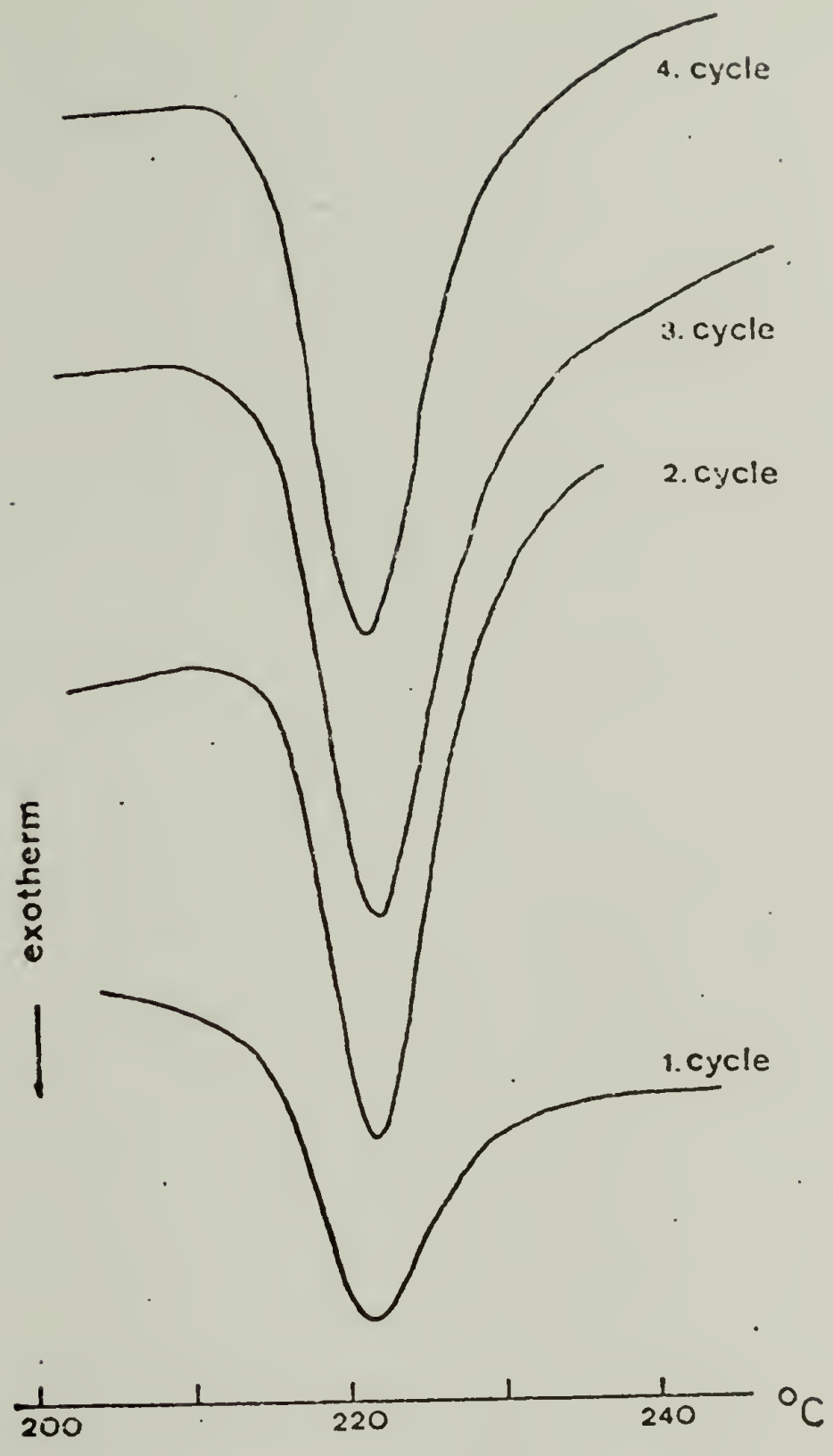


FIGURE 8. DSC-CURVE (CRYSTALLIZATION) OF OPTICALLY ACTIVE POLY-(-)-α-PHENYL-α-ETHYL-β-PROPIOLACTONE. (1. CYCLE ON RANGE 4, OTHERS ON RANGE 2).

therm peak which had approximately the size of both endotherm melting peaks taken together.

The racemic poly-α-phenyl-α-ethyl-β-propiolactone also showed two melting endotherms but at much lower temperatures than the isotactic polymer. Two endotherms for the former appeared at 59°C and 92°C (Figure 9), compared to 234°C and 248°C for the latter. The polymer obtained from a 25/75 mixture of the two isomers showed the same behavior as the racemic polymer (Figure 9).

Upon cooling at 10°/minute the racemic and the partially optically active polymer did not show any crystallization peak, neither did the melting endotherms reappear upon renewed heating. It might be possible that the cooling rate was too fast for recrystallization to occur and that annealing below the melting point would be needed.

The large difference in melting points between the optically active, isotactic polymer and the racemic and partially optically active polymer would have to be explained through the different stereoregularity of the polymers only. No solvent residues of any amount remained in the samples, since all were dried in the vacuum oven at 60°C, and according to viscosity data no large differences in molecular weight, which could account for the melting point depression, were apparent.

The melting point of a polymer is markedly dependent on stereoregularity. A method of estimating isotacticity from melting points has been suggested by Coleman[87]. Some measurements have been reported for comparison of melting points for atactic and isotactic polymers (see Table III).

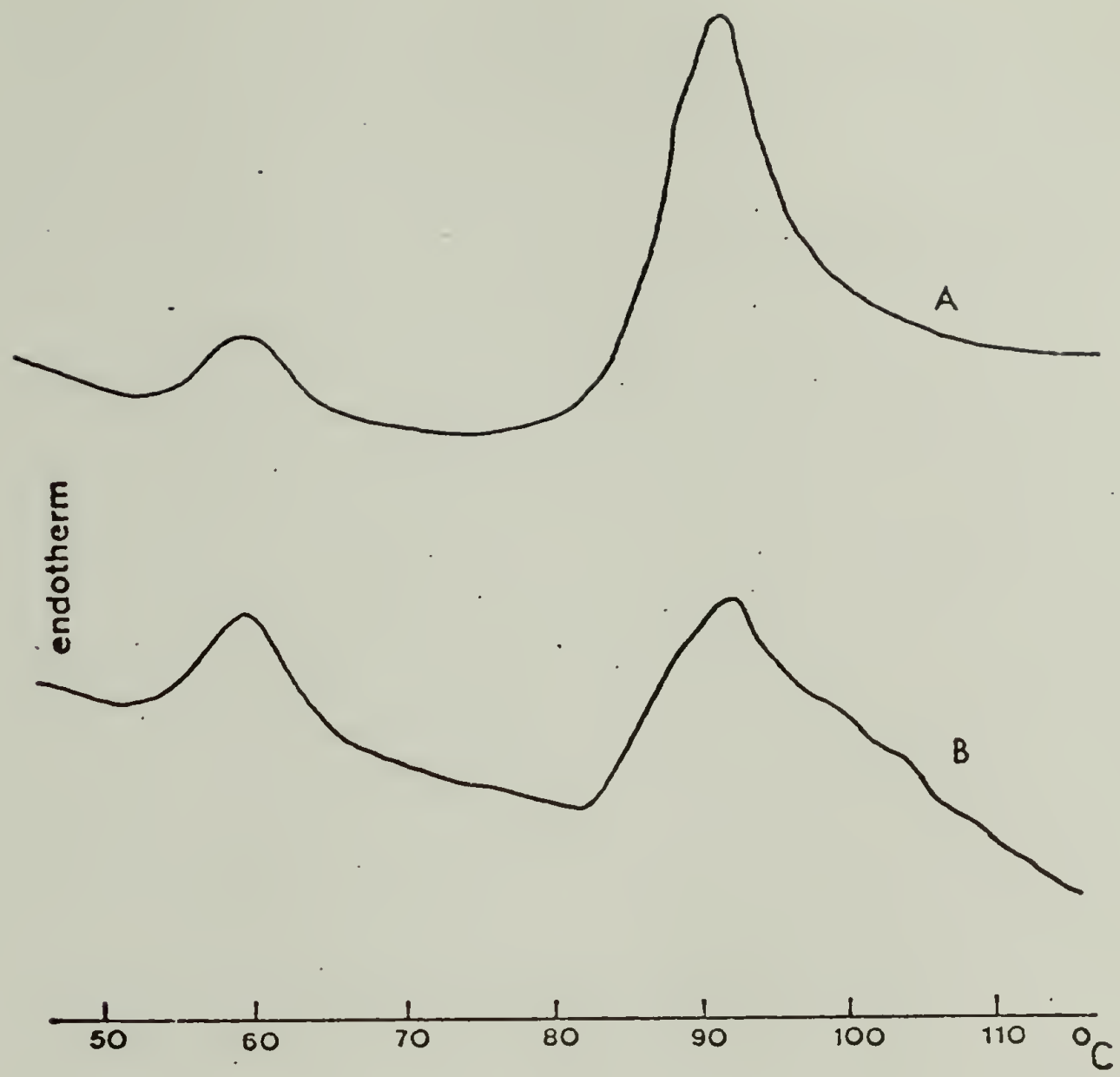


FIGURE 9. DSC-CURVE OF POLY-α-PHENYL-α-ETHYL-β-PROPIOLACTONE OBTAINED FROM RACEMIC AND APPROXIMATELY 47% OPTICALLY PURE MONOMER.

TABLE III

Melting Points of Atactic and Isotactic Polymers[88]

Polymer	Melting points, °C	
	Atactic[a]	Isotactic
Polypropylene	-35	160 - 170
Poly-1-butene	-42	120 - 130
Polystyrene	85	230

a) These values referred in reference 88 as "melting points", presumably are softening temperatures.

Natta[89] determined melting points for mixtures of tactic species of polypropylene. In Figure 10 the lowering of crystallinity as a function of the melting temperature is shown for stereoblock polymers and for mechanical mixtures of isotactic and atactic polypropylenes.

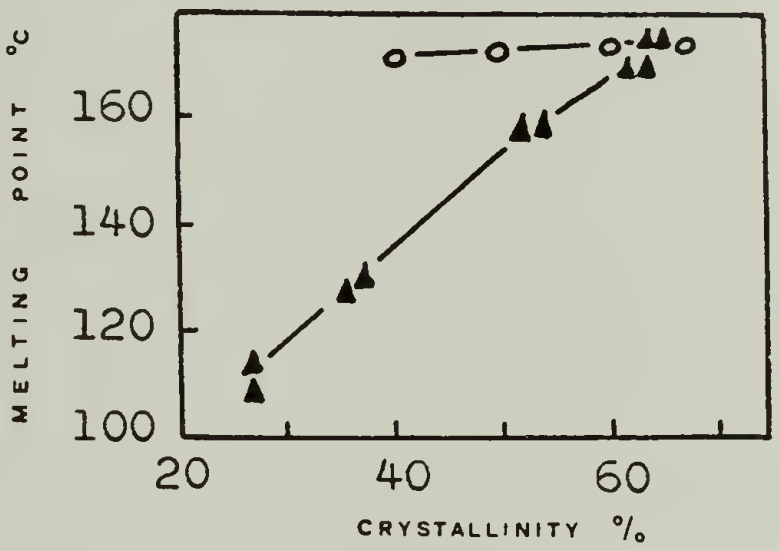


Figure 10. Melting temperature of mixtures of isotactic and atactic polypropylenes (o) and of stereoblock polypropylenes (▲) having different crystallinity. (ref. 89)

Stereoblock polymers of propylene show a melting temperature and a crystallinity depending on the average lengths of the isotactic sections of the chain.

A large difference in melting points was observed between the optically active, isotactic poly-α-phenyl-α-ethyl-β-propiolactone and the polymer obtained from racemic monomer (Table IV). The polymer obtained from a monomer mixture of approximately 25%(+) and 75%(-) -isomer showed also a markedly lowered melting point compared to the high optical purity material.

TABLE IV

Melting Points of Poly-α-phenyl-α-ethyl-β-propiolactone of Different Tacticities

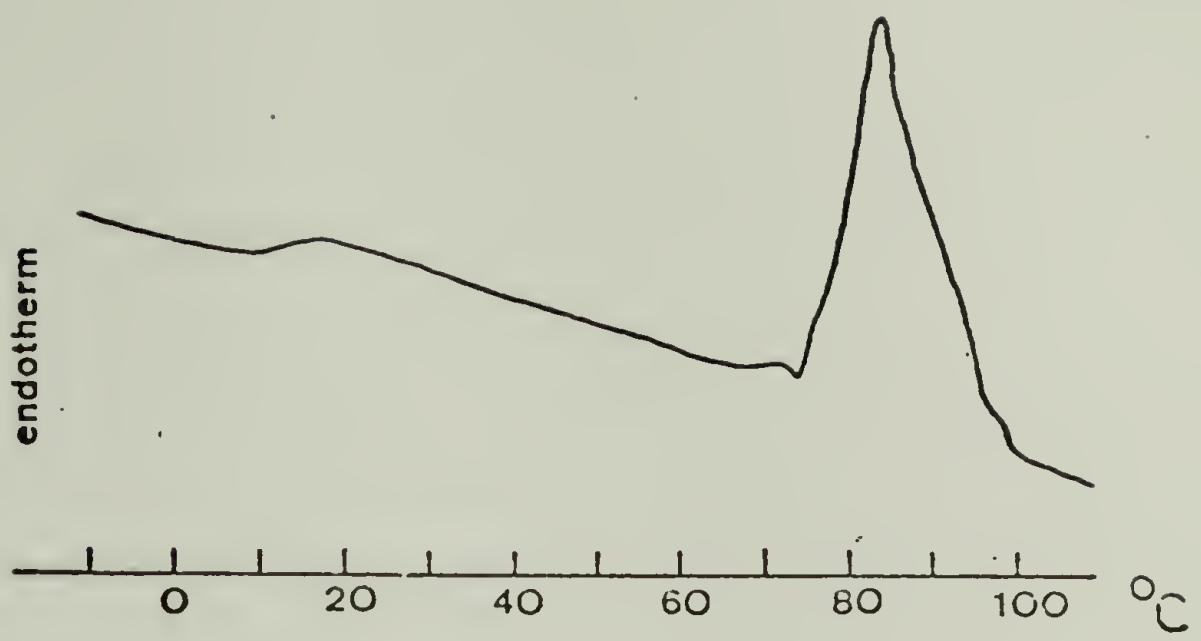
Monomer enantiomer composition		Melting point, °C[a]
(+)	(-)	
90%	10%	260
26.5%	73.5%	116
50%	50%	110

a) temperature where DSC-curve returns to base-line.

Overberger and Jabloner[90a] have shown that poly-(+)-β-methyl--ε-caprolactam melted at 135-145°C, whereas poly-(R)-(-)-β-methyl--ε-caprolactam melted at 225°C. This difference in melting point has been attributed to a difference in crystal structure as evidenced by the fact that the d spacings are quite different.

It has been demonstrated by Overberger[90b], in the case of poly-(R)-(+)-7-hydroxy-4-methylheptanoic acid, that the polymer with high optical purity and greater stereoregularity can crystallize whereas the incorporation of 10% of the enantiomeric monomer is sufficient to inhibit crystallization. This is probably true in the present case too. In the DSC study of the optically active poly-α-phenyl-α-ethyl-β-propiolactone, crystallization was obtained upon cooling whereas both the partially optically active and the racemic do not recrystallize upon cooling at 10°/minute.

The results for racemic poly-α-methyl-α-isopropyl-β-propiolactone are shown in Figure 11. Two fractions, one methanol soluble the other methanol insoluble were obtained. The methanol soluble fraction showed only an inflection in the DSC-curve around -5°C which probably corresponds to the glass-transition of this polymer. The methanol insoluble fraction however, had an endotherm peak at 85°C and an inflection in the curve at 17°C. The melting peak did not reappear in the second heating cycle, neither did a crystallization peak on cooling. Again, this is probably due to the slow crystallization of the polymer, which does not occur at a rate of cooling of 10°/minute.



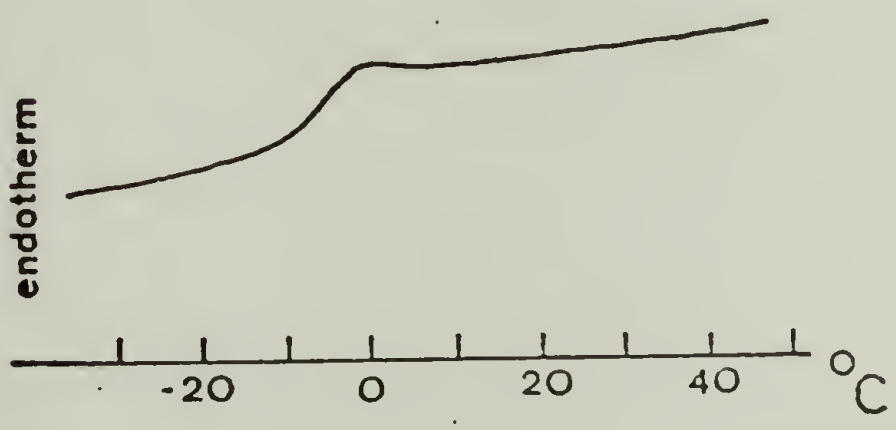


FIGURE 11. DSC-CURVES OF DIFFERENT FRACTIONS OF POLY-α-METHYL-α-ISOPROPYL-β-PROPIOLACTONE. METHANOL INSOLUBLE FRACTION (UPPER CURVE); METHANOL SOLUBLE FRACTION (LOWER CURVE).

Poly-α-methyl-α-isopropyl-β-propiolactone. Etienne and Fischer[4] have reported a melting point of 25°C for poly-α-methyl-α-isopropyl -β-propiolactone. They had obtained their polymer from a small amount of not completely purified monomer and cautiously mentioned that a higher molecular weight polymer could show a slightly higher melting point.

The poly-α-methyl-α-isopropyl-β-propiolactone obtained in the present study was fractionated into two fractions, one methanol soluble the other methanol insoluble. The methanol soluble fraction (90-80% of the total polymer) is a very viscous liquid at 30°C and has a tan color, whereas the methanol insoluble fraction (10-20% of the total polymer) is a fine, white powder. As has been reported earlier in this paper only the methanol insoluble fraction showed a crystalline melting at 100°C (return to baseline of DSC-curve) whereas the methanol soluble fraction exhibited only an inflection in the DSC-curve around -5°C, which probably corresponds to the T_g of this polymer

The IR- and NMR-spectra of both fractions were practically identical.

The difference in the behavior of the two fractions could be explained by their different molecular weights. The methanol insoluble fraction was shown to have a $\overline{M}_n$ of 8400, whereas the methanol soluble fraction had a $\overline{M}_n$ of 4700 only, corresponding to a $\overline{DP}_n$ of 65 and 36.

Thus, Fischer and Etienne had probably measured the melting point of a low molecular weight polymer.

Solution viscosity and molecular weights. The inherent viscosities of the polymers were measured in chloroform at 25°C. The results, together with the number average molecular weights obtained by vapor-phase osmometry, are shown in Table V and Table VI.

As can be seen from Table VI the molecular weight of the methanol insoluble fraction was nearly twice as large as the molecular weight of the methanol soluble fraction obtained in the same polymerization.

Because of the inconsistency of the measurements at low concentrations the inherent viscosities could not be extrapolated to zero concentration in order to obtain an intrinsic viscosity for the polymers. Thus, an inherent viscosity at one concentration only is reported in the above tables.

Infrared studies of the polymers. Infrared spectra of the polymers obtained from racemic and from optically active α-phenyl-α-ethyl-β-propiolactone showed no differences as seen by a comparison of Figures 12 and 13. The major absorption peak was at 1735 cm^{-1} and corresponds to the ester carbonyl stretching mode. A double peak at 1600 cm^{-1} is assigned to the phenyl ring and peaks at 2900-3000 cm^{-1} and 1450 cm^{-1} correspond to both the methyl and methylene groups. In the range of 1230-1130 cm^{-1} were two strong bands corresponding to the C-O-C stretch.

The infrared spectra for poly-α-methyl-α-isopropyl-β-propiolactone is shown in Figure 14. The major absorption, for the ester

TABLE V

Inherent Viscosity and Molecular Weight of

Poly-α-phenyl-α-ethyl-β-propiolactone

Monomer Isomer Mixture	Mol %[a] Initiator	Polym. Time (Days)	Polym. Temp.	$\frac{\ln \eta r}{c}$ (dl/g)[b] (conc. in g/dl)	$\bar{M}_n$ [c]
50%(+)/50%(-)	0.88	10	R.T.	0.065 (1.81)	9500
73%(+)/27%(-)	0.95	11	R.T.	0.056 (1.12)	7000
10%(+)/90%(-)	1.01	8	R.T.	0.063 (1.92)	7700

a) initiator: tetraethylammonium benzoate

b) in $CHCl_3$ at 25°C

c) by VPO in chloroform

TABLE VI

Inherent Viscosity and Molecular Weight of Poly-α-methyl-α-isopropyl-β-propiolactone

Sample	Mol % Initiator	Polym. Time	Polym. Temp	$\frac{\ln\eta r}{c}$ (dl/g) b) (conc. in g/dl)	$\bar{M}_n$ c)
racemic monomer	0.39	18 hrs.	75°C		
MeOH soluble fraction				0.06 (1.22)	4700
MeOH insol. fraction				0.07 (1.28)	8400

a) initiator: tetraethylammonium benzoate

b) in $CHCl_3$ at 25°C

c) by VPO in chloroform

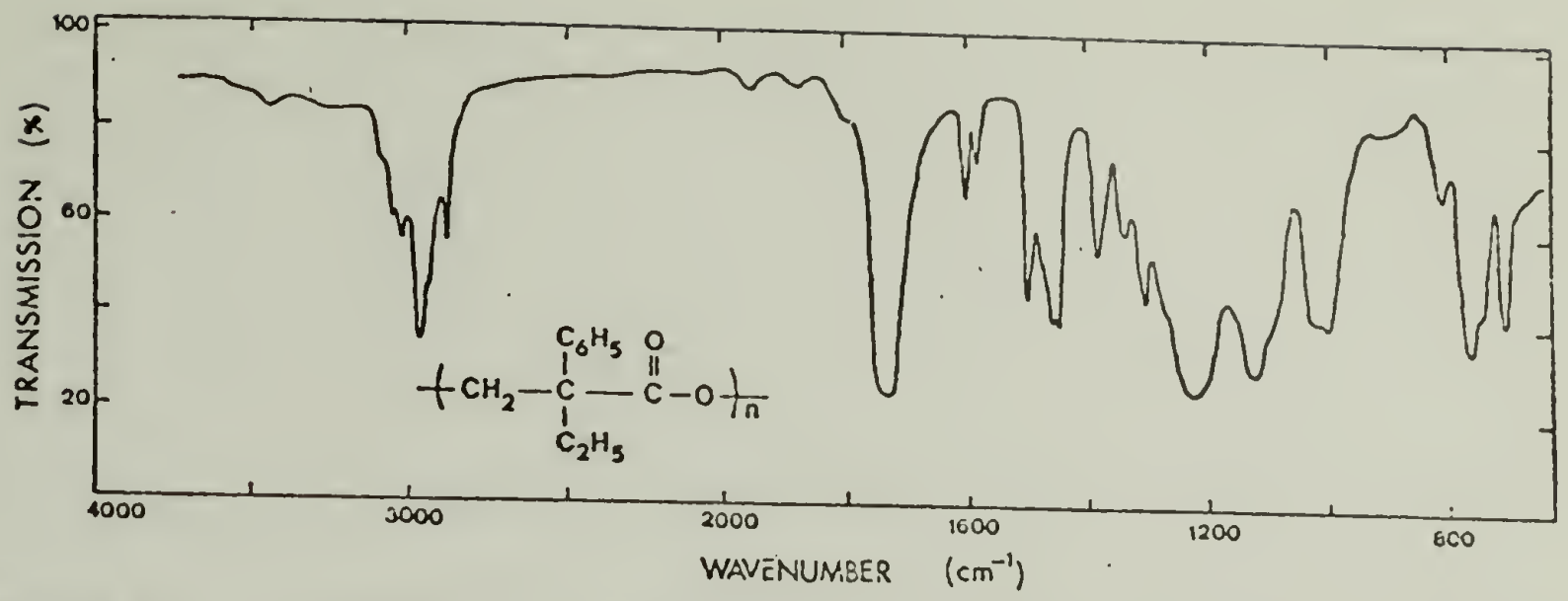


FIGURE 12. IR SPECTRUM OF RACEMIC POLY-α-PHENYL-α-ETHYL-β-PROPIOLACTONE CASTED AS THIN FILM ON A SALT-PLATE.

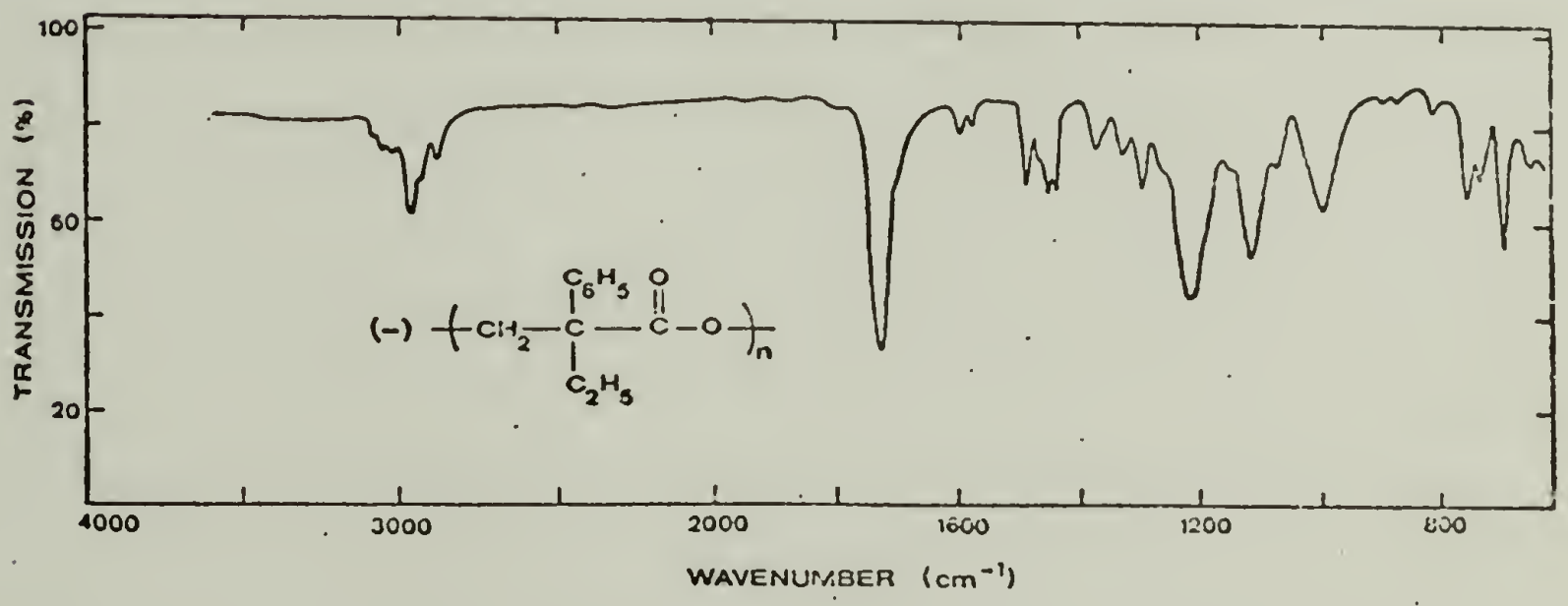


FIGURE 13. IR SPECTRUM OF OPTICALLY ACTIVE POLY-(-)-α-PHENYL-α-ETHYL-β-PROPIOLACTONE. CASTED AS THIN FILM ON A SALT-PLATE.

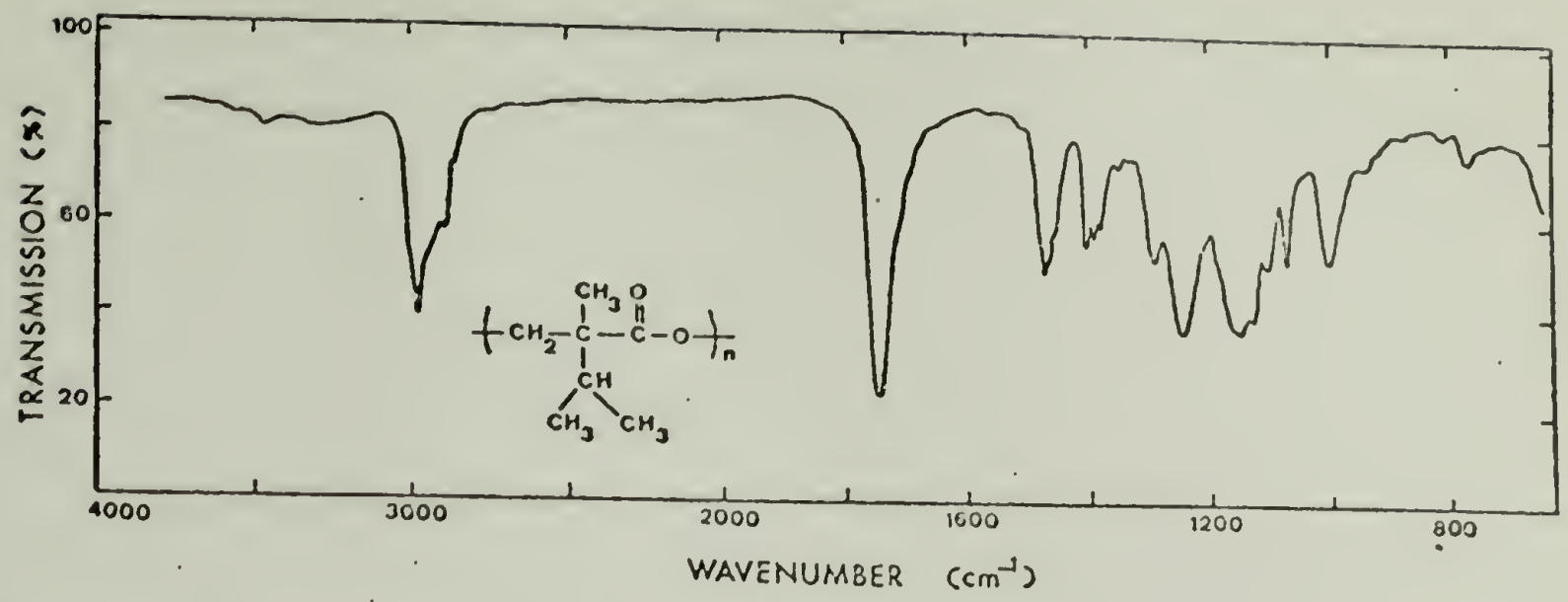


FIGURE 14. IR SPECTRUM OF POLY-α-METHYL-α-ISOPROPYL-β-AMINOPROPIOLACTONE. CASTED AS THIN FILM ON A SALT-PLATE.

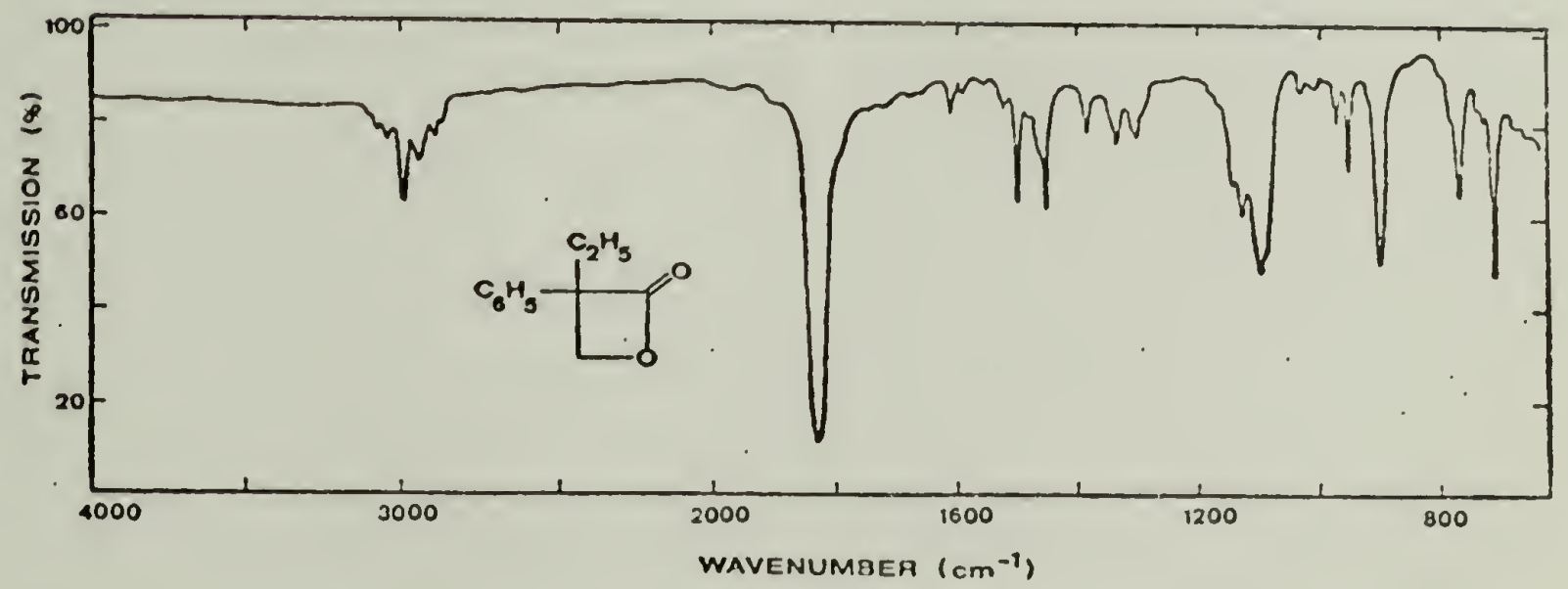


FIGURE 15. IR SPECTRUM OF α-PHENYL-α-ETHYL-β-PROPIOLACTONE (NEAT).

carbonyl was at 1735 cm^{-1}. Peaks between 2880-2980 cm^{-1} correspond to the stretching mode of methine, methylene and methyl groups which have also characteristic bands between 1470-1370 cm^{-1}. Two bands between 1240-1130 cm^{-1} were assigned to the C-O-C stretching frequency.

Practically no difference in the IR-spectra were observed for the methanol-soluble and methanol-insoluble fraction of poly-α-methyl-α-isopropyl-β-propiolactone.

The infrared spectra of the two monomers are shown in Figures 15 and 16. The absorption band for the carbonyl-group of these β-lactones is at 1825 cm^{-1} as compared to 1735 cm^{-1} for the polymers. This difference was used to monitor the polymerization by taking small samples out of the reaction mixture and checking the disappearance of the monomer peak during polymerization.

NMR studies of polymers and monomers. The NMR spectrum of the monomer, α-phenyl-α-ethyl-β-propiolactone is shown in Figure 17. It shows a triplet at 0.93 ppm, corresponding to the methyl group of the side chain. The methylene group of the side chain appears at 2 ppm as a quartet. The methylene protons of the lactone ring were not equivalent and appear as two sets of doublets at 4.3 ppm. The aromatic ring protons give rise to a singlet at 7.27 ppm.

The methyl and side chain methylene protons of the polymer (Figure 18) are shifted towards higher field compared to the monomer and appear at 0.5 ppm and 1.85 ppm. The methylene protons of the main chain have about the same chemical shift as the methylene protons of the lactone ring and appear at 4.35 ppm. The signal for the

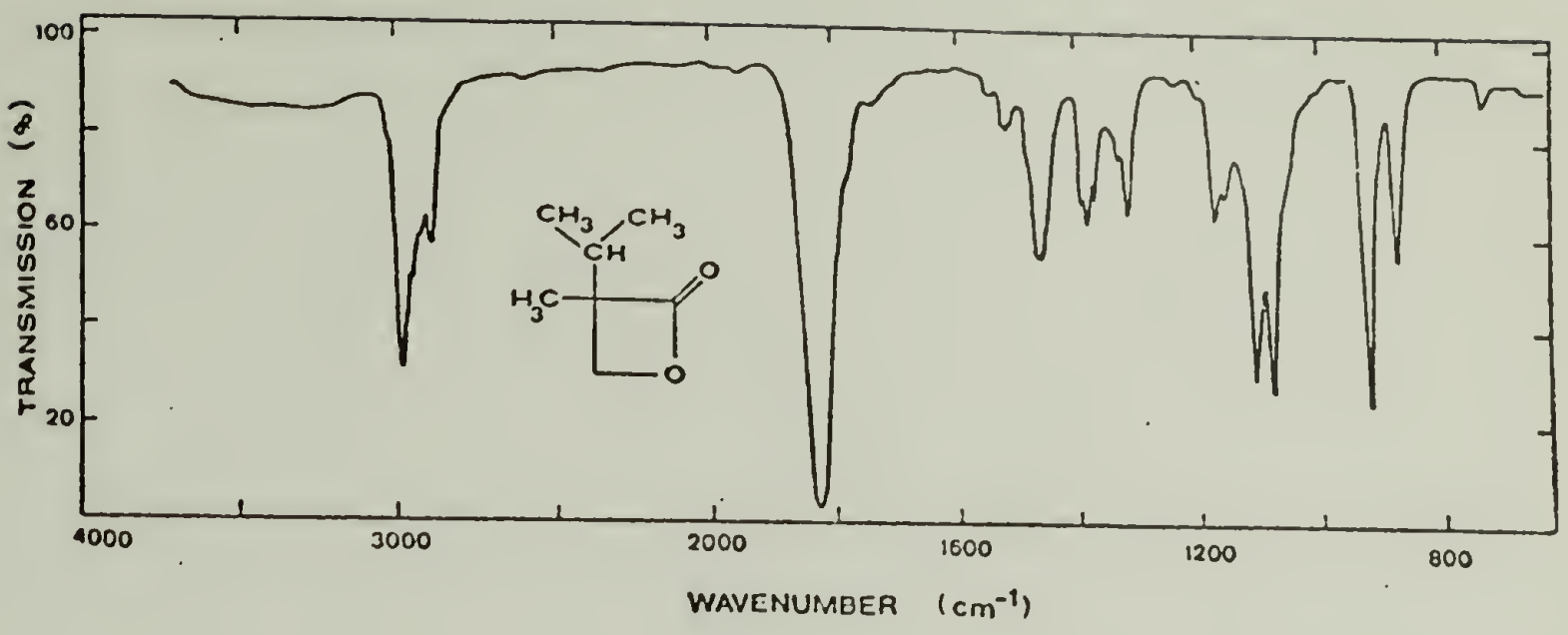


FIGURE 16. IR SPECTRUM OF α-METHYL-α-ISOPROPYL-β-PROPIOLACTONE (NEAT)

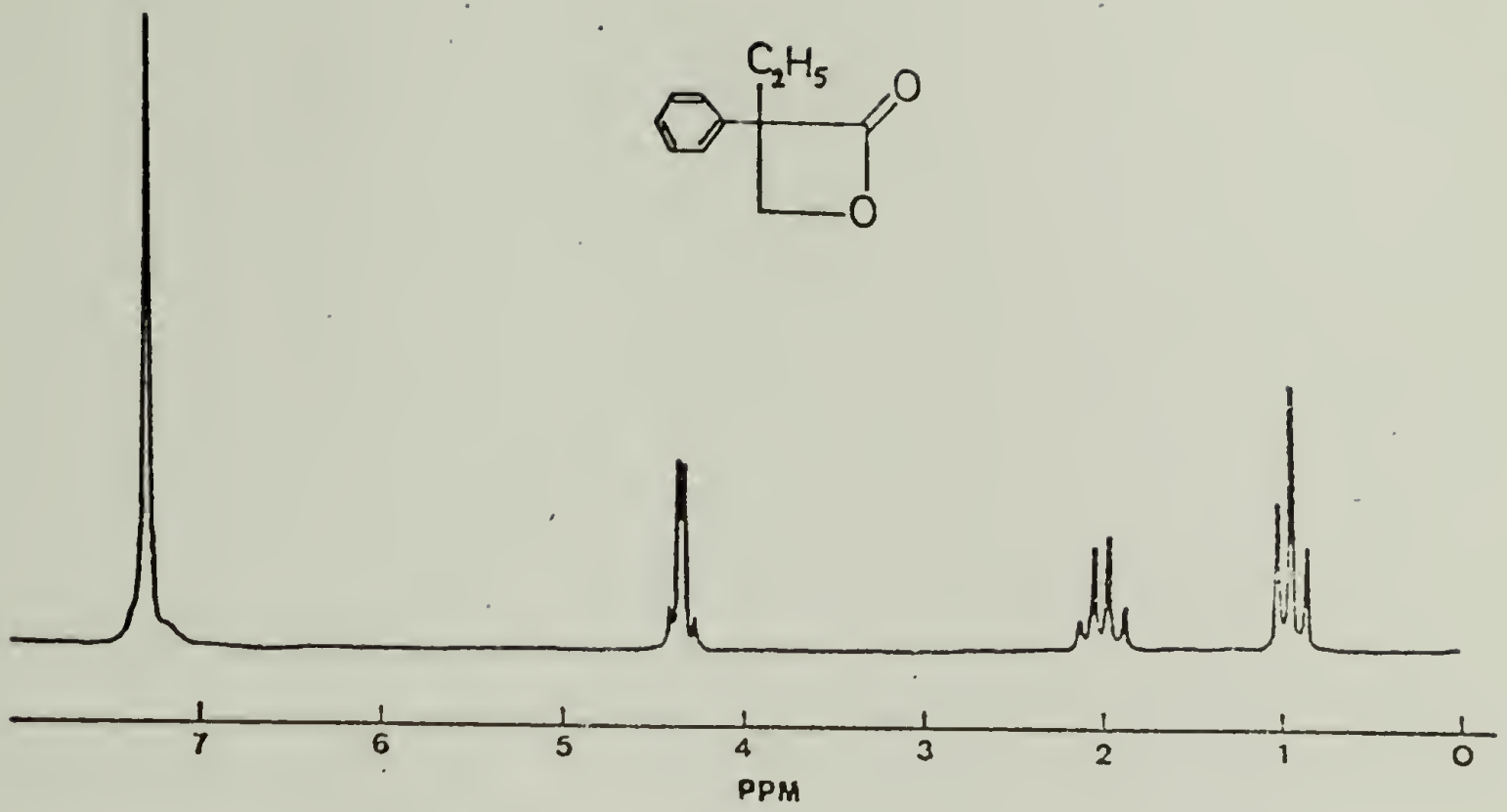


FIGURE 17. NMR SPECTRUM OF α-PHENYL-α-ETHYL-β-PROPIOLACTONE in CCl_4. RECORDED AT 35°C USING TMS AS INTERNAL STANDARD.

phenyl protons in the polymer is split into two signals, one at 6.9 ppm, corresponding to two protons and one at 7.2 ppm, corresponding to three protons.

There is practically no difference in the spectra of the racemic (Figure 18) and the optically active (Figure 19) polymers.

The NMR spectrum of the α-methyl-α-isopropyl-β-propiolactone monomer is shown in Figure 20. Two sets of doublets at 0.95 ppm and 1.03 ppm correspond to the two methyl groups of the isopropyl group. The methyl side group appears as a singlet at 1.32 ppm and a multiplet at 2 ppm is asigned to the methine proton of the isopropyl group. The two methylene protons of the lactone ring are not equivalent and appear as two sets of doublets at 3.85 and 4.05 ppm.

The methyl protons of the side chains of poly-α-methyl-α-isopropyl-β-propiolactone are shifted slightly towards higher field compared to the monomer (see Figure 21). The methyl side group appears at 1.1 ppm and two split signals at 0.95 ppm and 0.86 ppm are assigned to the methyl groups of the isopropyl side chain. The methine proton of the isopropyl group appears at 2 ppm and the signal at 4.1 ppm corresponds to the methylene protons of the main chain. As seen from Figure 21 there exists practically no difference in the NMR spectra of the methanol soluble and methanol insoluble fraction of poly-α-methyl-α-isopropyl-β-propiolactone.

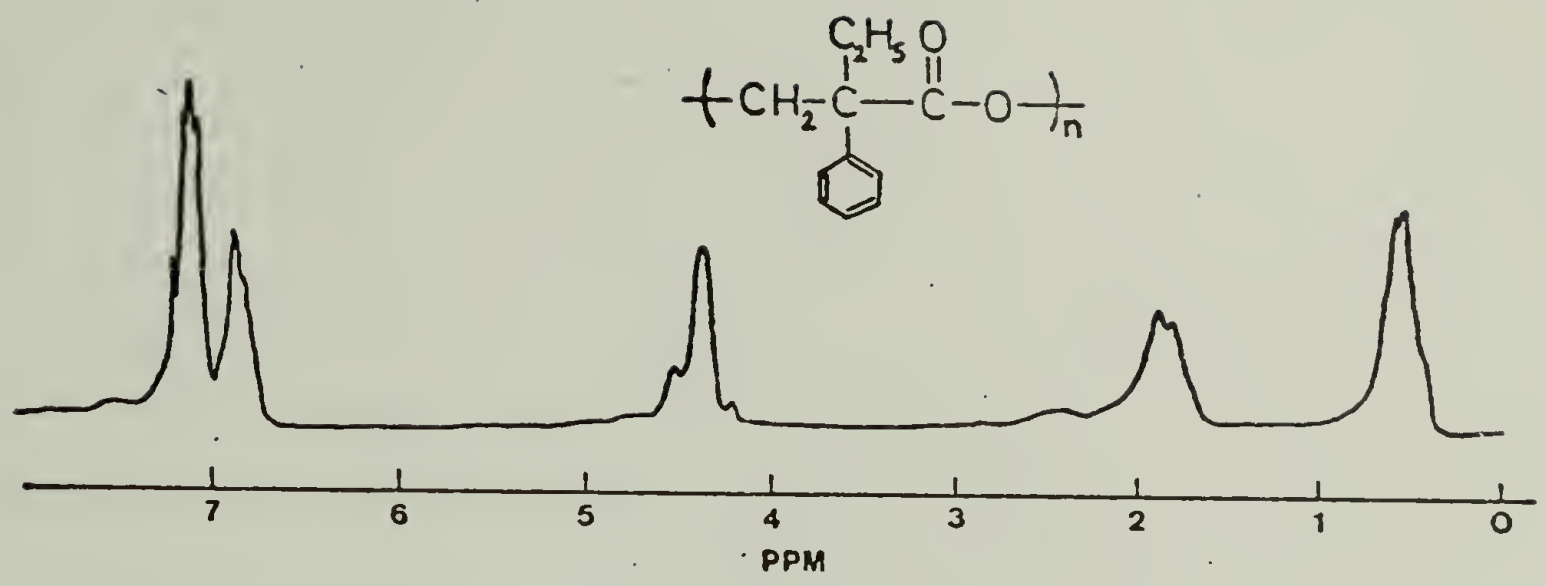


FIGURE 18. 90MHz-NMR SPECTRUM OF RACEMIC POLY-α-PHENYL-α-ETHYL -β-PROPIOLACTONE IN CHLOROFORM. RECORDED AT 35°C USING TMS AS INTERNAL STANDARD.

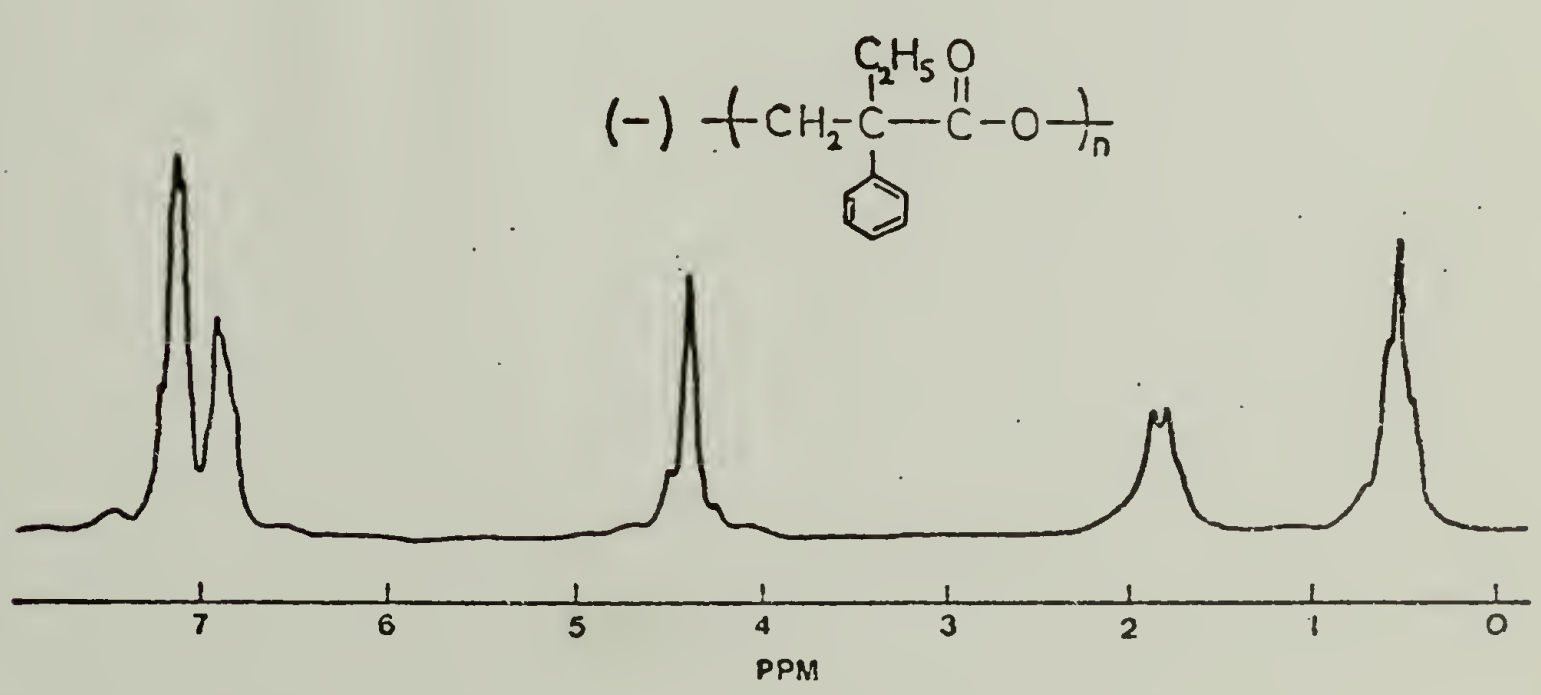


FIGURE 19. 90 MHz-NMR SPECTRUM OF OPTICALLY ACTIVE POLY-α-PHENYL-α-ETHYL-β-PROPIOLACTONE IN CHLOROFORM. RECORDED AT 35°C USING TMS AS INTERNAL STANDARD.

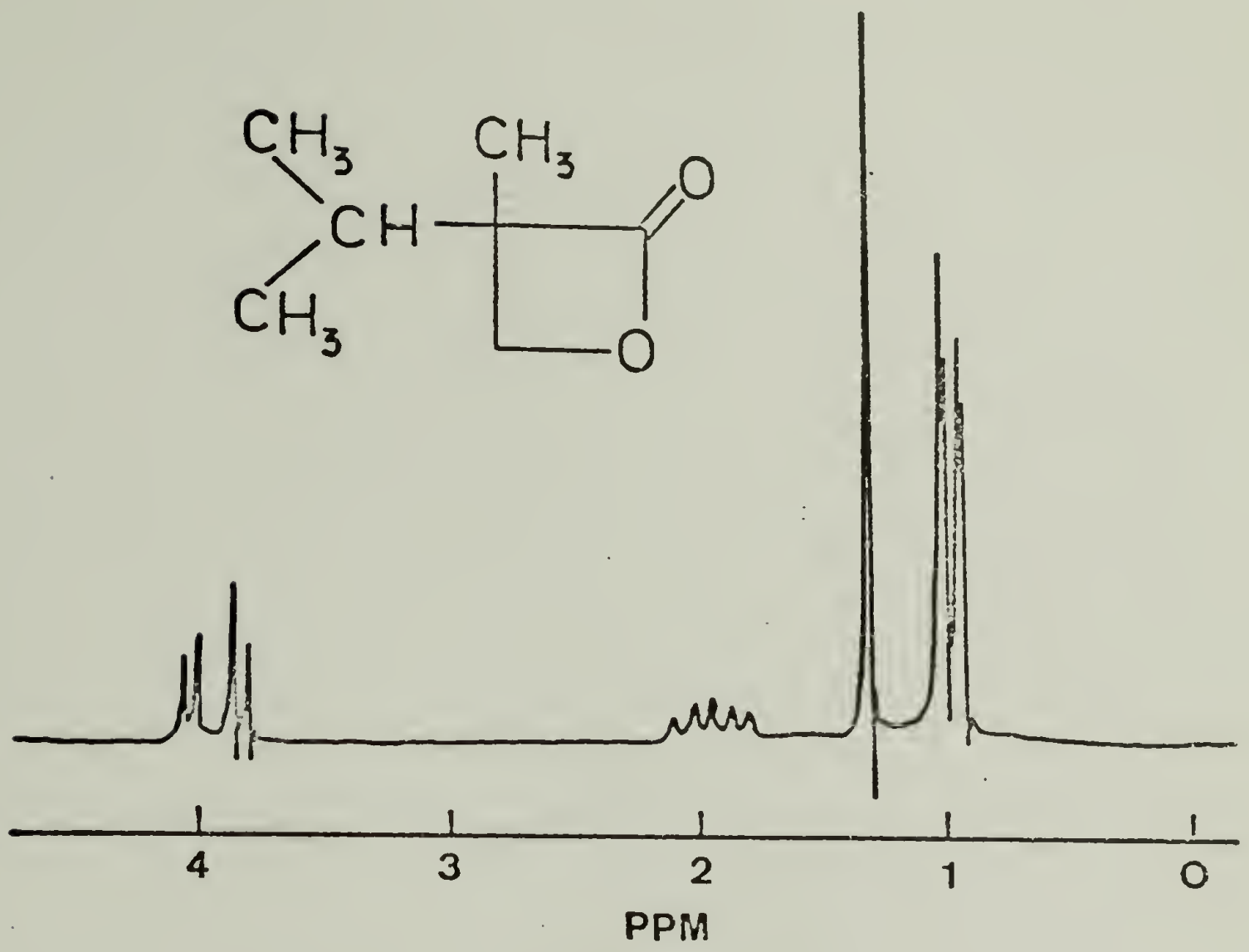


FIGURE 20. 90 MHz-NMR SPECTRUM OF α-METHYL-α-ISOPROPYL-β-LACTONE IN CCl_4. REORDERED AT 35°C USING TMS AS INTERNAL STANDARD.

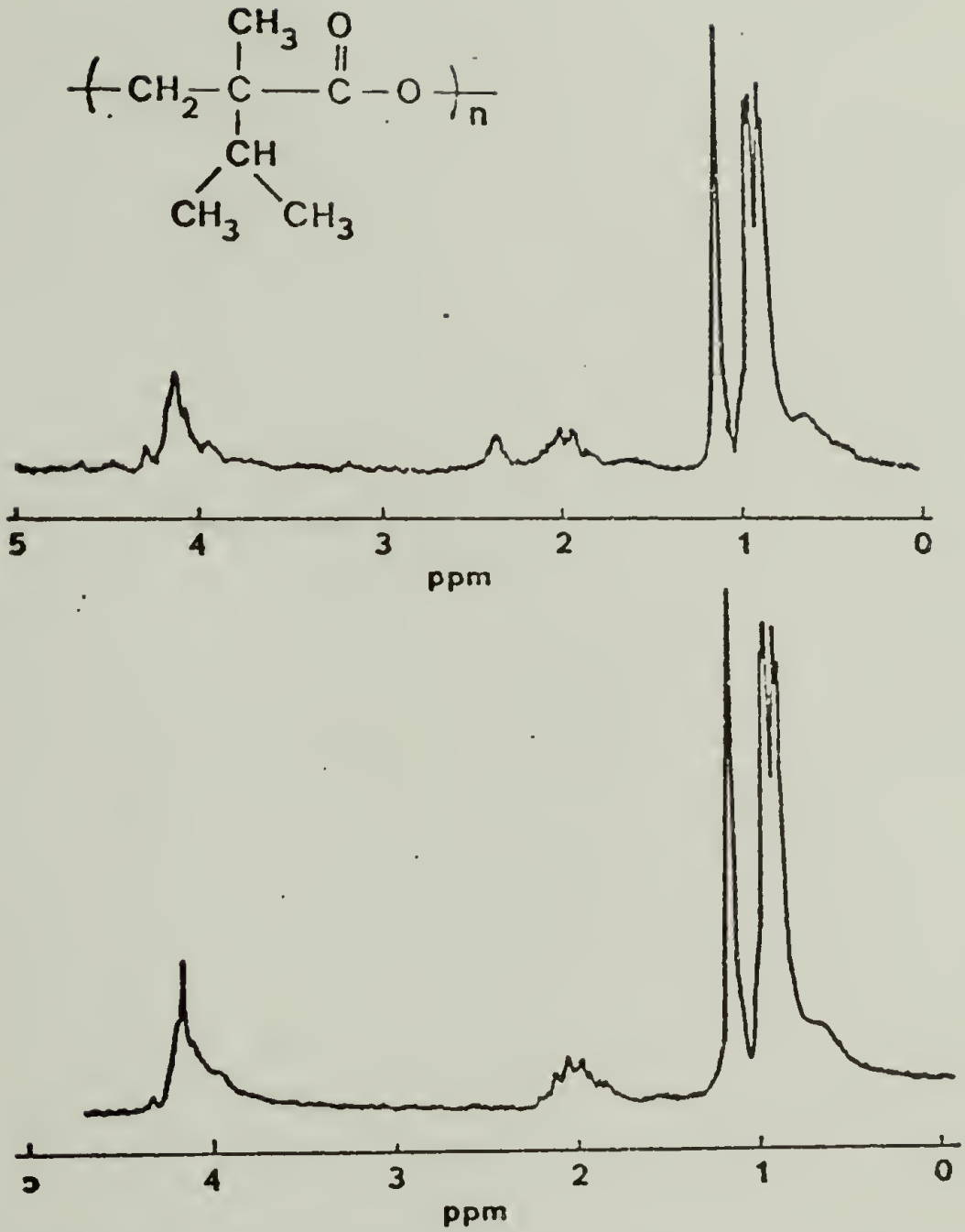


FIGURE 21. 90 MHz-NMR SPECTRUM OF POLY-α-METHYL-α-ISOPROPYL-β-PROPIOLACTONE IN CHLOROFORM. RECORDED AT 35°C USING TMS AS INTERNAL STANDARD. METHANOL INSOLUBLE FRACTION (UPPER CURVE); METHANOL SOLUBLE FRACTION (LOWER CURVE).

Wide angle X-ray measurements of poly-α-phenyl-α-ethyl-β-propiolactones. Measurements were performed with a General Electric GE XRD-5 goniometer in the symmetrical reflection technique. Cu-K_α radiation from a source of 16 mA and 50 kV was used. A high-resolution set-up (1° entrance slit, 0.1° detector slit) was used in order to obtain good resolution of the crystalline peaks. The samples, about 1 mm thick (pressed powder, unannealed) were measured from 2Θ = 4° to 2Θ = 25°. The samples were 40 mm long.

Optically active poly-(-)-α-phenyl-α-ethyl-β-propiolactone		Racemic poly-α-phenyl-α-ethyl-β-propiolactone	
Maxima 2Θ	Peak*	Maxima 2Θ	Peak*
9.5°	s	7.8	m
14.5°	m	9.2	s
15.3°	s	14.5	s
17.5°	w	15.0	m
19.5°	m	16.0	m
21.4°	w	19.5	m
		21.3	w

*s = sharp, m = medium, w = weak

Figure 22, curve c, shows the X-ray diffraction spectra of optically active poly-(-)-α-phenyl-α-ethyl-β-propiolactone (pressed powder, unannealed) and racemic poly-α-phenyl-α-ethyl-β-propiolactone (pressed powder, unannealed), curve b, as compared to the diffraction spectra of poly-α-methyl-α-propyl-β-propiolactone (curve d) and poly(pivalolactone)(curve a) taken from Allegrezza's thesis[6]. Both the optically active (curve c) and the racemic (curve b) poly-α-phenyl-α-ethyl-β-propiolactone had a high degree of crystallinity according to their X-ray diffraction.

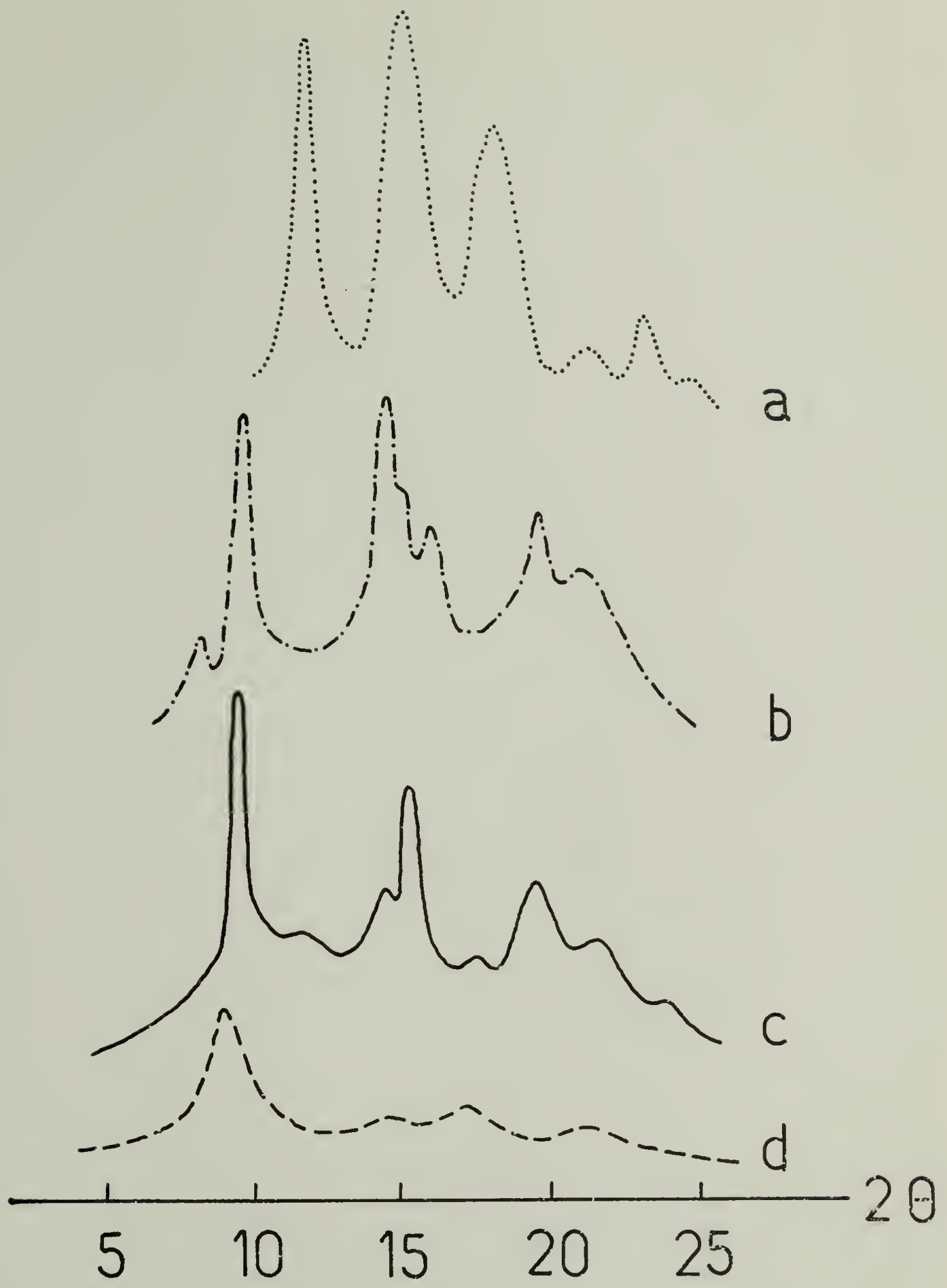
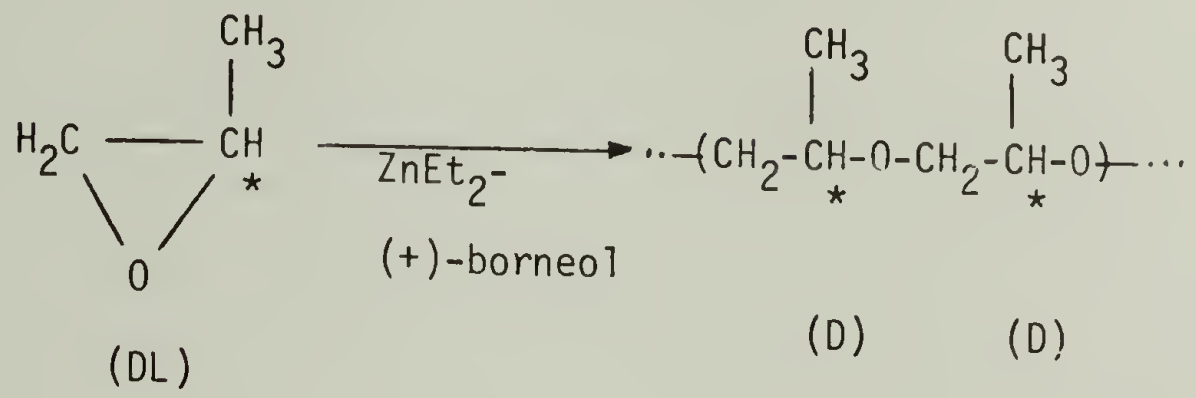


FIGURE 22. X-RAY DIFFRACTION OF DIFFERENT POLY-α,α-DISUBSTITUTED-β-PROPIOLACTONES. POLY(PIVALOLACTONE) (CURVE a), RACEMIC POLY-α-PHENYL-α-ETHYL-β-PROPIOLACTONE (CURVE b), OPTICALLY ACTIVE POLY-(-)-α-PHENYL-α-ETHYL-β-PROPIOLACTONE (CURVE c) AND POLY-α-METHYL-α-PROPYL-β-PROPIOLACTONE (CURVE d).

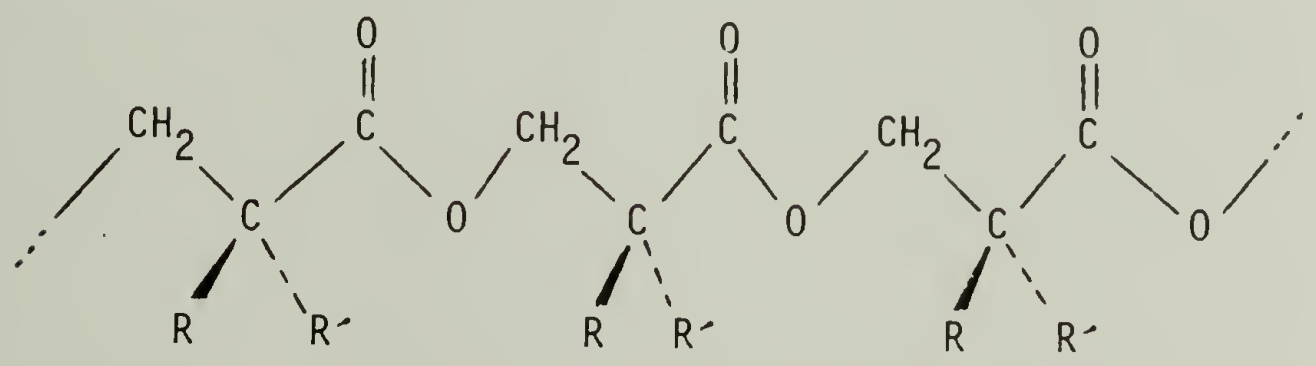
Stereoregularity, crystallinity and optical activity of polymers. For crystallization in polymers a high degree of regularity of the chemical and geometric structure is required. To obtain crystalline polymers, therefore, highly ordered sequences of monomeric units generally are required; in which case the polymer is said to be stereoregular. Stereoregularity in a polymer containing substituent groups is obtained if the configurations of the substituted carbon atoms in sequences of repeating units are either isotactic or syndiotactic or show any other ordered structure.

The first conditions for optical activity in polymers concerns the type of symmetry existing in the repeating unit. The repeating unit may not posses mirror symmetry; i.e., it must be asymmetric. The second condition for a polymer to be optically active is that the number of repeating units having an asymmetric structure of a given type, say D, differs from the number of repeating units of the L type. Otherwise the rotation caused by the D units will be balanced by an equal and opposite rotation caused by the L units. Thus a polymer obtained from a racemic monomer mixture will show no optical rotation, unless a stereoelective catalyst is used; i.e., a catalyst which preferentially selects one of the isomers over the other. An example of a stereoelective polymerization is the polymerization of DL-propylene oxide with diethylzinc - (+)-borneol as catalyst, carried out by Inoue et al.[91]. The poly-(propylene oxide) formed exhibited optical activity, dextrorotatory in chloroform and levorotatory in benzene. Tsuruta et al.[92] found that the recovered

monomer showed levorotation owing to the presence of excess L(-) monomer. From these results, they concluded that there is preferential incorporation of D(+)monomer into the polymer chain over L(-)monomer:

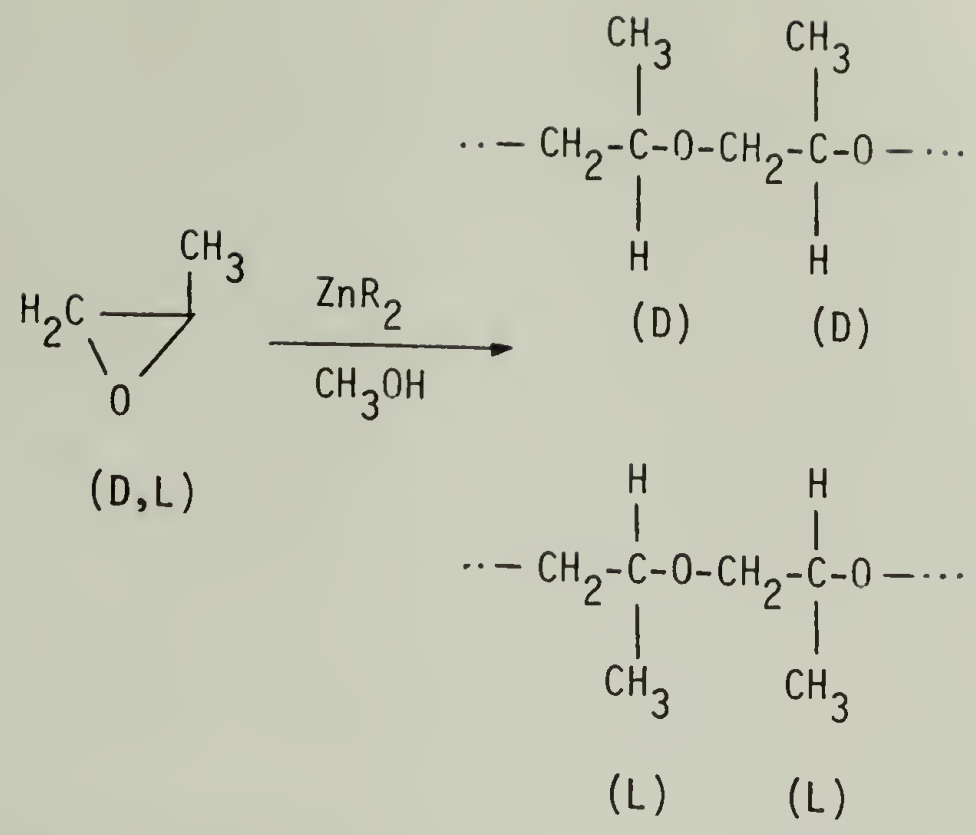


No rotation will be observed also if one has a mixture of pure D- and L- polymers (that is, pure isotactic polymers) or a polymer consisting of equal amounts of D- and L- blocks (blocks of isotactic configuration).



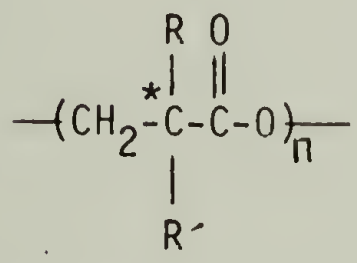
(An isotactic triad ≡ block of three successions D or L configuration.)

In order to obtain a mixture of pure D- and L-polymers a stereoselective initiator would have to be used. An example of stereoselective polymerization is the polymerization of DL-propylene oxide with zinc alkyl - methanol as initiator[92]:



(An excellent review on stereoselective and stereoelective polymerizations has been published by T. Tsuruta[93]).

In the present study the polyesters have a chiral center at the α-carbon:



This repeating unit has thus an intrinsic asymmetry, and optically active poly-α,α-disubstituted-β-lactones could be obtained using essentially three different methods: (1) polymerization of optically active monomers; (2) stereoelective polymerization of racemic monomers and (3) resolution of racemic mixtures of the polymer.

In the present work, method (1) was used because it was the one promising the best results. Method (2) was not purposely attempted because no stereoelective catalysts or mechanisms for the

polymerization of α,α-disubstituted-β-lactones are known to date. This method, however, has been successfully used in the case of poly(propylene oxide) and could possibly apply also to the β-lactone polymerization reactions.

Method (3) did not seem suitable because, for this method to work, one needs to have a mixture of pure D- and L- polymers, and for the polymers investigated in this study, this is probably not the case as discussed elsewhere in this paper. For other polymers this method has been successful, e.g. for racemic poly-4-methyl-1-hexene[70] and poly(DL-propylene oxide)[94].

The specific rotation [α] of a material varies as a function of the wavelength of the incident light. If the specific rotation is plotted against wavelength, the optical rotatory dispersion curve (ORD) is obtained. For a compound containing no chromophore in the region of wavelength in which it is examined, the optical activity will decrease in magnitude with increasing wavelength and a plain positive or plain negative ORD-curve is obtained, depending upon whether it rises or falls with decreasing wavelength. If one has a compound which contains one or several chromophores which give rise to an absorption in the wavelength examined, the ORD-curve will be anomalous and show one or several extrema (peaks, troughs or shoulders) at the wavelength where the chromopore absorbs.

For the region where no chromophore absorption bands are observed, Drude[95] proposed the following equation:

$$[\alpha] = \frac{A_o}{\lambda^2 - \lambda_o^2} \qquad (1)$$

where A is a constant, λ_o is the wavelength of the closest absorption maximum, and λ is the wavelength of the incident light. The above expression is referred to as the one-term Drude equation and applies for compounds having one chromophore. For compounds containing two different chromophores, two absorption maxima are obtained and a two-term Drude equation applies:

$$[\alpha] = \frac{A_1}{\lambda^2 - \lambda_o^2} + \frac{A_2}{\lambda^2 - \lambda_1^2} \qquad (2)$$

The first term corresponds to the rotatory contribution of the chromophore absorbing at λ_o and the second term refers to the second chromophore absorbing at λ_1.

By rearranging equation (1) one obtains:

$$[\alpha]\lambda^2 = A_o + \lambda_o^2[\alpha] \qquad (3)$$

Plotting $[\alpha]\lambda^2$ against $[\alpha]$ should give a straight line if the one-term Drude equation is obeyed. If a curvature is observed in such a plot this indicates that an anomalous behavior, such as a Cotton-effect (see p. 60), can be expected.

In the case of a polymer the total rotation can be formed by two contributions: one part is due to the asymmetric repeating unit, the other can come from the conformation of the macromolecule if a

regular or ordered conformation is formed; e.g. a helix. The conformational part of the rotation can be significant in the case of stereoregular polymers and can be used to determine a secondary structure such as a helix.

Moffitt and Yang[96] derived an expression for polypeptides and proteins having a helical conformation:

$$[m']_\lambda = [\alpha] \cdot \frac{3}{n^2 + 2} \cdot \frac{M_o}{100} = \frac{a_o \lambda_o^2}{\lambda^2 - \lambda_o^2} + \frac{b_o \lambda_o^4}{(\lambda^2 - \lambda_o^2)^2}$$

where n is the refractive index of the solvent; a_o, b_o and λ_o are constants; M_o is the molecular weight of the repeating unit and $[m']_\lambda$ is the molar rotation.

Multiplying both sides with $\lambda^2 - \lambda_o^2/\lambda_o^2$ one obtains:

$$[m']_\lambda \cdot \frac{\lambda^2 - \lambda_o^2}{\lambda_o^2} = a_o + b_o \cdot \frac{\lambda_o^2}{\lambda^2 - \lambda_o^2}$$

One then plots $[m']_\lambda \ \lambda^2 - \lambda_o^2/\lambda_o^2$ against $\lambda_o^2/\lambda^2 - \lambda_o^2$ and obtains a straight line if the Moffitt equation is obeyed. Validity of the Moffitt equation indicates the occurrence of a helical conformation.

When an optically active medium is traversed by a plane polarized light in the spectral range in which an optically active chromophore absorbs, not only does the plane of polarization rotate at an angle, but the resulting light is also elliptically polarized; that is, the medium exhibits circular dichroism (CD).

The molar ellipticity $[\theta]$ is defined by:

$$[\theta] = 2.303 \ \frac{4500}{\pi^1} \ (\varepsilon_L - \varepsilon_R)$$

where ε_L and ε_R are the molar extinction coefficients for left-and right-circularly polarized light.

The above equation can be rewritten to give:

$$[\theta] = 3300\ (\varepsilon_L - \varepsilon_R) = 3300 \cdot \Delta\varepsilon$$

CD measurements have been used in polymer chemistry especially for monitoring the helix-coil transition of polypeptides (see refs. 97, 98): Certain polypeptides and proteins exhibit a relatively large Cotton effect in the spectral region around 225 mm. This Cotton effect has been shown both to be related to the n-π* transition of the peptide group and to be conformation-dependent. Destruction of the α-helical conformation of synthetic polypeptides by means of pH changes, solvent changes, or thermal changes results in the loss of this Cotton effect.

The combination of unequal absorption (CD) and unequal velocity of transmission (ORD) of left and right circularly polarized light in the region in which optically active absorption bands are observed is a phenomenon called the Cotton effect. Figure 23 depicts the general dependence of CD and ORD upon wavelength in the region of an absorption band.

The CD-curve will have its maximum at the absorption maximum. The ORD-curve has a cross-over at the band center but extends with measurable intensity far out in both directions from the center. The CD-spectrum, on the other hand, can be observed only in the immediate neighborhood of the absorption band. The Cotton band shown in Figure 23 is positive: the rotation on the long wavelength side, and the CD-curve are positive at all points. For a negative Cotton band, these curves would be inverted.

Review on Optically Active Polyesters

Drew and Haworth[99], in 1927, synthesized the first optically active polyester known. They obtained a low molecular weight polymer (DP=10) from 2,3,4-trimethyl-l-arabonolactone and reported a specific rotation for the polymer of about one-fifth of that of the original lactone (+ 180° for the lactone).

Schulz and Schwaab[100] reported the optical rotatory dispersion of L-(-)-lactide and its polymer. The polymer softened between 175° and 190°C and had a η_{sp}/c-value of 0.29(l/g) (c=1 g/l) measured in chloroform at 25°C. The ORD of the L-(-)-lactide obeyed the one term Drude equation, while for the polymer the Moffitt-Yang equation was valid. The polymer showed a dispersion curve with a first extremum at 275 nm. At that time they concluded that the polymer possibly has a helical conformation in solution. Later, this was shown not to be the case: O-Acetyl-methyl-S-lactate was synthesized as model compound and its ORD compared to the polymer[101]. No appreciable difference in the behavior of the poly-S-lactic acid and

its model compound was found. These results suggested that the polymer may not be ordered in solution[101,102].

Overberger and co-workers[90], polymerized (R)-(+)-7-hydroxy-4-methylheptanoate of different optical purity. The polymer obtained from 80% optically pure starting material was pale yellow, very viscous liquid, $[\alpha]_D^{25}$= + 3.36°(c=3.4, benzene), with an intrinsic viscosity of 0.45 dl/g (benzene). The polymer did not crystallize when kept for two months at -78°C.

The polymer obtained from 96.7% optically pure starting material was a white solid, mp. 34-36°C, $[\alpha]_D^{25}$ = +8.55° (c=0.55, 2,2,2-trifluoroethanol), the intrinsic viscosity was 0.62 dl/g (benzene).

The polymer prepared from 80% optically pure starting material was expected to have less stereoregularity due to a random distribution of S and R monomer units along the chain.

They demonstrated that a material with high optical purity and greater stereoregularity could crystallize whereas the incorporation of 10% of the enantiomeric monomer was sufficient to inhibit crystallization. They attributed the differences in specific rotation, melting point and crystallinity to an increase in the stereoregularity of the polymer. The ORD of their polymer obeyed the Drude equation and they thus concluded that no secondary structure exists for this polymer in solution.

Overberger and Kaye[71] studied the ORD and conformation of poly-(methyl-ε-caprolactones) in solution. They detected no special con-

formation for these polyesters in solution. The Drude equation was obeyed in all solvents they studied.

Iwakura and co-workers[103] reported conformational studies of poly(L-α-hydroxyisovalerate). They prepared the polymer from L-α,α-diisopropylglycolide using zinc oxide as catalyst. Their results of ORD, CD and UV suggested that this polymer does not form any specific conformation such as a helical structure in the solvents examined. This conclusion was supported by the fact that the rotatory dispersion of the polymer was essentially the same as that of poly-(L-lactide).

Agostini[22,104] synthesized optically active poly-(β-hydroxy-butyrate). Besides the somewhat lower optical purity, the synthetically obtained polymer was similar in all respects to the naturally occurring polymer. He noted that both enantiomers of the monomer produced samples of poly(β-hydroxybutyrate) of positive rotation.

Delsarte and Weill[105] have investigated the conformation of poly(β-hydroxybutyrate) in solution. They measured the CD of the n - π* transition of the carbonyl chromophore in trifluoroethanol and compared it to values obtained for model compounds. They found that the n - π* rotatory strength in the polymer was twice as intense as in model compounds and concluded that the polymer must have a helical conformation in trifluoroethanol. Further proof of poly (β-hydroxybutyrate) retaining largely its helical conformation in solutions was brought by the same authors[106] using lanthanide-induced shifts in NMR.

Doak and Campbell[107] in their study of the effect of substituents upon melting points of linear polyesters synthesized polymers from d- and meso-tartaric acid and decamethylene glycol. The d-tartrate has the OH-groups oriented the same way in all structural units, while the meso-tartrate has the OH-groups oriented at random, depending upon the manner in which the acid units enter the polymer chain. They showed that the d-tartrate was crystalline, with a melting point of 66°C. The meso-tartrate was also crystalline, but melted at 33°C.

The same authors also prepared polyesters of tetramethylene glycol and α,β-dimethoxysuccinic acids. The d-α,β-dimethoxysuccinate was highly crystalline and melted at 92°C, whereas the meso-α,β-dimethoxysuccinate, prepared similarly, did not crystallize under similar conditions, presumably because of the random orientation of the substituent groups.

M. Yokouchi et al.[108] analyzed the molecular and crystal structure of naturally occurring optically active poly(β-hydroxybutyrate) by X-ray diffraction. They found that the polymer had a left-handed helical conformation with two repeating units per turn. Because the racemic polymer they synthesized showed the same X-ray diffraction as the naturally occurring optically active polymer, they concluded that the racemic polymer must have an isotactic configuration and consist of two kinds of crystallites, each composed only of left-handed helices of (R)-polymer chains, or only of right-handed helices of (S)-polymer chains.

Chiroptical properties of poly-(-)-α-phenyl-α-ethyl-β-propiolactone and its monomer. In the present study optically active poly-(-)-α-phenyl-α-ethyl-β-propiolactone was obtained by ring-opening polymerization of the corresponding lactone, using tetraethyl-ammonium benzoate as initiator.

Surprisingly the lactone of (-)-rotation gave a polymer of (+)-rotation. A similar behavior had been observed by Agostini[22] and by Overberger[71] in some cases. The optical rotatory dispersion (ORD) is given in Table VII and Figure 24 for both monomer and polymer.

The circular dichroism (CD) of the polymer and monomer in solution is shown in Figure 25. The dichroic bands at 250-270 nm can be assigned to the phenyl-chromophore. The CD band positions of the polymer obtained from monomer of (-)-rotation resemble those of the partially resolved (+)-monomer (see Figure 25). This bands are in the same region as those of the UV-spectra. (Figure 26).

Because no suitable solvent could be found for the polymer (that is, one which would not absorb near 220 nm), it was decided to make the low wavelength CD-measurements of the polymer in the solid state. For this purpose a thin film was cast on a quartz disk of 1/16 inch thickness. The disk was rotated in the holder and CD-curves were taken with the disk in different positions. This was to make sure that no artifacts due to orientation of the film were measured. All the CD-curves showed the same maximum at 220-223 nm (Figure 27). This positive Cotton-effect was assigned to the n - π* band due to the ester carbonyl and has been observed in other optically

TABLE VII

Optical Rotatory Dispersion of Poly-α-phenyl-α-ethyl--β-propiolactone and its Monomer

λ (nm)	$[\alpha]_D^{25}$ Polymer [a] (c=2.68)	$[\alpha]_D^{25}$ Monomer [a] (c=2)
589.00	---	- 54°
576.96	---	- 54°
546.07	+ 1.04°	- 61°
435.83	+ 9.35°	-104°
407.78	+14.31°	-123°
404.66	+14.88°	-126°
366.32	+24.20°	----

a) measured in chloroform at 25°C.

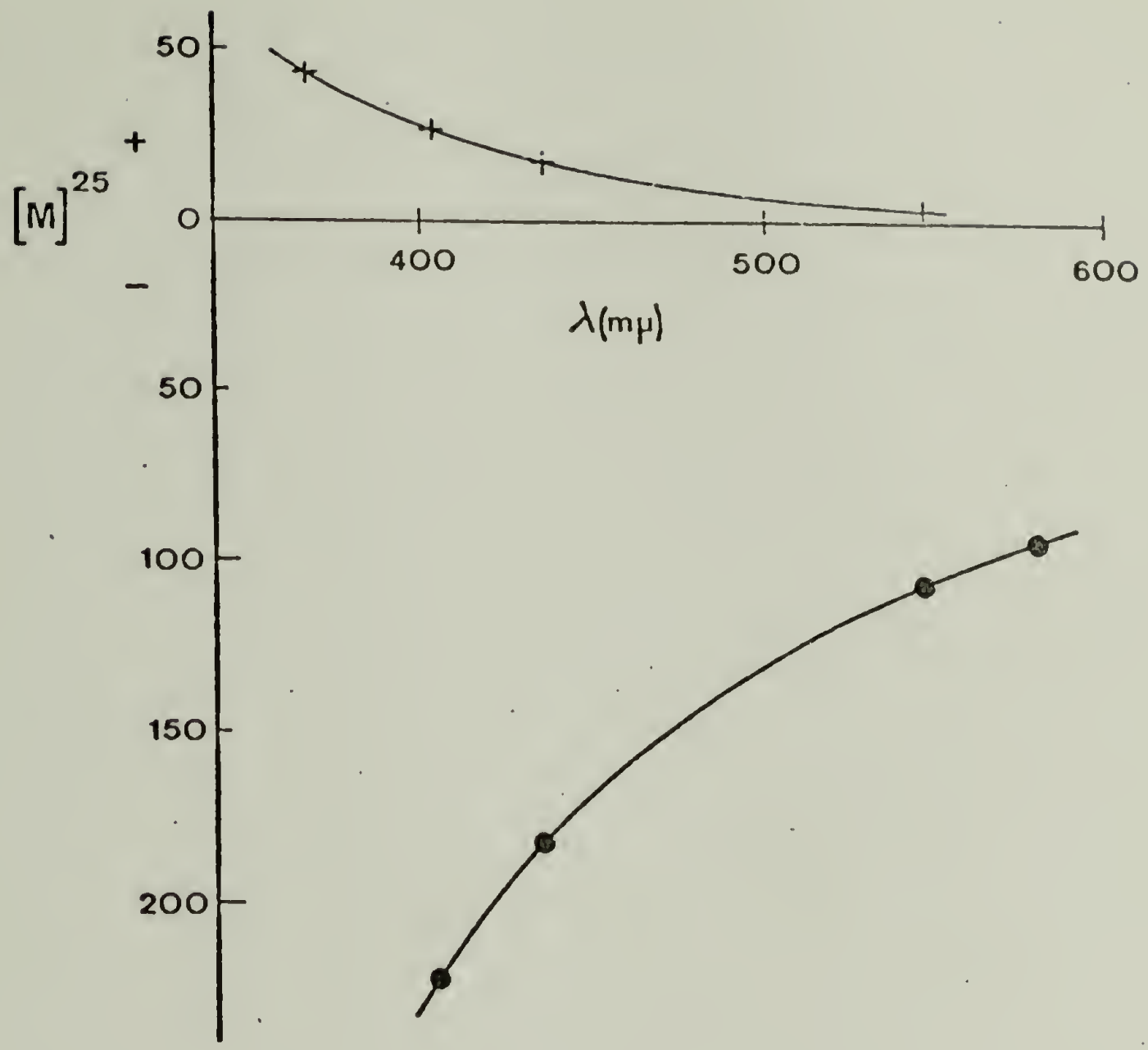


FIGURE 24. ORD OF (-)-α-PHENYL-α-ETHYL-β-PROPIOLACTONE (●) AND POLY-(-)-α-PHENYL-α-ETHYL-β-PROPIOLACTONE (+). MEASURED IN CHLOROFORM AT 25°C.

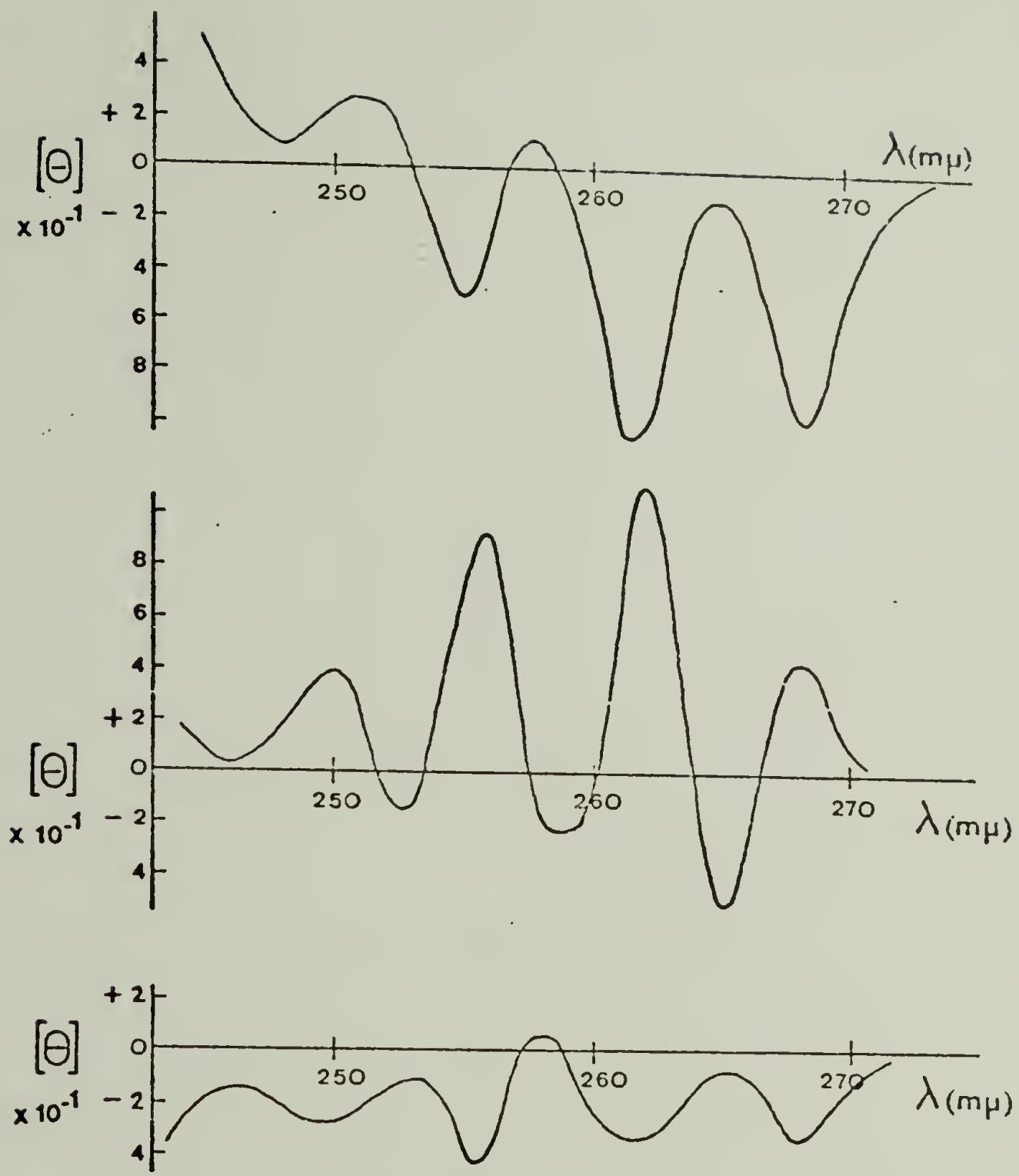


FIGURE 25. CD OF POLY-(-)-α-PHENYL-α-ETHYL-β-PROPIOLACTONE (UPPER CURVE), (-)-α-PHENYL-α-ETHYL-β-PROPIOLACTONE (MIDDLE CURVE) AND PARTIALLY RESOLVED (+)-α-PHENYL-α-ETHYL -β-PROPIOLACTONE (LOWER CURVE). THE POLYMER WAS MEASURED IN CHLOROFORM, THE MONOMERS IN ACETRONITRILE AT 25°C.

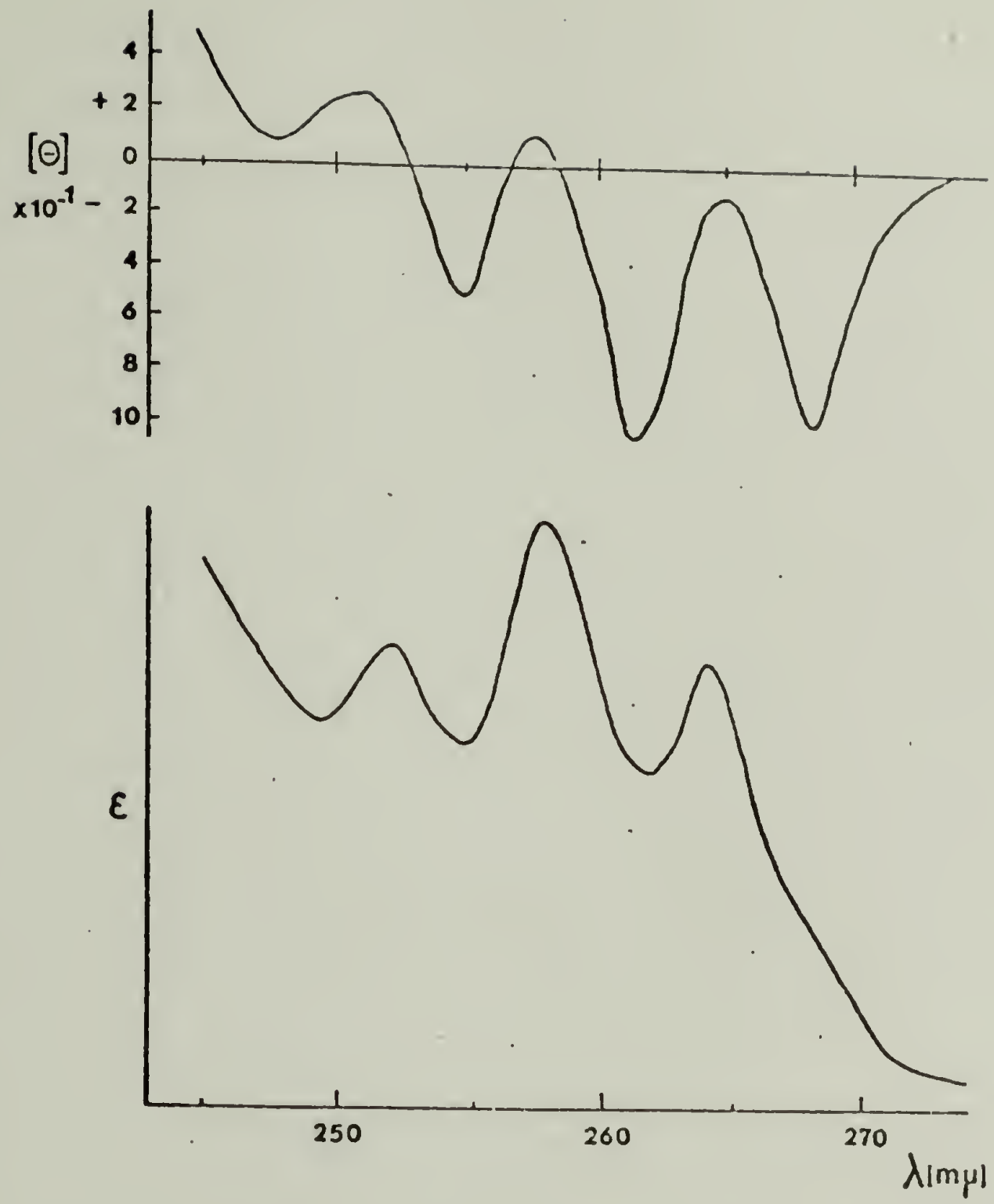


FIGURE 26. CD (UPPER CURVE) AND UV (LOWER CURVE) OF POLY-(-)-α-PHENYL-α-ETHYL-β-PROPIOLACTONE. CD MEASURED IN CHLOROFORM AT 25°C, UV AS THIN FILM CASTED ON A QUARTZ DISK.

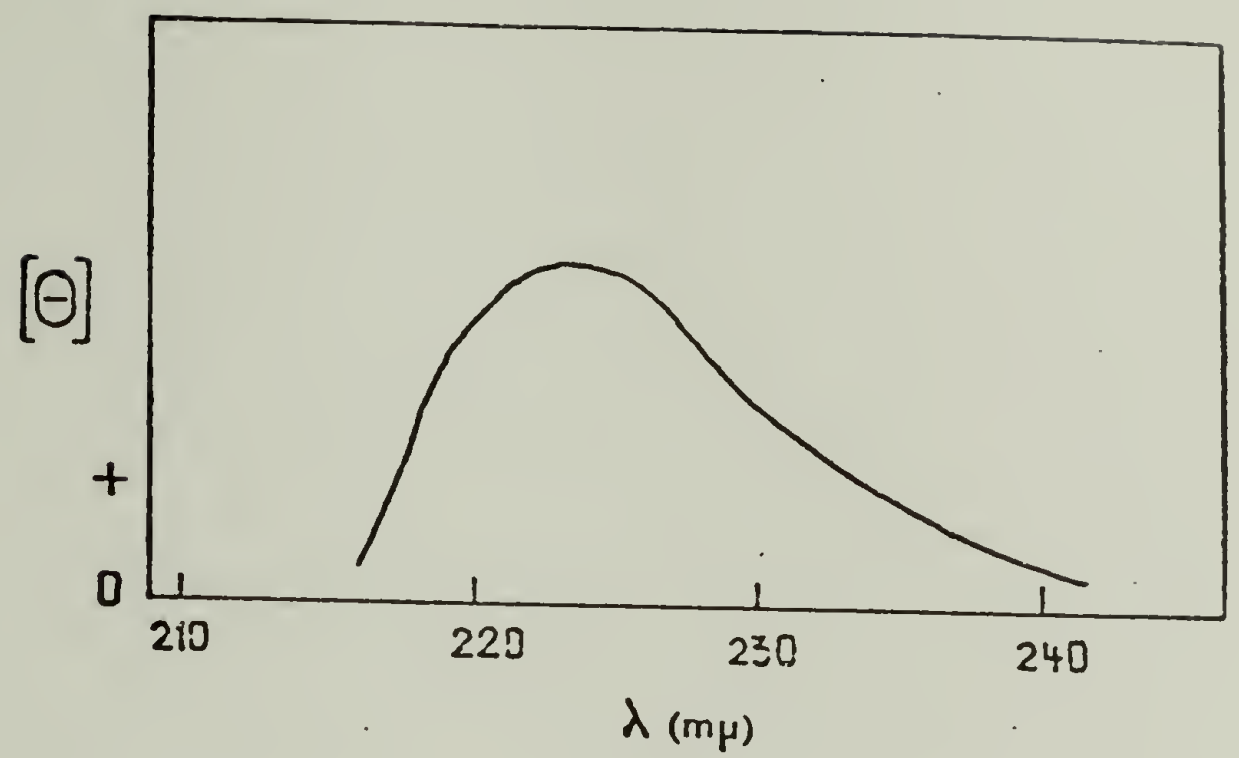


FIGURE 27. CD OF POLY-(-)-α-PHENYL-α-ETHYL-β-PROPIOLACTONE IN THE SOLID STATE SHOWING THE $n-\pi^*$ TRANSITION OF THE CARBONYL CHROMOPHORE. MEASURED AT 25°C AS THIN FILM CASTED ON A QUARTZ DISK.

active polyesters too.

The ORD of poly-(-)-α-phenyl-α-ethyl-β-propiolactone, in chloroform solution, is essentially the same in magnitude as that of the polymethyl-ε-caprolactones obtained by Overberger[71]. All other optically active polyesters studied by different investigators showed essentially the same behavior[100-106]. They all came to the conclusion that no specific conformation existed for these polyesters in solution.

The dichroic band of the phenyl-chromophore in the CD is rather small and indicates that probably no short range helical conformations are present for this polymer in chloroform, because if such a secondary structure would be present it would contribute to the absorption. In the present case, monomer and polymer show dichroic bands of different sign but of approximately same magnitude; if a helical conformation would be present a marked contrast in the CD spectra of the polymer and the monomer (as a bad model-compound) would be expected as, for example, is the case in the CD of poly-N-methyl-L-alanine and N-acetyl-N-methyl-L-alanine methyl ester (as model) in trifluoroethanol solution[109].

In order to be able to make more precise predictions a better model-compound, such as an open-chain ester, would have to be synthesized and examined.

Thus results of ORD and CD suggest that poly-(-)-α-phenyl-α-ethyl-β-propiolactone does not form any special conformation in chloroform. As mentioned above, no solvent which would not absorb above 220 nm, was found for the polymer. Solvents which were tried

but did not dissolve the polymer are: acetonitrile, 2,2,2-trifluoroethanol, tetrahydrofuran. Solvents which would absorb below 220 nm are listed in Table VIII. The optically active polymer was found to be soluble in chloroform, trifluoroacetic acid and hot benzene only.

If a suitable solvent can be found, which would allow to measure the CD and ORD of the polymer down to low wavelengths where the ester-chromophore absorbs (223 nm), one would be able to compare the conformation of the polymer in the solid state and in solution. In the solid state this polymer is probably in helical conformation as has been found for other polymers of this family[110-112], whereas in solution the above findings suggest that the polymer exists as random coil.

TABLE VIII

Solvents Absorbing at 220 nm or Below

Acetonitrile	180-195
Bis-2-methoxyethylether	
n-Butylalcohol	210-220
Butylether	
Cyclohexane	210-220
Cyclopentane	200-210
p-Dioxane	
Dodecane	
Glycerol	200-210
Heptane	
Hexafluoroisopropanol	
Hexane	200-210
Methane sulfonic acid	
2-Methylbutane	
Pentane	
iso-Pentyl alcohol	
Isopropyl alcohol	210-220
Tetramethylene sulfone	
2,2,2 Trifluoroethanol	
2,2,4 Trimethylpentane	200-210
THF	
Water	180-195
Sulfuric acid (96%)	180-195
Methanol	200-210
Ethyl ether	210-220

Summary and Conclusions

The crystalline properties of poly-α-phenyl-α-ethyl-β-propiolactones having different contents of isotactic configuration were studied.

A large difference in melting points was observed for the optically active polymer compared to the racemic and partially optically active polymer.

The chiroptical properties of the optically active poly-(-)-α-phenyl-α-ethyl-β-propiolactone were recorded in solution and in the solid state. No evidence for a secondary structure in chloroform solution was found.

X-ray diffraction of optically active and racemic poly-α-phenyl-α-ethyl-β-propiolactone showed that both polymers had a high degree of crystallinity. The differences in the crystalline peaks and in the melting points suggest that the optically active and the racemic polymer crystallize in different structures.

The aim of this work was to try to explain why poly-α, α-disubstituted-β-propiolactones could crystallize despite the fact that an asymmetric center is present in the main-chain if the two substituents are different. In Chapter I four options were given which could explain the crystallinity:

(1) there is a mixture of chirally homogeneous polymers;
or
(2) there are randomly formed sequences of sufficient length of either or both D or L units to permit

crystallization; or

(3) the polymer has a syndiotactic structure, which means alternating D and L monomer units; or

(4) there is no need of any stereoregularity in order for these polymers to be crystalline.

Based on the X-ray diffraction results (4) seems to be the most likely. It appears that the two different substitutents are interchangeable and that both D and L units can be accommodated in a crystal-lattice which, however, is different for the racemic polymer compared to the optically active polymer.

C H A P T E R I I I

EXPERIMENTAL PART

Measurement of chiroptical properties. The optical rotation dispersion curves (ORD) were measured on a Perkin-Elmer 141 MC polarimeter using chloroform as solvent for both α-phenyl-α-ethyl-β-propiolactone and its polymer.

Specific rotations of diastereomer salts were measured on a Kern-polarimeter, concentrations are given in g/dl.

The circular dichroisms were measured on a Cary-60 spectrophotometer using a 1-cm cell for solutions. Films were casted on quartz disks (1 inch diameter) from a solution of polymer in chloroform (2.5 mg/ml), using 4-6 drops. The quartz disks had a thickness of 1/16 inch. Measurements were made at ambient temperature under nitrogen.

Thermal transitions. The thermal measurements on the polymer samples were made with a Perkin-Elmer DSC 1-B differential scanning calorimeter. Polymer samples were weighed into a solids sample pan and run against an empty pan. Melting points are taken were the curves return to baseline.

Infrared measurements. IR measurements were made with a Perkin-Elmer 257 Grating Infrared Spectrophotometer. Polymer samples were casted as thin films on saltplates from a chloroform solution. Aminoacids were measured in KBr-pellets, all other compounds were measured between salt-plates.

NMR measurements. H^1-NMR of monomers and polymers were measured using a 90 MHz Perkin-Elmer R 32. All other compounds were measured on a 60 MHz Hitachi Perkin-Elmer R 24. Solvent for polymers was deutero chloroform, all other compounds were measured in carbon tetrachloride.

Optical purity measurements of the aminoesters, using NMR, were made on a 90 MHz Perkin-Elmer R 32, using carbon tetrachloride as solvent.

In all cases tetramethyl silane (TMS) was used as internal standard.

Ethyl-α-phenyl-cyanoacetate.[113] Sodium (24g, 1.05 mol) was suspended in the usual manner in 450 ml absolute toluene. The suspension was heated to 80°C and 85 ml absolute ethanol was added under stirring. As soon as almost all of the sodium had disappeared, a mixture of benzyl cyanide (117 g, 1 mol), diethyl carbonate (130 g, 1.1 moles) and 50 ml dry toluene was added. Under constantly stirring, the reaction-mixture was heated and the reflux condenser was arranged in such a way that in 2 hours time, 300 ml of solvent could be distilled off (mostly ethanol which is formed during the reaction). At the end, the vapor-temperature reached 108°C (toluene). During the reaction the sodium-salt of ethyl α-phenyl-cyanoacetate precipitated. At the end of the reaction time the mixture was allowed to cool to room temperature, and 600 ml of water and 120 ml of acetic acid were added. Two layers were formed and separated and the aqueous layer was extracted with 100 ml toluene. The combined toluene-phases were

washed with water and dried over sodium sulfate.

The solvent was then distilled off under vacuum (aspirator) and the residue fractionated under high vacuum to yield a clear, oily product: 165.6 g, 0.87 mol, 87% yield; bp 110-115°C (0.3 mm); nmr (CCl_4) 1.2 ppm(t,3H,CH_3), 4.15 ppm(q,2H,CH_2), 4.6 ppm(S,1H,CH) and 7.3 ppm(s,5H,C_6H_5). [Lit.[113]: 110-118°(0.5mm)]

Ethyl-α-phenyl-α-ethyl-cyanoacetate. This intermediate was prepared according to the method by E. Testa et al.[18] as follows:

Sodium (12.9 g, 0.56 mol) was dissolved in 225 ml absolute ethanol and heated to 50°C. Ethyl α-phenyl-cyanoacetate (106.5 g, 0.561 mol) was dissolved in 420 ml absolute ethanol and added to the sodium ethoxide solution. The temperature dropped to 35°C. Ethyl bromide (72 g, 0.66 mol) was added dropwise and the solution was refluxed for 90 minutes. After the reaction was completed, the precipitated sodium bromide was filtered off. All the solvent was evaporated from the reaction-mixture and the residue was taken up in ether and washed with water. The ether solution was dried over sodium sulfate. Fractionation was carried out under high vacuum to yield pure ethyl α-phenyl-α-ethyl-cyanoacetate: 79 g, 0.365 mol; 65% yield, bp 90-91°C (0.6 mm); nmr (CCl_4) 1.01 ppm(t,3H,CH_3), 1.2 ppm (t,3H,CH_3), 2.2 ppm(m,2H,CH_2), 4.15 ppm(q,2H,CH_2) and 7.3 ppm(m,5H, C_6H_5).

α-ethyl-α-phenyl-β-aminopropionicacid ethyl ester.[18] The following conditions for the preparation of this compound were slightly different than those used by Testa et al.:[18]

Ethyl α-phenyl-α-ethyl-cyanoacetate (60 g, 0.276 mol) in 100 ml absolute ethanol was reduced with hydrogen, using 30 g Raney-nickel (50%/50%) as catalyst.

A 1 liter autoclave was charged with the materials and pressurized with hydrogen-gas to 356 psi at 11°C. The autoclave was then heated without stirring to 80°C, which increased the pressure to 425 psi. Stirring was then started and the pressure dropped to 270 psi in 15 minutes time. After 2 hours the pressure had reached to 200 psi at 80°C. The autoclave was allowed to cool, the catalyst was then filtered off and all the ethanol was distilled off on a rotary evaporator. To the oily residue 50 ml water were added. The solution was acidified with 25 ccm conc. HCl and extracted with 100 ml benzene. The acidic, aqueous solution was made alkaline with saturated sodium carbonate solution and then extracted several times with benzene. The benzene solution was dried over sodium sulfate. Fractionation yielded: 49 g, 0.222 mol of pure product; bp 107-108°C (0.4 mm); nmr (CCl_4) o.7 ppm(s,2H,NH_2), 0.76 ppm(t,3H,CH_3), 1.12 ppm(t,3H,CH_3), 2.09 ppm(q,2H,CH_2), 3.08 ppm(s,2H,CH_2), 4.08 ppm(q,2H,CH_2) and 7.18 ppm(s,5H,C_6H_5). 80% yield.[Lit.[18]:108-114°C(0.5mm)]

α-phenyl-α-ethyl-β-aminopropionic acid. 10 g (0.045 mol) α-ethyl-α-phenyl-β-aminopropionic acid ethyl ester was dissolved in 200 ml conc. HCl. The mixture was refluxed for 10 hours, then let stand overnight. After evaporation to dryness, 30 ml water was added and the solution was again evaporated. Finally 25 ml water was added, and the solution was brought to pH 7 with conc. sodium

hydroxide solution. The aminoacid precipitated and was filtered off after the solution was allowed to cool in the refrigerator. The product was washed with 95% EtOH. Yield: 6 g (0.031 mol) α-phenyl -α-ethyl-β-aminopropionic acid; mp: 258-259°C (decomp.). 70% yield.

α-phenyl-α-ethyl-β-propiolactone.[20] In a 100 ml, 3-neck round-bottomed flask, fitted with a thermometer and a dropping funnel, was dissolved 4.8 g(0.0695 mol) of sodium nitrite in 12.5 ml water with stirring by a magnetic bar. The solution was cooled in an ice/H_2O bath to 0°-5°C after which a solution of 5 g (0.026 mol) of α-phenyl-α-ethyl-β-aminopropionic acid was slowly added, drop by drop, in 62.5 ml of 25% acetic acid. The addition was complete in about 1.5 hours. Stirring was continued for another hour at 0°-5°C, and the solution was then extracted with ether, washed with water and dried over sodium sulfate. The ether as well as most of the remaining acetic acid were distilled off on a rotary evaporator. The crude product was then fractionated under high vacuum to yield: 2.84 g (0.016 mol) α-phenyl-α-ethyl-β-propiolactone bp 82-85°C (0.25 mm); 62.5% yield, nmr (CCl_4) 0.93 ppm(t,3H,CH_3), 2.0 ppm (q,2H,CH_2), 4.33 ppm(2d, 2H,CH_2), 7.27 ppm(s,5H,C_6H_5).[Lit[20]:bp105°(0.8mm)]

Polymerization of α-Phenyl-α-Ethyl-β-Propiolactone

Purification of initiator. Tetraethylammonium benzoate was used as initiator. In order to get pure and dry initiator some re-crystallization solvents were tried including acetonitrile --- t-butyl alcohol and hexane --- benzene, but these were not successful.

The best method found was to add the salt into benzene, heat under stirring to obtain a suspension, and then let it cool in the refrigerator. Two layers were formed with the top layer being benzene. The lower layer did not recrystallize until a seed crystal was added upon which the initiator solidified. The crystals were stirred, filtered and washed with benzene, care being taken not to expose the initiator to air. The rest of the benzene was evaporated in a drying oven at 42°C under vacuum. After the initiator appeared to be dry, P_2O_5 was put into the oven and the initiator was dried some more at 42°C under vacuum over P_2O_5. A white powder was obtained and stored in the descicator (over P_2O_5) in a closed brown flask.

mp. : 72-75°C (sealed tube)

NMR : integral OK.

Purification of the solvent. THF was used as the reaction solvent. It was kept over calcium hydride for 24 hours and then distilled over $LiAlH_4$ and under nitrogen into a dry flask.

Poly-α-phenyl-α-ethyl-β-propiolactone. The polymerization was carried out at room-temperature under a positive nitrogen pressure in a flask closed with serum stoppers. The initiator was added to the flask under exclusion of air. The solvent, THF, was added using a syringe. The initiator was not soluble in THF so it was dispersed by stirring for a few minutes before adding the monomer.

Monomer: 1.07 g (6.1 mmol) α-phenyl-α-ethyl-β-propiolactone

Initiator: 0.0169 g (0.0675 mmol) tetraethylammonium benzoate

Solvent: 22.5 ml dry THF

The polymerization was followed by observing the characteristic carbonyl absorption bands in the IR of the monomer (1825 cm^{-1}) and polymer (1730 cm^{-1}). After 10 days the polymerization was stopped by adding 20 ml methanol. The suspension was then poured into 400 ml methanol and put in the refrigerator for one day after which the white powder was filtered off. The polymer was dried in the vacuum oven at 50°C. Yield: 1.02 g, 95% of theory. mp. 210°C (by DSC).

Resolution of α-ethyl-α-phenyl-β-aminopropionic acid ethyl ester[77] (see Figure 28). 150.5 g (0.4 mol) of dibenzoyl d-tartaric acid in 1200 ml methanol was added to a 3 liter, round-bottomed flask and heated to the boiling point. 88.5 g (0.4 mol) of α-ethyl -α-phenyl-β-aminopropionic acid ethyl ester in 100 ml methanol was added, the mixture was refluxed for 15 min., and then 800 ml methanol was distilled off. The solution was allowed to cool to room-temperature, and a crystalline mass started to precipitate and was filtered off after letting stand for 1.5 hours. The crystals were washed with two small portions of cold methanol and dried in the vacuum oven at 80°C.

Fraction (a): 56.5 g $[\alpha]_D^{19}$ = -73° (c=1.2, MeOH)

The mother liquor was heated on the steam bath until everything had redissolved and was then kept in the refrigerator for three days. The precipitated crystals were filtered off to yield:

Fraction (b_1): 26.4 g $[\alpha]_D^{19}$ = -72.5° (c=1, MeOH).

Methanol was then evaporated from the mother liquor until the solution had a volume of 950 ml. This was placed back in the re-

frigerator, and after two days fraction (b_2) was filtered off:
20.8 g $[\alpha]_D^{20}$ = -68.8° (c=1.2, MeOH).

Fraction (a) and (b_1) were combined together and recrystallized from 477 ml of methanol. After 3 hours, the crystals were filtered off to yield:

Fraction (e_1): 38.5 g $[\alpha]_D^{20}$ = -65° (c=1.1, MeOH).

Fraction (b_2) was added to the mother liquors of (a) and (b_1), and the solution was heated to the boiling point in order to dissolve everything. After one night in the refrigerator, the product was filtered off:

Fraction (e_2): 23 g $[\alpha]_D^{20}$ = -68.7° (c=1.2, MeOH).

Fraction (e_1) and (e_2) were recrystallized from 340 ml methanol to yield:

Fraction (h): 35 g $[\alpha]_D^{20}$ = -63.6°(c=1.1, MeOH).

Fraction (h) was recrystallized from 190 ml of methanol. After 30 min. fraction (i_1) was filtered off, after 1 hour fraction (i_2) and after 2.5 hours fraction (i_3).

Fraction (i_1): 19.5 g $[\alpha]_D^{21}$ = -59.7° (c=1.1, MeOH)

Fraction (i_2): 2.5 g $[\alpha]_D^{20}$ = -59.7° (c=1.1, MeOH)

Fraction (i_3): 1.5 g

The mother liquors of fraction (e_1) and (h) were added together and methanol was distilled off until the volume was 400 ml. The mixture was heated until everything went into solution and put in the refrigerator for 3 days. After this period of time, the crystalls obtained were filtered off and dried. They were added to the

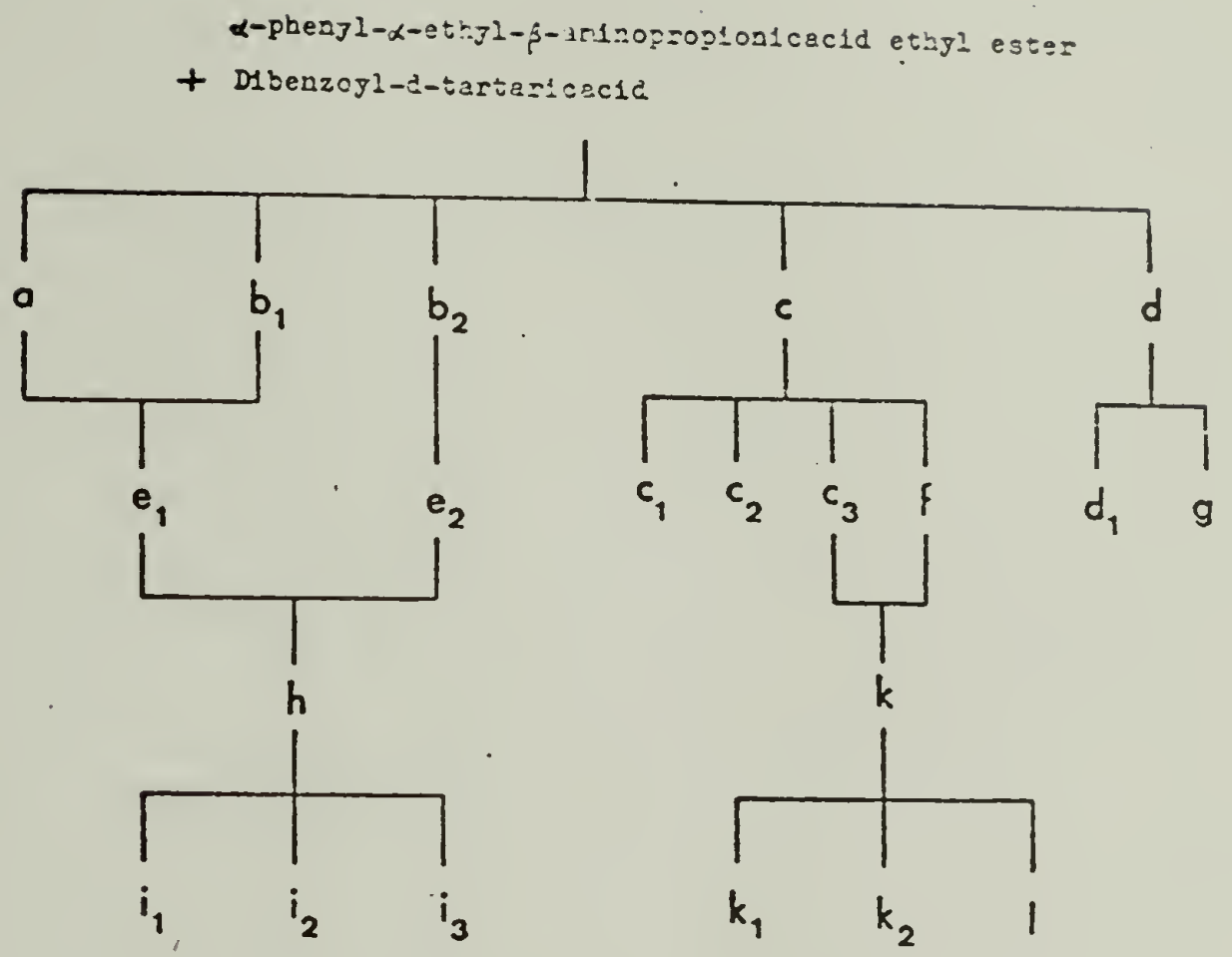


FIGURE 28. RESOLUTION OF α-PHENYL-α-ETHYL-β-AMINOPROPIONIC ACID ETHYL ESTER. CHART SHOWS HOW THE DIFFERENT FRACTIONS WERE OBTAINED.

mother liquor of fraction (i) (ca. 180 ml) and heated until everything had dissolved. After one hour the crystals obtained were filtered off:

Fraction (MM^1): 17.5 g $[\alpha]_D^{20}$ = -63.6° (c=1.1, MeOH).

Fractions (i_2), (i_3) and (MM^1) were added together and recrystallized from 125 ml methanol. After 30 min. the crystals were filtered off:

Fraction (MM^2): 11.5 g $[\alpha]_D^{22}$ = -60° (c=1.1, MeOH)

The mother liquors of fractions (a), (b_1) and (b_2) were added together and methanol was evaporated until only about 70 ml were left. The same amount of ether was then added and the precipitate filtered off to give:

Fraction (c): 61 g $[\alpha]_D^{20}$= -68.2° (c=1.1, MeOH).

The remaining solution was evaporated to dryness to give:

Fraction (d): 27 g $[\alpha]_D^{20}$ = -83.7° (c=1, MeOH)

Fraction (c) was recrystallized from 150 ml MeOH, this gave 4 fractions: (c_1), (c_2), (c_3) and (f).

The first fraction was filtered off after a certain time at room-temperature:

Fraction (c_1): 15 g $[\alpha]_D^{28}$ = -73° (c=2, MeOH).

The second fraction was filtered off after a certain time at room-temperature:

Fraction (c_2): 4.5 g $[\alpha]_D^{28}$ = -75° (c=2, MeOH)

The third filtered off after evaporating some solvent:

Fraction (c_3): 7 g $[\alpha]_D^{28}$ = -79° (c=2, MeOH).

After evaporating to dryness and addition of 50 ml ether, fraction (f) was obtained:

Fraction (f): 17 g $[\alpha]_D^{28}$ = -80° (c=2, MeOH).

Fraction (d) was recrystallized from 50 ml MeOH, to give fractions (d_1) and (g):

Fraction (d_1): 4.6 g $[\alpha]_D^{28}$ =-81.5° (c=2, MeOH).

After evaporating the supernatent liquid to dryness and treating with 50 ml ether fraction (g) was obtained:

Fraction (g): 10 g $[\alpha]_D^{28}$ = - 84° (c=2, MeOH).

Fractions (f) and (c_3) were combined and recrystallized from 75 ml methanol to give fractions (k_1), (k_2) and (l):

Fraction (k_1): 8.2 g $[\alpha]_D^{25}$ = -77.5° (c=2, MeOH).

Fraction (k_2): 1.8 g $[\alpha]_D^{25}$ = -80° (c=2, MeOH).

Fraction (l): 8.5 g $[\alpha]_D^{31}$ = -82.5° (c=2, MeOH).

(+)-α-phenyl-α-ethyl-β-aminopropionic acid ethyl ester.[77] The optically active (+)-aminoester was obtained by treating 19 g (0.0318 mol) of the (-) dibenzoyl-d-tartaric acid salt (Fraction (i_1)) $[\alpha]_D^{21}$ = -59.7° (c=1.1, MeOH) with 150 ml of saturated sodium carbonate solution. The liberated aminoester was extracted several times with ether. The ether solution was dried over sodium sulfate, filtered and evaporated on a rotary evaporator, and the remaining oil was fractionated under high vacuum to yield: 6.0 g (0.027 mol) (+)-α-phenyl-α-ethyl-β-aminopropionic acid ethyl ester. 85.5% yield.

bp 92-94° (0.35 mm) $[\alpha]_D^{21}$ =+24.8 (c=2, MeOH)

[Lit[77]: bp 111-114°; $[\alpha]_D^{30}$= 27.1° (c=2, MeOH)

(+)-α-phenyl-α-ethyl-β-aminopropionic acid. The optically active β-aminoacid was obtained from the aminoester in the same way as described for the racemic β-aminoacid. 5.2 g (0.0235 mol) (+)-α-phenyl-α-ethyl-β-aminopropionic acid ethyl ester in 100 ml conc. HCl gave: 3.55 g (0.0184 mol) (+)-α-phenyl-α-ethyl-β-amino-propionic acid. 78% yield. mp: 237-240° (decomp.).
R_f = 0.65 (butanol: acetic acid: water/4:1:1) $[\alpha]_D^{22}$ = +30° (c=1.5, H_2O).

Partially resolved (-)-α-phenyl-α-ethyl-β-aminopropionic acid ethyl ester. Fractions d_1, g and l (total 23.1 g (0.038 mol)) were given together and treated with ca. 250 ml saturated sodium carbonate solution. One extracted with ether and dried over sodium sulfate. Fractionation yielded: 6 g (0.027 mol) α-phenyl-α-ethyl -β-aminopropionic acid ethyl ester, 70% yield, bp 80-82°C (0.15 mm). $[\alpha]_D^{28}$ = -14.5° (c=2, MeOH).

Optical purity measurement by NMR (see p. 13) showed that 73.5% (-)-isomer and 26.5% (+)-isomer were present, corresponding to an optical purity of 47%.

(-)-α-phenyl-α-ethyl-β-propiolactone. The method was the same as used for the racemic compound (see p. 80). Thus, 3 g (0.0155 mol) (+)-α-phenyl-α-ethyl-β-aminopropionic acid gave 1.66 g (0.0095 mol) (-)-α-phenyl-α-ethyl-β-propiolactone, 61% yield, bp 84-86°C (0.25 mm).
$[\alpha]_D^{22}$ = -40° (c=1.5, MeOH)
$[\alpha]_D^{22}$ = -54° (c=2, chloroform).

Partially resolved (-)-α-phenyl-α-ethyl-β-aminopropionic acid. The procedure was the same as used for the racemic compound (see p. 79). Thus, 4.74 g (0.0214 mol) α-phenyl-α-ethyl-β-aminopropionic acid ethyl ester $[\alpha]_D^{28}$ = -14.5° (c=2, MeOH)) gave 2.64 g (0.0137 mol) of α-phenyl-α-ethyl-β-aminopropionic acid, 64% yield.

Partially resolved (+)-α-phenyl-α-ethyl-β-propiolactone. Again, the method was the same as used for the racemic compound. 2.3 g (0.012 mol) α-phenyl-α-ethyl-β-aminopropionic acid yielded 0.897 g (0.0051 mol) α-phenyl-α-ethyl-β-propiolactone, bp 80-82°C (0.23 mm), 42.5% yield.

Poly-(-)-α-phenyl-α-ethyl-β-propiolactone. The same conditions as for the polymerization of the racemic lactone were used. 0.81 ml = 0.765 g (4.35 mmol) (-)-α-phenyl-α-ethyl-β-propiolactone were given to a suspension of 0.0111 g (0.044 mmol) teraethylammonium benzoate in 15 ml dry THF.

The polymerization was carried out at room-temperature under dry nitrogen. After 8 days the polymerization was stopped by adding 20 ml methanol. The suspension was then poured into 400 ml methanol and put in the refrigerator overnight after which the white powder was filtered off. The polymer was dried in the vacuum oven at 45°C. Yield 0.599 g, 80% of theory, mp 260°C (by DSC).

$[\alpha]_{546}^{25}$ = +1.04° (c=2.68, chloroform)

$[\alpha]_{407}^{25}$ = +14.31° (c=2.68, chloroform).

Ethyl α-methyl-α-isopropylcyanoacetate. Ethyl α-methylcyano-acetate (127.1 g, 1 mol) was added with isopropyl bromide (155 g,

1.26 mol), into a 1-liter three-neck round-bottom flask, fitted with a condenser, a dropping funnel, a thermometer and a magnetic stirrer. A solution of 24.5 g (1.07 mol) of sodium in 500 ml dry ethanol was added slowly, and after the addition was completed, the reaction mixture was refluxed for 20 hours. Most of the ethanol was then distilled off, water was added, the organic layer separated and the aqueous solution extracted several times with ether. Fractionation yielded: 124 g (0.735 mol) of pure ethyl α-methyl-α-isopropylcyano-acetate, 73.5% yield, bp 55-56°C (0.4 mm); nmr (CCl_4) 1.0 ppm (d,3H, CH_3), 1.1 ppm (d,3H,CH_3), 1.3 ppm (t,3H,CH_3), 1.5 ppm (s,3H,CH_3) 2.1 ppm (m,1H,CH), 4.2 ppm (q,2H,CH_2).

α-Methyl-α-isopropyl-β-aminopropionic acid ethyl ester. Ethyl α-methyl-α-isopropylcyanoacetate (148.8 g, 0.855 mol) in 250 ml absolute ethanol was hydrogenated with 75 g Raney-nickel (50%/50%) catalyst. A 1-liter autoclave was charged with the reactants and pressurized with hydrogen gas to 1422 psi at 11°C. The autoclave was then heated without stirring to 60°C, which increased the pressure to 1600 psi. Stirring was then started, and the pressure dropped to 1200 psi in 1 minute while the temperature rose to 100°C. After 2 1/2 hours the pressure had reached 520 psi at 80°C. The autoclave was allowed to cool, and the catalyst was filtered off. Ethanol was distilled off on a rotary evaporator. Water was added and the solution was acidified with concentrated HCl. After extraction with ether, the acidic, aqueous solution was made alkaline with saturated sodium carbonate solution, and then extracted several times

again with ether. The ether solution was dried over sodium sulfate. Fractionation yielded: 127 g (0.735 mol) of α-methyl-α-isopropyl-β-aminopropionic acid ethyl ester, purity 95% (GC); bp 64-65°C (0.3 mm); yield 86% of theory, nmr (CCl_4) 0.9 ppm (s,2H,NH_2); 0.9 ppm (d,6H,$2CH_3$); 0.9 ppm (s,3H,CH_3), these three signals overlap; 1.2 ppm (t,3H,CH_3); 1.9 ppm (m,1H,CH); 2.7 ppm (m,2H,CH_2); 4.06 ppm (q,2H,CH_2).

α-Methyl-α-isopropyl-β-aminopropionic acid. 11 g (0.063 mol) α-methyl-α-isopropyl-β-aminopropionic acid ethyl ester was dissolved in 200 ml concentrated HCl. The mixture was refluxed for 10 hours and then allowed to stand overnight. After evaporation to dryness, 30 ml of water was added and again evaporated. Finally, 25 ml of water was added, and the solution was brought to pH 7 with concentrated sodium hydroxide solution. The aminoacid precipitated and was filtered off, after the solution was allowed to cool in the refrigerator, then washed with 95% ethanol and dried in a vacuum oven.

Yield: 7.0g (0.048 mol) α-methyl-α-isopropyl-β-aminopropionic acid, 76% of theory. Mp: 255-256°C (decomp.), turns brown at 203°C.

R_f = 0.61 (butanol: acetic acid: water = 4:1:1).

α-Methyl-α-isopropyl-β-propiolactone. 7.20 g (0.105 mol) sodium nitrite was dissolved in 30 ml water and cooled to 0-5°C. 6.00 g (0.0414 mol) α-methyl-α-isopropyl-β-aminopropionic acid was dissolved in 100 ml of 25% acetic acid, cooled to 3°C, and then added slowly and under stirring to the sodium nitrite solution. During the addition the temperature was maintained between 0° and 5°C

using an ice-water bath. After the addition was completed, the mixture was stirred for 60 minutes at 0-5°C then extracted twice with 50 ml ether and washed once with cold water. The etheral solution was dried over sodium sulfate. Most of the acetic acid still present in the etheral solution was distilled off, together with the ether, on a rotary evaporator. Fractionation yielded: 2.4 g (0.018 mol) α-methyl-α-isopropyl-β-propiolactone; bp 65-68° (4.3 mm); 45% yield, nmr (CCl_4) 0.95 ppm (d,3H,CH_3); 1.03 ppm (d,3H,CH_3); 1.32 ppm (s,3H, CH_3); 3.85 ppm (d,1H,CH_2); 4.05 ppm (d,1H,CH_2).

Second method. In this method the intermediate aminoacid was not isolated. Instead 21 g (0.121 mol) α-methyl-α-isopropyl-β-aminopropionic acid ethyl ester was refluxed for 28 hours in 100 ml diluted HCl (6 parts concentrated HCl + 4 parts water), then cooled to room temperature and neutralized with sodium hydroxide solution. To this neutral solution was added 75 ml glacial acetic acid to acidify. 13.5 g (0.195 mol) sodium nitrite was dissolved in 60 ml water and cooled to 0°C. From this point on the procedure was the same as above. Yield: 5.9 g (0.046 mol) α-methyl-α-isopropyl-β-propiolactone; bp 67-69°C (5.0 mm); 38% overall yield.

Poly-α-methyl-α-isopropyl-β-propiolactone. The polymerizations were carried out in bulk at 65-75°C under a dry nitrogen atmosphere in a flask closed with serum stoppers. The polymerization time was 18-24 hours. Tetraethylammonium benzoate was used as initiator. The polymerization was stopped by adding methanol to the reaction mixture. The suspension was then poured into a large quantity of

TABLE IX

Polymerization of α-methyl-α-isopropyl-β-propiolactone

Run	[M]/[I][a)]	Polym. Temp.	Polym. Time	Yield	Fraction Methanol[b)] -soluble	-insoluble
1	302	65°C	24 hrs.	99%	90.3%	9.7%
2	155	65°C	24 hrs.	99%	90.2%	9.8%
3	256	75°C	18 hrs.	94%	74.0%	26.0%

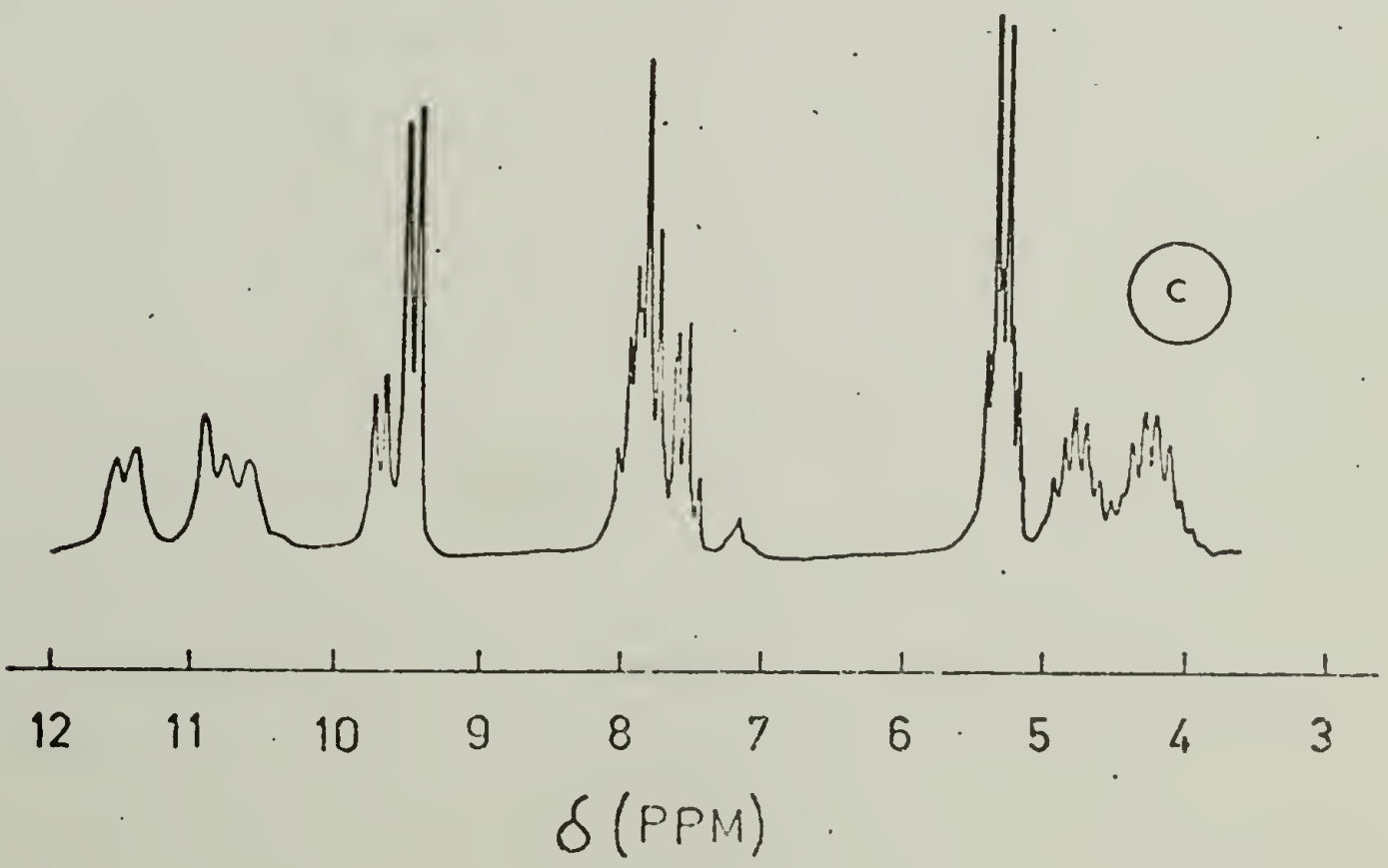
a) Molar ratio of monomer to initiator

b) Fraction of total polymer obtained

methanol and put in the refrigerator overnight, after which a fine, white powder was filtered off, yielding the methanol insoluble fraction. The methanol was distilled off to obtain a methanol-soluble fraction which was a very viscous liquid at 30°C. By freezing down to -60° this material solidified. Both methanol-soluble and methanol-insoluble fractions showed the same IR spectra. The results of different polymerization-runs are summarized in Table IX

Runs 1-3 were carried out using 12-24 mmoles of monomer. The methanol-insoluble fraction had a melting point of 99°C (by DSC); the methanol-soluble fraction did not show a crystalline melting point, a softening point at -5°C (by DSC) was observed only. For solution viscosity data see p. 40.

Calculation of optical purity from NMR. As mentioned in Chapter II, the optical purities of the α,α-disubstituted-β-aminopropionic acid ethyl esters were calculated using NMR. Below is the NMR spectrum of a CCl_4 solution of partially optically pure α-phenyl-α-ethyl-β-aminopropionic acid ethyl ester in the presence of europium (III)-shift reagent (from Figure 3, spectrum C):



The optical purity of the material was calculated by measuring the peak-heights of the signals for the ortho-hydrogen protons of the aromatic ring:

heights of signal for (+)-isomer:	16 mm	= 27%
heights of signal for (-)-isomer:	42 mm	= 73%
total	58 mm	=100%

This material consisted of 27% (+)-isomer and 73% (-)-isomer and had thus an optical purity of 46%.

CHAPTER IV

SUGGESTIONS FOR FUTURE WORK

Unfortunately the optically active poly-(-)-α-phenyl-α-ethyl-β-propiolactone was not soluble in a solvent which would allow to measure its ORD and CD in solution at low wavelength where the n - π* transition of the carbonyl chromophore occurs. If a solvent could be found, which would be transparent enough in the above mentioned region, additional information about the conformation of the polymer in solution could be obtained. A comparison of ORD and CD of the polymer in solution and in the solid state could bring further information concerning its conformation in these two states.

To be able to make more precise comparisons of the chiroptical properties of the polymer and a low molecular weight model compound, a straight-chain ester such as an optically active α-phenyl-α-ethyl-β-hydroxypropionic acid ethyl ester would have to be synthesized. The latter would serve as a better model than the α-phenyl-α-ethyl-β-propiolactone monomer used in this study.

The resolution of the α-methyl-α-isopropyl-β-aminopropionic acid ethyl ester could be tried using other resolving agents. This task is very time consuming and the chances of success are uncertain.

A more interesting subject would be the further study of the racemic poly-α-methyl-α-isopropyl-β-propiolactone. The methanol soluble and methanol insoluble fractions could be investigated in regard to tacticity and an explanation of their different thermal behavior could possibly be found.

As mentioned in Chapter I the synthesis used in this study can yield both α,α-disubstituted-β-propiolactones and α,α-disubstituted -β-propiolactams from the same intermediate aminoester. Polyamides from α,α-disubstituted-β-propiolactams form a new class of polymers which is currently under investigation in this laboratory [114,115]. Conformational studies of the poly-α,α-disubstituted-β-propiolactams by ORD and CD would be promising because these polymers dissolve in solvents which allow to measure the chiroptical properties at low wavelength. Many papers on the chiroptical properties of polypeptides have been published which would give ample data for comparison.

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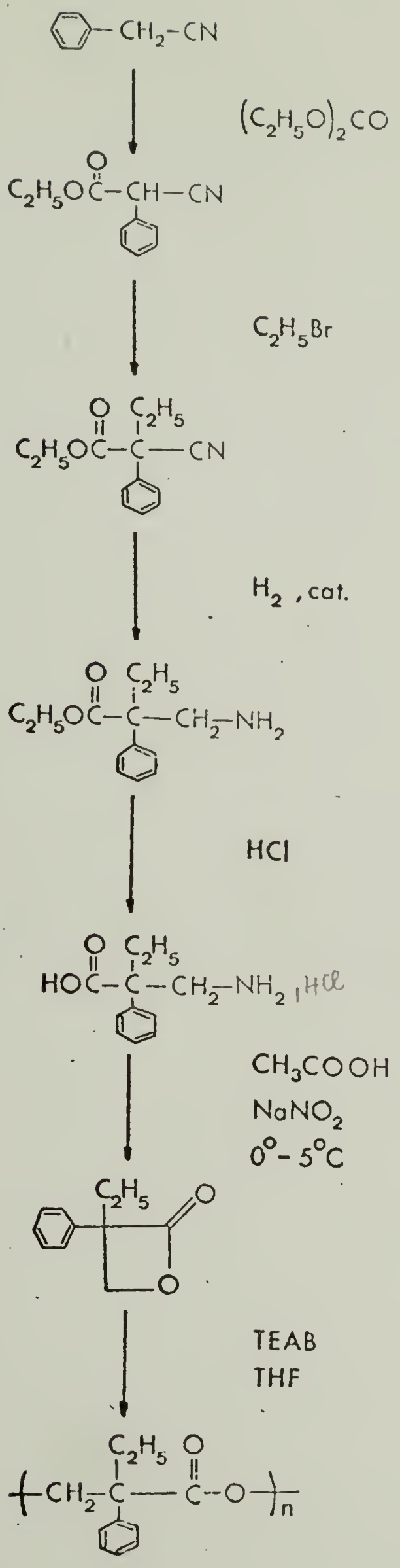
APPENDIX I

1. Synthesis of poly-α-phenyl-α-ethyl-β-propiolactone
2. Synthesis of poly-α-methyl-α-isopropyl-β-propiolactone.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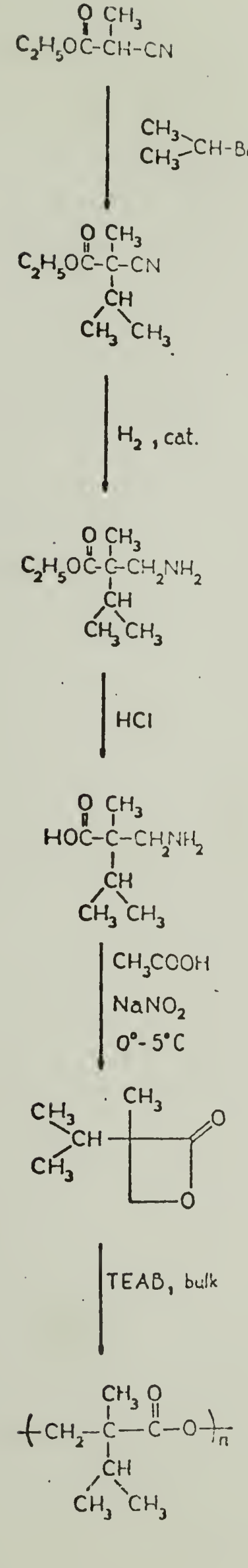
TEAB
THF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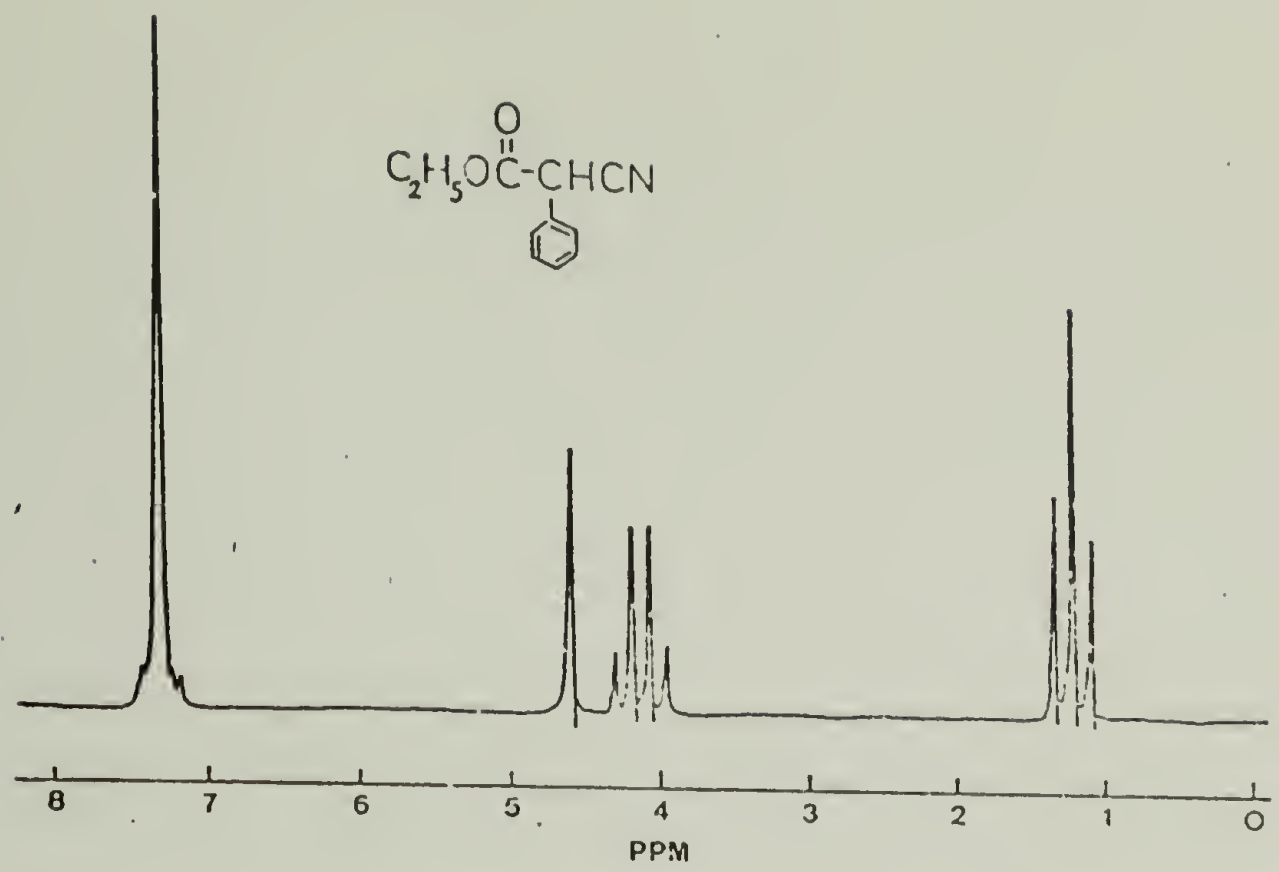
APPENDIX II

SPECTRAL DATA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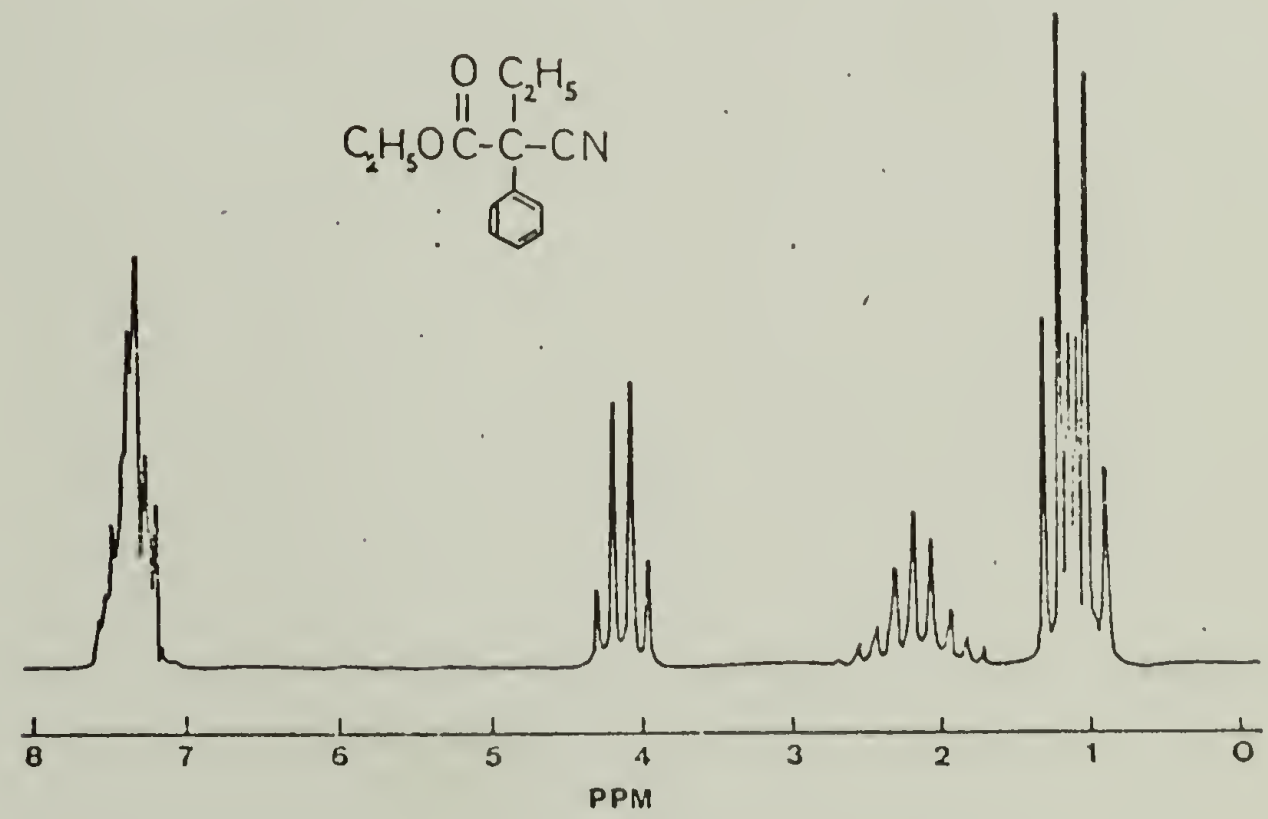
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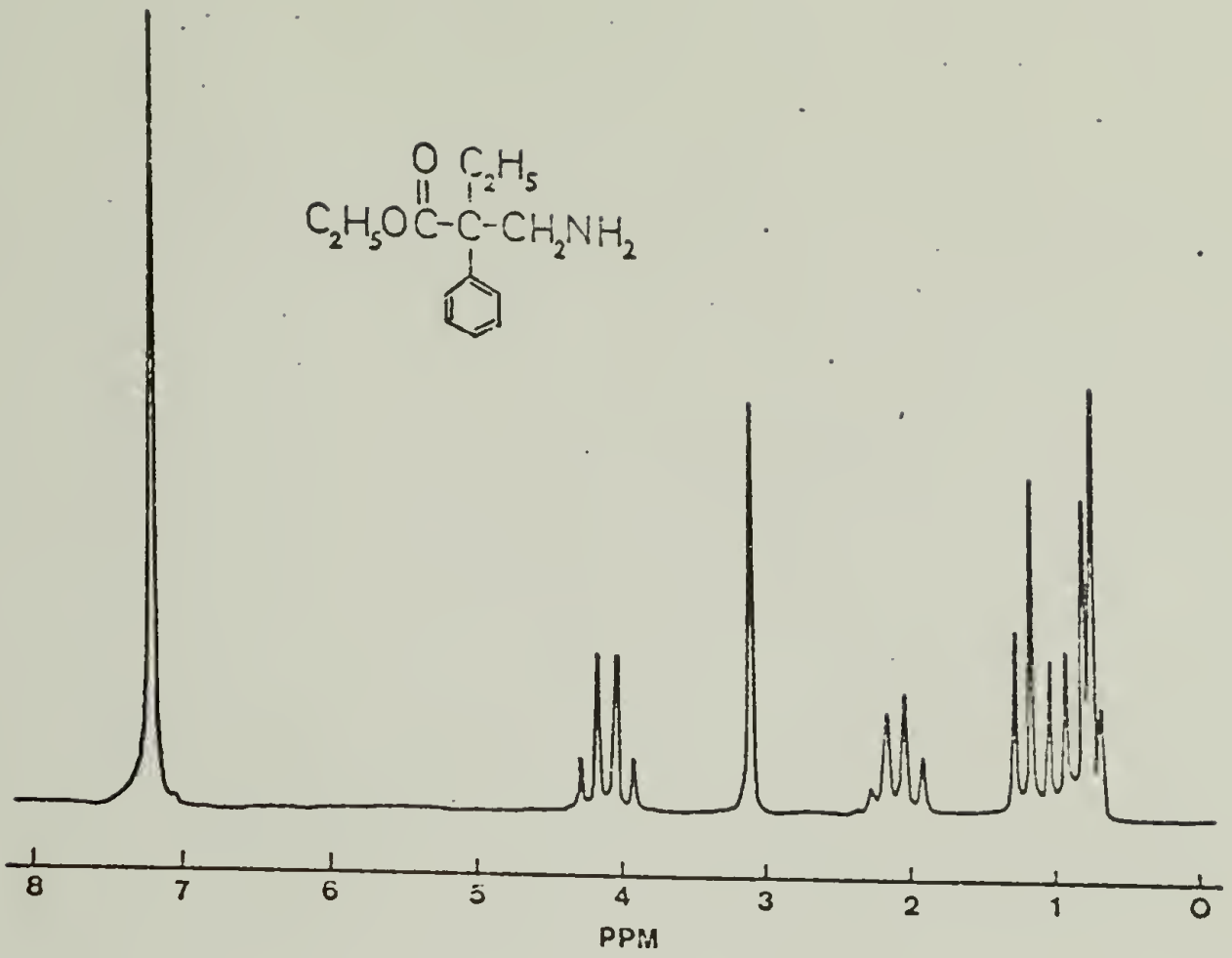
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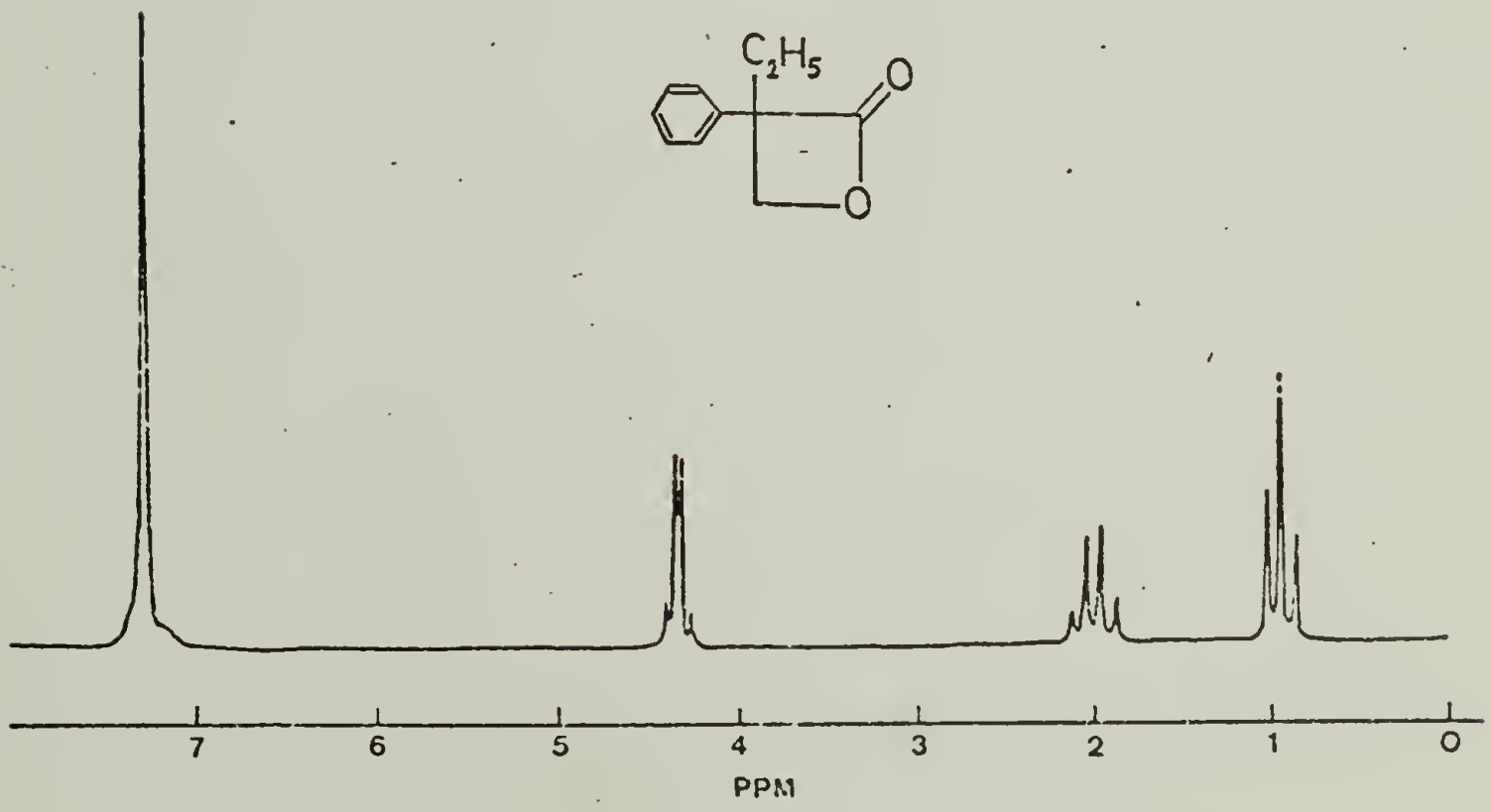
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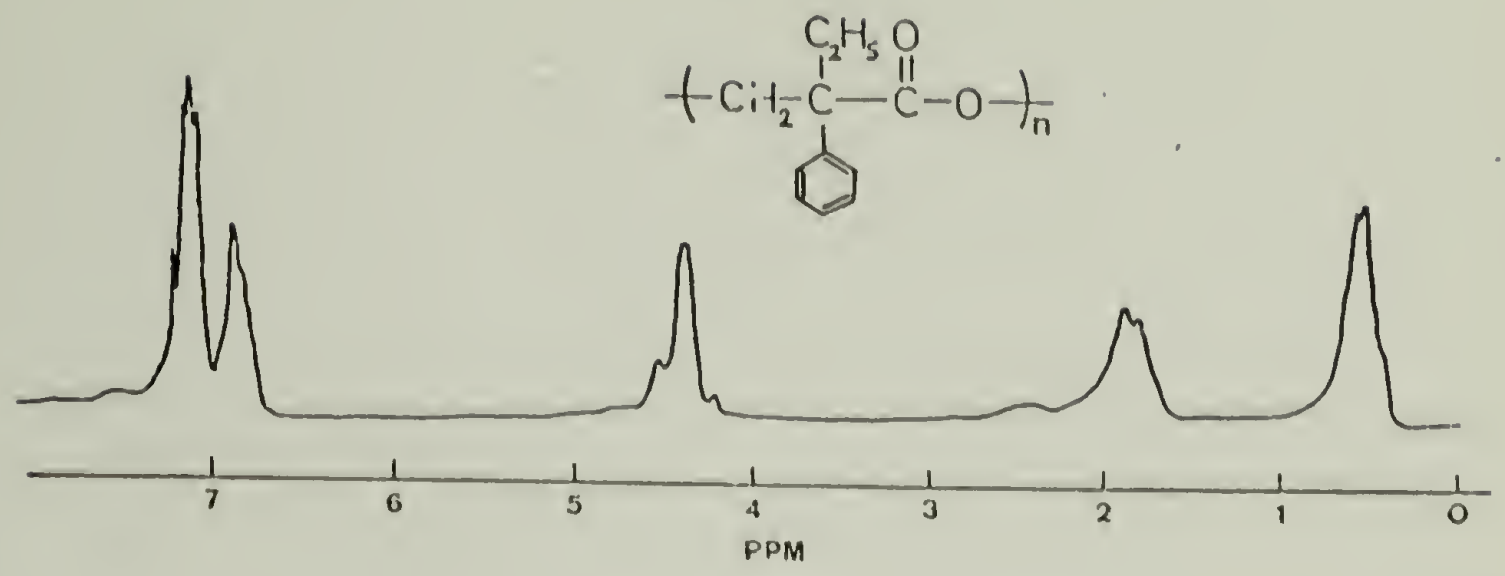
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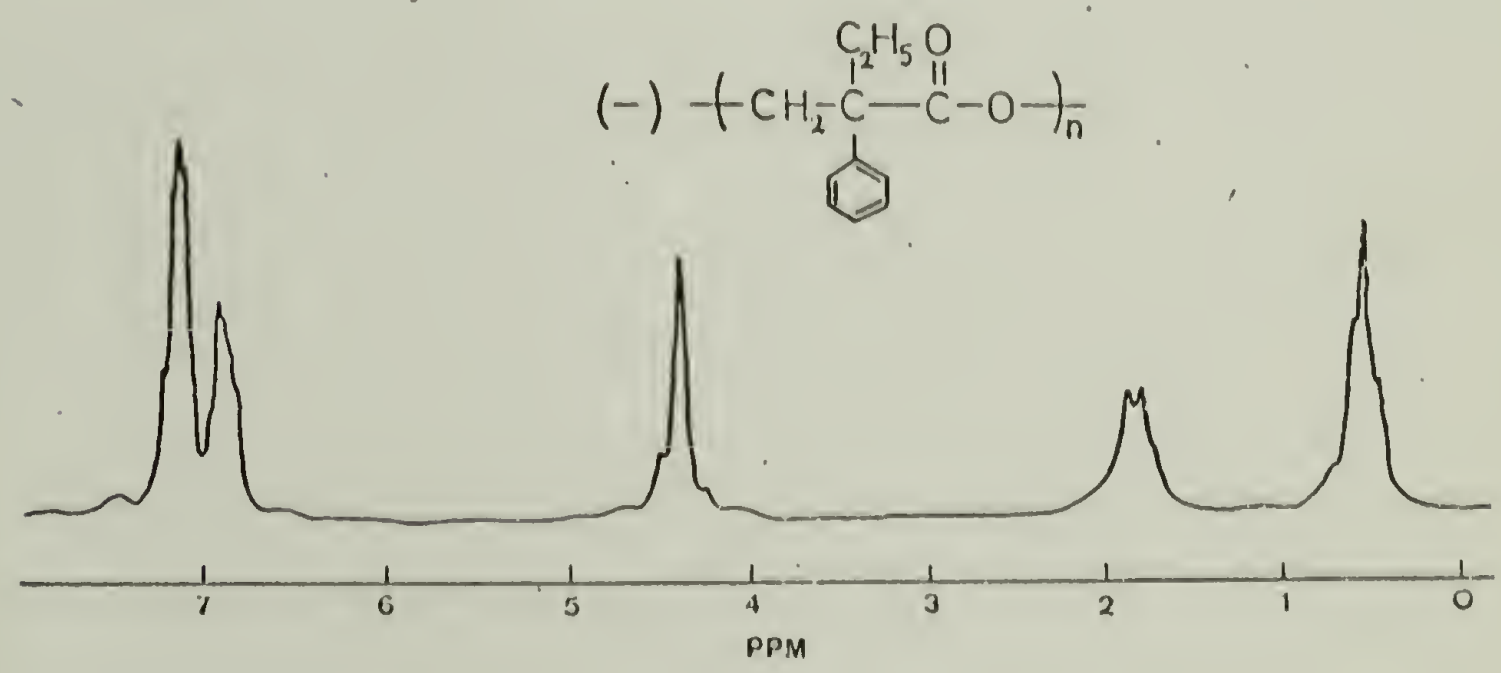
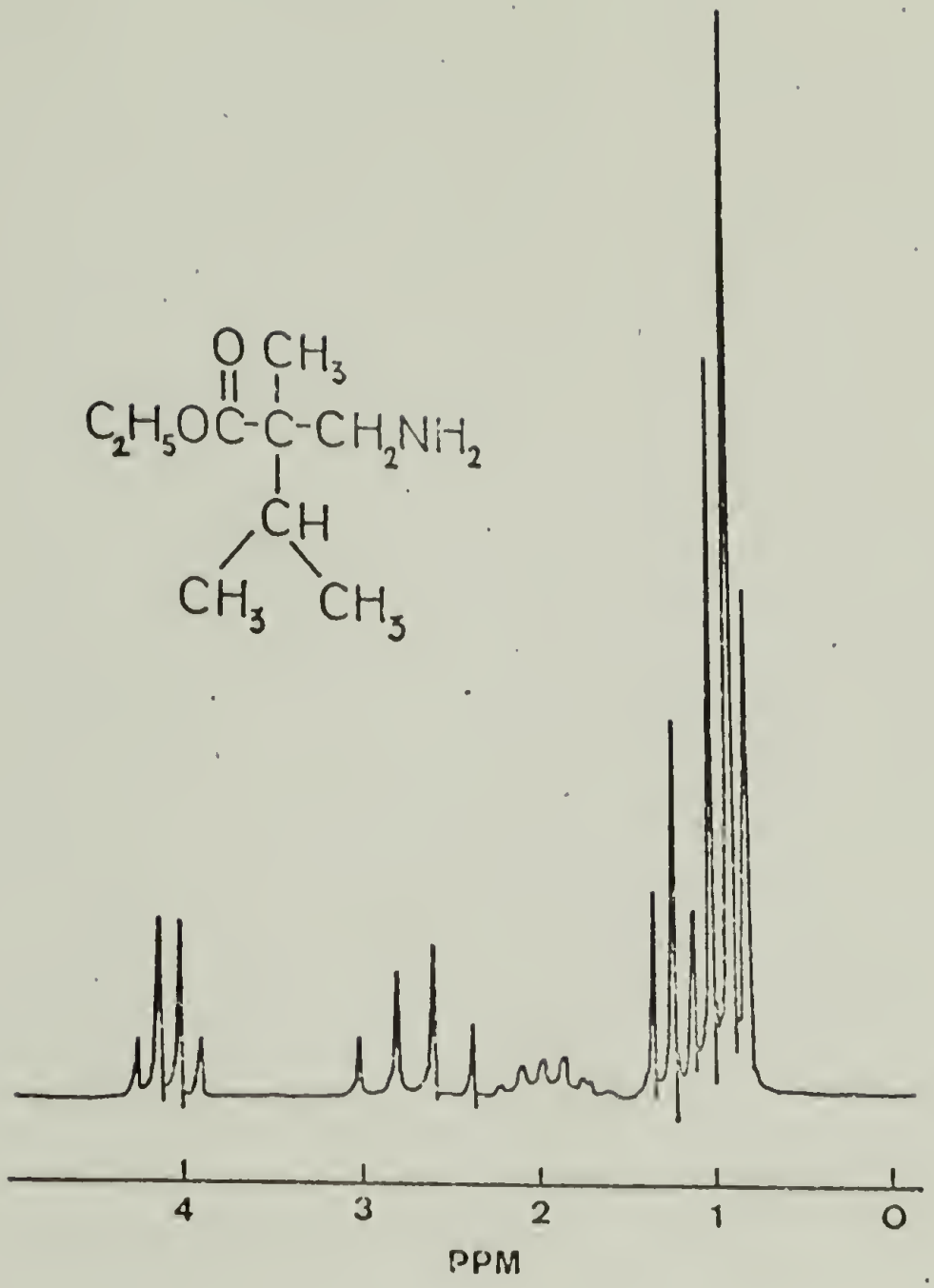
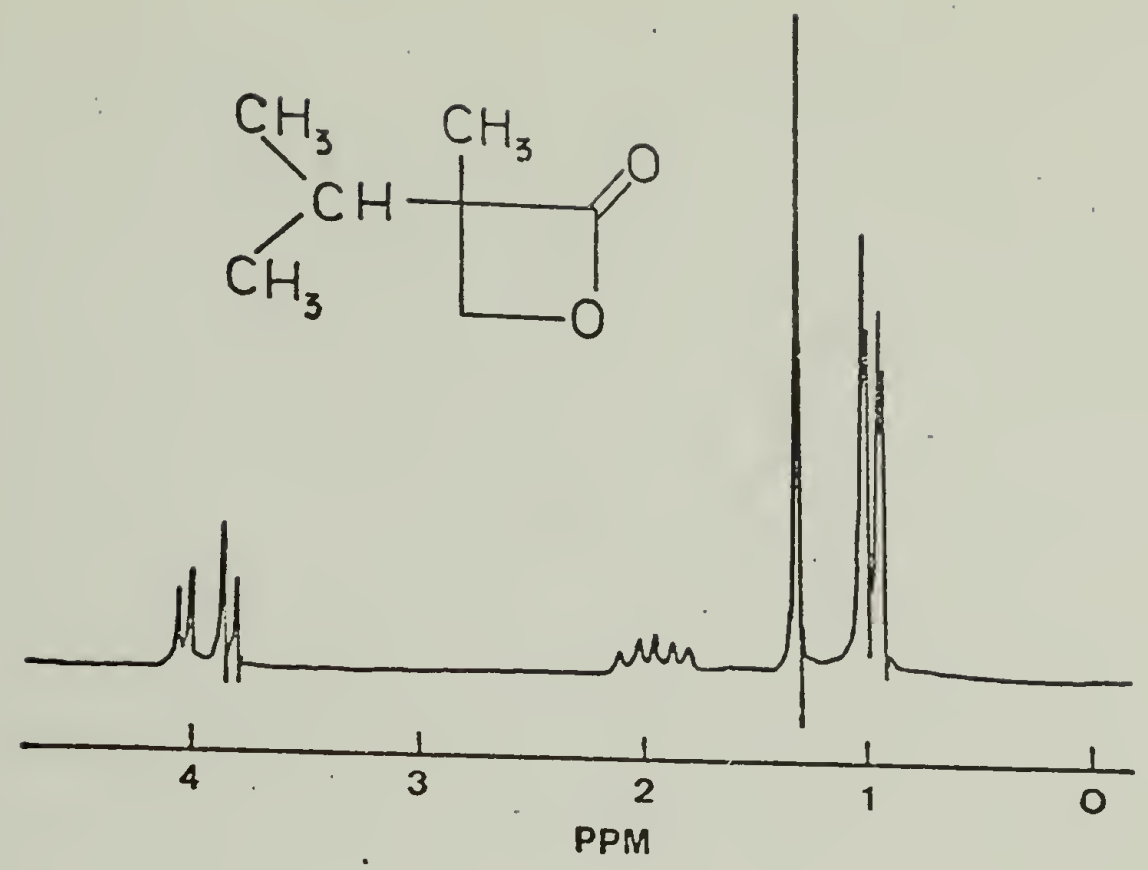
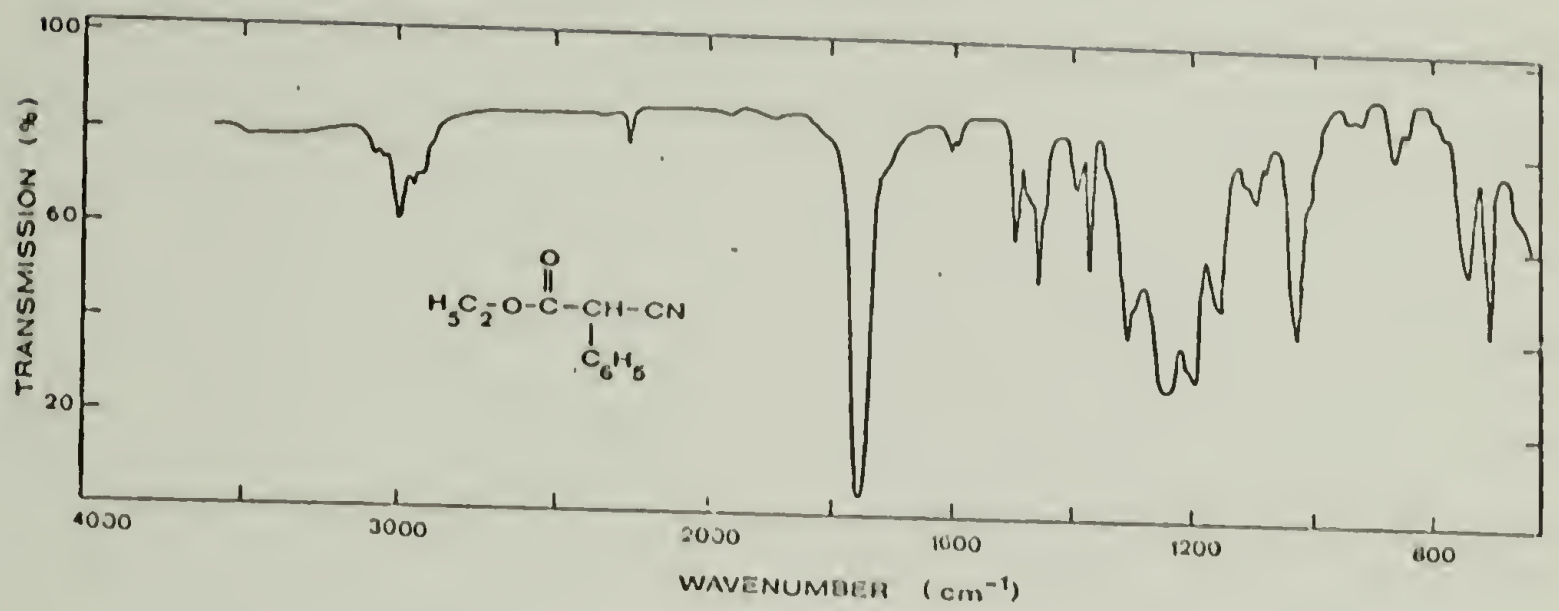
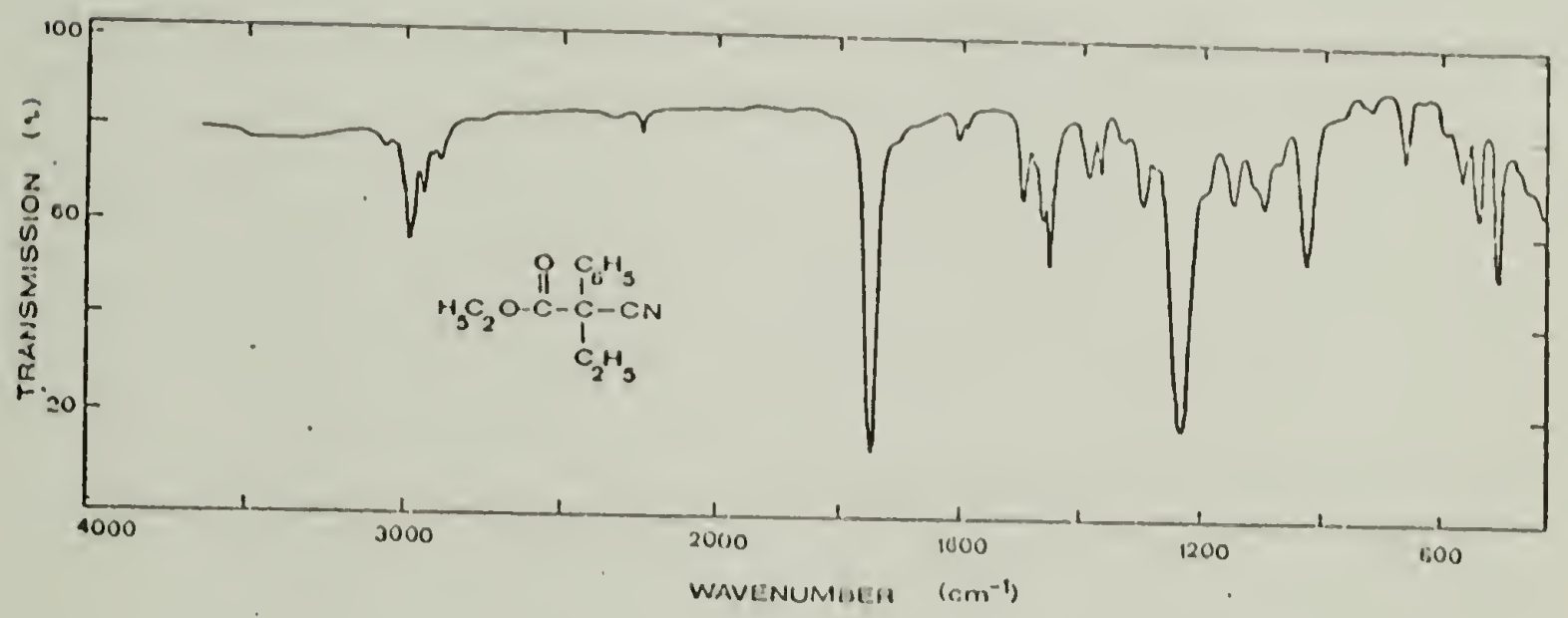
PPM

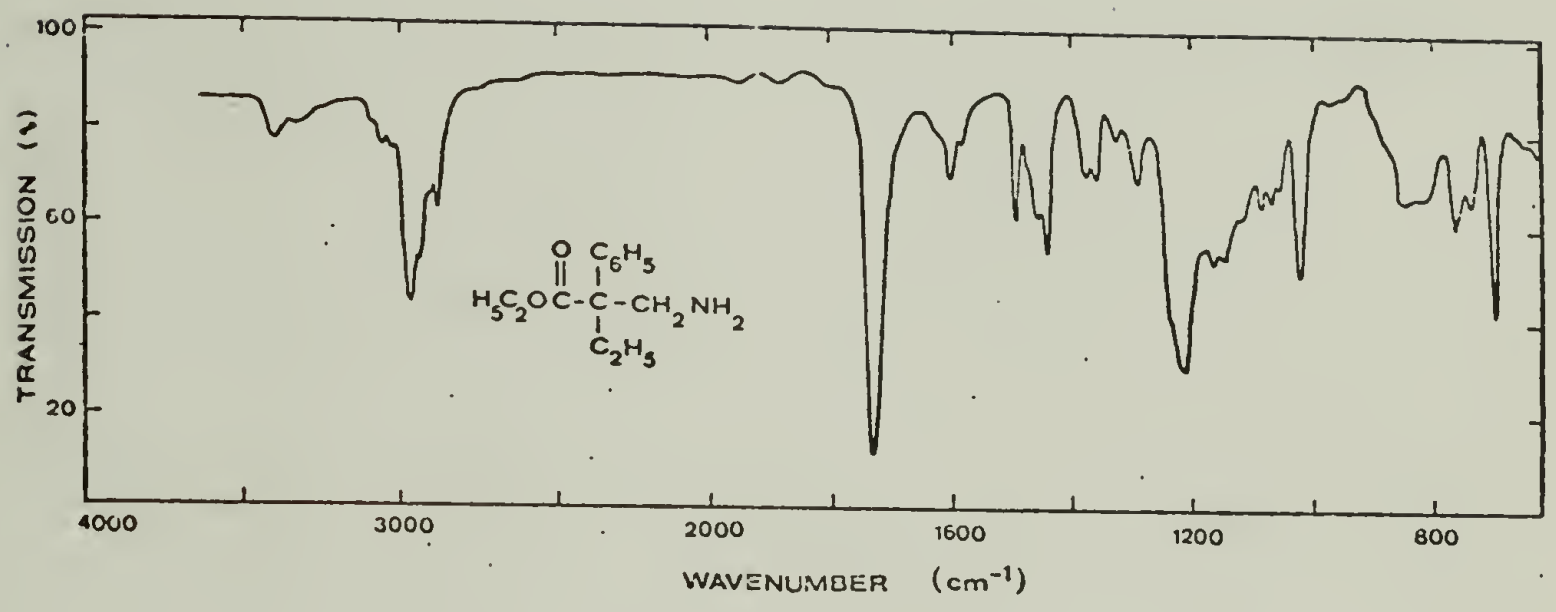

(-)
7
6
5
4
3
2
1
0
PPM

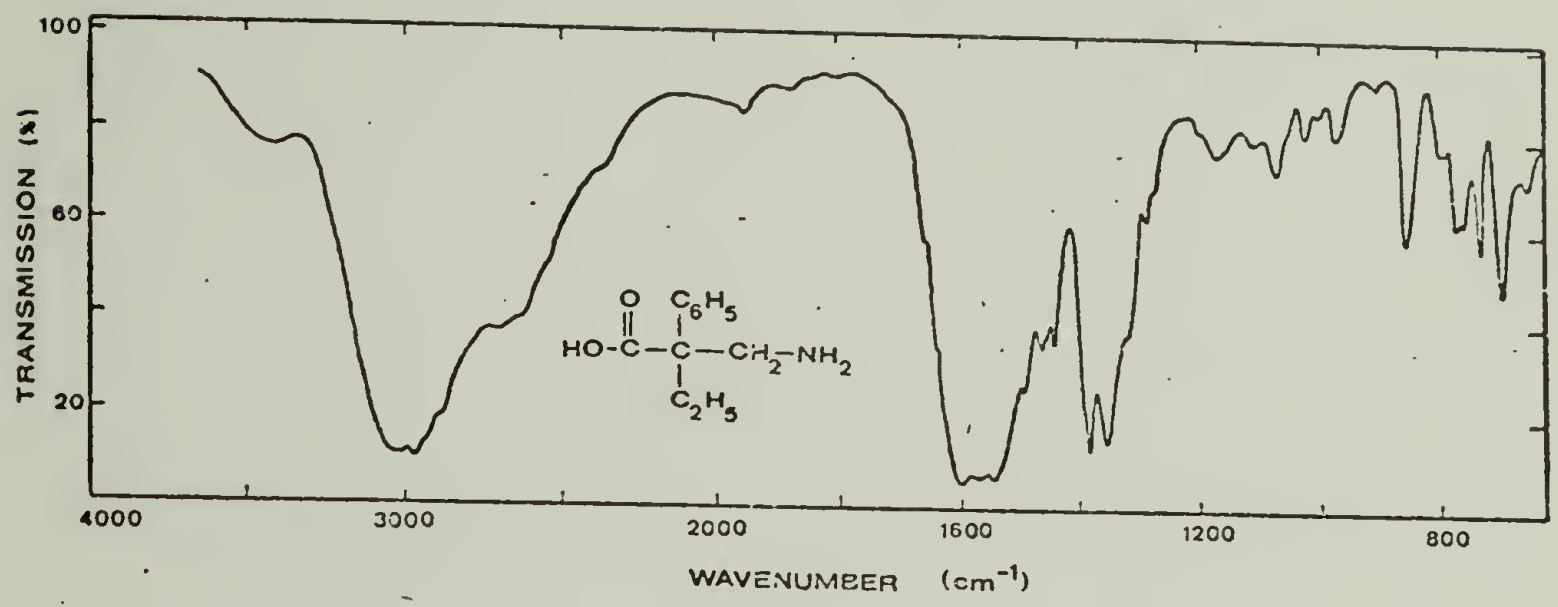

O CH3
C2H5OC-C-CH2NH2
CH
CH3 CH3
4
3
2
1
0
PPM

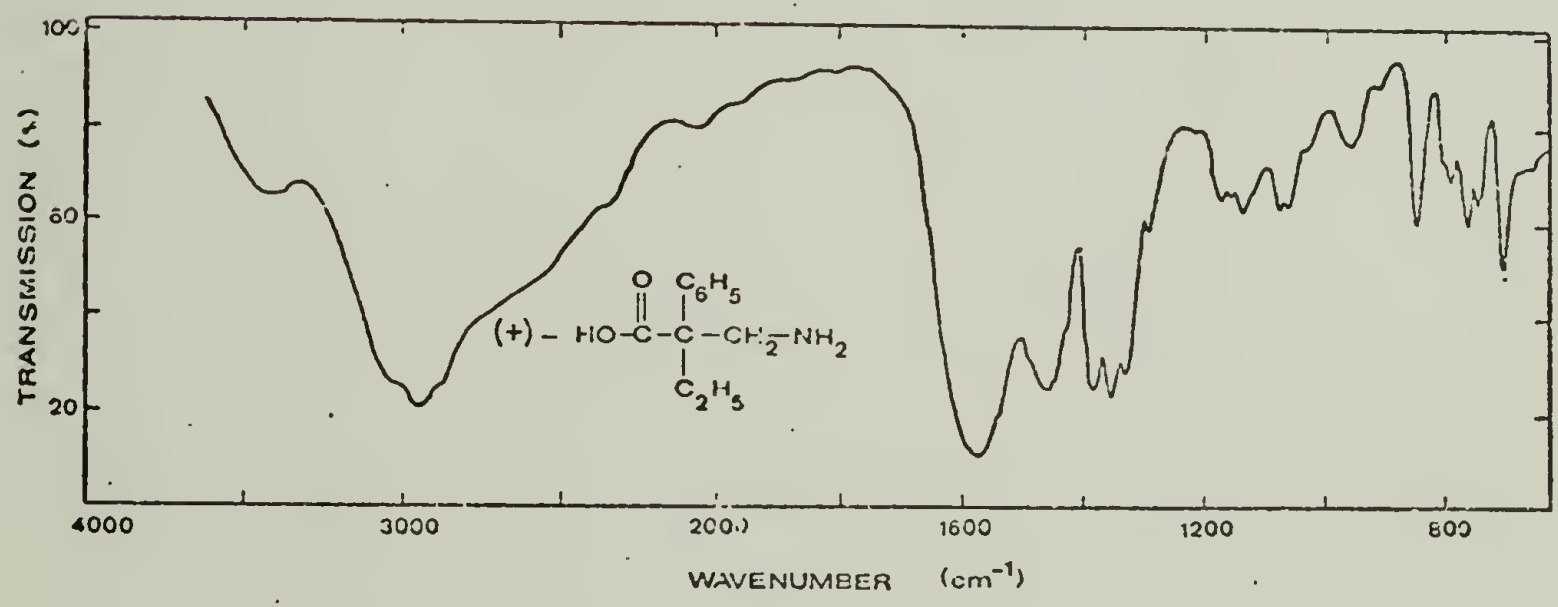

CH3
CH3
CH
CH3
O
O
4
3
2
1
0
PPM

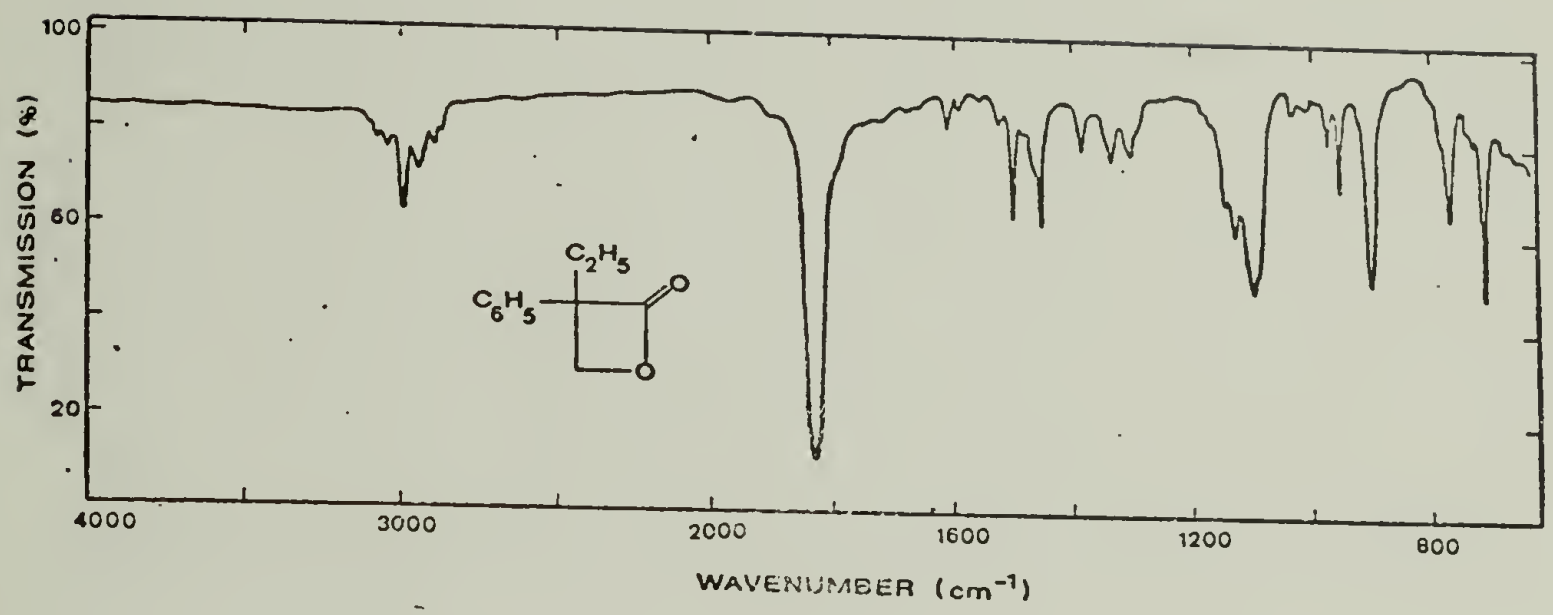

100
60
20
TRANSMISSION (%)
4000
3000
2000
1600
1200
800
WAVENUMBER (cm⁻¹)

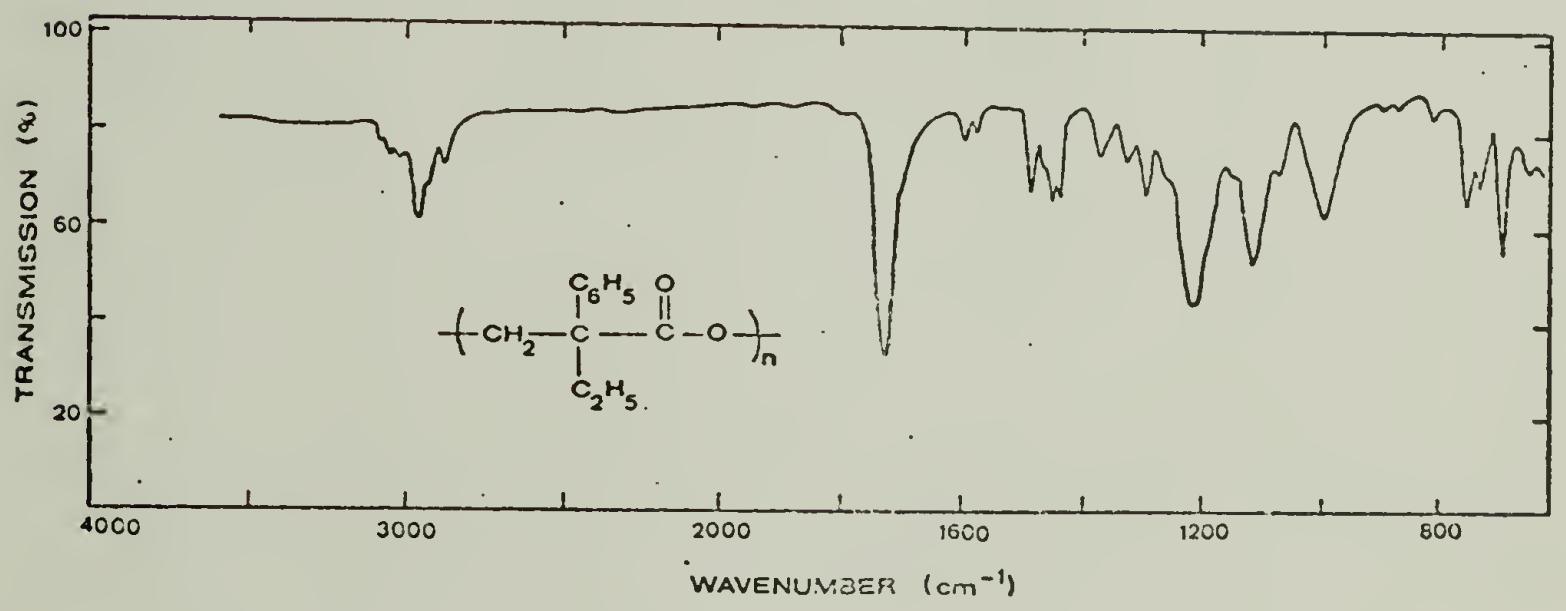

100
60
20
TRANSMISSION (%)
4000
3000
2000
1600
1200
600
WAVENUMBER (cm⁻¹)

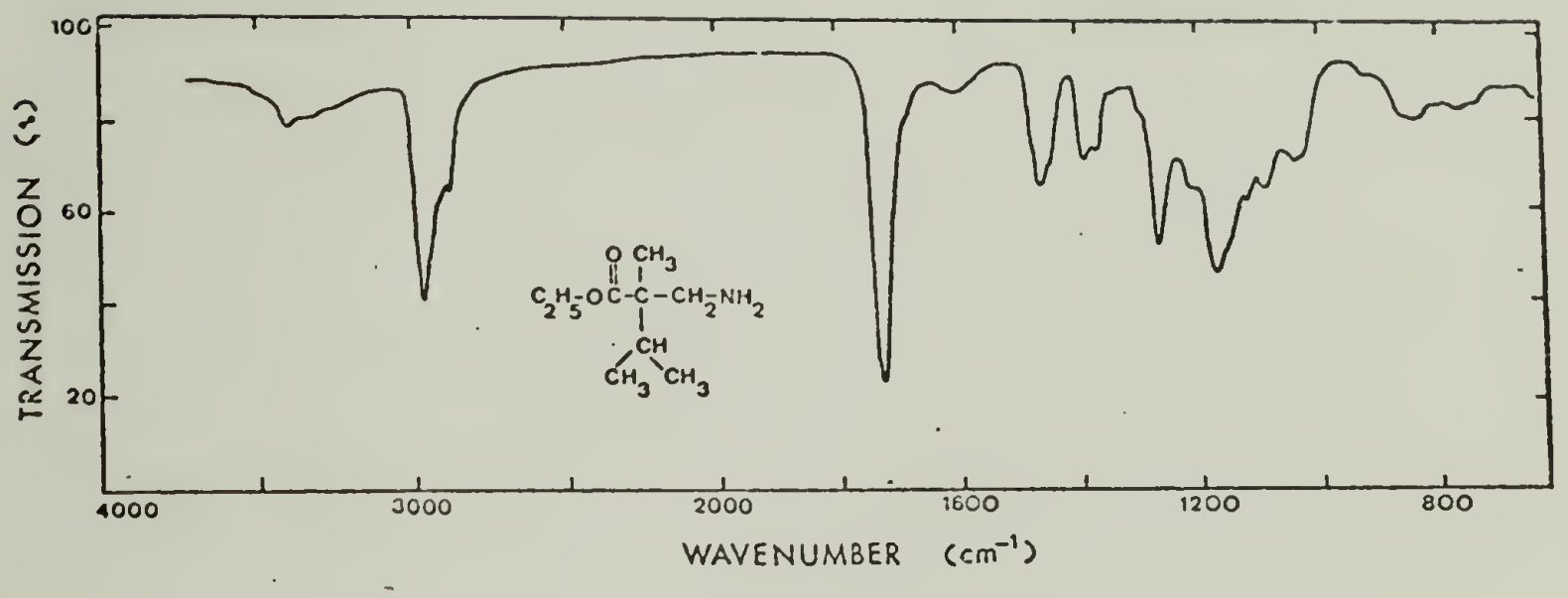

100
60
20
TRANSMISSION (%)
4000
3000
2000
1600
1200
800
WAVENUMBER (cm⁻¹)
O
C6H5
H5C2OC-C-CH2NH2
C2H5

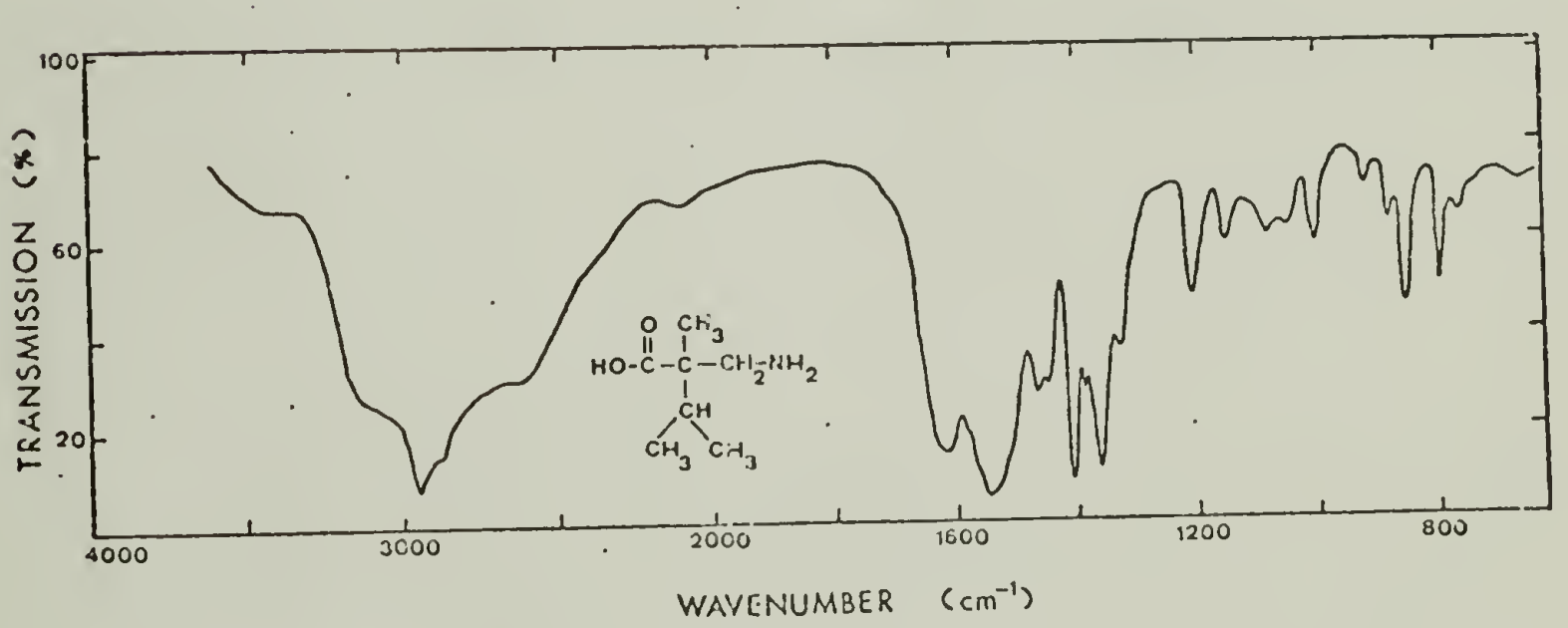

100
60
20
TRANSMISSION (%)
4000
3000
2000
1600
1200
800
WAVENUMBER (cm⁻¹)
O
C6H5
HO-C-C-CH2-NH2
C2H5

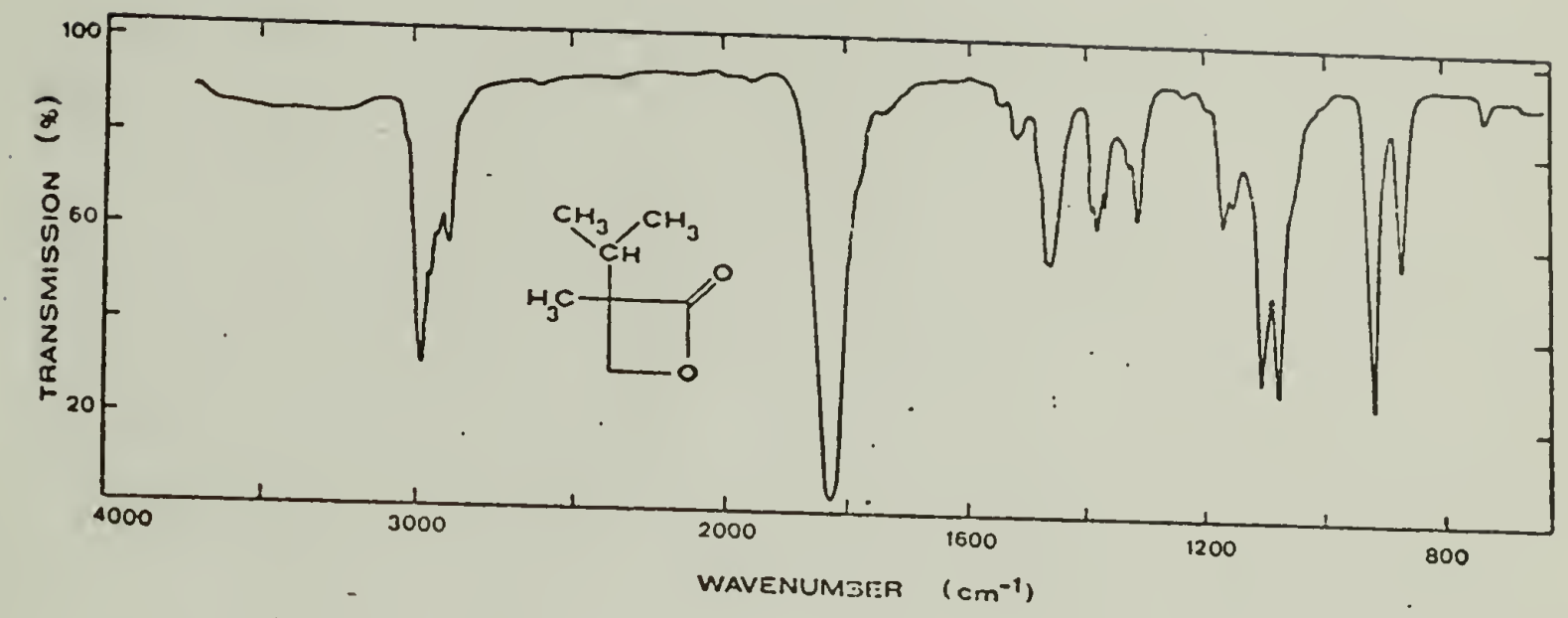

100
60
20
TRANSMISSION (%)
4000
3000
2000
1600
1200
800
WAVENUMBER (cm⁻¹)
(+) -
O
C6H5
HO-C-C-CH2-NH2
C2H5

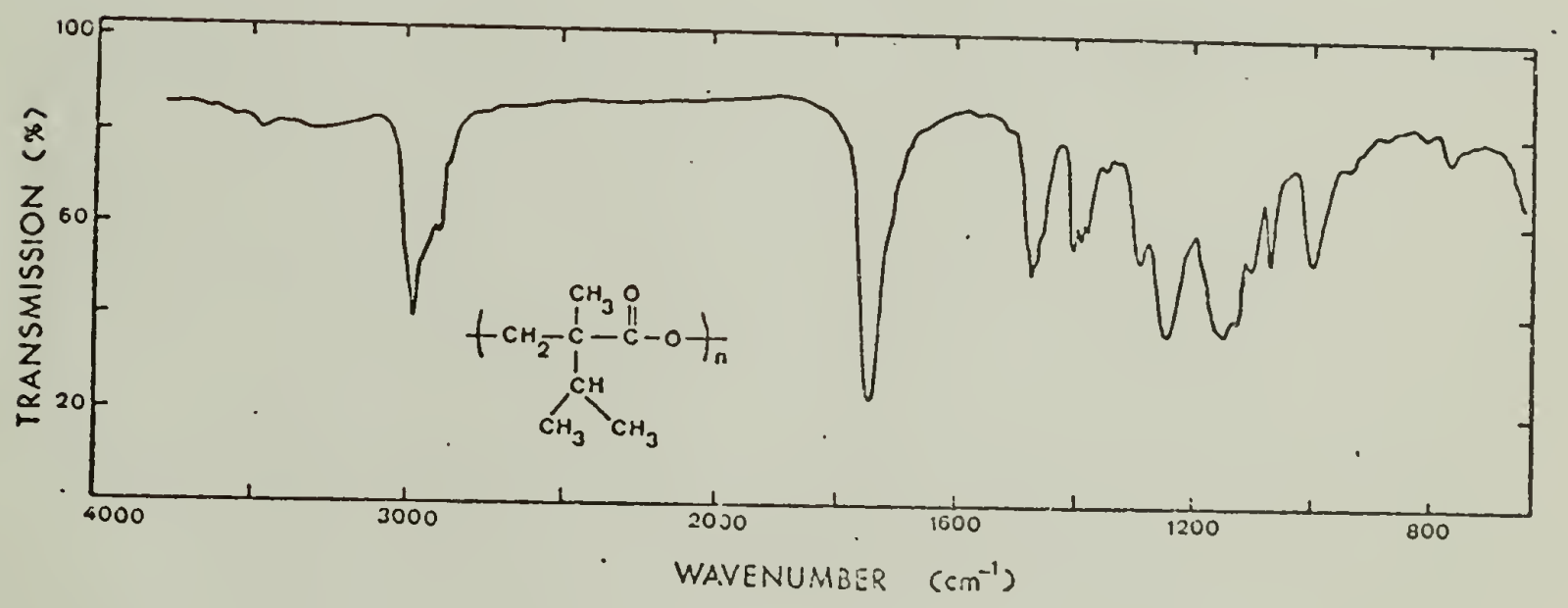

100
60
20
TRANSMISSION (%)
4000
3000
2000
1600
1200
800
WAVENUMBER (cm⁻¹)
C2H5
C6H5
O
O


100
60
20
TRANSMISSION (%)
4000
3000
2000
1600
1200
800
WAVENUMBER (cm⁻¹)
C6H5
O
CH2
C
C
O
n
C2H5


100
60
20
TRANSMISSION (%)
4000
3000
2000
1600
1200
800
WAVENUMBER (cm⁻¹)
O CH3
C2H5-O-C-C-CH2-NH2
CH
CH3 CH3


100
60
20
TRANSMISSION (%)
4000
3000
2000
1600
1200
800
WAVENUMBER (cm⁻¹)
O CH3
HO-C-C-CH2-NH2
CH
CH3 CH3


100
60
20
TRANSMISSION (%)
4000
3000
2000
1600
1200
800
WAVENUMBER (cm⁻¹)
CH3
CH3
CH
H3C
O
O


100
60
20
TRANSMISSION (%)
4000
3000
2000
1600
1200
800
WAVENUMBER (cm⁻¹)
CH3
O
CH2
C
C
O
n
CH
CH3
CH3