Helical Configuration of Poly(iminomethylenes). Screw Sense of Polymers Derived from Optically Active Alkyl Isocyanides[1,2]

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ABSTRACT: The synthesis of three poly(iminomethylenes), $[RN{=}C{<}]_n$, from optically active isocyanides is described. The group R includes (R)-$(CH_3)_2CHCH_2CH(CH_3)$, (R)-$(CH_3)_2CHCH(CH_3)$, and (R)-n-$C_6H_{13}CH(CH_3)$. From viscosity data it is estimated that MW's range from 20 000 to 70 000. The central chain of these polymers is a rigid helix. The optically active side chains induce a predominance of one helical screw sense. In the UV spectra of the polymers the $n{-}\pi^*$ transition of the $N{=}C$ chromophore of the helical main chain is present as a shoulder at 310 nm. In model compounds $RN{=}CH\text{-}t\text{-}C_4H_9$ this transition lies at an approximately 50 nm lower wavelength. The $n{-}\pi^*$ transition of the $N{=}C$ group is responsible for the CD spectrum in the region from 240 to 380 nm. The CD reveals a contribution from the side chains as well as from the excess helix. A comparison with the CD spectrum of enantiomerically pure (M)-poly($tert$-butyliminomethylene) proves the excess helix to be of M sense. This excess diminishes from approximately 62% in $R = (R)$-$(CH_3)_2CHCH(CH_3)$ to 20% in $R = (R)$-n-$C_6H_{13}CH(CH_3)$. This sequence is in agreement with predictions based on the polymerization mechanism.

Poly(isocyanides), more properly called poly(iminomethylenes), are obtained by the polymerization of isocyanides with nickel(II) catalysts[3]

$$nRN{=}C \xrightarrow{\text{Ni(II)}} (RN{=}C{<})_n$$
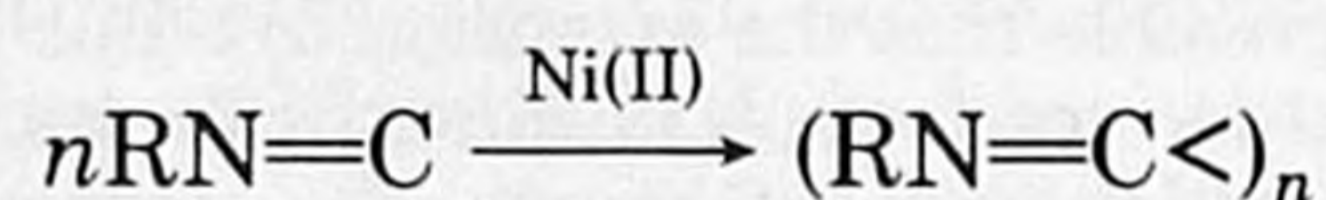
These polymers show atropisomerism, that is, stereoisomerism due to restricted rotation about single bonds,[4] and represent a rare case of this kind of isomerism in polymers.[5] They have a helical configuration and consequently are chiral. Poly($tert$-butyliminomethylene) has been completely resolved by column chromatography.[2,6] The support consisted of glass beads coated with poly[(S)-sec-butyliminomethylene]. The right-handed (P) helix could be assigned to the levorotatory enantiomer and the left-handed (M) one to the dextrorotatory enantiomer.[7]

This resolution of poly($tert$-butyliminomethylene) into enantiomers shows that polymerization of a nonchiral isocyanide gives a racemic mixture of P and M screws. However, when the monomer is one enantiomer of a chiral isocyanide, its polymer will be a mixture of diastereoisomers, and P and M screws will not be formed in equivalent amounts.

In a previous paper[8] we compared the optical rotation values of various chiral isocyanides with those of their corresponding polymers. This comparison strongly supported the hypothesis that optically active isocyanides do indeed polymerize screw sense selectively. The screw sense of the various polymers was tentatively deduced from the optical rotation values. From the polymerization mechanism, rules were derived by means of which the screw sense can be predicted when an optically active isocyanide is polymerized by nickel(II).

Optical rotation values have been used frequently to draw conclusions about conformations of polymer chains in solution.[9] However, in the present system one should be cautious about doing this, because poly(iminomethylenes) are highly rigid rod polymers.[10] The rigid environment in the system $(R^*N{=}C{<})_n$ might considerably affect the conformation of R^* and thus its contribution to the optical rotation. Therefore, when going from monomer to polymer the change in the optical rotation value is not necessarily due to the conformation of the polymer main chain exclusively.

More reliable information can be expected from circular dichroism (CD) data. Many of the polymers which we synthesized earlier had chromophores in their side chains. These chromophores might interfere with the helically arranged $C{=}N$ chromophores of the main chain. These polymers are therefore less suitable for CD spectral analysis. Poly(iminomethylenes) derived from optically active alkyl isocyanides do not have additional chromophores and are more appropriate for a CD study. One such polymer, poly(sec-butyliminomethylene), was synthesized earlier.[7] Its CD spectrum could not be recorded because of its complete insolubility in organic solvents. Yet its screw sense could be derived from the resolution process of poly($tert$-butyliminomethylene).[7] In this paper we describe the synthesis of three additional poly(alkyliminomethylenes) prepared from optically active alkyl isocyanides, compounds 4a–c of Scheme I. These polymers are soluble in apolar organic solvents. Their CD spectra are compared with the spectrum of poly($tert$-butyliminomethylene) (4d) and spectra of model compounds.

Results and Discussion

Synthesis. For the synthesis of polymers 4a–c as well as for their model compounds 5a–c one requires optically active amines as starting materials (Scheme I). 2-Octanamine (1a) was resolved through fractional crystallization of its bitartrate from water. After 12 crystallizations ${}^1H$ NMR shift experiments showed that 1a was optically pure with $[\alpha]^{22}_{578}$ $-6.92°$. The absolute configuration of this enantiomer has been established to be R.[11] (R)-3-Methyl-2-butanamine (1b) and (R)-4-methyl-2-pentanamine (1c) were prepared from the amino acids L-valine and L-leucine, respectively, as outlined in Scheme II. The carboxylic function of the latter compounds was esterified and subsequently reduced to the hydroxymethyl group with $LiAlH_4$. We found it convenient to attach a benzoyl group to the NH_2 group of 6, as this facilitates the isolation of alcohol 9 from the reaction mixture.[12] This benzoyl group is converted into a benzyl group during the reduction process. The latter group was removed by hydrogenolysis with palladium-on-carbon. The unprotected alcohol 10 was treated with HBr in acetic acid to give 11. In this reaction a small amount of bromine was added as a catalyst. The bromide 11 was subjected to hydrogenolysis in an aqueous

Table I
Molar Optical Rotations of Poly(iminomethylenes) 4,
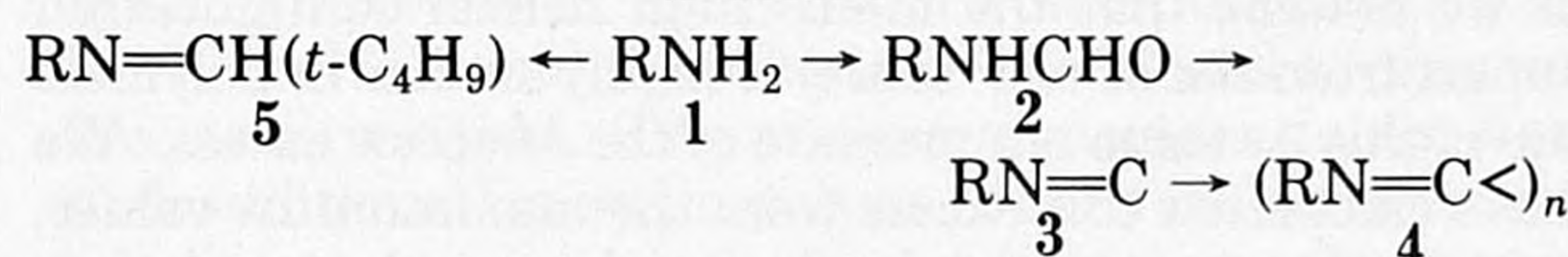$(RN{=}C{<})_n$, Their Monomers 3, RN=C, and Model
Imines 5, $RN{=}CH(t\text{-}C_4H_9)$

		$[M]^{22}_{578}$ ^{a}/deg		
	R	3	5	4 ^{b}
a	$(R)\text{-}n\text{-}C_6H_{13}CH(CH_3)$	−66.3	−34.5	+47.3
b	$(R)\text{-}(CH_3)_2CHCH(CH_3)$	−23.5	−76.1	−16.2
c	$(R)\text{-}(CH_3)_2CHCH_2CH(CH_3)$	−68.8	−58.2	+68.9
d	$(CH_3)_3C$			+46 ^{c}

^{a} In chloroform; 3, c 1.1–1.9; 4, c 0.25–0.8; 5, c 0.9–2.3.
^{b} Per repeating unit RN=C. ^{c} Taken from ref 2, M helix.

sodium acetate–acetic acid buffer with palladium-on-carbon as catalyst. After workup the desired amines were isolated as their HCl salts. It follows from Scheme II that, when we start from the L-amino acids **6**, the absolute configuration of the amines **1b** and **1c** is R.[13]
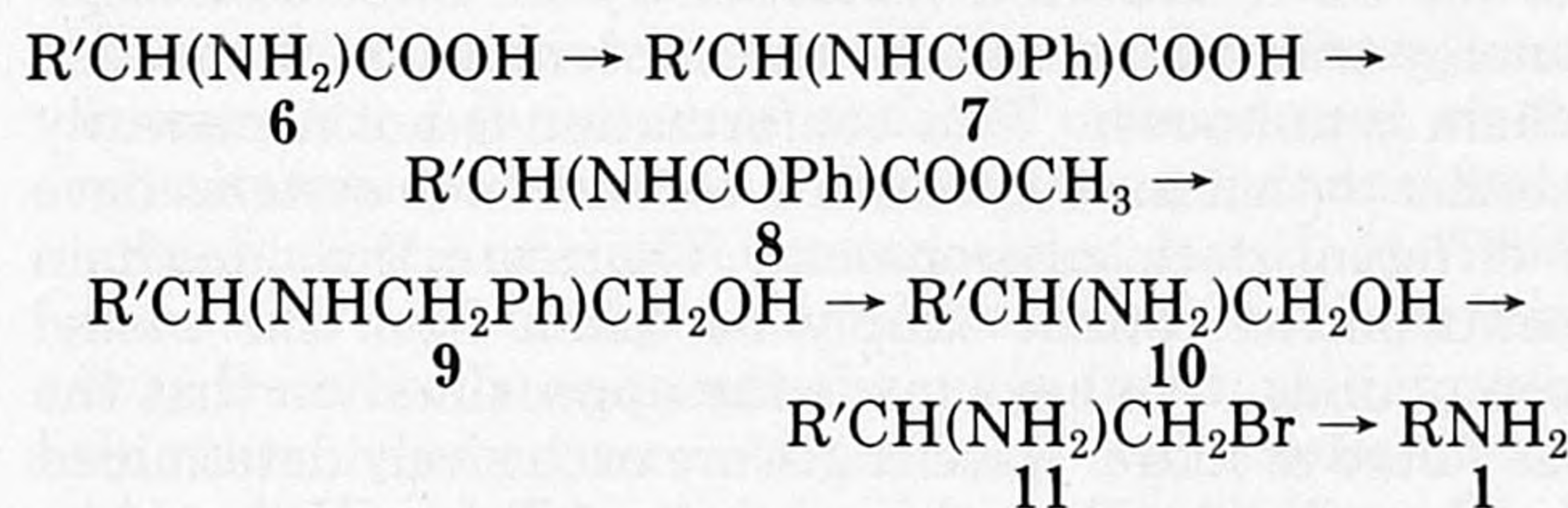
Scheme I

$$RN{=}CH(t\text{-}C_4H_9) \leftarrow RNH_2 \rightarrow RNHCHO \rightarrow$$
$$\quad 5 \qquad\qquad\quad 1 \qquad\qquad 2$$
$$RN{=}C \rightarrow (RN{=}C{<})_n$$
$$\quad 3 \qquad\quad 4$$

a, R = $(R)\text{-}n\text{-}C_6H_{13}CH(CH_3)$

b, R = $(R)\text{-}(CH_3)_2CHCH(CH_3)$

c, R = $(R)\text{-}(CH_3)_2CHCH_2CH(CH_3)$

d, R = $(CH_3)_3C$

Scheme II

$$R'CH(NH_2)COOH \rightarrow R'CH(NHCOPh)COOH \rightarrow$$
$$\quad 6 \qquad\qquad\qquad 7$$
$$R'CH(NHCOPh)COOCH_3 \rightarrow$$
$$\qquad\qquad 8$$
$$R'CH(NHCH_2Ph)CH_2OH \rightarrow R'CH(NH_2)CH_2OH \rightarrow$$
$$\quad 9 \qquad\qquad\qquad\qquad\qquad 10$$
$$R'CH(NH_2)CH_2Br \rightarrow RNH_2$$
$$\qquad 11 \qquad\qquad\quad 1$$

6e, R' = $(CH_3)_2CH$, valine

f, R' = $(CH_3)_2CHCH_2$, leucine

Upon treatment with an excess of ethyl formate the amines **1a–c** afforded the *N*-formyl derivatives **2a–c** (Scheme I). The isocyanides **3a** and **3c** were obtained in 85 and 70% yield, respectively, by dehydration of the corresponding formamides with phosphorus oxychloride and triethylamine at low temperatures.[14] Compound **3b** was prepared in 86% yield, using *p*-toluenesulfonyl chloride and quinoline as dehydrating agent. The latter procedure is the preferred one for relatively volatile isocyanides.[15] We assume that racemization does not occur in either procedure. With regard to the former procedure this assumption is based on our observation that retention occurs in molecules even more sensitive to racemization than the isocyanides described here. With respect to the second procedure, it is known[16] that optically active *sec*-butyl isocyanide retains its configuration under reaction conditions similar to those applied by us. The infrared absorption spectra of compounds **3a–c** showed characteristic isocyanide stretching vibrations at approximately 2140 cm⁻¹. At 578 nm the isocyanides have negative optical rotations (Table I). Their structures were confirmed by ¹H NMR.

The monomers were polymerized at room temperature by 0.1–1.0 mol % of nickel chloride either in methanol or without solvent. The yields of isolated polymer ranged from 60 to 95%. Polymers **4a–c** were pale yellow. They were soluble in petroleum ether, benzene, toluene, chlo-
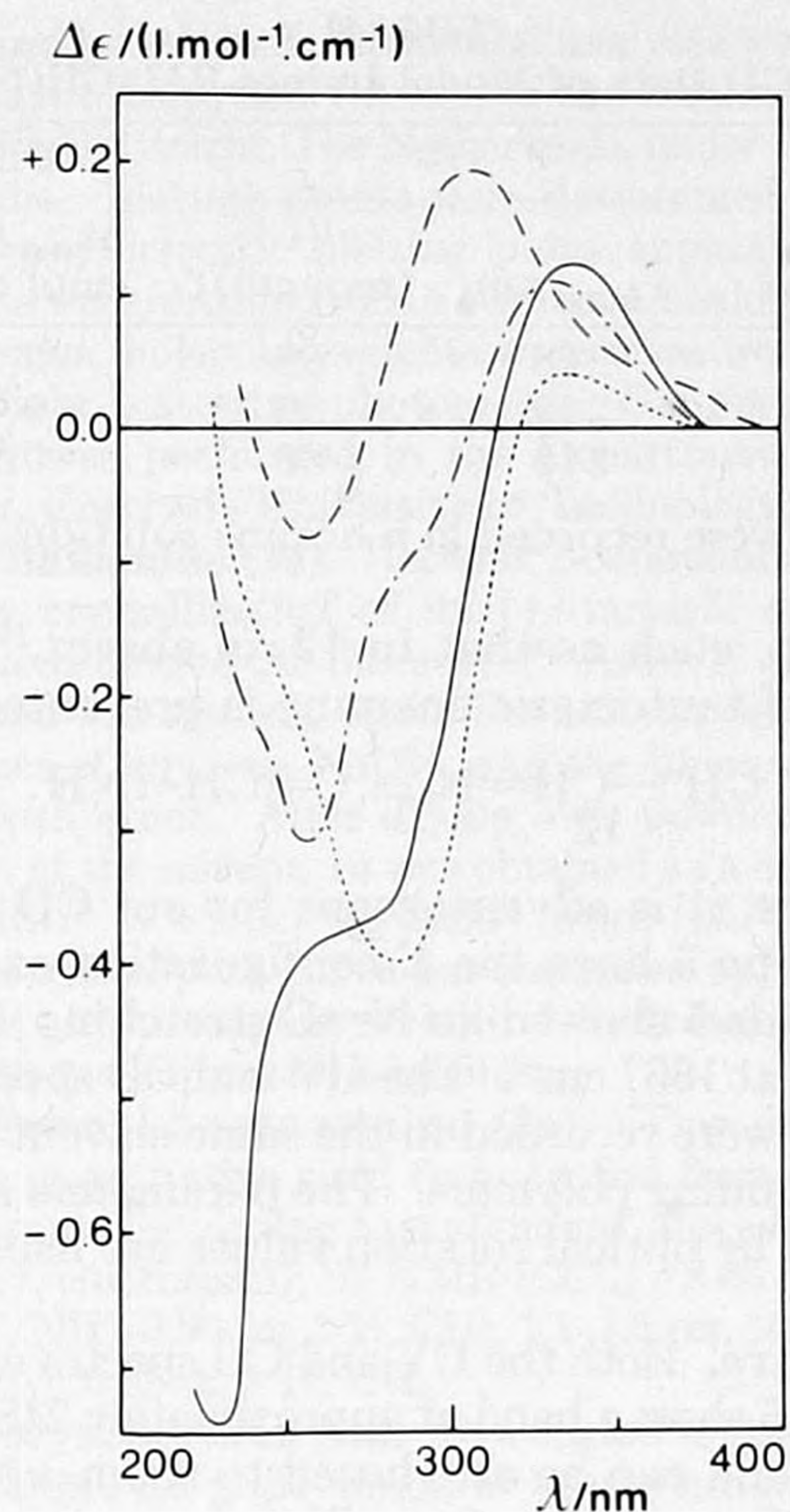
$\Delta\epsilon/(l.mol^{-1}.cm^{-1})$

Figure 1. CD spectra of poly(alkyliminomethylenes) in hexane solution: (···) **4a**; (—) **4b**; (−·−) **4c**; (−−−) **4d**.

rinated hydrocarbons, and tetrahydrofuran and insoluble in alcohols and water. Filtered and initially clear solutions of **4b** were unstable and gave deposits of polymer when allowed to stand for a short time. This behavior prevented the determination of the intrinsic viscosity of this compound. Polymers **4a** and **4c** showed intrinsic viscosities $[\eta]$ varying from 0.05 to 0.45 dL/g (toluene, 30.00 °C). In order to obtain an impression of the molecular weights corresponding to these viscosities we determined a Mark–Houwink relation. To this end a sample of racemic 2-isocyanooctane was prepared as indicated for the optically active compound **3a**. This racemic monomer was polymerized by nickel chloride under various conditions to give polymers having intrinsic viscosities from 0.43 to 1.6 dL/g (toluene, 30.00 °C). Their weight-average molecular weights were determined by light scattering and were found to vary from 65 000 to 140 000. The ratio of $\bar{M}_w/\bar{M}_n$ (gel permeation chromatography) for these polymers was about 6. From these data on the unfractionated samples the Mark–Houwink equation $[\eta] = 1.4 \times 10^{-9}\bar{M}_w^{1.75}$ was derived. Applying this equation to our optically active polymers **4a** and **4c**, we estimate that their viscosity-average molecular weights range from 20 000 to 70 000.

Compounds **4a–c** showed a distinct N=C stretching vibration in the infrared spectrum at about 1630 cm⁻¹. The UV spectra in hexane solution revealed a weak shoulder at about 310 nm ($\epsilon \simeq 60$ L/(mol·cm)) due to the n–π* transition of the N=C chromophore.[7] This shoulder is at the onset of a much stronger absorption band which has its maximum in the far-UV region. The CD spectra of the polymers were recorded in hexane and are presented in Figure 1. The optical rotation values are given in Table I.

As low molecular weight model compounds for our polymers the *N*-neopentylidene derivatives of amines **1**, compounds **5**, were synthesized. These compounds were selected because they can easily be prepared from pivaldehyde and **1**.[17,18] Moreover, with these imines the problem of aldol-type condensation is avoided because an
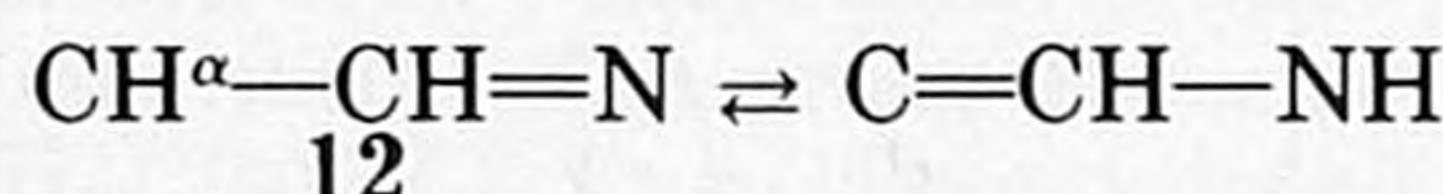
Table II
UV and CD Data of Model Imines RN=CH(t-C$_4$H$_9$)^a

compd	λ_{max}/nm	UV ϵ/(L/(mol·cm))	CD $\Delta\epsilon_{max}$/(L/(mol·cm))
5a	248	86	-0.71
5b	249	86	-0.98
5c	248	88	-0.91

^{a} Spectra were recorded in n-hexane solutions at 25 °C.

α-CH group, such as that in **12**, is absent.[19] Also the formation of tautomeric enamine is prevented[20]

$$\text{CH}^\alpha{-}\text{CH}{=}\text{N} \rightleftharpoons \text{C}{=}\text{CH}{-}\text{NH}$$
12

Furthermore, it is advantageous for our CD study that imines of type **5** have the E configuration exclusively.[21]

Compounds **5** showed an N=C stretching vibration in the infrared at 1667 cm^{-1}. The UV and CD spectra of these compounds were recorded in the same solvent as used for the corresponding polymers. The parameters are given in Table II. The optical rotation values are listed in Table I.

CD Spectra. Both the UV and CD spectra of the model compounds **5** show a band at approximately 248 nm (Table II). This band can be attributed to the n–π* transition of the N=C group.[20] Our (R)-imines show a simple, negative Cotton effect at the wavelength indicated. This result is in line with the ORD spectrum of (R)-N-neo-pentylidene-sec-butylamine, measured by Bonnett,[17] which also shows a negative Cotton effect at 245 nm.

In polymers **4a–c** the n–π* transition of the N=C group in the UV spectrum is shifted some 50 nm toward longer wavelength. The CD (Figure 1) in the region of 240–380 nm corresponds to this transition. At wavelengths λ < 240 nm the spectra are complicated by the onset of effects due to a transition of relatively high energy, most probably the π–π* transition of the N=C group. In the polymers both the chiral center in the side chain and the helical structure of the main chain will induce rotational power in the N=C chromophore.[22] The contribution by the chiral side chain reveals itself in the CD spectra (Figure 1) as a relatively large negative band with a maximum $\Delta\epsilon$ value at about 260 nm. The helicity of the main chain is manifested as a positive "couplet",[23] the positive part of which is visible as a band at about 325 nm. Such a positive couplet is also found in the CD spectrum of (M)-poly($tert$-butyliminomethylene) (**4d**). For comparison this spectrum is included in Figure 1. From the similarity of the couplets we conclude that polymers **4a–c** are predominantly in the M-helical configuration. The rotation data for these polymers (Table I) show appreciable shifts to positive values compared to the rotations of the model imines. This behavior suggests a dextrorotatory contribution by the helices. The combination of M-screw sense and dextrorotation is in line

Scheme III

13-($\underline{Z}$)   13-($\underline{E}$)

k_P k_M

($\underline{P}$)-Screw   ($\underline{M}$)-Screw

S=H, M=CH$_3$, L=R'
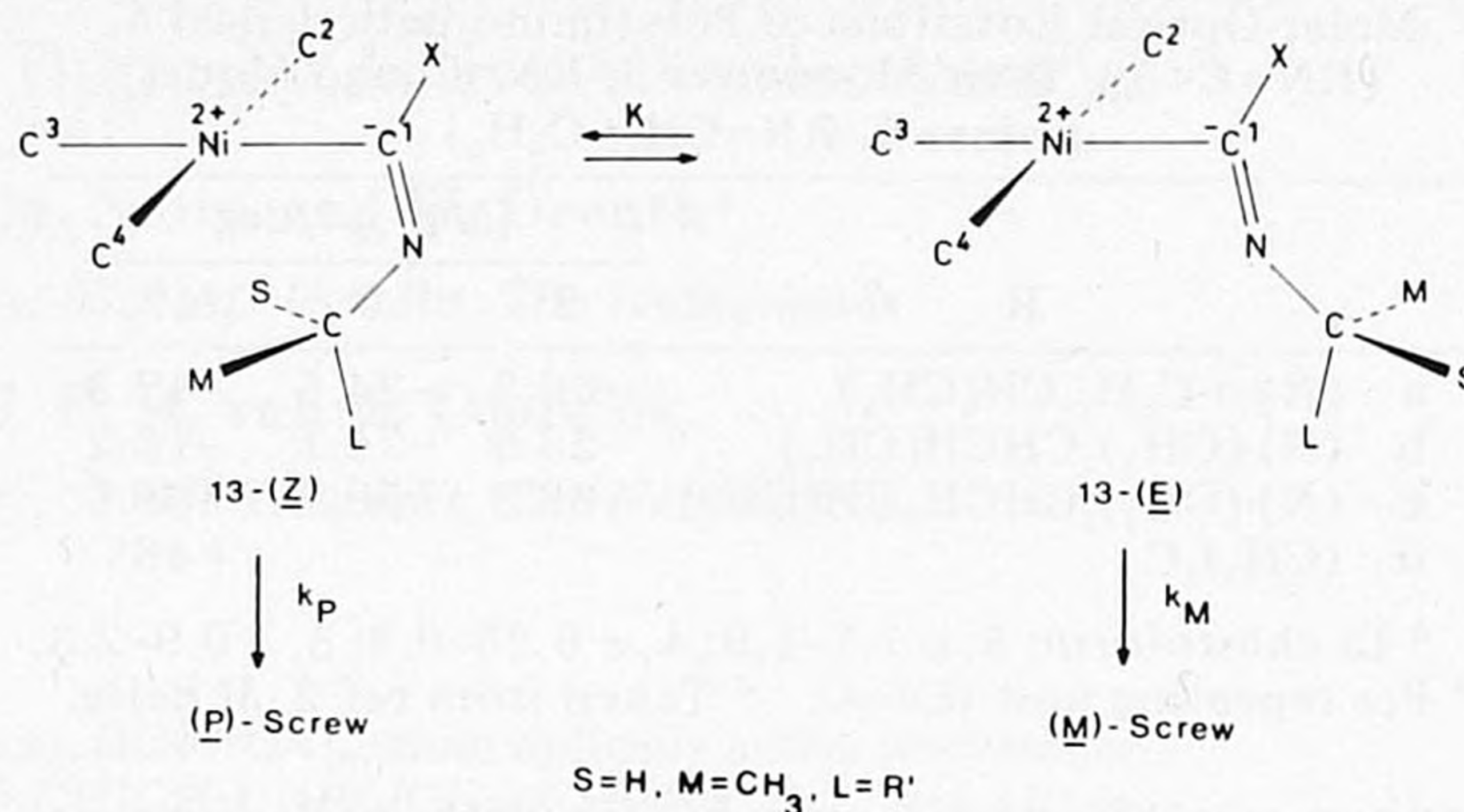
with what was found earlier for poly($tert$-butyliminomethylene).[7]

Figure 1 shows that the maximum $\Delta\epsilon$ value of the positive CD band at 320–340 nm varies for the three polymers. If we assume that the main-chain helical configuration (apart from the M or P sense) is highly similar in polymers **4a–c**, this $\Delta\epsilon$ value is a measure of the M-screw excess. We have calculated this excess from the maximum $\Delta\epsilon$ values, taking the $\Delta\epsilon$ of completely resolved poly($tert$-butyliminomethylene) as the calibration value[1] (Table III). Actually, for an accurate calculation the contributions made by the helical main chain[24] and the chiral side chain should be considered separately. However, this is not really possible since the latter contribution is difficult to quantify for two reasons: (a) the lower wavelength region of the CD spectrum is disturbed by the effects on high-energy transitions and (b) the conformation of the side chain is unknown. This conformation is not necessarily similar to that in compounds **5**, because both systems have a different steric environment. Therefore, the side-chain contribution cannot simply be taken from the model compounds. We have made the approximation that the $\Delta\epsilon$ values at longer wavelength are exclusively determined by the couplet. Thus, the numbers of Table III should be considered as useful only within the present series of polymers. They are probably lower limits.

The data in Table III show that the excess of M screws diminishes with decreasing bulkiness of R', as expressed by the λ steric constant[25] or approximately the Taft steric parameter.[26] The P excess in the polymer of (R)-sec-butyl isocyanide (R' = C$_2$H$_5$), which we synthesized earlier,[7] fits into this series. We will try to explain this result in terms of the polymerization mechanism.

It was suggested earlier[3,27] that polymerization of isocyanides by nickel(II) chloride proceeds via a circular sequence of insertion reactions around the nickel center ("merry-go-round" mechanism). The reaction starts from the square-planar complex Ni(CNR)$_4^{2+}$. In this complex π back-bonding from nickel to the isocyanide ligands is very small. The terminal carbon atom of such a ligand is

Table III
CD and Optical Rotation Data of Polymers [(R)-R'CH$_3$CHN=C<]$_n$ and of [t-C$_4$H$_9$N=C<]$_n$

R'	$\Delta\epsilon_{max}{}^a$/(L/(mol·cm))	$\Delta[M]^{22}_{578}{}^b$/deg	screw sense, % ee^c	$\lambda_{R'}{}^d$	$-(E_S)_{R'}{}^e$
C$_2$H$_5$			P^f	1.05	0.07
n-C$_6$H$_{13}$	0.040	81.8	M, 20	~1.1	0.30
i-C$_4$H$_9$	0.115	127.1	M, 56	1.20	0.93
i-C$_3$H$_7$	0.125	59.9	M, 62	1.27	0.47
(t-C$_4$H$_9$NC)$_n$	0.20	46	M, 100		

^{a} $\Delta\epsilon_{max}$ of positive band at 300–400 nm. ^{b} Difference between the molar optical rotation value of polymer 4 and that of model compound 5. ^{c} ee = enantiomeric excess of indicated screw, assuming complete stereoregular polymerization. ^{d} See ref 25. ^{e} Taft steric constant. See ref 26. ^{f} See ref 7.

easily attacked by a nucleophile X^- (e.g., Cl^-) giving rise to ion **13** (Scheme III). In **13** the carbanion $^-C^1(X)=$ N—C< is attached coordinatively to the nickel center. Its plane is approximately perpendicular to the $C^1C^2C^3C^4$ plane for steric reasons. There is free rotation around the bonds from Ni to C^2, C^3, and C^4, but not around that to C^1. Carbon atom C^1 has gained in nucleophilicity. As a nucleophile it is able to attack a neighboring isocyanide carbon. This attack is facilitated when a new ligand enters apically from above and coordinates to the nickel. The direction of attack determines the screw sense. Continuing the sequence $C^1 \rightarrow C^2 \rightarrow C^3$ in a merry-go-round fashion, a right-handed helix is obtained. In a similar way the sequence $C^1 \rightarrow C^4 \rightarrow C^3$ results in a left-handed helix.

In our earlier studies[8,27] we assumed that the group SMLC in **13** (the relative steric requirements of the substituents are denoted by small (S), medium (M), and large (L)) is predominantly in the Z position, (Z)-**13**. This assumption was probably correct, since at that time we had ligands $C^1(X)=NCR^1R^2R^3$ in which one of the substituents R^1, R^2, or R^3 could coordinate to nickel and in this way favor a Z position. The present monomers do not have such additional ligand properties. Therefore, we must now take into account both the Z and E isomers of polymerization intermediate **13**. It is known[28-30] that, in comparable metal complexes as well as in imines, the E/Z ratio varies with temperature, solvent, and substituents.

Let us consider conformation (Z)-**13**. The competition between the attack by C^1 on C^2 and on C^4 will depend on the relative energies of the respective transition states. These energies will be related to the steric interactions within the transition states. With regard to these interactions, the relative sizes and the arrangement of the substituents on the chiral carbon atom of ligand C^1 are of interest. In the case under consideration, S = H, M = CH_3, and L = R′. We have positioned the substituent L pointing away from the largest impediment in the transition state, viz., the nickel center. Attack by C^1 will preferentially occur at the least hindered side, i.e., in (Z)-**13** on C^2. A P screw will be formed (rate constant k_P).

For intermediate (E)-**13** we have to consider which of the two substituents on C^1, namely, nickel center or X, will interfere more severely with L in the transition state. In our opinion this will be X since this group is placed in a cis position with respect to SMLC. Reasoning in a similar way as indicated for (Z)-**13** one can derive that an M screw will be formed from (E)-**13** (rate constant k_M).

What will be the influence of R′ (=L) on the rate constants k_P and k_M and on the equilibrium constant K? Since R′ is far away from the reaction centers (C^1–C^2 in (Z)-**13** and C^1–C^4 in (E)-**13**) the effects of R′ on k_P and k_M will be relatively small. However, the effect on the equilibrium constant K will be relatively larger. With a sterically more demanding R′ (in Table III reading from top to bottom) the equilibrium will shift to the right since in (E)-**13** the steric interactions are less severe than in (Z)-**13**. Thus, the preference for M helices will increase in the same direction.

Experimental Section

Analytical Techniques. Infrared (IR) spectra were recorded on Perkin-Elmer 297 and 283 spectrophotometers. Ultraviolet (UV) spectra were obtained on a Perkin-Elmer 200 spectrophotometer. CD spectra were recorded on a home-built apparatus. This instrument measures the differential absorbance (ΔA) with a sensitivity better than 1×10^{-6}. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. ^{1}H NMR spectra were obtained on a Varian EM390 instrument. Chemical shifts (δ) are given in ppm downfield from internal tetramethylsilane. Abbreviations used are s = singlet, d = doublet, t = triplet, m =

multiplet, and br = broad. Elemental analyses were carried out by the Element Analytical Section of the Institute for Organic Chemistry TNO, Utrecht, The Netherlands, under the supervision of W. J. Buis. Melting points were determined on a Mettler FP5/FP51 photoelectric melting point apparatus. Solution viscosity data were obtained with a Cannon-Ubbelohde viscometer. Weight-average molecular weights were measured on a Fica 50 automatic light scattering photometer. Gel permeation chromatography was performed in the Department of Chemical Technology, Enschede University of Technology.

(R)-2-Octanamine (1a). Racemic 2-octanamine (Fluka) was resolved by crystallization of its (+)-tartaric acid salt from methanol, according to the literature.[31] After 12 crystallizations the compound was optically pure. The salt was decomposed with a 10% excess of aqueous NaOH, and the liberated amine was extracted with ether. After drying over powdered KOH and evaporation of the solvent, **1a** was obtained as a colorless liquid: yield 33% (lit.[31] 17%); $[\alpha]^{22}_{578}$ –6.92° (neat) [lit.[31] $[\alpha]^{17}_{578}$ –6.97° (neat)]. The optical purity of **1a** was confirmed by ^{1}H NMR, using the chiral shift reagent tris[3-(1-hydroxy-2,2-dimethylpropylidene)-D-camphorato]europium.

(R)-N-Formyl-2-octanamine (2a). This compound was obtained in quantitative yield from **1a** and from a 25% excess of ethyl formate, according to a standard procedure:[32] $[\alpha]^{22}_{578}$ +7.44° (c 2.7, chloroform); ^{1}H NMR (CCl$_4$) δ 8.00 (s, 1 H, CHO), 7.75 (d, 1 H, NH), 3.90 (m, 1 H, CH), 1.1–1.5 (m, 10 H, CH$_2$), 1.10 (d, 3 H, CH$_3$), 0.85 (t, 3 H, CH$_3$).

(R)-2-Isocyanooctane (3a). To a stirred solution of 5 g (31.8 mmol) of **2a** and 8.1 g (80 mmol) of triethylamine in 40 mL of methylene chloride was added dropwise at 0 °C 4.9 g (32 mmol) of POCl$_3$ in 10 mL of methylene chloride. The reaction mixture was stirred at 0 °C for 1 h. Subsequently, the temperature was raised to 20 °C and 7 g of anhydrous sodium carbonate in 30 mL of water was added slowly (foaming!) while stirring. After the mixture had been stirred for a further 15 min, it was diluted with water and extracted with methylene chloride. After drying over sodium sulfate and evaporation of the solvent, the residue was distilled under diminished pressure: yield 3.80 g (85%) of **3a**; bp 73–74 °C (8 mm); $[\alpha]^{22}_{578}$ –47.6° (c 1.9, chloroform); IR (CCl$_4$) 2140 (NC) cm^{-1}; ^{1}H NMR (CCl$_4$) δ 3.50 (m, 1 H, CH), 1.2–1.7 (m, 13 H, CH$_2$ and CH$_3$), 0.85 (m, 3 H, CH$_3$).

Poly[(R)-2-octaniminomethylene] (4a). To a stirred solution of 14 mg (0.060 mmol) of NiCl$_2$·6H$_2$O in 5 mL of methanol was added at ambient temperature 2.35 g (16.9 mmol) of **3a** all at once. Immediately an orange-red color appeared, followed by a cream-colored precipitate. After about 20 min the reaction mixture solidified. Stirring was stopped and the reaction mixture was kept at ambient temperature for 5 h. Subsequently, the methanol was evaporated under diminished pressure and the polymer dissolved in 25 mL of chloroform. This solution was added dropwise to 375 mL of vigorously stirred methanol–water (4:1 (v/v)). The precipitated polymer was collected by filtration, washed twice with methanol, and dried at reduced pressure at 50 °C over KOH; yield 2.15 g (90%) of **4a** (the polymer did not melt when heated to 300 °C); $[\alpha]^{22}_{578}$ +34° (c 0.8, chloroform); $[\eta]$ = 0.45 dL/g (toluene, 30.00 °C); IR (KBr) 1635 (N=C) cm^{-1}. Anal. Calcd for C$_9$H$_{17}$N: C, 77.63; H, 12.31; N, 10.06. Found: C, 77.23; H, 12.18; N, 10.06; O, 0.52 (corrected to (C + H + N) = 100%: C, 77.64; H, 12.24; N, 10.11). Thus the polymer contains a small amount of O; compare also ref 33 and 34.

N-Benzoyl-L-valine (7e)[35,36] and **N-Benzoyl-L-valine Methyl Ester (8e).**[36,37] These compounds were prepared starting from L-valine (**6e**, Fluka), according to standard procedures.

N-Benzyl-L-valinol (9e). This compound was prepared from **8e** with an excess of LiAlH$_4$ in boiling diethyl ether.[36,38]

(S)-2-Amino-3-methylbutanol (L-Valinol, 10e). This compound was prepared from **9e** by hydrogenolysis[39] in water–ethanol (1:4 (v/v)) at 60 °C. The HCl salt of **10e** was crystallized from methanol–ether: mp 120 °C (lit.[40] mp 117–118 °C); $[\alpha]^{20}_D$ +14.5° (c 2.0, water) [lit.[40] $[\alpha]^{20}_D$ +14.25° (c 5.5, water)]; ^{1}H NMR (CD$_3$OD) δ 4.8 (s, 4 H, NH$_3^+$ and OH), 3.5–3.9 (m, 2 H, CH$_2$), 2.95 (m, 1 H, CHN), 1.96 (m, 1 H, CH), 0.98 and 1.06 (2d, 6 H, (CH$_3$)$_2$C).

(S)-1-Bromo-3-methyl-2-butanamine (11e). This compound was synthesized in 70% yield by reaction of **10e** with a mixture of 40% HBr in acetic acid and 1 vol % of bromine in an autoclave

at 115 °C for 20 h.[13,41] The HBr salt of **11e** was used directly for the synthesis of **1b**.

(R)-3-Methyl-2-butanamine (1b). An amount of 19 g (77 mmol) of **11e** was subjected to catalytic reduction with 1 g of 10% palladium-on-carbon in a solution of 15 mL of acetic acid and 20 g of sodium acetate in 100 mL of water. After stirring for 4 h at room temperature and 1 atm of H_2 pressure, the calculated amount of H_2 was consumed. Subsequently, the catalyst was removed by filtration. The filtrate was rendered alkaline with an excess of NaOH and extracted with ether. After drying over KOH, HCl gas was led into the ether layer. The flocculent precipitate was collected by filtration and recrystallized from acetone–ether: yield 8.8 g (93%) of the HCl salt of **1b**; mp 216–217 °C (lit.[13] mp 205 °C); $[\alpha]^{22}_{578}$ +2.3° (c 0.7, methanol), $[\alpha]^{22}_{578}$ +3.25°, $[\alpha]^{22}_{546}$ +3.68° (c 0.3, water) [lit.[13] $[\alpha]^{17}_{546}$ +3.5° (c 6.5, water)]; ^{1}H NMR (CD$_3$OD) δ 3.15 (m, 1 H, CHN), 1.95 (m, 1 H, CH), 1.28 (d, 3 H, CH$_3$), 1.06 and 0.98 (2d, 6 H, (CH$_3$)$_2$C).

(R)-N-Formyl-3-methyl-2-butanamine (2b). Amine **1b** was liberated from its HCl salt with an excess of aqueous NaOH and formylated as indicated for the synthesis of **2a**: $[\alpha]^{22}_{578}$ –12.5° (c 1.2, chloroform); ^{1}H NMR (CCl$_4$) δ 8.00 (s, 1 H, CHO), 7.9 (br, 1 H, NH), 3.80 (m, 1 H, CHN), 1.70 (m, 1 H, CH), 1.05 (d, 3 H, CH$_3$), 0.90 (d, 6 H, (CH$_3$)$_2$C).

(R)-2-Isocyano-3-methylbutane (3b). This isocyanide was synthesized from **2b** according to the method of Schuster et al.[15] but at a lower pressure (0.1 mm) than recommended. After redistillation **3b** was obtained as a colorless liquid in a yield of 86%: $[\alpha]^{22}_{578}$ –24.2° (c 1.1, chloroform); IR (CCl$_4$) 2135 (NC) cm^{-1}; ^{1}H NMR (CCl$_4$) δ 3.47 (m, 1 H, CHN), 1.5–2.0 (m, 1 H, CH), 1.32 (m, 3 H, CH$_3$), 1.00 (d, 6 H, (CH$_3$)$_2$C).

Poly[(R)-3-methyl-2-butaniminomethylene] (4b). Monomer **4b** was polymerized with 0.1 mol % of NiCl$_2$·6H$_2$O in methanol as solvent as described for **4a**: yield 75% of pale yellow polymer; $[\alpha]^{22}_{578}$ –16.7° (c 0.5, chloroform); IR (KBr) 1628 (N=C) cm^{-1}. Anal. Calcd for C$_6$H$_{11}$N: C, 74.17; H, 11.41; N, 14.42. Found: C, 73.29; H, 10.84; N, 14.04; O, 1.83 (corrected to (C + H + N) = 100%: C, 74.65; H, 11.04; N, 14.30 (compare also **4a**)).

N-Benzoyl-L-leucine (7f), N-Benzoyl-L-leucine Methyl Ester (8f), and N-Benzoyl-L-leucinol (9f). These compounds were prepared starting from L-leucine (**6f**, Fluka) as indicated for compounds **7e**, **8e**, and **9e**, respectively.

(S)-2-Amino-4-methylpentanol (L-Leucinol, 10f). This compound was obtained from **9f** as indicated for the synthesis of **10e**: $[\alpha]^{22}_D$ +7° (c 1.7, methanol) [lit.[42] $[\alpha]^{19-20}_D$ +6.9° (c 0.8–2.25, ethanol)]; ^{1}H NMR (CD$_3$OD) δ 4.8 (s, 3 H, NH$_2$ and OH), 3.2–3.7 (m, 2 H, CH$_2$O), 2.95 (m, 1 H, CHN), 1.65 (m, 1 H, CH), 1.25 (m, 2 H, CH$_2$), 0.93 and 0.92 (2d, 6 H, (CH$_3$)$_2$C).

(S)-1-Bromo-4-methyl-2-pentanamine (11f). This compound was prepared from **10f** as indicated for the synthesis of **11e**. The HBr salt of **11f** was used directly for the synthesis of **1c**.

(R)-4-Methyl-2-pentanamine (1c). The synthesis of this compound was performed as indicated for **1b**. The HCl salt of **1c** exhibited the following: mp 190 °C; $[\alpha]^{22}_{578}$ +6.34° (c 0.5, methanol); ^{1}H NMR (CD$_3$OD) δ 4.9 (br, 3 H, NH$_3$$^+$), 3.35 (m, 1 H, CHN), 1.35–1.95 (m, 3 H, CH$_2$ and CH), 1.31 (d, 3 H, CH$_3$), 0.91 and 0.99 (2d, 6 H, (CH$_3$)$_2$C).

(R)-N-Formyl-4-methyl-2-pentanamine (2c). Amine **1c** was liberated from its HCl salt and formylated as indicated for the synthesis of **2a** and **2b**. Compound **2c** had the following: $[\alpha]^{22}_{578}$ –14.7° (c 1.0, chloroform); ^{1}H NMR (CCl$_4$) δ 8.07 (s, 1 H, CHO), 7.7 (br, 1 H, NH), 4.06 (m, 1 H, CHN), 1.15–1.80 (m, 3 H, CH$_2$ and CH), 1.10 (d, 3 H, CH$_3$), 0.90 (d, 6 H, (CH$_3$)$_2$C).

(R)-2-Isocyano-4-methylpentane (3c). This isocyanide was synthesized from **3b** with POCl$_3$ and triethylamine as described for the synthesis of **3a**: yield of colorless liquid 70%; $[\alpha]^{20}_{578}$ –61.9° (c 1.8, chloroform); IR (CCl$_4$) 2142 (NC) cm^{-1}; ^{1}H NMR (CCl$_4$) δ 3.64 (m, 1 H, CHN), 1.1–2.0 (m, 3 H, CH$_2$ and CH), 1.33 (m, 3 H, CH$_3$), 0.91 and 0.98 (2d, 6 H, (CH$_3$)$_2$C).

Poly[(R)-4-methyl-2-pentaniminomethylene] (4c). Monomer **3c** was polymerized with 0.4 mol % of NiCl$_2$·6H$_2$O without solvent as described for **4a**. The polymer was obtained as a yellow powder in a yield of 90%: $[\eta]$ = 0.15 dL/g (toluene, 30.00 °C); $[\alpha]^{22}_{578}$ +62° (c 0.23, chloroform); IR (KBr) 1630 (N=C) cm^{-1}. Anal. Calcd for C$_7$H$_{13}$N: C, 75.62; H, 11.79; N, 12.60. Found: C, 75.25; H, 11.64; N, 12.07; O, 1.14 (corrected to (C + H + N)

= 100%: C, 76.04; H, 11.76; N, 12.20 (compare also **4a** and **4b**)). Another sample of **3c** was polymerized with 1.0 mol % of NiCl$_2$·6H$_2$O in methanol as solvent: yield of isolated polymer 60%; $[\eta]$ = 0.05 dL/g (toluene, 30.00 °C); $[\alpha]^{22}_{578}$ +58° (c 0.34, chloroform). The polymer which had $[\eta]$ = 0.15 and $[\alpha]^{22}_{578}$ +62° was used for the CD measurements.

(R)-N-Neopentylidenamines (5). These compounds were synthesized from pivaldehyde and amines **1** according to a procedure described in literature.[17,18]

Compound **5a**: bp 55 °C (0.2 mm); $[\alpha]^{22}_{578}$ –27.3° (c 2.4, hexane) and $[\alpha]^{22}_{578}$ –17.5° (c 2.3, chloroform); IR (neat) 1667 (N=C) cm^{-1}; ^{1}H NMR (CCl$_4$) δ 7.42 (s, 1 H, =CH), 2.90 (m, 1 H, CHN), 1.03 (s, 9 H, t-C$_4$H$_9$), 0.75–1.60 (m, 16 H, remaining H's).

Compound **5b**: bp 72 °C (60 mm); $[\alpha]^{22}_{578}$ –50.3° (c 2.1, hexane) and $[\alpha]^{22}_{578}$ –49.0° (c 0.9, chloroform); IR (neat) 1668 (N=C) cm^{-1}; ^{1}H NMR (CCl$_4$) δ 7.41 (s, 1 H, =CH), 2.68 (m, 1 H, CHN), 1.6 (m, 1 H, CH), 1.05 (s, 9 H, t-C$_4$H$_9$), 1.03 (d, 3 H, CH$_3$), 0.77 and 0.85 (2d, 6 H, (CH$_3$)$_2$C).

Compound **5c**: bp 58 °C (12 mm); $[\alpha]^{22}_{578}$ –47.2° (c 1.7, hexane) and $[\alpha]^{22}_{578}$ –34.4° (c 1.1, chloroform); IR (neat) 1667 (N=C) cm^{-1}; ^{1}H NMR (CCl$_4$) δ 7.45 (s, 1 H, =CH), 3.04 (m, 1 H, CHN), 1.1–1.6 (m, 3 H, CH$_2$ and CH), 1.04 (d, 3 H, CH$_3$), 1.02 (s, 9 H, t-C$_4$H$_9$), 0.81 and 0.87 (2d, 6 H, (CH$_3$)$_2$C).

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Optically Active Polyampholytes Derived from L- and D-Carbylalanyl-L-histidine[1,2]

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ABSTRACT: Two optically active polymers with the general structure [>C=NCH(CH$_3$)C(O)NHCH-(COOH)CH$_2$Im]$_n$ were prepared by the polymerization of L- and D-carbylalanyl-L-histidine with catalytic amounts of nickel(II) chloride. The monomers were synthesized from the dipeptides L- and D-alanyl-L-histidine by converting the amino group of these compounds into an isocyano function. The polymer from D-alanyl-L-histidine has a pK_a(ImH$^+$) of 8.4. It shows a polyelectrolyte viscosity behavior. Its molar rotation is [M]$^{20}_{578}$ ≃ 0°. Its CD spectrum has a couplet indicative of a right-handed helix. The other polymer has a pK_a(ImH$^+$) of 9.4 and a nonpolyelectrolyte viscosity behavior. Its [M]$^{20}_{578}$ is +1025°. The CD spectrum contains a single positive band, which does not provide information about the screw sense.

Enzymes combine high catalytic activity with high selectivity.[3] Certain polymeric model systems, called synzymes, have equal or even greater activity.[4] Striking examples are the ethylenimine-based systems developed by Klotz et al.[5] and very recently by Kunitake et al.[6] The success in this field contrasts sharply with the little progress that has been made in imitating the enantioselectivity of enzymes.[4,7] In our opinion there is a lack of appropriate chiral polymers which can be tested as enantioselective catalysts.[4] We are currently investigating whether poly(isocyanides), more properly called poly(iminomethylenes), [RN=C<]$_n$, are useful as such polymers. These compounds are attractive for two reasons. First, they are readily obtainable from the monomeric isocyanides, RN=C, with nickel chloride or a nickel(II) complex as catalyst.[8] These monomers in turn can be prepared in great variety from the corresponding amines.[9] Second, poly(iminomethylenes) have a stable helical structure.[8] Left-handed and right-handed helices of poly(*tert*-butyliminomethylene) have been separated by resolution.[10,11] Preferential formation of one screw occurs in the polymerization of one enantiomer of a chiral monomer.[12]

In previous papers[13,14] we reported on the synthesis and catalytic activity of imidazole-containing poly(iminomethylenes) such as poly(carbylhistidine), 1, which could
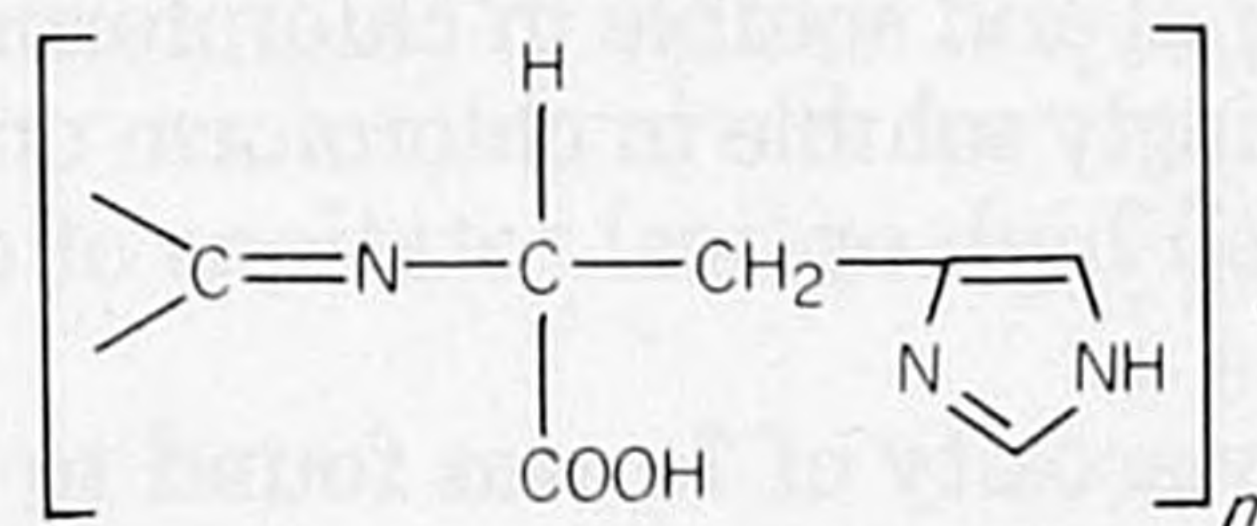
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be models for hydrolytic enzymes. We were unable to get 1 in optically active form because its carboxyl- and imid-

azole-protected monomer suffered from a rapid racemization. This was due to the presence of both a basic imidazole function in the molecule and two electron-withdrawing substituents at the chiral center, viz., the isocyano and carboxyl ester function.

We have now found that racemization problems can be avoided if one starts from isocyanides of dipeptides of histidine and other amino acids. The synthesis and physical properties of two polymers derived from such isocyanides, viz., poly(L-carbylalanyl-L-histidine) and poly(D-carbylalanyl-L-histidine), are described in this paper. Their catalytic activity in the hydrolysis of chiral esters will be described elsewhere.[15]

Results and Discussion

Synthesis. As far as we are aware, isocyanides derived from dipeptides containing histidine have not been described in the literature.[9,16] We have synthesized protected L- and D-carbylalanyl-L-histidine, compounds **6a** and **6b**, according to Scheme I.

Prior to the coupling of the amino acids, the carboxyl group of histidine and the amino group of alanine were protected as the methyl ester and the formamide group, respectively. The latter protecting group was chosen because it can be transformed directly into an isocyano function.[9] Dicyclohexylcarbodiimide in acetonitrile/*N,N*-dimethylformamide was used as coupling agent.[17] From the synthesis of 1 we learned[13] that it is necessary to protect the imidazole nucleus before converting the *N*-formyl function into an isocyano group. We chose the *p*-toluenesulfonyl (Tos) group as an imidazole protecting group in 4. This group is easily introduced and can be removed under mild conditions, as we found recently.[18] Moreover, a *p*-toluenesulfonyl group lowers the basicity of the imidazole nucleus, which reduces the chance of