Diastereoselective Synthesis of Actinobolin from D-Glucose by Application of a Novel [3 + 3] Annulation

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Received February 23, 1994[⊗]

The synthesis of 5,6-*O*-(2-propylidene)-*N*-desalanyl-*N*-[(4-methylphenyl)methanesulfonyl]actinobolin (**37**) is reported. The carbocyclic ring of **37** is constructed by a novel [3 + 3] annulation method involving sequential two-electron and one-electron allylation with the conjunctive reagent **5**. The 4-amino-4,6-dideoxy-D-galactose derivative **25** is efficiently prepared from D-glucose and coupled with **5**. The key step in the annulation is the diastereoselective 6-*endo-trig* radical cyclization of the unusual thiocarbamate **32**. The stereoselectivity is postulated to result from the acetonide protecting group in **32**. The conversion of **37** into actinobolin has been previously established.

The isolation,[1] characterization,[1a] and biological properties[2] of (+)-actinobolin (**1**), a metabolite of *Streptomyces griseoviridus* var *atropaciens*, were first reported in 1959. After several structural studies,[3] the complete structure[4] and absolute stereochemistry[5] of actinobolin was proposed and confirmed by X-ray crystallography.[6] Actinobolin is a broad-spectrum antibiotic[2a] with potent cariostatic activity[7] and has limited antitumor[2b,c] and antileukemic[2d] activity. Biological activity in bacteria[8] and tumors[9] is thought to result from inhibition of protein synthesis. Bactobolin (**2**)[10] is a close structural analogue to **1** but is much more potent in bioactivity.[11]

The structure and properties of actinobolin and bactobolin have attracted considerable synthetic interest.[12–17] Two syntheses of (+)-**1** from L-threonine have been reported;[12,15] a third synthesis involved separation of the diastereomers resulting from the acylation of racemic **3a** with L-alanine.[16] The *N*-acetyl-*N*-desalanyl derivative **3d**[18] has been prepared both in racemic[13] and in enantiomerically pure[14] forms. Despite the structural similarities between **1** and **2**, only the elegant route of Weinreb *et al.* has successfully produced bactobolin.[16b,19] In this paper we report the diastereoselective synthesis of (+)-actinobolin from D-glucose by application of a novel [3 + 3] annulation.[20]

Successful conversion of desalanyl derivatives **3** to actinobolin is possible only with certain *N*-protecting groups making **3b** or **3c** suitable synthetic targets.[12,15,16] A theme common to four[12–15] of the five successful syntheses of the actinobolin skeleton is the use of a Diels–Alder reaction to construct the carbocyclic ring.[21] We considered a disconnection of the skeleton involving the C_6–C_7, C_{4a}–C_{8a}, and C_1–O_2 bonds to produce a hexanal (**4**) and an acetoacetate fragment (see Scheme 1). Our synthetic approach envisaged a [3 + 3] annulation process that would couple the fully functionalized **4** (or derivative) with either an acetoacetate or an acetone[22] synthon to form the carbocyclic ring. The C_6–C_7 bond would be formed by nucleophilic addition to the hexanal carbonyl. Considerable literature precedent suggests

[⊗] Abstract published in *Advance ACS Abstracts,* July 1, 1994.

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(9) Smithers, D. L.; Bennett, L. L., Jr.; Struck, R. F. *Mol. Pharmacol.* **1969**, *5*, 433.

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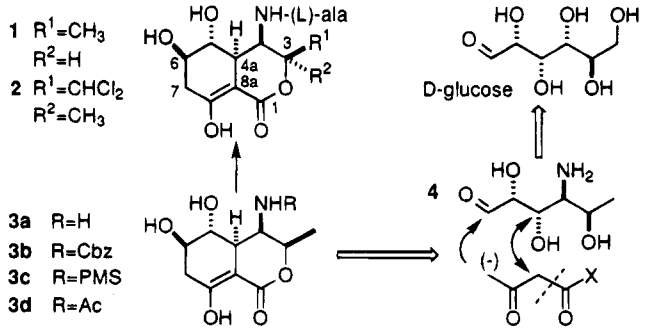
(21) The other successful synthesis[16] used 3-cyclohexenol as an intact progenitor to the carbocyclic ring.

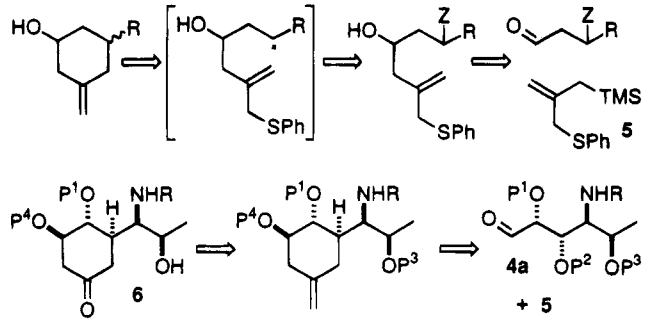
(22) An acetone synthon was feasible since the effective introduction of the C_1 carboxyl group onto the intact carbocyclic ring was established.[16]

0022-3263/94/1959-4230$04.50/0

Scheme 1



Scheme 2



that the desired stereochemical outcome would result from a chelation-controlled addition to the α-alkoxy aldehyde.[23] Formation of the C_{4a}—C_{8a} bond with the desired stereochemistry might, in principle, result from an S_N2 reaction of an enolate (or equivalent) onto a suitably configured leaving group at the β-position of the hexanal. Alternatively, this bond could be formed via an aldol-type reaction, a process which would require a subsequent reduction step. It should be noted that the desired stereochemistry at C_{4a} allows all substituents on the cyclohexane ring to assume an equatorial orientation. Thus, introduction of the C_{4a}-H by a reduction reaction proceeding via a radical or ionic intermediate might be expected to produce an excess of the product with the correct configuration.

One advantage of the above approach lies in the possibility of employing a hexose template to introduce the five contiguous stereogenic centers with the correct absolute configuration.[24] The structure and absolute stereochemistry of the hexanal required for an actinobolin synthesis is equivalent to a 4-amino-4,6-dideoxy-D-galactose. Although this hexose is not readily available, derivatives are easily prepared from D-glucose.[25]

There are relatively few methods available for the synthesis of six-membered carbocyclic rings by [3 + 3] annulation.[26] We are unaware of any close analogies to our proposed scheme where C—C bonds are formed by addition to an aldehyde carbonyl and nucleophilic substitution.[27] There are several examples of formation of six-membered rings by intramolecular enolate alkylaton on an epoxide or primary halide or tosylate.[28] Alkylation is difficult, however, when the leaving group is not primary.[28a] Our concern with the viability of either an inter- or intramolecular enolate alkylation led us to develop a free radical-based protocol for the formation of the C_{4a}—C_{8a} bond.[29] In a model study,[30] we described a new [3 + 3] annulation method using 3-(phenylthio)-2-[(trimethylsilyl)methyl]propene (**5**) as a conjuntive reagent. The process involved the preparation of 3-hydroxy-1-methylenecyclohexanes by sequential two-electron and one-electron allylation of β-substituted aldehydes with **5** (see Scheme 2). It was established that the addition of **5** to an aldehyde was amenable to chelation-controlled diastereoselectivity. Although the subsequent 6-*endo-trig* radical cyclization proceeded with poor stereoselectivity with the model substrates, we expected that a similar cyclization of the projected hexose-derived precursor would give the desired stereochemistry (*vide infra*).

Our initial goal was to prepare an intermediate analogous to **6** by a [3 + 3] annulation of **5** onto a suitably protected galactosamine derivative **4a** (see Scheme 2). The feasibility for further conversion of **6** into both actinobolin and bactobolin is established by analogy to Weinreb's syntheses.[16] The three secondary hydroxyl groups of **4a** require differential protection as each will serve a specific purpose: the C-2 group must provide for chelation-controlled addition to the aldehyde; the C-3 group will be used to generate a carbon-centered radical; the C-5 group will participate in an intramolecular delivery of the C-1 carboxy group of **3**.

The conversion of D-glucose into a 4-amino-4,6-dideoxy-D-galactose requires substitution of the C-4 hydroxy group with an amino group with inversion of configuration and reductive deoxygenation of the C-6 hydroxy group. These transformations are well precedented on a D-glucopyranoside framework.[25] Diol **7** is readily available from D-glucose;[31] the preparation of a suitably protected galactosamine derivative from **7** is illustrated in Scheme 3. In analogy with literature precedent,[32] selective 2-*O*-benzylation of **7** was achieved by treatment with Bu_2SnO followed by BnBr to give the known **8**[33] in 72% yield. Initially, we prepared the azide **14a** from **7** according to the known procedure.[25a] In our hands the conversion of **13a** into **14a** proceeded in modest yield

(23) See, for example: (a) Eliel, E. L. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1983; Vol. 2. (b) Nógrádi, M. *Stereoselective Synthesis*; VCH: Weinheim, Germany, 1987. (c) Reetz, M. T. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 556. (d) Danishefsky, S.; Pearson, W. H.; Harvey, D. F. *J. Am. Chem. Soc.* **1984**, *106*, 2456. (e) Keck, G. E.; Boden, E. P. *Tetrahedron Lett.* **1984**, *25*, 265.

(24) Hanessian, S. *Total Synthesis of Natural Products, The 'Chiron' Approach*; Organic Chemistry Series; Pergamon Press: New York, 1983; Vol. 3.

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(26) For a discussion and list of references see: (a) Seebach, D.; Missbach, M.; Calderari, G.; Eberle, M. *J. Am. Chem. Soc.* **1990**, *112*, 7625. See also: (b) Strauss, M.; Torres, *R. J. Org. Chem.* **1989**, *54*, 756. (c) Guyot, B.; Pornet, J.; Miginiac, L. *Tetrahedron* **1991**, *47*, 3981. (d) Degl'Innocenti, A.; Dembech, P.; Mordini, A.; Ricci, A.; Seconi, G. *Synthesis* **1991**, 267.

(27) An otherwise analogous method using 3-iodo-2-[(trimethylsilyl)-methyl]propene and α,β-epoxy aldehydes gives Felkin–Ahn diastereoselectivity and results in *cis*-1,2-cyclohexanediols. Molander, G.; Shubert, C. *J. Am. Chem. Soc.* **1987**, *109*, 576.

(28) (a) Caine, D. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: New York, 1991; Vol. 3, Chapter 1.01. (b) Ho, T.-L. *Carbocycle Construction in Terpene Synthesis*; VCH Publishers: New York, 1988.

(29) For free radical-based [3 + 3] annulation see: (a) Padwa, A.; Murphree, S. S.; Yeske, P. E. *Tetrahedron Lett.* **1990**, *31*, 2983. (b) Padwa, A.; Klein, D. N.; Murphree, S. S.; Yeske, P. E. *J. Org. Chem.* **1992**, *57*, 298. For a review of the use of radical reactions in the synthesis of natural products see: (c) Jasperse, C. P.; Curran, D. P.; Fevig, T. L. *Chem. Rev.* **1991**, *91*, 1237.

(30) Ward, D. E.; Kaller, B. F. *Tetrahedron Lett.* **1991**, *32*, 843.

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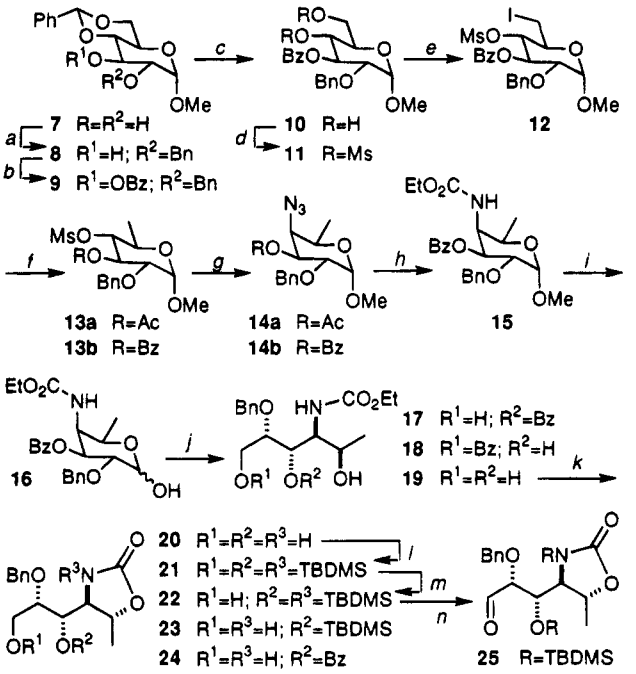
(33) (a) Küster, J. M.; Dyong, I. *Liebigs Ann. Chem.* **1975**, 2179. (b) Garegg, P. J.; Iversen, T.; Oscarson, S. *Carbohydr. Res.* **1976**, *50*, C12.

Scheme 3

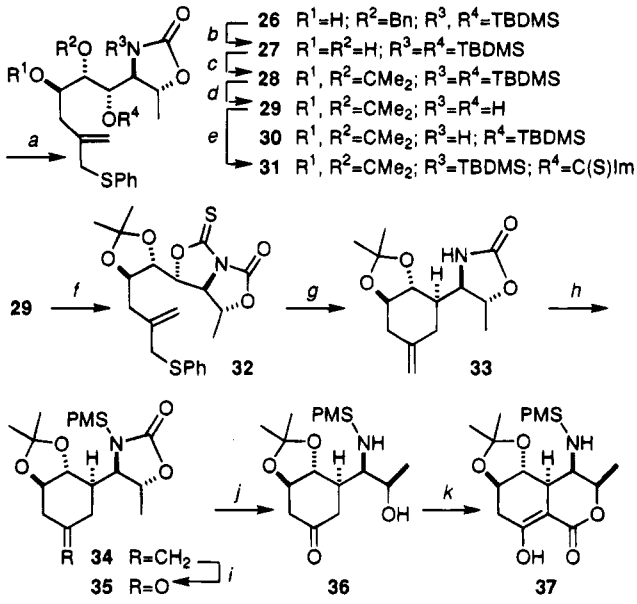


[a] Key: (a) Bu_2SnO; BnBr (72%); (b) BzCl, pyr (90%); (c) TFA, MeOH (94%); (d) MsCl, pyr (92%); (e) NaI, butanone (94%); (f) Zn, HOAc (91%); (g) NaN_3, DMF (90%); (h) (i) $SnCl_2$, Et_3N, PhSH; (ii) EtO_2CCl (72%); (i) TFA, Ac_2O; NaOH, H_2O_2, MeOH (92%); (j) $NaBH_4$, EtOH; (k) KH, PhH (84%); (l) TBDMSOTf, collidine (85%); (m) $HF_{(aq)}$, CH_3CN (78%); (n) $(COCl)_2$, DMSO; Et_3N (88%).

(50–60%) and was plagued by side reactions.[34] These problems were effectively resolved by using the 3-*O*-benzoyl derivative and **14b** was prepared from **7** in excellent overall yield. The azide **14b** was reduced[35] to the corresponding amine which was converted without isolation[36] into the ethyl carbamate **15** under Schotten–Baumann conditions.

Ring opening of the pyranoside acetal of **15** and protection of the resulting C_5 hydroxyl group would reveal a suitable hexanal fragment for annulation with **5**. With related compounds, the use of a dithioacetal to effect formation of open chain aldoses was inefficient due to difficulties encountered in regenerating the aldehydes.[37] We planned to effect ring opening of the pyranose by reduction to give the diol **17** and to achieve selective protection of the secondary alcohol by formation of a cyclic carbamate **24**; oxidation of **24** would give the desired substrate. The pyranose **16** was prepared from **15** by acetolysis followed by hydrolysis under mild conditions.[38] Surprisingly, treatment of **16** with $NaBH_4$ in ethanol failed to produce the expected **17** but instead gave a mixture of **18** and **19**. Despite various changes of solvent, temperature, or addition of buffers, we were unable to

Scheme 4



[a] Key: (a) **25**, **5**, $TiCl_4$, CH_2Cl_2 (87%); (b) BBr_3, CH_2Cl_2 (92%); (c) DMP, TsOH (74%); (d) TBAF, THF (87%); (e) TBDMSOTf, Et_3N; $Im_2C{=}S$, DMAP (52%); (f) $Im_2C{=}S$, PhH (64% from **26**); (g) $(Me_3Sn)_2$, Ph_2CO, $h\nu$ (40–50%); (h) BuLi, PMS-Cl (88%); (i) O_3, CH_2Cl_2/MeOH; DMS (75%); (j) NaOMe, MeOH (60%); (k) Im_2CO; NaH (76% from **34**).

prevent the migration and subsequent hydrolysis of the benzoyl group during reduction of **16**. Treatment of **18** or **19** or a mixture of the two with KH in refluxing benzene selectively formed the *trans* disubstituted oxazolidinone resulting from participation of the C_5 hydroxy group and removed the benzoate group to give **20**. The selective protection of the secondary alcohol of **20** would be a necessary prelude to oxidation. This group was rather hindered and the order of reactivity towards typical alkyl, silyl, and acyl halides was primary OH > NH > secondary OH. After considerable experimentation with sequential protection schemes,[39] we prepared **21** by persilylation of **20** followed by selective deprotection of the primary alcohol. Oxidation of **22** under Swern conditions gave the desired aldehyde **25**.

The synthesis of **25** from **7** (Scheme 3) proceeded in 16 steps and in 14% yield. We found it more efficient and much easier to directly use the crude reaction products and purify intermediates only where most convenient. In this way a 19% overall yield was achieved on a 5-g scale with only three chromatographic separations.

The aldehyde **25** smoothly coupled with allylsilane **5**[30] in the presence of $TiCl_4$ to give the alcohol **26** together with up to 10% of the debenzylated **27** (Scheme 4). Only a single diastereomer of **26** (and of **27**) was detected, and the stereochemistry was assigned on the basis of an expected[30,40] chelation-controlled addition. Completion of

(34) Several products arising from acetate hydrolysis and/or neighboring group participation of the acetate in the mesylate displacement were isolated.

(35) Bartra, M.; Romea, P.; Urpí, F.; Vilarrasa, J. *Tetrahedron* **1990**, *46*, 587.

(36) The amine was prone to O → N acyl migration to give the corresponding benzamide.

(37) Kaller, B. F. Ph.D. Thesis, University of Saskatchewan, 1993.

(38) Hydrolysis of the acetoxy pyranoside with $NaHCO_3$ in MeOH gave **16** along with significant amounts of decomposition products resulting from elimination of the benzoate group. For other examples of the use of alkaline hydrogen peroxide to hydrolyze esters in base-sensitive compounds see: (a) Corey, E. J. *et al. J. Am. Chem. Soc.* **1978**, *100*, 4620. (b) Woodward, R. B. *et al. J. Am. Chem. Soc.* **1981**, *103*, 3213.

(39) For example, it was possible to selectively silylate the primary OH and NH groups with TBDMSOTf in the presence of Et_3N (cf. collidine). Attempted protection of the remaining secondary OH group with MeI, BnBr, or p-(OMe)BnBr lead to N → O silyl migration and subsequent N-alkylation. Hydrolysis of the primary silyl ether (HF, CH_3CN) followed by Swern oxidation gave aldehydes which coupled effectively with **5** establishing the silyl ether as a compatible protecting group for our purposes. For the use of *N*-(trimethylsilyl)-2-oxazolidinone as silylating agent see: Aizpurua, J. M.; Palomo, C. *Can. J. Chem.* **1984**, *62*, 336.

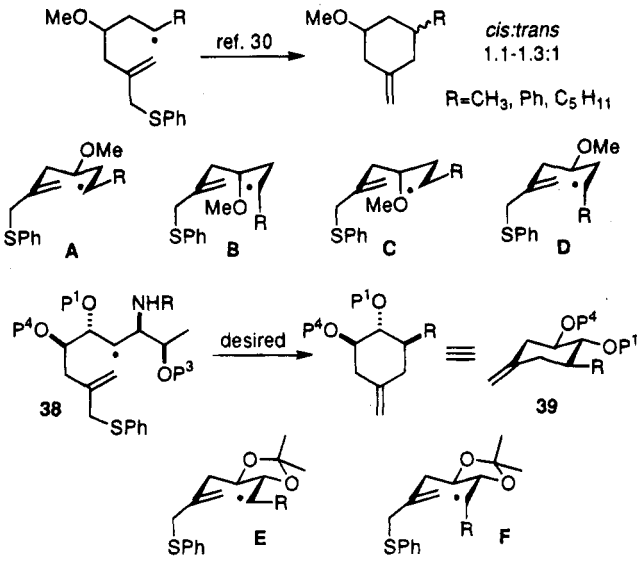


Figure 1. Chairlike transition states for 6-*endo-trig* radical cyclizations.

the [3 + 3] annulation process by a 6-*endo-trig* cyclization would be triggered by the generation of a carbon centered radical at C_{4a} (actinobolin numbering). We planned to protect the C_7-OH group and then selectively convert the *O*-silyl ether into a imidazole thiocarbamate, a group that proved efficacious in our model study.[30]

Poor stereoselectivity had been observed in radical cyclization of our model substrates.[30] These results could be explained by considering the four possible chairlike transition states (TS's) for cyclization (Figure 1). Transition state **A** leading to the *cis* product would expected to be the lowest in energy since both substituents are in a pseudoequatorial orientation. The lower energy TS of those (**C** and **D**) which lead to the *trans* product should be **C** since the *A* value[41] for the MeO group is less than that of the R substituent (CH_3, C_6H_5, or n-C_5H_{11}). The difference in energy between transition states **A** and **C** should be considerably less than the *A* value for the MeO group (0.75 kcal/mol) due to the relatively long carbon–carbon bond in the TS resulting in low selectivity.[42] We reasoned that the diastereoselectivity in the cyclization of **38** to **39** might be improved by reducing the number of TS's by restricting the available conformations. The use of a cyclic protecting group for the C_5,C_6 diol (actinobolin numbering) would necessitate the equatorial orientation of these two substituents and only two chairlike TS's for 6-*endo-trig* cyclization would be possible (**E** and **F**; Figure 1). The difference in energy between **E** and **F** should be related to the *A* value of the R group and thus be much greater than the difference in energy between **A** and **C**.[42]

Treatment of **26** with BBr_3 selectively removed the benzyl ether to give **27** which was converted into the acetonide **28**. We were unable to selectively hydrolize the *O*-silyl ether in the presence of the *N*-silyl group; **29** was readily prepared from **28** by reaction with TBAF. Treatment of **28** with 1,1′-(thiocarbonyl)diimidazole did not produce the expected **31** (R^3 = H) but yielded the unusual thiocarbamate **32**. Although the use of cyclic thionocarbonates as precursors for carbon radicals has been reported,[43] a similar use of cyclic thiocarbamates appears to be unprecedented. Irradiation of a benzene solution of **32** in the presence of $(Me_3Sn)_2$ and benzophenone[44] gave a 40–50% yield of **33**.[30] The stereochemistry of **33** was assigned on the basis of ^{1}H NMR which clearly indicated that the alkyl substituent of the cyclohexane ring was in an equatorial orientation ($J_{H\text{-}4a,H\text{-}5}$ = 10 Hz; $J_{H\text{-}4a,H\text{-}8a}$ = 3 Hz, 13 Hz). Despite considerable experimentation, the yield of **33** could not be improved although the reaction appeared to be very clean by TLC and by ^{1}H NMR. Reactions under various conditions were conducted in sealed tubes and monitored by ^{1}H NMR. Thiocarbamate **32** was largely consumed after 2–4 h of irradiation. Signals due to **33** slowly increased in intensity upon prolonged irradiation.[45] No other products could be detected, although the yield of **33** reached a maximum of only 50% by comparison to an internal standard. Treatment of the crude product with base did not improve the yield of **33** or reveal a new product.[46] Fractionation of the reaction mixture gave **33** along with a complex array of unidentified products. Stereoisomers of **33** were neither detected nor isolated. Reaction of the acyclic radical precursor **31** under the same conditions failed to produce **33**.

Treatment of **33** with (4-methylphenyl)methanesulfonyl chloride (PMS-Cl)[12,47] followed by ozonolysis of the exocyclic methylene group gave **35**. The cyclic carbamate of **35** was hydrolyzed by treatment with methoxide to give the alcohol **36**. The racemic form of **36** was previously converted into (+)-actinobolin by Weinreb *et al.*[16] We noted several differences when comparing the spectral data of **36** with those reported.[48] To further confirm the structure, **36** was cyclized via intramolecular acylation according to the known[16] procedure to give **37** ($[\alpha]_D$ = 5.2°; c = 0.23, $CHCl_3$). The spectral data for (+)-**37** agreed closely with those reported for (±)-**37**.

In conclusion, the preparation of **37** from **7** proceeds in 26 steps and 2.1% overall yield. The synthesis of **37** constitutes a formal synthesis of actinobolin since the efficient conversion of both racemic[16] and optically active[12] **37** into (+)-actinobolin hydrochloride has been described (HF, anisole; Cbz-L-alanine, DCC, Et_3N, DMF; H_2, Pd–C, HCl, MeOH; ca. 85% overall yield).

Experimental Section

General Methods. All solvents were distilled prior to use. Pyridine and Et_3N were distilled from CaH_2 and stored over KOH pellets. Anhydrous solvents were distilled under argon

(40) For a review on reactions of allyl silanes see: Fleming, I.; Dunoguès, J.; Smithers, R. *Org. React.* **1989**, *37*, 57.

(41) Hirsch, J. A. *Top. Stereochem.* **1967**, *1*, 199.

(42) At rt, a product ratio of 1.3:1 requires $\Delta\Delta G^{\ddagger}$ = 0.16 kcal/mol; a $\Delta\Delta G^{\ddagger}$ = 0.75 kcal/mol would give a 3.5:1 ratio. We estimate the *A* value for the R group in TS's **E** and **F** to be ≥2 kcal/mol (Et = 1.8 kcal/mol; *i*-Pr = 2.1 kcal/mol).[41]

(43) Ziegler, F. E.; Metcalf, C. A., III; Shulte, G. *Tetrahedron Lett.* **1992**, *33*, 3117.

(44) Neumann, W. P.; Hillgärtner, H.; Baines, K. M.; Dicke, R.; Vorspohl, K.; Kobs, U.; Nussbeutel, U. *Tetrahedron* **1989**, *45*, 951.

(45) The product was somewhat unstable to the reaction conditons; $t_{1/2}$ was ca. 3–4 days.

(46) We considered that generation of a radical from the cyclic carbamate could produce an *N*-acyl derivative.[43]

(47) Fukuda, T.; Kitada, C.; Fujino, M. *J. Chem. Soc., Chem. Commun.* **1978**, 220.

(48) In the ^{1}H NMR data several differences in chemical shifts were noted (e.g., δ 4.68 vs δ 5.25 for the NH). In the ^{13}C NMR we observed an unreported signal at δ 77.0 (obscured by $CDCl_3$ but readily detected in a *J*-modulated spectrum) and did not observe a reported signal at δ 8.13; all other signals matched closely. The discrepancies in the ^{1}H NMR might be due to concentration effects while the reported signal at δ_C 8.13 is likely an artifact (a similar high field signal is not reported for several analogous compounds). In principle, spectra from an enantiomerically pure sample can be different from those of a mixture of enantiomers; see: Tsai, W. L.; Hermann, K.; Hug, E.; Rohde, B.; Dreiding, A. S. *Helv. Chim. Acta* **1985**, *68*, 2238 and references cited therein.

as follows: $(CH_3)_2SO$ from CaH_2 under reduced pressure (10–15 Torr) and stored over 3-Å molecular sieves; Et_2O and tetrahydrofuran from benzophenone potassium ketyl; benzene, toluene, and CH_2Cl_2 from P_2O_5 and stored over 3-Å molecular sieves; MeOH from $Mg(OMe)_2$. Benzene solutions were degassed by bubbling argon through the solvent (solution) followed by three freeze–thaw cycles under high vacuum (0.01 Torr). Unless otherwise noted, other commercially available reagents were used as received. Unless otherwise noted, reactions were carried out under an atmosphere of argon, and reaction temperatures refer to the bath. Concentration refers to removal of volatiles at water aspirator pressure on a rotary evaporator.

Preparative TLC was carried out on glass plates (20 × 20 cm) precoated (0.25 mm) with silica gel 60 F_{254}. Materials were detected by visualization under an ultraviolet lamp (254 nm) and/or by treating a 1-cm vertical strip removed from the plate with a solution of phosphomolybdic acid (5%) containing a trace of ceric sulfate in aqueous sulfuric acid (5% v/v), followed by charring on a hot plate. Flash column chromatography (FCC) was performed according to Still *et al.*[49] with Merck silica gel 60 (40–63 μm). Medium-pressure chromatograpy (MPC) was performed with minor modifications of the procedure reported by Taber.[50] All mixed solvent eluents are reported as v/v solutions.

Spectral Data. Optical rotations were determined at ambient temperature on a Perkin-Elmer 141 polarimeter using a 1-mL, 10-dm cell; concentrations (*c*) are reported in g/100 mL. Low-resolution mass spectra (LRMS) were recorded on a single sectored, magnetic scanning MS-12. EI ionization was accomplished at 70 eV and CI at 50 eV with ammonia or isobutane as the reagent gas; only partial data are reported. IR spectra were recorded on a Fourier transform interferometer using a diffuse reflectance cell; only diagnostic peaks are reported. Unless otherwise noted, NMR spectra were measured in $CDCl_3$ solution at 300 MHz for ^1H and 75 MHz for ^{13}C. For ^1H NMR, residual $CHCl_3$ in $CDCl_3$ was employed as the internal standard (7.26 δ); for ^{13}C NMR, $CDCl_3$ was employed (77.0 δ). The ^1H NMR chemical shifts and coupling constants were determined assuming first-order behavior. Multiplicity is indicated by one or more of the following: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad), ap (apparent). The list of couplings contants (*J*) corresponds to the order of the multiplicity assignment. ^1H NMR spectra were normally obtained with a digital resolution of 0.244 Hz/pt (sweep width = 4000 Hz, FID = 32 K data points), and coupling constants are reported to the nearest 0.5 Hz. The ^1H NMR assignments were made on the basis of chemical shift and multiplicity and were confirmed, where necessary, by homonuclear decoupling and/or NOE experiments. The multiplicity of ^{13}C NMR signals refers to the number of attached H's (i.e., s = C, d = CH, t = CH_2, q = CH_3) and was determined by *J*-modulation.[51]

Methyl 2-*O*-Benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (8). A stirred suspension of Bu_2SnO (6.82 g, 27.4 mmol) and diol **7**[31] (5.10 g, 18.1 mmol) in 10% (v/v) methanolic benzene (300 mL) was heated under reflux for 3 h. The resulting colorless solution was cooled and concentrated to give a glassy white solid which was suspended in CH_3CN (210 mL). The mixture was heated under reflux and treated with three portions of $PhCH_2Br$ (6.5 mL, 54.6 mmol; ×3) at 2-h intervals. After 24 h, the solution was cooled and concentrated to provide an oil (40.1 g) which was mainly $PhCH_2Br$ (88% by mol; ^1H NMR) and contained alcohol **8** and the regioisomeric 3-*O*-benzyl ether (ca. 9:1, respectively; ^1H NMR). The product from a reaction conducted on smaller scale (0.364 g of **7**) was fractionated by FCC (22% EtOAc in toluene) to provide **8** as a white crystalline solid (0.349 g, 72%): mp 122–124 °C (lit.[33] mp 129.5 °C); IR ν_{max} 3465, 3038, 2927, 1086 cm^{-1}; ^1H NMR δ 7.55–7.28 (10, m), 5.52 (1H, s), 4.78 (1H, d, *J* = 12 Hz), 4.69 (1H, d, *J* = 12 Hz), 4.61 (1H, d, *J* = 3.5 Hz), 4.27 (1H, dd, *J* = 4.5, 10 Hz), 4.16 (1H, ddd, *J* = 2, 9.5, 9.5 Hz), 3.81 (1H, ddd, *J* = 5, 9.5, 9.5 Hz), 3.70 (1H, dd, *J* = 9.5, 10 Hz), 3.50 (1H, dd, *J* = 9.5, 9.5 Hz), 3.46 (1H, dd, *J* = 3.5, 9.5 Hz), 2.65 (1H, d, *J* = 2 Hz, OH); ^{13}C NMR δ 138.0 (s), 137.2 (s), 129.2 (d), 128.6 (d), 128.4 (d), 128.2 (d), 128.2 (d), 126.4 (d), 102.0 (s), 98.7 (d), 81.3 (d), 79.6 (d), 73.4 (t), 70.3 (d), 69.0 (t), 62.1 (d), 55.4 (q); LRMS (CI, NH_3) *m/z* (relative intensity) 390 ($[M + 18]^+$, 9), 373 ($[M + 1]^+$, 100), 341 (14), 121 (14), 91 (24).

Methyl 3-*O*-Benzoyl-2-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (9). PhCOCl (8.5 mL, 73.2 mmol) was added dropwise with stirring to a cooled (0 °C) solution of the above crude alcohol **8** (40.1 g) in pyridine (15 mL). The resulting viscous mixture was allowed to warm to rt and, after 4 h, was diluted with CH_2Cl_2, washed twice with HCl (6 M) and once with water, dried over Na_2SO_4, and concentrated to provide an oil (26.9 g) containing **9** which was used without further purification. The product from a reaction conducted on smaller scale (0.151 g of pure **8**; 2 equiv of PhCOCl) was fractionated by FCC (22% EtOAc in toluene) to provide **9** as a white crystalline solid (0.175 g, 90%): mp 118–120 °C; IR ν_{max} 2931, 1725, 1269 cm^{-1}; ^1H NMR δ 8.18–8.05 (2H, m), 7.45–7.35 (1H, m), 7.32–7.20 (12H, m), 5.85 (1H, dd, *J* = 9.5, 9.5 Hz), 5.48 (1H, s), 4.76 (1H, d, *J* = 4 Hz), 4.63 (2H, ap s), 4.31 (1H, dd, *J* = 5, 10 Hz), 3.98 (1H, ddd, *J* = 5, 9.5, 10 Hz), 3.75 (1H, dd, *J* = 9.5, 10 Hz), 3.73 (1H, dd, *J* = 4, 9.5 Hz), 3.71 (1H, dd, *J* = 9.5, 10 Hz), 3.45 (3H, s); ^{13}C NMR δ 165.5 (s), 137.6 (s), 137.1 (s), 133.8, 130.3 (d), 129.8 (s), 129.0 (d), 128.5 (d), 128.4 (d), 128.4 (d), 126.2 (d), 101.5 (d), 98.8 (d), 79.7 (d), 77.6 (d), 73.0 (t) 71.3 (d), 69.1 (t), 62.5 (d), 55.5 (q); LRMS (CI, NH_3) *m/z* (relative intensity) 494 ($[M + 18]^+$, 32), 477 ($[M + 1]^+$, 32), 445 (19), 371 (11), 105 (100).

Methyl 3-*O*-Benzoyl-2-*O*-benzyl-α-D-glucopyranoside (10). A mixture of CF_3COOH (1.6 mL) and the above crude acetal **9** (26.9 g) in 17% (v/v) aqueous MeOH (100 mL) was heated under reflux for 20 min. The solution was concentrated to a volume of ca. 50 mL and then diluted with CH_2Cl_2, washed with saturated $NaHCO_3$ (×3) and with water, dried over Na_2SO_4, and concentrated to give an oil (22.0 g) which contained the diol **10** which was used without further purification. The product from a reaction conducted on smaller scale (13 mg of pure **9**; 20 h at rt) was fractionated by preparative TLC (50% EtOAc in toluene) to provide **10** as a colorless oil (10 mg, 94%): IR ν_{max} 3458, 2929, 1723, 1273, 1057 cm^{-1}; ^1H NMR δ 8.05 (2H, m), 7.60 (1H, m), 7.45 (2H, m), 7.25–7.12 (5H, m), 5.52 (1H, dd, *J* = 9, 9.5 Hz), 4.73 (1H, d, *J* = 3.5 Hz), 4.66 (1H, d, *J* = 12 Hz), 4.63 (1H, d, *J* = 12 Hz), 3.95 (1H, m), 3.87 (2H, m), 3.74 (1H, m), 3.66 (1H, dd, *J* = 3.5, 9.5 Hz), 3.41 (3H, s); ^{13}C NMR δ 167.7 (s), 137.7 (s), 133.4 (d), 130.1 (d), 129.9 (d), 129.7 (s), 128.5 (d × 4), 128.0 (d), 97.9 (d), 76.6 (d), 76.2 (d), 73.0 (t), 71.3 (d), 70.2 (d), 62.1 (t), 55.4 (q); LRMS (CI, NH_3) *m/z* (relative intensity) 406 ($[M + 18]^+$, 64), 389 ($[M + 1]^+$, 23), 357 (38), 105 (100).

Methyl 3-*O*-Benzoyl-2-*O*-benzyl-4,6-bis-*O*-(methanesulfonyl)-α-D-glucopyranoside (11). MsCl (5.7 mL, 73 mmol) was added dropwise with stirring to a cooled (0 °C) solution of the above crude diol **10** (22.0 g) in pyridine (24 mL). After standing for 12 h at 3 °C, MeOH (30 mL) was added and the solution was stirred for 30 min at rt and concentrated. The residue was diluted with CH_2Cl_2, washed with 6 M HCl (×2), water, dried over Na_2SO_4, and concentrated. The resulting oil (27.0 g) containing **11** was used without further purification. The crude solid product obtained from a reaction conducted on smaller scale (0.951 g of pure **10**) was recrystallized from MeOH to provide **11** as a white crystalline solid (1.22 g, 92%): mp 132–134 °C; IR ν_{max} 2939, 1728, 1177 cm^{-1}; ^1H NMR δ 8.05 (2H, m), 7.62 (1H, m), 7.45 (2H, m), 7.25–7.12 (5H, m), 5.82 (1H, dd, *J* = 9.5, 9.5 Hz), 4.84 (1H, dd, *J* = 9.5, 9.5 Hz), 4.75 (1H, d, *J* = 3.5 Hz), 4.55 (2H, s), 4.50 (1H, dd, *J* = 2.5, 11.5 Hz), 4.41 (1H, dd, *J* = 3.5, 11.5 Hz), 4.10 (1H, ddd, *J* = 2.5, 3.5, 9.5 Hz), 3.66 (1H, dd, *J* = 3.5, 9.5 Hz), 3.44 (3H, s), 3.07 (3H, s), 2.34 (3H, s); ^{13}C NMR δ 165.5 (s), 137.1 (s), 133.5 (d), 129.9 (d), 129.4 (s), 128.6 (d), 128.5 (d), 128.2 (d), 128.0 (d), 97.7 (d), 76.6 (d), 74.3 (d), 73.2 (t), 71.3 (d), 67.2 (t), 67.0 (d), 56.0 (q), 38.9 (q), 37.6 (q); LRMS (CI, NH_3) *m/z* (relative intensity) 562 ($[M + 18]^+$, 10), 472 (36), 423 (8), 370

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(50) Taber, D. F. *J. Org. Chem.* **1982**, *47*, 1351.
(51) Brown, D. W.; Nakashima, T. T.; Rabenstein, D. L. *J. Magn. Reson.* **1981**, *45*, 302.

(28), 105 (100). Anal. Calcd for $C_{23}H_{28}O_{11}S_2$: C, 50.73; H, 5.18. Found: C, 50.98; H, 5.17.

Methyl 3-*O*-Benzoyl-2-*O*-benzyl-6-deoxy-6-iodo-4-*O*-(methanesulfonyl)-α-D-glucopyranoside (12). A stirred suspension of NaI (27.4 g, 183 mmol) and the above crude dimesylate **11** (27.0 g) in 2-butanone (100 mL) was heated under reflux for 2 h. The mixture was cooled and concentrated, and the residue was triturated with CH_2Cl_2. The combined organic extracts were washed with 10% (w/v) $Na_2S_2O_3$ (×2) and with water, dried over Na_2SO_4, and concentrated to provide an oil (25.4 g). The oil was fractionated by FCC (gradient elution 0–50% EtOAc in hexane) to give crude **12** as an oil (8.39 g). Crystallization from methanol gave pure iodide **12** as a white crystalline solid (5.00 g, 48% from diol **7**):[52] mp 118–120 °C; IR ν_{max} 2936, 1727, 1267, 1175 cm^{-1}; ^1H NMR δ 8.05 (2H, m), 7.58 (1H, m), 7.47 (2H, m), 7.22–7.12 (5H, m), 5.80 (1H, dd, J = 9.5, 10 Hz), 4.77 (1H, d, J = 3.5 Hz), 4.59 (1H, dd, J = 9.5, 10 Hz), 4.55 (2H, s), 3.82 (1H, ddd, J = 2.5, 8.5, 10 Hz), 3.66 (1H, dd, J = 3.5, 10 Hz), 3.62 (1H, dd, J = 2.5, 11 Hz), 3.47 (3H, s), 3.24 (1H, dd, J = 8.5, 11 Hz), 2.82 (3H, s); ^{13}C NMR δ 165.4 (s), 137.3 (s), 133.6 (d), 129.9 (d), 129.5 (s), 128.7 (d), 128.5 (d), 128.1 (d), 128.0 (d,), 97.5 (d), 78.5 (d), 77.0 (d), 73.0 (t), 71.0 (d), 68.4 (d), 56.1 (q), 38.9 (q), 4.6 (t); LRMS (CI, NH_3) m/z (relative intensity) 594 ([M + 18]$^+$, 18), 468 (20), 105 (100). Anal. Calcd for $C_{22}H_{25}IO_8S$: C, 45.84; H, 4.37. Found: C, 45.58; H, 4.18.

Methyl 3-*O*-Benzoyl-2-*O*-benzyl-6-deoxy-4-*O*-(methanesulfonyl)-α-D-glucopyranoside (13b). Powdered zinc (14.0 g) and glacial acetic acid (14.0 mL) were added to a stirred solution of iodide **12** (8.60 g, 14.9 mmol) in Et_2O (350 mL). After 5 h the mixture was filtered and the cake was washed repeatedly with Et_2O. The combined filtrate and washings was washed with 2 M NaOH (×2), aqueous $Na_2S_2O_3$ (10% w/v), and brine, dried over Na_2SO_4, and concentrated to provide crude **13b** as a yellowish solid (7.2 g) which was used without further purification. The solid product from a reaction conducted on smaller scale (0.840 mg of pure **12**) was recrystallized from MeOH to provide **13b** as a white crystalline solid (0.600 g, 91%): mp 128–130 °C; IR ν_{max} 2989, 2908, 1723, 1267, 1095 cm^{-1}; ^1H NMR δ 8.05 (2H, m), 7.61 (1H, m), 7.48 (2H, m), 7.25–7.12 (5H, m), 5.28 (1H, dd, J = 9.5, 9.5 Hz), 4.68 (1H, d, J = 3.5 Hz), 4.57 (2H, s), 4.49 (1H, dd, J = 9.5, 9.5 Hz), 3.97 (1H, dq, J = 9.5, 6.5 Hz), 3.63 (1H, dd, J = 3.5, 9.5 Hz), 3.43 (3H, s), 2.80 (3H, s), 1.37 (3H, d, J = 6.5 Hz); ^{13}C NMR δ 165.4 (s), 137.5 (s), 133.4 (d), 129.8 (d), 129.7 (s), 128.6 (d), 128.4 (d), 127.9 (d × 3), 97.3 (d), 80.7 (d), 77.4 (d), 72.7 (t), 71.5 (d), 65.0 (d), 55.4 (q), 38.8 (q), 18.0 (q); LRMS (CI, NH_3) m/z (relative intensity) 468 ([M + 18]$^+$, 45), 451 ([M + 1]$^+$, 9), 419 (26), 105 (100), 91 (62).

Methyl 4-Azido-3-*O*-benzoyl-2-*O*-benzyl-4,6-dideoxy-α-D-galactopyranoside (14b). A stirred suspension of NaN_3 (32.0 g, 192 mmol) and the above crude **13b** (7.20 g) in DMF (70 mL) was heated under reflux for 6 h. The cooled mixture was filtered and the cake washed repeatedly with 50% ether in hexane. The combined filtrate and washings was washed with water (×3), dried over Na_2SO_4, and concentrated to provide the crude azide **14b** (5.45 g) which was used without further purification. The product from a reaction conducted on smaller scale (85 mg of pure **13b**) was fractionated by preparative TLC (50% EtOAc in toluene) to provide **14b** as a colorless oil (68 mg; 90%): $[\alpha]_D$ −37° (c = 0.76, $CHCl_3$); IR ν_{max} 2934, 2108, 1724, 1267 cm^{-1}; ^1H NMR δ 8.10 (2H, m), 7.62 (1H, m), 7.48 (2H, m), 7.32–7.20 (5H, m), 5.67 (1H, dd, J = 3.5, 10.5 Hz), 4.71 (1H, d, J = 12.5 Hz), 4.64 (1H, d, J = 12.5 Hz), 4.70 (1H, d, J = 3.5 Hz), 4.15 (1H, dq, J = 1, 6.5 Hz), 4.01 (1H, dd, J = 1, 3.5 Hz), 4.00 (1H, dd, J = 3.5, 10.5 Hz), 3.40 (3H, s), 1.28 (3H, d, J = 6.5 Hz); ^{13}C NMR δ 165.6 (s), 137.9 (s), 133.4 (d), 130.0 (d), 129.8 (d), 129.5 (s), 128.5 (d), 128.4 (d), 127.9 (d), 98.4 (d), 73.8 (d), 73.2 (t), 72.4 (d), 65.1 (d), 64.3 (d), 55.5 (q), 17.1 (q); LRMS (CI, NH_3) m/z (relative intensity) 415 ([M + 18]$^+$, 82), 398 ([M + 1]$^+$, 7), 366 (53), 105 (100), 91 (65).

Methyl 4-Amino-3-*O*-benzoyl-2-*O*-benzyl-4,6-dideoxy-*N*-(ethoxycarbonyl)-α-D-galactopyranoside (15). A solution of the above crude azide **14b** (5.45 g) in CH_3CN (25 mL) was added rapidly to a stirred mixture of $SnCl_2$ (3.90 g, 20.6 mmol), Et_3N (8.6 mL, 62 mmol), and PhSH (8.5 mL, 82 mmol) in CH_3CN (200 mL). After 1 h, the solution was poured onto 2 M NaOH and the aqueous layer was extracted with CH_2Cl_2 (×2). The combined organic layers were concentrated to a volume of ca. 50 mL.[53] Saturated $NaHCO_3$ (50 mL) and ClCOOEt (13.1 mL, 137 mmol) were added to the rapidly stirred solution. After the mixture was stirred for 18 h, the aqueous layer was extracted with CH_2Cl_2 (×2) and the combined organic layers were concentrated to provide an oil (8.32 g) consisting of ClCOOEt and the carbamate **15** which was used without further purification. The product from a reaction conducted on smaller scale (0.380 g of pure **14b**) was fractionated by FCC (40% EtOAc in hexane) to provide **15** as a white crystalline solid (306 mg; 72%): mp 125–126 °C; IR ν_{max} 3361, 2980, 1721, 1274 cm^{-1}; ^1H NMR δ (* indicates minor rotamer) 8.00 (2H, m), 7.55 (1H, m), 7.44–7.22 (7H, m), 5.51 and 5.42* (1H, dd, J = 4.5, 10.5 Hz), 4.90 and 4.82* (1H, d, J = 10 Hz, NH), 4.73 (1H, d, J = 12 Hz), 4.62 (1H, d, J = 12 Hz), 4.68 (1H, d, J = 4 Hz), 4.65 and 4.23* (2H, m), 4.32 and 4.27* (1H, m), 3.98 (1H, m), 3.78* and 3.72 (1H, dd, J = 4, 10.5 Hz), 3.40 (3H, s), 1.22–1.12 (6H, m) and 0.77* (3H, t); ^{13}C NMR δ (major rotamer) 165.5 (s), 156.9 (s), 138.1 (s), 132.7 (d), 130.5 (s), 129.6 (d), 128.3 (d), 128.1 (d), 127.6 (d), 98.3 (d), 74.0 (d), 72.8 (t), 71.6 (d), 64.1 (d), 60.2 (t), 55.3 (q), 53.5 (d), 16.3 (q), 14.1 (q); δ (minor rotamer) 165.5 (s), 156.9 (s), 138.1 (s), 133.1 (d), 130.0 (s), 129.6 (d), 128.3 (d), 128.1 (d), 127.6 (d), 127.6 (d), 98.3 (d), 73.6 (d), 73.0 (t), 72.1 (d), 63.8 (d), 61.2 (t), 55.3 (q), 54.0 (d), 16.3 (q), 13.7 (q); LRMS (CI, NH_3) m/z (relative intensity) 461 ([M + 18]$^+$, 23), 444 ([M + 1]$^+$, 3), 412 (100), 105 (69), 91 (38). Anal. Calcd for $C_{24}H_{29}NO_7$: C, 65.00; H, 6.59; N, 3.16. Found: C, 64.79; H, 6.51; N, 3.04.

(1′*S*,2′*S*,4*R*,5*R*)-4-[2′-(Benzyloxy)-1′,3′-dihydroxypropyl]-5-methyl-2-oxazolidinone (20). A stirred solution of trifluoroacetic acid (4.90 mL) and the above crude ethyl carbamate **15** (8.32 g) in acetic anhydride (20 mL) was heated at 80 °C for 2 h. The cooled mixture was concentrated to provide the crude acetyl α-pyranoside[54] an oil (9.61 g) which was dissolved in THF (100 mL). Aqueous H_2O_2 (30%, 15.4 mL) and then 2 M NaOH (45.3 mL) were added. After the mixture was stirred for 1 h, brine was added and the mixture was extracted with ether (×3). The combined organic layers were dried over Na_2SO_4 and concentrated to provide the crude pyranose **16** as an oil (5.70 g).[55] Sodium borohydride (5.7 g, 151 mmol) was added to a solution of **16** (5.70 g) in EtOH (100 mL) at rt. After being stirred for 14 h, the mixture was concentrated to a volume of ca. 50 mL and filtered. The filter cake was washed repeatedly with CH_2Cl_2, and the combined filtrate and washings were cooled in an ice–water bath, and saturated NH_4Cl was carefully added (**Caution**: H_2 evolution). The mixture was extracted with CH_2Cl_2 (×3), and the combined organic layers were dried over Na_2SO_4 and concentrated to give a mixture[56] of **19** and **18** as an oil (5.87 g) which was used without further purification. A suspension of KH (35% in oil, 4.15 g, 36.2 mmol) and the crude alcohols **19** and **18** (5.87 g) in dry benzene (100 mL) was heated under reflux for 20 h. Saturated NH_4Cl was carefully added to the cooled reaction mixture (**Caution**: H_2 evolution). The aqueous layer was extracted with EtOAc (×3), and the combined organic layers were dried over Na_2SO_4 and concentrated to provide

(52) The product from a reaction conducted on a smaller scale (1.221 g of pure **11**) similarly gave **12** (1.215 g, 94%).

(53) The corresponding amine could be isolated at this point by preparative TLC (75% EtOAc in hexanes).[36]

(54) The ^1H and ^{13}C NMR spectra were complicated by the presence of carbamate rotamers (ca. 2:1). The anomeric configuration is assigned as α since the major rotamer shows $^3J_{H1-H2}$ = 3.5 Hz and the only signal attributable to an anomeric carbon appears at δ_C 90.0.

(55) The product from a reaction conducted on a smaller scale (0.418 g of pure **15**) was fractionated by FCC (50% ethyl acetate in hexane) to give **16** as a colorless oil (0.373 g, 92%): IR ν_{max} 3350, 2980, 1721, 1273 cm^{-1}; ^1H and ^{13}C NMR spectra are complex due to the mixture of anomers and carbamate rotamers; LRMS (CI, NH_3) m/z (relative intensity) 447 ([M + 18]$^+$, 9), 430 ([M + 1]$^+$, 20), 429 (17), 412 (76), 308 (62), 105 (71), 91 (100).

(56) The ratio of **19** to **18** was dependent on the reaction time: after 5 h, ca. 1:1; after 14 h, >5:1.

the crude oxazolidinone **20** as an oil (4.60 g). Fractionation by MPC (gradient elution 5–10% MeOH in CH_2Cl_2) gave **20** as a whitish solid (2.59 g, 61% from iodide **12**):[57] mp 112–114 °C (MeOH/hexane); IR ν_{max} 3297, 2882, 1730, 1055 cm^{-1}; ^1H NMR δ 6.94–6.77 (5H, m), 5.90 (1H, br s, NH), 4.31 (1H, d, J = 11.5 Hz), 4.15 (1H, d, J = 11.5 Hz), 4.21 (1H, dq, J = 4.5, 6.5 Hz), 3.47 (1H, dd, J = 6, 12 Hz), 3.39 (1H, dd, J = 4.5, 12 Hz), 3.27 (1H, dd, J = 2.5, 8 Hz), 3.17 (1H, ddd, J = 2.5, 4.5, 6 Hz), 3.09 (1H, ddd, J = 1, 4.5, 8 Hz), 0.93 (3H, d, J = 6.5 Hz); ^{13}C NMR δ 158.3 (s), 138.1 (s), 127.9 (d), 127.5 (d), 127.2 (s), 78.2 (d), 76.1 (d), 73.2 (d), 71.5 (t), 60.4 (t), 59.8 (d), 20.7 (q); LRMS (CI, NH_3) m/z (relative intensity) 299 ([M + 18]$^+$, 39), 282 ([M + 1]$^+$, 100), 108 (15), 91 (33).

(1′*S*,2′*R*,4*S*,5*R*)-4-[2′-(Benzyloxy)-1′,3′-bis[(*tert*-butyldimethylsilyl)oxy]propyl]-3-(*tert*-butyldimethylsilyl)-5-methyl-2-oxazolidinone (21). *tert*-Butyldimethylsilyl trifluoromethanesulfonate (5.90 mL, 25.7 mmol) was added dropwise with stirring to a cooled (0 °C) solution of diol **20** (1.85 g, 6.58 mmol) in 2,4,6-collidine (13 mL). The resulting solution was stirred at rt for 12 h and then was diluted with Et_2O/hexane (1:1), washed with 1 M HCl (×3), water, and concentrated. The resulting oil (5.01 g) containing the silyl ether **21** was used without further purification. The product from a reaction conducted on smaller scale (58 mg of **20**) was concentrated under high vacuum to give a crystalline solid (125 mg, quantitative) which was fractionated by MPC (40% EtOAc in hexane) to provide **21** as a white crystalline solid (108 mg; 85%): mp 111–113 °C; IR ν_{max} 2953, 2929, 2856, 1711, 838 cm^{-1}; ^1H NMR δ 7.33 (5H, m), 4.77 (1H, d, J = 12 Hz), 4.63 (1H, d, J = 12 Hz), 4.63 (1H, dq, J = 1.5, 6.5 Hz), 3.85 (1H, dd, J = 3.5 10.5 Hz), 3.78 (1H, d, J = 4.5 Hz), 3.64 (1H, d, J = 1.5 Hz), 3.54 (1H, dd, J = 7.5, 10.5 Hz), 3.43 (1H, ddd, J = 3.5, 4.5, 7.5 Hz), 1.31 (3H, d, J = 6.5 Hz), 0.97 (9H, s), 0.91 (9H, s), 0.87 (9H, s), 0.41 (3H, s), 0.22 (3H, s), 0.07 (6H, s), 0.04 (3H, s), −0.02 (3H, s); ^{13}C NMR δ 161.8 (s), 138.1 (s), 128.4 (d), 128.0 (d), 127.8 (d), 81.6 (d), 75.0 (d), 73.3 (t), 72.0 (d), 64.5 (d), 62.6 (t), 27.0 (q), 25.9 (q), 25.7 (q), 20.7 (q), 20.1 (s), 18.3 (s), 18.0 (s), −4.2 (q), −4.5 (q), −5.3 (q). LRMS (CI, NH_3) m/z (relative intensity) 624 ([M + 1]$^+$, 4), 510 (100), 452 (22), 132 (19), 108 (40), 91 (96). Anal. Calcd for $C_{32}H_{61}NO_5Si_3$: C, 61.6; H, 9.86; N, 2.25. Found: C, 61.7; H, 9.78; N, 2.32.

(1′*S*,2′*R*,4*S*,5*R*)-4-[2′-(Benzyloxy)-1′-[(*tert*-butyldimethylsilyl)oxy]-3′-hydroxypropyl]-3-(*tert*-butyldimethylsilyl)-5-methyl-2-oxazolidinone (22). Aqueous HF (25%, 0.50 mL) was added to a stirred solution of the above crude silyl ether **21** (2.49 g) in acetonitrile (77 mL), and the disappearance of **21** was carefully monitored by TLC (25% EtOAc in hexane). After ca. 2 h, saturated $NaHCO_3$ was added and the mixture was concentrated. The residue was diluted with CH_2Cl_2, washed twice with brine, dried over Na_2SO_4 and concentrated to provide an oil (1.92 g) which contained a 7–8:1 mixture of **22** and **23** (^1H NMR) and which was used without further purification. The product from a reaction conducted on smaller scale (80 mg of pure **21**) was fractionated by MPC (30% EtOAc in hexane) to provide **22** as a yellow oil (51 mg, 78%):[58] IR ν_{max} 3416, 2954, 2929, 2857, 1736, 1710, 837 cm^{-1}; ^1H NMR δ 7.36 (5H, m), 4.67 (1H, d, J = 12 Hz), 4.64 (1H, dq, J = 1, 6.5 Hz), 4.59 (1H, d, J = 12 Hz), 3.84 (1H, d, J = 5 Hz), 3.76 (1H, m), 3.72 (1H, d, J = 1 Hz), 3.60 (1H, m), 3.41 (1H, ddd, J = 5, 5, 5 Hz), 1.38 (3H, d, J = 6.5 Hz), 1.02 (9H, s), 0.87 (9H, s), 0.44 (3H, s), 0.26 (3H, s), 0.06 (3H, s), 0.01 (3H, s); ^{13}C NMR δ 162.1 (s), 137.5 (s), 128.6 (d), 128.2 (d), 128.0 (d), 79.9 (d), 75.1 (d), 72.6 (t), 72.6 (d), 63.6 (d), 59.4 (t), 27.0 (q), 25.7 (q), 20.8 (q), 20.1 (s), 17.9 (s), −4.2 (q), −4.3 (q), −4.5 (q), −4.7 (q); LRMS (CI, NH_3) m/z (relative intensity) 510 ([M + 1]$^+$, 100), 452 (17), 214 (21), 91 (53).

(1′*S*,2′*R*,4*S*,5*R*)-4-[2′-(Benzyloxy)-1′-[(*tert*-butyldimethylsilyl)oxy]-3′-oxopropyl]-3-(*tert*-butyldimethylsilyl)-5-methyl-2-oxazolidinone (25). Oxalyl chloride (0.66 mL, 7.7 mmol) was added dropwise via syringe to a solution of DMSO (0.92 mL, 13 mmol) in CH_2Cl_2 (25 mL) at −78 °C. After the mixture was stirred for 15 min, a solution of the above crude alcohol **22** (0.96 g) in CH_2Cl_2 (5 mL) was added dropwise via syringe to the Swern reagent. The resulting mixture was allowed to warm to −55 °C over 30 min, and then Et_3N (3.6 mL, 26 mmol) was added. After being stirred at −55 °C for 10 min, the mixture was allowed to slowly warm to rt and then was washed with 1 M HCl; the aqueous layer was extracted with CH_2Cl_2 (×2). The combined organic layers were dried over Na_2SO_4 and concentrated to give an oil (0.92 g) which was fractionated by MPC (20% EtOAc in hexane) to provide **21** (47 mg, 4.6%) and **25** as a yellowish oil (556 mg, 67% overall yield from diol **20**):[59] IR ν_{max} 2954, 2857, 1734, 837 cm^{-1}; ^1H NMR δ 9.83 (1H, d, J = 1 Hz), 7.42–7.27 (5H, m), 4.75 (1H, d, J = 12 Hz), 4.54 (1H, dq, J = 1.5, 6.5 Hz), 4.43 (1H, d, J = 12 Hz), 3.98 (1H, d, J = 5.5 Hz), 3.84 (1H, dd, J = 1, 5.5 Hz), 3.65 (1H, d, J = 1.5 Hz), 1.25 (3H, d, J = 6.5 Hz), 0.97 (9H, s), 0.86 (9H, s), 0.43 (3H, s), 0.22 (3H, s), 0.05 (3H, s), −0.03 (3H, s); ^{13}C NMR δ 201.8 (d), 161.6 (s), 136.5 (s), 128.7 (d), 128.5 (d), 128.1 (d), 84.0 (d), 76.0 (d), 72.8 (t), 71.8 (d), 62.8 (d), 26.9 (q), 25.6 (q), 20.3 (q), 20.2 (s), 17.9 (s), −4.2 (q), −4.3 (q), −4.7 (q), −4.7 (q); LRMS (CI, NH_3) m/z (relative intensity) 525 ([M + 18]$^+$, 19), 508 ([M + 1]$^+$, 50), 411 (23), 402 (29), 214 (28), 173 (25), 91 (100).

(1′*S*,2′*S*,3′*R*,4*S*,5*R*)-4-[2′-(Benzyloxy)-1′-[(*tert*-butyldimethylsilyl)oxy]-3′-hydroxy-5′-[(phenylthio)methyl]-5′-hexenyl]-3-(*tert*-butyldimethylsilyl)-5-methyl-2-oxazolidinone (26). A solution of $TiCl_4$ (8.8 mL, 0.25 M in CH_2Cl_2, 2.2 mmol) was added dropwise via syringe to a stirred solution of aldehyde **25** (0.556 g, 1.10 mmol) and allylsilane **5**[30] (1.39 mL, 5.48 mmol) in CH_2Cl_2 (15 mL) at 0 °C. After 3 h, the solution was poured onto saturated $NaHCO_3$, and the resulting emulsion was filtered through Celite, and the filter cake was washed repeatedly with CH_2Cl_2. The combined filtrate and washings was washed with saturated $NaHCO_3$ (×2) and water, dried over Na_2SO_4, and concentrated. The resulting oil (1.53 g) was fractionated by MPC (18% EtOAc in hexane) to give **27** (10 mg, 2%) and **26** as a colorless oil (0.646 g, 87%): IR ν_{max} 3401, 2953, 2928, 2856, 1731, 838 cm^{-1}; ^1H NMR δ 7.42–7.13 (10H, m), 4.94 (1H, br s), 4.79 (1H, d, J = 12 Hz), 4.77 (1H, s), 4.66 (1H, dq, J = 1, 6.5 Hz), 4.50 (1H, d, J = 12 Hz), 3.99 (1H, m), 3.88 (1H, d, J = 5 Hz), 3.80 (1H, d, J = 1 Hz), 3.54 (1H, d, J = 13 Hz), 3.48 (1H, d, J = 13 Hz), 3.23 (1H, d, J = 5 Hz), 2.33 (1H, dd, J = 9.5, 14 Hz), 2.13 (1H, dd, J = 4.5, 14 Hz), 1.84 (1H, d, J = 9 Hz, OH), 1.36 (3H, d, J = 6.5 Hz), 0.98 (9H, s), 0.89 (9H, s), 0.43 (3H, s), 0.24 (3H, s), 0.13 (3H, s), 0.06 (3H, s); ^{13}C NMR δ 162.2 (s), 141.0 (s), 136.9 (s), 135.8 (s), 130.3 (d), 128.9 (d), 128.7 (d), 128.6 (d), 128.5 (d), 126.6 (d), 116.7 (t), 81.1 (d), 74.5 (t), 74.4 (d), 73.5 (d), 66.1 (d), 62.3 (d, C-4), 40.9 (t), 40.4 (t), 27.0 (q), 25.8 (q), 21.0 (q), 20.2 (s), 17.9 (s), −4.0 (q), −4.2 (q), −4.2 (q), −4.6 (q); LRMS (CI, NH_3) m/z (relative intensity) 672 ([M + 1]$^+$, 14), 564 (36), 450 (25), 345 (37), 328 (25), 214 (33), 91 (100).

(1′*S*,2′*S*,3′*R*,4*S*,5*R*)-3-(*tert*-Butyldimethylsilyl)-4-[1′-[(*tert*-butyldimethylsilyl)oxy]-2′,3′-dihydroxy-5′-[(phenylthio)methyl]-5′-hexenyl]-5-methyl-2-oxazolidinone (27). A solution of BBr_3 (1.28 mL, 1.0 M in CH_2Cl_2, 1.28 mmol) was added rapidly via syringe to a stirred solution of the alcohol **26** (0.156 g, 0.23 mmol) in CH_2Cl_2 (20 mL) at rt. After 20 min, saturated $NaHCO_3$ and 10% sodium thiosulfate were added sequentially to the rapidly stirred solution. The organic layer was washed with saturated $NaHCO_3$ and with water, dried over Na_2SO_4, and concentrated to provide an oil (0.904 g) which was fractionated by FCC (25% EtOAc in hexane) to give **27** as a colorless oil (125 mg, 92%): $[\alpha]_D$ +5.3° (c = 0.77, $CHCl_3$); IR ν_{max} 3520, 3348, 2954, 2929, 2857, 1702, 838 cm^{-1}; ^1H NMR δ 7.37–7.18 (5H, m), 5.03 (1H, br s), 4.94 (1H, br s), 4.67 (1H, dq, J = 2, 6.5 Hz), 3.91 (1H, m), 3.86 (1H, d, J = 5 Hz), 3.59 (2H, ap s), 3.33 (1H, m), 2.58 (1H, m, OH), 2.46 (2H, ap d, J = 7 Hz), 2.18 (1H, m, OH), 1.34 (3H, d, J = 6.5 Hz), 0.99 (9H, s), 0.90 (9H, s), 0.46 (3H, s), 0.28 (3H, s), 0.13 (3H, s), 0.09 (3H,

(57) The product from a reaction conducted on a smaller scale (0.328 g of pure **16**) similarly gave **20** (0.181 g, 84%).

(58) Attempted chromatography of the product from larger scale reactions (e.g., 2 g of **21**) led to partial hydrolysis, and **22** was isolated in only 50–60% yield along with **20** and **23** (30–40%). Although **20** and **23** can easily be recycled, we found it more convenient to directly oxidize the crude product.

(59) Oxidations of pure **22** under the same conditions gave **25** in 85–90% yield.

s); ^{13}C NMR δ 162.7 (s), 140.9 (s), 135.8 (s), 130.2 (d), 128.9 (d), 126.5 (d), 116.9 (t), 76.5 (d), 73.5 (d), 73.1 (d), 66.7 (d), 63.7 (d), 40.5 (t), 40.2 (t), 27.0 (q), 25.8 (q), 21.2 (q), 20.2 (s), 18.0 (s), −4.2 (q × 2), −4.3 (q), −4.5 (q); LRMS (CI, NH_3) *m/z* (relative intensity) 582 ([M + 1]$^+$, 64), 474 (24), 361 (20), 360 (25).

(1′*S*,2′*S*,3′*R*,4*S*,5*R*)-3-(*tert*-Butyldimethylsilyl)-4-[1′-[(*tert*-butyldimethylsilyl)oxy]-2′,3′-(2″-propylidenedioxy)-5′-[(phenylthio)methyl]-5′-hexenyl]-5-methyl-2-oxazolidinone (28). A solution of the diol **27** (0.308 g, 0.53 mmol) and $TsOH·H_2O$ (10 mg, 0.053 mmol) in 2,2-dimethoxypropane (20 mL) was stirred for 18 h at rt. The mixture was diluted with CH_2Cl_2, washed with saturated $NaHCO_3$ (×2) and water, dried over Na_2SO_4, and concentrated to provide crude acetonide **28** (0.318 g) which was used without further purification. The product from a reaction conducted on smaller scale (0.135 g of **27**) was fractionated by FCC (gradient elution 10−50% EtOAc in hexane) to give **30** (10 mg, 8%) and **28** as a colorless oil (0.106 g, 74%): $[\alpha]_D$ −9.1° (*c* = 0.93, $CHCl_3$); IR ν_{max} 2930, 2857, 1738, 1207, 838 cm^{-1}; ^{1}H NMR δ 7.36−7.12 (5H, m), 5.01 (1H, br s), 4.93 (1H, br s), 4.84 (1H, dq, *J* = 2, 6.5 Hz), 3.95 (1H, ddd, *J* = 2.5, 8.5, 9 Hz), 3.84 (1H, d, *J* = 3.5 Hz), 3.64 (2H, m), 3.60 (1H, d, *J* = 2 Hz), 3.58 (1H, dd, *J* = 3.5, 8.5 Hz), 2.62 (1H, br d, *J* = 2.5, 15 Hz), 2.30 (1H, dd, *J* = 8.5, 15 Hz), 1.38 and 1.36 (each 3H, s), 1.34 (3H, d, *J* = 6.5 Hz), 0.99 (9H, s), 0.91 (9H, s), 0.46 (3H, s), 0.23 (3H, s), 0.12 (3H, s), 0.08 (3H, s); ^{13}C NMR δ 161.8 (s), 141.0 (s), 135.9 (s), 130.0 (d), 128.8 (d), 126.4 (d), 115.8 (t), 108.8 (s), 82.7 (d), 76.6 (d), 75.2 (d), 73.7 (d), 65.4 (d), 40.7 (t), 37.8 (t), 27.3 (q), 27.0 (q), 27.0 (q), 25.9 (q), 20.8 (q), 20.3 (s), 16.1 (s), −4.1 (q), −4.1 (q), −4.3 (q × 2); LRMS (CI, NH_3) *m/z* (relative intensity) 622 ([M + 1]$^+$, 88), 582 (34), 349 (29), 214 (100).

(1′*S*,2′*S*,3′*R*,4*S*,5*R*)-4-[1′-Hydroxy-5′-[(phenylthio)methyl]-2′,3′-(2″-propylidenedioxy)-5′-hexenyl]-5-methyl-2-oxazolidinone (29). A solution of Bu_4NF (hydrate) (0.350 g) and the above crude acetonide **28** (0.318 g) in THF (15 mL) was stirred at rt for 10 min. The mixture was diluted with H_2O and extracted with Et_2O (×3). The combined organic layers were dried over Na_2SO_4 and concentrated to provide the crude alcohol **29** as an oil (233 mg) which was used without further purification. The product from a reaction conducted on smaller scale (23 mg of pure **28**) was fractionated by preparative TLC (63% EtOAc in hexane) to give **29** as an off-white solid (14 mg, 87%): $[\alpha]_D$ +27° (*c* = 0.84, $CHCl_3$); IR ν_{max} 2982, 2930, 1734, 1227, 1060 cm^{-1}; ^{1}H NMR δ 7.36−7.15 (5H, m), 5.33 (1H, s, NH), 5.04 (1H, br s), 4.99 (1H, br s), 4.74 (1H, dq, *J* = 4.5, 6.5 Hz), 4.24 (1H, ddd, *J* = 5.5, 7, 8 Hz), 370−3.55 (4H, m), 3.51 (1H, dd, *J* = 3.5, 4.5 Hz), 2.55 (1H, dd, *J* = 7.5, 13.5 Hz), 2.48 (1H, dd, *J* = 5, 13.5 Hz), 1.47 (3H, d, *J* = 6.5 Hz), 1.42 (6H, s); ^{13}C NMR δ 159.8 (s), 140.7 (s), 136.0 (s), 130.2 (d), 128.8 (d), 126.4 (d), 116.3 (t), 109.5 (s), 79.9 (d), 76.6 (d), 75.1 (d), 70.0 (d), 62.1 (d), 40.7 (t), 37.3 (t), 27.3 (q), 26.8 (q), 21.2 (q); LRMS (EI) *m/z* (relative intensity) 393 ([M]$^+$, 62), 335 (67), 110 (100).

(1′*S*,2′*S*,3′*R*,4*S*,5*R*)-3,1′-*O*-(Thiocarbonyl)-4-[1′-hydroxy-5′-[(phenylthio)methyl]-2′,3′-(2″-propylidenedioxy)-5′-hexenyl]-5-methyl-2-oxazolidinone (32). A solution of 1,1′-(Thiocarbonyl)diimidazole (110 mg, 0.555 mmol) and the above crude alcohol 29 (233 mg) in benzene (15 mL) was heated under reflux in the dark. After 6 h, an additional portion of 1,1′-(thiocarbonyl)diimidazole (110 mg, 0.555 mmol) was added and refluxing continued overnight. The solution was washed with 1 M HCl, and the aqueous layer was extracted with Et_2O/hexane (1:1; ×3). The combined organic layers were dried over Na_2SO_4 and concentrated to provide an oil (218 mg) which was fractionated by MPC (gradient elution, 50−75% EtOAc in hexane) to give **32** as an oil (145 mg, 64% from diol 27): IR ν_{max} 2985, 1787, 1748, 1325, 1243, 1174 cm^{-1}; ^{1}H NMR δ 7.37−7.17 (5H, m), 5.06 (1H, br s), 5.00 (1H, br s), 4.98 (1H, dq, *J* = 7.5, 6.5 Hz), 4.73 (1H, d, *J* = 8 Hz), 4.61 (1H, dd, *J* = 7.5, 8 Hz), 4.42 (1H, ddd, *J* = 5.5, 7, 8.5 Hz), 3.67 (1H, d, *J* = 14 Hz), 3.64 (1H, d, *J* = 8.5 Hz), 3.56 (1H, d, *J* = 14 Hz), 2.60 (1H, dd, *J* = 7, 15 Hz), 2.47 (1H, dd, *J* = 5.5, 15 Hz), 1.54 (3H, d, *J* = 6.5 Hz), 1.40 and 1.39 (each 3H, s); ^{13}C NMR δ 182.4 (s), 149.8 (s), 140.1 (s), 135.7 (s), 130.1 (d), 129.0 (d), 126.6 (d), 116.7 (t), 111.0 (s), 79.2 (d), 79.2 (d), 74.2 (d), 73.6 (d), 65.6 (d), 40.9 (t), 36.4 (t), 27.5 (q), 26.1 (q), 20.6 (q); LRMS (CI, NH_3) *m/z* (relative intensity) 453 ([M + 18]$^+$, 54), 436 ([M + 1]$^+$, 45), 345 (75), 328 (52), 285 (100), 268 (70), 69 (66).

(1′*R*,2′*S*,3′*R*,4*S*,5*R*)-4-[5′-Methylidene-2′,3′-(2″-propylidenedioxy)cyclohexyl]-5-methyl-2-oxazolidinone (33). A degassed solution of $(Me_3Sn)_2$ (0.077 mL, 0.37 mmol), benzophenone (68 mg, 0.37 mmol), and **32** (73 mg, 0.17 mmol) in dry benzene (2 mL) was irradiated for 20 h in a Rayonet reactor (300 nm) at ca. 40 °C. MeOH (1 mL) was added, and the solution was stirred at rt for 30 min and then concentrated to provide an oil which was fractionated by MPC (50% EtOAc in hexane) to give **33** as a white crystalline solid (20 mg, 41%): mp 183−186 °C dec.; $[\alpha]_D$ +3° (*c* = 0.18, $CHCl_3$),[60] +19° (*c* = 0.23, MeOH); IR ν_{max} 3318, 2983, 2874, 1741, 1242, 1055 cm^{-1}; ^{1}H NMR δ 5.58 (1H, s, NH), 4.93 (2H, m), 4.69 (1H, dq, *J* = 5, 6.5 Hz), 3.42 (1H, dd, *J* = 5, 7 Hz), 3.38 (1H, ddd, *J* = 4.5, 8.5, 12 Hz), 3.18 (1H, dd, *J* = 8.5, 10 Hz), 2.73 (1H, dd, *J* = 4.5, 12 Hz), 2.41 (1H, dd, *J* = 3, 13 Hz), 2.20 (1H, dd, *J* = 12, 12 Hz), 1.87 (1H, dd, *J* = 13, 13 Hz), 1.77 (1H, dddd, *J* = 3, 7, 10, 13 Hz), 1.45 (3H, d, *J* = 6.5 Hz), 1.42 and 1.40 (each 3H, s); ^{13}C NMR δ 159.4 (s), 141.3 (s), 115.0 (t), 110.4 (s), 81.0 (d), 78.9 (d), 77.5 (d), 62.0 (d), 43.6 (d), 37.6 (t), 34.3 (t), 27.0 (q), 27.0 (q), 20.8 (q); LRMS (EI) *m/z* (relative intensity) 267 ([M]$^+$, 5), 252 (41), 149 (16), 148 (31), 100 (100).

(1′*R*,2′*S*,3′*R*,4*S*,5*R*)-4-[5′-Methylidene-2′,3′-(2″-propylidenedioxy)cyclohexyl]-5-methyl-3-[(4-methylphenyl)-methanesulfonyl]-2-oxazolidinone (34). BuLi (2.5 M in hexane) was added to a stirred solution of oxazolidinone **33** (6.0 mg, 0.022 mmol) and 1,10-phenanthroline (trace) in THF (1.0 mL) at 0 °C until a red color persisted. A solution of PMS-Cl[47] (8.4 mg, 0.041 mmol) in THF (0.2 mL) was added via syringe, and the solution was stirred for a further 30 min at 0 °C. The mixture was diluted with CH_2Cl_2,washed with NaOH (2 M), saturated NH_4Cl and water, dried over Na_2SO_4, and concentrated to provide an oil (10.5 mg) which was fractionated by preparative TLC (50% EtOAc in hexane) to give recovered **33** (1.8 mg, 30%) and **34** (6.1 mg, 62%): IR ν_{max} 2983, 2927, 2850, 1773, 1367, 1169, 1139 cm^{-1}; ^{1}H NMR δ 7.38 and 7.20 (each 2H, m), 4.92 and 4.77 (each 1H, d, *J* = 14 Hz), 4.88 and 4.81 (each 1H, br s), 4.66 (1H, dq, *J* = 1, 6.5 Hz), 3.85 (1H, dd, *J* = 1, 5 Hz), 3.32 (1H, ddd, *J* = 3.5, 8.5, 12.5 Hz), 3.19 (1H, dd, *J* = 8.5, 11 Hz), 2.67 (1H, brdd, *J* = 3.5, 12.5 Hz), 2.35 (3H, s), 2.21−1.98 (3H, m), 1.78 (1H, br dd, *J* = 13, 13 Hz), 1.40 and 1.37 (each 3H, s), 1.17 (3H, d, *J* = 6.5 Hz); LRMS (CI, NH_3) *m/z* (relative intensity) 453 ([M + 18]$^+$, 46), 436 ([M + 1]$^+$, 93), 285 (61), 268 (88), 105 (100).

(1′*R*,2′*S*,3′*R*,4*S*,5*R*)-4-[5′-Oxo-2′,3′-(2″-propylidenedioxy)cyclohexyl]-5-methyl-3-[(4-methylphenyl)methanesulfonyl]-2-oxazolidinone (35). A stream of ozone in oxygen was bubbled through a solution of **34** (12.1 mg, 0.028 mmol) in 20% methanolic CH_2Cl_2 (2.0 mL) at −78 °C until a blue color was observed. Oxygen was then bubbled through the solution until the blue color was discharged. Pyridine (0.1 mL) and dimethyl sulfide (0.1 mL) were added, and the solution was allowed to stand at 3 °C overnight. The solution was concentrated and the residue fractionated by preparative TLC (50% EtOAc in hexane) to give **35** (9.1 mg, 75%): IR ν_{max} 2985, 2931, 2871, 1773, 1719, 1370, 1361, 1141 cm^{-1}; ^{1}H NMR δ 7.40 and 7.32 (each 2H, m), 4.93 and 4.82 (each 1H, d, *J* = 14 Hz), 4.55 (1H, dq, *J* = 1, 6.5 Hz), 4.97 (1H, dd, *J* = 1, 3.5 Hz), 3.53 (1H, ddd, *J* = 5, 9, 13 Hz), 3.56 (1H, dd, *J* = 5, 13 Hz), 2.82 (1H, br dd, *J* = 5, 13 Hz), 2.37 (3H, s), 2.31 (1H, dd, *J* = 13, 13 Hz), 2.23−2.09 (2H, m), 1.88 (1H, m), 1.47 and 1.42 (each 3H, s), 1.22 (3H, s); ^{13}C NMR δ: 203.9 (s), 153.2 (s), 140.0 (s), 131.1 (d), 129.9 (d), 124.3 (s), 112.2 (s), 78.4 (d), 76.8 (d), 76.4 (d), 62.4 (d), 58.6 (t), 44.5 (t), 39.5 (t), 38.8 (d), 26.8 (q), 26.8 (q), 21.2 (q), 20.3 (q); LRMS (CI, NH_3) *m/z* (relative intensity) 455 ([M + 18]$^+$, 100), 438 ([M + 1]$^+$, 17), 287 (74), 105 (74).

(1′*S*,2′*R*,3′*R*,4*S*,5*R*)-5-[2′-Hydroxy-1′-[(4″-methylphenyl)methanesulfonamido]propyl]-3,4-(2-propylidenedioxy)cyclohexanone (36). Excess NaH (60% in oil; ca. 5 mg) was added to a stirred solution of **35** (10.9 mg, 0.025 mmol) in MeOH (1 mL). After 3 h, saturated NH_4Cl was carefully

(60) The previously reported[20] value of +10° was shown to be incorrect.

added, and the mixture was diluted with CH_2Cl_2. The organic solution was washed with saturated NH_4Cl and with brine, dried over Na_2SO_4, and concentrated to provide crude **36** as an oil (12.9 mg). The crude product appeared to be homogeneous by ^1H NMR (other than the oil from the NaH) and was used without further purification. The product from a reaction conducted on smaller scale (2.5 mg of **35**) was fractionated by preparative TLC (50% EtOAc in hexane) to give **36** (1.4 mg, 60%): IR ν_{max} 3500, 3284, 2984, 2930, 1714, 1230, 1127 cm^{-1}; ^1H NMR δ 7.25 and 7.20 (each 2H, m), 4.68 (1H, d, J = 9 Hz, NH), 4.32 (2H, ap s), 4.08 (1H, dq, J = 2, 6.5 Hz), 3.73 (1H, dd, J = 8.5, 11 Hz), 3.59 (1H, ddd, J = 4.5, 8.5, 13 Hz), 3.42 (1H, ddd, J = 2, 5.5, 9 Hz), 2.88 (1H, ddd, J = 2, 4.5, 14 Hz), 2.54 (1H, ddd, J = 2, 5, 16 Hz), 2.52 (1H, dd, J = 13, 14 Hz), 2.35 (3H, s), 2.15 (1H, dd, J = 12, 16 Hz), 1.91 (1H, dddd, J = 5, 5.5, 11, 12 Hz), 1.47 and 1.44 (each 3H, s), 1.31 (3H, d, J = 6.5 Hz); ^{13}C NMR δ: 205.6 (s), 138.8 (s), 130.6 (d), 129.6 (d), 126.0 (s), 111.9 (s), 79.5 (d), 77.0 (d), 67.7 (d), 60.3 (d), 60.3 (t), 44.7 (t), 41.6 (t), 39.3 (d), 26.9 (q), 26.9 (q), 21.1 (q × 2); LRMS (CI) *m/z* (relative intensity) 429 ($[M + 18]^+$, 25), 412 ($[M + 1]^+$, 24), 391 (19), 244 (100), 198 (52), 102 (62).

5,6-*O*-(2-Propylidene)-*N*-desalanyl-*N*-[(4-methylphenyl)-methanesulfonyl]actinobolin (37). 1,1'-Carbonyldiimidazole (8.0 mg, 0.049 mmol) was added to a solution of the above crude **36** (12.9 mg) in THF (0.5 mL), and the solution was stirred at rt for 18 h. Excess NaH (60% in oil; ca. 5 mg) was added, and the reaction mixture was stirred for 1 h. Saturated NH_4Cl was carefully added, and the mixture was diluted with water and extracted with EtOAc (×3). The combined organic layers was dried over Na_2SO_4, concentrated, and fractionated by preparative TLC (50% EtOAc in hexane) to give recovered **36** (7.3 mg, 71% from **35**) and **37** (2.4 mg, 22% from **35**): $[\alpha]_D$ +5.2° (c = 0.23, $CHCl_3$); IR ν_{max} 3226, 2985, 2925, 2854, 1775, 1721, 1644, 1331, 1146 cm^{-1}; ^1H NMR δ 12.77 (1H, s, OH), 7.29 and 7.19 (each 2H, m), 4.60 (1H, dq, J = 1.5, 6.5 Hz), 4.51 (1H, d, J = 10 Hz, NH), 4.48 and 4.25 (each 1H, d, J = 13 Hz), 4.10 (1H, ddd, J = 1.5, 3.5, 10 Hz), 3.83 (1H, ddd, J = 6, 9, 11 Hz), 3.57 (1H, dd, J = 9, 10 Hz), 2.96 (2H, m), 2.65 (1H, ddd, J = 3, 11, 17 Hz), 2.35 (3H, s), 1.48 and 1.42 (each 3H, s), 1.47 (3H, d, J = 6.5 Hz); ^{13}C NMR δ 176.5 (s), 170.4 (s), 138.9 (s), 130.5 (d), 129.6 (d), 125.4 (s), 112.2 (s), 89.7 (s), 78.2 (d), 76.2 (d), 74.0 (d), 60.4 (t), 50.5 (d), 41.0 (d), 34.9 (t), 27.0 (q), 26.8 (q), 21.2 (q), 17.9 (q); LRMS (CI, NH_3) *m/z* (relative intensity) 455 ($[M + 18]^+$, 24), 438 ($[M + 1]^+$, 80), 270 (100), 203 (25), 105 (76).

Acknowledgment. We thank Dr. Yuanzhu Gai for repeating the preparation of **33** from **20** and Dr. M. Soledade C. Pedras for obtaining optical rotations. Financial support from the Natural Sciences and Engineering Research Council (Canada) and the University of Saskatchewan is gratefully acknowledged.

Supplementary Material Available: ^1H NMR spectra for **8–16**, **20–22**, **25–29**, and **32–37** (22 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.