An Oxidative Mannich Cyclization Methodology for the Stereocontrolled Synthesis of Highly Functionalized Piperidines

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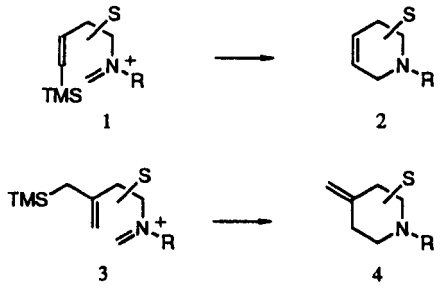
Studies focusing on the development and application of a new oxidative methodology for promoting Mannich cyclizations have been conducted. The general features of these processes were explored with selected α-silylamino and α-silylamido allyl- and vinylsilanes. Representative conditions for affecting conversion of the α-silylamine and -amide functionalities into intermediate *N*-alkyl and *N*-acyliminium cations involve either 9,10-dicyanoanthracene SET-sensitized photooxidation or ceric ammonium or tetra-*n*-butylammonium nitrate oxidations. The applicability of these procedures for promoting Mannich cyclizations was first demonstrated by the preparation of methylidenepiperidines and -hydroazepines. Further studies have led to observations which show that Mannich cyclizations of stereochemically labeled α-silylamino vinylsilanes proceed to furnish tetrahydropyridines. Also, unlike their amine analogues, α-silylamido (*E*)-vinylsilanes undergo cyclization to produce tetrahydropyridines with retention of absolute and relative stereochemistry. The differences are due to the fact that *N*-acyliminium cations serve as intermediates in reactions of the α-silylamide systems. Moreover, the oxidation procedure is ideally suited for intermediate *N*-acyliminium cation generation in stereocontrolled reactions of α-silylamido allylsilanes. Finally, the preparative utility of the new cyclization method, when used in conjunction with an α-amino acid based strategy for substrate generation, was demonstrated by applications in concise routes for the synthesis of the aza-sugars, (−)-1-deoxymannojirimycin and (+)-1-deoxyallonojirimycin.

Introduction

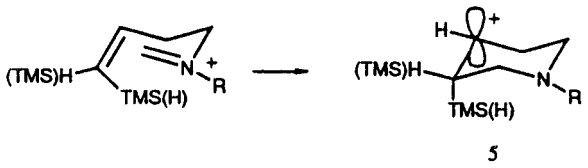
Mannich and related cyclization reactions of alkene-tethered iminium cations play important roles in the methodologies for preparation of functionalized five- and six-membered N-heterocyclic compounds.[2,3] For the specific case of piperidine ring construction, Mannich cyclizations of iminium salts which contain N-linked 1-(trimethylsilyl)buten-4-yl and 2-[(trimethylsilyl)methyl]buten-4-yl groups (**1** and **3**) are particularly attractive processes. As shown in Scheme 1, reactions of these substrates lead to regiocontrolled production of piperidines possessing either endo- (**2**) or exocyclic (**4**) unsaturation. Overman,[2] Grieco,[4] and Speckamp[5] have demonstrated that a number of classical methods can be used to generate the requisite iminium cation intermediates and that the cyclizations can be employed effectively in complex molecule synthesis.

However, the vinyl- and allylsilane versions of Mannich cyclizations have several potentially limiting features. For example, stereoelectronic requirements can reduce the versatility of the vinylsilane reactions. Overman[6] has shown that in certain cases, only *N*-[1-(trimethylsillyl)-buten-4-yl] substituted iminium salts with Z- and not E-double bond stereochemistry successfully undergo cyclization. This phenomenon has been attributed to stabilization of the transient piperidyl cation intermediates or transition states **5** by pseudoaxially rather than pseudoequatorially disposed β-TMS groups (Scheme 2). The negative impact that this has on synthetic applications stems from the fact that (*E*)-vinylsilanes generally are more easily accessed as compared to their Z-stereoisomers (see below).

Scheme 1



Scheme 2



Another potential limitation is the intervention of competitive aza-Cope rearrangements of *N*-butenyliminium cations. Extensive studies by Overman[3] indicate that *N*-(3-hydroxybuten-4-yl)-substituted systems un-

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(2) Overman, L. E.; Ricca, D. J. In *Comprehensive Organic Synthesis*; Heathcock, C. H., Trost, B. M., Fleming, I., Eds., Pergamon: Oxford, 1991; Vol. 2, pp 1007−1046.

(3) Overman, L. E. *Acc. Chem. Res.* **1992**, *25*, 352−359.

(4) (a) Grieco, P. A.; Fobare, W. F. *Tetrahedron Lett.* **1986**, *27*, 5067. (b) Grieco, P. A.; Fobare, W. F. *J. Chem. Soc., Chem. Commun.* **1987**, *185*.

(5) Speckamp, W. N.; Hiemstra, H. *Tetrahedron* **1985**, *41*, 4367.

(6) Flann, C.; Malone, T. C.; Overman, L. E. *J. Am. Chem. Soc.* **1987**, *109*, 6097. Overman, L. E.; Burk, R. M. *Tetrahedron Lett.* **1984**, *25*, 5739.

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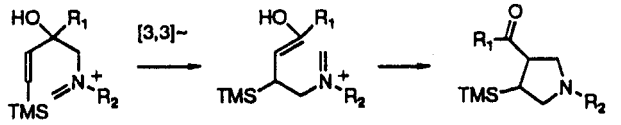
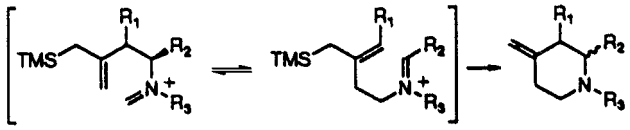
Scheme 3



Scheme 4



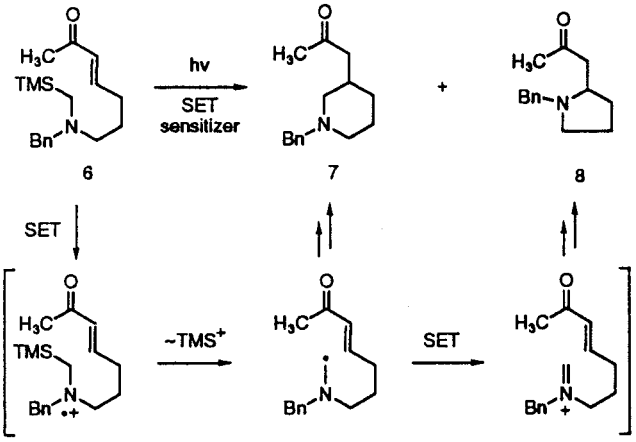
dergo this [3.3]-rearrangement process followed internal-enol Mannich addition to yield 3-acylpyrrolidines. While the two-step sequence in its own right is quite useful in the context of natural product syntheses, its operation (Scheme 3) would confound an approach to piperidine ring formation using hydroxy substituted vinyl- or allylsilanes. Moreover, rapid reversible aza-Cope rearrangement in stereochemically defined allyl and vinylsilane-tethered iminium cations could compromise absolute and/or relative stereochemical control in the Mannich cyclization process (Scheme 4).

Our interest in this area of chemistry arose out of earlier investigations of α-silylamine SET-photochemistry[7] in which we uncovered a novel methodology for iminium cation generation. The results of both exploratory[7] and mechanistic[8] efforts showed that photoinduced SET-oxidation of α-silylamines is rapidly followed by solvent-promoted desilylation to generate α-amino radicals in a highly regiocontrolled manner. In addition, we observed that α-amino radicals are efficiently transformed into iminium cations in the presence of mild oxidizing agents owing to their exceptionally low oxidation potentials (ca. −1 V).[9] An example of this is found in the 9,10-dicyanoanthracene (DCA)- or 3-methyllumiflavin-sensitized photoreactions of the silylamino enone **6** in which the product of α-amino radical cyclization (piperidine **7**) predominates at low sensitizer (i.e., oxidant) concentration and the product arising by iminium cation formation and hydrolysis (pyrrolidine **8**) becomes competitive at high oxidant concentration (Scheme 5).[7c,10]

These observations led to the proposal that α-silylamines would serve as useful precursors of iminium cations under mild oxidative conditions. The suggestion was initially tested by using the enone **6**. Metal cation (e.g., Hg(II), Pb(IV), and Mn(III)) as well as electrochemical oxidations of **6** were shown to lead to selective formation of the iminium cation derived pyrrolidine **8**.[11]

In the context of Mannich cyclization chemistry, we believed that an oxidative procedure for initiating iminium cation formation might serve as a useful alternative to the classical methods involving acid-catalyzed amine−

Scheme 5



aldehyde condensation, imine protonation, or silver-promoted α-cyanoamine elimination. This could be a particularly attractive procedure for *N*-acyliminium cation generation, where a more limited repertoire of preparative methodologies exist[12] and with which some of the potential limitations of the Mannich cyclization process might be overcome (see below).

Guided by these thoughts, we designed a broad study to (1) explore the scope and limitations of the oxidative method to promote Mannich cyclizations of vinyl- and allylsilane systems, (2) investigate and contrast stereochemical features of the oxidative *N*-acyl- and *N*-alkyliminium ion cyclizations, and (3) develop a new α-amino acid based strategy for polyhydroxylated piperidine synthesis. The results of this effort are reported below along with applications of the oxidative Mannich methodology to the preparation of selected aza-sugars.

Results and Discussion

General Features of the Oxidative Mannich Cyclization Process. Initial studies were conducted in order to determine the feasibility of the oxidative Mannich cyclization reaction and to probe several of its general features. The initial goal was to evaluate different oxidative conditions for iminium cation generation from α-silylamine precursors and the compatibility of these conditions with the presence of vinyl- and allylsilane functionality in potential Mannich cyclization substrates. For this purpose, three allylsilane derivatives, **13**−**15**, were prepared by the sequences shown in Scheme 6 which start with the known[13] silyl alcohols **9** and **10**.

Photooxidation of **14** was investigated first. Accordingly, irradiation (λ > 320 nm) of an MeCN solution containing saturated (excess) DCA and **14** leads to production of the methylidenepiperidine **16** in a 53% isolated yield (Scheme 7). Cyclization of **14** is also promoted by $(^nBu_4N)_2Ce(NO_3)_6$ (CTAN),[14] $Pb(OAc)_4$, and $Mn(OAc)_3$. For example, treatment of **14** with 2 equiv of CTAN in MeCN at 25 °C, followed by alumina chromatography, gives piperidine **16** in a 45% yield. A more quantitative evaluation of the efficiencies of these processes was obtained by comparing the GLC yields of **16** for the various reactions of **14** (see Table 1).

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(9) Wayner, D. D. M.; McPhee, D. J.; Griller, D. J. *J. Am. Chem. Soc.* **1988**, *110*, 132.

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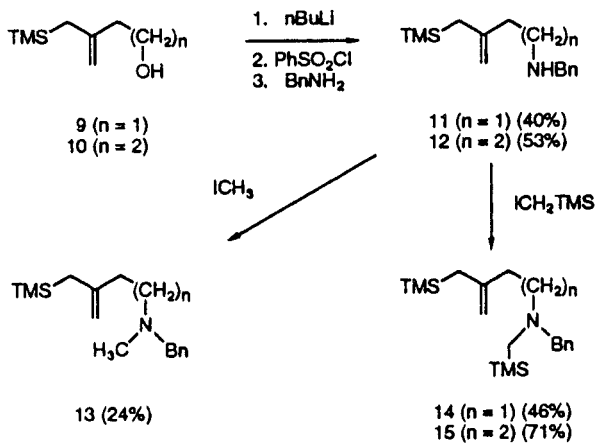
Scheme 6



Scheme 7

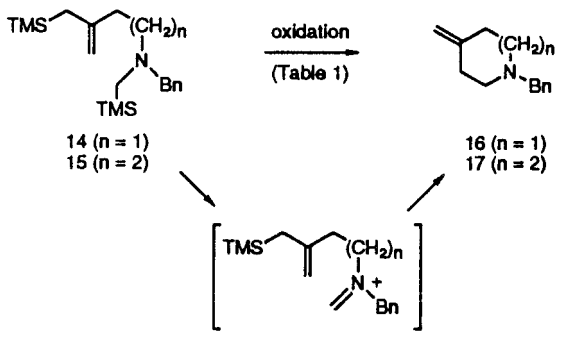


Table 1. The Efficiencies of Oxidative Mannich Cyclizations of Silylamino-Allylsilane 14

conditions[a]	time (h)	Glc yield (%)	isolated yield (%)
hν, saturated DCA	2	100	53
2 equiv CTAN	1	62	45
1 equiv $Pb(OAc)_4$	3	60	*b*
1 equiv $Mn(OAc)_3$	3	55	*b*
1 equiv $Hg(OAc)_2$	0.1	0	*b*

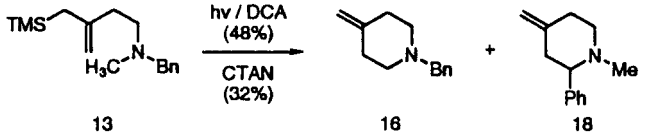
[a] All reactions were conducted in anhydrous MeCN at 25 °C. [b] Not determined.

The homologous silylamino-allylsilane **15** also participates in this cyclization reaction. Treatment of **15** in MeCN under the CTAN or DCA-photooxidation conditions results in its conversion to the hydroazepine derivative **17** in 62% and 60% yields, respectively.

Two features of these processes deserve brief comment. First, the reactions display high regioselectivities associated with iminium cation formation. Thus, oxidation occurs exclusively at the α-TMS center even when the relatively easily oxidized benzylic site is available. This selectivity is a result of the larger rates of tertiary aminium radical α-desilylation vs α-deprotonation.[8] Second, the yields of the oxidation reactions are modestly high despite the fact that the products are also tertiary amines. Clearly, the rates of oxidation of α-silylamines must exceed those of their non-silicon analogues, a point which has been discussed earlier in the context of our SET-photochemical studies.[7]

The unique function of the α-silylamine group in governing both efficiency and regiochemistry is demonstrated by the contrasting behavior of the amino-allylsilane **13** under the oxidative cyclization conditions (Scheme 8). Upon DCA-promoted photooxidation, this substance is converted to an ca. 1:3 mixture of piperidines

Scheme 8



16 and **18** in a combined 46% yield. Also, **16** and **18** are produced as a 1:1 mixture in a 32% yield when **13** is oxidized with CTAN.[15] Regiocontrol is lacking in these reactions and efficiencies are lower when compared to similar cyclizations starting with the silicon substituted substrate **14**.

Stereochemically More Complex α-Silylamino Allylsilanes. The results of the brief exploratory study gave impetus to our continuing work on this process. Our attention next turned to stereochemically and functionally more complex substrates. The subgoal of this work was to probe a general strategy for stereocontrolled, functionalized piperidine ring construction based on Mannich cyclizations of α-amino acid derived substrates. Accordingly, L-alanine was converted to the α-amino aldehyde **19** (>90% ee) by a procedure previously developed in our laboratory (Scheme 9).[16] Addition of 1-[(trimethylsilyl)methyl]-1-vinyllithium to **19** in THF at −78 °C gave the silylamino alcohol **20** as a single antidiastereomer[17] with no loss of enantiomeric purity and in a 65% yield. To block potential intervention of either iminium cation capture by the pendent alcohol or sequential aza-Cope/Mannich cyclization,[3] **20** was first transformed to the acetate derivative **21**.

Oxidative cyclization of **21** promoted by reaction with CTAN in MeCN at 25 °C, occurred efficiently (75%) to produce a mixture of separable stereoisomeric piperidines **22** and **25** in a 1:1.2 ratio. To gain information about the origin of the stereorandomization accompanying this reaction, the enantiomeric purities of **22** and **25** were determined by conversion to the respective alcohol derivatives **23** and **26** (KCN, MeOH) and then to the Mosher esters **24** and **27** ((*R*)- and (*S*)-methoxy(trifluoromethyl)phenylacetic acid (MTPAcOH), DCC). ^{1}H NMR analysis of the esters shows that the cis-piperidine **22** is produced in only a 4% ee while the trans-isomer **25** has a 24% ee.

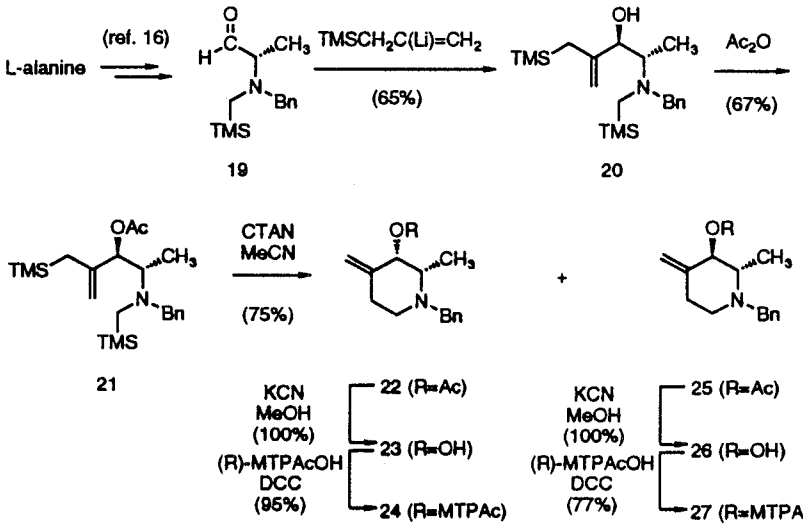
The extensive loss of both absolute and relative stereochemistry in the oxidation reaction of **21** suggests the possible operation of a competitive aza-Cope/C=N stereomutation process. A mechanism for this is outlined in Scheme 10. Cyclization of the initially formed iminium cation **28** should yield trans-piperidine **25** in an enantio- and diastereoselective manner. However, reversible [3.3]-rearrangement of **28** via the iminium cation **29** competes with this process and leads to complete randomization of stereochemistry and, as a result, production of both **22** and **25** in racemic forms.

(15) The different ratios of **16** and **18** arising from oxidation reactions under the photochemical and CTAN conditions is likely a result of the different relative rates of aminium radical deprotonation at the NCH_3 vs NCH_2Ph centers and the fact that the active base in each process is most likely different.

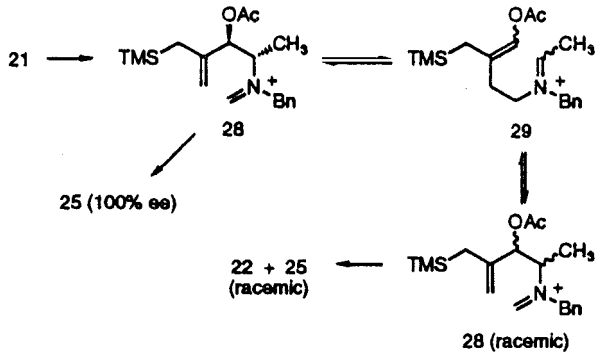
(16) Khim, S. K.; Cederstrom, E.; Ferri, D. C.; Mariano, P. S. *Tetrahedron* **1996**, *52*, 3195. Kim, S. K.; Wu, X.; Mariano, P. S. *Tetrahedron Lett.* **1996**, *37*, 571.

(17) (a) This stereochemical outcome is consistent with a simple Felkin−Ahn prediction and similar to that observed in other addition reactions of chiral α-amino carbonyl compounds (ref 17b). (b) Morrison, J. D.; Mosher, H. S. *Asymmetric Organic Reactions*; Prentice Hall: Englewood Cliffs, New Jersey, 1971; pp 103−107.

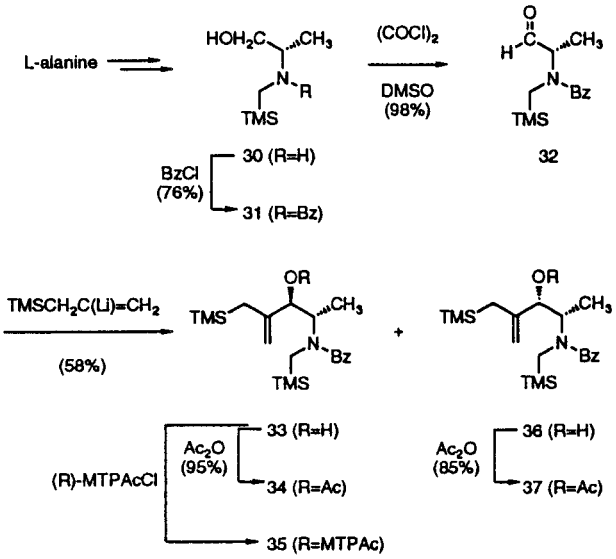
Scheme 9



Scheme 10



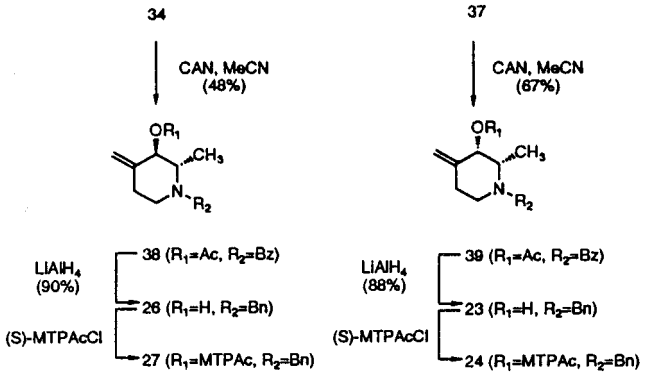
Scheme 11



Clearly, despite the high-yielding nature of the allylsilane-terminated Mannich cyclization reaction, its synthetic utility is compromised by the significant loss of absolute and relative stereochemistry. This pitfall should not be unique for the oxidative protocol but, rather, more generally associated with all allylsilane Mannich cyclizations. A possible solution to this problem, and one that emphasizes the specific advantages of the oxidative method, involves the use of *N*-acyl- rather than *N*-alkyliminium cation intermediates. We reasoned that destabilization of an iminium cation related to **28** (Scheme 10) by replacement of the *N*-Bn by a *N*-Bz group would enhance the rate of cyclization relative to aza-Cope rearrangement. If so, this change would result in a highly stereospecific process.

To evaluate this proposal, the diastereomeric α-silylamido allylsilanes **34** and **37** were prepared starting from the known,[16] L-alanine-derived amino alcohol **30** (Scheme 11). A distinguishing feature of this sequence is that the vinyllithium addition to aldehyde **32** (>90% ee) leads to both anti (52%) and syn (6%) amido alcohols **33** and **36** in only 50% ee (by ^{1}H NMR analysis of the Mosher ester **35** obtained by reaction with (*R*)-methoxy(trifluoromethyl)phenylacetyl chloride ((*R*)-MTPAcCl). Acylation of **33** and **36** provides the respective acetates **34** and **37** which were subjected to the oxidative cyclization protocol by using in this case[18] $(NH_4)_2Ce(NO_3)_6$ (CAN) as the oxidant. Each reaction occurs to yield a single piperidine with complete retention of the original diastereomeric and enantiomeric purity (Scheme 12). Specifically, CAN-promoted reaction of **34** yields the trans-piperidine **38** with an enantiomeric purity of 50% as determined by ^{1}H NMR analysis of the Mosher ester **27** of alcohol **26** (derived by $LiAlH_4$ reduction). Similarly, cyclization of the syn-diastereomer **37** yields cis-piperidine **39** exclusively with complete retention of enantiomeric purity.

Scheme 12



(18) We have found that CTAN and CAN are about as equally effective in promoting these processes.

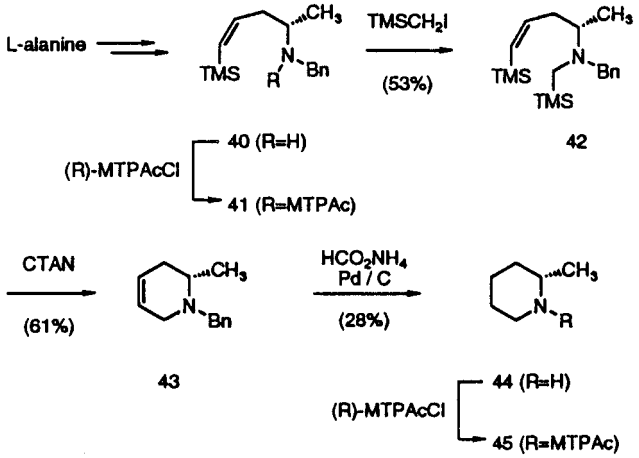
In accord with the mechanistically based prediction, cyclizations of allylsilane-terminated *N*-acyliminium cations proceed in a highly stereocontrolled fashion. Thus, *N*-acyl substituents appear to play a critical role in governing the relative rates of the aza-Cope and Mannich cyclization processes.[19] Moreover, the oxidative method appears to be ideally suited for generation of these types of "activated" iminium cations starting with *N*-(α-silyl)-amides or *N*-(α-silyl) carbamates.[20,21]

Vinylsilane Oxidative Mannich Cyclizations. An extensive effort by Overman and co-workers has provided a number of examples in which vinylsilanes serve as terminating groups (vinyl anion equivalents) in Mannich cyclization processes.[2,6,22] Two important findings of Overman's efforts, related to cyclizations which produce 1,2,5,6-tetrahydropyridine products, are the enhanced reactivity of (*Z*)- vs (*E*)-vinylsilanes and the loss of stereochemical integrity in reaction of enantiomerically pure substrates.[22c] The original aim of our investigations in this area was to determine if implementation of the oxidative methodology could lead to solutions of these two potentially detrimental problems. In the interim period, collaborative studies by Overman's and our group[23] led to a correction of the original conclusions about the stereochemical course of these processes. Our contribution to this study along with additional efforts which demonstrate the synthetic advantages of the oxidative protocol are presented below.

As pointed out above, one of the potentially useful characteristics of the oxidative Mannich cyclization process resides in the mild (25 °C, nonacidic) conditions needed for *N*-alkyl and *N*-acyliminium cation generation. As part of our preliminary thinking, we questioned whether the mild conditions could alter the stereochemical course of vinylsilane cyclizations. This is particularly true in the case of the photooxidative process which, in theory, could be conducted at low temperatures. To address this issue, we designed experiments in which the oxidative conditions are used to prepare the same types of iminium cation intermediates in the cyclizations originally studied by Overman and co-workers.[22c] For this purpose, the α-silylamino (*Z*)-vinylsilane **42** was synthesized by silylmethylation of the secondary amine **40** (Scheme 13), a substance prepared from L-alanine by a minor modification of the sequence reported earlier by Overman.[22c] Importantly, **40** generated in this manner has >95% ee as determined by both GLC and ^{1}H NMR analysis of its Mosher amide **41** (from reaction with (*R*)-MTPAcCl).

Treatment of **42** with 2 equiv of CTAN at 25 °C in anhydrous MeCN leads to production of optically active ($[\alpha]^{25}_D = +56°$) tetrahydropyridine **43** in 61% yield. To determine the enantiomeric purity of **43**, it is converted to the piperidine **44** by catalytic hydrogenolysis−hydrogenation. The Mosher amide **45** was then generated and

Scheme 13



analyzed by ^{1}H NMR. This procedure showed that **43** has a >90% ee and, thus, that the oxidative Mannich cyclization is highly enantiospecific. Contrary to the earlier report,[22c] we also found that **43**, generated by use of Grieco−Mannich cyclization conditions (aqueous formaldehyde, TFA, H_2O−THF, 25 °C), has a high enantiomeric purity ($[\alpha]^{25}_D = +56°$). These results in conjunction with those coming from parallel studies by the Overman group lead to a correction[23] of the original stereochemical conclusions about vinylsilane-terminated Mannich cyclizations. Specifically, these processes are highly enantiospecific and, consequently, can be applied in the stereocontrolled preparation of substituted tetrahydropyridines.

Information about the general synthetic potential of these cyclization reactions as well as their limitations has come from further studies with the functionally and stereochemically more complex α-silylamino vinylsilanes **50** and **52** and their amide analogues **59** and **63**. Preparation of **50** is accomplished by a route beginning with addition of lithium trimethylsilylacetylide to the L-alanine-derived aldehyde **19**. The process produces the propargylic alcohol **46** as a single anti-diastereomer[16] (Scheme 14). A number of reduction conditions were attempted to affect stereoselective conversion of **46** to the (*Z*)-vinylsilane **47**. In our hands, the best, but yet still not satisfactory, method employs controlled catalytic hydrogenation with 5% Pd/C in EtOAc at −10 °C. This reaction yields **47** (71%) along with its *E*-isomer **48** (28%) and a trace quantity of the saturated analogue **49**. Acetylation of **47** gives **50**, one of the substrates selected to further probe the oxidative cyclization methodology.

A more direct route is used to prepare the (*E*)-vinylsilane **48**. Thus, (*E*)-[(trimethylsilyl)vinyl]lithium, derived by tin−lithium exchange with the tin derivative **51**,[24] adds to aldehyde **19** to generate **48** (81%) which is then acetylated to give the *E*-substrate **52** (Scheme 14).

Oxidation of the silylamino (*E*)-vinylsilane **52** with 2 equiv of CTAN in anhydrous MeCN leads to only low yielding formation of the secondary amine **57** (Scheme 15). No trace of the piperidine **53** could be detected by ^{1}H NMR and TLC analysis of the crude product mixture. In contrast, the (*Z*)-vinylsilane **50** reacts under identical conditions (or with use of CAN as the oxidant) to yield the piperidine **53** along with the product of desilylmethylation, **54**.

(19) Personal communication from Professor L. E. Overman.

(20) Kim, H. J.; Yoon, U. C.; Jung, Y. S.; Park, N. S.; Cederstrom, E. M.; Mariano, P. S. (manuscript in preparation).

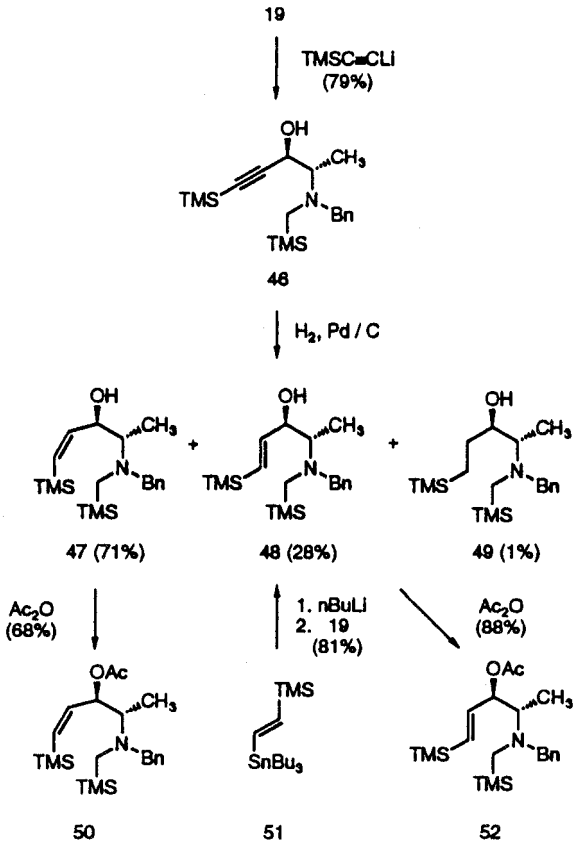
(21) (a) Narasaka (ref 21b) has also demonstrated that α-tin amides undergo oxidation to produce *N*-acyliminium cations. (b) Narasaka, K.; Kohno, Y.; Shimada, S. *Chem. Lett.* **1993**, 125.

(22) (a) Overman, L. E.; Bell, K. L.; Ito, F. *J. Am. Chem. Soc.* **1984**, *106*, 4192. (b) Overman, L. E.; Lin, N. H. *J. Org. Chem.* **1985**, *50*, 3669. (c) Daub, G. W.; Heerding, D. A.; Overman, L. E. *Tetrahedron* **1988**, *44*, 3919. (d) Overman, L. E.; Ricca, D. J. *J. Compr. Org. Synth.* **1991**, *2*, 1007.

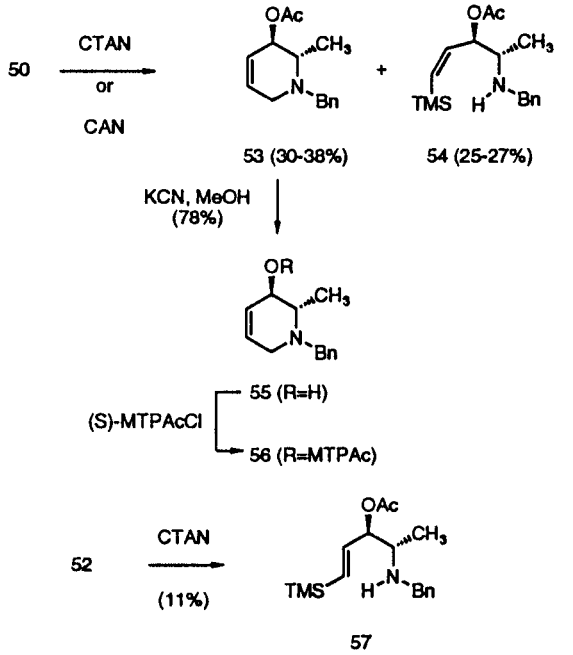
(23) Castro, P.; Overman, L. E.; Zhang, X. M.; Mariano, P. S. *Tetrahedron Lett.* **1993**, *34*, 5243.

(24) (a) Cunico, R. E.; Clayton, G. *J. Org. Chem.* **1976**, *41*, 1480. (b) Pillot, F. J.; Dunogues, J. P.; Calas, J.; Lapouyade, R. *Synth. Commun.* **1979**, *9*, 395.

Scheme 14

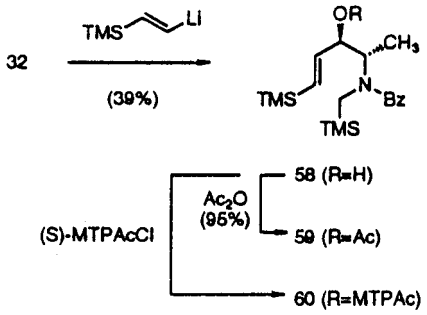


Scheme 15

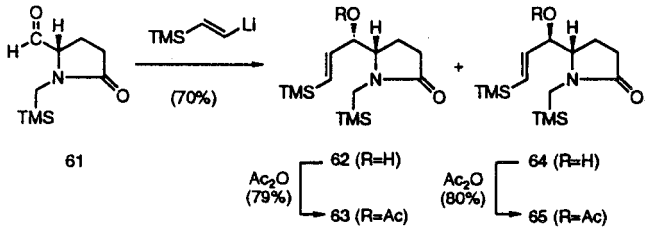


These results provide another example of the stereochemical requirements for six-membered ring forming, vinylsilane-terminated Mannich cyclizations (see above). Furthermore, they show that cyclization of the *Z*-substrate **50** occurs in an enantio- and diastereoselective manner. The former conclusion comes from the observation that **53** has a >90% ee (conversion of **53** to alcohol **55** and Mosher ester **56**) and the latter from the fact that **53** has trans C-5,C-6 stereochemistry.

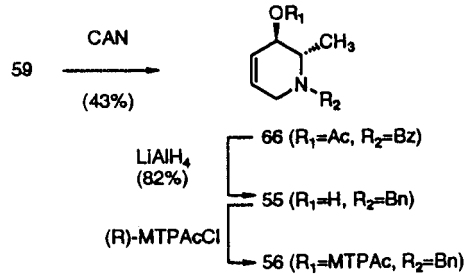
Scheme 16



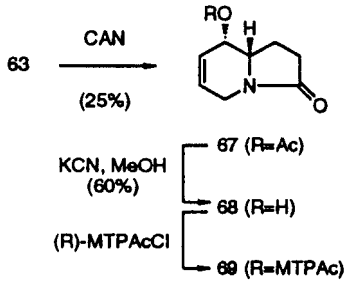
Scheme 17



Scheme 18



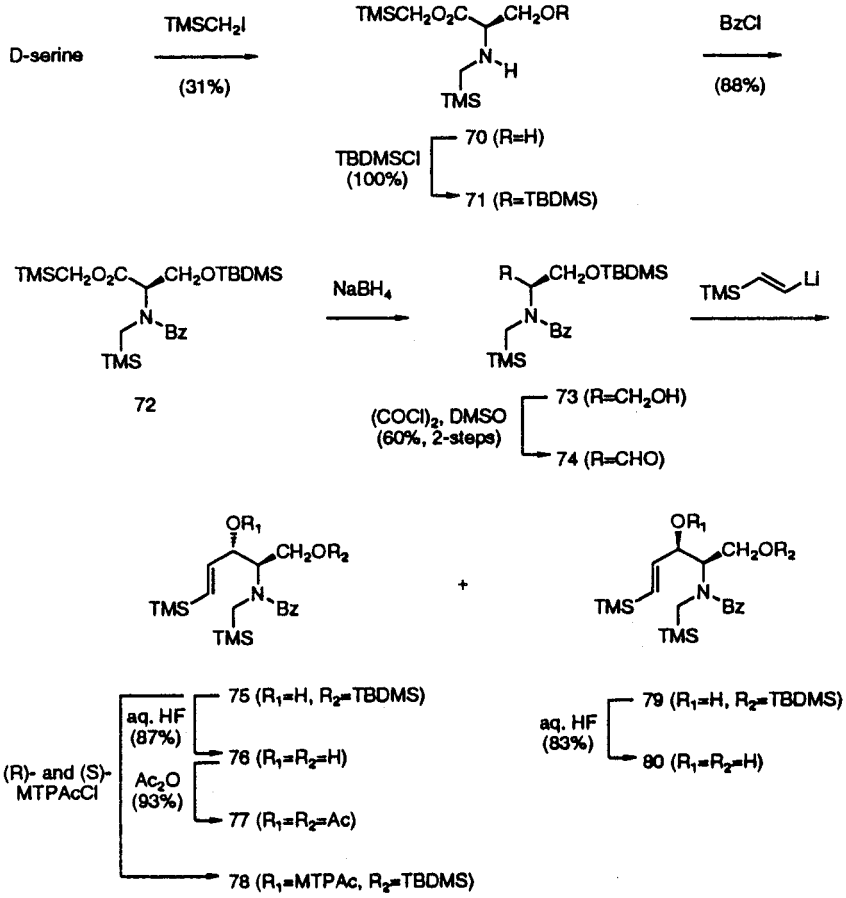
Scheme 19



We have already demonstrated how a change in the N-substituent from alkyl to acyl can markedly affect the enantio- and diastereoselectivities of allylsilane-terminated iminium cation cyclizations. The energetic origin of this effect (i.e., reactant vs transition state destabilization) suggests that it could also influence the reactivity of vinylsilane systems and, perhaps, alter the *Z*-stereochemical requirement. Support for this conjecture is found in the results of studies with the α-silylamides **59** and **63**. The benzamide derivative **59** is prepared by a two-step sequence (Scheme 16) beginning with addition of the (*E*)-vinyllithium reagent derived from **51** to aldehyde **32** followed by acetylation of the intermediate alcohol **58**. The enantiomeric purity of **59** was determined to be >90% by ^{1}H NMR analysis of the Mosher ester **60**.

Similarly, (*E*)-vinyllithium addition to the L-pyroglutamic acid derived aldehyde **61** (62% ee)[16] yields a separable 3.3:1 mixture of the allylic alcohols **62** and **64**

Scheme 20



(Scheme 17) which are then converted to the corresponding acetates **63** and **65**.

In contrast to the *N*-alkyl analogue, (*E*)-vinylsilane **59** is oxidized by CAN to produce the trans-tetrahydropyridine **66** with a >90% ee (by $LiAlH_4$ reduction to the *N*-benzyl alcohol **55** and Mosher ester **56**) (Scheme 18). The lactam-containing substrate **63** also undergoes oxidative Mannich cyclization forming the indolizidinone **67** (Scheme 19). The enantiomeric purity of **67** is determined by use of a sequence involving hydrolysis to form alcohol **68**, Mosher esterification giving **69**, and ^{1}H NMR analysis. The observed 62% ee for **67** matches that of the aldehyde precursor **61**. These results show that (*E*)-vinylsilanes serve as effective terminator groups in stereocontrolled, tetrahydropyridine Mannich cyclization processes of *N*-acyliminium cations.

Application to 1-Deoxy-Aza-Sugar Synthesis. The results presented above show that the oxidative Mannich cyclization process, when coupled with an α-amino acid based protocol for substrate synthesis, serves as a versatile method for the stereocontrolled preparation of highly functionalized piperidines. To demonstrate the synthetic potential of this chemistry, application to the synthesis of (−)-1-deoxymannojirimycin (**90**) and (+)-1-deoxyallonojirimycin (**91**), two biologically interesting aza-sugars,[27a−p] were explored. The sequences commence with the conversion of D-serine to the α-silylamido ester **70** (Scheme 20). Attempts to improve the 31% yield of this process by using alternative bases, solvents, and alkylating agents were unsuccessful. TBDMS protection of the primary alcohol group in **70** is followed by N-benzoylation and $NaBH_4$ reduction to provide alcohol **73**. Swern oxidation then gives aldehyde **74**. To assess if racemization occurs in these steps, **74** was immediately reduced with $NaBH_4$, and the resulting alcohol was converted to its Mosher ester. Analysis of this substance by ^{1}H NMR showed that **74** has a 70% ee.

Reaction of aldehyde **74** with *E*-[(trimethylsilyl)vinyl-]lithium yields two separable diastereomeric alcohols, **75** and **79**, in a 3.6:1 ratio. Initial assignment of syn-

(25) The ^{1}H NMR spectrum of **53** contains a small 2.0 Hz H-5,H-6 coupling and a modestly large 5.0 Hz H-4,H-5 coupling both of which are consistent with its existence in a Macromodel-calculated (ca. 2 kcal/mol) psuedo-diaxial conformation.

(26) Curiously, epimer **65** does not cyclize when treated with CAN. Instead, an MeCN (Ritter-type) trapping product is produced. Similarly, the diacetate of **80** does not undergo oxidative Mannich cyclization. Thus, it appears that other factors can also influence the rates of these processes.

(27) (a) Hughes, A. B.; Rudge, A. *J. Nat. Prod. Rep.* **1994**, *11*, 135. (b) Look, G. C.; Fotsch, C. H.; Wong, C. H. *Acc. Chem. Res.* **1993**, *26*, 182. (c) Vanden Borek, L. A.; Vremus, D. J.; Heskamp, B. M.; Van Breckel, C. A.; Tan, M. C.; Bolscher, J. G.; Ploegh, H. L., Van Kamenade, F. J.; de Goede, R. E.; Miedema, F. *Recl. Trav. Chim. Pays-Bas* **1993**, *112*, 82. (d) Winchester, B.; Fleet, G. W. *J. Glycobiology* **1992**, *2*, 199. (e) Tyms, A. S.; Taylor, D. L.; Sunkara, P. S.; Kang, M. S. *Glycoprotein Synthesis and Human Immunodeficiency Viruses*. In *Design of Anti-AIDS Drugs*; Declerq, E., Ed.; Elsevier: New York, 1990; pp 257−318. (f) Fleet, G. W. J.; Gough, M. J.; Shing, T. K. M. *Tetrahedron Lett.* **1984**, *25*, 4029. (g) Legler, G.; Julich, E. *Carbohydr. Res.* **1994**, *128*, 61. (h) Bernotas, R. C.; Ganem, B. *Tetrahedron Lett.* **1985**, *26*, 1123. (i) Fleet, G. W. J.; Smith, P. W. *Tetrahedron Lett.* **1985**, *26*, 1469. (j) Fleet, G. W. J.; Fellows, L. E.; Smith, P. W. *Tetrahedron Lett.* **1987**, *28*, 979. (k) Fleet, G. W. J.; Ramsden, N. G.; Witty, D. R. *Tetrahedron Lett.* **1988**, *29*, 2871. (l) Ikota, N. *Heterocycles* **1989**, *29*, 1469. (m) Iida, H.; Yamazaki, N.; Kibayashi, C. *J. Org. Chem.* **1987**, *52*, 3337. (n) Altenbach, H.-J.; Himmedldirk, K. *Tetrahedron* **1995**, *52*, 1077. (o) Fellow, L. E.; Bell, E. A.; Lynnm, D. G.; Nakanishi, K. *J. Chem. Soc., Chem. Commun.* **1979**, 977. (p) Myers, A. I.; Price, D. A.; Andres, C. J. *Synlett.* **1997**, *5*, 533.

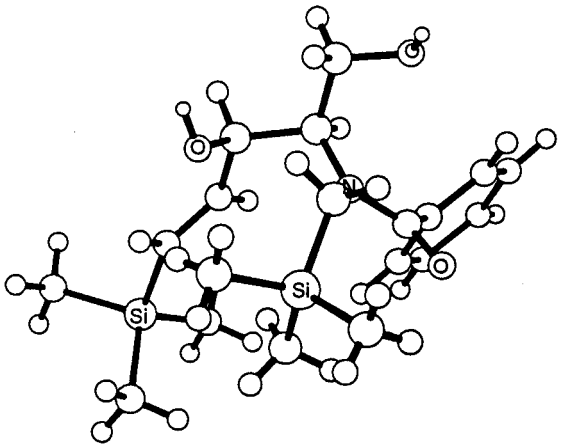
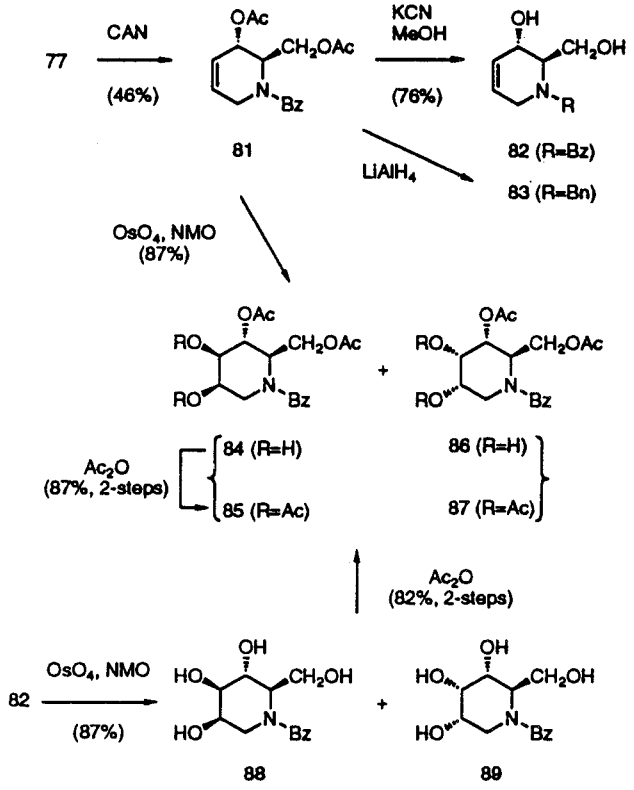


Figure 1. Chem-3D plot of the X-ray crystallographically determined structure of diol **80**.

Scheme 21



stereochemistry to **75**, the major isomer, is made by application of the Felkin−Ahn model.[17] X-ray crystallographic analysis (see Figure 1) of the diol **80**, derived by treatment[6] of the minor-isomer **79** with aqueous HF, provides unambiguous proof for this assignment. Also, Mosher ester (**78**) analysis of **75** shows that it retains a 70% ee, identical with that of the aldehyde **74**.

The α-silylamido vinylsilane **75** has the needed relative and absolute stereochemistry for use as an intermediate in the synthesis of the targeted aza-sugars. To prevent competitive reactions involving the free hydroxyl or desilylation to generate a free hydroxyl,[28] **75** is first transformed into the diacetate **77**. Oxidation of **77** with CAN leads to formation of the desired tetrahydropyridine

(28) Treatment of the monoacetate of **75** with CAN results in instantaneous O-desilylation.

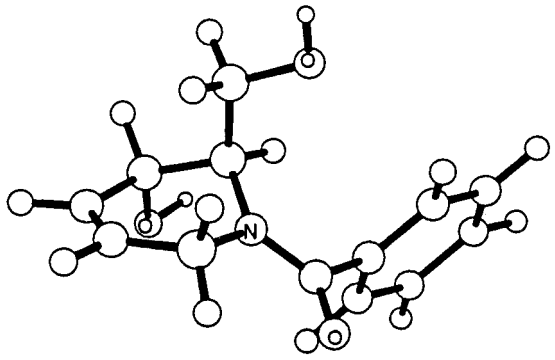


Figure 2. Chem-3D plot of the X-ray crystallographically determined structure of diol **82**.

81 (Scheme 21). The C-5,C-6 stereochemistry in **81** cannot be ascertained convincingly by using ^{1}H NMR spectroscopy owing to line broadening associated with slow amide rotation. Thus, **81** is converted to the *N*-benzyl diol **83** by $LiAlH_4$ reduction. ^{1}H NMR analysis of **83** reveals an H-5,H-6 coupling of 3.5 Hz consistent with the diequatorial disposition of these protons (see above).[25] X-ray crystallographic analysis of the related diol **82** (Figure 2), arising by methanolysis of **81**, confirmed the structure and stereochemistry of **81**.

The $\Delta^{2,3}$-unsaturation in tetrahydropyridines **81** and **82**, as planned, is useful for the stereocontrolled introduction of properly positioned hydroxyl functionality in the aza-sugar targets. Catalytic dihydroxylation[29] is ideal for approaches to aza-sugar targets with *cis*-2,3-diol stereochemistry. As outlined in Scheme 21, reaction of diacetate **81** with OsO_4/NMO in aqueous acetone yields a mixture of the diols **84** and **86** in a 3:2 ratio which are converted directly to the respective tetraacetates **85** and **87**. The degree of stereoselectivity in this process is unexpectedly low.[30] To evaluate whether a free hydroxyl at C-5 is a better stereochemical control element, diol **82** was subjected to dihydroxylation in the presence of the chiral ligand, hydroquinidine 1,4-phthalazinediyl diether, described by Sharpless.[31] Acetylation of the crude product mixture followed by separation yields the tetraacetates **85** and **87**, again in a 3:2 ratio. The diastereofacial selectivity of this dihydroxylation process could not be improved even when several other chiral ligands[31,32] are used.[33]

The tetraacetates **85** and **87** serve as direct precursors of the respective aza-sugars, (−)-1-deoxymannojirimycin and (+)-1-deoxyallonojirimycin (Scheme 22). Each trans-

(29) (a) VanRheenen, V.; Kelly, R. C.; Cha, D. Y. *Tetrahedron Lett.* **1976**, *23*, 1973. (b) Aube, J.; Ghosh, S.; Tanol, M. *J. Am. Chem. Soc.* **1994**, *116*, 9009.

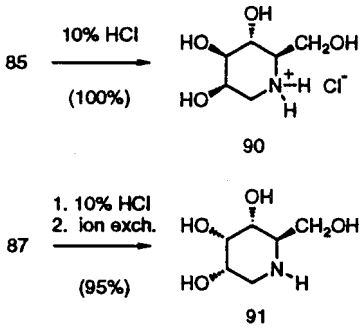
(30) (a) Cha, J. K.; Christ, W. J.; Kishi, Y. *Tetrahedron Lett.* **1983**, *24*, 3943. (b) Cha, J. K.; Christ, W. J.; Kishi, Y. *Tetrahedron* **1984**, *42*, 2247.

(31) (a) Sharpless, K. B.; Amberg, W.; Beller, M.; Chen, H.; Hartung, J.; Kawanami, Y.; Lubben, D.; Manoury, E.; Ogino, Y.; Shibata, T.; Ukita, T. *J. Org. Chem.* **1991**, *56*, 4585. (b) Cha, J. K.; Kim, N. O. *Chem. Rev. (Washington, D.C.)* **1995**, *95*, 1. (c) Oishi, T.; Iwakuma, T.; Hirama, M.; Ito, S. *Synlett* **1995**, 404. (d) Oishi, T.; Iida, K.-I.; Hirama, M. *Tetrahedron Lett.* **1993**, *34*, 3573. (e) Oishi, T.; Hirama, M. *J. Org. Chem.* **1989**, *54*, 5834. (f) Annunziata, R.; Cinquini, M.; Cozzi, F.; Raimondi, L. *Tetrahedron* **1987**, *44*, 6897. (g) Masamune, S.; Choy, W.; Petersen, J. S.; Sita, L. R. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 1.

(32) For example, hydroquinine 4-chlorobenzoate, hydroquinidine 4-chlorobenzoate, and hydroquinine 1,4-phthalazinediyl diether.

(33) When hydroquinine 1,4-phthalazinediyl diether is used in the catalytic hydroxylation reaction of **82**, the tetraacetates **85** and **87** are formed in a 2:3 ratio.

Scheme 22



formation is achieved by treatment with 10% HCl. 1-Deoxymannojirimycin hydrochloride (**90**) prepared in this manner is identical in all respects to the natural material[27f,o] except for its optical rotation ($[\alpha]^{26}_D = -7.7°$ vs $[\alpha]^{20}_D = -10.9°$) which reflects a 70% ee translated directly from aldehyde **74**. Likewise, synthetic (+)-1-deoxyallonojirimycin (**91**) has spectroscopic properties that match those reported for this substance,[27n] and its optical rotation $[\alpha]^{28}_D = +21.2°$ (vs $[\alpha]^{20}_D = +35.2°$)[27n] corresponds to a 70% ee.

Summary

The studies described above, related to the development of a new oxidative Mannich process, have provided an opportunity to probe several generally interesting features of the allylsilane and vinylsilane cyclizations. The results have led to the correction of an important stereochemical issue and the discovery of a technique to avoid stereochemical problems which have limited the synthetic application of this reaction. Finally, although the Mannich cyclization processes proceed with only modest efficiencies independent of the methods used for their initiation,[23] their application in α-amino acid based strategies for polyhydroxylated piperidine (and perhaps indolizidine) syntheses comprise new and generally concise approaches to these interesting substances.

Experimental Section

General Procedures. Unless otherwise noted, ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ solutions by using 200.13, 400.13, or 500.14 MHz operational frequencies for ^{1}H observations and 50.32 and 100.62 MHz for ^{13}C observations. Chemical shifts are reported in parts per million relative to $CDCl_3$ (7.24 ppm for ^{1}H NMR and 77.0 ppm for ^{13}C NMR) as the internal standard. ^{1}H NMR coupling constant determinations (*J* values reported in hertz) and nuclei assignments were aided by the use of homonuclear decoupling experiments. ^{13}C NMR resonance assignments were aided by use of the DEPT technique to determine numbers of attached hydrogens. Infrared (IR) spectra were obtained on samples which were prepared as neat oils (liquids) unless otherwise noted, and band assignments are in units of cm^{-1}. Mass spectrometric data determined by use of either the electron impact (EIMS), chemical ionization (CIMS), or fast atom bombardment (FAB) method are reported as *m*/*z* (relative intensity) and high-resolution mass spectral data (HRMS) are recorded as *m*/*z*. Optical rotations [α] were measured at 589 nm (sodium D line). All new compounds were obtained as oils in >90% purity (by ^{1}H and ^{13}C NMR) unless otherwise noted. Column chromatographic separations were performed by using EM Type 60 silica gel (230−400 mesh), Florisil (100−200 mesh), or Type F-20 Alumina (neutral, 80−120 mesh). Preparative TLC was performed on 20 × 20 cm plates coated with EM Type-60 GF-254 silica gel.

***N*-Benzyl-*N*-[2-[(trimethylsilyl)methyl]but-1-en-4-yl]-amine (11).** A solution of BuLi (2.1 mmol) in hexane was added to a solution of 3-[(trimethylsilyl)methyl]-3-buten-1-ol (**9**)[13] (250 mg, 1.71 mmol) in THF (3 mL) at −78 °C. After stirring at −78 °C for 0.5 h, benzenesulfonyl chloride (300 mg, 1.71 mmol) was added and the resulting mixture was warmed to 25 °C and stirred for 2.5 h. After concentration in vacuo, excess benzylamine in MeCN (5 mL) was added to the residue which was then stirred at reflux for 4 h, diluted with satd $NaHCO_3$, and extracted with ether. The extracts were dried and concentrated in vacuo to give a residue which was subjected to column chromatography (Florisil, 10% ether−hexanes) to afford 160 mg (40%) of the desired silylamine **11**: ^{1}H NMR 0.02 (s, 9 H, $SiMe_3$), 1.51 (s, 2 H, CH_2Si), 2.18 (t, *J* = 7.0, 2 H, CH_2C=), 2.73 (t, *J* = 7.0, 2 H, CH_2NH), 3.78 (s, 2 H, NCH_2Ph), 4.56, 4.61 (s, 2 H, vinyl), 7.30 (m, 5 H, ArH); ^{13}C NMR −1.4 ($SiMe_3$), 26.5 (CH_2Si), 38.4 (CH_2), 47.1 (CH_2N), 49.2 (CH_2Ph), 108.5 (CH_2=C), 126.8, 128.1, 128.3 (Ar), 140.4 (Ar C-*ipso*), 145.3 (CH_2=C); IR 1631, 1494, 1452, 1374, 1247, 1154; EIMS 247 (0.3), 196 (7), 188 (5), 186 (5), 172 (6), 150 (6), 120 (36), 91 (69); HRMS 247.1457, $C_{15}H_{25}NSi$ requires 247.1456.

***N*-Benzyl-*N*-[2-[(trimethylsilyl)methyl]pent-1-en-5-yl]-amine (12).** A solution of BuLi (0.52 mmol) was added to a solution of silyl alcohol **10**[13] (100 mg, 0.58 mmol) in THF (3 mL) at −78 °C. After stirring fo 30 min, benzenesulfonyl chloride (112 mg, 0.64 mmol) was introduced, and the resulting mixture was warmed to 25 °C and stirred for 3 h. To the residue obtained by concentration in vacuo was added excess benzylamine in MeCN (10 mL), and the resulting mixture was stirred at reflux for 3 h, diluted with satd $NaHCO_3$, and extracted with ether. The extracts were dried and concentrated in vacuo to afford a residue which was subjected to column chromatography (Florisil, 60% ether−hexanes) to give 80 mg (53%) of **12**. ^{1}H NMR 0.02 (s, 9 H, $SiMe_3$), 1.51 (s, 2 H, CH_2Si), 1.65 (m, 2 H, $(CH_2)_3$, 1.97 (t, *J* = 6.8, 2 H, =CCH_2-CH_2), 2.63 (t, *J* = 7.5, 2 H, CH_2N), 3.78 (s, 2 H, NCH_2Ph), 4.50, 4.57 (s, 2 H, vinylic), 7.30 (m, 5 H, Ar); ^{13}C NMR −1.3 ($SiMe_3$), 26.7 (CH_2), 28.2 (CH_2Si), 35.9 (CH_2=C), 49.2 (CH_2N), 54.0 (NCH_2PH), 107.0 (CH_2=C), 126.8, 128.1, 128.3 (Ar), 132.7 (Ar, C-*ipso*), 147.3 (=C); IR 3066, 3028, 2952, 1630; EIMS 261 (1), 133 (58), 121 (52), 91 (100); HRMS 261.1931, $C_{16}H_{27}NSi$ requires 261.1931.

***N*-Benzyl-*N*-methyl-*N*-[2-[(trimethylsilyl)methyl]buten-4-yl]amine (13).** Iodomethane (0.66 g, 4.6 mmol) in MeCN (10 mL) was added dropwise to a solution of **11** (1.0 g, 4.3 mmol) in MeCN (20 mL) at 0 °C. The resulting mixture was stirred at 25 °C for 12 h, diluted with water, and extracted with ether. The extracts were dried and concentrated in vacuo to give a residue which was subjected to column chromatography (Florisil, 10% ether−hexanes) to yield 0.26 g (24%) of **13**. ^{1}H NMR −0.05 (s, 9 H, TMS), 1.45 (s, 2 H, CH_2TMS), 2.15 (m, 5 H, NCH_3, CH_2), 2.45 (t, *J* = 8.7, 2 H, CH_2N), 3.45 (s, 2 H, NCH_2Ph), 4.48 and 4.52 (s, 2 H, CH_2, 7.20 (m, 5 H, Ar); ^{13}C NMR −1.4 (TMS), 27.0 (CH_2TMS), 35.9 (CH_2), 42.2 (NCH3), 56.2 (CH_2), 62.3 (NCH_2Ph), 107.5 (=CH_2), 126.9, 128.1, 129.1, 139.1 (Ar), 145.9 (C=); IR (neat) 3065, 2953, 2789, 1753, 1718, 1701, 1685, 1630; EIMS 261 (M, 3), 134 (54), 91 (50), 73 (13); HRMS 261.1909, $C_{16}H_{27}NSi$ requires 261.1912.

Irradiation of *N*-Benzyl-*N*-methyl-*N*-[2-[(trimethylsilyl)methyl]buten-4-yl]amine (13). A N_2-purged solution of **13** (30 mg, 0.12 mmol), saturated with 9,10-dicyanoanthracene in MeCN (80 mL), was irradiated for 3.5 h (85% coversion of **13**). Concentration of the photolyzate followed by preparative TLC (50% ether−hexanes) separation afforded piperidenes **16** (3 mg, 14%) and **18** (7.3 mg, 34%).

18: ^{1}H NMR 1.99 (s, 3 H, NCH_3), 2.13 (ddd, *J* = 3.0, 11.1, and 12.8, 1 H, H-5), 2.28 (m, 3 H, H-4, H-3), 2.47 (m, 1 H, H-4), 2.79 (dd, *J* = 3.5, 10.9, 1 H, H-1), 3.09 (ddd, *J* = 2.1, 4.9, and 9.8, 1 H, H-5), 4.67 and 4.71 (s, 2 H, =CH_2 7.21−7.28 (m, 5 H, Ar); ^{13}C NMR 34.7 (C-4), 43.8 (NCH_3), 44.0 (C-2), 57.9 (C-5), 61.1 (C-1), 107.8 (=CH_2), 126.1, 126.9, 128.5 133.5 (Ar), 146.5 (C3); IR (neat) 2925, 2853, 1728, 1685, 1560; EIMS 187 (M, 3), 91 (100), 71 (17); HRMS 187.1368, $C_{13}H_{17}N$ requires 187.1361.

***N*-Benzyl-*N*-[(trimethylsilyl)methyl]-*N*-[2-[(trimethylsilyl)methyl]but-1-en-4-yl]amine (14).** A solution of **11** (2.0 g, 85 mmol), iodo(methyltrimethyl)silane (2.7 g, 127 mmol), and K_2CO_3 (4.6 g, 425 mmol) in MeCN (100 mL) was stirred at reflux for 12 h, diluted with water, and extracted with ether. The extracts were dried and concentrated in vacuo to give a residue which was subjected to column chromatography (Florisil, 10% ether−hexanes) to afford 1.30 g (46%) of the desired aminoallylsilane **14**: ^{1}H NMR 0.02, 0.08 (s, 18 H, $SiMe_3$), 1.49 (s, 2 H, CH_2Si), 2.51 (t, J = 7.7, 2 H, CH_2N), 3.54 (s, 2 H, NCH_2Ph), 4.53 (d, J = 8.7, 2 H, vinyl), 7.35 (m, 5 H, ArH); ^{13}C NMR −1.3 ($SiMe_3$), 27.1 (CH_2SiMe_3), 35.4 (CH_2CH_2N), 45.9 (NCH_2Si), 56.0 (CH_2N), 62.0 (NCH_2Ph), 107.7 (=CH_2), 126.6, 128.0, 128.7 (Ar), 140.4 (Ar, C-*ipso*), 146.1 (C=CH_2); IR 3064, 3026, 2953, 2786, 1631; CIMS 334 (M + 1, 0.4), 206 (100), 91 (70), 73 (31); HRMS 333.2305, $C_{18}H_{35}NSi_2$ requires 333.2308.

CTAN Oxidation of Aminoallylsilane 14. Preparation of 4-Methylidenepiperidine 16. A solution of aminoallylsilane **14** (20 mg, 0.006 mmol), and $(^nBu_4N)_2Ce(NO_3)_6$ (108 mg, 0.12 mmol) in MeCN (5 mL) was stirred at 25 °C for 4 h, diluted with water, and extracted with $CHCl_3$. The extracts were dried and concentrated in vacuo giving a residue which after preparative TLC (30% ether−hexanes) separation afforded 5 mg (45%) of **16**. ^{1}H NMR 2.24 (t, J = 5.5, 4 H, $(CH_2CH_2)_2N$), 2.44 (t, J = 5.5 H, 4 H, $(CH_2)_2N$), 3.51 (s, 2 H, NCH_2Ph), 7.30 (m, 5 H, Ar); ^{13}C NMR 34.5 (CH_2C=), 54.9 (CH_2CH_2N), 62.9 (NCH_2Ph), 107.5 (C=CH_2), 126.9, 128.1, 129.0 (Ar), 138.6 (Ar C-*ipso*), 146.7 (C=CH_2); IR 3066, 3027, 2939, 2902, 2792, 2755; EIMS 187 (62), 186 (40), 111 (32), 91 (100); HRMS 187.1358, $C_{13}H_{17}N$ requires 187.1361.

Photooxidation of 14. A N_2-purged solution of **14** (20 mg, 0.006 mmol) saturated with DCA in MeCN (80 mL) was irradiated (Uranium glass filtered-light) for 2 h (90% conversion of **14** by GLC). Workup followed by preparative TLC (30% ether−hexanes) separation afforded the cyclized product **16** (6 mg, 53%).

***N*-Benzyl-*N*-[(trimethylsilyl)methyl]-*N*-[4-[(trimethylsilyl)methyl]-pentenyl]amine (15).** A solution of **12** (350 mg, 1.3 mmol), K_2CO_3 (724 mg, 6.5 mmol), and iodomethane (430 mg, 1.95 mmol) in MeCN (10 mL) was heated at reflux for 12 h and then diluted with water. The resulting mixture was extracted with ether, and the combined ethereal extracts were dried and concentrated in vacuo to give a brown oil which was subjected to column chromatography (florisil, 10% ether−hexanes) to yield 331 mg (71%) of **15**. ^{1}H NMR −0.08 (s, 9 H, $SiMe_3$), 0.03 (s, 9 H, $SiMe_3$), 1.49 (s, 2 H, CH_2=CCH_2-$SiMe_3$), 1.58 (m, 2 H, NCH_2CH_2), 1.92 (m, 4 H, NCH_2SiMe_3, CH_2C=CH_2), 2.31 (t, J = 7.1 Hz, 2 H, CH_2CH_2N), 3.47 (s, 2 H, NCH_2Ph), 4.47, 4.53 (s, 2 H, *vinyl*), 7.20−7.26 (m, 5 H, Ar*H*); ^{13}C NMR −1.3 ($SiMe_3$), 25.5 (CH_2CH_2N), 27.0 (CH_2=CCH_2-$SiMe_3$), 36.0 (CH_2=CCH_2 CH_2), 46.1 (NCH_2SiMe_3), 57.1 (CH_2CH_2N), 62.2 (NCH_2Ph), 106.6 (CH_2=C), 126.6, 128.0, 128.7 (aromatic), 140.6 (aromatic, *C-ipso*), 147.8 (CH_2=*C*); IR (neat) 3066, 3028, 2953, 2788, 1420,1248, 855 cm^{-1}; EIMS 347 (6), 332 (15), 274 (86), 206 (39), 91 (85), 73 (100); HRMS 347.2484, $C_{20}H_{37}NSi$ requires 347.2465.

CTAN Oxidation of Aminoallylsilane 15. Preparation of 4-Methylidenehydroazepine 17. Application of the same procedure was used for transformation of **14** to **16**, starting with the silylamine **15** (35 mg, 0.1 mmol), and resulted in the formation of hydroazepine **17** (11 mg, 62%): ^{1}H NMR 1.68 (m, 2 H, H-5, H-5′), 2.35 (t, J = 6.2, 2 H, H-4, H-4′), 2.39 (t, J = 5.5, 2 H, H-2, H-2′), 2.63 (qt, J = 5.3, 4 H, H-6, H-6′, H-1, H-1′), 3.62 (s, 2 H, NCH_2Ph), 4.68 (s, 1 H, vinyl), 4.70 (d, J = 0.9, 2 H, vinyl), 7.15−7.35 (m, 5 H, Ar); ^{13}C NMR 27.4 (C-5), 35.2 (C-4), 36.5 (C-2), 55.1 (C-6), 56.9 (C-1), 62.1 (NCH_2Ph), 110.5 (CH_2=C), 126.8, 128.1, 128.8 (Ar), 139.5 (Ar-*ipso*), 150.5 (C-3); IR 3065, 3026, 1933, 2807, 1685, 1638; EIMS 201 (13), 91 (100); HRMS 201.1514, $C_{14}H_{19}N$ requires 201.1517.

Photooxidation of 15. A N_2-purged solution of **15** (35 mg, 0.1 mmol) and excess DCA in MeCN (100 mL) was irradiated (Uranium glass filtered-light) for 1.5 h (70% conversion of **15** by GLC). Concentration of the photolyzate followed by preparative TLC (50% ether−hexanes) separation afforded 7 mg of **17**.

(3*R*,4*S*)-2-[(Trimethylsilyl)methyl]-3-hydroxy-4-[*N*-[(trimethylsilyl)methyl]-*N*-benzylamino]-1-pentene (20). To a solution of 2-(bromoallyl)trimethylsilane (1.8 g, 9.3 mmol) in THF (10 mL) at −78 °C was added n-BuLi (1.4 M in hexane, 6.5 mL, 9.1 mmol). The resulting mixture was stirred at −78 °C for 1 h. To this mixture was added a solution of **19** (1.2 g, 4.9 mmol) in THF (10 mL) at −78 °C. The reaction mixture was warmed to 25 °C, stirred for 5 h, diluted with satd NH_4Cl, and extracted with CH_2Cl_2. The extracts were washed with brine, dried, and concentrated in vacuo, giving a residue which was subjected to column chromatography (silica gel, hexane:EtOAc, 100:1) to give 1.1 g (65%) of **20**: $[\alpha]^{29}_D$ +2.9° (*c* 0.41); ^{1}H NMR −0.03 (s, 9H, TMS), 0.04 (s, 9H, TMS), 0.93 (d, J = 6.8, 3H, CH_3), 1.10 and 1.39 (ABq, J = 13.9, 2H, CH_2TMS), 2.04 and 2.22 (ABq, J = 14.8, 2H, NCH_2), 2.78 (dq, J = 3.2, 6.8, 1H, CHCH$_3$), 3.50 and 3.76 (ABq, J = 14.2, 2H, CH_2Ph), 4.05 (d, J = 3.2, 1H, CHOH), 4.62 (s, 1H, C=CH_2), 4.86 (s, 1H, C=CH_2), 7.27 (m, 5H, Ar); ^{13}C NMR −1.4 (TMS), −1.3 (TMS), 7.2 (CHCH$_3$), 23.2 (CH$_2$TMS), 41.7 (NCH$_2$TMS), 57.8 (CHCH$_3$), 58.5 (NCH$_2$Ph), 76.5 (CHOH), 107.2 (C=CH$_2$), 126.8, 128.2, 128.6, and 140.5 (Ar), 148.8 (C=CH$_2$); IR 2951, 1241, 839; CIMS 364 (M + 1, 12), 348 (28), 288 (36), 220 (100), 91 (84); HRMS 364.2501, $C_{20}H_{38}NOSi_2$ requires 364.2492.

(3*R*,4*S*)-2-[(Trimethylsilyl)methyl]-3-acetoxy-4-[*N*-[(trimethylsilyl)methyl]-*N*-benzylamino]-1-pentene (21). A solution of **20** (287 mg, 0.79 mmol), Ac_2O (0.15 mL, 1.6 mmol), and 4-DMAP (2 mg) in pyridine (5 mL) was stirred for 1 h at 25 °C, diluted with $CHCl_3$, washed with brine and water, dried, and concentrated in vacuo, giving a residue which was subjected to column chromatography (silica gel, hexane:ether, 100:1) to give 214 mg (67%) of **21**: $[\alpha]^{25}_D$ +13.1° (*c* 0.36); ^{1}H NMR −0.06 (s, 9H, TMS), −0.02 (s, 9H, TMS), 0.93 (d, J = 6.8, 3H, CHCH$_3$), 1.03 and 1.23 (ABq, J = 14.3, 2H, CH_2TMS), 1.96 (s, 2H, NCH_2), 1.99 (s, 3H, COCH$_3$), 2.79 (dq, J = 3.5, 6.8, 1H, CHCH$_3$), 3.46 and 3.55 (ABq, J = 13.9, 2H, CH_2Ph), 4.53 (s, 1H, C=CH_2), 4.66 (s, 1H, C=CH_2), 5.18 (d, J = 3.5, 1H, CHOCH$_3$), 7.15−7.30 (m, 5H, Ar); ^{13}C NMR −1.4 (2TMS), 7.7 (CHCH$_3$), 21.4 (COCH$_3$), 22.9 (CH$_2$TMS), 40.4 (NCH$_2$TMS), 55.0 (CHCH3), 58.0 (NCH$_2$Ph), 78.3 (CHOCOCH$_3$), 108.6 (C=CH$_2$), 126.8, 128.2, 128.8, and 140.4 (Ar), 144.7 (C=CH$_2$), 169.7 (*C*OCH3); IR 2953, 1739, 1371, 1234, 843; EIMS 405 (1), 220 (100), 91 (86); HRMS 405.2500, $C_{22}H_{39}NO_2Si_2$ requires 405.2519.

CTAN Oxidation of Aminoallylsilane 21. Preparation of 4-Methylidenepiperidinyl Acetates 22 and 25. A solution of **21** (43.0 mg, 0.11 mmol) and CTAN (211 mg, 0.21 mmol) in dry MeCN (20 mL) was stirred for 5 h at 25 °C, diluted with isopropyl alcohol and $CHCl_3$, washed with brine and water, dried, and concentrated in vacuo, giving a residue which was subjected to column chromatography (silica gel, hexane:ether, 10:1) to give 21 mg (75%) of a mixture of **22** and **25** in a 1:1.2 ratio (^{1}H NMR). These substances were separated by preparative TLC (silica gel, 5:1 hexanes−ether).

22: R_f 0.20 (5:1 hexanes−EtOAc); $[\alpha]^{25}$ −0.11° (*c* 0.90); ^{1}H NMR 0.93 (d, J = 6.5, 3H, CHCH_3), 2.09 (s, 3H, COCH_3), 2.23−2.34 (m, 2H, CH_2CH$_2$N), 2.43 (ddd, J = 11.4, 4.6, 4.6, 1H, Hb, CH_2N), 2.56 (ddd, J = 11.4, 9.7, 4.4, 1H, Ha, CH_2N), 3.12 (dq, J = 4.9, 6.5, 1H, CHCH$_3$), 3.62 and 3.66 (ABq, J = 13.6, 2H, CH_2Ph), 4.80 (d, J = 1.1, 1H, C=CH_2), 4.85 (s, 1H, C=CH_2), 5.42 (d, J = 4.9, 1H, CHOCOCH$_3$), 7.29 (m, 5H, Ar); ^{13}C NMR 6.9 (CHCH$_3$), 21.1 (COCH$_3$), 32.9 (CH$_2$CH$_2$N), 46.9 (CH$_2C$H$_2$N), 56.6 (CHCH$_3$), 58.0 (NCH$_2$Ph), 74.9 (CHOCOCH$_3$), 108.1 (C=CH$_2$), 127.0, 128.3, 128.6, and 139.1 (Ar), 142.0 (C=CH$_2$), 170.0 (COCH$_3$); IR 2966, 2931, 2814, 1743, 1655; EIMS 259 (28), 244 (74), 216 (55), 199 (81), 91 (100), 83 (37); HRMS 259.1577, $C_{16}H_{21}NO_2$ requires 259.1572.

25: R_f 0.18 (5:1 hexanes−EtOAc); ^{1}H NMR 1.05 (d, J = 6.5, 3H, CHCH_3), 2.12 (s, 3H, COCH_3), 2.15−2.20 (m, 1H, CH_2-CH$_2$N), 2.34 (m, 1H, CH_2CH$_2$N), 2.43 (m, 1H, CH$_2C$H$_2$N), 2.70 (ddd, J = 11.3, 7.3, 3.7, 1H, CH$_2C$H$_2$N), 2.79 (dq, J = 5.7, 6.4, 1H, CHCH$_3$), 3.46 and 3.84 (ABq, J = 13.7, 2H, CH_2Ph), 4.83 (s, 1H, C=CH_2), 4.87 (s, 1H, C=CH_2), 5.00 (d, J = 5.7, 1H, CHOCOCH$_3$), 7.20−7.34 (m, 5H, Ar); ^{13}C NMR 12.2 (CHCH$_3$), 21.2 (COCH$_3$), 31.6 (CH$_2$CH$_2$N), 49.2 (CH$_2C$H$_2$N), 57.5 (CH$_2$-Ph), 58.8 (CHCH$_3$), 77.0 (CHOCOCH$_3$), 110.4 (C=CH$_2$), 126.9,

128.2, 128.6, and 139.4 (Ar), 142.6 (*C*=CH_2), 170.3 (*C*OCH_3); EIMS 259 (5), 244 (28), 199 (32), 91 (100); HRMS 259.1568, $C_{16}H_{21}NO_2$ requires 259.1572.

Enantiomeric Purity Determination of 22. Preparation of Alcohol 23 and Mosher Ester 24. A solution of **22** (11 mg, 0.04 mmol) and KCN (1.3 mg, 0.02 mmol) in MeOH (2 mL) was stirred for 12 h at 25 °C, diluted with $CHCl_3$, washed with brine and water, dried, and concentrated in vacuo to give 12 mg (100%) of **23** which was used without further purification: ^{1}H NMR 1.08 (d, J = 6.5, 3H, CH_3), 2.08 (m, 2H, C$H_2$$CH_2$N), 2.33 (m, 1H, Hb, C$H_2$N), 2.63 (m, 1H, C$H$$CH_3$), 2.67 (m, 1H, Ha, C$H_2$N), 3.25 and 3.82 (ABq, J = 13.4, 2H, CH_2Ph), 3.97 (br d, J = 2.1, 1H, CHOH), 4.72 (s, 1H, C=CH_2), 4.81 (s, 1H, C=CH_2), 7.21 (m, 5H, Ar); ^{13}C NMR 12.0 (CH_3), 31.4 (*C*$H_2$$CH_2$N), 50.4 ($CH_2$*C*$H_2$N), 57.5 (*C*$H_2$Ph), 60.8 (*C*$HCH_3$), 75.2 (CHOH), 107.9 (C=*C*H_2), 127.0, 128.3, 128.7, and 139.3 (Ar), 147.4 (*C*=CH_2).

A solution of **23** (13 mg, 0.06 mmol), the Mosher acid (*R*)-MTPAcOH (70 mg, 0.30 mmol), DCC (80 mg, 0.40 mmol), and 4-DMAP (15 mg, 0.12 mmol) in CH_2Cl_2 (3 mL) was stirred at 25 °C for 12 h and concentrated in vacuo, giving a residue which was subjected to column chromatography (silica gel, hexane:ether, 10:1) to give (*R*)-Mosher ester **24**. The ee of **22** was determined to be ca. 4% by ^{1}H NMR analysis of **24**. Characteristic peaks in the ^{1}H and ^{13}C NMR spectra are as follows: ^{1}H NMR 0.86 (d, J = 6.6, 3H, CHCH_3), 1.01 (d, J = 6.6, 3H, CHCH_3), 3.56 (s, 3H, OCH_3), 3.57 (s, 3H, OCH_3), 4.77 (s, 1H, C=CH_2), 4.86 (s, 1H, C=CH_2), 4.92 (s, 1H, C=CH_2), 4.94 (s, 1H, C=CH_2), 5.64 (d, J = 4.1, 2H, CHOCO); ^{13}C NMR 8.5 (CH*C*H_3), 8.6 (CH*C*H_3), 109.8 (C=*C*H_2), 110.1 (C=*C*H_2); IR 2935, 1745, 1714, 1665, 1493, 1248, 1181; EIMS 433 (M, 16), 418 (73), 216 (50), 189 (84), 126 (100); HRMS 433.1866, $C_{24}H_{26}NO_3F_3$ requires 433.1865.

Enantiomeric Purity Determination of 25. Preparation of Alcohol 26 and Mosher Ester 27. By the procedure used to convert **22** to **23**, the ester **25** was transformed quantitativly to **26**: ^{1}H NMR 0.90 (d, J = 6.7, 3H, CHCH_3), 2.06 (m, 1H, C$H_2$$CH_2$N), 2.47 (m, 3H, C$H_2$$CH_2$N), 2.88 (dq, J = 3.9, 6.7, 1H, C$H$$CH_3$), 3.48 and 3.56 (ABq, J = 13.2, 2H, CH_2Ph), 3.69 (d, J = 3.9, 1H, CHOH), 4.79 (s, 1H, C=CH_2), 4.80 (s, 1H, C=CH_2), 7.26 (m, 5H, Ar); ^{13}C NMR 9 (CH_3), 30 (*C*$H_2$$CH_2$N), 46 ($CH_2$*C*$H_2$N), 58 (*C*$H_2$Ph), 59.8 (*C*$HCH_3$), 75.6 (CHOH), 110.6 (C=*C*H_2), 127.1, 128.3, 128.7, and 138.9 (Ar), 145.1 (*C*=CH_2).

A mixture of **26** (22 mg, 0.20 mmol), 4-DMAP (2 mg), Et_3N (0.03 mL, 0.20 mmol), and freshly prepared (see above) (*S*)-MTPAcCl (5 mg, 0.20 mmol) in CH_2Cl_2 (5 mL) was stirred for 12 h at 25 °C, diluted with $CHCl_3$, washed with brine and water, dried, and concentrated in vacuo, giving a residue which was subjected to column chromatography (silica gel, hexane: ether, 5:1) to give 34 mg (77%) of (*S*)-Mosher ester **27**. The ee of **25** was determined to be ca. 24% by ^{1}H and ^{13}C NMR spectral analysis **27**: $[\alpha]^{30}$ −10.4° (*c* 1.39); ^{1}H NMR 1.00 (d, J = 6.8, 3H, CHCH_3, major), 1.02 (d, J = 7.4, 3H, CHCH_3), 2.40 (m, 4H, CH_2CH_2), 3.09 (m, 1H, C$H$$CH_3$), 3.13−3.19 (m, 1H, C$H$$CH_3$), 3.50 and 3.66 (ABq, J = 13.8, 2H, CH_2Ph), 3.55 (s, 3H, OCH_3), 5.00 (br s, 1H, C=CH_2), 5.02 (s, 1H, C=CH_2), 5.23 (d, J = 6.0, 1H, CHOCO, minor), 5.24 (d, J = 5.9, 1H, CHOCO, major), 7.30 (m, 10H, Ar); ^{13}C NMR 9.5 (CH*C*H_3, major), 9.9 (CH*C*H_3, minor), 30.7 (*C*$H_2$$CH_2$N, minor), 30.8 (*C*$H_2$$CH_2$N, major), 46.6 ($CH_2$*C*$H_2$N, major), 46.7 ($CH_2$*C*$H_2$N, minor), 55.4 (*C*$HCH_3$, major), 55.5 (*C*$HCH_3$, minor), 57.3 (*C*HOCO, minor), 57.7 (*C*HOCO, major), 57.9 (*C*H_2Ph, minor), 58.0 (*C*H_2Ph, major), 79.8 (OCH_3), 114.3 (C=*C*H_2, major), 114.5 (C=*C*H_2, minor), 122.0 (*C*=CH_2, minor), 124.8 (*C*=CH_2, major), 126.8, 126.9, 127.4, 127.5, 128.1, 128.2, 128.4, 128.5, 129.4, and 129.5 (aromatic), 132.4, 139.2, 139.3, 140.4, 140.7, 141.1, and 141.4 (quart), 165.8 (C=O, minor), 166.0 (C=O, major); IR 2955, 1743, 1455, 1261, 1177; EIMS 433 (12), 418 (64), 216 (42), 146 (7), 91 (100); HRMS 433.1859, $C_{24}H_{26}NO_3F_3$ requires 433.1865.

(2*S*)-2-[*N*-Benzoyl-*N*-[(trimethylsilyl)methyl]amino]-1-propanol (31). A solution of amine **30**[16] (4.74 g, 29.4 mmol), triethylamine (6.14 mL, 44.1 mmol), and benzoyl chloride (3.76 mL, 32.3 mmol) in CH_2Cl_2 (100 mL) was stirred at 25 °C for 2 h and diluted with water. The CH_2Cl_2 layer was washed with brine and concentrated in vacuo to give a residue which was subjected to column chromatography (silica gel, 3:1 hexanes/EtOAc) to give 5.94 g (76%) of **31**. $[\alpha]^{26}$ +0.60° (*c* 7.54, $CHCl_3$); ^{1}H NMR 0.12 (s, 9H, TMS), 0.98 (d, J = 5.0, 3H, CHCH_3), 2.44 and 2.78 (ABq, J = 14.4, 2H, CH_2TMS), 3.26 (s, 1H, C$H$$CH_3$), 3.49 (s, 1H, C$H_2$OH), 3.89 (s, 1H, C$H_2$OH), 7.31 (s, 5H, Ar); ^{13}C NMR −0.8 (TMS), 15.0 (CH*C*H_3), 32.0 (*C*H_2TMS), 56.1 (C*H*CH_3), 63.3 (*C*H_2OH), 126.7, 128.3, 129.0 and 137.0 (Ar), 172.3 (C=O); IR 3351, 2951, 1596, 1456; EIMS 265 (8), 264 (37), 250 (33), 105 (100), 77 (35); HRMS 265.1491, $C_{14}H_{23}NO_2$-Si requires 265.1498.

(2*S*)-2-[*N*-Benzoyl-*N*-[(trimethylsilyl)methyl]amino]-propionaldehyde (32). To a solution of DMSO (1.49 mL, 35.1 mmol) in 15 mL of CH_2Cl_2 at −78 °C was added oxalyl chloride (0.92 mL, 10.5 mmol), and the resulting solution was stirred at −78 °C for 1 h. After addition of alcohol **31** (1.86 g, 7.0 mmol) in CH_2Cl_2 (6 mL), the mixture was stirred at −78 °C for 2 h, diluted with triethylamine (4.89 mL, 35.1 mmol) and stirred at 25 °C for 2 h, diluted with water, and extracted with CH_2Cl_2. The extracts were washed with brine, dried, and concentrated in vacuo to give 1.18 g (98%) of aldehyde **32** which was used without further purification owing to its instability. $[\alpha]^{26}$ −17.2° (*c* 1.90, $CHCl_3$); ^{1}H NMR (mixture of rotamers A/B = 3:1) −0.08 (s, 9H, TMS, B), 0.05 (s, 9H, TMS, A), 1.21 (s, 3H, CHCH_3, A), 1.39 (s, 3H, CHCH_3, B), 2.36 and 2.68 (ABq, J = 13.8, 2H, CH_2TMS, A), 2.75 and 3.01 (ABq, J = 13.8, 2H,CH_2TMS, B), 3.39 (s, 1H, C$H$$CH_3$, B), 4.24 (s, 1H, C$H$$CH_3$, A), 7.26 (m, 5H, Ar, A and B), 9.50 (m, 1H, CHO, A and B); ^{13}C NMR −1.4 (TMS, B), −1.1 (TMS, A), 11.1 (*C*H_3, B), 12.5 (*C*H_3, A), 35.7 (*C*H_2TMS, A), 41.6 (*C*H_2TMS, B), 63.2 (*C*H, B), 64.0 (*C*H, A), 126.1, 126.5, 128.2, 128.5, 129.4, 135.5 and 136.3 (Ar, A and B), 171.8 (C=O), 196.6 (CHO, B), 199.3 (CHO, A); IR 2948, 1727, 1622, 1447; EIMS 263 (11), 262 (44), 248 (32), 234 (27), 105 (100); HRMS 263.1353, $C_{14}H_{21}NO_2Si$ requires 263.1342.

Enantiomeric Purity Determination of Aldehyde 32. Preparation of Alcohol 30 and Its Mosher Ester. To a solution of crude aldehyde **32** (56 mg, 0.21 mmol) in Et_2O (2 mL) at 0 °C was added $LiAH_4$ (24 mg, 0.63 mmol). The mixture was stirred at 25 °C for 6 h, diluted with H_2O, and extracted with Et_2O. The extracts were washed with brine, dried, and concentrated in vacuo to give 41 mg (76%) of the known[16] 2-[*N*-benzyl-*N*-[(trimethylsilyl)methyl]amino]propan-1-ol. This substance was esterified with (*R*)-MTPAcCl (Aldrich) to provide the Mosher ester which ^{1}H NMR analysis showed to be >90% diastereomerically pure.

(3*R*,4*S*)- and (3*S*,4*S*)-2-[(Trimethylsilyl)methyl]-3-hydroxy-4-[*N*-[(trimethylsilyl)methyl]-*N*-benzoylamino]-1-pentene (33 and 36). To a solution of (2-bromoallyl)-trimethylsilane (1.63 g, 8.44 mmol) in THF (5 mL) was added *tert*-BuLi (1.5 M in pentane, 5.4 mL, 8.16 mmol) at −78 °C dropwise via a syringe. After stirring for 1 h, aldehyde **32** (0.74 g, 2.81 mmol) was added, and the mixture was stirred at −78 °C for 2 h, warmed to 25 °C, diluted with water, and extracted with CH_2Cl_2. The extracts were washed with brine, dried, and concentrated in vacuo to give a residue which was subjected to flash column chromatography (silica gel, 4:1 hexanes−EtOAc) to give 0.55 g (52%) of **33** and 0.07 g (6%) of **36**.

33: $[\alpha]^{25}$ +0.68° (*c* 7.51, $CHCl_3$); ^{1}H NMR −0.13 (s, 9H, TMS), 0.12 (s, 9H, TMS), 0.64 and 1.04 (ABq, J = 14.1, 2H, CH_2TMS), 1.12 (d, J = 6.3, 3H, CH_3), 2.69 and 3.06 (ABq, J = 14.5, 2H, NCH_2), 3.79 (m, 2H, CH and CHOH), 4.57 (s, 1H, =CH_2), 4.79 (s, 1H, =CH_2), 7.30 (m, 5H, Ar); ^{13}C NMR (mixture of rotamers A/B = 10:1) −2.6 (TMS, B), −1.6 (TMS, A), −0.7 (TMS, A), 0.2 (TMS, B), 12.2 (*C*H_3, A), 13.8 (*C*H_3, B), 21.8 (*C*H_2-TMS, A), 23.6 (*C*H_2TMS, B), 34.2 (N*C*H_2, A), 37.2 (N*C*H_2, B), 56.1 (*C*H, A), 59.0 (*C*H, B), 78.4 (*C*HOH, A), 78.9 (*C*HOH, B), 108.7 (=*C*H_2, A and B), 120.2, 126.5, 128.1, 128.5, 129.0, 132.3 and 137.3 (Ar, A and B), 147.4 (*C*=, A and B), 171.1 (C=O); IR 3351, 3074, 2951, 2362, 1598; CIMS 378 (M + 1, 1), 234 (91), 105 (100); HRMS 378.2273, $C_{20}H_{36}NO_2Si_2$ requires 378.2284.

36: $[\alpha]^{23}$ +4.47° (*c* 0.75, $CHCl_3$); ^{1}H NMR −0.10 (s, 9H, TMS), 0.16 (s, 9H, TMS), 1.00 (d, J = 6.2, 3H, CH_3), 1.13 and 1.19 (ABq, J = 14.3, 2H, CH_2TMS), 2.53 and 2.84 (ABq, J =

14.5, 2H, NCH_2), 3.81−3.87 (m, 2H, CHCH$_3$ and CHOH), 4.65 (s, 1H, =CH_2), 4.79 (s, 1H, =CH_2), 7.35 (m, 5H, Ar); ^{13}C NMR (mixture of rotamers A/B = 10:1) −2.3 (TMS, B), −1.6 (TMS, A), −0.9 (TMS, A), −0.4 (TMS, B), 15.2 (CH_3, B), 15.4 (CH_3, A), 20.9 (CH_2TMS, A), 26.0 (CH_2TMS, B), 32.3 (NCH_2, A), 33.6 (NCH_2, B), 57.4 (CH, A), 58.1 (CH, B), 75.8 (CHOH, B), 76.4 (CHOH, A), 111.3 (=CH_2, A and B), 126.3, 126.8, 128.0, 128.1, 128.3, 128.7 and 137.0 (Ar), 146.3 (C=, A and B), 172.5 (C=O); IR 3336, 3070, 2954, 1597; EIMS 377 (0.5), 234 (83), 105 (100), 77 (40); HRMS 377.2196, $C_{20}H_{35}NO_2Si_2$ requires 377.2206.

Enantiomeric Purity Determination of Alcohol 33. Preparation of Mosher Ester 35. A mixture of **33** (24 mg, 0.064 mmol), 4-DMAP (2 mg, 0.016 mmol), (*R*)-MTPAcCl (32 mg, 0.127 mmol) in CH_2Cl_2 (3 mL), and Et_3N (0.018 mL, 0.127 mmol) was stirred for 12 h at 25 °C, diluted with water, and extracted with CH_2Cl_2. The extracts were washed with brine, dried, and concentrated in vacuo to give the Mosher ester **35** as a 75:25 mixture (50 ee%) based upon ^{1}H NMR integration. Subjection to column chromatography (silica gel, 7:1 hexane/EtOAc) did not alter the diastereomer ratio and gave pure **35** Mosher ester (35 mg, 92%). ^{1}H NMR (3:1 mixture of diastereomers, A/B) −0.06 (s, 9H, TMS, A and B), 0.04 (s, 9H, TMS, B), 0.08 (s, 9H, TMS, A), 0.41 and 1.06 (ABq, J = 14.4, 2H, CH_2TMS, A), 0.51 and 1.13 (ABq, J = 14.4, 2H, CH_2TMS, B), 1.15 (d, J = 6.9, 3H, CH_3, B), 1.20 (d, J = 6.9, 3H, CH_3, A), 2.41 and 2.83 (ABq, J = 14.6, 2H, NCH_2, A), 2.43 and 2.87 (ABq, J = 14.6, 2H, NCH_2, B), 3.41 (s, 3H, OCH$_3$, A), 3.50 (s, 3H, OCH$_3$, B), 4.15 (m, 1H, CHCH$_3$, A and B), 4.56 (s, 1H, =CH_2, A), 4.60 (s, 1H, =CH_2, B), 4.66 (s, 1H, =CH_2, A and B), 5.02 (s, 1H, CHOCO, A), 5.14 (s, 1H, CHOCO, B), 7.38 (m, 10H, Ar, A and B); ^{13}C NMR −1.5 (TMS, A), −1.2 (TMS, B), −1.0 (TMS, A), −0.7 (TMS, B), 12.5 (CH_3, A), 12.7 (CH_3, B), 22.4 (CH_2TMS, A and B), 33.8 (NCH_2, A and B), 54.8 (OCH$_3$, A), 55.1 (CH, A), 55.2 (OCH$_3$, B), 55.3 (CH, B), 81.7 (CHOCO, B), 82.4 (CHOCO, A), 110.0 (CH_2=, A), 110.7 (CH_2=, B), 122.0 (COCH$_3$, A and B), 124.8 (CF$_3$, A and B), 126.5, 127.7, 127.9, 128.4, 128.6, 128.8, 129.5, 129.7, 129.8, 131.2, 131.6, 136.8 (Ar, A and B), 142.2 (=C, A), 142.5 (=C, B), 165.0 (CHOCO, A and B), 171.2 (NC=O, A and B); IR 2967, 1745, 1629; EIMS 593 (0.8), 360 (20), 234 (64), 130 (25), 105 (100); HRMS 593.2601, $C_{30}H_{42}NO_4F_3Si_2$ requires 593.2604.

(3*R*,4*S*)-2-[(Trimethylsilyl)methyl]-3-acetoxy-4-[*N*-[(trimethylsilyl)methyl]-*N*-benzoylamino]-1-pentene (34). A solution of allylic alcohol **33** (0.28 g, 0.74 mmol), pyridine (3 mL), acetic anhydride (0.38 g, 3.72 mmol), and 4-DMAP (3 mg) was stirred at 25 °C for 14 h, diluted with water, and extracted with CH_2Cl_2. The extracts were dried and concentrated in vacuo to give 0.30 g (95%) of **34**. This material was used without further purification. [α]^{22} −1.08° (*c* 7.91, CHCl$_3$); ^{1}H NMR −0.10 (s, 9H, TMS), 0.12 (s, 9H, TMS), 0.72 and 1.02 (ABq, J = 14.2, 2H, CH_2TMS), 1.18 (d, J = 6.8, 3H, CHCH_3), 2.03 (s, 3H, COCH$_3$), 2.55 and 2.94 (ABq, J = 14.6, 2H, NCH_2), 4.07 (dq, J = 6.8, 4.0, 1H, CHCH$_3$), 4.61 (s, 1H, =CH_2), 4.75 (s, 1H, =CH_2), 5.08 (d, J = 4.0, 1H, CHOCOCH$_3$), 7.35 (m, 5H, Ar); ^{13}C NMR −1.5 (TMS), −0.7 (TMS), 13.5 (CHCH$_3$), 21.2 (COCH$_3$), 21.7 (CH_2TMS), 34.0 (NCH$_2$), 54.8 (CHCH$_3$), 79.1 (CHOCOCH$_3$), 110.9 (=CH_2), 126.6, 128.6, 129.3 and 136.9 (Ar), 142.4 (C=), 169.3 (COCH$_3$), 171.5 (C=O); IR 2952, 1749, 1629; EIMS 419 (0.4), 234 (55), 105 (100); HRMS 419.2298, $C_{22}H_{37}NO_3Si_2$ requires 419.2312.

(3*S*,4*S*)-2-[(Trimethylsilyl)methyl]-3-acetoxy-4-[*N*-[(trimethylsilyl)methyl]-*N*-benzoylamino]-1-pentene (37). To a solution of allylic alcohol **36** (0.14 g, 0.37 mmol), pyridine (2 mL), acetic anhydride (0.19 g, 1.86 mmol), and 4-DMAP (3 mg) was stirred at 25 °C for 16 h, diluted with water, and extracted with CH_2Cl_2. The extracts were dried and concentrated in vacuo to give a residue which was subjected to chromatographic separation (silica gel, 9:1 hexanes/EtOAc) to afford 0.13 g (85%) of **37**: [α]^{24} −2.65° (*c* 3.75, CHCl$_3$); ^{1}H NMR −0.14 (s, 9H, TMS), 0.13 (s, 9H, TMS), 1.19 (d, J = 6.8, 3H, CHCH_3), 1.01 and 1.13 (ABq, J = 14.5, 2H, CH_2TMS), 2.08 (s, 3H, COCH$_3$), 2.36 and 2.85 (ABq, J = 14.6, 2H, NCH_2), 4.06 (dq, J = 9.7, 6.8, 1H, CHCH$_3$), 4.75 (s, 1H, =CH_2), 4.94 (s, 1H, =CH_2), 5.15 (d, J = 9.7, 1H, CHOCOCH$_3$), 7.31 (m, 5H, Ar); ^{13}C NMR −1.2 (TMS), −0.7 (TMS), 15.7 (CHCH$_3$), 20.4 (CH_2-TMS), 21.4 (COCH$_3$), 33.0 (NCH$_2$), 55.6 (CHCH$_3$), 78.1 (CHOCOCH$_3$), 114.9 (=CH_2), 126.9, 128.5, 129.2 and 137.3 (Ar), 142.0 (C=), 169.3 (COCH$_3$), 172.4 (NC=O); IR 2949, 1739, 1625; EIMS 419 (0.2), 234 (67), 105 (100), 7 (50); HRMS 419.2303, $C_{22}H_{37}NO_3Si_2$ requires 419.2312.

CAN Oxidation of 34. Preparation of *trans*-4-Methylidene Acetate 38. A solution of CAN (0.51 g, 0.93 mmol) and allylsilane **34** (0.13 g, 0.31 mmol) in MeCN (3 mL) was stirred for 20 h at 25 °C, diluted with 2-propanol and water, and extracted with CH_2Cl_2. The extracts were washed with brine, dried, and concentrated in vacuo to give a residue which was subjected to column chromatography (silica gel, 7:1 hexanes/EtOAc) to provide 0.041 g (48%) of **38**. [α]^{22} −1.91° (*c* 0.77, CHCl$_3$) ^{1}H NMR (CD$_3$CN at 70 °C) 1.18 (d, J = 7.1, 3H, CHCH_3), 1.99 (s, 3H, COCH$_3$), 2.19 (m, 1H, CH_2CH$_2$), 2.52 (td J = 13.4, 5.8, 1H, CH_2CH$_2$), 3.00 (m, 1H, CH_2N), 4.15 (m, 1H, CHCH$_3$), 4.46 (m, 1H, CH_2N), 4.96 (s, 1H, CHOCOCH$_3$), 5.10 (t, J = 1.7, 1H, =CH_2), 5.14 (t, J = 1.7, 1H, =CH_2), 7.41 (m, 5H, Ar); ^{13}C NMR (CD$_3$CN) 15.0 (CHCH$_3$), 21.2 (COCH$_3$), 29.9 (CH_2), 37.3 (CH$_2$), 54.9 (CH), 76.4 (CHO), 116.6 (=CH_2), 126.5, 128.5, 129.6 and 136.4 (Ar), 139.2 (C=), 169.5 (COCH$_3$), 171.5 (NC=O); IR 2978, 1726, 1632, 1415; EIMS 273 (14), 213 (56), 105 (100), 77 (54); HRMS 273.1378, $C_{16}H_{19}NO_3$ requires 273.1365.

CAN Oxidation of 37. Preparation of *cis*-4-Methylidene Acetate 39. A solution of CAN (130 mg, 0.236 mmol) and allylsilane **37** (33 mg, 0.079 mmol) in MeCN (3 mL) was stirred for 22 h at 25 °C, diluted with 2-propanol and water, and extracted with CH_2Cl_2. The extracts were washed with brine, dried, and concentrated in vacuo to give a residue which was subjected to column chromatography (silica gel, 7:1 hexanes/EtOAc) to provide 14 mg (67%) of **39**. [α]^{24} −2.26° (*c* 0.60, CHCl$_3$); ^{1}H NMR (C$_6$D$_6$, at 70 °C) 0.95 (d, J = 6.7, 3H, CHCH_3), 1.57 (s, 3H, COCH$_3$), 1.91 (m, 1H, CH_2), 1.99 (td J = 12.8, 5.5, 1H, CH_2), 2.66 (td, J = 12.8, 3.5, 1H, CH_2N), 3.03 (m, 1H, CH_2N), 4.75 (d, J = 1.4, 1H, =CH_2), 4.86 (d, J = 1.4, 1H, =CH_2), 4.86 (m, 1H, CHCH$_3$), 5.47 (d, J = 5.3, 1H, CHO), 7.21 (m, 5H, Ar); ^{13}C NMR (C$_6$D$_6$, at 70 °C) 11.1 (CHCH$_3$), 20.0 (COCH$_3$), 33.9 (CH_2), 39.9 (CH_2N), 51.1 (CH), 73.1 (CHO), 108.5 (=CH_2), 128.6 128.7, 129.6 and 137.3 (Ar), 140.8 (C=), 168.4 (COCH$_3$), 170.7 (NC=O); IR 2948, 1740, 1629; EIMS 273 (8), 213 (30), 105 (100); HRMS 273.1366, $C_{16}H_{19}NO_3$ requires 273.1365.

Enantiomeric Purity Determination of 38. Preparation of Alcohol 26 and Mosher Ester 27. To a solution of acetate **38** (70 mg, 0.256 mmol) in anhydrous Et_2O (3 mL) at 0 °C was added LAH (29 mg, 0.769 mmol). The resulting mixture was allowed to warm to 25 °C and stirred for 4 h, diluted with H_2O, and extracted with Et_2O. The organic extracts were washed with brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo to give 50 mg (90%) of alcohol **26**. The spectroscopic data for this compound were identical with those reported above.

A solution of **26** (12 mg, 0.055 mmol), 4-DMAP (2 mg), triethylamine (0.015 mL, 0.110 mmol), and (*S*)-MTPAcCl (28 mg, 0.110 mmol) in CH_2Cl_2 (3 mL) was stirred at 25 °C for 18 h, diluted with H_2O, and extracted with CH_2Cl_2. The extracts were washed with 5% HCl, saturated aqueous $NaHCO_3$ and H_2O, dried, and concentrated in vacuo to provide 24 mg (100%) of the (*S*)-Mosher ester **27** as a 75:25 mixture (50% ee) based upon ^{1}H NMR integration. Subjection to column chromatography (silica gel, 8:1 hexane/EtOAc) did not alter the diastereomer ratio and gave pure **27** (22 mg, 92%). [α]^{28} 23.7° (*c* 0.88, CHCl$_3$). The spectroscopic properties of this subtance were the same as those reported above.

Enantiomeric Purity Determination of 39. Preparation of Alcohol 23 and Mosher Ester 24. To a solution of acetate **39** (9 mg, 0.04 mmol) in Et_2O (2 mL) at 0 °C was added $LiAlH_4$ (6 mg, 0.15 mmol). The mixture was stirred for 4 h at 25 °C, diluted with H_2O, and extracted with Et_2O. The extracts were washed with brine, dried, and concentrated in vacuo to give 7 mg (88%) of alcohol **23**. The spectroscopic data for this compound were identical with those reported above.

A solution of **23** (5 mg, 0.02 mmol), 4-DMAP (1 mg), triethylamine (0.006 mL, 0.046 mmol), and (*S*)-MTPAcCl (12

mg, 0.046 mmol) in CH_2Cl_2 (3 mL) was stirred at 25 °C for 18 h, diluted with H_2O, and extracted with CH_2Cl_2. The extracts were washed with 5% HCl, saturated aqueous $NaHCO_3$, and H_2O, dried, and concentrated to provide 10 mg of the Mosher ester **24** as a 75:25 mixture of diastereomers (50% ee) based upon ^{1}H NMR integration. Subjection of this material to column chromatography (silica gel, 6:1 hexane/EtOAc) did not effect diastereomeric ratios and gave **24** (8 mg, 85%). The spectroscopic properties of this substance were the same as those reported above.

(4*S*)-*N*-Benzyl-*N*-[1(*Z*)-(trimethylsilyl)-1-penten-4-yl]-amine (40). (4*S*)-*N*-(*p*)-toluenesulfonyl)-*N*-[1(*Z*)-(trimethylsilyl)-1-penten-4-yl]amine (0.65 g, 2.1 mmol) and K_2CO_3 (1.46 g, 10.6 mmol) in DMF (20 mL) was stirred at 25 °C for 15 min. To this mixture was added benzyl bromide (0.47 g, 2.7 mmol) and DMF (5 mL), and the resulting mixture was stirred at 25 °C for 12 h and concentrated in vacuo. The residue was partitioned between water and CH_2Cl_2, and the CH_2Cl_2 phase was dried and concentrated in vacuo to give 0.76 g (92%) of the *N*-benzyl analogue which was used without further purification: $[\alpha]^{25}$ +12.9° (*c* 0.007, $CHCl_3$). ^{1}H NMR −0.08 (s, 9 H, $SiMe_3$), 0.98 (d, *J* = 6.9, 3 H, NCH), 2.00 (m, 2 H, =CCH_2), 2.41 (s, 3 H, CH_3), 3.98 (m, 1 H, $NCHCH_3$), 4.21 and 4.53 (ABq, *J* = 16.0, 2 H, NCH_2Ph), 5.40 (d, *J* = 14.1, 1 H, CH=CH), 5.99 (m, 1 H, CH=CH), 7.35 (m, 9 H, Ar), 7.68 (m, 1 H, Ar); ^{13}C NMR −0.1 ($SiMe_3$), 17.8 ($NCHCH_3$), 21.5 (CH_3), 39.8 (=CCH_2), 47.3 (NCH_2Ph), 54.3 ($NCHCH_3$), 127.1, 127.5, 128.4, 129.6 (Ar), 131.5 (CH=$CHSiMe_3$), 138.2, 138.4 (Ar-*ipso*), 143.0 (Ar-*ipso*), 144.4 (CH=$CHSiMe_3$); IR 3030, 2954, 1495, 1455, 1388; CIMS 402 (M + 1, 2), 288 (100); HRMS 402.1959, $C_{22}H_{32}NOSSi$ requires 402.1950.

A solution of this substance (750 mg, 1.88 mmol) in anhydrous MeOH (100 mL) containing 6% Na/Hg (7.2 g) and Na_2HPO_4 (1.6 g, 7.62 mmol) was stirred at reflux for 12 h, poured into water, decanted, and extracted with CH_2Cl_2. The extracts were washed with aqueous satd $NaHCO_3$ and brine, dried, and concentrated in vacuo to provide a residue which was subjected to flash column chromatography (silica, 20% ether−hexanes) to give **40** (371 mg, 80%): $[\alpha]^{25}$ −17.7° (*c* 0.025, $CHCl_3$); ^{1}H NMR 0.10 (s, 9 H, $SiMe_3$), 1.08 (d, *J* = 6.3, 3 H, $NCHCH_3$), 1.58 (br singlet, 1 H, NH), 2.26 (m, 2 H, $NCHCH_2$), 2.75 (tq, *J* = 6.3, 6.3, 1 H, NCH), 3.67 and 3.89 (ABq, *J* = 13.0, 2 H, NCH_2Ph), 5.57 (d, *J* = 14.4, 1 H, Me_3SiCH=CH), 6.26 (ddd, *J* = 7.2, 7.2, 14.4, 1 H, Me_3SiCH=CH), 7.30 (m, 5 H, Ar); ^{13}C NMR 0.2 ($SiMe_3$), 20.2 (CH_3), 40.7 ($NCHCH_2$), 51.4 (NCH_2Ph), 52.6 (NCH), 126.8, 128.0, 128.4 (Ar), 131.4 (CH=CH), 140.7 (Ar-*ipso*), 145.6 (CH=CH); IR 3085, 3062, 3027, 2958, 2896, 1605; CIMS 338 (M + 1, 9), 134 (100); HRMS 248.1830, $C_{15}H_{26}NSi$ requires 248.1835.

Enantiomeric Purity Determination of 40. Preparation of Mosher Amide 41. A mixture of (*R*)-MTPAcCl (prepared by refluxing 150 mg of (*R*)-MTPAcOH and excess thionyl chloride followed by removal of excess thionyl chloride in vacuo), **40** (30 mg, 0.12 mmol), 4-DMAP (30 mg, 0.24 mmol), and pyridine (0.5 mL) in CCl_4 (3 mL) was stirred at reflux for 12 h, cooled to 25 °C, diluted with satd $NaHCO_3$, and extracted with ether. The extracts were washed with brine, dried, and concentrated in vacuo. The resulting residue was subjected to preparative TLC (50% ether−hexanes) to give 20 mg (33%) of the desired Mosher amide **41**. The amine **40** was shown to have an ee >99% by capillary GC and 400 MHz NMR analysis of **41**: ^{1}H NMR (2:1 mixture of rotamers A and B) −0.02 (s, 9 H, $SiMe_3$, A) 0.02 (s, 9 H, $SiMe_3$, B), 0.26 (d, *J* = 6.7, 3 H, $NCHCH_3$, A), 1.18 (d, *J* = 6.8, 3 H, $NCHCH_3$, B), 2.10−2.25 (m, 2 H, $NCHCH_a$, A and B), 2.45 (m, 1 H, $NCHCH_3$, B), 2.74 (m, 1 H, $NCHCH_3$, B), 3.49 (m, 1 H, $NCHCH_b$, A), 3.74 (m, 6 H, OCH_3, A and B), 4.23 (m, $NCHCH_3$, 1 H, A), 4.84, 4.22 (ABq, *J* = 15.4, 2 H, NCH_2Ph, A), 4.72, 4.25 (AB, *J* = 15, 2 H, NCH_2Ph, B), 5.48 (d, *J* = 14.2, 1 H, Me_3SiCH=CH, A), 5.50 (d, *J* = 14.2, 1 H, Me_3SiCH=CH, B), 5.92 (ddd, *J* = 5.0, 9.0 and 14.2, 1 H, Me_3SiCH=CH, A), 6.12 (ddd, *J* = 7.1, 7.1 and 14.2, 1 H, Me_3SiCH=CH, B), 6.60−7.78 (m, 10 H, Ar−H, A and B); ^{13}C NMR −0.03 ($SiMe_3$, A), 0.03 ($SiMe_3$, B), 16.5 ($NCHCH_3$, A), 16.7 ($NCHCH_3$, B) 37.8 (Me_3SiCH=$CHCH_2$, B), 40.6 (Me_3SiCH=$CHCH_2$, A), 45.5 (NCH_2Ph, A), 50.9 (NCH_2Ph, B), 52.4 (OMe, A), 55.9 (OMe, B), 56.1 ($NCHCH_3$, B), 56.4 ($NCHCH_3$, A), 127.5, 128.0, 128.2, 128.3, 128.4, 128.5, 129.2, 129.3 (Ar, A and B), 131.6 (Me_3SiCH=CH, B), 132.1 (Me_3SiCH=CH, A), 134.0 (Ar-*ipso*, A), 134.2 (Ar-*ipso*, B), 136.2 (Ar-*ipso*, B), 139.1 (Ar-*ipso*, A), 143.9 (CH=CH, A), 145.4 (CH=CH, B), 165.9 (NC=O, B), 166.1 (NC=O, A); IR 3010, 2955, 1652,; CIMS 464 (5), 351 (15), 350 (72), 189 (100); HRMS 464.2211; $C_{25}H_{34}NSiF_3O_2$ requires 464.2222.

(4*S*)-*N*-Benzyl-*N*-[(trimethylsilyl)methyl]-*N*-[1(*Z*)-(trimethylsilyl)-1-penten-4-yl]amine (42). A solution of amine **40** (1.5 g, 6.03 mmol), (iodomethyl)trimethylsilane (6.5 g, 30 mmol) and K_2CO_3 (3.3 g, 30 mmol) in MeCN (25 mL) was stirred at reflux for 48 h, cooled to 25 °C, and partitioned between water and ether. The ethereal layer was washed with brine, dried, and concentrated in vacuo to provide a residue which was subjected to column chromatography (Florisil, 20% ether−hexane) to give **42** (1.07 g, 53%): $[\alpha]^{25}_D$ +27.1° (*c* 0.057, $CHCl_3$). ^{1}H NMR 0.05 (s, 9 H, $SiMe_3$), 0.02 (s, 9 H, $SiMe_3$), 0.91 (d, *J* = 6.5, 3 H, $NCHCH_3$), 1.92 and 1.88 (ABq, *J* = 14.8, 2 H, NCH_2Si), 2.05 (m, 1 H, NCHCH), 2.20 (m, 1 H, NCHCH), 2.70 (m, 1 H, NCH), 3.39 and 3.61 (ABq, *J* = 14.0, 2 H, NCH_2-Ph), 5.46 (d, *J* = 14.1, 1 H, CH=CH), 6.28 (m, 1 H, CH=CH), 7.15−7.23 (m, 5 H, Ar); ^{13}C NMR −1.4 ($SiMe_3$), 0.2 ($SiMe_3$), 12.9 ($NCHCH_3$), 37.0 (NCH_2SiMe_3), 40.3 ($NCHCH_2$), 55.7 (NCH), 56.8 (NCH_2Ph), 126.5 (CH=CH), 128.0, 128.5129.2 (Ar), 141.0 (Ar-*ipso*), 147.5 (CH=CH); IR 3027, 2957, 1640; CIMS 334 (M + 1, 14), 318 (32), 220 (100); HRMS 334.2388, $C_{19}H_{36}NSi_2$ requires 334.2386.

CTAN Oxidation of Aminovinylsilane 42. Preparation of Dimethyltetrahydropyridine 43. To a solution of aminovinylsilane **42** (100 mg, 0.3 mmol) in MeCN (5 mL) was added $(^nBu_4N)_2Ce(NO_3)_6$ (270 mg, 0.3 mmol) in anhydrous MeCN (5 mL). After stirring at 25 °C for 6 h, another 1 equiv of $(^nBu_4N)_2Ce(NO_3)_6$ was added, and the resulting mixture was stirred for 12 h, diluted with satd $NaHCO_3$, and extracted with ether. The extracts were washed with brine and concentrated in vacuo to give a residue which was subjected to preparative TLC (50% ether−hexanes) to afford 34 mg (61%) of **43**: $[\alpha]^{25}$ +56° (*c* 0.02, $CHCl_3$). ^{1}H NMR 1.08 (d, *J* = 6.5, 3 H, Me), 1.86 (m, 1 H, NCHCH), 2.30 (m, 1 H, NCHCH), 2.95 (m, 2 H, CH_2N), 3.45 and 3.78 (ABq, *J* = 13.3, 2 H, NCH_2Ph), 5.64 (m, 2 H, CH=CH), 7.27 (m, 5 H, Ar−H); ^{13}C NMR 14.5 (Me), 32.6 (C-5), 48.9 (NCH_2Ph), 51.0 (C-6), 57.9 (C-2), 124.1, 124.9 (vinyl), 126.8, 128.2, 128.8 (Ar), 139.4 (Ar-*ipso*); IR 3028, 2962, 2923, 2793; EIMS 187 (8), 172 (28), 134 (69), 132; HRMS 187.1362, $C_{13}H_{17}N$ requires 187.1360.

Enantiomeric Purity Determination of 43. Preparation of Mosher Amide 45. To a stirred suspension of **43** (110 mg, 0.54 mmol) and 10% Pd/C (110 mg) in dry methanol (3 mL) was added anhydrous ammonium formate (64 mg, 5.4 mmol). The resulting reaction mixture was stirred at reflux for 10 min and filtered, and the filtrate was concentrated in vacuo to afford 15 mg of 2,6-methyl-1,2,5,6-tetrahydropyridine (**44**) whose spectroscopic properties matched those of the commercial (Aldrich) substance.

A mixture of (*R*)-MTPAcCl (prepared by refluxing 150 mg of (*R*)-MTPAcOH in excess thionyl chloride for 5 h), **44** (15 mg), 4-DMAP (30 mg, 0.24 mmol), and pyridine (0.5 mL) in MeCN (2 mL) was stirred at reflux for 12 h, cooled to 25 °C, diluted with satd $NaHCO_3$, and extracted with ether. The extracts were washed with brine, dried, and concentrated in vacuo, giving a residue which was subjected to preparative TLC (50% ether−hexanes) to give 4 mg of the Mosher amide **45**. The tetrahydropyridine **43** was shown to have an ee of >98% by capillary GC and ^{1}H NMR (500 MHz) analysis of the Mosher amide **45**. The assignments and validity of the analysis were supported by comparisons of ^{1}H NMR spectra of both **45**, and the Mosher amide was prepared from (*R*)-MTPAcCl and racemic 2-methylpiperidine.

45: ^{1}H NMR (mixture of rotamers A/B = 2:1) 0.28 (d, *J* = 7.0, 3 H, CH_3, B), 1.18 (d, *J* = 7.0, 3 H, CH_3, A), 1.53 (m, 12 H, A and B), 2.63 (ddd, *J* = 3.0, 13.5 and 13.5, 1 H, B), 2.89 (ddd, *J* = 3.0, 10.3 and 10.3, 1 H, A), 3.61 (s, 3 H, OMe, A), 3.76 (s, 3 H, OMe, B). 3.72 (m, 1 H, A), 4.32 (m, 1 H, B), 4.54 (m, 1 H, B), 5.01 (m, 1 H, A). 7.40 (m, 10 H, Ar, A and B); ^{13}C NMR

14.3, 15.8, 18.3, 18.7, 24.0, 26.2, 29.6, 29.7, 30.9, 36.9, 39.5, 44.4, 47.8, 55.2, 126.8, 126.9, 128.1, 128.2, 129.1, 134.2, 163.9; IR 3063, 2942, 2867, 1650, 1453, 1428; EIMS 315 (1), 125 (100); HRMS 315.1456, $C_{16}H_{20}NF_3O_2$ requires 315.1446.

(3*R*,4*S*)-1-(Trimethylsilyl)-4-[*N*-benzyl-*N*-[(trimethylsilyl)methyl]amino]pent-1-yn-3-ol (46). To a solution of (trimethylsilyl)acetylene (6.6 mL, 46.0 mmol) in THF (20 mL) was added BuLi (1.6 M solution, 22 mL, 36.0 mmol) at −78 °C. After stirring for 2 h at −78 °C, a solution of **19** (2.97 g, 12.0 mmol) in THF (10 mL) was added. The resulting solution was stirred at −78 °C for 4 h, at 25 °C for 1 h, and diluted with ether and water. The ethereal layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo, giving a residue which was subjected to column chromatography (silica gel, hexane:EtOAc, 10:1) to give 3.36 g (79%) of **46** as a single diastereomer: $[\alpha]^{25}$ +9.0° (*c* 0.15); ^{1}H NMR 0.02 (s, 9H, TMS), 0.07 (s, 9H, TMS), 1.02 (d, *J* = 6.8, 3H, Me), 1.88 and 2.51 (ABq, *J* = 14.8, 2H, CH_2TMS), 2.82 (m, 1H, CH), 3.21 and 3.97 (ABq, *J* = 13.3, 2H, $PhCH_2$), 4.02 (d, *J* = 6.0, 1H, CHO), 7.28 (m, 5H, Ar); ^{13}C NMR −1.3 (TMS), −0.2 (TMS), 7.8 ($CHCH_3$), 41.4 (CH_2TMS), 57.2 ($CHCH_3$), 58.6 (CH_2Ph), 63.1 (CHOH), 90.7 (C≡*C*TMS), 106.2 (*C*≡CTMS), 127.2, 128.4, and 129.1 (Ar), 139.1 (Ar-*ipso*); IR 3018, 2960, 2400, 1251, 1216; CIMS 348 (M + 1, 1), 221 (28), 220 (99), 91 (100); HRMS 348.2174, $C_{19}H_{34}NOSi_2$ requires 348.2179.

(3*R*,4*S*)-1-(Trimethylsilyl)-4-[*N*-benzyl-*N*-[(trimethylsilyl)methyl]amino]-1(*Z*)-penten-3-ol (47). A suspension containing **46** (0.30 mmol) and 5 mg of 5% Pd/C in EtOAc at −10 °C was evacuated by water aspirator and stirred under a H_2 atmosphere for 3 h, filtered, and concentrated in vacuo, giving a residue which was subjected to column chromatography (silica gel, hexane:EtOAc, 70:1) to give (*Z*)-allylic alcohol **47** (71%), (*E*)-allylic alcohol **48** (28%), and saturated product **49** (1%).

47: $[\alpha]^{32}$ +25.8° (*c* 0.12); ^{1}H NMR 0.04 (s, 9H, TMS), 0.09 (s, 1H, TMS), 1.00 (d, *J* = 6.8, 3H, CH_3), 1.96 and 2.03 (ABq, *J* = 14.8, 2H, CH_2TMS), 2.82 (m, 1H, $CHCH_3$), 3.29 and 3.74 (ABq, *J* = 13.7, 2H, CH_2Ph), 4.03 (m, 1H, CHOH), 5.64 (dd, *J* = 14.3, 0.8, 1H, CH=C*H*TMS), 6.32 (dd, *J* = 14.3, 8.6, 1H, C*H*=CHTMS), 7.19−7.29 (m, 5H, Ar); ^{13}C NMR −1.2 (TMS), 0.5 (TMS), 7.9 ($CHCH_3$), 42.5 (CH_2TMS), 58.6 (NCH_2Ph), 59.8 ($CHCH_3$), 73.3 (*C*HOH), 127.0, 128.3, 128.8, and 139.8 (Ar), 132.1 (TMS*C*H=CH), 148.1 (TMSCH=*C*H); IR 2953, 1660, 1605; CIMS 350 (M + 1, 1), 220 (100), 91 (75); HRMS 350.2339, $C_{19}H_{36}NOSi_2$ requires 350.2336.

48: $[\alpha]^{25}$ +15.2° (*c* 0.61); ^{1}H NMR 0.03 (s, 18H, 2TMS), 1.01 (d, *J* = 6.8, 3H, $CHCH_3$), 1.91 and 2.02 (ABq, *J* = 14.7, 2H, CH_2TMS), 2.85 (dq, *J* = 6.8, 4.6, 1H, $CHCH_3$), 3.25 and 3.75 (ABq, *J* = 13.6, 2H, CH_2Ph), 3.89 (m, 1H, CHOH), 5.94 (dd, *J* = 18.8, 1.6, 1H, C*H*=CHCHOH), 6.19 (dd, *J* = 18.8, 4.6, 1H, CH=C*H*CHOH), 7.12−7.34 (m, 5H, Ar); ^{13}C NMR −1.3, and −1.2 (2TMS), 7.7 ($CHCH_3$), 42.1 (CH_2TMS), 58.4 (NCH_2Ph), 59.6 ($CHCH_3$), 74.7 (*C*HOH), 127.0, 128.3, 128.8, and 139.8 (Ar), 129.3 (*C*H=CHCHOH), 146.9 (CH=*C*HCHOH); IR 2954, 1634, 1247.

49: $[\alpha]^{31}$ +39.1° (*c* 0.24); ^{1}H NMR −0.04 (s, 9H, TMS), 0.04 (s, 9H, TMS), 0.26 (ddd, *J* = 13.6, 13.6, 4.3, 1H, TMSCH_2CH_2), 0.60 (ddd, *J* = 13.8, 13.8, 4.3, 1H, TMSCH_2CH_2), 0.99 (d, *J* = 6.7, 3H, CH_3), 1.16 (m, 1H, $TMSCH_2CH_2$), 1.79 (m, 1H, $TMSCH_2CH_2$), 1.94 and 1.98 (ABq, *J* = 14.8, 2H, CH_2TMS), 2.54 (dq, *J* = 6.7, 6.8, 1H, $CHCH_3$), 3.32 (m, 1H, CHOH), 3.32 and 3.69 (ABq, *J* = 13.7, 2H, CH_2Ph), 7.18−7.30 (m, 5H, Ar); ^{13}C NMR −1.8 (TMS), −1.2 (TMS), 7.3 (CH_3), 12.3 (TMSCH_2-CH_2), 28.6 ($TMSCH_2CH_2$), 41.8 (CH_2TMS), 58.3 (NCH_2Ph), 59.5 ($CHCH_3$), 76.3 (CHOH), 126.8, 128.2, 128.8, and 140.4 (Ar); IR 3420, 2953, 1651; EIMS 351 (1), 220 (100), 91 (88); HRMS 351.2414, $C_{19}H_{37}NOSi_2$ requires 351.2414.

(3*R*,4*S*)-1-(Trimethylsilyl)-3-acetoxy-4-[*N*-benzyl-*N*-[(trimethylsilyl)methyl]amino]-1(*Z*)-pentene (50). A solution of (*Z*)-allylic alcohol **47** (31 mg, 0.09 mmol) in $CHCl_3$ (10 mL) containing Ac_2O (0.01 mL, 0.01 mmol), pyridine (0.01 mL, 0.01 mmol), and 4-DMAP (2 mg) was stirred for 12 h at 25 °C, diluted with $CHCl_3$ (10 mL), and washed with brine and water. The $CHCl_3$ layer was dried and concentrated in vacuo, giving a residue which was subjected to column chromatography (silica gel, hexane:EtOAc, 20:1) to give 21 mg (60%) of **50**: ^{1}H NMR 0.01 (s, 9H, TMS), 0.06 (s, 9H, TMS), 0.99 (d, *J* = 6.6, 3H, $CHCH_3$), 1.97 (s, 3H, $COCH_3$), 1.95 and 2.01 (ABq, *J* = 14.7, 2H, CH_2TMS), 2.80 (m, 1H, $CHCH_3$), 3.32 and 3.68 (ABq, *J* = 13.9, 2H, CH_2Ph), 5.40 (dd, *J* = 9.4, 9.3, 1H, TMSC*H*=CH), 5.68 (d, *J* = 14.6, 1H, C*H*OAc), 6.17 (dd, *J* = 14.6, 9.4, 1H, TMSCH=C*H*), 7.20−7.31 (m, 5H, Ar); ^{13}C NMR −1.2 (TMS), 0.00 (TMS), 7.9 ($CHCH_3$), 21.5 (CO*C*H3), 41.5 (CH_2TMS), 57.7 (NCH_2Ph), 59.0 ($CHCH_3$), 76.2 (*C*HOAc), 126.8, 128.1, 128.8, and 140.2 (aromatic), 133.9 (TMS*C*H=CH), 144.2 (TMSCH=*C*H), 169.9 (*C*OCH_3); IR 2951, 1731, 1241, 857; CIMS 394 (M + 1, 1), 220 (100), 91 (82); HRMS 394.2606, $C_{21}H_{40}NO_2Si_2$ requires 394.2598.

CTAN Oxidation of Aminovinylsilane 50. Preparation of Tetrahydropyridinyl Acetate 53. To a solution of **50** (21 mg, 0.05 mmol) in MeCN (5 mL) was added a solution of $(^nBu_4N)_2Ce(NO_3)_6$ (107 mg, 0.11 mmol) in MeCN (5 mL) through a cannula. The resulting solution was stirred for 12 h at 25 °C, diluted with $CHCl_3$, and washed with brine and water. The $CHCl_3$ layer was dried and concentrated in vacuo, giving a residue which was subjected to column chromatography (silica gel, hexane:ether, 10:1) to give 4 mg (30%) of **53** and 4 mg (25%) of secondary amine **54**.

The same reaction was conducted by using CAN (160 mg, 0.029 mmol) as the oxidant and **50** (57 mg, 0.14 mmol) in dry MeCN (5 mL) for 24 h at 25 °C. Workup and purification in the same manner gave 25 mg (38%) of **53** and 12 mg (27%) of **54**.

53: $[\alpha]^{25}$ −57.4° (*c* 0.23); ^{1}H NMR 0.96 (d, *J* = 6.8, 3H, $CHCH_3$), 2.06 (s, 3H, $COCH_3$), 2.99 (dq, *J* = 6.8, 2.0, 1H, $CHCH_3$), 3.59 and 3.76 (ABq, *J* = 13.4, 2H, CH_2Ph), 4.91 (br t, *J* = 2.0, 1H, $CHCOCH_3$), 5.76 (m, 1H, C*H*=CH), 6.01 (m, 1H, CH=C*H*), 7.28 (m, 5H, Ar); ^{13}C NMR 8.6 ($CHCH_3$), 21.4 ($COCH_3$), 47.4 (CH_2N), 54.2 ($CHCH_3$), 57.7 (NCH_2Ph), 71.8 ($CHOCOCH_3$), 121.6 (*C*H=CH), 127.1, 128.3, 128.7, and 138.7 (Ar), 131.8 (CH=*C*H), 170.9 (*C*OCH_3); IR 2926, 1728, 1454, 1371; CIMS 246 (M + 1, 17), 186 (38), 170 (68), 134 (72), 91 (100); HRMS 246.1503, $C_{15}H_{20}NO_2$ requires 246.1494.

54: $[\alpha]^{22}$ +9.7° (*c* 0.17); ^{1}H NMR 0.13 (s, 9H, TMS), 1.08 (d, *J* = 6.5, 3H, $CHCH_3$), 2.04 (s, 3H, $COCH_3$), 2.83 (dq, *J* = 3.9, 6.5, 1H, $CHCH_3$), 3.78 and 3.83 (ABq, *J* = 13.2, 2H, CH_2Ph), 5.46 (ddd, *J* = 14.6, 3.9, 0.4, 1H, $CHOCOCH_3$), 5.79 (dd, *J* = 14.6, 0.4, 1H, CH=C*H*TMS), 6.21 (dd, *J* = 14.6, 9.2, 1H, C*H*=CHTMS), 7.28 (m, 5H, Ar); ^{13}C NMR 0.1 (TMS), 15.7 ($CHCH_3$), 21.3 ($COCH_3$), 51.2 (CH_2Ph), 55.5 ($CHCH_3$), 76.1 ($CHOCOCH_3$), 127.0, 128.1, 128.4, and 140.3 (aromatic), 135.3 (CH=*C*HTMS), 142.4 (*C*H=CHTMS), 170.1 (*C*OCH3); IR 2916, 1735, 1451, 1235; CIMS 306 (M + 1, 3), 220 (28), 134 (99), 91 (100); HRMS 306.1889, $C17H_{28}NO_2Si$ requires 306.1889.

Enantiomeric Purity Determination of 53. Preparation of Alcohol 55 and Mosher Ester 56. A solution of piperidine **53** (10 mg, 0.04 mmol) and KCN (1.5 mg, 0.02 mmol) in MeOH (2 mL) was stirred for 12 h at 25 °C and concentrated in vacuo. The residue was dissolved in $CHCl_3$ and washed with brine and water, dried, and concentrated in vacuo giving a residue which was subjected to column chromatography (silica gel, hexane:ether, 1:1) to give 6.5 mg (78%) of **55**: $[\alpha]^{26}_D$ −26.0° (*c* 0.2); ^{1}H NMR 0.91 (d, *J* = 6.8, 3H, $CHCH_3$), 2.87 (ddd, *J* = 17.7, 1.9, 1.2, 1H, =CHCH_2N), 2.99 (dq, *J* = 6.8, 1.9, 1H, $CHCH_3$), 3.05 (ddd, *J* = 17.7, 4.1, 1.9, 1H, =CHCH_2N), 3.64 (s, 2H, CH_2Ph), 3.67 (br s, 1H, C*H*OH), 5.78 (ddd, *J* = 9.8, 4.1, 1.9, C*H*=), 5.86 (dddd, *J* = 9.8, 4.0, 1.9, 1.2, 1H, =C*H*CHO), 7.22−7.33 (m, 5H, Ar); ^{13}C NMR 7.6 (CH_3), 47.4 (CH=$CHCH_2$N), 57.9 ($CHCH_3$), 58.8 (CH_2Ph), 68.8 (CHOH), 126.0 (*C*H=), 127.2 (=*C*HCHO), 128.4, 128.8, and 138.6 (Ar); IR 3400, 2953, 2925, 1707, 1454, 1370, 1138; EIMS 203 (11), 134 (51), 91 (100); HRMS 203.1314, $C_{13}H_{17}NO$ requires 203.1310.

To a mixture of piperidine alcohol **55** (20 mg, 0.10 mmol) and 4-DMAP (2 mg) was added a solution of freshly made (*S*)-MTPAcCl (52 mg, 0.20 mmol) in CH_2Cl_2 (5 mL). The resulting solution was treated with Et_3N (0.03 mL, 0.20 mmol) and stirred for 12 h at 25 °C, diluted with $CHCl_3$, and washed with brine and water. The $CHCl_3$ layer was dried and concentrated in vacuo, giving a residue which was subjected to column

chromatography (silica gel, hexane:ether, 5:1) to give 40 mg (95%) of the Mosher ester **56**. The enantiomeric purity of **53** was determined to be >90% by analysis of the ^{1}H NMR spectrum of **57**: ^{1}H NMR 1.01 (d, J = 6.8, 3H, CHCH_3), 2.94 and 2.99 (m, 1H, CH=CHCH_2N), 3.04 (m, 1H, CH=CHCH_2N), 3.08 (m, 1H, CHCH$_3$), 3.57 (s, 3H, OCH$_3$), 3.52 and 3.67 (ABq, J = 13.5, 2H, CH_2Ph), 5.11 (br s, 1H, =CHCHO), 5.86 (dddd, J = 10.0, 4.6, 2.5, 2.4, 1H, =CHCH$_2$N), 6.01 (dddd, J = 10.0, 3.8, 2.5, 1.7, 1H, CH=CHCH$_2$N), 7.16−7.24 (m, 5H, Ar), 7.35−7.38 (m, 3H, Ar), 7.57−7.59 (m, 2H, Ar); ^{13}C NMR 9.6 (CHCH$_3$), 47.1 (=CHCH$_2$N), 55.1 (CHCH$_3$), 55.4 (OCH$_3$), 57.9 (CH$_2$Ph), 74.5 (=CHCHO), 120.4 (=CHCH$_2$N), 126.9, 127.4, 128.2, 128.3, 128.5, and 129.5 (Ar), 132.9 (CH=), 166.4 (C=O), 122.0, 124.8, 132.5, and 138.7; EIMS 419 (2), 189 (87), 170 (53), 104 (25), 91 (100); HRMS 419.1714, $C_{23}H_{24}NO_3F_3$ requires 419.1708.

(3*R*,4*S*)-1-(Trimethylsilyl)-3-hydroxy-4-[*N*-benzyl-*N*-[(trimethylsilyl)methyl]amino]-1(*E*)-pentene (48). To a solution of (*E*)-1-(trimethylsilyl)-2-(tri-*n*-butylstannyl)ethene (1.5 g, 4.20 mmol) in THF (5 mL) was added n-BuLi (1.M in hexane, 2.3 mL, 3.70 mmol) at −78 °C. The resulting solution was warmed to 25 °C and stirred for 5 min, cooled to −78 °C, and treated with aldehyde **19** (0.7 g, 2.80 mmol). The resulting solution was stirred for 12 h, diluted with $CHCl_3$, washed with brine and water, dried, and concentrated in vacuo, giving a residue which was subjected to column chromatography (silica gel, hexane:EtOAc, 20:1) to give 794 mg (81%) of **48**: $[\alpha]^{25}$ +15.2° (*c* 0.61); ^{1}H NMR 0.03 (s, 18H, 2TMS), 1.01 (d, J = 6.8, 3H, CHCH_3), 1.91 and 2.02 (ABq, J = 14.7, 2H, CH_2TMS), 2.85 (dq, J = 6.8, 4.6, 1H, CHCH$_3$), 3.25 and 3.75 (ABq, J = 13.6, 2H, CH_2Ph), 3.89 (m, 1H, CHOH), 5.94 (dd, J = 18.8, 1.6, 1H, CH=), 6.19 (dd, J = 18.8, 4.6, 1H, =CHCHOH), 7.12−7.34 (m, 5H, Ar); ^{13}C NMR −1.3, and −1.2 (2TMS), 7.7 (CHCH$_3$), 42.1 (CH$_2$TMS), 58.4 (NCH_2Ph), 59.6 (CHCH$_3$), 74.7 (CHOH), 127.0, 128.3, 128.8, and 139.8 (Ar), 129.3 (CH=), 146.9 (=CHCHOH); IR 2954, 1634, 1247; CIMS 350 (M + 1, 1), 220 (100), 162 (2), 91 (75); HRMS 350.2339, $C_{19}H_{36}NOSi_2$ requires 350.2336.

(3*R*,4*S*)-1-(Trimethylsilyl)-3-acetoxy-4-[*N*-benzyl-*N*-[(trimethylsilyl)methyl]amino-1(*E*)-pentene (52). A solution of **48** (270 mg, 0.77 mmol), acetic anhydride (0.15 mL, 1.20 mmol), 4-DMAP (2 mg), and pyridine (0.1 mL, 1.20 mmol) in $CHCl_3$ (5 mL) was stirred for 12 h at 25 °C, washed with water, dried, and concentrated in vacuo, giving a residue which was subjected to column chromatography (silica gel, hexane:EtOAc, 20:1) to give 265 mg (88%) of **52**: $[\alpha]^{31}$ −22.6° (*c* 0.31); ^{1}H NMR 0.02 (s, 9H, TMS), 0.06 (s, 9H, TMS), 0.94 (d, J = 6.6, 3H, CHCH_3), 1.94 and 1.99 (ABq, J = 14.7, 2H, CH$_2$TMS), 2.04 (s, 3H, COCH$_3$), 2.78 (dq, J = 6.6, 8.3, CHCH$_3$), 3.35 and 3.69 (ABq, J = 13.8, 2H, CH_2Ph), 5.29 (m, 1H, CHOCOCH$_3$), 5.73 (dd, J = 18.8, 1.3, =CHTMS), 6.10 (dd, J = 18.8, 5.3 Hz, HC=CHTMS), 7.18−7.34 (m, 5H, Ar); ^{13}C NMR −1.3 (TMS), −1.2 (TMS), 7.9 (CHCH$_3$), 21.2 (COCH$_3$), 41.2 (CH$_2$TMS), 57.5 (NCH_2Ph), 58.4 (CHCH$_3$), 76.4 (CHOCOCH$_3$), 126.7, 128.1, 128.7, and 140.2 (Ar), 130.8 (=CHTMS), 143.4 (CH=CHTMS), 170.1 (COCH$_3$); IR 2955, 1739, 1668, 1373, 1247, 863, 839; CIMS 392 (M + 1, 3), 220 (100), 134 (22), 91 (24), 73 (86); HRMS 392.2442, $C_{21}H_{38}NO_2SiO_2$ requires 392.4411.

CTAN Oxidation of Aminovinylsilane 52. Preparation of Secondary Amine 57. A solution of $(Bu_4N)_2Ce(NO_3)_6$ (1 g, 1.20 mmol) and **52** (231 mg, 0.60 mmol) in dry MeCN (20 mL) was stirred for 12 h at 25 °C and concentrated in vacuo, giving a residue which was diluted with $CHCl_3$, washed with water and brine, and concentrated in vacuo, giving a residue which was subjected to column chromatography (silica gel, hexane:EtOAc, 10:1) to give 19 mg (11%) of **57**. $[\alpha]^{32}$ +41.6° (*c* 0.25); ^{1}H NMR (CD_3CN) 0.02 (s, 9H, TMS), 1.47 (d, J = 7.0, 3H, CH$_3$), 1.97 (s, 3H, COCH$_3$), 4.53 and 4.95 (ABq, J = 15.2, 2H, CH_2Ph), 4.64 (dq, J = 5.1, 7.0, 1H, CHCH$_3$), 5.49 (dd, J = 5.1, 4.3, 1H, CHOCO), 5.91 (s, 1H, TMSCH=), 5.93 (d, J = 4.3, 1H, TMSCH=CH), 7.08 (m, 2H, Ar), 7.24−7.37 (m, 3H, Ar); ^{13}C NMR (CD_3CN) −1.5 (TMS), 15.3 (CHCH$_3$), 21.1 (COCH$_3$), 48.5 (CH$_2$PH), 61.9 (CHCH$_3$), 77.6 (CHCO), 128.3, 128.4, 129.6, and 136.2 (Ar), 134.8 (TMSCH=), 141.1 (TMSCH=CH), 170.5 (COCH$_3$); IR 2955, 1746, 1446, 1372; EIMS 304 (M − 1, 6), 134 (61), 91 (100), 75 (33); HRMS 305.1816, $C_{17}H_{27}NO_2Si$ requires 305.1811.

(3*R*,4*S*)-1-(Trimethylsilyl)-3-hydroxy-4-[*N*-benzoyl-*N*-[(trimethylsilyl)methyl]amino]-1(*E*)-pentene (58). To a solution of (*E*)-1-(trimethylsilyl)-2-(tri-*n*-butylstannyl)ethene (0.51 g, 1.31 mmol) was added dropwise *tert*-BuLi (1.4 M in pentane, 0.81 mL) at −78 °C. The solution was stirred at 25 °C for 2 h. Aldehyde **32** (0.23 g, 0.87 mmol) was added at −78 °C, and the mixture was stirred for 12 h at 25 °C, diluted with water, and extracted with CH_2Cl_2. The extracts were washed with brine, dried, and concentrated in vacuo to give a residue which was subjected to column chromatography (silica gel, hexanes:EtOAc, 5:1) to afford 0.15 g (47%) of **58**: mp 151−153 °C; $[\alpha]^{20}$ −2.17° (*c* 2.34, $CHCl_3$); ^{1}H NMR 0.05 (s, 9H, TMS), 0.12 (s, 9H, TMS), 1.22 (d, J = 6.6, 3H, CH_3), 2.45 and 2.85 (ABq, J = 14.4, 2H, NCH_2), 3.75 (dq, J = 6.6, 5.0, 1H, CH), 4.00 (s, 1H, CHOH), 5.83 (s, 2H, =CH), 7.29 (m, 5H, Ar); ^{13}C NMR −1.4 (TMS), −0.6 (TMS), 15.1 (CH$_3$), 34.1 (NCH$_2$), 58.8 (CH), 76.4 (CHOH), 126.7, 128.5, 129.2, and 137.0 (Ar), 132.1 (CH=), 145.0 (=CH), 171.6 (C=O); IR 3327, 2952, 1592, 1244, 842; EIMS 363 (1), 234 (64), 105 (100); HRMS 363.2051, $C_{19}H_{33}NO_2Si_2$ requires 363.2050.

(3*R*,4*S*)-1-(Trimethylsilyl)-3-acetoxy-4-[*N*-benzoyl-*N*-[(trimethylsilyl)methyl]amino]-1(*E*)-pentene (59). A solution of alcohol **58** (84 mg, 0.23 mmol), Ac_2O (118 mg, 1.16 mmol), and 4-DMAP (5 mg) in pyridine (2 mL) was stirred at 25 °C for 18 h, diluted with water, and extracted with CH_2Cl_2. The extracts were dried and concentrated in vacuo to give 88 mg (95%) of **59** which was used without further purification. $[\alpha]^{22}$ −5.29° (*c* 2.52, $CHCl_3$); ^{1}H NMR −0.03 (s, 9H, TMS), 0.11 (s, 9H, TMS), 1.18 (d, J = 6.7, 3H, CH_3), 1.98 (s, 3H, COCH$_3$), 2.45 and 2.85 (ABq, J = 14.5, 2H, NCH_2), 3.95 (dq, J = 6.7, 6.0, 1H, CH), 5.22 (dd, J = 6.0, 5.7, 1H, CHO), 5.67 (dd, J = 18.7, 5.7, 1H, CH=), 5.84 (d, J = 18.7, 1H, =CH), 7.26−7.34 (m, 5H, Ar); ^{13}C NMR −1.5 (TMS), −0.6 (TMS), 15.5 (CHCH$_3$), 21.1 (CH$_3$), 34.1 (NCH$_2$), 57.1 (CH), 77.0 (CHOCOCH$_3$), 126.8, 128.5, 129.4, and 136.8 (Ar), 134.7 (=CH), 139.9 (CH=), 169.6 (COCH$_3$), 171.7 (NC=O); IR 2954, 1743, 1629, 1232, 840; EIMS 405 (5), 390, 234 (61), 105(100); HRMS 405.2136, $C_{21}H_{35}NO_3Si_2$ requires 405.2156.

Enantiomeric Purity Determination of 58. Preparation of Mosher Ester 60. A mixture of **58** (14 mg, 0.037 mmol), 4-DMAP (3 mg), triethylamine (0.03 mL, 0.074 mmol), and (*R*)-MTPAcCl (Aldrich) (19 mg, 0.074 mmol) in CH_2Cl_2 (3 mL) was stirred for 12 h at 25 °C, diluted with water, and extracted with CH_2Cl_2. The extracts were washed with brine, dried, and concentrated, giving a residue which was subjected to column chromatography (silica gel, hexanes:EtOAc, 5:1) to give 19 mg (89%) of Mosher ester **60**. The alcohol **58** was shown to have an enantiomeric excess of ca. 90% by ^{1}H NMR analysis of the **60**: ^{1}H NMR (mixture of diasteromers, A/B = ca. 10:1); 0.03 (s, 9H, TMS), 0.05 (s, 9H, TMS, B), 0.12 (s, 9H, TMS, A and B), 1.06 (d, J = 6.7, 3H, CH_3, B), 1.24 (d, J = 6.6, 3H, CH_3, A), 2.38 and 2.81 (ABq, J = 14.2, 2H, NCH_2, B), 2.40 and 2.84 (ABq, J = 14.5, 2H, NCH_2, A), 3.45 (s, 3H, OCH_3, A and B), 4.02 (m, 1H, CH, A and B), 5.41 (m, 1H, CHOCO, A and B), 5.53 (dd, J = 8.7, 7.1, 1H, CH=, A), 5.63 (dd, J = 8.7, 7.1, 1H, CH=, B), 5.94 (d, J = 8.7, 1H, =CH, A), 6.05 (d, J = 8.7, 1H, =CH, B), 7.23−7.39 (m, 10H, Ar, A and B); ^{13}C NMR −2.8 (TMS, B), −1.6 (TMS, A), −1.4 (TMS, B), −0.6 (TMS, A), 15.3 (CH$_3$, B), 15.7 (CH$_3$, A), 33.5 (TMSCH$_2$, B), 33.8 (TMSCH$_2$, A), 55.4 (OCH$_3$, B), 55.6 (OCH$_3$, A), 56.7 (CH, A), 56.8 (CH, B), 79.4 (CHOC, B), 79.6 (CHOC, A), 121.7 (CO), 124.6 (CF_3), 126.7, 127. 2, 127.3, 127.8, 128.4, 128.6, 129.6, 129.7, 131.7, and 136.5 (Ar, A and B), 137.9 (=CH, A and B), 138.6 (=CH, A and B), 165.6 (CHOCO), 171.6 (NC=O); IR 2944, 1745, 1629, 1241, 1163, 841; EIMS 579 (6), 234 (34), 130 (50), 105 (100); HRMS 579.2471, $C_{29}H_{40}NO_4F_3Si_2$ requires 579.2448.

CAN Oxidation of 59. Preparation of Tetrahydropyridinyl Acetate 66. A solution of CAN (325 mg, 0.59 mmol) and **59** (80 mg, 0.20 mmol) in MeCN (3 mL) was stirred for 24 h at 25 °C, diluted with 2-propanol and water, and extracted with CH_2Cl_2. The extracts were washed with brine, dried, and concentrated to give a residue which was subjected to column chromatography (silica gel, hexanes:EtOAc, 3:1) to provide 18 mg (43%) of **66**. $[\alpha]^{25}_D$ +6.57° (*c* 0.65, $CHCl_3$); ^{1}H NMR 1.14 (d, J = 6.5, 3H, CH_3), 2.02 (s, 3H, CH$_3$), 3.61 (d, J = 19.9, 1H,

CH_2N), 4.04 (dq, J = 6.5, 6.0, 1H, C*H*), 4.86 (s, 1H, C*H*O), 4.95 (d, J = 19.9, 1H, CH_2N), 4.87 (m, 1H, =CH), 6.12 (m, 1H, =CH), 7.30 (m, 5H, Ar); ^{13}C NMR 15.9 (CH_3), 21.0 (CH_3), 38.2 (NCH_2), 52.6 (*C*H), 69.4 (*C*HO), 120.4 (=*C*H), 126.6 128.5, 129.6, and 136.1 (Ar), 130.0 (*C*H=), 170.1 ($COCH_3$), 171.3 (NC=O); IR 1729, 1625, 1418, 1233; EIMS 259 (1), 105 (100), 77 (34); HRMS 259.1200, $C_{15}H_{17}NO_3$ requires 259.1209.

Enantiomeric Purity Determination of 66. Preparation of Tetrahydropyridinyl Alcohol 55 and Mosher Ester 56. To a solution of **66** (22 mg, 0.085 mmol) in Et_2O (2 mL) at 0 °C was added $LiAlH_4$ (10 mg, 0.255 mmol). The mixture was stirred at 25 °C and for 4 h, diluted with H_2O, and extracted with Et_2O. The extracts were washed with brine, driedn and concentrated in vacuo to give 14 mg (82%) of alcohol **55**. A solution of **55** (7 mg, 0.035 mmol), 4-DMAP (1 mg), (*R*)-MTPAcCl (Aldrich) (18 mg, 0.069 mmol), and triethylamine (0.010 mL, 0.069 mmol) in CH_2Cl_2 (3 mL) was stirred at 25 °C for 21 h, diluted with H_2O, and extracted with CH_2Cl_2. The extracts were washed with 5% HCl, satd $NaHCO_3$, and H_2O, dried, and concentrated to provide 14 mg of the Mosher ester **56** as an ca. 95:5 diastereomeric mixture (90 ee%) based upon ^{1}H NMR analysis. Subjection of this material to column chromatography (silica gel, hexane:EtOAc, 6:1) did not alter the diastereomeric ratio and gave pure **56** Mosher ester (11 mg, 77%).

(5*S*,6*R*)- and (5*S*,6*S*)-1-[(Trimethylsilyl)methyl]-5-[3-hydroxy-1-(trimethylsilyl)-1(*E*)-propen-3-yl]-2-pyrrolidone 62 and 64. To a solution of (*E*)-1-(trimethylsilyl)-2-(tri-*n*-butylstannyl)ethylene (4.4 mL, 4.6 g, 12 mmol) in THF (10 mL) at −78 °C was added n-BuLi (7.5 mL of 1.6 M hexane solution). The mixture was stirred at −78 °C for 2 h and at 25 °C for 11 h and cooled to −78 °C, and aldehyde **61** (1.1 g, 5.5 mmol) in THF (20 mL) was added. The mixture was stirred at 25 °C for 15 h, diluted with water, and extracted with CH_2Cl_2. The extracts were washed with brine and water, dried, and concentrated in vacuo to give a residue which was subjected to column chromatography (silica gel, ether:acetone, 4:1) to provide 495 mg (30%) of **62** and 150 mg (9%) of **64**.

62: mp 133−134 °C, Et_2O/hexane; $[\alpha]^{22}$ −11.5° (*c* 0.012, $CHCl_3$); ^{1}H NMR 0.03 (s, 9 H, $Si(CH_3)_3$), 1.93 (m, 2 H, CH_2), 2.19 (m, 2 H, CH_2), 2.44 and 3.26 (ABq, J = 15.3, and 2), 2.58 (s, 1 H, O*H*), 3.67 (ddd, J = 5.3, 4.1, and 2.9, 1 H, C*H*), 4.31 (d, J = 4.1, 1 H, C*H*OH), 5.97 (s, 2 H, C*H*=C*H*); ^{13}C NMR −1.3 ($Si(CH_3)_3$), −1.5 ($Si(CH_3)_3$), 20.0 (CH_2CH_2CH), 29.9 (CH_2CH_2-CH), 33.4 (NCH_2Si), 63.4 (CH_2CH_2CH), 74.2 (*C*HOH), 132.6 (CH=*C*H), 143.6 (*C*H=CH), 174.6 (NCO); IR 3220, 2994, 2955, 2898, 1652; CIMS 300 (M + 1, 0.8), 170 (100); HRMS 300.1788, $C_{14}H_{29}O_2NSi_2$ requires 300.1815.

64: mp 124−126 °C, Et_2O/acetone; $[\alpha]^{22}$ −13° (*c* 0.035, $CHCl_3$); ^{1}H NMR 0.06 (s, 9 H, TMS), 0.08 (s, 9 H, TMS), 1.69 (s, 1 H, O*H*), 1.85 (m, 1 H, CH_2), 1.95 (m, 1 H, CH_2), 2.123 (m, 1 H, CH_2), 2.40 (m, 1 H, CH_2), 2.37 and 3.33 (ABq, J = 15.2, 2 H, NCH_2), 3.56 (ddd, J = 9.3, 3.8, 2.1, 1 H, C*H*), 4.48 (dd, J = 4.3 and 2.1, 1 H, C*H*OH), 5.92 (dd, J = 18.9 and 4.3, 1 H, =C*H*), 6.04 (dd, J = 18.9 and 1.3, 1 H, TMSC*H*); ^{13}C NMR −1.4 (TMS), −1.3 (TMS), 17.9 (CH_2), 30.1 (CH_2), 32.0 (NCH_2), 63.7 (*C*H), 71.5 (*C*HOH), 132.4 (=*C*H), 143.5 (TMS*C*H=), 175.1 (NCO); IR 3322, 2954, 2896, 1651; CIMS 300 (M + 1, 2), 170 (100); HRMS 300.1813, $C_{14}H_{29}O_2NSi_2$ requires 300.1815.

(5*S*,6*R*)-1-[(Trimethylsilyl)methyl]-5-[3-acetoxy-1-(trimethylsilyl)-1(*E*)-propen-3-yl]-2-pyrrolidone (63). A solution of hydroxy-vinylsilane **62** (50 mg, 0.17 mmol), 4-DMAP (10 mg, 0.08 mmol), and acetic anhydride (0.20 mL, 0.22 g, 2.1 mmol) in pyridine (4 mL) was stirred at 25 °C for 16 h, diluted with water, and extracted with CH_2Cl_2. The extracts were washed with water, dried, and concentrated in vacuo to provide a residue which was subjected to column chromatography (silica gel, Et_2O:hexane, 1:3) to yield 45 mg (79%) of acetoxy-vinylsilane **63**: $[\alpha]^{23}$ −7.3° (*c* 0.06, $CHCl_3$); ^{1}H NMR 0.01 (s, 9 H, TMS), 0.05 (s, 9 H, TMS), 1.96 (m, 2 H, CH_2), 2.07 (s, 3 H, CH_3CO), 2.18 (m, 2 H, CH_2), 2.36 and 3.26 (ABq, J = 15.3, 2 H, NCH_2Si), 3.68 (ddd, J = 8.1, 3.1, and 2.9, 1 H, C*H*), 5.44 (dd, J = 4.6 and 3.1, 1 H, C*H*OH), 5.83 (dd, J = 18.8 and 4.6, 1 H, =C*H*), 5.91 (d, J = 18.8, 1 H, TMSC*H*=); ^{13}C NMR −1.6 (TMS), −1.4 (TMS), 19.6 (CH_2), 21.1 (CH_3CO), 29.6 (CH_2), 33.0 (NCH_2), 61.3 (*C*H), 74.2 (*C*HOAc), 135.0 (=*C*H), 137.9 (TMS*C*H=), 169.6 (CH_3CO), 174.2 (NCO); IR 2954, 2900, 1744, 1685, 1231, 842; CIMS 342 (M + 1, 3), 170 (100); HRMS 342.1938, $C_{16}H_{31}O_3NSi_2$ requires 342.1921.

CAN Oxidation of Vinylsilane 63. Preparation of Acetoxyindolizidinone 67. To a solution of CAN (472 mg, 0.86 mmol) in MeCN (1 mL) was added a solution of acetoxy-vinylsilane **63** (91 mg, 0.27 mmol) in MeCN (2 mL). The resulting mixture was stirred at 25 °C for 2 d, diluted with 2-propanol and water, and extracted with CH_2Cl_2. The extracts were dried and concentrated in vacuo to provide a residue which was subjected to column chromatography (silica gel, 100% Et_2O to 3:2 Et_2O/acetone) (resulting in significant product loss) to provide 13 mg (25%) of indolizidine **67**: $[\alpha]^{27}$ +190° (*c* 0.003, $CHCl_3$); ^{1}H NMR 1.86 (m, 1 H, CH_2), 2.03 (s, 3 H, CH_3OCO), 2.16 (m, 1 H, CH_2), 2.42 (m, 2 H, CH_2), 3.53 and 4.42 (ABq, J = 18.8, 2 H, NCH_2), 3.83 (ddd, J = 3.0, 3.6, and 8.6, C*H*), 5.15 (q, J = ca. 3, 1 H, C*H*OAc), 6.12 (d, J = 3.1, 2 H, =C*H*); ^{13}C NMR 19.8 (CH_2), 21.0 (CH_3CO), 30.1 (CH_2), 40.2 (NCH_2), 55.9 (C_2CH), 67.0 (*C*HOAc), 123.0 (*C*H=), 130.1 (=*C*H), 170.6 (OCO), 174.4 (NCO); IR 3234, 3090, 3035, 1934, 1854, 1618; EIMS 195 (M, 2), 155 (24), 126 (25), 84 (100); HRMS 195.0886, $C_{10}H_{13}NO_3$ requires 195.0895.

Enantiomeric Purity Determination of 67. Preparation of Alcohol 68 and Mosher Ester 69. A mixture of acetoxyindolizidone **67** (6 mg, 0.03 mmol) and KCN (2 mg, 0.03 mmol) in MeOH (2 mL) was stirred at 25 °C for 18 h and concentrated in vacuo providing a residue which was triturated with acetone. The triturate was concentrated in vacuo to provide 3 mg (60%) of hydroxyindolizidine **68**: $[\alpha]^{26}$ +66° (*c* 0.002, $CHCl_3$); ^{1}H NMR 2.12 (m, 1 H, CH_2), 2.28 (m, 1 H, CH_2), 2.36 (m. 1 H, CH_2), 2.50 (m, 1 H, CH_2), 3.53 (d, J = 19.7, 1 H, CH_2), 3.68 (ddd, J = 8.9, 4.2, 2.4, 1 H, C*H*), 3.98 (dd, 1 H, J = 5.1, 2.4, C*H*OH), 4.38 (ddd, J = 19.7, 3.2, 2.7, 1 H, NCH_2), 5.92 (ddd, J = 9.6, 3.2, 1.9, C*H*=), 6.10 (m, 1 H, =C*H*); ^{13}C NMR 19.0 (CH_2), 29.7 (CH_2), 40.3 (NCH_2), 58.0 (*C*H), 64.9 (CHOH), 127.1 (*C*H=), 128.2 (=*C*H), 175.4 (NCO); IR 3373, 2929, 2840, 1687, 1679, 1650; EIMS 153 (M, 7), 84 (100); HRMS 153.0783, $C_8H_{11}NO_2$ requires 153.0790.

A solution of 100 mg (0.40 mmol) of (*R*)-MTPAcCl (Aldrich), 4-DMAP (4 mg, 0.03 mmol), and indolizidine **68** (3 mg, 0.02 mmol) in 1:1 CH_3CN−pyridine (1 mL) was stirred at 75 °C for 12.5 h, cooled to 25 °C, diluted with satd $NaHCO_3$, and extracted with Et_2O. The extracts were washed with brine, dried, and concentrated in vacuo to provide a 4:1 mixture (63% de) of (*R*)-Mosher esters **69** (^{1}H NMR analysis). Subjection to preparative TLC (silica, Et_2O:acetone, 4:1) provided 7 mg (97%) of **69** again as a 4:1 diastereomeric mixture: $[\alpha]^{26}$ −8.3° (*c* 0.003, $CHCl_3$); ^{1}H NMR (mixture of (*R*)-Mosher diastereomers A/B) 1.1 (m, 2 H, CH_2, A and B), 2.17 (m, 2 H, CH_2, A and B), 2.25 (m, 4 H, CH_2, A and B), 3.36 (d, J = 0.9, 3 H, OCH_3, A), 3.42 (buried signal, 1 H, NCH_2, B), 3.49 (d, J = 1.4, 3 H, OCH_3, B), 3.54 (d, J = 19.6, 1 H, NCH_2, A), 3.83 (ddd, J = 7.4, 4.4, 3, 1 H, C*H*, B), 3.87 (ddd, J = 8.8, 3.9, 2.9, 1 H, C*H*, A), 4.37 (ddd, J = 19.6, 3.2, 1 Hz, 1 H, NCH_2, A), 4.44 (ddd, J = 20.6, 3, 1, 1 H, NCH_2, B), 5.21 (ddd, J = 5.9, ca. 3, 1, 1 H, C*H*OCO, B), 5.27 (ddd, J = 7.3, 2.9, 1, 1 H, C*H*OCO, A), 6.10 (m, 2 H, NCH_2CH, A and B), 6.16 (m, 2 H, C*H*, A and B), 7.40 (m, 6 H, Ar, A and B), 7.45 (m, 4 H, Ar, A and B); ^{13}C NMR 19.8 (CH_2, A), 19.9 (CH_2, B), 29.3 (CH_2, B), 29.4 (CH_2, A), 40.1 (NCH_2, A and B), 55.1 (*C*H, A and B), 55.6 (OCH_3, A), 55.7 (OCH_3, B), 69.8 (*C*HOCO, B), 70.0 (*C*HOCO, A), 121.8 (NCH_2CH=, A), 122.1 (NCH_2CH=, B), 126.8 (NCH_2CHCH, B), 127.7 (NCH_2-$CHCH$, A), 128.4 (B), 128.6 (A), 129.8 (A and B), 131.7 (A), 131.8 (B), 131.3 (A and B), 166.4 (OCO, A), 168.8 (OCO, B), 174.1 (NCO, B), 174.2 (NCO, A); IR 2954, 2849, 1755, 1729, 1695, 1654; EIMS 369 (2), 189 (100), 135 (24); HRMS 369.1183, $C_{18}H_{18}NO_3F_3$ requires 369.1182.

(Trimethylsilyl)methyl *N*-[(Trimethylsilyl)methyl]serinate (70). To a slurry of D-serine (5.25 g, 50 mmol) and K_2CO_3 (6.91 g, 50 mmol) in anhydrous DMF (150 mL) at 100 °C was added (trimethylsilyl)methyl iodide (21.4 g, 100 mmol). After stirring at 100 °C for 17 h, the reaction mixture was cooled to 25 °C, filtered, diluted with 5% $NaHCO_3$, and extracted with Et_2O. The extracts were washed with brine,

dried, and concentrated in vacuo to give a residue which was subjected to flash column chromatography (silica gel, hexane:EtOAc, 4:1) providing **70** (4.29 g, 31%): $[\alpha]^{26}$ +0.71° (*c* 0.05, $CHCl_3$); ^{1}H NMR 0.04 (s, 9H, TMS), 0.06 (s, 9H, TMS), 1.95 and 2.05 (ABq, *J* = 13.2, 2H, NCH_2TMS), 3.29 (dd, *J* = 7.1, 4.5, 1H, C*H*NH), 3.49 (dd, *J* = 10.5, 7.1, 1H, CH_2OH), 3.75 (dd, *J* = 10.5, 4.5, 1H, CH_2OH), 3.79 and 3.88 (ABq, *J* = 14.1, 2H, TMSCH_2O); ^{13}C NMR −3.2 (TMS), −2.8 (TMS), 38.3 (NCH_2TMS), 58.4 (TMSCH_2O), 61.8 (*C*H_2OH), 66.4 (*C*HNH), 173.6 (NC═O); IR 3431, 2955, 2901, 1730, 1244, 1169, 850; FABMS 278 (M + 1, 100), 246 (2), 190 (1); HRMS 277.1535, $C_{11}H_{27}O_3Si_2N$ requires 277.1530.

(Trimethylsilyl)methyl *N*-[(Trimethylsilyl)methyl]-*O*-(*tert*-butyldimethylsilyl)serinate (71). To a solution of primary alcohol **70** (0.44 g, 1.59 mmol) in DMF (2 mL) were added imidazole (0.27 g, 3.98 mmol) and *tert*-butyldimethylsilyl chloride (0.29 g, 1.91 mmol) at 25 °C. The resulting mixture was stirred at 25 °C for 18 h, diluted with water, and extracted with CH_2Cl_2. The combined organic extracted was washed with brine, dried over $MgSO_4$, and concentrated in vacuo to give a residue which was subjected to column chromatography (silica gel, hexane:EtOAc, 5:1) to provide 0.54 g (100%) product **71**: $[\alpha]^{22}_D$ +1.43° (*c* 0.09, $CHCl_3$); ^{1}H NMR 0.00 (s, 3H, SiCH_3), 0.01 (s, 3H, SiCH_3), 0.02 (s, 9H, TMS), 0.06 (s, 9H, TMS), 0.84 (s, 9H, C(CH_3)$_3$), 1.92 and 2.07 (ABq, *J* = 13.1 Hz, 2H, NCH_2-TMS), 3.26 (t, *J* = 4.8 Hz, 1H, C*H*N), 3.78 (d, *J* = 4.8 Hz, 2H, CH_2OTBDMS), 3.79 (s, 2H, TMSCH_2O); ^{13}C NMR −5.5 (Si-(CH_3)$_2$), −3.0 (TMS), −2.7 (TMS), 18.2 (*C*(CH_3)$_3$), 25.8 (C(*C*H_3)$_3$), 38.1 (NCH_2TMS), 57.7 (TMSCH_2O), 64.2 (*C*H_2OTBDMS), 67.0 (*C*HN); IR 3389 (br), 2956, 2840, 1733, 1464, 1242, 1110; CIMS *m*/*z* 392 (M + 1, 12), 376 (18), 362 (21), 334 (20), 261 (25), 260 (100), 246 (72); HRMS 392.2462, $C_{17}H_{42}NO_3Si_3$ requires 392.2473.

(Trimethylsilyl)methyl *N*-[(Trimethylsilyl)methyl]-*N*-benzoyl-*O*-(*tert*-butyldimethylsilyl)serinate (72). To a solution of **71** (2.08 g, 5.31 mmol) and triethylamine (0.50 mL, 5.31 mmol) in CH_2Cl_2 (50 mL) at 0 °C was added benzoyl chloride (0.62 mL, 5.31 mmol), and the resulting mixture was stirred at 0 °C for 15 min, diluted with H_2O, and extracted with CH_2Cl_2. The extracts were washed with brine, dried, and concentrated in vacuo to give a residue which was subjected to flash column chromatography (silica gel, hexane:EtOAc, 4:1) to give 1.83 g (88%) of benzamide **72** (11.2 g, 96%): $[\alpha]^{22}_D$ +0.60° (*c* 0.04, $CHCl_3$); ^{1}H NMR 0.00 (s, 3H, SiCH_3), 0.00 (s, 3H, SiCH_3), 0.05 (s, 9H, TMS), 0.12 (s, 9H, TMS), 0.84 (s, 9H, C(CH_3)$_3$), 2.63 (s, 2H, NCH_2), 3.74 and 3.84 (ABq, *J* = 14.1, 2H, CH_2O), 3.87 (d, *J* = 6.8, 2H, CH_2O), 4.60 (t, *J* = 6.8, 1H, C*H*N), 7.38 (m, 5H, Ar); ^{13}C NMR −5.6 (Si(CH_3)$_2$), −3.1 (TMS), −0.7 (TMS), 18.2 (*C*(CH_3)$_3$), 25.8 (C(CH_3)$_3$), 35.0 (NCH_2), 58.8 (CH_2O), 60.4 CH_2O), 64.4 (*C*HN), 127.4, 128.2, 129.4, and 136.1 (Ar), 169.9 (OC═O), 172.6 (NC═O); IR 2952, 2931, 2858, 1734, 1641; EIMS 495 (M, 37), 480 (88), 438 (30), 348 (25), 206 (84), 105 (100); HRMS 495.2652, $C_{24}H_{45}NO_4Si_3$ requires 495.2657.

(2*S*)-3-(*tert*-Butyldimethylsiloxy)-2-[*N*-[(trimethylsilyl)methyl]-*N*-benzoylamino]-1-propanol (73). A solution of ester **72** (1.02 g, 2.05 mmol) and $NaBH_4$ (0.16 g, 4.20 mmol) in absolute ethanol (5 mL) was stirred at 25 °C for 6 h, cooled to 0 °C, diluted with H_2O, and extracted with $CHCl_3$. The extracts were washed with brine, dried, and concentrated in vacuo to give 0.77 g (95%) of alcohol **73** which was used without further purification. Column chromatography (silica gel, hexane:EtOAc, 3:1) of this substance gave **73**: mp 91−92 °C (CH_2Cl_2/hexane); $[\alpha]^{23}$ −2.44° (*c* 0.05, $CHCl_3$); ^{1}H NMR −0.03 (s, 3H, SiCH_3), −0.01 (s, 3H, SiCH_3), 0.13 (s, 9H, TMS), 0.84 (s, 9H, C(CH_3)$_3$), 2.67 and 2.72 (ABq, *J* = 14.5, 2H, NCH_2), 3.60 (m, 4H, CH_2O and CH_2OH), 3.98 (m, 1H, C*H*N), 7.37 (m, 5H, Ar); ^{13}C NMR −5.6 (Si(*C*H_3)$_2$), −0.7 (TMS), 18.2 (*C*(CH$_3$)$_3$), 25.8 (C(*C*H$_3$)$_3$), 33.5 (NCH_2), 61.0 (CH_2), 61.7 (CH_2), 61.9 (*C*HN), 127.2, 128.3, 129.1, and 136.8 (Ar), 172.8 (NC═O); IR 3368, 2951, 2931, 2890, 2857, 1615; EIMS 395 (M, 14), 380 (58), 208 (65), 105 (100); HRMS 395.2316, $C_{20}H_{37}NO_3Si_2$ requires 395.2312.

(2*S*)-3-(*tert*-Butyldimethylsiloxy)-2-[*N*-[(trimethylsilyl)methyl]-*N*-benzoylamino]-1-propanol (74.) To a solution of DMSO (1.17 mL, 16.4 mmol) in CH_2Cl_2 (10 mL) at −78 °C was added oxalyl chloride (0.72 mL, 8.21 mmol). After stirring the resulting mixture at −78 °C for 1 h, a solution of alcohol **73** (2.16 g, 5.48 mmol) in CH_2Cl_2 (10 mL) was added, and the resulting mixture was stirred at −78 °C for 2.5 h, diluted with triethylamine (3.82 mL, 27.4 mmol), stirred at 25 °C for 2.5 h, diluted with H_2O, and extracted with CH_2Cl_2. The extracts were washed with brine, dried, and concentrated in vacuo to provide aldehyde **74** (2.11 g, 98%, ca. 85% pure by ^{1}H NMR) which was used without purification: ^{1}H NMR (mixture of rotamers A/B = 2:1) 0.11 (s, 9H, TMS, A and B), 0.13 (s, 6H, Si(CH_3)$_2$, A and B), 0.87 (s, 9H, C(CH_3)$_3$, A), 0.92 (s, 9H, C(CH_3)$_3$, B), 2.62 and 2.72 (ABq, *J* = 14.5, 2H, NCH_2, A), 3.08 and 3.25 (ABq, *J* = 14.6, 2H, NCH_2, B), 4.20 (m, 3H, CH_2O and C*H*N, A and B), 7.41 (m, 5H, Ar, A and B), 9.55 (s, 1H, CHO, A), 9.59 (s, 1H, CHO, A); ^{13}C NMR −5.6 (Si(CH_3)$_2$, A and B), −1.7 (TMS, B), −0.7 (TMS, A), 18.4 (*C*(CH_3)$_3$, A and B), 25.8 (C(*C*H$_3$)$_3$, A and B), 36.6 (NCH_2, A), 43.9 (N*C*H$_2$, B), 60.0 (*C*H$_2$O, A), 60.8 (*C*H$_2$O, B), 69.5 (*C*HN, B), 70.5 (*C*HN, A), 127.1, 128.5, 129.7, and 135.5 (Ar, A and B), 170.3 (NC═O, B), 172.7 (NC═O, A), 195.9 (CHO, B), 1985.7 (CHO, A); EIMS 393 (M, 10), 378 (37), 206 (28), 105 (100); HRMS 393.2159, $C_{20}H_{35}NO_3Si_2$ requires 393.2156.

Enatiomeric Purity Determination of 74. Preparation of Alcohol 73 and Its Mosher Ester. A solution of aldehyde **74** (72 mg, 0.183 mmol) and $NaBH_4$ (10 mg, 0.275 mmol) in absolute ethanol (1 mL) was stirred at 25 °C for 5 h, diluted with H_2O, and extracted with CH_2Cl_2. The extracts were washed with brine, dried, and concentrated in vacuo to provide 67 mg (92%) of alcohol **73**. A solution of **73** (32 mg, 0.081 mmol), 4-DMAP (1 mg), and triethylamine (0.055 mL, 0.396 mmol) and (*R*)-MTPAcCl (100 mg, 0.396 mmol) in CH_2Cl_2 (3 mL) was stirred at 25 °C for 18 h, diluted with H_2O, and extracted with CH_2Cl_2. The extracts were washed with 5% HCl, saturated aqueous $NaHCO_3$, and H_2O, dried, and concentrated to provide 41 mg (84%) of the (*R*)-Mosher ester diastereomer as a 85:15 mixture (70% ee) based upon ^{1}H NMR integration. Subjection of this substance to column chromatography (silica gel, hexane:EtOAc, 5:1) did not effect the diastereomeric ratios and gave pure esters: $[\alpha]^{30}$ −12.4° (*c* 9.67, $CHCl_3$); ^{1}H NMR (mixture of *R*−A/B = 85:15) −0.05 (s, 3H, SiCH_3, A and B), −0.02 (s, 3H, SiCH_3, A and B), 0.07 (s, 9H, TMS, A), 0.12 (s, 9H, TMS, B), 0.83 (s, 9H, C(CH_3)$_3$, A), 0.87 (s, 9H, C(CH_3)$_3$, B), 2.55 and 2.69 (ABq, *J* = 14.5, 2H, NCH_2, A), 2.57 and 2.68 (ABq, *J* = 14.6, 2H, NCH_2, B), 3.45 (s, 3H, OCH_3, A), 3.51 (s, 3H, OCH_3, B), 3.63 (m, 2H, CH_2O, A and B), 4.17 (m, 2H, CH_2O, A and B), 4.52 (m, 1H, C*H*N, A and B), 7.27 (m, 10H, Ar, A and B); ^{13}C NMR −5.7 (Si(CH_3)$_2$, A and B), −5.6 (Si(*C*H$_3$)$_2$, A and B), −0.7 (TMS, A), −0.6 (TMS, B), 18.2 (*C*(CH$_3$)$_3$, A and B), 25.8 (C(*C*H$_3$)$_3$, A and B), 33.4 (NCH_2, B), 33.6 (NCH_2, A), 55.5 (OCH_3, A), 55.7 (OCH_3, B), 58.8 (*C*HN, B), 59.0 (*C*HN, A), 61.5 (*C*H$_2$O, A), 61.6 (*C*H$_2$O, B), 63.6 (*C*H$_2$O, B), 63.7 (*C*H$_2$O, A), 121.8 (*C*CF$_3$, A and B), 124.7 (C*C*F$_3$, A and B), 126.9, 127.0, 127.1, 128.3, 128 5, 128.6, 129.1, 129.2, 129.7, 129.8, 131.8, 132.0, and 136.3 (Ar), 166.4 (OC═O, A), 166.5 (OC═O, B), 172.3 (NC═O, A and B); IR 2952, 2851, 1750, 1628; EIMS 611 (M, 32), 596 (60), 189 (48), 105 (100); HRMS 611.2711, $C_{30}H_{44}F_3NO_5Si_2$ requires 611.2710.

(3*S*,4*R*)- and (3*R*,4*R*)-1-(Trimethylsilyl)-4-[*N*-[(trimethylsilyl)methyl]-*N*-benzoylamino]-5-(*tert*-butyldimethylsiloxy)-1(*E*)-penten-3-ol (75 and 79). To a solution of (*E*)-1-(trimethylsilyl)-2-(tri-*n*-butylstannyl)ethene (4.18 g, 10.7 mmol) in THF (7 mL) was added a hexane solution of n-BuLi (6.24 mL, 1.55 M) at −78 °C. The resulting solution was stirred at −78 °C for 1 h and at 25 °C for 3 h and then cooled again to −78 °C before addition of a solution of aldehyde **74** (2.11 g, 5.37 mmol) in THF (15 mL). The mixture was stirred at −78 °C for 2 h, at 25 °C for 0.5 h, diluted with H_2O, and extracted with CH_2Cl_2. The extracts were washed with brine and H_2O, dried, and concentrated in vacuo to give a residue containing diastereomeric alcohols **75** and **79** (ca. 3.6:1) which was subjected to column chromatography (silica gel, hexane: EtOAc, 8:1) providing 1.24 g (47%) of **75** and 0.35 g (13%) of **79**.

75: mp 139−141 °C, (CH_2Cl_2/hexane); $[\alpha]^{26}$ +2.48° (*c* 0.02, $CHCl_3$); ^{1}H NMR 0.04 (s, 3H, SiCH_3), 0.07 (s, 3H, SiCH_3), 0.07

(s, 9H, TMS), 0.13 (s, 9H, TMS), 0.88 (s, 9H, C(CH_3)$_3$), 2.57 and 2.83 (ABq, J = 14.3, 2H, NCH_2), 3.87 (m, 3H, CH_2O and CHN), 4.26 (dd, J = 6.4, 4.6, 1H, CHOH), 5.87 (dd, J = 18.7, 4.6, 1H, =CH), 5.94 (d, J = 18.7, 1H, CH=), 7.40 (m, 5H, Ar); ^{13}C NMR −5.5 (Si(CH_3)$_2$), −1.4 (TMS), −0.4 (TMS), 18.2 (C(CH_3)$_3$), 25.9 (C(CH$_3$)$_3$), 34.8 (NCH$_2$), 62.5 (CH$_2$O), 63.9 (NCH), 74.5 (CHOH), 127.4, 128.2, 129.2, and 136.7 (Ar), 132.3 (=CH), 144.4 (CH=), 172.4 (NC=O); IR 3323, 2952, 2852, 1592; EIMS 493 (M, 0.8), 364 (82), 105 (100); HRMS 493.2867, $C_{25}H_{47}NO_3Si_3$ requires 493.2864.

79: mp 134−136 °C, (CH$_2$Cl$_2$/hexane); [α]^{26} +2.31° (*c* 0.05, CHCl$_3$); ^{1}H NMR −0.02 (s, 3H, SiCH_3), 0.00 (s, 3H, SiCH_3), 0.02 (s, 9H, TMS), 0.14 (s, 9H, TMS), 0.85 (s, 9H, C(CH_3)$_3$), 2.72 and 2.85 (ABq, J = 14.4, 2H, NCH_2TMS), 3.59 (dd, J = 10.9, 3.9, 1H, CH_2O), 3.67 (dd, J = 10.9, 7.9, 1H, CH_2O), 3.82 (ddd, J = 7.9, 3.9, and undetermined, 1H, CHN), 4.11 (t, J = 5.8, 1H, CHOH), 5.81 (dd, J = 18.7, 5.8, 1H, =CH), 5.89 (d, J = 18.7, 1H, CH=), 7.38 (m, 5H, Ar); ^{13}C NMR −5.6 (Si(CH$_3$)$_2$), −1.5 (TMS), −0.5 (TMS), 18.2 (C(CH$_3$)$_3$), 25.9 (C(CH$_3$)$_3$), 34.0 (NCH$_2$), 63.1 (CH$_2$O), 64.7 (NCH), 73.2 (CHOH), 127.7, 128.1, 129.0, and 136.9 (Ar), 133.8 (=CH), 144.4 (CH=), 173.3 (NC=O); IR 3302, 2951, 2858, 1590; EIMS 493 (M, 1), 478 (23), 364 (100), 105 (58); HRMS 493.2853, $C_{25}H_{47}NO_3Si_3$ requires 493.2864.

Enantiomeric Purity Determination of 75. Preparation of Mosher Esters 78. A solution of alcohol **75** (35 mg, 0.071 mmol), 4-DMAP (1 mg), triethylamine (0.06 mL, 0.426 mmol), and (*R*)-MTPAcCl (100 mg, 0.396 mmol) in CH$_2$Cl$_2$ (2 mL) was stirred at 25 °C for 17 h, diluted with H$_2$O, and extracted with CH$_2$Cl$_2$. The extracts were washed with satd NaHCO$_3$ and H$_2$O, dried, and concentrated in vacuo to give 33 mg of Mosher ester **78** as an 85:15 mixture (70% ee) based upon ^{1}H NMR integration. Subjection of this material to column chromatography (silica gel, hexane:EtOAc, 6:1) did not affect diastereomeric ratios and provided **78** (30 mg, 60%): [α]^{30} +1.90° (*c* 6.33, CHCl$_3$); ^{1}H NMR 0.03 (s, 3H, Si(CH$_3$)$_2$, A), 0.04 (s, 6H, Si(CH$_3$)$_2$, B), 0.04 (s, 9H, TMS, A), 0.06 (s, Si(CH$_3$)$_2$, A), 0.06 (s, 9H, TMS, B), 0.12 (s, 9H, TMS, B), 0.13 (s, 9H, TMS, A), 0.86 (s, 9H, C(CH$_3$)$_3$, B), 0.90 (s, 9H, C(CH$_3$)$_3$, A), 2.45 and 2.61 (ABq, J = 14.3, 2H, NCH_2, B), 2.48 and 2.64 (ABq, J = 14.2, 2H, NCH_2, A), 3.40 (s, 3H, OCH_3, A), 3.43 (s, 3H, OCH_3, B), 3.48 (dd, J = 10.8, 3.8, 1H, CH_2O, B), 3.66 (dd, J = 10.3, 9.3, 1H, CH_2O, B), 3.78 (m, 2H, CH_2O, A), 4.15 (m, 1H, CHN, B), 4.18 (m, 1H, CHN, A), 5.42 (t, J = 7.5, 1H, CHOH, A), 5.43 (t, J = 7.5, 1H, CHOH, B), 5.59 (dd, J = 18.6, 7.5, 1H, =CH, A), 5.67 (dd, J = 18.6, 7.5, 1H, =CH, B), 5.96 (d, J = 18.6, 1H, CH=, A), 6.04 (d, J = 18.6, 1H, CH=, B), 7.44 (m, 10H, Ar, A and B); ^{13}C NMR −5.6 (Si(CH$_3$)$_2$, B), −5.5 (Si(CH$_3$)$_2$, A and B), −1.7 (TMS, A and B), −0.3 (TMS, A and B), 18.3 (C(CH$_3$)$_3$, A and B), 25.9 (C(CH$_3$)$_3$, A and B), 33.6 (NCH$_2$, B), 33.9 (NCH$_2$, A), 55.3 (OCH_3, A and B), 59.9 (CH$_2$O, B), 60.3 (CH$_2$O, A), 62.5 (NCH, A and B), 77.2 (CHO, A and B), 121.7 (CCF$_3$, A), 121.8 (CCF$_3$, B), 124.5 (CCF$_3$, A), 124.7 (CCF$_3$, B), 127.2, 127.4, 127.7, 127.9, 128.2, 128.5, 129.4, 129.8, 131.4, 131.8, 136.2, and 136.3 (Ar), 138.1 and 138.3 (CH=CH, A), 138.4 and 139.2 (CH=CH, B), 165.4 (CC=O, A), 165.5 (CC=O, B), 172.7 (NC=O, B), 172.8 (NC=O, A); IR 2955, 2857, 1744, 1627; EIMS 709 (M, 1), 694 (20), 364 (23), 260 (42), 105 (100); HRMS 709.3275, $C_{35}H_{54}NO_5F_3Si_3$ requires 709.3262.

(3*S*,4*R*)-1-(Trimethylsilyl)-4-[*N*-[(trimethylsilyl)methyl]-*N*-benzoylamino]-1(*E*)-pentene-3,5-diol (76). A solution of allylic alcohol **75** (0.302 g, 0.613 mmol) and 0.2 mL of 48% HF−H$_2$O in CH$_3$CN (3 mL) was stirred at 25 °C for 0.5 h, made basic with NaHCO$_3$, and extracted with CHCl$_3$. The extracts were washed with brine, dried, and concentrated in vacuo to give a residue which was subjected to flash column chromatography (silica gel, hexane:EtOAc, 2:1) to provide **76** (0.202 g, 87%): [α]^{24} −1.46° (*c* 2.27, CHCl$_3$); ^{1}H NMR (mixture of rotamers A/B = 2.5:1) −0.04 (s, 9H, TMS, B); 0.05 (s, 9H, TMS, A), 0.11 (s, 9H, TMS, A and B), 2.53 and 2.80 (ABq, J = 14.3, 2H, NCH_2, A), 2.69 and 3.03 (ABq, J = 15.7, 2H, NCH_2, B), 3.71−3.85 (m, 2H, CH_2OH, A), 4.02 (m, 2H, CH_2OH, B), 4.16 (m, 1H, CHN, A and B), 4.79 (m, 1H, CHOH, A), 4.91 (m, 1H, CHOH, B), 5.80 (dd, J = 18.8, 4.4, 1H, =CH, A), 5.87 (d, J = 18.8, 1H, CH=, A), 6.07 (d, J = 18.5, 1H, CH=, B), 6.15 (dd, J = 18.5, 5.3, 1H, =CH, B), 7.33 (m, 5H, Ar); ^{13}C NMR −1.8 (TMS, B), −1.4 (TMS, A and B), −0.5 (TMS, B), 35.1 (NCH$_2$, A), 46.1 (NCH$_2$, B), 62.0 (CH$_2$OH, B), 62.4 (CH$_2$OH, A), 63.7 (NCH, A), 68.3 (NCH, B), 72.1 (CHOH, B), 74.4 (CHOH, A), 126.7, 127.1, 128.4, 128.5, 129.3, 129.6, 136.5, and 136.6 (Ar), 132.6 (=CH, A), 133.0 (=CH, B), 144.4 (CH=, A), 145.0 (CH=, B), 172.6 (NC=O, A), 172.8 (NC=O, B); IR 3359, 2949, 2892, 1593; EIMS 379 (M, 2), 250 (57), 105 (100); HRMS 379.1996, $C_{19}H_{33}NO_3Si_2$ requires 379.1999.

(3*S*,4*R*)-1-(Trimethylsilyl)-3,5-diacetoxy-4-[*N*-[(trimethylsilyl)methyl]-*N*-benzoylamino]-1(*E*)-pentene (77). A solution of diol **76** (1.45 g, 3.82 mmol), 4-DMAP (8 mg), and acetic anhydride (2.16 mL, 22.9 mmol) in pyridine (6 mL) was stirred at 25 °C for 17 h, diluted with H$_2$O, and extracted with CH$_2$Cl$_2$. The extracts were washed with brine, dried, and concentrated in vacuo to give a residue which was subjected to flash column chromatography (silica gel, hexane:EtOAc, 6:1) to provide 1.64 g (93%) **77**: [α]^{26} −3.87° (*c* 6.00, CHCl$_3$); ^{1}H NMR 0.06 (s, 9H, TMS), 0.12 (s, 9H, TMS), 2.02 (s, 3H, COCH_3), 2.09 (s, 3H, COCH_3), 2.55 and 2.75 (ABq, J = 14.3, 2H, NCH_2), 4.08 (dd, J = 11.5, 2.9, 1H, CH_2O), 4.18 (td, J = 7.8, 2.9, 1H, CHN), 4.27 (dd, J = 11.5, 9.2, 1H, CH_2O), 5.37 (t, J = 6.3, 1H, CHO), 5.72 (dd, J = 18.7, 6.3, 1H, =CH), 5.90 (d, J = 18.7, 1H, CH=), 7.36 (m, 5H, Ar); ^{13}C NMR −1.6 (TMS), −0.6 (TMS), 20.8 (COCH$_3$), 21.0 (COCH$_3$), 34.5 (NCH$_2$), 60.1 (CHN), 61.3 (CH$_2$O), 74.2 (CHO), 127.2, 128.5, 129.6, and 136.3 (Ar), 135.6 (=CH), 138.9 (CH=), 169.3 (OC=O), 170.2 (OC=O), 172.6 (NC=O); IR 2950, 2898, 1741, 1635; EIMS 463 (M, 1), 448 (28), 292 (28), 105 (100); HRMS 463.2213, $C_{23}H_{37}NO_5Si_2$ requires 463.2210.

CAN Oxidation of 77. Preparation of Tetrahydropyridinyl Diacetate 81. To a solution of CAN (0.533 g, 0.972 mmol) in dry MeCN (2 mL) was added a solution of **77** (0.225 g, 0.486 mmol) in MeCN (2 mL) at 25 °C. The mixture was stirred for 20 h at 40 °C, diluted with H$_2$O, and extracted with CHCl$_3$. The extracts were washed with brine, dried, and concentrated in vacuo to give a residue which was subjected to flash column chromatography (silica gel, hexane:EtOAc, 2:1) to provide **81** (71 mg, 46%): [α]^{25} +16.9° (*c* 1.63, CHCl$_3$); ^{1}H NMR 2.03 (s, 3H, COCH_3), 2.06 (s, 3H, COCH_3), 3.63 (d, J = 19.8, 1H, NCH_2), 3.91 (dd, J = 11.2, 5.1, 1H, CH_2O), 4.12 (dd, J = 11.2, 9.4, 1H, CH_2O), 4.30 (m, 1H, CHN), 4.86 (d, J = 19.8, 1H, NCH_2), 4.99 (d, J = 2.4, 1H, CHO), 5.91 (m, 1H, CH=), 6.16 (m, 1H, CH=), 7.39 (m, 5H, Ar); ^{13}C NMR 20.7 (COCH$_3$), 20.9 (COCH$_3$), 38.9 (NCH$_2$), 55.6 (NCH), 60.8 (CH$_2$O), 65.6 (CHO), 120.8 (CH=), 127.2, 128.4, 129.9, and 135.5 (Ar), 130.9 (=CH), 170.1 (COCH$_3$), 172.2 (NC=O); IR 1732, 1634; EIMS 317 (M, 0.2), 184 (22), 105 (100), 77 (48); HRMS 317.1264, $C_{17}H_{19}NO_5$ requires 317.1263.

(3*R*,4*R*)-1-(Trimethylsilyl)-4-[*N*-[(trimethylsilyl)methyl]-*N*-benzoylamino]-1(*E*)-pentene-3,5-diol (80). A solution of silyl ether **79** (0.413 g, 0.838 mmol) and 0.3 mL of 48% HF−H$_2$O in MeCN (4.5 mL) was stirred at 25 °C for 0.5 h, made basic with NaHCO$_3$, and extracted with CHCl$_3$. The extracts were washed with brine, dried, and concentrated in vacuo to give a residue which was subjected to flash column chromatography (silica gel, hexane:EtOAc, 2:1) to provide 0.264 g (83%) of **80**: mp 139−141 °C (CH$_2$Cl$_2$/hexane); [α]^{24} −2.93° (*c* 2.87, CHCl$_3$); ^{1}H NMR 0.03 (s, 9H, TMS), 0.15 (s, 9H, TMS), 2.77 and 2.85 (ABq, J = 14.3, 2H, NCH_2), 3.65 (m, 1H, CH$_2$OH), 3.88 (m, 1H, CH$_2$OH), 4.13 (m, 1H, CHN), 4.68 (s, 1H, CHOH), 5.80 (dd, J = 18.5, 5.1, 1H, =CH), 5.89 (d, J = 18.5, 1H, CH=), 7.34 (m, 5H, Ar); ^{13}C NMR −1.5 (TMS), −0.5 (TMS), 34.0 (NCH$_2$), 60.4 (CH$_2$OH), 64.4 (CHN), 73.6 (CHOH), 127.4, 128.4, 129.1, and 136.8 (Ar), 134.0 (=CH), 144.2 (CH=), 173.7 (NC=O); IR 3342, 2951, 2899, 1591, 1568; EIMS 379 (M, 1), 250 (24), 105 (100); HRMS 379.2001, $C_{19}H_{33}NO_3Si_2$ requires 379.1999.

Tetradydropyridinyl Diol 82. A solution of diacetate **81** (99 mg, 0.31) and KCN (13 mg, 0.20 mmol) in MeOH (2 mL) was stirred for 18 h at 25 °C, concentrated, diluted with CHCl$_3$, and washed with brine and H$_2$O. The CHCl$_3$ layer was dried and concentrated in vacuo to give 55 mg (76%) of the trans-diol **82** as a crystalline substance which was used without further purification: mp 173−174 °C (acetone/hexane); [α]^{24}

−44.3° (*c* 3.0, MeOH); ^{1}H NMR (d_6-acetone) 3.53 (m, 3H, CH_2-OH and CH_2N), 3.97 (t, J = 5.6, 1H, CHOH), 4.11 (s, 1H, CHCH_2O), 4.66 (d, J = 18.9, 1H, CH_2N), 5.91 (m, 2H, CH=CH), 7.37 (s, 3H, Ar), 7.57 (s, 2H, Ar); ^{13}C NMR 39.6 (*C*H_2N), 60.7 (*C*H_2OH), 62.6 (N*C*H or *C*HOH), 64.1(N*C*H or *C*HOH), 126.5 and 128.0 (*C*H=*C*H), 128.6, 129.0, 129.6, and 138.2 (Ar), 172.5 (NC=O); IR 3329, 1598, 1436; EIMS 233 (M, 1), 105 (100) 77 (39); HRMS 233.1046, $C_{13}H_{15}NO_3$ requires 233.1052.

X-ray Crystallographic Data for 80 and 82. A crystal was placed and optically centered on the Enraf-Nonius CAD-4 diffractometer. The crystals' final cell parameters and crystal orientation matrix were determined from 25 reflections and were confirmed with axial photographs. Data were collected [Mo Kα] with $\omega/2\theta$ scans over the range $2.34 < \theta < 22.5°$ with each scan recorded in 96 steps with the outermost 16 steps on each end of the scan being used for background determination. The diffractometer was controlled with a Digital Equipment Corporation MicroVAX II (MVII) computer and the Enraf-Nonius VAX\VMS CAD4 Express control program. Six standard reflections well dispersed in reciprocal space were monitored at 1 h intervals of X-ray exposure. Minor variations in intensity were observed; data were not corrected. An absorption correction was applied based upon six ψ-scans, each collected. Two forms of data were collected: the indices $\pm h$-k-l and their Friedel mates $\pm hkl$.

All crystallographic calculations were performed on a personal computer (PC) with a 486 DX2/66 processor and 20 Mb of extended memory. Data were corrected for Lorentz and polarization factors and reduced to F_o^2 and $\sigma(F_o^2)$ using the program XCAD4 (data reduction program written for a PC by Klaus Harms, 1993). Intensity statistics and systematic absences clearly determined the centrosymmetric monoclinic space group $P2_1/c$ (no. 14). The structure was determined by direct methods with the successful location of several oxygen, nitrogen, and carbon atoms using the program XS.[2] The structure was refined with XL (Siemens SHELXTL, version 5).

Summary of results for **80**: ($C_{19}H_{33}NO_3SI_2O_3$), M_r = 379.64, orthorhombic, crystal dimensions 0.55 × 0.275 × 0.125 mm, scan width (0.95 + 0.75 tan θ)°, variable scan speed of 4.1−5.1° min^{-1}, transmission factor range 0.9576 = 0.9800, 3637 reflections with 3099 unique [R(int) = 0.658], $P2_12_12_1$, a = 7.3246(6) Å, b = 10.5921(7) Å, c = 30.685(6) Å, V = 2380.7(5) Å^3, Z = 4, D_x = 1.059 g cm^{-3}, λ(Mo Kα) = 0.71073 Å, μ(Mo Kα) = 0.164 mm^{-1}, F(000) = 824, T = 153(2) K, $R(F)$ = 9.08%, $R(wF^2)$ = 16.16% (for all 3099 independent reflections) $R(F)$ = 6.45%, $R(wF^2)$ = 14.44% (for the 2462 reflections with $F_o > 4\sigma(F_o)$).

Summary of results for **82**: ($C_{13}H_{15}N_1O_3$), M_r = 233.26, monoclinic, crystal dimensions 0.325 × 0.150 × 0.050 mm, scan width (0.52 + 0.45 tan θ)°, variable scan speed of 2.0−3.3° min^{-1}, transmission factor range 0.9359=1.0000, 3189 reflections with 1511 unique [R(int) = 0.0597], $P2_1/c$, a = 9.0412(12) Å, b = 10.3876(12) Å, c = 12.3801(14) Å, b = 96.854(10)°, V = 1154.4(2) Å^3, Z = 4, D_x = 1.342 g cm^{-3}, λ(Mo Kα) = 0.71073 Å, μ(Mo Kα) = 0.096 mm^{-1}, F(000) = 496, T = 153 K, $R(F)$ = 10.19%, $R(wF^2)$ = 8.24% for all 1511 independent reflections.

Piperidinyl Tetracetates 85 and 87. To a stirred solution of diol **82** (0.01 mmol) and hydroquinidine 1,4-phthalazinediyl diether (0.01 mmol) in a 10:1 acetone:water mixture at 0 °C was added NMO (0.012 mmol) followed by 0.01 equiv of a 4 wt % solution of OsO_4 in water. The mixture was stirred for 17 h at 0 °C, quenched by addition of solid $Na_2S_2O_5$, stirred for 0.5 h, dried with Na_2SO_4, and filtered. The filtrate was concentrated in vacuo to give a residue, shown by ^{1}H NMR analysis to contain the tetrols **88** and **89**. A solution of this mixture, 4-DMAP (2 mg), and acetic anhydride (0.01 mL, 0.10 mmol) in pyridine (3 mL) was stirred at 25 °C for 17 h, diluted with H_2O, and extracted with $CHCl_3$. The extracts were washed with brine, dried, and concentrated in vacuo to give a residue which was subjected to flash column chromatography (silica gel, hexane:EtOAc, 2:1) to provide **85** (less polar, 33%) and **87** (more polar, 49%).

85: $[\alpha]^{30}$ −17° (*c* 8.0, $CHCl_3$); ^{1}H NMR (70 °C, CD_3CN) 1.95 (s, 3H, COCH_3), 2.02 (s, 3H, COCH_3), 2.07 (s, 3H, COCH_3), 2.11 (s, 3H, COCH_3), 3.33 (t, J = 12.3, 1H, CH_2N), 4.22 (m, 1H, CHN), 4.28 (dd, J = 11.7, 5.4, 1H, CH_2O), 4.51 (s, 1H, CH_2N), 4.64 (dd, J = 11.7, 9.0, 1H, CH_2O), 4.95 (d, 1H, J = 3.3, 1H, CHO), 5.06 (ddd, J = 11.3, 5.2, 3.3, 1H, NCH$_2$CHO), 5.32 (t, J = 3.3, 1H, NCHCHO), 7.45 (m, 5H, Ar); ^{13}C NMR 21.0 (CO*C*H$_3$), 21.1 (CO*C*H$_3$), 21.1 (CO*C*H$_3$), 21.2 (CO*C*H$_3$), 61.3 (*C*H$_2$O), 66.6 (*C*HO), 68.4 (*C*HO), 69.8 (*C*HO), 128.2, 129.7, 131.1, and 137.0 (Ar), 170.4 (OC=O), 170.4 (OC=O), 170.7 (OC=O), 171.4 (OC=O), 173.1 (NC=O); IR 1746, 1644; CIMS 436 (M + 1, 8), 302 (39), 242 (41), 105 (100) 77 (43); HRMS 436.1615, $C_{21}H_{26}NO_9$ requires 436.1608.

87: $[\alpha]^{30}$ −6.8° (*c* 9.3, $CHCl_3$); ^{1}H NMR (70 °C, CD_3CN) 1.95 (s, 3H, COCH_3), 2.04 (s, 3H, COCH_3), 2.05 (s, 3H, COCH_3), 2.07 (s, 3H, COCH_3), 3.44 (dd, J = 15.4, 1.3, 1H, CH_2N), 4.23 (dd, J = 11.8, 5.7, 1H, CH_2O), 4.43 (dd, J = 11.8, 8.1, 1H, CH_2O), 4.31 (m, 1H, CHN). 4.77 (s, 1H, CH_2N), 5.13 (m, 1H, NCH$_2$CHO), 5.18 (t, J = 2.8, 1H, NCHCHO), 5.21 (m, 1H, CHO), 7.43 (m, 5H, Ar); ^{13}C NMR 20.9 (CO*C*H$_3$), 21.1 (CO*C*H$_3$), 21.2 (CO*C*H$_3$), 21.2 (CO*C*H$_3$), 44.2 (*C*H$_2$N), 56.0 (N*C*HCH$_2$O), 61.9 (*C*H$_2$O), 68.1 (*C*HO), 68.1 (*C*HO), 68.4 (*C*HO), 128.1, 129.7, 130.8, and 137.3 (Ar), 170.7 (OC=O), 171.1 (OC=O), 171.2 (OC=O), 171.3 (OC=O), 173.3 (NC=O); IR 1740, 1641, 1421; CIMS 436 (M + 1, 1), 105 (100); HRMS 436.1594, $C_{21}H_{26}NO_9$ requires 436.1608.

(−)-1-Deoxymannojirimycin Hydrochloride (90). A solution of the teraacetate **85** (47 mg, 0.11 mmol) in 6 N HCl (2 mL) was stirred at reflux for 5 h and concentrated, and the residue was washed with ether, giving 24 mg (100%) of deoxymannojirimycin hydrochloride (**90**). The free amine of **90**: The spectroscopic data for this substance were the same as the previously reported.[27a−p] $[\alpha]^{26}_D$ −7.7° (*c* 6.0, MeOH); ^{1}H NMR 3.01 (ddd, J = 10.2, 6.7, 3.3, 1H, NCH), 3.09 (dd, J = 13.6, 0.9 Hz, 1H, NCH$_2$), 3.27 (dd, J = 13.6, 2.9, 1H, NCH$_2$), 3.55 (dd, J = 9.5, 2.9, 1H), 3.68 (dd, J = 12.5, 6.7, 1H, CH$_2$-OH), 3.71 (dd, J = 10.2, 9.5, 1H, C*H*OH), 3.83 (dd, J = 12.5, 3.3, 1H, CH$_2$OH), 4.10 (ddd, J = 2.9, 2.9, 0.9, 1H, C*H*OH); ^{13}C NMR 48.2 (NCH$_2$), 58.8 (CH$_2$OH), 61.0 (CHN), 66.4, 66.6 and 73.1 (CHOH); CIMS 164 (M + 1, 100), 130 (19), 102 (18), 60 (26); HRMS 164.0923, $C_6H_{14}NO_4$ requires 164.0923.

(+)-1-Deoxyallonojirimycin (91). A solution of tetraacetate **87** (44 mg, 0.10 mmol) in 6 N HCl (2 mL) was stirred at reflux for 5 h and concentrated, and the residue was washed with ether, giving 21 mg of the hydrochloride salt of deoxyallonojirimycin. Ion-exchange chromatography provided deoxyallonojirimycin (**91**). **91**·HCl: $[\alpha]^{29}_D$ +10.9° (*c* 6.3, MeOH); ^{1}H NMR 2.96 (t, J = 11.8, 1H, NCH_2), 3.10 (dd, J = 11.8, 4.9, NCH_2), 3.17 (ddd, J = 10.8, 5.1, 3.2, 1H, NCH), 3.67 (dd, J = 10.8, 2.3, 1H, C*H*OH), 3.70 (dd, J = 12.8, 5.1, 1H, CH_2OH), 3.77 (dd, J = 12.8, 3.2, 1H, CH_2OH), 3.85 (ddd, J = 11.8, 4.9, 2.5, 1H, C*H*OH), 4.01 (dd, J = 2.5, 2.3, 1H, C*H*OH); ^{13}C NMR 44.0 (*C*H$_2$N), 57.2 (*C*HN), 60.1 (*C*H$_2$OH), 67.0, 67.8 and 72.4 (*C*HOH); CIMS 164 (M + 1, 6), 133 (30), 132 (81), 86 (18), 60 (100); HRMS 164.0923, $C_6H_{14}NO_4$ requires 164.0923.

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Supporting Information Available: ^{1}H NMR spectroscopic data for the new substances described in this publication, the X-ray crystallographic data for **80** and **82** (91 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from ACS; see any current masthead page for ordering information.

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