# Atropisomerism in Polymers. Screw-Sense Selective Polymerization of Isocyanides by Inhibiting the Growth of One Enantiomer of a Racemic Pair of Helices

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**Abstract:** Isocyanides polymerize under the catalytic activity of Ni(II) to the corresponding poly(isocyanides): $n\mathrm{RN^+{\equiv}C^-} \xrightarrow{\mathrm{Ni(II)}} [\mathrm{RN{=}C{<}}]_n$. The polymers are of the rigid-rod type, and their molecules have a helical configuration as a result of hindered rotation in their carbon main chains. Upon polymerization, achiral isocyanides generally form a racemic mixture of left- and right-handed helices, whereas in the case of an optically active isocyanide one screw sense predominates. We describe a method for the preparation of a polymer with an excess of either left- or right-handed helices, starting from an achiral isocyanide. To this end, we added a slowly polymerizing optically active isocyanide as comonomer to a rapidly polymerizing achiral isocyanide. CD spectra and optical rotation indicate that the screw sense of the resulting polymer samples is opposite to the one preferred by the homopolymer of the optically active comonomer. A mechanism is proposed according to which the optically active comonomer is preferentially incorporated in one of the two helices formed from the achiral isocyanide, viz. the one that corresponds to its own homopolymer. The further growth of these helices is inhibited as a result of the low rate of polymerization of the optically active isocyanide, whereas the helices of the opposite screw sense can grow relatively unhindered.

Stereoisomerism resulting from restricted rotation around a single bond (atropisomerism) is a well-known phenomenon in organic chemistry.[2] In polymer chemistry this type of isomerism is very rare. Atropisomerism in polymers was demonstrated for the first time in 1974 in polymers of isocyanides.[3] It was shown that poly(*tert*-butyl isocyanide) $[>C{=}NC(CH_3)_3]_n$ could be resolved into fractions that displayed positive and negative optical rotations. Subsequent work revealed that the optical rotation is due to a 4:1 helical configuration of the polymer backbone (Figure 1).[4] To date, two other examples of atropisomerism in polymers have been reported. There is evidence that polychloral, prepared from chloral with a chiral initiator, forms a stable helix with a preference of one helical screw sense over the other.[5] Yuki et al.[6a-c] and later Cram and Sogah[6d] showed that bulky methacrylic acid esters polymerize in the presence of chiral anionic catalysts to give optically active polymers.

Poly(isocyanides) more systematically called poly(iminomethylenes) or poly(carbonimidoyls) are prepared from isocyanides by the catalytic action of protonic acids, Lewis acids, or nickel(II) salts.[7,8] The polymers are ususual in the sense that they carry a side chain on each atom of their main chain. This feature causes restricted rotation around the single bonds that connect the main-chain carbon atoms.[7,8] Two configurations are possible around each of the single bonds, viz. *R* or *S*.[2] If the poly(isocyanide) is highly isotactic (meaning that the configuration is the same around all the single bonds) a helix will be formed.[9] This helix is right-handed (*P*) if the aforementioned configurations are all *S* and left-handed (*M*) if they are all *R* (see Figure 1).

**Scheme I**

$$\mathrm{RNH_2} \rightarrow \underset{\mathbf{1}}{\mathrm{RNHCHO}} \rightarrow \underset{\mathbf{2}}{\mathrm{RN^+{\equiv}C^-}} \rightarrow \underset{\mathbf{3}}{[\mathrm{RN{=}C{<}}]_n}$$

**a**, R = (*S*)-*i*-$C_3H_7CH(COOCH_3)$
**b**, R = (*S*)-*i*-$C_3H_7CH(COO$-*i*-$C_3H_7)$
**c**, R = (*S*)-*i*-$C_3H_7CH(COO$-*t*-$C_4H_9)$
**d**, R = (2*S*,3*S*)-$C_2H_5CH(CH_3)$-$CH(COOCH_3)$
**e**, R = (*S*)-$CH_3CH(COOC_2H_5)$
**f**, R = (*S*)-$C_2H_5CH(CH_3)$
**g**, R = (*S*)-$C_6H_5CH(CH_3)$
**h**, R = (*R*)-$C_6H_5CH(CH_2OC(O)CH_3)$
**i**, R = (*R*)-*i*-$C_3H_7CH(CH_3)$
**j**, R = 4-$(CH_3)_2NC_6H_4$
**k**, R = 4-$CH_3OC_6H_4$
**l**, R = 4-$CH_3C_6H_4$
**m**, R = 2-$CH_3C_6H_4$
**n**, R = $C_6H_5$
**o**, R = 4-$ClC_6H_4$
**p**, R = 2,6-$Cl_2C_6H_3$
**q**, R = $C_6H_5CH_2$
**r**, R = *n*-$C_8H_{17}$
**s**, R = *i*-$C_3H_7$
**t**, R = *t*-$C_4H_9$

**Table I.** Chiroptical Properties of Homopolymers of Chiral Isocyanides $[RN{=}C{<}]_n$[a]

| | R | $[\alpha]^{20}_D$,[b] deg | screw sense[c] | $\bar{M}_v$[d] |
|---|---|---|---|---|
| **3a**, | (*S*)-*i*-$C_3H_7CH(COOCH_3)$ | -110 | *M* | *g* |
| **3b** | (*S*)-*i*-$C_3H_7CH(COO$-*i*-$C_3H_7)$ | -24 | *M* | 14 400 |
| **3c** | (*S*)-*i*-$C_3H_7CH(COO$-*t*-$C_4H_9)$ | 32.5 | *M* | *g* |
| **3d** | (2*S*,3*S*)-$C_2H_5CH(CH_3)CH(COOCH_3)$ | -32.2 | *M* | 32 500 |
| **3e** | (*S*)-$CH_3CH(COOC_2H_5)$ | -280 | *P* or *M*[f] | 71 700 |
| **3f** | (*S*)-$C_2H_5CH(CH_3)$ | *e* | *e* | *e* |
| **3g** | (*S*)-$C_6H_5CH(CH_3)$ | 350 | *M* | 93 500 |
| **3h** | (*R*)-$C_6H_5CH(CH_2OC(O)CH_3)$ | -82 | *P* | 26 300 |
| **3i** | (*R*)-*i*-$C_3H_7CH(CH_3)$ | -16.7 | *M* | *g* |

[a] Reaction conditions (monomer, mol % $NiCl_2$, solvent, temperature): **2a**, 10, neat, 20 °C; **2b** and **2c**, 0.5, neat, 45 °C; **2d**, 1.0, neat, 45 °C; **2e** and **2g**, 0.2, neat, 20 °C; **2f** 0.05, EtOH, 20 °C; **2h**, 0.15, MeOH, 20 °C; **2i**, 0.1, MeOH, 20 °C. [b] *c* 0.1, $CHCl_3$. [c] Derived from the CD spectra of the polymers. [d] Determined by measuring intrinsic viscosities (toluene at 30.00 °C): Mark-Houwink relation $[\eta] = 1.4 \times 10^9 \bar{M}_v^{1.75}$. [e] Polymer insoluble in organic solvents and water. [f] CD spectrum gives no decisive answer about the screw sense. [g] Not determined.

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(2) Eliel, E. L. *Stereochemistry of Carbon Compounds*; McGraw-Hill: New York, 1962; p 156.
(3) (a) Nolte, R. J. M.; Beijnen, A. J. M. v.; Drenth, W. *J. Am. Chem. Soc.* **1974**, *96*, 5932-5933. (b) The occurrence of a helical structure in polymers of isocyanides was suggested by Millich and co-workers in 1969; cf. ref 37.
(4) (a) Beijnen, A. J. M. v.; Nolte, R. J. M.; Drenth, W.; Hezemans, A. M. F. *Tetrahedron* **1976**, *32*, 2017-2019. (b) Millich, F. *Adv. Polym. Sci.* **1975**, *19*, 117-141.
(5) (a) Corley, L. S.; Vogl, O. *Polym. Bull. (Berlin)* **1980**, *3*, 211-217. (b) Vogl, O.; Jaycox, G. D. *CHEMTECH.* **1986**, 698-703.
(6) (a) Okamoto, Y.; Suzuki, K.; Ohta, K.; Hatada, K.; Yuki, H. *J. Am. Chem. Soc.* **1979**, *101*, 4763-4765. (b) Okamoto, Y.; Suzuki, K.; Yuki, H. *J. Polym. Sci., Polym Chem. Ed.* **1980**, *18*, 3043-3051. (c) Okamoto, Y.; Mohri, H.; Ishikura, M.; Hatada, K.; Yuki, H. *J. Polym. Sci., Polym. Symp.* **1986**, *n74*, 125-139. (d) Cram, D. J.; Sogah, D. Y. *J. Am. Chem. Soc.* **1985**, *107*, 8301-8302.
(7) Drenth, W.; Nolte, R. J. M. *Acc. Chem. Res.* **1979**, *12*, 30-35.
(8) Millich, F. *Macromol. Rev.* **1980**, *15*, 207-253.
(9) If the configurations around the single bonds are alternating *R* and *S*, a syndiotactic structure arises. If the configurations are randomly *R* and *S*, an atactic chain is formed. Strictly speaking, the terms isotactic, syndiotactic, and atactic cannot be used for polymers of the type described in this paper, as they refer to polymer chains that contain chiral centers.

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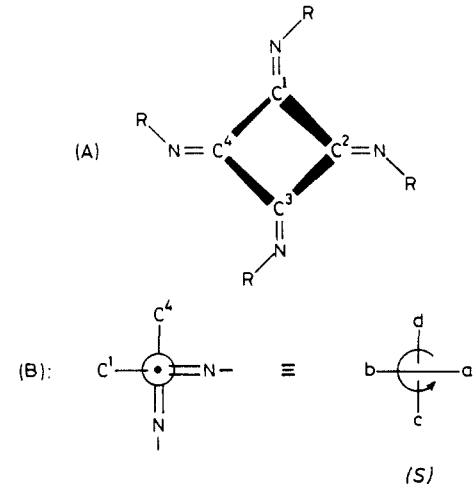


**Figure 1.** View along the helical axis of a poly(isocyanide) molecule with a right-handed screw sense. Unit 5 is behind unit 1, etc. (A) According to the Cahn–Ingold–Prelog nomenclature rules, the configuration around each of the single bonds connecting the main-chain carbon atoms is *S*; see the Newman projection along $C^2$–$C^3$. (B) a–d denotes the priority sequence.

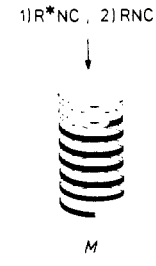


**Figure 2.** Screw-sense selective polymerization by adding an achiral isocyanide to an optically active living polymer.

The resolution of poly(*tert*-butyl isocyanide) into enantiomers indicates that polymerization of isocyanides proceeds stereoselectively to isotactic helical molecules. When the monomer is achiral, a racemic mixture of *P* and *M* screws is formed. 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 obtained in equal amounts. This feature was confirmed for approximately 20 different optically active isocyanides.[10-12] The present paper deals with the problem of how to obtain an excess of polymer molecules with one screw sense from an achiral monomer. Recently, we reported that stereoselective polymerization of achiral isocyanides can be achieved by using nickel(II) complexes as catalysts and optically active amines as initiators.[13] Here we describe a different procedure for obtaining optically active polymers from achiral isocyanides, i.e., by polymerizing a mixture of an achiral and a bulky optically active isocyanide.[14] Our initial objective was to make a living polymer of an optically active isocyanide with one particular screw sense. By adding a large amount of an achiral isocyanide, we expected the screw to grow further in the same direction (see Figure 2). However, a different reaction took place. The bulky optically active monomer selectively inhibited the growth of one of the polymer helices from the achiral isocyanide. Our procedure resembles the procedure used by Berkovitch-Yellin to regulate the growth of crystals by "tailor-made" inhibitors.[15]

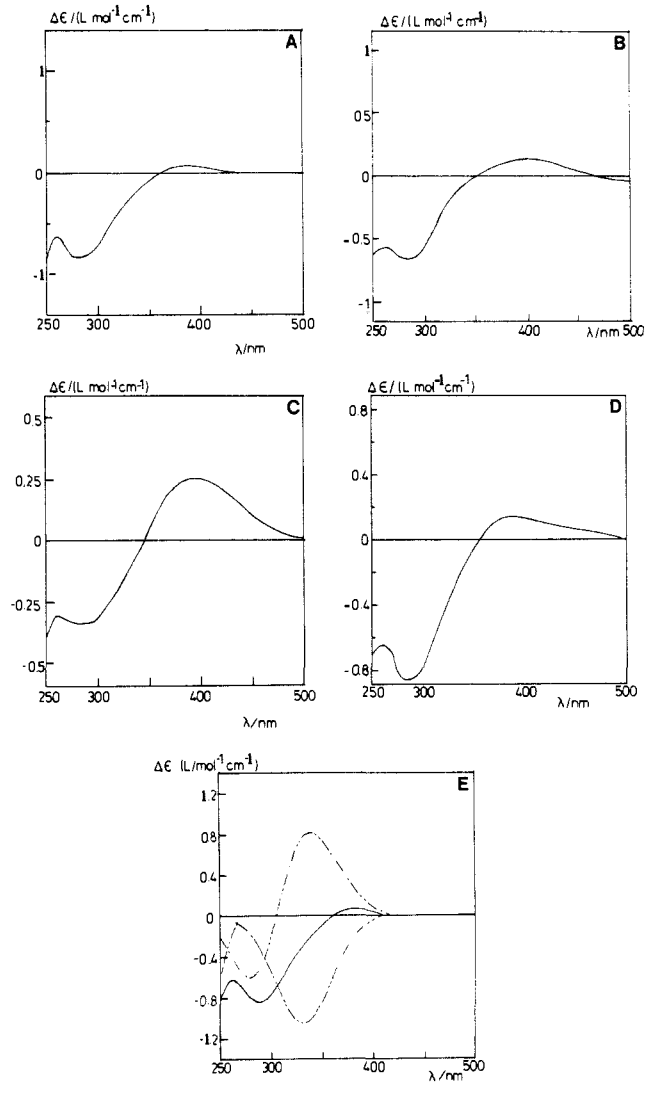


**Figure 3.** CD spectra of polymers **3a** (A), **3b** (B), **3c** (C), **3d** (D), and simulated spectrum of **3a** (E).

## Results

**Homopolymerization of Chiral Isocyanides.** The chiral isocyanides used in this study were synthesized from optically active amines and amino acids as generally outlined in Scheme I. (See also the Experimental Section.) Homopolymerization of these monomers was achieved by adding 0.1–10 mol % of $NiCl_2$ or $NiCl_2 \cdot 6H_2O$ as catalyst. The polymers were off-white or yellow solids. Their viscosity-average molecular weights ranged from 15 000 to 95 000 (Table I, footnote *b*). In the infrared spectra, N=C stretching vibrations were visible at 1620–1650 $cm^{-1}$. The optical rotation values of the polymers are presented in Table I. The CD spectra of polymers **3a–d** are shown in Figure 3. Those of **3e** and **3g–i** have been published in previous papers.[11] No CD spectrum could be recorded of polymer **3f**, since this compound was insoluble in organic solvents and water. The UV spectra of **3a–c** show a broad shoulder at 300–400 nm on the onset of a much larger band in the far-UV region. This shoulder is due to the n → π* transition of the N=C groups in the polymer backbone.

(10) (a) Nolte, R. J. M; Zwikker, J. W.; Reedijk, J.; Drenth, W. *J. Mol. Catal.* **1978**, *4*, 423–426. (b) Beijnen, A. J. M. v.; Nolte, R. J. M.; Zwikker, J. W.; Drenth, W. *J. Mol. Catal.* **1978**, *4*, 427–432.

(11) (a) Beijnen, A. J. M v.; Nolte, R. J. M.; Drenth, W.; Hezemans, A. M. F.; Coolwijk, P. J. F. M. v. d. *Macromolecules* **1980**, *13*, 1386–1391. (b) Beijnen, A. J. M v.; Nolte, R. J. M.; Naaktgeboren, A. J.; Zwikker, J. W.; Drenth, W.; Hezemans, A. M. F. *Macromolecules* **1983**, *16*, 1679–1689.

(12) (a) Nolte, R. J. M.; Zomeren, J. A. J. v.; Zwikker, J. W. *J. Org. Chem.* **1978**, *43*, 1972–1975. (b) Visser, H. G. J.; Nolte, R. J. M.; Zwikker, J. W.; Drenth, W. *J. Org. Chem.* **1985**, *50*, 3133–3137, 3138–3143.

(13) Kamer, P. C. J.; Nolte, R. J. M.; Drenth, W. *J. Chem. Soc., Chem. Commun.* **1986**, 1789–1791.

(14) For a preliminary report, see: Harada, T.; Cleij, M. C.; Nolte, R. J. M.; Hezemans, A. M. F.; Drenth, W. *J. Chem. Soc., Chem. Commun.* **1984**, 726–727.

(15) (a) Berkovitch-Yellin, Z.; Mil, J. v.; Addadi, L.; Idelson, M.; Lahav, M.; Leiserowitz, L. *J. Am. Chem. Soc.* **1985**, *107*, 3111–3122. (b) Berkovitch-Yellin, Z. *J. Am. Chem. Soc.* **1985**, *107*, 8239–8253.

**Table II.** Properties of Copolymers of 4-Methoxyphenyl Isocyanide (**2k**) and Chiral Isocyanides **2a–l**[a]

| | R in chiral monomer | incorp,[b] % | $[\alpha]^{20}_D$,[c] deg | screw sense[d] | $\bar{M}_v$[e] |
|---|---|---|---|---|---|
| **2a** | (*S*)-*i*-$C_3H_7CH(COOCH_3)$ | 23 | −520 | *P* | 42 000 |
| **2b** | (*S*)-*i*-$C_3H_7CH(COO$-*i*-$C_3H_7)$ | 19 | −413 | *P* | 42 000 |
| **2c** | (*S*)-*i*-$C_3H_7CH(COO$-*t*-$C_4H_9)$ | 15 | −350 | *P* | 44 000 |
| **2d** | (2*S*,3*S*)-$C_2H_5CH(CH_3)CH(COOCH_3)$ | 25 | −430 | *P* | 48 000 |
| **2e** | (*S*)-$CH_3CH(COOC_2H_5)$ | 39 | −200 | *P* | 46 000 |
| **2f** | (*S*)-$C_2H_5CH(CH_3)$ | 49 | 41[f] | *M* + *P* | *g* |
| **2g** | (*S*)-$C_6H_5CH(CH_3)$ | 46 | −45[f] | *M* + *P* | *g* |
| **2h** | (*R*)-$C_6H_5CH(CH_2OC(O)CH_3)$ | 32 | −9[f] | *M* + *P* | *g* |
| **2i** | (*R*)-*i*-$C_3H_7CH(CH_3)$ | 35 | −25[f] | *M* + *P* | *g* |

[a] Reaction conditions: molar ratio 4-methoxyphenyl isocyanide to chiral monomer, 1:1; catalyst, 1 mol % $NiCl_2$; neat; reaction temperature, 20 °C. [b] Percent incorporation of chiral monomers in polymer sample as calculated from elemental analysis and $^1H$ NMR. [c] Optical rotation of polymer sample (*c* 0.03, $CHCl_3$). [d] Derived from, the CD spectra of the polymers. [e] Determined by measuring intrinsic viscosities (toluene at 30.00 °C): Mark–Houwink relation $[\eta] = 1.4 \times 10^9 \bar{M}_v^{1.75}$. [f] Optical rotation is probably due to side chains of chiral monomer. [g] Not determined.

**Table III.** Properties of Copolymers of Achiral Isocyanides $RN^+{\equiv}C^-$ (**2j–t**) and the Chiral Isocyanides (*S*)-*i*-$C_3H_7CH(COOR')NC$ (**2a, 2b**)[a]

| | R in achiral monomer | R′ in chiral monomer | incorp,[b] % | $[\alpha]^{20}D$,[c] deg | screw sense[d] | $\bar{M}_v$[e] |
|---|---|---|---|---|---|---|
| **2j** | 4-$(CH_3)_2NC_6H_4$ | $CH_3$ | 13 | −250 | *P* | <5000 |
| **2k** | 4-$CH_3OC_6H_4$ | $CH_3$ | 23 | −520 | *P* | 42 000 |
| **2l** | 4-$CH_3C_6H_4$ | $CH_3$ | 31 | −550 | *P* | 36 000 |
| **2m** | 2-$CH_3C_6H_4$ | $CH_3$ | 31 | −340 | *P* | 33 000 |
| **2n** | $C_6H_5$ | $CH_3$ | 30 | −610 | *P* | 44 000 |
| **2o** | 4-$ClC_6H_4$ | $CH_3$ | 35 | −660 | *P* | 31 000 |
| **2p** | 2,6-$Cl_2C_6H_3$ | *i*-$C_3H_7$ | 37 | 0 | *P* + *M* | *f* |
| **2q** | $C_6H_5CH_2$ | *i*-$C_3H_7$ | 68 | −93 | *P* | *f* |
| **2r** | *n*-$C_8H_{17}$ | *i*-$C_3H_7$ | 58 | −58 | *P* | 35 000 |
| **2s** | *i*-$C_3H_7$ | *i*-$C_3H_7$ | 52 | −105 | *P* | 45 000 |
| **2t** | *t*-$C_4H_9$ | *i*-$C_3H_7$ | 52 | −37[g] | *P* + *M* | 16 000 |

[a] Reaction conditions: molar ratio achiral to chiral monomer, 1:1; catalyst, 1 mol % $NiCl_2$; neat; reaction temperature, 20 °C. [b] Percent incorporation of chiral monomer in polymer as calculated from elemental analysis and $^1H$ NMR. [c] Optical rotation of polymer (*c* 0.03, $CHCl_3$). [d] Derived from the CD spectra of the polymers. [e] Determined by measuring intrinsic viscosities (toluene at 30.00 °C): Mark–Houwink relation $[\eta] = 1.4 \times 10^9 \bar{M}_v^{1.75}$. [f] Not determined. [g] Optical rotation is probably due to side chain of chiral monomer **2b**.

This n → π* transition is responsible for the CD spectrum in the region 250–500 nm. In polymers of optically active isocyanides both the chiral center in the side chain and the helical structure of the main chain induce rotational power in the imino chromophore. In the spectra of the polymers of Table I, the side-chain contribution is manifested as a negative band in the range 250–350 nm. The screw senses of the polymers are derived from the couplet at ~350 nm in their CD spectra. We previously calculated the CD spectra of poly(isocyanides) with Tinoco's exciton theory[4,16,17] and the coupled oscillator theory of De Voe.[18–20] In this way it was derived that a positive couplet corresponds with an *M* helix and a negative couplet with a *P* helix. In its CD spectrum polymer **3c** clearly shows a positive couplet, indicative of an *M* helix. For polymers **3a** and **3b**, this couplet is partly obscured by the contribution of the chiral side chain (Figure 3). However, the CD spectra of **3a** and **3b** could be analyzed by simulation. For instance, in Figure 3 the calculated spectrum of **3a** is shown, divided into a contribution from the chiral side chain and from the helical main chain. As the resulting calculated curve is almost identical with the experimental curve, we conclude that this polymer also consists of *M* helices. The CD spectra of polymers **3e–i** have been discussed earlier.[11] For polymer **3e**, no definite conclusion about the screw sence could be made, as the couplet is completely obscured by the contribution from the chiral side chain. Even simulated CD spectra could give no decisive answer about the screw sense. The screw senses of polymers **3a–i** as derived from the CD spectra are given in Table I.

**Copolymerization.** The achiral isocyanide 4-methoxyphenyl isocyanide (**2k**) was polymerized neat by $NiCl_2$ in the presence of optically active isocyanides **2a–i**. The molar ratio of achiral to chiral monomer was 1:1. After workup, yellow to brown polymer samples were obtained, containing varying amounts of optically active monomer (Table II). The molecular weights of these samples amounted to $M_v \simeq 45\,000$. The optical rotation of the polymers varied with the type of optically active comonomer used. High negative optical rotations were obtained with the comonomers derived from the amino acids **2a–e** (Table II). Relatively low optical rotations were obtained with the comonomers **2f–i** (Table II). The CD spectra showed that the polymers derived from the latter comonomers consisted of a racemic mixtures of right- and left-handed screws; no couplets were visible in the CD spectra. This suggests that the low optical rotations of the polymers are due to the chirality of the side chains and not to the helical structure of the polymer main chain.

Various achiral isocyanides (**2j–t**) were polymerized by $NiCl_2$ in the presence of chiral isocyanide **2a** or **b** as described above (Table III). All the resulting polymers had negative optical rotations except for the one derived from 2,6-dichlorophenyl isocyanide (**2p**); for this polymer no optical rotation within experimental error could be measured. CD spectra (e.g. see Figures 4 and 5) confirmed that the negative optical rotations of the samples derived from **2j–o** and **2q–s** can be ascribed to right-handed helical structures of the polymer main chains. The CD spectra of the polymers resulting from the achiral aromatic isocyanides **2j–o** show a very clear negative couplet pointing to a *P* helix (Figure 4). For the monomers **2q–s** this negative couplet is partly obscured by the contribution from the incorporated chiral monomer (e.g. Figure 5A). The CD spectra of the polymer samples derived from **2q–s** and **2b** could be analyzed by subtracting the CD spectrum of the homopolymer of **2b**, corrected for the amount of incorporation of **2b** (see Figure 5B). Figure 5B clearly shows a negative couplet, thereby proving that the aliphatic isocyanides **2q–s** also form a *P* helix. An exception is the polymer derived from *tert*-butyl isocyanide (**2t**) and the chiral comonomer **2b**. This polymer showed a negative optical rotation but no couplet in the CD spectrum, indicating that is consists of a racemic mixture of *P* and *M* screws. The observed optical rotation is probably due to the chirality of the side chains originating from **2b**. Also, the polymer obtained from 2,6-dichlorophenyl isocyanide (**2p**) and

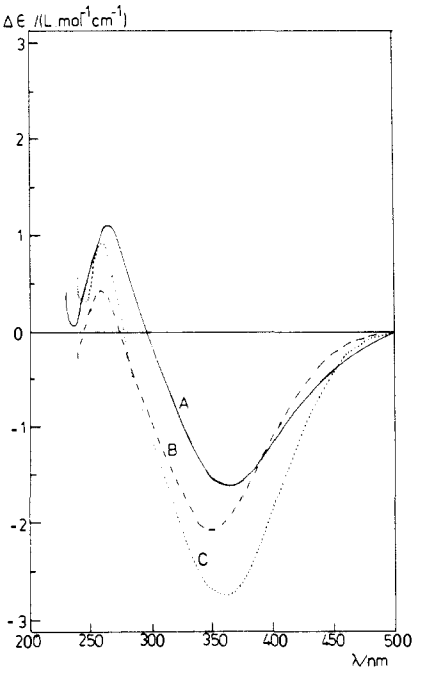


**Figure 4.** CD spectra of polymers **3k** (A, 19% incorporation of **2a**), **3n** (B, 23% incorporation of **2a**), and **3o** (C, 35% incorporation of **2a**). The observed couplets are indicative of right-handed helices.

(16) Tinoco, I. *Adv. Chem. Phys.* **1962**, *4*, 113–160.
(17) Tinoco, I. *J. Chim. Phys. Phys. Chim. Biol.* **1968**, *65*, 91–97.
(18) Huige, C. J. M. Thesis, University of Utrecht, 1985.
(19) De Voe, H. *J. Chem. Phys.* **1964**, *41*, 393–400.
(20) De Voe, H. *J. Chem. Phys.* **1965**, *43*, 3199–3208.

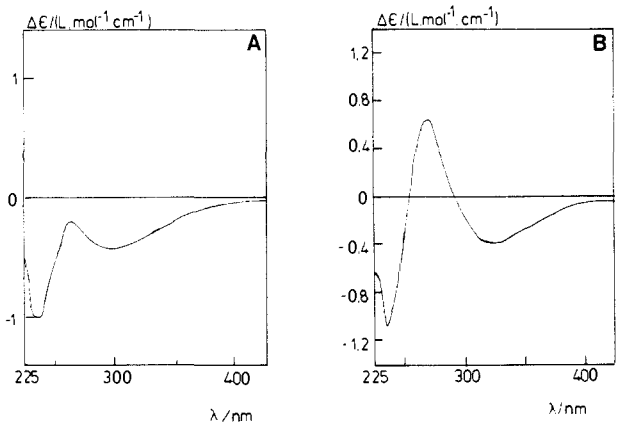


Figure 5. CD spectrum of polymer **3q** (A, 68% incorporation of **2b**) and simulated CD spectrum of polymer **3q** obtained by substracting the spectrum of polymer **3b** from A (B). The observed couplet is indicative of a right-handed helix.

**2b** did not show a couplet in the CD spectrum, indicating it to be a racemic mixture of screws as well.

The extent of asymmetric induction in the polymerization of 4-methoxyphenyl isocyanide (**2k**) by the chiral comonomer **2a** was measured as a function of the initial ratio of these isocyanides in the monomer mixture. The optical rotation of the polymer samples increased with increasing mole fraction of **2a** ($f_{2a}$) in the starting mixture up to a maximum value of 740° at $f_{2a} = 0.75$ and thereafter decreased. The percentage of monomeric units of **2a** that is incorporated in these samples increased with increasing $f_{2a}$. In Figure 6A the optical rotation of the polymer sample is presented as a function of the incorporation of the chiral comonomer. For comparison, the optical rotation of a mixture of homopolymers **3a** and **3k** is also presented (Figure 6B). From these curves the contribution of the achiral monomer to the optical rotation can be calculated (Figure 6C). Figure 6C also includes a number of corrected optical rotation values for the copolymerization of **2k** with **2b** and **2k** with **2c**. These values match the curve of **2k** and **2a**. As the CD spectrum is a better method for measuring the chiral induction, we determined the differential dichroic absorption coefficient ($\Delta\epsilon$) at 366 nm as a function of the incorporation of **2a** (Figure 6D). Both the optical rotation and the $\Delta\epsilon$ curves show a maximum at about 50% incorporation of **2a**.[21]

The copolymer mixture derived from 4-methoxyphenyl isocyanide (**2k**) and (*S*)-2-isocyanovaleric acid isopropyl ester (**2b**) was analyzed by chromatography over a Sephadex LH-60 column. Subsequently, the low molecular weight fractions were separated over a Sephadex LH-20 column. The results are presented in Table IV. The copolymer mixture consisted of high molecular weight fractions with a low content of chiral monomer and a high optical rotation and low molecular weight fractions with a high content of chiral monomer and a low optical rotation.

## Discussion

A convenient procedure for obtaining optically active polymers from achiral monomers is by copolymerization with optically active comonomers.[21,22] By the inductive effect of the chiral comonomer units, the achiral monomers can assume as secondary structure that corresponds to the structure of the main chain of the optically active homopolymer.[23] The data presented in the Results section indicate that an unusual reaction had taken place. The homopolymers from isocyanides **2a–e** form a left-handed helix (see

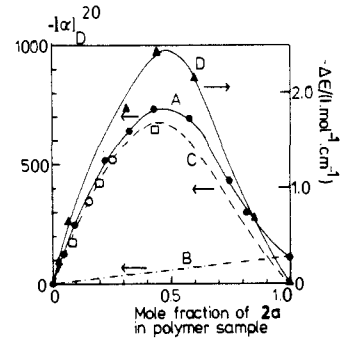


Figure 6. Optical rotation of the polymer obtained from **2a** and **2k** as a function of incorporation of **2a** (●) (A); optical rotation of a mixture of homopolymers **3a** and **3k** (B); contribution of the achiral monomer **2k** to the optical rotation of the polymer sample; some values for the copolymerization of **2b** and **2k** (□) and of **2c** and **2k** (○) (C); differential dichroic absorption coefficient at 366 nm as a function of incorporation of **2a** (▲) (D).

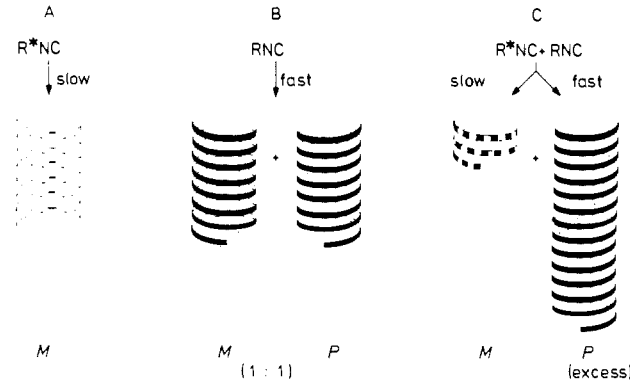


Figure 7. Stereoselective polymerization of achiral isocyanides in the presence of optically active isocyanides. For an explanation; see text.

Figure 3 and Table I). We, therefore, expected left-handed screws in our copolymer samples. However, when the achiral monomers **2j–o** and **2q–s** are polymerized in the presence of the chiral isocyanides **2a–c** a right-handed helix is formed (see Figure 4 and Table II). We explain these results as follows. The optically active isocyanides **2a–e** are bulky, slowly polymerizing monomers. From kinetic measurements we estimate their second-order rate constants in $v = k_2[\mathrm{Ni}][\mathrm{RNC}]$ to be $\ll 10^{-3}$ $M^{-1}\cdot s^{-1}$.[24] These monomers preferentially form an *M* screw (Figure 7A). The achiral monomers **2j–o** and **2q–s** polymerize rapidly. Their second-order rate constants are in the range $k_2 = 0.2\text{–}12$ $M^{-1}\cdot s^{-1}$.[24] These monomers form a racemic mixture of *M* and *P* screws (Figure 7B). When an achiral isocyanide, e.g., phenyl isocyanide (**2n**),

(21) For copolymers of other achiral and chiral monomers similar features have been observed. See: (a) Chiellini, E.; Solaro, R.; Colella, O.; Ledwith, A. *Eur. Polym. J.* **1978**, *14*, 489–496. (b) Chiellini, E.; Solaro, R.; Galli, G.; Ledwith, A. *Macromolecules* **1980**, *13*, 1654–1660. (c) Galli, G.; Solaro, R.; Chiellini, E.; Fernyhough, A.; Ledwith, A. *Macromolecules* **1983**, *16*, 502–507. (d) Altomare, A.; Carlini, C.; Ciardelli, F.; Pearce, E. M. *J. Polym. Sci., Polym. Chem. Ed.* **1983**, *21*, 1693–1698. (e) Altomare, A.; Carlini, C.; Panattoni, M.; Solaro, R. *Macromolecules* **1984**, *17*, 2207–2212.

(22) (a) Majundar, N.; Carlini, C. *Makromol. Chem.* **1980**, *181*, 201–214. (b) Majundar, N.; Carlini, C.; Bertucci, C. *Makromol. Chem.* **1982**, *183*, 2047–2057. (c) Altomare, A.; Carlini, C.; Ciardelli, F.; Solaro, R.; Rosato, N. *J. Polym. Sci., Polym. Chem. Ed.* **1984**, *22*, 1267–1280. (d) Yuki, H.; Ohta, K.; Okamoto, Y.; Hatada, K. *J. Polym. Sci., Polym. Lett. Ed.* **1977**, *15*, 589–593. (e) Chiellini, E.; Raspolli-Galleti, A. M.; Solaro, R. *Macromolecules* **1984**, *17*, 2212–2217. (f) Oishi, T.; Fujimoto, M. *J. Polym. Sci., Polym. Chem. Ed.* **1984**, *22*, 2789–2800. (g) Chiellini, E.; Solaro, R.; Galli, G.; Ledwith, A. *Adv. Polym. Sci.* **1984**, *62*, 143–169. (h) Wulff, G.; Zabrocki, K.; Hohn, J. *Angew. Chem.* **1978**, *90*, 567–568. (i) Douichi, T.; Yamaguchi, H. *Eur. Polym. J.* **1984**, *20*, 831–836. (j) Segre, A. L.; Delfini, M.; Paci, M.; Raspolli-Galetti, A. M.; Solaro, R. *Macromolecules* **1985**, *18*, 44–48. (k) Okada, M.; Summitomo, H. ; Hirasawa, T. *Macromolecules* **1985**, *18*, 2345–2349. (l) Altomare, A.; Carlini, C.; Ciardelli, F.; Panattoni, M.; Solaro, R.; Houben, J. L. *Macromolecules* **1985**, *18*, 729–734. (m) Oishi, T.; Okamoto, N.; Fujimoto, M. *J. Polym. Sci., Polym. Chem. Ed.* **1986**, *24*, 1185–1196. (n) Oishi, T.; Fujimoto, N. *J. Polym. Sci., Polym. Chem. Ed.* **1984**, *22*, 2789–2800. (o) Carlini, C.; Altomare, A.; Menconi, F.; Ciardelli, F. *Macromolecules* **1987**, *20*, 464–465.

(23) Ciardelli, F.; Salvadori, P. *Pure Appl. Chem.* **1985**, *57*, 931–940.

(24) (a) Nolte, R. J. M.; Drenth, W. *Recl. Trav. Chim. Pays-Bas* **1973**, *92*, 788–800. (b) Kamer, P. C. J.; Cleij, M. C.; Nolte, R. J. M.; Drenth, W., unpublished results.

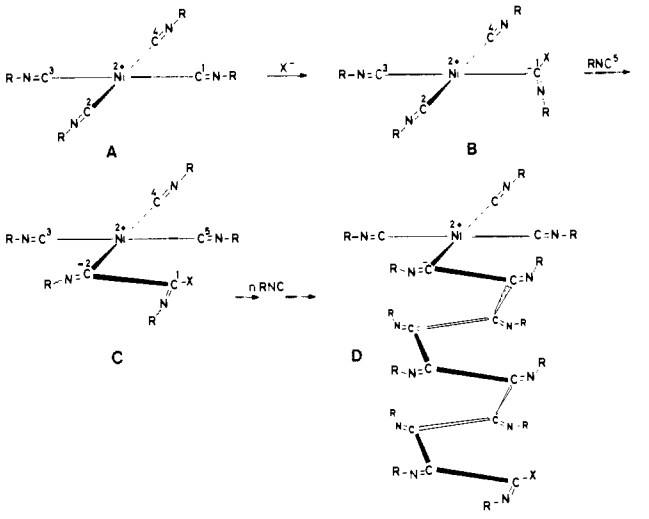

**Figure 8.** Mechanism of polymerization of isocyanides with Ni(II) as catalyst.

**Table IV.** Gel Permeation Chromatography of the Copolymer Mixture from 4-Methoxyphenyl Isocyanide and (*S*)-2-Isocyanoisovaleric Acid Isopropyl Ester[a]

| fraction | incorp,[b] % | $[\alpha]^{20}_D$,[c] deg | $\bar{M}_v$[d] |
|---|---|---|---|
| 1–9 | 17 | −460 | 58 600 |
| 10–14 | 20 | −440 | |
| 15–21 | 21 | −450 | 47 000 |
| 21a[e] | 24 | −430 | *g* |
| 21b[e] | 27 | −440 | *g* |
| 21c[e] | 30 | −390 | *g* |
| 21d[e] | 49 | −170 | *g* |
| 22[f] | 100 | −25 | 8800 |

[a] Sephadex LH 60 column unless otherwise indicated; eluent $CHCl_3$. [b] Percent incorporation of chiral monomer as derived from $^1H$ NMR. [c] Optical rotation of polymer sample (*c* 0.02, $CHCl_3$). [d] Determined by measuring intrinsic viscosities (toluene at 30.00 °C): Mark–Houwink relation $[\eta] = 1.4 \times 10^9 \bar{M}_v^{1.75}$. [e] Fraction 21 was subsequently separated on Sephadex LH 20. [f] Methanol-soluble fraction. [g] Not determined, due to small size of the samples. From the retention times the rank order of molecular weight is estimated to be 21a > 21b > 21c > 21d.

is polymerized in the presence of a chiral one, e.g., (*S*)-2-isocyanoisovaleric acid methyl ester (**2a**), the former isocyanide will start to form a racemic mixture of left- and right-handed screws. Monomer **2a** will have a preference for incorporation in the *M* helix of **2n**, and as a result, the growth of this helix will be slowed down. As far less of **2a** will be incorporated in the *P* helix of **2n**, this screw can grow relatively unhindered. Eventually, the *P* helix will consume most of the achiral phenyl isocyanide, and this screw sense will be predominantly formed (Figure 7C). This mechanism is supported by the fact that no chiral induction is observed when a combination of a fast polymerizing chiral (**2f–i**) and a fast polymerizing achiral monomer (**2k**) is used (Table II). Also, a combination of a slowly polymerizing chiral (**2b**) and a slowly polymerizing achiral monomer (**2p**, **2t**) yields a racemic mixture of *P* and *M* helices (Table III).

According to the mechanism shown in Figure 7, the copolymer sample is expected to have the following composition: high molecular weight fractions with high optical activity and a low content of chiral monomer; low molecular weight fractions with a high content of chiral monomer (which will eventually add up to 100%) and an optical rotation that will approach that of the homopolymer of the chiral isocyanide. Table IV shows that the results of the chromatography experiments are in line with the suggested mechanism.

Table II and Figure 6B reveal that the substituent R′ in the ester function COOR′ of isocyanides **2a–e** has no appreciable effect on the chiral induction, whereas the alkyl group at the chiral carbon atom does. We explain this in the following way. Previously, we have shown that the mechanism of polymerization of an isocyanide is a consecutive insertion process around the nickel(II) center.[7] The reaction starts from a square-planar nickel–isocyanide complex by attack of a nucleophile $X^-$ on one of the coordinated isocyanides (see Figure 8). In the resulting complex (Figure 8B) the plane of the ligand C(X)=NR is approximately perpendicular to the plane of the isocyanide carbons and nickel, with R in either the *E* or the *Z* configuration. There is no free rotation around the bond from $C^1$ to Ni for steric reasons. Carbon atom $C^1$ in Figure 8B has gained in nucleophilicity and can now attack a neighboring ligand. Such an attack is facilitated when a new isocyanide ligand $C^5$=NR is substituted for $C^1$(X)=NR. In the case of an achiral isocyanide the possibilities of attack on $C^2$ or $C^4$ are equal. In the case of a chiral isocyanide one of these attacks will predominate. In Figure 8C it has occurred on $C^2$. When the sequence of attack continues in the direction $C^1 \rightarrow C^2 \rightarrow C^3 \rightarrow C^4$, a left-handed helix is obtained. In a similar way, the sequence of attacks $C^1 \rightarrow C^4 \rightarrow C^3 \rightarrow C^2$ results in a right-handed helix.

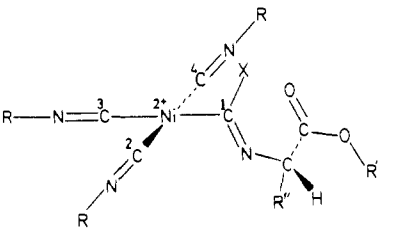

**Figure 9.** Intermediate in the polymerization of isocyanides **2a–e**.

For isocyanides **2a–e** the complex as shown in Figure 8B will have the *E* configuration, as these isocyanides have large substituents. The alkyl group at the chiral carbon atom is the most bulky substituent and will point away from the bulky nickel center (see Figure 9).[25] As a consequence, the ester function COOR′ is directed toward $C^4$ and the hydrogen atom toward $C^2$. This will result in the formation of a left-handed helix, as was experimentally confirmed. For steric reasons, the substituent R′ in COOR′ will point away from the reaction center and is expected to have no effect on the chiral induction. When the methyl group in **2e** is replaced by an isopropyl (**2a**) or *sec*-butyl (**2d**) group, an increase in stereoselectivity will be the result, in agreement with experiments.

As far as we know, the copolymerization mechanism presented here has no precedent in literature. It would be interesting to see whether our procedure can be applied to other copolymerization systems.

## Experimental Section

**Analytical Techniques.** Infrared (IR) spectra were recorded on Perkin-Elmer 297 and 283 spectrophotomers. Ultraviolet (UV) spectra were obtained on a Perkin-Elmer 200 spectrophotometer. CD spectra were recorded on a homemade apparatus. This instrument measures the differential absorbance ($\Delta\epsilon$) with a sensitivity of more than $1 \times 10^{-6}$. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. $^1H$ NMR spectra were obtained on a Varian EM 390 instrument. Chemical shifts ($\delta$) are given downfield from internal tetramethylsilane. Abbreviations used are s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and br = broad. Melting points were determined on a Mettler FP5/FP51 photoelectric melting point apparatus. Solution viscosity data were obtained with a Cannon-Ubbelohde viscometer.

***N*-Formyl-L-valine Methyl Ester (1a).** According to a literature procedure L-valine was esterified with methanol and freshly distilled $SOCl_2$ in quantitative yield.[26] Subsequent reaction with formic acid, sodium formate, and acetic anhydride,[27] gave *N*-formyl-L-valine methyl

(25) As a relative measure of steric hinder, the λ steric parameter can be used. See also: Kagan, H. B. *Stereochemistry*; Thieme: Stuttgart, 1977; Vol. 3, p 26. (R, λR): H, 0.00; $CH_3$, 1.00; $CH(CH_3)_2$, 1.27; $H_5C_2OCO$, 0.90.

(26) (a) Brenner, M.; Müller, H. R.; Pfister, R. W. *Helv. Chim. Acta* **1950**, *33*, 568–591. (b) Brenner, M.; Huber, W. *Helv. Chim. Acta* **1953**, *36*, 1109–1115.

(27) Jones, R. G. *J. Am. Chem. Soc.* **1949**, *71*, 644–647.

(28) Skorna, G.; Ugi, I. *Angew. Chem.* **1977**, *89*, 267–268. Urbau, R.; Marquarding, D.; Seidel, P.; Ugi, I.; Weindelt, A. *Chem. Ber.* **1977j**, *110*, 2012–2015.

ester: yield 80%; white crystals after recrystallization from $CCl_4$; $[\alpha]^{20}_D$ −27.2° (c 5, $CH_3OH$); mp 62.1 °C; IR (KBr) 1660 (NCHO), 1740 (C=O) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.0 (2 d, 6 H, $C(CH_3)_2$), 1.9–2.6 (m, 1 H, CH), 3.85 (s, 3 H, $OCH_3$), 4.8 (2 d, 1 H, CH), 6.75 (s, br, 1 H, NH), 8.5 (s, 1 H, CHO).

**(*S*)-2-Isocyanoisovaleric Acid Methyl Ester (2a).** This isocyanide was prepared from **1a** according to a modification of the procedure of Skorna and Ugi.[28] Into a round-bottomed flask, equipped with a magnetic stirrer and a $CO_2$/acetone reflux condenser kept at −30 °C, were brought 7.95 g (50.0 mmol) of **1a**, 25.5 mL (228 mmol) of dry *N*-methylmorpholine, and 100 mL of dry $CH_2Cl_2$. At a temperature of −30 to −40 °C, 3.62 mL (30.0 mmol) of diphosgene in 40 mL of dry $CH_2Cl_2$ was introduced into the stirred reaction mixture over a period of approximately 1 h. After the mixture was stirred for an additional 1 h, the cooling bath was removed, and 65 mL of water was immediately added to the mixture. Subsequently, the still cold organic layer was separated, shaken with 65 mL of an aqueous 7.5% $NaHCO_3$ solution, separated again, and dried over $Na_2SO_4$. The crude reaction product was purified by column chromatography (silica gel, $CH_2Cl_2$) and distilled in vacuo: bp 33 °C (0.5 mmHg); yield 5.2 g (74%) of a colorless liquid; $[\alpha]^{20}_D$ 5.5° (c 3.4, $CHCl_3$); IR (neat) 1750 (C=O), 2150 (N=C) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.1 (2 d, 6 H, $C(CH_3)_2$), 2.0–2.7 (m, 1 H, CH), 3.9 (s, 3 H, $OCH_3$), 4.3 (d, 1 H, CH).

***N*-Formyl-L-valine Isopropyl Ester (1b).** This compound was obtained from L-valine and 2-propanol as described for the synthesis of **1a**: yield 82% of a white solid; mp 105.9 °C; $[\alpha]^{20}_D$ −32.5° (c 1, $CH_3OH$); IR (KBr) 1680 (NHCH=O), 1740 (C=O); $^1H$ NMR ($CDCl_3$) δ 1.0 (2 d, 6 H, $CHCH(CH_3)_2$), 1.3 (d, 6 H, $C(CH_3)_2$), 1.7 (2 d, 1 H, $CHCH(CH_3)_2$), 1.9–2.6 (m, 1 H, $CHCH(CH_3)_2$), 5.2 (m, 1 H, $CO_2CH(CH_3)_2$), 7.1 (s, br, 1 H, NH), 8.45 (s, 1 H, CHO).

**(*S*)-2-Isocyanoisovaleric Acid Isopropyl Ester (2b).** This compound was obtained from *N*-formyl-L-valine isopropyl ester (**1b**) as described for **2a**. The reaction temperature was kept between −45 and −50 °C: yield 82%; colorless liquid; bp 60 °C (0.6 mmHg); $[\alpha]^{20}_D$ 32.7° (c 0.7, $C_6H_6$); IR ($CCl_4$) 2150 (N=C), 1755 (C=O) $cm^{-1}$; $^1H$ NMR ($CCl_4$) δ 1.05 (2 d, 6 H, $CHCH(CH_3)_2$), 1.4 (d, 6 H, $CO_2CH(CH_3)_2$), 1.9–2.6 (m, 1 H, $CHCH(CH_3)_2$), 4.15 (d, 1 H, CH), 5.2 (m, 1 H, $CO_2CH(CH_3)_2$).

***N*-Formyl-L-valine *tert*-Butyl Ester (1c).** L-Valine was esterified with *tert*-butyl acetate according to a literature procedure.[29] Subsequent N-formylation was carried out as described for **1a**: yield 52%; white solid; mp 65.4 °C; $[\alpha]^{20}_D$ −31.3° (c 1.7, $C_2H_5OH$); IR (KBr) 1660 (NHCH=O), 1737 (C=O) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.0 (2 d, 6 H, $CH(CH_3)_2$), 1.5 (s, 9 H, $C(CH_3)_3$), 1.9–2.6 (m, 1 H, $CH(CH_3)_2$), 4.6 (2 d, 1 H, CH), 6.4 (s, br, 1 H, NH), 8.35 (s, br, 1 H, CHO).

**(*S*)-2-Isocyanovaleric Acid *tert*-Butyl Ester (2c).** This compound was obtained from *N*-formyl-L-valine *tert*-butyl ester (**1c**) as described for **2a**. The reaction temperature was −40 °C: yield 70%; colorless liquid; bp 64 °C (0.65 mmHg); $[\alpha]^{20}_D$ 29.5 (c 0.7 $C_6H_6$); IR ($CCl_4$) 2150 (C=N), 1750 (C=O) $cm^{-1}$; $^1H$ NMR δ 0.85 (2 d, 6 H, $CH(CH_3)_2$), 1.35 (s, 9 H, $C(CH_3)_3$), 1.9–2.5 (m, 1 H, $CH(CH_3)_2$), 3.9 (d, 1 H, CH).

***N*-Formyl-L-isoleucine Methyl Ester (1d).** This compound was prepared from L-isoleucine as described for **1a**: yield 72%; white solid; mp 67.3 °C; $[\alpha]^{20}_D$ −8.8° (c 2, $CH_3OH$); IR (KBr) 1738 (C=O), 1650 (NHCHO) $cm^{-1}$; $^1H$ NMR ($CCl_4$) δ 1.0 (m, 8 H, $C_2H_5CCH_3$), 1.9 (m, 1 H, CH), 3.9 (s, 3 H, $OCH_3$), 4.7 (2 d, 1 H, CH), 7.65 (s, br, 1 H, NH), 8.35 (s, 1 H, CHO).

**(*S*)-2-Isocyano-3-methylpentanoic Acid Methyl Ester (2d).** This compound was obtained from *N*-formyl-L-isoleucine methyl ester (**1d**) as described for **1a**. The reaction temperature was −55 °C: yield 60%; colorless liquid; bp 44 °C (0.2 mmHg); $[\alpha]^{20}_D$ 35.0° (c 1.5, $C_6H_6$); IR ($CH_2Cl_2$) 1750 (C=O), 2145 (C=N) $cm^{-1}$; $^1H$ NMR ($CCl_4$) δ 0.8–1.6 (m, 8 H, $C_2H_5CH(CH_3)$), 1.7–2.3 (m, 1 H, CH), 3.75 (s, 3 H, $OCH_3$), 4.1 (d, 1 H, CH).

***N*-Formyl-L-alanine Ethyl Ester (1e).** This compound was prepared from L-alanine as described for **1a**. The colorless liquid was obtained in quantitative yield: $[\alpha]^{21}_{578}$ −69° (c 4, $C_2H_5OH$); IR (neat) 1675 (NHCO), 1740 (C=O) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.25 (t, 3 H, $CH_3$), 1.43 (d, 3 H, $CH_3$), 4.22 (q, 2 H, $CH_2$), 4.61 (m, 1 H, CH), 7.75 (br, 1 H, NH), 8.24 (s, 1 H, CHO).

**(*S*)-Carbethoxyethyl Isocyanide (2e).** This compound was synthesized from *N*-formyl-L-alanine ethyl ester (**1e**) as described for **2a**: yield 75%; $[\alpha]^{21}_{578}$ 16.7° (c 3.7, $CHCl_3$); IR ($CCl_4$) 1750 (C=O), 2140 (N=C) $cm^{-1}$; $^1H$ NMR ($CCl_4$) δ 1.37 (t, 3 H, $CH_3$), 1.65 (d, 3 H, $CH_3$), 4.25 (m, 1 H, CH), 4.30 (q, 2 H, $CH_2$).

**(*S*)-*N*-Formyl-*sec*-butylamine (1f).** *sec*-Butylamine was resolved through fractional crystallization of the hydrogen (+)-tartrate from water according to the literature.[30] The amine was liberated with an excess of 50% aqueous solution of sodium hydroxide and distilled from powdered potassium hydroxide, $[\alpha]^{20}_D$ 8.28° (neat). This amine was converted into the *N*-formyl-*sec*-butylamine with 10% excess of ethyl formate:[31] yield almost 100%; $[\alpha]^{20}_D$ 17.9° (c 4.9, $CHCl_3$).

**(*S*)-*sec*-Butyl Isocyanide (2f).** (*S*)-*N*-Formyl-*sec*-butylamine was converted into the isocyanide by the method of Casanova[32] but at a lower pressure (0.5 mmHg) than recommended: yield 95%; $[\alpha]^{22}_D$ 47.0° (c 1.8, $CHCl_3$); IR ($CCl_4$) 2142 (N=C) $cm^{-1}$; $^1H$ NMR ($CCl_4$) δ 1.05 (t, 3 H, $CH_3$), 1.25–1.90 (m, 5 H, $CH_2$ and $CH_3$), 3.58 (m, 1 H, CH).

**(*S*)-*N*-Formyl-1-phenylethylamine (1g).** 1-Phenylethylamine was resolved into its optical antipodes by a standard method.[33] The specific optical rotation of the *S* enantiomer was $[\alpha]^{22}_D$ −38.6° (neat) [lit.[33] $[\alpha]^{29}_D$ −39.4° (neat)]. This amine was N-formylated with a 10% excess of ethyl formate:[31] yield almost 100%; mp 46–48 °C (lit.[34] mp 46–47 °C); $[\alpha]^{22}_D$ −190° (c 1, $CH_3OH$) [lit.[35] $[\alpha]^{19}_D$ −178° (c 4.25, 96% $C_2H_5OH$)].

**(*S*)-1-Phenylethyl Isocyanide (2g).** This isocyanide was synthesized from **1g** according to the method of Appel et al.:[35] yield 50%; bp 95–96 °C (16 mmHg) [lit.[36] bp 93–94 °C (13 mmHg)]; $[\alpha]^{20}_D$ −40.9° (c 5, $CH_3OH$) [lit.[37] $[\alpha]^{27}_D$ −35.8° (neat)]; IR ($CCl_4$) 2140 (NC) $cm^{-1}$; $^1H$ NMR ($CCl_4$) δ 1.59 (m, 3 H, $CH_3$), 4.75 (m, 1 H, CH), 7.30 (s, 5 H, $C_6H_5$).

**(*R*)-2-Amino-2-phenylethanol.** This compound was prepared starting from (*R*)-(−)-α-aminophenylacetic acid (D-phenylglycine). The amino acid was esterified in methanol with dry HCl. The resulting ester was liberated from its HCl salt by dissolving it in an aqueous $Na_2CO_3$ solution; the free amine was extracted with benzene and dried over $Na_2SO_4$. After the solvent was evaporated, the residue was dissolved in diethyl ether and added dropwise to an excess of $LiAlH_4$ in diethyl ether. Subsequently, the mixure was refluxed for 2 h. After workup, the desired compound was obtained as light yellow crystals from ether/hexane: yield 65%; mp 76.0–76.5°C [lit.[38] 77–78 °C]; $[\alpha]^{22}_D$ −26.2° (c 1.0, $CH_3OH$) [lit.[38] $[\alpha]^{25}_D$ −27.2° (c 9.9, $CH_3OH$)]; $^1H$ NMR ($CDCl_3$) δ 2.66 (s, 3 H, $NH_2$ and OH), 3.35–3.85 (m, 2 H, $CH_2$), 3.98 (m, 1 H, CH), 8.32 (s, 5 H, $C_6H_5$).

**(*R*)-*N*-Formyl-2-amino-2-phenylethanol.** This formamide was synthesized with a 25% excess of ethyl formate:[31] yield 90%; mp 100 °C; $[\alpha]^{22}_{578}$ −149° (c 0.7, $CH_3OH$); IR (KBr) 1660 (NC=O) $cm^{-1}$.

**(*R*)-*N*-Formyl-*O*-acetyl-2-amino-2-phenylethanol (1h).** This compound was obtained from (*R*)-*N*-formyl-2-amino-2-phenylethanol by O-acetylating with acetic anhydride and a catalytic amount of pyridine at a temperature of 50°C for 24 h. The product was obtained as white crystals from ether: yield 95%; mp 67 °C; $[\alpha]^{22}_{578}$ −89.6° (c 1.0, $CHCl_3$); IR (KBr) 1745 (C=O), 1655 (NC=O) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.97 (s, 3 H, $CH_3$), 4.30 (d, 2 H, $CH_2$), 5.35 (m, 1 H, CH), 7.33 (s, 5 H, $C_6H_5$) 7.65 (br, d, 1 H, NH), 8.15 (s, 1 H, CHO).

**(*R*)-*O*-Acetyl-2-isocyano-2-phenylethanol (2h).** Formamide **1h** was converted into isocyanide **2h** at a reaction temperature of −20 °C as described for the synthesis of **2a**. Column chromatography (silica gel, $CHCl_3$) of the crude product afforded the pure isocyanide as a colorless liquid: yield 60%; $[\alpha]^{22}_{578}$ −68.5° (c 2.1, $CHCl_3$); IR ($CCl_4$) 2138 (NC), 1748 (C=O) $cm^{-1}$; $^1H$ NMR ($CCl_4$) δ 2.02 (s, 3 H, $CH_3$), 4.0–4.3 (m, 2 H, $CH_2$), 4.91 (m, 1 H, CH), 7.37 (s, 5 H, $C_6H_5$).

(*R*)-3-methyl-2-butanamine was prepared from L-valine according to the following sequence of reactions: L-valine → *N*-benzoyl-L-valine → *N*-benzoyl-L-valine methyl ester → *N*-benzyl-L-valinol → L-valinol → (*S*)-1-bromo-3-methyl-2-butanamine → (*R*)-3-methyl-2-butanamine.

***N*-Benzoyl-L-valine[39,40] and *N*-Benzoyl-L-valine Methyl Ester.[40,41]** These compounds were prepared starting from L-valine according to standard procedures.

***N*-Benzyl-L-valinol.** This compound was prepared from *N*-benzoyl-L-valine methyl ester with an excess of $LiAlH_4$ in boiling diethyl ether.[40,42]

**(*S*)-2-Amino-3-methylbutanol (L-valinol).** This compound was pre-

(29) Deimer, K. H.; Tham, P.; Stelzel, P. *Methoden Org. Chem.* (*Houben–Weyl*) **1974**, *15(1)*, 391.

(30) Thomé, L. *Chem. Ber.* **1903**, *36*, 582–584.
(31) Moffat, J.; Newton, M. V.; Papenmeier, G. J. *J. Org. Chem.* **1962**, *27*, 4058.
(32) Schuster, R. E.; Scott, J. E.; Casanova, J. *Org. Synth.* **1966**, *46*, 75–77.
(33) Ault, A. *Org. Synth.* **1969**, *49*, 93–98.
(34) Huisgen, R.; Rüchardt, C. *Justus Liebigs Ann. Chem.* **1956**, *601*, 21–39.
(35) Appel, R.; Kleinstück, R.; Ziehn, K.-D. *Angew. Chem.* **1971**, *83*, 143.
(36) Terashima, S.; Takashima, K.; Sato, T.; Yamada, S. *Chem. Pharm. Bull.* **1973**, *21*, 1135–1139.
(37) Millich, F.; Baker, G. K. *Macromolecules* **1969**, *2*, 122–128.
(38) Hunt, J. H.; Machale, D. *J. Chem. Soc.* **1957**, 2073–2077.
(39) Wunsch, E. *Methoden Org. Chem.* (*Houben-Weyl*) **1974**, *15*(1), 198.
(40) Bauer, H.; Adams, E.; Tabor, H. *Biochem. Prep.* **1955**, *4*, 46–50.
(41) Reference 40, p 316.
(42) Poindexter, G. S.; Meyers, A. I. *Tetrahedron Lett.* **1977**, 3527–3528.

pared from *N*-benzyl-L-valinol by hydrogenolysis[43] in water/ethanol (1:4, v/v) at 60 °C. The HCl salt was crystallized from methanol/diethyl ether: mp 120 °C (lit.[44] mp 117–118 °C); $[\alpha]^{20}_D$ 14.5° (*c* 2.0, water) [lit.[44] $[\alpha]^{20}_D$ 14.25° (*c* 5.5, water)]; $^1$H NMR ($CD_3OD$) δ 0.98 and 1.06 (2 d, 6 H,$CH_3)_2C$), 1.96 (m, 1 H, CH), 2.95 (m, 1 H, CHN), 3.5–3.9 (m, 2 H, $CH_2$), 4.8 (s, 4 H, $NH_3^+$ and OH).

**(*S*)-1-Bromo-3-methyl-2-butanamine.** This compound was synthesized in 70% yield by reaction of L-valinol with a mixture of 40% HBr in acetic acid and 1 vol % of bromine in an autoclave at 115 °C for 20 h.[45,46] The HBr salt of this compound was used directly for the synthesis of (*R*)-3-methyl-2-butanamine.

**(*R*)-3-Methyl-2-butanamine.** An amount of 19 g (77 mmol of (*S*)-1-bromo-3-methyl-2-butanamine 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 the resultant mixture was stirred for 4 h at room temperature under 1 atm $H_2$ 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 the extract was dried 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%); mp 216–217 °C (lit.[45] mp 205 °C); $[\alpha]^{22}_{578}$ 2.3° (*c* 0.7, $CH_3OH$), $[\alpha]^{22}_{578}$ 3.25°, $[\alpha]^{22}_{546}$ 3.68° (*c* 0.3, water) [lit.[45] $[\alpha]^{17}_{546}$ 3.5° (*c* 6.5, water)]; $^1$H NMR ($CD_3OD$) δ 0.98 and 1.06 (2 d, 6 H, $(CH_3)_2C$), 1.28 (d, 3 H, $CH_3$), 1.95 (m, 1 H, CH), 3.15 (m, 1 H, CHN).

**(*R*)-*N*-Formyl-3-methyl-2-butanamine (1i).** (*R*)-3-Methyl-2-butanamine was liberated from its HCl salt with an excess of aqueous NaOH and formylated as indicated for the synthesis of **1f**: $[\alpha]^{22}_{578}$ −12.5° (*c* 1.2, $CHCl_3$); $^1$H NMR ($CCl_4$) δ 0.90 (d, 6 H, $(CH_3)_2C$), 1.05 (d, 3 H, $CH_3$), 1.70 (m, 1 H, CH), 3.80 (m, 1 H, CHN), 7.9 (br, 1 H, NH), 8.00 (s, 1 H, CHO).

**(*R*)-2-Isocyano-3-methylbutane (2i).** This isocyanide was prepared from **1i** as described for the synthesis of **2f**. After redistillation, **2i** was obtained as a colorless liquid: yield 86%; $[\alpha]^{22}_{578}$ −24.2° (*c* 1.2, $CHCl_3$); IR ($CCl_4$) 2135 (NC) $cm^{-1}$; $^1$H NMR($CCl_4$) δ 1.00 (d, 6 H,$(CH_3)_2C$), 1.32 (m, 3 H, $CH_3$), 1.5–2.0 (m, 1 H, CH), 3.47 (m, 1 H, CHN).

The achiral isocyanides are known compounds and were prepared by the method of Ugi[28] (**2j–r**) and by the method of Casanova[32] (**2s**, **2t**).

**Homopolymerization. Poly[(*S*)-1-(methoxycarbonyl)-2-methylpropyl isocyanide] (3a).** Isocyanide **2a** were polymerized neat with 10 mol % $NiCl_2$ at ambient temperature. After 5 days, methanol/water (3:1, v/v) was added to the reaction mixture. The yellow polymer was collected by filtration, washed with methanol/water, and dried under reduced pressure at 50 °C: yield 15%; $[\alpha]^{20}_D$ −110° (*c* 0.1, $CHCl_3$); IR (KBr) 1735 (C=O), 1630 (C=N) $cm^{-1}$; $^1$H NMR ($CDCl_3$) δ 0–1.7, (br, 6 H, $CH_3$), 1.8–2.9 (br, 1 H, CH), 3.2–4.3 (br, 3 H, $OCH_3$), 4.0–5.3 (br, 1 H, CH).

**Poly[(*S*)-1-(isopropoxycarbonyl)-2-methylpropyl isocyanide] (3b).** Isocyanide **2b** was polymerized neat with 2.5 mol % $NiCl_2$ at 5 °C. After 3 days, methanol/water (2:1, v/v) was added, and the yellow polymer was collected by filtration, washed with methanol/water, and dried under reduced pressure at 50 °C: yield 60%; $[\alpha]^{20}_D$ −24° (*c* 0.1, $CHCl_3$); IR (KBr) 1730 (C=O), 1640 (N=C) $cm^{-1}$; $^1$H NMR ($CDCl_3$) δ 0–2.6 (br, 12 H, $CH_3$), 1.8–2.9 (br, 1 H, CH), 3.5–5.9 (br, 2 H, CH).

**Poly[(*S*)-(*tert*-butoxycarbonyl)-2-methylpropyl isocyanide] (3c).** Isocyanide **2c** was polymerized neat with 1 mol % $NiCl_2$ at 45 °C. After 4 days, methanol/water was added to the reaction mixture, and the yellow colored polymer was collected by filtration, washed with methanol/water, and dried under reduced pressure at 50 °C: yield 59%; $[\alpha]^{20}_D$ 32.5° (*c* 0.1, $CHCl_3$); IR (KBr) 1735 (C=O), 1640 (C=N) $cm^{-1}$; $^1$H NMR ($CDCl_3$) δ 0–1.2 (br, 6 H, $C(CH_3)_2$), 1.2–1.7 (br, 9 H, $C(CH_3)_3$), 1.5–2.7 (br, 1 H, CH), 3–5 (br, 1 H, CH).

**Poly[(1*S*,2*S*)-1-carbomethoxy-2-methylbutyl isocyanide] (3d).** Isocyanide **2d** was polymerized neat with 1 mol % $NiCl_2$ at 45 °C. After 5 days, methanol/water (3:1, v/v) was added to the reaction mixture. The yellow polymer was collected by filtration, washed with methanol/water, and dried under reduced pressure at 50 °C: yield 33%; $[\alpha]^{20}_D$ −32.2° (*c* 0.05, $CHCl_3$); IR (KBr) 1740 (C=O), 1640 (C=N) $cm^{-1}$; $^1$H NMR ($CDCl_3$) δ 0.2–2.7 (br, 9 H, $C_2H_5CH(CH_3)$), 2.8–3.8 (br, 3 H, $OCH_3$), 3.8–4.9 (br, 1 H, CH).

**Poly[(*S*)-1-carbethoxyethyl isocyanide] (3e).** Isocyanide **2e** was polymerized neat with 0.2 mol % $NiCl_2{\cdot}6H_2O$ at ambient temperature. After 5 days, the glassy reaction mixture was dissolved in a small amount of chloroform and added dropwise to an excess of vigorously stirred methanol/water (4:1, v/v). The precipitated yellow polymer was collected by filtration, washed with methanol/water, and dried under reduced pressure at 50 °C over KOH: yield 70%; $[\alpha]^{22}_{578}$ −280° (*c* 0.36, $CHCl_3$); IR (KBr) 1740 (C=O) 1638 (C=N) $cm^{-1}$.

**Poly[(*S*)-*sec*-butyl isocyanide] (3f).** Isocyanide **2f** (7.6 g, 91 mmol) was polymerized with 12 mg (0.05 mmol) of $NiCl_2{\cdot}6H_2O$ in 100 mL of ethanol at ambient temperature. The insoluble polymer was isolated and washed thoroughly with ethanol and chloroform: yield 95%; IR (KBr) 1634 (C=N) $cm^{-1}$.

**Poly[(*S*)-1-phenylethyl isocyanide] (3g).** Isocyanide **2g** was polymerized neat with 0.015 mol % $NiCl_2{\cdot}6H_2O$ at 0–5 °C: yield 90%; $[\alpha]^{20}_D$ −350° (*c* 1, $CHCl_3$); IR (KBr) 1624 (C=N) $cm^{-1}$; $^1$H NMR ($CDCl_3$) δ 1.15 (br, 3 H, $CH_3$), 5.0 (br, 1 H, CH), 6.9 (br, 5 H, $C_6H_5$).

**Poly[(*R*)-2-acetoxy-1-phenylethyl isocyanide] (3h).** Isocyanide **2h** was polymerized with 0.15 mol % $NiCl_2{\cdot}6H_2O$ in methanol at ambient temperature. The polymer was obtained as a bright yellow powder: yield 70% $[\alpha]^{22}_{578}$ −82° (*c* 0.5, $CHCl_3$); IR (KBr) 1745 (C=O), 1622 (C=N) $cm^{-1}$.

**Poly[(*R*)-1,2-dimethylpropyl isocyanide] (3i).** Monomer **2i** was polymerized with 0.1 mol % $NiCl_2{\cdot}6H_2O$ in methanol at ambient temperature: yield 75%; $[\alpha]^{22}_{578}$ −16.7° (*c* 0.5, $CHCl_3$); IR (KBr) 1628 (N=C) $cm^{-1}$.

**Copolymerization.** In a typical procedure, 133 mg of 4-methoxyphenyl isocyanide (**2k**) was mixed with 144 mg of (*S*)-2-isocyanoisovaleric acid methyl ester (**2a**) and polymerized with 1 mol % $NiCl_2$. After 16 h, methanol was added to the reaction mixture. The yellow polymer was collected by fiiltration, washed with methanol, and dried at reduced pressure at 50 °C: yield 158 mg (90% based on achiral monomer; 23 mol % incorporation of **2a**). The methanol-soluble fraction contained unreacted **2a** and the homopolymer **3a**. The physical properties of the copolymers are given in Tables II and III.

**Registry No. 1a**, 3154-46-9; **1b**, 99065-94-8; **1c**, 71738-70-0; **1d**, 3154-48-1; **1e**, 21683-14-7; **1f**, 61852-43-5; **1g**, 19145-06-3; **1h**, 87281-05-8; **1i**, 75240-52-7; **2a**, 63472-88-8; **(2a)(2k)** (copolymer), 112138-45-1; **(2a)(2j)** (copolymer), 112115-26-1; **(2a)(2l)** (copolymer), 112115-27-2; **(2a)(2m)** (copolymer), 112115-28-3; **(2a)(2n)** (copolymer), 112115-29-4; **(2a)(2o)** (copolymer), 112115-30-7; **2b**, 112115-11-4; **(2b)(2k)** (copolymer), 112115-18-1; **(2b)(2p)** (copolymer), 112138-46-2; **(2b)(2q)** (copolymer), 112115-31-8; **(2b)(2r)** (copolymer), 112115-32-9; **(2b)(2s)** (copolymer), 112115-33-0; **(2b)(2t)** (copolymer), 112115-34-1; **2c**, 112115-12-5; **(2c)(2k)** (copolymer), 112115-19-2; **2d**, 63643-98-1; **(2d)(2k)** (copolymer), 112115-20-5; **2e**, 68778-13-2; **(2e)(2k)** (copolymer), 112115-21-6; **2f**, 53368-88-0; **(2f)(2k)** (copolymer), 112115-22-7; **2g**, 21872-32-2; **(2g)(2k)** (copolymer), 112115-23-8; **2h**, 87281-06-9; **(2h)(2k)** (copolymer), 112115-24-9; **2i**, 75236-36-1; **(2i)(2k)** (copolymer), 112115-25-0; **3a**, 112115-14-7; **3b**, 112115-15-8; **3c**, 112115-16-9; **3d**, 112115-17-0; **3e**, 68778-14-3; **3f**, 53368-89-1; **3g**, 26714-26-1; **3h**, 87281-24-1; **3i**, 75236-37-2; $NiCl_2$, 7718-54-9; (L)-valine, 72-18-4; (L)-isoleucine, 73-32-5; (L)-alanine, 56-41-7; (*R*)-2-amino-2-phenylethanol, 56613-80-0; (*R*)-*N*-formyl-2-amino-2-phenylethanol, 87281-04-7; *N*-benzoyl-L-valine, 5699-79-6; *N*-benzoyl-L-valine methyl ester, 10512-91-1; *N*-benzyl-L-valinol, 42807-42-1; (L)-valinol, 2026-48-4; (*S*)-1-bromo-3-methyl-2-butanamine, 112115-13-6; (*R*)-3-methyl-2-butanamine, 34701-33-2.

(43) Hartung, W. H.; Simonoff, R. *Org. React.* (*N.Y.*) **1953**, *7*, 263–326.
(44) Karrer, P.; Portmann, P.; Suter, M. *Helv. Chim. Acta* **1949**, *32*, 1156–1157.
(45) Barrow, F.; Ferguson, G. F. *J. Chem. Soc.* **1935**, 410–418.
(46) Ison, R. R.; Cosy, A. F. *J. Med. Chem.* **1970**, *13*, 1027.