Optical Rotatory Dispersion Studies of Asymmetric Poly(thiol esters)

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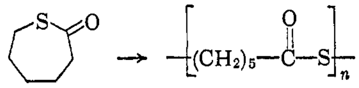
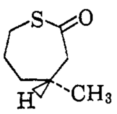
Abstract: Optically pure (*R*)-(+)-poly-β-methyl-ε-thiocaprolactone and (*R*)-(−)-poly-γ-methyl-ε-thiocaprolactone of high molecular weight were prepared by anionic ring-opening polymerization of the corresponding thiepan-2-ones. The γ-substituted polymer is crystalline, with a melting point of 62°, whereas the corresponding racemic material cannot be crystallized. In the optical rotatory dispersion spectra of each of the asymmetric polymers two Cotton effects were observed. As in the case of the monomers, they appear to arise from π-π* and n-π* transitions, respectively. (*R*)-(+)-Ethyl-6-acetylthio-3-methylthiohexanoate and (*R*)-(−)-ethyl-6-acetylthio-4-methylthiohexanoate were prepared as model compounds of the optically active polymers. A comparison of their optical rotatory dispersion spectra with those of the polymers indicates that the conformations around the asymmetric centers are the same in both types of compounds. This is confirmed by the observed Drude dispersion constants, and there is no evidence of any molecular dissymmetry in the polymers. It is therefore concluded that the two macromolecules, although of high molecular weight, optically pure, and structurally homogeneous, are too flexible to assume conformational order in dilute solution.

Synthetic optically active polymers have been prepared by a variety of methods.[2] Reactions of inactive polymers with small optically active molecules and addition polymerizations of optically active monomers (without asymmetric induction) generally produce polymers in which the asymmetric carbon atoms are located in the side chains. Macromolecules prepared by selective polymerization of one enantiomer from a racemic mixture and by asymmetric induction are rare; they are not optically pure but merely contain an excess of one configuration over the other. Condensation and ring-opening polymerizations of optically active monomers, however, may produce optically pure polymers whose asymmetric centers are located in the backbone. Most optically active macromolecules prepared by reactions of this type are synthetic analogs of biopolymers, such as polypeptides, polynucleotides, and polysaccharides, but optically pure poly-β-L-aspartic acid,[3] poly-L-lactide,[4] and polypropylenimine[5] were also synthesized. Condensation polymerizations with optically pure dialcohols[2] and diacids[6] are reported, and menthone lactam has been polymerized.[7] Several A–B-type polyamides and polyesters with optically active carbon atoms in the main chain have been studied in this laboratory.[8]

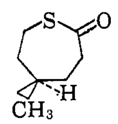
Recently, thiepan-2-one (I) was prepared and polymerized to the linear poly(thiol ester) II.[9] The methyl-substituted thiepan-2-ones III, IVa, and IVb are described elsewhere.[10] The present paper comprises a study of the polymers of III, IVa, and IVb. Their optical rotatory dispersion spectra are discussed, particular attention being given to the polymer conformation in dilute solution.



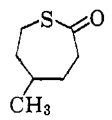
I II



III



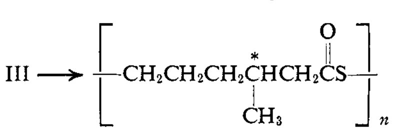
IVa
(optically active)



IVb
(racemic)

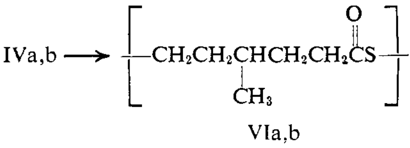
Results and Discussion

Polymers. The methyl-substituted thiolactones III, IVa, and IVb were polymerized with anionic catalysts in the same manner as I, the parent compound of these monomers.[9] The molecular weights of the resulting



$$\text{III} \longrightarrow \left[-\text{CH}_2\text{CH}_2\text{CH}_2\underset{\text{CH}_3}{\overset{*}{\text{C}}}\text{HCH}_2\overset{\text{O}}{\overset{\|}{\text{C}}}\text{S}- \right]_n$$

V



$$\text{IVa,b} \longrightarrow \left[-\text{CH}_2\text{CH}_2\underset{\text{CH}_3}{\text{C}}\text{HCH}_2\text{CH}_2\overset{\text{O}}{\overset{\|}{\text{C}}}\text{S}- \right]_n$$

VIa,b

a, optically active; b, racemic

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(2) R. C. Schulz and E. Kaiser, *Advan. Polymer Sci.*, 4 [2], 236 (1965).

(3) D. Balasubramanian and J. B. Applequist, Abstracts, 145th National Meeting of the American Chemical Society, New York, N. Y., 1963, p 67-C.

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(8) C. G. Overberger and H. Jabloner, *J. Amer. Chem. Soc.*, **85**, 3431 (1963); C. G. Overberger, S. Ozaki, and D. M. Braunstein, *Makromol. Chem.*, **93**, 13 (1966); C. G. Overberger and G. M. Parker, *J. Polymer Sci.*, *C*, in press; C. G. Overberger and H. Kaye, *J. Amer. Chem. Soc.*, **89**, 5649 (1967); C. G. Overberger and T. Takekoshi, *Macromolecules*, in press.

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(10) C. G. Overberger, and J. K. Weise, *ibid.*, submitted for publication.

polymers V, VIa, and VIb are high, although the intrinsic viscosities are somewhat lower than that of II (Table I). As in the case of II, partially halogenated hydrocarbons are the best solvents for the substituted polymers. However, the latter are in general more soluble and dissolve in dioxane and benzene as well.

Table I. Physical Properties of Poly-ε-thiolactones

Poly (thiol ester)	$[\eta]^{25}_{CHCl_3}$, dl/g	Mp, °C	Second-order transition
V	0.626	Amorphous	(tacky)
VIa (optically active)	0.421	62[a]	−50°, +20°[b]
VIb (racemic)	0.341	Amorphous	(tacky)

[a] Determined by differential thermal analysis; the value obtained with a polarizing hot-stage microscope was 62–64°. Both measurements are corrected and the polymer samples were not specially oriented. [b] The transition at −50° is more pronounced.

(*R*)-(+)-Poly-β-methyl-ε-thiocaprolactone (V) and (*R*)-(−)-poly-γ-methyl-ε-thiocaprolactone (VIa) are optically pure, since they are prepared from optically pure monomers (III and IVa, respectively), it having been shown that no racemization occurs during polymerization.[10] Further proof of their optical purity is provided by the close agreement of the molar rotations of the polymers with those of the model compounds prepared from the corresponding optically pure mercapto acids (IX and XII); if racemization had taken place during polymer synthesis, the molar rotations of the polymers would have been smaller than those of their models.

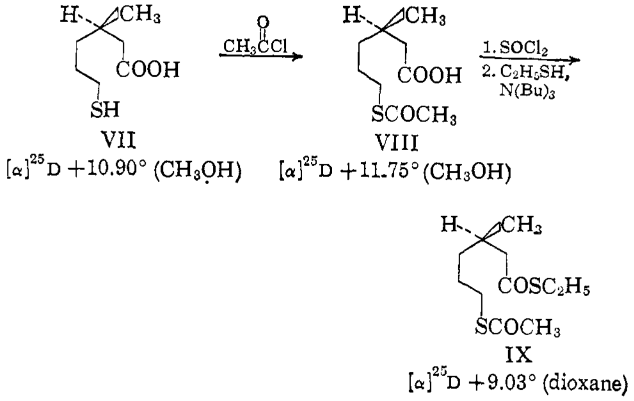
In a ring-opening polymerization there is but a single way in which the monomers can be incorporated into the chain. As a result, the positions of the asymmetric carbon atoms along the linear chain are regularly spaced and unambiguously defined. If, in addition, all asymmetric centers of a macromolecule are of the same configuration, a structurally homogeneous material is obtained. Thus V and VIa are homogeneous in structure.

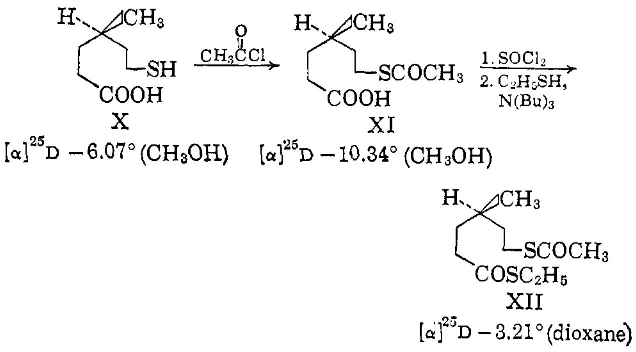
In the case of the γ-substituted macromolecules, this structural purity has a dramatic effect on the solid-state properties (Table I). Whereas the racemic VIb cannot be crystallized, the optically active VIa crystallizes readily after precipitation from solution. By means of a variable-temperature cell the infrared spectrum of a sample of VIa was recorded in both the crystalline and the amorphous (molten) states. In the crystalline state the bands are sharper, and many of them are shifted to higher or lower frequencies. In addition, there are bands which do not correspond to absorptions of the amorphous sample but are due to the crystalline order. Such bands were observed at 1428, 996, 920, and 618 cm^{-1}. Further evidence of the crystallinity of VIa is furnished by X-ray diffraction photographs. In a diagram of unoriented sample, diffractions corresponding to the following spacings were observed: d = 7.63 (medium), 5.16 (strong), 4.42 (very strong), 4.13 (medium), 3.85 (medium), 3.36 (weak), 2.71 (medium), 2.56 (weak), 2.24 (medium), 2.18 (weak), 2.09 (weak), 1.88 (weak), 1.71 (weak), and 1.63 Å (weak).

The melting point of the optically active γ-substituted VIa is considerably lower than that of the unsubstituted polythiocaprolactone II (108–109°).[9] In this respect poly(thiol esters) are analogous to polyesters rather than to polyamides. Poly-ε-caprolactone is crystalline, but the polyester corresponding to VIa is not.[8] In the amide series, on the other hand, the polymer corresponding to VIa melts at a slightly higher temperature than nylon 6.[8]

Model Compounds. For the purpose of optical rotatory dispersion studies, model compounds of the optically active polymers were prepared. Each of these models (IX and XII) consists of one structural unit with its respective thiol ester group at each end. They were obtained from the same mercapto acids that were used for the synthesis of the corresponding monomers (III and IVa, respectively).[10]

Mercapto acid VII was acetylated at its mercaptan function to yield thiol ester acid VIII. Conversion of VIII to IX proved difficult and was successful only when the intermediate acid chloride was isolated by distillation.[11] This method results in a poor yield of the acid chloride (46%), but the reaction with ethyl mercaptan in the presence of a tertiary amine proceeds well. Purification of (*R*)-(+)-ethyl-6-acetylthio-3-methylthiohexanoate (IX) was difficult; preparative vapor phase chromatography on silicone oil or Carbowax resulted in complete separation of the impurities, but the product decomposed partially before it was cooled in the collector.[12] Distillation also led to increased contamination. The product was obtained in >99% purity by slow molecular distillation at 40°.





By the same sequence of reactions mercapto acid X was converted to (*R*)-(−)-ethyl-6-acetylthio-4-methyl-

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[11] A. W. Ralston, E. W. Segebrecht, and S. T. Bauer, *J. Amer. Chem. Soc.*, 4, 502 (1939).

[12] Of the two decomposition products one was identified as the corresponding thiolactone III, the other is probably ethyl thiolacetate. We believe that these products result from intramolecular nucleophilic attack of one sulfur atom on the carbonyl carbon on the other thiol ester group.

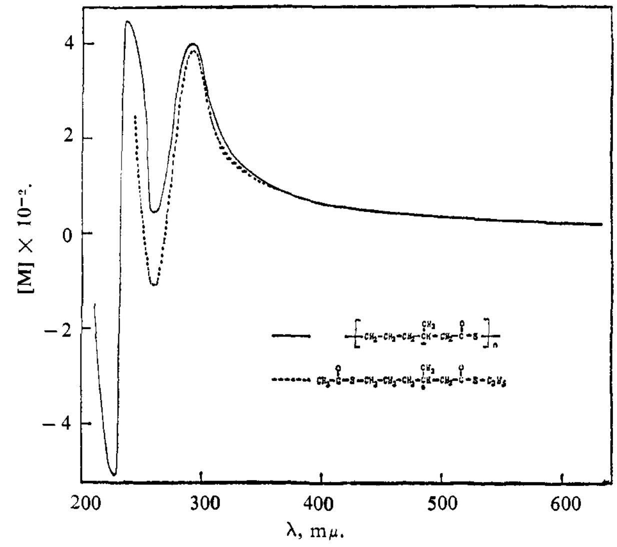

Figure 1. Optical rotatory dispersion of (*R*)-(+)-poly-β-methyl-ϵ-thiocaprolactone (V) and model compound (*R*)-(+)-ethyl 6-acetylthio-3-methylthiohexanoate (IX) in dioxane.

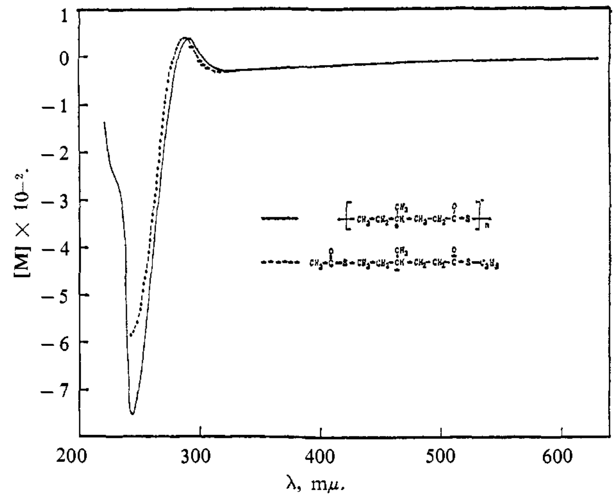

Figure 2. Optical rotatory dispersion of (*R*)-(−)-poly-γ-methyl-ϵ-thiocaprolactone (VIa) and model compound (*R*)-(−)-ethyl 6-acetylthio-4-methylthiohexanoate (XII) in dioxane.

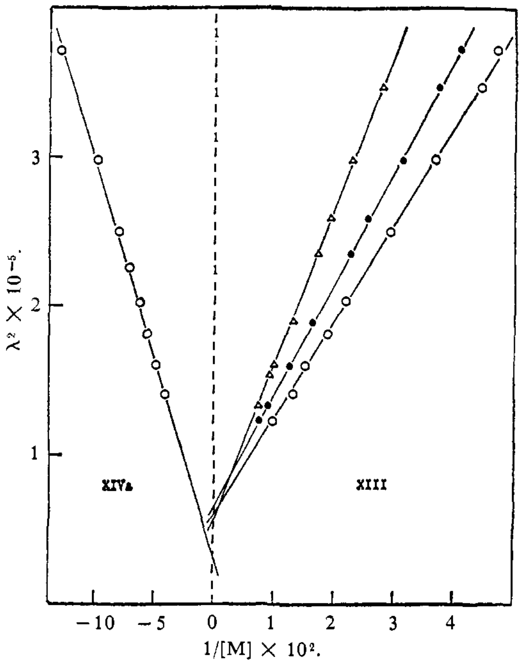

Figure 3. Drude dispersions of (*R*)-(−)-poly-γ-methyl-ϵ-thiolactone (VIa) and (*R*)-(+)-poly-β-methyl-ϵ-thiocaprolactone (V) in dioxane (○), tetrahydrofuran (●), and chloroform (△).

thiohexanoate (XII). This was purified by slow fractional distillation at 2×10^{-4} mm. The over-all yields of IX and XII from pulegone were 1.8 and 0.6%, respectively.

Ultraviolet and Optical Rotatory Dispersion Studies. The optical rotatory dispersion spectrum of (*R*)-(+)-poly-β-methyl-ϵ-thiocaprolactone (V, Figure 1) shows two positive Cotton effects. The one at lower wavelength is almost perfectly symmetrical and is centered around λ_0 232 mμ,[13] which agrees well with the ultraviolet absorption maximum and is very similar to the corresponding data of the monomer III.[10] The Cotton effect at higher wavelength is apparently centered around 278 mμ. The corresponding effect of the monomer shows a λ_0 of 284 mμ; since the amplitude is small and both Cotton effects are distorted by strong background curves of different intensity, the apparent shift is not significant. These analogies as well as the similarities of the ultraviolet absorption characteristics (Table II) show that the two Cotton effects exhibited by polymer V can, in all probability, be designated as $\pi-\pi^*$ and $n-\pi^*$ transitions as in the case of the monomer.

An examination of the optical rotatory dispersion and ultraviolet spectra of the γ-substituted polymer VIa (Figure 2 and Table III) leads to similar conclusions. In this case, however, the two Cotton effects are not easy to distinguish. Probably the troughs of the positive high-wavelength ($n-\pi^*$) and the negative low-wavelength ($\pi-\pi^*$) Cotton effects overlap in such a manner that only a single trough is apparent. This combined trough is indeed located at a higher wavelength than the corresponding extrema of the $\pi-\pi^*$ Cotton effects of the β-substituted polymer and of both monomers[10] as well as at a much lower wavelength than the corresponding extrema of the $n-\pi^*$ Cotton effects. The only peak visible in this spectrum seems to stem from the $n-\pi^*$ Cotton effect. The peak of the $\pi-\pi^*$ Cotton effect is indicated only by a shoulder. However, at this wavelength the reproducibility is only ±180°. A change in the slope of the curve was observed in each run, but it is not known whether it represents a shoulder or a peak.

In this connection it is to be noted that the Drude analysis (Tables II and III, Figure 3) shows a dispersion constant, λ_c, of 180 mμ (dioxane) for the γ-substituted polymer but λ_c 247 mμ (dioxane) for the β-substituted polymer. In each case the critical wavelength found for the model compound (IX or XII) is similar to that obtained for the polymer. We do not know whether this difference in the λ_c of the two polymers is related to the fact that the $n-\pi^*$ Cotton effects are apparently of the same sign (positive), whereas the $\pi-\pi^*$ Cotton effects are of opposite sign, or whether it reflects a large Cotton effect at lower wavelength in the case of the γ-substituted polymer. If the latter is the case, the discontinuity at 235 mμ (Figure 2) may indeed be a shoulder rather than a peak.[14]

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[13] λ_0 refers to the wavelength at which the rotation is zero.

Table II. Optical Rotatory Dispersion and Ultraviolet Absorption Data of (*R*)-(+)-Poly-β-methyl-ϵ-thiocaprolactone (V) and Model Compound IX in Dioxane

Measurement and compd	π–π^* transition[a] Trough	λ_0	Peak	n–π^* transition[a] Trough	Peak
ORD					
Polymer	228 $m\mu$ ($-508 \pm 150°$)	232 $m\mu$	236 $m\mu$ ($+447 \pm 150°$)	261 $m\mu$ ($+45°$)	292 $m\mu$ ($+398°$)
Model	...	...	...	260 $m\mu$ ($-108°$)	292 $m\mu$ ($+376°$)
Uv					
Polymer	λ_{max} 234 $m\mu$ (ϵ 3650)				
Model	λ_{max} 232 $m\mu$ (ϵ 7680)				
Drude analysis[b]					
Polymer		λ_c 247 $m\mu$ (dioxane) λ_c 254 $m\mu$ (THF) λ_c 239 $m\mu$ (chloroform)			
Model		λ_c 254 $m\mu$ (dioxane)			

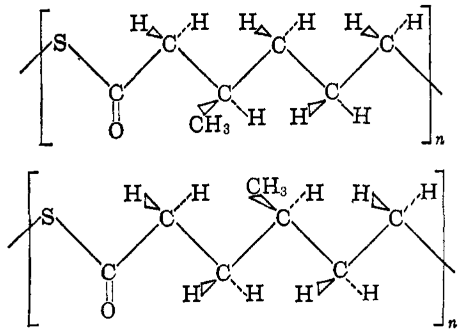
[a] This assignment is tentative; see text for discussion. [b] Only data recorded with a Rudolph spectropolarimeter, Model 80, were evaluated. The data were plotted according to Yang and Doty ($\lambda^2[M]$ *vs.* [M]) and the results checked by Lowry plots (λ^2 *vs.* 1/[M]) in all cases.

Table III. Optical Rotatory Dispersion and Ultraviolet Absorption Data of (*R*)-(−)-Poly-γ-methyl-ϵ-thiocaprolactone (VIa) and Model Compound XII in Dioxane

Measurement and compd	π–π^* transition[a] Shoulder	Trough	n–π^* transition[a] Peak	Trough
ORD				
Polymer	*Ca.* 235 $m\mu$ ($-247 \pm 180°$)	244 $m\mu$ ($-753 \pm 150°$)	292 $m\mu$ ($+38°$)	[323 $m\mu$] ($-31°$)
Model	...	...	287 $m\mu$ ($+38$)	[317 $m\mu$] ($-30°$)
Uv				
Polymer	λ_{max} 232 $m\mu$ (ϵ 4130)			
Model	λ_{max} 231 $m\mu$ (ϵ 8410)			
Drude analysis[b]				
Polymer	λ_c 180 $m\mu$ (dioxane)			
Model	λ_c 184 $m\mu$ (dioxane)			

[a] This assignment is tentative; see text for discussion. [b] Only data recorded with a Rudolph spectropolarimeter, Model 80, were evaluated. The data were plotted according to Yang and Doty ($\lambda^2[M]$ *vs.* [M]) and the results checked by Lowry plots (λ^2 *vs.* 1/[M]) in all cases.

The inversion of the sign of the π–π^* Cotton effect of polymer VIa as compared with that of V corresponds to the fact that in the acyclic case the asymmetric centers contribute normally. They are of opposite configuration (even though the configurational symbol is *R* for both).[15] If the polymers are considered as essentially *trans*-staggered chains



the methyl in each of the two polymers will be expected to have quite a different orientation to the chromophore and, in this extended conformation, the two asymmetric centers will be expected to give rise to Cotton effects of opposite sign. This has in fact been observed.

Whenever rotations of the model compounds could be measured reproducibly, they were almost equal to those of the polymers, provided that the optical rotations per active center (molar rotations) were compared. Only at wavelengths at which the absorption is high are appreciable differences noted. The Cotton effects are not very large, and the experimental error of the rotations in the absorption bands is considerable. In addition, the absorptions of the model compounds are even stronger than those of the polymers because they possess two chromophores per optically active center. Consequently, the inaccuracy of these measurements is twice as large as in the case of the polymers, and measurements near the maximum of the absorption band are meaningless for the model compounds.

Not only does each polymer exhibit a molar rotation of equal sign and comparable magnitude to those of the model compound, but models and polymers exhibit the same extrema and the same critical wavelengths. There is thus no evidence whatsoever of a contribution arising from molecular dissymmetry in the polymers. The slight differences in rotatory power appear to arise from the inevitable deviations in primary structure and not from the existence of any ordered secondary structures in the polymers. In the dynamic equilibria be-

(14) That another transition occurs near 180 $m\mu$ is probable because in the ultraviolet spectra of the monomers (in cyclohexane) an absorption of high extinction (ϵ >1000) was observed at λ_{max} 188 $m\mu$.[9]

(15) This effect is also discussed in connection with the cyclic monomers; *cf.* ref 10.

tween the various conformers minor changes of the equilibrium constants are likely to result and can fully account for the observed differences. For example, in the polymer steric interference with other parts of the same chain reduces the probability of certain conformations. As both polymers and models are very flexible and can rotate freely, the number of possible conformations is considerable. It must also be kept in mind that the local concentrations of polymer segments in a solvated polymer coil are much higher than the statistical macroscopic concentration of the polymer in solution. The nature of the solvent near the polymer chain is therefore altered. The resulting general solvent effect also contributes to the small differences that are found.

The results suggest not only that the types of conformers found in the polymers and their molecular models are the same, but also that all conformations in the immediate environment of the asymmetric centers are alike. The above optical rotatory dispersion studies in the range of visible and ultraviolet light have produced no evidence of conformations specific to the polymers. It is therefore concluded that the two macromolecules, although of high molecular weight, optically pure, and structurally homogeneous, are too flexible to assume conformational order in dilute solution.

Experimental Section[16]

(*R*)-(+)-Poly-β-methyl-ϵ-thiocaprolactone (V). (*R*)-(−)-4-Methylthiepan-2-one (III), 1.45 g (10 mmol), was treated with 0.2 mol % of potassium *t*-butoxide in a side-arm polymerization tube, as has been described previously for II, part B.[9] After 8 hr at 110–150°, the oil bath was heated to 190° for 30 min while the pressure in the polymerization tube was maintained at 0.1 mm. The nitrogen capillary was raised above the level of the polymer, and the broken glass sank to the bottom of the tube. The amorphous polymer was studied without further treatment, n^{25}D 1.5376, $[\eta]$ 0.626 dl/g, $[\alpha]^{25}$D +15.66° (*c* 0.029 g/ml, dioxane), $[\alpha]^{25}$D +18.62° (*c* 0.011 g/ml, tetrahydrofuran), $[\alpha]^{25}$D +24.97° (*c* 0.062 g/ml, chloroform); $\lambda_{\max}^{\text{dioxane}}$ 234 mμ (ϵ 3650); $\nu_{\max}$ 2955, 2925, 2870, 1685, 1455, 1408, 1377, 1348, 1292, 1269, 1253, 1163, 1097, 1012, 936, 760, and 630 cm^{-1}; τ 7.31 (2 H, multiplet), 7.41–7.79 (2 H, triplet), 7.86–8.92 (5 H, multiplet), and 9.14 (3 H, doublet).

Anal. Calcd for $(C_7H_{12}OS)_n$: C, 58.29; H, 8.39; S, 22.23. Found: C, 58.30; H, 8.59; S, 22.35.

Another sample of this polymer was prepared with 1.2 mol % of potassium *t*-butoxide in a sealed tube.[9] It was freed from monomer by precipitation with methanol, and the solvent was removed by heating under vacuum, yield 76%, $[\eta]$ 0.542 dl/g. This sample had the same physical and optical properties as the one described above.

(*R*)-(−)-Poly-γ-methyl-ϵ-thiocaprolactone (VIa). Freshly distilled (*R*)-(+)-5-methylthiepan-2-one (IVa), 2.44 g (16.9 mmol), was shaken with 1.1 mol % of *n*-butyllithium for 21 hr at room temperature as in the preparation of II, part C.[9] The partially solid polymer was dissolved in chloroform, and this solution was added dropwise to ether. The ether was decanted, and the sticky polymer was taken up in dioxane and precipitated with water. The water was in turn decanted and the polymer repeatedly rinsed with acetone and stirred overnight in the same solvent. The polymer had become a white solid, which was carefully decanted and dried in a desiccator under vacuum, yield 28%, mp 62° (by DTA), $[\eta]$ 0.421 dl/g; $[\alpha]^{25}$D −5.39° (*c* 0.207 g/ml, dioxane); $\lambda_{\max}^{\text{dioxane}}$ 232 mμ (ϵ 4130); infrared bands of the crystalline polymer (as film) at $\nu_{\max}$ 2955, 2920, 2865, 1685, 1475, 1428, 1400, 1378, 1280, 1252, 1208, 1172, 1140, 1088, 1018, 996, 963, 920, 848, 782, 682, and 618 cm^{-1}; bands of the amorphous (molten) polymer at $\nu_{\max}$ 2955, 2920, 2865, 1685, 1455, 1407, 1378, 1273, 1256, 1200, 1160, 1128, 1095, 1028, 980, 878, 768, and 703 cm^{-1}; τ 7.15 (2 H, triplet), 7.47 (2 H, triplet), 8.16–8.72 (5 H, multiplet), and 9.04 (3 H, doublet).

Anal. Calcd for $(C_7H_{12}OS)_n$: C, 58.29; H, 8.39; S, 22.23. Found: C, 58.26; H, 8.42; S, 22.15.

(±)-Poly-γ-methyl-ϵ-thiocaprolactone (VIb). (±)-5-Methylthiepan-2-one (IVb), 2.40 g (16.6 mmol), was polymerized with 1.9 mol % of *n*-butyllithium (in hexane) as in part C of the preparation of II,[9] *i.e.*, by shaking at room temperature for 36 hr. The liquid product was dissolved in 3.5 ml of dioxane and precipitated with 66.5 ml of methanol. The solvent was decanted and the polymer rinsed repeatedly with acetone. It was stirred for a week with acetone, then decanted and dried. It was finally dissolved in 2 ml of dioxane, filtered, and precipitated with 18 ml of ether. The solvent was decanted and completely removed under vacuum and trapped at liquid nitrogen temperature. The polymer was also held overnight at 70° (0.1 mm), yield 55%, $[\eta]$ 0.341 dl/g; $\lambda_{\max}^{\text{dioxane}}$ 232 mμ (ϵ 4130, dioxane); the infrared spectrum shows the same features as that of the optically active polymer (VIa) in the molten state, but it is better resolved. The nmr spectrum is identical with that of VIa.

Anal. Calcd for $(C_7H_{12}OS)_n$: C, 58.29; H, 8.39; S, 22.23. Found: C, 58.46; H, 8.36; S, 22.22.

(*R*)-(+)-6-Acetylthio-3-methylhexanoic Acid (VIII). (*R*)-(+)-6-Mercapto-3-methylhexanoic acid (VII),[10] 8.5 g (52 mmol), was placed in a 100-ml, three-necked flask equipped with thermometer, gas inlet, dropping funnel with side arm, drying tube, and magnetic stirrer. Sodium hydroxide, 4.4 g (0.11 mol), in 60 ml of water was added to dissolve the acid, and the temperature was held at 0 to 5° while acetyl chloride, 6.1 g (78 mmol), was added through the dropping funnel with vigorous stirring. After 1 hr, sulfuric acid, 10 g (0.1 mol), was added to the flask and the mixture extracted with ether. The extract was dried over magnesium sulfate and distilled to yield 7.7 g (76%) of colorless liquid. The product was found by vpc to be homogeneous on silicone oil (Dow Corning 710), retention time 20 min at 195°, bp 125° (0.08 mm), n^{25}D 1.4848, $[\alpha]^{25}$D +11.75° (*c* 0.036 g/ml, methanol); $\nu_{\max}$ 3050 (broad), 2960, 2930, 1710, 1410, 1378, 1690, 1353, 1285, 1215, 1236, 950, and 625 cm^{-1}.

Anal. Calcd for $C_9H_{16}O_3S$: C, 52.91; H, 7.90; S, 15.70. Found: C, 52.94; H, 8.17; S, 15.79.

(*R*)-(+)-Ethyl 6-Acetylthio-3-methylthiohexanoate (IX). (*R*)-(+)-6-Acetylthio-3-methylhexanoic acid (VIII), 2.8 g (14 mmol), was placed in a 50-ml, two-necked flask fitted with dropping funnel, thermometer, and magnetic stirrer. Thionyl chloride, 2.0 g (17 mmol) was added at 10° with stirring; the temperature was then raised to 40°. The dropping funnel was replaced by a distillation head, and vacuum was applied to remove the volatile materials completely. Short-path distillation gave 1.40 g (46%), bp 98° (0.2 mm); $\nu_{\max}$ 1690 (thiol ester C=O) and 1800 cm^{-1} (acid chloride C=O).

Tri-*n*-butylamine, 1.17 g (6.3 mmol), and ethyl mercaptan, 0.47 g (7.6 mmol), were placed under nitrogen in a 50-ml, three-necked flask fitted with dropping funnel, gas inlet, magnetic stirrer, and drying tube. At −10 to 0°, (*R*)-6-acetylthio-3-methylhexanoyl chloride, 1.40 g (6.3 mmol), in 20 ml of ether was added dropwise to the stirred mixture. The dropping funnel was replaced by a condenser, and stirring was contained for 2 hr, during which time the temperature rose to 30°. The mixture was cooled and dissolved in ether, washed with aqueous sodium carbonate, then with water until the latter remained neutral, and the ether solution dried and flash-distilled to give 1.2 g (76%). The distillate was fractionated with a Podbielniak column to give a product of 94% purity as determined by vpc. Attempts to purify it further by fractional distillation and preparative vpc led to increased contamination due to decomposition. Slow molecular distillation (3 days) at *ca.* 40° gave two fractions; one impurity was concentrated in the fraction obtained at 3 × 10^{-1} mm, the other in the residue. The fraction obtained at 1 × 10^{-4} mm was 99% pure as determined by vpc on silicone oil (Dow Corning 200), retention time 34 min at 195°

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(16) Melting points were measured with a Thomas-Hoover capillary melting-point apparatus and are corrected. Viscosities were measured in Ubbelohde viscometers each equipped with a sintered-glass filter at the bottom of a mixing bulb. Reagent grade chloroform was used at 25 ± 0.1°, and flow times were at least 85 sec. Elemental analyses were performed by Bernhardt Mikroanalytisches Laboratorium, Mülheim, Germany. Optical rotatory dispersions were measured with a Rudolph photoelectric spectropolarimeter, Model 80, and with a Cary 60 spectropolarimeter. Ultraviolet spectra were determined with a Cary 14 spectrophotometer; infrared spectra were recorded on Perkin-Elmer spectrophotometers, Model 12 or 521; the wave numbers reported are the $\nu_{\max}$ of the strong and medium bands, or important shoulders. Nmr spectra were taken with a Varian HR-60 spectrometer, in deuteriochloroform and with tetramethylsilane as internal standard. Perkin-Elmer vapor fractometers Model 154-D with packed columns 2 m in length were used for analytical vpc and a Wilkens Aerograph Model A-700 for preparative work. The reported retention times are for samples of 1 μl at pressures of 15 psi on the Perkin-Elmer instruments, with helium as carrier gas.

(helium pressure 20 psi), by 104–105° (0.1 mm), $n^{25}\text{D}$ 1.5037; $[\alpha]^{25}\text{D}$ +9.03° (c 0.065 g/ml, dioxane); $\lambda_{\max}^{\text{dioxane}}$ 232 mμ (ε 7680); $\nu_{\max}$ 2955, 2925, 2870, 1690, 1447, 1410, 1377, 1350, 1260, 1133, 1105, 1020, 995, and 628 cm^{-1}; τ 6.89–7.54 (4 H, multiplet), 7.15 (2 H, triplet), 7.66 (3 H, singlet), 8.17–8.55 (5 H, multiplet), 8.72 (3 H, triplet), and 9.08 (3 H, doublet).

Anal. Calcd for $C_{11}H_{20}O_2S_2$: C, 53.18; H, 8.12; S, 25.82. Found: C, 53.43; H, 8.14; S, 25.78.

(*R*)-(−)-6-Acetylthio-4-methylhexanoic Acid (XI). (*R*)-(−)-6-Mercapto-4-methylhexanoic acid (X),[10] 8.2 g (40 mmol), was dissolved in aqueous sodium hydroxide, allowed to react with 4.1 g (66 mmol) of acetyl chloride, and worked up as described above for VIII. Distillation gave 4.6 g (44%) of product, and 36% of the starting material was recovered. The product was found to be homogeneous by vpc on silicone oil (Dow Corning 710), retention time 21 min at 195°, bp 126° (0.07 mm), $n^{25}\text{D}$ 1.4870, $[\alpha]^{25}\text{D}$ −10.34° (c 0.86 g/ml, methanol); $\nu_{\max}$ 3050 (broad), 2965, 2935, 2875, 1710, 1690, 1450, 1380, 1355, 1283, 1135, 955, and 625 cm^{-1}; τ −1.02 (1 H, singlet), 7.12 (2 H, triplet), 7,64 (2 H, triplet), 7.72 (3 H, singlet), 8.20–8.98 (5 H, multiplet), and 9.07 (3 H, doublet).

Anal. Calcd for $C_9H_{16}O_3S$: C, 52.91; H, 7.90; S, 15.70. Found: C, 52.95; H, 7.78; S, 15.53.

(*R*)-(−)-Ethyl 6-Acetylthio-4-methylthiohexanoate (XII). (*R*)-(−)-6-Acetylthio-4-methylhexanoic acid (XI), 4.4 g (21.5 mmol), was treated with 3.1 g (25.8 mmol) of thionyl chloride according to the method described above for IX. Distillation gave 1.80 g (38%) of (*R*)-6-acetylthio-4-methylhexanoyl chloride, bp 93° (0.08 mm); $\nu_{\max}$ 1690 (thiol ester C=O) and 1800 cm^{-1} (acid chloride C=O).

The acid chloride, 1.80 g (8.1 mmol), was allowed to react with 0.60 g (9.70 mmol) of ethanethiol in the presence of 1.50 g (8.1 mmol) of tri-*n*-butylamine as described above for IX. Distillation gave 2.0 g (100% from acid chloride); two consecutive fractional distillations under high vacuum produced a sample which was found to be homogeneous by vpc on silicone oil (Dow Corning 200 and 710), retention times 33 min (195°) and 62 min (216°), respectively (helium pressure 20 psi), bp 105° (0.07 mm), bp 74–75° (2 × 10^{-4} mm), $n^{25}\text{D}$ 1.5057, $[\alpha]^{25}\text{D}$ −3.21° (c 0.22 g/ml, dioxane); $\lambda_{\max}^{\text{dioxane}}$ 231 mμ (ε 8410); $\nu_{\max}$ 2955, 2925, 2870, 1690, 1447, 1410, 1377, 1350, 1260, 1133, 1105, 1020, 955, and 628 cm^{-1}; τ 6.89–7.54 (4 H, multiplet), 7.15 (2 H, triplet), 7.66 (3 H, singlet), 8.17–8.55 (5 H, multiplet), 8.72 (3 H, triplet), and 9.08 (3 H, doublet).

Anal. Calcd for $C_{11}H_{20}O_2S_2$: C, 53.18; H, 8.12; S, 25.82. Found: C, 53.30; H, 8.04; S, 25.90.

Nuclear Magnetic Resonance Spectroscopy. Carbon-13 Spectra of Five-Membered Aromatic Heterocycles[1a]

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Abstract: High-resolution ^{13}C nmr spectra have been obtained for the five-membered nitrogen heterocycles and for furan, thiophene, and selenophene. All possible carbon–proton coupling constants have been observed and assigned to the proper protons. The chemical shifts and coupling constants are discussed both empirically and with respect to extended Hückel calculations. The chemical shifts follow variations in the local charge densities and the long-range carbon–proton coupling constants may be correlated with geometrically corresponding carbon–proton and proton–proton coupling constants in substituted ethylenes. Extended Hückel calculations seem uniformly poor in correlating spin–spin coupling constants in these systems.

There have been many nuclear magnetic resonance studies of the five-membered heterocycles because of their utility as models in the testing of semiempirical theoretical predictions. Difficulties arise in the study of the proton spectra of pyrrole and furan because their spectra are deceptively simple and it is not possible to extract the values of the various coupling constants directly from the spectra. Abraham and Bernstein[2] and Hoffman and Gronowitz[3] have studied corresponding substituted heterocycles and inferred values of the coupling constants by suitable interpolation of the observed substituent effects. Reddy and Goldstein[4] used the ^{13}C satellites of the proton spectra of the parent compounds to assign the various proton–proton coupling constants by requiring that the assigned values reproduce the ^{13}C-satellite spectra. In matching the outer satellite spectra by the method of effective chemical shifts, it was necessary to take account of differences between the long-range, carbon–proton couplings, although the outer satellite spectra are not sensitive to the absolute magnitudes of these couplings. Tori and Nakagawa[5] have reported a large number of one-bond, carbon–proton coupling constants for five- and six-membered heterocycles through observations of the ^{13}C satellites in the proton spectra.

Direct observation of ^{13}C spectra has been hampered by the low sensitivity of the ^{13}C nucleus to nmr detection and its low natural abundance. Page, Alger, and Grant[6] have measured the ^{13}C chemical shifts and one-bond, carbon–proton coupling constants in some heterocycles by a combination of complete proton decoupling techniques for determination of the carbon chemical shifts and rapid-passage, dispersion-mode conditions for determination of the one-bond, carbon–proton coupling constants in the ^{13}C spectrum. Neither technique allows the observation of the long-range, carbon–proton coupling constants. In the present research, high-resolution ^{13}C spectra have been obtained for a

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