by Grunwald and his co-workers. The substituent effect of 3-X-quinuclidines shows that a complex of a more basic amine dissociates more slowly, and the slope of a Brønsted type plot is $\beta_{diss} = -0.25 \pm 0.04$. Molecular mechanics calculations indicate that dispersion forces represent at most 40% of the activation energy for dissociation of the *N,N*-diethyl-*m*-toluidine–*tert*-butyl alcohol complex, and simple calculation of the cavity term suggests that this may be as important as the dispersion term for this complex. These results help in understanding the surprising effect of basicity change on the rate of phosphoryl transfer reactions[10] and other reactions with small intrinsic β_{nuc} values, as well as the effect of solvation in protic solvents in general.

Acknowledgment. This work was supported in part by grants from The National Institutes of Health (GM20888), the National Science Foundation (DMB-8715832), and the Swedish Natural Science Research Council. We are especially grateful to Dr. A. Redfield for invaluable assistance with the NMR experiments and for access to the 500-MHz instrument (NIH GM 20168) and to Dr. E. Grunwald for generous advice and discussions. We thank Dr. C. Grob, Basel, for sending us a preprint.

Registry No. 3-CN-Q, 51627-76-0; 3-Cl-Q, 42332-45-6; 3-OH-Q, 1619-34-7; Q, 100-76-5; 3-(Me_3N)-Q, 75-50-3; 3-CN-Q·HCl, 116599-22-5; Q·HCl, 39896-06-5; 3-OH-Q·HCl, 6238-13-7; 3-Cl-Q·HCl, 33601-77-3; Me_3N·HCl, 593-81-7; *p*-$MeC_6H_4NEt_2$, 91-67-8; *t*-BuOH, 75-65-0; H_2O, 7732-18-5; *p*-$MeC_6H_4SO_2CH_2NCO$, 10564-55-3; 3-oxo-quinuclidinium-*l*-*d*, 135144-20-6; 3,3-dihydroxy-d_2-quinuclidium-*l*-*d*, 135144-21-7; 3-quinuclidone, 3731-38-2.

Free-Radical Telomerization of Chiral Acrylamides: Control of Stereochemistry in Additions and Halogen-Atom Transfer

Ned A. Porter,* Robert Breyer, Elizabeth Swann, James Nally, Jyotsna Pradhan, Timothy Allen, and Andrew T. McPhail

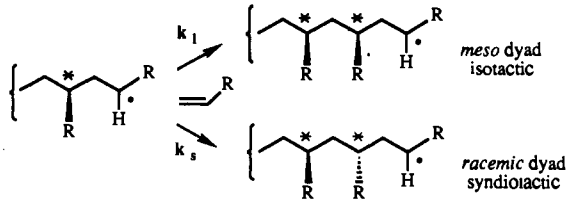
Contribution from the Department of Chemistry, Duke University, Durham, North Carolina 27706. *Received April 1, 1991*

Abstract: The free-radical reactions of carbon radicals substituted α to a chiral pyrrolidine amide have been studied. The pyrrolidine used was 2,5-dimethylpyrrolidine, available as either the *R,R* or *S,S* enantiomer from D- or L-alanine, and the radicals were generated (1) by tin radical abstraction of the halogen from the 2-iodobutyramide of the pyrrolidine, (2) by decomposition of a pyrrolidine amide substituted Barton ester **4**, and (3) by radical addition to the acrylamide of the pyrrolidine **3**. Addition of chiral α amide radicals to alkenes occurs with a selectivity of ~15:1 at room temperature, while bromine- and iodine-atom transfer to these radicals occurs with a selectivity of 10:1 at room temperature. Telomerization of the acrylamide **3** is achieved by photolysis of $BrCCl_3$ in the presence of acrylamide. Telomers are readily formed and the lower telomers, n = 1 to 5, were isolated and characterized. Halogens were removed from the telomers by reduction with tributyltin hydride and in this way, the major diastereomers of the n = 2 and n = 3 telomers were converted to known compounds. Chain-transfer constants for the $BrCCl_3$ telomerization were determined and they range from 0.3 to 0.5 for $C_n = C_2$ to C_5. An analysis of the chiral amide auxiliary is presented that may prove useful in the consideration of other auxiliary groups.

Control of stereochemistry in the free-radical addition reactions of vinyl monomers has been of interest since 1929 when Staudinger[1,2] pointed out that the tertiary carbons formed in vinyl polymerizations are asymmetric and can assume both the *meso* (isotactic) and *racemic* (syndiotactic) arrangements. Significant stereoregulation in free-radical addition to vinyl monomers has not been observed, atactic polymers generally resulting from free-radical polymerization.[3] The ratio of rate constants that determines the selectivity for methyl acrylate (R = COOMe) is $k_i/k_s = 1.1$ at 0 °C, for example, and the polymers that result are atactic. In an authoritative review of stereoregulation in polymerization, Pino and Suter suggest that "the perspectives for stereocontrol in free radical polymerization are not very promising" outside of work in "polymerization of monomers included in solid matrices which seem to be today (1976) the only way to obtain highly stereoregular polymers with radical polymerization."[4]

In the polymerization of achiral vinyl monomers, the important stereocontrol element for consideration is the stereogenic center nearest to the radical terminus of the growing chain. If this nearest "R" group were to control the face of the prochiral radical to which addition occurred, stereoregulation would be achieved. This nearest center effect on stereoselection, which is essentially a 1,3 steric interaction, is apparently small due to the conformational mobility of the chain, which does not "fix" the stereogenic center relative to the radical.

nearest chain stereogenic center control



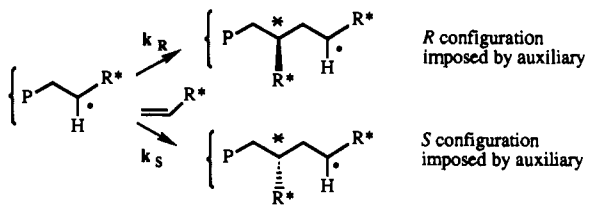
The use of chiral monomers that have an auxiliary group that exerts a biasing effect on the radical face selected for addition is an alternate approach to control polymer tacticity. In this strategy, the chirality of the auxiliary group, R*, would define the stereochemistry of the stereogenic center formed during each addition. If a monomer was chosen that carried with it the auxiliary, a controlling effect would be exerted in the radical addition and a controlling group would also be introduced at the growing radical terminus in each addition step, assuring control at the next step of chain growth in the serial addition sequence.

The use of an auxiliary to control the stereochemistry in the addition reactions of acyclic radicals like those in a growing vinyl free-radical polymer chain is a problem that has not been previously solved, and therefore advances in control of polymer

(1) Staudinger, H.; Ashdown, A. A.; Brunner, M.; Bruson, H. A.: Wehrli, S. *Helv. Chim. Acta* **1929**, *12*, 934.
(2) Staudinger, H. *Die Hochmolekularen Organischen Verbindungen*; Springer Verlag: Berlin, 1932.
(3) Bovey, F. A. *Chain Structure and Conformation of Macromolecules*: Academic Press: New York, 1982.
(4) Pino, P.; Suter, U. W. *Polymer* **1976**, *17*, 977.

0002-7863/91/1513-7002$02.50/0

chiral auxiliary control



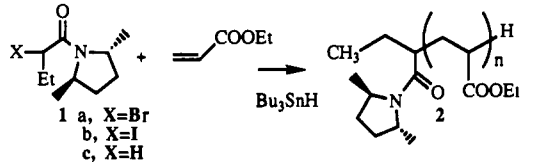
stereochemistry have awaited the development of an understanding of the fundamental elements of "acyclic stereoselection" in free-radical chemistry. While there have been impressive achievements in the control of stereochemistry in free-radical reactions involving cyclic radicals,[5] there has been, until recently, little success in the stereoregulation of reactions involving acyclic radicals.

In the past two years there have been reports of advances in the control of acyclic stereochemistry in radical addition reactions. Substitution of chiral amides onto the radical center undergoing addition has been reported to give rise to stereoselection in the new stereogenic center formed from the radical. We[6] and Giese[7] have utilized 2,5-dimethylpyrrolidine as a radical auxiliary, Curran has reported the use of a sultam derived from camphor[8,9] as an effective auxiliary in radical addition reactions, and other recent reports of acyclic stereocontrol in radical reactions have appeared.[10,11] Due to the potential impact of these recent discoveries on the control of free-radical polymer and oligomer stereochemistry, we have begun a program to examine amide auxiliaries as control elements in serial radical addition reactions. We have chosen to initially examine small oligomers and telomers of addition so that the addition compounds can be completely characterized by spectroscopic means such that the larger problem of polymer stereochemistry can be rationally approached. We report here the results of our studies of telomerization of the acrylamide derived from 2,5-dimethylpyrrolidine in the presence of the chain transfer agent bromotrichloromethane[12] or tin hydride/alkyl iodides. Small telomers of acrylamide can be formed with significant control of stereochemistry in both the radical addition reaction and, in the case of bromotrichloromethane, in the chain-transfer step.

Results

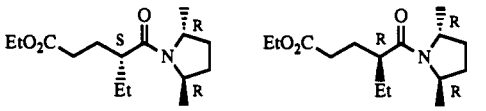
Two approaches were used to examine dimethylpyrrolidine amides as control elements in free-radical additions. In the first approach, amide-substituted radicals were produced by reaction of a halo- or thiopyridyl ester precursor with tin radicals, while in the second, bromotrichloromethane chain transfer telomerization of an acrylamide was initiated photochemically.

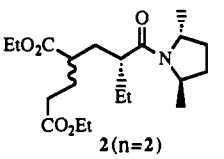
Reaction of the halide, **1a** or **1b**, or the thiopyridyl ester, **4**, with tin hydride in the presence of ethyl acrylate gave addition products **2**, into which one or more alkenes were incorporated. The reaction of ethyl acrylate with bromo amide **1a** was carried out by slow addition of 1 equiv of tributyltin hydride (via syringe pump) to a refluxing solution of the bromo amide and 10 equiv of ethyl acrylate in benzene. The optimum bromo amide concentration was found to be 0.16 M; more dilute and more concentrated reaction mixtures were attempted but these led to less of the desired addition adducts being formed. The product ratio was



found typically to be 35–50% of the monoadduct **2** (n = 1), 15–25% of the diadduct **2** (n = 2), and 20% of the reduced product **1c**.

The monoadduct isomers *S*-**2** (n = 1) and *R*-**2** (n = 1) were separated from the reduced material by preparative HPLC (50% hexane, 50% ethyl acetate elution) and the diastereomers were identified by independent synthesis from resolved 2-ethylglutaric acid.[13] The selectivity of the monoadduct isomer observed at 80 °C was 12:1 *S*:*R*. This ratio was determined by GC (*S*-**2** retention time 9.9 min and *R*-**2** retention time 10.0 min). The diadduct **2** (n = 2) (GC retention times for diastereomers 12.7 and 12.8 min) was obtained from the flash column as a 1/1 mixture of diastereomers and was characterized by NMR, IR, and MS, but no attempt was made to separate the mixture.





Identical ethyl acrylate addition reactions were carried out at lower temperatures with the Barton ester **4** as a radical precursor. The Barton ester was 0.01 M in benzene or dichloromethane (for low temperatures) and 20 equiv of ethyl acrylate, and 1 equiv of tributyltin hydride was added in one portion and the mixture irradiated. The irradiation was carried out with a 100-W tungsten lamp positioned 30 cm from the reaction vessel. Product ratios for temperatures of 80, 25, and −24 °C were obtained. The *S*:*R* ratios determined were 12:1 (80 °C), 25:1 (25 °C), and 36:1 (−24 °C). The yields of isolated monoadduct range from 30% (−24 °C) to 55% (25 °C) of **2** (n = 1) and traces of dimer were observed by GC. A reaction of −78 °C was attempted, but only trace amounts of adducts were observed by GC over an extended time period and the reaction proved to be too sluggish to be practical.

The reaction of acrylamide **3** with bromo amide **1a** was carried out by syringe addition of 1 equiv of tributyltin hydride to a refluxing benzene solution of the bromo amide **3** (16 mM) and 4 equiv of acrylamide **1a**. The products were purified by flash column (petroleum ether–ether, 10% gradient elution) and preparative HPLC (80% hexane, 20% 2-propanol elution). The product mixture was found to be 10% of the reduced product **1c**, 40% of monoadduct **5** (n = 2), and 20% of diadduct **5** (n = 3).

Analytical HPLC of the crude mixture showed the major diastereomer of **5** (n = 2) to elute before the minor isomer. The ratio was shown to be 25:1, as determined by analytical HPLC (4.5-cm column, 5% 2-propanol, 95% hexane elution). The stereochemistry of the diastereomers of **5** (n = 2) was determined by an independent synthesis using resolved ethylglutaric acid in a DCC coupling reaction with (*R*,*R*)-2,5-dimethylpyrrolidine. The major diastereomer of **5** (n = 2) formed had the *S* configuration at C-2 of the glutaric chain when the auxiliary used had the *R*,*R* configuration, 2*S*-**5** (n = 2).

One major diastereomer of **5** (n = 3) was formed and could be purified by HPLC. Single-crystal X-ray analysis of this

(5) Giese, B. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 969.
(6) Porter, N. A.; Swann, E.; Nally, J.; McPhail, A. T. *J. Am. Chem. Soc.* **1990**, *112*, 6740.
(7) Giese, B.; Zehnder, M.; Roth, M.; Zeitz, H. G. *J. Am. Chem. Soc.* **1990**, *112*, 6741.
(8) Curran, D. P.; Shen, W.: Zhang, J.; Heffner, T. A. *J. Am. Chem. Soc.* **1990**, *112*, 6738.
(9) See also Curran, D. P.; Heffner, T. A. *J. Org. Chem.* **1990**, *55*. 4585, for use of the same auxiliary in dipolar cycloadditions.
(10) Guindon, Y.; Lavallee, J.; Boisvert, L.; Chabot, C.; Delorme, D.; Yoakim, C.; Hall, D.; Lemieux, R.; Simoneau, B. *Tetrahedron Lett.* **1991**, *32*, 27.
(11) Crich, D.; Davies, J. W. *Tetrahedron Lett.* **1987**, *28*, 2205.
(12) Kimura, T.; Nakanishi, I.; Hamashima, M. *Polymer* **1986**, *18*, 689 and references cited.
(13) Jacques, J.; Gros, C.; Bourcier, S.; Brienne, M. J.; Toullec, J. *Absolute Configurations of 6000 Selected Compounds With One Asymmetric Carbon Atom. Stereochemistry*; Kagan, H., Ed.; Georg Thieme Publishers: Stuttgart, 1977; Vol. 4.

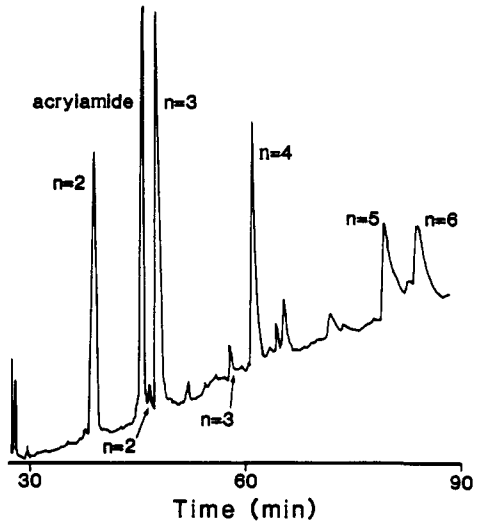
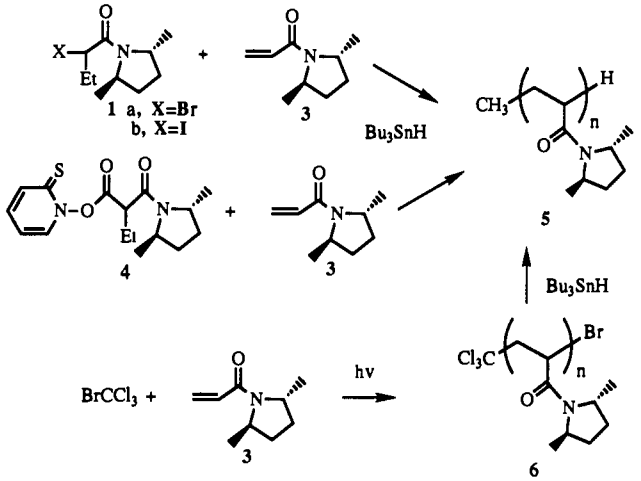
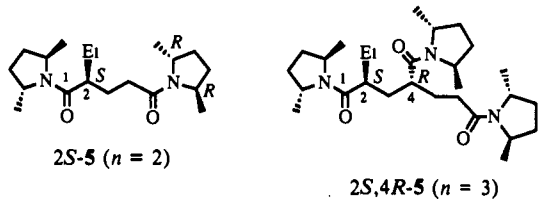


Figure 1. High-pressure liquid chromatogram of product mixture for $BrCCl_3$ telomerization of acrylamide 3. Chromatography conditions: gradient from 0 to 75% 2-propanol/hexane, UV detection at 214 nm.

Scheme I



product, published previously, determined the configuration of the two stereogenic centers formed in the addition.[6] This major diastereomer is designated as 2*S*,4*R*-**5** (n = 3).



Due to the fact that it was not possible to produce significant quantities of telomers **5** with $n > 3$ with this strategy, bromotrichloromethane chain transfer telomerization[12-14] was investigated. Photolysis of the acrylamide **3** in the presence of $BrCCl_3$ with a 450-W medium-pressure mercury lamp in hexane, benzene, chlorobenzene, or methylene chloride resulted in the complete consumption of the acrylamide and conversion to the telomer **6** in high yield. In hexane, the telomer product precipitates during photolysis while the telomers are soluble in benzene, chlorobenzene, or methylene chloride. No precipitate is formed if these solvents are used in the phototelomerization.

The lower telomers of **6** (n = 1-5) were examined by gradient HPLC (both analytical and preparative). A linear gradient of 2-propanol (0–75% in 75 min at 0.8 mL/min) in hexane was sufficient to resolve the telomers by analytical HPLC (retention times for major stereoisomers in min, n = 1 to n = 5, 10.76, 20.40, 29.9, 48.6, 60.6; the starting acrylamide eluted at 29.0 min). Large-scale preparative chromatography (2-propanol, 0–75% in 75 min at 20.0 mL/min) in hexane was sufficient to resolve the telomers (Figure 1) (retention times in minutes, n = 1 to n = 5, 24.0, 36.8, 46.8, 62.8, 84.0; the starting acrylamide eluted at 44.4 min).

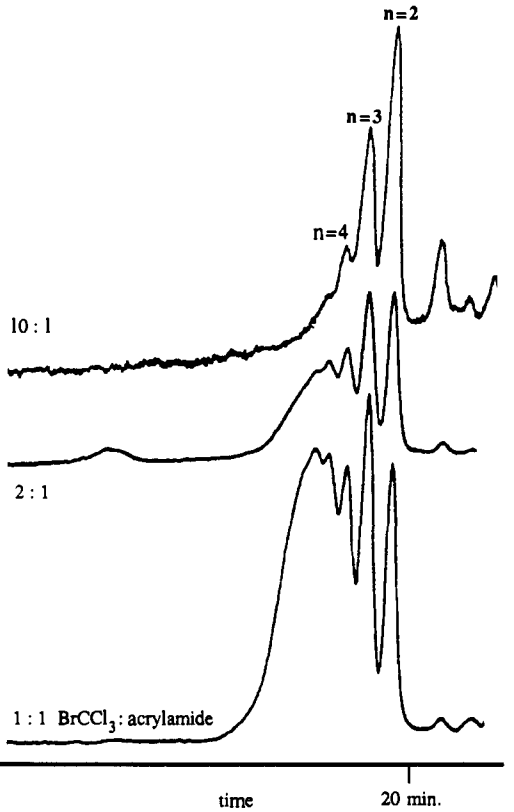


Figure 2. Gel permeation chromatogram of product mixture for $BrCCl_3$ telomerization of acrylamide 3.

Table I. Mole Fraction of Telomer **6** Present in Product Mixture[a]

	mole ratio of $BrCCl_3$:acrylamide		
telomer	1:1	2:1	10:1
n = 1	4.00×10^{-2}	8.70×10^{-2}	3.30×10^{-1}
n = 2	3.69×10^{-1}	4.52×10^{-1}	4.51×10^{-1}
n = 3	2.40×10^{-1}	2.32×10^{-1}	1.56×10^{-1}
n = 4	1.11×10^{-1}	9.18×10^{-2}	4.13×10^{-2}
n = 5	7.73×10^{-2}	5.55×10^{-2}	1.44×10^{-2}
n = 6	5.84×10^{-2}	3.56×10^{-2}	5.16×10^{-3}
n = 7	4.22×10^{-2}	2.17×10^{-2}	1.75×10^{-3}
n = 8	1.95×10^{-2}	1.26×10^{-2}	8.81×10^{-4}
n = 9	8.12×10^{-3}	3.37×10^{-3}	0
n = 10	4.55×10^{-3}	3.34×10^{-3}	0
n = 11	2.30×10^{-3}	1.15×10^{-3}	0

[a] >95 consumption of acrylamide.

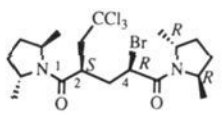
Gel permeation chromatography of **6** was conducted with THF as the eluent at 1.0 mL/min and a typical GPC chromatogram is presented in Figure 2. Known samples of **6** (n = 1 to n = 6) obtained from HPLC purification gave the GPC retention times for the telomers as follows: (in minutes) n = 1, 16.72; n = 2, 15.91; n = 3, 15.30; n = 4, 14.81; n = 5, 14.40; n = 6, 14.06. A plot of log (molecular weight) of the telomers vs retention time gave a correlation with an R^2 of 0.996.

Additional experiments conducted varying the ratio of acrylamide to $BrCCl_3$ from 1:1 to 1:10 (acrylamide to $BrCCl_3$). Telomer product distribution was determined by GPC for these different runs. A deconvolution program (based on the algoritum of Vaidya[15]) was used to aid in the determination of the mole-

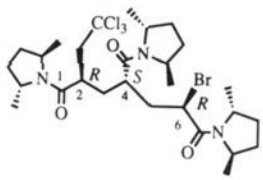
(14) Starks, C. M. *Free Radical Telomerization*; Academic Press: New York, 1974.

fraction distribution of the telomers. The mole fractions presented in Table I are based on the heights of peaks obtained from the deconvolution and are weighted by the number of monomer units included in the telomer to correct for the change in absorbance.

The stereochemistry of the major purified stereoisomer of the **6** ($n = 2$) telomer and the **6** ($n = 3$) telomer was established by removal of the halogens from the products by reaction with tributyltin hydride.[16] The stereochemistry of the products formed by this sequence, **5** ($n = 2$) and **5** ($n = 3$), have been previously established by independent synthesis and single-crystal X-ray analysis. Thus, the major $n = 2$ telomer of **6** was assigned the structure 2*S*,4*R*-**6** ($n = 2$) on the basis of its conversion to 2*S*-**5** ($n = 2$) in the reaction with tributyltin hydride. The major $n = 3$ telomer of **6** was assigned the structure 2*R*,4*R*,6*R*-**6** ($n = 3$) on the basis of its conversion to 2*S*,4*R*-**5** ($n = 3$) in the reaction with tributyltin hydride. The configuration of the carbon-bearing



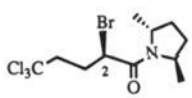
2*S*,4*R*-**6** ($n = 2$)



2*R*,4*S*,6*R*-**6** ($n = 3$)

bromine cannot be rigorously assigned for the **6** ($n = 2$) telomer and the **6** ($n = 3$) telomer by the tin hydride conversion to the **5** telomers. The stereochemistry of this center is assigned on the basis of the stereochemistry established for the reaction of structurally analogous radicals reacting with $BrCCl_3$; vide infra. The crude **6** telomer mixture was also reduced with tributyltin hydride, and the mixture of **5** telomers were analyzed by analytical HPLC and GC/MS. The ratio of diastereomers 2*S*-**5** ($n = 2$):2*R*-**5** ($n = 2$) was formed with a ratio in excess of 15:1. Four telomers of **5** ($n = 3$) were observed by gas chromatography and gas chromatography/mass spectrometry, and the major product, 2*S*,4*R*-**5** ($n = 3$), dominated the product mixture by ~30:2:2:<1. The stereochemistry of the three minor stereoisomers has not been assigned.

The observation of one major **6** stereoisomer for $n = 1$ to $n = 3$ in the $BrCCl_3$ telomerization of acrylamide **3** suggested that not only was the radical addition reaction stereoselective but also that the bromine atom transfer reaction was proceeding with selectivity. In fact, gas chromatography and gas chromatography/mass spectrometry of the telomerization product mixture showed two telomers with $n = 1$, **6** ($n = 1$), formed in a ratio of 9:1 at 6 °C. Since only one new stereogenic center is formed



2*R*-**6**(n=1)

in this product, and this center is formed in the bromine-atom chain transfer reaction, this step must be occurring with significant selectivity. To test this hypothesis, a series of reactions were carried out with the Barton ester precursor, **4**, in Barton–Hunsdiecker type decarboxylations in the presence of $BrCCl_3$ or iodoform.

Reactions were carried out by a previously reported method.[17] Typically the Barton ester **4** (8 mM concentration) in benzene or dichloromethane (for low-temperature reactions) was irradiated for 2 h with 1.1 equiv of $BrCCl_3$ or iodoform. The irradiation was carried out with a 300-W sunlamp positioned 30 cm from the reaction vessel. The reaction product mixture was purified by flash column chromatography (petroleum ether/ether, 1/1

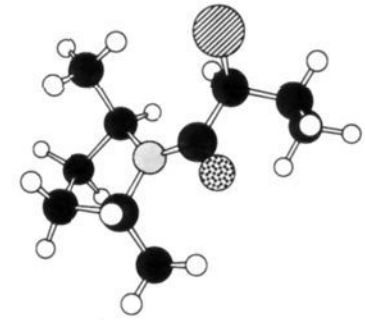


Figure 3. Diagram showing the solid-state conformation of the minor stereoisomer of **1a**; small circles represent hydrogen atoms.

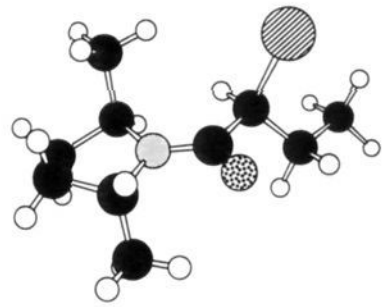
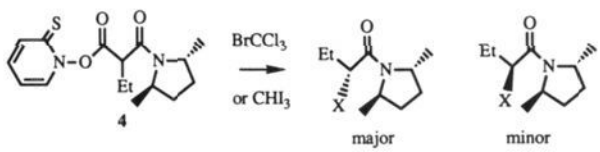


Figure 4. Diagram showing the solid-state conformation of the minor stereoisomer of **1b**; small circles represent hydrogen atoms.

elution) to give the bromo amide **1a** or the iodo amide **1b** in 55–75% isolated yield.



1a, X = Br; **1b**, X = I

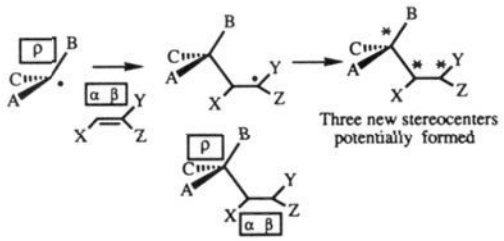
The stereoselectivity for formation of the bromide **1a** at 25 °C was found to be 11:1 for the major bromide (GC retention 6.2 min) to the minor bromide (GC retention time 7.2 min). The diastereomers from an independent synthesis were separated by preparative HPLC (3% 2-propanol, 97% hexane elution). The major and minor isomers eluted at 23 and 30 min, respectively. Crystals of the minor isomer were grown from ether and the stereochemistry was established by X-ray crystallography (Figure 3). Stereoselectivity observed for the formation of **1a** at 0 °C was 17:1.

The stereoselectivity for formation of the iodide **1b** at 25 °C was found to be 9:1 for the major iodide (GC retention 7.0 min) to the minor iodide (GC retention time 7.6 min). The diastereomers from an independent synthesis were separated by preparative HPLC (3% 2-propanol, 97% hexane elution); the major and minor isomers eluted at 23 and 28 min, respectively. The major iodo amide isomer was obtained as an oil while the minor isomer was obtained as needles. The crystals were grown in ether and the stereochemistry was established by X-ray crystallography (Figure 4).

Discussion

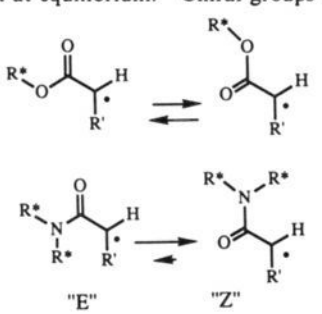
In radical addition to carbon–carbon double bonds there may be three new stereogenic centers formed if the alkene and the radical are suitably substituted. For example, if the addition of a prochiral radical to a trisubstituted alkene XCH=CYZ is followed by hydrogen-atom trapping, three adjacent stereogenic centers would result. Examples of acyclic stereocontrol in free-radical chemistry are rare[11,18] and there has been, until re-

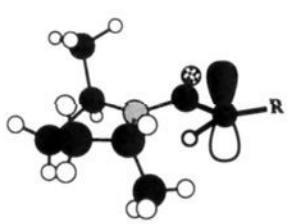
(15) Vaidya, R. A.; Hester, R. D. *J. Chromatogr.* **1984**, 231.
(16) Giese, B. *Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds*; New York: Pergamon Press, 1986.
(17) Barton, D. H. R.; Crich, D.; Motherwell, W. B. *Tetrahedron Lett.* **1983**, *24*, 4979.
(18) Hart, D. J.; Huang, H.-C. *Tetrahedron Lett.* **1985**, *26*, 3749.



cently, no general understanding of the factors that are important in controlling the ρ or α centers for acyclic systems. There has been some recent success in the control of stereochemistry at the α center,[19-23] and pyrrolidine amides substituted on the α carbon have been useful in defining the stereochemistry of that center in addition reactions.

One anticipates that approaches to the control of stereochemistry at the ρ and β centers should be similar since the β center is a radical in its stereochemically defining step. Critical to any strategy for ρ control is fixing the stereochemistry of any chiral group attached (relative to the radical center), and substitution by chiral amides suggested itself in analogy to the strategy developed for α control. In fact, Strub, Roduner, and Fischer[24] have studied α amide radicals by EPR and they have suggested that the preferred conformer of such radicals has the Z orientation, while analogous α ester radicals exist with Z and E geometric isomers present at equilibrium. Chiral groups attached to an





7

amide-substituted radical would therefore be fixed relative to the radical, while those attached to an ester radical would have more than one conformer contributing to the overall stereoselectivity. Fischer[24] also suggests that the barrier separating Z and E conformers of both α amide and α ester radicals is in excess of 11 kcal/mol.

The second bond that is important to fix in the α amide radical is the carbonyl–nitrogen partial double bond. It should be noted that there is a considerable barrier to rotation about this bond for amides (~18–20 kcal/mol) but the barrier to rotation about the analogous bond in an α amide radical is not known. In order to eliminate rotation about this bond from consideration, the C2 symmetric dimethylpyrrolidine was used as an amide substituent, the radical **7** resulting from this substitution. The two rotamers of the radical **7** are degenerate and the chirality of the amide is therefore fixed relative to the diastereotopic radical faces.[25] For the radical **7**, the proximate pyrrolidine methyl group, Z to the radical center, shields the bottom face of the radical from addition, while the remote pyrrolidine methyl substituent, E to the radical center, cannot effectively shield the top face of the radical. This differential shielding of the radical faces is at the heart of the selectivity observed in the reactions of radical **7**.

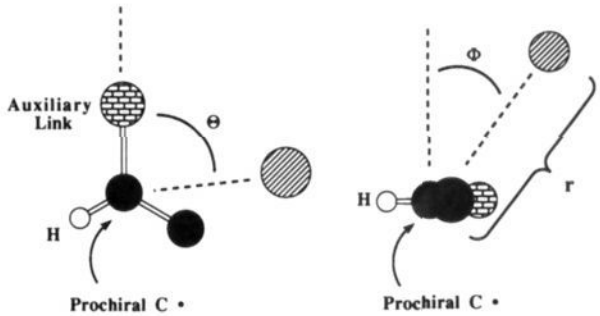


Figure 5. Polar coordinates for analysis of radical face-protecting groups.

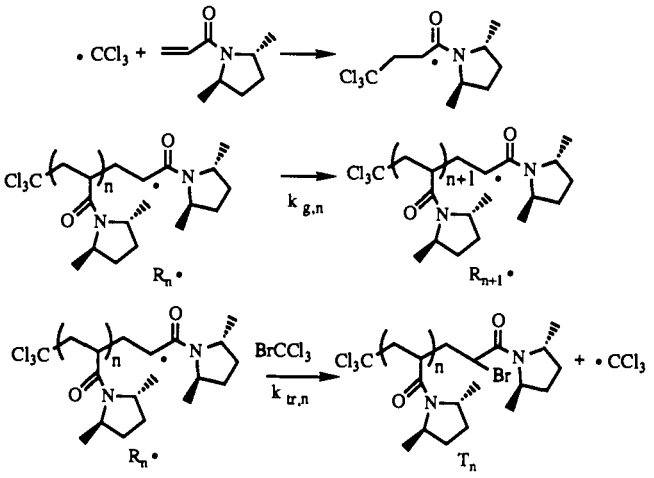
We have earlier proposed a set of polar coordinates to be considered for groups that shield the faces of alkenes and lead to α center selectivity.[23] The polar coordinates developed for α selectivity reflect the angle of approach of the radical to the alkene face on the basis of the presumed transition state of the addition reaction of nucleophilic radicals to electron-deficient alkenes.[26] It seems inappropriate to use the α center vector of approach coordinates for consideration of ρ selectivity, and the generalized polar coordinates of substituents relative to the radical face shown in Figure 5 are presented for use in consideration of ρ selectivity. In this analysis, Θ is the angle of the shielding group from the bond linking the auxiliary to the prochiral carbon in the plane of the radical, Φ is the angle between the shielding group and the axis perpendicular to the radical face, and r is the distance between the prochiral carbon and the shielding group. While the effect of Θ on the facial selectivity is unknown and may be highly dependent on the nature of the radical (i.e. nucleophilic, electrophilic, ambiphilic) and the reaction partner, one anticipates that selectivity will be dramatically dependent on Φ and r. If $\Phi = 0°$ or 180° for a group and r is small (2–4 Å), one expects good facial shielding while that would not be the case if $\Phi = 90°$ and/or r is large. If one assumes that the radical **7** has a structure close to the solid-state structure of an alkene with a pyrrolidine amide substituent,[23] then the proximate methyl of **7** has parameters $r = 3.3$ Å, $\Phi = 128°$, and $\Theta = -66°$, while the remote methyl has parameters of $r = 4.3$ Å, $\Phi = 68°$, and $\Theta = -17°$. The pyrrolidine methyl anti to the radical is at a greater distance from the prochiral carbon and has Φ closer to 90°than the pyrrolidine methyl Z to the radical center, and this is consistent with the facial selectivity observed in the addition reactions reported here.

Reaction of the radical **7** (from (*R*,*R*)-dimethylpyrrolidine) occurs preferentially from the *re* face for all the reactions described here. Thus, addition of **7** where R = Et to ethyl acrylate or to the acrylamide **3** occurs from the *re* face as does reaction of the same radical in halogen-atom transfers from $BrCCl_3$ or CHI_3. Similarly, radicals in the growing telomer chains from $BrCCl_3$-initiated telomerization all react predominately from the *re* face. Selectivity in the addition to alkenes is on the order of ~15:1 at room temperature while selectivity for halogen-atom transfer is approximately 10:1 at room temperature.

For $BrCCl_3$ telomerization, the stereochemical problem can be simplified by reaction of the original telomer mixture **6** with Bu_3SnH. This removes the stereogenic center at the carbon bearing Br in the initial telomer and also converts the $BrCCl_3$

(19) Porter, N. A.; Lacher, B.; Chang, V. H.-T.; Magnin, D. R. *J. Am. Chem. Soc.* **1989**, *111*, 8309.
(20) Scott, D. M.; McPhail, A. T.; Porter, N. A. *Tetrahedron Lett.* **1990**, *31*, 1679.
(21) Porter, N. A.; Scott, D. M.; Lacher, B.; Giese, B.; Zeitz, H. G.; Lindner, H. J. *J. Am. Chem. Soc.* **1989**, *111*, 8311.
(22) Porter, N. A.; Scott, D. M.; Rosenstein, I. J.; Giese, B.; Veit, A.; Zeitz, H. G. *J. Am. Chem. Soc.* **1991**, *113*, 1791.
(23) Porter, N. A.; Wu, W.-X.; McPhail, A. T. *Tetrahedron Lett.* **1991**, *32*, 707.
(24) Strub, W.; Roduner, E.; Fischer, H. *J. Phys. Chem.* **1987**, *91*, 4379 and references cited therein.
(25) Whitesell, J. K. *Chem. Rev.* **1989**, *89*, 21581.
(26) Spellmeyer, D. C.; Houk, K. N. *J. Org. Chem.* **1987**, *52*, 959.

Scheme II. $BrCCl_3$ Chain Transfer Scheme for Acrylamide 3



telomers to compounds **5** that have been previously characterized. The mixture of **5** obtained by Bu_3SnH reduction of **6** reflects the selectivity in the alkene addition reaction, and the product distribution for **5** ($n = 2$) and **5** ($n = 3$) suggests that the selectivity is independent of chain length. For **5** ($n = 2$), the ratio of the 2 diastereomers is ~15:1 and if this probability (0.94) is translated to the second step of addition, one expects a mixture of 4 diastereomers of **5** ($n = 3$) in a ratio of (0.94 × 0.94):(0.94 × 0.06):(0.06 × 0.94):(0.06 × 0.06) = 0.88:0.056:0.056:0.003. This is the approximate distribution of diastereomers formed (30:2:2:<1) on the basis of the GC and GC/MS analyses of the tin hydride reduction mixture of **6**. The selectivity of radical addition is apparently independent of chain length at the stage of $n = 2$ or $n = 3$.

The telomer product distribution can be controlled by the ratio of $BrCCl_3$ and the acrylamide used in the telomerization. This is apparent from the data presented in Table I where the product distribution for three different feed ratios is presented. For these experiments, where the telomerization was carried to greater than 95% completion based upon the limiting reagent, smaller telomers are favored when a higher $BrCCl_3$:acrylamide ratio is utilized. For example, a 10:1 ratio of $BrCCl_3$:acrylamide gives nearly 80% of the product mixture as $n = 1$ and $n = 2$ telomers, while these two compounds amount to only 40% of the mixture when the feed ratio is 1:1. The scheme for $BrCCl_3$ chain transfer telomerization is presented in Scheme II. Trichloromethyl radical is generated by photolysis and initiates the chain by addition to the acrylamide. The telomer length is defined by a ratio of the rate constants $k_{tr,n}/k_{g,n}$, the ratio of chain transfer to chain growth.

Chain transfer constants were determined at 0 °C in experiments carried out with 8 different feed ratios in which the reaction was kept to less than 10% (determined by gas chromatography monitoring of the starting acrylamide). Under these conditions the feed ratio is essentially constant during the course of the reaction, and R, the feed ratio, can be taken as the molar ratio at the start of the reaction.[27] Chain-transfer coefficients were calculated by using gel permeation chromatography peak height data with an in-house program based on the method of Vaidya.[15] These data were used to make plots of Ht_n/Ht_{n+1} (GPC peak height) vs R (molar feed ratio), from which C_2–C_5 were calculated.[28] It proved extremely difficult to accurately measure the amount of the $n = 1$ telomer in the reaction mixtures, especially at low feed ratios. This was due to both the small amount of telomer present and its proximity to starting materials in the chromatograms. The difficulty in measuring the amount of the $n = 1$ telomer made it very difficult to calculate C_1, but we estimate a value of ~0.03 for this chain transfer constant. Values determined for chain-transfer constants C_2–C_5 were as follows: $C_2 = 0.29 \pm 0.04$; $C_3 = 0.39 \pm 0.03$; $C_4 = 0.55 \pm 0.07$; and $C_5 = 0.50 \pm 0.17$.

We conclude that significant acyclic stereoselectivity is possible from addition of α amide radicals to alkenes or in halogen atom transfer reactions of these radicals. Acrylamides derived from chiral 2,5-dimethylpyrrolidine telomerize efficiently when photolyzed in the presence of $BrCCl_3$, and the ratio of rate constants for bromine-atom abstraction from $BrCCl_3$ to the rate constant for chain growth is on the order of 0.5 for telomers with $n > 3$. These data suggest that chiral amides may prove to be useful auxiliaries in the free-radical vinyl polymerization, and we are currently exploring this possibility.

Experimental Section

Tetrahydrofuran was freshly distilled from sodium benzophenone. Dichloromethane was distilled from calcium hydride and stored over molecular sieves. Gas chromatography was done on a Hewlett-Packard 5890A gas chromatograph with a flame-ionization detector coupled to a Hewlett-Packard 3393A integrator (conditions: 30-m SPB-1 column, 11 psi, 3 min at 100 °C to 280 °C at 15 °C/min). ^1H and ^{13}C NMR were run on either a Varian XL-300 or a General Electric QE-300 (TMS as internal standard). Mass spectra were acquired on either a VG 70-250 or an HP-5990. Flash chromatography was carried out with EM silica gel, 30–60-μm size. Analytical HPLC was performed on a Waters Model 600E gradient system with two tandem Beckman Ultrasphere Si (5 μ, 4.6 × 25 cm) columns using UV detection (Waters 441 UV detector). Preparative HPLC was done on a Waters 600E gradient system with a Dynamax 60A Si 83-121-C column and a UV detector. Gel permeation chromatography was done on a Waters Model 600E gradient system with two tandem Waters Ultrastyragel columns (8 μ, 500A, 100A, 7.8 × 300 mm). Melting points are uncorrected.

Syntheses. (2*R*,5*R*)-1-Acryloyl-2,5-dimethylpyrrolidine (3). The pyrrolidine salt[29,30] (0.701 g, 5.17 mmol) and 1,1,3,3-tetramethylguanidine (1.12 g, 10.24 mmol) were stirred at 0 °C for 30 min and then acryloyl chloride (0.508 g, 5.61 mmol) was slowly added. The resulting solution was stirred at 0 °C for an additional 2 h and then washed with 1 N HCl (2 × 5 mL) and a brine solution (1 × 10 mL). The organic phase was dried over $MgSO_4$. The solvent was removed and the residue was loaded directly onto a flash column (5 g of Si) and eluted with at first 10% ethyl acetate/hexane (50 mL) and then 30% ethyl acetate/hexane (50 mL), by which time all the acrylamide had eluted from the column. This provided 473 mg (61% yield) of pure product. The acrylamide was dissolved in 9 mL of benzene and then stored at −78 °C: ^1H NMR δ 6.48 (1 H, dd, 16.8 Hz, 9.5 Hz), 6.39 (1 H, dd, 16.7 Hz, 2.4 Hz, CH_2=C), 5.56 (1 H, dd, 9.5 Hz, 2.4 Hz, CH_2CH), 4.34 (1 H, quintet, 6.6 Hz, NCH), 4.16 (1 H, quintet, 6.6 Hz, NCH), 2.18 (2 H, m, NCH(CH3)CH_2), 1.61 (2 H, m, NCH(CH_3) CH_2CH_2), 1.22 (3 H, d, 6.4 Hz, CH_3), 1.18 (3 H, d, 6.6 Hz, CH_3); ^{13}C NMR δ 164.30 (C=O), 129.52 (C=C—C=O), 126.90 (C=C—C=O), 53.34, 53.20 (NCH(CH_3)CH_2), 30.73, 28.85 (NCH(CH_3)CH_2), 22.30, 19.15 (NCH(CH_3)CH_2); IR (film) 2955, 1645, 1610, 1425 cm^{-1}. Anal. Calcd for $C_9H_{15}ON$: C, 70.54; H, 9.87. Found: C, 70.40; H, 9.90.

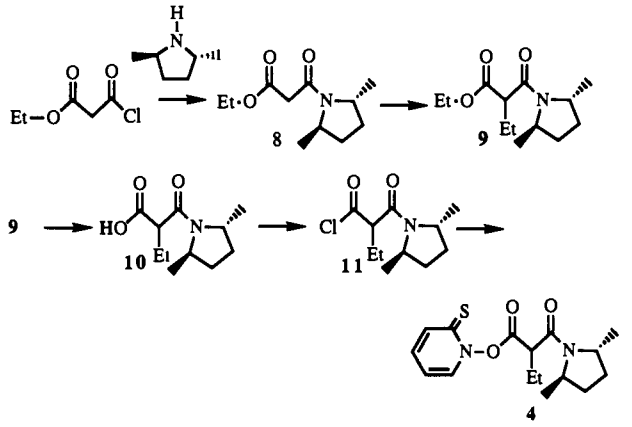
Bromo Amide 1a. The 2,5-dimethylpyrrolidine was liberated by dissolving the 2,5-dimethylpyrrolidine hydrochloride salt in dichloromethane and washing twice with sodium hydroxide (5 M). The organic layer was dried over potassium hydroxide pellets for 30 min.

To a stirring mixture of 2,5-dimethylpyrrolidine (0.73 g, 7.4 mmol) in dichloromethane (25 mL) and 1,1,3,3-tetramethylguanidine (0.85 g, 7.4 mmol) at 0 °C was added dropwise 2-bromobutyryl chloride (1.24 g, 6.7 mmol) as a solution in dichloromethane. After the addition was completed, the mixture was stirred at room temperature for 3 h. The organic layer was washed twice with dilute hydrochloric acid, dried over sodium sulfate, and concentrated to yield an oil. Purification by column chromatography (gradient elution, petroleum ether/ether, 75/25) gave the bromo amide **1a** as a diastereomeric mixture, 1.3 g, 83%. The diastereomers were separated by preparative HPLC, with a 3% 2-propanol, 97% hexane elution at 8 mL/min. The major and minor isomer eluted at 23 and 30 min, respectively: R_f 0.4 petroleum ether/ether, 1/1; GC major, minor, 6.2, 7.2 min. A single-crystal X-ray analysis established the configuration of the stereoisomers (Figure 3). The major isomer is designated *R*-**1a**, the minor isomer, *S*-**1a**.

(2*R*,5*R*,2′*R*)-*trans*-2,5-Dimethyl-1-(1′-oxo-2′-bromobutyl)pyrrolidine (*R*-1a): ^1H NMR δ 4.14 (2 H, t, 7.2 Hz, CHBr, m, NCH), 3.99 (1 H,

(27) Barson, C. A.; Luxton, A. R.; Robb, J. C. *Trans. Faraday Soc.* **1972**, *68*, 1666.
(28) Barson, C. A.; Mather, R. R.; Robb, J. C. *Trans. Faraday Soc.* **1970**, *66*, 2585.
(29) Schlessinger, R. H.; Iwanowicz, E. J. *Tetrahedron Lett.* **1987**, *28*, 2083.
(30) Harding, K. E.; Burks, S. R. *J. Org. Chem.* **1981**, *46*, 3920.

Scheme III. Synthetic Route to Barton Ester **4**



quintet, 6.6 Hz, NCH), 2.21–1.86 (4 H, m, NCH(CH_3)CH_2, CH_2CH$_3$), 1.55–1.44 (2 H, m, NCH(CH_3)CH$_2$CH_2), 1.08 (6 H, 2 d, 6.6 Hz, CH_3), 0.90 (3 H, t, 7.3 Hz, CH$_2$CH_3); ^{13}C NMR δ 167.24 (C=O), 53.53, 53.17 (NCH(CH_3)CH$_2$), 47.80 (CHBr), 30.65, 28.94, 27.71 (NCH(CH_3)CH_2, CH_2CH$_3$), 23.38, 17.45, 13.38 (CH_3); IR (film) 2950, 1635 cm^{-1}; MS (CI) 250 (97%), 248 (100) MH$^+$, 172 (0.2), 170 (11) -Br; HR (CI) MH$^+$ calcd 248.0645, found 248.0645. Anal. Calcd for $C_{10}H_{18}OBrN$: C, 48.38; H, 7.31. Found: C, 48.23; H, 7.28.

(2*R*,5*R*,2′*S*)-*trans*-2,5-Dimethyl-1-(1′-oxo-2′-bromobutyl)pyrrolidine (*S*-1a): ^{1}H NMR δ 4.21 (2 H, m, CHBr, NCH), 4.22 (1 H, quintet, 6.6 Hz, NCH), 2.18–1.87 (4 H, m, NCH(CH_3)CH_2, CH_2CH$_3$), 1.57–1.43 (2 H, m, NCH(CH_3)CH$_2$CH_2), 1.18 (3 H, d, 6.4 Hz, CH_3), 1.07 (3 H, d, 6.4 Hz, CH_3), 0.86 (3 H, t, 7.3 Hz, CH$_2$CH_3); ^{13}C NMR δ 167.51 (C=O), 54.24, 53.97 (NCH(CH_3)CH$_2$), 47.78 (CHBr), 31.11, 29.90, 28.75 (NCH(CH_3)CH_2, CH_2CH$_3$), 21.21, 18.93, 12.04 (CH_3); IR (film) 2950, 1635 cm^{-1}; MS (CI) 250 (97%), 248 (100) MH$^+$, 172 (0.2), 170 (14) -Br; HR (CI) MH$^+$ calcd 248.0645, found 248.0645. Anal. Calcd for $C_{10}H_{18}OBrN$: C, 48.38; H, 7.31. Found: C, 48.13; H, 7.39.

Iodo Amide 1b. The bromo amide **1a** (0.59 g, 2.4 mmol) and sodium iodide (1.96 g, 13.1 mmol) were refluxed in acetone (30 mL) for 2 h. The crude solution was washed with sodium thiosulfate, and the organic layer was dried over magnesium sulfate and reduced to an oil. Purification by column chromatography (petroleum ether/ether, 1/1 elution) yielded a diastereomeric mixture of iodo amide **1b** as a colorless oil, 0.65 g, 93%. The diastereomers were separated by preparative HPLC, with a 3% 2-propanol, 97% hexane elution at 8 mL/min. The major **1b** isomer was obtained as an oil and the minor isomer **1b** as a white crystalline solid, mp 76–78 °C. The major and minor isomers eluted at 23 and 28 min, respectively: R_f 0.4 petroleum ether/ether, 1/1; GC major, minor, 7.0, 7.6 min. A single-crystal X-ray analysis established the configuration of the stereoisomers. The major isomer is designated *R*-**1b**, the minor isomer, *S*-**1b**.

(2*RS*,5*RS*,2′*RS*)-*trans*-2,5-Dimethyl-1-(1′-oxo-2′-iodobutyl)-pyrrolidine (*R*-1b): ^{1}H NMR δ 4.25 (1 H, t, 7.4 Hz, CHI), 4.20 (1 H, quintet, 6.5 Hz, NC*H*(CH_3)CH$_2$), 3.90 (1 H, quintet, 6.6 Hz, NCH), 2.12 (4 H, m, CH_3CH_2, NCH(CH_3)CH_2), 1.56 (2 H, m, NCH(CH_3)CH$_2$CH_2), 1.18 (3 H, d, 6.4 Hz, CH_3), 1.09 (3 H, d, 6.7 Hz, CH_3), 0.92 (3 H, t, 7.3 Hz, CH_3CH$_2$); ^{13}C NMR δ 168.47 (C=O), 53.44 (NCH-(CH_3)CH$_2$), 30.53, 29.25, 28.86 (CH_3CH_2, NCH(CH_3)CH_2), 26.41, 23.12, 16.31, 14.29 (CH_3); IR (film) 2950, 1625 cm^{-1}; MS (CI) 296 (MH$^+$), 168. Anal. Calcd for $C_{10}H_{18}ONI$: C, 40.67; H, 6.15. Found: C, 40.80; H, 6.21.

(2*RS*,5*RS*,2′*SR*)-*trans*-2,5-Dimethyl-1-(1′-oxo-2′-iodobutyl)-pyrrolidine (*S*-1b): ^{1}H NMR δ 4.38 (1 H, dd, 6.7 Hz, CHI), 4.24 (1 H, quintet, 6.5 Hz, NCH), 4.03 (1 H, quintet, 6.6 Hz, NCH), 2.11 (4 H, m, CH_2CH$_3$, NCH(CH_3)CH_2), 1.58 (2 H, m, NCH(CH_3)CH$_2$CH_2), 1.26, 1.16 (6 H, 2d, 6.3 Hz, CH_3); ^{13}C NMR δ 168.96 (C=O), 54.39, 54.22 (NCH(CH_3)CH$_2$), 31.84, 31.23, 28.83 (CH_3CH_2, NCH(CH_3)-CH_2), 26.08, 20.51, 19.01, 13.91 (CH_3); IR (film) 2950, 1625 cm^{-1}; MS (CI) 296 (100%) MH$^+$, 170 (16), 168 (16). Anal. Calcd for $C_{10}H_{18}ONI$: C, 40.67; H, 6.15. Found: C, 40.78; H, 6.20.

Barton ester **4** was prepared by the approach outlined in Scheme III.

(2*RS*,5*RS*)-*trans*-2,5-Dimethyl-1-[1′,3′-dioxo-3′-ethoxypropyl]-pyrrolidine (8). To a stirring mixture of 2,5-dimethylpyrrolidine (1.3 g, 13 mmol) in dichloromethane (50 mL) and 1,1,3,3-tetramethylguanidine (1.6 g, 14 mmol) at 0 °C was added dropwise ethyl malonyl chloride (2.4 g, 16 mmol). After the addition was completed the mixture was stirred at room temperature for 3 h. The organic layer was washed twice with dilute hydrochloric acid, dried over sodium sulfate and concentrated to yield an oil. Purification by column chromatography (50% petroleum ether/50% ether elution) yielded the malonylamide as a colorless oil, 2.0 g, 73%: R_f 0.6 ether, GC 7.5 min; ^{1}H NMR δ 4.27 (2 H, q, 7.1 Hz, CH_3CH_2O, 1 H, m, NCH), 4.05 (1 H, quintet, 6.6 Hz, NCH), 3.45 (2 H, 2 d, 15.1 Hz, 14.9 Hz, COCH$_2$CO), 2.23 (2 H, m, NCH(CH_3)CH_2), 1.64 (2 H, m, NCH(CH_3)CH$_2$CH_2), 1.32 (3 H, t, 7.1 Hz, OCH$_2$CH_3), 1.24 (6 H, d, 6.3 Hz, CH_3); ^{13}C NMR δ 167.70 (C(=O)N), 164.10 (C(=O)O), 61.10 (OCH$_2$CH$_3$), 54.00, 53.29 (NCH(CH_3)CH$_2$), 42.14 (COCH$_2$CO), 30.66, 28.99 (NCH(CH_3)CH_2), 21.60, 18.59, 13.95; IR (film) 2950, 1740, 1640 cm^{-1}; MS (EI) 213 (M$^+$), 198 (M$^+$ - CH3), 98, 84; HR (CI) MH$^+$ calcd 214.1443, found 214.1446, error 1.3 ppm. Anal. Calcd for $C_{11}H_{19}O_3N$: C, 61.93; H, 8.98. Found: C, 61.80; H, 8.98.

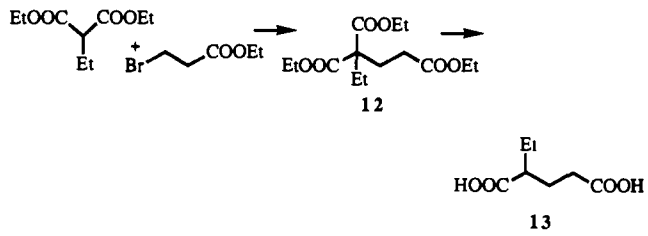
(2*RS*,5*RS*)-*trans*-2,5-Dimethyl-1-[1′,3′-dioxo-2′(*RS*/*SR*)-2′-ethyl-3′-ethoxypropyl]pyrrolidine (9). A potassium hydride dispersion in oil was washed with hexane three times to remove the mineral oil. Traces of hexane were removed under reduced pressure. The malonylamide **8** (1.46 g, 6.8 mmol) was added dropwise as a solution in dimethoxyethane (10 mL) to a stirring suspension of potassium hydride (0.41 g, 1.0 mmol) in dimethoxyethane (30 mL) at 0 °C. The mixture was stirred for 1 h while the mixture was allowed to warm up to room temperature. On recooling with ice, ethyl iodide (1.2 g, 7.5 mmol) was added dropwise. The mixture was stirred and allowed to warm up over a period of 2 h. Saturated ammonium chloride solution was added, and the layers were separated. The aqueous layer was extracted twice with ether. The combined organic layers were dried and concentrated to an oil. Column chromatography (gradient elution, 80% petroleum ether, 20% ether) yielded a diastereomeric mixture of the alkylated ester as a pale yellow oil, 1.27 g, 77%: R_f 0.7, 0.6 ether; GC 7.9, 8.2 min; ^{1}H NMR δ 4.18 (4 H, m, CH_3CH_2O, NCH), 3.42 (1 H, dd, 6.7 Hz, 7.3 Hz, COC*H*(Et)-CO), 2.10 (4 H, m, NCH(CH_3)CH_2, CH_2CH$_3$), 1.62 (2 H, m, NCH-(CH_3)CH$_2$CH_2), 1.25 (6 H, 4 d, 6.3 Hz, CH_3, 3 H, 2 t, 7.2 Hz, OCH$_2$CH_3), 0.98 (3 H, 2 t, 7.4 Hz, CH$_2$CH_3); ^{13}C NMR δ 169.99 (C(=O)N), 167.92 (C(=O)O), 60.91 (CH_3CH$_2$O), (54.11, 53.34), (53.26, 53.18), (52.09, 51.89) (NCH(CH_3)CH$_2$), (30.78, 30.63), (28.98, 28.96) (NCH(CH_3)CH$_2$), (23.47, 22.43), (21.79, 21.76), 18.76, 18.14), (14.04, 14.00), (12.15, 11.60); IR (film) 2950, 1745, 1645 cm^{-1}; MS (CI) 242 (MH$^+$), 228, 196; HR (CI) MH$^+$ calcd 242.1756, found 242.1755, error 0.5 ppm. Anal. Calcd for $C_{13}H_{23}O_3N$: C, 64.69; H, 9.61. Found: C, 64.52; H, 9.55.

(2*RS*,5*SR*)-*trans*-2,5-Dimethyl-1-[1′,3′-dioxo-2′(*RS*/*SR*)-2′-ethyl-3′-hydroxypropyl]pyrrolidine (10). To a stirring solution of the ester **9** (1.2 g, 4.9 mmol) in THF (25 mL) was added dropwise 2 M lithium hydroxide solution (8 mL). The mixture was allowed to stir at room temperature for 3 h. The solution was acidified with concentrated sulfuric acid and extracted with ether. The organic layers were combined and dried to yield a white crystalline solid, 1.02 g, 97%: mp 71–73 °C, R_f 0.1 ether; ^{1}H NMR δ 11.47 (1 H, s, OH), 4.19 (2 H, 4 quintets, 6.6 Hz, NCH), 3.36 (1 H, t, 6.8 Hz; dd, 5.4 Hz, COC*H*(Et)CO), 2.21 (2 H, m, NCH(CH_3)CH_2), 2.00 (2 H, m, CH_2CH$_3$), 1.68 (2 H, m, NCH-(CH_3)CH$_2$CH_2), 1.22 (6 H, 4 d, 6.8 Hz, CH_3), 1.07 (3 H, 2 t, 7.6 Hz, CH$_2$CH_3); ^{13}C NMR δ 171.95 (C(=O)N), 170.81 (C(=O)O), (54.63, 54.12), (54.27, 53.91) (NCH(CH_3)CH$_2$), 49.72 (COCH(Et)CO), (30.86, 30.50), (29.03, 28.70) (NCH(CH_3)CH_2), (27.30, 26.47), (22.09, 21.96), (18.62, 18.44), (11.81, 11.24); IR (film) 3445, 2950, 1725, 1635 cm^{-1}; MS (CI) 170 (MH$^+$ - CO$_2$). Anal. Calcd for $C_{11}H_{19}O_3N$: C, 61.93; H, 8.98. Found: C, 61.84; H, 9.00.

(2*RS*,5*SR*)-*trans*-2,5-Dimethyl-1-[1′,3′-dioxo-3′-chloro-2′(*RS*/*SR*)-2′-ethylpropyl]pyrrolidine (11). The amide acid **10** (0.21 g, 1 mmol) was refluxed in dichloromethane (5 mL) and thionyl chloride (0.24 g, 2 mmol) for 90 min. The reaction was monitored by IR. Excess thionyl chloride and dichloromethane were removed under reduced pressure to yield a pale brown crystalline solid, 0.19 g, 84%, as a mixture of diastereomers: ^{1}H NMR δ 4.09 (2 H, m, NCH), 3.36, 3.28 (1 H, t, 6.8 Hz; dd, 4.9 Hz, COCH), 2.14 (2 H, m, NCH(CH_3)CH_2), 1.93 (2 H, m, CH_2CH$_3$), 1.64 (2 H, m, NCH(CH_3CH$_2$CH_2), 6 H, 4 d, 6.6 Hz, CH_3), 1.07 (3 H, 2 t, 7.3 Hz, CH$_2$CH_3); IR (film) 2950, 1800, 1625 cm^{-1}.

Barton Ester 4. Mercaptopyridine 1-oxide sodium salt (0.14 g, 0.9 mmol) was added in one portion to a stirring solution of acid chloride **11** (0.19 g, 0.8 mmol) in dichloromethane (4 mL). The mixture was stirred at room temperature for 3 h in the dark. The crude mixture was concentrated and the residue was purified quickly by column chromatography (ether elution). A bright yellow crystalline solid was obtained, 0.23 g, 86%, as a mixture of diastereomers. The Barton ester was stored as a benzene solution at −78 °C: R_f 0.4 ethyl acetate; ^{1}H NMR δ 7.65, 7.25, 6.66 (4 H, m, aromatic), 4.59, 4.33, 4.12 (2 H, 3 quintets, 6.6 Hz, NCH), 3.98, 3.91 (1 H, t, 7.2 Hz; dd, 6.4 Hz, OCH), 2.31–1.99 (4 H, m, NCH(CH_3)CH_2, CH_2CH$_3$), 1.67 (2 H, m, NCH(CH_3)CH$_2$CH_2), 1.46, 1.26 (6 H, 4 d, 6.3 Hz, CH_3), 1.12 (3 H, 2 t, 7.4 Hz, CH$_2$CH_3); ^{13}C NMR δ (166.64, 165.86) (C=O), (165.74, 164.81) (C=O), (138.06, 137.62), (137.19, 137.01), 133.82 (122.84, 112.64), (54.67, 53.96),

Scheme IV. Synthetic Route to 2-Ethylglutaric Acid



12

13

(50.32, 49.95) ((NCH(CH$_3$)CH$_2$), (30.80, 30.70), (30.53, 29.14), (23.21, 22.67) (NCH(CH$_3$)CH$_2$, CH$_2$CH$_3$), (22.27, 22.06), (18.72, 18.10), (12.10, 11.31) (CH$_3$).

The synthetic approach to 2-ethylglutaric acid is outlined in Scheme IV. The synthesis of this acid was based on the approach of Kornfeld, Jones, and Parke,[31] and the resolution of the acid was analogous to the approach of Berner and Leonardsen.[32]

Diethyl 2-Ethyl-2-(ethoxycarbonyl)glutarate (12). Diethyl ethylmalonate (13 g, 0.07 mol) and ethyl 3-bromopropionate (5.6 g, 0.06 mol) were added dropwise as a mixture to a suspension of sodium hydride (2.6 g, 0.1 mol) in THF (150 mL) at room temperature. After the addition was completed the mixture was refluxed for 5 h. The crude mixture was filtered and the filtrate was washed with water, dried, and concentrated to yield 12.9 g, 63% of the triester **12** as a colorless oil: ^{1}H NMR δ 4.06 (6 H, m, OCH$_2$CH$_3$), 2.14 (4 H, m, CH$_2$CH$_2$), 1.83 (2 H, 2 q, 7.6 Hz, CH$_2$CH$_3$), 1.16 (9 H, 2 t, 7.1 Hz, OCH$_2$CH$_3$), 0.76 (3 H, 2 t, 7.6 Hz, CH$_2$CH$_3$); ^{13}C NMR δ 172.30 (C=O), 170.70 (C=O), 60.64, 59.96, 56.67 (OCH$_2$CH$_3$), 28.98, 26.52, 25.33 (CH$_2$) 13.64, 13.53, 7.89 (CH$_3$); IR (film) 2950, 1720 cm^{-1}; MS (CI) 289 (100) MH$^+$, 243 (29).

2-Ethylglutaric Acid (13). To the triester **12** (45.3 g, 0.16 mol) was added 5.5 M hydrochloric acid (330 mL). The mixture was refluxed for 20 h. The acid/water mixture was distilled off at atmospheric pressure. The resulting residue was dissolved in dichloromethane, dried, and concentrated. The crude product was recrystallized from petroleum ether and benzene. The diacid **13**, 19.3 g, was obtained in 83% yield: mp 55–57 °C; ^{1}H NMR δ 2.40 (1 H, t, 7.2 Hz, CHEt), 2.32 (2 H, m, OCCH$_2$), 1.93–1.44 (4 H, m, CH$_2$CH$_3$, CH(Et)CH$_2$), 0.91 (3 H, t, 7.4 Hz, CH$_2$CH$_3$); ^{13}C NMR δ 181.72 (C=O), 179.24 (C=O), 45.68 (CH), 31.37, 25.71, 24.56 (CH$_2$), 11.06 (CH$_3$); IR (film) 2950, 1700 cm^{-1}; MS (CI) 161 (46) MH$^+$, 143 (100), 115 (35).

Resolution of 2-Ethylglutaric Acid (13). Racemic glutaric acid **13** (10 g), strychnine (20.9 g), and water were mixed. The mixture was heated until the reactants dissolved and on cooling the (+)-glutaric acid strychnine salt crystallized. The salt was filtered off and recrystallized twice from hot water. Water and ammonium hydroxide solution were added to the (+) salt. The precipitated strychnine was filtered off and the filtrate acidified and extracted with ether. The (−) salt from the first filtration was treated with ammonium hydroxide, the strychnine removed, and the filtrate removed and extracted with ether. The (+)-(*S*)-2-ethylglutaric acid (*S*-**13**) was 66% optically pure (83:17) and the (−)-(*R*)-2-ethylglutaric acid (*R*-**13**) was 34% optically pure. Coupling of partially resolved 2-ethylglutaric acid with optically pure 2,5-dimethylpyrrolidine gave the diamides that were separated (isopropyl alcohol/hexane gradient) and fully characterized. Spectral data for the telomers **5** are given below.

1,1′-[(2′*S*)-2′-Ethylglutaryl]bis[(2*R*,5*R*)-*trans*-2,5-dimethylpyrrolidine] (2*S*-5 (*n* = 2)): ^{1}H NMR δ 4.27 (2 H, quintet, 6.4 Hz, NCH), 4.09 (1 H, quintet, 6.4 Hz, NCH), 3.96 (1 H, quintet, 6.4 Hz, NCH), 2.58 (1 H, m, CHEt), 2.41–1.96, 1.87–1.36 (14 H, NCH(CH$_3$)CH$_2$CH$_2$, COCH$_2$CH$_2$CHCH$_2$CH$_3$), 1.18 (12 H, 4 d, 6.4 Hz, CH$_3$), 0.96 (3 H, t, 7.4 Hz, CH$_2$CH$_3$); ^{13}C NMR δ 174.46 (C=O), 171.07 (C=O), 53.67, 53.19, 52.97 (NCH(CH$_3$)CH$_2$), 43.87 (CHEt), 31.47, 30.97, 30.93, 28.99, 28.96, 28.62 (NCH(CH$_3$)CH$_2$, COCH$_2$CH$_2$), 25.47 (CH$_2$CH$_3$), 22.46, 21.49, 19.21, 19.18, 12.19 (CH$_3$); IR (film) 2950, 1630 cm^{-1}; MS (CI) 323 (100) MH$^+$, 224 (39), 98 (12); HR (CI) MH$^+$ calcd 323.2698, found 323.2689, error 3.0 ppm; $[\alpha]^{20}_D$ −5.65° (*c* 0.17 CHCl$_3$).

1,1′-[(2′*R*)-2′-Ethylglutaryl]bis[(2*R*,5*R*)-*trans*-2,5-dimethylpyrrolidine] (2*R*-5 (*n* = 2)): ^{1}H NMR δ 4.29–4.12 (2 H, m, NCH), 4.05 (2 H, quintet, 6.6 Hz, NCH), 2.53 (1 H, m, CHEt), 2.43–1.50 (14 H, m, NCH(CH$_3$)CH$_2$CH$_2$, COCH$_2$CH$_2$CHCH$_2$CH$_3$) 1.16 (12 H, 4 d, 6.4 Hz, CH$_3$), 0.94 (3 H, t, 7.5 Hz, CH$_2$CH$_3$); ^{13}C NMR δ 174.07 (C=O), 171.45 (C=O), 53.44, 53.17, 53.00, 52.87 (NCH(CH$_3$)CH$_2$), 49.14, 44.07, 33.95, 32.70, 30.86, 30.82, 29.07, 28.95, 27.58, 27.07, 25.61, 24.94, 19.14 (CH$_3$); IR (film) 2950, 1630 cm^{-1}; MS (CI) 323 (100) MH$^+$; HR (CI) MH$^+$ calcd 323.2698, found 323.2692, error 2.0 ppm; $[\alpha]^{20}_D$ −15.0° (*c* 0.4 CHCl$_3$).

Hunsdiecker–Barton Decarboxylation. General Method for Reaction of Barton Ester 4 with Bromotrichloromethane. The carboxylic acid **10** (53 mg, 0.24 mmol) was dissolved in dichloromethane (5 mL) and treated with thionyl chloride (35 mL, 55.7 mg, 0.72 mmol) at reflux. When the reaction was complete (IR), the solvent was removed and the crystalline residue taken up in bromotrichloromethane (5 mL). This solution was then added dropwise to a refluxing suspension of *N*-hydroxypyridine-2-thione sodium salt (41 mg, 0.26 mmol) in the same solvent (5 mL). After 20 min, the mixture had turned dark brown and a granular precipitate had been deposited. The solvent was removed and the residue purified by chromatography (SiO$_2$, ether/petroleum, 1:3), affording the bromides **1a** as a clear oil (40 mg, 64%). ^{1}H and ^{13}C NMR spectra of the isolated products were identical with those described above. The diastereoisomeric ratio of the products in the crude mixture was determined to be 8:1 by GC analysis. Also isolated from this reaction was trichloromethyl 2-pyridyl sulfide (33.2 mg, 68%): ^{1}H NMR δ (CDCl$_3$) 8.8–8.7 (1 H, m), 7.90–7.79 (2 H, m), 7.48–7.40 (1 H, m).

In an alternative procedure, the acid chloride (28.5 mg, 0.123 mmol), prepared as above, was dissolved in bromotrichloromethane (1 mL) and added in one portion to a suspension of *N*-hydroxypyridine-2-thione sodium salt (25.0 mg, 0.148 mmol) in the same solvent (5 mL). This mixture was then protected from light and stirred for 4 h at room temperature. 4-(Dimethylamino)pyridine (1 mg, 0.008 mmol) was then added and the mixture irradiated for 2.5 h by a 300-W sunlamp. GC analysis after this time indicated the ratio of diastereoisomers of the bromide to be ca. 11:1. Chromatography (SiO$_2$, ether/petroleum ether, 1:3) gave the bromides as a mixture (18.0 mg, 59%) spectroscopically identical with that prepared above.

In an alternate procedure, the Barton ester **4**, prepared from the carboxylic acid **10** (54 mg, 0.23 mmol) as detailed above, was dissolved in bromotrichloromethane (5 mL) and irradiated at 0 °C by a 300-W sunlamp for 2.5 h. The bromide **1a** was formed as a mixture of diastereoisomers in a 17:1 ratio by GC. Chromatography (SiO$_2$, ether/petroleum ether 1:3) gave the bromides as a mixture (40 mg, 64%) spectroscopically identical with that prepared above.

General Method for Reaction of Barton Ester 4 with Iodoform. Barton ester **4** (25 mg, 0.07 mmol) and iodoform (33 mg, 0.08 mmol) in benzene (1 mL) (dichloromethane for low-temperature reactions) were irradiated with a 300-W sunlamp for 2 h. Typically the Barton ester **4** in benzene or dichloromethane (for low-temperature reactions) was irradiated for 2 h with 1.1 equiv of iodoform. The irradiation was carried out by a 300-W sunlamp positioned 30 cm from the reaction vessel. The reaction was purified by flash column chromatography (petroleum ether/ether, 1/1 elution) to give the iodo amide **1b** in 68% isolated yield.

BrCCl$_3$ Telomerization of (2*R*,5*R*)-1-Acryloyl-2,5-dimethylpyrrolidine (3). The acrylamide **3** (80.3 mg, 0.525 mmol), bromotrichloromethane (103.9 mg, 0.525 mmol), and dodecane (91.3 mg, 0.525 mmol, as an internal standard) were combined in an NMR tube and hexane (300 μL) was added. The solution was suspended in a jacketed vessel that was cooled to 6 °C. The sample was then irradiated for 50 min with a 450-W Hanovia medium-pressure mercury lamp. During the irradiation a white precipitate formed and the solution was filtered. The supernatant was irradiated for 40 additional min, by which time less than 1% of the acrylamide remained (as determined by GC analysis). The sample was again filtered and the solid material was collected and dissolved in CH$_2$Cl$_2$ and then separated by gradient HPLC and GPC.

6 *n* = 1 telomer: ^{1}H NMR δ 4.64 (1 H, dd, *J* = 8.25, 2.51 Hz, C(Br)H), 4.20 (dd, 1 H, *J* = 15.23, 8.25 Hz, CCl$_3$C(H)HCH), 4.22 (1 H, quintet, *J* = 6.75 Hz, NCH(CH$_3$)CH$_2$), 4.12 (1 H, quintet, *J* = 6.79 Hz, NCH(CH$_3$)CH$_2$), 3.24 (1 H, dd, *J* = 15.23, 2.51 Hz, CCl$_3$C(H)-HCH), 2.33–2.04 (2 H, m, NCH(CH$_3$)C(H)H), 1.71–1.52 (2 H, m, NCH(CH$_3$)C(H)H), 1.29 (3 H, d, *J* = 6.48 Hz, NCH(CH$_3$)CH$_2$), 1.15 (3 H, d, *J* = 6.48 Hz, NCH(CH$_3$)CH$_2$); ^{13}C NMR δ 165.53 (O=C), 96.79 (CCl$_3$), 57.40 (CH$_2$CCl$_3$), 54.06, 53.53 (NCH(CH$_3$)CH$_2$), 38.55 (C(H)Br), 30.84, 28.96 (NCH(CH$_3$)CH$_2$), 22.76, 17.11 (NCH(CH$_3$)C-H$_2$); MS (Cl. CH$_4$/NH$_3$) 351 (MH$^+$).

6 *n* = 2 telomer: ^{1}H NMR δ 4.63–4.35 (1 H, m, NCH(CH$_3$)CH$_2$), 4.32 (1 H, t, *J* = 7.39 Hz, C(Br)H), 4.25–4.15 (2 H, m, NCH(CH$_3$)-CH$_2$), 4.10–4.03 (1 H, m, NCH(CH$_3$)CH$_2$), 3.56–3.49 (1 H, dd, *J* = 15.02, 7.46, Hz, CCl$_3$C(H)HCH), 3.24–3.14 (1 H, m, CCl$_3$C(H)HCH), 2.78–2.72 (1 H, dd, *J* = 15.02, 3.95 Hz, CCl$_3$C(H)HCH), 2.56–2.34 (2 H, m, CCl$_3$C(H)HCHCH$_2$), 2.31–2.00 (4 H, m, NCH(CH$_3$)C(H)H), 1.66–1.49 (4 H, m, NCH(CH$_3$)C(H)H), 1.32–1.14 (12 H, 4 d, NCH-(CH$_3$)CH$_2$); ^{13}C NMR δ 170.66 (O=C (nearest to Br)), 166.20 (O=C (nearest to CCl$_3$)), 98.26 (CCl$_3$), 54.77 (CH$_2$CCl$_3$), 53.80, 53.73, 53.56, 53.48, (NCH(CH$_3$)CH$_2$), 42.60 (C(H)Br), 40.30 (CH), 37.56 (CH$_2$), 31.16, 30.78, 29.09, 28.90 (NCH(CH$_3$)CH$_2$), 23.31, 22.32, 18.74, 17.33

(31) Kornfeld, E. C.; Jones, R. G.; Parke, T. V. *J. Am. Chem. Soc.* **1949**, *71*, 150.

(32) Berner, E.; Leonardsen, R. *Liebigs Ann. Chem.* **1939**, *538*, 1.

($NCH(CH_3)CH_2$); IR 1637.73 (D<<bdO stretch), 1422.90 (C-N bending) cm^{-1}; MS (CI, CH_4/NH_3) 505 (MH^+); exact mass (CI) calcd for $C_{19}H_{31}O_2N_2Cl_3Br$ 505.0655, found 505.0602 (-2.4 ppm).

6 *n* = 3 telomer: ^1H NMR δ 4.44-4.35 (1 H, m, $NCH(CH_3)CH_2$), 4.34-4.28 (1 H, t, J = 7.39 Hz, C(Br)*H*), 4.25-4.14 (4 H, m, $NCH(CH_3)CH_2$), 3.98-3.90 (1 H, m, $NCH(CH_3)CH_2$), 3.36-3.28 (1 H, dd, J = 15.93, 6.00 Hz, $CCl_3C(H)HCH$), 3.23-3.14 (1 H, m, $CCl_3C(H)HCH$), 2.86-2.77 (1 H, dd, J = 15.93, 5.68 Hz, $CCl_3C(H)HCH$), 2.75-2.65 (1 H, m, CH), 2.40-2.29 (2 H, m, CH_2CHBr), 2.20-1.90 (6 H, m, $NCH(CH_3)C(H)H$), 1.66-1.49 (8 H, m, $NCH(CH_3)C(H)H$, CH_2), 1.32-1.14 (18 H, 4 d, $NCH(CH_3)CH_2$); ^{13}C NMR δ 172.02 (O=C), 171.22 (O=C (nearest to Br)), 166.65 (O=C (nearest to CCl_3)), 98.19 (CCl_3), 56.63 (CH_2CCl_3), 54.21, 54.14, 53.94, 53.89, 53.71, 53.51 ($NCH(CH_3)CH_2$), 44.71 (C(H)Br), 39.26 (CH), 38.80 (CH), 37.34 (CH_2), 35.60 (CH_2), 31.35, 31.13, 30.85, 29.18, 29.16, 29.01 ($NCH(CH_3)CH_2$), 25.52, 23.30, 22.59, 19.47, 19.00, 17.79 ($NCH(CH_3)CH_2$); IR 1636.52 (C=O stretch), 1422.63 (C-N bending) cm^{-1}; MS (CI, CH_4/NH_3) 658 (MH^+); exact mass (CI) calcd for $C_{28}H_{46}O_3N_3Cl_3Br$ 658.1768, found 658.1746 (-3.3 ppm).

6 *n* = 4 telomer: ^1H NMR δ 4.50-3.97 (9 H, m, $NCH(CH_3)CH_2$, CHBr), 3.41-3.35 (1 H, dd, J = 15.0, 6.17 Hz, $CCl_3C(H)HCH$), 3.20-3.17 (1 H, m, $CCl_3C(H)HCH$), 2.89-2.79 (1 H, dd, J = 15.0, 5.54 Hz, $CCl_3C(H)HCH$), 2.77-2.63 (1 H, m, CHC=O), 2.62-2.55 (1 H, m, CHC=O), 2.40-2.00 (10 H, m, $NCH(CH_3)C(H)H$, CH_2CHBr), 1.73-1.50 (12 H, m, $NCH(CH_3)C(H)H$, CH_2), 1.40-1.05 (24 H, md, $NCH(CH_3)CH_2$); ^{13}C NMR δ 172.61 (O=C), 172.35 (O=C), 171.41 (O=C (nearest to Br)), 166.48 (O=C (nearest to CCl_3)), 98.00 (CCl_3), 56.53 (CH_2CCl_3), 54.17, 53.91, 53.83, 53.79, 53.56, 53.43, 53.39, 53.31 ($NCH(CH_3)CH_2$), 44.93 (C(H)Br), 39.42 (CH), 38.80 (CH), 37.79 (CH), 37.39 (CH_2), 36.37 (CH_2), 36.01 (CH_2), 31.16, 30.92, 30.60, 29.03, 28.92, 28.89, 28.82, 28.78 ($NCH(CH_3)CH_2$), 19.46, 19.21, 19.11, 18.94, 18.18, 17.72, 17.68 ($NCH(CH_3)CH_2$); MS (CI, CH_4/NH_3) 811 (MH^+); exact mass (CI) calcd for $C_{37}H_{60}O_4N_4Cl_3Br$ 811.2921, found 811.29028 (-2.4 ppm).

6 *n* = 5 telomer: ^1H NMR δ 4.40-3.87 (11 H, m, $NCH(CH_3)CH_2$, CHBr), 3.26 (1 H, dd, J = 14.9, 5.73 Hz, $CCl_3C(H)HCH$), 3.20-3.08 (1 H, m, $CCl_3C(H)HCH$), 2.80 (1 H, dd, J = 14.9, 5.63 Hz, $CCl_3C(H)HCH$), 2.71-2.60 (1 H, m, CHC=O), 2.59-2.42 (2 H, m, CHC=O), 2.39-1.90 (2 H, m, $NCH(CH_3)C(H)H$), 1.75-1.45 (2 H, m, $NCH(CH_3)C(H)H$), 1.28-1.05 (30 H, md, $NCH(CH_3)CH_2$); ^{13}C NMR δ 172.73 (O=C), 172.62 (O=C), 172.52 (O=C), 171.39 (O=C (nearest to Br)), 166.40 (O=C (nearest to CCl_3)), 98.28 (CCl_3), 56.75 (CH_2CCl_3), 45.35 (C(H)Br), 39.42 (CH), 38.68 (CH), 37.80 (CH), 37.70 (CH), 37.52 (CH_2), 36.27 (CH_2), 36.45 (CH_2), 36.17 (CH_2); MS (CI, CH_4/NH_3) 964 (MH^+).

Removal of Halogens from the *n* = 2 Telomer with $[CH_3(CH_2)_3]_3SnH$. The **6** *n* = 2 telomer (12.6 mg, 0.025 mmol, 0.025 M) was dissolved in 1 mL of benzene; $(CH_3(CH_2)_3)_3SnH$ (69.8 mg, 0.24 mmol, 0.24 M) and AIBN (3 mg, 0.24 mmol, 0.24 M) were added, and the solution was heated under reflux for a total of 8 h. After 2 h an additional 2 mg of AIBN was added; this was repeated at 5 h and at this time an additional 30 μL of $(CH_3(CH_2)_3)_3SnH$ was added. After 8 h the benzene was removed under vacuum. The residue was taken up in 1.5 mL of *tert*-butyl methyl ether and 100 mg of KF was added. The resulting suspension was stirred at room temperature overnight and then filtered. The solvent was removed and the residue taken up in 20% 2-propanol/hexane and then analyzed by gradient HPLC (linear gradient from 0% to 75% 2-propanol/hexane at 0.8 mL/min) and purified by preparative HPLC (gradient similar to above but at 8 mL/min). The major product isolated in this way (3.6 mg, 45% yield, additional material used in chromatography increased the yield to >50%) was identical with the compound 2*S*-**5** (*n* = 2) prepared independently.

Removal of Halogens from the *n* = 3 Telomer with $[CH_3(CH_2)_3]_3SnH$. The **6** *n* = 3 telomer (9.6 mg, 0.015 mmol, 0.015 M) was dissolved in 1 mL of benzene; $(CH_3(CH_2)_3)_3SnH$ (69.8 mg, 0.24 mmol, 0.24 M) and AIBN (3 mg, 0.24 mmol), 0.24 M) were added, and the solution was heated under reflux for a total of 8 h. After 2 h an additional 2 mg of AIBN was added; this was repeated at 5 h and at this time an additional 30 μL of $(CH_3(CH_2)_3)_3SnH$ was added. After 8 h the benzene was removed under vacuum. The residue was taken up in 1.5 mL of *tert*-butyl methyl ether and 100 mg of KF was added. The resulting suspension was stirred at room temperature overnight and then filtered. The solvent was removed and the residue taken up in 20% 2-propanol/hexane and then analyzed by gradient HPLC (linear gradient from 0% to 75% 2-propanol/hexane at 0.8 mL/min) and purified by preparative HPLC (gradient similar to above but at 8 mL/min). The product isolated in this way, 2*S*,4*R*-**5** (*n* = 3), was identical with a compound prepared independently: ^1H NMR δ 4.46 (1 H, quintet, 6.6 Hz, $NCH(CH_3)CH_2$, 4.27 (3 H, m, $NCH(CH_3)CH_2$), 3.99 (2 H, m, $NCH(CH_3)CH_2$), 2.59 (1 H, m, CHEt), 2.53-1.44 (21 H, m, $NCH(CH_3)CH_2$, C(=O)CH_2C-H_2CHCH_2, CH_2CH_3), 1.24-1.16 (18 H, m, CH_3), 0.95 (3 H, t, 7.4 Hz, CH_2CH_3); ^{13}C NMR δ 174.21, 174.07, 170.66 (C=O), 53.58, 53.51, 53.25, 52.94, 52.90 ($NCH(CH_3)CH_2$), 42.12, 40.10 (C(=O)CHR), 35.06, 31.56, 31.07, 31.00, 30.92, 29.09, 28.99, 28.89, 28.53, 25.97 (CH_2), 22.49, 22.15, 21.47, 19.31, 19.24, 19.09, 12.11 (CH_3); MS (CI) 476 (MH^+) calcd 476.3851, found 476.3865, error 2.7 ppm; X-ray data previously published. Both GC and HPLC indicated a high isomeric purity >20:1.

Single-Crystal X-ray Analyses of 1a and 1b. Crystal data: **1a**, $C_{10}H_{18}BrNO$, MW = 248.17; monoclinic, space group $P2_1/c$; a = 12.120 (2) Å, b = 9.480 (1) Å, c = 10.682 (2) Å, β = 91.87 (2)° (from 25 orientation reflections, 30° < θ < 35°); V = 1226.7 (6) Å^3; Z = 4; d_{calcd} = 1.344 g cm^{-3}, μ (Cu Kα radiation, l = 1.5418 Å) = 43.3 cm^{-1}; crystal dimensions 0.10 × 0.22 × 0.60 mm; **1b**, $C_{10}H_{18}INO$, MW = 295.17; orthorhombic space group *Pbca*; a = 10.754 (1) Å, b = 24.066 (3) Å, c = 9.617 (1) Å (from 25 orientation reflections, 40° < θ < 45°); V = 2488.9 (8) Å^3; Z = 8; d_{calcd} = 1.575 g cm^{-3}; μ (Cu Kα) = 202 cm^{-1}; crystal dimensions 0.07 × 0.07 × 0.50 mm. Intensity data ($+h$, $+k$, $\pm l$, θ_{max} = 65°; 1948 nonequivalent reflections for **1a**; $+h$, $+k$, $+l$, θ_{max} = 75°, 2553 reflections for **1b**), recorded on an Enraf-Nonius CAD-4 diffractometer (Cu Kα radiation, graphite monochromator), were corrected for the usual Lorentz and polarization effects; an empirical absorption correction was applied to each data set and a linear decay correction (net loss 11%) was also made to the data for **1b**. Both crystal structures were solved by the heavy-atom approach.[33] Initial bromine- and iodine-atom coordinates were derived from Patterson maps. Weighted F_o and difference Fourier syntheses yielded approximate coordinates for the other non-hydrogen atoms; the methyl group of the bromopropyl moiety in **1a** was found to be disordered over two positions. Hydrogen atoms, except those associated with the disorder of the bromopropyl group in **1a**, were incorporated at their calculated positions in the full-matrix least-squares refinement of non-hydrogen atom positional and anisotropic thermal parameters. An extinction correction was added as a variable in the later least-squares cycles. The refinements converged at R = 0.083 (R_w = 0.115, GOF = 3.1)[34] for **1a** and R = 0.038 (R_w = 0.051, GOF = 1.4) for **1b** over 906 and 1232 reflections, respectively, with $I > 3.0\sigma(I)$. For structure-factor calculations, neutral atom scattering factors and their anomalous dispersion corrections were taken from ref 35. Final difference Fourier syntheses revealed no unusual features.

Supplementary Material Available: ORTEP diagrams and tables of crystallographic data, atomic positional and thermal parameters, and bond lengths and angles for **1a** and **1b** (11 pages); listings of observed and calculated structure factor amplitudes for **1a** and **1b** (16 pages). Ordering information is given on any current masthead page.

(33) Crystallographic calculations were performed on PDP11/44 and MicroVAX computers by use of the Enraf-Nonius Structure Determination Package (SDP).

(34) $R = S||F_o| - |F_c||/S|F_o|$; $R_w = [Sw(|F_o| - |F_c|)^2/Sw|F_o|^2]^{1/2}$; SwD^2 [$w = 1/s^2(|F_o|)$], $D = (|F_o| - |F_c|)$ was minimized; GOF (goodness-of-fit) = $[SwD^2/(N_{observations} - N_{parameters})]^{1/2}$.

(35) *International Tables for X-Ray Crystallography*; Kynoch: Birmingham, England, 1974; Vol. IV.