Anal. Calcd for $C_{28}H_{48}O_6$: C, 70.00; H, 10.10. Found: C, 69.80; H, 10.00.

A similar Baeyer–Villiger reaction starting with the tetraacetate **5d** (100 mg) afforded the tetraacetoxy lactone **4d** (80 mg): mp 172–174 °C (from hexane); NMR δ 5.24 (1 H, m, 3β-H; $W_{1/2}$ = 8 Hz, 5.20 (1 H, dd, 22-H; J = 7 and 3 Hz), 5.08 (1 H, dd, 22-H; J = 3.5 and 3 Hz), 4.86 (1 H, m, 2β-H; $W_{1/2}$ = 12 Hz), 4.18 (1 H, dd, 8β-H; J = 10.5 and 8.4 Hz), 2.72 (1 H, dd, 6β-H; J = 10 and 15 Hz), 2.08 (6 H, s, 2 × CH_3CO), 2.05 (3 H, s, CH_3CO), 1.99 (3 H, s, CH_3CO), 1.06 (3 H, s, 19-CH_3), 0.65 (3 H, s, 18-CH_3).

Anal. Calcd for $C_{36}H_{56}O_{10}$: C, 66.60; H, 8.70. Found: C, 66.50; H, 8.60.

Saponification of **4d** (70 mg) followed by acydification afforded the tetrahydroxy lactone **4b** (55 mg): mp 97 °C (sinterizes), 146 °C (clarifies) (from hexane); IR 1730, 1710, 1695 cm^{-1}; NMR (C_5D_5N) δ 4.18 (1 H, dd, 8β-H; J = 10.5 and 8.4 Hz), 2.72 (1 H, dd, 6β-H; J = 10 and 15 Hz); mass spectrum, m/e 462 ($M^+ - H_2O$).

Anal. Calcd for $C_{28}H_{48}O_6$: C, 70.00; H, 10.10. Found: C, 69.85; H, 9.90.

Acknowledgment. This work was supported by the Italian Research Council (Progetto Finalizzato Chimica Fine e Secondaria).

Registry No. **4a**, 93782-67-3; **4b**, 93805-92-6; **4c**, 93782-68-4; **4d**, 93782-69-5; **5a**, 90965-40-5; **5b**, 90965-39-2; **5c**, 93782-70-8; **5d**, 93782-71-9; **7**, 93782-72-0; **8**, 93782-73-1; **8** (detosylated), 10123-90-7; **9**, 93806-01-0; **10**, 93782-74-2; **11**, 93782-75-3; **12a**, 72050-71-6; **12b**, 72050-72-7; **12b** (thioketal), 93782-76-4; **13a**, 72050-69-2; **13b**, 72050-70-5; $HSCH_2CH_2SH$, 540-63-6.

α-Amino Acids as Chiral Educts for Asymmetric Products. Chirospecific Syntheses of Methyl L-Sibirosaminide and Its C-3 Epimer from L-Allothreonine

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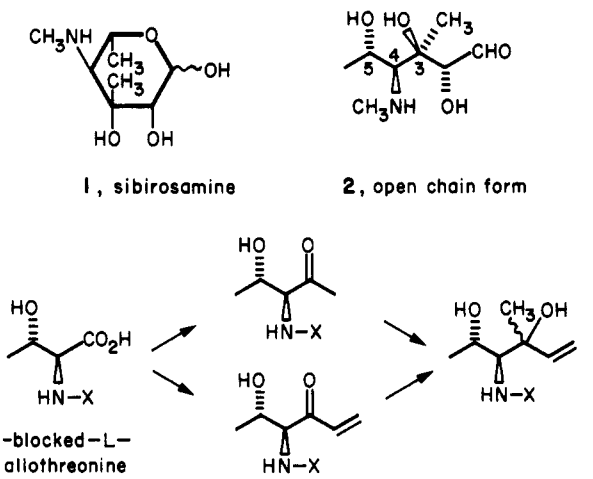
Efficient syntheses of methyl L-sibirosaminide and its C-3 epimer are described using L-allothreonine as the chiral educt. Amino acylations of organometallics with the lithium salt of *N*-(phenylsulfonyl)-L-allothreonine constitute the key carbon–carbon bond-forming steps. The resulting methyl and vinyl ketones are then converted to tertiary alcohols by a second organometallic addition, and the order of addition controls the stereochemistry at the new chiral center. Stereocontrolled functionalization of the vinyl group then leads to the amino sugars. Elaboration to the C-3 epimer of sibirosamine was achieved via a Pummerer oxidation route, while in the preparation of sibirosamine itself a selective tetraol oxidation route was used.

Largely due to their occurrence in important antibiotics,[1,2] amino sugars have elicited a substantial interest as synthetic targets for organic synthesis.[3] The challenge of creating several adjacent, functionalized chiral centers in a stereo- and enantioselective manner is chemically intriguing, and the emerging importance of the biological role of amino sugars[4] adds to the impetus for efficient construction of these molecules.

The problem of enantioselection in amino sugar synthesis is usually overcome by choosing a carbohydrate or other chiral precursor,[5,6] or occasionally by resolution of a racemic intermediate.[7] There appears to be no reported case, however, of the preparation of an amino sugar from an amino acid with retention of the amino group and its chiral integrity. This is probably due to the lack of methods for forming carbon–carbon bonds with amino acids while maintaining optical purity.

Recently, we have demonstrated some very versatile methods for performing just these operations. These methods are based on either Freidel–Crafts type amino acylations of aromatic substrates with amino acid chlorides,[8] or on the amino acylations of organometallics with lithium salts of amino acids.[8,9] The latter method appeared to be aptly suitable as the basis for a chirospecific route to amino sugar syntheses, and we set out to experimentally determine the feasibility of this concept.

Scheme I. Relationship of Sibirosamine and L-Allothreonine



Sibirosamine (**1**), derived from the potent antitumor antibiotic sibiromycin,[10,11] was chosen as our prototypical target for several reasons. First, our proposed methodology is made starkly suitable by the structural resemblance of

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0022-3263/85/1950-0325$01.50/0

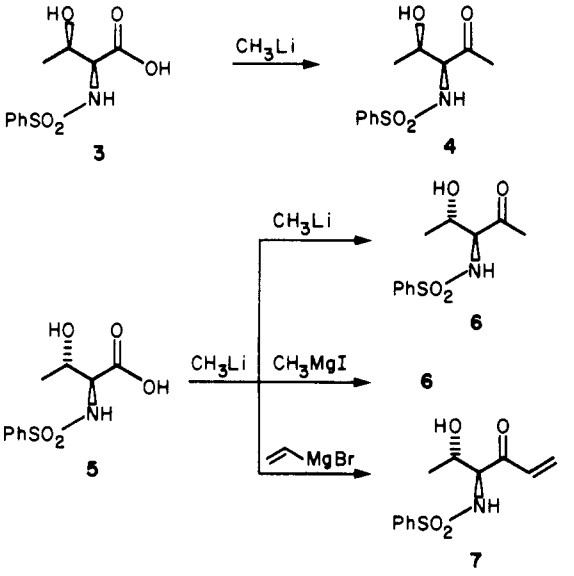
the C-3 to C-6 portion of sibirosamine (open chain form, **2**) to L-allothreonine. Second, any epimeric variation at C-4 and C-5 would be readily accomodated by choosing the proper alternate stereoisomer of threonine, all of which are readily available in optically pure form.[12] Third, the branching methyl at C-3 allows us to explore the formation of two carbon–carbon bonds from the amino acid carboxyl in a stereocontrolled manner. Fourth, sibirosamine has previously been synthesized only as the unnatural D-enantiomer.[13,14] Since a carbohydrate precursor was used, the natural L-form may be less accessible by that route. Fifth, a careful stereochemical analysis of our intermediates would allow independent evaluation of the recent revision[14] of the relative stereochemistry at C-3 in sibirosamine which was based on established stereoselective synthetic methods and comparison of synthetic and natural materials. Finally, the biological properties of sibiromycin enhance the interest in the availability of its constituent amino sugar. We now report our results which clearly demonstrate the utility and efficiency of the amino acid route to amino sugars.

Results and Discussion

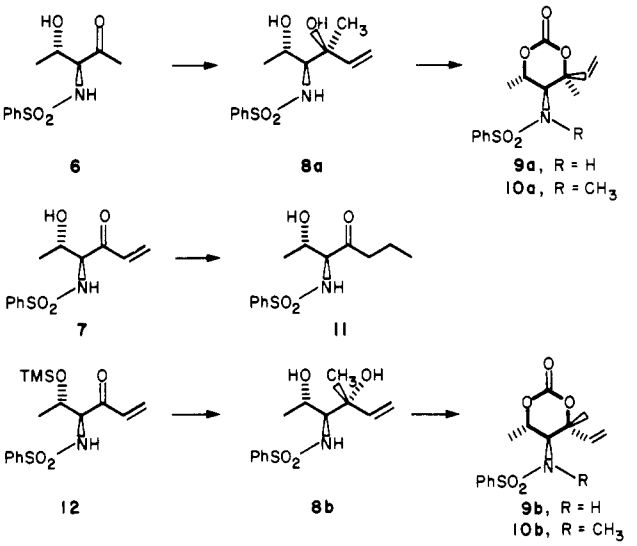
α-Amino Ketones from Threonines. The attachment of a methyl group and a two carbon fragment to the carboxyl group of L-allothreonine conceptually provides the complete carbon skeleton of sibirosamine (Scheme I). We considered the vinyl group as a suitable two carbon fragment since (a) it should be easily elaborated by a variety of oxygenation procedures and (b) the vinyl Grignard reagent[15] is easily handled. We proposed that the order in which the methyl and vinyl groups were added would be a significant factor in the stereochemical outcome and could be the key to controlling C-3 stereochemistry in our synthesis. Thus both routes shown in Scheme I were to be pursued. On the basis of earlier results,[8,9,16] we chose the phenylsulfonyl groups as the nitrogen protecting group and prepared a quantity of *N*-(phenylsulfonyl)-L-allothreonine by a modified Schotten–Bauman procedure. The amino acid was prepared by a modified literature procedure.[12]

We had earlier formed the methyl ketone **4** from N-protected L-threonine (**3**) by simply stirring with excess methyllithium at room temperature. When these same conditions were applied to *N*-(phenylsulfonyl)-L-allothreonine (**5**) the yield was severely diminished (from 70% to 30%), and the isolation was complicated by the presence of several byproducts. This reaction was improved, however, by treating the lithium salt of **5** (made by adding 250 mol% of methyllithium to a THF solution of **5**) with excess methylmagnesium iodide and stirring at a slightly higher temperature. Thus the methyl ketone **6** could be obtained from the reaction mixture by a simple crystallization after an aqueous isolation in 64% yield, allowing for 42% recovery of starting material. If the reaction time is lengthened or the temperature raised further to consume all the starting material, then the isolation is more difficult and the yield is not significantly improved. The vinyl ketone **7** was prepared in much the same way by substituting vinylmagnesium bromide for the methyl Grignard reagent. It should be noted that α-epimerization of ketone **6** can take place during the aqueous quench of the reaction mixture if the quenching solution is not kept acidic. This leads to contamination of **6** with the enantiomer of **4**. The problem, however, is completely avoided by pouring the reaction mixture slowly into excess cold 2 M H_3PO_4. These transformations are outlined in Scheme II.

Scheme II. Formation of α-Amino Ketones from Threonines



Scheme III. Stereospecific Formation of Tertiary Alcohols



Formation of Tertiary Alcohols and Stereochemical Analysis. Treatment of ketone **6** with vinylmagnesium bromide provided a single isomer of the tertiary alcohol **8a** (Scheme III). Some of the starting ketone (~20%) was present in the product; therefore, after crystallizing as much **8a** as possible from the mixture the mother liquors were resubjected to the Grignard reaction after which the ketone had been completely consumed. With this simple recycle step a total yield of 83% of pure tertiary alcohol was obtained. If the presence of **6** (after the first treatment) is due to enolization, then it is clear that enolization occurs regiospecifically toward the methyl group since no epimerization takes place. This is in accordance with our observation that ketones **4** and **6** can be added to excess LDA and recovered unchanged after quenching.

In order to obtain the epimeric tertiary alcohol, vinyl ketone **7** was treated with methyllithium. This led, unexpectedly, to the nearly exclusive (15/1) formation of

(12) Elliot, D. F. *J. Chem. Soc.* **1950**, 62.
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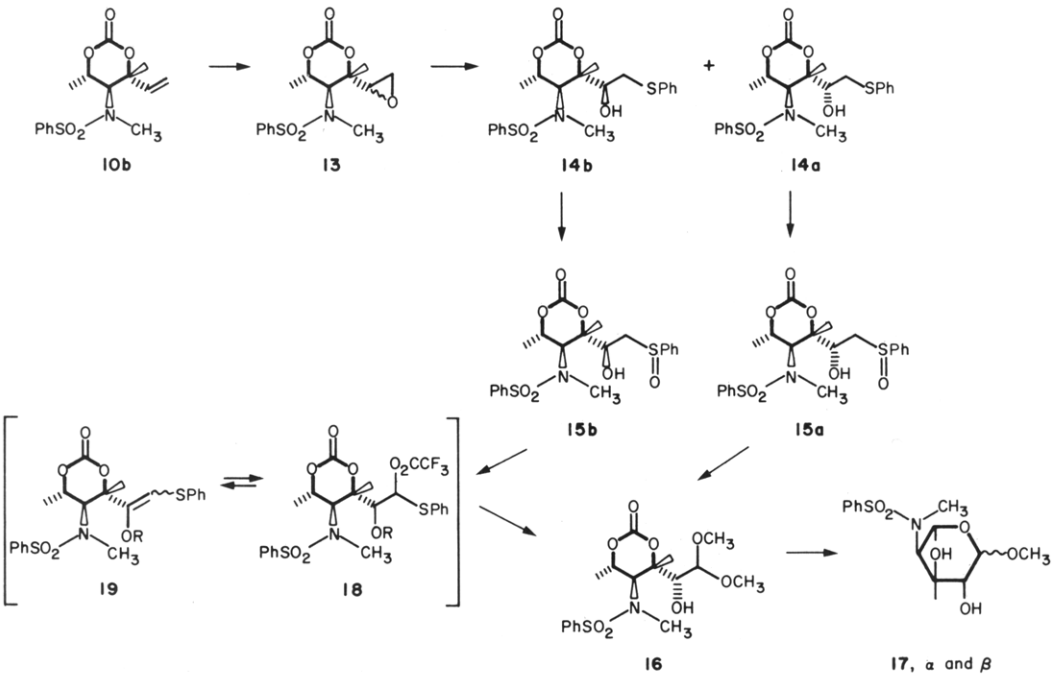
Scheme IV. Pummerer Route to Episibirosaminide 17



propyl ketone **11** by 1,4-addition, the minor product being the desired tertiary alcohol **8b**. Treatment of **7** with methylmagnesium iodide resulted in the formation of an insoluble precipitate and, after quenching, starting material was recovered. Results were more satisfactory after blocking the hydroxyl group. Thus treatment of trimethylsilyl ether **12** with methyllithium in ether provided vinyl tertiary alcohol **8b** as the major product. A trace of the epimer **8a** was also formed as well as about 20% of 1,4-addition product **11**. Treatment of **12** with methylmagnesium iodide gave inferior stereoselection (**8b**/**8a**, 4/1 compared to 12/1 for the lithium reagent).

In order to determine the relative stereochemistry, the two tertiary alcohols were converted into their corresponding cyclic carbonates **9a** and **9b**, as shown in scheme III. A recent report[17] appeared to indicate that in six-membered cyclic carbonates, an axial substituent would have an ^{1}H NMR absorption at higher field than a similar equatorial substituent. We reasoned that structure **9a** should have an axial vinyl group, allowing the other three substituents to be equatorial. Similarly **9b** should have an axial methyl group (at the tertiary alcohol center), allowing three equatorial substituents as well. This analysis is based on the assumption that the cyclic carbonates exist in the chair conformation with the maximum number of equatorial substituents.

This rationalization led us to (temporarily) misassign the stereochemistry in structures **9a** and **9b** and thus **8a** and **8b**. The correct assignment became clear when *N*-methyl derivative **10b** was subjected to an X-ray crystallographic structure determination which proved it to have the relative stereochemistry shown in Scheme III and Figure 1. The discrepancy with the NMR analysis was also clarified since the crystal structure shows the ring of **10b** to be nearly planar. The tertiary carbinol carbon is the only ring atom substantially out of the plane, placing the vinyl group in a pseudoaxial position. The bond from the vinyl group to the ring is nearly perpendicular to the plane of the ring. Thus, while simple methyl-substituted

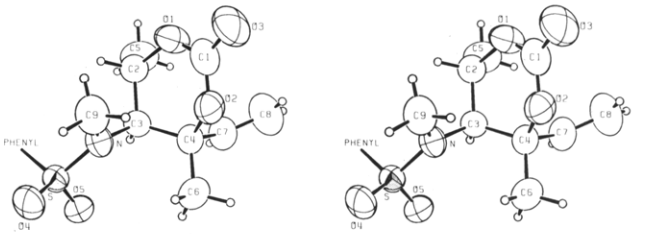


Figure 1. ORTEP drawing of cyclic carbonate **10b** from X-ray study. The phenyl group has been deleted for clarity. The numbering system only serves to correlate Figure 1 with the data in Table II and in the supplementary material; C-4 is equivalent to C-3 of the sibirosamine derivatives.

cyclic carbonates may exist in stable chair conformations,[17] bulkier substituents or heteroatoms apparently perturb the geometry in these systems so that this NMR chemical shift analysis of stereochemistry is unreliable.

Elaboration of Cyclic Carbonate 10b to Methyl *N*-(Phenylsulfonyl)-3-episibirosaminide (17) via the Pummerer Reaction. Since **10b** was first assigned the stereochemistry of **10a** (^{1}H NMR assignment, prior to X-ray analysis), it was chosen for elaboration to the amino sugar (Scheme IV). Epoxidation with MCPBA proceeded smoothly to give epoxide **13** as a 2.5/1 ratio of inseparable epimers. This relatively nonstereoselective reagent was used in order to prepare both epimers for a rapid comparative characterization. The plan was to open the epoxides with a sulfur nucleophile in order to investigate the Pummerer route to the aldehyde oxidation state, a route which was applied recently in the synthesis of carbohydrates.[18,19] Treating the epimeric epoxides with thiophenoxide gave completely selective ring opening by attack at the primary carbon, affording phenyl sulfides **14a** and **14b**. We have no basis for assigning the stereochemistry of the new hydroxyl group, but for purposes of the discussion we have assumed the major isomer of the 2.5/1

(17) Pihlaja, K.; Teinonen, K.-J.; Äyräs, P. *Suom. Kemistil. B* **1970**, *43*, 41.

(18) Ko, S. Y.; Lee, A. W. M.; Masamune, S.; Reed, L. A., III; Sharpless, K. B.; Walker, F. J. *Science (Washington, D.C.)* **1983**, *220*, 949.

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mixture to have structure **14a**. The phenyl sulfides were separated by chromatography and individually elaborated as follows.

The sulfides were easily oxidized to the sulfoxides **15a** and **15b** with sodium periodate. These sulfoxides were each clearly mixtures of sulfoxide epimers as expected and as shown by doubling of ^1H NMR signals. Heating **15a** (or its *O*-acetyl derivative) in acetic anhydride and sodium acetate as previously described[18,19] resulted in a complex mixture of products. We suggest that the difficulty lies with the ease of formation of a tertiary carbonium ion under these conditions at the site of the branching methyl group. The hexoses prepared by similar methods were all straight chain molecules.[18] Furthermore, the adjacent nitrogen could afford some assistance in carbonium ion formation. Seeking a milder method, we explored the action of trifluoroacetic anhydride (TFAA) on the sulfoxides. Treatment of **15a** with excess TFAA at 0 °C to room temperature followed by mercury-assisted methanolysis afforded dimethyl acetal **16** in good yield. The stereochemistry of the hydroxyl group was determined by conversion to the 3-episibirosamine derivative **17**. This was accomplished by stirring in methanolic sodium methoxide to cleave the carbonate followed by acidification which instantly led to the methyl glycoside as a mixture of α- and β-anomers.

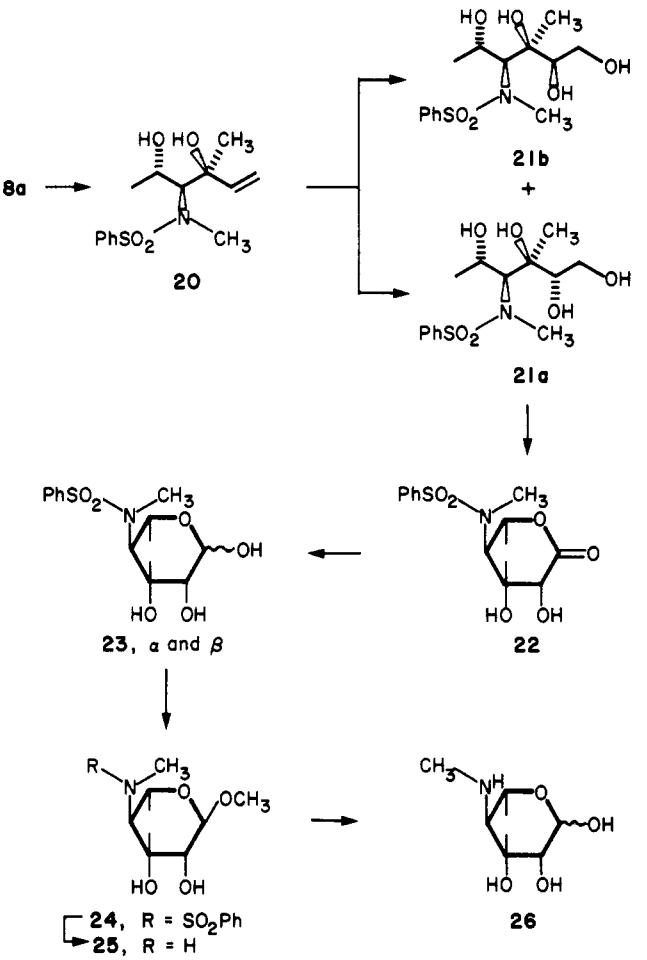
The *N*-tosyl analogue of **17** has been previously prepared,[14] and the almost total identity of NMR data between the two derivatives (in both anomers) leaves no doubt about the stereochemical assignment at C-2 in **17**. The stereochemical arrangement at C-3, C-4, and C-5 is completely unambiguous based on the X-ray structure of **10b**. Since **17** corresponds to the stereochemistry that has now been assigned at the C-3 epimer of sibirosamine, this work provides confirmation of the recent reassignment of C-3 stereochemistry in natural sibirosamine.[14]

Since sulfoxide **15b** was also in hand, we sought to elaborate it to the C-2 epimer of **17**. However, the Pummerer reaction of **15b** led to dimethyl acetal **16**, identical with that obtained from **15a**. Obviously, some process is in effect which funnels either C-2 epimer of **15** into the single C-2 epimer **16**. This could occur as shown in Scheme IV. Here the initial Pummerer rearrangement product **18** (R = $COCF_3$ or H) eliminates trifluoroacetic acid to form **19**. Readdition of a proton (from either CF_3CO_2H or CH_3OH) to C-2 is then stereospecific, leading only to **16** and none of the C-2 epimer. Since the acetic anhydride mediated Pummerer has no efect on the stereochemistry of the adjacent center,[18,19] these results must be rationalized on the basis of the better leaving ability of trifluoroacetate compared with acetate itself.

While this C-2 funneling process fortuitously leads to the correct C-2 configuration for 3-episibirosamine, we did not wish to rely on this stereomutable approach in the synthesis of the natural isomer of sibirosamine. Therfore, after failing to find a suitable protection scheme which would allow the normal acetic anhydride Pummerer route to succeed with our branched substrates, we turned our attention to a different method.

Elaboration of 8a to Sibirosamine via the Selective Oxidation Route. The approach ultimately taken in our synthesis of sibirosamine is shown in Scheme V. This route relies on the stereoselective dihydroxylation of olefin **20** to tetraol **21a**, followed by the highly selective oxidation of the primary hydroxyl group[20,21] to afford lactone **22**. The need for O-protection was thus completely circumvented.

Scheme V. Selective Oxidation Route to Sibirosamine



N-Methylation of **8a** with methyl iodide and potassium carbonate in acetone led to significant *O*-methylation; however, when the solvent was changed to isopropyl alcohol, N-methylated derivative **20** was isolated in 85% yield as analytically pure crystalline material. Catalytic osmylation[22] of **20** provided a 4/1 mixture of tetraols **21a** and **21b** which were easily separable by chromatography. The major isomer (**21a**) was crystallized to give a 64% yield of analytically pure material. The minor isomer (**21b**) was isolated in 15% yield as an oil. The assignments are based on the following conversion of **21a** to sibirosamine.

Platinum-catalyzed oxidation[20,21] of tetraol **21a** with O_2 proceeded cleanly to afford lactone **22** in over 90% yield. We have also recently used this process in the conversion of amino alcohols to amino acids with very satisfactory results.[16] In this case traces of the anomeric lactols **23** were also noted. Without purification, the lactone was reduced (diisobutylaluminum hydride) to the lactols **23** which were crystallized as the anomeric mixture. The lactols were converted by the action of acidic methanol to a single anomer of methyl glycoside **24** in high yield. ^1H NMR data of **24** were compared with data for the *N*-tosyl analogue prepared from natural sibiromycin[14] and found to be in excellent agreement. These spectra were substantially different from either anomer of C-3 epimer **17**. The fact that **24** is obtained as a single anomer is also in agreement with the properties of the natural product.[14]

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(22) VanRheenen, V.; Kelly, R. C.; Cha, D. Y. *Tetrahedron Lett.* **1976**, 1973.

N-Deprotection was accomplished by the rapid reductive cleavage of the phenylsulfonyl group with sodium in liquid ammonia.[23] A single anomer of the free amine **25** again was isolated in 82% yield as an oil. The 250-MHz ^1H NMR spectrum of this product appears very clean, and the high-resolution mass spectrum confirms the molecular formula. In an attempt to obtain the free sugar, the methyl glycoside was treated with 6 N HCl. While the product could be detected by ^1H NMR, byproducts also were formed, and the unstable amino sugar could not be isolated in pure form. The 4-amino sugar probably forms pyrroles by cyclization of the amino group with the aldehyde carbon followed by dehydration and aromatization.

Summary

The methyl glycosides of L-sibirosamine and its C-3 epimer have been prepared by two different routes from the epimeric diols **8a** and **8b**. It seems likely that both the Pummerer route and the selective tetraol oxidation route could be used to prepare either epimer of the amino sugars, although the two routes were selectively applied in this demonstration of the present methodology. Stereocontrol is exerted at each new chiral center formed (C-2 and C-3), and the stereochemistry at C-4 and C-5 are set by the choice of starting threonine. Thus, any of the eight possible diastereomers of the amino sugar should be available in either the D or L form by proper application of this process. Amino acids clearly should be useful for other chirospecific amino sugar syntheses as well.

Experimental Section

General Methods. Ether and tetrahydrofuran (THF) were distilled from sodium/benzophenone immediately before use. Methylene chloride was distilled from P_2O_5. Solutions of reaction mixtures in organic solvents were dried over Na_2SO_4. Organometallic reactions were carried out under N_2, reagents and solvent being transferred by syringe. Methyllithium and methylmagnesium iodide were used as ether solutions. Vinylmagnesium bromide was used as a THF solution.[15] Platinum oxide (used for preparing platinum oxidation catalyst) was prepared from ammonium chloroplatinate as described[24,25] in a platinum vessel.[21] ^1H NMR spectra were recorded in $CDCl_3$ unless otherwise noted and are reported in ppm downfield of internal tetramethylsilane (δ units). The X-ray crystallographic structure of **10b** was determined by using the MULTAN 11/82 program.

***N*-(Phenylsulfonyl)-L-threonine (3).** L-Threonine (1.19 g, 10 mmol) was dissolved in H_2O (15 mL) and treated with Na_2CO_3 (3.18 g, 30 mmol) followed by phenylsulfonyl chloride (2.65 g, 15 mmol). The mixture was stirred at room temperature for 5 h, then washed with Et_2O, acidified to pH 2, and extracted with EtOAc. The solvent was dried and evaporated and the residue was crystallized (EtOAc/petroleum ether) to yield 1.68 g, 65% yield, of **3**: mp 146–148 °C; ^1H NMR (acetone-d_6) δ 1.16 (d, 3 H, J = 7 Hz), 3.86 (m, 1 H), 4.2 (m, 1 H), 6.29 (d, 1 H, J = 9), 7.55 (m, 3 H), 7.86 (m, 2 H); $[\alpha]^{25}_D$ +10.6° (c 3.2, MeOH). Anal. ($C_{10}H_{13}NO_5S$) C, H, N.

***N*-(Phenylsulfonyl)-L-allothreonine (5).** Methyl *cis*-L-2-phenyl-5-methyl-2-oxazoline-4-carboxylate (27.2 g, 0.124 mol) was hydrolyzed with 6 N HCl as reported.[12] After removal of benzoic acid and evaporation of the HCl, the residue was dissolved in water (600 mL), treated with Na_2CO_3 (39.3 g, 0.372 mol) and benzenesulfonyl chloride (23.6 mL, 0.186 mol), and stirred vigorously for 4 h. Isolation was carried out as above to yield **5**: 21.8 g, 67% yield; mp 176–177 °C (lit.[16] mp 175–177 °C, D isomer); $[\alpha]^{23}_D$ +17.1° (c 2.0, MeOH) (lit.[16] $[\alpha]_D$ −16.8°, D isomer).

(3*S*,4*R*)-*N*-(Phenylsulfonyl)-3-amino-4-hydroxy-2-pentanone (4). *N*-(Phenylsulfonyl)-L-threonine (**3**, 1.04 g, 4.0 mmol) was dissolved in THF (50 mL), cooled to −78 °C, and treated with MeLi (1.29 M, 24 mmol) dropwise over 20 min. The mixture was allowed to warm to room temperature and stirred for 2 h, and then it was poured into 2 M H_3PO_4 (25 mL) at 0 °C and extracted with EtOAc (4×). The organic extracts were combined, washed with $NaHCO_3$ (saturated), dried, and evaporated. Crystallization (EtOAc) of the residue provided 0.75 g, 73% yield, of **4**: mp 174–176 °C; ^1H NMR (5% Me_2SO-d_6 in $CDCl_3$) δ 1.08 (d, 3 H, J = 6.2 Hz), 2.19 (s, 3 H), 3.72 (m, 1 H), 4.17 (m, 1 H), 4.27 (d, 1 H, J = 6, OH), 6.80 (d, 1 H, J = 7, NH), 7.56 (m, 3 H), 7.84 (m, 2 H); $[\alpha]^{23}_D$ +49.1° (c 1.0, MeOH). Anal. ($C_{11}H_{15}NO_4S$) C, H, N.

(3*S*,4*S*)-*N*-(Phenylsulfonyl)-3-amino-4-hydroxy-2-pentanone (6). *N*-(Phenylsulfonyl)-L-allothreonine (**5**, 2.50 g, 9.6 mmol) was dissolved in THF (110 mL), cooled to −78 °C, and treated with MeLi (1.5 M, 24.1 mmol) dropwise over 10 min. After being stirred for 15 min, the mixture was allowed to warm to 0 °C when MeMgI (1.0 M, 24.1 mmol) was added and the mixture was stirred at 35 °C for 24 h. Isolation as above provided 0.92 g, 37% yield, of **6**: mp 145–146 °C (EtOAc/hexanes); ^1H NMR (5% Me_2SO-d_6 in $CDCl_3$) δ 1.13 (d, 3 H, J = 6.4 Hz), 2.07 (s, 3 H), 3.65 (d, 1 H, J = 6.7, OH), 3.81 (dd, 1 H, J_1 = 7.9, J_2 = 4.6), 3.94 (m, 1 H), 6.49 (d, 1 H, J = 7.9, NH), 7.54 (m, 3 H), 7.86 (m, 2 H); $[\alpha]^{23}_D$ +9.6° (c 1.0, MeOH). Anal. ($C_{11}N_{15}NO_4S$) C, H, N.

From the $NaHCO_3$ washings 1.05 g (42%) of **5**, unchanged in melting point and $[\alpha]_D$, was recovered by acidification and extraction.

(4*S*,5*S*)-*N*-(Phenylsulfonyl)-4-amino-5-hydroxy-1-hexen-3-one (7) was prepared in the same manner as ketone **6** by substituting vinylmagnesium bromide for MeMgI. The yield of **7** was 35–40% with about 40% of starting material being recovered: mp 121–122 °C ($CHCl_3$/hexanes); ^1H NMR δ 1.09 (d, 3 H, J = 6.4 Hz), 4.09 (m, 1 H), 4.30 (m, 1 H), 5.84 (m, 2 H, includes NH), 6.33 (m, 2 H), 7.53 (m, 3 H), 7.84 (m, 2 H); $[\alpha]^{23}_D$ +45.4° (c 1.2, MeOH). Anal. ($C_{12}H_{15}NO_4S$) C, H, N.

(3*S*,4*S*,5*S*)-*N*-(Phenylsulfonyl)-4-amino-3,5-dihydroxy-3-methyl-1-hexene (8a). Ketone **6** (3.02 g, 11.7 mmol) in THF (30 mL) was added dropwise to vinylmagnesium bromide (70 mmol in 140 mL THF) at −10 °C. After 15 min of stirring, the reaction was allowed to warm to room temperature and stirred an additional 15 min. The mixture was poured into cold 2 M H_3PO_4 (100 mL) and extracted with EtOAc (3×), the extracts were washed with $NaHCO_3$ (saturated), dried, and evaporated, and the residue was crystallized (EtOAc/hexanes) to give 2.18 g of **8a**. The mother liquors were evaporated and the residue was resubjected to the Grignard reaction ($^1/_3$ scale). Aqueous isolation and chromatography (silica gel, $CHCl_3$/EtOAc, 80/20) provided a further 0.60 g of **8a**: total yield, 2.78 g, 83%; mp 123–124 °C; ^1H NMR δ 1.20 (d, 3 H, J = 6.5 Hz), 1.24 (s, 3 H), 2.53 (s, 1 H), 2.88 (d, 1 H, J = 7.2), 3.26 (m, 1 H), 4.01 (m, 1 H), 4.80 (d, 1 H, J = 8.9), 4.92 (dd, 1 H, J_1 = 10.7, J_2 = 0.9), 5.16 (dd, 1 H, J_1 = 17.2, J_2 = 0.9), 5.52 (dd, 1 H, J_1 = 10.5, J_2 = 17.2), 7.56 (m, 3 H), 7.86 (m, 2 H); $[\alpha]^{23}_D$ −51.5° (c 2.3, MeOH). Anal. ($C_{13}H_{19}NO_4S$) C, H, N.

(5*S*,6*S*)-*N*-(Phenylsulfonyl)-5-amino-6-hydroxy-4-heptanone (11). Vinyl ketone **7** (75 mg, 0.28 mmol) in THF (3 mL) was added dropwise to MeLi (1.4 mmol in 7 mL THF) at −78 °C. The mixture was stirred at −78 °C for 1 h, then at room temperature for 30 min. The usual isolation provided 80 mg of material which appeared to be 90% **11** by ^1H NMR analysis: ^1H NMR δ 0.69 (t, 3 H, J = 7.4 Hz), 1.10 (d, 3 H, J = 6.3), 1.38 (m, 2 H), 2.20 (m, 2 H), 2.38 (m, 1 H), 4.03 (m, 2 H), 5.91 (d, 1 H, J = 7.7), 7.57 (m, 3 H), 7.83 (m, 2 H).

(4*S*,5*S*)-*N*-(Phenylsulfonyl)-4-amino-5-[(trimethylsilyl)oxy]-1-hexen-3-one (12). Vinyl ketone **7** (1.81 g, 6.74 mmol) was dissolved in THF (50 mL) and cooled to 0 °C. Trimethylsilyl chloride (1.28 mL, 10.1 mmol) was added followed by Et_3N (1.41 mL, 10.1 mmol). The mixture was stirred for 20 min at 0 °C and then distributed between EtOAc and 1 M NaH_2PO_4, the organic phase was washed ($NaHCO_3$, saturated), dried, and evaporated, and the resulting residue of **12** (2.30 g, 100% yield) was sufficiently pure for further use: ^1H NMR δ −0.02 (s, 9 H), +1.25 (d, 3 H, J = 6.1 Hz), 3.82 (m, 1 H), 4.02 (m, 1 H), 5.48 (d, 1 H, J = 9.3), 5.64 (dd, 1 H, J_1 = 10.5, J_2 = 1.1), 6.04 (dd, 1 H, J_1 = 17.4, J_2 = 1.2), 6.32 (dd, 1 H, J_1 = 10.5, J_2 = 17.4), 7.50 (m, 3 H), 7.80 (m, 2 H).

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(3*R*,4*S*,5*S*)-*N*-(Phenylsulfonyl)-4-amino-3,5-dihydroxy-3-methyl-1-hexene (8b). To ketone **12** (2.00 g, 5.86 mmol), dissolved in ether (30 mL) and cooled to −78 °C, was added dropwise MeLi (1.5 M, 27 mmol). The mixture was stirred at −78 °C for 1.5 h and then at room temperature for 30 min. Isolation as before provided a mixture of **8b**, **8a**, and **11** in a 12/1/4 ratio. Chromatography (silica gel, CH_2Cl_2/EtOAc, 4/1) provided 1.17 g (70% yield) of a 12/1 mixture of **8b**/**8a** which could not be separated until after conversion to the cyclic carbonates. Peaks corresponding to **8a** are not listed in the NMR data: ^{1}H NMR δ 1.04 (s, 3 H), 1.16 (d, 3 H, J = 6.5 Hz), 2.68 (s, 1 H), 2.82 (d, 1 H, J = 7.6), 3.31 (m, 1 H), 3.96 (m, 1 H), 5.08 (dd, 1 H, J_1 = 10.7, J_2 = 1.0), 5.27 (dd, 1 H, J_1 = 17.2, J_2 = 1.0), 5.88 (dd, 1 H, J_1 = 10.7, J_2 = 17.2).

Cyclic Carbonates 9a and 9b. The diols (either pure **8a** or the 12/1 mixture of **8b**/**8a**) were dissolved in CH_2Cl_2 and cooled to 0 °C. Pyridine (400 mol%) was added, and phosgene was slowly bubbled in for 10 min. After a further 45 min at 0 °C the mixture was flushed with N_2 and quenched with aqueous $NaHCO_3$ (saturated). The organic phase was dried and evaporated. In this way pure **8a** led to **9a** which was isolated by chromatography (silica gel, CH_2Cl_2/EtOAc, 4/1) and crystallization (EtOAc/hexanes) in 75–80% yield. The 12/1 mixture of **8b**/**8a** led to a 12/1 mixture of **9b**/**9a** which was separated by chromatography (silica gel, CH_2Cl_2/EtOAc, 9/1). Crystallization (EtOAc/hexanes) gave analytically pure **9b** in 70–75% yield.

9a: mp 178–181 °C; ^{1}H NMR δ 1.09 (d, 3 H, J = 6.3 Hz), 1.32 (s, 3 H), 3.50 (m, 1 H), 4.20 (m, 1 H), 5.07 (d, 1 H, J = 9.9), 5.39 (d, 1 H, J = 17.2), 5.42 (d, 1 H, J = 11.0), 5.88 (dd, 1 H, J_1 = 17.2, J_2 = 11.0), 7.60 (m, 3 H), 7.92 (m, 2 H); $[\alpha]^{23}_D$ −83.2° (*c* 1.1, Me_2SO). Anal. ($C_{14}H_{17}NO_5S$) C, H, N.

9b: mp 210–214 °C; ^{1}H NMR δ 1.31 (d, 3 H, J = 6.5 Hz), 1.42 (s, 3 H), 3.53 (m, 1 H), 4.30 (m, 1 H), 4.97 (d, 1 H, J = 9.8), 5.00 (d, 1 H, J = 10.8), 5.28 (d, 1 H, J = 17.3), 5.59 (dd, 1 H, J_1 = 10.8, J_2 = 17.3), 7.58 (m, 3 H), 7.83 (m, 2 H); $[\alpha]^{23}_D$ −40.1° (*c* 1.2, Me_2SO). Anal. ($C_{14}H_{17}NO_5S$) C, H, N.

***N*-Methyl Cyclic Carbonate 10b.** Compound **9b** (249 mg, 0.80 mmol) was dissolved in acetone (15 mL) and treated with K_2CO_3 (442 mg, 3.2 mmol) and MeI (0.20 mL, 3.2 mmol). The mixture was stirred at room temperature for 3 h, filtered, and evaporated, and the residue was distributed between water and EtOAc. The organic phase was dried and evaporated to leave a crystalline mass of 258 mg, 99% yield. Crystallization ($CHCl_3$/hexanes) provided analytically pure material suitable for X-ray structure determination: mp 110–111 °C; ^{1}H NMR δ 1.28 (d, 3 H, J = 5.7 Hz), 1.48 (s, 3 H), 2.91 (s, 3 H), 4.2–4.3 (m, 2 H), 5.27 (dd, 1 H, J_1 = 10.9, J_2 = 0.9), 5.48 (dd, 1 H, J_1 = 17.2, J_2 = 0.9), 5.92 (dd, 1 H, J_1 = 10.9, J_2 = 17.2), 7.5–7.7 (m, 3 H), 7.8 (m, 2 H); $[\alpha]^{23}_D$ −31.3° (*c* 1.1, MeOH). Anal. ($C_{15}H_{19}NO_5S$) C, H, N.

Epoxides 13. Cyclic carbonate **10b** (244 mg, 0.75 mmol) and MCPBA (388 mg, 2.25 mmol) were refluxed in CH_2Cl_2 (10 mL) for 4 days. The mixture was diluted with EtOAc, washed (1 × $NaHSO_3$, 2 × $NaHCO_3$), and dried, the solvent was evaporated, and the residue was purified by radial chromatography (silica gel, CH_2Cl_2/EtOAc, 9/1) to provide the epoxides **13** as a 2.5/1 epimeric mixture: 243 mg, 95% yield; ^{1}H NMR (major epimer) δ 1.08 (d, 3 H, J = 6.3 Hz), 1.55 (s, 3 H), 2.8–2.9 (m, 1 H), 2.92 (s, 3 H), 3.0 (m, 1 H), 3.4 (m, 1 H), 4.2–4.4 (m, 2 H), 7.5–7.7 (m, 3 H), 7.8–7.9 (m, 2 H); ^{1}H NMR (minor epimer) δ 1.13 (d, 3 H, J = 6.4), 1.49 (s, 3 H), 2.8–3.0 (m, 2 H), 2.91 (s, 3 H), 3.3 (m, 1 H), 4.1 (d, 1 H, J = 8), 4.2–4.4 (m, 1 H), 7.5–7.7 (m, 3 H), 7.8–7.9 (m, 2 H).

Phenyl Sulfides 14a and 14b. The 2.5/1 mixture of epoxides **13** (243 mg, 0.71 mmol) was treated with a solution made by adding MeLi (0.071 mmol, 10 mol%) to thiophenol (80.4 μL, 0.78 mmol) in THF (15 mL). The mixture was stirred at room temperature for 16 h, the solvent was evaporated, and the residue was dissolved in EtOAc and washed with 10% Na_2CO_3 (4×), dried, and evaporated. Radial chromatography (silica gel, EtOAc/CH_2Cl_2, 10/90) provided the phenyl sulfides **14a** and **14b** as a 2.5/1 mixture of 295 mg, 91% yield. The mixture was separated by preparative HPLC (EtOAc/isooctane, 20/80).

14a: mp 116–117 °C; $[\alpha]^{24}_D$ −2.8° (*c* 0.7, MeOH); ^{1}H NMR δ 1.01 (d, 3 H, J = 5.9 Hz), 1.29 (s, 3 H), 2.82 (s, 3 H), 3.09 (dd, 1 H, J_1 = 7.8, J_2 = 14.0), 3.33 (dd, 1 H, J_1 = 6.6, J_2 = 14.0), 4.09 (d, 1 H, J = 9.2), 4.2 (m, 1 H), 5.36 (dd, 1 H, J_1 = 6.6, J_2 = 7.7), 7.3–7.5 (m, 3 H), 7.5–7.7 (m, 5 H), 7.8–8.0 (m, 2 H). Anal. ($C_{21}H_{25}NO_6S_2$) C, H, N.

14b: mp 173–175 °C; $[\alpha]^{24}_D$ −41° (*c* 0.5, MeOH); ^{1}H NMR δ 0.97 (d, 3 H, J = 6.2 Hz), 1.41 (s, 3 H), 2.85 (s, 3 H), 3.61 (d, 2 H, J = 7.0), 4.15 (m, 1 H), 4.31 (d, 1 H, J = 9.4), 4.48 (t, 1 H, J = 7.0), 7.3–7.7 (m, 8 H), 7.8–8.0 (m, 2 H). Anal. ($C_{21}H_{25}NO_6S_2$) C, H, N.

Sulfoxides 15a. Phenyl sulfide **14a** (91 mg, 0.20 mmol) was dissolved in MeOH (12 mL) and treated with $NaIO_4$ (67 mg, 0.32 mmol) in H_2O (2 mL). The mixture was stirred at room temperature for 24 h and then distributed between water and $CHCl_3$. The organic phase was dried and evaporated, and the residue was purified by radial chromatography (silica gel, EtOAc/CH_2Cl_2, 1/1). The product (94 mg, 100% yield), which was obtained as an oil, was a 2/1 mixture of sulfoxide epimers: ^{1}H NMR (major epimer) δ 0.82 (d, 3 H, J = 6.1 Hz), 1.39 (s, 3 H), 2.82 (s, 3 H), 2.9–3.2 (m, 2 h), 3.92 (d, 1 H, J = 9.2), 4.2 (m, 1 H), 5.88 (dd, 1 H, J_1 = 2.6, J_2 = 10.5), 7.5–7.9 (m, 10 H); ^{1}H NMR (minor epimer) δ 0.84 (d, 3 H, J = 5.9), 1.43 (s, 3 H), 2.79 (s, 3 H), 3.2–3.4 (m, 2 H), 3.89 (d, 1 H, J = 8.5), 4.2 (m, 1 H), 5.63 (dd, 1 H, J_1 = 4.7, J_2 = 7.8), 7.5–7.9 (m, 10 H).

Sulfoxides 15b. These were obtained as a 3/2 mixture of sulfoxide epimers from **14b** in the same manner as above: ^{1}H NMR (major epimer) δ 0.84 (d, 3 H, J = 5.9 Hz), 1.52 (s, 3 H), 2.77 (s, 3 H), 3.05 (dd, 1 H, J_1 = 1.8, J_2 = 13.0), 3.87 (dd, 1 H, J_1 = 11.3, J_2 = 13.0), 3.94 (d, 1 H, J = 9.9), 4.1 (m, 1 H), 5.02 (dd, 1 H, J_1 = 11.1, J_2 = 1.8), 7.4–7.9 (m, 10 H); ^{1}H NMR (minor epimer) δ 0.89 (d, 3 H, J = 5.7), 1.43 (s, 3 H), 2.78 (s, 3 H), 3.2–3.5 (m, 2 H), 4.1 (m, 1 H), 4.12 (d, 1 H, J = 10), 4.59 (dd, 1 H, J_1 = 4, J_2 = 9), 7.5–7.9 (m, 10 H).

Dimethyl Acetal 16. Sulfoxide **15a** (18 mg, 0.038 mmol) was dissolved in CH_2Cl_2 (4 mL), cooled to 0 °C, and treated with trifluoroacetic anhydride (95 μL, 0.67 mmol). The solution was stirred at 0 °C for 30 min and then at room temperature for another 30 min. Methanol (5 mL) was added, followed by methanesulfonic acid (1 drop) and mercuric acetate (30 mg). The mixture was stirred a further 10 min, then poured into saturated $NaHCO_3$, and extracted with $CHCl_3$. The extracts were dried and evaporated and the residue was purified by radial chromatography (silica gel, EtOAc/CH_2Cl_2, 15/85) to give the pure dimethyl acetal **16**, which crystallized on standing: 12 mg, yield 78%; mp 156–157 °C; $[\alpha]^{24}_D$ −20° (*c* 0.2, MeOH); ^{1}H NMR δ 0.99 (d, 3 H, J = 6.1 Hz), 1.32 (s, 3 H), 2.83 (s, 3 H), 3.48 (s, 3 H), 3.51 (s, 3 H), 4.11 (d, 1 H, J = 9.3), 4.2–4.35 (m, 1 H), 4.49 (d, 1 H, J = 7.7), 5.28 (d, 1 H, J = 7.7), 7.5–7.7 (m, 3 H), 7.8–7.9 (m, 2 H). Anal. ($C_{17}H_{25}NO_8S$) C, H, N.

Under the same conditions, sulfoxide **15b** gave the same dimethyl acetal **16**.

Methyl *N*-(Phenylsulfonyl)-3-episibirosaminide, α- and β-Anomers (17). Dimethyl acetal **16** (8 mg, 19 μmol) was dissolved in MeOH (2 mL) and treated with sodium methoxide (1 M in MeOH, 38 μL). The mixture was stirred at room temperature for 24 h, then methanesulfonic acid (3 drops) was added, and stirring was continued another 15 min. The mixture was poured into $NaHCO_3$ (saturated) and extracted with $CHCl_3$, and the extracts were dried and evaporated to give a mixture of anomers of **17** as an oil: 7 mg, 100% yield; ^{1}H NMR (α anomer) δ 1.04 (d, 3 H, J = 6.2 Hz), 1.19 (s, 3 H), 2.95 (s, 3 H), 3.44 (s, 3 H), 3.48 (br s, 1 H), 3.9–4.2 (m, 1 H), 4.06 (d, 1 H), 4.68 (br s, 1 H), 7.4–7.65 (m, 3 H), 7.8–7.9 (m, 2 H); ^{1}H NMR (β anomer) δ 0.83 (d, 3 H, J = 6.1), 1.40 (s, 3 H), 2.93 (s, 3 H), 3.37 (br s, 1 H), 3.51 (s, 3 H), 3.88 (d, 1 H, J = 10.1), 3.9–4.2 (m, 1 H), 4.79 (d, 1 H, J = 1.0), 7.4–7.65 (m, 3 H), 7.8–7.9 (m, 2 H).

(3*S*,4*S*,5*S*)-*N*-(Phenylsulfonyl)-*N*,3-dimethyl-4-amino-3,5-dihydroxy-1-hexene (20). Diol **8a** (2.00 g, 7.01 mmol), K_2CO_3 (4.84 g, 35 mmol), and MeI (2.18 mL, 35 mmol) were stirred in isopropyl alcohol (125 mL) at 65 °C for 36 h. The solvent was evaporated, the residue was partitioned between water and $CHCl_3$, the aqueous phase was reextracted with $CHCl_3$, and the organic phases were combined, dried, and evaporated. The residue was chromatographed (silica gel, EtOAc/$CHCl_3$, 1/9) and crystallized to give **20**: 1.75 g, 83% yield; mp 96–97 °C; ^{1}H NMR δ 0.96 (d, 3 H, J = 6.2 Hz), 1.41 (s, 3 H), 2.75 (s, 3 H), 3.14 (d, 1 H, J = 3.2, OH), 3.27 (s, 1 H, OH), 3.91 (d, 1 H, J = 8.8), 4.05 (m, 1 H), 5.14 (dd, 1 H, J_1 = 1.0, J_2 = 10.8), 5.35 (dd, 1 H, J_1 = 1.0, J_2 = 17.2), 6.01 (dd, 1 H, J_1 = 10.8, J_2 = 17.4), 7.5–7.7 (m, 3 H), 7.8–7.9

(m, 2 H); $[\alpha]^{23}_D$ -39.1° (*c* 1.6, MeOH). Anal. ($C_{14}H_{21}NO_4S$) C, H, N.

(2*S*,3*R*,4*S*,5*S*)- and (2*R*,3*R*,4*S*,5*S*)-*N*-(Phenylsulfonyl)-*N*,3-dimethyl-4-aminohexane-1,2,3,5-tetrols (21a and 21b). Olefin **20** (1.48 g, 4.94 mmol) and *N*-methylmorpholine *N*-oxide·H_2O (1.34 g, 9.89 mmol) were dissolved in acetone/H_2O (8/1, 120 mL), treated with OsO_4 (25 mg/mL in *tert*-butyl alcohol, 5 mL, 0.49 mmol), and stirred at room temperature for 48 h. Sodium dithionite (1.72 g), in a small amount of water was added and stirring was continued for 30 min. The precipitated osmium was filtered off, the filtrate was evaporated, and the residue was dissolved in 0.25 M H_3PO_4 and extracted with $CHCl_3$/*i*-PrOH (4/1, 5×). The solvent was dried and evaporated, and the residue was chromatographed (silica gel, EtOAc/$CHCl_3$, 1/1 elutes **21a**; EtOAc elutes **21b**). The first fraction was crystallized (EtOAc/hexanes) to give **21a**: 1.05 g, 64% yield; mp 179–180 °C; ^{1}H NMR (CD_3OD) δ 1.01 (d, 3 H, *J* = 6.3 Hz), 1.30 (s, 3 H), 3.01 (s, 3 H), 3.59 (m, 1 H), 3.88 (m, 4 H), 7.5–7.7 (m, 3 H), 7.8–7.9 (m, 2 H); $[\alpha]^{25}_D$ -17.0° (*c* 2, MeOH). Anal. ($C_{14}H_{23}NO_6S$) C, H, N.

The second fraction gave **21b** as an oil: 0.27 g, 16% yield; ^{1}H NMR (CD_3OD) δ 1.00 (d, 3 H, *J* = 5.8 Hz, 1.28 (s, 3 H), 2.90 (s, 3 H), 3.57–3.81 (m, 2 H), 4.03 (m, 2 H), 7.5–7.7 (m, 3 H), 7.8–7.9 (m, 2 H).

(2*R*,3*R*,4*S*,5*S*)-*N*-(Phenylsulfonyl)-*N*,3-dimethyl-4-amino-2,3,5-trihydroxyhexanoic Acid δ-Lactone (22). Platinum oxide (395 mg) was reduced in H_2O (30 mL) under 45 psi H_2 pressure for 20 min. The catalyst suspension was added to **21a** (790 mg, 2.37 mmol) in H_2O (180 mL), oxygen was passed through the stirred mixture at 60 °C for 2 h, the catalyst was filtered off, NaCl (3 g) was added, and the solution was extracted with $CHCl_3$/*i*-PrOH (4/1, 5×). The extracts were dried and the solvents were evaporated to leave 706 mg (91% yield) of **22** containing a trace of lactols **23**. The product was used in the next step without further purification: ^{1}H NMR δ 1.07 (d, 3 H, *J* = 6.1 Hz), 1.30 (s, 3 H), 2.84 (s, 3 H), 4.14 (d, 1 H, *J* = 9.8), 4.19 (s, 1 H), 4.4 (m, 1 H), 7.5–7.7 (m, 3 H), 7.8–8.0 (m, 2 H); $[\alpha]^{23}_D$ -74.0° (*c* 1.3, MeOH).

***N*-(Phenylsulfonyl)sibirosamine (23).** Lactone **22** (639 mg, 1.94 mmol), dissolved in THF and cooled to -45 °C, was treated with diisobutylaluminum hydride (1.4 M in hexane, 6.93 mL, 9.7 mmol). The solution was stirred at -45 °C for 3.5 h and then quenched with MeOH (20 mL) containing CH_3SO_3H (2 mL). After warming to room temperature, the mixture was poured into $CHCl_3$ and excess saturated $NaHCO_3$, the mixture was filtered, and the layers were separated. The aqueous phase was reextracted with $CHCl_3$ and $CHCl_3$/*i*-PrOH (4/1), the combined extracts were dried, and the solvents were evaporated to leave a residue (600 mg) which was crystallized (EtOAc/hexanes) to give 485 mg (75% yield) of the lactols as a nearly 1/1 α,β-anomeric mixture: mp 180–188 °C; ^{1}H NMR δ 0.53 (d, $^3/_2$ H, *J* = 6.2 Hz), 0.59 (d, $^3/_2$ H, *J* = 5.9), 1.32 (s, $^3/_2$ H), 1.45 (s, $^3/_2$ H), 2.87 (s, $^3/_2$ H), 2.92 (s, $^3/_2$ H), 3.60 (br s, 1 H), 3.72 (m, 1 H), 4.0–4.2 (m, 1 H), 4.81 (br s, $^1/_2$ H), 5.23 (br s, $^1/_2$ H), 7.5–7.7 (m, 3 H), 7.8–7.9 (m, 2 H); $[\alpha]^{23}_D$ -46.6° (*c* 1.4, MeOH). Anal. ($C_{14}H_{21}NO_6S$) C, H, N.

Methyl *N*-(Phenylsulfonyl)sibirosaminide (24). *N*-(Phenylsulfonyl)sibirosamine (**23**, α- and β-anomers, 339 mg, 1.02 mmol) was dissolved in MeOH (8 mL), CH_3SO_3H (5 drops) was added, and the solution was refluxed for 45 min, then poured into $NaHCO_3$ (saturated), and extracted with $CHCl_3$ and $CHCl_3$/*i*-PrOH (4/1). The extracts were dried and evaporated and the residue was chromatographed (silica gel, $CHCl_3$/EtOAc, 4/1) and crystallized (EtOAc/hexanes) to give 315 mg, 89% yield, of **24**: mp 115–116 °C; ^{1}H NMR δ 0.53 (d, 3 H, *J* = 5.7 Hz), 1.38 (s, 3 H), 2.90 (s, 3 H), 3.25 (br s, 1 H, OH), 3.34 (s, 3 H), 3.55 (d, 1 H, *J* = 1.3), 3.69 (d, 1 H, *J* = 9.9), 3.74 (m, 1 H), 4.33 (br s, 1 H, OH), 4.69 (d, 1 H, *J* = 1.2), 7.5–7.7 (m, 3 H), 7.8–7.9 (m, 2 H); $[\alpha]^{23}_D$ -89.3° (*c* 1.8, MeOH). Anal. ($C_{15}H_{23}NO_6S$) C, H, N.

Methyl Sibirosaminide (25).[11] Phenylsulfonyl derivative **24** (148 mg, 0.43 mmol) was placed in a flask equipped with a dry ice condensor. Anhydrous ammonia (10 mL) was condensed into the flask, small pieces of sodium were added to the stirred solution until a deep blue color persisted for 5 min, and then NH_4Cl was added to destory the blue color. The ammonia was evaporated with a stream of nitrogen, and the residue was dissolved in saturated $NaHCO_3$ (2 mL) and extracted with $CHCl_3$ and $CHCl_3$/*i*-PrOH (4/1) alternating for a total of eleven extractions. The dried (K_2CO_3) extracts were evaporated to leave a residue of nearly pure amine **25** as an oil: 72 mg, 82% yield; ^{1}H NMR (CD_3OD) δ 1.21 (s, 3 H), 1.27 (d, 3 H, *J* = 6.3 Hz), 2.35 (d, 1 H, *J* = 9.9), 2.48 (s, 3 H), 3.32 (s, 3 H), 3.36 (d, 1 H, *J* = 1.3), 3.56 (dq, 1 H, J_1 = 6.3, J_2 = 9.9), 4.59 (d, 1 H, *J* = 1.0); in D_2O/DCl the ^{1}H NMR spectrum is essentially identical with that reported[11] for the glycoside hydrochloride; $[\alpha]^{23}_D$ -77.0° (*c* 1.5, MeOH); mass spectrum, exact mass calcd for $C_9H_{19}NO_4$ *m*/*z* 205.1314, found 205.1317.

Sibirosamine·HCl (26). Methyl sibirosaminide (**25**, 10 mg, 50 μmol) was dissolved in 6 N DCl in D_2O. The solution was heated at 60 °C and monitored by ^{1}H NMR ever 2 h. After 6 h, the methyl glycoside was cleaved to the extent of about 50%. The anomeric protons of the free sugar appeared as slightly broadened singlets at 5.05 and 5.17 ppm in a ratio of 2/1. Other signals were obscured by byproducts and starting material. Further heating or storage of the sample led to continually decreasing amounts of product with formation of UV absorbing (254 nm) material.

X-ray Crystallographic Analysis. Large, clear, colorless crystals of **10b** were obtained by slow crystallization from $CHCl_3$/hexanes. Fragments cleaved from some of these crystals were mounted on glass fibers using polycyanoacrylate cement. Preliminary precession photographs indicated orthorhombic Laue symmetry and yielded preliminary cell dimensions. Systematic absences were consistent only with space group $P2_12_12_1$ (No. 19).

The crystal used for data collection was then transferred to our Enraf-Nonius CAD-4 diffractometer[26] and centered in the beam. Automatic peak search and indexing procedures yielded the same reduced primitive cell as found from the photographs. The final cell parameters and specific data collection parameters are given in Table I.

Table I. Crystal and Data Collection Parameters for Compound 10b, $C_{15}H_{19}NO_5S$

Crystal Parameters at 25 °C[a,b]	
a = 8.2136 (5) Å	space group, $P2_12_12_1$ (No. 19)
b = 11.1000 (14) Å	formula weight = 325.39 amu
c = 18.2287 (21) Å	*Z* = 4
V = 1661.9 (3)	size of crystal, 0.28 × 0.30 × 0.32 mm
d(obsd) =	*d*(calcd) = 1.30 g cm^{-3}
μ(calcd) = 2.06 cm^{-1}	

Data Measurement Parameters[26]

radiation, Mo Kα (λ = 0.71073 A)
monochromator, highly oriented graphite (2θ = 12.2°)
detector, crystal scintillation counter with PHA
reflections measured, +*h*,+*k*,+*l*
2θ range, 3–45 scan type: θ-2θ
scan speed, 0.60–6.7 (θ deg/min)
scan width, Δθ = 0.5 + 0.347 tan θ
background, measured over an additional 0.25 (Δθ) at each end of the scan
aperture - crystal = 173 mm vertical aperture = 3.0 mm
horizontal aperture = 2.0 + 1.0 tan θ mm (variable)
no. of reflections collected, 1288
no. of unique reflections, 1269
intensity standards, (4,0,0), (0,8,0), (0,0,12), measured every 2 h of X-ray exposure time; over the data collection period no decrease in intensity was observed
orientation, 3 reflections were checked after every 250 measurements; crystal orientation was redetermined if any of the reflections were offset from their predicted positions by more than 0.1°; reorientation was not needed during data collection

[a] Unit cell parameters and their esd's were derived by a least-squares fit to the setting angles of the unresolved Mo Kα components of 24 reflections with 2θ between 27° and 31°. [b] In this and all subsequent tables and esd's of all parameters are given in parentheses, right justified to the least significant digit(s) given.

(26) Instrumentation at the University of California chemistry department X-ray crystallographic facility (CHEXRAY) consists of two Enraf-Nonius CAD-4 diffractometers, one controlled by a DEC PDP 8/a with an RK05 disk and the other by a DEC PDP 8/e with an RL01 disk. Both use Enraf-Nonius software as described in the CAD-4 Operation Manual, Enraf-Nonius, Delft, Nov, 1977, updated Jan, 1980.

Table II. Positional Parameters and Their Estimated Standard Deviations[a]

atom	x	y	z	B, Å²
S	0.00987 (9)	−0.28966 (7)	0.24879 (4)	4.24 (1)
O1	−0.0962 (3)	−0.3982 (2)	−0.0037 (1)	6.06 (6)
O2	0.1756 (3)	−0.3698 (2)	0.0156 (1)	5.43 (5)
O3	0.0623 (4)	−0.3279 (3)	−0.0898 (1)	8.03 (7)
O4	0.0682 (3)	−0.1747 (2)	0.2711 (1)	5.81 (5)
O5	0.0838 (3)	−0.3958 (2)	0.2778 (1)	5.38 (5)
N	0.0261 (3)	−0.2950 (2)	0.1602 (1)	4.39 (5)
C1	0.0488 (5)	−0.3649 (3)	−0.0280 (2)	5.69 (8)
C2	−0.1366 (4)	−0.4190 (3)	0.0736 (2)	4.58 (7)
C3	0.0127 (4)	−0.4115 (2)	0.1233 (1)	3.82 (6)
C4	0.1681 (4)	−0.4441 (3)	0.0818 (2)	4.59 (7)
C5	−0.2260 (5)	−0.5365 (4)	0.0767 (2)	7.0 (1)
C6	0.3217 (4)	−0.4128 (4)	0.1234 (2)	6.48 (9)
C7	0.1718 (5)	−0.5747 (3)	0.0609 (2)	6.17 (9)
C8	0.2125 (7)	−0.6172 (4)	−0.0036 (2)	9.5 (1)
C9	0.0161 (5)	−0.1823 (3)	0.1169 (2)	5.70 (8)
C10	−0.1983 (3)	−0.2972 (3)	0.2707 (2)	4.05 (6)
C11	−0.2617 (5)	−0.3963 (4)	0.3039 (3)	7.4 (1)
C12	−0.4248 (6)	−0.3986 (4)	0.3233 (3)	9.1 (1)
C13	−0.5208 (4)	−0.3049 (4)	0.3082 (2)	7.1 (1)
C14	−0.4620 (4)	−0.2099 (4)	0.2725 (2)	7.08 (9)
C15	−0.2992 (4)	−0.2025 (4)	0.2532 (2)	5.80 (8)

[a] Anisotropically refined atoms are given in the form of the isotropic equivalent thermal parameter defined as

$$(4/3)[a^2B(1,1) + b^2B(2,2) + c^2B(3,3) + ab(\cos\gamma)B(1,2) + ac(\cos\beta)B(1,3) + bc(\cos\alpha)B(2,3)]$$

Structure Determination. The 1288 raw intensity data were converted to structure factor amplitudes and their estimated standard deviations by correction for scan speed, background, and Lorentz and polarization effects.[27-29] No correction for crystal decomposition was necessary. Inspection of the azimuthal scan data[30] showed a variation $I_{min}/I_{max} = 0.97$ for the average curve. No correction for absorption was applied. Removal of systematically absent data left 1269 unique data.

The structure was solved by using MULTAN 11/82[29] and refined via standard least-squares and Fourier techniques. The enantiomer was fixed by reference to the known absolute configuration around C-2 and C-3. In a difference Fourier map calculated following refinement of all non-hydrogen atoms with anisotropic thermal parameters, peaks corresponding to the expected positions of most of the hydrogen atoms were found. Hydrogens were included in the structure factor calculations in their expected positions based on idealized bonding geometry but were not refined in at least squares. They were assigned isotropic thermal parameters 1–2A^2 larger than the equivalent Biso of the atom to which they were bonded. Inspection of the low-angle, high-intensity data indicated that a correction for secondary extinction was necessary. A secondary extinction coefficient[31] was included in the least-squares refinement.

The final residuals[32] for 200 variables refined against the 1123 data for which $F^2 > 3\sigma(F^2)$ were $R = 2.81\%$, $wR = 4.04\%$ and GOF = 1.823. The R value for all 1269 data was 3.63%.

The quality minimized by the least-squares program was $\sum w(|F_o| - |F_c|)^2$, where w is the weight of a given observation. The p factor,[32] used to reduce the weight of intense reflections, was set to 0.035 for the final cycles of refinement. The analytical forms of the scattering factor tables for the neutral atoms were used[33] and all non-hydrogen scattering factors were corrected for both the real and imaginary components of anomalous dispersion.[34]

Inspection of the residuals ordered in ranges of sin θ/λ, $|F_o|$, and parity and value of the individual indexes showed no unusual features or trends. the largest peak in the final difference Fourier map had an electron density of 0.13 e^-/A^3.

The positional parameters of the non-hydrogen atoms are given in Table II.

Acknowledgment. The crystal structure analysis was performed by Dr. F. J. Hollander, staff crystallographer at the University of California, Berkeley, X-ray Crystallographic Facility (CHEXRAY).

Registry No. **3**, 93474-55-6; **4**, 93474-56-7; **5**, 93474-57-8; **6**, 93474-58-9; **7**, 93474-59-0; **8a**, 93474-60-3; **8b**, 93601-09-3; **9a**, 93474-61-4; **9b**, 93601-10-6; **10b**, 93474-62-5; **11**, 93474-63-6; **12**, 93474-64-7; **13** (isomer A), 93474-65-8; **13** (isomer B), 93601-11-7; **14a**, 93474-66-9; **14b**, 93601-12-8; **15a** (isomer A), 93474-67-0; **15a** (isomer B), 93601-13-9; **15b** (isomer A), 93601-14-0; **15b** (isomer B), 93601-15-1; **16**, 93474-68-1; **17** (α-isomer), 93474-69-2; **17** (β-isomer), 93474-70-5; **20**, 93474-71-6; **21a**, 93474-72-7; **21b**, 93601-16-2; **22**, 93474-73-8; **23** (α-isomer), 93474-74-9; **23** (β-isomer), 93474-75-0; **24**, 93474-76-1; **25**, 93601-17-3; **26**, 93601-18-4; L-threonine, 72-19-5; methyl *cis*-L-2-phenyl-5-methyl-2-oxazoline-4-carboxylate, 82659-84-5; vinylmagnesium bromide, 1826-67-1; thiophenol, 108-98-5; L-allothreonine, 28954-12-3; MeMgI, 917-64-6.

Supplementary Material Available: Tables of general temperature factor expressions, thermal vibration amplitudes, unrefined hydrogen positional parameters, intramolecular distances, intramolecular angles and torsional angles (4 pages). Ordering information is given on any current masthead page.

(27) All calculations were performed on a PDP 11/60 equipped with 128 kilowords of memory, twin RK07 28 MByte disk drives, Versatec printer/plotter and TU10 tape drive with locally modified Nonius-SDP[3] software operating under RSX-11M.

(28) Structure Determination Package User's Guide, 1982, B. A. Frenz and Associates, College Station, TX 77840.

(29) The data reduction formulae are

$$F_o^2 = \frac{\omega}{Lp}(C - 2B)$$

$$\sigma_0(F_o^2) = \frac{\omega}{Lp}(C + 4B)^{1/2}$$

$$F_o = (F_o^2)^{1/2}$$

$$\sigma_0(F) = \frac{\sigma_0(F_o^2)}{2F_o}$$

where C is the total count in the scan, B the sum of the two background counts, ω the scan speed used in deg/min, and

$$\frac{1}{Lp} = \frac{\sin 2\theta\,(1 + \cos^2 2\theta_m)}{1 + \cos^2 2\theta_m - \sin^2 2\theta}$$

is the correction for Lorentz and polarization effects for a reflection with scattering angle 2θ and radiation monochromatized with a 50% perfect single-crystal monochrometer with scattering angle $2\theta_m$.

(30) Reflections used for azimuthal scans were located near $\chi = 90°$ and the intensities were measured at 10° increments of rotation of the crystal about the diffraction vector.

(31) Zachariesen, W. H. *Acta Crystallogr.* **1963**, *16*, 1139.

(32)

$$R = \frac{\sum||F_o| - |F_c||}{\sum|F_o|}$$

$$wR = \left\{\frac{\sum w(|F_o| - |F_c|)^2}{\sum wF_o^2}\right\}^{1/2}$$

$$\text{GOF} = \left\{\frac{\sum w(|F_o| - |F_c|)^2}{(n_o - n_v)}\right\}^{1/2}$$

where n_o is the number of observations, n_v the number of variable parameters, and the weights w were given by

$$w = \frac{4F_o^2}{\sigma^2(F_o^2)},\quad \sigma^2(F_o^2) = \{\sigma_0^2(F_o^2) + (pF^2)^2\}$$

where p is the factor used to lower the weight of intense reflections.

(33) Cromer, D. T.; Waber, J. T. "International Tables for X-ray Crystallography"; The Kynoch Press: Birmingham, England, 1974; Vol. IV, Table 2.2B.

(34) Cromer, D. T. Reference 33, Table 2.3.1.