Optically Active Polyisocyanates. II

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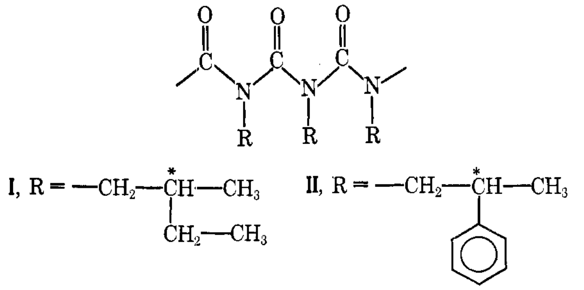
ABSTRACT: Optically active poly[(*S*)-(+)-2-methylbutyl isocyanate] has been synthesized. The optically active polymer has inherently symmetric chromophores in the main chain which acquire optical activity from dissymmetric perturbations by the side chains. A comparison of the dichroic differences between poly[(*S*)-(+)-2-methylbutyl isocyanate] and its model compound indicates that dissymmetry in the polymer backbone contributes to the circular dichroism spectrum of the optically active polymer. The nuclear magnetic resonance spectra of this polymer and of its racemic modification show similar complex patterns. The spectra also reveal nonequivalent protons for both methylene groups bonded to the asymmetric carbon atoms in the side chain. A comparison is also made between the rotatory properties of this polymer and an optically active polyisocyanate containing aromatic side chains.

In our continuing study of optically active polyisocyanates, we synthesized poly[(*S*)-(+)-2-methylbutyl isocyanate]. The polymer contains asymmetric carbon atoms in its side chains, and consists wholly of an amide-like backbone.



The chromophores in the polymer are closely related to those in peptides. Dissymmetric perturbations of the amide chromophores of the main chain arise solely from side-chain effects.

We carried out circular dichroism (CD) and nuclear magnetic resonance (nmr) studies of the polymer and its model compound. As in the case of optically active aromatic polymer poly[(+)-2-phenylpropyl isocyanate] (II), which was reported previously,[1] the aliphatic polymer poly[(*S*)-(+)-2-methylbutyl isocyanate] (I) is soluble only in chloroform and sulfuric acid. The present paper reports the synthesis of the optically active poly[(*S*)-(+)-2-methylbutyl isocyanate] and the stereochemical implications indicated by circular dichroism and nuclear magnetic resonance spectroscopy.

Experimental Section

Synthesis of Optically Active Aliphatic Polymer Poly[(*S*)-(+)-2-methylbutyl isocyanate]. (1) Synthesis of (*S*)-(+)-2-Methylbutanal. (*S*)-(−)-2-Methylbutanol (40 g, 0.45 mol) was oxidized by a mixture of sodium dichromate dihydrate (49.4 g, 0.17 mol), 98% sulfuric acid (30 ml), and water (90 ml) under a nitrogen atmosphere.[2,3] The aldehyde was removed by distillation as formed and collected. The organic layer was separated, dried by molecular sieves, and distilled under nitrogen to give 12.5 g of crude (*S*)-(+)-2-methylbutanal (bp 90–100°). The aldehyde fraction was again dried by molecular sieves and the fraction boiling between 92 and 95° at atmospheric pressure was collected (9.4 g, 24.1%), $[\alpha]^{23}\text{D}$ +17.4°, neat. This material contained some starting material, but was used without further purification.

(2) Synthesis of (*S*)-(+)-2-Methylbutanal Oxime. The method reported by Bousquet for the preparation of heptanal oxime was adopted.[4] A solution of hydroxylamine hydrochloride (71.6 g, 1.03 mol) in water (123 ml) and (*S*)-(+)-2-methylbutanal (70.7 g, 0.822 mol) was placed into a 2-l., three-necked, round-bottomed flask fitted with a mechanical stirrer, a thermometer, and a dropping funnel. A solution of anhydrous sodium carbonate (54.5 g, 0.514 mol) in water (103 ml) was added to the mixture while it was stirred. The rate of addition was such that the temperature of the reaction mixture did not rise above 45°. Stirring was continued at room temperature for 1 hr after complete addition of the sodium carbonate solution. Afterward, the oily layer was separated and washed with two 30-ml portions of water. Distillation provided (*S*)-(+)-2-methylbutanal oxime (42 g, 50.6%, bp 146°), $[\alpha]^{23}\text{D}$ +14°, neat.

(3) Reduction of (*S*)-(+)-2-Methylbutanal Oxime to (*S*)-(−)-2 Methylbutylamine. Anhydrous ether (700 ml) and powdered lithium aluminum hydride (30 g, 0.792 mol) were placed into a three-necked, 3-l., round-bottomed flask fitted with a reflux condenser protected from atmospheric moisture with a drying tube containing calcium chloride, a pressure-compensated dropping funnel, and a mechanical stirrer. The slurry was stirred while (*S*)-(+)-2-methylbutanal oxime (40 g, 0.396 mol) was added slowly through the dropping funnel, causing the mixture to boil. After the addition of oxime was completed, the reaction mixture was allowed to reflux for 1 hr. Afterward, the mixture was cooled with ice water, and the excess lithium aluminum hydride was decomposed by gradual addition of water (80 ml). Later a 20% solution of sodium potassium tartrate (250 ml) and a 10% solution of sodium hydroxide (50 ml) were added.[5] After separating the ether layer, the thick slurry was extracted with ether several times. The combined ether extracts were dried over potassium carbonate. After removal of ether, distillation provided (*S*)-(−)-2-methylbutylamine (21.4 g, 62.2%, bp 94.5°, $n^{24}\text{D}$ 1.4116), $[\alpha]^{23}\text{D}$ −5.24°, neat.

(4) Synthesis of the Monomer. (*S*)-(+)-2-Methylbutyl isocyanate was prepared according to the method given by Rossi and coworkers.[6] Concentrated hydrochloric acid (19.4 ml) was added to a suspension of (*S*)-(−)-2-methylbutylamine (20 g, 0.229 mol) in water (168 ml). The mixture was warmed to 80° and sodium cyanate (15.1 g) was added. The mixture was held at 80° for 15 min and then cooled to room temperature. Concentrated hydrochloric acid (46.4 ml) and benzene (84.2 ml) were added. After chilling to less than 10°, a solution of sodium nitrite (16 g in 84.2

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[1] M. Goodman and S. C. Chen, *Macromolecules*, 3, 398 (1970).

[2] A. Abe and M. Goodman, *J. Polym. Sci., Part A*, 1, 2193 (1963).

[3] C. Weygand, "Organic Preparations," Interscience, New York, N. Y., 1945, p 143.

[4] E. W. Bousquet, "Organic Syntheses," Collect. Vol. II, A. H. Blatt, Ed., Wiley, New York, N. Y., 1946, p 313.

[5] D. R. Smith, M. Maienthal, and J. Tipton, *J. Org. Chem.*, **17**, 294 (1952).

[6] S. Rossi, A. Riva, and B. Piantanida, *Chim. Ind. (Milan)*, **42**, 1243 (1960); *Chem. Abstr.*, **55**, 25850*h* (1961).

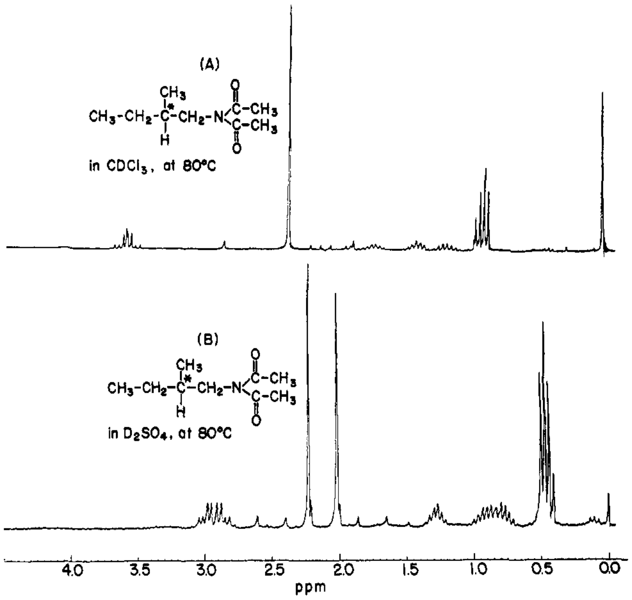


Figure 1. Nuclear magnetic resonance spectra (220 MHz) of optically active aliphatic model compound (*S*)-(−)-*N*,*N*-diacetyl-2-methylbutylamine (a) in deuteriochloroform, (b) in deuteriosulfuric acid.

ml of water) was added. When the addition was complete, the benzene layer was decanted and the aqueous layer was extracted with benzene. The combined extract was dried over sodium sulfate. After removal of benzene, distillation provided (*S*)-(+)-2-methylbutyl isocyanate (5.4 g, 21%, bp 112–113° (180 mm), $n^{24}{}_D$ 1.4227), $[\alpha]^{25}{}_D$ +3.08° (*c* 0.78, chloroform). *Anal.* Calcd for $C_6H_{11}NO$: C, 63.71; H, 9.74; N, 12.39. Found: C, 63.76; H, 9.98; N, 12.60.

(5) Polymerization. Polymerization was carried out in a serum-capped Pyrex glass tube. The tube was flamed while being swept with dry helium in order to ensure maximum dryness. Dry *N*,*N*-dimethylformamide (2 ml) was added to the tube and cooled with Dry Ice–acetone. (*S*)-(+)-2-Methylbutyl isocyanate (0.5 ml) was added. Afterward, a saturated solution of sodium cyanide in dry DMF (0.5 ml) was added dropwise from a syringe. The polymerization was terminated by adding methanol (5 ml). The polymer was isolated by filtration, washed with large amounts of methanol, and dried at 40° under vacuum, giving poly[(*S*)-(+)-2-methylbutyl isocyanate]: $[\alpha]^{25}{}_D$ +160°, $[M]^{25}{}_D$ +180.8° (*c* 0.005, chloroform). *Anal.* Calcd for $C_6H_{11}NO$: C, 63.71; H, 9.74; N, 12.39. Found: C, 63.68; H, 9.82; N, 12.38.

(6) Synthesis of Model Compound (*S*)-(−)-*N*,*N*-Diacetyl-2-methylbutylamine. Synthesis of the model compound was accomplished by using the method reported earlier.[1] Ketene, generated by the pyrolysis of acetone, was introduced into a hexane solution (30 ml) of (*S*)-(−)-2-methylbutylamine (4.189 g, 0.048 mol) at room temperature. The temperature of the mixture increased gradually as ketene was added. When the temperature started decreasing, the introduction of ketene was temporarily stopped. One drop of concentrated sulfuric acid was added at room temperature and the flow of ketene was resumed. The temperature rose again. When the temperature began falling, the diacetylation was complete. The mixture was washed with saturated sodium bicarbonate solution and water until the washings showed neutrality. The product was dried over magnesium sulfate and distilled: bp 89–90° (3 mm), $[\alpha]^{25}{}_D$ −6°, $[M]^{25}{}_D$ −10.3° (*c* 0.15, chloroform). *Anal.* Calcd for $C_9H_{17}NO_2$: C, 63.15; H, 9.94; N, 8.18. Found: C, 63.14; H, 10.00; N, 8.29.

Physical Measurements. Circular dichrosim (CD) measurements were carried out on a Cary 60 automatic recording spectropolarimeter equipped with a Cary CD attachment. A 450-W Osram xenon lamp was used as the light source. CD spectra were obtained at room temperature with 1.00- and 0.2-mm fused silica cells. Specific rotations were measured on a Perkin-Elmer 141 polarimeter. A sodium lamp was used as the light source. The cell length was 1 dm and the concentrations were varied, as indicated for each sample. Nuclear magnetic resonance spectra were obtained with a Varian HR 220-MHz spectrometer, using Wilmad superconducting grade sample tubes. Resonances are expressed in parts per million relative to tetramethylsilane as the internal standard.

Table I

Type of proton	Nature of peaks	Chemical shift, ppm	Area
N-Methylene	Multiplet	3.58	2
Diacetyl	Singlet	2.37	6
Methinyl	Multiplet	1.73	1
Methylene	Two discrete multiplets	1.48, 1.25	1 for each proton
Methyl	Quadruplet	0.95	6

Results and Discussion

We find large contributions from the aromatic chromophores to the side-chain Cotton effects in optically active poly[(+)-2-phenylpropyl isocyanate]. In order to separate the aromatic effects from the main-chain conformational effects, we prepared an optically active aliphatic polyisocyanate, poly [(*S*)-(+)-2-methylbutyl isocyanate], and its model compound, (*S*)-(−)-*N*,*N*-diacetyl-2-methylbutylamine. In addition, we also synthesized a racemic modification of the aliphatic polymer.

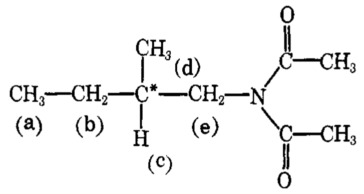
Both the optically active and the racemic polymers show crystallinity by X-ray diffraction. The optically active polymer melts at approximately 220°, about 10° higher than the racemic polymer.

We investigated the nuclear magnetic resonance spectrum of the aliphatic model compound at 220 MHz (Figure 1). The nmr spectrum of the model compound in deuteriochloroform shows the results given in Table I. We believe the quadruplet can be resolved into a low-field triplet and a high-field doublet, suggesting that simple splitting rules apply to the two methyl groups.

Protonation of the model compound has interesting effects. The nmr spectrum of the model compound in deuteriosulfuric acid shows a multiplet between 2.80 and 3.05 ppm assigned to the *N*-methylene protons. The combined signal from the two acetyl groups appears as two singlets, 0.21 ppm apart, with similar intensities, indicating monoprotonation of the imide. The methinyl proton shows absorption bands at 1.27 ppm, and the methylene protons of the ethyl group show a multiplet between 0.66 and 1.05 ppm. In deuteriochloroform, the two methyl peaks can be viewed as overlapping low-field doublet and high-field triplet.

Based on valence-bond calculations, Karplus[7] obtained an approximate equation relating the coupling constant, J_{HH}, between two protons on adjacent tetrahedral carbon atoms to the dihedral angle, ϕ, between the carbon–hydrogen bonds in the functional form, $A \cos^2 \phi + B$.

In the aliphatic model compound



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[7] M. Karplus, *J. Chem. Phys.*, 30, 11 (1959).

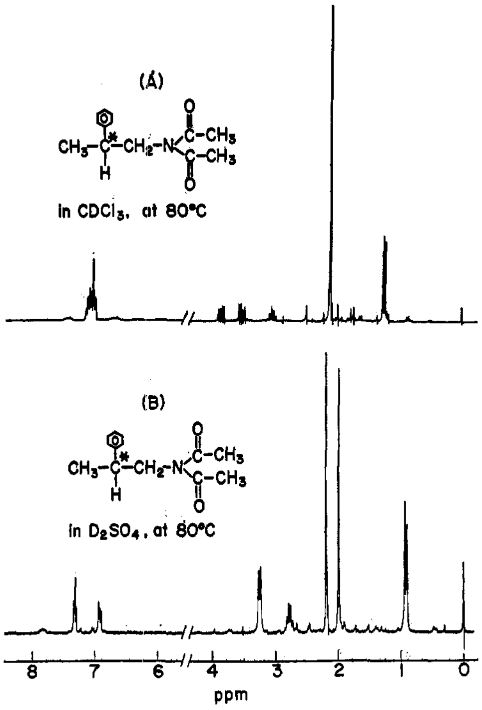

Figure 2. Nuclear magnetic resonance spectra (220 MHz) of optically active aromatic model compound (+)-*N*,*N*-diacetyl-2-phenylpropylamine (a) in deuteriochloroform, (b) in deuteriosulfuric acid.

we assume that CH_3(a) or CH_3(d) is in three equally populated rotamer conformations; therefore, $\phi = 60°, -60°$, and 180°.

From experiment, $J_{dc} = 7$ Hz and $J_{ab} = 7$ Hz. The Karplus equations are as follows.

$$J_{HH} = A \cos^2\phi + B \qquad 0° \leq \phi \leq 90°$$

$$J_{HH} = A' \cos^2\phi + B \qquad 90° \leq \phi \leq 180°$$

To compute average coupling

$$\langle J \rangle = (1/3)(A \cos^2 60° + B + A \cos^2 -60° + B + A' \cos^2 180° + B) = (1/3)(0.5A + A' + 3B)$$

From the literature, we can assume that B is negligible.[8] This gives $\langle J \rangle = 0.17A + 0.33A'$.

It is found experimentally that A' is approximately 20% larger than A.[9] Thus $A' \simeq 1.2A$, and we obtain $\langle J \rangle = 0.57A$.

Since $J_{\mathrm{exptl}} = 7$ Hz, then $A = 12.3$ and $A' = 14.7$. These Karplus coefficients are in the range commonly used in the literature.[9-11]

Since $J_{ec} = 7$ Hz and $J_{bc} = 7$ Hz, the same types of rotamers (giving $\phi = 60°, -60°$, and 180°) are also present about the CH_2(b)–C* and C*–CH_2(e) bonds.

We also carried out nmr measurements of (+)-*N*,*N*-diacetyl-2-phenylpropylamine, an optically active aromatic model compound for poly[(+)-2-phenylpropyl isocyanate] (II) (Figure 2). The nmr spectrum of the model compound in deuteriochloroform provides the information given in Table II.

TABLE II

Type of proton	Nature of peaks	Chemical shift, ppm	Area
Aromatic	Multiplet	7.06	5
N-Methylene	Two discrete multiplets	3.82, 3.50	1 for each proton
Methinyl	Multiplet	3.05	1
Diacetyl	Singlet	2.12	6
Methyl	Doublet	1.25	3

In deuteriosulfuric acid, the model compound shows significantly different features in the nmr spectrum. The phenyl protons exhibit two resonance bands. The methylene protons appear as a doublet. The two acetyl groups now have separate resonances of comparable intensities. As in the aliphatic model compound, monoprotonation seems to prevail.

Integration of the phenyl-proton signal shows that two protons have been exchanged with deuterium. After 48 hr, the nmr spectrum of the same compound no longer shows a signal from the phenyl protons. The rest of the spectrum remains unchanged. The hydrogen exchange between aromatic compounds and acid solvents has also been studied by Lauer and coworkers.[12] They concluded that deuteration occurred in the aromatic ring, and none in the side chain.

The nmr spectra of the optically active aliphatic polymer and the racemic polymer are similar in deuteriochloroform and in deuteriosulfuric acid (Figures 3 and 4). Since polymer molecules have lower segmental mobility, broader absorption bands are observed in their resonance spectra. Integration of the bands shows areas in the ratios of approximately 2:1:2:6, attributable to *N*-methylene, methinyl, methylene, and a combination of two methyl groups.

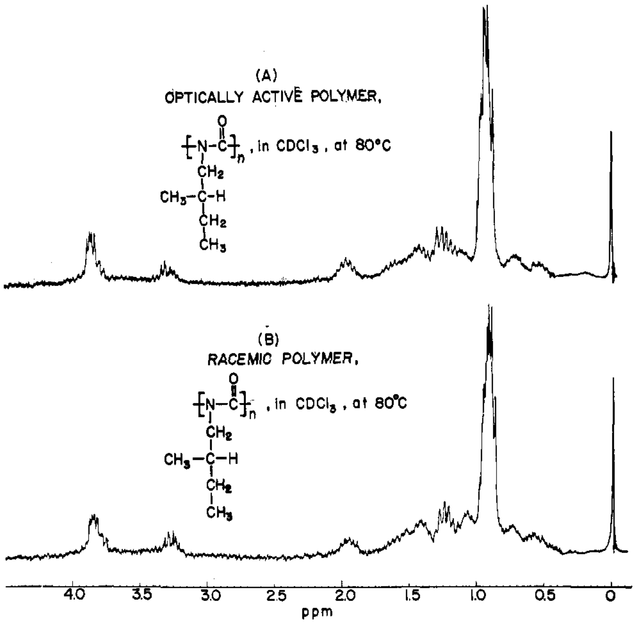

Figure 3. Nuclear magnetic resonance spectra (220 MHz) of (a) optically active aliphatic polymer poly[(*S*)-(+)-2-methylbutyl isocyanate] and (b) racemic polymer; both polymers are in deuteriochloroform.

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[8] L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, Oxford, England, 1969, p 281.

[9] R. J. Abraham and J. S. E. Holker, *J. Chem. Soc.*, 806 (1963).

[10] K. L. Williamson and W. S. Johnson, *J. Amer. Chem. Soc.*, **83**, 4623 (1961).

[11] R. U. Lemieux and J. W. Lown, *Tetrahedron Lett.*, 1229 (1963).

[12] W. M. Lauer, G. W. Matson, and G. Stedman, *J. Amer. Chem. Soc.*, **80**, 6433 (1958).

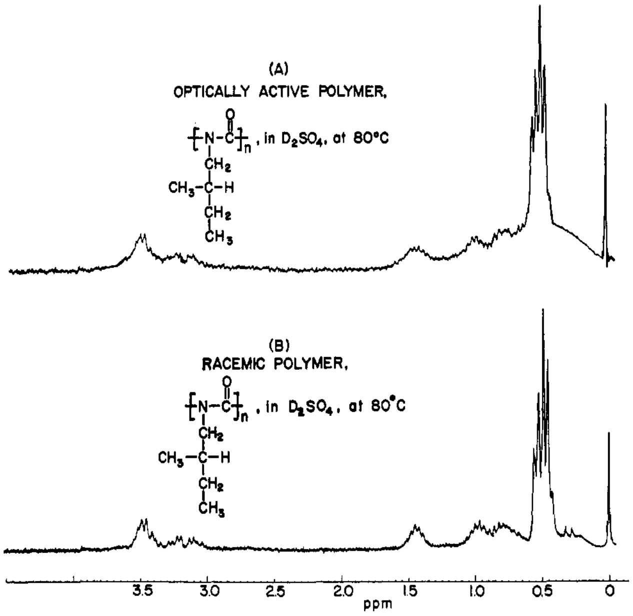

Figure 4. Nuclear magnetic resonance spectra (220 MHz) of (a) optically active polymer poly[(*S*)-(+)-2-methylbutyl isocyanate] and (b) racemic polymer; both polymers are in deuteriosulfuric acid.

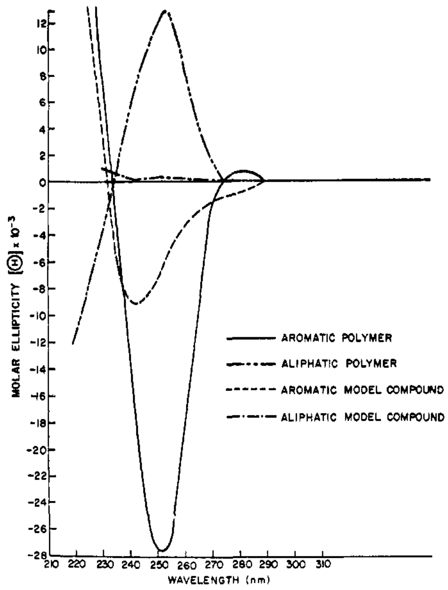

Figure 6. Circular dichroism spectra of the optically active aromatic polymer poly[(+)-2-phenylpropyl isocyanate] and its model compound (+)-*N*,*N*-diacetyl-2-phenylpropylamine, and of the optically active aliphatic polymer poly[(*S*)-(+)-2-methylbutyl isocyanate] and its model compound, (*S*)-(−)-*N*,*N*-diacetyl-2-methylbutylamine, in chloroform.

The widths of the nmr bands of the optically active aliphatic polymer and the racemic polymer are similar. In contrast, the nmr bands of the optically active aromatic polymer are sharper than those of its racemic modification. Since the nature of the nmr signals of a polymer in dilute solution is determined only by protons in the same polymer chain or the surrounding solvent molecules and is not sensitive to interaction with protons in the other polymer molecules, we believe that the racemic aliphatic isocyanate polymerizes by a stereoselective route.[13] Such polymerizations lead to mixtures of poly(*R*-)- and poly(*S*-)- isocyanates. As a result, the nmr spectrum of the racemic aliphatic polymer will be essentially identical with that obtained from the optically active polymer.

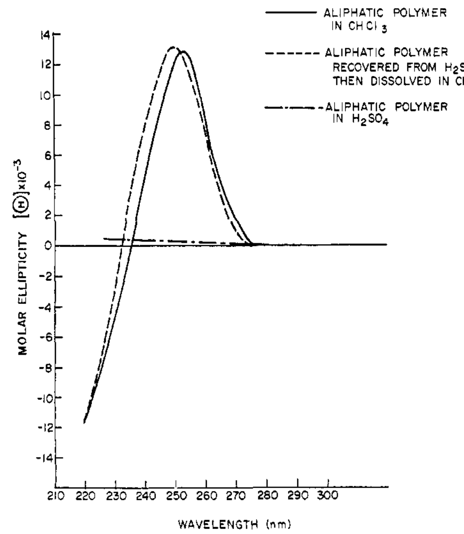

Figure 5. Circular dichroism spectra of the optically active polymer poly[(*S*)-(+)-2-methylbutyl isocyanate] in sulfuric acid and in chloroform, and of the same polymer recovered from sulfuric acid solution and then dissolved in chloroform.

We also measured the circular dichroism (CD) spectra of the optically active aliphatic polyisocyanate. The CD spectrum of the aliphatic polymer in sulfuric acid exhibits no peaks (Figure 5). Interactions between amides and sulfuric acid result in protonation.[1] If protonation were to occur to a substantial extent, then the dichroic band representing $n \rightarrow \pi^*$ transition should be almost totally eliminated. In sulfuric acid, the $n \rightarrow \pi^*$ transition band does indeed disappear. Bovey[14] reported the disappearance of the $n \rightarrow \pi^*$ band for D-oxolupanine, a diamide, in sulfuric acid, and attributed this phenomenon to protonation of the amide group.

In chloroform (Figure 6), the aliphatic polymer shows a circular dichroic band which is strongly positive and is centered at 253 nm with a crossover at 235 nm. The beginning of a region of negative dichroism below 235 nm is also observed. This positive dichroism band with a molar ellipticity of about +13,000 (deg cm^2)/dmol can be assigned to the $n \rightarrow \pi^*$ transition of the amide chromophore.

We have been able to recover the optically active aliphatic polyisocyanate from sulfuric acid solution by reprecipitating with methanol, a nonsolvent. The CD spectrum of the recovered polymer in chloroform gives essentially the same pattern as the optically active polymer dissolved directly in chloroform (Figure 5). The positive dichroism band of the recovered polymer has a molar ellipticity of about +13,180 (deg cm^2)/dmol, compared with +13,000 (deg cm^2)/dmol for the polymer dissolved directly in chloroform.

As in the aromatic polyisocyanate, the aliphatic polyisocyanate also has enhanced rotational strength compared with its model compound. Table III shows the differences in optical rotatory properties of these two polymers.

In the aliphatic polymer, the main chain has inherently symmetric chromophores which acquire optical activity from

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(13) P. Pino, F. Ciardelli, and G. Montagnoli, *J. Polym. Sci., Part C*, No. 16, 3265 (1968).

(14) F. A. Bovey, *Pure Appl. Chem.*, 16, 417 (1968).

TABLE III
ROTATORY PROPERTIES OF POLYMERS AND THEIR MODEL COMPOUNDS

		CD bands[a]	
	$[\alpha]^{25}\text{D}$,[a] deg	$\lambda_{\max}$, nm	Ellipticity[b]
Aromatic polyisocyanate	−468.8	280	+1,000
		252	−28,000
(+)-*N*,*N*-Diacetyl-2-phenylpropylamine[c]	+114.4	243	−9,100
Aliphatic polyisocyanate	+160	253	+12,900
(*S*)-(−)-*N*,*N*-Diacetyl-2-methylbutylamine[c]	−6	250	+192

[a] In chloroform. [b] The molecular weight of the repeating unit of the polymer and the molecular weight of the entire model compound were used in calculating the molar ellipticities of the polymer and the model compound, respectively. [c] Model compound.

dissymmetric perturbations of their environment by the side chains.

In the aromatic polymer, in addition to dissymmetric perturbation of inherently symmetric chromophores, Cotton effects also arise from interactions among the aromatic side chains. These interactions are responsible for the larger magnitudes of the side-chain Cotton effects for the aromatic polymer, as compared with the aliphatic polymer where no side-chain optical activity contribution can occur in this spectral region. In the aliphatic model compound, (*S*)-(−)-*N*,*N*-diacetyl-2-methylbutylamine, essentially no rotation is observed. In the aromatic model compound, (+)-*N*,*N*-diacetyl-2-phenylpropylamine, we observe an aromatic rotatory contribution which is enhanced in the polymer (*cf.* Table III). Quantitatively, the aromatic model compound cannot really represent the polymer, since the model compound has a 2:1 ratio of the carbonyl groups to nitrogen, in contrast to a 1:1 ratio in the polymer. Although the model compound is not exactly analogous to the polymer, we believe this model compound is satisfactory in giving a qualitative picture of the rotatory contributions.

The optical activity of the polyisocyanates originates in asymmetric sites in their side chains. The enhancement in optical activity of the polymers, compared to their model compounds, can be explained by conformational selections and preferences induced in the main chains by the optically active side chains. A conformational preference may result from favored spatial arrangement from the asymmetric side chain. The basis for this reasoning is a restriction on accessible conformations of the polymers because of steric interference on the side chains carrying centers of asymmetry. This steric interference will limit the range of accessible conformations of the polymer. With fewer conformations contributing to the measured optical rotation, the probability of conformation averaging decreases. Therefore, the overall rotation would be expected to be enhanced.

X-Ray diffraction studies on crystalline poly(*n*-butyl isocyanate) by Shmueli, Traub, and Rosenheck[15] showed that the polymer has a helical structure. Construction of a molecular model of poly(*n*-butyl isocyanate) also indicates that regular planar arrangement of the polymer chain would be unstable because of steric hindrance.

The main chain of our polymers cannot assume a planar structure because of similar steric factors noted above for poly(*n*-butyl isocyanate). Macromolecules containing very bulky side chains cannot assume a completely random structure, since steric hindrance will lead to specific conformational preferences. This propensity can lead to order or periodicity in the main chain, in the side chain of a polymer, or in a combination of both.[16] The optically active polyisocyanates show side-chain Cotton effects, which indicates that the aromatic chromophores are in somewhat different dissymmetric environments in the model compound and the polymer. Molecular models of our polymers show that the bulky side groups arrange themselves with some order. We are proposing that a helical conformation exists in the optically active polyisocyanates. The neighboring amide groups are no longer planar in order to relieve the large steric hindrance of neighboring side chains.

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(15) U. Shmueli, W. Traub, and K. Rosenheck, *J. Polym. Sci., Part A-2*, 7, 515 (1969).

(16) D. F. Bradley, M. Goodman, A. Felix, and R. Records, *Biopolymers*, 4, 607 (1966).