Tandem Inter [4 + 2]/Intra [3 + 2] Cycloadditions of Nitroalkenes. The Bridged Mode (*β*-Tether)†

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A new variation of the tandem inter [4 + 2]/intra [3 + 2] cycloaddition of nitroalkenes has been developed. This method involves the Lewis acid-promoted [4 + 2] cycloaddition of nitro olefins **12** with 1-alkoxy-1,4-dienes **3**. The resulting nitronates **13**, bearing a C(5) tethered dipolarophile, undergo thermal, intramolecular [3 + 2] cycloaddition to afford stable tricyclic nitroso acetals **14**, which can be subsequently reduced to unveil a new carbocycle **16**. Thus, in three steps, highly functionalized aminocyclopentanes can be stereoselectively constructed in high yield.

Introduction

The hetero-Diels−Alder reaction constitutes a powerful method for the construction of a diverse array of heterocyclic compounds.[1] This process allows for the rapid and predictable formation of complex ring systems with remarkably high regio-, diastereo-, and enantiocontrol. The utility of this method can be further enhanced if the resulting cycloadduct is poised to undergo a second reaction in tandem. Tandem pericyclic reactions are extremely valuable for the expedient and efficient construction of highly functionalized polycyclic compounds.[2] In these laboratories, the tandem [4 + 2]/[3 + 2] cycloaddition of nitroalkenes and nitronates has been developed as a general approach for the synthesis of a variety of cyclic, nitrogen-containing systems.[3] In this sequence, the Lewis acid-promoted [4 + 2] cycloaddition provides nitronic esters which undergo [3 + 2] cycloaddition with appropriate dipolarophiles to afford polycyclic nitroso acetals. Depending on the choice of the dienophile and dipolarophile, a wide variety of highly substituted nitroso acetals can be formed. In the realm of inter [4 + 2]/intra [3 + 2] nitroalkene tandem cycloadditions, threedistinct subclasses have evolved. The first two subclasses, termed the *fused* and *spiro modes*, employ substrates in which the dipolarophile is tethered at the *β*- and α-positions of the nitroalkene, respectively, Scheme 1. The third subclass involves a relatively new construction entitled the *bridged mode*.[4] The fundamental difference in this class is that the dipolarophile is attached to the vinyl ether or dienophile, as opposed to the nitroalkene. In the α-tether bridged mode, the intermediate nitronate bears a C(6) olefin which undergoes an intramolecular [3 + 2] cycloaddition to afford the bridged nitroso acetal. Importantly, the utility of the tandem process has been illustrated for all three subclasses by the reduction of the polycyclic nitroso acetals into hydroxy lactams and aminocyclohexanes.

A recent communication from these laboratories disclosed the development of a new variant of the bridged-mode tandem sequence in which the dipolarophile is attached to the *β*-position of the vinyl ether, Scheme 2.[5] Thus, intermolecular [4 + 2] cycloaddition affords a nitronate with the dipolarophile tethered to the C(5) position. Subsequent dipolar cycloaddition provides a novel bridged nitroso acetal which upon reduction reveals a highly substituted aminocyclopentane.[6]

Since these products have a structural motif that is common to a variety of known glycosidase inhibitors,[7] a general and stereoselective method for the synthesis of these compounds would be useful. This full report details our efforts on the *β*-tethered bridged-mode process ([4 + 2]/[3 + 2]/cleavage) with achiral vinyl ethers and simple nitro olefins.

Results

Synthesis of 1-Alkoxy-1,4-pentadienes. To explore the scope and limitation of the *β*-bridged-mode tandem

† Tandem [4 + 2]/[3 + 2] Cycloadditions of Nitroalkenes. 19.

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(6) For a review of a 1,3-dipolar cycloaddition approach to substitued aminocyclopentanols see: Padwa, A.; Schoffstall, A. M. In *Advances in Cycloadditions*; Curran, D. P., Ed.; JAI Press: Greenwich 1990; Vol. 2, pp 1−89.

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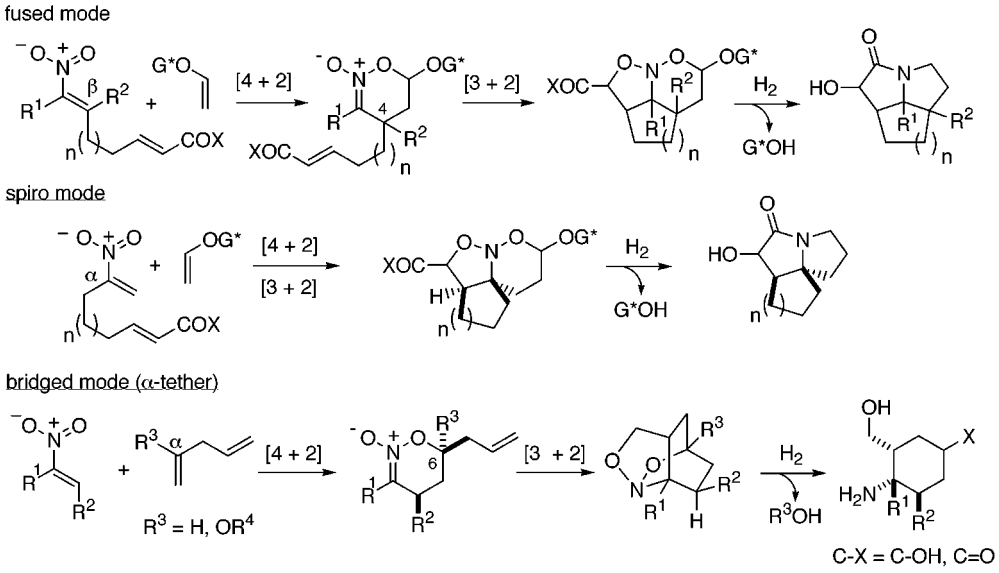
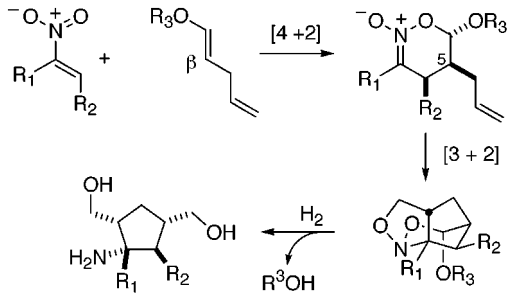
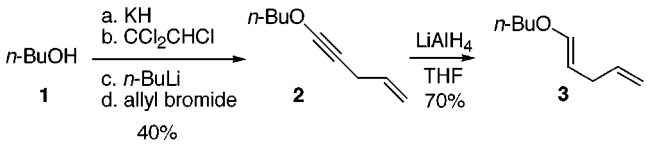
Scheme 1



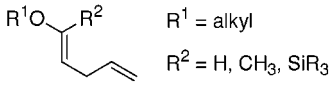
Scheme 2



Scheme 3

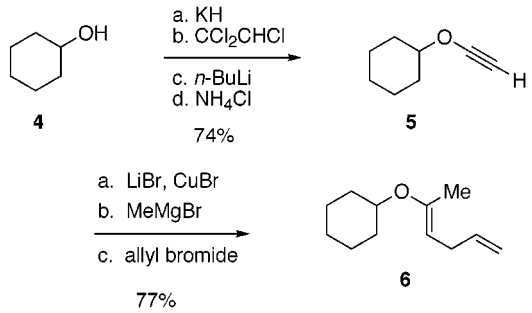


process, a variety of dienophile/dipolarophile components were prepared. In all cases, the dienophile (enol ether) was β-substituted with a simple allyl group (dipolarophile) in a trans configuration. In the inital survey, a simple butyl ether was employed, while in a subsequent investigation a chiral auxiliary was appended. For most studies, a disubstituted dienophile (R^2 = H) was used, though a brief examination of substitutent effects (R^2 = Me, Me_3Si) will be mentioned.



Following the method of Greene,[8] the potassium alkoxide of **1** was treated sequentially with trichloroethylene and *n*-butyllithium, to afford, after quenching with allyl bromide, the acetylenic ether **2** in 40% yield, Scheme 3. Lithium aluminum hydride reduction of **2** provided exclusively the trans-vinyl ether **3** in 70% yield.[9]

Scheme 4



Preparation of the disubstituted vinyl ether **6** was accomplished in two steps starting from cyclohexanol (**4**). The potassium alkoxide of **4** was combined with trichloroethylene and *n*-butyllithium, to afford, after quenching with saturated aqueous ammonium chloride solution, the acetylenic ether **5** in 74% yield, Scheme 4. Methylcupration of alkynyl ether **5** followed by trapping the vinyl cuprate with allyl bromide provided the disubstituted vinyl ether **6** in 77% yield.[10]

The silyl-substituted vinyl ethers **7** and **11** were prepared as outlined in Scheme 5. The simple vinyl ether **7** was accessed through metalation of *n*-butyl vinyl ether followed by quenching with trimethylsilyl chloride.[11] Synthesis of the α-silyl-β-allyl vinyl ether **11** was accomplished as reported by Ito from a novel silastannation procedure.[12] Palladium-mediated reaction of silylstannane **9** with ethoxy acetylene (**8**) provided the vinylstannane **10**, which was subsequently coupled with allyl bromide to afford the desired silyl-substituted pentadiene **11** in moderate yield.

Cycloadditions of Nitroalkene 12 and Vinyl Ether 3. (*E*)-2-Methyl-2-nitrostyrene (**12**)[13] was chosen as the test nitro olefin for orienting experiments with the vinyl ether **3**. A variety of Lewis acids were found to be useful in promoting the [4 + 2] cycloaddition, Table 1. Titanium

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Scheme 5

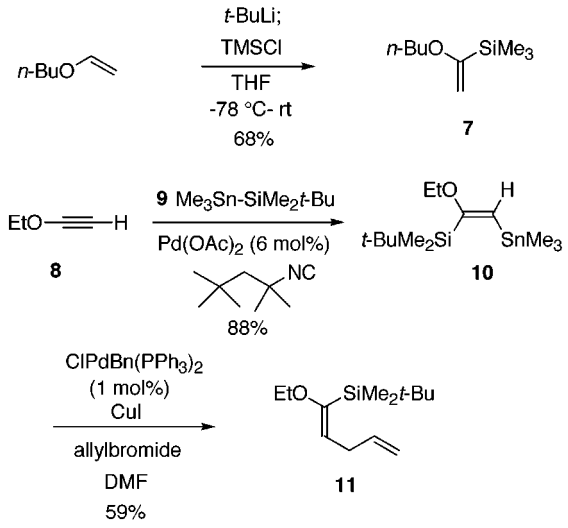
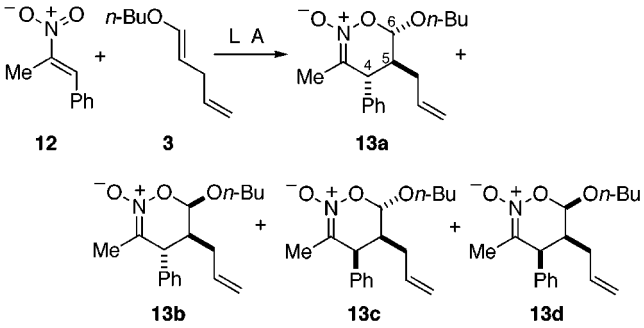


Table 1. [4 + 2] Cycloadditions of Nitroalkene 12 with Vinyl Ether 3



Lewis acid (equiv)	*T*, °C	yield, %	**13a**/**13b**/-**13c**/**13d**[a]	endo/exo (**13a** + **13b**/-**13c** + **13d**)[a]
Ti(O-*i*-Pr)$_2$Cl$_2$ (6)	−30	97	14/98/1/0	112/1
SnCl$_4$ (2)	−78	91	1/4.9/11.5/1.3	1/2.2
MAD (3)	−20	94	3.9/0/1/0	3.9/1

[a] Determined by isolation and by ^{1}H NMR integration.

diisopropoxide dichloride (Ti(O-*i*-Pr)$_2$Cl$_2$) effected a highly selective cycloaddition affording in 97% yield a mixture of three diastereomeric nitronates **13a**, **13b**, and **13c** in a ratio of 14/98/1 (**13a**/**13b**/**13c**). An interesting switch in diastereoselectivity was observed when tin(IV) chloride (SnCl$_4$) was used as the Lewis acid promoter. In this case a diastereomeric mixture of four nitronates (1/4.9/11.5/1.3, **13a**/**13b**/**13c**/**13d**) was obtained in 91% yield. Additionally, an aluminum-based Lewis acid, methylaluminum bis(2,6-di-(*tert*-butyl)-4-methylphenyloxide) (MAD), provided a 3.9/1 mixture of only two diastereomeric nitronates **13a** and **13c** in 94% yield.

The Lewis acid-promoted [4 + 2] cycloaddition of nitroalkene **12** with enol ether **3** should only produce twodiastereomeric nitronates **13a** and **13c**, which result from endo- and exo-mode approaches of the vinyl ether to the nitroalkene, respectively. The other two diastereomers **13b** and **13d** are believed to have arisen from epimerization of the anomeric center (C(6)) under the reaction conditions.[14] The stereostructural assignments of **13a**−**d** draw on ample precedent and chemical correlation. The assignment of the trans C(4)/C(5) configuration for **13a** and **13b** was made on the basis of the following: (1) both **13a** and **13b** were subsequently converted to the same aminocyclopentane **16**, (2) the diagnostic resonance at HC(4) in nitronates **13a** and **13b** displays a significant upfield chemical shift (0.5−1.1 ppm) with respect to the same proton in nitronates **13c** and **13d**, Figure 1, and (3) Ti(O-*i*-Pr)$_2$Cl$_2$-promoted cycloadditions of very similar partners have been shown to proceed via an endo-(alkoxy) [4 + 2] transition structure.[15] Thus, it is reasonable to conclude that nitronates **13a** and **13b**, which were formed with high selectivity in a Ti(O-*i*-Pr)$_2$Cl$_2$-promoted reaction (Table 1), arose from an endo-(alkoxy) mode process and must contain a trans C(4)/C(5) relationship. By default, the minor product of this reaction **13c** must have a cis C(4)/C(5) relationship and be designated as resulting from an exo-(alkoxy) mode cycloaddition.[16] The suggestion that it bore a trans C(5)/C(6) relationship was supported by its formation from an MAD-promoted reaction. Aluminum-based Lewis acids have never been observed to cause epimerization of the products in nitroalkene cycloadditions. Only two diastereomers, **13a** and **13c**, were produced from the MAD-promoted reaction, and they are assigned to be the unepimerized C(4)/C(5) trans and C(4)/C(5) cis nitronates, respectively. Significantly, the major diastereomer was found to be identical to **13a** formed in the "Ti"-promoted reaction, thereby allowing the assignment of **13b** as the C(4)/C(5) trans, C(5)/C(6) cis isomer. Finally, diastereomer **13d**, which was produced as a minor product from a SnCl$_4$-promoted [4 + 2] reaction, must possess a C(4)/C(5) cis, C(5)/C(6) cis relationship, i.e., exo-mode cycloaddition, affording **13c**, followed by epimerization of the anomeric center.

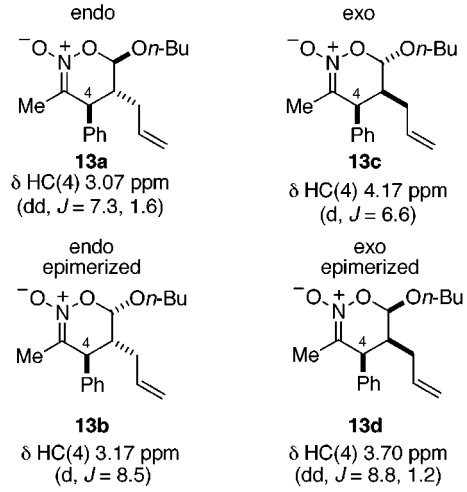


Figure 1. ^{1}H NMR chemical shift data for HC(4) of nitronates **13a**−**d**.

As was the case in the α-tethered bridged-mode cycloadditions,[4] thermal activation was required to effect the intramolecular [3 + 2] cycloaddition. Thus, the desired nitroso acetal **14a** was obtained in good yield (79%) by heating a dilute solution (0.01 M) of **13a** in

(14) The nitroalkene and vinyl ether are presumed to retain their stereochemical integrity under the reaction condition.

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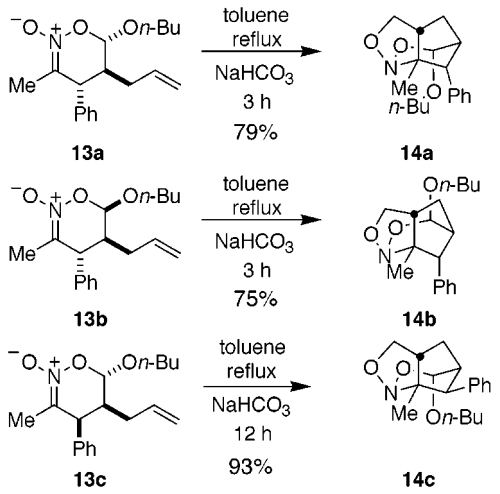
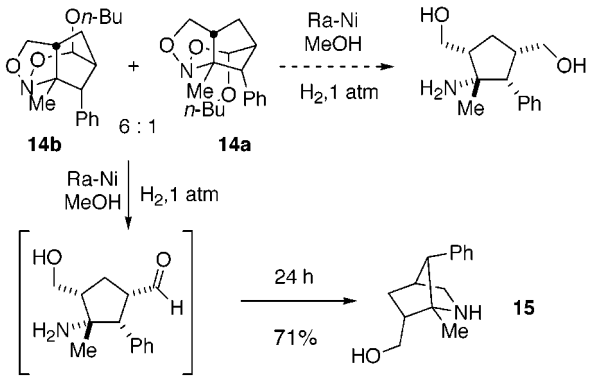
(16) This was subsequently confirmed by correlation of the end product **17** to an identical material derived from a nitroso acetal related to **14c** whose structure was established by X-ray crystallography, see accompanying paper in this issue and Denmark, S. E.; Swiss, K. A.; Dixon, J. D. *Acta Crystallogr. C* **1996**, *C52*, 2561.

Scheme 6



Scheme 7

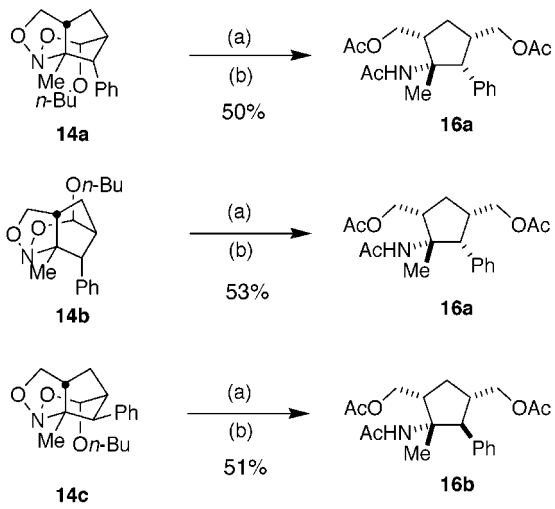


toluene at reflux for 3 h in the presence of sodium bicarbonate,[17] Scheme 6. The sodium bicarbonate serves to neutralize acid resulting from the slow decomposition of nitronates and/or nitroso acetals. In a similar fashion, nitronates **13b** and **13c** smoothly underwent [3 + 2] cycloaddition to afford their corresponding diastereomeric nitroso acetals **14b** and **14c** in good to excellent yield.

Reduction of Nitroso Acetals 14a−c. After demonstrating the feasibility of the β-bridged-mode tandem process, our attention was focused on the unmasking of the nitroso acetals. Initial efforts at hydrogenolytic cleavage of a mixture of nitroso acetals **14b** and **14a** using the standard Raney nickel protocol (W-2 Ra−Ni/1 atm of hydrogen) failed to provide the desired aminocyclopentanedimethanol, Scheme 7. Unexpectedly, the interesting bicyclic amine **15** was obtained in good yield. Furthermore, bicyclic amines were obtained as the major products from the reduction of pure nitroso acetals **14a**, **14b**, and **14c**. Several experimental variations of the reduction were employed to circumvent the formation of amine **15**, including the use of higher hydrogen pressures, more activated Raney nickel, and additives such as chloroplatinic acid. Unfortunately, none of the modifications prevented intramolecular reductive amination which lead to the construction of bicyclic amine **15**.[18]

Since bicyclic amine **15** must arise from condensation and reduction of an intermediate amino aldehyde, we sought a new reagent combination that would intercept the aldehyde before imine formation could occur. Consequently, we were delighted to find that the addition of sodium borohydride to a solution of the nitroso acetal **14a** and Raney nickel, under an atmosphere of hydrogen in ethanol at room temperature, provided the desired aminocyclopentane **16a** in moderate yield (50% after acylation), Scheme 8. Similarly, the diastereomeric nitroso acetal **14b** was reduced to the same aminocyclopentane triacetate **16a** in 53% yield over the two steps. Finally, nitroso acetal **14c** was hydrogenated in the presence of Raney nickel and sodium borohydride to provide, after acylation, the epimeric aminocyclopentane triacetate **16b** in 51% yield.

Scheme 8



(a) Raney nickel, EtOH, H_2, $NaBH_4$; (b) Ac_2O, pyridine

Cycloadditions of Nitroalkene 12 with Vinyl Ethers 6, 7, and 11. An alternative strategy to avoid the formation of bicyclic amine in the hydrogenolysis entailed the use of a disubstituted enol ether as the dienophile/dipolarophile component in the tandem process. It was speculated that during the hydrogenolysis the intermediate amino *ketone* would be less prone to undergo intramolecular imine formation as readily as an intermediate amino aldehyde. The $Ti(O\text{-}i\text{-}Pr)_2Cl_2$-promoted [4 + 2] cycloaddition of nitroalkene **12** with enol ether **6** provided a 5/1 mixture of diastereomeric nitronates **17a** and **17b** in moderate yield, Scheme 9.[19] The major diastereomer, which arose from an endo(alkoxy)-mode cycloaddition, was heated in toluene at reflux for 12 h to afford the desired nitroso acetal **18** in 72% yield. Unfortunately, hydrogenation of nitroso acetal **18** using Raney nickel and hydrogen provided, after acylation, a complex mixture of bicyclic amines **19** and desired aminocyclopentane derivatives **20** in low yield. Additionally, a stable bicyclic *imine* could be isolated from these reactions in varying amounts. While this alternate strategy provided small quantities of the desired aminocyclopentanes, the formation of unwanted bicyclic amine still predominated in the hydrogenolysis.

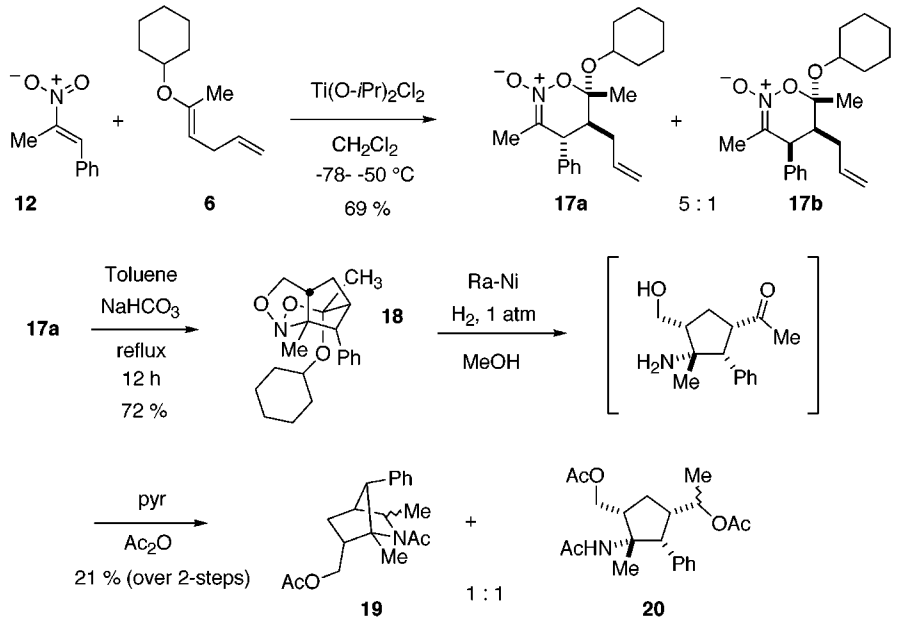
In a similar vein, we evaluated the use of silyl-substituted vinyl ethers as a means to achieve our goal

(17) The presence of an insoluble base such as $NaHCO_3$ in [3 + 2] cycloadditions was critical for the success of these reactions, since the resulting nitroso acetals are acid labile.

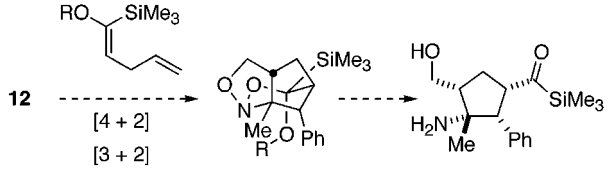
(18) Additionally, the use of lithium aluminum hydride as a reducing agent was explored but the starting nitroso acetal remained unchanged even in a refluxing solution of THF.

(19) The stereochemical assignment of the nitronates was based on previous results that $Ti(O\text{-}i\text{-}Pr)_2Cl_2$ promotes endo selective [4 + 2] cycloadditions and the relative chemical shift of the C(4) proton in the nitronate as discussed above.

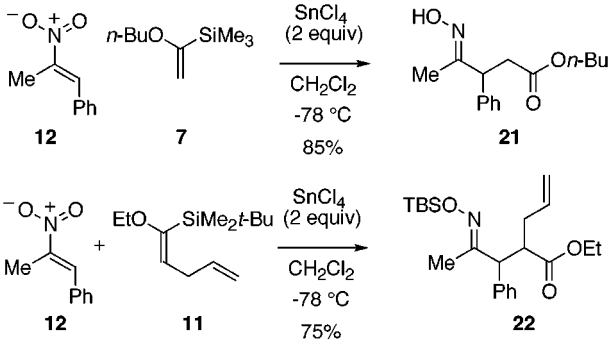
Scheme 9



Scheme 10



Scheme 11



of accessing aminocyclopentanes. It was envisioned that during the reduction of a silyl-substituted nitroso acetal, formed via a tandem [4 + 2]/[3 + 2] cycloaddition, the intermediate acyl silane would be too sterically encumbered to undergo intramolecular condensation, Scheme 10. Furthermore, it was hoped that the acyl silane moiety would provide a convenient handle for further functional group manipulations.

Curiously, the $SnCl_4$-promoted [4 + 2] cycloaddition of nitroalkene **12** with vinyl ether **7** did not provide the expected nitronate, Scheme 11. Instead, an 85% yield of the substituted oxime **21** was obtained.[20] Similarly, the [4 + 2] cycloaddition of nitroalkene **12** with *tert*-butyldimethylsilyl-substituted pentadiene **11** afforded a product that is believed to be the silylated oxime **22**. Interestingly, other Lewis acids such as Ti(O-*i*-Pr)$_2$Cl$_2$ and MAD failed to promote this reaction.

(20) The identity of **21** was secured by 1-D and 2-D NMR spectroscopy as well as other analytical techniques.

Discussion

Epimerization. The tendency for epimerization at C(6) when Ti(O-*i*-Pr)$_2$Cl$_2$ or $SnCl_4$ was used as the Lewis acid promoter is believed to result from trace amounts of acid that are generated from hydrolysis of these Lewis acids by adventitious moisture or enol ether decomposition.[21] The driving force for the epimerization of **13a** to **13b** is clearly due to the formation of a thermodynamically more stable nitronate. If the preferred conformation of **13a** is a half-chair with the oxygen substituent in an axial position for anomeric stabilization, then epimerization of **13a** places the phenyl and allyl substituents equatorially, relieving serious 1,3-diaxial interaction and leading to a more stable nitronate, **13b**, Figure 2. The driving force for epimerization of **13c** to **13d** is not so obvious; however, this isomerization may be attributed to the relief of $A^{1,2}$ strain in **13c**.[22]

[4 + 2] Cycloaddition: Endo/Exo Selectivity. The stereochemical course of the [4 + 2] cycloaddition is governed by the orientation of the vinyl ether (exo or endo) in its approach to the nitroalkene. Importantly, the Lewis acid employed in the cycloaddition has an enormous influence on endo/exo selectivity. Previous investigations from these laboratories have documented that Ti(O-*i*-Pr)$_2$Cl$_2$ promotes endo selective [4 + 2] cycloadditions.[3b,23] This phenomenon has been attributed to a favorable Coulombic interaction between the electron-rich oxygen atom of the vinyl ether and the electron-

(21) It should be noted that alkylaluminum-derived Lewis acids can also serve as Bronsted bases. Snider, B. B. *Acc. Chem. Res.* **1980**, *13*, 426.

(22) Since this epimerization is only observed when $SnCl_4$ is used as the Lewis acid and only a small quantity of product is formed, generation of nitronate **13d** may not be due to a simple epimerization. Perhaps, under the $SnCl_4$-promoted [4 + 2] cycloaddition conditions, isomerization of a small amount of the trans-vinyl ether **3** to a cis-vinyl ether followed by and an exo mode cycloaddition could give rise to nitronate **13d**. In the presence of MAD and Ti(O-*i*-Pr)$_2$Cl$_2$, the stereochemical integrity of the vinyl ether is maintained; however, the stereochemical integrity of the vinyl ether in the presence of $SnCl_4$ has never been addressed.

(23) (a) Denmark, S. E.; Senanayake, C. B. W. *J. Org. Chem.* **1993**, *58*, 8, 1853. (b) Denmark, S. E.; Thorarensen, A. *J. Org. Chem.* **1994**, *59*, 5672. (c) Denmark, S. E.; Schnute, M. E.; Marcin, L. R.; Thorarensen, A. *J. Org. Chem.* **1995**, *60*, 3205.

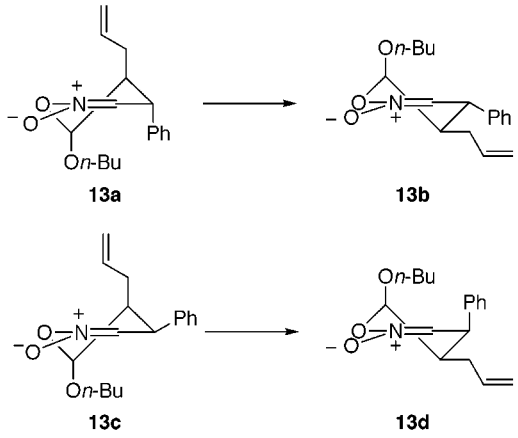


Figure 2. Proposed stable conformations of nitronates **13a**−**d** (the C(2)-methyl group is omitted for clarity).

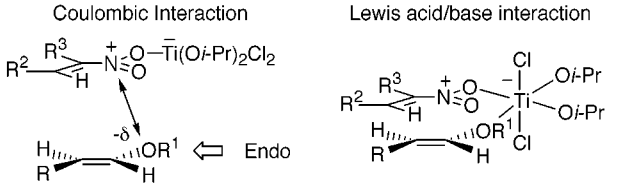


Figure 3. Preferred endo approach of the vinyl ether to the nitroalkene−Lewis acid complex.

deficient nitroalkene, Figure 3. Alternatively, an association of the vinyl ether oxygen with the coordinatively unsaturated titanium Lewis acid may be considered.

Interestingly, the MAD-promoted [4 + 2] cycloaddition of **12** with **3** favored an endo transition structure. While the ability of MAD to promote selective endo-mode cycloadditions has precedence,[4] the nature of this selectivity is intriguing when considering the significant steric bulk of this Lewis acid. The predominance for exo selectivity in the cycloaddition of **12** with **3** when promoted by $SnCl_4$ is also consistent with other results from these laboratories.[4,24] The origin of this selectivity might be a conformational change of the vinyl ether (*s*-trans/*s*-cis) in the presence of $SnCl_4$ or from the formation of bulky hexacoordinate tin complexes. In any case, this interesting reversal in selectivity is the subject of more detailed investigations that will be reported in the accompanying paper in this issue.

[3 + 2] Cycloaddition. The nitroso acetals arose from a single stereochemical pathway which was dictated by the geometrical constraints on the dipolarophile. Specifically, the allyl group approached the nitronate moiety in an endo, syn-cofacial fashion with the methylene terminus attached to the oxygen of the dipole. No other arrangement is geometrically feasible. The activation energy required for the [3 + 2] cycloaddition is dependent on the reactivity of the dipolarophile and the accessibility of a reactive conformation of the nitronate. The effects of dipolarophile geometry and substitution on the rate of the intramolecular [3 + 2] cycloaddition of cyclic nitronates has been studied in detail.[25] This investigation revealed that the rate of cycloaddition with unactivated, monosubstituted dipolarophiles is much slower than with disubstituted dipolarophiles. Thus, the intramolecular [3 + 2] cycloaddition of nitronates **13a**−**c** and **17a** is an energetically costly processes since it involves the reaction of an unactivated, monosubstituted dipolarophile. The difference in rates of cycloaddition of trans C(4)/C(5) nitronates (**13a/b**) and cis C(4)/C(5) nitronate **13c** was noted previously, in the related bridged-mode (α-tether) cycloadditions.[4b] While the effect observed herein is much less dramatic, we again suspect that the avoidance of $A^{1,2}$ strain between the methyl and phenyl substitutents allows for more facile access to the reactive conformers in **13a/b**.

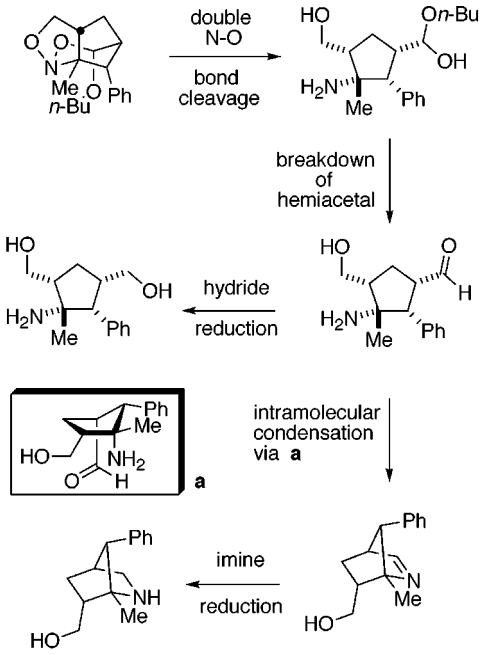


Figure 4. Proposed mechanism for the hydrogenolysis.

The generation and stability of the unique skeleton of the nitroso acetals are quite remarkable since the tricyclic core appears to be a very strained framework. Additionally, the nitroso acetals are thermally stable and less acid labile than the corresponding tricyclic nitroso acetals derived from the bridged mode (α-tether).[4] The conformation (chair or boat) of the oxazine ring in the various nitroso acetals has not been unambiguously determined and has been drawn with the oxygen axial in all cases.[26] The factors that are believed to influence the preferred conformation of the oxazine ring include anomeric stabilization and 1,3-diaxial interactions. The optimum conformation would be one in which the oxygen substituent would be placed axial in order to enjoy anomeric stabilization, while not experiencing interactions with a neighboring axially standing substituent. In many of the nitroso acetals, the benefit of the anomeric stabilization cannot be experienced without the adverse 1,3-diaxial interactions. Thus, the conformation of the oxazine ring in these cases cannot be predicted.

Hydrogenolysis. A suggested mechanism for the formation of the bicyclic amine and aminocyclopentane derivative from the Raney nickel reduction of the nitroso acetal is outlined in Figure 4. Double N−O bond cleavage of the nitroso acetal affords, after breakdown of the

(24) Denmark, S. E.; Schnute, M. E. *J. Org. Chem.* **1994**, *59*, 4576.
(25) Denmark, S. E.; Senanayake, C. B. W. *Tetrahedron* **1996**, *35*, 11579.

(26) X-ray crystal structure analysis of several chiral nitroso acetals from the β-tether tandem process indicate that the oxygen substituent prefers to be axial so that anomeric stabilization is gained, cf. ref 16.

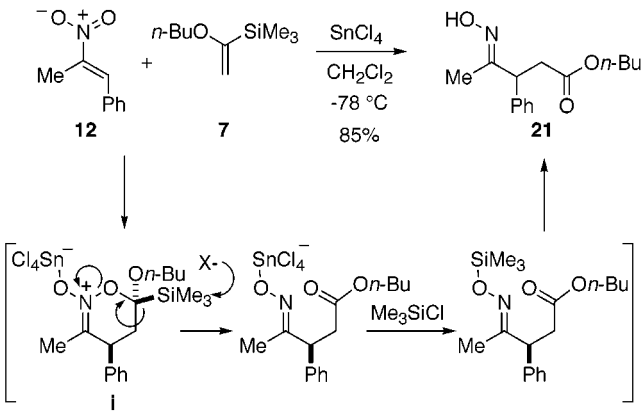


Figure 5. Proposed mechanism for the formation of oximes.

intermediate hemiacetal, an amino aldehyde which is capable of reacting through two different pathways. The first involves the reduction of the aldehyde with a hydride source to provide the desired aminocyclopentane. The second pathway entails the intramolecular condensation of the amino aldehyde followed by reduction of the imine to afford the bicyclic amine. The intramolecular condensation of intermediate amino aldehydes, generated from the reduction of a variety of nitroso acetals and nitronates, is a very important event in the formation of a variety of polycyclic nitrogen-containing compounds and pyrrolidines.[3,15,23−25] In the reduction of the tricyclic nitroso acetals, it was initially thought that the intramolecular condensation would be energetically disfavored since a strained bicyclic system would be produced. However, by looking at a low-energy conformation of the five-membered ring (structure a) it can be seen that the aldehyde and the amine are placed pseudoaxially and are poised to undergo a facile intramolecular imine formation.

The combined use of Raney nickel and sodium borohydride in the hydrogenolysis was successful in the generation of our desired aminocyclopentane derivatives. The presence of sodium borohydride in the reaction mixture serves to reduce the intermediate aldehyde before an intramolecular condensation can occur. Additionally, the combination of sodium borohydride and Raney nickel may be creating a new nickel species that serves as the reducing agent which cleaves the N−O bonds of the nitroso acetal. It is well established that adding sodium borohydride to nickel acetate or nickel chloride generates nickel boride which is a powerful reducing agent.[27]

Oxime Formation. The unexpected generation of oxime **22** from the $SnCl_4$-promoted [4 + 2] cycloaddition of nitro olefin **12** with silyl-substituted vinyl ether **7** is rationalized as outlined in Figure 5. Intermediate i is ideally set up for a silyl-Kornblum-type[28] fragmentation to produce the ester oxime **21**. Presumably, the immediate product is the silyl oxime as was seen for **22** which was generated from nitroalkene **12** and silyl-substituted pentadiene **11** in a similar fashion. However, the *tert*-butyldimethylsilyl group is maintained in the final product **22**, due to the robust nature of this silyl group under acidic conditions. The product oximes are versatile 1,4-dicarbonyl compounds that are not easily generated by other methods.

(27) For review on nickel boride see: Ganem, B.; Osby, J. O. *Chem. Rev.* **1986**, *86*, 763.
(28) Kornblum, N.; Brown, R. A. *J. Am. Chem. Soc.* **1964**, *86*, 2681.

Conclusion

The feasibility of the bridged (β-tether) mode tandem inter [4 + 2]/intra [3 + 2] cycloaddition process has been demonstrated. Simple 1-alkoxy-1,4-pentadienes as well as 1-alkoxy-1-alkyl-1,4-pentadiene function effectively as the dienophile/dipolarophile component in the tandem sequence. Good to excellent selectivities and yields were obtained in the [4 + 2] cycloaddition when promoted by a variety of Lewis acids. The intramolecular [3 + 2] cycloadditions proceeded with good yields affording stable, bridged nitroso acetals. Hydrogenolytic unmasking of the nitroso acetals was successfully accomplished using a combination of Raney nickel and sodium borohydride to provide the target aminocyclopentanes. Further studies on the application of this tandem sequence for the asymmetric preparation of aminocyclopentane derivatives will be addressed in the following report.

Experimental Section

General. See Supporting Information.

Materials. See Supporting Information.

1-Butyloxypent-4-ene-1-yne (2). To a room temperature suspension of prewashed (5 × 20 mL hexanes) potassium hydride (3.5 g, 87.3 mmol, 2 equiv) in THF (90 mL) was added a solution of *n*-butanol **1** (4.04 mL, 43.63 mmol) in THF (90 mL) via cannula. The suspension was stirred at room temperature for 1 h and then cooled to −60 °C. A solution of trichloroethylene (5.2 mL, 43.63 mmol, 1 equiv) in THF (50 mL) was then added via cannula to the cold reaction mixture. After the addition, the reaction was allowed to warm to room temperature and stir for 2 h. The resulting dark brown mixture was recooled to −78 °C, and *n*-butyllithium (67 mL, 104.7 mmol, 2.4 equiv) was added via cannula. The reaction was allowed to warm to −10 °C over a 2 h period and was then recooled to −78 °C. A solution of allyl bromide (19 mL, 218.2 mmol, 5 equiv) in hexamethylphosphoramide (HMPA) (10 mL) was added to the cold reaction via cannula, and the reaction was allowed to warm to room temperature and stir for 4 h. Reaction mixture was quenched with aqueous NH_4Cl (20 mL), diluted with pentane (150 mL), and washed with water (3 × 150 mL). The aqueous phase was back extracted with pentane (2 × 100 mL), and the combined organic layer was washed with brine (100 mL), dried (Na_2SO_4), filtered, and concentrated to provide a dark brown oil. The crude organic concentrate was purified by basic alumina (activity III) chromatography (pentane) and then by silica gel (pretreated with Et_3N (2 mL/300 mL of hexane)) column chromatography (hexane). Residual solvent was removed at 25 °C with an 80 mbar vacuum to provide 2.4 g (40%) of alkynyl ether **2** as a light yellow liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.83 (ddt, J = 16.8, 10.0, 5.0, 1 H), 5.29 (dq, J = 16.9, 2.0, 1 H), 5.06 (dq, J = 10.0, 1.8, 1 H), 4.00 (t, J = 6.2, 2 H), 2.90 (dt, J = 5.2, 2.0, 2 H), 1.74−1.67 (m, 2 H), 1.45−1.36 (m, 2 H), 0.94 (t, J = 7.4, 3 H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 134.29, 114.94, 91.82, 78.15, 33.59, 30.73, 21.63, 18.57, 13.61; IR (neat) 2962, 2937, 2275, 1237, 1212, 937, 914; TLC R_f 0.30 (hexane).

1-Butyloxy-1,4-pentadiene (3). Lithium aluminum hydride (98 mg, 25.87 mmol, 4 equiv) was added to a solution of the acetylenic ether (−)-**2** (89 mg, 6.47 mmol) in THF (64 mL). The suspension was heated to reflux for 45 min. After the solution was cooled to room temperature, the excess hydride was quenched with water (0.98 mL), 15% $NaOH/H_2O$ (0.98 mL), and finally water (1.86 mL). The suspension was stirred at room temperature approximately 30 min, and the white salts were removed by filtration, washing with EtOAc (100 mL). Concentration afforded a light yellow oil. The crude

organic concentrate was purified by basic alumina (activity III) chromatography (pentane), and the residual solvent was removed at 25 °C with a 60 mbar vacuum to provide 635 mg (70%) of vinyl ether **3** as a clear liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.25 (d, J = 12.7, 1 H), 5.87−5.77 (m, 1 H), 5.07−5.01 (m, 1 H), 4.98−4.94 (m, 1 H), 4.75 (dt, J = 12.7, 7.1, 1 H), 3.65 (t, J = 6.6, 2 H), 2.68−2.64 (m, 2 H), 1.65−1.58 (m, 2 H), 1.44−1.35 (m, 2 H), 0.93 (t, J = 7.5, 3 H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 147.13, 138.17, 114.36, 101.19, 68.86, 31.94, 31.33, 19.16, 13.82; IR (neat) 2960, 2935, 2874, 1655, 1175; MS (70 eV) 141 (M^+ + 1, 7), 83 (100); TLC R_f 0.36 (hexane).

1-Cyclohexyloxyacetylene (5). To a room temperature suspension of prewashed (5 × 20 mL of hexanes) potassium hydride (2.0 g, 49.9 mmol, 2 equiv) in THF (45 mL) was added a solution of cyclohexanol **4** (2.6 mL, 24.9 mmol) in THF (45 mL) via cannula. The suspension was stirred at room temperature for 1.5 h and then cooled to −60 °C. A solution of trichloroethylene (2.98 mL, 24.9 mmol, 1 equiv) in THF (27 mL) was then added via cannula to the cold reaction mixture. After the addition, the reaction was allowed to warm to room temperature and stir for 2 h. The resulting dark brown mixture was recooled to −78 °C, and *n*-butyllithium (40 mL, 62.3 mmol, 2.5 equiv) was added via cannula. The reaction was allowed to warm to −10 °C over a 2 h period and was then quenched with ammonium chloride (30 mL). The reaction mixture was diluted with pentane (100 mL) and washed with water (3 × 100 mL). The aqueous phase was back extracted with pentane (2 × 100 mL), and the combined organic layer was washed with brine (100 mL), dried (Na_2SO_4), filtered, and concentrated to provide a dark brown oil. The crude organic concentrate was purified by basic alumina (activity III) chromatography (pentane). Residual solvent was removed at 25 °C with a 60 mbar vacuum to provide 2.28 g (74%) of alkynyl ether **5** as a light brown liquid: ^{1}H NMR (499.7 MHz, $CDCl_3$) δ 4.11−4.06 (m, 1 H), 1.99−1.96 (m, 2 H), 1.79−1.73 (m, 2 H), 1.65−1.58 (m, 2 H), 1.53−1.48 (m, 2 H), 1.37−1.25 (m, 3 H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 89.89, 86.49, 30.74, 27.03, 25.04, 23.09; IR (neat) 3320, 2942, 2938, 2862, 2143; MS (CI) 125 (M^+ + 1, 0.2), 83 (100); TLC R_f 0.33 (hexane); HRMS (FAB) calcd for $C_8H_{11}O$ 123.08079, found 123.08099.

1-Cyclohexyloxy-1-methyl-1,4-pentadiene (6). Lithium bromide (547 mg, 6.3 mmol, 1.26 equiv) was placed under vacuum and flame dried until the internal temperature was approximately 150 °C. Copper bromide (904 mg, 6.3 mmol, 1.26 equiv) was then added, and the solids were placed under vacuum for 20 min. Tetrahydrofuran (23 mL) was added, the suspension was cooled to −90 °C, and a solution of methylmagnesium bromide (2.0 mL, 6.0 mmol, 1.2 equiv) in THF (5 mL) was added dropwise via cannula. After 15 min, a solution of acetylenic ether **5** (620 mg, 5.0 mmol) in THF (1 mL) was added dropwise and the reaction was allowed to warm to −78 °C. After 1 h, a solution of allyl bromide (0.93 mL, 10.0 mmol, 2 equiv) in THF (1 mL) was slowly added dropwise and the mixture was allowed to warm to 0 °C over a 2 h period. The reaction was allowed to stir for an additional 1 h between 0 °C and room temperature and was then quenched with saturated aqueous NH_4Cl (20 mL). The mixture was diluted with pentane (100 mL) and was washed with water (3 × 100 mL). The aqueous phase was back extracted with pentane (3 × 50 mL), and the combined organic layers were washed with brine (75 mL), dried (Na_2SO_4), filtered, and concentrated with care (compound is volatile). The crude organic concentrate was purified by basic alumina (activity III) chromatography (pentane). Residual solvent was removed at 25 °C with a 60 mbar vacuum to provide 698 mg (77%) of vinyl ether **6** as a clear liquid: ^{1}H NMR (499.7 MHz, $CDCl_3$) δ 5.86−5.78 (m, 1 H), 5.02 (dd, J = 17.0, 1.6, 1 H), 4.94 (dd, J = 10.0, 1.5, 1 H), 4.43 (t, J = 7.5, 1 H), 3.94−3.89 (m, 1 H), 2.72 (dd, J = 7.0, 6.6, 2 H), 1.93−1.90 (m, 2 H), 1.74−1.72 (m, 5 H), 1.55−1.53 (m, 1 H), 1.40−1.22 (m, 5 H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 151.35, 138.23, 113.69, 95.92, 73.21, 31.75, 31.25, 25.77, 24.01, 16.39; IR (neat) 2933; MS (CI) 181 (M^+ + 1, 0.6), 83 (100); TLC R_f 0.33 (hexane); HRMS (FAB) calcd for $C_{12}H_{21}O$ 181.15863, found 181.15924.

(1-Butoxyvinyl)trimethylsilane (7). To a −78 °C solution of butyl vinyl ether (4.14 mL, 32 mmol, 1.6 equiv) in THF (12 mL) was slowly added *tert*-butyllithium (20.0 mL, 26 mmol, 1.3 equiv) over a period of 1.5 h. The resulting, bright-yellow, heterogeneous mixture was allowed to warm to 0 °C over a 3 h period and was then recooled to −78 °C. Trimethylsilyl chloride (2.54 mL, 20 mmol) was added dropwise via syringe, and the reaction was allowed to warm to room temperature and stir for 3 h. The reaction mixture was quenched with saturated aqueous NH_4Cl (20 mL), diluted with pentane (75 mL), and washed with saturated aqueous NH_4Cl (3 × 100 mL). The aqueous phase was back-extracted with pentane (2 × 50 mL) and the combined organic layers were washed with brine (50 mL) and then were dried (K_2CO_3), filtered, and concentrated. The crude organic concentrate was purified by bulb-to-bulb distillation to afford 2.36 g (68%) of analytically pure **7** as a clear thin oil: bp 55 °C (5.0 Torr); ^{1}H NMR (499.7 MHz, $CDCl_3$) δ 4.55 (d, J = 1.7 1 H), 4.26 (d, J = 1.7 1 H), 3.63 (t, J = 6.3, 2 H), 1.68−1.62 (m, 2 H), 1.46−1.38 (m, 2 H), 0.94 (t, J = 7.4, 3 H), 0.11 (s, 9 H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 170.15, 93.21, 66.13, 31.09, 19.42, 13.86, −2.38; IR (neat) 2960, 2936, 1584, 1249, 1216; MS (CI) 173 (M^+ + 1, 8), 57 (100). Anal. Calcd for $C_9H_{20}OSi$ (172.34): C, 62.72; H, 11.70. Found: C, 62.62; H, 11.86.

***rel*-(4*R*,5*S*,6*S*)-6-Butyloxy-3-methyl-4-phenyl-5-(2-propenyl)-5,6-dihydro-4*H*-[1,2]-oxazine *2*-Oxide (13a).** Trimethylaluminum (2.0 M in toluene, 2.19 mL, 4.38 mmol, 3.0 equiv) was added dropwise to a solution of 2,6-di-*tert*-butyl-4-methylphenol (1.93 g, 8.76 mmol, 6.0 equiv) in toluene (8 mL) at room temperature. Gas evolution (CH_4) was observed, and the resulting clear solution was stirred at room temperature for 45 min. The Lewis acid solution (MAD) was transferred, via cannula, to a second reaction vessel containing a −78 °C solution of nitroalkene **12** (238 mg, 1.46 mmol) and vinyl ether **3** (410 mg, 2.92 mmol, 2 equiv) in toluene (3 mL). The resulting dark green solution was allowed to warm slowly to −35 °C and was left to stir for 12 h (the color faded to a light yellow), after which time the reaction was quenched with H_2O (8 mL). The mixture was diluted with CH_2Cl_2 (150 mL) and was washed with water (3 × 150 mL). The aquous layers were back-extracted with CH_2Cl_2 (3 × 75 mL), and the combined organic phases were washed with brine (100 mL) and then were dried (Na_2SO_4), filtered, and concentrated in vacuo. The crude material was purified by silica gel column chromatography (hexane/EtOAc, 4/1) to afford 256 mg of nitronate **13a**, 80 mg of a 20/1 (**13a**/ **13c**) mixture of **13a** and **13c**, and 82 mg of nitronate **13c**. The overall yield of the reaction was 418 mg (94%) with an overall selectivity of 3.9/1 (**13a**/**13c**) (selectivity reflects the endo/exo ratio). An analytical sample of **13a** was obtained by recrystallization (pentane). Nitronate **13c** was found to be identical by ^{1}H NMR to nitronate **13c** obtained from the $Ti(O\text{-}i\text{-}Pr)_2Cl_2$- and $SnCl_4$-promoted [4 + 2] cycloadditions. Data for **13a**: mp 36−37.5 °C (pentane); ^{1}H NMR (400 MHz, C_6D_6) δ 7.05−6.96 (m, 3 H), 6.89−6.86 (m, 2 H), 5.51−5.41 (m, 1 H), 4.95−4.86 (m, 2 H), 4.83 (d, J = 4.6, 1 H), 4.08 (dt, J = 9.5, 6.5, 1 H), 3.36 (dt, J = 9.5, 6.6, 1 H), 3.07 (dd, J = 7.3, 1.6, 1 H), 2.16−2.10 (m, 1 H), 2.04−1.97 (m, 1 H), 1.90−1.82 (m, 1 H), 1.68 (d, J = 1.7, 3 H), 1.51−1.44 (m, 2 H), 1.34−1.20 (m, 2 H), 0.81 (t, J = 7.3, 3 H); ^{13}C NMR (100.6 MHz, C_6D_6) δ 140.09, 134.65, 129.11, 128.94, 127.47, 120.88, 118.03, 105.62, 69.65, 47.80, 45.87, 35.14, 31.75, 19.45, 16.84, 13.91; IR (CCl_4) 2961, 2935, 1613, 1273, 1116, 922, 894; MS (CI) 304 (M^+ + 1, 100); TLC R_f 0.17 (hexane/EtOAc, 2/1). Anal. Calcd for $C_{18}H_{25}NO_3$ (303.405): C, 71.26; H, 8.31; N, 4.62. Found: C, 71.41; H, 8.20; N, 4.77.

***rel*-(4*R*,5*S*,6*R*)-6-Butyloxy-3-methyl-4-phenyl-5-(2-propenyl)-5,6-dihydro-4*H*-[1,2]-oxazine *2*-Oxide (13b).** Titanium(IV) chloride (0.503 mL, 4.59 mmol, 3.0 equiv) was added to a solution of titanium(IV) isopropoxide (1.37 mL, 4.59 mmol, 3.0 equiv) in CH_2Cl_2 (7 mL) at room temperature. The resulting solution was allowed to stir for 30 min and was then added via cannula to a −50 °C solution of nitroalkene **12** (250 mg, 1.53 mmol) and **3** (429 mg, 3.06 mmol, 2.0 equiv) in CH_2Cl_2 (2.0 mL). The resulting dark brown reaction mixture was allowed to warm slowly to −35 °C, was left to stir for 16

h, and was then warmed further to −25 °C for 8 h. The reaction mixture was quenched (at −25 °C) with a methanolic sodium hydroxide solution (1 N, 8 mL) and then was diluted with CH_2Cl_2 (150 mL) and washed with water (3 × 150 mL). The aqueous layers were back-extracted with CH_2Cl_2 (3 × 70 mL), and the combined organic phases were washed with brine (100 mL) and then were dried (Na_2SO_4), filtered, and concentrated to afford a yellow oil. The crude material was purified twice by silica gel column chromatography (hexane/EtOAc, 4/1 (500 mL), 3/1 (400 mL), 2/1) to afford 256 mg of nitronate **13b**, 180 mg of a 2.2/1 (**13b**/**13a**) mixture of **13b** and **13a**, 13 mg of a 10/1 (**13b**/**13c**) mixture of **13b** and **13c**, and 3 mg of nitronate **13c**. The overall yield of the reaction was 452 mg (97%) with an overall selectivity of 98/14/1 (**13b**/**13a**/**13c**) and an endo/exo ratio of 112/1 (**13a** + **13b**/**13c**). An analytical sample of **13b** was obtained by recrystallization (pentane). Nitronates **13a** and **13c** were found to be identical by ^{1}H NMR to nitronates **13a** and **13c** obtained from the MAD- and $SnCl_4$-promoted [4 + 2] cycloadditions. Data for **13b**: mp 39−40.5 °C (pentane); ^{1}H NMR (400 MHz, C_6D_6) δ 6.99−6.96 (m, 3 H), 6.70−6.78 (m, 2 H), 5.28−5.17 (m, 1 H), 5.02 (d, J = 1.7, 1 H), 4.89−4.81 (m, 2 H), 4.00 (dt, J = 9.8, 6.3, 1 H), 3.37 (dt, J = 9.8, 6.3, 1 H), 3.18−3.16 (m, 1 H), 2.00−1.90 (m, 3 H), 1.69 (d, J = 1.7, 3 H), 1.54−1.40 (m, 2 H), 1.38−1.20 (m, 2 H), 0.84 (t, J = 7.3, 3 H); ^{13}C NMR (100.6 MHz, C_6D_6) δ 140.19, 134.87, 129.13, 128.80, 127.63, 119.05, 117.54, 102.16, 69.08, 47.37, 42.90, 33.69, 31.78, 19.51, 17.57, 13.89; IR (CCl_4) 2961, 2935, 1618, 1277, 1272, 1238, 921, 897; MS (CI) 304 (M^+ + 1, 100); TLC R_f 0.22 (hexane/EtOAc, 2/1). Anal. Calcd for $C_{18}H_{25}NO_3$ (303.405): C, 71.26; H, 8.31; N, 4.62. Found: C, 71.52; H, 8.43; N, 4.88.

***rel*-(4*S*,5*S*,6*S*)-6-Butyloxy-3-methyl-4-phenyl-5-(2-propenyl)-5,6-dihydro-4*H*-[1,2]-oxazine 2-Oxide (13c) and *rel*-(4*S*,5*S*,6*R*)-6-Butyloxy-3-methyl-4-phenyl-5-(2-propenyl)-5,6-dihydro-4*H*-[1,2]-oxazine 2-Oxide (13d).** Tin(IV) chloride (0.29 mL, 2.44 mmol, 2 equiv) was added to a −78 °C solution of nitroalkene **12** (200 mg, 1.22 mmol) in CH_2Cl_2 (10 mL), and the resulting bright yellow complex was left to stir for 15 min. A solution of vinyl ether **3** (342 mg, 2.44 mmol, 2.0 equiv) in CH_2Cl_2 (2 mL) was added slowly over a 20 min period to the cold reaction mixture via syringe. The reaction was left to stir at −78 °C for an additional 15 min and was then quenched with a methanolic sodium hydroxide solution (1 N, 4 mL). The mixture was diluted with CH_2Cl_2 (150 mL) and washed with water (3 × 150 mL). The aqueous phase was back-extracted with CH_2Cl_2 (3 × 50 mL), and the combined organic layers were washed with brine (100 mL) and then were dried (Na_2SO_4) and concentrated to afford a cloudy oil. The crude organic concentrate was purified by silica gel column chromatography (hexane/EtOAc, 4/1) to afford 199 mg of nitronate **13c**, 77 mg of a 7.5/1 (**13b**/**13c**) mixture of **13b** and **13c**, 38 mg of a 1.1/1 (**13a**/**13b**) mixture of **13a** and **13b**, and 24 mg of nitronate **13d**. The overall yield of the reaction was 338 mg (91%) with an overall selectivity of 1/5/11.5/1.3 (**13a**/**13b**/**13c**/**13d**) and an endo/exo ratio of 2.2/1 (**13c** + **13d**/**13a** + **13b**). An analytical sample of **13c** was obtained by recrystallization (pentane/TBME). Nitronates **13a** and **13b** were found to be identical by ^{1}H NMR to nitronates **13a** and **13b** obtained from the MAD- and Ti(O-*i*-Pr)$_2$Cl$_2$-promoted [4 + 2] cycloadditions. Data for **13c**: mp 82−83 °C (pentane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.26 (m, 3 H), 7.11−7.08 (m, 2 H), 5.54−5.43 (m, 1 H), 5.19 (d, J = 2.0, 1 H), 5.04−4.99 (m, 2 H), 4.17 (d, J = 6.6, 1 H), 4.01 (dt, J = 9.5, 6.6, 1 H), 3.64 (dt, J = 9.5, 6.3, 1 H), 2.11−1.97 (m, 2 H), 1.92 (d, J = 1.6, 3 H), 1.72−1.56 (m, 3 H), 1.37 (sept, J = 7.3, 2 H), 0.92 (t, J = 7.4, 3 H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 136.42, 134.79, 129.31, 128.71, 127.51, 122.55, 118.22, 103.23, 69.10, 44.75, 38.87, 32.11, 31.42, 19.12, 18.23, 13.74; IR (CCl_4) 3004, 2962, 2935, 1613, 881; MS (CI) 304 (M^+ + 1, 100); TLC R_f 0.31 (hexane/EtOAc, 2/1). Anal. Calcd for $C_{18}H_{25}NO_3$ (303.405): C, 71.26; H, 8.31; N, 4.62. Found: C, 71.13; H, 8.39; N, 4.92. Data for **13d**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31−7.25 (m, 5 H), 5.73−5.63 (m, 1 H), 5.17 (d, J = 2.9, 1 H), 5.04 (d, J = 10.0, 1 H), 4.95 (dd, J = 17.1, 12, 1 H), 4.06 (dt, J = 9.3, 6.4, 1 H), 3.70 (dd, J = 8.8, 1.2, 1 H), 3.47 (dt, J = 9.3, 6.7, 1 H), 2.54−2.47 (m, 1 H), 2.04−1.97 (m, 1 H), 1.87 (d, J = 1.2, 3 H), 1.66−1.51 (m, 3 H), 1.38−1.24 (m, 2 H), 0.89 (t, J = 7.3, 3 H); TLC R_f 0.11 (hexane/EtOAc, 2/1).

***rel*-(1*R*,6*S*,7*S*,8*R*,9*S*)-6-Butyloxy-9-methyl-8-phenyl-4-aza-3,5-dioxatricyclo[5.2.1.0^{4,9}]decane (14a).** A solution of nitronate **13a** (162 mg, 0.53 mmol) in toluene (10 mL) was added to a suspension of sodium bicarbonate (314 mg, 3.73 mmol, 7 equiv) in toluene (43 mL), and the mixture was heated to reflux for 3.5 h. After the solution was cooled to room temperature, the reaction mixture was concentrated (until only ca. 10 mL remained) and then was filtered through a cotton pipet plug, eluting with TBME (20 mL). The crude organic concentrate was purified by column chromatography on basic (III) alumina (hexane/TBME 7/1) to provide 173 mg (79%) of analytically pure nitroso acetal **14a** as a white solid: mp 85−86 °C (hexane/TBME); ^{1}H NMR (400 MHz, C_6D_6) δ 7.68−7.66 (m, 2 H), 7.26−7.22 (m, 2 H), 7.13−7.09 (m, 1 H), 4.69 (d, J = 1.0, 1 H), 4.05 (t, J = 8.3, 1 H), 3.79 (dd, J = 8.0, 3.7, 1 H), 3.72 (dt, J = 9.3, 6.5, 1 H), 3.06 (dt, J = 9.3, 6.4, 1 H), 2.70 (d, J = 4.5, 1 H), 2.33 (t, J = 5.2, 1 H), 1.95−1.90 (m, 1 H), 1.48 (ddd, J = 13.2, 10.3, 6.0, 1 H), 1.22−1.14 (m, 5 H), 1.03−0.93 (m, 3 H), 0.71 (t, J = 7.5, 3 H); ^{13}C NMR (100.6 MHz, C_6D_6) δ 138.43, 130.94, 128.48, 126.35, 106.32, 81.07, 77.68, 68.06, 51.50, 49.16, 45.66, 35.45, 32.09, 22.59, 19.55, 14.17; IR (CCl_4) 2959, 2935, 2872; MS (CI) 304 (M^+ + 1, 100); TLC R_f 0.45 (hexane/EtOAc, 2/1). Anal. Calcd for $C_{18}H_{25}NO_3$ (303.405): C, 71.26; H, 8.31; N, 4.62. Found: C, 71.35; H, 8.31; N, 4.74.

***rel*-(1*R*,6*R*,7*S*,8*R*,9*S*)-6-Butyloxy-9-methyl-8-phenyl-4-aza-3,5-dioxatricyclo[5.2.1.0^{4,9}]decane (14b).** A solution of nitronate **13b** (230 mg, 0.79 mmol) in toluene (10 mL) was added to a suspension of sodium bicarbonate (466 mg, 5.3 mmol, 7 equiv) in toluene (70 mL) and the mixture was heated to reflux for 3 h. After the solution was cooled to room temperature, the reaction mixture was concentrated (until only ca. 10 mL remained) and then was filtered through a cotton pipet plug, eluting with TBME (20 mL). The brown organic concentrate was purified by column chromatography on basic (III) alumina (hexane/TBME 7/1) to provide 173 mg (75%) of nitroso acetal **14b** as a white solid. An analytical sample of **14b** was obtained by recrystallization (pentane): mp 63−65 °C (pentane); ^{1}H NMR (400 MHz, C_6D_6) δ 7.67 (d, J = 7.6, 2 H) 7.24−7.20 (m, 2 H), 7.12−7.08 (m, 1 H), 4.67 (d, J = 5.4, 1 H), 4.10 (d, J = 6.8, 2 H), 3.76 (dt, J = 9.5, 6.6, 1 H), 3.00 (dt, J = 9.5, 6.4, 1 H), 2.77 (d, J = 4.2, 1 H), 2.33 (q, J = 4.9, 1 H), 2.13−2.08 (m, 1 H), 1.98 (d, J = 12.7, 1 H), 1.42−1.30 (m, 3 H), 1.25−1.15 (m, 2 H), 0.77 (t, J = 7.3, 3 H); ^{13}C NMR (100.6 MHz, C_6D_6) δ 137.00, 130.46, 128.44, 126.78, 101.40, 79.85, 77.27, 68.28, 53.27, 49.86, 45.79, 32.06, 30.43, 22.06, 19.66, 13.95; IR (CCl_4) 2960, 2935, 2875, 1090; MS (CI) 304 (M^+ + 1, 100); TLC R_f 0.59 (hexane/EtOAc, 2/1). Anal. Calcd for $C_{18}H_{25}NO_3$ (303.405): C, 71.26; H, 8.31; N, 4.62. Found: C, 71.38; H, 8.41; N, 4.78.

***rel*-(1*R*,6*S*,7*S*,8*S*,9*S*)-6-Butyloxy-9-methyl-8-phenyl-4-aza-3,5-dioxatricyclo[5.2.1.0^{4,9}]decane (14c).** A solution of nitronate **13c** (136 mg, 0.45 mmol) in toluene (10 mL) was added to a suspension of sodium bicarbonate (264 mg, 3.14 mmol, 7 equiv) in toluene (35 mL), and the mixture was heated to reflux for 18 h. After the solution was cooled to room temperature, the reaction was concentrated (until only ca. 10 mL remained) and the reaction mixture was filtered through a cotton pipet plug, eluting with TBME (20 mL). The crude organic concentrate was purified by column chromatography on basic (III) alumina (hexane/TBME 7/1) to provide 127 mg (93%) of analytically pure nitroso acetal **14c** as a white solid: mp 58−60 °C (pentane); ^{1}H NMR (400 MHz, C_6D_6) δ 7.12−7.02 (m, 5 H), 4.67 (d, J = 2.4, 1 H), 4.26−4.24 (m, 2 H), 4.11 (t, J = 7.8, 1 H), 4.04 (dt, J = 9.6, 6.7, 1 H), 3.39 (dt, J = 9.5, 6.6, 1 H), 2.14−2.07 (m, 3 H), 1.62−1.55 (m, 2 H), 1.43−1.24 (m, 3 H), 1.04 (s, 3 H), 0.86 (t, J = 7.3, 3 H); ^{13}C NMR (100.6 MHz, C_6D_6) δ 140.90, 129.06, 128.77, 126.86, 106.08, 87.92, 79.63, 67.70, 47.70, 46.04, 44.66, 36.08, 32.14, 20.01, 19.77, 14.09; IR (CCl_4) 2959, 2938, 2875, 1096, 1078; MS (CI) 304 (M^+ + 1, 89), 230 (100); TLC R_f 0.50 (hexane/EtOAc, 2/1).

Anal. Calcd for $C_{18}H_{25}NO_3$ (303.405): C, 71.26; H, 8.31; N, 4.62. Found: C, 71.26; H, 8.31; N, 4.84.

***rel*-(1*R*,2*S*,4*R*,7*S*)-2-Hydroxymethyl-1-methyl-7-phenyl-6-aza-bicyclo[2.2.1]hexane (15).** A mixture 6/1 (**13b**/**13a**) of nitroso acetals **13a** and **13b** (110 mg, 0.363 mmol) was added to a suspension of prewashed (5 × 5 mL MeOH) Raney nickel (amount that would fit on a tip of a spatula) in MeOH (8 mL). The reaction was placed under 1 atm of H_2 at room temperature for 24 h. The Raney nickel was removed by filtering the reaction mixture through a cotton pipet plug, washing with copious amounts of MeOH, and concentrating. The crude organic concentrate was purified by column chromatography on neutral (III) alumina ($CHCl_3$/MeOH, 32/1) to provide 56 mg (71%) of bicyclic amine **15** as a clear viscous oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34−7.30 (m, 2 H), 7.25−7.21 (m, 3 H), 4.43 (s, 1 H), 4.18 (dd, J = 11.6, 2.3, 1 H), 3.71 (dd, J = 11.6, 2.9, 1 H), 3.41 (dt, J = 10.3, 3.4, 1 H), 2.89 (d, J = 10.5, 1 H), 2.81 (s, 1 H), 2.66 (t, J = 3.9, 1 H), 2.04−1.96 (m, 1 H), 1.89−1.83 (m, 1 H), 1.78 (dd, J = 11.5, 5.1, 1 H), 1.35 (s, 3 H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 137.78, 128.59, 128.26, 126.41, 69.24, 62.25, 57.97, 51.54, 46.37, 42.05, 31.67, 16.59; IR (CCl_4) 3689, 3583, 3011, 2997, 2966, 2896, 1453, 1102, 980, 830; TLC R_f 0.22 ($CHCl_3$/MeOH, 32/1) [alumina plate].

[(1*S*,3*R*,4*S*,5*R*)-4-(Acetylamino)-4-methyl-5-phenyl]-1,3-cyclopentanedimethanol Diacetate (16a). Nitroso acetal **14a** (107 mg, 0.355 mmol) was added to a suspension of prewashed (5 × 15 mL MeOH) Raney nickel (amount that would fit on a tip of a spatula) in EtOH (35 mL). Sodium borohydride (54 mg, 1.42 mmol, 4 equiv) was directly added to the reaction mixture and was then immediately placed under 1 atm of H_2. After 1.5 h, a solution of sodium borohydride (54 mg, 1.42 mmol, 4 equiv) in EtOH (1 mL) was added to the reaction while it was under 1 atm of H_2. After an additional 2 h, a solution of sodium borohydride (54 mg, 1.42 mmol, 4 equiv) in EtOH (1 mL) was again added and the reaction was allowed to stir 2.5 h further. The Raney nickel was removed by filtering the reaction mixture through a cotton pipet plug, washing with copious amounts of MeOH, and concentrating. The crude material was dissolved in pyridine (3 mL), and acetic anhydride (3 mL) and was left to stir at room temperature for 8 h. The excess pyridine and acetic anhydride were removed in vacuo, using an external trap, providing a brown oil. The crude organic concentrate was purified by silica gel column chromatography (EtOAc/hexane, 1/1) to afford 62 mg (49% over two steps) of aminocyclopentane triacetate **16a**, which was found to be identical by ^{1}H NMR to the triacetate derived from the reduction and acylation of nitroso acetal **14b**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 77.34−7.30 (m, 2 H), 7.28−7.24 (m, 1 H), 7.21−7.19 (m, 2 H), 5.73 (s, 1 H), 4.40 (dd, J = 11.3, 6.1, 1 H), 4.23 (dd, J = 11.5, 7.5, 1 H), 3.79 (d, J = 6.4, 2 H), 3.35 (d, J = 9.0, 1 H), 2.81−2.70 (m, 1 H), 2.49−2.41 (m, 1 H), 2.19−1.12 (m, 1 H), 2.10 (s, 3 H), 1.98 (s, 3 H), 1.79 (s, 3 H), 1.71 (s, 3 H), 1.71−1.64 (m, 1 H); TLC R_f 0.23 (EtOAc/hexanes, 2/1).

[(1*S*,3*R*,4*S*,5*R*)-4-(Acetylamino)-4-methyl-5-phenyl]-1,3-cyclopentanedimethanol Diacetate (16a). Nitroso acetal **14b** (129 mg, 0.42 mmol) was added to a suspension of prewashed (5 × 10 mL MeOH) Raney nickel (amount that would fit on a tip of a spatula) in EtOH (35 mL). Sodium borohydride (65 mg, 1.70 mmol, 4 equiv) was directly added to the reaction mixture and was then immediately placed under 1 atm of H_2. After approximately 1 h, a solution of sodium borohydride (65 mg, 1.70 mmol, 4 equiv) in EtOH (1 mL) was added to the reaction while it was under 1 atm of H_2. After an additional hour, a solution of sodium borohydride (65 mg, 1.70 mmol, 4 equiv) in EtOH (1 mL) was again added and the reaction was allowed to stir 4 h further. The Raney nickel was removed by filtering the reaction mixture through a cotton pipet plug, washing with copious amounts of MeOH, and concentrating. The crude material was dissolved in pyridine (5 mL) and acetic anhydride (5 mL) and was left to stir at room temperature for 18 h. The excess pyridine and acetic anhydride were removed in vacuo, using an external trap, providing a brown oil. The crude organic concentrate was purified twice by silica gel column chromatography (EtOAc/hexane, 1/1) to afford 80 mg (53% over two steps) of aminocyclopentane triacetate **16a**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34−7.30 (m, 2 H), 7.28−7.24 (m, 1 H), 7.21−7.19 (m, 2 H), 5.73 (s, 1 H), 4.40 (dd, J = 11.3, 6.1, 1 H), 4.23 (dd, J = 11.5, 7.5, 1 H), 3.79 (d, J = 6.4, 2 H), 3.35 (d, J = 9.0, 1 H), 2.81−2.70 (m, 1 H), 2.49−2.41 (m, 1 H), 2.19−1.12 (m, 1 H), 2.10 (s, 3 H), 1.98 (s, 3 H), 1.79 (s, 3 H), 1.71 (s, 3 H), 1.71−1.64 (m, 1 H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 170.80, 170.34, 169.34, 136.69, 129.91, 128.37, 127.11, 65.10, 64.64, 63.73, 60.21, 49.11, 39.36, 31.97, 28.10, 24.24, 20.90, 20.82; IR (CCl_4) 1745, 1235; MS (FAB) 362 (M^+ + 1, 67), 302 (100); TLC R_f 0.23 (EtOAc/hexanes, 2/1); HRMS (FAB) calcd for $C_{20}H_{28}N_5O$ 362.19675, found 362.19710.

[(1*S*,3*R*,4*S*,5*S*)-4-(Acetylamino)-4-methyl-5-phenyl]-1,3-cyclopentanedimethanol Diacetate (16b). Nitroso acetal **14c** (200 mg, 0.66 mmol) was added to a suspension of prewashed (5 × 10 mL MeOH) Raney nickel (amount that would fit on a tip of a spatula) in EtOH (35 mL). Sodium borohydride (99 mg, 2.64 mmol, 4 equiv) was directly added to the reaction mixture and was then immediately placed under 1 atm of H_2. After approximately 1 h, a solution of sodium borohydride (99 mg, 2.64 mmol, 4 equiv) in EtOH (1 mL) was added to the reaction while it was under 1 atm of H_2. The reaction was allowed to stir 2 h further. The Raney nickel was removed by filtering the reaction mixture through a cotton pipet plug, washing with copious amounts of MeOH, and concentrating. The crude material was dissolved in pyridine (8 mL) and acetic anhydride (8 mL) and was left to stir at room temperature for 18 h. The excess pyridine and acetic anhydride were removed in vacuo, using an external trap, providing a brown oil. The crude organic concentrate was purified by silica gel column chromatography (EtOAc/hexane, 1/1) to afford 122 mg (51% over two steps) of aminocyclopentane triacetate **16b** along with 28 mg of an unidentified byproduct: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35−7.31 (m, 2 H), 7.28−7.24 (m, 1 H), 7.17−7.14 (m, 2 H), 5.43 (s, 1 H), 4.16 (*A*B*X*, J_{ab} = 11.0, J_{ax} = 5.6, 1 H), 4.16 (A*B*X, J_{bx} = 7.4, 1 H), 4.07 (*A*B*X*, J_{ab} = 10.2, J_{ax} = 3.5, 1 H), 3.91 (A*B*X, J_{bx} = 6.3, 1 H), 3.42 (d, J = 11.2, 1 H), 2.73−2.63 (m, 1 H), 2.58−2.51 (m, 1 H), 2.23−2.15 (m, 1 H), 2.07 (s, 3 H), 1.92 (s, 3 H), 1.82 (s, 3 H), 1.70−1.62 (m, 1 H), 1.06 (s, 3 H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 171.03, 171.00, 169.90, 138.11, 128.95, 128.50, 127.19, 66.95, 65.43, 63.86, 54.52, 46.59, 39.56, 30.20, 24.22, 23.47, 21.04, 20.60; IR (CCl_4) 1742, 1686, 1683, 1366, 1233; MS (FAB) 362 (M^+ + 1, 78), 302 (100); TLC R_f 0.31 (EtOAc/hexanes, 2/1); HRMS (FAB) calcd for $C_{20}H_{28}N_5O$ 362.19675, found 362.19710

***rel*-(4*R*,5*S*,6*S*)-6-Cyclohexyloxy-3,6-dimethyl-4-phenyl-5-(2-propenyl)-5,6-dihydro-4*H*-[1,2]-oxazine 2-Oxide (17a) and *rel*-(4*R*,5*R*,6*R*)-6-Cyclohexyloxy-3,6-dimethyl-4-phenyl-5-(2-propenyl)-5,6-dihydro-4*H*-[1,2]-oxazine 2-Oxide (17b).** Titanium(IV) chloride (0.329 mL, 3.00 mmol, 3.0 equiv) was added to a solution of titanium(IV) isopropoxide (0.892 mL, 3.00 mmol, 3.0 equiv) in CH_2Cl_2 (9 mL) at room temperature. The resulting solution was allowed to stir for 30 min and was then added via cannula to a −78 °C solution of nitroalkene **12** (163 mg, 1.00 mmol) and **6** (325 mg, 1.80 mmol, 1.8 equiv) in CH_2Cl_2 (3.0 mL). The resulting dark reaction mixture was left to stir at −78 °C for 2 h and was then warmed to −50 °C for 5 h. The reaction mixture was quenched with a methanolic sodium hydroxide solution (1 N, 8 mL) and then was diluted with CH_2Cl_2 (150 mL) and washed with water (3 × 100 mL). The aqueous layers were back-extracted with CH_2Cl_2 (3 × 50 mL), and the combined organic phases were washed with brine (75 mL), dried (Na_2SO_4), filtered, and concentrated to afford a yellow oil. The crude material was purified by silica gel column chromatography (hexane/EtOAc, 5/1 (600 mL), 4/1) to afford 39 mg of analytically pure nitronate **17b** and 197 mg of analytically pure **17a** to give a combined yield of 236 mg (69%) and an overall endo/exo ratio of 5/1 (**17a**/**18b**). Data for **17a**: ^{1}H NMR (499.7 MHz, $CDCl_3$) δ 7.35−7.28 (m, 3 H), 7.20−7.18 (m, 2 H), 5.72−5.63 (m, 1 H), 4.94−4.90 (m, 2 H), 4.06−4.01 (m, 1 H), 3.47 (d, J = 10.2, 1 H), 2.25−2.12 (m, 3 H), 1.83−1.68 (m, 7 H), 1.58−1.19 (m, 9 H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 139.47, 136.07, 129.04, 128.99, 127.73, 124.48,

116.69, 106.89, 70.87, 48.25, 47.69, 33.89, 33.57, 32.80, 25.51, 24.03, 20.96, 17.24; IR (CCl_4) 2934, 1621, 1271, 1237; MS (FAB) 344 ($M^+ + 1$, 100); TLC R_f 0.23 (hexane/EtOAc, 2/1). Anal. Calcd for $C_{21}H_{29}NO_3$ (343.47): C, 73.44; H, 8.51; N, 4.08. Found: C, 73.58; H, 8.63; N, 4.16. Data for **17b**: ^{1}H NMR (499.7 MHz, $CDCl_3$) δ 7.34−7.31 (m, 2 H), 7.28−7.26 (m, 1 H), 7.13−7.12 (m, 2 H), 5.30−5.22 (m, 1 H), 4.75−4.70 (m, 2 H), 4.42 (d, J = 6.0, 1 H), 4.07−4.02 (m, 1 H), 2.11−2.00 (m, 3 H), 1.95 (d, J = 1.3, 3 H), 1.79−1.67 (m, 4 H), 1.53−1.49 (m, 4 H), 1.41−1.15 (m, 5 H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 137.25, 137.05, 129.70, 128.67, 127.33, 123.29, 115.58, 107.37, 70.66, 46.27, 44.54, 34.31, 33.64, 30.68, 25.42, 24.30, 24.24, 20.49, 18.24; IR (Neat) 2934; MS (FAB) 344 ($M^+ + 1$, 100); TLC R_f 0.34 (hexane/EtOAc, 2/1). Anal. Calcd for $C_{21}H_{29}NO_3$ (343.47): C, 73.44; H, 8.51; N, 4.08. Found: C, 73.29; H, 8.59; N, 4.94.

***rel*-(1*R*,6*S*,7*S*,8*R*,9*S*)-6-Cyclohexyloxy-6,9-dimethyl-8-phenyl-4-aza-3,5-dioxatricyclo[5.3.1.0^{4,9}]decane (18).** Sodium bicarbonate (262 mg, 3.12 mmol, 7 equiv) was added to a solution of nitronate **17a** (153 mg, 0.445 mmol) in toluene (45 mL), and the suspension was heated to reflux for 12 h. After being cooled to room temperature, the concentrated reaction mixture was redissolved in benzene (10 mL), filtered through a cotton pipet plug, followed by washing the plug with excess benzene and reconcentrating. The crude material was purified by basic alumina (activity III) chromatography (hexane/EtOAc, 8/1) to afford 110 mg (72%) of analytically pure nitroso acetal **18** as a white crystalline solid: mp 150−157 °C (hexane/EtOAc); ^{1}H NMR (499.7 MHz, C_6D_6) δ 7.61 (bs, 2 H), 7.21−7.18 (m, 2 H), 7.08−7.05 (m, 1 H), 4.28 (dd, J = 6.8, 3.5, 1 H), 4.09 (dd, J = 9.1, 6.8, 1 H), 3.86−3.80 (m, 1 H), 2.82 (d, J = 4.0, 1 H), 2.33−2.17 (m, 4 H), 1.66−1.42 (m, 4 H), 1.35−1.24 (m, 6 H), 1.19−1.03 (m, 3 H), 0.79 (s, 3 H); ^{13}C NMR (125.7 MHz, C_6D_6) δ 139.66, 130.81, 128.31, 126.57, 102.86, 78.36, 77.48, 70.59, 54.26, 51.85, 50.98, 35.07, 33.92, 31.26, 25.98, 25.88, 24.85, 24.68, 21.97; IR (neat) 2937; MS (FAB) 344 ($M^+ + 1$, 68), 171 (100); TLC R_f 0.56 (hexane/EtOAc, 2/1). Anal. Calcd for $C_{21}H_{29}NO_3$ (343.47): C, 73.44; H, 8.51; N, 4.08. Found: C, 73.22; H, 8.60; N, 3.91.

rel*-(1*R*,2*S*,4*R*,5*R*,7*S*)-2-Hydroxymethyl-1,5-dimethyl-7-phenyl-6-azabicyclo[2.2.1]hexane and *rel*-(1*R*,2*S*,4*S*,5*S*,7*S*)-2-Hydroxymethyl-1,5-dimethyl-7-phenyl-6-aza-bicyclo-[2.2.1]hexane (19) and *rel*-[(1*S*,3*R*,4*R*,5*R*,6*R*)-4-(Acetylamino)-4,6-dimethyl-5-phenyl]-1,3-cyclopentanedimethanol Diacetate and *rel*-[(1*S*,3*R*,4*S*,5*R*,6*S*)-4-(Acetylamino)-4,6-dimethyl-5-phenyl]-1,3-cyclopentanedimethanol Diacetate (20).** Nitroso acetal **18** (91 mg, 0.26 mmol) was added to a suspension of prewashed (4 × 10 mL of MeOH) Raney nickel (amount that would fit on a tip of a spatula) in MeOH (10 mL). The reaction was placed under 1 atm of H_2 at room temperature for 24 h. The Raney nickel was removed by filtering the reaction mixture through a cotton pipet plug, washing with copious amounts of MeOH, and concentrating. The crude material was dissolved in pyridine (3 mL) and acetic anhydride (3 mL) and was left to stir at room temperature for 4.5 h. The excess pyridine and acetic anhydride were removed in vacuo to provide a brown oil. The crude organic concentrate was purified by silica gel column chromatography (EtOAc/hexane, 2/1) to provide a complex mixture of four compounds. Separation of the two main components was accomplished using MPLC (silica gel; hexane/*i*-PrOH, 85:15) which afforded 10 mg of a 1.4/1 mixture of diastereomeric bicyclic amines **19** at C(5) and 10 mg of a 7.3/1 mixture of diastereomeric triacetates **20** at C(6). The combined yield of the reaction over two steps was 20 mg (21%). Data for **19**: ^{1}H NMR (499.7 MHz, C_6D_6) δ 7.14−7.04 (m, 5 H), 4.51 (dd, J = 11.2, 6.6, 0.59 H), 4.31−4.21 (m, 1.41 H), 3.96 (dd, J = 11.2, 9.2, 0.41 H), 3.44−3.41 (m, 0.59 H), 2.46 (s, 0.59 H), 2.40 (s, 0.41 H), 2.09−2.03 (m, 0.59 H), 1.97 (s, 1.23 H), 1.95−1.88 (m, 2.18 H), 1.78 (s, 1.77 H), 1.72 (s, 1.77 H), 1.64−1.57 (m, 1.82 H), 1.49−1.31 (m, 2 H), 1.26 (d, ***J = , 1.77 H), 1.10 (dd, J = 13.3, 4.8, 0.41 H), 0.79 (d, J = 6.2, 1.23 H); MS (FAB) 316 ($M^+ + 1$, 100); TLC R_f 0.32 (EtOAc/hexane). Data for **21**: ^{1}H NMR (499.7 MHz, C_6D_6) δ 7.12−7.02 (m, 5 H), 5.74 (s, 0.12 H), 5.25 (s, 0.88 H), 4.91 (t, J = 6.6, 0.12 H), 4.54 (dd, J = 11.5, 6.0, 0.012 H), 4.47−4.41 (m, 1.76 H), 4.29 (dd, J = 11.3, 7.3, 0.88 H), 4.25 (dd, J = 11.3, 7.5, 0.12 H), 3.34 (d, J = 7.9, 0.88 H), 2.92 (d, J = 9.5, 0.12 H), 2.32−2.24 (m, 1.76 H), 2.15−2.08 (m, 0.24 H), 1.89 (s, 0.36 H), 1.79 (s, 2.64 H), 1.72 (s, 2.64 H), 1.64−1.54 (m, 1.36 H), 1.51 (s, 2.64 H), 1.46−1.35 (m, 0.9 H), 1.26 (s, 2.64 H), 1.02 (d, J = 6.0, 2.64 H), 0.95 (d, J = 6.2, 0.36 H), 0.91−0.86 (m, 0.88 H); MS (FAB) 376 ($M^+ + 1$, 42), 316 (100); TLC R_f 0.32 (EtOAc/hexane, 2/1)

4-Hydroxyimino-3-phenylpentanoic Acid Butyl Ester (21). To a −78 °C solution of nitroalkene **12** (100 mg, 0.613 mmol) in CH_2Cl_2 (4 mL) was added $SnCl_4$ (0.143 mL, 1.23 mmol, 2.0 equiv). The resulting, bright-yellow complex was allowed to stir for 15 min, and then a solution of silane **7** (317 mg, 1.84 mmol, 3 equiv) in CH_2Cl_2 (1 mL) was slowly added dropwise via syringe. The reaction was left to stir at −78 °C for 30 min and subsequently quenched with 1 N NaOH/CH_3-OH(4 mL). The cold reaction mixture was diluted with CH_2-Cl_2 (150 mL) and was washed with water (3 × 100 mL). The aqueous phase was back-extracted with CH_2Cl_2 (3 × 50 mL), and the combined organic layers were washed with brine (100 mL), dried (Na_2SO_4), filtered, and concentrated to afford a light yellow oil. The crude organic concentrate was purified by silica gel column chromatography (hexane/EtOAc 7/1, 6/1) to provide 137 mg (85%) of oxime **21** as white solid: mp 64−65 °C (hexane/EtOAc); ^{1}H NMR (499.7 MHz, $CDCl_3$) δ 7.33−7.30 (m, 3 H), 7.27−7.23 (m, 2 H), 4.07−3.96 (M, 3 H), 3.04 (dd, J = 15.9, 8.6, 1 H), 2.65 (dd, J = 15.9, 6.9, 1 H), 1.76 (s, 3 H), 1.56−1.50 (m, 2 H), 1.33−1.25 (m, 2 H), 0.88 (t, J = 7.5, 3 H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 172.06, 158.37, 139.83, 128.77, 128.06, 127.32, 64.37, 48.02, 38.09, 30.55, 18.99, 13.63, 13.53; IR ($CHCl_3$) 3504, 3475, 3420, 3401, 3361; MS (FAB) 264 ($M^+ + 1$, 100); TLC R_f 0.22 (hexane/EtOAc, 4/1). Anal. Calcd for $C_{15}H_{21}NO_3$ (263.33): C, 68.42; H, 8.04; N, 5.32. Found: C, 68.43; H, 7.91; N, 5.38.

4-[Dimethyl-(1,1-dimethylethyl)]-silyloxyimino-2-(3-propenyl)-3-phenylpentanoic Acid Ethyl Ester (22). To a −78 °C solution of nitroalkene **12** (24 mg, 0.146 mmol) in CH_2Cl_2 (2 mL) was added tin tetrachloride (43 μL, 0.291 mmol, 2.0 equiv). The resulting, bright-yellow complex was allowed to stir for 15 min, and then a solution of vinyl silane **11** (66 mg, 0.291 mmol, 2.0 equiv) in CH_2Cl_2 (1 mL) was slowly added dropwise via syringe. The reaction was stirred at −78 °C for 15 min and subsequently quenched with a 1 N NaOH/CH_3OH solution (3 mL). The cold reaction mixture was diluted with CH_2Cl_2 (100 mL) and washed with water (3 × 100 mL). The aqueous phase was back-extracted with CH_2Cl_2 (3 × 50 mL), and the combined organic layers were washed with brine (100 mL), dried (Na_2SO_4), filtered, and concentrated to afford a light yellow oil. The crude product was purified by silica gel column chromatography (hexane/EtOAc 50/1) to provide 42.4 mg (75%) of a 7/1 mixture of oxime **22** and an unidentified compound as a clear oil: ^{1}H NMR (499.7 MHz, $CDCl_3$) δ 7.27−7.20 (m, 5 H), 5.81−5.73 (m, 1 H), 5.05 (dd, J = 17.0, 1.5, 1 H), 5.00 (dd, J = 11.2, 0.9, 1 H), 3.81−3.75 (m, 2 H), 3.61 (d, J = 11.5, 1 H), 3.32−3.27 (m, 1 H), 2.59−2.55 (m, 1 H), 3.39−3.33 (m, 1 H), 1.72 (s, 3 H), 0.96 (s, 9 H), 0.87 (t, J = 7.1, 3 H) 0.19 (s, 3 H), 1.72 (s, 3 H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 173.98, 160,01, 138.79, 135.19, 128.68, 128.30, 127.19, 116.74, 59.91, 54.21, 48.41, 35.65, 26.17, 18.11, 14.13, 13.86, −5.07; IR (neat) 1737, 876, 839; MS (FAB) 390 ($M^+ + 1$, 100); TLC R_f 0.15 (hexane/EtOAc, 40/1); HRMS (FAB) calcd for $C_{22}H_{36}NO_3Si$ 390.24645, found 390.24630.

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Supporting Information Available: General experimental and materials as well as complete ^{1}H NMR, ^{13}C NMR, IR, and MS data for all characterized compounds (22 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 the ACS; see any current masthead page for ordering information.

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