(C-4), 60.98, 59.59, 55.76 (OMe).

3-Deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*erythro*-hex-3-enofuranose (16): mp 50–51 °C (lit.[19] mp 50–52 °C); $[\alpha]^{20}_D$ = 23° (*c* 1.8, $CHCl_3$) [lit.[19] $[\alpha]_D$ = 21° (*c* 1)]; IR 1662 cm^{-1} (s); ^1H NMR δ 6.06 (d, 1 H, H-1, J_{12} = 5.1), 5.28 (dd, 1 H, H-2, J_{23} = 1.4), 5.23 (dd, 1 H, H-3, J_{35} = 1.2), 4.57 (ddd, 1 H, H-5, J_{56_a} = J_{56_b} = 6.2), 4.13 and 3.95 (d AB system, 2 H, H-6_a, H-6_b, J_{AB} = 6.7), 1.45, 1.43, 1.37 (3 H, s, Me); ^{13}C NMR δ 160.11 (C-4), 112.17, 110.22 (=C= isopropylidene), 108.64 (C-1), 98.99 (C-3), 83.39, 71.34 (C-2, C-5), 67.25 (C-6), 28.22, 27.92, 26.20, 25.51 (Me isopropylidene).

Reductions of Deoxy Halo Sugars by Zinc/Silver–Graphite. General Procedure. The reductions of the corresponding deoxy halo sugars (5.0 mmol) by zinc/silver–graphite (7.35 mmol) and workup of the reaction mixtures followed the same procedure as described for C_8K.

5,6-Dideoxy-2,3,4-tri-*O*-methyl-D-*xylo*-hex-5-enose (2): oil; $[\alpha]^{20}_D$ = 31.4° (*c* 1.7, $CHCl_3$); IR 1730 cm^{-1} (s); ^1H NMR δ 9.73 (s, 1 H, CHO), 5.83 (d X part of an ABX, 1 H, H-5, J_{45} = 7.8, J_{56_a} = 10.5, J_{56_b} = 14.9), 5.34 (AB part of the ABX, 2 H, H-6_a, H-6_b, J_{AB} = 16.0), 3.81 (dd, 1 H, H-3, J_{23} = 4.4, J_{34} = 7.8), 3.74 (d, 1 H, H-2), 3.54 (dd, 1 H, H-4), 3.49, 3.43, 3.24 (s, 3 H, OMe); ^{13}C NMR δ 201.12 (CHO), 134.81 (C-5), 119.07 (C-6), 84.38, 84.29, 81.83 (C-2, C-3, C-4), 60.37, 59.10, 56.54 (OMe).

6-*O*-Benzyl-4,5-dideoxy-2,3-di-*O*-methyl-L-*threo*-hex-4-enose (10): oil; $[\alpha]^{20}_D$ = 75.7° (*c* 4, $CHCl_3$); IR 1735 cm^{-1} (s); ^1H NMR δ 9.74 (d, CHO(*E*), $J_{CHO,2}$ = 1.4), 9.71 (d, CHO(*Z*), $J_{CHO,2}$ = 1.2), 7.25–7.38 (m, 5 H, Ph), 5.86–6.00 (m, 1 H, H-5), 5.75 (dd, H-4(*E*), J_{45} = 15.8, J_{34} = 7.2), 5.63 (dd, H-4(*Z*), J_{45} = 9.8, J_{34} = 9.4), 4.52 (s, 2 H, CH_2Ph), 4.35 (dd, H-3(*Z*), J_{23} = 4.0), 4.05–4.18 (m, 2 H, H-6_a, H-6_b), 4.01 (dd, H-3(*E*), J_{23} = 3.7), 3.61 (dd, H-2(*E*), $J_{2,CHO}$ = 1.4), 3.57 (dd, H-2(*Z*), $J_{2,CHO}$ = 1.2), 3.56, 3.51, 3.27, 3.22 (OMe, (*Z*) and (*E*)), *Z*:*E* = 1.1:1; ^{13}C NMR δ 202.91, 202.78 (CHO), 132.43, 132.39, 128.79, 128.65, 128.60, 128.13, 127.94, 127.88 (C-4, C-5, Ph), 88.07, 87.91 (C-2), 81.95, 77.12 (CH_2Ph), 72.89, 72.50 (C-3), 69.91, 66.09 (C-6), 59.71, 59.61, 57.20, 56.97 (OMe).

Methyl 6-*O*-benzyl-3,4-dideoxy-2-*O*-methyl-α-D-*erythro*-hex-3-enopyranoside (11): oil; $[\alpha]^{20}_D$ = −4.7° (*c* 3.0, $CHCl_3$); ^1H NMR δ 7.25–7.35 (m, 5 H, Ph), 5.82 and 5.76 (d AB system, 2 H, H-3, H-4, J_{AB} = 10.8, J_{45} = 1.2, J_{23} = 0.8), 5.03 (d, 1 H, H-1, J_{12} = 4.1), 4.63 and 4.58 (AB system, 2 H, CH_2Ph), 4.35 (ddd, 1 H, H-5, J_{56_a} = 2.7, J_{56_b} = 3.9), 3.98 (dd, 1 H, H-2), 3.52 (dd, 2 H, H-6_a, H-6_b), 3.52, 3.44 (s, 3 H, OMe); ^{13}C NMR δ 138.27, 128.57, 127.85, 127.58, 124.70 (C-3, C-4, Ph), 97.02 (C-1), 73.64, 73.41, 72.31, (C-2, C-5, CH_2Ph), 68.29 (C-6), 56.84, 56.12 (OMe).

3,4-Dideoxy-5,6-*O*-isopropylidene-D-*erythro*-hex-3-enitol (15): oil $[\alpha]^{20}_D$ = 31.3° (*c* 7.5, CH_2Cl_2); IR 3700–3080 cm^{-1} (b s); ^1H NMR δ 5.85 (dd, 1 H, H-4, J_{34} = 11.2, J_{45} = 6.0), 5.55 (dd, 1 H, H-3, J_{23} = 8.1), 4.47 (ddd, 1 H, H-2, J_{12} = 7.1, $J_{1a,2}$ = 5.8), 4.26 and 4.13 (d AB system, 2 H, H-1, H-1_a, J_{AB} = 13.2), 4.07 and 4.03 (d AB system, 2 H, H-6_a, H-6_b, J_{AB} = 6.3, J_{56_a} = J_{56_b} = 1.3), 3.93 (ddd, 1 H, H-5), 3.02, 2.4 (b s, 1 H each, OH, disappears on addition of D_2O), 1.44, 1.36 (s, 3 H, Me isopropylidene); ^{13}C NMR δ 132.62, 131.02 (C-3, C-4), 109.79 (=C= isopropylidene), 78.14, 68.31, 66.07, 58.57 (C-1, C-2, C-5, C-6), 26.53, 25.22 (Me isopropylidene).

4,5-Dideoxy-2,3-*O*-isopropylidene-D-*erythro*-pent-4-enonic acid (18): oil; $[\alpha]^{20}_D$ = −28° (*c* 10, acetone); IR 3600–2880 (b s), 1715 cm^{-1} (m); ^1H NMR δ 9.8 (b s, 1 H, COOH, disappears on addition of D_2O), 5.80 (X part of an ABX system, 1 H, H-4, J_{34} = 6.8, J_{45_a} = J_{45_b} = 15), 5.42 and 5.38 (AB part of the ABX system, 2 H, H-5_a, H-5_b, J_{AB} = 16), 4.86 (dd, 1 H, H-3, J_{23} = 6.7), 4.71 (d, 1 H, H-2), 1.63, 1.42 (s, 3 H, Me isopropylidene); ^{13}C NMR δ 174.18 (COOH), 136.69 (C-4), 119.74 (C-5), 111.42 (=C= isopropylidene), 78.55, 77.28 (C-2, C-3), 28.21, 25.39 (Me isopropylidene).

1,5-Anhydro-4,6-*O*-benzylidene-1,2-dideoxy-D-*ribo*-hex-1-enitol (20): mp 83–84 °C (lit.[17] mp 83.5 °C); $[\alpha]^{20}_D$ = 219° (*c* 3.2, ethanol) [lit.[17] $[\alpha]^{25}_D$ = 209.5° (*c* 2, ethanol)]; IR 3620–3200 (b s), 1635 cm^{-1} (s); ^1H NMR δ 7.25–7.40 (m, 5 H, Ph), 6.37 (d, 1 H, H-1, J_{12} = 6.0), 5.6 (s, 1 H, H benzylidene), 4.9 (dd, 1 H, H-2, J_{23} = 6), 4.2 (m, 2 H, H-3, H-5), 4.43 and 3.90 (d AB system, 2 H, H-6_a, H-6_b, J_{56_a} = 4.5, J_{56_b} = 9, J_{AB} = 11), 3.73 (dd, 1 H, H-4, J_{34} = 3, J_{45} = 9.5), 2.9 (b s, 1 H, OH, disappears on addition of D_2O); ^{13}C NMR δ 146.19 (C-1), 137.28, 129.42, 128.51, 126.42 (Ph), 101.85, 101.26 (C-2, C benzylidene), 78.25, 68.62, 64.01 (C-3, C-4, C-5), 60.11 (C-6).

Preparation of Bis(methyl 6-deoxy-2,3,4-tri-*O*-methyl-α-D-glucopyranosid-6-yl) (4). A solution of **1a** (1.04 g, 3 mmol) in anhydrous THF (20 mL) was droped into a suspension of magnesium–graphite (7.65 mmol) in THF (25 mL) at ambient temperature under argon, and the mixture was refluxed for 3 h. After cooling, filtration, washing of insolubles with THF (50 mL), and evaporation, column chromatography with toluene/ethyl acetate (3/1) as eluant yields **4** (0.45 g, 68%) and 0.05 g (8%) of methyl 6-deoxy-2,3,4-tri-*O*-methyl-α-D-*gluco*-pyranoside and only traces of **2**. **4**: mp 86–87 °C; $[\alpha]^{20}_D$ = 158° (*c* 1.1, $CHCl_3$); ^1H NMR δ 4.77 (d, 1 H, H-1, J_{12} = 3.6), 3.61, 3.54, 3.51, 3.39 (s, 3 H, OMe), 3.38–3.58 (m, 2 H, H-4, H-5), 3.17 (dd, 1 H, H-2, J_{23} = 9.7), 2.84 (dd, 1 H, H-3, J_{34} = 9.7), 1.89 (m, 1 H, H-6_a), 1.64 (m, 1 H, H-6_b); ^{13}C NMR δ 97.41 (C-1), 84.31, 83.79, 82.33 (C-2, C-3, C-4), 69.70 (C-5), 60.92, 60.73, 59.03, 55.18 (OMe), 27.52 (C-6).

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Synthesis and Reactivity of β-Lactones Derived from L-Threonine and Related Amino Acids

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The synthesis and nucleophilic ring opening of optically pure N-protected α-amino-β-alkyl β-lactones was investigated. Treatment of *N*-BOC-L-threonine (**8**) and *N*-BOC-L-*allo*-threonine (**9**) under modified Mitsunobu conditions (Ph_3P, dimethyl azodicarboxylate, −78 °C) gives stereospecific (anti) decarboxylative elimination to afford *N*-BOC-aminopropenes **10** and **11**, respectively, in contrast to cyclization of *N*-BOC-L-serine to its β-lactone under these conditions. However, the corresponding *N*-(phenylsulfonyl) derivatives **12**, **13**, and **16** cyclize to chiral β-lactones **14**, **15**, and **17**, respectively, in 40–55% yield by using carboxyl group activation by 4-bromobenzenesulfonyl chloride in pyridine. Nitrogen (pyrazole, benzylamine), oxygen (hydroxide, acetate), and carbon (EtMgCl, $CuBr{\cdot}SMe_2$) nucleophiles prefer to attack at the carbonyl carbon, in contrast to their reactions (except that of hydroxide) with β-butyrolactone and serine β-lactones. However, β-lactones **14**, **15**, and **17** are opened at the β-carbon with inversion of configuration by some sulfur (thiourea) and halogen (magnesium chloride, bromide, iodide) nucleophiles to N-protected optically pure β-substituted amino acids in good yield.

The importance of α-amino acids has prompted the recent development of numerous methods for their stereospecific synthesis.[1] In earlier work we have shown that N-protected derivatives **1** of serine can be cyclized under

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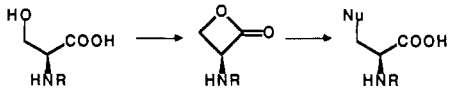
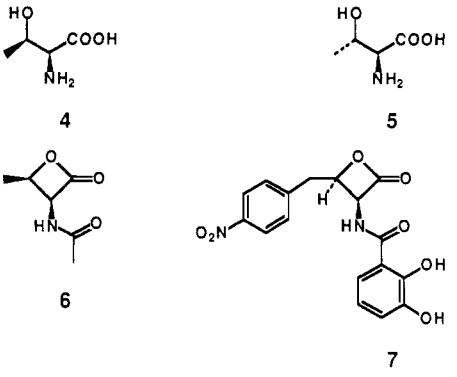
modified Mitsunobu conditions (Ph_3P, dialkyl azodicarboxylate, <−40 °C) to β-lactones **2**, which afford access to stereochemically pure α-amino acids **3** upon reaction



1 **2** **3**

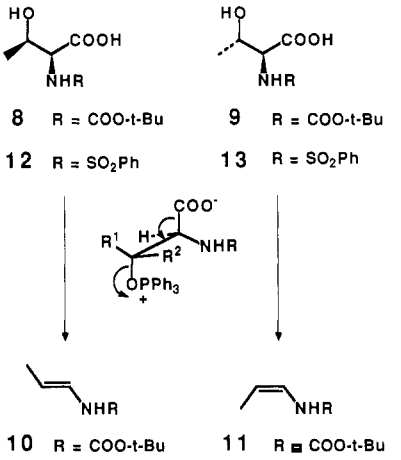
with a variety of carbon or heteroatom nucleophiles.[2] Since a large number of interesting amino acids bear two substituents at the β-carbon,[3] it appeared that analogous β-lactone formation from other β-hydroxy amino acids could provide a route to such substances with control of chirality at both centers. This approach seems especially promising because a number of methods for production of the enantiomerically pure hydroxy compounds have been developed.[4] In addition, the commercial availability of the pure L and D isomers of both threonine (**4**) and *allo*-threonine (**5**) suggests that many β-methyl amino acids not occur naturally[3a] or are useful tools for biochemical studies (e.g., β-halo-α-aminobutyrates[5]) might be easily obtained by this approach.



4 **5**

6 **7**

Interestingly, a number of β-substituted-α-amino β-lactone derivatives (e.g., *N*-acetyl-L-threonine β-lactone (**6**) and obafluorin (**7**) are microbial metabolites with antibiotic activity.[6] The combined presence of both a β-substituent and a protected α-amino group has hindered previous chemical syntheses of such lactones; usual cyclization yields are often 1% or less.[6b,7] In the present work we describe improved syntheses of optically pure N-protected β-lactones derived from **4**, **5**, and a related amino acid and examine the reactions of these lactones with several heteroatom and carbon nucleophiles.



8 R = COO-t-Bu **9** R = COO-t-Bu

12 R = SO_2Ph **13** R = SO_2Ph

10 R = COO-t-Bu **11** R = COO-t-Bu

Figure 1. Decarboxylative elimination of N-protected threonine and *allo*-threonine derivatives at −78 °C under Mitsunobu conditions.

Results and Discussion

Initial attempts to cyclize the *N*-(*tert*-butoxycarbonyl) (BOC) derivatives **8** and **9** of L-threonine and L-*allo*-threonine using the low temperature (−78 °C) Mitsunobu conditions that were successful for the corresponding serine derivatives[2a,d] gave only stereospecific decarboxylative anti elimination to form **10** (88%) and **11** (78%), respectively (Figure 1).[8] Since earlier experiments show that Mitsunobu cyclization of β-hydroxy acids bearing a protected α-amino substituent proceeds exclusively by hydroxyl group activation[2c] (in contrast to certain alkyl-substituted analogues[9]), it appears that replacement of hydrogen by methyl hinders nucleophilic displacement sufficiently to completely shift partitioning of the key phosphonium intermediate toward elimination. Hence a reagent that gives carboxyl group activation seemed essential.[7,10]

All attempts to cyclize N-protected threonine derivatives having a carbonyl group directly attached to nitrogen generated complex mixtures containing little if any desired product if carboxyl group activation was used, presumably because of competing oxazolinone (azlactone) formation.[7,11] The *N*-(phenylsulfonyl) derivatives[12] **12** and **13** were examined to prevent this involvement of the protecting group in the reaction. Although reaction of **12** with a large number of reagents commonly used for β-lactone formation[13,14] fails to produce significant amounts of the desired material, treatment with 4-bromobenzenesulfonyl chloride

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Table I. Nucleophilic Opening of β-Substituted β-Lactones 14, 15, and 17[a]

reactants	product[a,b]					% yield[c]
		R^3	R^4	X	Y	
14, thiourea	19	Me	H	$H_2N{=}C(NH_2)S^+$	O^-	70
14, LiSH	20	H	Me	HO	SH	84
14, NaSH	20	H	Me	HO	SH	86
14, NaOAc	21	H	Me	AcO	OH	
						51[d]
	22	Me	H	AcO	OH	
14, pyrazole	23	H	Me	HO	pyrazolyl	75
14, $PhCH_2NH_2$	24	H	Me	HO	$NHCH_2Ph$	72
14, EtMgCl, $CuBr{\cdot}SMe_2$	25	H	Me	HO	Et	30
	26					38
14, $MgBr_2{\cdot}Et_2O$	27	Me	H	Br	OH	99
15, $MgBr_2{\cdot}Et_2O$	28	H	Me	Br	OH	77
14, $MgI_2{\cdot}Et_2O$	29	Me	H	I	OH	83
14, $MgCl_2{\cdot}Et_2O$, Bu_4NCl	30	Me	H	Cl	OH	78
17,[e] $MgBr_2{\cdot}Et_2O$	31[e]	Et	H	Br	OH	80

[a] For structures, see Figure 2. [b] All compounds were isolated as single pure isomers except for 21 and 22. [c] Isolated yield. [d] A 7:1 mixture of 21 and 22 was isolated. [e] Compound 17 has 2R, 3S configuration; 31 has 2S,3R configuration (enantiomeric to that in Figure 2).

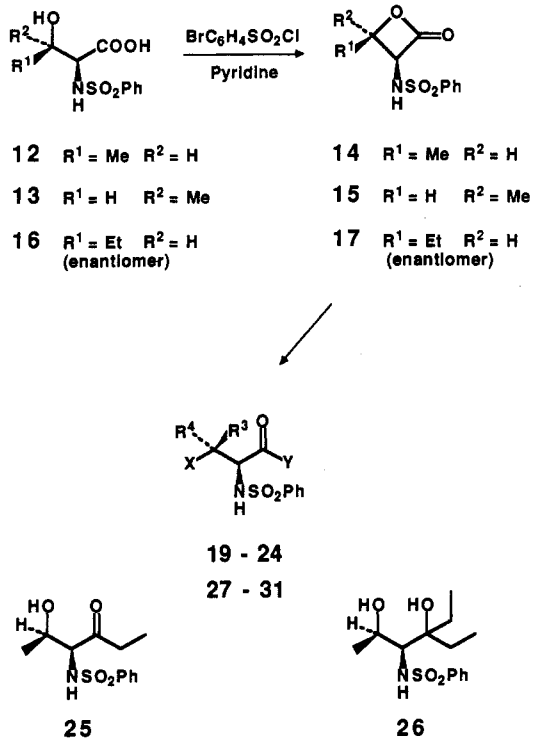

Figure 2. Formation and ring opening of β-lactones 14, 15, and 17. See Table I for structures of products 19–24 and 27–31.

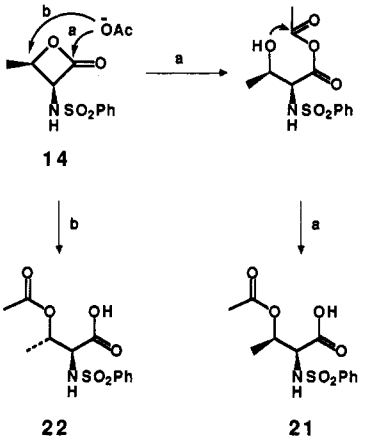

Figure 3. Mechanism for cleavage of 14 by sodium acetate in acetic acid.

in pyridine at −40 to −10 °C gives the corresponding lactone 14 in 40–55% isolated yield (Figure 2). The cyclization conditions are fairly specific; for example, variations in solvent composition (e.g., THF or MeCN as cosolvents), in activating reagent (e.g., use of benzenesulfonyl chloride), or in temperature drastically lower the yield of 14. Conversion of the *allo*-threonine derivative 13 to its β-lactone 15 proceeds analogously. The stereochemistry of each lactone was confirmed from its ^1H NMR spectrum[15] and by hydrolysis with aqueous base. Since it is known that under these conditions ring opening occurs by attack at the carbonyl without alteration of the configuration at the β-carbon,[2c,16] the transformation of 14 to 12 and of 15 to 13 without loss of optical purity verifies the structural assignment. Compound 16, derived from (2R,3S)-2-amino-3-hydroxypentanoic acid (18),[17] cyclizes to β-lactone 17 in 39% isolated yield.

Since recent investigations demonstrate that β-butyrolactones are readily attacked by a variety of nucleophiles at the β-carbon,[16d,18] it seemed likely that the protected

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(16) (a) Olson, A. R.; Hyde, J. L. *J. Am. Chem. Soc.* **1941**, *63*, 2459–2461. (b) Long, F. A.; Purchase, M. *J. Am. Chem. Soc.* **1950**, *72*, 3267–3273. (c) Wynberg, H.; Staring, E. G. J. *J. Chem. Soc., Chem. Commun.* **1984**, 1181–1182. (d) Griesbeck, A.; Seebach, D. *Helv. Chim. Acta* **1987**, *70*, 1326–1332.
(17) Compound 18 was obtained by condensation of propionaldehyde with the chiral glycine enolate derivative of Seebach and co-workers.[4c]
(18) For examples of attack by carbon nucleophiles, see: Fujisawa, T.; Sata, T.; Kawara, T.; Noda, A.; Obinata, T. *Tetrahedron Lett.* **1980**, *21*, 2553–2554.

threonine β-lactone **14** and *allo*-threonine β-lactone **15** would behave similarly and afford the desired amino acid derivatives in analogy to the serine β-lactones.[2] However, this is true only with certain nucleophiles; in many cases reaction proceeds instead at the carbonyl carbon (Table I). Although condensation of **14** with thiourea generates a single diastereomer of the expected[2d] isothiouronium salt **19**, a precursor of β-methylcysteine,[19] the use of LiSH or NaSH gives **20** by attack at the carbonyl. Reaction of isomerically pure **14** with sodium acetate in acetic acid produces diastereomeric acetates **21** and **22** in a 7:1 ratio; hydrolysis of this mixture with aqueous base generates the N-protected threonine **12** and *allo*-threonine **13** in the same ratio. This shows that the predominant reaction of acetate is at the carbonyl carbon of the β-lactone, which is followed by ensuing acyl transfer (probably intramolecular) to the β-oxygen to give **21** (Figure 3). Ring opening of **14** by nitrogen nucleophiles like pyrazole and benzylamine also occurs primarily (if not exclusively) at the carbonyl to form amides **23** and **24**. Similarly, copper-catalyzed organometallic reactions under a variety of conditions fail to give any trace of ring cleavage at the β-carbon, in contrast to the behavior of the serine β-lactone **2**.[2b] Instead, treatment of **14** with ethylmagnesium chloride in the presence of catalytic $CuBr{\cdot}SMe_2$ affords ketone **25** and alcohol **26**.[20] Apparently the additional steric and/or electron-withdrawing effect of the α-nitrogen substituent on the β-lactone ring suffices to alter the course of reaction from that observed with the less-substituted β-butyrolactone[16d,18] and serine β-lactones.[2]

However, reactions of **14**, **15**, and **17** with anhydrous magnesium halides (chloride, bromide, iodide) proceed at the β-carbon to give single isomers (>98% by ^1H NMR) of β-haloamino acid derivatives **27–31** in good yield. The stereochemistry of these products was assigned by comparison of relative proton chemical shifts and coupling patterns of diastereomers **27** and **28** with those of **12** and **13** as well as with the other β-substituted α-amino acid derivatives. The results indicate clean inversion of configuration at the β-carbon. This reaction is quite rapid except with magnesium chloride, in which case added chloride is necessary to achieve conversion at a reasonable rate. Since the *N*-(phenylsulfonyl) group can be readily removed by concentrated halogen acids,[21] this method should provide useful access to stereochemically pure β-halo amino acids for biological studies.[5]

In summary, the present results offer an improved synthesis of β-lactones derived from β-substituted-β-hydroxy α-amino acids and demonstrate that such cyclizations are best accomplished by carboxyl group activation of derivatives that do not have a carbonyl group directly attached to nitrogen. Although the unexpected tendency of these β-lactones to undergo carbonyl attack limits their utility for synthesis of new amino acids compared to the serine β-lactones,[2] they do provide a route to stereochemically pure protected α-amino acids bearing a sulfur or halogen at the β-position. Recent preparation of stable salts of α-amino-β-propiolactone[2a] suggests that a more easily removable nitrogen protecting group on β-substituted-α-amino β-lactones could be exchanged to generate naturally occurring β-lactone antibiotics. This possibility is currently being investigated.

Experimental Section

General procedures and instrumentation have been described previously.[2,5a]

(*E*)-1-[(*tert*-Butoxycarbonyl)amino]propene (10).[8] Dimethyl azodicarboxylate (0.60 mL, 5.5 mmol) was added dropwise over 5 min to a solution of triphenylphosphine (1.44 g, 5.5 mmol) in THF (25 mL) at −78 °C. The mixture was stirred 15 min at −78 °C, BOC-L-threonine (**8**) (1.10 g, 5.01 mmol) was added dropwise in THF (25 mL) over 10 min at −78 °C, and the solution was stirred for 20 min at −78 °C and 1.5 h at 25 °C. No β-lactone (λ_{max} = 1820 cm^{-1}) could be detected at any time during the reaction by IR spectroscopy. Unreacted triphenylphosphine was consumed by addition of a few microliters of dimethyl azodicarboxylate. The mixture was separated on a column (120 × 5 cm) of silica gel (40–63 μm) with ethyl acetate/hexane (1/3) to afford 0.69 g (88%) of **10**. This product is sensitive to acid and moisture and decomposes slowly in $CDCl_3$ (50% in 3 days): mp 65.0–65.5 °C; IR ($CHCl_3$ cast), 1693, 1679, 1521, 1307 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 6.60 (br s, 1 H, N*H*), 6.45 (t, 1 H, *J* = 13 Hz, NC*H*), 5.06–4.84 (dq, 1 H, *J* = 6.4, 13 Hz, C*H*CH_3), 1.62 (d, 3 H, *J* = 6.4 Hz, CHC*H*$_3$), 1.47 (s, 9 H, *t*-Bu); ^{13}C NMR (90.56 MHz, $CDCl_3$) δ 152.84 (s), 124.62 (d), 104.20 (d), 79.84 (s), 28.17 (q), 14.37 (q); exact mass 157.1106 (157.1103 calcd for $C_8H_{15}NO_2$). Anal. Calcd for $C_8H_{15}NO_2$: C, 61.12; H, 9.62; N, 8.91. Found: C, 61.03; H, 9.59; N, 8.85.

(*Z*)-1-[(*tert*-Butoxycarbonyl)amino]propene (11).[8] Reaction of dimethyl azodicarboxylate (72 μL, 0.66 mmol), triphenylphosphine (174 mg, 0.66 mmol), and BOC-*allo*-L-threonine (**9**) (97 mg, 0.44 mmol) according to the procedure described for **10** gave 54 mg (78%) of **11**. No β-lactone was detected by IR or TLC during the reaction. This material was considerably more labile than **10** and decomposed in $CDCl_3$ (~50% in 8 h). For **11**: mp 74.5–75.0 °C; IR ($CHCl_3$ cast) 1677, 1515 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.42 (t, 1 H, *J* = 10.0 Hz, NC*H*), 6.14 (s, 1 H, N*H*), 4.70–4.56 (m, 1 H, C*H*CH_3), 1.56 (dd, 3 H, *J* = 7.3, 1.6 Hz, C*H*$_3$), 1.49 (s, 9 H, *t-Bu*); ^{13}C NMR (75.46 MHz, $CDCl_3$) δ 152.85 (s), 123.16 (d), 101.91 (d), 80.33 (s), 28.32 (q), 10.53 (q); exact mass 157.1102 (157.1103 calcd for $C_5H_{15}NO_2$).

(3*S*,4*R*)-3-[(Phenylsulfonyl)amino]-4-methyl-2-oxetanone (14). A solution of *N*-(phenylsulfonyl)-L-threonine[12] (**12**) (2.07 g, 8.0 mmol) in anhydrous pyridine (28 mL) was cooled to −43 °C and a cold (4 °C) solution of 4-bromobenzenesulfonyl chloride (4.04 g, 15.8 mmol) in anhydrous pyridine (28 mL) was added over 10 min. The mixture was stirred at −43 °C for 45 min, allowed to warm up to −10 °C, and poured on crushed ice (ca. 50 g). This was acidified with concentrated HCl to pH ~2. The acidic solution was extracted with EtOAc (3 × 25 mL). The combined extracts were dried, concentrated in vacuo, and purified by flash chromatography[22] (hexane/EtOAc, 65/35) to afford 1.05 g (54%) of **14**: mp 113–114 °C; $[\alpha]^{25}_D$ +24.7° (*c* 1, CH_2Cl_2); IR ($CHCl_3$ cast) 3280, 1826, 1162, 1092 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) δ 7.5–7.9 (m, 5 H, Ar*H*), 5.8 (d, 1 H, *J* = 9 Hz, N*H*), 5.1 (dd, 1 H, *J* = 9, 6 Hz, HNC*H*), 4.8–4.9 (m, 1 H, C*H*CH_3), 1.4 (d, 3 H, *J* = 6 Hz, C*H*$_3$); MS (CI, NH_3) *m/z* 259 (M·NH_4^+, 100%). Anal. Calcd for $C_{10}H_{11}NO_4S$: C, 49.79; H, 4.60; N, 5.80; S, 13.28. Found: C, 49.70; H, 4.51; N, 5.71; S, 12.96.

(3*S*,4*S*)-3-[(Phenylsulfonyl)amino]-4-methyl-2-oxetanone (15). Reaction of *N*-(phenylsulfonyl)-L-allothreonine[12] (**13**) (259 mg, 1.0 mmol) and 4-bromobenzenesulfonyl chloride (0.512 g, 2.0 mmol) in anhydrous pyridine (7 mL) as described for **14** gave 133 mg of **15** (55%): mp 114–115 °C; $[\alpha]^{22}_D$ −19.6° (*c* 0.5, CH_2Cl_2); IR ($CHCl_3$ cast) 3280, 1832, 1157 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) δ 7.5–8.0 (m, 5 H, Ar*H*), 6.4 (d, 1 H, *J* = 7 Hz, N*H*), 4.6–4.7 (dq, 1 H, *J* = 3.8, 7 Hz, C*H*CH_3), 4.4–4.5 (dd, 1 H, *J* = 3.8, 7 Hz, HNC*H*), 1.58 (d, 3 H, *J* = 7 Hz, C*H*$_3$); MS (CI, NH_3) *m/z* 259

(19) For conversion of isothiouronium salts to free thiols, see: Cossar, B. C.; Fournier, J. O.; Fields, D. W.; Reynolds, D. D. *J. Org. Chem.* **1962**, *27*, 93–95.

(20) Use of a full equivalent of $CuBr{\cdot}SMe_2$ at −23 °C gave no reaction after several hours. Reaction of **14** with $Bu_2Cu(CN)Li_2$ afforded products of attack at the carbonyl carbon. Attempts to couple the β-bromo compound **27** with $Bu_2Cu(CN)Li_2$ at −21 °C overnight gave almost exclusively (*E*)-2-(phenylsulfonyl))amino)-2-butenoic acid (**32a**) (<1% *Z* isomer, 51% isolated yield) and unreacted starting material (40%). Similar reaction at 0 °C for 3 h followed by warming to 20 °C overnight produced the *E* isomer **32a** (44%) as well as the *Z* isomer **32b** (8%). This failure to couple contrasts behavior of other types of secondary bromides: Lipshutz, B. H.; Wilhelm, R. S.; Kozlowski, J. A.; Parker, D. *J. Org. Chem.* **1984**, *49*, 3928–3938.

(21) Roemelle, R. C.; Rapoport, H. *J. Org. Chem.* **1988**, *53*, 2367–2371.

(22) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2925.

(M·NH_4^+). Anal. Calcd for $C_{10}H_{11}NO_4S$: C, 49.79; H, 4.60; N, 5.80; S, 13.28. Found: C, 49.91; H, 4.74, N, 5.79; S, 13.29.

(2*R*,3*S*)-2-Amino-3-hydroxypentanoic Acid (18). The procedure of Seebach and co-workers[4c] was used to prepare (2*R*,5*R*,1′*S*)-1-benzoyl-2-*tert*-butyl-5-(1′-hydroxypropyl)-3-methylimidazolidin-4-one from lithium diisopropylamide (made from diisopropylamine (0.45 mL, 3.2 mmol), and BuLi (2.0 mL, 1.6 M, 3.2 mmol)), (2*R*)-1-benzoyl-2-*tert*-butyl-3-methylimidazolidin-4-one[4c] (0.78 g, 3.0 mmol), and propionaldehyde (0.36 mL, 5.0 mmol). This material was purified by flash chromatography[22] (hexane/ethyl acetate, 55/45) to give 798 mg (84%): IR ($CHCl_3$ cast) 3400, 1682, 1637 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) δ 7.4–7.7 (m, 5 H, Ar*H*), 5.7 (s, 1 H, NC*H*N), 4.46 (d, 1 H, *J* = 4 Hz, NC*H*CO), 4.14 (d, 1 H, *J* = 11 Hz, OH), 3.08 (s, 3 H, NCH_3), 2.9–3.0 (m, 1 H, CHOH), 1.2–1.3 (m, 1 H, C*H*HCH_3), 1.06 (s, 9 H $C(CH_3)_3$), 0.8–1.0 (m, 1 H, CH*H*CH_3), 0.72 (t, 3 H, *J* = 7 Hz, CH_3); MS (CI, NH_3) *m/z* 319 (MH^+, 100%). Anal. Calcd for $C_{18}H_{26}N_2O_3$: C, 67.92; H, 8.23; N, 8.80. Found: C, 67.81; H, 8.18; N, 8.73.

This imidazolidinone (0.73 g, 2.3 mmol) was refluxed in 6 N HCl (25 mL) for 22 h. The cooled solution was extracted with ether (3 × 20 mL). The aqueous phase was concentrated to give a solid, which was purified by ion exchange chromatography (AG 50 × 8, H^+ form, 2% aqueous NH_3 as eluent) to furnish 278 mg (91%) of **18**: mp 225–227 °C dec; IR (KBr cast) 3399, 1669, 1637, 1583, 1528 cm^{-1}; ^1H NMR (D_2O), 200 MHz) δ 3.96–4.08 (m, 1 H, C*H*OH, 3.7 (d, 1 H, *J* = 4.5 Hz, NHC*H*), 1.5–1.8 (m, 2 H, CH_2), 1.0 (t, 3 H, *J* = 7.5 Hz, CH_3); FAB MS (glycerol, HCl) *m/z* 134 (M·H^+). Anal. Calcd for $C_5H_{11}NO_3$: C, 45.11; H, 8.33; N, 10.52. Found: C, 44.75; H, 8.24; N, 10.64.

(2*R*,3*S*)-2-[(Phenylsulfonyl)amino]-3-hydroxypentanoic Acid (16). Reaction of **18** (253 mg, 1.9 mmol), Na_2CO_3 (0.6 g, 5.7 mmol), and benzenesulfonyl chloride (0.36 mL, 2.9 mmol) using the literature procedure[12] gave, after recrystallization from ethyl acetate/petroleum ether, 331 mg of **16** (64%): mp 138–140 °C; $[\alpha]^{23}_D$ −17.4° (*c* 0.5, acetone); IR (KBr cast) 3512, 3328, 1743, 1707, 1328, 1170 cm^{-1}; ^1H NMR (d_6-acetone, 360 MHz) δ 7.5–8.0 (m, 5 H, ArH), 6.35 (d, 1 H, *J* = 9 Hz, N*H*), 3.9–4.0 (m, 2 H, NC*H*, C*H*OH), 2.4–3.4 (br s, COOH), 1.5–1.7 (m, 2 H, CH_2), 0.92 (t, 3 H, *J* = 7.5 Hz, CH_3); FAB MS (glycerol, HCl) *m/z* 274 (M·H^+, 100%). Anal. Calcd for $C_{11}H_{15}NO_5S$: C, 48.35; H, 5.53; N, 5.13; S, 11.72. Found: C, 48.57; H, 5.66; N, 5.47; S, 11.78.

(3*R*,4*S*)-3-[(Phenylsulfonyl)amino]-4-ethyl-2-oxetanone (17). Reaction of **16** (137 mg, 0.50 mmol) and 4-bromobenzenesulfonyl chloride (256 mg, 1.0 mmol) in anhydrous pyridine (3.5 mL) as described for **14** gave 50 mg (39%) of **17**: mp 123–125 °C; $[\alpha]^{23}_D$ −34.6° (*c* 0.5, CH_2Cl_2); IR ($CHCl_3$ cast) 3261, 1824, 1345, 1157, 1091 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) δ 7.5–8.0 (m, 5 H, Ar*H*), 5.48 (d, 1 H, *J* = 9 Hz, H*H*), 5.1 (dd, 1 H, *J* = 6, 9 Hz, NHCH), 4.55–4.64 (m, 1 H, C*H*O), 1.64–1.82 (m, 2 H, CH_2), 1.06 (t, 3 H, *J* = 7 Hz, CH_3); MS (CI, NH_3) *m/z* 273 (M·NH_4^+, 100%). Anal. Calcd for $C_{11}H_{13}NO_4S$: C, 51.76; H, 5.13; N, 5.49; S, 12.55. Found: C, 51.78; H, 5.18; N, 5.47; S, 12.39.

(2*R*,3*S*)-2-[(Phenylsulfonyl)amino]-3-isothioureidobutanoic Acid (19). A solution of **14** (108 mg, 0.45 mmol) in anhydrous acetonitrile (3 mL) was treated with thiourea (38 mg, 0.5 mmol), and the suspension was heated at 60 °C for 72 h. The mixture was cooled to 20 °C and filtered to give 100 mg (70%) of **19** as an internal salt: mp 174–175 °C dec; $[\alpha]^{23}_D$ +36.4° (*c* 0.5, 1 N HCl); IR (KBr cast) 3348, 2400–3200 (br), 1659, 1611, 1581, 1390, 1348, 1169 cm^{-1}; ^1H NMR (D_2O, DCl, 360 MHz) δ 7.5–7.9 (m, 5 H, ArH), 4.4 (d, 1 H, *J* = 7 Hz, C*H*N), 4.25 (dq, 1 H, *J* = 7, 6.5 Hz, C*H*CH_3), 1.32 (d, 3 H, *J* = 6.5 Hz, CH_3); FAB MS (glycerol, HCl) *m/z* 318 (MH^+, 100%). Anal. Calcd for $C_{11}H_{15}N_3O_4S_2$: C, 41.62; H, 4.76; N, 13.24; S, 20.20. Found: C, 41.64; H, 4.83; N, 13.12; S, 20.13.

(2*S*,3*R*)-2-[(Phenylsulfonyl)amino]-3-hydroxybutanethioic Acid (20). To a solution of **14** (0.12 g, 0.50 mmol) in THF (5 mL) at 0 °C was added a suspension of LiSH in THF (0.5 mmol (prepared from BuLi and H_2S)) over 5 min. The resulting pale yellow mixture was stirred at 0 °C for 10 min and then acidified to pH 3 with 1 N H_3PO_4. The aqueous phase was saturated with NaCl and extracted with EtOAc (3 × 10 mL). The combined extracts were dried (Na_2SO_4) and concentrated in vacuo to a solid that was recrystallized from EtOAc/hexane to give 115 mg of **20** (84%): mp 139–141 °C; $[\alpha]^{22}_D$ −34.6° (*c*, 1, acetone); IR (KBr cast) 3514, 3280, 1692, 1447, 1328, 1165 cm^{-1}; ^1H NMR (d_6-acetone, 360 MHz) 7.6–8.0 (m, 5 H, ArH), 6.8 (d, 1 H, *J* = 8 Hz, N*H*), 4.6–5.3 (br, 1 H, OH), 4.3 (dq, 1 H, *J* = 3, 6 Hz, C*H*CH_3), 4.0 (dd, 1 H, *J* = 3, 8 Hz, NHC*H*), 2.6–3.2 (br, 1 H, SH), 1.02 (d, 3 H, *J* = 6 Hz, CH_3); MS (CI, NH_3) *m/z* 276 (MH^+, 97%). Anal. Calcd for $C_{10}H_{13}NO_4S_2$: C, 43.63; H, 4.76; N, 5.09; S, 23.27. Found: C, 43.63; H, 4.88; N, 4.97; S, 23.03. A similar reaction of **14** with NaSH in H_2O/THF gave **20** in 86% yield.

(2*S*,3*R*)-2-[(Phenylsulfonyl)amino]-3-acetoxybutanoic Acid (21) and Its 2*S*,3*S* Isomer 22. A solution of **14** (241 mg, 1 mmol) and sodium acetate (0.41 g, 5 mmol) in glacial acetic acid (5 mL) was heated at 55–60 °C for 24 h. The mixture was cooled to 20 °C, and the solvent was removed in vacuo. The residue was dissolved in 0.1 N HCl (20 mL), and the solution was acidified to pH ~3 with 1 N HCl and extracted with EtOAc (3 × 10 mL). The combined extracts were dried (Na_2SO_4) and concentrated to give a syrup that was purified by medium pressure liquid chromatography (MPLC) (RP-8; H_2O/CH_3CN, 7/3, v/v) to give **21** and **22** as a 7:1 mixture of diastereomers 155 mg (51%): mp 98–100 °C; IR ($CHCl_3$ cast) 2900–3600 (br), 1742, 1330, 1237, 1166 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) major diastereomer **21** (2*S*,3*R*) δ 7.4–8.0 (m, 5 H, Ar*H*), 5.5–6.0 (br, 1 H, COOH), 5.42 (d, 1 H, *J* = 10 Hz, N*H*), 5.3 (dq, 1 H, *J* = 2.5, 6 Hz, C*H*OAc) 4.0 (dd, 1 H, *J* = 2.5, 10 Hz, C*H*NH), 2.0 (s, 3 H, $COCH_3$), 1.3 (d, 3 H, *J* = 6 Hz, CH_3); minor diastereomer **22** (2*S*,3*S*) δ 7.4–8.0 (m, 5 H, ArH), 5.56 (d, 1 H, *J* = 9 Hz, N*H*), 5.1 (dq, 1 H, *J* = 4, 6.2 Hz, C*H*OAc), 4.3 (dd, 1 H, *J* = 4, 9 Hz, C*H*NH), 2.0 (s, 3 H, $COCH_3$), 1.24 (d, 3 H, *J* = 6.2 Hz, CH_3); MS (CI, NH_3), *m/z* 319 (M·NH_4^+, 100%). Anal. Calcd for $C_{12}H_{15}NO_6S$: C, 47.84; H, 5.02; N, 4.65; S, 10.63. Found: C, 47.63; H, 4.84; N, 4.61; S, 10.45. Hydrolysis (NaOH, H_2O/THF, 20 °C) gave a mixture of **12** and **13** in a 7:1 ratio.

(2*S*,3*R*)-1-[2-[(Phenylsulfonyl)amino]-3-hydroxy-1-oxobutyl]pyrazole (23). A solution of **14** (0.12 g, 0.5 mmol) and pyrazole (70 mg, 1.0 mmol) in anhydrous CH_3CN (7 mL) was heated at 60 °C for 4 days. The solvent was removed in vacuo, and the residue was taken up in ether/CH_2Cl_2 (3/1, 30 mL). The resulting suspension was washed with water (3 × 10 mL). The organic phase was dried (Na_2SO_4) and concentrated to give 116 mg of **23** (75%) as an analytically pure solid: mp 155–157 °C; $[\alpha]^{23}_D$ +42.8° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$ cast) 3280, 1735, 1383, 1350 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) δ 8.0–6.4 (m, 8 H, ArH), 6.8 (d, 1 H, *J* = 10.5 Hz, N*H*), 5.2 (dd, 1 H, *J* = 10.5, 3 Hz, NHC*H*), 4.3 (dq, 1 H, *J* = 6, 3 Hz, C*H*CH_3), 1.34 (d, 3 H, *J* = 6 Hz, CH_3); FAB MS (glycerol, formic acid) *m/z* 310 (MH^+). Anal. Calcd for $C_{13}H_{15}N_3O_4S$: C, 50.48; H, 4.89; N, 13.59; S, 10.35. Found: C, 50.43; H, 4.85; N, 13.29; S, 10.03.

(2*S*,3*R*)-*N*-Benzyl-2-[(phenylsulfonyl)amino]-3-hydroxybutanamide (24). A solution of benzylamine (0.17 mL, 0.50 mmol) in acetonitrile (5 mL) at −30 °C was treated with a solution of **14** (0.24 g, 0.50 mmol) in acetonitrile (5 mL). The mixture was slowly warmed to room temperature and then stirred overnight. The solvent was removed in vacuo, the residue was dissolved in CH_2Cl_2 (25 mL), and this was washed with water (2 × 10 mL). The CH_2Cl_2 layer was dried (Na_2SO_4) and concentrated in vacuo to give a solid residue, which was recrystallized from EtOAc/hexane to give 0.25 g of **24** (72%): mp 139–140 °C; $[\alpha]^{23}_D$ −35.8° (*c* 0.5, $CHCl_3$); IR ($CHCl_3$ cast) 3000–3600 (br), 1650, 1447, 1320, 1164, 1091 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) δ 7.15–7.9 (m, 10 H, Ar*H*), 7.0 (br t, 1 H, N*H*CH_2), 5.78 (br, d, 1 H, *J* = 5.5 Hz, N*H*CH), 4.3–4.4 (m, 3 H, C*H*CH_3, CH_2Ph), 3.6–3.7 (m, 1 H, CHNH), 2.65 (br s, 1 H, OH), 0.9 (d, 3 H, *J* = 6.5 Hz, CH_3); exact mass 348.1143 (348.1143 calcd for $C_{17}H_{20}N_2O_4S$). Anal. Calcd for $C_{17}H_{20}N_2O_4S$: C, 58.60; H, 5.79; N, 8.04; S, 9.20. Found: C, 58.62; H, 5.80; N, 8.08; S, 9.11.

(4*S*,5*R*)-4-[(Phenylsulfonyl)amino]-5-hydroxyhexan-3-one (25) and (2*R*,3*S*)-3-[(Phenylsulfonyl)amino]-4-ethyl-2,4-hexanediol (26). A solution of **14** (0.24 g, 1.0 mmol) and CuBr·SMe_2[23] (40 mg, 0.20 mmol) in THF (10 mL) containing dimethyl sulfide (1 mL) was cooled to −23 °C, and a solution of ethylmagnesium chloride in ether (2.8 mL, 4.9 mmol) was added over 5 min. The mixture was maintained at −23 °C for 15 min and poured into cold (4 °C) degassed 0.5 M HCl (30 mL).

(23) Theis, A. B.; Townsend, C. A. *Synth. Commun.* **1981**, *11*, 157–166.

Methanol (8 mL) was added, and the mixture was stirred under Ar for 25 min. The resulting precipitate of CuCl was filtered, and the filtrate was extracted with EtOAc (3 × 25 mL). The combined extracts were washed with saturated EDTA solution (3 × 10 mL) and brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by MPLC (RP-8, CH_3CN/H_2O, 3/7, v/v) to give **25** (80 mg, 30%) and **26** (110 mg, 38%).

For **25**: mp 132–133 °C; $[\alpha]^{24}_D$ +23.8° (*c* 0.5, $CHCl_3$); IR ($CHCl_3$ cast) 3487, 3283, 1720, 1447, 1325, 1312, 1166 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) δ 7.5–7.9 (m, 5 H, ArH), 5.8 (br s, 1 H, N*H*), 4.2–4.3 (m, 1 H, C*H*OH), 3.82 (br s, 1 H, C*H*NH), 2.5–2.6 (m, 1 H, CH_2CH$_3$), 2.2–2.3 (m, 1 H, CH_2CH$_3$), 1.24 (d, 3 H, CHCH_3), 0.86 (t, 3 H, CH$_2$CH_3); MS (CI, NH_3) *m/z* 289 (M·NH_4^+).

For **26**: IR ($CHCl_3$ cast) 3100–3600, 2972, 2949, 2934, 2884, 1447, 1325, 1156 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) δ 7.4–7.9 (m, 5 H, ArH), 5.3–5.4 (br s, 1 H, NH), 4.3 (q, 1 H, *J* = 6.0 Hz, C*H*CH$_3$), 3.25 (d, 1 H, *J* = 8.5 Hz, C*H*NH), 2.4–2.9 (br, 1 H, OH), 1.65–1.8 (m, 1 H, CH_2CH$_3$), 1.5–1.6 (m, 1 H, CH_2CH$_3$), 1.25–1.5 (m, 2 H, CH_2CH$_3$), 1.0 (d, 3 H, *J* = 6 Hz, CHCH_3), 0.85 (t, 3 H, *J* = 7.5 Hz, CH_3), 0.68 (t, 3 H, *J* = 7.5 Hz, CH_3); MS (CI, NH_3) *m/z* 319 (M·NH_4^+, 100%). Anal. Calcd for $C_{14}H_{23}NO_4S$: C, 55.79; H, 7.69; N, 4.65; S, 10.63. Found: C, 55.84; H, 7.56; N, 4.52; S, 10.44.

(2*R*,3*S*)-2-[(Phenylsulfonyl)amino]-3-bromobutanoic Acid (27). To a suspension of anhydrous $MgBr_2$·OEt_2 (4.0 mmol, prepared from Mg metal (0.10 g, 4.0 mmol) and 1,2-dibromoethane (freshly distilled, 0.36 mL, 4.0 mmol)) in anhydrous ether (16 mL) at room temperature was added a solution of **14** (241 mg, 1.00 mmol) in anhydrous ether (25 mL) over 5 min. The mixture was stirred at room temperature for 10 min, cooled in an ice bath, and treated with 1 N H_3PO_4 (20 mL). The ether phase was separated, and the aqueous phase was extracted with ether (3 × 10 mL). The combined ether extracts were dried (Na_2SO_4) and concentrated in vacuo to give 0.32 g (99%) of pure **27**. Recrystallization could be effected from EtOAc/hexane (88% recovery): mp 140–142 °C; $[\alpha]^{22}_D$ +37.6° (*c* 1, $CHCl_3$); IR ($CHCl_3$ cast) 2900–3350, 1724, 1334 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz), δ 7.5–7.6, 7.8–7.9 (m, 5 H, Ar*H*), 5.55 (d, 1 H, *J* = 9 Hz, N*H*), 4.0–4.5 (br, 1 H, COO*H*), 4.3 (dq, 1 H, *J* = 4.4, 7 Hz, C*H*CH$_3$), 4.2 (dd, 1 H, *J* = 4.4, 9 Hz, C*H*N), 1.75 (d, 3 H, *J* = 7 Hz, CH_3); FAB MS (glycerol/formic acid) *m/z* 322, 324 ($MH^+(^{79}Br)(^{81}Br)$). Anal. Calcd for $C_{10}H_{12}NO_4SBr$: C, 37.27; H, 3.72; N, 4.35; S, 9.94; Br, 24.84. Found: C, 37.33; H, 3.62; N, 4.31; S, 9.77; Br, 24.80.

(2*R*,3*R*)-2-[(Phenylsulfonyl)amino]-3-bromobutanoic Acid (28). This was prepared from $MgBr_2$·OEt_2 (1.0 mmol) in anhydrous ether (4.0 mL) and **15** (60 mg, 0.25 mmol) in anhydrous ether (8 mL) as described for conversion of **14** to **27**. The yield of **28** after recrystallization from EtOAc/hexane was 62 mg (77%): mp 163–165 °C; $[\alpha]^{22}_D$ −9.1° (*c* 1, $CHCl_3$); IR (KBr cast) 3320, 1700, 1338, 1171, 1142 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.5–7.9 (m, 5 H, ArH), 5.4 (d, 1 H, *J* = 10 Hz, N*H*), 5.3–5.8 (br, 1 H, COO*H*), 4.5 (dq, 1 H, *J* = 2.5, 7 Hz, C*H*CH$_3$), 4.2 (dd, 1 H, *J* = 2.5, 10 Hz, C*H*N), 1.75 (d, 3 H, *J* = 7 Hz, CH_3); FAB MS (glycerol/formic acid) *m/z* 322, 324 ($MH^+(^{79}Br)(^{81}Br)$). Anal. Calcd for $C_{10}H_{12}NO_4SBr$: C, 37.27; H, 3.72; N, 4.35; S, 9.94; Br, 24.84. Found: C, 37.12; H, 3.75; N, 4.43; S, 10.24; Br, 24.96.

(2*R*,3*S*)-2-[(Phenylsulfonyl)amino]-3-iodobutanoic Acid (29). This was prepared from anhydrous MgI_2·OEt_2 (0.55 mmol, prepared from Mg metal (24 mg, ~1.0 mmol) and 1,2-diiodoethane (155 mg, 0.55 mmol)) in anhydrous ether (7 mL, protected from light) and **14** (120 mg, 0.50 mmol) in anhydrous ether (10 mL) as described for **27** to give an oil that solidified at −20 °C. This was dissolved in a minimum amount of EtOAc, and excess hexane (ca. 15 vol) was added to give, after cooling, 154 mg of crystalline **29** (83%): mp 149–150 °C; $[\alpha]^{22}_D$ +50.8° (*c* 1, $CHCl_3$); IR ($CHCl_3$ cast) 2800–3500 (br), 1722, 1162, 1091 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) δ 7.5–7.9 (m, 5 H, ArH), 6.4 (d, 1 H, *J* = 8.5 Hz, N*H*), 4.4 (dq, 1 H, *J* = 4.2, 6.5 Hz, C*H*CH$_3$), 3.9 (dd, 1 H, *J* = 4.2, 8.5 Hz, C*H*NH), 1.95 (d, 3 H, *J* = 6.5 Hz, CH_3); FAB MS (glycerol, HCl) *m/z* 370 (MH^+). The compound was light sensitive and satisfactory analysis could not be obtained.

(2*R*,3*S*)-2-[(Phenylsulfonyl)amino]-3-chlorobutanoic Acid (30). To a suspension of anhydrous $MgCl_2$ (94 mg, 1.0 mmol) in ether (10 mL) was added a solution of **14** (120 mg, 0.50 mmol) in anhydrous ether (11 mL). Tetrabutylammonium chloride (132 mg, 0.50 mmol) was added, and the mixture was stirred at room temperature for 2 weeks. The solvent was removed in vacuo, the residue was taken up in 1 N H_3PO_4 (10 mL), and the solution was extracted with EtOAc (3 × 15 mL). The combined EtOAc extracts were stirred with a slurry of excess aqueous ion exchange resin (AG 50 × 8 (H^+ form)), dried (Na_2SO_4), and concentrated in vacuo. The residue was recrystallized from EtOAc/hexane to give 108 mg of **30** (78%): mp 129–131 °C; $[\alpha]^{23}_D$ +35.7° (*c* 1, $CHCl_3$); IR ($CHCl_3$ cast) 3340, 3200–3400 (br), 1725, 1334, 1166, 1091 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) δ 7.5–7.9 (m, 5 H, ArH), 6.8–7.2 (br, 1 H, COO*H*), 5.62 (d, 1 H, *J* = 9.3 Hz, N*H*), 4.2–4.3 (m, 2 H, C*H*CH$_3$, NC*H*CO), 1.6 (d, 3 H, *J* = 6.5 Hz, CH_3); FAB MS (glycerol/formic acid) *m/z* 278 (MH^+). Anal. Calcd for $C_{10}H_{12}NO_4SCl$: C, 43.40; H, 4.34; N, 5.06; S, 11.57; Cl, 12.84. Found: C, 43.22; H, 4.27; N, 4.79; S, 11.53; Cl, 12.67.

(2*S*,3*R*)-2-[(Phenylsulfonyl)amino]-3-bromopentanoic Acid (31). This was prepared from anhydrous $MgBr_2$·OEt_2 (0.65 mmol) in anhydrous ether (3.0 mL) and **17** (41 mg, 0.16 mmol) in anhydrous ether (7 mL) as described for conversion of **14** to **27**. The yield of **31** was 44 mg (80%) after recrystallization: mp 142–143 °C; $[\alpha]^{23}_D$ −36.8° (*c* 0.5, $CHCl_3$); IR ($CHCl_3$ cast) 3290, 1707, 1450, 1342, 1166 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) δ 7.5–7.9 (m, 5 H, ArH), 5.54 (d, 1 H, *J* = 9 Hz, N*H*), 4.3 (dd, 1 H, *J* = 4, 9 Hz, C*H*NH), 4.0–4.1 (m, 1 H, C*H*Br), 3.4–4.0 (br, COO*H*), 1.9–2.1 (m, 2 H, CH_2CH$_3$), 1.08 (t, 3 H, *J* = 7.5 Hz, CH_3); FAB MS (glycerol, HCl) *m/z* 336, 338 ($MH^+(^{79}Br)(^{81}Br)$). Anal. Calcd for $C_{11}H_{14}NO_4SBr$: C, 39.28; H, 4.20; N, 4.17; S, 9.54; Br, 23.53. Found: C, 38.85; H, 4.25; N, 4.01; S, 9.76; Br, 23.38.

(*E*)-2-[(Phenylsulfonyl)amino]-2-butenoic Acid (32a) and Its *Z* Isomer 32b. To a solution of $Bu_2Cu(CN)Li_2$ (prepared from CuCN (143 mg, 1.60 mmol) and BuLi (3.2 mmol) over 40 min at −23 °C) in THF (5 mL) at −78 °C was added a solution of **27** (240 mg, 0.75 mmol) in THF (6 mL). The mixture was warmed to 0 °C for 3 h and then to room temperature overnight. The mixture was quenched and extracted as described for preparation of **25** to give an oil that was purified by MPLC (RP-8, CH_3CN/H_2O, 3/7, v/v, 0.1%, CF_3COOH). Concentration of the fractions in vacuo gave 80 mg of the *E* isomer **32a** (44%) and 15 mg of the *Z* isomer **32b** (8%).[20] A similar reaction of **27** at −21 °C for 22 h gave only the *E* isomer **32a** (40%) and unreacted **27** (51%). Less than 1% *Z* isomer could be detected under the latter conditions.

For *E* isomer **32a**: mp 104–106 °C; IR ($CHCl_3$ cast) 2800–3600 (br), 1697, 1443, 1409, 1155, 1090 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) δ 7.5–7.8 (m, 5 H, ArH), 6.75 (q, 1 H, *J* = 8 Hz, CH_3CH), 6.5 (br s, 1 H, N*H*), 2.1 (d, 3 H, *J* = 8 Hz, CH_3); FAB MS (glycerol, HCl) *m/z* 242 (MH^+). Anal. Calcd for $C_{10}H_{11}NO_4S$: C, 49.79; H, 4.60; N, 5.80; S, 13.28. Found: C, 49.84; H, 4.31; N, 5.67; S, 13.00.

For *Z* isomer **32b**: IR ($CHCl_3$ cast) 2800–3600 (br), 1686, 1403, 1332, 1279, 1169, 1147; ^1H NMR ($CDCl_3$, 360 MHz) δ 7.5–7.8 (m, 5 H, ArH), 7.1 (q, 1 H, $CH_3CH{=}C<$), 6.0 (br s, 1 H, N*H*), 2.08 (d, 3 H, CH_3), FAB MS (glycerol, HCl) *m/z* 242 (MH^+).

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