An Enantioselective Ring Expansion Route Leading to Furanose and Pyranose Nucleosides Featuring Spirodiketopiperazines at the Anomeric Position

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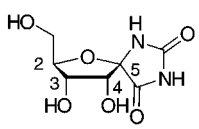
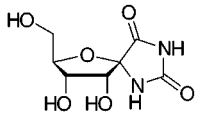
A study directed at the enantioselective synthesis of spirodiketopiperazine homologues of hydantocidin is described. Furanoid glycals, systems that are amenable to C-5 metalation in the presence of *tert*-butyllithium, are readily coupled to N-protected 2,3-azetidinediones provided that at least 1 equiv of BF_3·OEt_2 is present to curb enolization. The resulting 1:1 mixtures of carbinols undergo smooth ring expansion to spirocyclic keto amides when heated with pyridinium *p*-toluenesulfonate in benzene. 1,2-Acyl shifts operate exclusively. Since attempts to engage these products in Beckmann rearrangement proved singularly unsuccessful, recourse was alternatively made to new methodology based upon sequential Baeyer−Villiger oxidation and ammonolysis. The data show that the first of these steps occurs with exclusive migration of the quaternary carbon. Furthermore, nucleophilic attack by NH_3 can be directed regioselectively to the anomeric region. If heating is supplied during acid-promoted cyclization to the spirodiketopiperazines, spiropyranose derivatives are produced in a complementary process. The central issue of this synthesis effort was the utilization of 4-phenylseleno-substituted furanoid glycals so as to ultimately enable introduction of the cis-diol functionality at C-3 and C-4 (hydantocidin numbering).

(+)-Hydantocidin (**1**) is an architecturally unusual spirohydantoin D-ribofuranose nucleoside recently isolated from fermentation broths of *Streptomyces hygroscopicus* SANK 63584,[1] Tu-2474,[2] and A1491.[3] This



(+)-**1**



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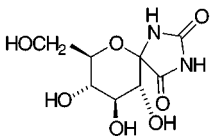

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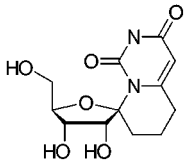

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substance was quickly recognized to be an extremely potent herbicide devoid of toxicity to animals and microorganisms.[1,4] This plant-growth regulator functions as a proherbicide to a metabolite that inhibits purine biosynthesis at the adenylosuccinate synthase site.[5] These observations have understandably stimulated considerable interest not only in the synthesis of **1**[6] but also in a variety of its analogues. Included in this group are the levorotatory C-5 epimer (**2**),[7] several deoxy derivatives,[4,8] as well as carbocyclic[9] and sulfur-containing isosteres.[10] Additional preparative work has focused on the elaboration of pyranose derivatives of various types (e.g., **3**)[11] or of more diverse spiroheterocyclic subunits (e.g., **4**).[12]

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(2) Ciba-Geigy, DE Pat. 41 29 616 A, 10/09/1990.

(3) Mitsubishi Kasei, Jpn. Pat. 04222589 A, 19/12/1990.

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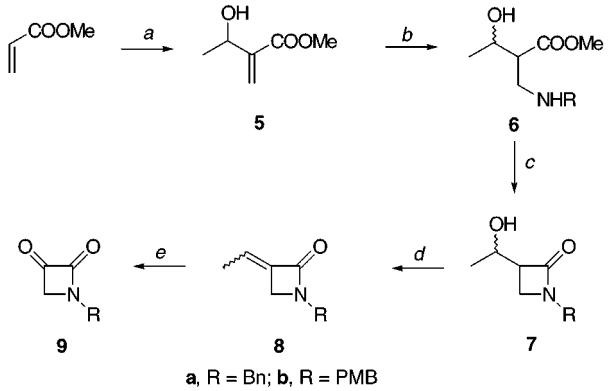
The fact that naturally occurring[13] and synthetic diketopiperazines[14] constitute a class of bioactive peptides[15] has not escaped attention. Fleet and co-workers have recently reported the incorporation of a spirodiketopiperazine ring into the anomeric position of furanose[16] and pyranose sugars[17] in an effort to mimic **1**. Our interest in constrained nucleosides of this type arose in the same context[18] and as a result of new ring expansion methodology being developed in this laboratory.[19] This paper explores the synthesis of a member of this compound class in which an acid-catalyzed rearrangement of a 3-hydroxy β-lactam and the ammonolysis of a spiro keto lactone are featured.

Results and Discussion

Coupling of Furanoid Glycals to N-Protected Azetidinediones. *N*-*p*-Methoxybenzyl-2,3-azetidinedione (**9b**) was prepared starting from methyl acrylate and acetaldehyde in a manner parallel to that developed earlier for the *N*-benzyl derivative **9a** (Scheme 1).[20,21] Entirely comparable yields were realized in steps *b*−*e*.

Scheme 1[a]



[a] Key: (a) CH_3CHO, DABCO, MeOH; (b) $ArCH_2NH_2$, MeOH; (c) *t*-BuMgCl, THF; (d) MsCl, Et_3N, CH_2Cl_2; DBU; (e) $NaIO_4$, (OsO_4), MeOH, H_2O.

Possible complications associated with the addition of carbon nucleophiles to α-keto-β-lactams have been alluded to by Palomo and co-workers.[22] These include a pronounced tendency to undergo enolization[23] and, in protic solvents, hemiacetal formation. Our investigation into both of these concerns revealed that **9a** was 70% enolized in $CDCl_3$ at room temperature (^{1}H NMR analysis). In D_2O, only the keto form was observed. The addition of Lewis acids, most notably boron trifluoride etherate, to $CDCl_3$ solutions likewise had the effect of driving the equilibrium strongly in the keto direction. As a consequence, all of the addition reactions reported herein were performed in the presence of $BF_3{\cdot}OEt_2$.

Furthermore, as the double bond cleavage in **8** is performed in aqueous methanol, the oxidation results in initial formation of the methyl hemiketal derivative. To avoid low yields in the ensuing glycal coupling step, care must be exercised to ensure complete removal of the methanol, either by prolonged warming under high vacuum or by recrystallization.

(*S*)-(+)-Dihydro-5-(hydroxymethyl)-2-(3,4)-furanone (**10**) was prepared in 97% enantiomeric excess from L-glutamic acid according to precedent.[24,25] Although the robust trityl protecting group was utilized in the early phases of this investigation, recourse was subsequently made to the *tert*-butyldimethylsilyl alternative in order to facilitate later unmasking of this hydroxyl.[26]

Dibal-H reduction of **10a** and **10b** followed by acetylation of the resulting lactols and vacuum pyrolysis in a Kugelrohr apparatus[27] gave rise efficiently to **12a** and **12b**, respectively (Scheme 2). In keeping with the kinetic acidity exhibited by the parent dihydrofuran[28] and alkyl derivatives thereof,[27b] **12a** and **12b** could be metalated at C-5 by exposure to *tert*-butyllithium at low temperature. Deprotonation α to silicon is reportedly a problem in the presence of this alkyllithium.[29] However, a deuterium labeling study designed to measure the regiochemistry and extent of lithiation of **12b** under standard conditions (*t*-BuLi, 30 min at −78 °C followed by 30 min at −20 to 0 °C to give a near-colorless solution) revealed that the dihydrofuran undergoes approximately 90% deprotonation at C-1 during this time frame. No deuteration of the CH_3Si groups was noted. Also, exposure

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(24) Ezquerra, J.; He, W.; Paquette, L. A. *Tetrahedron Lett*. **1990**, *31*, 6979 and relevant references therein.

(25) It is strongly recommended that the carboxy lactone precursor to **10** *not* be purified by distillation (165 °C, 0.1 Torr) as this appears to be the main cause of a loss in optical purity in subsequent intermediates (variations from 92 to 30% ee have been measured). This unwanted consequence can be avoided by utilizing the unpurified acid directly in further transformations or by recrystallization of the material from benzene. If the crude material is used, it should be dried sufficiently ($MgSO_4$, then azeotropic removal of benzene solvent) prior to subsequent reduction with the borane−dimethyl sulfide reagent. The reduction of crude acid is even more vigorous, and **great care** must be taken to ensure controlled addition of reducing agent so as to avoid an uncontrollable exotherm. HPLC analysis of **10** prepared in this manner demonstrates that if these precautions are taken the original optical purity of the L-glutamic acid (97% ee) is retained.

(26) The triisopropylsilyl and *tert*-butyldiphenylsilyl groups were introduced with equal success. In retrospect, the high crystallinity and UV activity imparted by the TBDPS functionality to its derivatives may cause its selection to be the most practical one.

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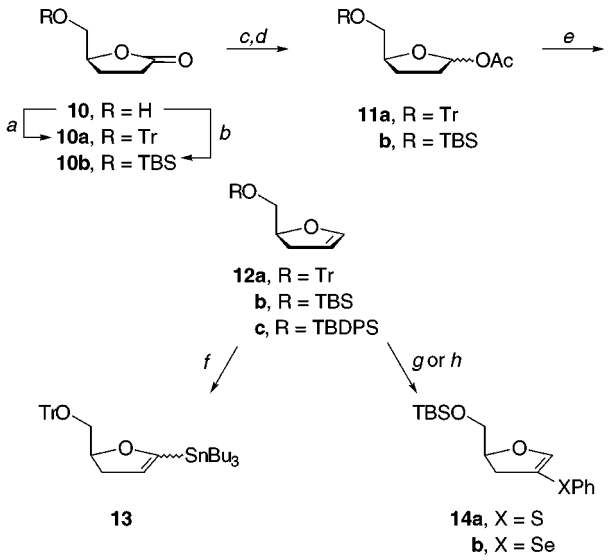
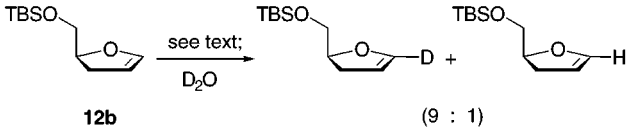
Scheme 2[a]



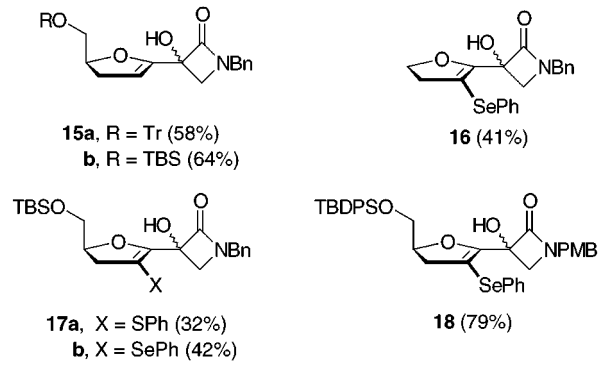
[a] Key: (a) TrCl, DMAP, Et_3N; (b) TBSCl, imid, DMF; (c) Dibal-H, CH_2Cl_2, Et_2O; (d) Ac_2O, py, CH_2Cl_2; (e) 190 °C 0.5 (**11a**) or 70 Torr (**11b**); (f) *t*-BuLi, THF, −78 °C; *n*-Bu_3SnCl; (g) PhSCl, THF, −78 °C; KO-*t*-Bu; (h) PhSeCl, THF, −78 °C; KO-*t*-Bu.

of the lithium derivative of **12a** to excess tri-*n*-butyltin chloride afforded **13** in 60% yield. Subsequent transmetalation of this stannane with *n*-butyllithium made possible clean reconversion to the lithium species without contamination by an excess of *n*-BuLi.[18b]



The formation of **14a** from **12b** via an intermediate chloro sulfide adduct with subsequent dehydrochlorination by means of DBU proved troublesome, giving rise to a complex reaction mixture from which only 17% of the desired product could be retrieved. However, the replacement of DBU by potassium *tert*-butoxide significantly improved the yield (87%) and rate of this conversion. Application of this modification to the phenylselenenyl derivative afforded **14b** without difficulty (78% yield).

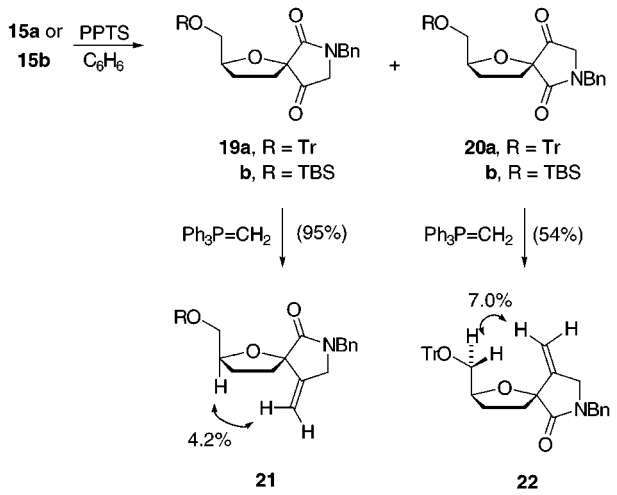
In every case examined, coupling of the lithiated dihydrofuran to **9a** and **9b** at low temperature in THF containing boron trifluoride etherate gave the desired epimeric mixture of carbinols, i.e., **15**−**18**. Considerable variation



in yield was noted, a phenomenon that was directly linked to the quantity of furanoid glycal recovered. Quenching of the lithiated intermediate by the enol tautomer of the 2,3-azetidinedione or incomplete lithiation during the preceding operation are believed to be contributory factors. The adducts proved not to be extraordinarily sensitive and were generally amenable to full characterization as inseparable 1:1 diastereomeric mixtures.

Isomerization of the 3-Hydroxyazetidinones. Pyridinium *p*-toluenesulfonate in benzene solution proved suitable for promoting the key spirocyclization−ring expansion transformation. When **15a** was stirred at 20 °C for 24 h under these conditions, the chromatographically purified lactams **19a** and **20a** were obtained in a 1:2 ratio and a combined isolated yield of 51% (Scheme 3). The rearrangement of **15b**, performed at the reflux

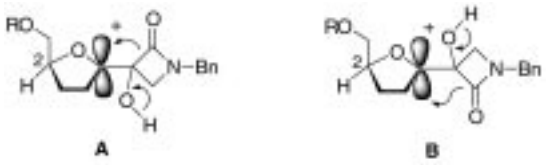
Scheme 3



temperature for a shorter time period (80 min), proceeded more efficiently (92%) to deliver **19b** and **20b**. Like **15a**, **15b** afforded the more polar spirocyclic isomer predominantly (1:1.6). Stereochemical distinction between **19a** and **20a** was achieved by their independent Wittig olefination. Access to **21** and **22** in this manner was followed by detailed analysis of NOE effects in C_6D_6 solution (see formulas). Other revealing ^1H NMR changes were fully consistent with the indicated structural assignments. Thus, the $\Delta\nu_{AB}$ of the protons in the TrOCH_2− group was more than doubled following the conversion of **20a** (53.4 Hz) to **22** (108.8 Hz). The associated effects in **19a** and **21** are only marginal (29.3 Hz → 26.5 Hz). Of equal importance was the fact that chemical shift and infrared data showed the carbonyl groups not to be vicinal. The relative configuration at the spirocyclic center in **19b** and **20b** was initially assigned by analogy and later confirmed unambiguously by X-ray crystallography (see below).

The available evidence supports the working assumption that expansion of the azetidinone ring proceeds exclusively with migration of the carbonyl carbon. This selectivity in favor of 1,2-acyl transfer conforms to observations recorded for many related acid-catalyzed isomerizations, the most exhaustively studied of which relate to α,β-epoxy ketones.[30] Once the glycal double bond has been protonated with formation of the cyclic oxonium

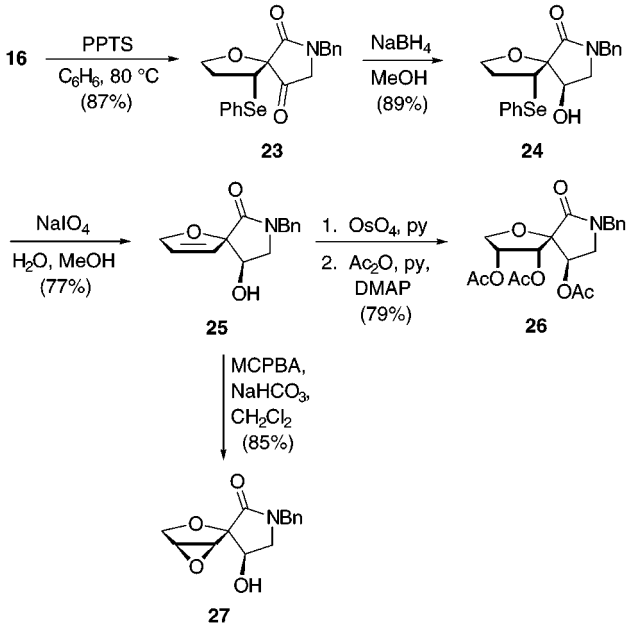
(30) Rosowsky, A. In *Heterocyclic Compounds with Three- and Four-Membered Rings, Part One*, Weissberger, A., Ed.; Interscience: New York, 1964; pp 253−261.



ion, the acyl shift can occur either syn (as in **A**) or anti to the substituent residing at C-2 (see **B**). The intuitive expectation based on steric considerations is that pathway **A** should be impeded to some degree. Significantly, the partitioning of these reaction trajectories gives no evidence of being linked to the diastereomeric ratio present in the starting 3-hydroxy-β-lactams **15**−**18**.

Comparable rearrangement of the model system **16** resulted in efficient conversion to **23** as the only product (Scheme 4). The structural features of **23** were originally

Scheme 4



deduced on the assumption that the 1,2-acyl shift would be directed by the phenylseleno substituent (possibly via an episelenonium ion), such that they would have an anti relationship. Conclusive proof of this assignment began with chemoselective sodium borohydride reduction of the ketone carbonyl in **23**. Hydride delivery under these circumstances is relegated predominantly to the π-surface distal to the selenide substituent. Indeed, **24** predominates by a ratio of 5:1. Selenoxide elimination then afforded olefin **25**, the hydroxyl group in which was utilized to effect syn delivery of OsO_4[31] and *m*-chloroperbenzoic acid.[32] Conversion to the triol occurred in a few hours with a selectivity of 4.7:1. Subsequent acetylation of the major isomer furnished the highly crystalline triacetate **26**, the stereochemical features of which were corroborated by X-ray structural analysis (Figure 1). The hydroxyl group in **25** also cleanly directs epoxidation to provide **27**.[33]

(31) The most successful conditions found for these dihydroxylations are those reported by: Paquette, L. A.; Lowinger, T. B.; Bolin, D. G.; Branan, B. M. *J. Org. Chem.* **1996**, *61*, 7486.

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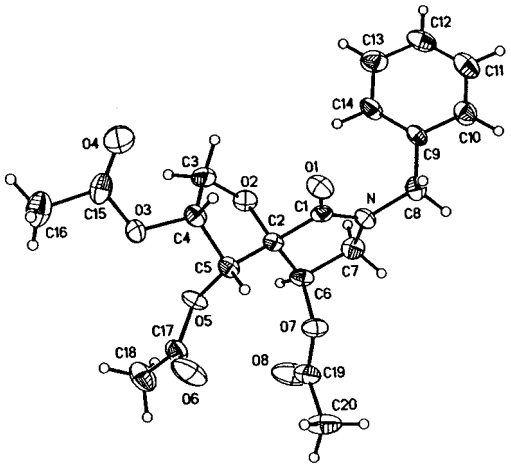
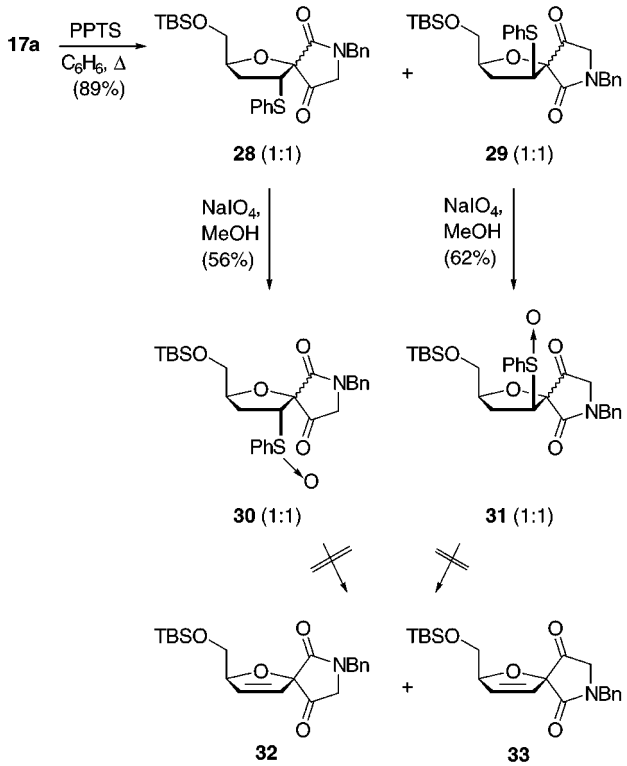


Figure 1. Computer-generated perspective drawing of **26** as determined by X-ray crystallography.

The acid-catalyzed isomerization of **17a** occurs at a considerably slower rate than the unsubstituted analogue **15b** under comparable conditions (48 h versus 80 min). This phenomenon may result because **17a** offers two possible sites for protonation. Although placement of the positive charge adjacent to oxygen is more likely, competitive protonation with generation of a sulfur-stabilized cation would obviate the course of the reaction. A similar rate reduction in spirocyclization is not observed for **16**, **17b**, and **18** since Se-stabilized carbocation generation is less likely. Notwithstanding, comparable yields are realized. Chromatographic purification of this reaction mixture gave two fractions defined as **28** and **29**, ^{1}H NMR analysis of which indicated the presence in each of two coeluting anomers in the approximate ratio of 1:1 (Scheme 5). Whether these anomers vary at C-5 (the spirocyclic center) or at the adjacent sulfur-substituted position would be demonstrated by their conversion to the 3,4-

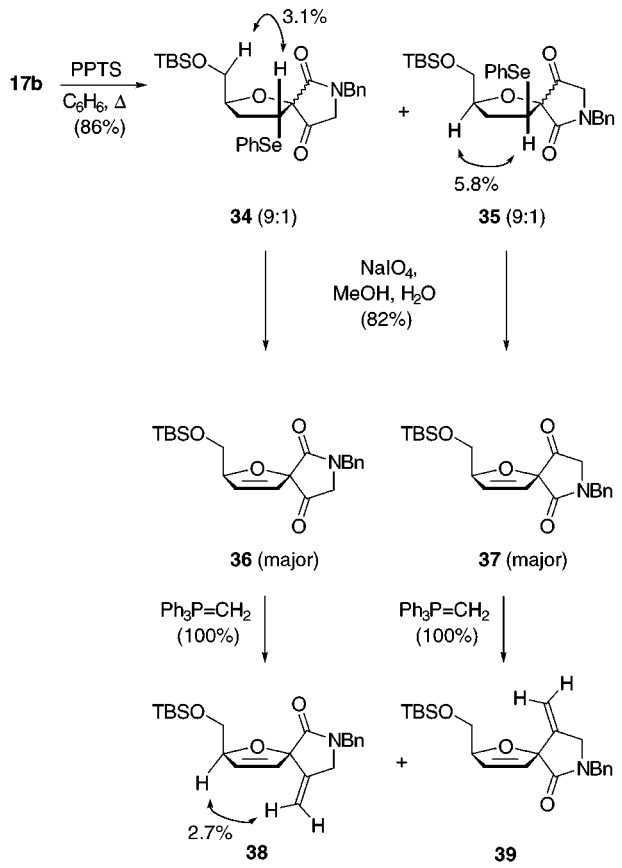
Scheme 5



dehydro analogues via *syn*-sulfoxide elimination. The inefficiencies experienced for the conversions of **28** and **29** into **30** and **31**, respectively, arise in large part because of the low solubilities of these substances in the aqueous methanol reaction medium. Still more problematic was the thermal extrusion step. No reaction was observed in refluxing toluene (111 °C) or chlorobenzene (132 °C) after extended heating (up to 48 h), and only substrate decomposition was seen in refluxing 1,2-dichlorobenzene (180 °C). For these reasons, the greater ease of selenoxide elimination as foreshadowed by the conversion of **24** to **25** was now exploited.

As before, the exposure of **17b** to PPTS in hot benzene afforded all four isomers, albeit with a greater preponderance for two of the four possibilities (approximate ratio 9:1:1:9). This mixture could be separated chromatographically into two fractions denoted as **34** and **35**, each of which consisted of a major and minor component (ratio 9:1, Scheme 6). Subsequent oxidation of each of these

Scheme 6



fractions with sodium metaperiodate gave the corresponding olefin as a diastereomeric mixture (9:1), thus indicating that the two components of each fraction are epimeric at the spirocyclic center. Fortuitously, since **36** and **37** are separable by chromatography, no need exists to deal directly with the **34/35** mixtures.

NOE analysis of the major anomer of **35** indicated that the $TBSOCH_2$ and PhSe substituents have a syn relationship. For the purpose of ascertaining the absolute configuration of the spirocyclic center, **36** and **37** were converted to their *exo*-methylene derivatives and subjected to NOE analysis as before. The structural assignment to **38** is fully consistent with that inferred from the crystal structure of its oxime derivative (see below).

In light of the stereoselectivity exhibited during the rearrangement of **17b**, it may be concluded that there is no facial preference associated with initial protonation of the double bond. The direct consequence of this lack of discrimination is the positioning of the PhSe group on both faces of the furanose ring. After the protonation step, however, the incoming acyl migrant exhibits almost complete selectivity for the face opposite to that occupied by the selenium, possibly because of the transient intervention of an episelenonium intermediate.

Elaboration of the Spirodiketopiperazine Ring. Dideoxy spironucleoside **19b** proved amenable to oximation as long as pyridine (and not sodium acetate) was present. A single geometric isomer was formed (Scheme 7). As a result of the sensitivity of the TBS protecting group to cleavage in the presence of hydroxylamine hydrochloride, this functionality can be preserved or removed at this stage depending on the order of addition of the reagents. The significantly reduced accessibility to the carbonyl group in **20b** required that high-pressure conditions be utilized to obtain **42**. In contrast, the dehydro congeners **36** and **37** undergo rapid oximation at room temperature.

X-ray crystallographic analysis of **44** revealed the presence of an "α-face" oxime with geometry well suited for the planned regioselective Beckmann rearrangement. The presence of an intramolecular hydrogen bond was also noted (Figure 2). Catalytic hydrogenation of **44** gave rise to **40**, thereby intercorrelating all necessary stereochemical assignments.

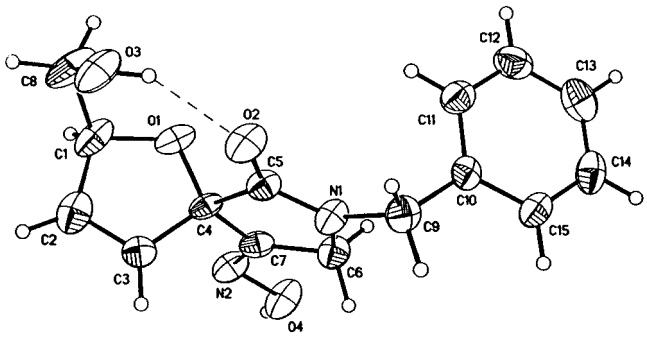


Figure 2. Computer-generated perspective drawing of **44** as determined by X-ray crystallography.

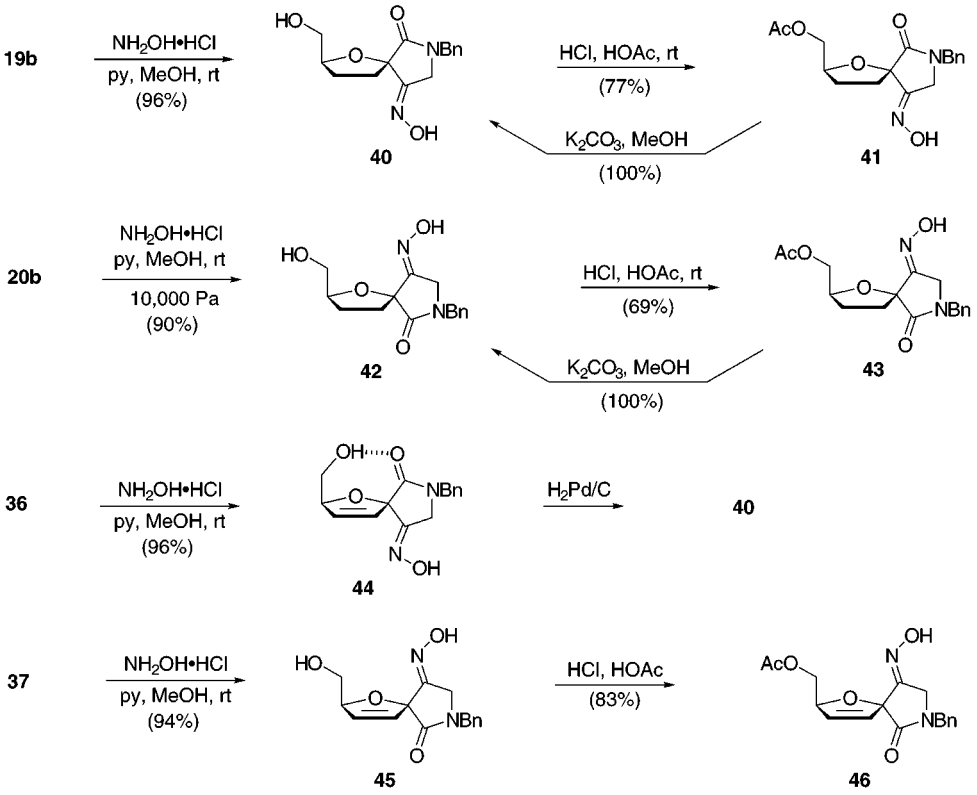
Exposure of either **41** or **42** to widely varying concentrations of hydrogen chloride in acetic acid failed to induce Beckmann rearrangement.[34,35] A ring-expanded diketopiperazine was likewise not obtained when these conditions were applied to **45**. On the basis of spectroscopic evidence, the crystalline products recovered from these attempts proved to be the simple O-acylated derivatives. Treatment of these products with potassium carbonate in aqueous methanol resulted in reconversion to the starting oximes.

When more forcing conditions such as saturated HCl in $HOAc/Ac_2O$ for 1 week or activation of **46** with phosphorus pentachloride in $CHCl_3$ at 0 °C led to no recognizable reaction or in slow decomposition, attention was turned to activation with sulfonyl chlorides.[36] To test this strategy, oximes which retained the TBS protecting

(34) (a) Donaruma, L. G.; Heldt, W. Z. *Org. React.* **1960**, *11*, 1. (b) Gawley, R. E. *Org. React.* **1988**, *35*, 1.

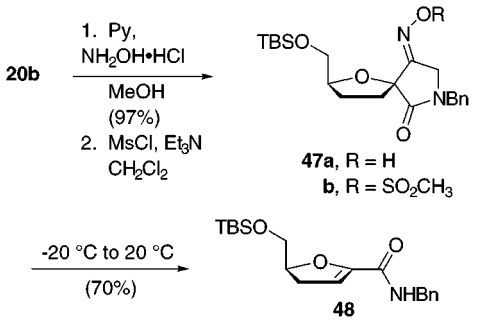
(35) McCarty, C. G. In *Chemistry of the Carbon−Nitrogen Double Bond*, Patai, S., Ed.; Interscience: New York, 1970; pp 408−439.

Scheme 7



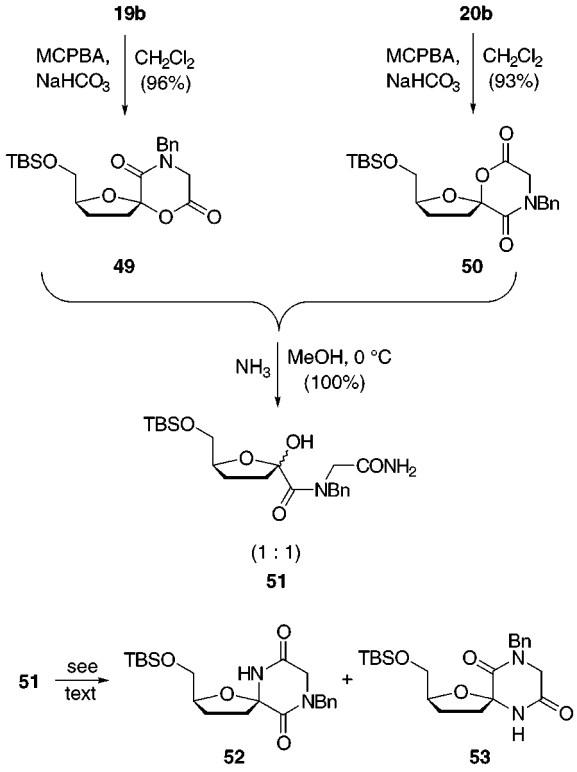
group were required as substrates. When pyridine addition was carried out prior to introduction of the hydroxylamine hydrochloride, **47a** was conveniently generated from **20b**. Although tosylation of this intermediate proved to be sluggish, the derived mesylate **47b** did form at a convenient rate (Scheme 8). Attempted in situ rearrangement merely by allowing the reaction mixture to warm to 20 °C resulted in an unexpected Beckmann fragmentation. Amide **48** was recovered as the only product. In all likelihood, such undesirable fragmentations were expected to be an unavoidable property of these systems. Therefore, an alternative strategy was sought in order to circumvent the problem.

Scheme 8



The diketopiperazine ring was successfully installed by means of the protocol outlined in Scheme 9. Baeyer–Villiger oxidation of all spiro systems examined in this study proceeded rapidly and with complete regioselectivity[37] to form the corresponding spirolactones, thereby intimating exclusive quaternary carbon migration. The requisite formal O to NH exchange was achieved simply by ammonolysis, a process that bears some similarity to the regioselective deprotection of a polyacetylated sugar at its anomeric center,[38] followed by acid-promoted recyclization. The conversion of **19b** and **20b** into **49** and **50**, respectively, with efficiencies approaching 100% is

Scheme 9

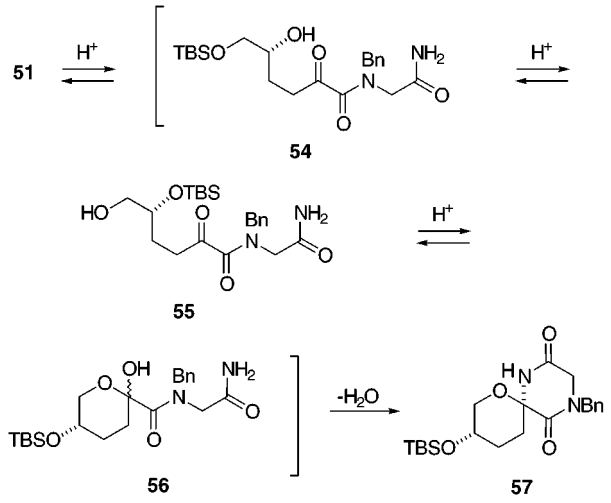


(36) Corey, E. J.; Ueda, Y.; Ruden, R. A. *Tetrahedron Lett.* **1975**, 4347.

(37) Paquette, L. A.; Kinney, M. J.; Dullweber, U. *J. Org. Chem.* **1997**, *62*, 1713.

illustrative of the first step. Subsequent ring cleavage of either product with NH_3 furnished the lactol amide **51** as a 1:1 mixture of epimers. The ring closure of this material, in a reaction patterned after the spiroketalization of a keto diol,[39] has been scrutinized under various conditions. In $CDCl_3$ solution, spontaneous cyclization can be observed by ^1H NMR to proceed to a 1:1 mixture of **52** and **53** with a half-life of approximately 72 h. Alternatively, this process can be completed within 48 h in 95% yield by stirring in benzene containing PPTS and 4 Å molecular sieves. Although 1:1 mixtures again result, the diastereomers are chromatographically separable. At 80 °C, ring closure is complete within 1 h. However, under these more forcing conditions, approximately 30% of a new product with an R_f midway between those of **52** and **53** is generated. Spectroscopic analysis (including NOE) clearly defines this product to be the pyranose spirodiketopiperazine **57** (Scheme 10). The competing

Scheme 10

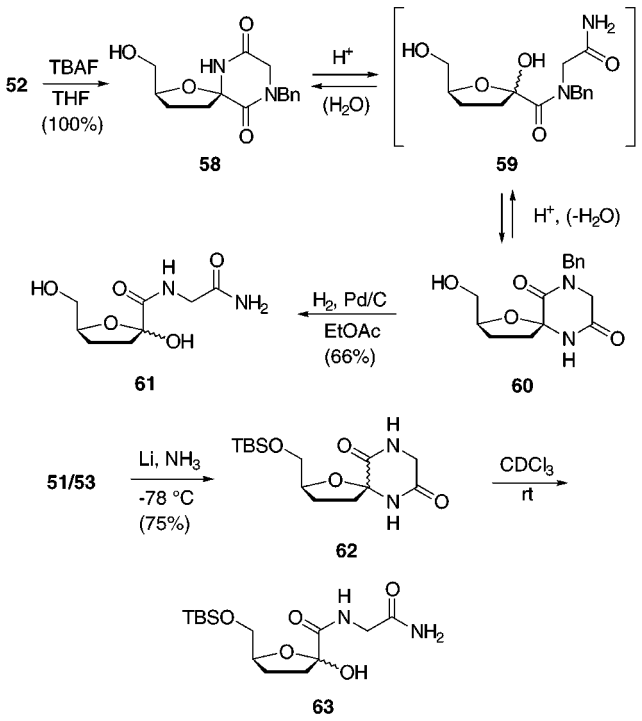


mechanism associated with the appearance of **57** likely involves preliminary equilibration of **51** with its open-chain tautomer **54** followed by primary to secondary silyl group migration as in **55**, and relactonization to the corresponding pyran **57**, possibly via an *N*-acyliminium ion intermediate. The sterically unfavorable migration of the TBS group is considered to be driven by subsequent formation of the assumedly more thermodynamically stable spiro[5,5]pyranose ring resident in **57**.

The effect of prolonged heating on lactol **51** is very predominant conversion to **57**. This being the case, **49**, **50**, and analogues thereof may serve as useful precursors to pyranose as well as furanose systems. Furthermore, this observation raises intriguing questions relating to the dynamic properties and configurational stabilities of these spirocyclic nucleosides.

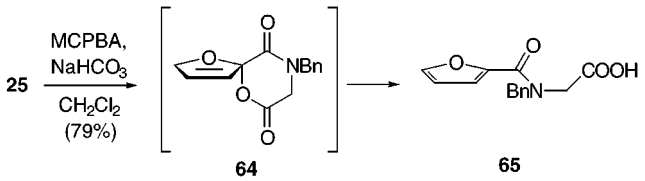
When attempted hydrogenolytic debenzylation of **52** (10% Pd/C in methanol) was found to cause partial loss of the silyl ether protecting group, the order of deprotection was reversed (Scheme 11). Quantitative desilylation was effected with TBAF in THF, but with partial epimer-

Scheme 11



ization (**58/60** = 5:1), likely due to the presence of adventitious moisture in the commercial fluoride reagent. The potential for configurational lability within **58** was further demonstrated by epimerization of the 5:1 anomeric mixture to the 1:1 level upon heating at 50 °C with PPTS in benzene. The anomers are indistinguishable by TLC. A related base-catalyzed isomerization of hydantocidin to the thermodynamically more stable 2-epi derivative is precedented.[7a] Attempted N-deprotection of this mixture by hydrogenolysis proceeded very sluggishly over several days to give **61** and not the intact diketopiperazine. Consequently, recourse was made to lithium in liquid ammonia for this purpose.[40] The debenyzylation proceeded rapidly (<5 min) to give the mixture **62** and a trace of ring-opened compound (≡ **63**). The latter was readily cyclized to **62**. As foreshadowed by earlier results, samples of **62** underwent hydrolysis to **63** in a matter of hours when stored at 0 °C in $CDCl_3$.

Arrival at Fully Functionalized Furanose Systems. The relatively low reactivity of **25**, **36**, and **37** toward osmylation led us to consider elaboration of the spirodiketopiperazine ring prior to olefin dihydroxylation. As anticipated, the peracid oxidation of **25** occurred very cleanly and rapidly (<2 min at −5 °C) as evidenced by TLC analysis. However, the resulting **64** turned out to be unstable upon attempted chromatography. During purification in this manner, complete conversion to furan **65** materialized. This option was therefore not further investigated.



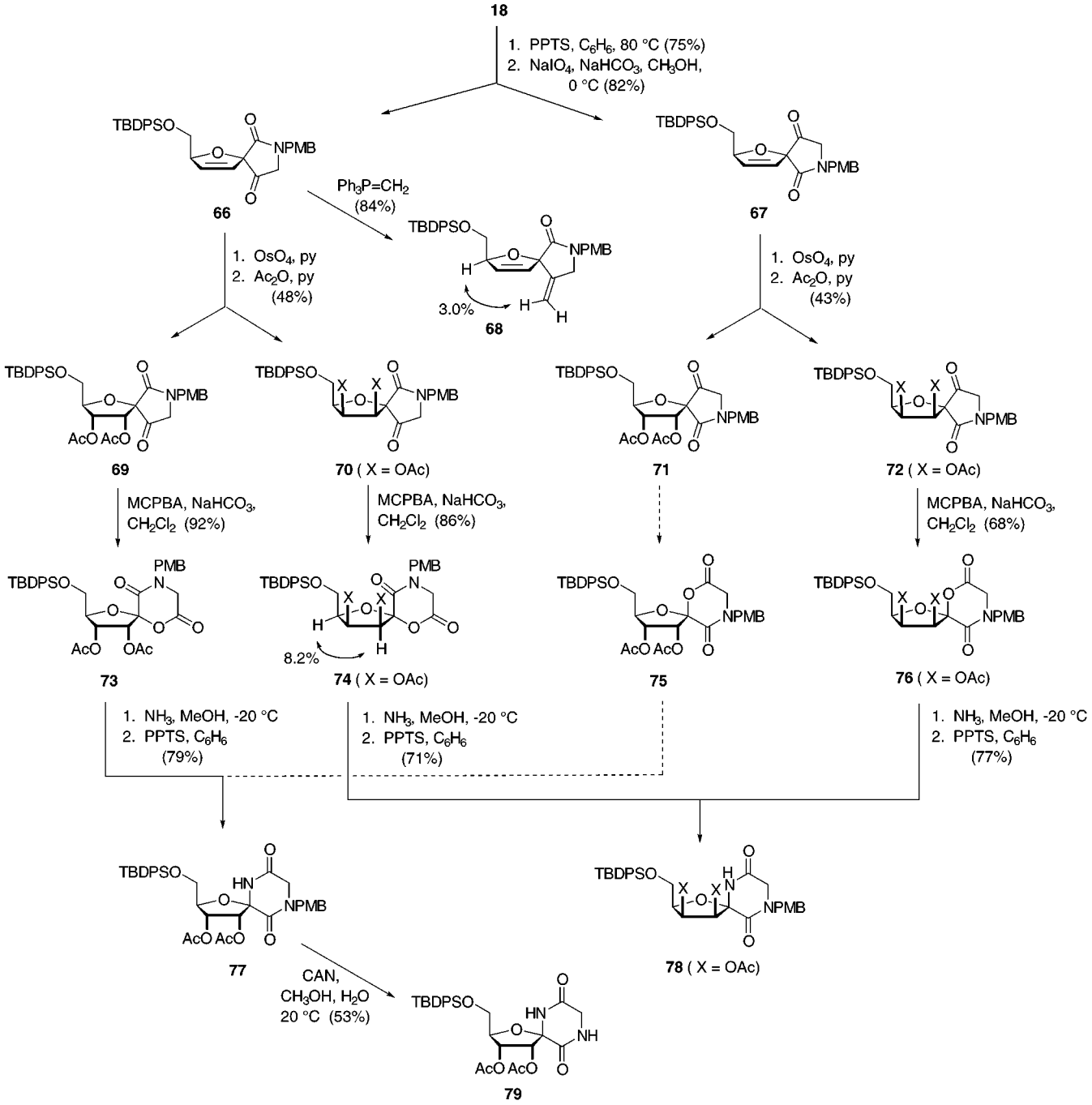
At this stage, attention was directed to **18**, acid-catalyzed rearrangement of which in the predescribed

(38) (a) Mehta, S.; Jordan, K. L.; Weimar, T.; Kreis, U. C.; Batchelor, R. J.; Einstein, F. W. B.; Pinto, B. M. *Tetrahedron*: *Asymmetry* **1994**, *5*, 2367. (b) Excoffier, G.; Gagnaire, D.; Utille, J.-P. *Carbohydr. Res.* **1975**, *39*, 368.

(39) Perron, F.; Albizati, K. F. *Chem. Rev.* **1989**, *89*, 1617.

(40) Kocienski, P. J.; Street, S. D. A.; Yeates, C.; Campbell, S. F. *J. Chem. Soc., Perkin Trans. 1* **1987**, 2171.

Scheme 12



manner provided a mixture of four ring-expanded selenides (ratio 10:1:1:10). Their direct oxidation with sodium periodate in the presence of sodium bicarbonate at 0 °C proceeded cleanly and allowed for the chromatographic separation of **66** from **67** (Scheme 12). Relative stereochemistry was determined by the conversion of **66** to its *exo*-methylene derivative **68**, which exhibited the diagnostic NOE shown.

Dihydroxylation of **66** proceeded with disappointing π-facial stereoselectivity (1:4 ratio of **69:70**) despite the presence of two groups having face-directing potential. Acetylation of this mixture gave the separable diacetates **69** and **70**. Both of these intermediates underwent facile and clean Baeyer−Villiger oxidation to form the corresponding spirolactones **73** and **74**. The latter exhibits a stereochemically diagnostic NOE effect. The ammonolysis of **73** occurred regioselectively without cleavage of the C-3 and C-4 acetates, due to the greater reactivity of the anomeric carboxylate, giving a mixture of lactol amides (1:1 by ^{1}H NMR). Subsequent acid-promoted ring closure resulted in formation of the single spirodiketopiperazine **77** in good yield. The anologous transformation of **74** likewise gave rise to an anomerically pure spiroamide, viz. **78**. In neither case has the absolute configuration of the anomeric center been unequivocally defined.

Additionally, **67** was converted via an identical pathway into **71** and **72** (ratio 1:3). Transformation of the major diastereomer into **76** allowed for the ultimate production of **78**. In the final synthetic maneuver, **77** was found to undergo sluggish oxidative debenzylation with ceric ammonium nitrate.[41]

In summary, application of the oxonium ion-initiated pinacol rearrangement to carbinols **15**−**18** easily obtained by the coupling of 5-lithiated furanoid glycals to 2,3-azetidinediones serves as a useful device for accessing spirocyclic keto lactams such as **19** and **20**. Added versatility is gained when a 4-phenylseleno substituent is present, since this modification allows for the ready introduction of a double bond as in **25**, **36**, **37**, **66**, and **67**. Possibilities for differentiating the two anomeric series at this stage have been identified. The optimal version of the end game involves Baeyer−Villiger oxidation of the derived diacetates followed by regioselective amination of the anomeric carbon. This chemistry defines a concise de novo strategy for the construction of hydantocidin homologues based on L-glutamic acid as the starting material. Further details on the biological actions of these and other compounds will be published elsewhere.

Experimental Section

General Information. Melting points are uncorrected. Magnetic stirring was used for all reactions. Yields were calculated for material judged to be homogeneous by TLC and NMR. Thin-layer chromatography was performed on Merck Kieselgel 60 F_{254} aluminum-backed plates. Flash column chromatography was accomplished in glass columns with Woelm silica gel (230−400 mesh). Solvents were reagent grade and in most cases dried prior to use. The high-resolution mass spectra were obtained at The Ohio State University Chemical Instrumentation Center. Elemental analyses were performed by the Scandinavian Microanalytical Laboratory, Herlev, Denmark, and Atlantic Microlab, Norcross, GA.

3-Ethylidene-1-(*p*-methoxybenzyl)-2-azetidinone (8b). A solution of **5**[20] (49.8 g, 0.38 mol) in methanol (385 mL) was treated dropwise with *p*-methoxybenzylamine (50 mL, 0.38 mol) and stirred for 24 h prior to concentration in vacuo. Flash chromatography of the residue on silica gel (elution with ethyl acetate) gave **6b** as a faintly yellowish oil (100 g, 98%); IR (neat, cm^{-1}) 3325, 1730, 1607; ^1H NMR (200 MHz, $CDCl_3$) δ 7.16 (d, $J = 8.8$ Hz, 2 H), 6.81 (d, $J = 8.8$ Hz, 2 H), 4.22−4.12 (m, 1 H), 3.74 (s, 3 H), 3.66 (s, 2 H), 3.65 (s, 3 H), 3.09−2.90 (m, 2 H), 2.47−2.38 (m, 1 H), 1.13 (d, $J = 6.3$ Hz, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 173.4, 158.6, 130.0, 129.2, 113.6, 69.1, 55.0, 53.0, 51.6, 50.7, 48.2, 21.7; MS *m*/*z* (M^+) calcd 267.1471, obsd 267.1460.

Anal. Calcd for $C_{14}H_{21}NO_4$: C, 62.90; H, 7.92. Found: C, 63.22; H, 8.15.

A procedure entirely parallel to that developed for the preparation of **7a**[20] was employed. From 56.0 g (0.21 mmol) of **6b**, 28.0 g of magnesium turnings, and 120 mL of *tert*-butyl chloride was obtained 48.6 g (98%) of **7b** as a colorless oil: IR (neat, cm^{-1}) 3412, 1729, 1612; ^1H NMR (200 MHz, $CDCl_3$) δ 7.11 (d, $J = 12.0$ Hz, 2 H), 6.78 (d, $J = 12.0$ Hz, 2 H), 4.30 (d, $J = 16$ Hz, 1 H), 4.19 (d, $J = 16$ Hz, 2 H), 4.20−3.97 (m, 1 H), 3.72 (s, 3 H), 3.62 (d, $J = 4.0$ Hz, 1 H), 3.14−2.80 (m, 2 H), 1.18 (d, $J = 9.0$ Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ168.3, 159.0, 129.3, 127.4, 114.0, 64.8, 56.8, 55.1, 45.2, 41.0, 21.3; MS *m*/*z* (M^+) calcd 235.1208, obsd 235.1215.

Anal. Calcd for $C_{13}H_{17}NO_3$: C, 66.36; H, 7.28. Found: C, 66.08; H, 7.53.

A similar procedure to that used for **8a**[20] was followed. Reaction of **7b** (48.6 g, 0.206 mmol) in CH_2Cl_2 (750 mL) with methanesulfonyl chloride (20 mL) followed by DBU (35 mL) in benzene (500 mL) gave **8b** as a pale yellow oil (37.1 g, 83%) following chromatography on silica gel (elution with 50% ethyl acetate in hexanes); IR (neat, cm^{-1}) 1743, 1612, 1513; ^1H NMR (300 MHz, $CDCl_3$) δ (major isomer) 7.15 (d, $J = 8.7$ Hz, 2 H), 6.84 (d, $J = 8.7$ Hz, 2 H), 6.12 (m, 1 H), 4.39 (s, 2 H), 3.77 (s, 3 H), 3.57 (m, 2 H), 1.66 (d, $J = 7.0$ Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (major isomer) 163.7, 159.0, 138.1, 136.7, 129.3, 121.1, 114.0, 55.2, 46.1 45.2, 14.1; MS *m*/*z* (M^+) calcd 217.1103, obsd 217.1109.

Anal. Calcd for $C_{13}H_{15}NO_2$: C, 71.87; H, 6.96. Found: C, 71.65; H, 7.04.

1-(*p*-Methoxybenzyl)-2,3-azetidinedione (9b). The procedure developed for **9a**[20] was followed. From 30.0 g (0.138 mmol) of **8b** in methanol (900 mL) and distilled water (500 mL), finely ground sodium periodate (80.0 g), and osmium tetraoxide (40 mg) was obtained 23.1 g (82%) of **9b** as a crystalline solid: mp 96−97.5 °C (from ethyl acetate); IR (neat, cm^{-1}) 3325, 1730, 1607; ^1H NMR (300 MHz, $CDCl_3$) δ 7.19 (d, $J = 8.6$ Hz, 2 H), 6.89 (d, $J = 8.6$ Hz, 2 H), 4.69 (s, 2 H), 3.79 (s, 3 H), 3.76 (s, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.0, 163.3, 159.7, 129.8, 125.4, 114.5, 58.8, 55.3, 46.4; MS *m*/*z* (M^+) calcd 205.0739, obsd 205.0758.

Anal. Calcd for $C_{11}H_{11}NO_3$: C, 64.38; H, 5.40. Found: C, 64.74; H, 5.53.

(*S*)-2,3-Dihydro-2-[(trityloxy)methyl]furan (12a). A solution of the lactol from **10a**[42] (750 mg, 2.08 mmol) in pyridine (25 mL) was treated with acetic anhydride (0.5 mL, 5.20 mmol), stirred overnight, diluted with ether (50 mL), washed with saturated $NaHCO_3$ solution (2×) and brine, dried, and evaporated in vacuo. Chromatographic purification on silica gel (elution with 10% ethyl acetate in hexanes) gave **11a** (620 mg, 74%) as a 1:3 mixture of α- and β-anomers: ^1H NMR (300 MHz, $CDCl_3$) δ (less polar anomer) 7.46−7.16 (series of m, 15 H), 6.38 (d, $J = 6.5$ Hz, 1 H), 4.45 (m, 1 H), 3.14 (AB, $J = 4.6$, 3.2 Hz, $\Delta\nu = 14.3$ Hz, 2 H), 2.23−2.10 (m, 2 H), 2.05 (s, 3 H), 2.02−1.61 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (less polar anomer) 170.5, 143.9, 128.2, 127.7, 127.0, 99.5, 86.6, 79.3, 65.6, 31.8, 25.3, 21.4; $[\alpha]_D^{20}$ +11.76 (*c* 1.27, CH_2Cl_2).

Anal. Calcd for $C_{26}H_{26}O_4$: C, 77.59; H, 6.51. Found: C, 77.47; H, 6.59.

A 850 mg (2.48 mmol) sample of **11a** was heated at 190 °C and 0.5 Torr in a Kugelrohr apparatus for 90 min. The resulting clear oil was purified on silica gel (eluting with 10% ethyl acetate and 2% triethylamine in hexanes) to provide 660 mg (91%) of **12a**, which exhibited spectra identical to those reported in the literature.

***tert*-Butyl[[(*S*)-2,3-dihydro-2-furyl]methoxy]dimethylsilane (12b).** A solution of (*S*)−(+)-**10b** (20.0 g, 0.087 mmol) in ether (200 mL) and CH_2Cl_2 (200 mL) was blanketed with N_2, cooled to −78 °C, and treated dropwise with Dibal-H (130.0 mL of 1 M in hexanes, 0.13 mol). The reaction mixture was maintained at −78 °C for 3 h, quenched with methanol (30 mL), and allowed to warm gradually to room temperature. After dilution with saturated Rochelle's salt solution and another hour of stirring, the product was extracted into ether (3 × 150 mL), and the combined organic extracts were dried and concentrated to give the lactol as a colorless oil (20.1 g, 100%).

A solution of the lactol (40.0 g, 0.17 mmol) in CH_2Cl_2 (500 mL) and pyridine (50 mL) was treated with acetic anhydride (19.3 g, 0.19 mol), stirred for 48 h, and processed in the predescribed manner to furnish **11b** (45.4 g, 96%). Heating of a 2.7 g (9.8 mmol) sample of this material as detailed earlier for **12a** gave **12b** (2.03 g, 96%) as a volatile colorless oil that was used without further purification.

***tert*-Butyl[[(*S*)-2,3-dihydro-4-(phenylthio)-2-furyl]methoxy]dimethyl silane (14a).** A cold (−78 °C), magnetically stirred solution of **12b** (1.54 g, 7.20 mmol) in THF (15 mL) was treated dropwise with phenylsulfenyl chloride until a faint yellow coloration just persisted (ca 1 mL). The reaction mixture was agitated for 15 min prior to the addition of finely divided potassium *tert*-butoxide (1.18 g, 1.5 equiv) with vigorous stirring, allowed to warm to room temperature during 1 h, and added to a mixture of ethyl acetate (40 mL) and saturated $NaHCO_3$ solution (40 mL). The separated aqueous layer was extracted with ethyl acetate (3 × 50 mL), and the combined organic phases were dried and concentrated. Purification of the residue by chromatography on silica gel (elution with 5% ethyl acetate in hexanes) gave **14a** as a colorless oil

(41) Shin, C.-g.; Okamoto, T.; Yoshimura, J.; Hashimoto, H.; Suzuki, T.; Yamaura, M. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 1413.

(42) These assignments could be reversed.

(2.06 g, 89%): IR (neat, cm^{-1}) 1693, 1607, 1472; ^1H NMR (300 MHz, $CDCl_3$) δ 7.31−7.23 (m, 5 H), 6.66 (t, J = 2.0 Hz, 1 H), 4.85−4.75 (m, 1 H), 3.75 (d, J = 4.8 Hz, 2 H), 2.71 (ddd, J = 14.6, 10.4, 2.0 Hz, 1 H), 2.57 (ddd, J = 14.6, 7.8, 2.0 Hz, 1 H), 0.91 (s, 9 H), 0.089 (s, 3 H), 0.085 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.9, 128.9, 127.1, 125.5, 102.6, 83.7, 77.3, 77.24, 77.21, 76.7, 65.0, 34.2, 25.9, 25.6, 18.4, −5.3; MS m/z (M^+) calcd 322.1423, obsd 322.1458; $[\alpha]_D^{25}$ +48.7 (c 3.7, $CHCl_3$).

Anal. Calcd for $C_{17}H_{26}O_2SSi$: C, 63.31; H, 8.12. Found: C, 63.08; H, 8.35.

***tert*-Butyl[[(*S*)-2,3-dihydro-4-(phenylseleno)-2-furyl]-methoxy]dimethylsilane (14b).** A solution of **12b** (1.84 g, 8.60 mmol) in dry THF (40 mL) was cooled to −78 °C, treated dropwise with a solution of phenylselenenyl chloride (1.65 g, 8.61 mmol) in THF (5 mL) until a faint yellow color persisted, and stirred for 30 min prior to the addition of finely divided potassium *tert*-butoxide (1.30 g, 1.5 equiv) with vigorous stirring. Workup in a manner identical to that just described afforded 2.48 g (78%) of **14b** as a colorless oil: IR (neat, cm^{-1}) 1609, 1578, 1475; ^1H NMR (300 MHz, $CDCl_3$) δ 7.42−7.38 (m, 2 H), 7.29−7.18 (m, 3 H), 6.61 (t, J = 2.1 Hz, 1 H), 4.77 (m, 1 H), 3.74 (m, 2 H), 2.76 (ddd, J = 14.8, 10.4, 2.1 Hz, 1 H), 2.60 (ddd, J = 14.8, 7.7, 2.1 Hz, 1 H), 0.91 (s, 9 H), 0.88 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.2, 129.9, 129.2, 126.3, 97.6, 83.5, 65.0, 36.2, 25.9 (2 C), 18.4, −5.3; MS m/z (M^+) calcd 370.0867, obsd 370.0886; $[\alpha]_D^{25}$ +46.7 (c 1.23, $CHCl_3$).

Anal. Calcd for $C_{17}H_{26}O_2SeSi$: C, 55.27; H, 7.09. Found: C, 55.54; H, 7.36.

***tert*-Butyl[[(*S*)-2,3-dihydro-4-(phenylseleno)-2-furyl]-methoxy]diphenylsilane.** A solution of **10** (55.0 g, 0.47 mol) and imidazole (65.0 g, 0.95 mol) in DMF at 20 °C was treated portionwise with *tert*-butyldiphenylsilyl chloride (130.0 g, 0.47 mol). The reaction mixture was stirred for 48 h with warming to 60 °C for the last 4 h and prior to the addition of saturated $NaHCO_3$ solution (2 L) and extraction with ether (4 × 600 mL). The combined organic phases were dried and concentrated to give a white solid (126.3, 75%), which was dissolved in CH_2Cl_2 (600 mL) under N_2, cooled to −78 °C and treated dropwise with Dibal-H (180 mL of 1.0 M in hexanes, 0.18 mol). The reaction mixture was maintained at −78 °C for 16 h prior to quenching with methanol (20 mL) and gradual warming to room temperature. Following the addition of saturated Rochelle salt solution and overnight stirring, the product was extracted into ether (3 × 150 mL), and the combined organic phases were dried and concentrated to give the lactol as a colorless oil (56.1 g, 97%).

A 52.0 g (0.146 mol) sample of this material was dissolved in CH_2Cl_2 (500 mL) and pyridine (50 mL), treated with acetic anhydride (25 mL) and DMAP (500 mg), and stirred for 48 h. After the removal of all volatiles in vacuo, the residue was purified by flash chromatography on silica gel (elution with 10% ethyl acetate in hexanes) to give the acetate as a colorless oil (53.4 g, 92%).

A 55.0 g (0.138 mol) sample of this oil was heated in 5 g lots in a Kugelrohr apparatus at 185−190 °C and 70 Torr. The distillate was purified in flash chromatography (SiO_2, elution with 2% ethyl acetate in hexanes) to give **12c** as a thick colorless oil (42.7 g, 91%).

A cold (−78 °C) solution of **12c** (22.2 g, 0.066 mol) in dry THF (800 mL) was treated dropwise with a solution of phenylselenenyl chloride (12.5 g, 0.066 mol) in THF (50 mL) until a faint yellow coloration just persisted. The reaction mixture was allowed to stir at this temperature for 30 min prior to the addition of finely divided potassium *tert*-butoxide under conditions of vigorous agitation, allowed to warm to room temperature over 2 h, and poured into ethyl acetate (1 L) and water (600 mL). The separated aqueous phase was extracted with ethyl acetate (3 × 10 mL), and the combined organic phases were dried and concentrated to give 27.2 g (84%) of a pale yellow oil that was used directly.

General Procedure for the Coupling of Furanoid Glycals to N-Protected Azetidine-2,3-diones. A. 1-Benzyl-3-[(*S*)-4,5-dihydro-5-[(trityloxy)methyl]-2-furyl]-3-hydroxy-2-azetidinone (15a). A solution of **12a** (1.00 g, 2.92 mmol) in dry THF (5 mL) under argon at −78 °C was treated dropwise with a solution of *tert*-butyllithium in pentane (2.60 mL of 1.7 M, 4.38 mmol). The solution was stirred for 1 h at this temperature prior to warming quickly to −10 °C whereupon the solution became clear. The reaction mixture was returned to −78 °C, transferred via a cold cannula into a stirred solution of **9a** (400 mg, 2.28 mmol) and boron trifluoride etherate (4.66 mL of 0.49 M solution in ether, 2.28 mmol) in THF (15 mL), and stirred at −78 °C for 30 min and at −10 °C for 30 min before being quenched with saturated $NaHCO_3$ solution (5 mL). The product was extracted into ether (3 × 30 mL), the combined extracts were dried, concentrated, and passed through a small pad of silica gel (washed with 30% ethyl acetate and 2% triethylamine in hexanes) to deliver 830 mg (58%) of **15a**. A total of 407 mg of **12a** was recovered: ^1H NMR (300 MHz, $CDCl_3$) δ 7.70−6.95 (m, 20 H), 5.25−5.10 (m, 1 H), 4.95−4.68 (m, 1 H), 4.28−4.05 (m, 2 H), 3.65−3.28 (m, 2 H), 3.28−3.06 (m, 3 H), 2.65−2.28 (dd, J = 14, 5.5 Hz, 2 H); MS m/z (M^+) calcd 517.2253, obsd 517.2269.

B. 1-Benzyl-3-[(*S*)-5-[(*tert*-butyldimethylsiloxy)methyl]-4,5-dihydro-2-furyl]-3-hydroxy-2-azetidinone (15b). The coupling of **12b** (1.14 g, 5.33 mmol) to **9a** (789 mg, 4.51 mmol) in this manner afforded 1.12 g (64%) of **15b** alongside 271 mg of recovered **12b**. For the 1:1 mixture of diastereomers: IR (neat, cm^{-1}) 3378, 1740, 1670, 1471; ^1H NMR (300 MHz, $CDCl_3$) δ 7.37−7.20 (m, 5 H), 5.08−5.05 (m, 1 H), 4.73−4.65 (m, 1 H), 4.48−4.42 (m, 2 H), 4.17 and 4.11 (br s, 1 H), 3.74−3.59 (m, 2 H), 3.48 (d, J = 5.3 Hz, 0.5 H), 3.47 (d, J = 5.4 Hz, 0.5 H), 3.25 (d, J = 5.4 Hz, 0.5 H), 3.24 (d, J = 5.3 Hz, 0.5 H), 2.77−2.66 (m, 1 H), 2.57−2.46 (m, 1 H), 0.89 and 0.87 (s, 9 H), 0.06, 0.05, 0.04, 0.03 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.2, 168.0, 153.3, 134.7, 128.6, 128.5, 128.0, 127.8, 127.7, 97.3, 82.5, 82.4, 81.5, 81.4, 65.0, 64.9, 53.3, 45.7, 32.1, 32.0, 25.9, 25.84, 25.81, −5.29, −5.31, −5.35; MS m/z (M^+) calcd 389.2022, obsd 389.2022; $[\alpha]_D^{25}$ +39.2 (c 1.3, $CHCl_3$).

Anal. Calcd for $C_{21}H_{31}NO_4Si$: C, 64.75; H, 8.03. Found: C, 64.69; H, 7.96.

C. 1-Benzyl-3-[4,5-dihydro-3-(phenylseleno)-2-furyl]-3-hydroxy-2-azetidinone (16). A stirred solution containing 2,3-dihydrofuran (35 mL) in THF (1000 mL) at −78 °C was treated dropwise with a solution of phenylselenenyl chloride (50.0 g, 0.26 mol) and stirred for 1 h prior to the addition of potassium *tert*-butoxide (34.95 g, 0.312 mol) in several portions. The resulting slurry was gradually warmed to room temperature during 1 h, poured into water (1 L), and extracted with ether (4 × 150 mL). The combined extracts were dried and concentrated prior to distillation in a Kugelrohr apparatus. There was obtained 53.0 g (90%) of the 4-phenylseleno derivative as a pale yellow oil: bp 160−165 °C (0.7 Torr); IR (neat, cm^{-1}) 1604, 1575, 1476, 1438; ^1H NMR (300 MHz, $CDCl_3$) δ 7.44−7.40 (m, 2 H), 7.30−7.18 (m, 3 H), 6.65 (t, J = 2.0 Hz, 1 H), 4.48 (t, J = 9.5 Hz, 2 H), 2.74 (td, J = 9.5, 2.0 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.7, 131.0, 130.0, 129.1, 126.4, 98.3, 71.6, 34.5; MS m/z (M^+) calcd 225.9897, obsd 225.9888.

Anal. Calcd for $C_{10}H_{10}OSe$: C, 53.35; H, 4.48. Found: C, 53.37; H, 4.52.

Coupling of the above selenide (8.15 g, 36.2 mmol) to **9a** (6.02 g, 34.4 mmol) as indicated above provided for the recovery of 2.17 g (27%) of unreacted dihydrofuran and isolation of **16** (5.95 g, 41%) as a colorless solid: mp 87−92 °C dec; IR (neat, cm^{-1}) 3398, 1760; ^1H NMR (300 MHz, $CDCl_3$) δ 7.50−7.21 (m, 10 H), 4.53−4.25 (m, 5 H), 3.73 (d, J = 5.4 Hz, 1 H), 3.28 (d, J = 5.4 Hz, 1 H), 2.82 (t, J = 9.8 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.9, 155.2, 134.7, 131.0, 129.4, 128.9, 128.8, 128.5, 128.1, 128.0, 127.9, 127.8, 127.3, 95.6, 83.8, 70.2, 53.7, 45.8, 37.1; MS m/z (M^+) calcd 401.0530, obsd 401.0522.

Anal. Calcd for $C_{20}H_{19}NO_3Se$: C, 59.88; H, 4.79. Found: C, 59.97; H, 4.71.

1-Benzyl-3-[(*S*)-5-[(*tert*-butyldimethylsiloxy)methyl]-4,5-dihydro-3-(phenylthio)-2-furyl]-3-hydroxy-2-azetidinone (17a). Metalation of **14a** (1.80 g, 5.59 mmol) and coupling with **9a** (880 mg, 5.00 mmol) as detailed earlier returned 620 mg of unreacted **14a** and afforded 1.38 g (56%) of **17a** as a colorless oil: IR (neat, cm^{-1}) 3378, 1767, 1473; ^1H

NMR (300 MHz, $CDCl_3$) δ 7.38−7.18 (m, 10 H), 4.79−4.71 (m, 1 H), 4.51−4.40 (m, 2 H), 3.76−3.65 (m, 3 H), 3.48 (d, J = 7.0 Hz, 1 H), 2.81−2.67 (m, 2 H), 0.88 and 0.87 (2s, total 9 H), 0.06, 0.04, 0.02 (3s, total 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.7, 133.9, 129.2, 128.7, 128.3, 128.2, 128.1, 127.7, 126.6, 99.9, 81.7, 64.5, 53.6, 53.5, 45.8, 36.5, 25.8, 25.7, 18.3, −5.4; MS m/z (M^+) calcd 497.2056, obsd 497.2067; $[\alpha]_D^{25}$ +28.7 (c 1.35, $CHCl_3$).

Anal. Calcd for $C_{27}H_{35}NO_4SSi$: C, 65.16; H, 7.09. Found: C, 65.19; H, 7.02.

1-Benzyl-3-[(*S*)-5-[(*tert*-butyldimethylsiloxy)methyl]-4,5-dihydro-3-(phenylseleno)-2-furyl]-3-hydroxy-2-azetidinone (17b). Metalation of **14b** (5.80 g, 15.7 mmol) and addition of the lithium derivative of **9a** (2.74 g, 15.7 mmol) in the conventional way returned 1.27 g of unreacted **14b** and provided 6.06 g (71%) of **17b** as a colorless gum: IR (neat, cm^{-1}) 3381, 1766; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50−7.44 (m, 2 H), 7.36−7.18 (m, 8 H), 4.71−4.62 (m, 1 H), 4.51−4.36 (m, 2 H), 3.77−3.65 (m, 3 H), 3.26 (m, 1 H), 2.94−2.62 (m, 2 H), 1.25 (br s, 1 H), 0.87 and 0.85 (2s, total 9 H), 0.05, 0.04, 0.03, 0.01 (4s, total 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.9, 166.7, 154.8, 154.6, 134.8, 131.0, 130.9, 129.4, 129.0, 128.7, 128.4, 128.1, 127.7, 127.2, 94.8, 84.0, 83.8, 81.9, 64.6, 64.5, 53.6, 53.5, 45.8, 39.1, 38.7, 25.84, 25.81, 18.3, −5.4; MS m/z (M^+) calcd 545.1501, obsd 545.1457; $[\alpha]_D^{25}$ +15.3 (c 2.5, $CHCl_3$).

3-[(*S*)-5-[(*tert*-Butyldiphenylsiloxy)methyl]-4,5-dihydro-3-(phenylseleno)-2-furyl]-3-hydroxy-1-(*p*-methoxybenzyl)-2-azetidinone (18). Furanoid glycal **12c** (22.2 g, 66 mmol) was exposed sequentially to phenylselenenyl chloride (12.5 g, 66 mmol) in cold (−78 °C) THF (850 mL) and then to potassium *tert*-butoxide as described earlier for **16**. The selenide was obtained as a faint yellow oil (27.2 g, 84%): IR (neat, cm^{-1}) 1608, 1578, 1475; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75−7.61 (m, 4 H), 7.42−7.23 (m, 8 H), 7.23−7.17 (m, 3 H), 6.62 (br s, 1 H), 4.86−4.79 (m, 1 H), 3.80−3.72 (m, 2 H), 2.83−2.63 (m, 2 H), 1.09 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.2, 135.6, 135.5, 133.4, 131.5 (2 C), 129.9, 129.7, 129.13, 129.08, 127.7, 126.2, 97.6, 83.4, 65.5, 36.2, 26.82, 26.76, 19.3; MS m/z (M^+) calcd 494.1180, obsd 494.1198; $[\alpha]_D^{25}$ +35.2 (c 0.8, $CHCl_3$).

Anal. Calcd for $C_{27}H_{30}O_2SeSi$: C, 65.70; H, 6.13. Found: C, 65.77; H, 6.07.

Lithiation of this furanoid glycal (10.0 g, 20.2 mmol) and coupling to **9b** (4.16 g, 20.3 mmol) as described earlier returned 5.1 g (51%) of unreacted seleno derivative and gave 11.24 g (79%) of **18** as a colorless gum: IR (neat, cm^{-1}) 3396, 1758, 1514; ^{1}H NMR (300 MHz, $CDCl_3$) δ (single isomer) 7.71−7.20 (m, 15 H), 7.14 (d, J = 8.7 Hz, 2 H), 6.78 (d, J = 8.7 Hz, 2 H), 4.77−4.71 (m, 1 H), 4.53 (s, 1 H), 4.42 (d, J = 15.0 Hz, 1 H), 4.27 (d, J = 15.0 Hz, 1 H), 3.81−3.74 (m, 2 H), 3.76 (s, 3 H), 3.70 (d, J = 5.3 Hz, 1 H), 3.23 (d, J = 5.3 Hz, 1 H), 2.85 (dd, J = 15.1, 11.2 Hz, 1 H), 2.74 (dd, J = 15.1, 8.0 Hz, 1 H), 1.09 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (single isomer) 166.4, 159.1, 154.8, 135.5, 133.1, 132.8, 130.9, 129.9, 129.7, 129.5, 129.3, 129.1, 127.7, 127.07, 127.06, 126.7, 114.1, 114.0, 94.6, 83.4, 81.8, 65.2, 55.2, 53.4, 45.2, 39.0, 26.7, 19.24, 19.19; MS m/z (M^+) calcd 699.1765, obsd 699.1722; $[\alpha]_D^{25}$ +17.6 (c 1.2, $CHCl_3$).

Anal. Calcd for $C_{38}H_{41}NO_2SeSi$: C, 65.32; H, 5.91. Found: C, 65.30; H, 5.91.

(2*S*,5*S*)-7-Benzyl-2-[(trityloxy)methyl]-1-oxa-7-azaspiro-[4.4]nonane-6,9-dione (19a) and (2*S*,5*R*)-Benzyl-2-[(trityloxy)methyl]-1-oxa-7-azaspiro[4.4]nonane-6,9-dione (20a). A solution of **15a** (830 mg, 1.60 mmol) in benzene (60 mL) was treated with pyridinium *p*-toluenesulfonate (30 mg), stirred overnight at room temperature, washed with saturated $NaHCO_3$ solution, dried, and concentrated. Chromatography of the residue on silica gel (elution with 30% ethyl acetate in hexanes) provided 255 mg (35%) of the less polar isomer **20a**, 102 mg (14%) of the more polar **19a**, and 69 mg (10%) of a 1:1 mixture of both.

For **19a**: colorless oil; IR (neat, cm^{-1}) 1779, 1709; ^{1}H NMR (300 MHz, C_6D_6) δ 7.68−6.91 (series of m, 20 H), 4.55 (m, 1 H), 4.17 (AB, J = 14.9 Hz, $\Delta\nu$ = 115.4 Hz, 2 H), 3.45 (AB, J = 5.3, 9.8 Hz, $\Delta\nu$ = 53.4 Hz, 2 H), 2.87 (AB, J = 7.4 Hz, $\Delta\nu$ = 28.1 Hz, 2 H), 2.01−1.59 (m, 4 H); ^{13}C NMR (75 MHz, C_6D_6) δ 206.5, 170.6, 144.7, 135.7, 129.3−127.1 (multiple signals), 87.1, 82.6, 81.3, 66.4, 52.6, 46.1, 32.9, 28.7; MS m/z (M^+) calcd 517.2253, obsd 517.2253; $[\alpha]_D^{20}$ −28.6 (c 1.41, $CHCl_3$).

For **20a**: colorless oil; IR (neat, cm^{-1}) 1768, 1684; ^{1}H NMR (300 MHz, C_6D_6) δ 7.67−6.89 (m, 20 H), 4.73−4.65 (m, 1 H), 4.12 (AB, J = 14.6 Hz, $\Delta\nu$ = 127.9 Hz, 2 H), 3.36 (AB, J = 4.2, 9.8 Hz, $\Delta\nu$ = 29.3 Hz, 2 H), 2.91 (AB, J = 17.3 Hz, $\Delta\nu$ = 21.7 Hz, 2 H), 2.01−1.62 (m, 4 H); ^{13}C NMR (75 MHz, C_6D_6) δ 205.6, 171.3, 144.7, 135.7, 129.3−127.1 (multiple signals), 87.0, 82.5, 81.4, 66.3, 52.7, 46.1, 33.5, 28.7; MS m/z (M^+) calcd 517.2253, obsd 517.2253; $[\alpha]_D^{20}$ +18.2 (c 1.82, $CHCl_3$).

Anal. Calcd for $C_{34}H_{31}NO_4$: C, 78.89; H, 6.04. Found: C, 78.62; H, 6.00.

(2*S*,5*S*)-7-Benzyl-2-[(*tert*-butyldimethylsiloxy)methyl]-1-oxa-7-azaspiro[4.4]nonane-6,9-dione (19b) and (2*S*,5*R*)-Benzyl-2-[(*tert*-butyldimethylsiloxy)methyl]-1-oxa-7-azaspiro[4.4]nonane-6,9-dione (20b). A solution of **15b** (700 mg, 1.78 mmol) in benzene (50 mL) containing 70 mg of pyridinium *p*-toluenesulfonate was heated at 75−80 °C for 80 min under N_2. The cooled reaction mixture was quenched with saturated $NaHCO_3$ solution and processed as described above to furnish 273 mg of the less polar **20b**, 165 mg of **19b**, and 210 mg of the mixture (92% total).

For **19b**: colorless oil; IR (neat, cm^{-1}) 1778, 1694; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38−7.22 (m, 5 H), 4.65 (d, J = 14.6 Hz, 1 H), 4.58 (d, J = 14.6 Hz, 1 H), 4.51 (m, 1H), 3.77 (dd, J = 10.6, 5.3 Hz, 1 H), 3.70−3.59 (m, 3 H), 2.34−1.96 (m, 4 H), 0.89 (s, 9 H), 0.060 (s, 3 H), 0.056 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.0, 171.5, 134.6, 129.0, 128.4, 128.2, 83.7, 81.4, 65.3, 52.8, 46.5, 33.6, 28.4, 18.4, −5.3; MS m/z (M^+) calcd 389.2022, obsd 389.2047; $[\alpha]_D^{25}$ +4.5 (c 2.0, $CHCl_3$).

For **20b**: colorless oil; IR (neat, cm^{-1}) 1776, 1688; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37−7.19 (m, 5 H), 4.60 (s, 2 H), 4.41 (m, 1 H), 3.83 (dd, J = 10.5, 5.5 Hz, 1 H), 3.67 (dd, J = 10.5, 6.5 Hz, 1 H), 3.66 (s, 2 H), 2.28−1.97 (m, 4 H), 0.89 (s, 9 H), 0.08 (s, 3 H), 0.06 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.5, 171.0, 134.6, 129.0, 128.8, 128.4, 83.6, 81.3, 65.4, 52.8, 46.5, 33.0, 28.4, 25.93, 25.89, 25.86, 18.4, −5.3; MS m/z (M^+) calcd 389.2022, obsd 389.2047; $[\alpha]_D^{25}$ −5.1 (c 2.3, $CHCl_3$).

Anal. Calcd for $C_{21}H_{31}NO_4Si$: C, 64.75; H, 8.03. Found: C, 64.61; H, 7.95.

(2*S*,5*R*)-7-Benzyl-9-methylene-2-[(trityloxy)methyl]-1-oxa-7-azaspiro[4.4]nonan-6-one (22). A slurry of methyltriphenylphosphonium iodide (234 mg, 0.58 mmol) in dry THF (10 mL) was cooled to 0 °C, treated with *n*-butyllithium (0.45 mL of 1.3 M in hexanes, 0.58 mmol), stirred at this temperature for 20 min and at room temperature for 30 min, and returned to −78 °C. A solution of **20a** (30 mg, 0.58 mmol) in dry THF (2 mL) was introduced dropwise, and the reaction mixture was stirred at −78 °C for 30 min, allowed to reach rt overnight, quenched with saturated $NaHCO_3$ solution, and diluted with ether. The separated organic phase was dried and evaporated to leave a residue, chromatography of which on silica gel (elution with 20% ethyl acetate in hexanes) yielded 16 mg (54%) of **22** as a colorless oil: IR (neat, cm^{-1}) 1703, 1448; ^{1}H NMR (300 MHz, C_6D_6) δ 7.69−6.95 (m, 20 H), 5.17 (t, J = 2.2 Hz, 1 H), 4.70 (d, J = 1.8 Hz, 1 H), 4.45 (m, 1 H), 4.18 (AB, J = 14.7 Hz, $\Delta\nu$ = 43.4 Hz, 2 H), 3.63 (AB, J = 9.5, 6.3, 4.9 Hz, $\Delta\nu$ = 108.9 Hz, 2 H), 3.24 (AB, J = 1.8, 2.2, 13.5 Hz, $\Delta\nu$ = 39.0 Hz, 2 H), 2.26−2.02 (m, 2 H), 1.82−1.71 (m, 1 H), 1.63−1.52 (m, 1 H); ^{13}C NMR (75 MHz, C_6D_6) δ 173.6, 145.4, 134.0, 136.7, 129.7−127.1 (multiple signals), 120.1, 115.8, 109.5, 87.1, 84.7, 81.2, 67.5, 48.5, 46.5, 36.8, 29.3; MS m/z (M^+) calcd 515.2460, obsd 515.2456; $[\alpha]_D^{20}$ −33.9 (c 0.59, $CHCl_3$).

(2*S*,5*S*)-7-Benzyl-9-methylene-2-[(trityloxy)methyl]-1-oxa-7-azaspiro[4.4]nonan-6-one (21). The analogous olefination of **19a** gave rise to **21** in 95% yield: IR (neat, cm^{-1}) 1703, 1596, 1078; ^{1}H NMR (300 MHz, C_6D_6) δ 7.81−7.11 (m, 20 H), 5.54 (s, 1 H), 4.98 (m, 1H), 4.89 (s, 1 H), 4.34 (AB, J = 14.7 Hz, $\Delta\nu$ = 60.4 Hz, 2 H), 3.44 (AB, J = 3.9, 9.7 Hz, $\Delta\nu$ = 26.5 Hz, 2 H), 3.39 (AB, J = 13.8 Hz, $\Delta\nu$ = 24 Hz, 2 H), 2.40−2.25 (m, 2 H), 1.92−1.82 (m, 2 H); ^{13}C NMR (75 MHz, C_6D_6) δ 174.3, 144.9, 144.8, 136.7, 129.3, 128.9, 128.5, 128.3, 128.0,

127.8, 127.7, 127.1, 110.0, 86.9, 80.5, 66.5, 48.6, 46.4, 36.5, 28.6; MS *m/z* (M^+) calcd 515.2460, obsd 515.2448; $[\alpha]_D^{20}$ +23.1 (*c* 0.92, $CHCl_3$).

Anal. Calcd for $C_{35}H_{33}NO_3$: C, 81.52; H, 6.45. Found: C, 81.68; H, 6.38.

(4*R,5*S**)-7-Benzyl-4-(phenylseleno)-1-oxa-7-azaspiro-[4.4]nonane-6,9-dione (23).** A solution of **16** (4.20 g, 10.5 mmol) in dry benzene (35 mL) was treated with pyridinium *p*-toluenesulfonate (200 mg, 0.79 mmol) and stirred at 80 °C under N_2 for 90 min. The cooled mixture was filtered and concentrated to leave a solid. Recrystallization of this material from ethyl acetate afforded isomerically pure **23** (3.67 g, 87%) as a white amorphous solid: mp 121−123 °C; IR (neat, cm^{-1}) 1775, 1703; ^1H NMR (300 MHz, $CDCl_3$) δ 7.50−7.45 (m, 2 H), 7.35−7.24 (m, 6 H), 7.18−7.14 (m, 2H), 4.61 (d, J = 14.8 Hz, 1 H), 4.34−4.18 (m, 2 H), 4.07−4.00 (m, 1 H), 4.01 (d, J = 14.8 Hz, 1 H), 3.67 (d, J = 17.3 Hz, 1 H), 3.54 (d, J = 17.3 Hz, 1 H), 2.63−2.53 (m, 1 H), 2.45−2.31 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.6, 169.6, 134.1, 132.7, 129.5, 128.9, 128.4, 128.1, 128.0, 83.1, 70.0, 53.9, 46.5, 42.7, 32.9 (1 C not observed); MS *m/z* (M^+) calcd 401.0530, obsd 401.0546.

Anal. Calcd for $C_{20}H_{19}NO_3Se$: C, 59.84; H, 4.77. Found: C, 59.74; H, 4.81.

(4*R,5*S**,9*R**)-7-Benzyl-9-hydroxy-4-(phenylseleno)-1-oxa-7-azaspiro[4.4]nonan-6-one (24).** A vigorously stirred solution of **23** (2.83 g, 7.06 mmol) in methanol (75 mL) was treated with sodium borohydride (320 mg, 8.46 mmol) in one portion, stirred for 15 min, and quenched with water (2 mL). The mixture was concentrated in vacuo and subjected to chromatography on silica gel (elution with 60% ethyl acetate in hexanes) to give **24** (2.52 g, 89%) as a colorless, crystalline solid: mp 131−132 °C; IR (neat, cm^{-1}) 3474, 1694, 1478; ^1H NMR (300 MHz, $CDCl_3$) δ 7.59−7.54 (m, 2 H), 7.34−7.21 (m, 8 H), 4.49 (d, J = 15.0 Hz, 1 H), 4.41 (d, J = 15.0 Hz, 1 H), 4.29 (dd, J = 5.2, 5.2 Hz, 1 H), 4.16−4.03 (m, 2 H), 3.99 (dd, J = 6.5, 4.3 Hz, 1 H), 3.53 (dd, J = 10.3, 5.2 Hz, 1 H), 3.23 (dd, J = 10.3, 2.5 Hz, 1 H), 3.09−2.97 (m, 1 H), 2.38−2.30 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.7, 135.5, 133.8, 129.5, 128.7, 128.1, 127.8, 127.6, 99.6, 89.2, 72.5, 68.0, 51.6, 46.7, 45.6, 35.4; MS *m/z* (M^+) calcd 403.0686, obsd 403.0671.

Anal. Calcd for $C_{20}H_{21}NO_3Se$: C, 59.70; H, 5.26. Found: C, 59.59; H, 5.31.

(5*R,9*S**)-7-Benzyl-9-hydroxy-1-oxa-7-azaspiro[4.4]non-3-en-6-one 25).** A solution of sodium metaperiodate (2.44 g, 11.4 mmol) in distilled water (25 mL) was added dropwise to a solution of **24** (2.30 g, 5.71 mmol) in methanol (100 mL). The resulting slurry was stirred for 12 h prior to the addition of Celite (5 g), filtration, and concentration to one-fourth of the original volume in vacuo. The resulting sludge was extracted with ethyl acetate (3 × 30 mL), and the combined extracts were dried and concentrated to leave a residue that was purified chromatographically (silica gel, elution with ethyl acetate). There was isolated 1.07 g (77%) of **25** as an amorphous white powder: mp 119−120 °C); IR (neat, cm^{-1}) 3400, 1698; ^1H NMR (300 MHz, $CDCl_3$) δ 7.33−7.18 (m, 5 H), 6.22 (m, 1 H), 5.78 (m, 1 H), 4.91 (dt, J = 13.0, 2.2 Hz, 1 H), 4.73 (dt, J = 13.0, 1.8 Hz, 1 H), 4.43 (s, 2 H), 4.29 (t, J = 6.8 Hz, 1 H), 3.44 (dd, J = 10.0, 7.3 Hz, 1 H), 3.04 (dd, J = 10.0, 6.2 Hz, 1 H), 3.06−2.45 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.6, 135.6, 131.7, 131.0, 128.8, 128.1, 127.7, 123.1, 96.1, 76.7, 72.1, 49.9, 46.8; MS *m/z* (M^+) calcd 245.1052, obsd 245.0989.

Anal. Calcd for $C_{14}H_{15}NO_3$: C, 68.56; H, 6.16. Found: C, 68.25; H, 6.17.

(3*R,4*R**,5*R**,9*R**)-7-Benzyl-3,4,9-trihydroxy-1-oxa-7-azaspiro[4.4]nonan-6-one 3,4,9-Triacetate (26).** A vigorously stirred solution of **25** (650 mg, 2.65 mmol) in pyridine (2.0 mL) at 0 °C was treated with finely ground osmium tetraoxide (675 mg, 2.66 mmol) and stirred for 12 h prior to concentration in vacuo. The resulting dark brown glass was redissolved in CH_2Cl_2 (10 × 10 mL), stirred with saturated $NaHSO_3$ solution (5 mL) for 2 h, filtered through a pad of Celite, and exhaustively extracted with CH_2Cl_2 (10 × 10 mL). The combined extracts were dried and evaporated to give the triol (623 mg, 84%) as a viscous gum. A 210 mg (0.752 mmol) portion of this material was dissolved in pyridine (1 mL), treated with acetic anhydride (0.4 mL) and DMAP (10 mg) in CH_2Cl_2 (10 mL), stirred for 24 h, and concentrated. The residue was subjected to flash chromatography on silica gel (elution with 50% ethyl acetate in hexanes), the process yielding both pure triacetates. Isomer **26** (197 mg) predominated over its diastereomer (48 mg).

For **26**: colorless crystals; mp 139−140 °C; IR (neat, cm^{-1}) 1751, 1702; ^1H NMR (300 MHz, $CDCl_3$) δ 7.31−7.21 (m, 3 H), 7.16−7.12 (m, 2 H), 5.86−5.80 (m, 1 H), 5.74 (d, J = 4.8 Hz, 1 H), 5.22 (d, J = 3.8 Hz, 1 H), 4.51 (d, J = 14.9 Hz, 1 H), 4.38−4.32 (m, 2 H), 3.81 (dd, J = 8.2, 7.5 Hz, 1 H), 3.61 (dd, J = 11.5, 3.8 Hz, 1 H), 2.97 (d, J = 11.5 Hz, 1 H), 2.02 (s, 3 H), 1.99 (s, 3 H), 1.90 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.6, 169.4, 169.2, 169.1, 135.0, 128.8, 127.9, 127.8, 87.4, 72.3, 71.6, 70.6, 69.8, 51.1, 46.4, 20.6, 20.4, 20.3; MS *m/z* (M^+) calcd 405.1424, obsd 405.1436.

Anal. Calcd for $C_{20}H_{23}NO_8$: C, 59.25; H, 5.72. Found: C, 59.37; H, 5.75.

(1*R,2*R**,4′*R**,5*R**)-1′-Benzyl-4′-hydroxyspiro[3,6-dioxabicyclo[3.1.0]hexane-2,3′-pyrrolidin]-2′-one (27).** A magnetically stirred slurry of **25** (200 mg, 0.82 mmol) and finely ground $NaHCO_3$ (150 mg) in CH_2Cl_2 (5 mL) at 0 °C was treated portionwise with *m*-chloroperbenzoic acid (300 mg of 70% purity, 1.5 equiv) and allowed to react at room temperature for 6 days. The reaction mixture was filtered and concentrated to leave a residue that was chromatographed on silica gel (elution with 50% ethyl acetate in hexanes). There was recovered 132 mg of unreacted **25** and 47 mg (85%) of **27** as a colorless gum: ^1H NMR (300 MHz, $CDCl_3$) δ 7.56−7.19 (m, 5H), 4.46 (s, 2 H), 4.46 (m, 1 H), 4.23 (d, J = 10.0 Hz, 1 H), 4.17 (d, J = 10.0 Hz, 1 H), 3.96 (dd, J = 5.0, 16.2 Hz, 2 H), 3.57−3.51 (m, 1 H), 3.17 (dd, J = 11, 3.5 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.8, 135.2, 128.8, 128.0, 127.9, 86.6, 70.1, 68.3, 56.6, 55.6, 51.2, 46.6; MS *m/z* (M^+) calcd 261.1001, obsd 261.1013.

Acid-Catalyzed Isomerization of 17a. A solution of **17a** (350 mg, 0.70 mmol) in benzene (20 mL) was treated with pyridinium *p*-toluenesulfonate (350 mg), blanketed with nitrogen, and heated at 75−80 °C for 48 h. The cooled reaction mixture was quenched with saturated $NaHCO_3$ solution (1 mL), and the separated organic phase was dried and concentrated. Careful chromatography of the residual oil on silica gel (elution with 10% ethyl acetate in hexanes) afforded the faster eluting fraction **28** (105 mg, 1:1 mixture of two isomers), the more polar fraction **29** (137 mg, 1:1 of two isomers), and a mixed fraction (71 mg) for an overall yield of 89%.

For **28**: IR (neat, cm^{-1}) 1742, 1693; ^1H NMR (300 MHz, $CDCl_3$) δ 7.38−7.06 (m, 10 H), 4.63−4.56 (m, 2 H), 4.32−4.23 (m, 1 H), 3.99−3.92 (m, 0.5 H), 3.89−3.83 (m, 1 H), 3.78−3.72 (m, 1 H), 3.80−3.70 (m, 0.5 H), 3.61 (d, J = 17.2 Hz, 0.5 H), 3.49 (d, J = 17.2 Hz, 0.5 H), 3.42 (d, J = 17.7 Hz, 0.5 H), 2.97 (d, J = 17.7 Hz, 0.5 H), 2.58−2.32 (m, 2 H), 0.93 (s, 4.5 H), 0.89 (s, 4.5 H), 0.12 (s, 1.5 H), 0.09 (s, 1.5 H), 0.08 (s, 1.5 H), 0.07 (s, 1.5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.0, 169.2, 168.8, 134.5, 134.1, 133.7, 131.4, 130.9, 129.7, 129.3, 129.2, 129.1, 129.0, 128.92, 128.86, 128.4, 128.2, 128.1, 127.7, 127.2, 83.6, 83.4, 82.5, 81.1, 66.3, 65.8, 64.9, 53.9, 53.6, 53.4, 48.9, 46.6, 46.5, 36.4, 33.8, 26.1, 26.0, 25.94, 25.87, 25.84, 25.78, 18.4, 18.32, 18.27, 15.3, −5.2, −5.3, −5.5; MS *m/z* (M^+) calcd 497.2056, obsd 497.2041; $[\alpha]_D^{25}$ +12.7 (*c* 1.2, $CHCl_3$).

Anal. Calcd for $C_{27}H_{35}NO_4SSi$: C, 65.16; H, 7.09. Found: C, 65.06; H, 7.13.

For **29**: mp 69−76 °C; IR (neat, cm^{-1}) 1742, 1693; ^1H NMR (300 MHz, $CDCl_3$) δ 7.38−7.08 (m, 10 H), 4.64−4.55 (m, 2 H), 4.56−4.48 (m, 0.5 H), 4.31−4.26 (m, 0.5 H), 3.99−3.92 (m, 0.5 H), 3.87−3.45 (m, 4.5 H), 2.54−2.46 (m, 1 H), 2.19−2.03 (m, 1 H), 0.90 (s, 4.5 H), 0.89 (s, 4.5 H), 0.063 (s, 3 H), 0.061 (s, 1.5 H), 0.059 (s, 1.5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.7, 169.6, 134.6, 133.7, 133.5, 131.1, 130.9, 129.8, 129.4, 129.1, 129.0, 128.92, 128.87, 128.8, 128.5, 128.2, 128.11, 128.05, 127.5, 127.4, 83.9, 83.1, 82.0, 81.4, 68.1, 65.8, 65.7, 65.1, 54.0, 53.7, 52.1, 50.6, 46.5, 46.4, 38.7, 35.7, 34.4, 28.9, 25.9, 25.8, 23.7, 18.4, 18.3, 15.3, 14.2, 11.0, −5.3, −5.4, −5.6; MS *m/z* (M^+) calcd 497.2056, obsd 497.2049; $[\alpha]_D^{25}$ −29.3 (*c* 1.8, $CHCl_3$).

Anal. Calcd for $C_{24}H_{35}NO_4SSi$: C, 65.16; H, 7.09. Found: C, 65.06; H, 7.13.

Acid-Catalyzed Isomerization of 17b. Comparable treatment of **17b** (800 mg, 1.47 mmol) in benzene (25 mL) provided 327 mg of the less polar **34** (9:1 mixture of two isomers) and 364 mg of the slower eluting **35** (9:1 mixture of two isomers) in an overall 86% yield. These fractions were individually subjected to oxidative elimination.

(2*S*,5*S*)-7-Benzyl-2-[(*tert*-butyldimethylsiloxy)methyl]-1-oxa-7-azaspiro[4.4]non-3-ene-6,9-dione (36). A solution of **34** (500 mg, 0.92 mmol) in methanol (35 mL) was vigorously agitated with a solution of sodium metaperiodate (0.59 g, 2.8 mmol) in water (5.9 mL) for 1 h, filtered, and concentrated in vacuo. The residue was taken up in ethyl acetate (30 mL), and the separated organic phase was allowed to stand at room temperature for 2 h to complete the elimination. After solvent evaporation, the residue was chromatographed on silica gel (elution with 40% ethyl acetate in hexanes) to give **36** of 90% isomeric purity as a colorless gum (292 mg, 82%): IR (neat, cm^{-1}) 1789, 1713; ^1H NMR (300 MHz, $CDCl_3$) δ 7.38−7.21 (m, 5 H), 6.31 (dd, J = 1.5 6.1 Hz, 1 H), 5.65 (dd, J = 2.1, 6.1 Hz, 1 H), 5.26 (m, 1 H), 4.65 (s, 2 H), 3.89−3.63 (m, 4 H), 0.89 (s, 9 H), 0.07 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.1, 168.9, 134.1, 128.7, 128.3, 127.7, 123.8, 90.1, 90.0, 87.9, 76.6, 67.0, 54.6, 52.9, 46.9, 46.8, 26.0, 25.9, 18.3, 14.2, −5.3, −5.4; MS m/z (M^+) calcd 383.1917, obsd 383.1936; $[\alpha]_D^{25}$ +2.3 (c 1.4, $CHCl_3$).

(2*S*,5*R*)-7-Benzyl-2-[(*tert*-butyldimethylsiloxy)methyl]-1-oxa-7-azaspiro[4.4]non-3-ene-6,9-dione (37). Comparable oxidation of **35** (100 mg) provided **37** in 82% yield as a single diastereomer: IR (neat, cm^{-1}) 1782, 1715; ^1H NMR (300 MHz, $CDCl_3$) δ 7.40−7.25 (m, 5 H), 6.34 (dd, J = 6.1, 1.5 Hz, 1 H), 5.65 (dd, J = 6.1, 2.2 Hz, 1 H), 5.19 (m, 1 H), 4.67 (d, J = 14.5 Hz, 1 H). 4.61 (d, J = 14.5 Hz, 1 H), 3.96 (dd, J = 10.0, 6.2 Hz, 1 H), 3.79 (d, J = 17.5 Hz, 1 H), 3.74 (dd, J = 10.0, 6.8 Hz, 1H), 3.67 (d, J = 17.5 Hz, 1 H), 0.90 (s, 9 H), 0.090 (s, 3 H), 0.089 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.5, 168.7, 134.5, 134.2, 129.1, 128.5, 128.3, 123.7, 100.0, 90.2, 67.3, 52.9, 46.9, 25.9, 18.3, −5.3, −5.4; MS m/z (M^+) calcd 383.1917, obsd 383.1870; $[\alpha]_D^{25}$ −82.9 (c 1.0, $CHCl_3$).

Anal. Calcd for $C_{22}H_{29}NO_3Si$: C, 68.53; H, 8.11. Found: C, 68.37; H, 7.98.

(2*S*,5*S*)-7-Benzyl-2-[(*tert*-butyldimethylsiloxy)methyl]-9-methylene-1-oxa-7-azaspiro[4.4]non-3-en-6-one (38). Olefination of **36** (30 mg, 78 μmol) with methylenetriphenylphosphorane in a manner analogous to that described above [from 430 mg (1.06 mmol) of the iodide salt] followed by chromatography on silica gel (elution with 35% ethyl acetate in hexanes) furnished **38** in quantitative yield (27 mg): ^1H NMR (300 MHz, $CDCl_3$) δ 7.37−7.23 (m, 5 H), 6.26 (dd, J = 1.5, 6.0 Hz, 1 H), 5.65 (dd, J = 2.0−6.0 Hz, 1 H), 5.34 (t, J = 2.3 Hz, 1 H), 5.24 (t, J = 1.9 Hz, 1 H), 5.05 (m, 1 H), 4.56 (d, J = 14.6 Hz, 1 H), 4.50 (d, J = 14.6 Hz, 1 H), 3.99 (dd, J = 9.8, 6.0 Hz, 1 H), 3.90 (dt, J = 13.8, 2.1 Hz, 1 H), 3.82 (d, J = 13.8, 2.1 Hz, 1 H), 3.75 (dd, J = 9.8, 7.2 Hz, 1 H),0.91 (s, 9 H), 0.87 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.5, 142.1, 135.5, 131.8, 128.8, 128.3, 127.8, 112.9, 100.0, 91.7, 88.4, 77.3, 77.21, 77.17, 67.8, 48.7, 47.0, 26.0, 18.4, −5.2, −5.3.

(2*S*,5*R*)-7-Benzyl-2-[(*tert*-butyldimethylsiloxy)methyl]-9-methylene-1-oxa-7-azaspiro[4.4]non-3-en-6-one (39). A procedure identical to that used above was employed. From 430 mg (1.06 mmol) of methyltriphenylphosphonium iodide and 27 mg (70 μmol) of **37** was isolated 27 mg (100%) of **39** as a colorless gum: ^1H NMR (300 MHz, $CDCl_3$) δ 7.33−7.23 (m, 5 H), 6.19 (dd, J = 1.3, 6.0 Hz, 1 H), 5.66 (dd, J = 2.3, 6.0 Hz, 1 H), 5.47 (t, J = 2.3 Hz, 1 H), 5.25 (t, J = 1.9 Hz, 1 H), 5.21 (m, 1 H), 4.57 (d, J = 14.6 Hz, 1 H), 4.51 (d, J = 14.6 Hz, 1 H), 3.92−3.80 (m, 3 H), 3.68 (dd, J = 10.6, 5.5 Hz, 1 H), 0.89 (s, 9 H), 0.061 (s, 3 H), 0.060 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.9, 142.1, 135.5, 131.7, 128.8, 128.5, 128.3, 127.8, 113.6, 88.1, 77.2, 66.1, 48.8, 46.9, 25.9, 18.4, −5.3.

(2*S*,5*S*)-7-Benzyl-2-(hydroxymethyl)-1-oxa-7-azaspiro[4.4]nonane-6,9-dione 9-Oxime (40). A solution of **19b** (110 mg, 0.28 mmol) in methanol (5 mL) was treated with hydroxylamine hydrochloride (300 mg, 4.3 mmol), and the mixture was stirred at room temperature for 1 h prior to the addition of pyridine (0.5 mL). After 12 additional hours, the solvent was evaporated, and the residue was purified chromatographically (silica gel, elution with ethyl acetate) to give **40** (79 mg, 96%) as colorless crystals: mp 137−139 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 8.45 (br s, 1 H), 7.35−7.22 (m, 5 H), 4.55−4.45 (m, 1 H), 4.58 (d, J = 14.5 Hz, 1 H), 4.51 (d, J = 14.5 Hz, 1 H), 4.08−3.87 (m, 3 H), 3.57 (dd, J = 12.2, 2.0 Hz, 1 H), 2.51−2.28 (m, 2 H), 2.22−2.18 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.9, 157.2, 134.8, 128.9, 128.4, 128.1, 82.8, 82.1, 63.6, 46.9, 44.5, 36.3, 25.5; MS m/z (M^+) calcd 290.1267, obsd 290.1268; $[\alpha]_D^{25}$ −20.2 (c 0.64, $CHCl_3$).

Anal. Calcd for $C_{15}H_{18}N_2O_4$: C, 62.05; H, 6.25. Found: C, 61.78; H, 6.31.

(2*S*,5*R*)-7-Benzyl-2-(hydroxymethyl)-1-oxa-7-azaspiro[4.4]nonane-6,9-dione 9-Oxime (42). A solution of **20b** (109 mg, 0.28 mmol) in methanol (5 mL) was treated with finely powdered hydroxylamine hydrochloride (300 mg, 4.3 mmol), stirred for 1 h, treated with pyridine (0.5 mL), sealed in a high-pressure reactor, and subjected to 10 000 Pa for 20 h. Workup in the predescribed manner furnished 73 mg (90%) of **42**: IR (neat, cm^{-1}) 3210, 1698, 1667; ^1H NMR (300 MHz, $CDCl_3$) δ 7.36−7.21 (m, 5 H), 4.59−4.49 (m, 1 H), 4.59 (d, J = 14.6 Hz, 1 H), 4.49 (d, J = 14.6 Hz, 1 H), 4.09 (d, J = 16.4 Hz, 1 H), 4.00 (dd, J = 12.2, 1.7 Hz, 1 H), 3.83 (d, J = 16.4 Hz, 1 H), 3.55 (dd, J = 12.2, 1.5 Hz, 1 H), 2.57−2.13 (m, 4 H), 1.25 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.9, 157.2, 134.8, 128.9, 128.4, 128.1, 82.8, 82.1, 62.6, 46.9, 44.5, 36.6, 25.6, 25.5.

Anal. Calcd for $C_{15}H_{18}N_2O_4$: C, 62.04; H, 6.25. Found: C, 61.78; H, 6.31.

(2*S*,5*R*)-7-Benzyl-2-(hydroxymethyl)-1-oxa-7-azaspiro[4.4]non-3-ene-6,9-dione 9-Oxime (44). A solution of **36** (70 mg, 0.18 mmol) and hydroxylamine hydrochloride (300 mg, 4.31 mmol) in methanol (5 mL) was stirred at room temperature for 1 h prior to the addition of pyridine (0.5 mL). The reaction was allowed to proceed for 12 h prior to solvent evaporation and chromatographic purification (silica gel, elution with ethyl acetate). There was obtained 50 mg (96%) of **44** as a colorless glass that was directly hydrogenated.

(2*S*,5*R*)-7-Benzyl-2-(hydroxymethyl)-1-oxa-7-azaspiro[4.4]non-3-ene-6,9-dione Oxime (45). Reaction of **37** (50 mg, 0.13 mmol) with hydroxylamine hydrochloride (300 mg, 4.31 mmol) and pyridine (0.5 mL) in methanol (5 mL) in the manner described above afforded 35 mg (94%) of **45** as a white solid that was directly acetylated.

(2*S*,5*S*)-7-Benzyl-2-(hydroxymethyl)-1-oxa-7-azaspiro[4.4]non-3-ene-6,9-dione 9-Oxime, Acetate (46). In a typical procedure, a solution of hydrogen chloride in glacial acetic acid (no less than 0.1 g/mL) was prepared at 0 °C. The oxime (30−120 mg) was treated with 2 mL of this solution and stirred at room temperature for 8 h to 7 days (TLC analysis). The solution was then concentrated, and the residue was purified by column chromatography on silica gel (elution with ethyl acetate). The yields varied from 69% for **43** to 77% for **41** to 83% in the present example.

For **46**: colorless solid: mp 156−161 °C; IR (neat, cm^{-1}) 3571, 3500−3100, 1713; ^1H NMR (300 MHz, $CDCl_3$) δ 8.65 (br s, 1 H), 7.37−7.23 (m, 5 H), 6.17 (dd, J = 6.0, 1.5 Hz, 1 H), 5.76 (dd, J = 6.0, 2.3 Hz, 1 H), 5.33 (m, 1 H), 4.60 (ABq, J = 11.0 Hz, 2 H), 4.27 (dd, J = 11.5, 3.6 Hz, 1 H), 4.09 (dd, J = 11.5, 6.5 Hz, 1 H), 4.04 (d, J = 16.4 Hz, 1 H), 3.97 (d, J = 16.4 Hz, 1 H), 2.06 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.1, 169.8, 153.8, 134.7, 129.1, 128.9, 128.5, 128.4, 128.1, 127.8, 89.4, 86.1, 66.5, 47.1, 45.2, 20.9; MS m/z (M^+) calcd 318.1341, obsd 318.1311; $[\alpha]_D^{25}$ −26.3 (c 0.9, $CHCl_3$).

(*S*)-*N*-Benzyl-5-[(*tert*-butyldimethylsiloxy)methyl]-4,5-dihydro-2-furamide (48). A solution of **20b** (803 mg, 2.06 mmol) in methanol (20 mL) was treated with pyridine (5 mL) followed by hydroxylamine hydrochloride (500 mg, 7.2 mmol), and the resulting mixture was pressurized at 10 000 Pa for 48 h. Workup in the predescribed manner gave amorphous powdery **47a** as a 1:1 mixture of diastereomers (786 mg, 97%). A sample of this material (220 mg, 0.54 mmol) was dissolved

in cold (−20 °C) CH_2Cl_2 (8 mL) containing triethylamine (190 μL) and treated with methanesufonyl chloride (46 μL, 1.1 equiv). The reaction mixture was stirred at this temperature for 2 h and concentrated. The residue was purified by chromatography on silica gel (elution with 20% ethyl acetate in hexanes) to give **48** (132 mg, 70%): IR (neat, cm^{-1}) 1647, 1435, 1253; ^1H NMR (300 MHz, $CDCl_3$) δ 7.40−7.26 (m, 5 H), 5.78 (t, J = 2.6 Hz, 1 H), 4.85−4.71 (m, 3 H), 4.14 (br s, 1 H), 3.70 (m, 2 H), 2.80 (ddd, J = 16.8, 2.8, 10.4 Hz, 1 H), 2.63 (ddd, J = 16.8, 7.6, 2.9 Hz, 1 H), 0.84 (s, 9 H), 0.02 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.6, 134.9, 129.0, 128.3, 128.2, 109.5, 83.4, 64.7, 31.6, 25.7, 18.2, −5.5 (1 C not observed); MS m/z (M^+) calcd 347.1916, obsd 347.1904; $[\alpha]_D^{25}$ +27.3 (c 1.4, $CHCl_3$).

(2*S*,5*S*)-9-Benzyl-2-[(*tert*-butyldimethylsiloxy)methyl]-1,6-dioxa-9-azaspiro[4.5]decane-7,10-dione (49). A cold (−5 °C) stirred solution of **19b** (178 mg, 0.46 mmol) in CH_2Cl_2 (10 mL) was treated with finely ground $NaHCO_3$ (230 mg, 3.0 mmol) and then *m*-chloroperbenzoic acid (200 mg, 0.82 mmol). After 30 min at this temperature, saturated $NaHSO_3$ solution (5 mL) was introduced, and stirring was maintained for a further 10 min prior to extraction with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were dried and concentrated to leave **49** (169 mg, 96%) as a colorless oil: IR (neat, cm^{-1}) 1769, 1690; ^1H NMR (300 MHz, $CDCl_3$) δ 7.38−7.21 (m, 5 H), 4.74 (d, J = 14.8 Hz, 1 H), 4.49 (d, J = 14.8 Hz, 1 H), 4.48−4.41 (m, 1 H), 4.26 (d, J = 17.5 Hz, 1 H), 3.85 (d, J = 17.5 Hz, 1 H), 3.63 (d, J = 4.8 Hz, 2 H), 3.07−2.94 (m, 1 H), 2.30−2.17 (m, 2 H), 3.06−1.94 (m, 1 H), 0.89 (s, 9 H), 0.05 (s, 3 H), 0.03 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.4, 162.7, 134.7, 129.0, 128.2, 128.0, 108.4, 83.6, 64.5 49.6, 48.3, 32.7, 25.8, 25.6, 18.3, −5.35, −5.44; MS m/z (M^+) calcd 389.2022, obsd 389.1972; $[\alpha]_D^{25}$ +11.9 (c 1.4, $CHCl_3$).

Anal. Calcd for $C_{21}H_{31}NO_4Si$: C, 62.19; H, 7.71. Found: C, 62.10; H, 7.66.

(2*S*,5*R*)-9-Benzyl-2-[(*tert*-butyldimethylsiloxy)methyl]-1,6-dioxa-9-azaspiro[4.5]decane-7,10-dione (50). Comparable oxidation of **20b** (280 mg, 0.72 mmol) with *m*-CPBA (320 mg, 1.3 mmol) in the presence of powdered $NaHCO_3$ (360 mg, 4.3 mmol) afforded 272 mg (93%) of **50** as a colorless solid: mp 54−56 °C; IR (neat, cm^{-1}) 1767, 1692; ^1H NMR (300 MHz, $CDCl_3$) δ 7.35−7.31 (m, 5 H), 4.72 (d, J = 14.8 Hz, 1 H), 4.51 (d, J = 14.8 Hz, 1 H), 4.49−4.37 (m, 1 H), 4.23 (d, J = 17.5 Hz, 1 H), 3.85 (d, J = 17.5 Hz, 1 H), 3.67 (d, J = 5.3 Hz, 2 H), 2.99−2.91 (m, 1 H), 2.31−2.24 (m, 1 H), 2.22−2.12 (m, 1 H), 2.06−1.93 (m, 1 H), 0.87 (s, 9 H), 0.03 (s, 3 H), 0.02 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.0, 163.0, 134.6, 129.0, 128.2, 128.0, 107.7, 85.1, 65.8, 49.6, 48.2, 33.3, 26.0, 25.8, 18.3, −5.4, −5.5; MS m/z (M^+) calcd 404.2131, obsd 404.2072; $[\alpha]_D^{25}$ −14.8 (c 1.6, $CHCl_3$).

Anal. Calcd for $C_{21}H_{31}NO_4Si$: C, 62.19; H, 7.71. Found: C, 62.03; H, 7.62.

(2*S*,5*S*)-9-Benzyl-2-[(*tert*-butyldimethylsiloxy)methyl]-1-oxa-6,9-diazaspiro[4.5]decane-7,10-dione (52) and (2*S*,5*R*)-9-Benzyl-2-[(*tert*-butyldimethylsiloxy)methyl]-1-oxa-6,9-diazaspiro[4.5]decane-7,10-dione (53). A solution of either **49** or **50** (200 mg, 0.49 mmol) in distilled methanol (1.0 mL) at 0 °C was treated with a saturated solution of ammonia in methanol (9.0 mL, saturated at 0 °C for 30 min), stirred for 30 min, and concentrated in vacuo to give **51** as a viscous oil (207 mg, 100%), which was used directly.

The above lactol (830 mg, 1.98 mmol) was dissolved in benzene (15 mL) containing 4 Å molecular sieves (200 mg) and pyridinium *p*-toluenesulfonate (30 mg) and heated at 90 °C under N_2 for 1 h. Chromatography of the product mixture on silica gel (elution with ethyl acetate) afforded 280 mg (35%) of **52**, 279 mg (35%) of **53**, and 230 mg (30%) of **57**.

For **52**:[42] colorless crystals; mp 127−129 °C; IR (neat, cm^{-1}) 3381, 1693; ^1H NMR (300 MHz, $CDCl_3$) δ 7.53 (br s, 1 H), 7.33−7.21 (m, 5 H), 4.59 (s, 2 H), 4.35−4.25 (m, 1 H), 4.01 (d, J = 17.7 Hz, 1 H), 3.74 (d, J = 17.7 Hz, 1 H), 3.71 (dd, J = 10.9, 3.8 Hz, 1 H), 3.61 (dd, J = 10.9, 3.5 Hz, 1 H), 2.93−2.83 (m, 1 H), 2.34−2.21 (m, 1 H), 2.08−1.90 (m, 2 H), 0.89 (s, 9 H), 0.07 (s, 3 H), 0.06 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.2, 165.1, 135.1, 128.9, 128.1, 128.0, 89.9, 82.0, 65.3, 49.8, 49.4, 35.8, 28.0, 25.7, 18.0, −5.5; MS m/z (M^+) calcd 404.2131, obsd 404.2150.

Anal. Calcd for $C_{21}H_{32}N_2O_4Si$: C, 62.34; H, 7.98. Found: C, 62.41; H, 7.99.

For **53**:[42] colorless crystals; mp 107−108 °C; IR (neat, cm^{-1}) 3381, 1693; ^1H NMR (300 MHz, $CDCl_3$) δ 8.23 (br s, 1 H), 7.33−7.22 (m, 5 H), 4.58 (s, 2 H), 4.23 (m, 1 H), 4.08 (d, J = 17.6 Hz, 1 H), 3.68 (d, J = 17.6 Hz, 1 H), 3.64 (dd, J = 10.6, 5.6 Hz, 1 H), 3.56 (dd, J = 10.6, 5.5 Hz, 1 H), 2.99−2.88 (m, 1 H), 2.18−1.98 (m, 2 H), 1.86−1.82 (m, 1 H), 0.88 (s, 9 H), 0.044 (s, 3 H), 0.035 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.4, 164.8, 135.3, 128.9, 128.1, 128.0, 89.9, 81.3, 65.3, 49.6 (2 C), 34.3, 28.2, 25.9, 18.4, −5.3; MS m/z (M^+) calcd 404.2131, obsd 404.2150; $[\alpha]_D^{25}$ −19.4 (c 1.0, $CHCl_3$).

Anal. Calcd for $C_{21}H_{32}N_2O_4Si$: C, 62.34; H, 7.98. Found: C, 62.41; H, 7.99.

For **57**: colorless crystalline solid; mp 142−148 °C; IR (neat, cm^{-1}) 3399, 3221, 1684; ^1H NMR (300 MHz, $CDCl_3$) δ 7.95−7.83 (br s, 1 H), 7.37−7.20 (m, 5 H), 4.78 (d, J = 14.8 Hz, 1 H), 4.43 (d, J = 14.8 Hz, 1 H), 4.09 (d, J = 17.2 Hz, 1 H), 3.83−3.76 (m, 1 H), 3.71−3.63 (m, 2 H), 3.42 (dd, J = 12.5, 10.0 Hz, 1 H), 2.56 (ddd, J = 14.4, 4.7, 4.6 Hz, 1 H), 2.19−2.11 (m, 1 H), 1.83 (dt, J = 14.4, 4.6 Hz, 1 H), 1.73−1.60 (m, 1 H), 0.87 (s, 9 H), 0.06 (s, 3 H), 0.05 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.1, 164.7, 135.2, 128.0, 127.90, 127.87, 80.7, 66.5, 65.2, 49.9, 49.7, 27.9, 27.8, 25.7, 18.0, −4.8; MS m/z (M^+) calcd 404.2131, obsd 404.2150.

Anal. Calcd for $C_{21}H_{32}N_2O_4Si$: C, 62.34; H, 7.98. Found: C, 62.42; H, 7.93.

(2*S*,5*S*)-9-Benzyl-2-(hydroxymethyl)-1-oxa-6,9-diazaspiro[4.5]decane-7,10-dione (58) and (2*S*,5*R*)-9-Benzyl-2-(hydroxymethyl)-1-oxa-6,9-diazaspiro[4.5]decane-7,10-dione (60). A solution of **52** (171 mg, 0.42 mmol) in THF (5.0 mL) was treated with tetra-*n*-butylammonium fluoride hydrate (144 mg, 0.55 mmol) at 0 °C, stirred for 2 h, and concentrated in vacuo. Chromatography of the residue (silica gel, elution with ethyl acetate) furnished a 5:1 mixture of **58** and **60** as evidenced by integration of the proton at C-2. Heating this mixture with pyridinium *p*-toluenesulfonate (30 mg) in benzene (5 mL) to 50 °C for 1 h altered the ratio to the 1:1 level. For this mixture: IR (neat, cm^{-1})3379, 3600−3200, 3229, 1682; ^1H NMR (300 MHz, $CDCl_3$) δ 8.24 (br s, 0.5 H), 8.12 (br s, 0.5 H), 7.31−7.15 (m, 5 H), 4.61−4.51 (m, 2 H), 4.42−4.34 (m, 0.5 H), 4.34−4.32 (m, 0.5 H), 4.02−3.94 (m, 1 H), 3.76−3.68 (m, 2 H), 3.50−3.41 (m, 1 H), 2.87−2.76 (m, 1 H), 2.53 (br s, 1 H), 2.21−2.08 (m, 1 H), 2.06−1.84 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.3, 165.9, 165.0, 164.9, 135.0, 134.7, 128.92, 128.86, 128.1, 128.0, 127.9, 90.0, 89.9, 82.13, 82.09, 64.9, 63.6, 50.1, 49.8, 49.31, 49.26, 35.9, 35.8, 27.1, 26.4; MS m/z (M^+) calcd 290.1266, obsd 290.1275; $[\alpha]_D^{25}$ +12.1 (c 1.7, $CHCl_3$).

(2*S*,5*S*)-2-[(*tert*-Butyldiphenylsiloxy)methyl]-7-(*p*-methoxybenzyl)-1-oxa-7-azaspiro[4.4]non-3-ene-6,9-dione (66) and (2*S*,5*R*)-2-[(*tert*-Butyldiphenylsiloxy)methyl]-7-(*p*-methoxybenzyl)-1-oxa-7-azaspiro[4.4]non-3-ene-6,9-dione (67). A solution of **18** (8.90 g, 11.5 mmol) in dry benzene (500 mL) was treated with freshly dried pyridinium *p*-toluenesulfonate (1.0 g), heated to 80 °C for 4 h, cooled, washed with 1 M $NaHCO_3$ solution (100 mL), and concentrated. The residue was subjected to flash chromatography on silica gel (elution with 30% ethyl acetate in hexanes) to give two separable fractions, each consisting of two isomeric selenides (total 5.96 g, 75%).

For **A**: IR (neat, cm^{-1}) 1776, 1704; ^1H NMR (300 MHz, $CDCl_3$) δ 7.68−7.63 (m, 4 H), 7.48−7.29 (m, 11 H), 7.08 (m, 2 H), 6.81 (m, 2 H), 4.59−4.52 (m, 2 H), 4.13−4.06 (m, 1 H), 3.93 (d, J = 14.5 Hz, 1 H), 3.80−3.79 (m, 2 H), 3.77 (s, 3 H), 3.65 (d, J = 17.3 Hz, 1 H), 3.52 (d, J = 17.3 Hz, 1 H), 2.66−2.59 (m, 1 H), 2.51−2.43 (m, 1 H), 1.07 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.2, 168.5, 159.4, 135.7, 135.5, 133.3, 133.1, 130.3, 129.8, 129.7, 129.2, 128.3, 127.74, 127.64, 127.6, 126.2, 114.2, 99.9, 84.0, 81.0, 65.2, 55.2, 53.7, 45.9, 45.8, 41.4, 34.1, 26.9, 19.2; FAB MS m/z (M^+ + 1) calcd 700.19, obsd 700.33; $[\alpha]_D^{25}$ +13.0 (c 2.45, $CHCl_3$).

For **B**: IR (neat, cm^{-1}) 1776, 1704; ^1H NMR (300 MHz, $CDCl_3$) δ 7.68−7.63 (m, 4 H), 7.48−7.29 (m, 11 H), 7.08 (m, 2 H), 6.81 (m, 2 H), 4.57 (d, J = 14.5 Hz, 1 H), 4.55−4.45 (m, 1 H), 4.13−4.06 (m, 1 H), 3.92 (d, J = 14.5 Hz, 1 H), 3.94−3.74 (m, 2 H), 3.77 (s, 3 H), 3.64 (d, J = 17.3 Hz, 1 H), 3.49 (d, J = 17.3 Hz, 1 H), 2.64−2.55 (m, 1 H), 2.22−2.10 (m, 1 H), 1.06 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.3, 169.5, 159.4, 135.6, 133.42, 133.40, 132.6, 129.6, 129.5, 128.2, 127.9, 127.7, 127.64, 127.60, 127.5, 126.2, 114.2, 83.5, 82.1, 66.2, 55.3, 53.8, 45.9, 42.9, 36.1, 28.5, 26.8, 19.2; FAB MS m/z ($M^+ + 1$) calcd 700.19, obsd 700.33; $[\alpha]_D^{25}$ −4.2 (c 1.35, $CHCl_3$).

Anal. Calcd for $C_{38}H_{41}NO_5SeSi$: C, 65.32; H, 5.91. Found: C, 65.28; H, 5.91.

A solution of the **A/B** mixture (8.90 g, 12.8 mmol) in methanol (350 mL) at 0 °C was treated with finely ground $NaHCO_3$ (10.0 g), and the resulting slurry was treated dropwise with a solution of sodium metaperiodate (8.20 g, 38.5 mmol) in distilled water (20 mL). After being stirred for 12 h, the reaction mixture was filtered through a Celite pad, and the filtrate was concentrated to approximately half-volume prior to being partitioned between saturated $NaHCO_3$ solution and ethyl acetate. The separated aqueous phase was extracted with ethyl acetate, and the combined organic layers were dried and concentrated. Flash chromatography of the residue on silica gel (elution with 30% ethyl acetate in hexanes) resulted in the separation of **66** from **67** (5.69 g total, 82%).

For **66**: IR (neat, cm^{-1}) 1782, 1707, 1612, 1513; ^1H NMR (300 MHz, $CDCl_3$) δ 7.71−7.25 (m, 10 H), 7.19 (d, J = 8.6 Hz, 2 H), 6.88 (d, J = 8.6 Hz, 2 H), 6.37 (dd, J = 6.1, 4.1 Hz, 1 H), 5.65 (dd, J = 6.1, 2.1 Hz, 1 H), 5.26 (m, 1 H), 4.59 (d, J = 14.5 Hz, 1 H), 4.53 (d, J = 14.5 Hz, 1 H), 4.05 (dd, J = 10.0, 5.9 Hz, 1 H), 3.83 (dd, J = 10.0, 7.2 Hz, 1 H), 3.80 (s, 3 H), 3.76 (d, J = 17.5 Hz, 1 H), 3.65 (d, J = 17.5 Hz, 1 H), 1.09 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.7, 168.4. 159.5, 135.54, 135.49, 134.2, 133.4, 133.3, 129.8, 129.6, 127.7, 126.4, 123.8, 114.4, 90.1, 89.8, 67.7, 55.2, 52.7, 46.2, 26.8, 19.2; MS m/z ($M^+ - 1$) calcd 541.2285, obsd 541.2313; $[\alpha]_D^{25}$ −102 (c 1.8, $CHCl_3$).

Anal. Calcd for $C_{32}H_{35}NO_5Si$: C, 70.95; H, 6.51. Found: C, 70.83; H, 6.47.

For **67**: IR (neat, cm^{-1}) 1783, 1703, 1611, 1513; ^1H NMR (300 MHz, $CDCl_3$) δ 7.69−7.25 (m, 10 H), 7.19 (d, J = 8.6 Hz, 2 H), 6.88 (d, J = 8.6 Hz, 2 H), 6.33 (dd, J = 6.0, 1.5 Hz, 1 H), 5.63 (dd, J = 6.0, 2.1 Hz, 1 H), 5.38−5.33 (m, 1 H), 4.58 (s, 2 H), 3.92 (dd, J = 10.2, 5.9 Hz, 1 H), 3.78 (dd, J = 10.2, 7.0 Hz, 1 H), 3.80 (s, 3 H), 3.71 (d, J = 17.2 Hz, 1 H), 3.64 (d, J = 17.2 Hz, 1 H), 1.06 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.9, 168.8, 159.6, 135.61, 135.55, 134.0, 133.4, 133.2, 129.9, 129.68, 129.66, 127.7, 126.4, 123.9, 114.4, 90.1, 89.9, 67.5, 55.3, 52.7, 46.3, 26.8, 19.2; MS m/z ($M^+ - 1$) calcd 541.2285, obsd 541.2288; $[\alpha]_D^{25}$ −12.7 (c 1.8, $CHCl_3$).

(2*S*,5*S*)-2-[(*tert*-Butyldiphenylsiloxy)methyl]-7-(*p*-methoxybenzyl)-9-methylene-1-oxa-7-azaspiro[4.4]nonan-6-one (68). Reaction of **66** (50 mg, 0.093 mmol) with the ylide prepared from methyltriphenylphosphonium iodide (400 mg) and *n*-butyllithium (0.4 mL) in THF (13 mL) according to the predescribed procedure gave, after chromatography on silica gel (elution with 40% ethyl acetate in hexanes), 42 mg (84%) of **68** as a colorless oil: IR (neat, cm^{-1}) 1702, 1513; ^1H NMR (300 MHz, $CDCl_3$) δ 7.71−7.25 (m, 10 H), 7.19 (d, J = 8.5 Hz, 2 H), 6.88 (d, J = 8.6 Hz, 2 H), 6.34 (dd, J = 6.0, 1.5 Hz, 1 H), 5.66 (dd, J = 6.0, 2.0 Hz, 1 H), 5.34 (m, 1 H), 5.24 (t, J = 2.3 Hz, 1 H), 5.14−5.08 (m, 1 H), 4.49 (d, J = 24.5 Hz, 1 H), 4.43 (d, J = 14.5 Hz, 1 H), 4.07 (dd, J = 9.7, 5.7 Hz, 1 H), 3.89−3.72 (m, 3 H), 3.79 (s, 3 H), 1.09 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.2, 159.2, 142.2, 135.58, 135.56, 133.7, 133.6, 132.0, 129.6, 128.2, 127.8, 127.6, 114.1, 112.8, 91.8, 88.0, 68.5, 55.3, 48.5, 46.4, 27.0, 26.0, 19.3; MS m/z (M^+) calcd 541.2648, obsd 541.2670; $[\alpha]_D^{25}$ +27.1 (c 2.1, $CHCl_3$).

(2*R*,3*S*,4*R*,5*S*)-2-[(*tert*-Butyldiphenylsiloxy)methyl]-3,4-dihydroxy-7-(*p*-methoxybenzyl)-1-oxa-7-azaspiro[4.4]-nonane-6,9-dione, Diacetate (Ester) (69) and (2*R*,3*R*,4*S*,5*S*)-2-[(*tert*-Butyldiphenylsiloxy)methyl]-3,4-dihydroxy-7-(*p*-methoxybenzyl)-1-oxa-7-azaspiro[4.4]nonane-6,9-dione, Diacetate (Ester) (70). Prototypical Procedure. A stirred solution of **66** (1.01 g, 1.88 mmol) in THF (40 mL) and pyridine (10 mL) was cooled to 0 °C, treated with a solution of osmium tetraoxide (476 mg, 1.88 mmol) in the minimum amount of pyridine, allowed to warm to room temperature during 4 h, and concentrated in vacuo (bath temperature <50 °C). The resulting dark brown foam was taken up in CH_2Cl_2 (100 mL), treated with saturated $NaHSO_3$ solution (1 mL), stirred vigorously overnight, filtered through a pad of Celite, and extracted repeatedly with CH_2Cl_2 (8 × 40 mL). The combined extracts were dried and concentrated. The residual glass was taken up in CH_2Cl_2 (50 mL), treated with acetic anhydride (3 mL), pyridine (6 mL), and DMAP (50 mg), stirred overnight, and concentrated. The product was chromatographed on silica gel (elution with 30% ethyl acetate in hexanes) to furnish 122 mg of **69** and 472 mg of **70** (48% total).

For **69**: IR (neat, cm^{-1}) 1782, 1681; ^1H NMR (300 MHz, $CDCl_3$) δ 7.70−7.64 (m, 4 H), 7.44−7.43 (m, 6 H), 7.20−7.16 (m, 2 H), 6.88−6.84 (m, 2 H), 5.43 (t, J = 6.4 Hz, 1 H), 5.20 (d, J = 6.3 Hz, 1 H), 4.69−4.64 (m, 1 H), 4.53 (d, J = 14.4 Hz, 1 H), 4.48 (d, J = 14.4 Hz, 1 H), 3.91−3.83 (m, 2 H), 3.87 (d, J = 17.3 Hz, 1 H), 3.80 (s, 3 H), 3.57 (d, J = 17.3 Hz, 1 H), 2.11 (s, 3 H), 2.05 (s, 3 H), 1.07 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.1, 172.1, 170.5, 169.9, 166.8, 159.5, 135.6, 133.1, 132.9, 130.0, 129.74, 129.72, 127.4, 126.4, 114.3, 97.6, 83.3, 81.9, 73.8, 71.4 62.9, 55.3, 53.0, 46.0, 26.8, 26.7, 20.6, 20.4, 19.2; FAB MS m/z ($M^+ + 1$) calcd 659.26, obsd 659.28.

Compound **70** was subjected directly to peracid oxidation.

(2*R*,3*S*,4*R*,5*S*)-2-[(*tert*-Butyldiphenylsiloxy)methyl]-3,4-dihydroxy-9-(*p*-methoxybenzyl)-1,6-dioxa-9-azaspiro-[4.5]decane Diacetate (Ester) (73). A stirred slurry of **69** (300 mg, 4.6 mmol) and finely ground $NaHCO_3$ (150 mg) in CH_2Cl_2 (20 mL) was treated with *m*-CPBA (225 mg of 70% purity, 2 equiv) and stirred for 20 in prior to dilution with more CH_2Cl_2 (10 mL) and $NaHSO_3$ solution (5 mL). The predescribed workup led to the isolation of 282 mg (92%) of **73** after chromatography on silica gel (elution with 30% ethyl acetate in hexanes): white foam; IR (neat, cm^{-1}) 1756, 1695, 1514; ^1H NMR (300 MHz, $CDCl_3$) δ 7.68−7.63 (m, 4 H), 7.49−7.33 (m, 6 H), 7.19−7.15 (m, 2 H), 6.89−6.85 (m, 2 H), 5.62 (d, J = 5.2 Hz, 1 H), 5.47 (dd, J = 5.2, 7.4 Hz, 1 H), 4.69 (d, J = 14.5 Hz, 1 H), 4.64−4.60 (m, 1 H), 4.25 (d, J = 14.5 Hz, 1 H), 4.12 (d, J = 17.8 Hz, 1 H), 3.96 (d, J = 17.8 Hz, 1 H), 3.92 (dd, J = 11.5, 4.5 Hz, 1 H), 3.84 (dd, J = 11.4, 4.4 Hz, 1 H), 3.80 (s, 3 H), 2.10 (s, 3 H), 2.06 (s, 3 H), 1.07 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.9, 169.6, 162.6, 160.5, 159.7, 135.6, 132.98, 132.8, 130.0, 129.8, 127.8, 126.1, 114.4, 104.3, 83.8, 75.0, 70.5, 63.2, 55.3, 49.1, 47.2, 26.7, 20.6, 20.4, 19.2; FAB MS m/z ($M^+ + 1$) calcd 676.25, obsd 676.34; $[\alpha]_D^{25}$ +40.2 (c 0.9, $CHCl_3$).

(2*R*,3*R*,4*S*,5*S*)-2-[(*tert*-Butyldiphenylsiloxy)methyl]-3,4-dihydroxy-9-(*p*-methoxybenzyl)-1,6-dioxa-9-azaspiro-[4.5]decane Diacetate (Ester) (74). Comparable oxidation of **70** (122 mg, 1.87 mmol) delivered 107 mg (86%) of **74** as a white foam: ^1H NMR (300 MHz, $CDCl_3$) δ 77.71−7.60 (m, 4 H), 7.45−7.32 (m, 6 H), 7.25−7.15 (m, 2 H), 6.89−6.83 (m, 2 H), 6.09 (d, J = 6.3 Hz, 1 H), 5.62 (t, J = 6.3 Hz, 1 H), 4.67 (d, J = 14.6 Hz, 1 H), 4.43 (d, J = 14.6 Hz, 1 H), 4.32−4.28 (m, 1 H), 4.02 (d, J = 18.0 Hz, 1 H), 3.84 (d, J = 18.0 Hz, 1 H), 3.86−3.78 (m, 2 H), 3.79 (s, 3 H), 2.08 (s, 3 H), 2.07 (s, 3 H), 1.05 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.9, 169.8, 163.3, 160.8, 159.7, 135.7, 132.9, 132.8, 130.0, 129.6, 127.71, 127.68, 126.0, 114.5, 102.4, 83.1, 74.7, 63.8, 55.3, 49.1, 46.9, 26.7, 20.7, 20.4, 19.2; FAB MS m/z ($M^+ + 1$) calcd 676.25, obsd 676.34; $[\alpha]_D^{25}$ +13.1 (c 1.0 $CHCl_3$).

(2*R*,3*S*,4*R*,5*R*)-2-[(*tert*-Butyldiphenylsiloxy)methyl]-3,4-dihydroxy-7-(*p*-methoxybenzyl)-1-oxa-7-azaspiro[4.4]-nonane-6,9-dione, Diacetate (Ester) (71) and (2*R*,3*R*,4*S*,5*R*)-2-[(*tert*-Butyldiphenylsiloxy)methyl]-3,4-dihydroxy-7-(*p*-methoxybenzyl)-1-oxa-7-azaspiro[4.4]nonane-6,9-dione, Diacetate (Ester) (72). A 1.02 g (1.92 mmol) sample of **67** was osmylated and acetylated in a manner directly paralleling that described above for **66**. There was isolated 132 mg of **71** and 395 mg of **72** (43% total).

For **71**: IR (neat, cm^{-1}) 1750, 1697; ^1H NMR (300 MHz, $CDCl_3$) δ 7.67−7.63 (m, 4 H), 7.39−7.26 (m, 6 H), 7.14 (d, J =

8.5 Hz, 2 H), 6.83 (d, J = 8.5 Hz, 2 H), 5.69 (t, J = 5.2 Hz, 1 H), 5.55 (d, J = 6.7 Hz, 1 H), 4.67 (dd, J = 5.2, 4.5 Hz, 1 H), 4.52 (d, J = 14.5 Hz, 1 H), 4.43 (d, J = 14.5 Hz, 1 H), 3.99−3.92 (m, 4 H), 3.78 (s, 3 H), 2.04 (s, 3 H), 1.98 (s, 3 H), 1.03 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.9, 169.8, 163.4, 159.7, 159.4, 135.6, 135.5, 133.1, 132.9, 127.8, 126.1, 114.4, 103,6, 80.7, 77.3, 70.3, 61.3, 55.3, 49.0, 47.3, 26.6, 20.5, 20.4, 19.2; FAB MS m/z ($M^+ + 1$) calcd 676.25, obsd 676.38.

Compound **72** was subjected directly to peracid oxidation.

(2*R*,3*R*,4*S*,5*R*)-2-[(*tert*-Butyldiphenylsiloxy)methyl]-3,4-dihydroxy-9-(*p*-methoxybenzyl)-1,6-dioxa-9-azaspiro-[4.5]decane-7,10-dione, Diacetate (Ester) (76). Oxidation of **72** (66 mg, 0.14 mmol) with buffered *m*-CPBA according to the general procedure afforded 47 mg (68%) of **76**: IR (neat, cm^{-1}) 1750, 1697; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67−7.63 (m, 4 H), 7.46−7.36 (m, 6 H), 7.14 (d, J = 8.7 Hz, 2 H), 6.83 (d, J = 8.7 Hz, 2 H), 5.69 (t, J = 5.2 Hz, 1 H), 5.54 (dd, J = 0.6, 5.2 Hz, 1 H), 4.71−4.65 (m, 1 H), 4.52 (d, J = 14.5 Hz, 1 H), 4.43 (d, J = 14.5 Hz, 1 H), 3.98−3.95 (m, 4 H), 3.78 (s, 3 H), 2.04 (s, 3 H), 1.98 (s, 3 H), 1.03 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.8, 163.4, 159.7, 159.4, 135.6, 135.5, 133.1, 132.9, 129.8, 127.8, 126.2, 114.4, 103.6, 80.7, 77.2, 76.7, 70.3, 61.3, 55.3, 49.0, 47.3, 26.7, 20.5, 19.2; FAB MS m/z ($M^+ + 1$) calcd 676.25, obsd 676.34; $[\alpha]_D^{25}$ +4.2 (c 0.1, $CHCl_3$).

(2*R*,3*S*,4*R*,5*S*)-2-[(*tert*-Butyldiphenylsiloxy)methyl]-3,4-dihydroxy-9-(*p*-methoxybenzyl)-1-oxa-6,9-diazaspiro-[4.5]decane-7,10-dione, Diacetate (Ester) (77). A solution of **73** (262 mg, 3.79 mmol) in $CHCl_3$ (25 mL) was cooled to −20 °C prior to the addition of a saturated solution of ammonia in methanol (4 mL). The progress of reaction was monitored periodically by TLC until complete disappearance of starting material (spot to spot). The mixture was concentrated in vacuo to remove all traces of methanol. The residual foam was taken up in benzene (20 mL), admixed with 4 Å molecular sieves (500 mg) and pyridinium *p*-toluenesulfonate (50 mg), and stirred at room temperature for 24 h. Filtration, concentration, and chromatography on silica gel (elution with 50% ethyl acetate in hexanes) followed to give **77** (201 mg, 79%) as a white foam: IR (neat, cm^{-1}) 1748, 1698; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71−7.65 (m, 4 H), 7.44−7.33 (m, 6 H), 7.19−7.16 (m, 2 H), 6.87−6.84 (m, 2 H), 6.10 (d, J = 6.7 Hz, 1 H), 5.61 (dd, J = 2.7, 6.7 Hz, 1 H), 4.82 (d, J = 17.8 Hz, 1 H), 4.44−4.40 (m, 1 H), 4.38 (d, J = 14.6 Hz, 1 H), 4.17 (d, J = 17.8 Hz, 1 H), 3.91 (d, J = 17.8 Hz, 1 H), 3.80 (s, 3 H), 3.94−3.75 (m, 2 H), 2.13 (s, 3 H), 2.12 (s, 3 H), 1.11 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.3, 169.7, 169.0, 164.8, 160.3, 159.7, 135.7, 135.6, 132.7, 129.8, 129.71, 129.65, 127.8, 127.7, 126.3, 114.5, 103.7, 87.1, 62.9, 55.3, 49.3, 47.5, 26.6, 20.7, 20.3, 19.1; FAB MS m/z ($M^+ + 2$) calcd 676.27, obsd 676.33; $[\alpha]_D^{25}$ +4.2 (c 1.7, $CHCl_3$).

(2*R*,3*R*,4*S*,5*S*)-2-[(*tert*-Butyldiphenylsiloxy)methyl]-3,4-dihydroxy-9-(*p*-methoxybenzyl)-1-oxa-6,9-diazaspiro-[4.5]decane-7,10-dione, Diacetate (Ester) (78). Comparable ammonolysis of **74** or **76** afforded **78** in 71% and 77% yield, respectively: white foam; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67−7.57 (m, 4 H), 7.46−7.33 (m, 6 H), 7.15 (m, 2 H), 6.86 (m, 2 H), 6.08 (d, J = 5.0 Hz, 1 H), 5.80 (dd, J = 4.2, 5.0 Hz, 1 H), 4.68 (d, J = 14.5 Hz, 1 H), 4.59−4.52 (m, 1 H), 4.41 (d, J = 14.5 Hz, 1 H), 4.00 (d, J = 17.9 Hz, 1 H), 3.85 (d, J = 17.9 Hz, 1 H), 3.93−3.80 (m, 2 H), 3.79 (s, 3 H), 2.05 (s, 3 H), 2.04 (s, 3 H), 1.01 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.8, 169.1, 161.3, 159.7, 135.5, 135.4, 130.0, 129.9, 129.7, 127.83, 127.78, 114.5, 101.9, 82.0, 61.4, 55.3, 49.2, 47.0, 26.7, 20.5, 20.3, 19.1; FAB MS m/z ($M^+ + 2$) calcd 676.27, obsd 676.33.

(2*R*,3*S*,4*R*,5*S*)-2-[(*tert*-Butyldiphenylsiloxy)methyl]-3,4-dihydroxy-1-oxa-6,9-diazaspiro[4.5]decane-7,10-dione, Diacetate (Ester) (79). A solution of **77** (105 mg, 0.16 mmol) in water (0.25 mL) and acetonitrile (3.5 mL) was treated with ceric ammonium nitrate (500 mg, ca. 6 equiv) and stirred for 6 h before being partitioned between saturated $NaHCO_3$ solution (5 mL) and ethyl acetate (10 mL). The resulting emulsion was filtered and extracted repeatedly with ethyl acetate. The combined organic phases were dried and concentrated to leave a residue that was chromatographed on silica gel (gradient elution with 30−100% ethyl acetate in hexanes) to give anisaldehyde (7 mg), unreacted **77** (61 mg, 58%), and **79** (19 mg, 53%) as a white foam: IR (neat, cm^{-1}) 1748, 1725, 1603; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69−7.64 (m, 4 H), 7.43−7.33 (m, 6 H), 6.00 (d, J = 6.6 Hz, 1 H), 5.61 (dd, J = 2.4, 6.6 Hz, 1 H), 4.46−4.45 (m, 1 H), 4.24 (dd, J = 17.8, 9.7 Hz, 1 H), 4.05 (dd, J = 17.8, 4.3 Hz, 1 H), 3.89−3.79 (m, 2 H), 2.13 (s, 3 H), 2.12 (s, 3 H), 1.09 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.3, 169.0, 164.6, 162.3, 135.7, 132.7, 132.6, 129.9, 129.8, 127.8, 127.7, 103.5, 87.4, 77.2, 71.5, 69.9, 63.0, 43.9, 26.8, 26.7, 20.7, 19.1; FAB MS m/z ($M^+ + 2$) calcd 556.21, obsd 556.31.

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Supporting Information Available: High-field ^{1}H and ^{13}C NMR spectra of key compounds lacking elemental analysis, along with tables giving the crystal data and structure refinement information, bond lengths and bond angles, atomic and hydrogen coordinates, and isotropic and anisotropic displacement coordinates for **26** and **44**. This material is available free of charge via the Internet at http://pubs.acs.org.

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