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Enantiospecific Synthesis of a Protected Equivalent of APTO, the β-Amino Acid Fragment of Microsclerodermins C and D, by Aziridino-γ-lactone Methodology

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Dedicated to the memory of Christian Marazano[†]

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The efficient synthesis of a protected form of (2*S*,3*R*,4*S*,5*S*,7*E*)-3-amino-8-phenyl-2,4,5-trihydroxyoct-7-enoic acid (APTO), the α-hydroxy β-amino acid component of microsclerodermins C and D, 23-membered cyclic peptides isolated from lithistid sponges, is described. The strategy is based on the preparation of the aziridino-γ-lactone **46** from L-gulose by a procedure previously developed in our laboratory for simpler substrates. Regioselective opening of the aziridine at C-2 by acetate anion, an intrinsic reactivity pattern of aziridino-γ-lactones, followed by a Heck reaction to install the terminal phenyl group, provides lactone **48**. This, a lactonized form of APTO, can be considered an activated building block for the synthesis of microsclerodermins C and D or their analogues, as demonstrated by its subsequent reaction with a benzylamine to give the carboxamide **51**. This represents the first example of the use of an aziridino-γ-lactone for the stereoselective synthesis of an α-substituted β-amino acid derivative.

Introduction

Lithistid sponges, found mainly in the waters of New Caledonia and the Philippines, are a source of a wide array of well-known bioactive metabolites, such as discodermolide, acetogenins, and swinholide.[1] Another family of metabolites, the microsclerodermins, has been isolated from these sponges by Faulkner and co-workers and is receiving increasing attention. The nine members of this family (microsclerodermins A–I) each contain a 23-membered cyclic peptide structure composed of six different amino acids.[2] Common to all the microsclerodermins so far identified are the amino acids glycine, *N*-methylglycine, and (3*R*)-4-amino-3-hydroxybutyric acid (GABOB). Structural differences originate from the presence of variously substituted tryptophan and 3-aminopyrrolidone derivatives, as well as a complex 3-amino-2,4,5-trihydroxy acid unit attached to an unsaturated hydrocarbon chain terminating in an aryl moiety. The last of these has been identified as (2*S*,3*R*,4*S*,5*S*,7*E*)-3-amino-2,4,5-trihydroxy-8-phenyloct-7-enoic acid (APTO, **3**) in the case of microsclerodermins C and D (Figure 1, **1** and **2**, respectively).

The structural complexity of the microsclerodermins, as well as their significant antifungal and cytotoxic activities, have spurred efforts to develop synthetic routes to these molecules. So far, only one total synthesis, that of microsclerodermin E, has been reported.[3] In that study, Zhu and Ma prepared a protected and reduced (terminal hydroxy group) form of (2*S*,3*R*,4*S*,5*S*,7*E*,9*E*)-3-amino-10-(4-ethoxyphenyl)-2,4,5-trihydroxydeca-7,9-dienoic acid (AETD, **4**) in 16 steps and 10% overall yield starting from γ-gluconolactone.

Shioiri and co-workers[4] have synthesized four constituent building blocks of microsclerodermins A and B, one of which was the protected trihydroxy β-amino acid (2*S*,3*R*,4*S*,5*S*,6*S*,11*E*)-3-amino-2,4,5-trihydroxy-12-(4-methoxyphenyl)-6-methyldodec-11-enoic acid (AMMTD, **5**) prepared in over 30 steps starting from methyl (*R*)-3-*O*-TBDPS-2-methylpropionate. These authors have not reported the assembly of these fragments into microsclerodermins A and B. Chandrasekhar and Sultana[5] have also described the synthesis of a reduced form of protected AMMTD in 27 steps starting from (–)-(*S*)-citronellol, in which the hydroxy groups were introduced by iterative ster-

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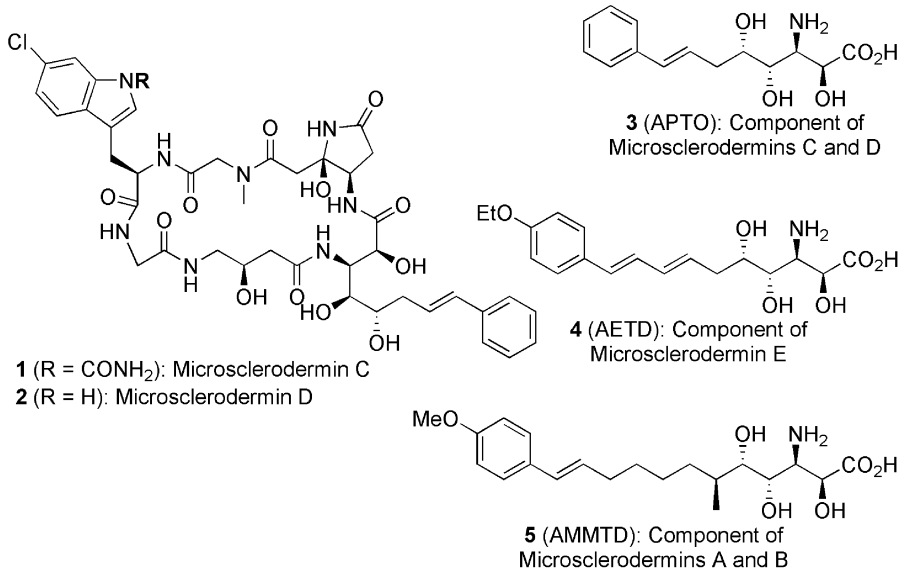
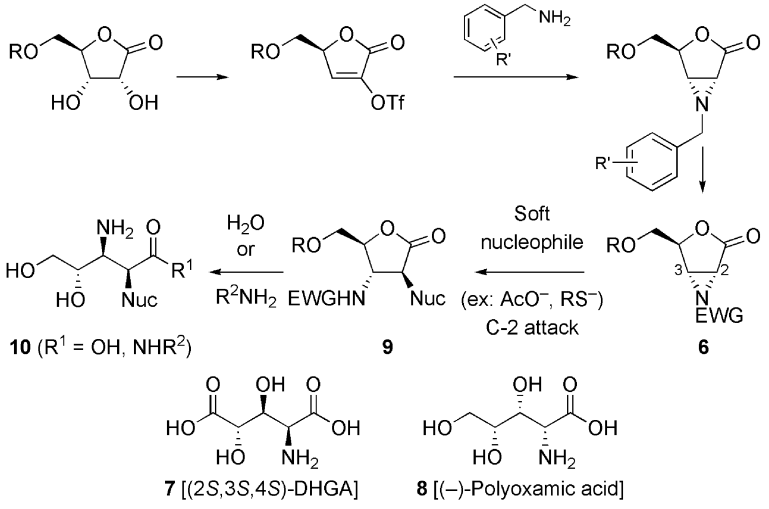


Figure 1. Microsclerodermins C and D and β-amino acid components.

eoselective dihydroxylations. Preparations of both protected APTO and AETD in 12 steps were recently reported by McLeod and co-workers,[6] in this case with the use of successive aminohydroxylation and dihydroxylation reactions to introduce these functional groups with the correct stereochemistry. Finally, Aitken and co-workers have developed a five-step synthesis of APTO and AETD by a two-carbon homologation of chiral sulfinimines derived from 2-deoxy-D-ribose acetonide.[7]

Here we wish to report the use of aziridino-γ-lactones for the enantiospecific synthesis of a protected lactone form of APTO that can be used directly for subsequent peptide synthesis. We have previously demonstrated that stereochemically pure and synthetically useful aziridino-γ-lactones (**6**, Scheme 1) can be easily and efficiently prepared in three steps starting from 5-*O*-protected ribonolactones by triflation of the diol, followed by Michael-type addition of a benzylamine and replacement of the benzyl moiety by an electron-withdrawing group.[8] A key feature of this strategy is the diastereoselectivity of the addition, which is governed by the chirality at C-4. The usefulness of aziridino-γ-lactones for the preparation of naturally occurring non-proteinogenic α-amino acid derivatives is attested by our recent syntheses of (2*S*,3*S*,4*S*)-dihydroxyglutamic acid (DHGA, **7**) [9] and (–)-polyoxamic acid (**8**).[10] These syntheses were made possible by the propensity of aziridino-γ-lactones to react with hard nucleophiles (i.e., alcohols) exclusively at C-3. In contrast, soft nucleophiles such as thiols and acetate react regioselectively at C-2, thereby giving access to 2-substituted 3-aminobutyrolactones **9**.[11] Such compounds can be regarded (after lactone hydrolysis) as protected and activated forms of α-substituted β-amino acids (**10**, R^1 = OH). Alternatively, opening of the lactone by the amine function of an amino acid or a peptide would give access to the corresponding α-substituted β-amino carboxamides (**10**, R^1 = NHR^2). We thus decided to exploit this property of azirid-

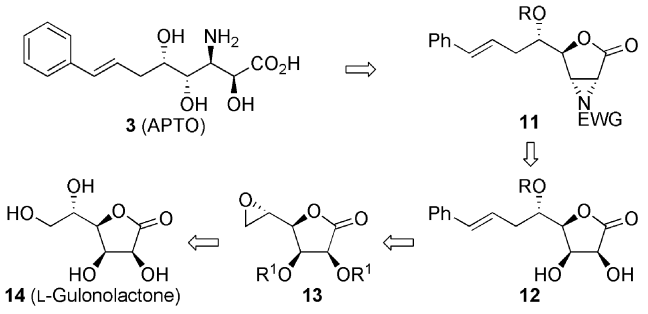


Scheme 1. Previous results.

ino-γ-lactones to synthesize an optically pure α-substituted β-amino acid derivative for the first time. In particular, the preparation of a protected and activated form of APTO suitable for eventual use in the total synthesis of microsclerodermins C and D was targeted.

Results and Discussion

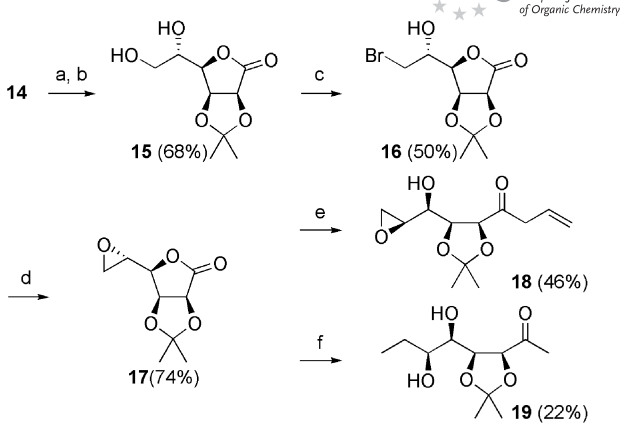
We first envisaged that APTO (**3**) should be accessible from an aziridino-γ-lactone of general structure **11** by regioselective opening of the aziridine at C-2 by acetate, lactone hydrolysis, and deprotection (Scheme 2). Aziridino-γ-lactone **11** should in turn be preparable by our chemistry from the starting protected dihydroxybutyrolactone **12** (the stereochemistry at C-2 and C-3 being unimportant) incorporating the required 1-hydroxy-4-phenylprop-3-enyl chain at C-4. This chain should be introducible by opening of the C-5–C-6 epoxide **13** by a vinylmetal reagent, followed by Heck arylation. From this analysis, commercially available L-gulonolactone (**14**) appeared to be an appropriate starting material for the preparation of epoxide **13** with the correct configuration at C-4 and C-5.



Scheme 2. First synthetic strategy.

In our initial approach, the key C-5–C-6 epoxide **17** was prepared by first protecting the hydroxy groups of L-gulonolactone (**14**) as the diacetonide, followed by selective deprotection of the C-5 and C-6 hydroxy groups with aqueous acetic acid to give the monoacetonide **15** (Scheme 3).[12] Treatment of **15** with carbon tetrabromide and triphenylphosphane in THF provided the C-6 bromo derivative **16** in 50% yield, and this was cyclized to provide the epoxide **17** by use of cesium fluoride in acetone at reflux.[13] In their synthetic route to (–)-muracaticin, Depezay and coworkers[14] had reported the preparation of the 2,3-dideoxy analogue of epoxide **17** and the regioselective opening of the epoxide ring with excess cuprate generated from undecanylmagnesium chloride and $LiCuCl_4$.

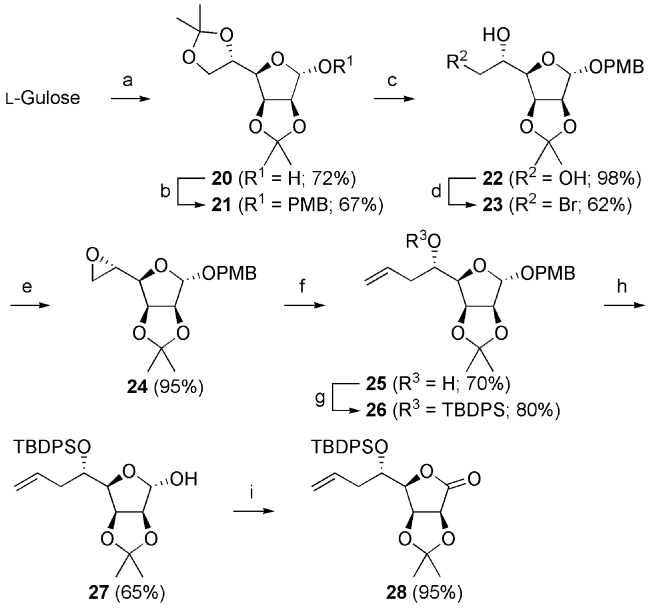
In model experiments, epoxide **17** was then treated in THF at –78 °C with the cuprate generated from allylmagnesium bromide and $LiCuCl_4$. However, in contrast to the result obtained with the 2,3-dideoxy analogue, only the product of lactone opening, compound **18**, was obtained. Similarly, use of CuI to generate the cuprate of methyllithium led to opening both of the epoxide and of the lactone to give the oxo diol **19**, though in low yield (22%), with no trace of the product only of epoxide opening.



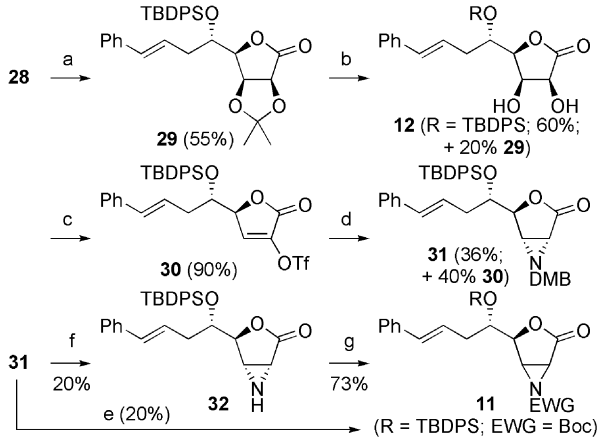
Scheme 3. Preparation and reactivity of epoxide **17**. Reagents and conditions: (a) 2,2-dimethoxypropane, TsOH, acetone, room temp., 36 h; (b) AcOH/H_2O (7:1), 30 °C, 16 h; (c) CBr_4, PPh_3, THF, 0 °C, 2 h then room temp., 10 h; (d) CsF, acetone, reflux, 5 h; (e) allylmagnesium bromide, $LiCuCl_4$ (0.3 equiv.), THF, –35 °C, 30 min, then addition of **17** at –78 °C, 10 min; (f) MeLi, CuI (0.5 equiv.), Et_2O, 0 °C, 15 min, then addition of **17** in THF, 0 °C, 1 h.

Because selective epoxide opening of **17** by an organocuprate seemed compromised at this point, we decided to avoid this competitive lactone opening by using L-gulose as starting material, at the expense of additional protection/deprotection/oxidation steps at the anomeric center. L-Gulose diacetonide **20** was thus prepared,[15] and the product was converted into the *p*-methoxybenzyl (PMB) glycoside **21** (Scheme 4). Selective deprotection of the 5,6-diol with aqueous acetic acid gave **22**, which was transformed first into the C-6 bromide **23** and then into the epoxide **24** under the same conditions as previously. The epoxide **24** now cleanly reacted with the cuprate generated in situ from vinylmagnesium bromide and catalytic copper iodide to give the epoxide-opening product **25** regioselectively and in 70% yield. The resulting secondary hydroxy function was protected with a *tert*-butyldiphenylsilyl group to give **26**. Treatment of glycoside **26** with DDQ in dichloromethane/water (10:1) at room temperature efficiently removed the PMB group,[16,17] and the resulting compound **27** was oxidized with TPAP in acetonitrile in the presence of NMO[11b–11d,18] to give lactone **28** in 95% yield.

With lactone **28** to hand, several options were open to us for the subsequent synthetic route to APTO, notably with respect to the order of introduction of the terminal phenyl moiety and the C-2 acetate (through opening of the 2,3-aziridino-γ-lactone prepared by our methodology). We first explored the viability of initially introducing the phenyl group. As shown in Scheme 5, Heck coupling[19] between iodobenzene and the olefinic lactone **28** was found to proceed reasonably well, the expected product **29** being isolated in 55% yield. From this compound, preparation of the aziridino-γ-lactone **31** was achieved by first removing the 2,3-di-*O*-isopropylidene group. This proved to be particularly delicate, because all the classical hydrolytic conditions[20] gave only very low yields of the desired diol, sometimes with, but more often without, recovery of starting material. Finally, the most satisfactory conditions found required



Scheme 4. Preparation of lactone **28**. Reagents and conditions: (a) 2,2-dimethoxypropane, TsOH, acetone, room temp., 36 h; (b) PMBCl, NaH, DMF, room temp., 2.5 h; (c) $AcOH/H_2O$ (4:1), 30 °C, 18 h; (d) CBr_4, PPh_3, THF, 0 °C to room temp., 10 h; (e) CsF, acetone, reflux, 6 h; (f) vinylmagnesium bromide, CuI (0.3 equiv.), THF, –25 °C to room temp., 2 h; (g) TBDPSCl, imidazole, DMF, 0 °C to room temp., 22 h; (h) DDQ, CH_2Cl_2/H_2O (10:1), room temp., 20 h; (i) TPAP, NMO, CH_3CN, room temp., 3 h.

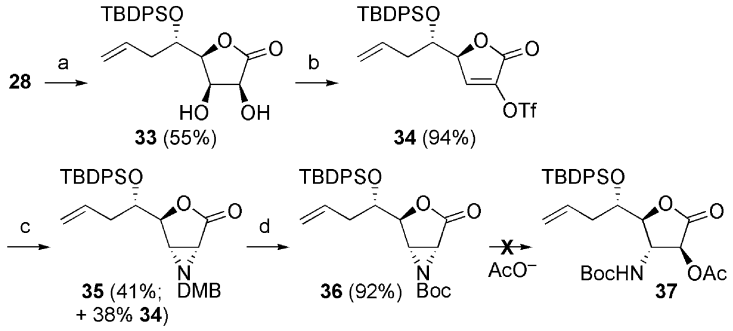


Scheme 5. Preparation of aziridino-γ-lactone **11**. Reagents and conditions: (a) $Pd(OAc)_2$ (0.05 equiv.), PPh_3 (0.1 equiv.), Et_3N (1.3 equiv.), PhI (1.3 equiv.), DMF, 110 °C, 20 h; (b) $AcOH/H_2O$ (4:1), Dean–Stark, 85 °C, 24 h; (c) Tf_2O, pyridine, CH_2Cl_2, –78 °C to 0 °C, 4 h; (d) DMB-NH_2, DMF, –60 °C, 30 min; (e) DDQ, CH_2Cl_2/H_2O (10:1), room temp., 24 h, then Boc_2O (5 equiv.), DMAP (0.2 equiv.), Et_3N (10 equiv.), CH_3CN, room temp., 48 h; (f) CAN, CH_3CN/H_2O (5:1), room temp., 2 h; (g) Boc_2O (5 equiv.), DMAP (0.2 equiv.), Et_3N (10 equiv.), CH_3CN, room temp., 1.5 h.

heating of a solution of **29** in 80% acetic acid at 85 °C for 24 h with continual removal of water by use of a Dean–Stark apparatus. This afforded diol **12** in 60% yield and recovery of 20% of the starting acetonide. Longer reaction times resulted in lower yields both of the diol and of recovered starting material. Diol **12** was next transformed into the monotriflate **30** in 90% yield by treatment, first at –78 °C and then at 0 °C, with 2.7 equiv. of triflic anhydride in the presence of pyridine in dichloromethane.[8,10] Treatment of triflate **30** with a very slight excess of 3,4-dimethoxybenzylamine[8,10] at –60 °C for 30 min provided aziridino-γ-lactone **31** in only 36% yield, although 40% of the starting material was recovered and could be recycled. Attempts to drive the reaction to completion (i.e., by increasing reaction times, temperature, or equivalents of DMB-amine) led in all cases to concomitant and irreversible opening of the lactone ring by the amine (vide infra). The ^1H NMR spectrum of compound **31** displayed resonances for 3-H and 2-H at δ = 2.54 and 2.63 ppm, respectively, characteristic of *N*-alkylaziridino-γ-lactones.[8]

As demonstrated previously, efficient and regioselective opening of the aziridine ring of an aziridino-γ-lactone is best achieved when the aziridine nitrogen atom is protected by an electron-withdrawing group.[11] We thus proceeded to convert the *N*-DMB derivative **31** into its *N*-Boc analogue **11** by our previously described one-pot procedure.[10,23] Compound **31** was first treated with 1 equiv. of DDQ at room temperature in a dichloromethane/water (10:1) mixture over 24 h.[10,17,24] Excess Boc anhydride and triethylamine were then added to the reaction mixture, together with a catalytic amount of DMAP. After 48 h at room temperature, the expected *N*-Boc aziridine **11** was obtained, but in only 20% yield and accompanied by many unidentified by-products, with no starting material remaining. Because modification of the reaction conditions had no beneficial effects on the yield of **11**, we decided to isolate the intermediate deprotected amine in order to determine which step posed a problem. Treatment of the *N*-DMB derivative **31** with DDQ under the same conditions as before allowed isolation of amine **32** in less than 20% yield, but the product was very difficult to purify. On the other hand, use of ceric ammonium nitrate (CAN)[17,24] instead of DDQ for the oxidative cleavage facilitated isolation of the product by chromatography on silica gel, although the yield of *N*-deprotected aziridine **32** was again in the 20% range. Because the free NH function of aziridine **32** could subsequently be transformed to give the *N*-Boc derivative **11** in high yield (73%), we concluded that inefficient removal of the DMB group was responsible for the low overall yield of the two-step process.

As a result, and suspecting that the styrene moiety of compound **31** may interfere with the intermediates formed during the cleavage of the DMB group with DDQ or CAN, we decided to investigate our second synthetic option: that is, installation of the phenyl moiety *after* formation and opening of the aziridine. The acetonide protecting group of compound **28** was thus removed with acetic acid/water as before to afford diol **33** in 55% yield (Scheme 6). Treatment of this with 2.2 equiv. of triflic anhydride and pyridine in dichloromethane provided the expected monotriflate **34** in 94% yield, and this was then treated with DMB-amine in DMF at –60 °C to give aziridino-γ-lactone **35** in 41% yield, with 38% of the starting material being recovered after



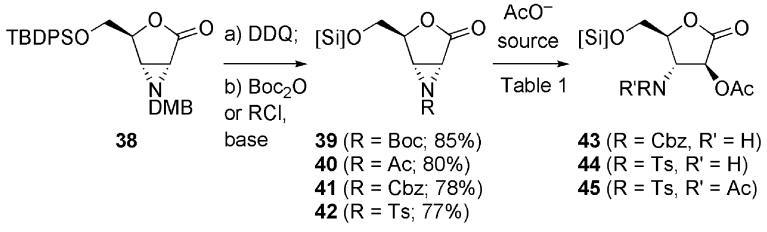
Scheme 6. Preparation and reactivity of aziridino-γ-lactone **36**. Reagents and conditions: (a) $AcOH/H_2O$ (4:1), Dean–Stark, 85 °C, 24 h; (b) Tf_2O, pyridine, CH_2Cl_2, –78 °C to –25 °C, 3 h; (c) DMB-NH_2, DMF, –60 °C, 30 min; (d) DDQ, CH_2Cl_2/H_2O (10:1), room temp., 24 h, then Boc_2O, DMAP, Et_3N, room temp., 24 h.

chromatography of the reaction mixture. The DMB group of **35** was then removed with DDQ in dichloromethane/water (10:1), and the resulting free amine was immediately protected by addition of Boc anhydride, triethylamine, and a catalytic amount of DMAP directly to the reaction mixture. The *N*-Boc-aziridino-γ-lactone **36** was thus obtained with an excellent yield of 92% from **35**, thereby corroborating the hypothesis that the poor yields of **11** obtained from derivative **31** by the same series of operations (Scheme 5) were indeed due to the presence of the terminal phenyl group in **31**. In its ^1H NMR spectrum, compound **36** displayed a downfield shift of the 2-H and 3-H resonances to δ = 3.30 and 3.25 ppm relative to the *N*-alkylaziridine-γ-lactones, again typical of their *N*-carbamoyl analogues.[11]

We then investigated the critical opening of the aziridine ring of **36** with an acetate anion source, which from our previous work with analogous but simpler systems was expected to occur regioselectively at C-2 to give **37**.[11b] However, treatment of **36** with acetic acid, potassium acetate, or cesium acetate in a variety of solvents and at various temperatures led only to degradation of the starting material and formation of a multitude of products that were not identified.

It thus seemed advisable at this point to optimize the aziridine ring-opening on a model aziridino-γ-lactone, in which the *N*-protecting/activating group could be easily varied. For this purpose, the 5-*O*-TBDPS-aziridino-γ-lactone **38**, the preparation of which we have previously reported,[10,23] seemed particularly suitable, this substrate differing from **35** only by the absence of the terminal allyl group. Compound **38** was thus easily transformed into the *N*-Boc, *N*-acetyl, *N*-Cbz,[10] and *N*-tosyl derivatives **39**–**42**, respectively, by treatment with DDQ, followed in the same pot with the appropriate acylating or sulfonylating agent (Scheme 7).

Each of these four aziridino-γ-lactones was then treated with different sources of acetate anion. In the case of *N*-Boc derivative **39**, treatment with excess acetic acid in chloroform in the presence of boron trifluoride–diethyl ether at room temperature gave no ring-opened product (Table 1, Entry 1), whereas heating of the reaction mixture at 50 °C for 24 h led only to degradation products (Entry 2). The same observations were made when potassium acetate or cesium acetate in DMF were used to effect aziridine ring opening (Entries 3 and 4). These results obtained with the model *N*-Boc-protected aziridino-γ-lactone **39** are thus similar to those seen with the APTO precursor **36**. Although the *N*-acetyl derivative **40** also proved to be unsatisfactory with cesium acetate (Entry 5), better results were obtained with the *N*-Cbz derivative **41**. In this case, both acetic acid in the presence of boron trifluoride–diethyl ether at 50 °C and cesium acetate in DMF, also at 50 °C, gave the desired C-2 acetate derivative **43** in 48% and 42% yields, respectively (Entries 6 and 7). Finally, the best results were obtained with *N*-tosylaziridine **42**. In this case, efficient aziridine opening could be achieved at room temperature with cesium acetate in DMF to give **44** in 49% yield (Entry 8). The expected regioselective opening of the aziridine ring by acetate at C-2 was clearly indicated by the COSY and HMBC NMR spectra of **44**.[25] Interestingly, with a procedure recently described by Fan and Hou,[26] treatment of **42** with tri-*n*-butylphosphane and acetic anhydride led both to regioselective opening of the aziridine ring and to acetylation of the amine, providing **45** in 58% yield (Entry 9).



Scheme 7. Preparation and reactivity of aziridino-γ-lactones **39**–**42**.

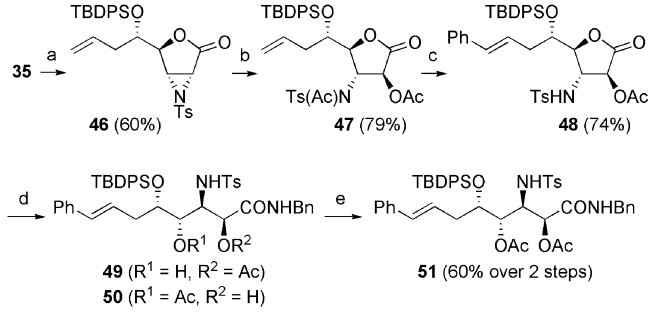
Table 1. Nucleophilic opening of aziridino-γ-lactones **39**–**42** by a variety of acetate anion sources.

Entry	Compound	Conditions	Results[a]
1	**39**	AcOH (5 equiv.), $CHCl_3$, $BF_3{\cdot}OEt_2$, room temp.,15 h	–[b]
2	**39**	AcOH/$CHCl_3$ (1:1), $BF_3{\cdot}OEt_2$, 50 °C, 24 h	–[c]
3	**39**	AcOK, DMF, room temp. to 90 °C	–[c]
4	**39**	AcOCs (5 equiv.), DMF, 50 °C	–[c]
5	**40**	AcOCs, DMF, 50 °C, 2 h	–[c]
6	**41**	AcOH/$CHCl_3$, $BF_3{\cdot}OEt_2$, 50 °C, 20 h	**43** (48%)
7	**41**	AcOCs, DMF, 50 °C, 2 h	**43** (42%)
8	**42**	AcOCs, DMF, room temp., 2 h	**44** (49%)
9	**42**	PBu_3 (0.2 equiv.), Ac_2O (3 equiv.), toluene, 110 °C, 2 h	**45** (58%)
10	**42**	PBu_3 (0.2 equiv.), Ac_2O (3 equiv.), microwaves, toluene, 130 °C, 30 min	**45** (72%)

[a] Values in parentheses are for isolated yields. [b] No reaction. [c] Degradation of starting materials.

When the same reaction was performed under microwave irradiation conditions, compound **45** was obtained in an optimal yield of 72% (Entry 10).

Because the *N*-tosylaziridine derivative **42** had given the best results in these model studies, the *N*-tosylaziridino-γ-lactone **46** was prepared by sequential treatment of the *N*-DMB precursor **35** with DDQ and tosyl chloride (Scheme 8). Treatment of **46** with 20 mol-% tri-*n*-butylphosphane and excess acetic anhydride in toluene under microwave irradiation conditions then afforded the 2-*O*-acetyl-3-*N*-acetyl-3-*N*-tosyl derivative **47** in 79% yield. Regioselective opening of the aziridine at C-2 was clearly indicated by the COSY ^{1}H NMR spectra of **47** (see Supporting Information).



Scheme 8. Preparation of the protected equivalent of APTO **51**. Reagents and conditions: (a) DDQ, CH_2Cl_2/H_2O (10:1), room temp., 20 h, then TsCl, pyridine, room temp., 2 h; (b) PBu_3 (0.2 equiv.), Ac_2O (3 equiv.), microwaves, toluene, 90 °C, 2 h; (c) $Pd(OAc)_2$ (0.1 equiv.), PPh_3 (0.2 equiv.), Et_3N (5 equiv.), PhI (1.3 equiv.), DMF, 110 °C, 24 h; (d) $BnNH_2$, THF, room temp., 2 h; (e) Ac_2O, pyridine, 0 °C to room temp., 18 h.

Finally, installation of the terminal phenyl moiety on compound **47** by means of a Heck reaction was studied. Whereas use of iodobenzene with 1 equiv. of triethylamine afforded the desired styrene derivative as a mixture of *N*-acetylated and *N*-deacetylated products, use of excess triethylamine (5 equiv.) ensured complete removal of the *N*-acetyl group to give lactone **48** in 74% yield. Compound **48** is a protected form of APTO that can be used directly for the formation of a carboxamide (e.g., peptide) bond as suggested by the following result. Treatment of **48** with benzylamine in THF at room temperature over 2 h provided a mixture of *N*-benzylcarboxamides **49** and **50** resulting from scrambling of the acetate group between the C-2 and C-4 hydroxy groups. Treatment of the mixture with acetic anhydride in pyridine then gave the diacetate **51** in 60% yield over the two steps. This thus represents the synthesis of a protected form of APTO that can be employed directly for the subsequent total synthesis of microsclerodermins C and D.

Conclusions

Here we report the first use of an aziridino-γ-lactone for the enantiospecific synthesis of an α-substituted β-amino acid derivative. From the gulonolactone derivative **33**, easily obtained from L-gulose by standard chemical transformations, the aziridino-γ-lactone **46** was efficiently prepared by a methodology previously developed by us for simpler substrates. From the known reactivity of aziridino-γ-lactones, conditions that allowed chemo- and regioselective opening of the aziridine at C-2 with acetate anion were found. The final product, lactone **48**, is a protected form of APTO, the α-hydroxy β-amino acid component of microsclerodermins C and D. As shown by its reaction with benzylamine to give APTO benzylamide, lactone **48** can be regarded as a convenient, activated building block for the eventual synthesis of microsclerodermins C and D or their analogues. This objective is presently being pursued by us.

Experimental Section

General Remarks: Melting points, measured in capillary tubes and recorded with a Büchi B-540 melting point apparatus, are uncorrected. IR spectra were recorded with a Perkin–Elmer Spectrum BX FT-IR spectrometer. Optical rotations were determined with a JASCO P-1010 polarimeter. ^{1}H and ^{13}C NMR spectra were recorded with Bruker spectrometers, namely Avance 300 and 500 (300 and 500 MHz, respectively). Chemical shifts (δ) are reported in parts per million (ppm) with reference to tetramethylsilane (TMS) as internal standard. NMR experiments were carried out in deuteriochloroform ($CDCl_3$) or in deuteriobenzene (C_6D_6). The following abbreviations are used for the ^{1}H multiplicities: s: singlet, d: doublet, t: triplet, q: quartet, m: multiplet. Coupling constants (J) are reported in Hertz (Hz). Mass spectra were obtained with an LCT (Micromass) instrument by electrospray ionization and with a time-of-flight analyzer (ESI-MS) for high-resolution mass spectra (HRMS). Thin-layer chromatography was performed on silica gel 60 plates with a fluorescent indicator and visualized under a UVP

Mineralight UVGL-58 lamp (254 nm) and with a solution of phosphomolybdic acid in ethanol (7%). Flash chromatography was performed with silica gel 60 (40–63 μm, 230–400 mesh ASTM) at medium pressure (200 mbar). All solvents were distilled and stored over molecular sieves (4 Å) before use. All reagents were obtained from commercial suppliers, unless otherwise stated. Organic extracts were, in general, dried with magnesium sulfate ($MgSO_4$) or sodium sulfate (Na_2SO_4). Elemental analyses were performed at the ICSN, CNRS, Gif-sur-Yvette, France.

5,6-Anhydro-2,3-*O*-isopropylidene-L-gulono-γ-lactone (17): Cesium fluoride (1.3 g, 8.54 mmol, 3 equiv., dried beforehand at 150 °C in vacuo overnight) was added to a solution of **16** (0.8 g, 2.85 mmol) in dry acetone (13 mL). The reaction mixture was heated at reflux for 5 h, active charcoal was added, the mixture was filtered, and the filtrate was concentrated to dryness under vacuum. The crude product was dissolved in hot chloroform. Active charcoal was again added, the mixture was filtered, and the solvent was evaporated in vacuo to give epoxide **17** (0.42 g, 2.1 mmol, 74%) as a white solid; R_f = 0.54 (EtOAc/heptane, 2:1). $[a]_D^{20}$ = +74 (c = 1.4, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 1.41 (s, 3 H, CH_3), 1.52 (s, 3 H, CH_3), 2.74 (dd, $J_{6,5}$ = 2.6, $J_{6,6}$ = 4.5 Hz, 1 H, 6-H), 2.96 (t, $J_{6',6}$ = $J_{6',5}$ = 4.5 Hz, 6′-H), 3.35 (m, 1 H, 5-H), 4.04 (m, 1 H, 4-H), 4.84 (m, 2 H, 2-H, 3-H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 25.7, 26.6 [C(CH_3)$_2$], 43.0 (C-6), 49.6 (C-5), 75.8, 76.3 (C-2, C-3), 80.9 (C-4), 114.7 [C(CH_3)$_2$], 173.1 (C=O, lactone) ppm. FTIR: $\tilde{\nu}$ = 2987, 1786 (C=O, lactone), 1379, 1197, 1114 cm^{-1}. HRMS (ESI$^+$): calcd. for [$C_9H_{12}O_5Na$ + MeOH]$^+$ 255.0845; found 255.0846.

Compound 18: Allylmagnesium bromide (0.58 mL, 1.16 mmol of a 2 M solution in THF) was added dropwise at –35 °C under argon to a solution of $LiCuCl_4$ [1.9 mL, 0.19 mmol of a 0.1 M solution in THF, prepared from a mixture of $CuCl_2$ (1 mol) and LiCl (2 mol)]. After 30 min of stirring at –35 °C, the reaction mixture was cooled to –78 °C, and a solution of epoxide **17** (77 mg, 0.39 mmol) in THF (5 mL) was added. The mixture was stirred at –78 °C for 10 min, quenched with saturated aqueous NH_4OAc, and extracted with diethyl ether (4 × 5 mL). The organic extracts were combined, washed with saturated aqueous NaCl, and dried with $MgSO_4$, and the solvents were evaporated under vacuum. The crude product was purified by flash chromatography on silica gel (heptane/EtOAc, 8:1) to furnish compound **18** (43 mg, 0.18 mmol, 46%) as a white solid; R_f = 0.5 (EtOAc/heptane, 4:3); m.p. 85–87 °C. $[a]_D^{20}$ = –26 (c = 1.11, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.33 (s, 3 H, CH_3), 1.51 (s, 3 H, CH_3), 2.50 (dd, $J_{7,8}$ = 8.8, $J_{7,7'}$ = 13.9 Hz, 1 H, 7-H), 2.64 (dd, $J_{1,2}$ = 2.7, $J_{1,1'}$ = 4.6 Hz, 1 H, 1-H), 2.72 (dd, $J_{7,8}$ = 5.8, $J_{7,7'}$ = 13.9 Hz, 1 H, 7′-H), 2.90 (t, $J_{1',1}$ = $J_{1',2}$ = 4.6 Hz, 1 H, 1′-H), 3.23 (m, 1 H, 2-H), 3.58 (dd, $J_{3,4}$ = 3.9, $J_{3,2}$ = 7.3 Hz, 1 H, 3-H), 4.48 (d, $J_{5,4}$ = 5.8 Hz, 1 H, 5-H), 4.81 (dd, $J_{4,3}$ = 3.9, $J_{4,5}$ = 5.8 Hz, 1 H, 4-H), 5.24 (m, 2 H, 9-H, 9′-H), 5.95 (m, 1 H, 8-H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 24.6, 25.9 [C(CH_3)$_2$], 39.6 (C-7), 43.6 (C-1), 49.8 (C-2), 81.0, 81.4 (C-3, C-4), 85.1 (C-5), 112.8 [C(CH_3)$_2$], 120.4 (C-9), 131.7 (C-8), 199.0 (C=O, ketone) ppm. FTIR: $\tilde{\nu}$ = 3412 (OH), 1735 (C=O, ketone), 1641 (C=C), 1376, 1211, 1101 cm^{-1}. ESI-MS: m/z = 225 [M + H – H_2O]$^+$, 243 [M + H]$^+$, 265 [M + Na]$^+$, 281 [M + K]$^+$.

Compound 19: MeLi (1.5 mL, 2.4 mmol, from a 1.6 M solution in diethyl ether) was added under argon at 0 °C to a suspension of CuI (229 mg, 1.2 mmol) in diethyl ether (1 mL). After the mixture had been stirred at 0 °C for 15 min, a solution of epoxide **17** (80 mg, 0.4 mmol) in THF (7 mL) was added dropwise, and stirring was continued at 0 °C for 1 h. The reaction was quenched with saturated aqueous NH_4Cl and the mixture extracted with diethyl ether (3 × 10 mL). The organic extracts were dried with $MgSO_4$ and filtered, and the solvents were evaporated to dryness under vacuum. The crude product was purified by flash chromatography on silica gel (heptane/EtOAc, 4:1) to furnish **19** (20 mg, 0.09 mmol, 22%) as a pale yellow oil; R_f = 0.40 (EtOAc/heptane, 2:1). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.01 (t, $J_{7,6}$ = 7.4 Hz, 3 H, 7-H), 1.42, 1.44 [2 × s, 6 H, C(CH_3)$_2$], 1.57 (m, 2 H, 6-H, 6′-H), 3.38 (m, 1 H, 5-H), 3.85 [s, 3 H, C(O)CH_3], 4.10 (dd, $J_{4,5}$ = 2.9, $J_{4,3}$ = 7.7 Hz, 1 H, 4-H), 4.24 (dd, $J_{3,2}$ = 4.2, $J_{3,4}$ = 7.7 Hz, 1 H, 3-H), 4.37 (m, 1 H, 2-H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 10.2 (C-7), 27.0, 27.3 [C(CH_3)$_2$], 27.6 (C-6), 52.8 ($COCH_3$), 71.1 (C-2), 71.8 (C-5), 78.4 (C-3), 79.3 (C-4), 109.9 [C(CH_3)$_2$], 172.5 (C=O, lactone) ppm. FTIR: $\tilde{\nu}$ = 3445 (OH), 2931, 1742 (C=O, ketone), 1215, 1074 cm^{-1}. ESI-MS: m/z = 255 [M + Na]$^+$, 271 [M + K]$^+$, 287 [M + Na + MeOH]$^+$.

2,3:5,6-Di-*O*-isopropylidene-1-*O*-(4-methoxybenzyl)-L-gulose (21): A solution of lactol **20** (3.08 g, 11.8 mmol) in DMF (30 mL) was added at room temperature under argon to a suspension of NaH (0.94 mg, 23.7 mmol) in anhydrous DMF (30 mL). After 3 h of stirring, the reaction was quenched by slow addition of water. The mixture was extracted with CH_2Cl_2 (3 × 25 mL), the organic extracts were combined and dried with $MgSO_4$, and the solvents were evaporated to dryness under vacuum. The crude product was purified by flash chromatography on silica gel (heptane/EtOAc, 5:1) to afford compound **21** (3.01 g, 7.9 mmol, 67%) as a pasty white solid; R_f = 0.70 (EtOAc/heptane 1:1). $[a]_D^{20}$ = +52 (c = 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.27, 1.41, 1.45, 1.48 [s, 12 H, 2 × C(CH_3)$_2$], 3.72 (m, 1 H, 6-H), 3.80 (s, 3 H, OCH_3), 3.99 (dd, $J_{4,3}$ = 3.2, $J_{4,5}$ = 8.4 Hz, 1 H, 4-H), 4.22 (m, 1 H, 6′-H), 4.40 (m, 1 H, 5-H), 4.45 (d, J = 11.7 Hz, 1 H, OCH_2Ar), 4.64 (m, 2 H, 2-H, 3-H), 4.69 (d, J = 11.7 Hz, 1 H, OCH_2Ar), 5.17 (s, 1 H, 1-H), 6.87 (d, 2 H, 2′-H, 6′-H), 7.25 (d, J = 7.4 Hz, 2-H, 3′-H, 5′-H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 24.7, 25.4, 25.9, 26.8 [C(CH_3)$_2$], 55.2 (OCH_3), 66.0 (C-6), 68.8 (OCH_2Ar), 75.6 (C-5), 79.8 (C-3), 82.1 (C-4), 85.1 (C-2), 105.4 (C-1), 109.7, 112.8 [C(CH_3)$_2$], 113.8 (C-2′, C-6′), 129.4 (C-1′), 129.7 (C-3′, C-5′), 159.3 (C-4′) ppm. FTIR: $\tilde{\nu}$ = 2987, 2937, 1613 (C=C), 1514, 1374, 1249, 1084, 1011, 848 cm^{-1}. ESI-MS: m/z = 403 [M + Na]$^+$. $C_{20}H_{28}O_7$ (380.18): calcd. C 63.14, H 7.42; found C 62.77, H 7.54.

2,3-*O*-Isopropylidene-1-*O*-(4-methoxybenzyl)-L-gulose (22): Compound **21** (2.99 g, 7.9 mmol) was dissolved in a mixture of acetic acid/H_2O (4:1, 20 mL), and the mixture was stirred at 30 °C for 18 h. The solution was concentrated to dryness under vacuum. To remove traces of acetic acid, the resulting oil was dissolved in n-butanol (35 mL) and toluene (35 mL), and the solvents were again removed in vacuo to furnish diol **22** (2.61 g, 7.7 mmol, 98%) as a white solid, homogeneous by TLC. For analytical purposes, an aliquot of the crude product was purified by flash chromatography on silica gel (heptane/EtOAc, 1:1); R_f = 0.10 (EtOAc/heptane, 1:1); m.p. 119–125 °C (decomp.). $[a]_D^{20}$ = +80 (c = 1.11, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.29, 1.46 [s, 6 H, 2 × C(CH_3)$_2$], 2.08 (t, J = 6.3 Hz, 1 H, OH), 3.64 (t, J = 6.3 Hz, 1 H, OH), 3.74 (d, $J_{6,5}$ = $J_{6',5}$ = 4.8 Hz, 2 H, 6-H, 6′-H), 3.79 (s, 3 H, OCH_3), 4.00 (dd, $J_{4,3}$ = 3.6, $J_{4,5}$ = 5.3 Hz, 1 H, 4-H), 4.12 (m, 1 H, 5-H), 4.51 (2 × d, J = 11.5 Hz, 2 H, OCH_2Ar), 4.30 (d, $J_{2,3}$ = 5.9 Hz, 1 H, 2-H), 4.76 (dd, $J_{3,4}$ = 3.6, $J_{3,2}$ = 5.9 Hz, 1 H, 3-H), 5.13 (s, 1 H, 1-H), 6.87 (d, J = 8.0 Hz, 2 H, H arom), 7.24 (d, J = 8.0 Hz, 2 H, H arom) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 24.3, 25.8 [C(CH_3)$_2$], 55.2 (OCH_3), 63.5 (C-6), 68.8 (OCH_2Ar), 70.6 (C-5), 79.1 (C-4), 80.3 (C-3), 85.3 (C-2), 104.9 (C-1), 112.7 [C(CH_3)$_2$], 113.8 (C-2′, C-6′), 129.2 (C-1′), 129.7 (C-3′, C-5′), 159.3 (C-4′) ppm. FTIR: $\tilde{\nu}$ = 3500, 3350 (OH), 2931, 1612 (C=C), 1514, 1376, 1249, 1081, 1009, 820 cm^{-1}. ESI-MS: m/z = 363 [M + Na]$^+$, 379

$[M + K]^+$. $C_{17}H_{24}O_7$ (340.15): calcd. C 59.99, H 7.11, O 32.90; found C 59.82, H 7.27, O 33.18.

6-Bromo-6-deoxy-2,3-*O*-isopropylidene-1-*O*-(4-methoxybenzyl)-L-gulose (23): Triphenylphosphane (2.53 g, 9.9 mmol) and carbon tetrabromide (2.52 g, 7.6 mmol) were added at 0 °C under argon to a solution of diol **22** (2.58 g, 7.6 mmol) in THF (25 mL). The reaction mixture was allowed to come to room temperature over 2 h, and stirring was continued for 10 h. The mixture was diluted with diethyl ether (25 mL) and filtered, and the solvents were evaporated to dryness. The crude product was purified by flash chromatography on silica gel (heptane/EtOAc, 5:1) to afford the product **23** (1.9 g, 2.2 mmol, 62%) as a colorless oil; R_f = 0.60 (EtOAc/heptane 1:1). $[\alpha]_D^{20}$ = +63 (c = 0.9, $CHCl_3$). ^1H NMR ($CDCl_3$, 250 MHz): δ = 1.30, 1.47 [s, 6 H, 2×C(CH_3)$_2$], 3.22 (d, $J_{OH,5}$ = 2.7 Hz, 1 H, OH), 3.62 (d, $J_{6,5}$ = $J_{6',5}$ = 5.0 Hz, 2 H, 6-H, 6′-H), 3.82 (s, 3 H, OCH_3), 4.17 (m, 1 H, 4-H), 4.22 (m, 1 H, 5-H), 4.53 (2×d, J = 11.3 Hz, 2 H, OCH_2Ar), 4.64 (d, $J_{2,3}$ = 6.0 Hz, 1 H, 2-H), 4.80 (dd, $J_{3,4}$ = 3.6, $J_{3,2}$ = 5.8 Hz, 1 H, 3-H), 5.15 (s, 1 H, 1-H), 6.90 (d, J = 8.0 Hz, 2 H, H arom), 7.27 (d, J = 8.0 Hz, 2 H, H arom) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 24.3, 25.8 [C(CH_3)$_2$], 34.3 (C-6), 55.2 (OCH_3), 68.8 (OCH_2Ar), 69.9 (C-5), 79.5 (C-4), 80.1 (C-3), 85.4 (C-2), 104.7 (C-1), 112.9 [C(CH_3)$_2$], 113.9 (C-2′, C-6′), 129.1 (C-1′), 129.8 (C-3′, C-5′), 159.4 (C-4′) ppm. FTIR: $\tilde{\nu}$ = 3474 (OH), 2989, 2934, 1613, 1514, 1377, 1250, 1081, 1024, 821 cm^{-1}. HRMS (ESI^+): calcd. for $[C_{17}H_{23}BrO_6Na]^+$ 425.0576; found 425.0563.

5,6-Anhydro-2,3-*O*-isopropylidene-1-*O*-(4-methoxybenzyl)-L-gulose (24): Cesium fluoride (2.8 g, 18.4 mmol, dried beforehand at 150 °C in vacuo overnight) was added to a solution of **23** (1.86 g, 4.6 mmol) in dry acetone (25 mL). The reaction mixture was heated at reflux for 6 h, active charcoal was added, the mixture was filtered, and the filtrate was concentrated to dryness under vacuum. The crude product was dissolved in hot chloroform, active charcoal was again added, and, after filtration, the solvent was evaporated in vacuo to give epoxide **24** (1.41 g, 4.4 mmol, 95%) as a white solid; R_f = 0.60 (EtOAc/CH_2Cl_2 2:98); m.p. 87–89 °C. $[\alpha]_D^{20}$ = +74 (c = 1.4, $CHCl_3$). ^1H NMR ($CDCl_3$, 250 MHz): δ = 1.32, 1.49 [s, 6 H, C(CH_3)$_2$], 2.43 (dd, $J_{6,6'}$ = 2.7, $J_{6,5}$ = 4.8 Hz, 1 H, 6-H), 2.89 (t, $J_{6',6}$ = $J_{6',5}$ = 4.5 Hz, 1 H, 6′-H), 3.26 (m, 1 H, 5-H), 3.54 (dd, $J_{4,3}$ = 3.7, $J_{4,5}$ = 7.0 Hz, 1 H, 4-H), 3.75 (s, 3 H, OCH_3), 4.52 (2×d, J = 11.9 Hz, 2 H, OCH_2Ar), 4.64 (d, $J_{2,3}$ = 5.7 Hz, 1 H, 2-H), 4.74 (dd, $J_{3,2}$ = 5.9, $J_{3,4}$ = 3.8 Hz, 1 H, 3-H), 5.14 (s, 1 H, 1-H), 6.85 (d, J = 8.0 Hz, 2 H, H arom), 7.25 (d, J = 8.0 Hz, 2 H, H arom) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 24.7, 26.0 [C(CH_3)$_2$], 43.6 (C-6), 50.0 (C-5), 55.3 (OCH_3), 68.6 (OCH_2Ar), 80.6 (C-4), 82.4 (C-3), 85.1 (C-2), 105.2 (C-1), 112.8 [C(CH_3)$_2$], 113.9 (C-2′, C-6′), 129.1 (C-1′), 129.8 (C-3′, C-5′), 159.4 (C-4′) ppm. FTIR: $\tilde{\nu}$ = 2991, 2937, 1613 (C=C), 1515, 1376, 1250, 1081, 1020, 856, 821 cm^{-1}. ESI-MS: m/z = 345 $[M + Na]^+$, 361 $[M + K]^+$. $C_{17}H_{22}O_6$ (322.14): calcd. C 63.34, H 6.88, O 29.78; found C 63.57, H 6.97, O 29.91.

4′-Methoxybenzyl 2,3-*O*-Isopropylidene-6,7,8-trideoxy-β-L-*gulo*-oct-7-enofuranoside (25): Vinylmagnesium bromide (12.7 mL of a 1 M solution in THF) was added at –25 °C under argon to a solution of copper iodide (240 mg, 1.26 mmol) in THF (20 mL). After the mixture had been stirred for 15 min, a solution of epoxide **24** (1.36 g, 4.2 mmol) in THF (10 mL) was added dropwise. The reaction mixture was allowed to come to room temperature, and stirring was continued for 1.5 h. The reaction was quenched with saturated aqueous NH_4OAc, and the mixture was extracted with diethyl ether (3×30 mL). The organic phases were combined, washed with saturated aqueous NaCl, dried with $MgSO_4$, and filtered, and the solvents were evaporated to dryness under vacuum. The crude product was purified by flash chromatography on silica gel (EtOAc/CH_2Cl_2, 1:99) to afford the alcohol **25** (1.03 g, 2.95 mmol, 70%) as a white solid; R_f = 0.40 (EtOAc/CH_2Cl_2, 2:98); m.p. 39–40 °C. $[\alpha]_D^{20}$ = +73 (c = 1.54, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.31, 1.48 [s, 6 H, 2×C(CH_3)$_2$], 2.44 (m, 2 H, 6-H, 6′-H), 3.01 (s, 1 H, OH), 3.81 (s, 3 H, OCH_3), 3.90 (m, 1 H, 4-H), 4.11 (m, 1 H, 5-H), 4.51 (d, J = 11.3 Hz, 2 H, OCH_2Ar), 4.64 (d, $J_{2,3}$ = 5.9 Hz, 1 H, 2-H), 4.75 (dd, $J_{3,2}$ = 5.9, $J_{3,4}$ = 3.5 Hz, 1 H, 3-H), 5.15 (m, 3 H, 1-H, 8-H, 8′-H), 5.90 (m, 1 H, 7-H), 6.82 (d, J = 8.0 Hz, 2 H, H arom), 7.28 (d, J = 8.0 Hz, 2 H, H arom) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 24.4, 25.8 [C(CH_3)$_2$], 37.9 (C-6), 55.2 (OCH_3), 68.7 (OCH_2Ar), 69.2 (C-5), 80.5, 80.7 (C-3, C-4), 85.5 (C-2), 104.7 (C-1), 112.7 [C(CH_3)$_2$], 113.9 (C-2′, C-6′), 117.6 (C-8), 129.2 (C-1′), 129.8 (C-3′, C-5′), 134.4 (C-7), 159.4 (C-4′) ppm. FTIR: $\tilde{\nu}$ = 3456 (OH), 2937, 1613, 1376, 1249, 1081, 1022, 854 cm^{-1}. HRMS $(ESI)^+$: calcd. for $[C_{19}H_{26}O_6Na]^+$ 373.1627; found 373.1606.

4-Methoxybenzyl 5-*O*-*tert*-Butyldiphenylsilyl-2,3-*O*-isopropylidene-6,7,8-trideoxy-β-L-*gulo*-oct-7-enofuranoside (26): Imidazole (354 mg, 5.2 mmol) and *tert*-butyldiphenylsilyl chloride (0.67 mL, 2.6 mmol) were added under argon at 0 °C to a solution of alcohol **25** (0.92 g, 2.6 mmol) in DMF (6.7 mL). The reaction mixture was allowed to come to room temperature, and, after 20 h of stirring, the mixture was diluted with water (10 mL) and EtOAc (10 mL). The organic phase was separated, and the aqueous phase was extracted with EtOAc (2×10 mL). The organic phases were combined, washed with water (2×10 mL), dried with $MgSO_4$, and filtered, and the solvents were evaporated to dryness under vacuum. The crude product was purified by flash chromatography on silica gel (heptane/EtOAc, 8:1) to furnish the silylated compound **26** (1.18 g, 2.01 mmol, 77%) as a colorless oil; R_f = 0.70 (EtOAc/heptane, 3:5). $[\alpha]_D^{20}$ = +55 (c = 1.7, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.08 [s, 9 H, SiC(CH_3)$_3$], 1.13, 1.20 [s, 6 H, 2×C(CH_3)$_2$], 2.32 (m, 2 H, 6-H, 6′-H), 3.81 (s, 3 H, OCH_3), 4.03 (m, 1 H, 4-H), 4.21 (m, 2 H, 5-H, OCHHAr), 4.46 (d, J = 11.5 Hz, 1 H, OCHHAr), 4.53 (m, 1 H, 2-H), 4.59 (m, 1 H, 3-H), 4.86 (s, 1 H, 1-H), 5.05 (m, 2 H, 8-H, 8′-H), 6.08 (m, 1 H, 7-H), 6.84 (d, J = 8.0 Hz, 2 H, H arom), 7.25 (d, J = 8.0 Hz, 2 H, H arom), 7.30–7.40 (m, 6 H, H arom), 7.70–7.85 (m, 4 H, H arom) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 19.6 [SiC(CH_3)$_3$], 25.3, 26.0 [C(CH_3)$_2$], 27.1 [SiC(CH_3)$_3$], 37.9 (C-6), 55.3 (OCH_3), 68.0 (OCH_2Ar), 71.5 (C-5), 79.5 (C-3), 82.9 (C-4), 85.6 (C-2), 104.3 (C-1), 112.2 [C(CH_3)$_2$], 113.8 (C-2′, C-6′), 117.1 (C-8), 127.2, 127.3, 127.7, 129.2 (C arom), 129.5 (C-1′), 129.8 (C-3′, C-5′), 134.3 (C-7), 134.4, 134.7, 135.2 (C arom), 159.3 (C-4′) ppm. FTIR: $\tilde{\nu}$ = 3071, 2934, 2857, 1613, 1514, 1428, 1250, 1110, 1082, 822, 703 cm^{-1}. ESI-MS: m/z = 611 $[M + Na]^+$. $C_{35}H_{44}O_6Si{\cdot}0.1C_7H_{16}$ (598.30): calcd. C 71.63, H 7.62; found C 72.01, H 7.65.

5-*O*-*tert*-Butyldiphenylsilyl-2,3-*O*-isopropylidene-6,7,8-trideoxy-β-L-*gulo*-oct-7-enofuranose (27): DDQ (613 mg, 2.7 mmol) was added in small portions to a solution of **26** (1.12 g, 1.8 mmol) in CH_2Cl_2/H_2O (10:1, 19.8 mL). The dark green solution was stirred at room temperature for 20 h. The resulting reddish-brown mixture was diluted with saturated aqueous $NaHCO_3$ (20 mL) and CH_2Cl_2 (20 mL). The organic phase was separated, and the aqueous phase was extracted with CH_2Cl_2 (2×20 mL). The organic phases were combined, dried with $MgSO_4$, and filtered, and the solvents were evaporated to dryness under vacuum. The crude product was purified by flash chromatography on silica gel (heptane/EtOAc, 10:1) to furnish lactol **27** (0.53 g, 1.1 mmol, 63%) as a colorless oil; R_f = 0.20 (AcOEt/heptane, 1:5). $[\alpha]_D^{20}$ = +40 (c = 1.40, $CHCl_3$). ^1H NMR ($CDCl_3$, 250 MHz): δ = 1.05 [s, 9 H, SiC(CH_3)$_3$], 1.11, 1.20 [s, 6 H, 2×C(CH_3)$_2$], 2.35 (m, 2 H, 6-H, 6′-H), 4.01 (dd, $J_{4,3}$ = 3.2, $J_{4,5}$ = 8.7 Hz, 1 H, 4-H), 4.16 (m, 2 H, 5-H, OH), 4.43 (d, $J_{2,3}$

= 5.8 Hz, 1 H, 2-H), 4.58 (dd, $J_{3,4}$ = 3.3, $J_{3,2}$ = 5.8 Hz, 1 H, 3-H), 4.99 (s, 1 H, 1-H), 5.04 (m, 2 H, 8-H, 8′-H), 6.08 (m, 1 H, 7-H), 7.30–7.76 (m, 10 H, H arom) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 19.4 [Si*C*$(CH_3)_3$], 25.2, 25.8 [C(*C*$H_3)_2$], 26.9 [SiC(*C*$H_3)_3$], 37.7 (C-6), 71.6 (C-5), 79.4 (C-3), 82.9 (C-4), 85.7 (C-2), 100.4 (C-1), 112.2 [*C*$(CH_3)_2$], 116.9 (C-8), 126.7, 127.0, 128.9, 129.0 (C arom), 134.4 (C-7), 135.7, 135.9 (C arom) ppm. FTIR: $\tilde{\nu}$ = 3411 (OH), 3072, 2934, 1428, 1109, 1085, 703 cm^{-1}. ESI-MS: *m*/*z* = 453 [M – CH_3]$^+$. $C_{27}H_{36}O_5Si$ (468.23): calcd. C 69.20, H 7.74; found C 69.49, H 8.11.

5-*O*-*tert*-Butyldiphenylsilyl-2,3-*O*-isopropylidene-6,7,8-trideoxy-β-L-*gulo*-oct-7-eno-1,4-lactone (28): *N*-Methylmorpholine *N*-oxide (82 mg, 0.7 mmol, dried beforehand in vacuo at 90 °C) and molecular sieves (4 Å, 240 mg, finely crushed and oven-dried) were added successively at 20 °C under argon to a solution of lactol **27** (218 mg, 0.47 mmol) and tetrapropylammonium perruthenate (25 mg, 0.07 mmol) in acetonitrile (6 mL). After 3 h of stirring, the reaction mixture was concentrated to dryness under vacuum. The resulting residue was filtered through a pad of silica gel (eluent EtOAc), and the filtrate was concentrated in vacuo to furnish lactone **28** (124 mg, 0.27 mmol, 95%) as a colorless oil; R_f = 0.16 (EtOAc/heptane, 1:5). $[\alpha]_D^{20}$ = +36 (*c* = 0.96, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 1.08 [s, 9 H, SiC(C*H*$_3)_3$], 1.11, 1.28 [s, 6 H, 2 × C(C*H*$_3)_2$], 2.29 (m, 2 H, 6-H, 6′-H), 4.11 (m, 1 H, 5-H), 4.41 (dd, $J_{4,3}$ = 3.4, $J_{4,5}$ = 8.9 Hz, 1 H, 4-H), 4.59 (dd, $J_{3,4}$ = 3.4, $J_{3,2}$ = 5.4 Hz, 1 H, 3-H), 4.72 (d, $J_{2,3}$ = 5.4 Hz, 1 H, 2-H), 5.07 (m, 2 H, 8-H, 8′-H), 6.05 (m, 1 H, 7-H), 7.29–7.79 (m, 10 H, H arom) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 19.3 [Si*C*$(CH_3)_3$], 26.0, 26.3 [C(*C*$H_3)_2$], 26.8 [SiC(*C*$H_3)_3$], 37.0 (C-6), 70.8 (C-5), 75.2 (C-3), 79.2 (C-2), 81.9 (C-4), 113.7 [*C*$(CH_3)_2$], 117.7 (C-8), 127.2, 127.3, 129.4 (C arom), 133.2 (C-7), 135.7, 136.1 (C arom), 173.2 (C=O) ppm. FTIR: $\tilde{\nu}$ = 3072, 2933, 2858, 1790 (C=O), 1428, 1110, 1085, 703 cm^{-1}. ESI-MS: *m*/*z* = 489 [M + Na]$^+$, 505 [M + K]$^+$, 521 [M + Na + MeOH]$^+$. $C_{27}H_{34}O_5Si$ (466.22): calcd. C 69.49, H 7.34; found C 69.39, H, 7.48.

(7*E*)-5-*O*-*tert*-Butyldiphenylsilyl-2,3-*O*-isopropylidene-8-phenyl-6,7,8-trideoxy-β-L-*gulo*-oct-7-eno-1,4-lactone (29): $Pd(OAc)_2$ (9 mg, 0.04 mmol), triphenylphosphane (21 mg, 0.08 mmol), triethylamine (73 μL, 0.52 mmol), and iodobenzene (58 μL, 0.52 mmol) were added to a solution of lactone **28** (188 mg, 0.40 mmol) in DMF (2.5 mL). After 20 h of stirring at 110 °C under argon, the mixture was diluted with EtOAc (10 mL) and water (10 mL). The organic phase was separated, and the aqueous phase was extracted with EtOAc (2 × 10 mL). The organic phases were combined, washed with water (2 × 10 mL), and dried with $MgSO_4$, and the solvents were evaporated to dryness under vacuum. The crude product was purified by flash chromatography on silica gel (heptane/EtOAc, 10:1) to furnish the acetonide **29** (119 mg, 0.22 mmol, 55%) as a pale yellow oil; R_f = 0.15 (EtOAc/heptane 1:5). $[\alpha]_D^{20}$ = +36 (*c* = 0.6, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.11 [s, 9 H, SiC(C*H*$_3)_3$], 1.15, 1.29 [s, 6 H, 2 × C(C*H*$_3)_2$], 2.49 (m, 2 H, 6-H, 6′-H), 4.18 (m, 1 H, 5-H), 4.43 (dd, $J_{4,3}$ = 3.3, $J_{4,5}$ = 8.8 Hz, 1 H, 4-H), 4.63 (dd, $J_{3,4}$ = 3.4, $J_{3,2}$ = 5.3 Hz, 1 H, 3-H), 4.71 (d, $J_{2,3}$ = 5.3 Hz, 1 H, 2-H), 6.35–6.41 (m, 2 H, 7-H, 8-H), 7.21–7.77 (m, 15 H, H arom) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 19.4 [Si*C*-$(CH_3)_3$], 26.1, 26.5 [C(*C*$H_3)_2$], 27.0 [SiC(*C*$H_3)_3$], 36.3 (C-6), 71.5 (C-5), 75.4 (C-3), 76.3 (C-2), 82.1 (C-4), 113.8 [*C*$(CH_3)_2$], 124.9 (C-8), 125.9, 127.2, 128.4, 129.5, 129.6 (C arom), 132.7 (C-8), 134.0, 135.9, 136.2, 136.9 (C arom), 173.3 (C=O) ppm. FTIR: $\tilde{\nu}$ = 3072, 3050, 2956, 2933, 2858, 1789 (C=O), 1428, 1186, 1110, 703 cm^{-1}. HRMS (ESI)$^+$: calcd. for $[C_{33}H_{38}O_5SiNa]^+$ 565.2386; found 565.2385.

(7*E*)-5-*O*-*tert*-Butyldiphenylsilyl-8-phenyl-6,7,8-trideoxy-β-L-*gulo*-oct-7-eno-1,4-lactone (12): A solution of acetonide **29** (486 mg, 0.9 mmol) in aqueous AcOH (80%, 4 mL) was stirred at 90 °C in a Dean–Stark apparatus for 24 h. The reaction mixture was concentrated to dryness under vacuum, the residue was dissolved in EtOAc (10 mL), and the solution was neutralized with saturated aqueous $NaHCO_3$ (10 mL). The organic phase was separated, and the aqueous phase was extracted with EtOAc (2 × 10 mL). The organic phases were combined, washed with water (2 × 10 mL), dried with $MgSO_4$, and filtered, and the solvents were evaporated to dryness under vacuum. The crude product was purified by flash chromatography on silica gel (heptane/EtOAc, 2:1) to furnish the diol **12** (271 mg, 0.54 mmol, 60%) as a pasty white solid; R_f = 0.20 (EtOAc/heptane, 3:4). $[\alpha]_D^{20}$ = +39 (*c* = 1.26, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.12 [s, 9 H, SiC(C*H*$_3)_3$], 2.44 (m, 2 H, 6-H, 6′-H), 4.18 (m, 1 H, 5-H), 4.33–4.47 (m, 3 H, 2-H, 3-H, 4-H), 6.17–6.34 (d, $J_{8,7}$ = 16.0 Hz, 2 H, 7-H, 8-H), 7.19–7.79 (m, 15 H, H arom) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 19.3 [Si*C*$(CH_3)_3$], 26.8 [SiC(*C*$H_3)_3$], 36.2 (C-6), 68.8, 71.0, 71.6 (C-2, C-3, C-5), 82.5 (C-4), 124.6 (C-7), 125.9, 127.2, 127.4, 128.4, 129.6, 129.7 (C arom), 132.9 (C-8), 135.8, 136.0, 136.29, 136.8 (C arom), 175.1 (C=O) ppm. FTIR: $\tilde{\nu}$ = 3432 (OH), 3071, 2929, 2856, 1781 (C=O, lactone), 1427, 1190, 1109, 702 cm^{-1}. HRMS (ESI)$^+$: calcd. for $[C_{30}H_{34}O_5SiNa]^+$ 525.2073; found 525.2062.

(5*S*,6*S*)-6-[1-(*tert*-Butyldiphenylsilyloxy)-4-phenylbut-3-enyl]-3-(trifluoromethylsulfonyl)furan-2(5*H*)-one (30): Pyridine (0.34 mL, 4.2 mmol) and trifluoromethanesulfonic anhydride (0.33 mL, 1.94 mmol) were added at –78 °C under argon to a solution of diol **12** (295 mg, 0.59 mmol) in CH_2Cl_2 (8 mL). After 15 min of stirring at –78 °C, the reaction mixture was warmed to 0 °C. After 4 h of stirring, the mixture was poured into cold diethyl ether (10 mL). The precipitated salts were filtered, and the filtrate was concentrated in vacuo at 0 °C. The crude product was purified by flash chromatography on silica gel (EtOAc/heptane, 1:4) to furnish the triflate **30** (327 mg, 0.53 mmol, 90%) as a pale yellow oil; R_f = 0.65 (EtOAc/heptane 1:2). $[\alpha]_D^{20}$ = +22 (*c* = 1.00, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.07 [s, 9 H, SiC(C*H*$_3)_3$], 2.50 (m, 2 H, 7-H, 7′-H), 4.09 (m, 1 H, 6-H), 5.03 (m, 1 H, 5-H), 5.98 (m, 1 H, 8-H), 6.34 (d, $J_{9,8}$ = 16.0 Hz, 1 H, 9-H), 6.78 (d, $J_{4,5}$ = 1.7 Hz, 1 H, 4-H), 7.20–7.72 (m, 15 H, H arom) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 19.2 [Si*C*$(CH_3)_3$], 26.8 [SiC(*C*$H_3)_3$], 36.8 (C-7), 72.0 (C-6), 79.7 (C-5), 123.8 (C-7), 126.1, 127.6, 127.9, 128.1, 128.5, 130.2, 130.4, 132.5, 132.7 (C arom, *C*F_3), 134.4 (C-9), 135.8, 135.9, 136.2, 136.3, 136.7, 137.6 (C arom, C-4), 163.6 (C=O) ppm. FTIR: $\tilde{\nu}$ = 2931, 2858, 1796 (C=O), 1435 (SO_2), 1220, 1138 (SO_2), 1112, 1108, 702 cm^{-1}. ESI-MS: *m*/*z* = 639 [M + Na]$^+$, 655 [M + K]$^+$. $C_{31}H_{31}F_3O_6SSi$ (616.16): calcd. C 60.37, H 5.07; found C 60.14, H 5.19.

(1*R*,4*S*,5*S*)-4-[(1*S*)-1-(*tert*-Butyldiphenylsilyloxy)-4-phenylbut-3-enyl]-6-(3′,4′-dimethoxybenzyl)-3-oxa-6-azabicyclo[3.1.0]hexan-2-one (31): 3,4-Dimethoxybenzylamine (88 μL, 0.58 mmol) was added dropwise under argon to a solution of triflate **30** (325 mg, 0.53 mmol) in DMF (3.8 mL), maintained at –60 °C. The reaction mixture was stirred at –60 °C for 30 min, diluted with EtOAc (5 mL) and then with water (5 mL). The layers were separated, and the aqueous layer was extracted with EtOAc (2 × 5 mL). The organic extracts were combined and dried with $MgSO_4$, and the solvents were evaporated to dryness under vacuum. The resulting oily residue was purified by flash chromatography on silica gel (heptane/EtOAc, 4:1) to afford aziridino-γ-lactone **31** (122 mg, 0.19 mmol, 36%) as a white solid, together with recovered starting material (121 mg, 0.21 mmol, 40%); R_f = 0.51 (EtOAc/heptane, 3:4). $[\alpha]_D^{20}$ = +55 (*c* = 1.00, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz):

δ = 0.96 [s, 9 H, SiC(CH_3)$_3$], 2.28 (m, 1 H, 8-H), 2.52 (m, 1 H, 8′-H), 2.54 (d, $J_{5,1}$ = 4.4 Hz, 1 H, 5-H), 2.63 (d, $J_{1,5}$ = 4.4 Hz, 1 H, 1-H), 3.17 (d, J = 13.2 Hz, 1 H, NCH_2Ar), 3.54 (d, J = 13.2 Hz, 1 H, NCH_2Ar), 3.79 (s, 6 H, OCH_3), 3.86 (m, 1 H, 7-H), 4.32 (d, $J_{4,5}$ = 2.0 Hz, 1 H, 4-H), 5.80 (m, 1 H, 9-H), 6.18 (d, $J_{10,9}$ = 15.8 Hz, 1 H, 10-H), 6.65–7.65 (m, 18 H, H arom) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 19.2 [SiC(CH$_3$)$_3$], 26.7 [SiC(CH$_3$)$_3$], 36.3 (C-6), 40.1 (C-5), 44.1 (C-1), 55.8 (OCH_3), 60.8 (NCH_2Ar), 73.0 (C-7), 80.6 (C-4), 110.9, 111.1 (C-2′, C-5′), 120.0 (C-6′), 124.2 (C-9), 125.8, 127.2, 127.6, 127.8, 128.3, 129.8, 130.0 (C arom), 133.6 (C-10), 135.7 (C arom), 149.1, 149.6 (C-3′, C-4′), 172.0 (C=O) ppm. FTIR: $\tilde{\nu}$ = 2933, 1857, 1779 (C=O, lactone), 1516, 1427, 1112, 703 cm^{-1}. ESI-MS: m/z = 656 [M + Na]$^+$.

(1*R*,4*S*,5*S*)-4-[(1*S*)-1-(*tert*-Butyldiphenylsilyloxy)-4-phenylbut-3-enyl)]-3-oxa-6-azabicyclo[3.1.0]hexan-2-one (32): Ceric ammonium nitrate (188 mg, 0.34 mmol) was added at room temperature to a solution of **31** (103 mg, 0.16 mmol) in MeCN/H_2O (5:1, 2.2 mL). After 2 h of stirring, the orange mixture was concentrated to dryness under vacuum, the residue was dissolved in diethyl ether (5 mL), and the solution was neutralized with saturated aqueous $NaHCO_3$. The organic phase was separated, and the aqueous phase was extracted with diethyl ether (3 × 5 mL). The organic phases were combined, dried with $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel (EtOAc/heptane, 1:4 + 1% Et_3N) to afford aziridine **32** (15 mg, 0.032 mmol, 20%) as a colorless oil; R_f = 0.47 (EtOAc/heptane, 3:4). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.05 [s, 9 H, SiC(CH_3)$_3$], 2.34 (m, 1 H, 8-H), 2.48–2.65 (m, 3 H, 8′-H, 1-H, 5-H), 3.95 (m, 1 H,7-H), 4.42 (s, 1 H, 4-H), 5.85 (dt, J = 7.5, J = 7.5, J = 15.8 Hz, 1 H, 9-H), 6.21 (d, J = 15.8 Hz, 1 H, 10-H), 7.13–7.71 (m, 15 H, H arom) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 19.3 [SiC(CH$_3$)$_3$], 26.8 [SiC(CH_3)$_3$], 31.9 (C-8), 32.4 (C-1), 36.6 (C-5), 73.5 (C-7), 76.6 (C-4), 126.0 (C-9), 127.5, 127.7, 128.0, 128.5, 130.3 (C arom), 133.9 (C-10), 135.8, 135.9 (C arom), 172.2 (C=O) ppm. FTIR: $\tilde{\nu}$ = 3350 (NH), 2926, 2855, 1785 (C=O, lactone), 1112, 702 cm^{-1}. ESI-MS: m/z = 484 [M + H]$^+$.

(1*R*,4*S*,5*S*)-6-(*tert*-Butoxycarbonyl)-4-[(1*S*)-1-(*tert*-butyldiphenylsilyloxy)-4-phenylbut-3-enyl]-3-oxa-6-azabicyclo[3.1.0]hexan-2-one (11): Boc_2O (45 mg, 0.21 mmol), DMAP (1 mg, 8.0 μmol), and triethylamine (56 μL, 0.4 mmol) were successively added at room temperature under argon to a solution of aziridine **32** (20 mg, 0.04 mmol) in CH_3CN (1 mL). After 1.5 h of stirring, the solution was concentrated to dryness. The crude product was diluted with EtOAc (5 mL), the solution was neutralized with saturated aqueous $NaHCO_3$, and the organic phase was separated. The aqueous phase was extracted with EtOAc (3 × 5 mL), and the organic phases were combined, dried with $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel (heptane/EtOAc, 6:1) to furnish compound **11** (17 mg, 0.029 mmol, 73%) as a colorless oil; R_f = 0.70 (EtOAc/heptane, 2:3). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.05 [s, 9 H, SiC(CH_3)$_3$], 1.41 [s, 9 H, OC(CH_3)$_3$], 2.33 (m, 1 H, 8-H), 2.59 (m, 1 H, 8′-H), 3.28 (d, J = 3.0 Hz, 1 H, 1-H), 3.36 (d, J = 3.0 Hz, 1 H, 5-H), 3.94 (m, 1 H, 7-H), 4.73 (d, J = 3.9 Hz, 1 H, 4-H), 5.79 (m, 1 H, 9-H), 6.17 (d, J = 15.9 Hz, 1 H, 10-H), 7.11–7.76 (m, 15 H, H arom) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 19.3 [SiC(CH$_3$)$_3$], 26.8 [SiC(CH$_3$)$_3$], 27.7 [OC(CH$_3$)$_3$], 34.0 (C-8), 37.8 (C-1), 42.9 (C-5), 73.5 (C-7), 76.6 (C-4), 83.5 [OC(CH$_3$)$_3$], 123.7 (C-9), 127.4, 127.8, 128.1, 128.4, 128.8, 130.3, 130.9 (C arom), 134.2 (C-10), 135.8, 135.9 (C arom), 155.9 (C=O, carbamate), 172.8 (C=O) ppm. FTIR: $\tilde{\nu}$ = 3350 (NH), 2926, 2855, 1785 (C=O lactone), 1112, 702 cm^{-1}. ESI-MS: m/z = 606 [M + Na]$^+$.

5-*O*-*tert*-Butyldiphenylsilyl-6,7,8-trideoxy-β-L-*gulono*-oct-7-eno-1,4-lactone (33): A solution of acetonide **28** (1.02 g, 2.33 mmol) in aqueous AcOH (80%, 10 mL) was stirred at 90 °C in a Dean–Stark apparatus for 24 h. The mixture was concentrated to dryness under vacuum, the residue was dissolved in EtOAc (10 mL), and the solution was neutralized with saturated aqueous $NaHCO_3$ (25 mL). The organic phase was separated, and the aqueous phase was extracted with EtOAc (2 × 25 mL). The organic phases were combined, washed with water (2 × 25 mL), dried with $MgSO_4$, and filtered, and the solvents were evaporated to dryness. The crude product was purified by flash chromatography on silica gel (heptane/EtOAc, 2:1) to furnish the diol **33** (516.8 mg, 1.21 mmol, 55%) as a white solid; R_f = 0.40 (EtOAc/heptane, 1:1); m.p. 136–137 °C. $[a]_D^{20}$ = +13.3 (c = 1.10, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.11 [s, 9 H, SiC(CH_3)$_3$], 2.27 (m, 2 H, 6-H), 3.2 (br. s, 1 H, OH), 4.17 (br. s, 1 H, OH), 4.30 (m, 3 H, 3-H, 4-H, 5-H), 4.42 (d, $J_{2,3}$ = 4.1 Hz, 1 H, 2-H), 5.02 (m, 2 H, 8-H), 5.92 (m, 1 H, 7-H), 7.3–7.9 (m, 10 H, H arom) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 19.6 [SiC(CH$_3$)$_3$], 27.2 [SiC(CH$_3$)$_3$], 37.2 (C-6), 69.1 (C-3), 70.1, 70.2 (C-5, C-2), 83.3 (C-4), 118.4 (C-8), 127.6, 127.7, 129.8 (C arom), 133.3 (C-7), 134.3, 136.1, 136.3 (C arom), 176.1 (C=O) ppm. FTIR: $\tilde{\nu}$ = 3415 (OH), 3071, 2931, 2856, 1773 (C=O), 1427, 1192, 1106, 702 cm^{-1}. HRMS (ESI)$^+$: calcd. for [$C_{24}H_{30}O_5SiNa$]$^+$ 449.1760; found 449.1772.

(5*S*,6*S*)-6-[1-(*tert*-Butyldiphenylsilyloxy)but-3-enyl]-3-(trifluoromethylsulfonyl)furan-2(5*H*)-one (34): Pyridine (758 μL, 9.42 mmol) and trifluoromethanesulfonic anhydride (734 μL, 4.33 mmol) were added at –78 °C under argon to a solution of diol **33** (574 mg, 1.35 mmol) in CH_2Cl_2 (18 mL). After 15 min of stirring at –78 °C, the reaction mixture was warmed to 0 °C. After 4 h, the mixture was poured into cold diethyl ether (25 mL). The precipitated salts were filtered, and the filtrate was concentrated in vacuo at 0 °C. The crude product was purified by flash chromatography on silica gel to furnish the triflate **34** (688 mg, 1.27 mmol, 94%) as a pale yellow oil; R_f = 0.50 (EtOAc/heptane, 1:4). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.06 [s, 9 H, SiC(CH_3)$_3$], 2.28 (m, 1 H, 7-H), 2.45 (m, 1 H, 7′-H), 4.02 (m, 1 H, 6-H), 5.02 (m, 3 H, 9-H, 9′-H, 5-H), 5.61 (m, 1 H, 8-H), 6.79 (d, $J_{4,5}$ = 1.8 Hz, 1 H, 4-H), 7.36–7.68 (m, 10 H, H arom) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 19.4 [SiC(CH$_3$)$_3$], 28.0 [SiC(CH$_3$)$_3$], 38.0 (C-7), 71.9 (C-6), 79.8 (C-5), 119.4 (C-9), 127.6, 127.7, 129.8 (C arom), 133.3 (C-8), 134.3, 136.1 (C arom), 136.3 (C-4) 176.1 (C=O, lactone) ppm. FTIR: $\tilde{\nu}$ = 2931, 2858, 1793 (C=O, lactone), 1428, 1218, 1102, 702 cm^{-1}. HRMS (ESI)$^+$: calcd. for [$C_{25}H_{27}F_3O_6SSiNa$]$^+$ 563.1148; found 563.1163.

(1*R*,4*S*,5*S*)-4-[(1*S*)-1-(*tert*-Butyldiphenylsilyloxy)but-3-enyl]-6-(3′,4′-dimethoxybenzyl)-3-oxa-6-azabicyclo[3.1.0]hexan-2-one (35): 3,4-Dimethoxybenzylamine (211 μL, 1.4 mmol) was added dropwise under argon to a solution of triflate **34** (688 mg, 1.27 mmol) in DMF (9.1 mL), maintained at –60 °C. The reaction mixture was stirred at –60 °C for 30 min and was diluted with EtOAc (12 mL) and then with water (12 mL). The layers were separated, and the aqueous layer was extracted with EtOAc (2 × 12 mL). The organic extracts were combined and dried with $MgSO_4$, and the solvents were evaporated to dryness under vacuum. The resulting oily residue was purified by flash chromatography on silica gel (heptane/EtOAc, 4:1) to afford aziridino-γ-lactone **35** (290 mg, 0.52 mmol, 41%) as a colorless viscous oil, together with recovered starting material **34** (260 mg, 0.48 mmol, 38%); R_f = 0.50 (heptane/EtOAc, 4:1). $[a]_D^{20}$ = +10 (c = 0.9, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.04 [s, 9 H, SiC(CH_3)$_3$], 2.21 (m, 1 H, 8-H), 2.46 (m, 1 H, 8′-H), 2.60 (d, J = 4.4 Hz, 1 H, 1-H), 2.66 (d, J = 4.4 Hz, 1 H, 5-H), 3.26 (d, J = 13.2 Hz, 1 H, NCH_2Ar), 3.59 (d, J = 13.2 Hz, 1 H, NCH_2Ar), 3.87 (m, 7 H, 2 × OCH_3, 7-H), 4.34 (d, $J_{7,4}$ = 2.5 Hz, 1

H, 4-H), 4.92 (m, 1 H, 10-H), 4.96 (m, 1 H, 10′-H), 5.53 (m, 1 H, 9-H), 6.72–7.70 (m, 13 H, H arom) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 19.5 [Si*C*$(CH_3)_3$], 27.1 [SiC(*C*$H_3)_3$], 37.6 (C-8), 40.6 (C-1), 44.5 (C-5), 56.2 (O*C*H_3), 61.2 (NH*C*H_2Ar), 73.1 (C-7), 80.9 (C-4), 118.8 (C-10), 127.3, 128.0, 130.1, 130.3 (C arom), 133.2 (C-9), 133.3, 136.0, 136.1, 148.3, 148.4 (C arom), 172.9 (C=O, lactone) ppm. FTIR: $\tilde{\nu}$ = 2931, 2854, 1774 (C=O, lactone), 1515, 1427, 1111, 702 cm^{-1}. HRMS (ESI)$^+$: calcd. for [$C_{33}H_{39}NO_5SiNa$]$^+$ 580.2495; found 580.2445.

(1*R*,4*S*,5*S*)-6-(*tert*-Butoxycarbonyl)-4-[(1*S*)-1-(*tert*-butyldiphenylsilyloxy)but-3-enyl]-3-oxa-6-azabicyclo[3.1.0]hexan-2-one (36): A solution of aziridine **35** (20.7 mg, 0.038 mmol) and DDQ (8.7 mg, 0.038 mmol) in a mixture of CH_2Cl_2 (0.4 mL) and water (0.04 mL) was stirred at room temperature for 24 h. Triethylamine (16 μL, 0.11 mmol), DMAP (0.2 mg, 2 μmol), and Boc_2O (33.4 mg, 0.15 mmol) were then successively added. The reaction mixture was stirred at room temperature for 24 h and was then diluted with CH_2Cl_2 (0.3 mL) and water (0.5 mL). The aqueous layer was separated, and the organic layer was successively washed with saturated aqueous $NaHCO_3$ (1 mL), water (1 mL), and saturated aqueous NaCl (1 mL). The organic phase was dried with $MgSO_4$ and filtered, and the solvents were evaporated to dryness under vacuum. The resulting residue was purified by column chromatography on silica gel (EtOAc/heptane, 1:6) to afford compound **36** (18.1 mg, 0.036 mmol, 92%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.03 [s, 9 H, SiC$(CH_3)_3$], 1.43 [s, 9 H, OCO$(CH_3)_3$], 2.17 (m, 1 H, 8-H), 2.50 (m, 1 H, 8′-H), 3.25 (d, J = 3.2 Hz, 1 H, 1-H), 3.30 (d, J = 3.2 Hz, 1 H, 5-H), 3.84 (ddd, J = 10.2, 4.3 and 1.5 Hz, 1 H, 7-H), 4.70 (d, J = 1.5 Hz, 1 H, 2-H), 4.92 (m, 1 H, 10-H), 5.44 (m, 1 H, 9-H), 7.35–7.75 (m, 10 H, H arom) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 19.4 [Si*C*$(CH_3)_3$], 27.0 [SiC(*C*$H_3)_3$], 27.9 [OCO(*C*$H_3)_3$], 37.8 (C-8), 38.1 (C-5), 43.0 (C-1), 73.4 (C-7), 76.7 (C-2), 83.6 [O*C*O$(CH_3)_3$], 119.3 (C-10), 127.9, 128.2, 130.2, 130.5 (CH arom), 132.5 (C-9), 135.9, 136.0 (CH arom), 157.2 (C=O, carbamate), 172.9 (C=O, lactone) ppm. FTIR: $\tilde{\nu}$ = 3070, 2929, 2856, 1793 (C=O, lactone), 1730 (C=O, carbamate), 1149, 1112, 702 cm^{-1}. HRMS (ESI)$^+$: calcd. for [$C_{29}H_{37}NO_5SiNa$]$^+$ 530.2339; found 530.2315.

(1*R*,4*S*,5*S*)-6-(*tert*-Butoxycarbonyl)-4-[(*tert*-butyldiphenylsilyloxy)methyl]-3-oxa-6-azabicyclo[3.1.0]hexan-2-one (39): A solution of aziridine **38** (870 mg, 1.65 mmol) and DDQ (382 mg, 1.65 mmol) in a mixture of CH_2Cl_2 (17 mL) and water (1.7 mL) was stirred at room temperature for 24 h. Triethylamine (0.7 mL, 5.00 mmol), DMAP (10 mg, 0.08 mmol), and Boc_2O (1.47 g, 6.7 mmol) were then successively added. The reaction mixture was stirred at room temperature for 24 h and was then diluted with CH_2Cl_2 (10 mL) and water (20 mL). The aqueous layer was separated, and the organic layer was successively washed with saturated aqueous $NaHCO_3$ (30 mL), water (30 mL), and saturated aqueous NaCl. The organic phase was dried with $MgSO_4$ and filtered, and the solvents were evaporated to dryness under vacuum. The resulting residue was purified by column chromatography on silica gel (EtOAc/heptane, 1:4) to afford compound **39** (0.66 g, 1.42 mmol, 85%) as a colorless oil; R_f = 0.77 (EtOAc/heptane, 3:4). ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 0.97 [s, 9 H, SiC$(CH_3)_3$], 1.40 [s, 9 H, OCO$(CH_3)_3$], 3.35 (2 × d, $J_{1,5}$ = 3.1 Hz, 2 H, 1-H, 5-H), 3.71 (dd, $J_{4,7}$ = 1.5, $J_{7,7'}$ = 11.6 Hz, 1 H, 7-H), 3.95 (dd, $J_{4,7'}$ = 2.9, $J_{7,7'}$ = 11.6 Hz, 1 H, 7′-H), 4.68 (m, 1 H, 4-H), 7.2–7.6 (m, 10 H, H arom) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 19.1 [Si*C*$(CH_3)_3$], 26.6 [SiC(*C*$H_3)_3$], 27.7 [OCO(*C*$H_3)_3$], 38.0 (C-5), 41.1 (C-1), 63.5 (C-7), 76.3 [O*C*O$(CH_3)_3$], 83.5 (C-4), 127.8, 127.9, 130.1, 131.8, 132.5 (CH arom), 135.5, 135.6 (C arom), 157.1 (C=O, carbamate), 169.2 (C=O, lactone) ppm. FTIR: $\tilde{\nu}$ = 3070, 2930, 1793 (C=O, lactone), 1727 (C=O, carbamate), 1149, 1112, 702 cm^{-1}. ESI-MS: m/z = 468 [M + H]$^+$, 490 [M + Na]$^+$, 506 [M + K]$^+$. $C_{26}H_{33}NO_5Si$ (467.21): calcd. C 66.78, H 7.11, N 3.00; found C 66.82, H 7.24, N 2.77.

(1*R*,4*S*,5*S*)-6-Acetyl-4-[(*tert*-butyldiphenylsilyloxy)methyl]-3-oxa-6-azabicyclo[3.1.0]hexan-2-one (40): A solution of aziridine **38** (540 mg, 1.00 mmol) and DDQ (227 mg, 1.00 mmol) in a mixture of CH_2Cl_2 (60 mL) and water (6 mL) was stirred at room temperature for 24 h. Pyridine (4.0 mL, 49.4 mmol) and acetic anhydride (0.94 mL, 10.00 mmol) were then successively added. The reaction mixture was stirred at 5 °C for 24 h, and CH_2Cl_2 (10 mL) was added, followed by aqueous HCl (10% v/v, 10 mL). The aqueous layer was separated, and the organic layer was successively washed with aqueous HCl (10% v/v, 10 mL), saturated aqueous $NaHCO_3$ (10 mL), and water (10 mL). The organic phase was dried with $MgSO_4$ and filtered, and the solvents were evaporated to dryness under vacuum. The resulting residue was purified by column chromatography on silica gel (EtOAc/heptane, 1:4) to afford compound **40** (327 mg, 0.8 mmol, 80%) as a colorless oil; R_f = 0.61 (EtOAc/heptane, 4:3). $[\alpha]_D^{20}$ = –22.0 (c = 1.6, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.99 [s, 9 H, C(C*H*$_3)_3$], 2.03 (s, 3 H, CH_3), 3.49 (s, 2 H, 1-H, 5-H), 3.74 (dd, $J_{4,7}$ = 1.8, $J_{7,7'}$ = 11.8 Hz, 1 H, 7-H), 3.97 (dd, $J_{4,7'}$ = 2.78, $J_{7,7'}$ = 11.8 Hz, 1 H, 7′-H), 4.73 (m, 1 H, 4-H), 7.2–7.6 (m, 10 H, H arom) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 19.9 [Si*C*$(CH_3)_3$], 23.1 (CO*C*H_3), 26.4 [C(*C*$H_3)_3$], 37.4 (C-5), 41.9 (C-1), 63.2 (C-7), 88.5 (C-4), 127.7, 127.8, 129.9, 130.0 (CH arom), 135.2, 135.4 (C arom), 168.9 (C=O, lactone), 179.0 (C=O, amide) ppm. FTIR: $\tilde{\nu}$ = 3070, 2930, 1785 (C=O, lactone), 1710 (C=O, amide), 1427, 1112, 701 cm^{-1}. ESI-MS: m/z = 410 [M + H]$^+$, 432 [M + Na]$^+$, 448 [M + K]$^+$. $C_{23}H_{27}NO_4Si{\cdot}0.4H_2O$ (416.37): calcd. C 66.29, H 6.72, N 3.36; found C 66.44, H 6.71, N 3.22.

(1*R*,4*S*,5*S*)-6-(Benzyloxycarbonyl)-4-[(*tert*-butyldiphenylsilyloxy)methyl]-3-oxa-6-azabicyclo[3.1.0]hexan-2-one (41): A solution of aziridine **38** (1.7 g, 3.3 mmol) and DDQ (0.75 g, 3.3 mmol) in a mixture of CH_2Cl_2 (33 mL) and water (3 mL) was stirred at room temperature for 24 h. Pyridine (4.0 mL, 49.4 mmol), benzyl chloroformate (0.95 mL, 6.6 mmol), and DMAP (81 mg, 0.66 mmol) were then successively added. The reaction mixture was stirred at room temperature for 2 h, and CH_2Cl_2 (10 mL) was added, followed by aqueous HCl (10% v/v, 20 mL). The aqueous layer was separated, and the organic layer was successively washed with aqueous HCl (10% v/v, 30 mL), saturated aqueous $NaHCO_3$ (30 mL), and water (30 mL). The organic phase was dried with $MgSO_4$ and filtered, and the solvents were evaporated to dryness under vacuum. The resulting residue was purified by column chromatography on silica gel (EtOAc/heptane, 1:4) to afford compound **41** (1.29 g, 2.57 mmol, 78%) as a colorless oil. R_f = 0.70 (EtOAc/heptane, 3:4). $[\alpha]_D^{20}$ = –2.0 (c = 1.5, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.97 [s, 9 H, C$(CH_3)_3$], 3.45 (2 × d, $J_{1,5}$ = 3.1 Hz, 2 H, 1-H, 5-H), 3.71 (dd, $J_{4,7}$ = 1.8, $J_{7,7}$ = 11.8 Hz, 1 H, 7-H), 3.93 (dd, $J_{4,7'}$ = 2.7, $J_{7,7'}$ = 11.8 Hz, 1 H, 7′-H), 4.62 (m, 1 H, 4-H), 5.10 (2 × d, J = 11.9 Hz, 2 H, PhC*H*$_2$), 7.2–7.7 (m, 15 H arom) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 19.2 [Si*C*$(CH_3)_3$], 26.7 [C(*C*$H_3)_3$], 37.9 (C-5), 42.3 (C-1), 63.5 (C-7, *C*H$_2$Ph), 69.3 (C-4), 128.1, 128.5, 128.7, 130.2, 131.9, 132.5 (CH arom), 134.8, 135.5, 135.7 (C arom), 158.5 (C=O, carbamate), 168.9 (C=O, lactone) ppm. FTIR: $\tilde{\nu}$ = 3070, 2930, 1792 (C=O, lactone), 1734 (C=O, carbamate), 1112, 701 cm^{-1}. ESI-MS: m/z = 502 [M + H]$^+$, 524 [M + Na]$^+$, 540 [M + K]$^+$. $C_{29}H_{31}NO_5Si$ (501.20): calcd. C 69.43, H 6.23, N 2.79; found C 69.12, H 6.14, N 2.59.

(1*R*,4*S*,5*S*)-4-[(*tert*-Butyldiphenylsilyloxy)methyl]-6-tosyl-3-oxa-6-azabicyclo[3.1.0]hexan-2-one (42): A solution of aziridine **38** (1.97 g,

3.8 mmol) and DDQ (866 mg, 3.8 mmol) in a mixture of CH_2Cl_2 (39 mL) and water (3.9 mL) was stirred at room temperature for 24 h. Pyridine (4.6 mL, 15.3 mmol) and tosyl chloride (2.9 g, 15.3 mmol) were then successively added. The reaction mixture was stirred at room temperature for 2 h, and CH_2Cl_2 (12 mL) was added, followed by aqueous HCl (10% v/v, 24 mL). The aqueous layer was separated, and the organic layer was successively washed with aqueous HCl (10% v/v, 30 mL), saturated aqueous $NaHCO_3$ (20 mL), and water (20 mL). The organic phase was dried with $MgSO_4$ and filtered, and the solvents were evaporated to dryness under vacuum. The resulting residue was purified by column chromatography on silica gel (EtOAc/heptane, 1:4) to afford compound **42** (1.52 g, 2.9 mmol, 77%) as a white solid; R_f = 0.7 (EtOAc/heptane, 3:4); m.p. 133–134 °C. $[\alpha]_D^{20}$ = +8.0 (c = 1.01, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.05 [s, 9 H, SiC(CH_3)$_3$], 2.48 (s, 3 H, PhCH_3), 3.73 (d, J = 5.0 Hz, 1 H, 1-H), 3.82 (dd, J = 2.1, J = 11.7 Hz, 1 H, 7-H), 3.94 (dd, J = 3.2, J = 11.7 Hz, 1 H, 7′-H), 3.99 (d, J = 5.0 Hz, 1 H, 5-H), 4.56 (m, 1 H, 4-H), 7.3–7.9 (m, 14 H, H arom) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 19.1 [SiC(CH_3)$_3$], 21.8 (PhCH_3), 26.7 [SiC(CH_3)$_3$], 40.0 (C-1), 43.5 (C-5), 63.2 (C-7), 79.7 (C-4), 128.0, 128.1, 128.1, 130.1, 130.2, 130.2, 135.5, 135.6 (CH arom), 131.7, 132.3, 133.7 (C arom), 145.8 (SO_2C arom), 168.2 (C=O, lactone) ppm. FTIR: $\tilde{\nu}$ = 3071, 2930, 1799 (C=O, lactone), 1427, 1339, 1161 (SO_2), 1112, 704 cm^{-1}. ESI-MS: m/z = 544 [M + Na]$^+$, 576 [M + Na + MeOH]$^+$. $C_{28}H_{31}NO_5SSi$ (521.17): calcd. C 64.46, H 5.99, N 2.68, S 6.15; found C 64.51, H 5.92, N 2.69, S 5.97.

(3*S*,4*R*,5*S*)-3-Acetoxy-4-[(benzyloxycarbonyl)amino]-5-[(*tert*-butyldiphenylsilyloxy)methyl]tetrahydrofuran-2-one (43): $BF_3{\cdot}Et_2O$ (34 μL, 0.27 mmol) was added at 0 °C under argon to a solution of **41** (104 mg, 0.21 mmol) in a mixture of acetic acid (1 mL) and chloroform (1 mL). The reaction mixture was stirred at 50 °C for 20 h and then diluted with EtOAc (10 mL) and neutralized with aqueous $NaHCO_3$ (10%, 10 mL). The aqueous layer was extracted with EtOAc (2 × 1 mL), the combined organic phases were dried with $MgSO_4$ and filtered, and the solvents were evaporated under vacuum. The resulting residue was purified by column chromatography on silica gel (heptane/EtOAc, 3:1) to afford **43** (58 mg, 0.10 mmol, 48%) as a colorless oil; R_f = 0.50 (EtOAc/heptane, 1:1). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.98 [s, 9 H, SiC(CH_3)$_3$], 2.11 [s, 3 H, OC(O)CH_3], 3.78 (dd, $J_{4,5}$ = 1.9, $J_{5,5'}$ = 12.1 Hz, 1 H, 5-H), 3.91 (dd, $J_{4,5'}$ = 2.3, $J_{5,5'}$ = 12.1 Hz, 1 H, 5′-H), 4.37 (m, 1 H, 4-H), 4.44 (m, 1 H, 3-H), 5.02 (m, 3 H, CH_2Ph, 2-H), 5.70 (d, J = 8.4 Hz, 1 H, NH), 7.3–7.7 (m, 15 H, H arom) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 19.3 [SiC(CH_3)$_3$], 20.6 [OC(O)CH_3], 26.7 [SiC(CH_3)$_3$], 53.7 (C-3), 61.8 (C-5), 67.4 (CH_2Ph), 71.6 (C-2), 80.1 (C-4), 127.9, 128.3, 128.7, 130.0, 132.5, 132.8, 135.8 (CH arom), 155.7 (C=O, carbamate), 169.5 (C=O, ester), 170.3 (C=O, lactone) ppm. FTIR: $\tilde{\nu}$ = 3351 (NH), 1800 (C=O, lactone), 1755 (C=O, ester), 1730 (C=O, carbamate), 1527 (C=O, carbamate), 1428, 1112, 702 cm^{-1}. ESI-MS: m/z = 562 [M + H]$^+$, 584 [M + Na]$^+$, 600 [M + K]$^+$. $C_{31}H_{35}NO_7Si{\cdot}H_2O$ (579.22): calcd. C 64.25, H 6.39; found C 63.93, H 6.02.

(3*S*,4*R*,5*S*)-3-Acetoxy-5-[(*tert*-butyldiphenylsilyloxy)methyl]-4-(tosylamino)tetrahydrofuran-2-one (44): Cesium acetate (90 mg, 0.47 mmol) was added to a solution of **42** (54.6 mg, 0.093 mmol) in DMF (0.3 mL). The reaction mixture was stirred at room temperature for 2 h and was then diluted with EtOAc (0.5 mL) and water (0.5 mL). After separation of the phases, the organic layer was extracted with water (2 × 0.5 mL). The combined organic extracts were dried with $MgSO_4$ and filtered, and the solvents were evaporated under vacuum. The resulting residue was purified by column chromatography on silica gel (heptane/EtOAc, 3:1) to furnish **44** (26.5 mg, 0.046 mmol, 49%) as a colorless oil; R_f = 0.5 (heptane/EtOAc, 3:1). $[\alpha]_D^{20}$ = +13.6 (c = 1.95, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.04 [s, 9 H, SiC(CH_3)$_3$], 1.93 [s, 3 H, OC(O)CH_3], 2.44 (s, 3 H, PhCH_3), 3.91 (d, $J_{6,5}$ = 1.5 Hz, 2 H, 6-H), 4.36 (m, 2 H, 4-H, 5-H), 5.55 (d, $J_{3,4}$ = 9.2 Hz, 1 H, 3-H), 5.91 (d, J = 6.1 Hz, 1 H, NH), 7.20–7.75 (m, 14 H, H arom) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 19.6 [SiC(CH_3)$_3$], 20.3 [OC(O)CH_3], 21.7 (PhCH_3), 26.8 [SiC(CH_3)$_3$], 54.5 (C-4), 60.8 (C-6), 72.2 (C-3), 81.1 (C-5), 127.5, 127.9, 128.0, 129.8, 129.9, 130.0, 130.1 (CH arom), 132.4, 133.0 (C arom), 134.9, 135.7, 135.9, (CH arom), 136.8 (C arom), 144.1 (SO_2CArCH$_3$), 168.6 (C=O, lactone), 170.3 (C=O, ester) ppm. FTIR: $\tilde{\nu}$ = 3277 (NH), 2929, 2856, 1799 (C=O, lactone), 1754 (C=O, ester), 1427, 1111, 703 cm^{-1}. HRMS (ESI)$^+$: calcd. for [$C_{30}H_{35}NO_7SSiNa$]$^+$ 604.1801; found 604.1806.

(3*S*,4*R*,5*S*)-3-Acetoxy-4-[(acetyl)(tosyl)amino]-5-[(*tert*-butyldiphenylsilyloxy)methyl]tetrahydrofuran-2-one (45): Acetic anhydride (91.2 μL, 0.96 mmol) and tributylphosphane (16 μL, 64 μmol) were successively added, in a glass tube under argon, to a solution of **42** (167.7 mg, 0.32 mmol) in freshly distilled toluene (1 mL). The tube was sealed, placed in a microwave oven, and heated at 130 °C for 30 min. The reaction mixture was diluted with water (1 mL). After separation of the phases, the aqueous phase was extracted with EtOAc (2 × 1 mL). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ (1 mL), water (1 mL), and saturated aqueous NaCl. The organic phase was dried with $MgSO_4$ and filtered, and the solvents were evaporated under vacuum. The resulting oil was purified by column chromatography on silica gel (heptane/EtOAc, 4:1) to furnish **45** (144.2 mg, 0.23 mmol, 72%) as a colorless oil; R_f = 0.5 (heptane/EtOAc, 4:1). $[\alpha]_D^{20}$ = +24 (c = 1.12, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.10 [s, 9 H, SiC(CH_3)$_3$], 1.94 [s, 3 H, OC(O)CH_3], 2.44 (s, 3 H, PhCH_3), 2.51 [3 H, NC(O)CH_3], 3.80 (dd, J = 1.9, J = 11.9 Hz, 1 H, 6-H), 3.94 (dd, J = 1.6, J = 11.9 Hz, 1 H, 6′-H), 4.64 (m, 1 H, 5-H), 5.27 (m, 1 H, 4-H), 5.96 (d, $J_{3,4}$ = 5.4 Hz, 1 H, 3-H), 7.26–7.85 (m, 14 H, H arom) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 19.4 [SiC(CH_3)$_3$], 20.4 [OC(O)CH_3], 21.8 (PhCH_3), 26.0 [NC(O)CH_3], 26.8 [SiC(CH_3)$_3$], 59.3 (C-4), 62.3 (C-6), 70.3 (C-3), 80.8 (C-5), 127.8, 128.0, 130.1, 130.4 (CH arom), 132.1, 132.9, 135.5 (C arom), 135.7, 135.8 (CH arom), 146.0 (SO_2CArCH$_3$), 169.3 (C=O, ester), 170.2 (C=O, lactone), 171.2 (C=O, carbamate) ppm. FTIR: $\tilde{\nu}$ = 2930, 2857, 1791 (C=O, lactone), 1752 (C=O, ester), 1693 (C=O, amide), 1427, 1365, 1187, 1104, 926, 701 cm^{-1}. HRMS (ESI)$^+$: calcd. for [$C_{32}H_{37}NO_8S$-SiNa]$^+$ 646.1907; found 646.1933.

(1*R*,4*S*,5*S*)-4-[(1*S*)-1-(*tert*-Butyldiphenylsilyloxy)but-3-enyl]-6-tosyl-3-oxa-6-azabicyclo[3.1.0]hexan-2-one (46): DDQ (103.4 mg, 0.46 mmol) was added at room temperature to a solution of aziridino-γ-lactone **35** (254 mg, 0.46 mmol) in CH_2Cl_2 (4.6 mL) and H_2O (0.46 mL). After the mixture had been stirred for 24 h, pyridine (0.55 mL, 6.83 mmol) and tosyl chloride (347.3 mg, 1.82 mmol) were added. After 2 h, the mixture was diluted with CH_2Cl_2 (5 mL) and water (5 mL). The phases were separated, and the organic phase was washed successively with water (2 × 10 mL) and with saturated aqueous NaCl (10 mL), dried with $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (EtOAc/heptane, 1:4) to afford compound **46** (157.1 mg, 0.28 mmol, 60%) as a viscous colorless oil; R_f = 0.60 (EtOAc/heptane, 1:4). $[\alpha]_D^{20}$ = +12 (c = 0.72, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.06 [s, 9 H, SiC(CH_3)$_3$], 2.20 (m, 1 H, 8-H), 2.45 (m, 1 H, 8′-H), 2.49 (s, 3 H, PhCH_3), 3.64 (d, J = 4.9 Hz, 1 H, 1-H), 3.83 (d, J = 4.9 Hz, 1 H, 5-H), 3.90 (m, 1 H, 7-H), 4.47 (d, J = 2.0 Hz, 1 H, 4-H), 4.94 (m, 1 H, 10-H), 5.00 (m, 1 H, 10′-H), 5.48 (m, 1 H, 9-H), 7.35–7.86 (m, 14 H, H arom) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 19.6 [SiC(CH_3)$_3$], 21.8 (PhCH_3), 27.0

[SiC(CH_3)$_3$], 37.5 (C-8), 40.3 (C-1), 43.7 (C-5), 72.8 (C-7), 80.2 (C-4), 119.4 (C-10), 128.0, 128.3, 130.2, 130.5, 132.4 (C-9), 133.0, 133.9, 135.9, 136.0, 145.9, (SO_2CArCH_3), 168.4 (C=O, lactone) ppm. FTIR: $\tilde{\nu}$ = 2928, 2856, 1792 (C=O, lactone), 1427, 1337, 1159, 702 cm^{-1}. HRMS (ESI)$^+$: calcd. for [$C_{31}H_{35}NO_5SSiNa$]$^+$ 584.1903; found 584.1921.

(3*S*,4*R*,5*S*)-3-Acetoxy-4-[(acetyl)(tosyl)amino]-5-[(1*S*)-1-(*tert*-butyldiphenylsilyloxy)but-3-enyl]tetrahydrofuran-2-one (47): Acetic anhydride (29.4 μL, 0.31 mmol) and tri-*n*-butylphosphane (5.1 μL, 21 μmol) were added to a solution of **46** (58.3 mg, 0.1 mmol) in toluene (340 mL), placed in a glass tube under argon. The tube was sealed and heated at 90 °C in a microwave oven for 2 h. After cooling, the reaction mixture was concentrated in vacuo, the resulting crude product was suspended in water (0.5 mL) and stirred for 10 min, and then EtOAc (0.5 mL) was added. After separation of the phases, the aqueous phase was extracted with EtOAc (2 × 0.5 mL). The organic phases were combined and washed with saturated aqueous $NaHCO_3$ (5 mL), water (5 mL), and saturated aqueous NaCl, dried with $MgSO_4$, and filtered, and the solvents were evaporated to dryness under vacuum. The crude product was purified by preparative TLC on silica gel (heptane/EtOAc, 2:1) to furnish compound **47** (52.5 mg, 0.079 mmol, 79%) as a viscous colorless oil; R_f = 0.55 (heptane/EtOAc, 2:1). $[\alpha]_D^{20}$ = +45.8 (*c* = 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.07 [s, 9 H, SiC(CH_3)$_3$], 1.98 [s, 3 H, OC(O)CH_3], 2.08 (m, 1 H, 7-H), 2.43 (m, 1 H, 7′-H), 2.48 (s, 3 H, PhCH_3), 2.50 [s, 3 H, NC(O)CH_3], 3.92 (ddd, *J* = 0.7, *J* = 3.8, *J* = 10.8 Hz, 1 H, 6-H), 4.56 (ddd, *J* = 0.7, *J* = 4.8 Hz, 1 H, 5-H), 4.76 (m, 1 H, 9-H), 4.88 (m, 1 H, 9′-H), 5.28 (m, 1 H, 8-H), 5.33 (dd, *J* = 5.21, *J* = 4.84 Hz, 1 H, 4-H), 6.01 (d, $J_{3,4}$ = 5.21 Hz, 1 H, 3-H), 7.3–7.9 (m, 14 H, H arom) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 19.6 [Si*C*(CH_3)$_3$], 20.5 [OC(O)*C*H$_3$], 21.8 (Ph*C*H$_3$), 26.0 [NC(O)*C*H$_3$], 26.9 [SiC(*C*H$_3$)$_3$], 37.7 (C-7), 60.4 (C-4), 70.3 (C-3), 73.2 (C-6), 81.0 (C-5), 119.4 (C-9), 127.7, 127.8, 128.1, 129.9, 130.2, 130.5, 132.5, 132.6 (C arom), 133.7 (C-8), 135.9, 136.0, 145.9 (SO_2CArCH_3), 169.2 (C=O, acetate), 170.4 (C=O, lactone), 171.2 (C=O, amide) ppm. FTIR: $\tilde{\nu}$ = 2930, 2856, 1794 (C=O, lactone), 1755 (C=O, ester), 1694 (C=O, amide), 1427, 1367, 1189, 1111, 704 cm^{-1}. HRMS (ESI)$^+$: calcd. for [$C_{35}H_{41}NO_8SSiNa$]$^+$ 686.2211; found 686.2220.

(3*S*,4*R*,5*S*)-3-Acetoxy-5-[(1*S*,3*E*)-1-(*tert*-butyldiphenylsilyloxy)-4-phenylbut-3-enyl]-4-(tosylamino)tetrahydrofuran-2-one (48): Palladium diacetate (1.2 mg, 5.3 μmol), triphenylphosphane (2.8 mg, 10.6 μmol), triethylamine (36 μL, 265 μmol), and iodobenzene (7.7 μL, 69 μmol) were added successively at room temperature under argon to a solution of **47** (35 mg, 53 μmol) in DMF (183 μL). The reaction mixture was heated to 110 °C and stirred for 24 h. The mixture was then diluted with EtOAc (5 mL) and water (5 mL). After separation of the phases, the aqueous phase was extracted with EtOAc (2 × 5 mL). The organic phases were combined, dried with $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by flash chromatography (EtOAc/heptane, 7:3) to afford **48** (27.3 mg, 39 μmol, 74%) as a colorless oil; R_f = 0.50 (EtOAc/heptane, 7:3). $[\alpha]_D^{20}$ = +54 (*c* = 0.75, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.02 [s, 9 H, SiC(CH_3)$_3$], 1.87 [s, 3 H, OC(O)CH_3], 2.29 (m, 1 H, 7-H), 2.39 (s, 3 H, PhCH_3), 2.47 (m, 1 H, 7′-H), 4.17 (dd, $J_{6,7'}$ = 4.6, $J_{6,7}$ = 10.1 Hz, 1 H, 6-H), 4.36 (d, $J_{5,4}$ = 7.3 Hz, 1 H, 5-H), 4.48 (m, 1 H, 4-H), 5.50 (d, $J_{3,4}$ = 8.9 Hz, 1 H, 3-H), 5.66 (m, 1 H, 8-H), 6.13 (d, $J_{9,8}$ = 15.9 Hz, 1 H, 9-H), 7.13–7.85 (m, 19 H, H arom) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 19.6 [Si*C*(CH_3)$_3$], 20.2 [OC(O)*C*H$_3$], 21.7 (Ph*C*H$_3$), 27.0 [SiC(*C*H$_3$)$_3$], 37.3 (C-7), 55.4 (C-4), 71.2 (C-6), 72.4 (C-3), 81.3 (C-5), 123.9 (C-8), 126.3, 127.4, 127.9, 128.1, 128.6, 129.9, 130.0, 130.2, 130.5, 133.1, 133.7 (C arom), 134.2 (C-9), 136.0, 136.9, 137.3 (C arom), 144.0 (SO_2CArCH_3), 168.8 (C=O, lactone), 169.9 (C=O, acetate) ppm. FTIR: $\tilde{\nu}$ = 2924, 2853, 1797, 1754 (C=O), 1427, 1111, 703 cm^{-1}. HRMS (ESI)$^-$: calcd. for [$C_{39}H_{43}NO_7SSi$ – H]$^-$ 696.2451; found 696.2435.

(2*S*,3*R*,4*S*,5*S*,7*E*)-2,4-Diacetoxy-*N*-benzyl-5-(*tert*-butyldiphenylsilyloxy)-8-phenyl-3-(tosylamino)oct-7-enamide (51): Benzylamine (4 μL, 32 μmol) was added at room temperature under argon to a solution of **48** (20 mg, 29 μmol) in THF (0.2 mL). After 2 h of stirring, the solvent was evaporated to dryness under vacuum. The resulting crude product was purified by flash chromatography on silica gel (EtOAc/heptane, 3:7) to furnish a mixture of 2-*O*- and 4-*O*-monoacetylated derivatives **49** and **50** (18.1 mg). The mixture was dissolved in pyridine (0.4 mL), and acetic anhydride was added (0.4 mL). After 18 h of stirring, the reaction mixture was concentrated to dryness under vacuum, and the crude product was purified by preparative TLC on silica gel (EtOAc/heptane, 3:7) to furnish the benzamido APTO derivative **51** (14.6 mg, 16.4 μmol, 60%) as a colorless oil; R_f = 0.65 (EtOAc/heptane, 1:1). $[\alpha]_D^{20}$ = +45.3 (*c* = 0.6, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.82 [s, 9 H, SiC(CH_3)$_3$], 1.66, 1.70 (2 × s, 6 H, 2 × CH_3CO), 1.86 (m, 2 H, 6-H), 2.10 (s, 3 H, PhCH_3), 3.92 (dd, *J* = 5.0, *J* = 14.8 Hz, 1 H, CH_2Ph), 4.10 (m, 1 H, 5-H), 4.12 (dd, *J* = 6.3, *J* = 14.8 Hz, 1 H, CH_2Ph), 4.17 (m, 1 H, 3-H), 4.72 (dd, *J* = 3.5, *J* = 6.0 Hz, 1 H, 4-H), 5.08 (d, *J* = 3.8 Hz, 1 H, 2-H), 5.44 (dt, *J* = 7.9, *J* = 15.8 Hz, 1 H, 7-H), 5.65 (d, 1 H, N*H*Ts), 5.70 (d, *J* = 15.8 Hz, 1 H, 8-H), 5.86 (t, *J* = 5.4 Hz, 1 H, N*H*Bn), 6.74–7.62 (m, 24 H, H arom) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 20.6, 20.7 (2 × *C*H$_3$CO), 26.9 (Ph*C*H$_3$), 36.6 (C6), 43.5 (*C*H$_2$Bn), 54.8 (C-3), 71.8 (C-2), 72.9 (C-4), 73.1 (C-5), 124.1 (C-7), 126.1, 127.1, 127.2, 127.4, 127.6, 127.7, 127.8, 127.9, 128.0, 128.1, 128.3, 128.7, 129.6, 129.8, 130.0, 133.0 (C arom), 133.3 (C-8), 134.0, 135.8, 135.9, 137.1, 137.2 (C arom), 167.3, 168.9 (2 × CH$_3$*C*O), 169.8 (*C*ONHPh) ppm. FTIR: $\tilde{\nu}$ = 3282, 2924, 2854, 1745, 1683, 1598, 1522, 1495, 1426, 1370, 1331, 1224, 1157, 1057, 965, 814, 740, 700, 667 cm^{-1}. HRMS (ESI)$^+$: calcd. for [$C_{48}H_{54}N_2O_8SSiNa$]$^+$ 869.3234; found 869.3268.

Supporting Information (see footnote on the first page of this article): NMR spectra of compounds **35**, **39**–**42**, **44**–**46**, **47**, **48**, **51**.

Acknowledgments

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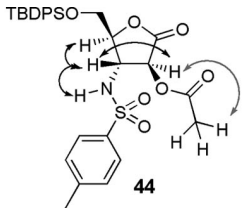

44

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