Total Synthesis of Calicheamicin γ_1^I. 3. The Final Stages

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Received February 25, 1993

Abstract: The first total synthesis of calicheamicin γ_1^I (**1**) has been achieved. The stereoselective glycosidation, joining the appropriately functionalized aglycon **3** with the oligosaccharide fragment **2**, was realized using Schmidt's trichloroacetimidate methodology. Segment **4**, equipped with the photolabile 2-nitrobenzyl group at the reducing end, was synthesized using similar chemistry to that applied to the synthesis of its methyl glycoside counterpart (see accompanying paper). Stereoselective reduction of oxime **31**, obtained from the coupling product, with $NaCNBH_3$ in the presence of $BF_3 \cdot OEt_2$, late in the synthetic scheme, generated the desired alkoxylamine **32** and its A-4 isomer **32-epi**. Installment of the allylic trisulfide and appropriate deprotections allowed transformation of **32** and **32-epi** to calicheamicin γ_1^I (**1**) and its A-4 epimer **1-epi**, respectively.

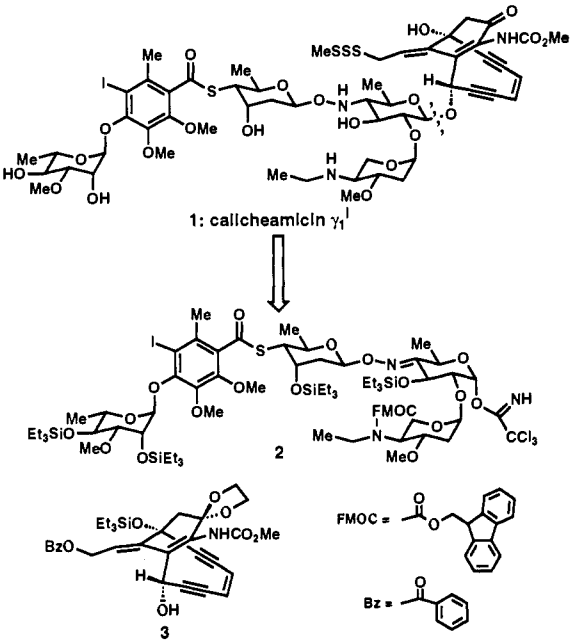
Introduction

The two preceding papers in this issue described the development of strategies for the construction of the oligosaccharide[1] and aglycon[2] fragments of calicheamicin γ_1^I (**1**),[3] respectively. In this paper, we describe the details of the final stages of the total synthesis of this remarkable natural product, culminating in enantiomerically pure calicheamicin γ_1^I (**1**). The strategy for the completion of the synthesis involved, as already briefly mentioned in the first paper of this series,[1] coupling of suitable precursors of the oligosaccharide and aglycon regions of the molecule followed by elaboration to the final target.

Results and Discussion

Strategy. Calicheamicin's molecular complexity dictated the need for a convergent strategy. Inspection of its structure revealed the glycoside bond linking the oligosaccharide and aglycon domains as the most appealing bond for retrosynthetic disconnection (Scheme I). Projections regarding the nature of the reagents and conditions for the final stages of the synthesis and the sensitivity of the functional groups present in the molecule led to the definition of intermediates **2** and **3** as the requisite precursors of the two domains. The triethyl silyl groups were chosen over other silyl groups as the best balanced compromise between stability and ease of removal. The trichloroacetimidate was selected as the activating group of the reducing end of the sugar on the basis of its generally high coupling yields associated with its use and ease of formation from the corresponding lactol. The latter is easily obtained by mild photolysis of an *o*-nitrobenzyl group, which serves as a reliable protecting group (of this key anomeric position) during the aryl tetrasaccharide construction. Protection of the secondary amine of the E-ring was accomplished using the FMOC group which is ideal for the final step due to the ease by which it is cleaved. A price had to be paid, however, for the potential of rotamers at the N–FMOC bond which would complicate the NMR spectra of intermediates, although higher temperatures could eliminate this problem. Having settled on the final synthetic plan, we proceeded to the execution phase of the synthesis, as described below.

Scheme I. Retrosynthetic Analysis of Calicheamicin γ_1^I (**1**)



Preparation of Key Intermediates 2 and 3. Following the general strategy and procedures for the synthesis of the β-methyl glycoside of the calicheamicin γ_1^I oligosaccharide,[1] we synthesized β-*o*-nitrobenzyl glycoside **4**[4] (Scheme II) in gram quantities. Schemes III and IV summarize the sequences leading to this intermediate. Photodeprotection of **4** in aqueous THF using a Hanovia mercury lamp at 0 °C produced a 1:1 mixture (by ^1H NMR) of lactols **5** (82% yield, plus 16% starting material, chromatographically purified). Employing Schmidt's procedure,[5] lactol **5** was converted to the labile trichloroacetimidate **2** in high yield (*ca.* 2:1 ratio, α/β-anomers by ^1H NMR). The crude trichloroacetimidate

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(1) Groneberg, R. D.; Miyazaki, A.; Stylianides, N. A.; Schulze, T. J.; Stahl, W.; Schreiner, T.; Suzuki, T.; Iwabuchi, Y.; Smith, A. L.; Nicolaou, K. C. *J. Am. Chem. Soc.*, first of three papers in this series.

(2) Nicolaou, K. C.; Smith, A. L.; Pitsinos, E. N.; Hwang, C.-K.; Mizuno, Y.; Saimoto, H.; Scarlato, G. R.; Suzuki, T. *J. Am. Chem. Soc.*, second of three papers in this series.

(3) For preliminary communication, see: Nicolaou, K. C.; Hummel, C. W.; Pitsinos, E. N.; Nakada, M.; Smith, A. L.; Shibayama, K.; Saimoto, H. *J. Am. Chem. Soc.* **1992**, *114*, 10082.

(4) Nicolaou, K. C.; Schreiner, E. P.; Stahl, W. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 585. Nicolaou, K. C.; Schreiner, E. P.; Iwabuchi, Y.; Suzuki, T. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 340.

(5) (a) Grandler, G.; Schmidt, R. R. *Carbohydr. Res.* **1985**, *135*, 203. (b) Schmidt, R. R. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 212 (review).

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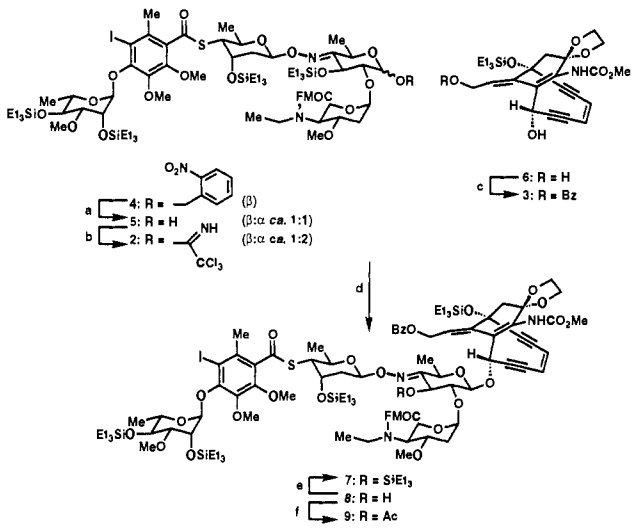
Scheme II[a]



[a] Reagents and conditions: (a) *hν*, THF–H_2O (10:1), 15 min, 0 °C, 82% (plus 16% of recovered **4**); (b) NaH (catalytic), excess Cl_3CCN, CH_2Cl_2, 0 °C, 2 h; (c) 2.4 equiv of benzoyl chloride, 4.5 equiv of pyr, CH_2Cl_2, −15 °C, 2 h, 84%; (d) 1.0 equiv of **2**, 1.6 equiv of **3**, 3.0 equiv of $BF_3{\cdot}Et_2O$, CH_2Cl_2, −40 °C, 1.75 h, 76% (40% of **7** plus 36% of **8**, over two steps); (e) 2.0 equiv of Et_3SiOTf, 4.0 equiv of $^iPr_2NEt$, CH_2Cl_2, 0 °C, 20 min, 99%; (f) 10 equiv of Ac_2O, 18 equiv of $^iPr_2NEt$, DMAP (catalytic), CH_2Cl_2, 0 °C, 1.5 h, 98%.

was then dried azeotropically with toluene at ambient temperature and used directly in the coupling step.

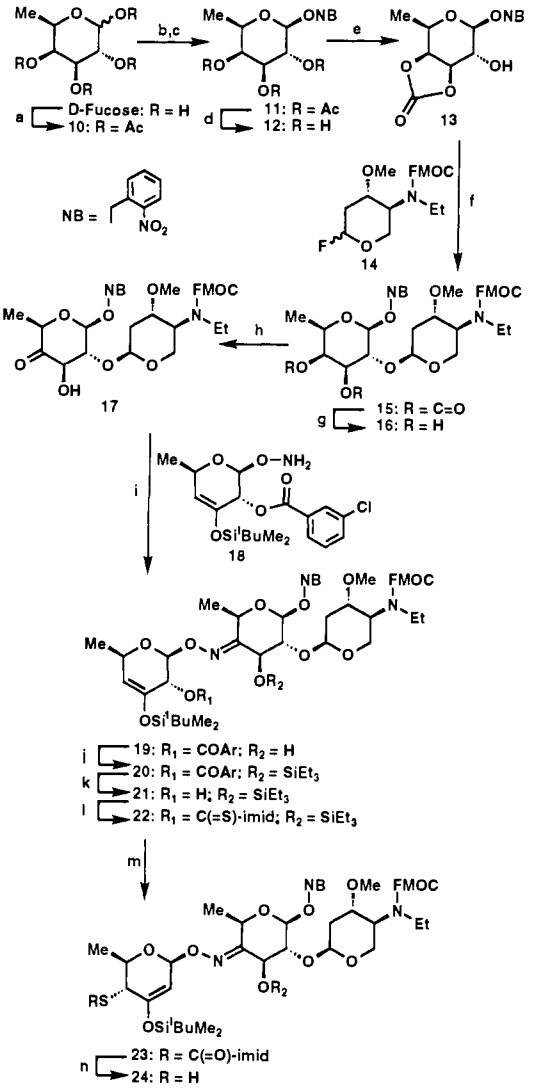
The required aglycon intermediate **3** was prepared (also in gram quantities) as shown in Scheme II from diol **6**, obtained enroute to calicheamicinone, as described in the preceding paper.[2] Thus, selective benzoylation (1.2 → 2.4 equiv of PhCOCl, excess pyridine until all starting material was consumed) of the primary hydroxyl group in **6** resulted in 84% yield of monobenzoate **3** plus a dibenzoylated compound. The two compounds were separated chromatographically, and the dibenzoate was converted back to diol **6** for recycling with excess DIBAL. The stage was now set for the crucial coupling reaction of the two fragments.

Coupling of Oligosaccharide and Aglycon Fragments 2 and 3. Components **2** and **3** (1.4 equiv) reacted under strictly anhydrous conditions and in the presence of $BF_3{\cdot}Et_2O$ in CH_2Cl_2 at −40 °C to afford, after 1.75 h,[4,6] a 40% yield of coupled product **7** as a single isomer (presumed at this stage, and later proven, to be the β-anomer) plus a 36% yield of a monodesilylated coupled product, **8** (Scheme II). Silylation of **8** under standard conditions led to **7** in quantitative yield. Acetylation of **8** with Ac_2O–$^iPr_2NEt$–DMAP in CH_2Cl_2 gave a monoacetate which was assigned structure **9** from its ^1H NMR data. The sensitivity of the A-ring silyl ether relative to that of the others is presumably due to its proximity to the oxime, which serves as the complexation center for $BF_3{\cdot}Et_2O$. The ratio of the two products **7**:**8** depended on the reaction time.

Introduction of the First Sulfur Atom. Having achieved the construction of the basic skeleton of calicheamicin γ_1^I (containing all necessary carbon atoms), we then turned our attention to the installation of the remaining functionalities in a stepwise fashion. The initial objective was the introduction of the first sulfur atom at the allylic position of the aglycon domain. To this end, the benzoate group was removed from compound **7** by careful treatment with DIBAL, avoiding attack at all other carbonyl sites. Steric shielding of the thioester carbonyl was particularly pivotal in the preservation of this functionality, although excessive amounts of DIBAL resulted in degradation of the compound, presumably *via* cleavage of this group. The liberated allylic

(6) Halcomb, R. L.; Boyer, S. H.; Danishefsky, S. J. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 338.

Scheme III[a]



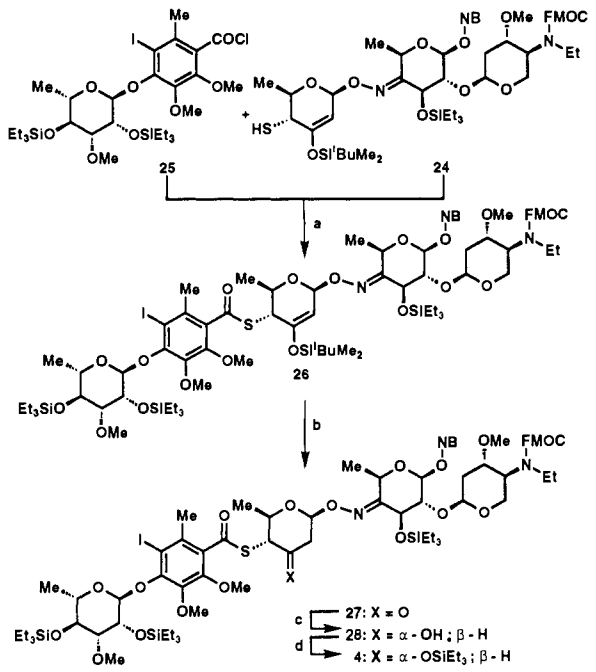
[a] Reagents and conditions: (a) 6.0 equiv of Ac_2O, 8.0 equiv of Et_3N, DMAP (catalytic), CH_2Cl_2, 0 → 25 °C, 18 h, 99%; (b) HBr–AcOH, CH_2Cl_2–Ac_2O, 0 °C, 2.0 h; (c) 1.5 equiv of *o*-nitrobenzyl alcohol, 1.4 equiv of Ag_2CO_3, 4-Å molecular sieves, CH_2Cl_2, 25 °C, 18 h, 87% (over two steps); (d) NaOMe (catalytic), MeOH, 25 °C, 0.5 h, 100%; (e) 2.5 equiv of CDI, MeCN, 100 °C, and then 5% HCl, 75 °C, 15 min, 66%; (f) 1.0 equiv of **14**, 1.2 equiv of **13**, 3.0 equiv of $AgClO_4$, 3.0 equiv of $SnCl_2$, 4-Å molecular sieves, THF, −78 → −15 °C, 18 h; (g) NaH (catalytic), THF–$(CH_2OH)_2$ (20:1), 0 °C, 15 min, 63% (over two steps); (h) 1.1 equiv of $^nBu_2SnO$, MeOH, reflux, 1.0 h, and then 1.5 equiv. of $^nBu_3SnOMe$, 1.0 equiv of Br_2, CH_2Cl_2, 25 °C, 5 min, 93%; (i) 1.0 equiv of **17**, 1.2 equiv of **18**, PPTS (catalytic), PhH, 25 °C, 18 h, 70%; (j) 1.5 equiv of 2,6-lutidine, 1.2 equiv of Et_3SiOTf, CH_2Cl_2, −78 °C, 1.5 h, 93%; (k) 2.3 equiv of DIBAL, CH_2Cl_2, −78 °C, 0.5 h, 99%; (l) 4.0 equiv of thiocarbonyldiimidazole, MeCN, 25 °C, 1.5 h, 92%; (m) PhMe, reflux, 0.75 h, 82%; (*n*) 1.0 equiv of NaSMe, 40 equiv of EtSH, CH_2Cl_2, 25 °C, 1.5 h, 95%.

alcohol **29** (Scheme V) reacted smoothly in a Mitsunobu reaction with AcSH according to the Danishefsky protocol,[7] leading to the requisite thioacetate **30** in 96% yield. At this point, it was decided that the reduction of the oxime bond should precede the installation of the trisulfide moiety, fearing destruction of the latter under the reduction conditions, although these fears have not been experimentally verified as yet.

Reduction of the Oxime Bond. Lack of success in our initial attempts to reduce stereoselectively the oxime bond in model

(7) Cabal, M. P.; Coleman, R. S.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1990**, *112*, 3253. Haseltine, J. N.; Cabal, M. P.; Mantlo, N. B.; Iwasawa, N.; Yamashita, D. S.; Coleman, R. S.; Danishefsky, S. J.; Schulte, G. K. *J. Am. Chem. Soc.* **1991**, *113*, 3850. Volante, R. P. *Tetrahedron Lett.* **1981**, *22*, 3119.

Scheme IV[a]



[a] Reagents and conditions: (a) 1.0 equiv of **24**, 1.1 equiv of **25**, 2.1 equiv of DMAP, CH_2Cl_2, 0 °C, 1 h, 78%; (b) 1.05 equiv of TBAF, 5.0 equiv of AcOH, THF, –23 °C, 0.5 h; (c) 3.0 equiv of K-Selectride, DME-THF, –78 °C, 0.5 h, 69% (over two steps); (d) 3.0 equiv of Et_3SiOTf, 6.0 equiv of $^iPr_2NEt$, CH_2Cl_2, 0 °C, 0.5 h, 97%.

systems prompted us to liberate all hydroxyl groups prior to attempting this operation. Thus, **30** was converted to pentol **31** in 94% yield by exposure to excess HF·pyr in THF–CH_2Cl_2. The reduction of **31** with $NaCNBH_3$–BF_3·Et_2O in THF (–40 °C) led to a mixture of **32** (4α-isomer, major) and **32-epi** (4β-isomer, minor) in 96% total yield (based on 83% conversion). Use of both enantiomers of Corey's oxazaborolidine reagent[8] in the same reduction furnished only **32-epi** along with recovered starting material, whereas the use of sodium or tetramethylammonium triacetoxyborohydride/AcOH combinations resulted in no reaction. Flash column chromatography separated the desired isomer **32** from its 4β-epimer (**32-epi**) but, unfortunately, not from the remaining starting material (**31**), necessitating further purification at a subsequent step. At this stage, it was also realized that protection of the free hydroxyl groups was desirable for the pending steps leading to the establishment of the trisulfide unit. To this end, the mixture of **32** + **31** (Scheme VI) was persilylated by exposure to Et_3SiOTf–$^iPr_2NEt$ in CH_2Cl_2, leading not to the desired pentaslilyl ether but rather to an unstable hexasilylated silyl compound, in which a nitrogen–silicon bond had been formed. Treatment of this crude product with excess AcOH/H_2O in EtOAc, however, easily cleaved this labile bond and furnished pentasilyl ether **33**, together with the oxime derivative **30**, in 75% total yield.

Installment of the Trisulfide Moiety. Having secured a suitable precursor, we then focused our attention on the task of completing the trisulfide moiety as part of the quest for the target molecule. Using excess *N*-(methyldithio)phthalimide (PhthNSSMe)[9] and following the studies of Magnus with model systems,[10] Danishefsky with racemic calicheamicinone,[7] and ours with optically active calicheamicinone,[11] we successfully installed the remaining two sulfur atoms capped with a methyl group *via* the intermediacy of the corresponding thiol. Thus, reaction of the mixture of thioacetates **33** and its oxime counterpart **30** (*ca.* 3:1) was treated with 3.0 equiv of DIBAL in CH_2Cl_2 at –90 °C to afford **34** and its corresponding oxime derivative. Treatment of this crude reaction mixture with excess PhthNSSMe in CH_2Cl_2 resulted in a separable mixture of trisulfides **35** and **36** in 77% total overall yield from the corresponding thioacetate mixture (**33** + **30**). Chromatographic separation of the two compounds allowed for the final deprotections to be carried out on pure **35**.

Final Deprotections. Total Synthesis of Calicheamicin γ_1^I (1). The successful synthesis of **35** left us with the liberation of calicheamicin γ_1^I (**1**) from its protected form as the only remaining task in the total synthesis. Upon careful consideration of the three types of protecting groups present in **35**, the following sequence of removal was chosen. First, the silyl ethers were cleaved by exposure to HF·pyr to afford pentol **37** (Scheme VII) in 90% yield. Second, the ethylene glycol ketal was removed by treatment with TsOH·H_2O in aqueous THF, leading to calicheamicin γ_1^I FMOC derivative **38** in 69% yield. Finally, the FMOC protecting group was induced to depart from the molecule by exposure to Et_2NH in aqueous THF, furnishing calicheamicin γ_1^I (**1**) in 90% yield. The synthetic material exhibited identical physical and spectroscopic data [TLC, HPLC, $[\alpha]^{25}_D$, ^1H and ^{13}C NMR, mass spectra, and IR and UV spectra] with those of an authentic sample.

Synthesis of A-4-*epi*-calicheamicin γ_1^I (1-epi). A 4-*epi*-thioacetate **32-epi** was taken through the same sequence as described above to furnish A-4-*epi*-calicheamicin γ_1^I (**1-epi**) via intermediates **33-epi**–**38-epi**, as summarized in Scheme VIII.

Conclusion

When the molecular structure of calicheamicin γ_1^I (**1**) was announced in 1987, synthetic chemists around the world were immediately stunned, challenged, and left in wonderment over its fascinating and unusual molecular architecture, particularly in the absence of an X-ray crystallographic proof. Six years later, in 1993, this molecule and its relatives still continue to fascinate not only chemists but also biologists with their interesting chemical and biological properties. However, with the total synthesis of calicheamicin γ_1^I (**1**) completed, the correctness of its molecular structure is no longer in doubt. During this synthesis, we have learned a great deal about synthetic strategy, about stability of unusual functionalities, and about the interaction of this molecule and its regional domains with DNA. Much more will be learned by studying the designed molecules now available through the established synthetic sequence and by applying the developed chemistry to other systems.

The chemistry described in this series of papers demonstrated the advanced state of the art of modern organic synthesis. Many of the concepts proposed in the original strategy were proven useful in the practical execution of the plan, while a number of new ideas had to be adopted to solve unexpected problems. Among the characteristics and highlights of this total synthesis are the following: (i) a short and efficient synthesis of the aromatic C-ring and the observation, by X-ray crystallographic analysis, that such compounds crystallize in separate enantiomeric forms, even though at first glance they appear achiral; (ii) the development of new strategies for the stereoselective construction of the unusual NH–O–β glycoside bond linking rings A and B; (iii) a stereospecific [3,3]-sigmatropic rearrangement involving a thionoimidazolide–vinyl ether functionality for the introduction of the novel B-ring functional groups; (iv) the use of an oxime linkage as both a

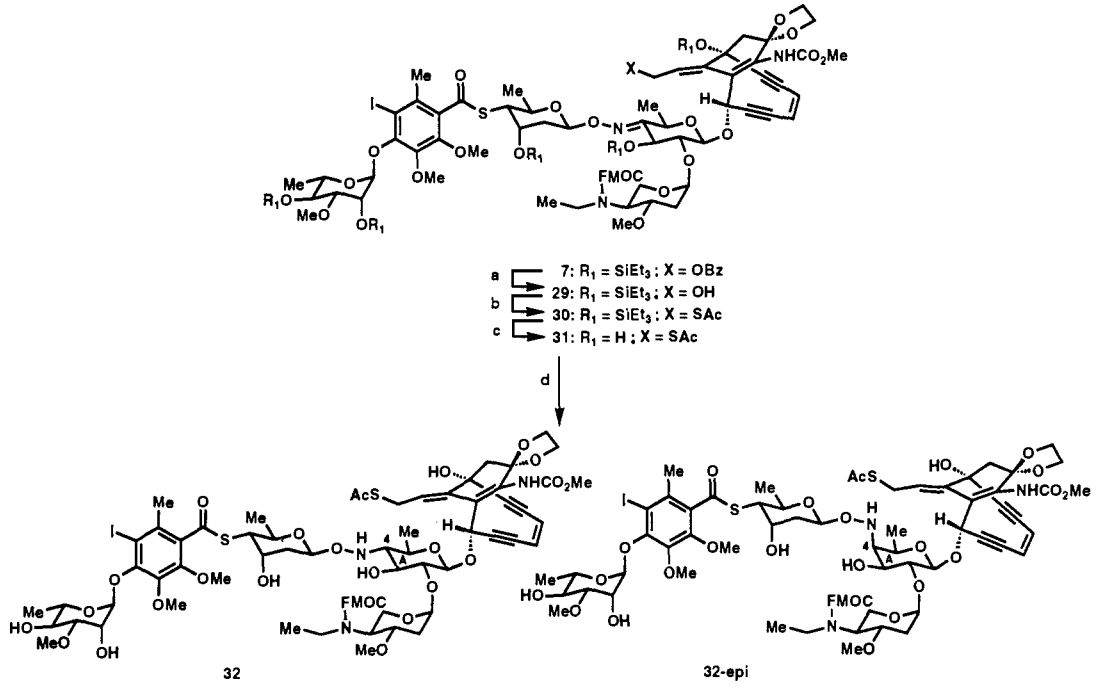
(8) Corey, E. J.; Bakshi, R. K.; Shibata, S.; Chen, C.-P.; Singh, V. K. *J. Am. Chem. Soc.* **1987**, *109*, 7925. Jones, T. K.; Mohan, J. J.; Xavier, L. C.; Blacklock, T. J.; Mathre, D. J.; Sohar, P.; Turner Jones, E. T.; Reamer, R. A.; Roberts, F. E.; Grabowski, E. J. J. *J. Org. Chem.* **1991**, *56*, 763. We thank Dr. I. Shinkai of Merck Sharp and Dohme, Rahway, NJ, for generous gifts of (+)- and (–)-oxazaborolidine reagents.

(9) (a) Harpp, D. N.; Ash, D. K. *Int. J. Sulfur Chem., Part A* **1971**, *1*, 211. (b) Sullivan, A. B.; Boustany, K. *Int. J. Sulfur Chem., Part A* **1971**, *1*, 207.

(10) Magnus, P.; Lewis, R. T.; Bennett, F. *J. Chem. Soc., Chem. Commun.* **1989**, 916.

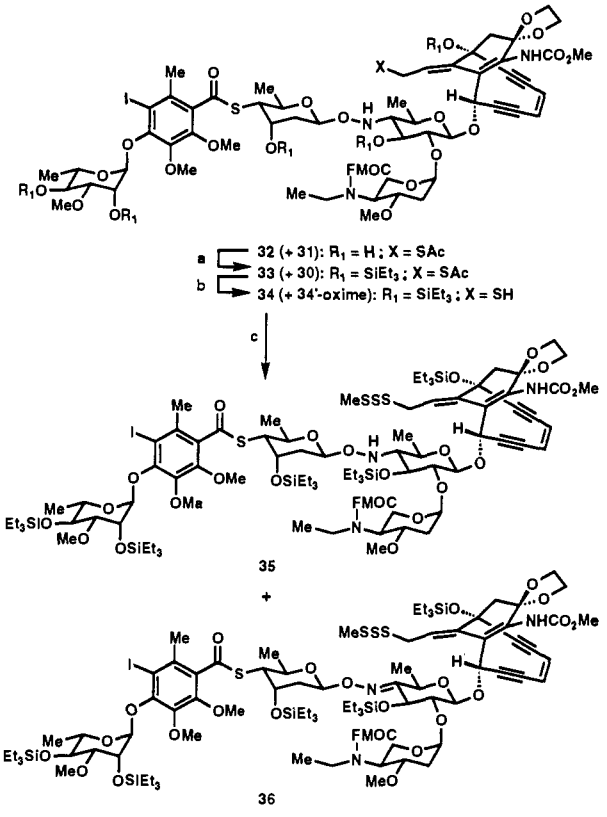
(11) Smith, A. L.; Hwang, C.-K.; Pitsinos, E.; Scarlato, G.; Nicolaou, K. C. *J. Am. Chem. Soc.* **1992**, *114*, 3134.

Scheme V[a]



[a] Reagents and conditions: (a) 3 equiv of DIBAL, CH_2Cl_2, −78 °C, 1 h, 91%; (b) 15 equiv of PPh_3, 12 equiv of DEAD, 14 equiv of AcSH, THF, 0 °C, 15 min, 96%; (c) excess HF·pyr, THF–CH_2Cl_2 (6:1), 0 → 25 °C, 3 h, 94%; (d) 40 equiv of $NaCNBH_3$, 15 equiv of $BF_3{\cdot}OEt_2$, THF −40 °C, 3.5 h, 96% (2:1 mixture of isomers, 83% conversion).

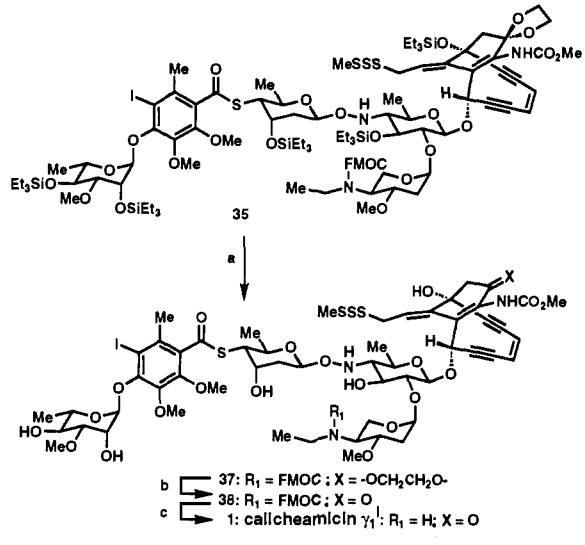
Scheme VI[a]



[a] Reagents and conditions: (a) 20 equiv of Et_3SiOTf, 39 equiv of $^iPr_2NEt$, CH_2Cl_2, 0 °C, 45 min; and then excess AcOH, EtOAc–H_2O (200:1), 25 °C, 8 h, 75%; (b) 3 equiv of DIBAL, CH_2Cl_2, −90 °C, 50 min; (c) 7 equiv of *N*-(methyldithio)phthalimide, CH_2Cl_2, 0 → 25 °C, 15 h (**35**, 57% and **36**, 20%, over two steps).

masking device for the NH–O moiety until late in the sequence and a bridging device to join the A–E ketone and the B-ring alkoxylamine; (v) the utilization of a strategy based on a nitrile

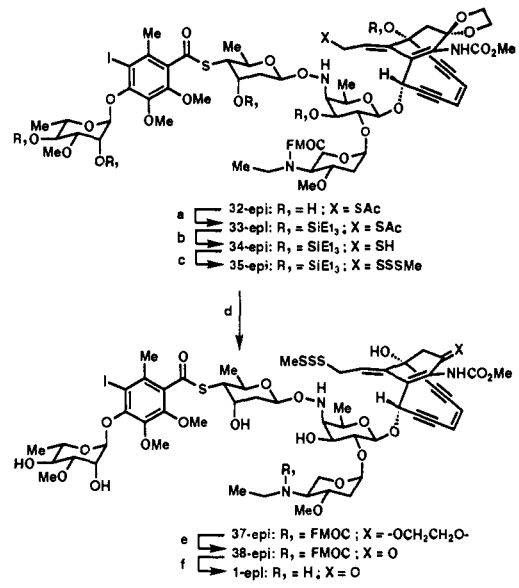
Scheme VII[a]



[a] Reagents and conditions: (a) HF·pyr, THF–CH_2Cl_2 (5:1), 0 → 25 °C, 18 h, 90%; (b) 1.0 equiv of $TsOH{\cdot}H_2O$, THF–H_2O (50:1), 25 °C, 23 h, 69% (based on recovered **37**); (c) Et_2NH–THF–H_2O (5:25:1), 25 °C, 2 h, 90%.

oxide/olefin intramolecular cycloaddition reaction to form the cyclohexenone ring of the calicheamicinone domain and the conservation and conversion of the original nitrogen to the urethane nitrogen of the target molecule; (vi) the use of a chiral allylborane in an asymmetric induction process to install, in high enantiomeric excess, the first controlling stereocenter, leading to an enantiomerically pure calicheamicinone fragment; (vii) an intramolecular acetylide–aldehyde condensation as the key reaction to construct the 10-membered enediyne ring; (viii) a stereoselective and efficient glycosidation reaction as the key coupling process for joining the oligosaccharide and aglycon fragments of the target molecule, based on Schmidt's trichloroacetimidate methodology; (ix) a stereoselective reduction of the oxime functionality to generate the requisite NH–O bond late in the synthesis; and (x)

Scheme VIII[a]



[a] Reagents and conditions: (a) 20 equiv of Et_3SiOTf, 40 equiv of $^iPr_2NEt$, CH_2Cl_2, 0 °C, 1 h, and then excess AcOH, EtOAc–H_2O (100:1), 25 °C, 24 h, 79%; (b) 3.0 equiv of DIBAL, CH_2Cl_2, –90 °C, 0.5 h; (c) 20 equiv of *N*-(methyldithio)phthalimide, CH_2Cl_2, 0 → 25 °C, 35 h, 98% (over two steps); (d) HF·pyr, THF–CH_2Cl_2 (5:1), 0 → 25 °C, 15 h, 96%; (e) 2.0 equiv of TsOH·H_2O, THF–H_2O (20:1), 25 °C, 31 h, 61%; (f) Et_2NH–THF–H_2O (5:25:1), 25 °C, 2.5 h, 51%.

a carefully chartered functional group installation–deprotection sequence in the final stages of the synthesis.

Besides confirming the molecular structure of calicheamicin γ_1^I (**1**), the total synthesis established a realistic synthetic approach to the natural product. Most significantly, complex-designed calicheamicins are now accessible by this route, as demonstrated in this paper. Additional examples of designed molecules of this class which cannot be accessed from the natural compound are currently under construction by total synthesis. The exploration of the chemistry and biology of such molecules will certainly enrich our understanding of the mechanism of action of these fascinating compounds and may provide new leads for drug discovery and development.

Experimental Section

General Techniques. NMR spectra were recorded on Bruker AMX-500, AM-300, or AM-250 instruments. The following abbreviations were used to explain the multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; b, broad; obs, obscured. IR spectra were recorded on Nicolet 205 or Perkin-Elmer 1600 series FT-IR spectrophotometers. Melting points were obtained on a Thomas-Hoover Unimelt apparatus and are uncorrected. Optical rotations were recorded using a Perkin-Elmer 241 polarimeter. High-resolution mass spectra (HRMS) were recorded on a VG ZAB-ZSE mass spectrometer under fast atom bombardment (FAB) conditions.

All reactions were monitored by thin-layer chromatography carried out on 0.25-mm E. Merck silica gel plates (60F-254) using UV light, 7% ethanolic phosphomolybdic acid, or *p*-anisaldehyde solution and heat as a developing agent. E. Merck silica gel (60, particle size 0.040–0.063 mm) was used for flash column chromatography. Tetrahydrofuran (THF) and ethyl ether were distilled from sodium–benzophenone and methylene chloride; benzene and toluene were distilled from calcium hydride.

All reactions were carried out under an argon atmosphere with anhydrous, freshly distilled solvents under anhydrous conditions, unless otherwise noted. Yields refer to chromatographically and spectroscopically (^1H NMR) homogeneous materials, unless otherwise stated.

1,2,3,4-Tetra-*O*-acetyl-D-fucopyranose (10). A suspension of D-fucose (21.5 g, 131 mmol) in CH_2Cl_2 (500 mL) was treated with triethylamine (146 mL, 1.05 mol), acetic anhydride (74 mL, 786 mmol), and 4-(dimethylamino)pyridine (1.6 g, 13.1 mmol) at 0 °C. After 10 min, the reaction mixture was allowed to warm to room temperature and stirred for 18 h. The reaction mixture was diluted with EtOAc (800 mL) and washed with H_2O (500 mL), saturated aqueous $NaHCO_3$ (4 × 300 mL), and brine (300 mL), dried ($MgSO_4$), concentrated, and purified by flash chromatography (silica, 50% ethyl acetate in petroleum ether) to give tetraacetate **10** (43.6 g, 99%, mixture of α/β-anomers): R_f = 0.38 (5% ethyl ether in methylene chloride); $[\alpha]^{23}_D$ +92.5° (*c* 1.85, CH_2Cl_2); IR (film) ν_{max} 2988, 1750, 1435, 1372, 1235, 1139, 1077, 1014, 972, 939, 899, 819 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.10 (m, 1 H, H-1), 5.16–5.04 (m, 3 H, H-2, H-3, H-4), 4.10 (m, 1 H, H-5), 1.99–1.78 (series of s, 12 H, 4 × CH_3CO), 0.95 (m, 3 H, H-6); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.9, 169.5, 169.4, 168.6, 89.3, 70.1, 67.3, 66.7, 66.0, 20.3, 20.1, 20.0, 15.4.

2-Nitrobenzyl 2,3,4-Tri-*O*-acetyl-β-D-fucopyranose (11). To a cooled solution of tetraacetate **10** (43.2 g, 130 mmol) in CH_2Cl_2 (200 mL) and Ac_2O (20 mL) was added dropwise 30% HBr–AcOH (150 mL) over 1.5 h, and the mixture was stirred for an additional 0.5 h at room temperature under argon. The reaction mixture was concentrated *in vacuo*, and the resulting orange oil was azeotroped with toluene (3×). The residue was dissolved in dry CH_2Cl_2 (500 mL), treated with powdered, activated 4-Å molecular sieves (30 g), and stirred for 10 min at room temperature under argon before addition of *o*-nitrobenzyl alcohol (29.5 g, 193 mmol). The mixture was stirred for 20 min followed by treatment with Ag_2CO_3 (50.5 g, 183 mmol). The reaction mixture was stirred at ambient temperature for 18 h. The reaction mixture was then diluted with CH_2Cl_2 (500 mL) and filtered through a pad of Celite. The filtrate was washed with saturated aqueous $NaHCO_3$ (500 mL) and brine (500 mL). The organic phase was dried (Na_2SO_4), concentrated, and purified by flash column chromatography (silica, 40–70% ethyl ether in petroleum ether) to yield *o*-nitrobenzyl glycoside **11** (48.27 g, 87% over two steps) as a white foam: R_f = 0.17 (silica, 50% ethyl ether in petroleum ether); $[\alpha]^{23}_D$ +1.9° (*c* 1.45, $CHCl_3$); IR (film) ν_{max} 2984, 2940, 1748, 1529, 1368, 1225, 1070, 732 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.00–7.98 (m, 1 H, aromatic), 7.67–7.65 (m, 1 H, aromatic), 7.59–7.55 (m, 1 H, aromatic), 7.40–7.36 (m, 1 H, aromatic), 5.26–5.19 (m, 3 H, H-2, H-4, CH_2Ph), 5.00 (dd, *J* = 10.5, 3.4 Hz, 1 H, H-3), 4.96 (d, *J* = 14.8 Hz, 1 H, CH_2Ph), 4.58 (d, *J* = 7.9 Hz, 1 H, H-1), 3.83 (b q, *J* = 6.4 Hz, 1 H, H-5), 2.11, 1.99, 1.92 (3 × s, 3 × 3 H, CH_3CO), 1.18 (d, *J* = 6.4 Hz, 3 H, H-6); ^{13}C NMR (125 MHz, C_6D_6) δ 177.4, 169.9, 169.5, 146.7, 133.6, 133.5, 128.5, 128.0, 124.5, 100.4, 71.0, 70.0, 69.1, 68.7, 67.8, 20.6, 20.4 (2), 15.7; HRMS (FAB) calcd for $C_{19}H_{23}NO_{10}Cs$ (M + Cs) 558.0376, found 558.0376.

Compounds **12**, **13**, **15–17**, **19–24**, and **26–28** were prepared according to the procedures reported in the accompanying paper[1] describing the synthesis of the methyl glycoside counterpart of **28**. Selected compounds from this group exhibited the following physical properties.

12: R_f = 0.25 (silica, 10% methanol in methylene chloride); $[\alpha]^{23}_D$ –10.6° (*c* 0.96, THF); IR (film) ν_{max} 3382, 2920, 2853, 1524, 1343, 1068, 722 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.02 (dd, *J* = 8.2, 1.2 Hz, 1 H, aromatic), 7.82 (d, *J* = 7.8 Hz, 1 H, aromatic), 7.61 (dt, *J* = 7.6, 1.2 Hz, 1 H, aromatic), 7.42 (t, *J* = 7.8 Hz, 1 H, aromatic), 5.22 (d, *J* = 14.8 Hz, 1 H, CH_2Ph), 5.03 (d, *J* = 14.8 Hz, 1 H, CH_2Ph), 4.35 (d, *J* = 7.7 Hz, 1 H, H-1), 3.80–3.60 (m, 4 H, H-2, H-3, H-4, H-5), 3.45 (b s, 1 H, O*H*), 3.19 (b s, 1 H, O*H*), 2.81 (b s, 1 H, O*H*), 1.31 (d, *J* = 6.5 Hz, 3 H, H-6); ^{13}C NMR (125 MHz, DMSO-d_6) 146.8, 134.7, 134.0, 128.9, 128.3, 124.5, 103.1, 73.5, 71.1, 70.4, 70.2, 66.2, 16.7; HRMS (FAB) calcd for $C_{13}H_{17}NO_7Cs$ (M + Cs) 432.0059, found 432.0072.

13: R_f = 0.65 (10% methanol in methylene chloride); $[\alpha]^{23}_D$ +26.1° (*c* 1.29, THF); IR (film) ν_{max} 3406, 1795, 1535, 1522, 1360, 1341, 1304, 1176, 1137, 1074, 1032, 873 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.05 (d, *J* = 7.2 Hz, 1 H, aromatic), 7.75 (d, *J* = 7.8 Hz, 1 H, aromatic), 7.65 (t, *J* = 7.5 Hz, 1 H, aromatic), 7.46 (t, *J* = 7.5 Hz, 1 H, aromatic), 5.23 (d, *J* = 14.5 Hz, 1 H, CH_2Ph), 5.06 (d, *J* = 14.5 Hz, 1 H, CH_2Ph), 4.69 (dd, *J* = 7.2, 7.2 Hz, 1 H, H-3), 4.58 (dd, *J* = 7.2, 2.0 Hz, 1 H, H-4), 4.52 (d, *J* = 7.1 Hz, 1 H, H-1), 3.95 (dq, *J* = 6.5, 2.0 Hz, 1 H, H-5), 3.83 (dd, *J* = 7.1, 6.9 Hz, 1 H, H-2), 1.44 (d, *J* = 6.5 Hz, 3 H, H-6); ^{13}C NMR (125 MHz, $CDCl_3$) 133.5, 129.7, 128.6, 124.6, 101.3, 78.4, 71.5, 68.2, 67.9, 16.2; HRMS (FAB) calcd for $C_{14}H_{15}NO_8Cs$ (M + Cs) 457.9852, found 457.9861.

15: R_f = 0.36 (40% ethyl acetate in benzene); $[\alpha]^{23}_D$ –30.8° (*c* 1.51, $CHCl_3$); IR (film) ν_{max} 2935, 1805, 1693, 1526, 1449, 1421, 1360, 1345, 1275, 1142, 1074, 1025, 737 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6, 340 K) δ 8.02 (d, *J* = 8.1 Hz, 1 H, aromatic), 7.84 (d, *J* = 7.5 Hz, 2 H, aromatic), 7.77 (d, *J* = 7.6 Hz, 1 H, aromatic), 7.73–7.69 (m, 1 H, aromatic), 7.61–7.52 (m, 1 H, aromatic), 7.39 (t, *J* = 7.2 Hz, 2 H, aromatic), 7.33–7.28 (m, 2 H, aromatic), 5.18 (b s, 1 H, E-1), 5.07 (d, *J* = 14.5 Hz, 1 H, CH_2Ph), 5.00 (d, *J* = 14.6 Hz, 1 H, CH_2Ph), 4.99

(dd, J = 7.7, 2.8 Hz, 1 H, A-3), 4.84 (dd, J = 7.7, 1.9 Hz, 1 H, A-4), 4.78 (d, J = 5.9 Hz, 1 H, A-1), 4.42–4.34 (m, 2 H, CH_2-FMOC), 4.24 (t, J = 6.0 Hz, 1 H, benzylic-FMOC), 4.05 (dq, J = 6.6, 1.9 Hz, 1 H, A-5), 3.80–3.60 (m, 4 H, A-2, E-3, E-5, E-5′), 3.29 (dd, J = 10.7, 4.6 Hz, 1 H, E-4), 3.17 (s, 3 H, CH_3O), 2.82 (b m, 2 H, CH_2N), 2.29 (m, 1 H, E-2$_{eq}$), 1.45 (m, 1 H, E-2$_{ax}$), 1.27 (d, J = 6.6 Hz, 3 H, A-6), 0.69 (b s, 3 H, CH_3CH$_2$N); ^{13}C NMR (125 MHz, $CDCl_3$) 155.4, 153.7, 146.7, 144.0, 141.3, 134.0, 133.8, 128.9, 128.4, 128.3, 127.9, 127.6, 127.0, 125.2, 125.0, 124.8, 124.5, 119.9, 99.5, 98.0, 97.3, 77.6, 76.9, 76.6, 73.4, 71.5, 67.5, 67.4, 66.8, 66.7, 60.7, 60.1, 59.9, 56.9, 56.4, 55.7, 47.2, 42.2, 35.5, 35.0, 16.5, 16.4, 14.5; HRMS (FAB) calcd for $C_{37}H_{40}N_2O_{12}Cs$ (M + Cs) 837.1636, found 837.1635.

16: R_f = 0.27 (80% ethyl acetate in benzene); $[\alpha]^{23}_D$ –44.6° (c 1.13, $CHCl_3$); IR (film) ν_{max} 3417, 3066, 2931, 1698, 1613, 1578, 1524, 1479, 1450, 1423, 1359, 1341, 1275, 1067, 995, 733 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, 340 K) δ 8.02–7.99 (m, 1 H, aromatic), 7.86–7.82 (m, 3 H, aromatic), 7.73–7.69 (m, 1 H, aromatic), 7.60–7.49 (m, 3 H, aromatic), 7.41–7.37 (m, 2 H, aromatic), 7.32–7.27 (m, 2 H, aromatic), 5.38 (b s, 1 H, E-1), 5.07 (d, J = 14.9 Hz, 1 H, CH_2Ph), 4.97 (d, J = 14.9 Hz, 1 H, CH_2Ph), 4.43 (d, J = 7.5 Hz, 1 H, A-1), 4.38–4.30 (m, 2 H, CH_2-FMOC), 4.22 (t, J = 6.0 Hz, 1 H, benzylic-FMOC), 3.84 (dd, J = 10.0, 10.0 Hz, 1 H, E-5$_{ax}$), 3.72 (b s, 1 H, E-3), 3.61–3.52 (m, 3 H, A-2, A-3, A-5), 3.43 (b d, J = 2.8 Hz, 1 H, A-4), 3.18–3.02 (m, 3 H, OH, E-4), 3.16 (s, 3 H, CH_3O), 2.74 (b s, 2 H, CH_2N), 2.34 (m, 1 H, E-2$_{eq}$), 1.35 (m, 1 H, E-2$_{ax}$), 1.14 (d, J = 6.4 Hz, 3 H, A-6), 0.60 (m, 3 H, CH_3-CH$_2$N); ^{13}C NMR (125 MHz, DMSO-d_6) 155.1, 146.8, 144.0, 143.9, 143.7, 140.8, 140.7, 134.1, 133.9, 133.8, 128.6, 128.5, 128.4, 128.3, 127.6, 127.5, 127.0, 125.1, 124.7, 124.6, 124.4, 120.0, 100.7, 97.3, 79.2, 74.4 (2), 74.3, 71.5, 71.2, 70.2, 66.1, 66.0, 58.9, 54.8, 46.7, 34.6, 16.4, 14.2, 13.9; HRMS (FAB) calcd for $C_{36}H_{42}N_2O_{11}Cs$ (M + Cs) 811.1843, found 811.1851.

19: R_f = 0.12 (5% acetone in methylene chloride); $[\alpha]^{23}_D$ –107.3° (c 1.35, $CHCl_3$); IR (film) ν_{max} 3343, 2932, 1728, 1695, 1527, 1424, 1343, 1252, 1130, 1085, 1043, 987, 839, 739 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, 340 K) δ 8.02–7.27 (series of multiplets, 16 H, aromatic), 5.51 (dd, J = 5.6, 2.2 Hz, 1 H, B-2), 5.42 (d, J = 5.6 Hz, 1 H, B-1), 5.18 (d, J = 1.9 Hz, 1 H, B-4), 5.12 (b s, 1 H, E-1), 5.08 (d, J = 14.5 Hz, 1 H, CH_2Ph), 4.91 (d, J = 14.5 Hz, 1 H, CH_2Ph), 4.71 (q, J = 6.7 Hz, 1 H, A-5), 4.55 (ddq, J = 6.6, 2.2, 1.9 Hz, 1 H, B-5), 4.48 (d, J = 6.3 Hz, 1 H, A-1), 4.42–4.32 (m, 2 H, CH_2-FMOC), 4.22 (t, J = 6.0 Hz, 1 H, benzylic-FMOC), 4.11 (m, 1 H, A-3), 3.85 (dd, J = 6.2, 2.2 Hz, 1 H, A-2), 3.80–3.60 (m, 3 H, E-3, E-5, E-5′), 3.22 (m, 1 H, E-4), 3.15 (s, 3 H, CH_3), 2.82 (m, 2 H, CH_2N), 2.22 (m, 1 H, E-2$_{eq}$), 1.46 (m, 1 H, E-2$_{ax}$), 1.30 (d, J = 6.7 Hz, 3 H, A-6), 1.23 (d, J = 6.6 Hz, 3 H, B-6), 0.86 (m, 3 H, CH_3CH$_2$N), 0.77 (s, 9 H, (CH_3)$_3$CSi), 0.17 (s, 3 H, CH_3-Si), 0.11 (s, 3 H, CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.5, 160.8, 160.6, 155.9, 155.6, 146.6, 144.3, 144.2, 144.1, 144.0, 143.8, 141.3, 134.5, 134.2, 133.8, 133.7, 133.3, 131.4, 129.7, 128.3, 128.2, 127.9 (2), 127.6, 126.9, 125.3, 125.1, 124.8, 124.6, 119.9, 110.4, 102.8, 102.4, 96.8, 76.6, 71.9, 71.6, 70.2, 69.4, 68.7, 68.2, 67.5, 67.4, 67.3, 66.8, 60.5, 59.8, 56.1, 55.7, 47.2 (2), 35.1, 34.9, 29.7, 25.3, 22.4, 18.8, 17.8, 14.6, 14.5, –4.6, –4.7; HRMS (FAB) calcd for $C_{55}H_{66}ClN_3O_{15}SiCs$ (M + Cs) 1204.3006, found 1204.3006.

20: R_f = 0.21 (40% ethyl ether in petroleum ether); $[\alpha]^{23}_D$ –94.8° (c 1.05, $CHCl_3$); IR (film) ν_{max} 2955, 2928, 2855, 1732, 1698, 1667, 1577, 1527, 1463, 1426, 1364, 1342, 1306, 1277, 1252, 1156, 1124, 1083, 983, 839, 741 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, 340 K) δ 8.00 (d, J = 7.9 Hz, 1 H, aromatic), 7.90–7.82 (m, 4 H, aromatic), 7.76–7.67 (d, J = 7.9 Hz, 1 H, aromatic), 7.63–7.49 (m, 4 H, aromatic), 7.38 (b t, J = 7.4 Hz, 2 H, aromatic), 7.29 (m, 2 H, aromatic), 5.51 (ddd, J = 5.7, 2.1, 0.7 Hz, 1 H, B-2), 5.42 (d, J = 5.7 Hz, 1 H, B-1), 5.18 (dd, J = 1.8, 0.7 Hz, 1 H, B-4), 5.13 (b s, 1 H, E-1), 5.08 (d, J = 14.5 Hz, 1 H, CH_2Ph), 4.91 (d, J = 14.5 Hz, 1 H, CH_2Ph), 4.71 (q, J = 6.7 Hz, 1 H, A-5), 4.55 (ddq, J = 6.6, 2.2, 1.8 Hz, 1 H, B-5), 4.48 (d, J = 6.3 Hz, 1 H, A-1), 4.40–4.31 (m, 2 H, CH_2-FMOC), 4.22 (t, J = 6.0 Hz, 1 H, benzylic-FMOC), 4.12 (d, J = 1.9 Hz, 1 H, A-3), 3.85 (dd, J = 6.3, 2.0 Hz, 1 H, A-2), 3.68 (b m, 3 H, E-3, E-5, E-5′), 3.22 (m, 1 H, E-4), 3.15 (s, 3 H, CH_3O), 2.82 (b m, 2 H, CH_2N), 2.22 (m, 1 H, E-2$_{eq}$), 1.42 (m, 1 H, E-2$_{ax}$), 1.29 (d, J = 6.7 Hz, 3 H, A-6), 1.23 (d, J = 6.6 Hz, 3 H, B-6), 0.91 (t, J = 7.9 Hz, 9 H, Si(CH$_2$CH_3)$_3$), 0.77 (s, 9 H, Si(CH_3)$_3$), 0.70–0.61 (b m, 3 H, CH_3CH$_2$N), 0.47 (q, J = 7.9 Hz, 6 H, Si(CH_2CH$_3$)$_3$), 0.17 (s, 3 H, CH_3Si), 0.11 (s, 3 H, CH_3Si); ^{13}C NMR (125 MHz, DMSO-d_6) δ 163.9, 161.4, 155.1, 146.9, 144.0, 143.9, 143.8, 143.1, 140.9, 140.7, 133.9, 133.8, 133.6 (2), 131.1, 131.0, 128.9, 128.7, 128.6, 128.5, 128.2, 127.9, 127.6, 127.5, 127.0, 125.3, 125.1, 125.0, 124.7, 124.6, 124.4, 120.0, 111.1, 101.7, 101.3, 94.4, 77.9, 71.2, 70.9, 69.8, 68.8, 68.1, 68.0, 67.9, 66.8, 66.5, 66.1, 58.8, 54.9, 46.7, 34.5, 25.1, 21.9, 21.0, 17.7, 17.4, 14.2, 14.1, 6.8, 5.9, 5.7, 3.9, –4.9, –5.0; HRMS (FAB) calcd for $C_{61}H_{80}ClN_3O_{15}Si_2Cs$ (M + Cs) 1318.3871, found 1318.3871.

21: R_f = 0.41 (70% ethyl ether in petroleum ether); $[\alpha]^{23}_D$ = –55.3° (c 0.60, $CHCl_3$); IR (film) ν_{max} 3452, 2955, 2932, 2877, 2858, 1703, 1682, 1612, 1527, 1451, 1422, 1362, 1342, 1275, 1256, 1213, 1157, 1085, 1060, 1019, 839 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, 340 K) δ 8.05–7.25 (series of multiplets, 12 H, aromatic), 5.13 (d, J = 4.0 Hz, 1 H, B-1), 5.11 (m, 1 H, E-1), 5.10 (d, J = 14.3 Hz, 1 H, CH_2Ph), 5.10 (obs, 1 H, OH), 4.94 (d, J = 14.3 Hz, 1 H, CH_2Ph), 4.90 (d, J = 2.0 Hz, 1 H, B-4), 4.72 (q, J = 6.3 Hz, 1 H, A-5), 4.54 (d, J = 5.3 Hz, 1 H, A-1), 4.41–4.31 (m, 3 H, B-5, CH_2-FMOC), 4.27 (d, J = 1.8 Hz, 1 H, A-3), 4.22 (t, J = 6.0 Hz, 1 H, benzylic-FMOC), 3.87 (dd, J = 5.3, 1.8 Hz, 1 H, A-2), 3.80–3.60 (m, 4 H, B-2, E-3, E-5, E-5′), 3.25 (m, 1 H, E-4), 3.17 (s, 3 H, CH_3O), 2.95–2.80 (m, 2 H, CH_2N), 2.22 (m, 1 H, E-2$_{eq}$), 1.45 (m, 1 H, E-2$_{ax}$), 1.43 (d, J = 6.3 Hz, 3 H, A-6), 1.13 (d, J = 6.5 Hz, 3 H, B-6), 0.98–0.90 (m, 18 H, Si(CH$_2$CH_3)$_3$, (CH_3)$_3$CSi), 0.70 (b s, 3 H, CH_3CH$_2$N), 0.64 (q, J = 7.5 Hz, 6 H, Si(CH_2CH$_3$)$_3$), 0.08 (s, 3 H, CH_3Si), 0.06 (s, 3 H, CH_3Si); ^{13}C NMR (125 MHz, DMSO-d_6) δ 158.8, 155.0, 154.9, 147.4, 147.0, 146.8, 144.0, 143.9 (2), 140.9, 140.7, 133.9, 133.8, 133.5, 128.7, 128.6, 128.5, 127.6, 127.5, 127.0, 125.1, 124.7 (2), 124.4, 120.0, 108.8, 104.7, 101.8, 94.5, 78.0, 71.0, 70.4, 68.7, 67.7, 66.8, 66.7, 66.6, 66.1, 65.9, 59.0, 55.0, 46.7, 34.6, 25.6, 22.6, 18.2, 17.9, 14.2, 6.8, 6.6, 5.7, 4.4, 4.0, –4.4, –4.7; HRMS (FAB) calcd for $C_{54}H_{77}N_3O_{14}Si_2Cs$ (M + Cs) 1180.3998, found 1180.3963.

26: R_f = 0.52 (40% ethyl ether in petroleum ether); $[\alpha]^{23}_D$ = +13.4° (c 0.56, $CHCl_3$); IR (film) ν_{max} 2948, 2876, 1696, 1526, 1451, 1416, 1356, 1237, 1142, 1095, 1012, 908, 833 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, 340 K) δ 8.00 (d, J = 7.6 Hz, 1 H aromatic), 7.83 (d, J = 7.6 Hz, 2 H, aromatic), 7.77 (d, J = 8.2 Hz, 1 H, aromatic), 7.70 (d, J = 7.9 Hz, 1 H, aromatic), 7.60–7.50 (m, 3 H, aromatic), 7.38 (t, J = 7.5 Hz, 2 H, aromatic), 7.29 (m, 2 H, aromatic), 5.74 (d, J = 2.5 Hz, 1 H, B-1), 5.37 (d, J = 2.0 Hz, 1 H, D-1), 5.13–5.09 (m, 3 H, B-2, E-1, CH_2Ph), 4.96 (d, J = 14.5 Hz, 1 H, CH_2Ph), 4.71 (q, J = 6.6 Hz, 1 H, A-5), 4.53 (d, J = 5.8 Hz, 1 H, A-1), 4.43 (m, 1 H, D-2), 4.37 (m, 1 H, CH_2-FMOC), 4.34 (dd, J = 10.6, 6.0 Hz, 1 H, CH_2-FMOC), 4.24 (d, J = 1.7 Hz, 1 H, A-3), 4.23 (t, J = 6.0 Hz, 1 H, benzylic-FMOC), 4.13 (m, 1 H, B-5), 4.06 (m, 1 H, D-5), 4.01 (d, J = 3.2 Hz, 1 H, B-4), 3.86 (dd, J = 5.6 1.7 Hz, 1 H, A-2), 3.81 (s, 3 H, CH_3O), 3.81–3.65 (b m, 3 H, E-3, E-5, E-5′), 3.77 (s, 3 H, CH_3O), 3.69 (dd, J = 9.0, 9.0 Hz, 1 H, D-4), 3.53 (dd, J = 9.0, 2.6 Hz, 1 H, D-3), 3.39 (s, 3 H, CH_3), 3.25 (m, 1 H, E-4), 3.15 (s, 3 H, CH_3O), 3.10 (obs, 1 H, CH_2N), 2.84 (b m, 1 H, CH_2N), 2.31 (s, 3 H, ArCH_3), 2.22 (m, 1 H, E-2$_{eq}$), 1.48 (m, 1 H, E-2$_{ax}$), 1.43 (d, J = 6.7 Hz, 3 H, B-6), 1.42 (d, J = 6.7 Hz, 3 H, A-6), 1.15 (d, J = 6.2 Hz, 3 H, D-6), 0.98–0.90 (series of m, 26 H, 3 × Si(CH$_2$CH_3)$_3$, C(CH_3)$_3$), 0.74–0.59 (series of m, 21 H, 3 × Si(CH_2CH$_3$)$_3$, CH_3CH$_2$N), 0.24 (s, 3 H, CH_3Si), 0.21 (s, 3 H, CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 193.5, 159.0, 158.9, 152.4, 150.7, 149.4, 146.4, 144.1, 144.0, 143.2, 141.3, 134.8, 133.8, 133.6, 129.9, 128.5, 128.4, 128.0, 127.6, 127.0 (2), 125.4, 125.1, 124.8, 124.7, 124.4, 119.9 (2), 104.7, 103.0, 102.9, 102.6, 102.3, 98.5, 98.4, 95.4, 95.2, 93.8, 81.4, 79.2, 79.0, 74.5, 72.4, 72.3, 71.9, 71.7, 71.6, 71.4, 69.8, 69.7, 68.6, 67.7, 67.5, 66.8, 61.6, 60.8, 59.8, 57.3, 56.1, 55.7, 47.5, 47.2 (2), 35.2, 35.0, 25.6, 25.4, 20.9, 18.4, 18.0, 14.6, 14.4, 7.0, 6.8, 6.7, 5.2, 4.9, 4.6, –4.4, –4.6; HRMS (FAB) calcd for $C_{83}H_{126}IN_3O_{21}SSi_4Cs$ (M + Cs) 1904.5781, found 1904.5605.

28: R_f = 0.22 (40% ethyl ether in petroleum ether); $[\alpha]^{23}_D$ –32.1° (c 0.81, $CHCl_3$); IR (film) ν_{max} 3458, 2951, 2879, 1684, 1528, 1455, 1417, 1240, 1143, 1085, 1012, 736 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, 340 K) δ 8.01 (m, 1 H, aromatic), 7.83 (d, J = 7.5 Hz, 2 H, aromatic), 7.78 (d, J = 7.7 Hz, 1 H, aromatic), 7.69 (m, 1 H, aromatic), 7.61–7.48 (m, 3 H, aromatic), 7.38 (t, J = 7.4 Hz, 2 H, aromatic), 7.29 (m, 2 H, aromatic), 5.41–5.36 (m, 2 H, B-1, D-1), 5.12 (d, J = 14.5 Hz, 1 H, CH_2Ph), 5.12 (b s, 1 H, E-1), 4.95 (d, J = 14.5 Hz, 1 H, CH_2Ph), 4.80 (q, J = 6.7 Hz, 1 H, A-5), 4.61 (d, J = 5.9 Hz, 1 H, A-1), 4.44 (m, 1 H, D-2), 4.40–4.30 (m, 2 H, CH_2-FMOC), 4.28 (b s, 1 H, A-3), 4.22 (t, J = 6.0 Hz, 1 H, benzylic-FMOC), 4.18 (b s, 1 H, B-3), 4.07 (m, 1 H, B-5), 3.99 (m, 1 H, D-5), 3.86 (b d, J = 5.8 Hz, 1 H, A-2), 3.85–3.60 (b m, 3 H, E-3, E-5, E-5′), 3.82 (s, 3 H, CH_3O), 3.77 (s, 3 H, CH_3O), 3.70 (dd, J = 9.0, 9.0 Hz, 1 H, D-4), 3.63 (dd, J = 10.5, 2.6 Hz, 1 H, B-4), 3.54 (dd, J = 9.0, 2.3 Hz, 1 H, D-3), 3.39 (s, 3 H, CH_3O), 3.24 (m, 1 H, E-4), 3.15 (s, 3 H, CH_3O), 2.83 (b m, 2 H, CH_2N), 2.31 (s, 3 H, ArCH_3), 2.23 (m, 1 H, E-2$_{eq}$), 2.00 (m, 1 H, B-2$_{eq}$), 1.87 (m, 1 H, B-2$_{ax}$), 1.46 (m, 1 H, E-2$_{ax}$), 1.43 (d, J = 6.7 Hz, 3 H, A-6), 1.26 (d, J = 6.2 Hz, 3 H, B-6), 1.16 (d, J = 6.2 Hz, 3 H, D-6), 0.98–0.90 (m, 27 H, 3 × Si(CH$_2$CH_3)$_3$), 0.78–0.58 (m, 21 H, 3 × Si(CH_2CH$_3$)$_3$, CH_3-CH$_2$N); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.0, 160.2, 160.9, 155.7,

152.4, 150.5, 146.4, 144.1, 144.0, 143.1, 141.3, 134.7, 133.8, 133.6, 133.3, 130.1, 128.4, 128.2, 128.0, 127.6, 127.5, 126.9, 125.3, 125.1, 124.8, 124.7, 124.4, 119.9, 119.8, 104.7, 102.6, 102.3, 99.5, 95.7, 95.6, 93.9, 81.3, 79.0, 78.7, 72.4, 72.2, 71.9, 71.7, 71.3, 71.2, 69.4, 69.3, 68.6, 68.2, 67.5 (2), 67.4, 66.8, 61.6, 60.8, 60.4, 59.8, 57.3, 56.1, 55.7, 51.7, 47.2, 36.9, 35.1, 35.0, 29.7, 25.4, 19.3, 18.6, 18.0, 14.6, 14.4, 6.9, 6.7, 5.1, 4.8, 4.6; HRMS (FAB) calcd for $C_{77}H_{114}IN_3O_{21}SSi_4Cs$ (M + Cs) 1792.5073, found 1792.5168.

Silyl Ether 4. A solution of alcohol **28** (533 mg, 0.32 mmol) in CH_2Cl_2 (10 mL) was treated at 0 °C with diisopropylethylamine (0.336 mL, 1.9 mmol) and triethylsilyl trifluoromethanesulfonate (0.218 mL, 0.96 mmol) and stirred at that temperature for 30 min. The reaction mixture was diluted with EtOAc (100 mL) and washed with water (50 mL), saturated aqueous $NaHCO_3$ (50 mL), and brine (50 mL). The organic layer was dried ($MgSO_4$), concentrated, and purified by flash column chromatography (silica, 30% ethyl ether in petroleum ether) to yield pure silyl ether **4** (551 mg, 97%) as a white foam: R_f = 0.58 (50% ethyl ether in petroleum ether); $[\alpha]^{25}_D$ −17.7° (*c* 0.31, CH_2Cl_2); IR (film) ν_{max} 2950, 2875, 1700, 1460, 1240, 1180 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6, 340 K) δ 8.04–7.27 (series of m, 12 H, aromatic), 5.39 (dd, *J* = 6.2, 6.2 Hz, 1 H, B-1), 5.37 (d, *J* = 2.1 Hz, 1 H, D-1), 5.12 (d, *J* = 14.1 Hz, 1 H, C*H*$_2$Ph), 5.11 (b s, 1 H, E-1), 4.96 (d, *J* = 14.1 Hz, 1 H, C*H*$_2$Ph), 4.80 (q, *J* = 6.6 Hz, 1 H, A-5), 4.60 (d, *J* = 6.3 Hz, 1 H, A-1), 4.42 (dd, *J* = 2.1, 2.1 Hz, 1 H, D-2), 4.40 (m, 1 H, B-3), 4.39–4.31 (m, 2 H, C*H*$_2$-FMOC), 4.27 (d, *J* = 1.4 Hz, 1 H, A-3), 4.22 (t, *J* = 6.0 Hz, 1 H, benzylic-FMOC), 4.06 (dq, *J* = 9.2, 6.0 Hz, 1 H, D-5), 3.99 (dq, *J* = 10.0, 6.0 Hz, 1 H, B-5), 3.86 (dd, *J* = 6.3, 1.4 Hz, 1 H, A-2), 3.81 (s, 3 H, C*H*$_3$O), 3.77 (s, 3 H, C*H*$_3$O), 3.76–3.63 (m, 3 H, E-3, E-5, E-5′), 3.69 (dd, *J* = 9.2, 8.9 Hz, 1 H, D-4), 3.68 (dd, *J* = 10.0, 2.9 Hz, 1 H, B-4), 3.54 (dd, *J* = 8.9, 2.1 Hz, 1 H, D-3), 3.39 (s, 3 H, C*H*$_3$O), 3.24 (m, 1 H, E-4), 3.17 (s, 3 H, C*H*$_3$O), 2.83 (b m, 2 H, C*H*$_2$N), 2.31 (s, 3 H, ArC*H*$_3$), 2.23 (m, 1 H, E-2$_{eq}$), 1.97 (m, 2 H, B-2$_{eq,ax}$), 1.46 (m, 1 H, E-2$_{ax}$), 1.43 (d, *J* = 6.6 Hz, 3 H, A-6), 1.28 (d, *J* = 6.0 Hz, 3 H, B-6), 1.17 (d, *J* = 6.0 Hz, 3 H, D-6), 0.98–0.91 (m, 36 H, 4 × Si(CH$_2$C*H*$_3$)$_3$), 0.75–0.59 (m, 27 H, 4 × Si(C*H*$_2$CH$_3$)$_3$, C*H*$_3$CH$_2$N); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.9, 160.0, 159.9, 155.7, 152.3, 150.5, 146.4, 144.1, 144.0, 143.2, 141.3, 134.7, 133.8, 133.6, 133.3, 130.4, 128.4, 128.3, 128.0, 127.6, 127.5, 126.9, 125.4, 125.1, 124.8, 124.7, 124.4, 119.9 (2), 104.7, 102.5, 102.2, 100.0, 95.7, 95.5, 93.8, 81.4, 79.1, 78.8, 72.4, 72.3, 71.9, 71.7, 71.4, 71.3, 70.6, 70.1, 69.5 (2), 68.6, 67.5 (2), 67.4, 66.8, 61.5, 60.8, 60.4, 59.8, 57.3, 56.1, 55.7, 51.4, 47.2, 38.3, 35.1, 35.0, 29.7, 25.3, 18.8, 18.6, 18.0, 14.6, 14.4, 7.0, 6.8, 6.7 (2), 6.6, 5.8, 5.2, 4.9, 4.8, 4.6; HRMS (FAB) calcd for $C_{83}H_{128}IN_3O_{21}SSi_4Cs$ (M + Cs) 1906.5937, found 1906.5981.

Lactol 5. A solution of *o*-nitrobenzyl glycoside **4** (480 mg, 0.27 mmol) in THF–H_2O (176 mL, 10:1) was cooled to 0 °C and irradiated for 15 min with a 450-W mercury Hanovia lamp equipped with a Pyrex filter. The reaction mixture was concentrated *in vacuo*, and the residue was dissolved in EtOAc (150 mL) and washed with brine (75 mL). The aqueous phase was extracted with EtOAc (75 mL), and the combined organic phases were dried ($MgSO_4$) and concentrated. The residue was purified by flash column chromatography (silica, 40–60% ethyl ether in petroleum ether) to yield a 1:1 (α/β) anomeric mixture of lactol **5** (0.364 g, 82%) as a white foam along with recovered **4** (0.077 g, 16%). **5**: R_f = 0.38 (silica, 60% ethyl ether in petroleum ether); ^1H NMR (500 MHz, DMSO-d_6, 340 K) δ 7.85 (d, *J* = 7.5 Hz, 2 H, aromatic), 7.64 (d, *J* = 7.3 Hz, 2 H, aromatic), 7.39 (t, *J* = 7.3 Hz, 2 H, aromatic), 7.31 (t, *J* = 7.4 Hz, 2 H, aromatic), 5.40–5.37 (m, 1 H, B-1(α/β)), 5.37 (d, *J* = 1.7 Hz, 1 H, D-1), 5.25 (m, 0.5 H, O*H*(β)), 5.08 (b s, 1 H, E-1), 4.93 (q, *J* = 6.9 Hz, 0.5 H, A-5(β)), 4.68 (q, *J* = 6.6 Hz, 0.5 H, A-5(α)), 4.44–4.40 (m, 4 H, D-2, B-3, C*H*$_2$-FMOC), 4.34 (d, *J* = 3.4 Hz, 0.5 H, A-1(β)), 4.28 (t, *J* = 6.0 Hz, 1 H, benzylic-FMOC), 4.17 (s, 0.5 H, A-1(α)), 4.06 (dq, *J* = 9.0, 6.2 Hz, 1 H, D-5), 4.02–3.97 (m, 1 H, B-5(α/β)), 3.92 (m, 1 H), 3.82–3.65 (m, 4 H), 3.81 (2 × s, 2 × 1.5 H, C*H*$_3$O-(α/β)), 3.77 (s, 3 H, C*H*$_3$O), 3.69 (dd, *J* = 9.1, 9.1 Hz, 1 H, D-4), 3.54 (dd, *J* = 9.0, 2.5 Hz, 1 H, D-3), 3.39 (s, 3 H, C*H*$_3$O), 3.28 (m, 1 H, E-4), 3.17 (b s, 3 H, C*H*$_3$O), 3.17–2.95 (obs, 2 H, C*H*$_2$N), 2.31 (s, 3 H, ArC*H*$_3$), 2.27–2.21 (m, 1 H, E-2$_{eq}$(α/β)), 1.98–1.94 (m, 2 H, B-2$_{eq,ax}$), 1.44 (m, 1 H, E-2$_{ax}$), 1.41 (d, *J* = 6.6 Hz, 1.5 H, A-6(α), 1.37 (d, *J* = 6.9 Hz, 1.5 H, A-6(β)), 1.29 (d, *J* = 6.1 Hz, 3 H, B-6), 1.16 (d, *J* = 6.2 Hz, 3 H, D-6), 0.98–0.91 (m, 36 H, 4 × Si(CH$_2$C*H*$_3$)$_3$), 0.85 (obs, 3 H, C*H*$_3$-CH$_2$N), 0.66–0.58 (m, 24 H, 4 × Si(C*H*$_2$CH$_3$)$_3$).

Benzoate 3. A solution of diol **6**[2] (1.4 g, 2.9 mmol) in CH_2Cl_2 (65 mL) was treated at −15 °C with pyridine (1.05 mL, 13.0 mmol) followed by dropwise addition of benzoyl chloride (0.4 mL, 3.4 mmol). The mixture was stirred for 1 h at −15 °C and treated with an additional 1.2 equiv of benzoyl chloride (0.4 mL, 3.4 mmol). The reaction was closely monitored by TLC, and once the starting material was consumed, the reaction was quenched with MeOH (0.5 mL) and stirring was continued for 20 min at 25 °C. The mixture was then poured into brine (50 mL) and diluted with CH_2Cl_2 (100 mL), and the layers were separated. The aqueous phase was back-extracted with CH_2Cl_2 (100 mL), and the combined organic layers were dried (Na_2SO_4), concentrated, and purified by flash column chromatography (silica, 50–70% ethyl ether in petroleum ether) to yield allylic benzoate **3** (1.44 g, 84%) as a white foam along with the corresponding dibenzoate (~13%). **3**: R_f = 0.39 (silica, 80% ethyl ether in petroleum ether); $[\alpha]^{25}_D$ −270° (*c* 0.36, CH_2Cl_2); IR (C_6H_6) ν_{max} 3090, 3070, 3035, 2955, 2876, 1815, 1722, 1480, 1271, 1225, 1166, 1110, 1035, 740 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 8.07 (m, 2 H, aromatic), 7.05 (m, 1 H, aromatic), 6.98 (m, 2 H, aromatic), 6.74 (dd, *J* = 7.6, 5.0 Hz, 1 H, C=C*H*CH$_2$), 6.18 (b s, 1 H, N*H*), 6.04 (d, *J* = 5.0 Hz, 1 H, C*H*C≡C), 5.71 (m, 1 H, CH$_2$C*H*=C), 5.43–5.35 (m, 3 H, CH$_2$C*H*=C, 2 × CH=C*H*), 3.99 (b s, 1 H, O*H*), 3.28–3.15 (m, 4 H, OCH$_2$CH$_2$O), 3.23 (s, 3 H, C*H*$_3$O), 2.57 (AB q, *J* = 13.8 Hz, Δν = 128 Hz, 2 H, C*H*$_2$), 1.09 (t, *J* = 7.9 Hz, 9 H, Si(CH$_2$C*H*$_3$)$_3$), 0.92–0.80 (m, 6 H, Si(C*H*$_2$-CH$_3$)$_3$); ^{13}C NMR (125 MHz, C_6D_6) δ 166.3, 155.0, 139.2, 132.3, 132.0, 131.3, 130.0, 124.3, 124.0, 123.3, 105.3, 101.8, 86.3, 86.0, 65.1 (2), 65.0, 64.2, 52.7, 7.4, 6.7; HRMS (FAB) calcd for $C_{32}H_{37}NO_8SiCs$ (M + Cs) 724.1343, found 724.1351.

Preparation and Coupling of Trichloroacetimidate 2 with the Aglycon Precursor 3. A solution of lactol **5** (0.810 g, 0.494 mmol) in CH_2Cl_2 (8 mL) was treated with trichloroacetonitrile (1.49 mL, 14.9 mmol) and NaH (5 mg, 60% dispersion in mineral oil) at 0 °C. The mixture was allowed to warm to ambient temperature over a period of 2 h with stirring. The solution was diluted with Et_2O (25 mL) and filtered through Celite under argon. The filtrate was concentrated *in vacuo* to yield an anomeric mixture of the crude imidate **2** as a yellow foam (*ca.* 2:1, α/β). This material was immediately combined with aglycon alcohol **3** (457 mg, 0.774 mmol) and azeotroped with toluene (3 × 15 mL). This mixture was dissolved in CH_2Cl_2 (20 mL) and transferred, *via* canula, to a flask containing powdered, activated 4-Å molecular sieves (2 g). The resulting mixture was stirred at 25 °C for 20 min and then cooled to −78 °C. $BF_3{\cdot}OEt_2$ (0.182 g, 1.48 mmol) was then slowly added to the mixture. The reaction mixture was then allowed to warm to −40 °C over a period of 1.75 h, the reaction was quenched with solid $NaHCO_3$ (0.5 g), and the mixture was stirred for an additional 10 minutes at −40 °C. This mixture was then diluted with Et_2O (50 mL) and filtered through Celite. The filtrate was washed with saturated aqueous $NaHCO_3$ (50 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL), and the combined organic layers were washed with brine (50 mL), dried ($MgSO_4$), and concentrated. Purification by flash column chromatography (silica, 50–80% ethyl ether in petroleum ether) provided the coupled compound **7** (666 mg, 40%) and the monodesilylated coupled compound **8** (566 mg, 36%) as white foams. **7**: R_f = 0.09 (silica, 50% ethyl ether in petroleum ether); $[\alpha]^{26}_D$ −83.3° (*c* 1.1, $CHCl_3$); IR (KBr) ν_{max} 2955, 2912, 2878, 1720, 1702, 1457, 1416, 1385, 1382, 1322, 1274, 1239, 1143, 1087, 1014, 964, 938, 907, 882, 826, 803, 740, 677 cm^{-1}; ^1H NMR (500 MHz, C_6D_6, 340 K) δ 8.12–8.10 (m, 2 H, aromatic), 7.65–7.57 (m, 4 H, aromatic), 7.23–7.15 (m, 4 H, aromatic), 7.10–7.02 (m, 3 H, aromatic), 6.74 (dd, *J* = 8.1, 3.7 Hz, 1 H, C=C*H*CH$_2$), 6.34 (d, *J* = 1.2 Hz, 1 H, C*H*C≡C), 5.81 (dd, *J* = 9.9, 2.0 Hz, 1 H, B-1), 5.76 (d, *J* = 1.9 Hz, 1 H, D-1), 6.75 (dd, *J* = 13.9, 3.7 Hz, 1 H, C*H*$_2$-OBz), 5.59 (dd, *J* = 13.9, 8.1 Hz, 1 H, CH$_2$-OBz), 5.47 (d, *J* = 9.4 Hz, 1 H, C*H*=CH), 5.44 (dd, *J* = 9.4, 1.2 Hz, 1 H, C*H*=CH), 5.39 (b s, 1 H, E-1), 5.17 (q, *J* = 6.8 Hz, 1 H, A-5), 5.11 (b m, 1 H), 4.68 (b m, 1 H), 4.66 (b s, 1 H, A-1), 4.59 (dd, *J* = 2.7, 1.9 Hz, 1 H, D-2), 4.45–4.38 (m, 2 H, D-5, C*H*O), 4.33–4.24 (m, 4 H, B-3, B-5, C*H*Os), 4.14 (m, 1 H, C*H*O), 4.05 (dd, *J* = 9.1, 9.0 Hz, 1 H, D-4), 4.02 (dd, *J* = 10.4, 2.5 Hz, 1 H, B-4), 3.86 (dd, *J* = 9.0, 2.7 Hz, 1 H, D-3), 3.80 (m, 1 H), 3.72 (s, 3 H, C*H*$_3$O), 3.55 (s, 3 H, C*H*$_3$O), 3.54 (s, 4 H, C*H*Os), 3.39 (m, 5 H, C*H*Os), 3.36 (s, 3 H, C*H*$_3$O), 3.14 (s, 3 H, C*H*$_3$O), 2.61 (AB q, *J* = 13.4 Hz, Δν = 173 Hz, 2 H, C*H*$_2$), 2.46 (s, 3 H, ArC*H*$_3$), 2.37 (m, 1 H, E-2$_{eq}$), 2.02 (m, 1 H, B-2$_{eq}$), 1.88 (obs, 1 H, B-2$_{ax}$), 1.86 (d, *J* = 6.8 Hz, 3 H, A-6), 1.57 (d, *J* = 6.3 Hz, 3 H, B-6), 1.51 (m, 1 H, E-2$_{ax}$), 1.41 (d, *J* = 6.2 Hz, 3 H, D-6), 1.13–0.54 (series of m, 78 H, 5 × Si(C*H*$_2$CH$_3$)$_3$, C*H*$_3$CH$_2$N); ^{13}C NMR (125 MHz, C_6D_6) δ 192.1, 166.2, 160.5, 160.0, 156.2, 152.6, 151.3. 144.9, 144.5, 144.2, 143.7, 141.8, 141.7, 141.5, 137.7, 133.8, 132.3 (2), 131.5, 130.0–127.2 (aromatic/solvent), 125.8, 125.7, 125.6, 124.9, 123.8, 123.6, 120.1 (2), 105.8, 104.9, 104.5, 103.9, 103.7, 102.7, 100.6, 100.4, 97.3, 96.9, 94.6, 86.9, 85.4, 82.0, 73.0, 72.9, 72.5, 72.3, 71.6, 71.0, 70.9, 70.8, 69.6, 69.0, 67.6, 67.5, 65.9, 65.2, 64.8, 64.6, 61.5, 61.4, 60.5 (2), 57.0, 55.1, 52.5 (2), 52.1, 47.7, 38.7, 36.3, 35.8, 30.3, 25.6, 19.8, 19.6, 19.2,

18.5, 15.1, 7.4, 7.3, 7.1 (3), 6.7, 5.7, 5.3, 5.2 (2); HRMS (FAB) calcd for $C_{108}H_{158}IN_3O_{26}SSi_5Cs$ (M + Cs) 2345.783, found 2345.790. **8**: R_f = 0.09 (silica, 70% ethyl ether in petroleum ether); ^{1}H NMR (500 MHz, DMSO-d_6, 340 K) δ 7.94–7.25 (series of m, 14 H, N*H*, aromatic), 6.16 (dd, J = 8.2, 4.2 Hz, 1 H, C=C*H*CH$_2$), 6.07 (d, J = 9.6 Hz, 1 H, C*H*=CH), 6.00 (dd, J = 9.6, 1.3 Hz, 1 H, C*H*=CH), 5.76 (b s, 1 H, C*H*C≡C), 5.49 (b s, 1 H, C*H*O), 5.39–5.35 (m, 2 H, B-1, D-1), 5.32 (dd, J = 14.7, 4.2 Hz, 1 H, C*H*$_2$-OBz), 5.15 (b s, 1 H, E-1), 4.99 (dd, J = 14.7, 8.2 Hz, 1 H, C*H*$_2$-OBz), 4.74 (q, J = 6.8 Hz, 1 H, A-5), 4.69 (d, J = 5.3 Hz, 1 H, A-1), 4.43–4.33 (m, 4 H, D-2, C*H*Os), 4.24 (m, 2 H, C*H*O), 4.16 (b s, 1 H, C*H*O), 4.09–3.95 (m, 4 H, C*H*Os), 3.90–3.72 (m, 6 H, C*H*Os), 3.81 (s, 3 H, C*H*$_3$O), 3.77 (s, 3 H, C*H*$_3$O), 3.71–3.67 (m, 2 H, C*H*Os), 3.59 (s, 3 H, C*H*$_3$O), 3.54 (d, J = 9.0, 2.8 Hz, 1 H, D-3), 3.39 (s, 3 H, C*H*$_3$O), 3.32 (m, 1 H), 3.15 (s, 3 H, C*H*$_3$O), 3.15–3.00 (obs, 2 H, C*H*$_2$N), 2.30 (s, 3 H, ArC*H*$_3$), 2.25 (AB q, J = 13.7 Hz, $\Delta\nu$ = 225 Hz, 2 H, C*H*$_2$), 2.22 (m, 1 H, E-2$_{eq}$), 1.95 (m, 2 H, B-2$_{eq,ax}$), 1.49 (d, J = 6.8 Hz, 3 H, A-6), 1.27 (d, J = 6.4 Hz, 3 H, B-6), 1.16 (d, J = 6.4 Hz, 3 H, D-6), 0.98–0.90 (m, 36 H, 4 × Si(CH$_2$C*H*$_3$)$_3$), 0.85 (b m, 3 H, C*H*$_3$CH$_2$N), 0.70–0.58 (m, 24 H, 4 × Si(C*H*$_2$CH$_3$)$_3$); HRMS (FAB) calcd for $C_{102}H_{144}IN_3O_{26}SSi_4Cs$ (M + Cs) 2231.696, found 2231.698.

Silylation of Compound 8. A solution of monodesilylated compound **8** (104 mg, 0.050 mmol) in CH_2Cl_2 (5 mL) was treated at 0 °C with diisopropylethylamine (0.036 mL, 0.20 mmol) and triethylsilyl trifluoromethanesulfonate (0.023 mL, 0.10 mmol) and stirred for 20 min at that temperature. The reaction mixture was diluted with EtOAc (25 mL) and washed with water (25 mL), saturated aqueous $NaHCO_3$ (25 mL), and brine (25 mL). The organic layer was dried ($MgSO_4$), concentrated, and purified by flash column chromatography (silica, 50–60% ethyl ether in petroleum ether) to yield pure pentasilylated compound **7** (109 mg, 99%).

Acetylation of Compound 8. A solution of monodesilylated compound **8** (13.5 mg, 6.4 μmol) in CH_2Cl_2 (3 mL) was treated with diisopropylethylamine (20 μL, 0.115 mmol), Ac_2O (6 μL, 0.064 mmol), and DMAP (catalytic) at 0 °C, and the resulting mixture was stirred at that temperature for 1.5 h. The reaction mixture was diluted with CH_2Cl_2 (20 mL) and washed with saturated aqueous $NaHCO_3$ (20 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 20 mL), and the combined organic layers were washed with brine (20 mL), dried ($MgSO_4$), and concentrated. The residue was purified by flash column chromatography (silica, 70% ethyl ether in petroleum ether) to give acetate **9** (13.7 mg, 98%): R_f = 0.28 (silica, 70% ethyl ether in petroleum ether); ^{1}H NMR (500 MHz, DMSO-d_6, 340 K) δ 7.93–7.26 (series of m, 14 H, N*H*, aromatic), 6.17 (dd, J = 7.9, 4.1 Hz, 1 H, C=C*H*CH$_2$), 6.08 (d, J = 9.5 Hz, 1 H, C*H*=CH), 6.00 (dd, J = 9.5, 1.4 Hz, 1 H, C*H*=CH), 5.80 (b s, 1 H, C*H*C≡C), 5.40–5.35 (m, 2 H, B-1, D-1), 5.27 (dd, J = 14.5, 4.1 Hz, 1 H, C*H*$_2$-OBz), 5.25 (s, 1 H, A-3), 5.18 (b s, 1 H, E-1), 4.92 (dd, J = 14.5, 7.9 Hz, 1 H, C*H*$_2$-OBz), 4.80 (q, J = 6.7 Hz, 1 H, A-5), 4.75 (d, J = 5.0 Hz, 1 H, A-1), 4.43–4.32 (m, 4 H, D-2, C*H*Os), 4.24 (m, 1 H, C*H*O), 4.14 (b s, 1 H, C*H*O), 4.09–3.99 (m, 3 H, C*H*Os), 3.90–3.72 (m, 6 H, C*H*Os), 3.81 (s, 3 H, C*H*$_3$O), 3.77 (s, 3 H, C*H*$_3$O), 3.71–3.67 (m, 2 H, C*H*Os), 3.57 (s, 3 H, C*H*$_3$O), 3.54 (d, J = 9.0, 2.4 Hz, 1 H, D-3), 3.39 (s, 3 H, C*H*$_3$O), 3.32 (m, 1 H), 3.15 (s, 3 H, C*H*$_3$O), 3.15–3.00 (obs, 2 H, C*H*$_2$N), 2.30 (s, 3 H, ArC*H*$_3$), 2.26 (obs AB q, J = 13.7 Hz, $\Delta\nu$ = 227 Hz, 2 H, C*H*$_2$), 2.22 (m, 1 H, E-2$_{eq}$), 2.05 (s, 3 H, C*H*$_3$CO), 1.96 (m, 2 H, B-2$_{eq,ax}$), 1.47 (m, 1 H, E-2$_{ax}$), 1.45 (d, J = 6.7 Hz, 3 H, A-6), 1.27 (d, J = 6.3 Hz, 3 H, B-6), 1.16 (d, J = 6.2 Hz, 3 H, D-6), 0.98–0.90 (m, 36 H, 4 × Si(CH$_2$C*H*$_3$)$_3$), 0.85 (b m, 3 H, C*H*$_3$CH$_2$N), 0.70–0.58 (m, 24 H, 4 × Si(C*H*$_2$CH$_3$)$_3$); HRMS (FAB) calcd for $C_{104}H_{146}IN_3O_{27}SSi_4Cs$ (M + Cs) 2272.7041, found 2272.7040.

Preparation of Compound 29. A solution of benzoate **7** (14.1 mg, 6.3 μmol) in CH_2Cl_2 (1 mL) at –78 °C was treated with DIBAL (0.019 mL of a 1.0 M solution in CH_2Cl_2, 0.019 mmol) and stirred for 1 h at that temperature. The reaction was quenched at –78 °C with MeOH (0.2 mL, added dropwise), the cooling bath was removed, the reaction mixture was diluted with EtOAc (5 mL), and saturated aqueous Rochelle salt (5 mL) was added. The mixture was vigorously stirred for 30 min until two phases became clear, poured into brine (10 mL), and extracted with EtOAc (3 × 10 mL). The combined organic extracts were dried ($MgSO_4$), concentrated, and purified by flash column chromatography (silica, 70% ethyl ether in petroleum ether) to give alcohol **29** (12.2 mg, 91%) as a white foam: R_f = 0.29 (silica, 70% ethyl ether in petroleum ether): $[\alpha]^{26}_D$ –84.3° (c 1.2, $CHCl_3$); IR (neat) ν_{max} 3338, 2954, 2912, 2878, 1737, 1682, 1456, 1416, 1394, 1324, 1279, 1237, 1143, 1086, 1013, 965, 907, 740 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6, 340 K) δ 7.60–7.57 (m, 4 H, aromatic), 7.23–7.15 (m, 4 H, aromatic), 6.68 (dd, J = 8.7, 6.8 Hz, 1 H, C=C*H*CH$_2$), 6.39 (d, J = 1.2 Hz, 1 H, C*H*C≡C), 5.81 (dd, J = 9.9, 2.0 Hz, 1 H, B-1), 5.76 (d, J = 2.0 Hz, 1 H, D-1), 5.49 (d, J = 9.4 Hz, 1 H, C*H*=CH), 5.42 (dd, J = 9.4, 1.3 Hz, 1 H, C*H*=CH), 5.27 (b d, J = 2.1 Hz, 1 H, E-1), 5.16 (b m, 1 H), 5.11 (q, J = 6.6 Hz, 1 H, A-5), 4.78 (m, 1 H), 4.78 (b m, 1 H), 4.60 (d, J = 2.2 Hz, 1 H, A-1), 4.59 (dd, J = 2.7, 2.0 Hz, 1 H, D-2), 4.55 (m, 1 H), 4.41 (m, 1 H, D-5), 4.37–4.33 (m, 3 H), 4.29–4.22 (m, 2 H, B-3, B-5), 4.13 (m, 1 H), 4.05 (dd, J = 9.2, 9.1 Hz, 1 H, D-4), 4.02 (dd, J = 10.3, 2.5 Hz, 1 H, B-4), 3.86 (dd, J = 9.1, 2.7 Hz, 1 H, D-3), 3.72 (s, 3 H, C*H*$_3$O), 3.72 (obs, 1 H), 3.55 (s, 3 H, C*H*$_3$O), 3.53 (s, 3 H, C*H*Os), 3.36 (s, 3 H, C*H*$_3$O), 3.36 (obs, 4 H, C*H*Os), 3.13 (s, 3 H, C*H*$_3$O), 2.57 (AB q, J = 13.4 Hz, $\Delta\nu$ = 188 Hz, 2 H, C*H*$_2$), 2.56 (m, 1 H), 2.45 (s, 3 H, ArC*H*$_3$), 2.32 (m, 1 H, E-2$_{eq}$), 2.01 (m, 1 H, B-2$_{eq}$), 1.86 (m, 1 H, B-2$_{ax}$), 1.79 (d, J = 6.6 Hz, 3 H, A-6), 1.57 (d, J = 6.3 Hz, 3 H, B-6), 1.51 (m, 1 H, E-2$_{ax}$), 1.41 (d, J = 6.2 Hz, 3 H, D-6), 1.25–0.53 (series of m, 78 H, 5 × Si(C*H*$_2$C*H*$_3$)$_3$, C*H*$_3$-CH$_2$N); ^{13}C NMR (125 MHz, C_6D_6) δ 192.2, 159.9, 159.5, 156.1, 153.0, 152.7, 151.3, 145.0, 144.5, 143.7, 141.8, 137.3, 133.8, 131.5, 130.0–127.4 (aromatic/solvent), 127.4, 127.3, 125.9, 125.6, 125.5, 124.5, 124.1, 123.5, 123.3, 120.1 (2), 106.0, 104.9, 104.0, 103.3, 102.5, 102.4, 100.7, 100.6, 96.6, 96.1, 94.6, 87.2, 84.9, 82.0, 73.1, 72.9, 72.5, 72.1, 71.7, 71.1, 70.8, 69.7, 69.0, 67.6, 67.2, 65.2, 65.1, 64.9, 64.7, 61.5, 61.4, 60.8, 60.6, 60.5, 57.1, 53.0, 52.8, 52.5, 52.0, 47.8, 39.1, 38.7, 36.2, 35.8, 30.7, 30.4, 30.2, 25.7, 19.8, 19.3, 19.3, 18.5, 15.2, 7.5, 7.4, 7.1, 6.7, 5.7, 5.3, 5.2, 5.1; HRMS (FAB) calcd for $C_{101}H_{154}IN_3O_{25}SSi_5Cs$ (M + Cs) 2241.756, found 2241.763.

Preparation of Thioaectate 30. A solution of triphenylphosphine (0.27 g, 1.0 mmol) in THF (3.5 mL) at 0 °C was treated with diethyl azodicarboxylate (0.130 mL, 0.83 mmol), and the resulting mixture was stirred at that temperature for 30 min. AcSH (0.065 mL, 0.91 mmol) was added dropwise at 0 °C followed by alcohol **29** (142 mg, 0.067 mmol) in THF (2.5 mL + 1.0 mL washing), and the solution was stirred at the same temperature for 15 min. The reaction mixture was poured into saturated aqueous $NaHCO_3$ (25 mL) and extracted with EtOAc (25 mL). The organic layer was washed with saturated aqueous $NaHCO_3$ (25 mL) and brine (25 mL), dried ($MgSO_4$), concentrated, and purified by flash column chromatography (silica, 30–55% ethyl ether in petroleum ether) to yield thioacetate **30** (140 mg, 96%) as a white foam: R_f = 0.34 (silica, 60% ethyl ether in petroleum ether): $[\alpha]^{26}_D$ –107.2° (c 1.7, $CHCl_3$); IR (KBr) ν_{max} 3440, 2955, 2878, 1739, 1688, 1633, 1457, 1418, 1384, 1323, 1239, 1087, 1015, 908, 881, 802, 740, 670, 572, 527, 464 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6, 340 K) δ 7.64–7.58 (m, 4 H, aromatic), 7.24–7.16 (m, 4 H, aromatic), 6.53 (dd, J = 7.8, 6.1 Hz, 1 H, C=C*H*CH$_2$), 6.29 (d, J = 0.9 Hz, 1 H, C*H*C≡C), 5.81 (dd, J = 9.9, 2.0 Hz, 1 H, B-1), 5.76 (d, J = 2.0 Hz, 1 H, D-1), 5.46 (d, J = 9.4 Hz, C*H*=CH), 5.43 (dd, J = 9.4, 1.1 Hz, 1 H, C*H*=CH), 5.30 (b s, 1 H, E-1), 5.13 (q, J = 6.7 Hz, 1 H, A-5), 5.05 (b m, 1 H), 4.61 (d, J = 2.8 Hz, 1 H, A-1), 4.59 (dd, J = 2.7, 2.0 Hz, 1 H, D-2), 4.49 (b m, 1 H), 4.43–4.30 (m, 4 H, D-5, C*H*$_2$S, C*H*O), 4.29–4.24 (m, 2 H, B-3, B-5), 4.15 (m, 1 H), 4.05 (dd, J = 9.1, 9.0 Hz, 1 H, D-4), 4.03 (dd, J = 10.5, 2.5 Hz, 1 H, B-4), 3.86 (dd, J = 9.1, 2.7 Hz, 1 H, D-3), 3.74 (obs, 1 H), 3.72 (s, 3 H, C*H*$_3$O), 3.55 (s, 3 H, C*H*$_3$O), 3.52 (s, 3 H, C*H*Os), 3.39 (m, 4 H, C*H*Os), 3.36 (s, 3 H, C*H*$_3$O), 3.14 (s, 3 H, C*H*$_3$O), 2.59 (AB q, J = 13.4 Hz, $\Delta\nu$ = 192 Hz, 2 H, C*H*$_2$), 2.46 (s, 3 H, ArC*H*$_3$), 2.37 (m, 1 H, E-2$_{eq}$), 2.02 (m, 1 H, B-2$_{eq}$), 1.96 (s, 3 H, C*H*$_3$CO), 1.87 (obs, 1 H, B-2$_{ax}$), 1.86 (d, J = 6.7 Hz, 3 H, A-6), 1.57 (d, J = 6.3 Hz, 3 H, B-6), 1.53 (m, 1 H, E-2$_{ax}$), 1.41 (d, J = 6.2 Hz, 3 H, D-6), 1.15–0.55 (series of m, 78 H, 5 × Si(C*H*$_2$C*H*$_3$)$_3$, C*H*$_3$CH$_2$N); ^{13}C NMR (125 MHz, C_6D_6) δ 194.6, 192.1, 160.6 (2), 156.3, 156.1, 154.9, 152.7, 151.3, 145.1, 145.0, 144.9, 144.4, 143.7, 141.9, 141.7, 137.7, 137.5, 133.8, 151.5 (2), 130.4–127.8 (aromatic/solvent), 127.5, 127.4, 127.2, 125.9, 125.8, 125.7, 125.6, 125.3, 123.9, 123.6, 120.1 (2), 106.1, 104.9 (2), 103.2, 101.4, 100.7, 100.5, 97.2, 96.5, 94.6, 86.8, 85.4, 82.0, 78.9, 73.1, 72.9, 72.7, 72.2, 71.7, 71.3, 71.0, 70.8, 69.8, 69.6, 69.0, 67.6, 67.4, 65.2, 65.0, 64.9, 64.5, 63.3, 62.2, 61.6, 61.5, 60.6, 60.5, 58.1, 57.0, 55.4, 52.6, 52.4, 52.1, 47.8, 47.7, 38.6, 36.0, 30.7, 30.4, 30.3, 30.2, 29.9, 25.6, 25.1, 19.6, 19.5, 19.2, 18.5, 15.2, 14.2, 14.0, 7.5, 7.3, 7.2, 7.1, 7.0, 6.8, 5.7, 5.3 (2), 5.2; HRMS (FAB) calcd for $C_{103}H_{156}IN_3O_{25}S_2Si_5Cs$ (M + Cs) 2299.744, found 2299.737.

Preparation of Pentol 31. A solution of compound **30** (0.900 g, 0.415 mmol) in THF–CH_2Cl_2 (49 mL, 6:1) was placed in a plastic vial and cooled to 0 °C. To this solution was added HF·pyr (6.3 mL) dropwise, and the resulting mixture was allowed to warm to 25 °C over a period of 3 h. The reaction mixture was then diluted with EtOAc (100 mL) and the reaction carefully quenched with saturated aqueous $NaHCO_3$ (100 mL). The organic layer was washed with additional $NaHCO_3$ (2 × 100 mL) and brine (100 mL), and the combined aqueous phases were extracted with EtOAc (100 mL). The organic layers were then combined, washed with brine (100 mL), dried ($MgSO_4$), and concentrated *in vacuo*. Flash

column chromatography (silica, ethyl acetate → 5% methanol in ethyl acetate) gave compound **31** (0.626 g, 94%) as a white solid: R_f = 0.22 (silica, ethyl acetate); $[\alpha]^{26}_D$ −127.2° (*c* 1.5, $CHCl_3$); IR (KBr) ν_{max} 3442, 2936, 1736, 1680, 1456, 1420, 1320, 1281, 1237, 1196, 1148, 1076, 1019, 962, 913, 826, 800, 742, 671, 599 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, 340 K) δ 7.86–7.84 (m, 2 H, aromatic), 7.78 (b s, 1 H, N*H*), 7.64–7.62 (m, 2 H, aromatic), 7.41–7.37 (m, 2 H, aromatic), 7.33–7.29 (m, 2 H, aromatic), 6.03–5.90 (m, 3 H, 2 × C*H*═CH, C═C*H*CH_2), 5.72 (b s, 1 H, C*H*C≡C), 5.44 (d, *J* = 1.9 Hz, 1 H, D-1), 5.45–5.38 (m, 3 H, B-1, O*H*, C*H*O), 5.12 (b s, 1 H, E-1), 4.84 (d, *J* = 4.4 Hz, 1 H, O*H*), 4.81 (d, *J* = 5.2 Hz, 1 H, O*H*), 4.72 (q, *J* = 6.8 Hz, 1 H, A-5), 4.63 (d, *J* = 5.3 Hz, 1 H, A-1), 4.45–4.35 (b m, 2 H), 4.29–4.26 (m, 2 H, D-2, C*H*O), 4.18–4.14 (m, 2 H, B-3, C*H*O), 4.04–3.90 (m, 5 H, B-5, D-5, C*H*Os), 3.87–3.67 (m, 6 H), 3.82 (s, 3 H, CH_3O), 3.78 (s, 3 H, CH_3O), 3.63 (dd, *J* = 10.5, 2.8 Hz, 1 H, B-4), 3.61–3.55 (m, 3 H, D-3, C*H*Os), 3.47 (m, 1 H, D-4), 3.43 (s, 3 H, CH_3O), 3.28 (b s, 1 H), 3.18–3.05 (obs, 5 H), 2.30 (s, 6 H, ArCH_3, CH_3CO), 2.22 (m, 1 H, E-2$_{eq}$), 2.18 (AB q, *J* = 13.7 Hz, Δν = 216 Hz, 2 H, CH_2), 1.99 (m, 1 H, B-2$_{eq}$), 1.87 (m, 1 H, B-2$_{ax}$), 1.49 (d, *J* = 6.8 Hz, 3 H, A-6), 1.44 (m, 1 H, E-2$_{ax}$), 1.26 (d, *J* = 6.4 Hz, 3 H, B-6), 1.15 (d, *J* = 6.2 Hz, 3 H, D-6), 0.84 (b s, 3 H, C$H_3$$CH_2$N); ^{13}C NMR (125 MHz, DMSO-d_6) δ 195.4, 192.4, 160.4, 155.7, 154.8, 151.8, 149.9, 144.1, 144.0, 143.9, 143.8, 142.9, 140.9, 140.9, 140.7, 138.5, 132.4, 130.0, 128.8, 127.6, 127.5, 127.0, 124.8 (2), 123.3, 122.5, 120.1, 120.0, 104.4, 104.2, 100.4, 100.3, 99.6, 95.6, 94.4, 86.2, 83.2, 80.2, 79.2, 71.3, 71.2, 70.1, 69.9, 69.2, 69.0, 68.4, 67.0, 66.4, 66.3, 64.9, 64.7, 61.5, 60.8, 56.5, 54.6, 52.0, 50.8, 49.5, 46.8, 46.7, 37.6, 35.1, 30.4, 29.2, 24.9, 18.7, 18.5, 17.8, 14.5, 14.3; HRMS (FAB) calcd for $C_{73}H_{86}IN_3O_{25}S_2Cs$ (M + Cs) 1728.3091, found 1728.3143.

Reduction of Oxime 31. A solution of oxime **31** (105 mg, 65.7 μmol) in CH_2Cl_2 (9 mL) at −65 °C was sequentially and dropwise treated with BF_3·OEt_2 (3.75 mL of a 0.26 M solution in CH_2Cl_2, 0.975 mmol) and $NaCNBH_3$ (2.6 mL of a 1.0 M solution in THF, 2.6 mmol). The mixture was warmed to −40 °C and stirred for 3.5 h. The reaction was then quenched with solid $NaHCO_3$ (0.55 g), and the solution was diluted with CH_2Cl_2 (25 mL) and saturated aqueous $NaHCO_3$ (25 mL) and then allowed to warm to 25 °C. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were washed with brine (25 mL), dried ($MgSO_4$), and concentrated. Flash column chromatography (silica, methylene chloride: ethyl acetate:methanol 6:3:0.3) gave compound **32** (56.7 mg, 54%) and recovered oxime **31** (17.9 mg, 11 μmol) as a coeluting mixture (*ca.* 3:1) along with the less polar product **32-epi** (27.3 mg, 26%). Although **32** and **31** were carried on as a mixture (which was separated at a subsequent step), a sample of this mixture was resubjected to the reduction conditions in order to obtain a more enriched sample of **32**. The following data for compound **32** were obtained using a ~6:1 mixture of **32**:**31**: R_f = 0.15 (silica, methylene chloride:ethyl acetate:methanol 6:3:0.3); $[\alpha]^{24}_D$ −125.7° (*c* 1.01, EtOH); IR (KBr) ν_{max} 3448, 2934, 1676, 1452, 1426, 1320, 1240, 1195, 1074, 917, 826, 802, 742, 682, 622 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, 340 K) δ 7.86–7.84 (m, 2 H, aromatic), 7.65–7.62 (m, 3 H, N*H*, aromatic), 7.41–7.37 (m, 2 H, aromatic), 7.33–7.29 (m, 2 H, aromatic), 6.90 (b s, 1 H, N*H*O), 6.16 (b s, 1 H), 6.00–5.89 (m, 3 H, 2 × C*H*═CH, C═C*H*CH_2), 5.80 (b s, 1 H, C*H*C═C), 5.44 (d, *J* = 1.8 Hz, 1 H, D-1), 5.32 (d, *J* = 4.0 Hz, 1 H, O*H*), 5.30 (b s, 1 H, E-1), 5.03 (d, *J* = 5.8 Hz, 1 H, O*H*), 4.97 (dd, *J* = 10.2, 1.8 Hz, 1 H, B-1), 4.84 (d, *J* = 4.5 Hz, 1 H, O*H*), 4.81 (d, *J* = 5.3 Hz, 1 H, O*H*), 4.52 (d, *J* = 7.4 Hz, 1 H, A-1), 4.50–4.32 (b m, 2 H), 4.29–4.26 (m, 2 H, D-2, C*H*O), 4.11 (m, 1 H, B-3), 4.03–3.89 (m, 5 H, B-5, D-5, C*H*$_2$S, C*H*Os), 3.88–3.77 (m, 6 H), 3.82 (s, 3 H, CH_3O), 3.77 (s, 3 H, CH_3O), 3.61–3.51 (m, 5 H, A-5, B-4, D-3, C*H*Os), 3.47 (ddd, *J* = 9.3, 9.2, 5.2 Hz, 1 H, D-4), 3.43 (s, 3 H, CH_3O), 3.38 (m, 1 H), 3.25 (m, 1 H), 3.20–3.05 (obs, 5 H), 2.43 (obs, 1 H, E-2$_{eq}$), 2.30 (2 × s, 6 H, ArCH_3, CH_3CO), 2.28 (obs, 1 H, A-4), 2.19 (AB q, *J* = 13.7 Hz, Δν = 212 Hz, 2 H, CH_2), 1.88 (m, 1 H, B-2$_{eq}$), 1.69 (m, 1 H, B-2$_{ax}$), 1.35 (m, 1 H, E-2$_{ax}$), 1.28 (2 × d, *J* = 6.2 Hz, 6 H, A-6, B-6), 1.15 (d, *J* = 6.2 Hz, 3 H, D-6), 0.86 (b s, 3 H, C$H_3$$CH_2$N); ^{13}C NMR (125 MHz, DMSO-d_6) δ 195.6, 195.5, 195.4, 192.5, 155.6, 154.8, 151.8, 149.9, 144.0 (2), 143.9, 142.9, 140.9, 140.8, 138.5, 138.3, 132.4, 130.1, 127.7, 127.6, 127.1, 127.0, 125.3, 125.2, 124.9, 124.8, 123.2, 122.6, 120.1, 104.7, 104.2, 101.3, 100.1, 97.7, 97.1, 94.4, 85.9, 83.0, 80.3, 71.3, 70.2, 70.0, 69.7, 69.4, 69.2, 69.0, 67.5, 67.2, 67.0, 66.4 (2), 64.7, 61.6, 60.9, 56.5, 54.8, 51.9, 51.1, 50.0, 46.8, 46.7, 37.7, 35.2, 30.4, 29.2, 24.9, 18.8, 18.6, 17.9, 14.5, 14.3; HRMS (FAB) calcd for $C_{73}H_{88}IN_3O_{25}S_2Cs$ (M + Cs) 1730.3247, found 1730.3190. **32-epi**: R_f = 0.17 (silica, methylene chloride:ethyl acetate:methanol 6:3:0.3); $[\alpha]^{25}_D$ −104.8° (*c* 0.5, $CHCl_3$); IR (KBr) ν_{max} 3427, 2931, 1678, 1455, 1421, 1321, 1238, 1074, 1025, 999, 914, 742, 627 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, 340 K) δ 7.86–7.84 (m, 2 H, aromatic), 7.65–7.62 (m, 3 H, N*H*, aromatic), 7.41–7.38 (m, 2 H, aromatic), 7.33–7.29 (m, 2 H, aromatic), 6.72 (b s, 1 H, N*H*O), 5.99–5.88 (m, 3 H, 2 × C*H*═CH, C═C*H*CH_2), 5.79 (b, s, 1 H, C*H*C≡C), 5.45 (d, *J* = 1.9 Hz, 1 H, D-1), 5.30 (d, *J* = 4.2 Hz, 1 H, B-3-O*H*), 5.30–5.21 (m, 2 H, E-1, C*H*O), 5.14 (dd, *J* = 10.2, 1.7 Hz, 1 H, B-1), 4.83 (d, *J* = 4.1 Hz, 1 H, D-2-O*H*), 4.79 (d, *J* = 5.1 Hz, 1 H, D-4-O*H*), 4.48 (d, *J* = 7.4 Hz, 1 H, A-1), 4.35 (m, 1 H), 4.29–4.25 (m, 2 H, D-2, C*H*O), 4.10 (m, 1 H, B-3), 4.03–3.94 (m, 3 H, B-5, D-5, C*H*O), 3.92 (m, 1 H), 3.86–3.75 (m, 5 H), 3.82 (s, 3 H, CH_3O), 3.78 (s, 3 H, CH_3O), 3.70 (m, 1 H), 3.64 (b q, *J* = 6.5 Hz, 1 H, A-5), 3.61–3.54 (m, 4 H, B-4, D-3, C*H*Os), 3.47 (ddd, *J* = 9.3, 9.2, 5.2 Hz, 1 H, D-4), 3.43 (s, 3 H, CH_3O), 3.37 (m, 1 H, A-2), 3.30–3.00 (m, 6 H), 2.37 (m, 1 H, E-2$_{eq}$), 2.30 (s, 6 H, ArCH_3, CH_3CO), 2.20 (AB q, *J* = 13.7 Hz, Δν = 211 Hz, 2 H, CH_2), 1.86 (m, 1 H, B-2$_{eq}$), 1.67 (m, 1 H, B-2$_{ax}$), 1.36 (m, 1 H, E-2$_{ax}$), 1.29 (d, *J* = 6.2 Hz, 3 H, B-6), 1.20 (d, *J* = 6.5 Hz, 3 H, A-6), 1.15 (d, *J* = 6.2 Hz, 3 H, D-6), 0.86 (b s, 3 H, C$H_3$$CH_2$N); ^{13}C NMR (125 MHz, DMSO-d_6) δ 195.5, 195.4, 192.5, 155.6, 154.9, 151.8, 149.9, 144.0 (2), 143.9, 142.9, 140.9, 140.7 (2), 138.4, 132.4, 130.1, 127.6 (2), 127.1, 127.0, 125.3, 125.2, 124.9, 124.8, 123.1, 122.5, 120.1, 104.7, 104.2, 101.4, 100.0, 99.9, 97.4, 96.9, 94.4, 85.9, 82.9, 80.2, 71.4 (2), 71.3, 70.1, 69.3, 69.2, 68.9, 67.1, 66.4 (2), 64.7, 64.6, 64.3, 61.5, 60.8, 59.8, 56.5, 54.8, 51.9, 51.1, 50.0, 46.7 (2), 38.0, 35.2, 30.3, 29.1, 24.9, 18.7, 17.8, 17.7, 14.5, 14.3, 14.1; HRMS (FAB) calcd for $C_{73}H_{88}IN_3O_{25}S_2Cs$ (M + Cs) 1730.3247, found 1730.3303.

Preparation of Pentasilyl Ether 33. A solution of pentol **32** (+ **31**, ca. 3:1 mixture, 235 mg, 0.147 mmol) in CH_2Cl_2 (15 mL) cooled to 0 °C was treated with diisopropylethylamine (1.0 mL, 5.74 mmol) and triethylsilyl trifluoromethanesulfonate (0.65 mL, 2.93 mmol), and the mixture was stirred for 45 min. The reaction mixture was diluted with EtOAc (50 mL) and washed with water (25 mL), saturated aqueous $NaHCO_3$ (25 mL), and brine (25 mL). The organic layer was dried ($MgSO_4$) and concentrated to yield the crude product along with a hexasilylated compound. This mixture was dissolved in EtOAc–H_2O (20 mL, 200:1) and treated with AcOH (0.10 mL) at 25 °C. After the solution was stirred for 8 h, the reaction was quenched with solid $NaHCO_3$ (1.3 g) and the solution was diluted with EtOAc (30 mL) and washed with saturated aqueous $NaHCO_3$ (25 mL) and brine (25 mL). The organic phase was dried ($MgSO_4$), concentrated, and purified by flash column chromatography (silica, 50–60% ethyl ether in petroleum ether) to yield compound **33** (240 mg, 75%, contaminated with oxime **30**) as a white foam: R_f = 0.37 (silica, 60% ethyl ether in petroleum ether); MS (FAB) calcd for $C_{103}H_{158}IN_3O_{25}S_2Si_5Cs$ (M + Cs) 2302, found 2302. This compound was taken on to the next step without further characterization.

Preparation of Thiol 34. A solution of thioacetate **33** (+ **30**, *ca.* 3:1 by ^{1}H NMR) (48 mg, 0.022 mmol) in CH_2Cl_2 (5 mL) at −90 °C was treated with DIBAL (0.070 mL of a 1.0 M solution in CH_2Cl_2, 0.070 mmol), and the mixture was stirred for 50 min. The reaction was quenched with MeOH (1.5 mL), the cooling bath was removed, and the reaction mixture was diluted with EtOAc (10 mL). Saturated aqueous Rochelle salt (10 mL) was added, and the mixture was vigorously stirred for 10 min until the two phases became clear. The organic layer was extracted with saturated aqueous Rochelle salt (2 × 10 mL). The aqueous phases were combined and extracted with EtOAc (2 × 15 mL). The combined organic layers were dried ($MgSO_4$) and concentrated to afford crude thiol **34**.

Preparation of Trisulfides 35 and 36. Crude thiol **34** (+ **34′**-oxime, *ca.* 3:1) was dissolved in CH_2Cl_2 (5 mL) at 0 °C, and *N*-(methyldithio)-phthalimide (36 mg, 0.16 mmol) was added. The solution was stirred for 15 h at 0 → 25 °C, concentrated to 1 mL, and applied directly to a flash chromatography column (silica, 30–60% ethyl ether in petroleum ether) to give trisulfide **35** (28 mg, 57%) as a white foam. Also isolated from this column was the more polar oxime trisulfide **36** (10 mg, 20%). **35**: R_f = 0.13 (silica, 50% ethyl ether in petroleum ether); $[\alpha]^{25}_D$ −100.76° (*c* 0.525, $CHCl_3$); IR (neat) ν_{max} 3019, 2956, 1681, 1455, 1216, 1083 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6, 340 K) δ 7.68–7.58 (m, 4 H, aromatic), 7.23–7.08 (m, 4 H, aromatic), 6.76 (obs, 1 H, C═C*H*CH_2), 6.74 (b s, 1 H, N*H*O), 6.37 (b s, 1 H, C*H*C≡C), 5.77 (s, 1 H, D-1), 5.50–5.43 (m, 3 H, 2 × C*H*═CH, E-1), 5.29 (b d, 1 H, B-1), 4.90–4.70 (b m, 1 H), 4.59 (m, 1 H, D-2), 4.45–4.37 (m, 3 H, 2 × CH_2CH═C, D-5), 4.33–4.29 (m, 2 H, C*H*Os), 4.19–4.13 (m, 3 H, B-3, B-5, C*H*O), 4.06 (dd, *J* = 9.1, 9.1 Hz, 1 H, D-4), 3.93 (dd, *J* = 10.7, 1.8 Hz, 1 H, B-4), 3.89–3.83 (m, 2 H, A-5, C*H*O), 3.87 (dd, *J* = 9.0, 1.9 Hz, 1 H, D-3), 3.81–3.76 (b s, 1 H, C*H*O), 3.74 (s, 3 H, CH_3O), 3.56 (s, 3 H, CH_3O), 3.55–3.52 (m, 3 H), 3.47–3.38 (m, 4 H), 3.36 (s, 3 H, CH_3O), 3.30–3.15 (m, 2 H), 3.22 (s, 3 H, CH_3O), 2.69 (AB q, *J* = 13.6 Hz, Δν = 184 Hz, 2 H, CH_2), 2.60

(m, 2 H, E-2_{eq}, A-4), 2.47 (s, 3 H, ArCH_3), 2.30 (s, 3 H, SSSCH_3), 1.90 (m, 1 H, B-2_{eq}), 1.74 (m, 1 H, B-2_{ax}), 1.65 (m, 1 H, E-2_{ax}), 1.60 (d, J = 5.7 Hz, 3 H, A-6), 1.56 (d, J = 6.1 Hz, 3 H, B-6), 1.42 (d, J = 6.2 Hz, 3 H, D-6), 1.20–0.55 (series of m, 78 H, 5 × Si(CH_2CH_3)$_3$, CH_3-CH_2N); ^{13}C NMR (125 MHz, $CDCl_3$) δ 193.3, 156.0, 152.3, 150.5, 144.3, 143.6, 143.2, 141.4, 141.3, 137.6, 135.3, 133.3, 130.9, 130.6, 128.8, 127.8, 127.7, 127.1, 126.9, 125.2, 124.8, 124.5, 123.7, 123.0, 120.0, 119.9, 105.5, 104.7, 103.4, 102.6, 99.8, 99.6, 99.3, 93.9, 86.3, 85.0, 83.1, 81.4, 72.5, 72.4, 72.3, 72.2, 70.6, 70.2, 69.5, 68.9, 68.6, 68.1, 67.6, 67.4, 65.3, 64.4, 61.5, 60.8, 59.8, 57.3, 56.7, 52.5, 51.7, 47.1, 38.7, 38.6, 38.2, 36.8, 30.3, 29.3, 28.9, 25.3, 23.7, 23.0, 22.8, 18.7, 18.5, 18.0, 14.1, 14.0, 11.0, 7.1, 7.0, 6.9, 6.8, 6.2, 5.2 (2), 4.9 (2); HRMS (FAB) calcd for $C_{102}H_{158}IN_3O_{24}S_4Si_5Cs$ (M + Cs) 2336.7064, found 2336.7114.

Preparation of Pentol 37. A solution of **35** (9.0 mg, 4 μmol) in THF–CH_2Cl_2 (1.2 mL, 5:1) was placed in a plastic vial and cooled to 0 °C. This solution was treated dropwise with HF·pyr (0.10 mL) and stirred at 0 → 25 °C for 18 h. The mixture was diluted with EtOAc (10 mL), and the reaction was carefully quenched with saturated aqueous $NaHCO_3$ (5 mL). The organic layer was washed with additional $NaHCO_3$ (2 × 10 mL) and brine (10 mL), and the combined aqueous phases were reextracted with EtOAc (20 mL). The organic layers were then combined, dried ($MgSO_4$), concentrated, and purified by flash column chromatography (silica, 5% methanol in ethyl acetate) to give compound **37** (6 mg, 90%) as a white solid: R_f = 0.13 (silica, methylene chloride:ethyl acetate:methanol 6:3:0.3): $[\alpha]^{25}_D$ –51.24° (c 0.445, $CHCl_3$); IR (KBr) ν_{max} 3426, 2932, 1676, 1452, 1320, 1238, 1156, 1071, 911, 757, 621 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, 340 K) δ 7.86–7.84 (m, 2 H, aromatic), 7.65–7.63 (m, 3 H, NH, aromatic), 7.41–7.37 (m, 2 H, aromatic), 7.33–7.29 (m, 2 H, aromatic), 6.90 (b s, 1 H, NHO), 6.19 (dd, J = 8.8, 6.2 Hz, 1 H, C=CHCH$_2$), 5.99 (d, J = 9.4 Hz, 1 H, CH=CH), 5.91 (dd, J = 9.4, 1.2 Hz, 1 H, CH=CH), 5.85 (b s, 1 H, CHC≡C), 5.44 (d, J = 1.4 Hz, 1 H, D-1), 5.38–5.30 (m, 2 H, E-1, CHO), 4.97 (b d, J = 10.1 Hz, 1 H, B-1), 4.54 (d, J = 7.2 Hz, 1 H, A-1), 4.48–4.32 (m, 2 H, CHOs), 4.29–4.25 (m, 2 H, D-2, CHO), 4.11 (b s, 1 H, B-3), 4.06–3.97 (m, 2 H, CH_2CH=C, D-5), 3.95–3.90 (m, 3 H, B-5, CHOs), 3.90–3.65 (m, 6 H, A-3, CHOs), 3.82 (s, 3 H, CH_3O), 3.78 (s, 3 H, CH_3O), 3.62–3.50 (m, 6 H, A-5, B-4, D-3, CHOs), 3.46 (dd, J = 9.4, 9.3 Hz, 1 H, D-4), 3.43 (s, 3 H, CH_3O), 3.39 (dd, J = 7.1, 6.8 Hz, 1 H, A-2), 3.33 (b s, 1 H), 3.25–3.05 (obs, 6 H), 2.56 (s, 3 H, SSSCH_3), 2.50 (obs, 1 H, E-2_{eq}), 2.30 (s, 3 H, ArCH_3), 2.27 (obs, 1 H, A-4), 2.22 (AB q, J = 13.6 Hz, $\Delta\nu$ = 201 Hz, 2 H, CH_2), 1.88 (m, 1 H, B-2_{eq}), 1.69 (m, 1 H, B-2_{ax}), 1.38 (m, 1 H, E-2_{ax}), 1.28 (d, J = 6.0 Hz, 3 H, B-6), 1.26 (d, J = 7.0 Hz, 3 H, A-6), 1.15 (d, J = 6.2 Hz, 3 H, D-6), 0.86 (b s, 3 H, CH_3CH$_2$N); ^{13}C (125 MHz, $CDCl_3$) δ 191.9, 156.0, 155.8, 151.5, 150.6, 144.3, 143.4, 143.0, 141.4, 141.3, 137.4, 133.4, 130.2, 127.8 (2), 127.1, 126.9, 125.6, 125.1, 124.8, 123.6, 123.2, 120.1, 119.9, 105.6, 103.4, 103.2, 102.6, 99.8, 99.2, 98.1, 93.5, 85.8, 80.8 (2), 72.1, 71.1, 71.0, 70.8, 70.4, 69.0, 68.7, 68.4, 67.9, 67.7, 67.0, 65.3, 64.4, 61.7, 60.9, 59.7, 57.2, 56.7, 52.5, 51.6, 49.9, 47.1, 39.2, 36.8, 36.3, 29.7, 25.3, 22.5, 19.0, 17.6 (2), 17.5, 14.3; HRMS (FAB) calcd for $C_{72}H_{88}IN_3O_{24}S_4Cs$ (M + Cs) 1766.2740, found 1766.2789.

Preparation of Enone 38. A solution of ketal **37** (7.0 mg, 4.2 μmol) in THF (0.5 mL) and H_2O (1 drop) was treated with TsOH (0.080 mL of a 0.055 M solution in THF, 4.4 μmol), and the mixture was stirred at 25 °C for 23 h. The product was purified by preparative TLC (direct application, silica, methylene chloride:ethyl acetate:methanol 6:3:0.3) affording ketone **38** (4.0 mg, 69%) as a white solid and starting ketal **37** (1 mg, 0.6 μmol). **38**: R_f = 0.12 (silica, methylene chloride:ethyl acetate: methanol 6:3:0.3); ^{1}H NMR (500 MHz, DMSO-d_6, 340 K) δ 8.27 (b s, 1 H, NHO), 7.86–7.84 (m, 2 H, aromatic), 7.66–7.62 (m, 2 H, aromatic), 7.41–7.37 (m, 2 H, aromatic), 7.33–7.28 (m, 2 H, aromatic), 6.32 (dd, J = 8.3, 7.0 Hz, 1 H, CH$_2$CH=C), 6.09 (d, J = 9.5 Hz, 1 H, CH=CH), 6.07 (b s, 1 H, CHC≡C), 5.99 (dd, J = 9.5, 1.5 Hz, 1 H, CH=CH), 5.44 (d, J = 1.5 Hz, 1 H, D-1), 5.37 (d, J = 1.6 Hz, 1 H, E-1), 4.96 (dd, J = 10.2, 1.9 Hz, 1 H, B-1), 4.58 (d, J = 7.5 Hz, 1 H, A-1), 4.41 (m, 2 H), 4.29–4.25 (m, 3 H, D-2, CHOs), 4.11 (m, 1 H, B-3), 4.00 (m, 1 H, D-5), 3.93 (m, 1 H, B-5), 3.90–3.75 (m, 3 H), 3.82 (s, 3 H, CH_3O), 3.77 (s, 3 H, CH_3O), 3.77 (dd, J = 9.8 Hz, 1 H, A-3), 3.59–3.54 (m, 4 H, A-5, B-4, D-3, CHO), 3.48–3.36 (m, 5 H, D-4, A-2, CHOs), 3.43 (s, 3 H, CH_3O), 3.25–3.05 (obs, 3 H), 3.18 (s, 3 H, CH_3O), 2.75 (AB q, J = 17.3 Hz, $\Delta\nu$ = 195.2 Hz, 2 H, CH_2), 2.47 (s, 3 H, SSSCH_3), 2.42 (m, 1 H, E-2_{eq}), 2.30 (s, 3 H, ArCH_3), 2.26 (dd, J = 9.8, 9.8 Hz, 1 H, A-4), 1.87 (m, 1 H, B-2_{eq}), 1.69 (m, 1 H, B-2_{ax}), 1.38 (m, 1 H, E-2_{ax}), 1.28 (d, J = 6.2 Hz, 3 H, B-6), 1.26 (d, J = 6.6 Hz, 3 H, A-6), 1.15 (d, J = 6.2 Hz, 3 H, D-6), 0.86 (b s, 3 H, CH_3CH$_2$N); HRMS (FAB) calcd for $C_{70}H_{84}IN_3O_{23}S_4Cs$ (M + Cs) 1722.2478, found 1722.2409.

Preparation of Calicheamicin γ_1^I (1). A solution of FMOC derivative **38** (4 mg, 2.5 μmol) in THF–H_2O (0.52 mL, 25:1) at 25 °C was treated with excess diethylamine (0.1 mL), and the mixture was stirred for 2 h. The reaction mixture was diluted with Et_2O–CH_2Cl_2 (1:1, 5 mL) and dried with Na_2SO_4. The mixture was decanted, and the solution was concentrated. Flash column chromatography (silica, methylene chloride: ethyl acetate:methanol 5:4:0.6) gave calicheamicin γ_1^I (**1**; 3.1 mg, 90%). Further purification was performed on a reverse phase C_{18} HPLC column, t_R = 18 ± 0.5 min [Vidac, 1.0 × 25 cm, using a linear gradient of 90:10 (0.2 M NH_4OAc:CH_3CN) to 10:90 (0.2 M NH_4OAc:CH_3CN) over 20 min with a flow rate of 3.5 mL/min].[12] After aqueous extraction to remove salts, pure calicheamicin γ_1^I (**1**) was precipitated from ethyl acetate solution with hexanes to yield a white solid: R_f = 0.22 (methylene chloride: ethyl acetate:methanol 5:4:0.6); $[\alpha]^{25}_D$ –100.5° (c 0.2, EtOH); IR (neat) ν_{max} 3408, 2978, 2921, 2845, 1715, 1682, 1453, 1410, 1390, 1319, 1238, 1070, 908, 731 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.40 (dd, J = 7.4, 7.4 Hz, 1 H, C=CHCH$_2$), 6.21 (d, J = 1.4 Hz, 1 H, CHC≡C), 5.87 (d, J = 9.5 Hz, 1 H, CH=CH), 5.80 (dd, J = 9.5, 1.7 Hz, 1 H, CH=CH), 5.72 (d, J = 1.4 Hz, 1 H, D-1), 5.68 (d, J = 2.9 Hz, 1 H, E-1), 5.02 (dd, J = 10.1, 1.8 Hz, 1 H, B-1), 4.66 (d, J = 7.7 Hz, 1 H, A-1), 4.46 (m, 1 H, D-2), 4.31 (m, 1 H, B-3), 4.18 (dq, J = 9.5, 6.2 Hz, 1 H, D-5), 4.06 (dq, J = 11.0, 6.2 Hz, 1 H, B-5), 4.01 (dd, J = 9.7, 9.7 Hz, 1 H, A-3), 3.88–3.78 (m, 5 H, A-2, A-5, D-3, 2 × CH_2CH=C), 3.87 (s, 3 H, ArOCH_3), 3.82 (s, 3 H, ArOCH_3), 3.76 (dd, J = 11.0, 2.5 Hz, 1 H, B-4), 3.70 (b s, 3 H, NHCO$_2$CH_3), 3.62 (dd, J = 9.5, 9.5 Hz, 1 H, D-4), 3.61–3.56 (obs, 2 H, E-5, E-5′), 3.56 (s, 3 H, CH_3O-D ring), 3.50 (m, 1 H, E-3), 3.41 (s, 3 H, CH_3O-E ring), 2.99 (AB q, J = 16.7 Hz, $\Delta\nu$ = 176 Hz, 2 H, CH_2), 2.71 (b m, 1 H, CH_2N), 2.64 (m, 1 H, E-4), 2.48 (s, 3 H, SSSCH_3), 2.48 (obs, 1 H, CH_2N), 2.36 (dd, J = 9.7, 9.7 Hz, 1 H, A-4), 2.34 (obs, 1 H, E-2_{eq}), 2.34 (s, 3 H, ArCH_3), 2.03 (m, 1 H, B-2_{eq}), 1.77 (m, 1 H, B-2_{ax}), 1.48 (m, 1 H, E-2_{ax}), 1.40 (d, J = 6.2 Hz, 3 H, B-6), 1.35 (d, J = 6.2 Hz, 3 H, A-6), 1.29 (d, J = 6.2 Hz, 3 H, D-6), 1.17 (t, J = 7.1 Hz, 3 H, CH_3CH$_2$N); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.6, 192.0, 151.5, 150.6, 143.0, 133.4, 130.2, 124.4, 123.5, 102.5, 100.8, 99.6, 99.5, 97.3, 93.5, 88.1, 82.8, 80.8, 75.9, 72.1, 71.7, 71.1, 70.4, 69.7, 69.1, 68.5, 68.4, 67.0, 61.7, 61.3, 60.9, 57.2, 56.3, 52.8, 51.6, 42.3, 39.0, 36.8, 34.1, 25.3, 22.8, 18.9, 17.6, 14.6; HRMS (FAB) calcd for $C_{55}H_{74}IN_3O_{21}S_4Cs$ (M + Cs) 1500.1797, found 1500.1833.

Compounds 33-epi–35-epi, 37-epi, 38-epi, and 1-epi. Compounds **33-epi–35-epi, 37-epi, 38-epi** and **1-epi** were prepared in a similar manner as described for compounds **33–35, 37, 38**, and **1**, respectively. They exhibited the following physical data.

33-epi: R_f = 0.31 (silica, benzene:ethyl acetate 10:1); $[\alpha]^{23}_D$ –123.1° (c 0.975, $CHCl_3$); IR (KBr) ν_{max} 3423, 2954, 2879, 1733, 1686, 1457, 1417, 1323, 1277, 1238, 1086, 1009, 963, 908, 738 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6, 340 K) δ 7.75–7.55 (m, 4 H, aromatic), 7.30–7.10 (m, 4 H, aromatic), 7.07 (b s, 1 H), 6.62 (t, J = 8.4 Hz, 1 H, C=CHCH$_2$), 6.43 (s, 1 H, CHC≡C), 5.76 (s, 1 H, D-1), 5.57 (b d, J = 10.1 Hz, 1 H, B-1), 5.43–5.38 (m, 2 H, CH=CH), 5.21 (b s, 1 H, E-1), 4.70 (m, 1 H, CHO), 4.60 (b m, 1 H, CHO), 4.57 (m, 1 H, D-2), 4.53 (m, 1 H, D-5), 4.48–4.38 (m, 3 H, CHOs), 4.28–4.20 (m, 2 H, B-5, CHOs), 4.10 (dd, J = 9.2, 9.2 Hz, 1 H, D-4), 4.06–4.00 (m, 3 H, B-4, CHOs), 3.86 (dd, J = 9.2, 2.5 Hz, 1 H, D-3), 3.85–3.79 (m, 2 H, CHOs), 3.67 (s, 3 H, CH_3O), 3.66 (obs, 1 H), 3.56 (b s, 2 H, CHOs), 3.46 (s, 3 H, CH_3O), 3.46–3.25 (m, 6 H, CHOs), 3.30 (s, 3 H, CH_3O), 3.21 (d, J = 4.8 Hz, 1 H, CHO), 3.15 (s, 3 H, CH_3O), 3.05 (b m, 2 H, CH_2N), 2.77 (AB q, J = 13.6 Hz, $\Delta\nu$ = 244 Hz, 2 H, CH_2), 2.55 (m, 1 H, E-2_{eq}), 2.44 (s, 3 H, ArCH_3), 2.00 (s, 3 H, CH_3CO), 1.90 (m, 1 H, B-2_{eq}), 1.75 (m, 1 H, B-2_{ax}), 1.61 (d, J = 6.1 Hz, 3 H, B-6), 1.54 (d, J = 6.4 Hz, 3 H, A-6), 1.51 (m, 1 H, E-2_{ax}), 1.46 (d, J = 6.2 Hz, 3 H, D-6), 1.16–0.48 (series of m, 78 H, 5 × Si(CH_2CH_3)$_3$, CH_3CH$_2$N); ^{13}C NMR (125 MHz, C_6D_6) δ 195.0, 192.2, 156.2, 152.6, 151.3, 145.1, 144.1, 143.7, 141.9, 141.7, 137.5, 136.4, 135.7, 133.8, 131.6, 127.6 (2), 127.4, 127.1, 125.8, 125.6, 125.4, 123.7, 123.4, 120.2, 120.1, 106.2, 104.9, 104.8, 103.2, 100.6, 100.2, 100.1, 94.5, 86.5, 85.2, 82.0, 78.8, 75.0, 73.1, 72.9, 72.6, 71.7, 71.3, 70.7, 70.3, 70.2, 69.0, 67.5, 65.5, 65.4, 64.3, 61.5, 60.5, 60.4, 57.0, 56.5, 52.3, 47.7, 39.0, 37.3, 30.4, 30.2, 30.0, 25.6, 19.2, 18.5 (2), 14.1, 7.5, 7.3, 7.2, 7.1, 7.0, 6.8, 5.7, 5.5, 5.3, 5.2; HRMS (FAB) calcd for $C_{103}H_{158}IN_3O_{25}S_2Si_5Cs$ (M + Cs) 2300.7571, found 2300.7406.

35-epi: R_f = 0.41 (silica, benzene:ethyl acetate 10:1); $[\alpha]^{23}_D$ –89.7° (c 1.0, $CHCl_3$); IR (KBr) ν_{max} 3420, 3213, 3063, 2925, 2879, 1742, 1680, 1458, 1417, 1381, 1309, 1279, 1238, 1086, 1009, 909, 739 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6, 340 K) δ 7.75–7.55 (m, 4 H, aromatic), 7.25–

(12) Lee, M. D.; Manning, J. K.; Williams, D. R.; Kuck, N. A.; Testa, R. T.; Borders, D. B. *J. Antiobiot.* **1989**, *42*, 1070.

7.10 (m, 4 H, aromatic), 7.04 (b s, 1 H), 6.79 (m, 1 H, C=C*H*CH_2), 6.43 (s, 1 H, C*H*C≡C), 5.76 (d, J = 1.7 Hz, 1 H, D-1), 5.59 (dd, J = 10.0, 1.5 Hz, 1 H, B-1), 5.43–5.39 (m, 2 H, C*H*=C*H*), 5.14 (b d, 1 H, E-1), 4.69 (m, 1 H), 4.60 (b m, 1 H), 4.57 (m, 1 H, D-2), 4.53 (m, 1 H, D-5), 4.49 (m, 1 H), 4.39 (b m, 1 H), 4.31 (m, 1 H, B-5), 4.23 (b m, 1 H), 4.10 (dd, J = 9.2, 9.2 Hz, 1 H, D-4), 4.09–4.02 (m, 3 H), 3.99 (b m, 1 H), 3.86 (dd, J = 9.2, 2.6 Hz, 1 H, D-3), 3.83 (dd, J = 9.5, 5.2 Hz, 1 H, C*H*O), 3.75–3.67 (m, 2 H), 3.67 (s, 3 H, CH_3O), 3.57 (bs, 1 H), 3.46 (s, 3 H, CH_3O), 2.45–3.24 (m, 4 H), 3.30 (s, 3 H, CH_3O), 3.18 (d, J = 5.0 Hz, 1 H), 3.15 (s, 3 H, CH_3O), 3.10 (obs, 2 H, CH_2N), 2.79 (AB q, J = 13.6 Hz, $\Delta\nu$ = 229 Hz, 2 H, CH_2), 2.53 (m, 1 H, E-2$_{eq}$), 2.43 (s, 3 H, ArCH_3), 2.31 (s, 3 H, SSSCH_3), 1.90 (m, 1 H, B-2$_{eq}$), 1.74 (m, 1 H, B-2$_{ax}$), 1.68 (d, J = 6.2 Hz, 3 H, B-6), 1.52 (obs, 1 H, E-2$_{ax}$), 1.51 (d, J = 6.4 Hz, 3 H, A-6), 1.46 (d, J = 6.2 Hz, 3 H, D-6), 1.19–0.49 (series of m, 78 H, 5 × Si(CH_2CH_3)$_3$), CH_3CH_2N); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.3, 167.3, 156.2, 152.6, 151.3, 145.1, 144.1, 143.7, 141.9, 141.7, 135.6, 133.9, 133.5, 133.1, 131.6, 127.1, 126.1, 125.8, 123.6, 123.5, 123.0, 120.2, 120.1, 110.4, 106.2, 104.9, 103.2, 100.6, 100.1 (2), 94.5, 86.5, 85.1, 82.0, 79.0, 74.9, 73.1, 72.9, 72.6, 71.8, 71.6, 70.7, 70.3, 70.1, 69.0, 67.5, 65.5, 65.2, 64.3, 61.5, 60.5, 60.3, 57.0, 56.6, 52.3, 47.7, 39.4, 39.0, 37.3, 32.3, 30.4, 30.2, 25.6, 23.1, 22.8, 19.3, 18.5, 18.4, 14.3, 14.1, 7.6, 7.4, 7.2 (2), 7.0, 6.8, 5.7, 5.5, 5.3, 5.2; HRMS (FAB) calcd for $C_{102}H_{158}IN_3O_{24}S_4Cs$ (M + Cs) 2336.7064, found 2336.6831.

37-epi: This compound was purified by reverse phase C_{18} HPLC column, t_R = 22.7 ± 0.5 min [Vidac, 1.0 × 25 cm, using a linear gradient of 90:10 (0.2 M NH_4OAc:CH_3CN) to 10:90 (0.2 M NH_4OAc:CH_3CN) over 30 min with a flow rate of 3.5 mL/min: R_f = 0.24 (silica, methylene chloride:ethyl acetate:methanol 6:3:0.3); $[\alpha]^{23}_D$ −85.4° (c 0.82, $CHCl_3$); IR (KBr) ν_{max} 3434, 2932, 1678, 1453, 1419, 1386, 1320, 1236, 1196, 1149, 1075, 960, 914, 742 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, J = 7.5 Hz, 2 H, aromatic), 7.63–7.57 (m, 2 H, aromatic), 7.42–7.37 (m, 2 H, aromatic), 7.34–7.27 (m, 2 H, aromatic) 6.48 (dd, J = 9.1, 6.4 Hz, 1 H, C=C*H*CH_2), 5.80 (d, J = 9.4 Hz, 1 H, C*H*=CH), 5.77 (b d, 1 H, C*H*=CH), 5.75 (b s, 1 H, C*H*C≡C), 5.73 (b s, 1 H, D-1), 5.34 (b s, 1 H, E-1), 5.16 (b d, J = 11.2 Hz, 1 H, B-1), 4.80 (b s, 1 H), 4.48 (m, 1 H, D-2), 4.45 (d, J = 7.6 Hz, 1 H, A-1), 4.35 (t, J = 11.2 Hz, 1 H), 4.32–4.27 (m, 2 H), 4.20 (m, 1 H, B-5 or D-5), 4.11–4.01 (m, 3 H, B-5 or D-5, C*H*Os), 3.97–3.92 (m, 2 H), 3.89 (s, 3 H, CH_3O), 3.85 (obs, 1 H), 3.84 (s, 3 H, CH_3O), 3.76–3.72 (m, 3 H), 3.68–3.61 (m, 4 H), 3.57 (s, 3 H, CH_3O), 3.50–3.41 (m, 5 H), 3.36–3.29 (m, 3 H), 3.30 (s, 3 H, CH_3O), 3.20 (b m, 2 H, CH_2N), 2.55 (s, 3 H, SSSCH_3), 2.50 (AB q, J = 13.9 Hz, $\Delta\nu$ = 229 Hz, 2 H, CH_2), 2.50 (m, 1 H, E-2$_{eq}$), 2.42 (b d, 1 H, A-4 or O*H*), 2.36 (s, 3 H, ArCH_3), 2.33 (b s, 1 H), 2.18 (b s, 1 H), 2.04 (m, 1 H, B-2$_{eq}$), 1.76 (m, 1 H, B-2$_{ax}$), 1.48 (m, 1 H, E-2$_{ax}$), 1.40 (d, J = 6.2 Hz, 3 H, B-6), 1.37 (d, J = 6.5 Hz, 3 H, A-6), 1.31 (d, J = 6.2 Hz, 3 H, D-6), 1.08 (m, 3 H, CH_3CH_2N); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.0, 156.0, 151.4, 150.6, 144.3, 143.3, 143.0, 141.4, 141.2, 134.1, 133.4, 130.3, 128.3, 128.0, 127.8 (2), 127.6, 127.1, 127.0, 126.9, 125.3, 125.2, 124.7, 123.6, 123.2, 120.1, 105.5, 103.3, 102.9, 102.5, 101.1, 99.5, 98.0, 93.5, 85.8, 80.8, 79.8, 74.6, 72.0, 71.1, 70.5, 70.4, 70.2, 69.8, 68.9, 68.3, 67.8, 66.9, 65.8, 65.3, 64.4, 61.7, 60.9, 59.7, 57.2, 56.6, 52.4, 51.7, 49.9, 47.2, 47.0, 39.5, 37.0, 36.4, 29.7, 25.3, 22.5, 19.0, 17.5, 17.2, 14.2; HRMS (FAB) calcd for $C_{78}H_{88}IN_3O_{24}S_4Cs$ (M + Cs) 1766.2470, found 1766.2655.

1-epi: R_f = 0.10 (silica, methylene chloride:ethyl acetate:methanol 5.5:4:0.5); $[\alpha]^{20}_D$ −176.4° (c 0.53, $CHCl_3$); IR (KBr) ν_{max} 3436, 2927, 1680, 1455, 1389, 1321, 1240, 1077, 914, 825 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.39 (d, J = 9.2, 5.6 Hz, 1 H, C=C*H*CH_2), 6.39 (obs, 1 H, NH), 6.18 (d, J = 1.5 Hz, 1 H, C*H*C≡C), 5.90 (d, J = 9.5 Hz, 1 H, C*H*=CH), 5.82 (dd, J = 9.5, 1.7 Hz, 1 H, C*H*=CH), 5.73 (d, J = 3.5 Hz, 1 H, E-1), 5.71 (d, J = 1.4 Hz, 1 H, D-1), 5.13 (dd, J = 10.1, 1.5 Hz, 1 H, B-1), 4.51 (d, J = 7.7 Hz, 1 H, A-1), 4.46 (m, 1 H, D-2), 4.27 (m, 1 H, B-3), 4.17 (dq, J = 9.5, 6.2 Hz, 1 H, D-5), 4.02 (dq, J = 10.9, 6.2 Hz, 1 H, B-5), 3.96 (m, 1 H), 3.86 (s, 3 H, CH_3O), 3.83–3.80 (obs, 1 H), 3.81 (s, 3 H, CH_3O), 3.76 (obs, 1 H, CH_2CH=C), 3.74–3.68 (m, 7 H, A-5, B-4, E-5, CH_3O, C*H*O), 3.65–3.58 (m, 2 H, A-2, E-5), 3.62 (dd, J = 9.5, 9.5 Hz, 1 H, D-4), 3.55 (s, 3 H, CH_3O), 3.45 (m, 1 H, E-3), 3.31 (b d, 1 H, A-4), 2.96 (AB q, J = 16.8 Hz, $\Delta\nu$ = 191 Hz, 2 H, CH_2), 2.68 (b m, 1 H, CH_2N), 2.61 (m, 1 H, E-4), 2.48 (s, 3 H, SSSCH_3), 2.48 (obs, 1 H, CH_2N), 2.33 (s, 3 H, ArCH_3), 2.32 (obs, 1 H, E-2$_{eq}$), 2.02 (m, 1 H, B-2$_{eq}$), 1.73 (m, 1 H, B-2$_{ax}$), 1.45 (m, 1 H, E-2$_{ax}$), 1.39 (d, J = 6.5 Hz, 3 H, A-6), 1.35 (d, J = 6.2 Hz, 3 H, B-6), 1.28 (d, J = 6.2 Hz, 3 H, D-6), 1.16 (t, J = 7.1 Hz, 3 H, CH_3CH_2N); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.5, 192.0, 151.5, 150.6, 143.0, 133.4, 130.3, 128.3, 126.5, 124.8, 123.2, 102.5, 101.2, 101.1, 99.5, 97.0, 93.5, 88.0, 82.8, 80.8, 75.6, 75.1, 72.1, 71.4, 71.1, 70.4, 68.9, 68.3, 67.0, 66.3, 61.7, 61.3, 60.9, 57.2, 56.3, 54.5, 52.9, 51.7, 42.4, 39.4, 37.0, 34.1, 31.9, 29.7, 27.2, 25.3, 22.7, 18.9, 17.6, 17.2, 14.4; HRMS (FAB) calcd for $C_{55}H_{74}IN_3O_{21}S_4Cs$ (M + Cs) 1500.1797, found 1500.1706.

Acknowledgment. We express our many thanks to Drs. Robert Babine, May Lee, George Ellestad, and Donald Borders of the Lederle group for originally bringing this fascinating molecule to our attention in 1986, for continuous discussions during the period of this project, and for a generous sample of calicheamicin γ_1^I. Our thanks are also due to Drs. Gary Siuzdak, Dee H. Huang, and Raj Chadha of The Scripps Research Institute for mass spectroscopic, NMR spectroscopic, and X-ray crystallographic assistance, respectively. This work was financially supported through a NATO (SERC, U.K.) fellowship (to A.L.S.), through a visiting scientist fellowship from Toray Co., Japan (to K.S.), through a visiting scientist fellowship from Takeda Co., Japan (to H.M.), through an Alexander von Humboldt Fellowship (to K.-U.B.), and by the National Institutes of Health (U.S.A.), The Scripps Research Institute, University of California, San Diego, Merck Sharp and Dohme, Schering Plough, Lederle Laboratories, and Pfizer Co.