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A Flexible Approach toward Trisubstituted Piperidines and Indolizidines: Synthesis of 6-*epi*-Indolizidine 223A

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2,5,6-Trisubstituted piperidines are readily prepared by a combination of an *aza*-Achmatowicz oxidation of a furyl-substituted benzenesulfonamide followed by a conjugate addition to the resulting 2*H*-pyridone and subsequent addition of various nucleophiles to a transient *N*-sulfonyliminium ion. The stereochemistry of the conjugate addition product is the result of axial attack from the face opposite the diaxial substituents at C_2 and C_6. This can be attributed to steric hindrance between the pseudoaxially oriented 2,6-substituents and the equatorially approaching nucleophile, thereby leading to the exclusive formation of the kinetically favored axial 1,4-adduct. Indolizidine alkaloid 223A was isolated from a skin extract of a Panamanian population of the dendrobatid *Dendrobates pumilio* Schmidt (Dendrobatidae). Synthesis of the originally proposed structure of this alkaloid was achieved in 13 steps in 13.1% overall yield by using an *aza*-Achmatowicz oxidative rearrangement and a diastereoselective 1,4-conjugate addition as the key steps. The structure of the natural 223A alkaloid (**5b**) differs from that of the *epi*-isomer **5a** synthesized in this study in the configuration at the 6-position of the indolizidine ring.

Nitrogen-containing saturated heterocyclic systems are important core structures in organic chemistry because of their presence in many natural products.[1] For this reason, simple procedures for the formation of substituted piperidines and pyrrolidines are highly desirable.[2] *Aza*-fused bicyclic alkaloids having indolizidine or quinolizidine ring systems have also been the targets of many synthetic efforts due to their interesting and potent biological activities including antiviral, antitumor, and glucosidate inhibitions.[3] The bicyclic structural motifs of these alkaloids are found in a variety of terrestrial and marine sources such as bacteria, fungi, higher plants, invertebrates, and vertebrates.[4] Accordingly, novel strategies for the stereoselective synthesis of six-membered *aza*-bicyclic systems continue to receive attention from the synthetic community.[5−13] In the past, addition of organometallic reagents to *N*-acyl pyridinium salts,[14] hetero-Diels−Alder reactions of imines,[15] Lewis acid or electrophile-induced cyclizations of imines or iminium ions,[16] and reactions of bicyclo cyano piperidines and lactams[17] have been employed for this purpose. Most of

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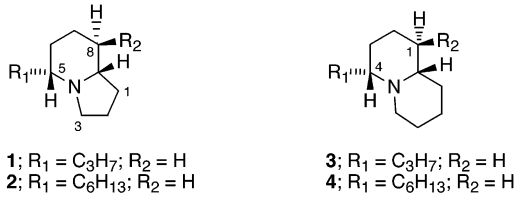


FIGURE 1. Indolizidine (**1**) and quinolizidine (**3**) scaffolds.

the known indolizidine alkaloids are either 3,5- or 5,8-substituted (Figure 1).[18]

Quite a number of indolizidine alkaloids have been isolated from the skin secretions of neotropical frogs,[19] and some have been shown to function as noncompetitive blockers for muscle-type and ganglionic nicotinic receptor channels.[20] Of these, indolizidines 167B (**1**) and 209D (**2**), structurally simple bicyclic gephyrotoxin alkaloids possessing a single substituent at C_5 of the indolizidine skeleton,[21] were isolated in minute quantities from unidentified dendrobatid frogs in a single population and have been attractive synthetic targets.[22,23] In 1997, a new subclass of amphibian alkaloids (223A) was isolated from a skin extract of a Panamanian population of the frog dendrobatid *Dendrobates pumilio* Schmidt (Dendrobatidae).[24] Three homologues of indolizidine 223A were also detected with different substituents, but their relative stereochemical structures have yet to be determined. Alkaloid 223A possesses the relatively rare 5,6,8-trisubstituted indolizidine ring. The structure of 223A was originally postulated as **5a** based upon GC-MS, GC-FTIR, and ^{1}H NMR spectral studies.[24] In a subsequent report published last year, the original proposed configuration at the 6-position of 223A was found to be incorrect and the structure was subsequently revised to **5b**.[25] The relative stereochemistry of natural 223A was established

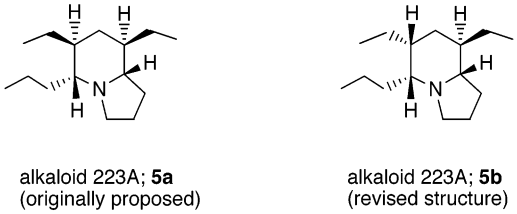
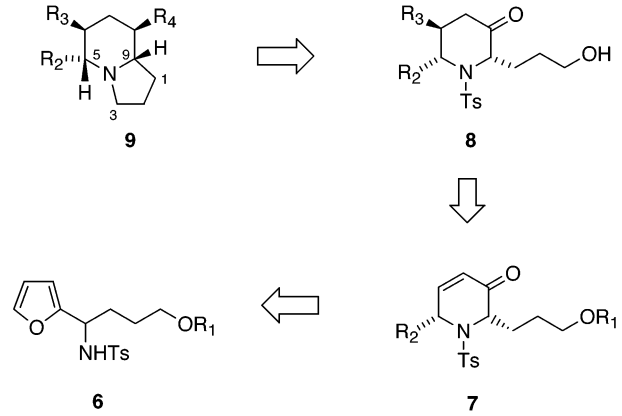


FIGURE 2. Structures of indolizidine 223A.

SCHEME 1



by a total synthesis, using a series of Michael-type conjugate additions to enaminoesters as the key steps.[26]

A critical problem in the total synthesis of various indolizidine alkaloids involves setting the stereocenters in the piperidine ring. When we initiated our work in this area in early 2001, our synthetic goal was to develop a stereoselective synthesis of **5a** since that was the presumed structure of 223A at that point in time.[24] We envisioned an approach to indolizidines such as **9** (Scheme 1) that is based on an *aza*-Achmatowicz oxidation reaction, a process defined as the conversion of furylamides such as **6** into 1,6-dihydro-2*H*-pyridin-3-ones (i.e., **7**).[27] This novel oxidative rearrangement has been used for the synthesis of azasaccharides,[28] izidine structures, β-lactam intermediates, and unusual amino acids and, we believe, possesses significant potential for the preparation of a variety of piperidine-based alkaloids.[29] In this paper we describe the successful application of this approach for the synthesis of 6-*epi*-indolizidine 223A (**5a**).

Results and Discussion

aza-Achmatowicz products incorporate functionality that is easily modified and can be utilized to construct complex nitrogen heterocycles. In his early studies of the *aza*-Achmatowicz reaction, Ciufolini reported that carbamate protected furfurylamines are somewhat unstable and readily hydrolyze to 3-hydroxypyridines under typical oxidation conditions.[27] Independent work by Zhou[30] and Altenbach,[31] however, showed that a sulfonamide

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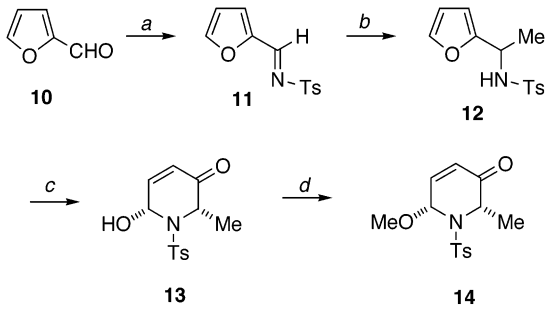
SCHEME 2[a]

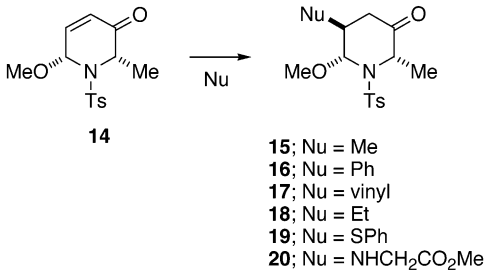


[a] Reagents and conditions: (a) $TsNH_2$, $BF_3{\cdot}OEt_2$, heat, 80%; (b) MeMgI, THF, 0 °C, 95%; (c) *m*-CPBA, CH_2Cl_2, 0 °C, 85%; (d) $(MeO)_3CH$, $BF_3{\cdot}OEt_2$, CH_2Cl_2, 0 °C, 85%.

protecting group was nicely compatible with the *aza*-Achmatowicz oxidation reaction. Consequently, we chose to work with an *N*-tosyl protecting group because of its robust nature and the ease of purification of the resulting products. To test our strategy for the eventual synthesis of indolizidine 223A, we needed to evaluate the stereochemical aspects of the proposed 1,4-conjugate addition to the dihydro-2*H*-pyridone intermediate (i.e., **7** → **8**) (Scheme 1).

Preparation of a model furyl sulfonamide (i.e., **12**) was first carried out to probe the stereochemical issues that we would need to deal with in our planned approach toward indolizidine alkaloid 223A. The synthesis of **12** was readily accomplished by condensation of furfural (**10**) with *p*-toluenesulfonamide, using $BF_3{\cdot}OEt_2$ as the catalyst (80% yield) (Scheme 2). Treatment of the resulting imine **11** with methylmagnesium iodide produced **12** in 95% yield. Sulfonylamide **12** was oxidatively rearranged by using *m*-CPBA in the *aza*-Achmatowicz reaction to furnish hemiaminal **13** in 85% yield. Conversion of the hydroxyl to the corresponding methoxy group was carried out by using trimethylorthoformate and catalytic $BF_3{\cdot}OEt_2$ which afforded 6-methoxy-2-methyl-1-(toluene-4-sulfonyl)-1,6-dihydro-2*H*-pyridin-3-one (**14**) in 85% yield. The stereochemical assignment of **14** as the cis-isomer is based on NMR spectroscopic analysis (1D-NOE). The exclusive formation of **14** can be rationalized by assuming that $A^{1,3}$-strain of the tosyl group forces the methoxy and methyl groups to adopt a pseudoaxial orientation. It should be noted that this stereochemistry (vide infra) does not follow from previous literature results with related systems.[32,33] The earlier reports have either suggested that the *trans*-dihydropyridinone isomer results from the oxidative cyclization,[32] or else the configuration of the product was not unequivocally elucidated.[33] The ^1H NMR data for dihydropyridinone **14** was consistent with those of similar compounds determined to have the cis-stereochemistry at C_2 and C_6.[34,35]

SCHEME 3[a]



entry	nucleophile (Nu)	yield %
1	$Me_2Cu(CN)Li$	90[a]
2	$Ph_2Cu(CN)Li$	90[b]
3	$(vinyl)_2CuMgBr$	87[c]
4	$(Et)_2CuMgBr$	85[d]
5	PhSH	85[e]
6	$H_2NCH_2CO_2Me$	60[f]

[a] Reagents and conditions: (a) MeLi, CuCN, Et_2O, −78 °C; (b) PhLi, CuCN, THF, −78 °C; (c) vinylMgBr, CuI, THF, −78 °C; (d) EtMgBr, CuI, THF, −78 °C; (e) PhSH, MeOH, 0 °C; (f) $NH_2CH_2CO_2Me$, Et_3N, MeOH, rt.

Treatment of 2*H*-pyridinone **14** with various cuprate reagents (Scheme 3, entries 1−4) proved to be remarkably stereoselective, providing the Michael adducts **15**−**18** in pure diastereomeric form and in high yield. Thiophenol and glycine methyl ester also furnished 1,4-addition products **19** and **20** in high yield.[36] The stereochemistry of the Michael addition products was unambiguously assigned on the basis of NMR spectroscopic analysis as well as an X-ray crystal structure of compound **15**. The stereochemistry of the conjugate addition product is the result of axial attack from the face opposite the diaxial substituents at C_2 and C_6. This may be attributed to steric hindrance between the pseudoaxially oriented 2,6-substituents and the equatorially approaching nucleophile, thereby leading to the exclusive formation of the kinetically favored axial 1,4-adduct.[37] It should be noted that related conjugate additions in the literature with dihydropyranulosides as substrates generally led to the formation of a mixture of diastereomers.[38] More than likely, the absence of a tosyl group makes the molecule more flexible, thereby permitting attack from both sides of the π-bond.[38]

Stereoselective functionalization of the pyridinone ring at the 6-position was accomplished by treating the heterocyclic system with allyl trimethylsilane under the influence of $BF_3{\cdot}OEt_2$ at 0 °C (Scheme 4). For example, the reaction of compound **14** with $CH_2{=}CHCH_2SiMe_3$ and $BF_3{\cdot}OEt_2$ afforded **21** in 85% yield. Similarly, treating **15** and **18** with allyl silane under comparable reaction conditions furnished **22** and **23** in 85% yield, respectively. Isopropenyl acetate reacted with **15** in the presence of $BF_3{\cdot}OEt_2$ to give ketone **24** in 85% isolated yield. In all

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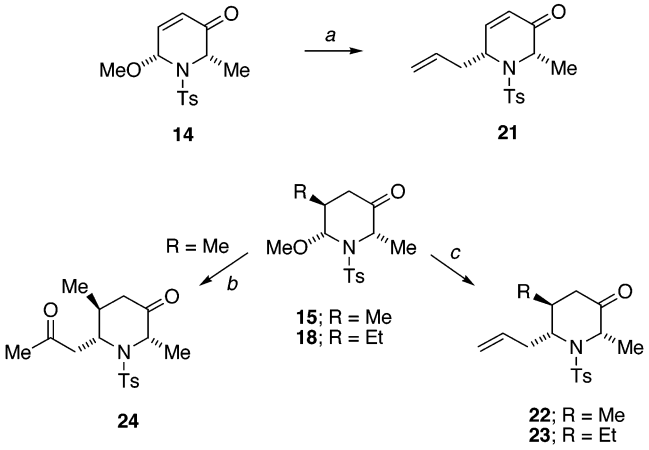
SCHEME 4[a]



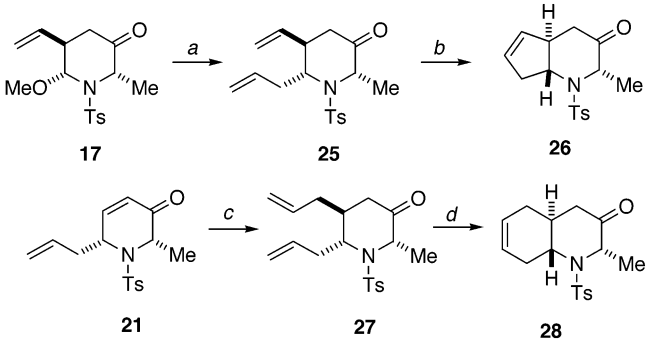
[a] Reagents and conditions: (a) $CH_2{=}CHCH_2SiMe_3$, $BF_3{\cdot}OEt_2$, CH_2Cl_2, 0 °C, 85%; (b) $CH_2{=}C(OAc)Me$, $BF_3{\cdot}OEt_2$, CH_2Cl_2, 0 °C, 70%; (c) $CH_2{=}CHCH_2SiMe_3$, $BF_3{\cdot}OEt_2$, CH_2Cl_2, 0 °C, 85%.

of the above examples, a single diastereomer was isolated whose stereochemistry was assigned as the 2,6-cis-disubstituted isomer. This assignment rests on literature analogy[39] and is also consistent with a NOE enhancement between the hydrogens on the C_2-methyl group and the methylene hydrogens of the allyl side chain at C_6. As suggested by others,[40] the preference for the 2,6-cis-disubstituted product can be rationalized by the $A^{1,3}$-strain present between the tosyl and methyl groups thereby causing the tosyl group to shield the opposite face of the molecule. The steric bulk associated with the tosyl group directs the attack of the nucleophile on the iminium ion to the side of the C_2-methyl group, leading to the formation of the cis-product.

In the past few years, the use of the ring-closing metathesis reaction (RCM)[41] for creating heterocyclic systems[42] from acyclic diolefins has increased enormously as a result of the ruthenium alkylidene catalysts that have been developed by Grubbs and co-workers.[41] Prompted by the ease with which pyridinones **25** and **27** can be prepared (Scheme 5), we decided to investigate their ring-closing olefin metathesis chemistry. The key cyclization reaction of **25** and **27** was performed with the Grubbs ruthenium benzylidene catalyst $Cl_2(PCy_3)_2$-Ru=CHPh (3 mol %) in CH_2Cl_2 under an atmosphere of nitrogen. Dienes **25** and **27** were completely consumed within 3 h at room temperature furnishing the hexahydro-1*H*-pyridine and octahydroquinoline ring systems **26** and **28** in 60 and 80% yield, respectively.

The above model studies show that 2-methyl-6-methoxy-2,6-dihydro-2*H*-pyridin-3-one (**14**) readily undergoes conjugate addition with various nucleophiles to deliver cis-substituted 2,6-piperidines. The resulting products can be further utilized as precursors for *N*-sulfonyliminium ions by reaction with various nucleophiles in the presence of a Lewis acid. The stereochemistry associated with the conjugate additions was established by X-ray analysis and is believed to arise from $A^{1,3}$-strain between the tosyl and adjacent substituents. Encouraged by these results we decided to apply the method toward the synthesis of the originally proposed indolizidine alkaloid 223A (**5a**).

SCHEME 5[a]



[a] Reagents and conditions: (a) $CH_2{=}CHCH_2SiMe_3$, $BF_3{\cdot}OEt_2$, CH_2Cl_2, 0 °C, 80%; (b) Grubbs catalyst, CH_2Cl_2, 25 °C, 60%; (c) $CH_2{=}CHCH_2SiMe_3$, $TiCl_4$, CH_2Cl_2, 0 °C, 90%; (d) Grubbs catalyst, CH_2Cl_2, 25 °C, 80%.

Synthesis of 6-*epi*-Indolizidine 223A (5a). The scarcity of 5,6,8-trisubstituted indolizidines as natural products and the uncertainty surrounding the originally proposed structure of indolizidine 223A (**5a**) prompted us to attempt its synthesis. With the model conjugate addition studies of dihydropyridone **14** in hand, we turned our attention to the synthesis of the structurally more complex dihydro-2*H*-pyridone **32**, which bears the requisite three-carbon side chain at the C_2-position of the ring necessary for the eventual preparation of **5a** (see Scheme 1). Our initial efforts to prepare furyl sulfonamide **30** using the Grignard reagent derived from a silyl-protected 3-bromopropan-1-ol as outlined in Scheme 2 furnished a complex mixture of products. Instead, we opted to synthesize **30** by first preparing the benzophenone-derived imine **29**. Treatment of this compound with *n*-BuLi followed by reaction of the resulting lithiate with 1-bromo-3-*tert*-butyldiphenyl-siloxypropane afforded the expected alkylated imine. A subsequent hydrolysis was followed by treatment of the resulting amine with tosyl chloride, which gave sulfonamide **30** in 66% overall yield from furfurylamine (Scheme 6). Oxidative rearrangement of **30** by treatment with 1.2 equiv of *m*-CPBA in CH_2Cl_2 for 4 h at room temperature yielded the 6-hydroxy-2,6-dihydropyridinone **31** as a single diastereomer. Compound **31** reacted with allyl silane under the influence of $BF_3{\cdot}OEt_2$ to produce the desired dihydropyridinone **32** in 64% yield over two steps.[43] The stereochemical assignment of **32** as the cis-isomer is based on NMR spectroscopic analysis (1D-NOE). We believe that the steric bulk of the tosyl group directs the attack of the nucleophile of the intermediate *N*-sulfonyliminium ion to the side of the C_2-substituent group, resulting in the formation of the cis-product.

(39) Shono, T.; Matsumara, Y.; Tsubata, K.; Uchida, K. *J. Org. Chem.* **1986**, *51*, 2590.

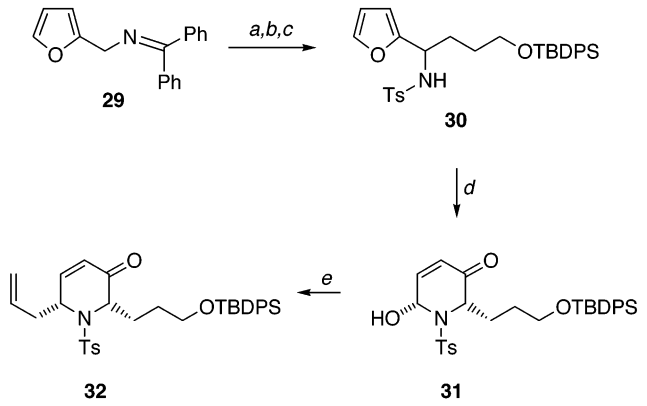
(40) Hopman, J. C. P.; van de Berg, E.; Ollero, L. O.; Hiemstra, H.; Speckamp, W. N. *Tetrahedron Lett.* **1995**, *36*, 4315.

(41) Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413.

(42) For several examples of the synthesis of piperidines via olefin metathesis, see: Fu, G. C.; Grubbs, R. H. *J. Am. Chem. Soc.* **1992**, *114*, 7324. Huwe, C. M.; Kiehl, O. C.; Blechert, S. *Synlett.* **1996**, 65. Rutjes, F. P. J. T.; Schoemaker, H. E. *Tetrahedron Lett.* **1997**, *38*, 677. Jo, E.; Na, Y.; Chang, S. *Tetrahedron Lett.* **1999**, *40*, 5581.

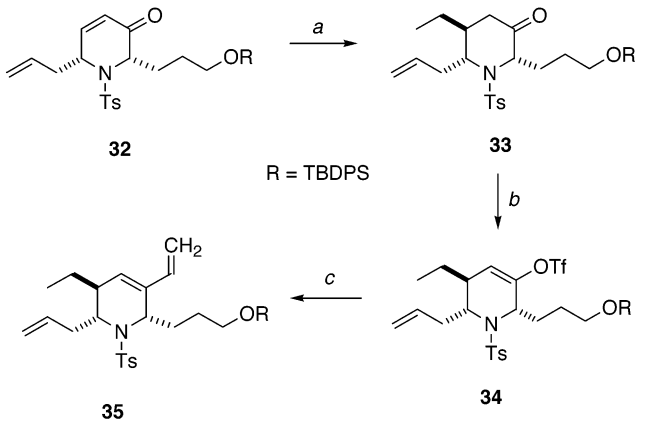
(43) So as to shorten the overall synthesis, the crude hemiaminal **31** was treated directly with $BF_3{\cdot}OEt_2$ and allyl silane instead of converting it to the corresponding methoxy derivative as had been done with the related hemiaminal **13**.

SCHEME 6[a]



[a] Reagents and conditions: (a) *n*-BuLi, THF, $BrCH_2CH_2CH_2OTB$-DPS, 86%; (b) 1 N HCl, acetone, 95%; (c) TsCl, NEt_3, CH_2Cl_2, 90%; (d) *m*-CPBA, CH_2Cl_2; (e) $CH_2{=}CHCH_2SiMe_3$, $BF_3{\cdot}OEt_2$, CH_2Cl_2, 0 °C, 64% over two steps.

SCHEME 7[a]

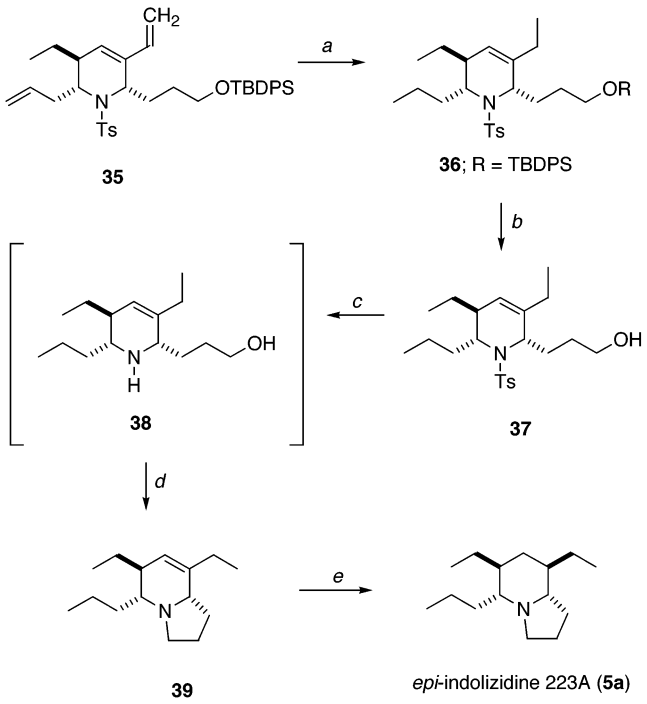


[a] Reagents and conditions: (a) $(Et)_2CuMgBr$, THF, 0 °C, 90%; (b) $PhNTf_2$, NaHMDS, −78 °C, 95%; (c) $CH_2{=}CHSnBu_3$, $Pd(PPh_3)_4$, LiCl, THF, 85%.

The next step involved Michael addition of an ethyl group onto the β-position of the enone π-system. We were pleased to find that the reaction of **32** with $(Et)_2CuMgBr$ in THF at −78 °C gave the 1,4-conjugate addition product **33** as a single diastereomer in 90% yield (Scheme 7). The stereochemistry of **33** was determined by the ^1H NMR coupling constants and NOE enhancements. The high diastereoselectivity encountered in the formation of **33** can be rationalized by axial attack of the organo-cuprate reagent from the face opposite the diaxial substituents at C_2 and C_6 as was similarly observed in our model studies with dihydropyridinone **14**.

To install the remaining carbon functionality present in indolizidine 223A, we needed to convert the keto group into a C_3-ethyl substituent and also control the stereochemistry at this carbon site. Our first attempts involved a Wittig or Julia olefination reaction at the ketonic center. However, all of our efforts to carry out this transformation failed and only recovered starting material was obtained. The low reactivity of pyridinone **33** is probably related to the fact that the substituent groups at C_2, C_3, and C_6 are all in an axial orientation thereby creating a sterically crowded environment around the carbonyl group. After considerable experimentation, we

SCHEME 8[a]



[a] Reagents and conditions: (a) PtO_2, H_2, EtOH, 95%; (b) TBAF, THF, 90%; (c) Na, $C_{10}H_8$, −78 °C; (d) CBr_4, PPh_3, Et_3N, 50% over three steps; (e) PtO_2, H_2, EtOH, 90%.

settled on a sequence that involved converting **33** to the corresponding vinyl triflate (**34**). This turned out to be an extremely facile process and proceeded in excellent yield. Thus, treatment of pyridinone **33** with *N*-phenyltrifluoromethane sulfonimide[44] in THF at −78 °C with NaHMDS afforded triflate **34** in 95% yield. Installation of a C_2-carbon group was accomplished by using the standard Stille coupling conditions[45] of vinyl tributyltin, $Pd(PPh_3)_4$, and lithium chloride, which afforded triene **35** in 85% yield (Scheme 7).

With ready access to triene **35**, we initially opted to reduce all of the π-bonds present in the molecule. Our first efforts were directed toward catalytic hydrogenation using palladium on charcoal as the catalyst. However, all of our attempts to fully reduce triene **35** with this catalyst as well as other platinum, rhodium, and iridium catalysts failed to give any detectable quantities of the desired tetrasubstituted piperidine. Fortunately, reduction of triene **35** to 1,2,3,6-tetrahydropyridine **36** with 1 atm of hydrogen and PtO_2 over a 36-h period proceeded smoothly and in 95% yield (Scheme 8). Final cyclization of the indolizidine core was accomplished by first removal of the silyl group with TBAF. The next step involved cleavage of the *N*-tosyl functionality. Removal of *N*-tosyl groups is substrate dependent and often requires harsh conditions such as HBr/AcOH.[46] We found, however, that cleavage of the sulfonyl group from **37** occurred easily when sodium naphthalenide (3 equiv) in THF was used.[47]

(44) McMurry, J. E.; Scott, W. J. *Tetrahedron Lett.* **1983**, *24*, 979.
(45) Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508.
(46) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*; Wiley: New York, 1991; pp 379−381.
(47) Ji, S.; Gortler, L. B.; Waring, A.; Battisti, A.; Bank, S.; Closson, W. D.; Wriede, P. *J. Am. Chem. Soc.* **1967**, *89*, 5311.

Rather than isolate and purify the expected secondary amine **38**, we simply converted the hydroxyl group into the corresponding bromide with carbon tetrabromide and triphenylphosphine. Addition of an excess of triethylamine resulted in spontaneous cyclization to give **39** in 50% overall yield for the 3-step sequence starting from **36**. Reduction of the double bond present in **39** proceeded without difficulty. Thus, subjection of a sample of **39** to an atmosphere of hydrogen with PtO_2 as the catalyst proceeded from the least hindered side and furnished racemic *epi*-indolizidine 223A (**5a**) in 98% yield (Scheme 8). The ^{1}H and ^{13}C NMR and IR spectra of **5a** did not match the literature values originally reported by Daly and co-workers.[24] That our synthesis has delivered the originally proposed structure[24] is beyond doubt, given the excellent agreement between our data and the spectroscopic properties reported by Professor Toyooka for *epi*-indolizidine 223A (**5a**) in the recent 2002 communication (see Supporting Information).[25,48]

In conclusion, we have described a 13-step synthesis of *epi*-indolizidine 223A (**5a**) in 13.1% overall yield. The approach involves a flexible combination of an *aza*-Achmatowicz oxidative rearrangement followed by a stereoselective allylsilane addition to a *N*-sulfonyliminium ion and a subsequent 1,4-conjugate addition. These synthetic studies have allowed us to define the scope of the *aza*-Achmatowicz reaction and to optimize the diastereoselective introduction of substituents at the 5-, 6-, and 8-positions of the indolizidine skeleton. Further application of this strategy for related indolizidine alkaloids is under study and will be reported at a later date.

Experimental Section

***N*-(1-Furan-2-ylethyl)-4-methylbenzenesulfonamide (12).** A 28.1-g (292 mmol) sample of 2-furfural (**10**), 300 mL of toluene, 40.0 g (234 mmol) of *p*-toluenesulfonamide, and 0.5 g (3 mmol) of *p*-toluenesulfonic acid were placed in a round-bottom flask with a Dean−Stark trap and heated at reflux for 10 h. The reaction turned a deep brown color. After 10 h, charcoal was added to the hot solution and the mixture was stirred for 1 h and filtered. The solvent was removed under reduced pressure to give *N*-1-furan-2-ylmethylene-4-methylbenezenesulfonamide (**11**) as a tan solid. Recrystallization from benzene gave 62.0 g (85%) of **11** as pure brown crystal: mp 100−101 °C (lit.[49] mp 101−102 °C); IR (thin film) 1605, 1542, 1467, 1319, 1289, 1089, and 1023 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.41 (s, 3H), 6.63 (dd, 1H, J = 2.8 and 1.6 Hz), 7.33 (m, 3H), 7.73 (d, 1H, J = 1.6 Hz), 7.86 (dd, 2H, J = 6.8 and 2.8 Hz) and 8.80 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 113.7, 124.7, 128.0, 128.2, 129.7, 135.1, 144.5, 149.7, 155.6.

The above compound (1.0 g, 4.0 mmol) was dissolved in 15 mL of THF and cooled to 0 °C and then methylmagnesium bromide (2.7 mL of a 3.0 M solution (8.0 mmol)) was added to the solution. The reaction was quenched with a saturated aqueous $NaHCO_3$ solution (30 mL) and 30 mL of ether was added. The solution was extracted with ether, the layers were separated, and the organic layer was dried ($MgSO_4$). Concentration under reduced pressure and purification by silica gel chromatography gave 1.0 g (95%) of benzenesulfonamide **12**: mp 72−73 °C (lit.[50] mp 72−73 °C); IR (thin film) 1599, 1427, 1333, 1152, and 1093 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.41 (d, 3H, J = 7.2 Hz), 2.37 (s, 3H), 4.52 (dq, 1H, J = 14.8, 7.2 and 7.2 Hz), 5.37 (d, 1H, J = 8.4 Hz), 5.97 (dd, 1H, J = 3.2 and 0.8 Hz), 6.12 (dd, 1H, J = 3.2 and 1.6 Hz), 7.14 (dd, 1H, J = 1.6 and 0.8 Hz), 7.21 (d, 2H, J = 8.4 Hz), and 7.68 (d, 2H, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.7, 21.4, 47.2, 106.0, 109.9, 126.9, 129.3, 137.5, 141.7, 143.0, and 154.0.

6-Methoxy-2-methyl-1-(toluene-4-sulfonyl)-1,6-dihydro-2*H*-pyridin-3-one (14). A 0.39-g (1.1 mmol) sample of sulfonamide **12**, 4 mL of CH_2Cl_2, and 0.39 g (2.3 mmol) of *m*-CPBA were placed in a round-bottom flask and the mixture was stirred for 2 h. The reaction was quenched with a saturated aqueous $NaHCO_3$ solution (15 mL) and 15 mL of ether was added. The solution was extracted with ether, the layers were separated, and the organic layer was dried ($MgSO_4$). Concentration under reduced pressure followed by purification by silica gel chromatography gave 0.27 g (85%) of 6-hydroxy-2-methyl-1-(toluene-4-sulfonyl)-1,6-dihydro-2*H*-pyridin-3-one (**13**): IR (thin film) 1686, 1597, 1165, and 1066 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.59 (d, 3H, J = 7.2 Hz), 2.38 (s, 3H), 3.82 (br s, 1H), 4.36 (q, 1H, J = 7.2 Hz), 5.90 (dd, 1H, J = 4.8 and 1.2 Hz), 5.96 (dd, 1H, J = 10.0 and 1.2 Hz), 6.86 (dd, 1H, J = 10.4 and 4.8 Hz), 7.25 (d, 2H, J = 8.4 Hz), and 7.62 (d, 2H, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 22.1, 57.0, 73.3, 126.2, 126.7, 130.0, 136.5, 143.5, 144.3, and 195.3.

The above 6-hydroxy-2*H*-pyridin-3-one (1.0 g, 3.5 mmol) was dissolved in 20 mL of CH_2Cl_2 and trimethyl orthoformate (780 μL, 7.1 mmol) and $BF_3{\cdot}OEt_2$ (45 μL, 0.36 mmol) were added to the solution. The solution was stirred for 3 h at 0 °C and quenched with a saturated aqueous $NaHCO_3$ solution (25 mL) and 40 mL of ether was added. The solution was extracted with ether, the layers were separated, and the organic layer was dried ($MgSO_4$). Concentration under reduced pressure and purification by silica gel chromatography gave 0.89 g (85%) of **14**: mp 113−115 °C; IR (thin film) 1692, 1597, 1340, 1080, and 1014 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.56 (d, 3H, J = 7.6 Hz), 2.38 (s, 3H), 3.57 (s, 3H), 4.30 (q, 1H, J = 7.6 Hz), 5.58, (dd, 1H, J = 4.8 and 0.8 Hz), 5.82 (dd, 1H, J = 10.4 and 0.8 Hz), 6.82 (dd, 1H, J = 10.4 and 4.8 Hz), 7.24 (dd, 2H, J = 8.0 and 1.2 Hz), and 7.56 (dd, 2H, J = 8.0 and 1.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.8, 21.5, 56.0, 57.2, 80.7, 126.6, 126.8, 130.0, 136.1, 142.5, 144.1, and 195.5. Anal. Calcd for $C_{14}H_{17}NO_4S$: C, 56.93; H, 5.81; N, 4.75. Found: C, 56.81; H, 5.69; N, 4.70.

6-Methoxy-2,5-dimethyl-1-(toluene-4-sulfonyl)piperidin-3-one (15). In a 10-mL round-bottom flask under nitrogen was added CuCN (0.1 g, 1.1 mmol) and 2 mL of THF and the mixture was cooled to −78 °C. A solution of MeLi (2.2 mL of 1.0 M ether solution) was added dropwise and the solution was allowed to warm to 0 °C over 20 min. The solution was cooled to −78 °C, compound **14** (0.25 g, 0.85 mmol) in 2 mL of THF was added, and the mixture was stirred at −78 °C for 45 min. The solution was quenched with a saturated aqueous NH_4Cl solution (20 mL) and 20 mL of ether was added. The solution was extracted with ether, the layers were separated and washed with a saturated aqueous $NaHCO_3$ solution, and the organic layer was dried ($MgSO_4$). Concentration under reduced pressure and purification by silica gel chromatography gave 0.24 g (90%) of **15**: mp 108−110 °C; IR (thin film) 1728, 1455, 1349, 1164, and 1093 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.78 (d, 3H, J = 7.2 Hz), 1.42 (d, 3H, J = 7.2 Hz), 1.64 (dd, 1H, J = 15.2 and 8.4 Hz), 2.22 (m, 1H), 2.35 (s, 3H), 2.51 (dd, 1H, J = 15.2 and 4.8 Hz), 3.44 (s, 3H), 4.08 (q, 1H, J = 7.2 Hz), 4.94 (dd, 1H, J = 4.0 and 0.8 Hz), 7.24 (d, 2H, J = 8.4 Hz), and 7.64 (d, 2H, J = 8.4 Hz);^{13}C NMR (100 MHz, $CDCl_3$) δ 18.2, 19.7, 21.4, 34.7, 40.0, 55.5, 59.1, 89.4, 127.0, 129.8, 137.0, 143.9, and 207.9. Anal. Calcd for $C_{15}H_{21}NO_4S$: C, 57.86; H, 6.80; N, 4.50. Found: C, 57.72; H, 6.61; N, 4.43.

6-Methoxy-2-methyl-5-phenyl-1-(toluene-4-sulfonyl)piperidin-3-one (16). In a 10-mL round-bottom flask under nitrogen was added CuCN (0.08 g, 0.83 mmol) and 2 mL of THF and the mixture was cooled to −78 °C. A solution of PhLi (2.2 mL of 0.75 M ether solution) was added dropwise and the solution was allowed to warm to 0 °C over 20 min. The solution

(48) We wish to thank Professor Naoki Toyooka for providing us with photocopies of the proton and carbon NMR spectra of synthetic *epi* (**5a**) and revised (**5b**) indolizidine alkaloids 223A.

(49) Trost, B. M.; Marrs, C. *J. Org. Chem.* **1991**, *56*, 6468.

(50) Zhou, W. S.; Lu, Z. H.; Wang, Z. M. *Tetrahedron* **1993**, *49*, 2641.

was cooled to −78 °C, compound **14** (0.19 g, 0.64 mmol) in 2 mL of THF was added, and the mixture was stirred at −78 °C for 45 min. The solution was quenched with a saturated aqueous NH_4Cl solution (20 mL) and 20 mL of ether was added. The solution was extracted with ether, the layers were separated and washed with a saturated aqueous $NaHCO_3$ solution, and the organic layer was dried ($MgSO_4$). Concentration under reduced pressure and purification by silica gel chromatography gave 0.22 g (90%) of **16**: mp 109−111 °C; IR (thin film) 1732, 1597, 1353, 1165, and 1094 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.59 (d, 3H, J = 7.2 Hz), 2.22 (dd, 1H, J = 15.6 and 10.4 Hz), 2.38 (s, 3H), 2.59 (dd, 1H, J = 15.6 and 4.8 Hz), 3.37 (ddd, 1H, J = 10.4, 5.2, and 4.8 Hz), 3.46 (s, 3H), 4.16 (q, 1H, J = 7.2 Hz), 5.36 (dd, 1H, J = 5.2 and 1.2 Hz), 7.05−7.03 (m, 2H), 7.38 (dd, 2H, J = 7.6 and 2.0 Hz), 7.17 (d, 2H, J = 7.6 Hz), and 7.27−7.25 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.6, 21.4, 31.9, 45.2, 55.7, 58.9, 90.2, 127.0, 127.2, 127.3, 128.9, 129.9, 136.4, 139.7, 143.8, and 208.6. Anal. Calcd for $C_{20}H_{23}NO_4S$: C, 64.32; H, 6.21; N, 3.75. Found: C, 64.29; H, 6.02; N, 3.81.

6-Methoxy-2-methyl-1-(toluene-4-sulfonyl)-5-vinylpiperidin-3-one (17). In a 10-mL round-bottom flask under nitrogen was added CuI (0.2 g, 1.0 mmol) and 3 mL of THF and the mixture was cooled to −78 °C. Vinylmagnesium bromide (2.7 mL of a 0.8 M THF solution (2.1 mmol)) was added dropwise and the solution was allowed to warm to −20 °C over 20 min. The solution was cooled to −78 °C, compound **14** (0.21 g, 0.7 mmol) in 3 mL of THF was added, and the mixture was stirred at −78 °C for 1 h. The reaction was quenched with a saturated aqueous NH_4Cl solution (20 mL) and 20 mL of ether was added. The solution was extracted with ether, the layers were separated and washed with saturated aqueous $NaHCO_3$ solution, and the organic layer was dried ($MgSO_4$). Concentration under reduced pressure and purification by silica gel chromatography gave 0.2 g (87%) of **17**: IR (thin film) 1731, 1452, 1354, 1330, 1164, and 1093 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.48 (d, 3H, J = 7.2 Hz), 1.90 (dd, 1H, J = 15.6 and 4.8 Hz), 2.38 (s, 3H), 2.58 (dd, 1H, J = 15.6 and 4.8 Hz), 2.82 (m, 1H), 3.48 (s, 3H), 4.10 (q, 1H, J = 7.2 Hz), 4.91 (d, 1H, J = 10.4 Hz), 4.94 (d, 1H, J = 17.2 Hz), 5.10 (d, 1H, J = 4.4 Hz), 5.44 (ddd, 1H, J = 17.2, 10.4, and 6.8 Hz), 7.25 (d, 2H, J = 8.4 Hz), and 7.64 (d, 2H, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.9, 21.5, 37.3, 43.5, 55.5, 59.2, 87.8, 117.2, 127.2, 129.7, 136.0, 136.9, 144.0, and 207.5; FAB HRMS calcd for $[(C_{16}H_{21}NO_4S) + Li]^+$ 330.1351, found 330.1361.

5-Ethyl-6-methoxy-2-methyl-1-(toluene-4-sulfonyl)piperidin-3-one (18). In a 25-mL round-bottom flask under nitrogen was added CuI (0.39 g, 2.0 mmol) and 5 mL of THF and the mixture was cooled to −78 °C. Ethylmagnesium bromide (3.9 mL of a 1.0 M ether solution (3.9 mmol)) was added dropwise and the solution was allowed to warm to −20 °C over 20 min. The solution was cooled to −78 °C, compound **14** (0.5 g, 1.7 mmol) in 5 mL of THF was added, and the mixture was stirred at −78 °C for 1 h. The reaction was quenched with a saturated aqueous NH_4Cl solution (20 mL) and 20 mL of ether was added. The solution was extracted with ether, the layers were separated and washed with saturated aqueous $NaHCO_3$ solution, and the organic layer was dried ($MgSO_4$). Concentration under reduced pressure and purification by silica gel chromatography gave 0.47 g (85%) of **18**: IR (thin film) 1731, 1597, 1459, 1352, 1163, and 1093 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.82 (t, 3H, J = 7.2 Hz), 1.09 (m, 1H), 1.29 (m, 1H), 1.42 (d, 3H, J = 7.6 Hz), 1.59 (dd, 1H, J = 15.2 and 10.0 Hz), 1.95 (m, 1H), 2.36 (s, 3H), 2.40 (dd, 1H, J = 15.2 and 5.2 Hz), 3.43 (s, 3H), 4.09(q, 1H, J = 7.2 Hz), 5.00 (dd, 1H, J = 4.4 and 0.8 Hz), 7.25 (d, 2H, J = 8.0 Hz), and 7.64 (d, 2H, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.1, 19.2, 21.4, 25.9, 38.4, 41.5, 55.3, 59.0, 88.5, 126.9, 129.8, 136.9, 143.9, and 208.3; FAB HRMS calcd for $[(C_{16}H_{23}NO_4S) + Li]^+$ 332.1508, found 332.1513.

6-Methoxy-2-methyl-5-phenylsulfanyl-1-(toluene-4-sulfonyl)piperidin-3-one (19). In a 10-mL round-bottom flask under nitrogen was added compound **14** (0.1 g, 0.34 mmol), 5 mL of MeOH, and thiophenol (105 μL, 1.0 mmol). The mixture was stirred for 6 h at room temperature. The reaction mixture was concentrated under reduced pressure and purified by silica gel chromatography to give 0.12 g (85%) of **19**: IR (thin film) 1730, 1597, 1439, 1347, 1164, 1094, and 1068 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.52 (d, 3H, J = 7.2 Hz), 2.39 (s, 3H), 2.79 (dd, 1H, J = 15.2 and 4.4 Hz), 2.97 (dd, 1H, J = 15.6 and 8.8 Hz), 3.52 (s, 3H), 3.53 (ddd, 1H, J = 8.8, 4.4, and 2.0 Hz), 4.06 (q, 1H, J = 7.2 Hz), 5.41 (dd, 1H, J = 4.4 and 2.0 Hz), 7.23 (d, 2H, J = 8.0 Hz), 7.40−7.34 (m, 5H), and 7.61 (d, 2H, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.6, 21.5, 39.4, 47.5, 55.7, 59.0, 87.4, 127.5, 128.4, 129.3, 129.7, 133.5, 136.2, 144.0, and 205.5; FAB HRMS calcd for $[(C_{20}H_{23}NO_4S_2) + Li]^+$ 412.1229, found 412.1221.

[2-Methoxy-6-methyl-5-oxo-1-(toluene-4-sulfonyl)piperidin-3-ylamino]acetic Acid Methyl Ester (20). In a 10-mL round-bottom flask under nitrogen was placed compound **14** (0.1 g, 0.34 mmol), 5 mL of MeOH, glycine methyl ester hydrochloride (0.17 g, 1.4 mmol), and triethylamine (284 μL, 2.0 mmol). The mixture was stirred for 10 h at room temperature. The reaction was quenched with a saturated aqueous NH_4Cl solution (15 mL) and 15 mL of ether was added. The solution was extracted with ether, the layers were separated and washed with a saturated aqueous $NaHCO_3$ solution, and the organic layer was dried ($MgSO_4$). Concentration under reduced pressure and purification by silica gel chromatography gave 0.08 g (60%) of [2-methoxy-6-methyl-5-oxo-1-(toluene-4-sulfonyl)piperidin-3-ylamino]acetic acid methyl ester **20**: IR (thin film) 1740, 1597, 1438, 1331, 1210, 1163, and 1095 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.47 (d, 3H, J = 7.2 Hz), 2.06 (dd, 1H, J = 15.2 and 7.0 Hz), 2.38 (s, 3H), 2.87 (dd, 1H, J = 15.2 and 4.4 Hz), 3.24 (dd, 1H, J = 7.0 and 4.4 Hz), 3.27 (d, 2H, J = 2.6 Hz), 3.50 (s, 3H), 3.70 (s, 3H), 4.05 (q, 1H, J = 7.2 Hz), 5.15 (d, 1H, J = 2.6 Hz), 7.25 (d, 2H, J = 8.0 Hz), and 7.75 (d, 2H, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.9, 21.5, 38.7, 48.0, 52.0, 55.4, 57.4, 59.4, 86.3, 127.5, 129.7, 136.8, 143.8, 172.2, and 206.0; FAB HRMS calcd for $[(C_{17}H_{24}N_2O_6S) + Li]^+$ 391.1515, found 391.1515.

6-Allyl-2-methyl-1-(toluene-4-sulfonyl)-1,6-dihydro-2*H*-pyridin-3-one (21). In a 10 mL round-bottom flask under nitrogen was placed compound **14** (0.58 g, 2.0 mmol), 7 mL of CH_2Cl_2, allyl trimethylsilane (625 μL, 3.93 mmol), and $BF_3 \cdot OEt_2$ (250 μL, 1.96 mmol). The mixture was stirred for 2 h at 0 °C. The reaction mixture was quenched with a saturated aqueous NH_4Cl solution (15 mL) and 30 mL of ether was added. The solution was extracted with ether, the layers were separated and washed with a saturated aqueous $NaHCO_3$ solution, and the organic layer was dried ($MgSO_4$). Concentration under reduced pressure and purification by silica gel chromatography gave 0.51 g (85%) of **21**: mp 78−80 °C; IR (thin film) 1686, 1597, 1398, 1357, 1333, 1167, 1120, 1095, and 1044 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.49 (d, 3H, J = 7.2 Hz), 2.36 (s, 3H), 2.52 (m, 1H), 2.71 (m, 1H), 4.47 (q, 1H, J = 7.2 Hz), 4.58 (m, 1H), 5.18 (ddd, 1H, J = 17.2, 3.2, and 1.6 Hz), 5.19 (d, 1H, J = 10.4 Hz), 5.79 (dd, 1H, J = 10.4 and 2.0 Hz), 5.91 (m, 1H), 6.82 (dd, 1H, J = 10.4 and 4.4 Hz), 7.22 (d, 2H, J = 8.4 Hz), and 7.58 (d, 2H, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 21.6, 41.7, 53.5, 56.9, 119.0, 124.8, 126.7, 129.9, 133.2, 136.2, 143.8, 147.8, and 194.8. Anal. Calcd for $C_{16}H_{19}NO_3S$: C, 62.93; H, 6.28; N, 4.59. Found: C, 62.77; H, 6.12; N, 4.49.

6-Allyl-2,5-dimethyl-1-(toluene-4-sulfonyl)piperidin-3-one (22). In a 5-mL round-bottom flask under nitrogen was placed compound **15** (0.024 g, 0.08 mmol), 1 mL of CH_2Cl_2, allyl trimethylsilane (25 μL, 0.15 mmol), and $BF_3 \cdot OEt_2$ (20 μL, 0.15 mmol). The mixture was stirred for 2 h at 0 °C. The reaction mixture was quenched with a saturated aqueous NH_4Cl solution (15 mL) and 30 mL of ether was added. The solution was extracted with ether, the layers were separated and washed with a saturated aqueous $NaHCO_3$ solution, and the organic layer was dried ($MgSO_4$). Concentration under

reduced pressure and purification by silica gel chromatography gave 0.0.2 g (85%) of **22**: IR (thin film) 1728, 1455, 1336, 1162, and 1093 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.93 (d, 3H, J = 6.4 Hz), 1.42 (d, 3H, J = 7.2 Hz), 1.48 (dd, 1H, J = 15.6 and 11.2 Hz), 1.94 (m, 1H), 2.17 (dd, 1H, J = 15.6 and 3.6 Hz), 2.42 (s, 3H), 2.56 (m, 2H), 3.70 (q, 1H, J = 6.8 Hz), 4.31 (q, J = 7.2 Hz), 5.11 (m, 2H), 5.91 (dddd, 1H, J = 16.8, 10.4, 7.2, and 7.2 Hz), 7.30 (d, 2H, J = 8.0 Hz), and 7.69 (d, 2H, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.6, 21.5, 32.2, 43.1, 58.9, 59.7, 117.9, 127.1 (2C), 129.9 (2C), 134.7, 136.7, 143.8, and 209.3; FAB HRMS calcd for $[(C_{17}H_{23}NO_3S) + Li]^+$ 328.1559, found 328.1551.

6-Allyl-5-ethyl-2-methyl-1-(toluene-4-sulfonyl)piperidin-3-one (23). In a 5-mL round-bottom flask under nitrogen was placed compound **18** (0.05 g, 0.15 mmol), 1.5 mL of CH_2Cl_2, allyl trimethylsilane (50 μL, 0.31 mmol), and $BF_3{\cdot}OEt_2$ (20 μL, 0.15 mmol). The mixture was stirred for 2 h at 0 °C. The reaction mixture was quenched with a saturated aqueous NH_4Cl solution (15 mL) and 30 mL of ether was added. The solution was extracted with ether, the layers were separated and washed with a saturated aqueous $NaHCO_3$ solution, and the organic layer was dried ($MgSO_4$). Concentration under reduced pressure and purification by silica gel chromatography gave 0.043 g (85%) of **23**: IR (thin film) 1728, 1598, 1458, 1338, 1163, and 1093 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.78 (t, 3H, J = 7.2 Hz), 1.18 (m, 2H), 1.42 (d, 3H, J = 7.6 Hz), 1.57 (dd, 1H, J = 14.8, and 11.2 Hz), 1.72 (m, 1H), 2.28 (dd, 1H, J = 14.8 and 4.0 Hz), 2.42 (s, 3H), 2.47 (m, 1H), 2.48 (dd, 1H, J = 14.4 and 7.2 Hz), 3.82 (m, 1H), 4.32 (q, 1H, J = 7.6 Hz), 5.10 (m, 2H), 5.88 (dddd, 1H, J = 17.6, 10.4, 7.2, and 7.2 Hz), 7.30 (d, 2H, J = 8.4 Hz), and 7.69 (d, 2H, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.8, 20.1, 21.5, 27.1, 39.5, 40.2, 41.5, 57.3, 59.1, 117.9, 127.1, 129.8, 134.7, 137.0, 143.7, and 209.5; FAB HRMS calcd for $[(C_{18}H_{25}NO_3S) + Li]^+$ 342.1715, found 342.1711.

2,5-Dimethyl-6-(2-oxo-propyl)-1-(toluene-4-sulfonyl)piperidin-3-one (24). In a 25-mL round-bottom flask under nitrogen was placed compound **15** (0.18 g, 0.56 mmol), 5 mL of CH_2Cl_2, isopropenyl acetate (125 μL, 1.12 mmol), and $BF_3{\cdot}OEt_2$ (70 μL, 0.56 mmol). The mixture was stirred for 2 h at 0 °C. The reaction mixture was quenched with a saturated aqueous NH_4Cl solution (15 mL) and 30 mL of ether was added. The solution was extracted with ether, the layers were separated and washed with a saturated aqueous $NaHCO_3$ solution, and the organic layer was dried ($MgSO_4$). Concentration under reduced pressure and purification by silica gel chromatography gave 0.13 g (70%) of **24**: IR (thin film) 1720, 1597, 1553, 1455, 1357, 1336, 1164, and 1122 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 0.83 (d, 3H, J = 7.2 Hz), 1.43 (dd, 1H, J = 15.6 and 3.6 Hz), 1.47 (d, 3H, J = 7.2 Hz), 1.89 (m, 1H), 2.17 (dd, 1H, J = 15.6 and 3.6 Hz), 2.25 (s, 3H), 2.41 (s, 3H), 2.77 (dd, 1H, J = 16.8 and 7.2 Hz), 3.09 (dd, 1H, J = 17.4 and 3.6 Hz), 4.00 (ddd, 1H, J = 7.2, 7.2, and 3.6 Hz), 4.40 (q, 1H, J = 7.2 Hz), 7.30 (d, 2H, J = 8.0 Hz), and 7.66 (d, 2H, J = 8.0 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 19.5, 21.2, 21.5, 29.7, 33.7, 42.9, 51.8, 54.7, 59.0, 127.0, 130.0, 136.2, 143.9, 205.5, and 208.6; FAB HRMS calcd for $[(C_{17}H_{23}NO_4S) + Li]^+$ 344.1508, found 344.1501.

6-Allyl-2-methyl-1-(toluene-4-sulfonyl)-5-vinyl-piperidin-3-one (25). In a 25-mL round-bottom flask under nitrogen was placed compound **17** (0.29 g, 0.90 mmol), 8.0 mL of CH_2Cl_2, allyl trimethylsilane (285 μL, 1.80 mmol), and $BF_3{\cdot}OEt_2$ (170 μL, 1.35 mmol). The mixture was stirred for 2 h at 0 °C. The reaction mixture was quenched with a saturated aqueous NH_4Cl solution (15 mL) and 30 mL of ether was added. The solution was extracted with ether, the layers were separated and washed with a saturated aqueous $NaHCO_3$ solution, and the organic layer was dried ($MgSO_4$). Concentration under reduced pressure and purification by silica gel chromatography gave 0.24 g (80%) of **25**: IR (thin film) 1728, 1683, 1641, 1452, 1337, and 1093 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.44 (dd, 3H, J = 7.6 Hz), 1.64 (dd, 1H, J = 15.6 and 12.4 Hz), 2.15 (dd, 1H, J = 15.6 and 3.6 Hz), 2.41 (s, 3H), 2.49 (m, 2H), 2.61 (m, 1H), 3.86 (dd, 1H, J = 12.4 and 6.4 Hz), 4.31 (q, 1H, J = 7.6 Hz), 5.00 (m, 2H), 5.12 (m, 2H), 5.49 (ddd, 1H, J = 16.8, 10.0, and 7.2 Hz), 5.90 (dddd, 1H, J = 17.2, 10.0, 7.2, and 7.2 Hz), 7.29 (d, 2H, J = 8.0 Hz), and 7.68 (d, 2H, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.6, 21.5, 40.7, 41.2, 41.6, 57.7, 58.9, 117.2, 118.1, 127.2, 129.9, 134.5, 136.4, 138.0, 143.9, and 208.7; FAB HRMS calcd for $[(C_{18}H_{23}NO_3S) + Li]^+$ 340.1559, found 340.1560.

2-Methyl-1-(toluene-4-sulfonyl)-1,2,4,4a,7,7a-hexahydro-[1]pyridin-3-one (26). In a 10-mL round-bottom flask under nitrogen was placed compound **25** (0.05 g, 0.15 mmol), 2 mL of CH_2Cl_2, and Grubb's catalyst (6.2 mg, 0.008 mmol). The reaction mixture was stirred for 6 h at 25 °C. The reaction mixture was filtered through a plug of silica gel, concentrated under reduced pressure, and purified by silica gel chromatography to give 0.03 g (60%) of **26**: IR (thin film) 1724, 1598, 1448, 1351, 1167, and 1060 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 1.60 (d, 3H, J = 7.2 Hz), 2.13 (dd, 1H, J = 18.6 and 13.8 Hz), 2.41 (s, 3H), 2.69 (m, 2H), 2.79 (dd, 1H, J = 18.6 and 5.4 Hz), 2.90 (ddd, 1H, J = 15.6, 5.4, and 3.0 Hz), 3.26 (m, 1H), 4.16 (q, 1H, J = 7.2 Hz), 5.66 (d, 1H, J = 6.0 Hz), 5.87 (ddd, 1H, J = 6.0, 4.0, and 3.0 Hz), 7.31 (d, 2H, J = 8.4 Hz), and 7.65 (d, 2H, J = 8.4 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.5, 23.6, 39.1, 41.1, 43.5, 63.4, 63.9, 127.5, 130.1, 130.2, 131.9, 133.3, 144.1, and 207.8; FAB HRMS calcd for $[(C_{16}H_{19}NO_3S) + Li]^+$ 312.1246, found 312.1258.

5,6-Diallyl-2-methyl-1-(toluene-4-sulfonyl)piperidin-3-one (27). In a 25-mL round-bottom flask under nitrogen was placed compound **21** (0.13 g, 0.40 mmol), 4.0 mL of CH_2Cl_2, allyl trimethylsilane (100 μL, 0.614 mmol), and $TiCl_4$ (50 μL, 0.45 mmol). The mixture was stirred for 2 h at 0 °C. The reaction mixture was quenched with a saturated aqueous NH_4Cl solution (15 mL) and 30 mL of ether was added. The solution was extracted with ether, the layers were separated and washed with a saturated aqueous $NaHCO_3$ solution, and the organic layer was dried ($MgSO_4$). Concentration under reduced pressure and purification by silica gel chromatography gave 0.13 g (90%) of **27**: IR (thin film) 1728, 1641, 1598, 1444, 1337, 1164, and 1093 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.40 (d, 3H, J = 7.6 Hz), 1.59 (dd, 1H, J = 15.2 and 10.8 Hz), 1.89 (m, 2H), 2.23 (dd, 1H, J = 15.2, and 4.0 Hz), 2.41 (s, 3H), 2.48 (m, 2H), 3.84 (dd, 1H, J = 6.8 Hz), 4.33 (q, 1H, J = 7.6 Hz), 5.12−4.95 (m, 4H), 5.53 (dddd, 1H, J = 17.2, 10.4, 7.6, and 7.6 Hz), 5.85 (dddd, 1H, J = 16.4, 10.6, 7.2, and 7.2 Hz), 7.29 (d, 2H, J = 8.0 Hz), and 7.68 (d, 2H, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.0, 21.5, 37.5, 38.3, 40.4, 41.5, 56.9, 59.1, 118.0, 118.3, 127.1, 129.8, 133.9, 134.6, 136.9, 143.8, and 209.2; FAB HRMS calcd for $[(C_{19}H_{25}NO_3S) + Li]^+$ 354.1715, found 354.1711.

2-Methyl-1-(toluene-4-sulfonyl)-1,4,4a,5,8,8a-hexahydro-2*H*-quinolin-3-one (28). In a 10-mL round-bottom flask under nitrogen was placed compound **27** (0.045 g, 0.13 mmol), 2 mL of CH_2Cl_2, and Grubb's catalyst (5.5 mg, 0.007 mmol). The reaction mixture was stirred for 6 h at 25 °C, filtered through a plug of silica gel, concentrated under reduced pressure, and purified by silica gel chromatography to give 0.03 g (80%) of **28**: IR (thin film) 1728, 1597, 1437, 1359, 1338, 1311, 1166, and 1099 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.15 (dd, 1H, J = 16.4 and 14.4 Hz), 1.48 (d, 3H, J = 7.6 Hz), 1.80 (m, 1H), 2.03 (m, 1H), 2.13 (dd, 1H, J = 16.4 and 2.4 Hz), 2.19 (m, 1H), 2.28 (m, 1H), 2.41 (s, 3H), 2.88 (ddd, 1H, J = 16.4, 5.6, and 5.6 Hz), 3.50 (ddd, 1H, J = 10.8, 10.8, and 4.8 Hz), 4.39 (q, 1H, J = 7.6 Hz), 5.62 (m, 1H), 5.69 (m, 1H), 7.29 (d, 2H, J = 8.4 Hz), and 7.64 (d, 2H, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 22.1, 32.7, 33.1, 36.4, 42.6, 57.2, 59.4, 125.3, 126.5, 126.9, 130.0, 135.8, 143.8, and 208.9; FAB HRMS calcd for $[(C_{17}H_{21}NO_3S) + Li]^+$ 326.1402, found 326.1411.

Benzhydrylidene-furan-2-ylmethylamine (29). A 50-g (515 mmol) sample of furfurylamine, 1 L of toluene, benzophenone (78 g (430 mmol)), and $BF_3{\cdot}OEt_2$ (5.5 mL (43 mmol)) were placed in a 2-L round-bottom flask with a Dean−Stark trap

and heated at reflux for 12 h. The solvent was removed under reduced pressure to give imine **29** as a yellow solid. Recrystallization from MeOH gave 101 g (90%) of pure white crystals: mp 51−53 °C (lit.[51] mp 52−53 °C); IR (thin film) 1623, 1576, 1446, 1290, and 1006 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.57 (s, 2H), 6.24 (dd, 1H, J = 3.2 and 0.8 Hz), 6.34 (dd, 1H, J = 3.2 and 2.0 Hz), 7.25 (m, 2H), 7.35 (m, 4H), 7.48 (m, 3H), 7.67 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 51.1, 106.3, 110.2, 127.7, 128.0, 128.6, 130.1, 136.3, 139.5, 141.6, 153.7, and 169.9. Anal. Calcd for $C_{18}H_{15}NO$: C, 82.73; H, 5.79; N, 5.36. Found: C, 82.85; H, 5.85; N, 5.43.

Benzhydrylidene-[4-(*tert*-butyldiphenylsilanyloxy)-1-furan-2-ylbutyl]amine. In a 250-mL round-bottom flask under nitrogen was added the above compound (5.0 g, 23 mmol) to 75 mL of THF and the mixture was cooled to −78 °C. A solution of *n*-BuLi (10.2 mL of a 2.5 M hexane solution) was added dropwise and the solution was stirred for 30 min. A sample of 1-bromo-3-*tert*-butyldiphenylsilanyloxypropane (9.6 g, 25 mmol) was added and the solution was stirred at 0 °C for 4 h. The reaction was quenched with a saturated aqueous $NaHCO_3$ solution (50 mL) and 50 mL of ether was added. The solution was extracted with ether, the layers were separated, and the organic layer was dried ($MgSO_4$). Concentration under reduced pressure and purification by silica gel chromatography gave 11 g (86%) of the titled compound: IR (thin film) 1661, 1622, 1446, 1428, 1316, 1278, 1111, and 1001 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.05 (s, 9H), 1.45 (m, 2H), 1.58 (m, 2H), 2.05 (m, 2H), 3.62 (t, 1H, J = 6.8 Hz), 4.49 (dd, 1H, J = 7.2 and 5.6 Hz), 6.15 (d, 1H, J = 3.2 Hz), 6.32 (dd, 1H, J = 3.2 and 2.0 Hz), 7.20 (m, 1H), 7.38 (m, 10H), 7.65 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 19.2, 22.6, 26.8, 29.2, 31.5, 60.1, 63.7, 105.3, 109.9, 127.5, 127.9, 128.3, 128.4, 128.7, 129.5, 130.0, 130.1, 132.4, 134.0, 135.5, 136.7, 139.8, 141.4, 156.7, and 168.4; FAB HRMS calcd for $[(C_{37}H_{39}NO_2Si) + Li]^+$ 564.2910, found 564.2902.

4-(*tert*-Butyldiphenylsilanyloxy)-1-furan-2-ylbutylamine. A 3.2-g (5.8 mmol) sample of the above compound, 30 mL of acetone, and 30 mL of 1 N HCl were placed in a round-bottom flask and the mixture was stirred for 2 h. The reaction was quenched with solid K_2CO_3 until a pH of 7−8 and then 100 mL of ether was added. The solution was extracted with ether, the layers were separated, and the organic layer was dried ($MgSO_4$). Concentration under reduced pressure gave 2.2 g (95%) of the titled compound: IR (thin film) 1663, 1428, 1111, and 1008 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.06 (s, 9H), 1.56 (m, 2H), 2.00 (m, 2H), 3.68 (t, 1H, J = 6.4 Hz), 4.49 (dd, 1H, J = 7.6 and 6.0 Hz), 6.11 (d, 1H, J = 3.6 Hz), 6.29 (dd, 1H, J = 3.6 and 2.0 Hz), 7.32 (dd, 1H, J = 2.0 and 0.8), 7.39 (m, 5H), 7.67 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.2, 26.8, 31.4, 57.9, 63.7, 105.1, 109.9, 127.6, 129.5, 133.9, 135.5 (2C), 141.3, and 156.4; FAB HRMS calcd for $[(C_{24}H_{31}NO_2Si) + Li]^+$ 400.2284, found 400.2300.

***N*-[4-(*tert*-Butyldiphenylsilanyloxy)-1-furan-2-ylbutyl]-4-methylbenzenesulfonamide (30).** The above compound (2.2 g, 5.5 mmol) was dissolved in 25 mL of CH_2Cl_2 and triethylamine (1.6 mL, 11.7 mmol) and *p*-toluenesulfonyl chloride (2.2 g, 11.7 mmol) were added to the solution at room temperature. The solution was stirred for 12 h and quenched with a saturated aqueous $NaHCO_3$ solution (30 mL) and 75 mL of ether was added. The solution was extracted with ether, the layers were separated, and the organic layer was dried ($MgSO_4$). Concentration under reduced pressure and purification by silica gel chromatography gave 2.7 g (90%) of **30** as a yellow solid: mp 89−90 °C; IR (thin film) 3268, 1472, 1428, 1332, 1161, 1111, 1094, and 1010 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.03 (s, 9H), 1.48 (m, 2H), 1.88 (m, 2H), 2.36 (s, 3H), 3.59 (t, 2H, J = 6.4 Hz), 4.42 (dd, 1H, J = 15.6 and 7.2 Hz), 4.92 (d, 1H, J = 8.4 Hz), 5.89 (d, 1H, J = 3.2 Hz), 6.11 (dd, 1H, J = 3.2 and 1.6 Hz), 7.13 (dd, 1H, J = 2.0 and 0.8 Hz), 7.17 (d, 2H, J = 8.0 Hz), 7.39 (m, 6H), 7.62 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.1, 21.4, 26.8, 28.5, 31.4, 51.6, 63.1, 106.7, 109.9, 126.9, 127.6, 129.3, 129.6, 133.7, 135.5, 141.8, 142.9, and 152.9. Anal. Calcd for $C_{31}H_{37}NO_4SSi$: C, 67.97; H, 6.81; N, 2.56. Found: C, 67.76; H, 6.80; N, 2.57.

6-Allyl-2-[3-(*tert*-butyldiphenylsilanyloxy)-propyl]-1-(toluene-4-sulfonyl)-1,6-dihydro-2*H*-pyridin-3-one (32). A 0.5-g (0.9 mmol) sample of compound **30**, 5 mL of CH_2Cl_2, and *m*-CPBA (0.19 g, 1.1 mmol) were placed in a round-bottom flask and the mixture was stirred for 4 h. The reaction mixture was quenched with a saturated aqueous $NaHCO_3$ solution (15 mL) and 15 mL of ether was added. The solution was extracted with ether, the layers were separated, and the organic layer was dried ($MgSO_4$). Concentration under reduced pressure gave 0.4 g (80%) of 2-[3-(*tert*-butyldiphenylsilanyloxy)propyl]-6-hydroxy-1-(toluene-4-sulfonyl)-1,6-dihydro-2*H*-pyridin-3-one (**31**). This compound was immediately used in the next step without purification.

The above 6-hydroxy-2*H*-pyridin-3-one **31** (0.4 g, 0.7 mmol) was dissolved in 5 mL of CH_2Cl_2 and allyl trimethylsilane (232 μL, 1.46 mmol) and $BF_3{\cdot}OEt_2$ (150 μL, 1.46 mmol) were added to the solution. The solution was stirred for 3 h at 0 °C and quenched with a saturated aqueous $NaHCO_3$ solution (25 mL) and 40 mL of ether was added. The solution was extracted with ether, the layers were separated, and the organic layer was dried ($MgSO_4$). Concentration under reduced pressure and purification by silica gel chromatography gave 0.34 g (80%) of **32**: IR (thin film) 1686, 1428, 1359, 1335, 1165, and 1111 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.05 (s, 9H), 1.87 (m, 4H), 2.37 (s, 3H), 2.50 (m, 1H), 2.77 (m, 1H), 3.72 (m, 2H), 4.41 (dd, 1H, J = 10.0 and 5.6 Hz), 4.54, (dddd, 1H, J = 6.4, 4.4, 4.4, and 2.0 Hz), 5.17 (m, 2H), 5.77 (dd, 1H, J = 10.4 and 2.0 Hz), 5.94 (dddd, 1H, J = 16.8, 10.4, 7.2, and 7.2 Hz), 6.74 (dd, 1H, J = 10.8 and 4.8 Hz), 7.23 (d, 2H, J = 8.0 Hz), 7.41 (m, 6H), 7.58 (d, 2H, J = 8.0 Hz), and 7.67 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.1, 21.5, 26.8, 28.7, 31.3, 41.1, 53.7, 61.5, 62.9, 119.0, 124.9, 126.7, 127.6, 129.5, 129.9, 133.4, 133.6, 135.5, 136.2, 143.8, 146.8, and 194.3; FAB HRMS calcd for $[(C_{34}H_{41}NO_4SSi) + Li]^+$ 594.2686, found 594.2698.

6-Allyl-2-[3-(*tert*-butyldiphenylsilanyloxy)propyl]-5-ethyl-1-(toluene-4-sulfonyl)piperidin-3-one (33). In a 50-mL round-bottom flask under nitrogen was added CuI (0.4 g, 2.2 mmol) and 20 mL of THF, and the mixture was cooled to −78 °C. Ethylmagnesium bromide (3.7 mL of a 1.0 M ether solution (3.7 mmol)) was added dropwise and the solution was allowed to warm to 0 °C over 20 min. The solution was cooled to −78 °C, compound **32** (1.1 g, 1.9 mmol) in 5 mL of THF was added, and the mixture was stirred at −78 °C for 1 h. The reaction was quenched with a saturated aqueous NH_4Cl solution (30 mL) and 30 mL of ether was added. The solution was extracted with ether, the layers were separated and washed with saturated aqueous $NaHCO_3$ solution, and the organic layer was dried ($MgSO_4$). Concentration under reduced pressure and purification by silica gel chromatography gave 1.0 g (90%) of **33**: IR (thin film) 1725, 1428, 1341, 1163, and 1111 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 0.77 (t, 3H, J = 7.8 Hz), 1.04 (s, 9H), 1.69 (m, 4H), 1.91 (m, 2H), 2.17 (dd, 1H, J = 15.6 and 3.0 Hz), 2.40 (s, 3H), 2.54 (m, 4H), 3.66 (m, 2H), 3.74 (dd, 1H, J = 15.0 and 6.6 Hz), 4.18 (dd, 1H, J = 9.6 and 5.4 Hz), 5.10 (m, 2H), 5.98 (dddd, 1H, J = 17.4, 9.6, 7.2, and 7.2 Hz), 7.27 (d, 2H, J = 7.8 Hz), 7.39 (m, 6H), 7.65 (m, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 19.2, 21.5, 26.6, 26.8, 29.1, 30.3, 30.6, 38.5, 40.4, 41.6, 57.7, 62.9, 63.6, 117.5, 127.2, 127.6, 129.6, 129.9, 133.7, 135.2, 135.6, 136.6, 143.8, and 209.5; FAB HRMS calcd for $[(C_{36}H_{47}NO_4SSi) + Li]^+$ 624.3155, found 624.3125.

Trifluoromethanesulfonic Acid 6-Allyl-2-[3-(*tert*-butyldiphenylsilanyloxy)propyl]-5-ethyl-1-(toluene-4-sulfonyl)-1,2,5,6-tetrahydropyridin-3-yl Ester (34). In a 10-mL round-bottom flask under nitrogen was added compound **33** (0.23 g, 0.36 mmol), *N*-phenyltrifluoromethanesulfonimide (0.26 g, 0.73 mmol), and 4 mL of THF, and the solution was cooled to −78 °C. A solution of NaHMDS (0.5 mL of 1.0 M THF solution (0.47 mmol)) was added dropwise and the

(51) Popandova-Yambolieva, K. *Synth. Commun.* **1990**, *20*, 1857.

mixture was stirred at −78 °C for 3 h and at room temperature for 9 h. The reaction was quenched with a saturated aqueous solution of $NaHCO_3$ (20 mL) and 20 mL of ether was added. The solution was extracted with ether, the layers were separated, and the organic layer was dried ($MgSO_4$). Concentration under reduced pressure and purification by silica gel chromatography gave 0.26 g (95%) of **34**: IR (thin film) 1422, 1343, 1213, 1142, and 1111 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.70 (t, 3H, J = 6.8 Hz), 0.92 (m, 2H), 1.05 (s, 9H), 1.83 (m, 2H), 2.00 (m, 1H), 2.10 (dd, 1H, J = 6.8 and 6.4 Hz), 2.28 (m, 1H), 2.38 (s, 3H), 2.46 (m, 1H), 3.66 (m, 2H), 3.82 (dd, 1H, J = 10.4 and 4.4 Hz), 4.59 (dd, 1H, J = 6.4 and 5.6 Hz), 5.05 (d, 1H, J = 16.8 Hz), 5.09 (d, 1H, J = 10.0 Hz), 5.70 (d, 1H, J = 5.2 Hz), 5.74 (dddd, 1H, J = 17.2, 10.4, 8.4, and 5.6 Hz), 7.24 (d, 2H, J = 8.0 Hz), 7.40 (m, 6H), 7.67 (m, 4H), 7.71 (d, 2H, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.7, 19.1, 21.4, 26.6, 26.8, 30.4, 32.8, 39.7, 41.1, 53.3, 54.1, 63.4, 118.3, 118.4 (q, 1C, J = 318.7 Hz), 118.5, 127.2, 127.6, 129.5, 133.8, 134.8, 135.5 (2C), 138.1, 143.6, and 146.7; FAB HRMS calcd for $[(C_{37}H_{46}NF_3O_6S_2Si) + Li]^+$ 756.2648, found 756.2651.

2-Allyl-6-[3-(*tert*-butyldiphenylsilanyloxy)propyl]-3-ethyl-1-(toluene-4-sulfonyl)-5-vinyl-1,2,3,6-tetrahydropyridine (35). A 0.23-g (0.3 mmol) sample of compound **34**, lithium chloride (0.05 g, 1.2 mmol), palladium tetrakistriphenylphosphine (0.04 g, 0.03 mmol), 5 mL of THF, and vinyl tributyltin (350 μL, 1.2 mmol) were placed in a 10-mL round-bottom flask and heated to reflux for 12 h. The reaction was quenched with saturated aqueous $NaHCO_3$ (15 mL) and 25 mL of ether was added. The solution was extracted with ether, the layers were separated, and the organic layer was dried ($MgSO_4$). Concentration under reduced pressure and purification by column chromatography gave 0.16 g (85%) of **35**: IR (thin film) 1428, 1338, 1159, 1111, and 1036 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 0.72 (t, 3H, J = 7.2 Hz), 0.96 (m, 2H), 1.06 (s, 9H), 1.64 (m,1H), 1.82 (m, 2H), 1.98 (m, 2H), 2.37 (s, 3H), 2.46 (m, 1H), 2.63 (m, 1H), 3.61 (ddd, 1H, J = 9.0, 4.8, and 4.8 Hz), 3.70 (ddd, 1H, J = 10.8, 5.4 and 5.4 Hz), 3.76 (ddd, 1H, J = 10.2, 7.2 and 4.8 Hz), 4.74 (dd, 1H, J = 10.8 and 3.6 Hz), 5.05 (m, 3H), 5.17 (d, 1H, J = 17.4 Hz), 5.43 (d, 1H, J = 3.6 Hz), 5.89 (dddd, 1H, J = 15.6, 11.4, 8.4, and 6.6 Hz), 6.13 (dd, 1H, J = 18.0 and 11.4 Hz), 7.18 (d, 2H, J = 8.4 Hz), 7.39 (m, 6H), 7.60 (d, 2H, J = 8.4 Hz), 7.68 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 11.2, 19.2, 21.4, 26.8, 27.4, 29.9, 31.4, 39.2, 43.2, 52.8, 55.5, 63.6, 111.9, 117.5, 127.4, 127.6, 129.0, 129.2, 133.9, 135.3, 135.5, 136.5, 137.8, 138.1, and 142.8; FAB HRMS calcd for $[(C_{38}H_{49}NO_3SSi) + Li]^+$ 624.3362, found 634.3372.

6-[3-(*tert*-Butyldiphenylsilanyloxy)propyl]-3,5-diethyl-2-propyl-1-(toluene-4-sulfonyl)-1,2,3,6-tetrahydropyridine (36). A 0.21-g (0.33 mmol) sample of compound **35**, platinum oxide (0.01 g, 0.017 mmol), and 5 mL of EtOH were placed in a 10-mL round-bottom flask. The flask was evacuated and filled with hydrogen via a balloon and stirred under an atmosphere of hydrogen for 24 h. The solution was filtered through a pad of Celite and concentration under reduced pressure and purification by column chromatography gave 0.2 g (95%) of **36**: IR (thin film) 1458, 1331, 1158, 1111, and 1036 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 0.77 (t, 3H, J = 7.2 Hz), 0.91 (t, 3H, J = 7.8 Hz), 0.97 (t, 3H, J = 7.2 Hz), 1.05 (s, 9H), 1.40 (m, 2H), 1.52 (m, 2H), 1.62 (m, 2H), 1.75 (m, 3H), 1.91 (m, 2H), 2.00 (m, 1H), 2.37 (s, 3H), 3.64 (m, 2H), 3.69 (m, 2H), 4.16 (dd, 1H, J = 7.2 and 4.8 Hz), 5.19 (d, 1H, J = 3.6 Hz), 7.19 (d, 2H, J = 7.8 Hz), 7.39 (m, 6H), and 7.67 (m, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 11.8, 12.0, 13.9, 19.2, 20.4, 21.4, 26.8, 27.2, 27.7, 30.8, 32.3, 39.6, 40.2, 54.7, 55.6, 63.6, 120.7, 127.2, 127.5, 129.1, 129.4, 133.9, 135.5, 138.8, 139.1, and 142.5; FAB HRMS calcd for $[(C_{38}H_{53}NO_3SSi) + Li]^+$ 638.3675, found 638.3650.

3-[3,5-Diethyl-6-propyl-1-(toluene-4-sulfonyl)-1,2,5,6-tetrahydropyridin-2-yl]propan-1-ol (37). In a 10-mL round-bottom flask under nitrogen was placed compound **36** (0.05 g, 0.08 mmol), 1.0 mL of THF, and TBAF (0.16 mL of a 1.0 M THF solution (0.16 mmol)). The mixture was stirred for 2 h at room temperature. The reaction was quenched with a saturated aqueous solution of $NaHCO_3$ (10 mL) and 20 mL of ether was added. The solution was extracted with ether, the layers were separated, and the organic layer was dried ($MgSO_4$). Concentration under reduced pressure and purification by silica gel chromatography gave 0.04 g (90%) of **37**: IR (thin film) 3510, 1458, 1331, and 1158 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 0.71 (t, 3H, J = 6.6 Hz), 0.90 (t, 3H, J = 7.8 Hz), 0.92 (t, 3H, J = 7.8 Hz), 1.90−1.40 (m, 12H), 1.98 (m, 1H), 2.36 (s, 3H), 3.65 (m, 4H), 4.16 (dd, 1H, J = 6.6 and 6.0 Hz), 5.15 (d, 1H, J = 3.6 Hz), 7.20 (d, 2H, J = 7.8 Hz), and 7.62 (d, 2H, J = 7.8 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 11.8, 12.0, 14.0, 20.5, 21.4, 27.3, 27.8, 30.7, 32.6, 39.8, 40.2, 54.8, 55.3, 62.7, 120.8, 127.2, 129.2, 138.7, 138.9, and 142.8; FAB HRMS calcd for $[(C_{22}H_{35}NO_3S) + Li]^+$ 400.2498, found 400.2488.

6,8-Diethyl-5-propyl-1,2,3,5,6,8a-hexahydroindolizine (39). In a 25-mL round-bottom flask under nitrogen was added sodium metal (0.028 g, 1.2 mmol) and 5 mL of THF, then naphthalene (0.16 g, 1.2 mmol) was added to the mixture. The solution was stirred for 1 h during which time a dark green color appeared. The solution was cooled to −78 °C and compound **37** (0.16 g, 0.41 mmol) was added to the solution. The reaction mixture was stirred at −78 °C for 1 h, the reaction was quenched with water (10 mL), and 10 mL of ether was added. The solution was extracted with ether, the layers were separated, and the organic layer was dried ($MgSO_4$). Concentration under reduced pressure gave 3-(3,5-diethyl-6-propyl-1,2,5,6-tetrahydropyridin-2-yl)propan-1-ol (**38**) that was immediately used in the next step without purification.

A sample of the above compound (0.4 mmol), 5 mL of CH_2Cl_2, carbon tetrabromide (0.18 g, 0.53 mmol), and triphenylphosphine (0.14 g, 0.53 mmol) were placed in a 10-mL round-bottom flask and stirred for 6 h. The reaction mixture was quenched with triethylamine (570 μL, 4.07 mmol) and the solution was stirred for 30 min. The solution was washed with aqueous saturated $NaHCO_3$ and extracted with ether, the layers were separated, and the organic layer was dried ($MgSO_4$). Concentration under reduced pressure and purification by column chromatography gave 0.045 g (50%) of **39**: IR (thin film) 2961, 1459, 1377, 1251, 1171, and 1143 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.90 (t, 3H, J = 7.6 Hz), 0.91 (t, 3H, J = 7.2 Hz), 1.01 (t, 3H, J = 7.6 Hz), 1.27−1.17 (m, 2H), 1.58−1.46 (m, 4H), 1.80−1.68 (m, 2H), 2.02−1.91 (m, 4H), 2.10−2.05 (m, 1H), 2.19−2.14 (m, 1H), 2.31 (q-like, 1H, J = 8.4 Hz), 2.91 (m, 1H), 2.94 (ddd, 1H, J = 8.4, 8.4, and 4.0 Hz), and 5.29 (dd, 1H, J = 2.0 and 1.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.6, 12.4, 14.7, 18.9, 21.6, 25.0, 26.1, 27.6, 34.0, 39.4, 48.1, 61.5, 63.8, 122.1, and 140.2; FAB HRMS calcd for $[(C_{15}H_{27}N) + Li]^+$ 222.2222, found 222.2223.

6-*epi*-Indolizidine 223A (5a). A 0.03-g (0.14 mmol) sample of compound **39**, platinum oxide (2 mg), and 2 mL of EtOH were placed in a 10-mL round-bottom flask. The flask was evacuated and filled with hydrogen via a balloon and was stirred under an atmosphere of hydrogen for 24 h. The solution was filtered through a pad of Celite and concentration under reduced pressure and purification by column chromatography gave 0.03 g (98%) of 6-*epi*-indolizidine 223A (**5a**): IR (thin film) 1459, 1378, 1325, 1171, 1047, and 933 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 0.60 (q, 1H, J = 12.0 Hz), 0.88 (t, 9H, J = 7.2 Hz), 1.06 (m, 2H), 1.75−1.17 (br m, 13H), 1.92 (dt, 3H, J = 13.2, and 3.6 Hz), 3.15 (t, 1H, J = 8.4 Hz); ^1H NMR (400 MHz, D_2O/DCl) δ 0.90−0.83 (m, 9H), 1.00 (q, 1H, J = 12.4 Hz), 1.20 (m, 2H), 1.35 (m, 1H), 1.55 (m, 3H), 1.65 (m, 2H), 1.73 (m, 2H), 2.00 (m, 3H), 2.31 (m, 1H), 2.98−2.88 (m, 2H), 3.04 (q, 1H, J = 10.0 Hz), 3.65 (ddd, 1H, J = 10.0, 10.0, and 3.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.1 (2C), 14.8, 17.9, 20.8, 24.7, 26.1, 28.9, 33.1, 35.3, 40.0, 42.4, 52.1, 67.4, and 70.0; ^{13}C NMR (100 MHz, D_2O/DCl) δ 9.7, 9.9, 13.8, 16.6, 19.3, 23.4, 24.8, 26.9, 29.9, 32.9, 38.2, 39.6, 51.4, 67.8, and 71.8; FAB HRMS calcd for $[(C_{15}H_{29}N) + H]^+$ 224.2378, found 224.2378.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra for new compounds lacking elemental analyses. This material is available free of charge via the Internet at http://pubs.acs.org.

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