Tandem Inter [4 + 2]/Intra [3 + 2] Cycloadditions of Nitroalkenes. Asymmetric Synthesis of Highly Functionalized Aminocyclopentanes Using the Bridged Mode (β-Tether) Process†

Scott E. Denmark* and Julie A. Dixon

Roger Adams Laboratory, Department of Chemistry, University of Illinois, Urbana, Illinois 61801

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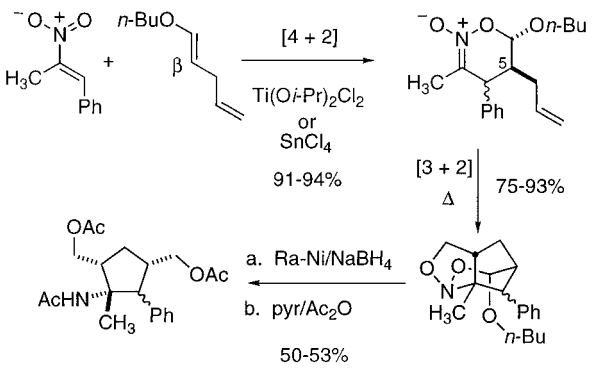
An asymmetric, tandem inter [4 + 2]/intra [3 + 2] bridged mode (β-tether) cycloaddition of nitroalkenes has been developed. This new sequence involves the Lewis acid-promoted [4 + 2] cycloaddition of nitro olefins with enantiopure 1-alkoxy-1,4-dienes. The resulting nitronates, bearing a C(5) tethered dipolarophile, undergo thermal, intramolecular [3 + 2] cycloaddition to afford stable tricyclic nitroso acetals, which can be subsequently reduced to provide interesting aminocyclopentanes. Thus, in three steps, highly functionalized, enantiomerically enriched aminocyclopentanes can be constructed with good yield and high ee. Additionally, the Lewis acid was found to impart a remarkable influence on the stereochemical outcome of the [4 + 2] cycloaddition.

Introduction

Asymmetric variants of the hetero-Diels−Alder reaction can be used to assemble a variety of chiral, nonracemic heterocyclic frameworks with good enantioselectivity.[1] As part of our research program involving inverse electron-demand nitroalkene cycloadditions, we have developed asymmetric, tandem [4 + 2]/[3 + 2] cycloadditions using nitro olefins and chiral vinyl ethers.[2] This process allows for the rapid and predictable construction of highly functionalized nitrogen-containing compounds with high diastereo- and enantioselectivity.

The preceding report in this issue detailed the development of the bridged-mode (β-tether) tandem inter [4 + 2]/intra [3 + 2] cycloaddition of (*E*)-2-methyl-2-nitrostyrene with 1-butoxy-1,4-pentadiene, Scheme 1.[3]

Scheme 1



The tandem cycloadducts were reduced to afford, after protection, highly functionalized aminocyclopentanedimethanol triacetates.

Aminocyclopentanols comprise an important structural motif which is common to a variety of biologically interesting compounds including glycosidase inhibitors and carbocyclic nucleosides, Figure 1. Aminocyclopentitol-derived natural products such as mannostatin A,[4] allosamizoline,[5] and trehazolin[6] have been reported to be potent glycosidase inhibitors.[7] Since glycosidase-processing enzymes perform critical roles in intra- and intercel-

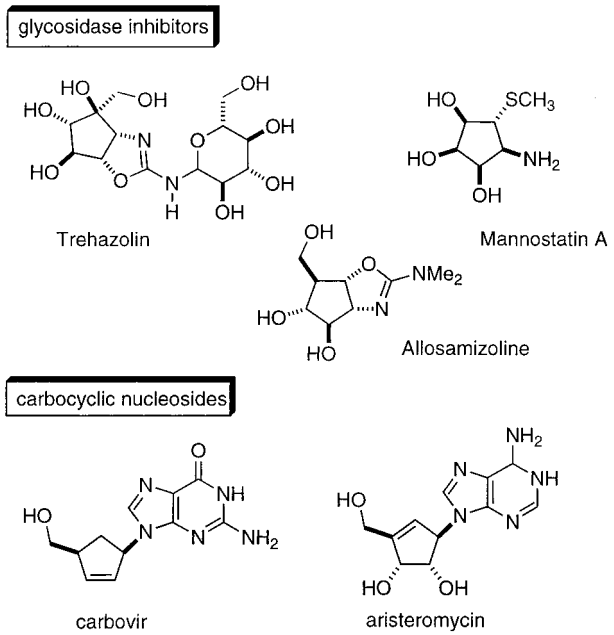


Figure 1. Selected aminocyclopentanol-derived natural products and carbocyclic nucleosides.

† Tandem [4 + 2]/[3 + 2] Cycloadditions of Nitroalkenes. 20.

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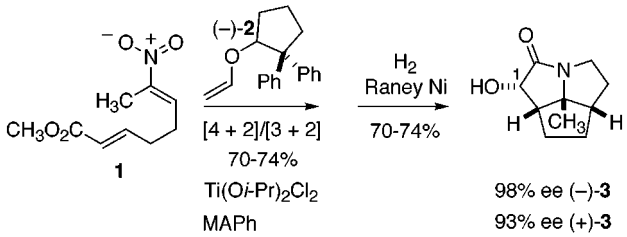
lular transport and signal transduction, inhibition of these enzymes has therapeutic ramifications on immunology, virology, and oncology.[8] Additionally, carbocyclic nucleosides have received considerable attention due to their remarkable antiviral and antitumor activities.[9] More specifically, carbovir[10] and aristeromycin[11] have shown potent and selective anti-HIV activity. Current interest in aminocyclopentanols stems not only from their interesting biological activity but also from a synthetic point of view. The high degree of functionality poses a significant challenge and creates opportunity for the development of new methods to construct these frameworks in enantiomerically enriched form.

This paper provides a detailed account of our studies on the asymmetric, bridged-mode (β-tether) tandem sequence ([4 + 2]/[3 + 2]/cleavage) employing nitroalkenes and enantiomerically enriched 1-alkoxy-1,4-pentadienes. Additionally, a novel influence of the Lewis acid on the stereochemical outcome of the [4 + 2] cycloaddition will be addressed. A preliminary report on the asymmetric bridged-mode (β-tether) process has appeared.[12]

Background

Asymmetric Tandem Cycloadditions. Enantiomerically enriched, chiral vinyl ethers have served admirably as the 2π components in asymmetric tandem cycloadditions.[2] For example, tandem [4 + 2]/[3 + 2] cycloadditions of nitroalkene **1** with enantiopure vinyl ether (−)-**2**, derived from (−)-2,2-diphenylcyclopentanol, afford intermediate nitroso acetals with exceptional diastereoselectivity when promoted by $Ti(O\text{-}i\text{-}Pr)_2Cl_2$ or methylaluminum bis(2,6-diphenylphenoxide) (MAPh), Scheme 2.[2c] After hydrogenolytic unmasking of the nitroso acetals, the α-hydroxy lactam **3** is produced with high enantiomeric purity (98−93% ee), whose absolute configuration is dependent upon the Lewis acid promoter employed in the initial [4 + 2] cycloaddition. This remarkable Lewis acid dependence on the stereochemical outcome of the [4 + 2] cycloaddition has been attributed to a switch in the approach (endo/exo) of one face of the vinyl ether to the enantiotopic faces of the Lewis acid−

Scheme 2



nitroalkene complex.[2b] Interestingly, a number of Lewis acid dependent reversals in selectivity have been documented for a variety of reactions including asymmetric Diels−Alder,[13] aldol,[14] and 1,4-addition reactions.[15] In some examples, the switch in selectivity is rationalized by invoking different coordination modes of the Lewis acids, while in other systems the reversal is believed to result from differing steric requirements of the Lewis acids.

Synthesis of Aminocyclopentanols. The first and most common approach for the asymmetric construction of aminocyclitols involves the fragmentation and functional group manipulation of natural carbohydrates. Several syntheses of trehazolin aglycon, allosamizoline, mannostatin A, and various aminocyclopentitol derivatives utilize carbohydrate precursors such as D-glucose, D-ribose, D-glucosamine, and D-ribonolactone.[16] Additionally, a variety of carbocyclic nucleosides have been prepared from D-ribose, D-glucono-δ-lactone, and other chiral precursors such as amino acids.[17]

Another common strategy for the preparation of aminocyclopentane moieties is the use of heteroatomic cycloaddition reactions. The key step in a number of aminocyclopentanol syntheses involves asymmetric hetero-Diels−Alder reactions of substituted cyclopentadienes and enantiopure acylnitroso species, Scheme 3.[18] Hydrogenolytic cleavage of the resulting cycloadducts followed by dihydroxylation provides the desired aminocyclopentitols or nucleosides. Additionally, intramolecular

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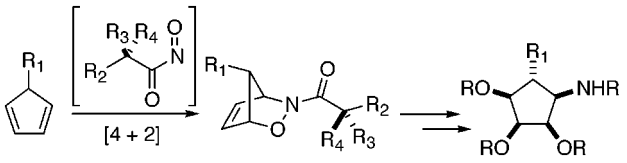
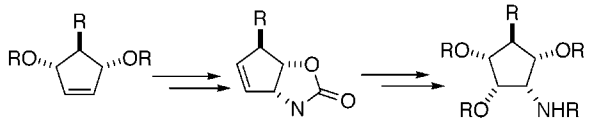
Scheme 3



nitrile oxide, nitrone, and oxime cycloadditions have been used in the preparation of aminocyclopentanols.[19]

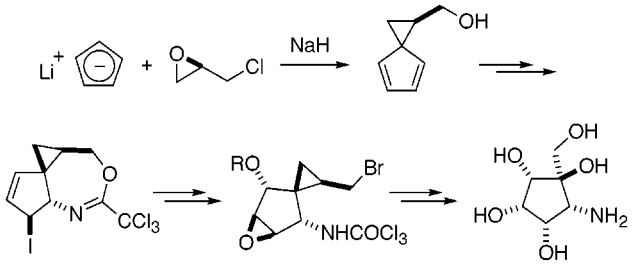
A third approach for the asymmetric synthesis of aminocyclopentitols and carbocyclic nucleosides involves the desymmetrization of functionalized cyclopentenyl-1,4-*meso*-diols, using enzyme-mediated hydrolyses[20] or palladium-catalyzed asymmetric allylic alkylations,[21] Scheme 4. Subsequent functionalization of the double bond affords highly oxygenated aminocyclopentanes.

Scheme 4



The last method reported for the asymmetric construction of aminocyclopentitols uses a cyclopropylcyclopentadiene as the key intermediate, Scheme 5. This interesting species is generated from the reaction of epichlorohydrin with lithium cyclopentadienide.[22] Amidohydroxylation and functionalization provided the aglycon of trehazolin.

Scheme 5

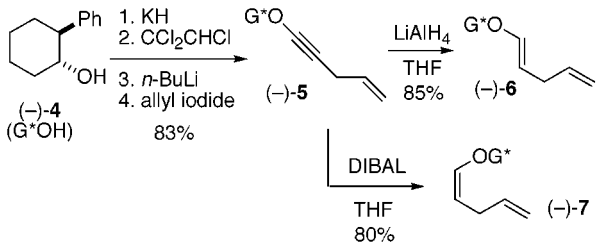


While there are various methods for the asymmetric preparation of aminocyclopentanoid products, several limitations still remain. For example, many of the routes employ a preexisting cyclopentane ring that limits the range of functionality and substitution which can be efficiently incorporated. In addition, some of the cyclopentane ring systems are created using carbohydrate precursors. While these are often inexpensive staring materials, they frequently require the use of many additional steps for the installation, removal, and interconversion of various functional groups. Thus, a more concise and general method for the asymmetric synthesis of aminocyclopentanols would still have merit.

Results

Synthesis of 1-Alkoxy-1,4-pentadienes. Preparation of chiral, nonracemic dienophiles for use in the β-bridged-mode tandem process was accomplished in two steps from (−)-(1*R*,2*S*)-phenylcyclohexanol ((−)-**4**). Following the method of Greene,[23] the potassium salt of (−)-**4** (>99% ee) was combined sequentially with trichloroethylene and *n*-butyllithium, to afford, after quenching with allyl iodide, the acetylenic ether (−)-**5** in 83% yield, Scheme 6. Lithium aluminum hydride reduction of (−)-**5** provided exclusively the trans vinyl ether (−)-**6** in 85% yield.[24] Alternatively, the cis vinyl ether (−)-**7** was stereoselectively obtained from a diisobutylaluminum hydride (DIBAL) reduction of (−)-**5**. Additionally, trans vinyl ethers, derived from 2,2-diphenylcyclopentanol and 2-(1-methyl-1-phenylethyl)cyclohexanol (TCC), were prepared in a similar fashion.

Scheme 6



Cycloadditions and Reductions of Nitro Olefin 8 with Trans Vinyl Ether (−)-6. The [4 + 2] cycloaddition of nitroalkene **8**[25] with (−)-**6** was efficiently promoted by $SnCl_4$ to afford a mixture of diastereomeric nitronates **9a**, **9b**, and **9d** (32/2/1) in 93% yield, Table 1. Diastereomers **9a** and **9b** possess a cis relationship between the C(4)-phenyl and C(5)-allyl substituents and are believed to retain the trans relationship of the vinyl ether. Thus, they must arise from an endo-(allyl), exo-(alkoxy) mode cycloaddition. The trans (C(4)/C(5)) nitronate **9d**, whose stereostructure was secured through X-ray analysis[26] may result from an endo-(alkoxy), exo-(allyl) mode reaction, which provides nitronate **9c**, followed by epimerization of the C(6) acetal center. Alternatively, an isomerization of the trans vinyl ether to a cis vinyl ether followed by an exo-(alkoxy) mode cycloaddition may be operative.[27] The nitronic ester subunits of **9a** and **9b** are enantiomorphic and arise from exo-mode cycloadditions from combinations of unlike (*ul*)[28] diastereotopic faces of

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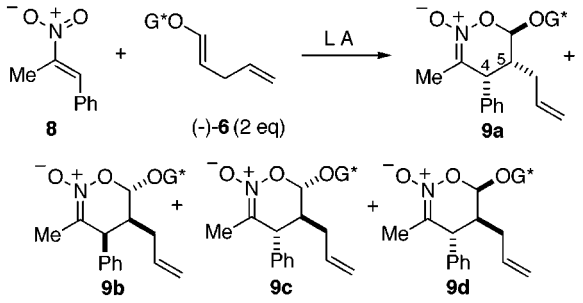
(27) The recovered vinyl ether (−)-**6** from the $SnCl_4$-promoted cycloaddition, had isomerized to approximately 3/1 (trans/cis) ratio.

Table 1. Asymmetric [4 + 2] Cycloadditions with 8 and (−)-6



Lewis acid (equiv)	*T*, °C	yield, %	**9a**/**9b**/**9c**/**9d**[a]
$SnCl_4$ (1)	−78	93	32/2/0/1
MAPh (3)	−25	95	1/15/1.8/0

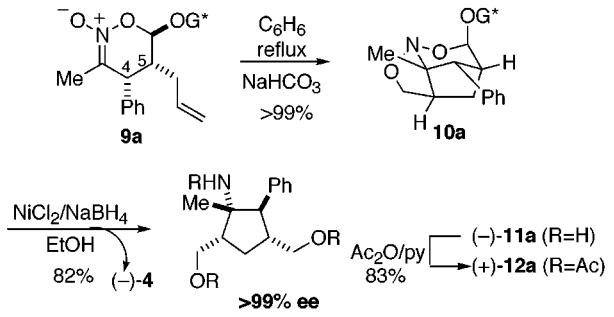
[a] Determined by isolation and by ^1H NMR integration.

the chiral vinyl ether and the nitroalkene.[29] Therefore, the overall diastereofacial selectivity of the cycloaddition in the exo series is 15/1 (**9a**/**9b**).

In view of our previous observations on the influence of Lewis acids on the stereochemical course of [4 + 2] cycloaddition, we next examined the reaction of **8** with (−)-**6** promoted by MAPh.[30] The diastereomeric nitronates **9a**, **9b**, and **9c** were formed in excellent yield (95%), however this time in a ratio of 1/15/1.8, Table 1. Thus, the reaction was again exo-(alkoxy) selective (exo/endo, >8.8/1 (**9a** + **9b**/**9c**), but remarkably, the major diastereomer from the MAPh-promoted cycloaddition corresponded to the minor exo diastereomer obtained in the $SnCl_4$-promoted cycloaddition. The use of $Ti(O\text{-}i\text{-}Pr)_2Cl_2$ as the Lewis acid promoter in the [4 + 2] cycloaddition of **8** with (±)-**6** provided a complex mixture of several diastereomeric nitronates.[31]

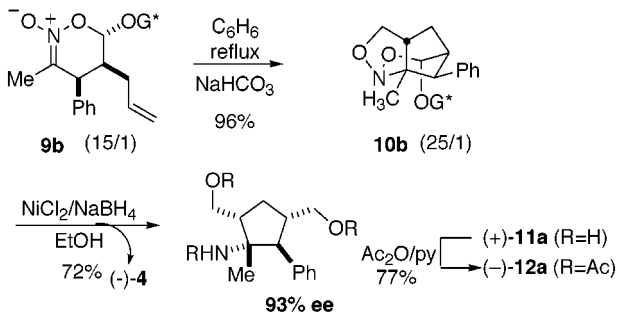
Intramolecular [3 + 2] cycloaddition of **9a** (obtained from the $SnCl_4$ cycloaddition) in refluxing benzene provided the tricyclic nitroso acetal **10a** as a crystalline solid in quantitative yield. The full stereostructure of **10a** was secured through single-crystal X-ray analysis of (±)-**20a** that was obtained from a $SnCl_4$-promoted tandem cycloaddition of nitroalkene **8** with enol ether (±)-**6**.[32] The nitroso acetals were reduced in an improved procedure with nickel boride[33] (instead of the conventional Raney nickel) to afford amino diol (−)-**11a** in 82% yield along with 94% of the recovered alcohol (−)-**4**. To facilitate purification and allow for the determination of enantiomeric purity, the amino diol (−)-**11a** was peracylated to provide the triacetate (+)-**12a** in 83% yield and >99% enantiomeric excess (ee).[34]

Scheme 7



Using a similar sequence of events as outlined above, a 15/1 mixture of nitronates **9b** and **9a** (obtained from an MAPh cycloaddition) was heated in benzene to afford a 25/1 mixture of nitroso acetals **10b** and **10a** in 96% yield. Unmasking of the nitroso acetals with nickel boride provided a single amino diol (+)-**11a** in 72% yield (along with a 94% recovery of (−)-**4**). The triacetate

Scheme 8



(−)-**12a** obtained from acylation of (+)-**11a** was found to be of 93% ee but was levorotatory and thus belonged to the opposite configurational series as the triacetate derived from the $SnCl_4$-promoted tandem process. *Therefore, from a single, chiral, nonracemic auxiliary, either enantiomer of the final amino diol can be obtained by appropriate selection of the Lewis acid in the tandem sequence.*

Optimization of the [4 + 2] Cycloaddition of 8 with (−)-6. During the investigation into the asymmetric bridged-mode (*β*-tether) tandem process, we discovered an unusual stoichiometry dependence on the diastereoselectivity of the $SnCl_4$-promoted [4 + 2] cycloaddition. In the reaction of nitro olefin **8** with vinyl ether (−)-**6**, when 2 equiv of (−)-**6** was added to a solution of 1 equiv of $SnCl_4$ and nitroalkene **8**, a >30/1 (**9a** + **9b**)/(**9c** + **9d**) ratio of diastereomeric nitronates was obtained in 96% yield, Table 2, entry 1. However, if only 1 equiv of vinyl ether was added to a solution containing nitroalkene and 2 equiv of $SnCl_4$, then the diastereoselectivity eroded to 5/1 (**9a** + **9b**)/(**9c** + **9d**), entry 2. Since the change in the reagent stoichiometry had such a dramatic influence on the diastereoselectivity of the reaction, other experiments were conducted to gain insight into the origin of this dependence. In entries 3 and 4, the stoichiometry of the vinyl ether and $SnCl_4$ change relative to the amount of nitroalkene used in the cycloaddition. Interestingly, this variation appears to have a small effect on the diastereomeric ratio, 10/1 vs >20/1 (**9a** + **9b**)/(**9c** + **9d**), for these reactions.

The use of a substoichiometric amount of $SnCl_4$ to promote the [4 + 2] cycloaddition provided the diaster-

(28) (a) Seebach, D.; Prelog, V. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 654. (b) For an excellent discussion of the stereochemical terminology, see: Helmchen, G. In *Stereoselective Synthesis, Methods of Organic Chemistry (Houben-Weyl)*; Edition E21; Helmchen, G., Hoffman, R., Mulzer, J., Schaumann, E., Eds.; Thieme: Stuttgart, 1996; Vol. 1, p 1.

(29) The topicity is defined at the *β*-carbons of the reactive components.

(30) Methylaluminum bis(2,6-diphenylphenoxide). Maruoka, K.; Yamamoto, H. *Tetrahedron* **1988**, *44*, 5001.

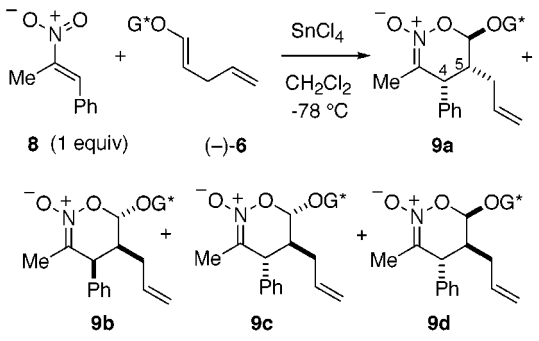
(31) Chiral vinyl ethers, derived from 2,2-diphenylcyclopentanol and TCC, were explored in the [4 + 2] cycloaddition; however, they offered no particular advantage with respect to their preparation, yield, and selectivity.

(32) Dixon, J. A.; Swiss, K. A.; Denmark, S. E. *Acta Crystallogr. C* *52*, **1996**, 2561.

(33) For review on nickel boride see: Ganem, B.; Osby, J. O. *Chem. Rev.* **1986**, *86*, 763.

(34) Determined by chiral stationary phase HPLC, see Supporting Information for details.

Table 2. Stoichiometry Dependence of Diastereoselectivity in the [4 + 2] Cycloaddition of 8 with (−)-6



entry	equiv, **6**	equiv, $SnCl_4$	yield, %	ratio[a] (**9a** + **9b**)/(**9c** + **9d**)
1	2	1[b]	96	>30/1
2	1	2[b]	89	5/1
3	2	2[b]	90	10/1
4	1	1[b]	76	>20/1
5	1	0.5[b]	80	>30/1
6	1	1[c]	88	>30/1

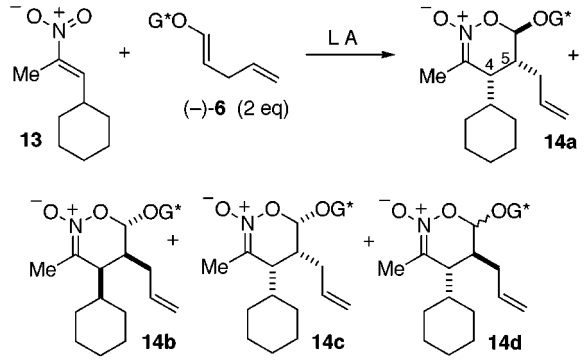
[a] Ratios were determined by ^{1}H NMR integration. [b] Vinyl ether was added to a solution of nitroalkene and $SnCl_4$. [c] $SnCl_4$ was added to a solution of nitroalkene and vinyl ether.

eomeric nitronates in good yield with high diastereoselectivity (>30 /1, (**9a** + **9b**)/(**9c** + **9d**)), entry 5. Last, by changing the order of addition for this reaction (adding the $SnCl_4$ to a solution of vinyl ether and nitro olefin) a high diastereomeric ratio (>30 /1, (**9a** + **9b**)/(**9c** + **9d**)) could also be obtained for this reaction, entry 6. Overall two trends may be visible from these experiments. First, the use of 1 equiv or less of $SnCl_4$ is necessary for good selectivity in the cycloaddition. Second, the use of excess vinyl ether (−)-**6** provides greater yields for this reaction.

Cycloadditions and Reductions of Nitro Olefin 13 with Vinyl Ether (−)-6. To investigate the generality of the bridged-mode (β-tether) tandem process and the Lewis acid dependent switch in diastereofacial selectivity, nitroalkene **13**[25] was used as the 4π component in the tandem process. The $SnCl_4$-promoted [4 + 2] cycloaddition of **13** with (−)-**6** afforded a mixture of diastereomeric nitronates **14a**, **14b**, and **14c** (6.9/1/3.4) in 80% yield, Table 3. All three nitronate **14a, 14b**, and **14c** possess a cis relationship between the C(4)-phenyl and C(5)-allyl substituents; however, only nitronates **14a** and **14b** retain the trans relationship of the vinyl ether. The stereostructure of **14c** was secured through X-ray analysis of the resulting nitroso acetal **15c**.[26] Additionally, all three nitronates were converted into the same aminocyclopentane triacetate after [3 + 2] cycloaddition, reduction, and protection (vide infra). Since nitronates **14a**, **14b**, and **14c** have a cis configuration between C(4) and C(5), they are believed to arise from an endo-(allyl), exo-(alkoxy) mode cycloaddition. Again, the nitronic ester subunits of **14a** and **14b** are enantiomorphic and arise from exo-(alkoxy) mode cycloadditions from unlike (*ul*)[28] combinations of the diastereotopic faces of the chiral vinyl ether and the nitroalkene.[29] The all-cis relationship in **14c** may result from epimerization of the C(6) acetal center of **14a** under the reaction conditions. Interestingly, the cycloaddition is completely exo selective with the overall diastereofacial selectivity being 10.3/1 (**14a** + **14c**/**14b**).

The MAPh-promoted [4 + 2] cycloaddition of **13** with vinyl ether (−)-**6** provided a 3/19/1 mixture of diastereomeric nitronates **14a**, **14b**, and **14d** in excellent yield (95%), Table 3. The nitronate **14d** is assigned as having a trans relationship between the C(4) and C(5) substituents and thus may result from an exo-(allyl), endo-(alkoxy) mode reaction. The overall exo/endo-(alkoxy) selectivity of the cycloaddition is 22/1 (**14b** + **14a**/ **14d**) while the diastereofacial selectivity in the exo manifold is 6.7/1 (**14b**/**14a**). Once again, the major diastereomer from the MAPh-promoted cycloaddition corresponded to the minor exo-(alkoxy) diastereomer obtained in the $SnCl_4$-promoted cycloaddition

Table 3. Asymmetric [4 + 2] Cycloadditions with 13 and (−)-6

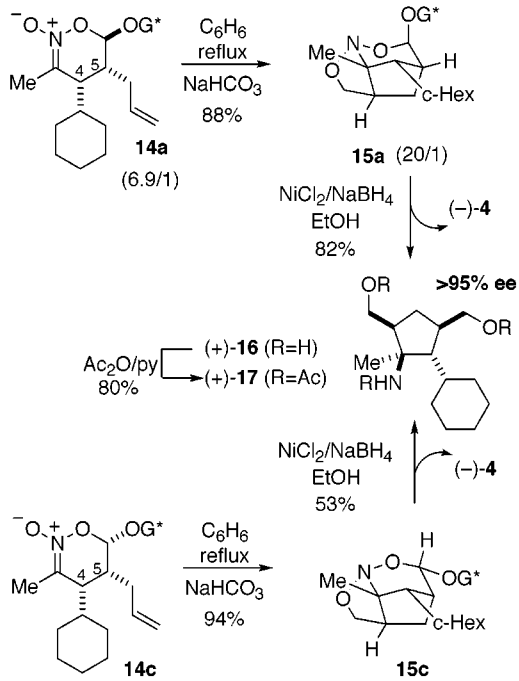


Lewis acid (equiv)	*T*, °C	yield, %	**14a**/**14b**/**14c**/**14d**[a]
$SnCl_4$ (1)	−78	80	6.9/1/3.4/0
MAPh (4)	0	90	3/19/0/1

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

Intramolecular [3 + 2] cycloaddition of **14a** and **14c** in refluxing benzene provided the diastereomeric nitroso acetals **15a** and **15c** in 88% and 94% yields, respectively (Scheme 9), and the full stereostructure of **15c** was

Scheme 9

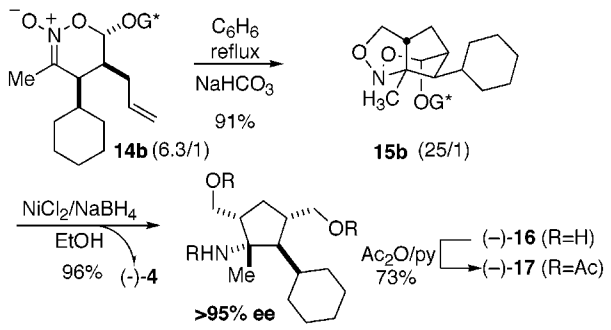


secured through single-crystal X-ray analysis.[26] Nickel boride reduction of nitroso acetals **15a** and **15c** provided the same enantiomerically enriched amino diol (+)-**16** in

53−82% yield. After acylation, the triacetate (+)-**17** was found to be enantiomerically enriched to the extent of >95% ee.[34]

The intramolecular dipolar cycloaddition of **14b** was effected by refluxing a dilute solution in benzene, to provide the desired nitroso acetal **15b** in 91% yield, Scheme 10. Subsequent nickel boride reduction (96%)

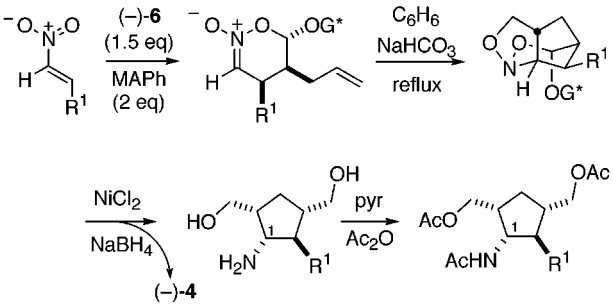
Scheme 10



followed by acylation afforded the triacetate (−)-**17** in 73% yield and >95% ee. Again, from a single, enantiopure auxiliary, either enantiomer of the final amino diol can be obtained by appropriate selection of the Lewis acid in the tandem sequence.

Cycloadditions and Reductions of Nitroalkenes 18 and 19 with (−)-6. To further probe the generality of the bridged-mode tandem [4 + 2]/[3 + 2] reaction, trans 2-substituted nitro olefins containing aromatic and heteroatom substituents were tested in the reaction sequence. MAPh was chosen as the Lewis acid for these reactions since it promotes highly selective cycloadditions and is a relatively mild reagent. Thus, the [4 + 2] cycloadditions of **18**[25] and **19**[35] with (−)-**6** afforded mixtures of nitronates **20** and **21** in good to excellent yields (68−92%), Table 4. In both cases the major

Table 4. Tandem [4 + 2]/[3 + 2] Cycloaddition and Reduction Sequence



nitroalkene (R^1)	nitronate yield,[a] %	nitroso acetal yield, % (dr)	amino diol yield, %	triacetate yield, % (ee, %)[d]
18 (Ph)	**20** 92	**22** 87 (25/1)	**24** 82[b]	(−)-**26** 59[b] (95)[e]
19 (OBz)	**21** 68	**23** − (nd)	**25a** 61[c]	(−)-**27a** 68 (>98)

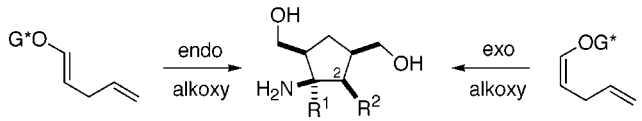
[a] Isolated as a mixture of diastereomers. [b] Isolated as 3.5:1 mixture of epimeric amino diols at C(1). [c] Yield over two steps. [d] Determined by CSP HPLC. [e] ee of major isomer **26a**.

nitronate is believed to have arisen from an endo-(allyl), exo-(alkoxy) mode cycloaddition; however, the exact diastereomeric ratios could not be determined at this stage due to the propensity of the nitronates to slowly undergo [3 + 2] cycloaddition at room temperature.

Consequently, the mixtures of nitronates **20** and **21** were heated to effect the intramolecular dipolar cycloadditions affording a 25/1 mixture of diastereomeric nitroso acetals **22a/b** in 87% yield and intermediate nitroso acetals **23** which were unstable to purification and were used directly in the next reaction. Nickel boride reduction of the nitroso acetals **22a/b** afforded the desired amino diol **24** as 3/1 mixture of C(1) epimers in 82% yield.[36] Subsequent acylation of **24** provided triacetates (−)-**26a** and **26b** in 59% yield. The major epimer (−)-**26a** was found to be of 95% ee.[31] Similarly, nickel boride reduction of nitroso acetal **23** provided the desired amino diol **25a** in 61% yield over two steps. After acylation (68%), the triacetate (−)-**27a** was found to be enriched to the extent of >98% ee.[34]

Cycloadditions and Reductions of 8 and 19 with Cis Vinyl Ether (−)-7. To access a C(2) diastereomeric amino diol using the bridged-mode tandem process, we required either an endo-(alkoxy) selective [4 + 2] cycloaddition using a trans vinyl ether or an exo-(alkoxy) selective cycloaddition with a cis vinyl ether, Scheme 11.

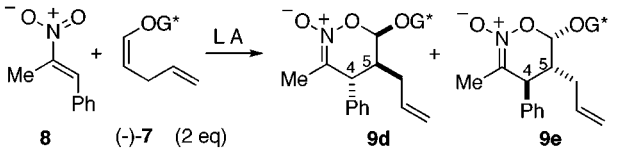
Scheme 11



Since most of the asymmetric [4 + 2] cycloadditions in the bridged-mode series are highly exo selective, we chose to investigate the use of cis vinyl ethers as the dienophile/dipolarophile component.

The $SnCl_4$-promoted [4 + 2] cycloaddition of nitroalkene **8** with cis vinyl ether (−)-**7** afforded a 11/1 mixture of diastereomeric nitronates **9d** and **9e** in excellent yield (93%), Table 5.[37] Diastereomers **9d** and **9e** possess a

Table 5. Asymmetric [4 + 2] Cycloadditions with 8 and (−)-7



Lewis acid (equiv)	*T*, °C	yield, %	**9d**/**9e**[a]
$SnCl_4$ (1)	−78	93	11/1
MAPh (3)	−30	70	1/8

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

trans relationship between the C(4)-phenyl and C(5)-allyl substituents and retain the cis relationship of the vinyl ether. Thus, they must arise from endo-(allyl), exo-(alkoxy) mode cycloadditions. Interestingly, the major nitronate **9d** obtained from this reaction corresponded to a minor diastereomer found in the $SnCl_4$-promoted [4 + 2] cycloaddition of **8** with trans vinyl ether (−)-**6**. The stereostructural assignment of the nitronate **9e** was made by analogy to the cycloadditions of the trans vinyl ether series and was later confirmed by X-ray analysis of nitroso acetal **10e**. Overall, the cycloaddition is

(35) Denmark, S. E.; Thorarensen, A. *J. Org. Chem.* **1994**, *59*, 5672.

(36) Epimeric ratios ranging from 3.5 to 20/1 have been obtained for this reaction.

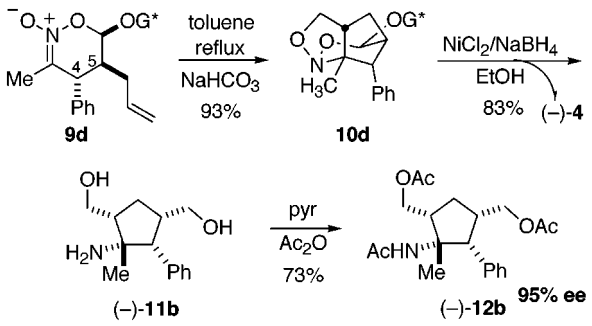
(37) The recovered vinyl ether (−)-**7** from the $SnCl_4$-promoted cycloaddition had isomerized to an approximately 1.4/1 (cis/trans) ratio.

completely exo selective with the diastereofacial selectivity being 11/1 (**9d**/**9e**).

The MAPh-promoted [4 + 2] cycloaddition of **8** with enol ether (−)-**7** again provided a mixture of nitronates **9d** and **9e** now in a ratio of 1/8 (**9d**/**9e**) in 70% yield, Table 5. The major diastereomer from the MAPh-promoted cycloaddition corresponded to the minor diastereomer obtained in the $SnCl_4$-promoted cycloaddition.

Intramolecular [3 + 2] cycloaddition of **9d** in refluxing toluene provided the tricyclic nitroso acetal **10d** in 93% yield, Scheme 12. Reduction of nitroso acetal **10d** using

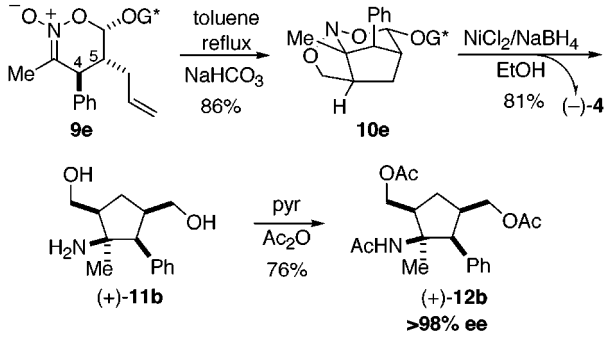
Scheme 12



nickel boride afforded the amino diol (−)-**11b** in 83% yield along with 94% of the recovered alcohol (−)-**4**. Subsequent acetylation of (−)-**11b** generated the triacetate (−)-**12b** in 73% yield. The extent of enantiomeric purity of (−)-**12b** was determined to be 95% ee.[38]

Nitronate **9e** was smoothly transformed in refluxing toluene into the desired nitroso acetal **10e** in 86% yield, Scheme 13. The full stereostructure of **10e** was secured

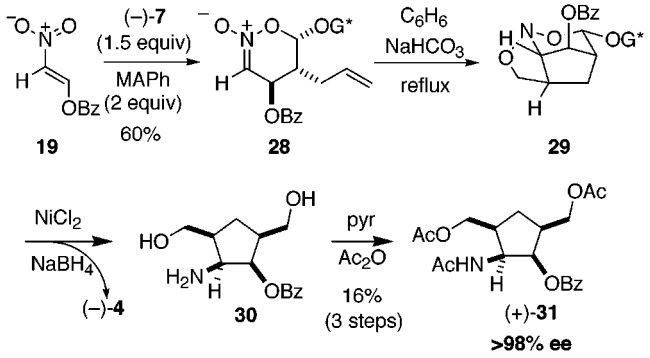
Scheme 13



through single-crystal X-ray analysis[26] of (±)-**10e** generated from a MAPh-promoted tandem sequence. Unmasking of the nitroso acetal with nickel boride provided amino diol (+)-**11b** in 81% yield (along with a 92% recovery of (−)-**4**). The triacetate (+)-**12b**, obtained from acylation of (+)-**11b**, was found to be >98% ee.[38] Again, the triacetate from this sequence belonged to the opposite enantiomeric series as the triacetate resulting from the $SnCl_4$-promoted tandem process.

To incorporate additional oxygen functionality into this amino diol series, we chose to examine the asymmetric [4 + 2] cycloaddition of nitro olefin **19** with the cis-enol ether (−)-**7**. The MAPh-promoted [4 + 2] cycloaddition of **19** with (−)-**7** produced a mixture of somewhat unstable nitronates **28** in 60% yield, Scheme 14. The

Scheme 14



major nitronate **28a** is believed to have arisen from an exo-(alkoxy) mode cycloaddition; however, the precise diastereomeric ratio for this cycloaddition could not be determined due to difficulties in removing small amounts of decomposed products. The intramolecular [3 + 2] cycloaddition of **28** did not proceed as readily as for the trans vinyl ether series. Higher temperatures and/or longer reaction times were necessary to effect the [3 + 2] cycloaddition, which in turn caused considerable decomposition.[39] Nonetheless, the unstable nitroso acetal **29** could be directly subjected to nickel boride reduction. Subsequent acylation of amino diol **30** provided the desired triacetate (+)-**31** in 16% yield (over three steps) and in >98% ee.[34]

Discussion[40]

Asymmetric [4 + 2] Cycloadditions. From the analysis of previous asymmetric tandem nitroalkene cycloadditions, two principle factors have been identified that govern the stereochemical course of the reaction.[2] The first factor involves the orientation (exo or endo) of the chiral vinyl ether in its approach to the nitroalkene. This feature determines the relative topicity of the reacting termini and establishes the stereochemical relationship between C(4) and C(5) (and de facto, C(4) and C(6)). The second factor entails the stereodifferentiation of the chiral vinyl ether for one π-face (*si* or *re*) of the nitroalkene.[41] This component governs the relative topicity of the C(5) (and de facto C(6)) center with respect to the chiral auxiliary, i.e., the absolute configurational series of the final aminocyclopentanedimethanol. For the purposes of this analysis these factors will be discussed individually; however, they are in actuality highly interdependent.

To facilitate the following discussion, some important stereochemical information is outlined in Figure 2. The prochiral descriptors are uniquely defined at the reacting components as follows: at the 2-position of the 1-nitroalkene and the C(3) and C(4) positions of the vinyl ether. Reaction of the C(4) *si* face of the vinyl ether with the *re* face of the nitro olefin would result in an unlike combination and is designated as *ul*. Alternatively, if the reaction took place on the C(4) *re* face of a vinyl ether with the *re* face of the nitroalkene, then that combination would be

(38) Determined by chiral stationary phase supercritical fluid chromotography (SFC), see Supporting Information for details.

(39) Various solvent and temperatures were tried to optimize the yield and minimize decompostion of this reaction.

(40) A detailed discussion of the [3 + 2] cycloaddition and nitroso acetal stability as well as the mechanism of hydrogenolysis can be found in the preceding paper.

(41) The *re* and *si* faces are defined at the β-carbon atom of the niroalkene.

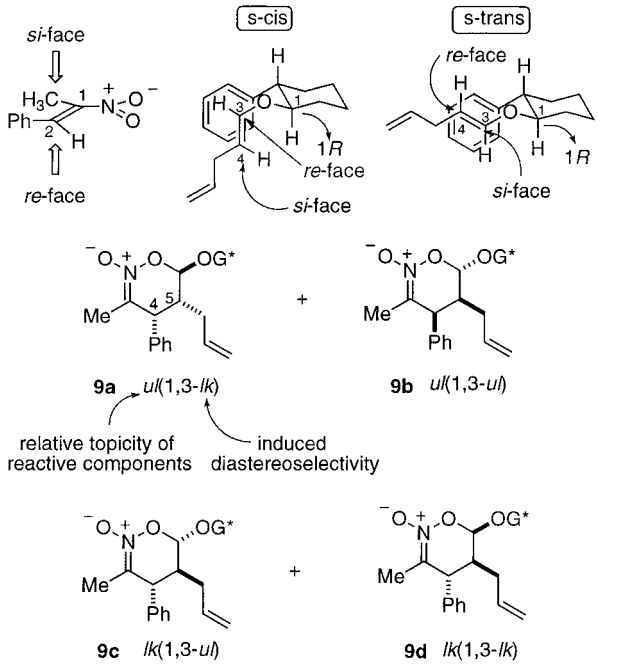


Figure 2. Stereochemical definitions in asymmetric [4 + 2] cycloaddition.

termed like (*lk*). A second stereochemical component to this definition involves the asymmetric induction of the chiral auxiliary. In this case, the configuration of the auxiliary at C(1) is compared to the prochiral descriptor of the olefin at C(3). For example, if the (1*R*,2*S*)-phenylcyclohexanol-derived vinyl ether (−)-**6** reacts at the (C(3)) *si* face, then the relative induction would be denoted as 1,3-*ul* (1*R* of the auxiliary with the *si* face of the olefin).

From consideration of the these factors, unified models have been developed to rationalize the stereochemical course of Lewis acid-promoted [4 + 2] cycloadditions involving both the trans vinyl ether (−)-**6** and cis vinyl ether (−)-**7**. The reactive conformation of the vinyl ether (−)-**6** in the $SnCl_4$-promoted [4 + 2] cycloaddition with nitroalkene **8** can be inferred through analysis of the X-ray crystal structure of nitroso acetal (±)-**10a**. The structure of (±)-**10a** would uniquely arise from a cis relationship between the phenyl (C(4)) and the allyl group (C(5)) in nitronate **9a**, which can only be established by an endo-mode orientation of the allyl appendage with respect to the nitro olefin in the [4 + 2] cycloaddition (i.e., *ul* topicity). Moreover, since the relative configuration of the auxiliary ((1*R**,2*S**)-2-phenylcyclohexanol) is known, the relative configurations of C(4) and C(5) in **9a** can be assigned as 4*R**,5*R**. To obtain the 4*R**,5*R** configuration, the C(3) *re* face of the enol ether **6** must approach the *re* face of the nitroalkene **8**. This approach would necessitate 1,3-*lk* induction (i.e., 1*R* auxiliary, *re* face vinyl ether). Previous analysis of molecular and computational models revealed that the C(3) *re* face of trans vinyl ethers derived from (1*R*,2*S*)-**4** are most accessible in the limiting *s*-cis reactive conformation, Figure 3. Moreover, the difference in ground-state energies of the *s*-cis and *s*-trans conformations was found to be negligible. Additionally, the preference for the vinyl ether to react in a *s*-cis conformation by an exo approach appears to be a general characteristic for $SnCl_4$-promoted reactions.[2g,3]

The MAPh-promoted cycloaddition of nitro olefin **8** with vinyl ether (−)-**6** afforded **9b** as the major nitronate, which bore a C(4)/C(5) cis, C(5)/C(6) trans relationship and therefore also arose from an endo-(allyl), exo-(alkoxy) [4 + 2] cycloaddition (*ul* topicity). However, this nitronate belongs to the opposite configurational family as **9a** (as evidenced by its ultimate conversion to (−)-**12a**). Therefore, **9b** must arise from the combination of the C(3) *si* face of (−)-**6** with the *si* face of **8** (i.e., 1,3-*ul* induction, 1*R* auxiliary, *si* face vinyl ether). To accommodate this pairwise combination, the vinyl ether (1*R*,2*S*)-**6** must react via the *s*-trans conformation as depicted in Figure 4. It has been well established that MAPh promotes predominately exo-(alkoxy) mode, *s*-trans cycloadditions, presumably due to the size of this bulky Lewis acid.[2]

The influence of the Lewis acid on the stereochemical outcome of the asymmetric [4 + 2] cycloaddition of nitro olefins and chiral vinyl ethers has been well documented.[2a−c,g] The Lewis acid-dependent reversal of stereoselectivity observed between $Ti(O\text{-}i\text{-}Pr)_2Cl_2$ and MAPh in the fused mode tandem process has been attributed to a switch in the relative topicity (endo/exo) of the vinyl ether and the Lewis acid−nitroalkene complex.[2b,c] In both of these cases, the relative sense of asymmetric induction at the chiral vinyl ether is the same. In the current study, we have discovered a new mode of Lewis acid-dependent stereoselection, which preserves the relative topicity of the reactive partners but alters the sense of asymmetric induction at the chiral vinyl ether. At this

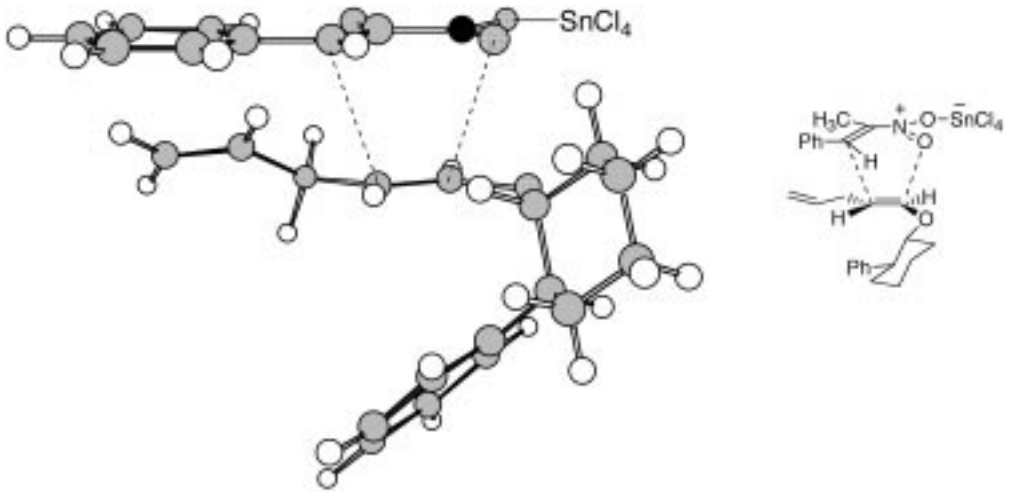


Figure 3. Proposed model of the $SnCl_4$-promoted asymmetric [4 + 2] cycloaddition.

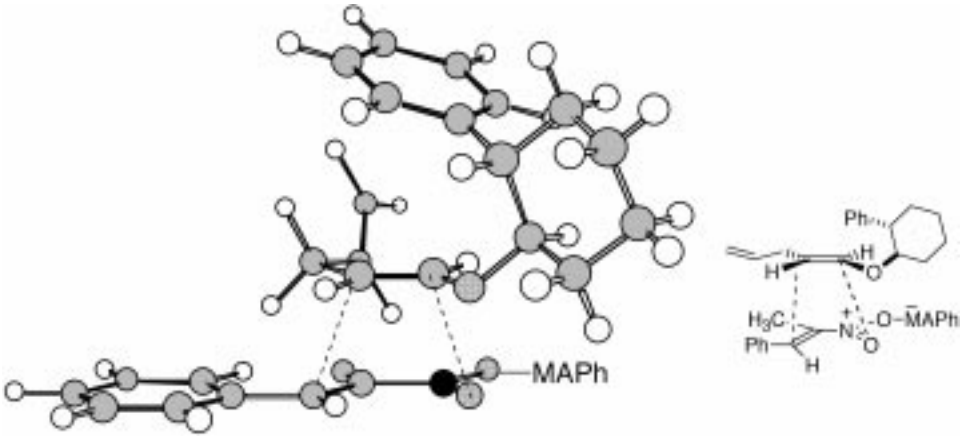


Figure 4. Proposed model of the MAPh-promoted asymmetric [4 + 2] cycloaddition.

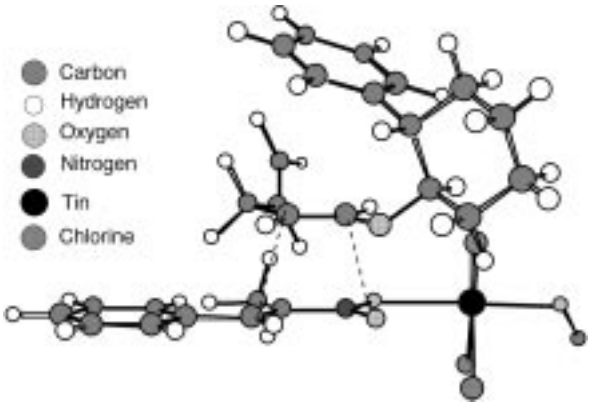


Figure 5. Approach of vinyl ether (−)-**6** in an *s*-trans conformation to the $SnCl_4$•**8** complex.

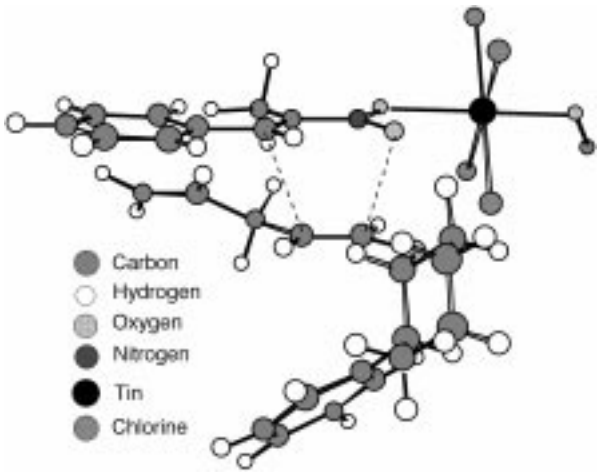


Figure 6. Approach of vinyl ether (−)-**6** in an *s*-cis conformation to the $SnCl_4$•**8** complex.

time, a clear understanding for the change in vinyl ether conformation with the two different reagents is lacking primarily due to the paucity of structural information on the nitroalkene/Lewis acid complexes. However, one plausible explanation may involve the sensitivity of the enol ether geometry to the steric environment of the different Lewis acid−nitroalkene complexes. It has been concluded that when MAPh and $Ti(O\text{-}i\text{-}Pr)_2Cl_2$ are used to promote nitroalkene [4 + 2] cycloadditions, the vinyl ether prefers to react in an *s*-trans conformation (1,3-*ul*).[2b,c] Alternatively, it appears that when $SnCl_4$ is used as the promoter, the vinyl ether prefers to react through an *s*-cis orientation (1,3-*lk*). We suspect that the switch from a *s*-trans to the *s*-cis reactive conformation may be attributed to nonbonding interactions of the approaching enol ether with a $SnCl_4$−nitroalkene complex. Models of the two limiting conformations (*s*-trans and *s*-cis) of the vinyl ether (−)-**6** with the $SnCl_4$−**8** complex are shown in Figures 5 and 6.[42] The tin atom is postulated to be hexacoordinate having another nitro olefin, product nitronate, or vinyl ether as the sixth ligand (the sixth ligand on tin in Figures 5 and 6 is depicted as methanol for simplicity). We assume that tin is octahedrally disposed since $SnCl_4$ is most commonly found in the hexacoordinate state when complexed with basic ligands.[43]

Shown in Figure 5 is the approach of vinyl ether (−)-**6** (in an *s*-trans conformation) to the $SnCl_4$•**8** complex. In this orientation, the methine hydrogen of the auxiliary appears to experience severe nonbonding interactions with one of the chlorine atoms of the Lewis acid. However, if the vinyl ether adopts an *s*-cis conformation, then the steric interactions are relieved, Figure 6.

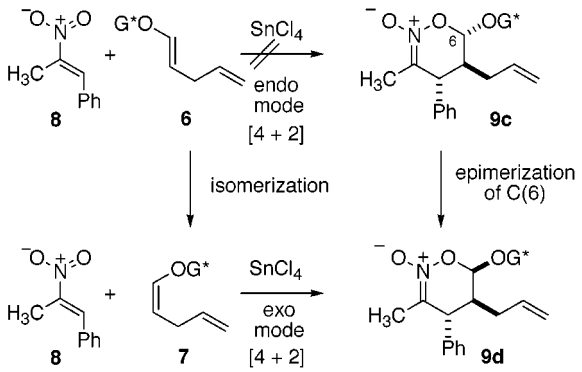
This rationale can be used to explain the stereochemical outcome of the [4 + 2] cycloadditions of nitronate **8** with the cis vinyl ether (−)-**7**. Again, in the $SnCl_4$-promoted cycloaddition, the enol ether (−)-**7** is believed to react through an *s*-cis conformation in an exo-(alkoxy) mode approach to the nitro olefin. In the MAPh-promoted reaction, the vinyl ether is believed to adopt an *s*-trans orientation as it approaches the nitroalkene/MAPh complex in an exo fashion.

Stoichiometry Studies. During the optimization of the $SnCl_4$-promoted [4 + 2] cycloaddition of **8** with (−)-**6**, it was noticed that diastereoselectivity eroded when more than 1 equiv of $SnCl_4$ was added. In particular, the amount of **9d** increased as the concentration of $SnCl_4$ increased, while the amount of diastereomer **9c** that was produced remained virtually unchanged. The most likely explanation for this observation is that **9d** is not a result of an endo-mode cycloaddition of **8** and vinyl ether (−)-**6** which is followed by epimerization of C(6) but from an exo-mode cycloaddition of the cis vinyl ether (−)-**7**, Scheme 15.

(42) The models were constructed using modified X-ray crystallographic data from Lewis, F. D.; Oxman, J. D.; Huffman, J. C. *J. Am. Chem. Soc.*, **1984**, *106*, 466.

(43) (a) Satchell, D. P. N.; Wardell, J. P. *Proc. Chem. Soc.* **1963**, 86. (b) Dumas, J. M.; Gomel, M. *Bull. Chem. Soc. Fr.* **1974**, 1885. (c) Merbach, A. E.; Knight, C. T. G. *Inorg. Chem.* **1985**, *24*, 576.

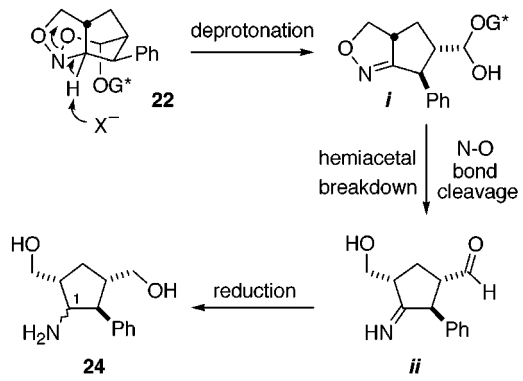
Scheme 15



In the presence of $SnCl_4$, the trans vinyl ether **6** was observed to partially isomerize to the cis vinyl ether **7**. This was discovered when unreacted vinyl ether (−)-**6** was recovered from the $SnCl_4$-promoted cycloaddition and it was found to have isomerized to a 3/1 (**6**/**7**) ratio. An exo-mode [4 + 2] cycloaddition of enol ether **7** gives rise to the requisite nitronate **9d**. Thus, if more than 1 equiv of $SnCl_4$ is used in the reaction, there is likely to be a greater propensity for the trans isomer **6** to isomerize to the cis derivative **7**, leading to increased production of diastereomeric nitronate **9d**.

Hydrogenolysis. The suggested mechanism for the nickel boride reduction of the nitroso acetals to the corresponding amino diols is similar to the mechanism proposed for the Raney nickel and sodium borohydride reduction of the achiral nitroso acetals (see the preceding paper).[3] A plausible explanation for the formation of epimeric C(1) amino diols **24** from the reduction of nitroso acetal **22** is outlined in Scheme 16. Deprotonation of

Scheme 16



nitroso acetal **22**, with concomitant β-alkoxy elimination under the mildly basic reaction conditions (i.e., $NaB(OMe)_4$), could provide the dihydroisoxazole intermediate i. This intermediate may subsequently undergo a N−O bond cleavage and breakdown of the hemiacetal, to provide the imino aldehyde ii. Reduction of the aldehyde followed by the unselective saturation of the imine provides the C(1) epimeric amino diols **24**. Alternatively, single N−O bond cleavage may occur prior to deprotonation and reduction.

Conclusion

An asymmetric variant of the tandem [4 + 2]/[3 + 2] cycloaddition process has been developed which provides access to highly substituted aminocyclopentanes. Enantiomerically enriched *trans*- and *cis*-1-alkoxy-1,4-pentadienes serve admirably as the dienophile/dipolarophile components in the bridged-mode (β-tether) sequence. A variety of nitroalkenes, including mono- and disubstituted as well as oxygen functionalized substrates, participate in the sequence, affording intermediate nitronates and nitroso acetals in good yields and high diastereoselectivities. Hydrogenolysis of the nitroso acetals provides goods yields of highly enantiomerically enriched aminocyclopentanes. Importantly, by changing the Lewis acid from $SnCl_4$ to MAPh in the tandem sequence, enantiomeric amino diols can be obtained using a single enantiomer of the chiral vinyl ether. Further studies on the application of this process toward the synthesis of aminocyclopentanoid natural products are in progress.

Experimental Section

General. See Supporting Information.

Materials. See Supporting Information.

1-[(1*R*,2*S*)-(2-Phenylcyclohexyl)oxy]pent-4-en-1-yne (5). A solution of (−)-(1*R*,2*S*)-phenylcyclohexanol ((−)-**4**) (3.84 g, 22.2 mmol, 1.0 equiv, >99% ee) in THF (39 mL) was added to a suspension of prewashed (5 × 10 mL of hexanes) potassium hydride (1.87 g, 46.62 mmol, 2.1 equiv) in THF (39 mL) at room temperature. Hydrogen evolution was observed, and the reaction mixture was stirred at room temperature for 3 h. The potassium alkoxide was then cooled to −78 °C, and a solution of trichloroethylene (2.78 mL, 23.31 mmol, 1.1 equiv) in THF (26 mL) was added via cannula. After the addition was complete, the mixture was immediately warmed to room temperature and was stirred for 13 h. The resulting dark mixture was cooled to −78 °C, and *n*-butyllithium (41.0 mL, 53.3 mmol, 2.4 equiv) was added slowly via cannula and was warmed slowly to 0 °C over a period of 2.5 h. The mixture was stirred for an additional 30 min at 0 °C and was then recooled to −78 °C. A solution of allyl iodide (6.0 mL, 66.6 mmol, 3 equiv) in HMPA (10 mL) was added via cannula to the cold reaction mixture and was stirred betweeen −70 and −50 °C for 1 h. After being warmed to 0 °C and stirring at that temperature for 3 h, the mixture was quenched with a saturated ammonium chloride solution (50 mL). The mixture was diluted with pentane (100 mL) and was washed with water (3 × 75 mL). The aqueous phase was back-extracted with pentane (3 × 75 mL), and the combined organic phases were washed with brine (100 mL), dried (Na_2SO_4), and filtered through a pad of basic alumina activity III, washing with pentane (100 mL). Concentration of the filtrate afforded a brown oil which was purified by column chromatography (basic alumina (III), pentane) to provide 4.42 g (83%) of a 20:1 mixture of (−)-**5** to [(1*R*,2*S*)-(2-phenylcyclohexyl)oxy]ethyne as a light yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34−7.31 (m, 2 H), 7.26−7.22 (m, 3 H) 5.80 (ddt, J = 15.6, 10.2, 5.1, 1 H), 5.25 (dq, J = 17.2, 1.8, 1 H), 5.04 (dq, J = 10.2, 1.6, 1 H), 4.05 (td, J = 10.8, 4.4, 1 H), 2.86 (dt, J = 5.1, 1.8, 2 H), 2.78−2.73 (m, 1 H), 2.45−2.41 (m, 1 H) 1.96−1.91 (m, 2 H), 1.78−1.75 (m, 1 H), 1.68−1.60 (m, 1 H), 1.57−1.30 (m, 3 H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 142.71, 134.48, 128.39, 127.54, 126.58, 114.90, 89.58, 88.66, 49.01, 35.37, 33.84, 30.97, 25.55, 24.69, 21.78; IR ($CHCl_3$) 2940, 2268; MS (FAB) 241 (M^+ + 1, 4), 159 (100); TLC R_f 0.38 (hexane/EtOAc, 20/1); optical rotation $[\alpha]^{25}_D$ = −66.8° (c = 1.1, $CHCl_3$); HRMS (FAB) calcd for $C_{17}H_{20}O$ 241.15924, found 241.15900.

***trans*-1-[(1*R*,2*S*)-(2-Phenylcyclohexyl)oxy]-1,4-pentadiene ((−)-6).** Lithium aluminum hydride (2.8 g, 72.52 mmol, 4 equiv) was added to a solution of the acetylenic ether (−)-**5** (4.36 g, 18.13 mmol) in THF (180 mL). The suspension was heated to reflux for 1.5 h. After the solution was cooled to room temperature, the excess hydride was quenched with water (2.9 mL), 15% NaOH/H_2O (2.9 mL), and finally water (5.8 mL). The suspension was stirred at room temperature

for ca. 30 min, and the white salts were removed by filtration, washing with EtOAc (100 mL). Concentration of the filtrate afforded a light yellow oil, which was purified by silica gel column chromatography (10:1 hexane/benzene) to provide 1.57 g of analytically pure vinyl ether (−)-**6** and 2.16 g of a 16:1 mixture of (−)-**6** to [(1*R*,2*S*)-2-(phenylcyclohexyl)oxy]ethene (85% yield overall): ^{1}H NMR (499.7 MHz, $CDCl_3$) δ 7.30−7.26 (m, 2 H), 7.21−7.17 (m, 3 H) 5.82 (d, J = 12.4, 1 H), 5.72−5.64 (m, 1 H), 4.94−4.87 (m, 2 H), 4.67 (dt, J = 12.3, 7.1, 1 H), 3.73 (td, J = 10.2, 4.4, 1 H), 2.63 (ddd, J = 12.4, 10.4, 3.8, 1 H), 2.48 (td, J = 7.3, 1.3, 2 H), 2.24−2.18 (m, 1 H), 1.93−1.83 (m, 2 H) 1.77−1.73 (m, 1 H), 1.54−1.46 (m, 1 H), 1.43−1.29 (m, 3 H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 146.25, 143.84, 138.09, 128.22, 127.66, 126.19, 114.28, 102.89, 82.30, 50.43, 34.07, 32.33, 31.63, 25.87, 24.84; IR (neat) 2931, 1670, 1121; MS (CI, CH_4) 243 (M^+ + 1, 11), 159 (100); TLC R_f 0.39 (hexane/EtOAc, 20/1); optical rotation $[\alpha]^{24}_D$ = −16.1° (c = 1.3, $CHCl_3$). Anal. Calcd for $C_{17}H_{22}O$ (242.364): C, 84.25; H, 9.15. Found: C, 84.22; H, 9.22.

***cis*-1-[(1*R*,2*S*)-(2-Phenylcyclohexyl)oxy]-1,4-pentadiene ((−)-7).** A solution of acetylenic ether (−)-**5** (2.5 g, 10.4 mmol) in THF (20 mL) was added to a solution of diisobutylaluminum hydride (5.56 mL, 31.2 mmol, 3 equiv) in THF (70 mL). The reaction mixture was heated to reflux for 1.5 h. After the solution was cool to room temperature, the reaction was quenched with an aqueous solution of sodium potassium tartrate (20 mL). The gelatinous mixture was stirred at room temperature for ca. 3 h. The mixture was diluted with EtOAc (100 mL) and washed with water (3 × 50 mL). The aqueous phase was back-extracted with EtOAc (3 × 50 mL), and the combined orgainc layers were washed with brine (75 mL), dried ($MgSO_4$), filtered, and concentrated to afforded a yellow oil. Purification by silica gel column chromatography (hexane/benzene, 13/1) provided 2.02 g of analytically pure vinyl ether (−)-**7** in 80% yield as a clear oil: ^{1}H NMR (499.7 MHz, $CDCl_3$) δ 7.30−7.26 (m, 2 H), 7.23−7.17 (m, 3 H) 5.80−5.78 (m, 1 H), 5.67−5.59 (m, 1 H), 4.90−4.82 (m, 2 H), 4.14−4.09 (m, 1 H), 3.61 (td, J = 10.0, 4.2, 1 H), 2.67−2.54 (m, 3 H), 2.17−2.14 (m, 1 H), 1.93−1.87 (m, 2 H) 1.78−1.76 (m, 1 H), 1.59−1.51 (m, 1 H), 1.49−1.31 (m, 3 H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 144.34, 143.82, 137.74, 128.12, 127.79, 126.17, 113.66, 103.46, 84.02, 50.48, 33.46, 32.85, 38.22, 25.81, 24.90; IR (neat) 2931, 1661, 1102; MS (CI, CH_4) 243 (M^+ + 1, 2), 159 (100); TLC R_f 0.18 (hexane/benzene, 10/1); optical rotation $[\alpha]^{22}_D$ = −141.16° (c = 0.93, $CHCl_3$). Anal. Calcd for $C_{17}H_{22}O$ (242.364): C, 84.25; H, 9.15. Found: C, 84.10; H, 9.06.

General Procedure for $SnCl_4$-Promoted [4 + 2] Cycloadditions (General Procedure I). The preparation of **9a** from **8** will serve to illustrate the general procedure utilized.

(4*R*,5*R*,6*R*)-3-Methyl-4-phenyl-5-(2-propenyl)-6-[(1*R*,2*S*)-(2-phenylcyclohexyl)oxy]-5,6-dihydro-4*H*-[1,2]-oxazine 2-Oxide (9a). Tin tetrachloride (0.13 mL, 1.09 mmol, 1 equiv) was added to a −78 °C solution of nitroalkene **8** (179 mg, 1.09 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 (−)-**6** (525 mg, 2.17 mmol, 2.0 equiv) in CH_2Cl_2 (2 mL) was added rapidly to the cold reaction mixture via syringe, and the yellow color faded as the vinyl ether was added. The reaction was left to stir at −78 °C for an additional 5 min and was then quenched with 1 N NaOH/MeOH (4 mL). The mixture was diluted with CH_2Cl_2 (150 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 (75 mL), dried (Na_2SO_4), and concentrated. The crude organic concentrate was purified by silica gel column chromatography (hexane/EtOAc, 5/1 (600 mL), 4/1) to afford 401 mg of **9a** as a 15:1 (**9a**:**9b**) mixture by ^{1}H NMR integration and 12 mg of nitronate diastereomers **9c** and **9d**. An analytical sample of **9a** was obtained after recrystallization (hexane/TBME) to afford a white crystalline solid. Nitronate **9b** was found to be identical by ^{1}H NMR to the major nitronate **9b** obtained from a MAPh-promoted [4 + 2] cycloaddition. Data for **9a**: mp 126−127 °C (TBME/hexane); ^{1}H NMR (499.7 MHz, C_6D_6) δ 7.35−7.33 (m, 2 H), 7.30−7.27 (m, 2 H), 7.02−6.98 (m, 1 H) 6.94−6.92 (m, 3 H), 6.56−6.54 (m, 2 H), 5.51 (d, J = 1.6, 1 H), 5.27−5.19 (m, 1 H), 4.93 (d, J = 17.0, 1 H), 4.86 (d, J = 10.1, 1 H), 4.32 (td, J = 10.2, 4.0, 1 H), 3.63 (dd, J = 6.8, 1.5, 1 H), 2.57 (ddd, J = 12.4, 10.6, 3.7, 1 H), 2.18−2.15 (m, 1 H), 2.02−1.95 (m, 1 H), 1.77−1.68 (m, 2 H), 1.62−1.56 (m, 1 H) 1.52−1.49 (m, 4 H), 1.45−1.41 (m, 1 H), 1.36−1.27 (m, 1 H), 1.11−0.98 (m, 3 H); ^{13}C NMR (125.6 MHz, C_6D_6) δ 144.62, 137.68, 135.72, 129.53, 128.65, 128.29, 128.04, 127.16, 126.27, 118.37, 117.63, 97.03, 75.96, 51.35, 44.39, 38.98, 34.81, 32.25, 30.34, 26.24, 24.50, 18.19; IR ($CHCl_3$) 3012, 2939, 1232; MS (FAB) 406 (M^+ + 1, 100); TLC R_f 0.33 (hexane/EtOAc, 2/1); optical rotation $[\alpha]^{23}_D$ = −220.6° (c = 1.0, $CHCl_3$). Anal. Calcd for $C_{26}H_{31}NO_3$ (405.534): C, 77.01; H, 7.71; N, 3.45. Found: C, 77.06; H, 7.72; N, 3.48.

(4*R*,5*S*,6*R*)-3-Methyl-4-phenyl-5-(2-propenyl)-6-[(1*R*,2*S*)-(2-phenylcyclohexyl)oxy]-5,6-dihydro-4*H*-[1,2]-oxazine 2-Oxide (9d). According to general procedure 1, tin tetrachloride (0.47 mL, 4.0 mmol, 2 equiv) was added to a −78 °C solution of nitroalkene **8** (326 mg, 2.0 mmol) in CH_2Cl_2 (15 mL) and the resulting complex was left to stir for 15 min. A solution of vinyl ether (−)-**6** (605 mg, 2.5 mmol, 1.5 equiv) in CH_2Cl_2 (5 mL) was added slowly dropwise to the cold reaction mixture via syringe. The reaction was left to stir at −78 °C for an additional 10 min and was then quenched with 1 N NaOH/MeOH (5 mL). After an aqueous extractive workup, the crude organic concentrate was purified by silica gel column chromatography (hexane/EtOAc, 6/1 (700 mL), 5/1) to afford 0.572 g of **9a** as a 13:1 (**9a**:**9b**) mixture by ^{1}H NMR integration, 125 mg of **9d**, and 0.080 g of a mixure of **9c** and **9d**. The overall yield of the reaction was 777 mg (96%) with a ratio of 3/1 for (**9a** + **9b**)/(**9c** + **9d**)). An analytical sample of **9d** was obtained by recrystallization (hexane). Nitronates **9a**, **9b**, and **9c** were found to be identical by ^{1}H NMR to the nitronates obtained from the previous $SnCl_4$ reaction and the MAPh-promoted [4 + 2] cycloadditions. Data for **9d**: mp 104−105 °C (hexane); ^{1}H NMR (400 MHz, C_6D_6) δ 7.35−7.29 (m, 4 H), 7.05−7.01 (m, 1 H), 6.94−6.92 (m, 3 H) 6.58−6.56 (m, 2 H), 5.33 (d, J = 1.5, 1 H), 5.29−5.19 (m, 1 H), 4.86 (dd, J = 19.2, 10.8, 2 H), 4.30 (td, J = 10.3, 3.9, 1 H), 2.76 (d, J = 9.0, 1 H), 2.52 (td, J = 13.1, 3.5, 1 H), 2.11−2.07 (m, 1 H), 1.92−1.81 (m, 3 H), 1.73−1.68 (m, 1 H), 1.56−1.53 (m, 1 H) 1.46−1.44 (m, 1 H), 1.37−1.27 (m, 4 H), 1.12−0.94 (m, 3 H); ^{13}C NMR (100.6 MHz, C_6D_6) δ 144.61, 140.18, 134.88, 129.00, 128.80, 128.62, 128.04, 127.49, 126.21, 118.82, 117.49, 96.07, 75.60, 51.38, 46.63, 42.13, 34.85, 33.41, 30.39, 26.30, 24.54, 17.52; IR ($CHCl_3$) 2938, 1619, 1232, 895; MS (FAB) 406 (M^+ + 1, 99), 159 (100); TLC R_f 0.26 (hexane/EtOAc, 2/1); optical rotation $[\alpha]^{25}_D$ = −337.8° (c = 1.0, $CHCl_3$). Anal. Calcd for $C_{26}H_{31}NO_3$ (405.534): C, 77.01; H, 7.71; N, 3.45. Found: C, 77.15; H, 7.74; N, 3.63.

General Procedure for MAPh-Promoted [4 + 2] Cycloadditions (General Procedure II). The preparation of **9b** from **8** will serve to illustrate the general procedure utilized.

(4*S*,5*S*,6*S*)-3-Methyl-4-phenyl-5-(2-propenyl)-6-[(1*R*,2*S*)-(2-phenylcyclohexyl)oxy]-5,6-dihydro-4*H*-[1,2]-oxazine 2-Oxide (9b). Trimethylaluminum (2.0 M in toluene, 1.7 mL, 3.40 mmol, 2.0 equiv) was added dropwise to a solution of 2,6-diphenylphenol (1.67 g, 6.8 mmol, 4.0 equiv) in CH_2Cl_2 (12 mL) at room temperature. Gas evolution (CH_4) was observed as the resulting light yellow solution stirred at room temperature for 40 min. The Lewis acid solution (MAPh) was transferred, via cannula, to a second reaction vessel containing a −78 °C solution of nitroalkene **8** (277 mg, 1.7 mmol) and vinyl ether (−)-**16** (751 mg, 3.09 mmol, 1.8 equiv) in CH_2Cl_2 (5 mL). The resulting, dark brown solution was allowed to warm slowly to −25 °C over a period of 1 h and was then left to stir at −25 °C for 4 h (the color faded to a light brown), after which time the reaction was quenched with H_2O (8 mL). The mixture was diluted with CH_2Cl_2 (150 mL) and washed with water (3 × 100 mL). The aquous layers were back-extracted with CH_2Cl_2 (3 × 50 mL), and the combined organic phases were washed with brine (75 mL), dried ($NaSO_4$), filtered, and concentrated in vacuo. The crude material was purified by silica gel column chromatography (hexane/EtOAc, 6/1 (700 mL), 5/1 (600 mL), 4/1) and radial chromotography (hexane/EtOAc, 5/1) of mixed fractions obtained in the column chromatography to afford 590

mg of nitronates **9b** and **9a** and 67 mg of **9c**. The ratio of diastereomeric nitronates **9b**, **9a**, and **9c** was found to be 15/1/1.8 (**9b**/**9a**/**9c**) overall by a combination of ^{1}H NMR integration and isolated yield. An analytical sample of the 15/1 mixture of nitronates **9b** and **9a** could not be obtained since formation of the nitroso acetal occurred during the removal of residual solvent from the sample. Nitronate **9a** was found to be identical by ^{1}H NMR to the nitronate obtained from the $SnCl_4$-promoted [4 + 2] cycloaddition. Data for **9b**: ^{1}H NMR (499.7 MHz, C_6D_6) δ 7.10−7.03 (m, 2 H), 7.02−6.92 (m, 6 H), 6.62−6.60 (m, 2 H), 5.51 (d, J = 1.6, 0.06 H), 4.93−4.85 (m, 1 H), 4.76−4.72 (m, 2 H), 4.57 (d, J = 2.2, 0.94 H), 3.94 (d, J = 7.1, 0.94 H), 3.76 (td, J = 10.8, 4.6, 1 H), 3.63 (d, J = 6.8, 0.06 H), 2.63−2.60 (m, 1 H), 2.50−2.45 (m, 1 H), 1.80 (s, 3 H), 1.78−1.71 (m, 1 H), 1.67−1.59 (m, 3 H) 1.55−1.44 (m, 2 H), 1.38−1.21 (m, 3 H), 1.07−1.00 (m, 1 H); ^{13}C NMR (125.7 MHz, C_6D_6) δ 144.39, 137.55, 135.50, 129.46, 128.72, 128.56, 128.29, 127.24, 126.59, 119.10, 117.19, 104.07, 82.81, 52.09, 45.03, 39.05, 34.68, 33.18, 32.26, 25.97, 25.25, 18.15; MS (FAB) 406 (M^+ + 1,100); TLC R_f 0.33 (hexane/EtOAc, 2/1).

General Procedure for [3 + 2] Cycloadditions of Nitronates (General Procedure III). The preparation of **10a** from **9a** will serve to illustrate the general procedure utilized.

(1*S*,6*R*,7*R*,8*R*,9*R*)-9-Methyl-8-phenyl-6-[(1*R*,2*S*)-(2-phenylcyclohexyl)oxy]-4-aza-3,5-dioxatricyclo[5.2.1.0^{4,9}]-decane (10a). A solution of nitronate **9a** (397 mg, 0.98 mmol) in benzene (10 mL) was added to a suspension of sodium bicarbonate (576 mg, 6.86 mmol, 7 equiv) in benzene (90 mL), and the mixture was heated to reflux for 10 h. After cooling to room temperature, the mixture was concentrated and the sodium bicarbonate was removed by filtration through a cotton pipet plug, washing with TBME (25 mL). Purification of the residue by column chromatography using basic alumina (III) (hexane/TBME, 6/1) afforded the nitroso acetal **10a** as a white foam. An analytical sample of **10a** as a clear glass (396 mg, 100%) was obtained by heating the foam in vacuo for 7 days at 70 °C: ^{1}H NMR (400 MHz, C_6D_6) δ 7.48−7.46 (m, 2 H), 7.37−7.33 (m, 2 H), 7.17−7.11 (m, 3 H), 7.07−7.03 (m, 1 H), 6.83−6.81 (m, 2 H) 4.97 (d, J = 2.7, 1 H), 4.53−4.47 (m, 1 H), 4.25−4.23 (m, 1 H), 4.10−4.06 (m, 1 H), 3.40 (s, 1 H), 2.68−2.61 (m, 1 H), 2.20−2.18 (m, 1 H), 2.04−1.99 (m, 2 H), 1.92−1.90 (m, 1 H) 1.82−1.78 (m, 1 H), 1.63−1.60 (m, 1 H)), 1.51−1.48 (m, 1 H), 1.44−1.35 (m, 1 H), 1.25−1.11 (m, 4 H) 0.89 (s, 3 H); ^{13}C NMR (100.6 MHz, C_6D_6) δ 145.43, 141.17, 129.11, 128.80, 128.56, 128.46, 126.70, 126.05, 99.86, 88.29, 79.82, 73.63, 51.66, 46.93, 45.78, 44.42, 35.98, 35.32, 30.70, 26.59, 24.82, 19.74; IR ($CHCl_3$) 3010, 2937, 1076; MS (FAB) 406 (M^+ + 1, 51), 159 (100); TLC R_f 0.50 (hexane/EtOAc, 2/1); optical rotation $[\alpha]^{23}_D$ = −220.0° (c = 1.0, $CHCl_3$). Anal. Calcd for $C_{26}H_{31}NO_3$ (405.534): C, 77.01; H, 7.71; N, 3.45. Found: C, 76.90; H, 7.81; N, 3.41.

General Procedure for Nickel Boride Reduction of Nitroso Acetals (General Procedure IV). The preparation of (−)-**11a** from **10a** will serve to illustrate the general procedure utilized.

[(1*R*,3*S*,4*R*,5*R*)-4-Amino-4-methyl-5-phenyl]-1,3-cyclopentanedimethanol ((−)-11a). Nickel chloride (87 mg, 0.678 mmol, 1.1 equiv) was added to a solution of nitroso acetal **10a** (250 mg, 0.616 mmol) in ethanol (12 mL) at room temperature (reaction does not need to be run under N_2). Sodium borohydride (70 mg, 1.83 mmol, 3 equiv) was added to the suspension, and a black precipitate formed rapidly with concomitant hydrogen evolution. After 15 min, another 3 equiv of $NaBH_4$ (70 mg) was added. After 40 min, the ethanol was removed in vacuo to provide a black solid. The crude organic concentrate was purified by silica gel column chromatography ($CHCl_3$/MeOH, 10/1 (100 mL), then $CHCl_3$/MeOH/NH_4OH, 10/5/1) to afford 119 mg (82% yield) of amino diol (−)-**11a** as a light brown solid and 100 mg (94% yield) of recovered (−)-(1*R*,2*S*)-phenylcyclohexanol ((−)-**4**). Recrystallization (acetonitrile) of the amino diol afford a white microcrystalline material. The ^{1}H NMR, ^{13}C NMR, and MS of amino diol (−)-**11a** were identical to the data obtained for amino diol (+)-**11a** which is derived from a tandem sequence using MAPh as the Lewis acid in the [4 + 2] cycloaddition. However, the signs of the rotation of the two amino diols are opposite. Data for (−)-**11a**: ^{1}H NMR (499.7 MHz, CD_3OD) δ 7.32−7.29 (m, 2 H), 7.24−7.21 (m, 3 H), 3.75 (dd, J = 10.8, 7.1, 1 H), 3.66 (dd, J = 10.8, 5.7, 1 H), 3.52 (dd, J = 10.3, 3.7, 1 H), 3.34 (dd, J = 10.5, 3.7, 1 H), 2.70 (d, J = 10.7, 1 H), 2.50 (ddddd, J = 10.7, 9.2, 7.9, 6.7, 3.7, 1 H), 2.16 (dt, J = 12.8, 7.9, 1 H), 2.01 (tdd, J = 8.5, 7.1, 5.6, 1 H), 1.48 (dt, J = 12.8, 9.2, 1 H), 0.84 (s, 3 H); ^{13}C NMR (125.7 MHz, CD_3OD) δ 141.25, 130.28, 129.24, 127.70, 65.34, 64.22, 62.66, 60.72, 51.15, 44.98, 31.24, 27.55; MS (FAB) 236 (M^+ + 1, 100); TLC R_f 0.49 ($CHCl_3$/CH_3OH/NH_4OH, 10/5/1); optical rotation $[\alpha]^{25}_D$ = −39.7° (c = 0.25, CH_3-OH).

General Procedure for Acylation of Amino Diols (General Procedure V). The preparation of (+)-**12a** from (−)-**11a** will serve to illustrate the general procedure utilized.

[(1*R*,3*S*,4*R*,5*R*)-4-(Acetylamino)-4-methyl-5-phenyl]-1,3-cyclopentanedimethanol Diacetate ((+)-12a). The amino diol (−)-**11a** (18 mg, 0.077 mmol) was dissolved in pyridine (1 mL) and acetic anhydride (1 mL) and was left to stir at room temperature for 1.5 h. The light yellow reaction mixture was concentrated in vacuo to afford a yellow oil. The crude organic concentrate was purified by silica gel column chromatography (EtOAc/hexane, 1/1) to provide 23 mg (83%) of triacetate (+)-**12a** as clear oil. The enantiomeric excess was determined to be >99% by chiral HPLC. Data for (+)-**12a**: ^{1}H NMR (499.7 MHz, $CDCl_3$) δ 7.35−7.32 (m, 2 H), 7.28−7.25 (m, 1 H), 7.17−7.15 (m, 2 H, 5.39 (s, 1 H), 4.16 (*A*BX, J_{ab} = 11.0, J_{ax} = 5.6, 1 H), 4.16 (A*B*X, J_{bx} = 7.4, 1 H), 4.08 (*AB*X, J_{ab} = 10.2, J_{ax} = 3.5, 1 H), 3.92 (A*B*X, J_{bx} = 6.3, 1 H), 3.43 (d, J = 11.2, 1 H), 2.73−2.65 (m, 1 H), 2.58−2.53 (m, 1 H), 2.23−2.17 (m, 1 H), 2.08 (s, 3 H), 1.93 (s, 3 H), 1.83 (s, 3 H), 1.70−1.64 (m, 1 H), 1.07 (s, 3 H); TLC R_f 0.31 (EtOAc/hexane, 2/1); optical rotation $[\alpha]^{23}_D$ = 41.5° (c = 1.06, $CHCl_3$); chiral HPLC ((*R*,*R*)-Whelk-O1, (*i*-PrOH/hexanes, 55/45), 0.5 mL/min); t_R (+)-**12a** 17.32 min (>99%), >99% ee.

(1*R*,6*S*,7*S*,8*S*,9*S*)-9-Methyl-8-phenyl-6-[(1*R*,2*S*)-(2-phenylcyclohexyl)oxy]-4-aza-3,5-dioxatricyclo[5.2.1.0^{4,9}]-decane (10b). According to general procedure III, a 15/1 (**9b**/**9a**) mixture of nitronate **9b** (506 mg, 1.37 mmol) was added to a suspension of sodium bicarbonate (806 mg, 9.6 mmol, 7 equiv) in benzene (137 mL) and the mixture was heated to reflux for 18 h. Purification by column chromotography basic alumina (III) (hexane/TBME, 6/1) afforded the nitroso acetal **10b** as a 25/1 (**10b**/**10a)** mixture. Nitroso acetal **10b** was obtained analytically pure as a white solid (536 mg, 96% yield) by heating the foam in vacuo for 6 days at 80 °C: ^{1}H NMR (499.7 MHz, C_6D_6) δ 7.11−7.02 (m, 8 H), 6.98−6.96 (m, 2 H) 4.98 (d, J = 2.9, 0.05 H), 4.27 (d, J = 2.2, 0.95 H), 4.12 (s, 1 H), 4.08 (dd, J = 7.7, 2.7, 1 H), 4.01 (dd, J = 7.7, 7.7, 1 H), 3.74 (td, J = 10.4, 4.4, 1 H), 2.73−2.70 (m, 1 H), 2.56−2.51 (m, 1 H), 2.01−1.96 (m, 1 H), 1.90−1.83 (m, 2 H) 1.71−1.62 (m, 3 H), 1.50−1.48 (m, 1 H), 1.42−1.34 (m, 1 H), 1.28−1.20 (m, 1 H), 1.34−1.05 (m, 1 H) 1.01 (s, 3 H), 0.97−0.92 (m, 1 H); ^{13}C NMR (125.6 MHz, C_6D_6) δ 145.07, 140.82, 129.08, 128.69, 128.34, 128.78, 126.76, 126.31, 106.81, 87.39, 81.60, 79.38, 51.85, 47.76, 45.87, 44.83, 35.81, 35.16, 33.20, 26.18, 25.43, 19.97; IR ($CHCl_3$) 3025, 3021, 3012, 2936; MS (FAB) 406 (M^++1, 44), 159 (100); TLC R_f 0.48 (hexane/EtOAc, 2/1); optical rotation $[\alpha]^{23}_D$ = −11.0° (c = 1.1, $CHCl_3$). Anal. Calcd for $C_{26}H_{31}NO_3$ (405.534): C, 77.01; H, 7.71; N, 3.45. Found: C, 77.24; H, 7.65; N, 3.54.

(1*S*,3*R*,4*S*,5*S*)-4-Amino-4-methyl-5-phenyl]-1,3-cyclopentanedimethanol ((+)-11a). According to general procedure IV, nickel chloride (155 mg, 1.10 mmol, 1.1 equiv) was added to a solution of nitroso acetal **10b** (405 mg, 1.0 mmol) in ethanol (20 mL). $NaBH_4$ (125 mg, 3.3 mmol, 3 equiv) was added to the suspension, and after 15 min, additional $NaBH_4$ (125 mg, 3.3 mmol, 3 equiv) was added. After 30 min, the ethanol was removed in vacuo providing a black solid. The crude organic concentrate was purified by silica gel column chromatography ($CHCl_3$/MeOH, 10/1 (100 mL), then $CHCl_3$/MeOH/NH_4OH, 10/5/1) to afford 169 mg (72% yield) of amino diol (+)-**11a** as a light brown solid and 162 mg (94% yield) of recovered (−)-(1*R*,2*S*)-phenylcyclohexanol ((−)-**4**). An analytical sample of (+)-**11a** was obtained by recrystallization (aceto-

nitrile) to provide a white microcrystalline material. The analytical data for (+)-**11a**, except for the sign of the rotation, was identical to the data obtained for amino diol (−)-**11a** which was derived from a tandem sequence using $SnCl_4$ as the Lewis acid in the [4 + 2] cycloaddition. Data for (+)-**11a**: mp 189−191 °C (CH_3CN); ^{1}H NMR (499.7 MHz, CD_3OD) δ 7.32−7.30 (m, 2 H), 7.24−7.20 (m, 3 H), 3.75 (dd, J = 10.8, 7.1, 1 H), 3.65 (dd, J = 10.8, 5.7, 1 H), 3.52 (dd, J = 10.3, 3.7, 1 H), 3.34 (dd, J = 10.5, 3.7, 1 H), 2.70 (d, J = 10.7, 1 H), 2.49 (ddddd, J = 10.7, 9.2, 7.9, 6.7, 3.7, 1 H), 2.16 (dt, J = 12.8, 7.9, 1 H), 2.01 (tdd, J = 8.5, 7.1, 5.6, 1 H), 1.48 (dt, J = 12.8, 9.2, 1 H), 0.83 (s, 3 H); ^{13}C NMR (125.7 MHz, CD_3OD) δ 140.33, 129.26, 128.21, 126.65, 64.61, 63.31, 61.50, 59.85, 50.21, 43.96, 30.33, 26.75; IR (KBr) 3318, 3271, 3264, 3257, 2956, 2922, 2898, 1040, 1036, 1013; MS (FAB) 236 (M^+ + 1, 100); TLC R_f 0.49 ($CHCl_3$/CH_3OH/NH_4OH, 10/5/1); optical rotation $[\alpha]^{25}_D$ = 31.9° (c = 0.75, CH_3OH). Anal. Calcd for $C_{14}H_{21}NO_2$ (235.33): C, 71.46; H, 8.99; N, 5.95. Found: C, 71.48; H, 9.10; N, 5.97.

[(1*S*,3*R*,4*S*,5*S*)-4-(Acetylamino)-4-methyl-5-phenyl]-1,3-cyclopentanedimethanol Diacetate ((−)-12a). According to general procedure V, the amino diol (+)-**11a** (25 mg, 0.106 mmol) was dissolved in pyridine (1.5 mL) and acetic anhydride (1.5 mL) and was left to stir at room temperature for 1.5 h. Purification by silica gel column chromatography (Et_2O) to provide 29 mg (77%) of triacetate (−)-**12a** as clear oil. The enantiomeric excess was determined to be 95% by chiral HPLC. Data for (−)-**12a**: ^{1}H NMR (499.7 MHz, $CDCl_3$) δ 7.35−7.32 (m, 2 H), 7.28−7.25 (m, 1 H), 7.17−7.15 (m, 2 H), 5.39 (s, 1 H), 4.16 (*A*BX, J_{ab} = 11.0, J_{ax} = 5.6, 1 H), 4.16 (A*B*X, J_{bx} = 7.4, 1 H), 4.08 (*A*BX, J_{ab} = 10.2, J_{ax} = 3.5, 1 H), 3.92 (A*B*X, J_{bx} = 6.3, 1 H), 3.43 (d, J = 11.2, 1 H), 2.73−2.65 (m, 1 H), 2.58−2.53 (m, 1 H), 2.23−2.17 (m, 1 H), 2.08 (s, 3 H), 1.93 (s, 3 H), 1.83 (s, 3 H), 1.70−1.64 (m, 1 H), 1.07 (s, 3 H); TLC R_f 0.31 (EtOAc/hexane, 2/1); optical rotation $[\alpha]^{23}_D$ = −40.3° (c = 1.45, $CHCl_3$); chiral HPLC ((*R*,*R*)-Whelk-O1, (*i*-PrOH/hexanes, 55/45), 0.5 mL/min) t_R (−)-**12a** 14.58 min (96.3%), t_R (+)-**12a** 17.98 min (3.7%), 93% ee.

(4*S*,5*R*,6*R*)-4-Cyclohexyl-3-methyl-5-(2-propenyl)-6-[(1*R*,2*S*)-(2-phenylcyclohexyl)oxy]-5,6-dihydro-4*H*-[1,2]-oxazine 2-Oxide (14a) and (4*S*,5*R*,6*S*)-4-Cyclohexyl-3-methyl-5-(2-propenyl)-6-[(1*R*,2*S*)-(2-phenylcyclohexyl)-oxy]-5,6-dihydro-4*H*-[1,2]-oxazine 2-Oxide (14c). According to general procedure I, tin tetrachloride (0.117 mL, 1.0 mmol, 1 equiv) was added to a −78 °C solution of nitroalkene **13** (169 mg, 1.0 mmol) in CH_2Cl_2 (10 mL) and the resulting colorless complex was left to stir for 15 min. A solution of vinyl ether (−)-**6** (485 mg, 2.0 mmol, 2.0 equiv) in CH_2Cl_2 (1 mL) was added rapidly to the cold reaction mixture via syringe, and the reaction mixture turned slightly brown. The reaction was left to stir at −78 °C for an additional 5 min and was then quenched with 1 N NaOH/MeOH (4 mL). After extractive aqueous workup (do not heat when concentrating solvent), the crude organic concentrate was purified by silica gel column chromatography (hexane/EtOAc, 8/1 (900 mL), 6/1 (700 mL), 2/1) to afford 229 mg of **14a** as a 6.9/1 (**14a**/**14b**) mixture by ^{1}H NMR integration and 99 mg of nitronate diastereomers **14c**. The overall yield of the reaction was 328 mg (80%) with an overall selectivity of 6.9/1/3.4 (**14a**/**14b**/**24c**). Nitronate **14b** was found to be identical by ^{1}H NMR to the nitronate **14b** obtained from a MAPh-promoted [4 + 2] cycloaddition. Data for **14a**: ^{1}H NMR (499.7 MHz, C_6D_6) δ 7.18−7.03 (m, 5 H), 5.52−5.45 (m, 0.11 H), 5.32−5.24 (m, 0.89 H), 4.90−4.87 (m, 2 H), 4.52 (d, J = 5.5, 1 H), 3.68 (td, J = 10.4, 4.2, 1 H), 3.04−3.02 (m, 1 H), 2.51−2.46 (m, 1 H), 1.92−0.73 (m, 25 H); TLC R_f 20 (hexane/EtOAc, 3/1). Data for **14c**: ^{1}H NMR (499.7 MHz, $CDCl_3$)) δ 7.31−7.26 (m, 2 H), 7.23−7.19 (m, 3 H), 5.35−5.26 (m, 1 H), 4.85 (d, J = 10.5, 1 H), 4.83 (d, J = 3.4, 1 H), 4.72 (d, J = 17.0, 1 H), 3.78−3.68 (m, 1 H), 2.52−2.45 (m, 2 H), 2.04−2.02 (m, 4 H), 1.94−1.61 (m, 10 H), 1.57−1.35 (m, 5 H), 1.33−1.04 (m, 5 H), 0.93−0.85 (m, 1 H); ^{13}C NMR (125.7 MHz, $CDCl_3$)) δ 144.44, 135.84, 128.44, 127.87, 126.51, 123.96, 116.52, 106.22, 84.45, 51.75, 44.19, 38.08, 36.34, 35.92, 34.73, 34.02, 30.54, 30.05, 27.15, 27.04, 26.18, 25.68, 24.97, 21.11 (CH_3); IR ($CHCl_3$) 2934; MS (FAB) 412 (M^+ + 1, 87), 159 (100); TLC R_f 0.16 (hexane/EtOAc, 3/1).

(4*R*,5*S*,6*S*)-4-Cyclohexyl-3-methyl-5-(2-propenyl)-6-[(1*R*,2*S*)-(2-phenylcyclohexyl)oxy]-5,6-dihydro-4*H*-[1,2]-oxazine 2-Oxide (14b). According to general procedure II, a solution of MAPh (2.0 mmol, 2.0 equiv) in CH_2Cl_2 (10 mL) was transferred, via cannula, to a second reaction vessel containing a −60 °C solution of nitroalkene **13** (169 mg, 1.0 mmol) and vinyl ether (−)-**6** (364 mg, 1.5 mmol, 1.5 equiv) in CH_2Cl_2 (5 mL). The resulting dark brown solution was allowed to warm slowly to −5 °C over a 3 h period and was then left to stir at −5−0 °C for 66 h (the color faded to a light brown), after which time the reaction was quenched with H_2O (6 mL). After an aqueous extractive workup, the crude material was purified by silica gel column chromatography (hexane/EtOAc, 8/1 (900 mL), 7/1 (800 mL), 6/1) to afford 353 mg of approximately 7/1 (**14b**/**14a**) mixture of **14b** and **14a** and 16 mg of **14d**. The exo/endo selectivity for the reaction was determined to be approxiamately 22/1 ((**14b** + **14a**)/**14d**). An analytical sample of the 7/1 mixture of nitronates **14b** and **14a** could not be obtained since formation of the nitroso acetal **15b** occurred during the removal of residual solvent from the sample. Data for **14b**: ^{1}H NMR (499.7 MHz, C_6D_6) δ 7.18−7.03 (m, 5 H), 5.52−5.45 (m, 0.11 H), 5.32−5.24 (m, 0.89 H), 4.90−4.87 (m, 2 H), 4.52 (d, J = 5.5, 1 H), 3.68 (td, J = 10.4, 4.2, 1 H), 3.04−3.02 (m, 1 H), 2.51−2.46 (m, 1 H), 1.92−0.73 (m, 25 H); TLC R_f 0.20 (hexane/EtOAc, 3/1).

(1*S*,6*R*,7*R*,8*S*,9*R*)-8-Cyclohexyl-9-methyl-6-[(1*R*,2*S*)-(2-phenylcyclohexyl)oxy]-4-aza-3,5-dioxatricyclo[5.2.1.0^{4,9}]-decane (15a). According to general procedure III, a 6.9/1 mixture of nitronates **14a** and **14b** (288 mg, 0.554 mmol) was added to a suspension of sodium bicarbonate (47 mg, 0.554 mmol, 1 equiv) in benzene (56 mL) and the mixture was heated to reflux for 15 min. Purification by column chromatography on basic alumina (III) (hexane/TBME, 10/1) afforded 201 mg (88% yield) of analytically pure nitroso acetal **15a** (determined to be a 20/1 (**15a**/**15b**) mixture by ^{1}H NMR integration) as a clear glass: ^{1}H NMR (499.7 MHz, C_6D_6) δ 7.42−7.40 (m, 2 H), 7.32−7.28 (m, 2 H), 7.14−7.11 (m, 1 H), 4.98 (d, J = 2.3, 1 H), 4.40 (td, J = 10.5, 4.2, 1 H), 4.17 (dd, J = 7.7, 2.7, 1 H), 4.09 (dd, J = 7.9, 7.7, 1 H), 2.60 (ddd, J = 12.4, 10.8, 3.7, 1H), 2.23−2.19 (m, 1 H), 1.92 (d, J = 4.9, 1 H), 1.86−1.81 (m, 1 H), 1.80−1.76 (m, 2 H), 1.65−1.54 (m, 5 H) 1.49−1.46 (m, 1 H), 1.41−0.94 (m, 14 H), 0.86−0.77 (m, 1 H), 0.66−0.58 (m, 1 H); ^{13}C NMR (125.6 MHz, C_6D_6) δ 145.30, 128.74, 128.25, 125.82, 100.30, 88.06, 79.57, 73.61, 51.45, 44.86, 44.08, 40.55, 37.02, 36.45, 35.29, 33.32, 30.77, 29.60, 26.97, 26.83, 26.69, 26.56, 24.83, 18.94; IR ($CHCl_3$) 2933; MS (FAB) 412 (M^+ + 1, 88), 159 (100); TLC R_f 0.48 (hexane/EtOAc, 3/1); optical rotation $[\alpha]^{24}_D$ = −143.3° (c = 0.98, $CHCl_3$). Anal. Calcd for $C_{26}H_{37}NO_3$ (411.59): C, 75.87; H, 9.06; N, 3.40. Found: C, 75.86; H, 9.18; N, 3.39.

(1*S*,6*S*,7*R*,8*S*,9*R*)-8-Cyclohexyl-9-methyl-6-[(1*R*,2*S*)-(2-phenylcyclohexyl)oxy]-4-aza-3,5-dioxatricyclo[5.2.1.0^{4,9}]-decane (15c). According to general procedure III, nitronate **14c** (99 mg, 0.240 mmol) was added to a suspension of sodium bicarbonate (141 mg, 1.68 mmol, 7 equiv) in benzene (24 mL) and the mixture was heated to reflux for 1.5 h. Purification by column chromatography on basic alumina (III) (10:1 hexane/TBME) afforded 93 mg (94% yield) of analytically pure nitroso acetal **15c** as a white crystalline solid: mp 113−115 °C (TBME/hexane); ^{1}H NMR (499.7 MHz, C_6D_6) δ 7.16−7.13 (m, 2 H), 7.10−7.06 (m, 3 H), 4.50 (d, J = 6.0, 1 H), 4.32 (dd, J = 7.0, 3.9, 1 H), 4.16 (dd, J = 9.0, 7.1, 1 H), 3.66 (td, J = 10.5, 4.4, 1 H), 2.68−2.65 (m, 1H), 2.49−2.43 (m, 1 H), 2.05−2.01 (m, 1 H), 1.94 (d, J = 13.0, 1 H), 1.78 (t, J = 5.9, 1 H), 1.70−1.57 (m, 3 H) 1.53−1.45 (m, 6 H), 1.39−1.31 (m, 1 H), 1.27−0.94 (m, 10 H), 0.88−0.81 (m, 1 H), 0.70−0.63 (m, 1 H), 0.51−0.44 (m, 1 H); ^{13}C NMR (125.6 MHz, C_6D_6) δ 144.92, 128.34, 128.29, 127.49, 106.46, 84.35, 82.57, 78.35, 52.06, 48.70, 48.59, 40.92, 36.07, 34.70, 34.21, 33.09, 29.73, 29.70, 26.85, 26.53, 26.48, 26.16, 25.33, 21.23; IR ($CHCl_3$) 2933; MS (FAB) 412 (M^+ + 1, 83), 159 (100); TLC R_f 0.46 (hexane/EtOAc, 3/1); optical rotation $[\alpha]^{24}_D$ = 59.90° (c = 1.01, $CHCl_3$). Anal. Calcd for $C_{26}H_{37}NO_3$ (411.59): C, 75.87; H, 9.06; N, 3.40. Found: C, 75.80; H, 9.06; N, 3.28.

[(1*R*,3*S*,4*R*,5*S*)-4-Amino-5-cyclohexyl-4-methyl]-1,3-cyclopentanedimethanol ((+)-16). According to general pro-

cedure IV, nickel chloride (64 mg, 0.490 mmol, 1.2 equiv) was added to a solution of nitroso acetal **15a** (168 mg, 0.408 mmol) in ethanol (9 mL). $NaBH_4$ (93 mg, 2.45 mmol, 6 equiv) was added to the suspension, and after ca. 15 min $NaBH_4$ (93 mg, 2.45 mmol, 6 equiv) was added. After ca. 40 min, the ethanol was removed in vacuo providing a black solid. Purification by silica gel column chromatography ($CHCl_3$/MeOH, 10/1 (100 mL), then $CHCl_3$/MeOH/NH_4OH, 10/5/1) afforded 81 mg (82% yield) of amino diol (+)-**16** as a white foam and 63 mg (90%) of recovered (−)-(1*R*,2*S*)-phenylcyclohexanol ((−)-**4**). The analytical data for (+)-**16**, except for the sign of the rotation, was identical to the data obtained for amino diol (−)-**16** which was derived from a tandem sequence using MAPh as the Lewis acid in the [4 + 2] cycloaddition. Data for (+)-**16**: ^{1}H NMR (499.7 MHz, CD_3OD) δ 3.72−3.64 (m, 3 H), 3.40 (dd, J = 10.1, 5.0, 1 H), 2.23−2.17 (m, 1 H), 1.97−1.85 (m, 3 H), 1.77−1.74 (m, 2 H), 1.68−1.47 (m, 6 H), 1.38−1.11 (m, 8 H); ^{13}C NMR (125.7 MHz, CD_3OD) δ 67.46, 65.66, 61.75, 58.70, 50.24, 39.34, 38.45, 33.72, 29.46, 28.92, 27.19, 26.51, 26.47, 19.37; IR (KBr) 3318, 3271, 3264, 3257, 2956, 2922, 2898, 1040, 1036, 1013; MS (FAB) 236 (M^+ + 1, 100); TLC R_f 0.57 ($CHCl_3$/CH_3OH/NH_4OH, 10/5/1); optical rotation $[\alpha]^{22}_D$ = 27.1° (c = 1.0, CH_3OH); HRMS (FAB) Calcd for $C_{14}H_{28}NO_2$, 242.21200; Found, 242.21210.

[(1*R*,3*S*,4*R*,5*S*)-4-Acetylamino-5-cyclohexyl-4-methyl]-1,3-cyclopentanedimethanol Diacetate ((+)-17). According to general procedure V, amino diol (+)-**16** (71 mg, 0.294 mmol) was dissolved in pyridine (4 mL) and acetic anhydride (4 mL) and was left to stir at room temperature for 1.5 h. Purification by silica gel column chromatography (Et_2O) provided 87 mg (80%) of analytically pure triacetate (+)-**17** as a clear oil. The enantiomeric excess was determined to be 95% by chiral HPLC. The analytical data for (+)-**17**, except for the sign of the rotation, were identical to the data obtained for triacetate (−)-**17** which was derived from a tandem sequence using MAPh as the Lewis acid in the [4 + 2] cycloaddition. Data for (−)-**17**: ^{1}H NMR (499.7 MHz, $CDCl_3$) δ 5.63 (s, 1 H), 4.13 (dd, J = 10.1, 4.8, 1 H), 4.10 (dd, J = 11.3, 4.1, 1 H), 4.03 (dd, J = 11.3, 6.8, 1 H), 3.85 (dd, J = 10.6, 8.6, 1 H), 2.39−2.34 (m, 1 H), 2.26−2.18 (m, 1 H), 2.07 (s, 3 H) 2.05 (s, 3 H), 2.04−1.98 (m, 1 H), 1.92 (s, 3 H), 1.79 (dd, J = 7,7, 4.2, 1 H), 1.75−1.72 (m, 2 H), 1.66−1.64 (m, 3 H), 1.60−1.54 (m, 1 H), 1.51−1.46 (m, 1 H) 1.43 (s, 3 H), 1.34−1.20 (m, 2 H), 1.16−1.01 (m, 3 H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 171.17, 170.90, 169.43, 69.13, 65.05, 64.48, 54.07, 46.47, 37.88, 36.36, 33.89, 30.25, 30.05, 26.86, 26.42, 26.23, 24.49, 20.99, 20.96, 20.20; TLC R_f 0.36 (EtOAc/hexane, 2/1); optical rotation $[\alpha]^{23}_D$ = 25.3° (c = 0.80, $CHCl_3$); chiral HPLC (Chiralcel OJ, (hexane/*i*-PrOH, 95/5), 0.4 mL/min); t_R (−)-**17** 42.19 min (2.2%), t_R (+)-**17** 63.40 min (97.8%), 95% ee.

[(1*R*,3*S*,4*R*,5*S*)-4-Acetylamino-5-cyclohexyl-4-methyl]-1,3-cyclopentanedimethanol Diacetate ((+)-17). According to general procedure IV, nickel chloride (20 mg, 0.155 mmol, 1.2 equiv) was added to a solution of nitroso acetal **15c** (53 mg, 0.129 mmol) in ethanol (4 mL). $NaBH_4$ (29 mg, 1.54 mmol, 6 equiv) was added to the suspension, and after 15 min, $NaBH_4$ (29 mg, 1.54 mmol, 6 equiv) was added. After 1 h, the ethanol was removed in vacuo providing a black solid. Purification by silica gel column chromatography ($CHCl_3$/MeOH, 10/1 (100 mL) then $CHCl_3$/MeOH/NH_4OH, 10/5/1) afforded 17 mg (53% yield) of amino diol (+)-**16** as a white foam and 16 mg (72%) of recovered (−)-(1*R*,2*S*)-phenylcyclohexanol ((−)-**4**).

According to general procedure V, amino diol (+)-**16** (17 mg, 0.069 mmol) was dissolved in pyridine (2.0 mL) and acetic anhydride (2.0 mL) and was left to stir at room temperature for 2.0 h. Purification by silica gel column chromatography (Et_2O) provided 20 mg (79%) of analytically pure triacetate (+)-**17** as a clear oil. The analytical data for (+)-**17**, except for the sign of the rotation, were identical to the data obtained for triacetate (−)-**17** which was derived from a tandem sequence using MAPh as the Lewis acid in the [4 + 2] cycloaddition. Data for (+)-**17**: ^{1}H NMR (499.7 MHz, $CDCl_3$) δ 5.64 (s, 1 H), 4.13 (dd, J = 10.1, 4.8, 1 H), 4.10 (dd, J = 11.3, 4.1, 1 H), 4.03 (dd, J = 11.3, 6.8, 1 H), 3.85 (dd, J = 10.6, 8.6, 1 H), 2.39−2.33 (m, 1 H), 2.26−2.18 (m, 1 H), 2.06 (s, 3 H), 2.05 (s, 3 H) 2.02−1.98 (m, 1 H), 1.92 (s, 3 H), 1.80−1.78 (m, 1 H), 1.74−1.72 (m, 2 H), 1.66−1.63 (m, 3 H), 1.59−1.53 (m, 1 H), 1.51−1.45 (m, 1 H) 1.43 (s, 3 H), 1.33−1.19 (m, 2 H), 1.15−1.01 (m, 3 H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 171.17, 170.90, 169.43, 69.13, 65.05, 64.49, 54.08, 46.47, 37.88, 36.36, 33.89, 30.25, 30.05, 26.85, 26.42, 26.22, 24.48, 20.99, 20.96, 20.19; IR ($CHCl_3$) 1732, 1265, 1243; MS (FAB) 368 (M^+ + 1, 100); TLC R_f 0.36 (EtOAc/hexane, 2/1); optical rotation $[\alpha]^{22}_D$ = 23.4° (c = 0.83, $CHCl_3$). Anal. Calcd for $C_{20}H_{33}NO_5$ (367.49): C, 65.37; H, 9.05; N, 3.81. Found: C, 65.11; H, 9.25; N, 3.61.

(1*R*,6*S*,7*S*,8*R*,9*S*)-8-Cyclohexyl-9-methyl-6-[(1*R*,2*S*)-(2-phenylcyclohexyl)oxy]-4-aza-3,5-dioxatricyclo[5.2.1.0^{4,9}]-decane (15b). According to general procedure III, a 7:1 mixture of nitronates **14b** and **14a** (353 mg, 0.858 mmol) was added to a suspension of sodium bicarbonate (216 mg, 2.57 mmol, 3 equiv) in benzene (85 mL) and the mixture was heated to reflux for 2 h. Purification by column chromatography on basic (III) alumina (hexane/Et_2O, 7/1) afforded 280 mg of analytically pure nitroso acetal **15b** (determined to be a >25:1 (**15b**/**15a**) mixture by ^{1}H NMR integration) as a clear viscous oil along with 43 mg of nitroso acetal **15a** as a clear glass for a combined yield of 91%: ^{1}H NMR (499.7 MHz, C_6D_6) δ 7.20−7.15 (m, 3 H), 7.09−7.06 (m, 2 H) 4.97 (d, J = 2.7, 0.05 H), 4.27 (d, J = 2.9, 0.95 H), 4.03−3.98 (m, 2 H). 3.67 (td, J = 10.5, 4.4, 1 H), 2.67−2.64 (m, 1 H), 2.57 (d, J = 5.4, 1 H), 2.53−2.48 (m, 1 H), 1.83−1.70 (m, 1 H), 1.70−1.53 (m, 8 H) 1.5−1.43 (m, 2 H), 1.36 (dq, J = 12.9, 3.4, 1 H), 1.26−0.92 (m, 11 H), 0.85−0.82 (m, 1 H), 0.67 (dq, J = 11.9, 3.2, 1 H); ^{13}C NMR (125.6 MHz, C_6D_6) δ 145.33, 128.39, 128.24, 126.26, 107.47, 87.10, 81.79, 79.18, 51.94, 45.50, 45.21, 40.84, 37.03, 36.26, 35.20, 33.72, 33.41, 29.97, 26.97, 26.85, 26.66, 26.21, 25.41, 19.43; IR ($CHCl_3$) 2932; MS (FAB) 412 (M^+ + 1, 65), 159 (100); TLC R_f 0.48 (hexane/EtOAc, 3/1); optical rotation $[\alpha]^{23}_D$ = 1.0° (c = 1.0, $CHCl_3$). Anal. Calcd for $C_{26}H_{37}NO_3$ (411.59): C, 75.87; H, 9.06; N, 3.40. Found: C, 75.96; H, 9.28; N, 3.12.

[(1*S*,3*R*,4*S*,5*R*)-4-Amino-5-cyclohexyl-4-methyl]-1,3-cyclopentanedimethanol ((−)-16). According to general procedure IV, nickel chloride (93 mg, 0.714 mmol, 1.2 equiv) was added to a solution of nitroso acetal **15b** (245 mg, 0.595 mmol) in ethanol (11 mL). $NaBH_4$ (68 mg, 1.79 mmol, 3 equiv) was added to the suspension, and after 15 min, $NaBH_4$ (68 mg, 1.79 mmol, 3 equiv) was added. After 40 min, the ethanol was removed in vacuo providing a black solid. Purification by silica gel column chromatography ($CHCl_3$/MeOH, 10/1 (100 mL), then $CHCl_3$/MeOH/NH_4OH, 10/5/1) afforded 138 mg (96% yield) of amino diol (−)-**16** as a white foam and 0.101 g (98%) of recovered (−)-(1*R*,2*S*)-phenylcyclohexanol ((−)-**4**). The analytical data for (−)-**16**, except for the sign of the rotation, were identical to the data obtained for amino diol (+)-**16** which was derived from a tandem sequence using $SnCl_4$ as the Lewis acid in the [4 + 2] cycloaddition. Data for (−)-**16**: ^{1}H NMR (499.7 MHz, CD_3OD) δ 3.85 (dd, J = 11.5, 3.5, 1 H), 3.73 (dd, J = 11.6, 3.9, 1 H), 3.66 (dd, J = 9.9, 2.4, 1 H), 3.46 (dd, J = 9.9, 3.1, 1 H), 2.38−2.37 (m, 1 H), 2.03−1.93 (m, 2 H), 1.88−1.65 (m, 6 H), 1.58−1.46 (m, 5 H), 1.42−1.11 (m, 5 H); ^{13}C NMR (125.7 MHz, CD_3OD) δ 65.90, 64.14, 59.52, 56.96, 48.36, 38.34, 38.12, 32.74, 28.23, 27.29, 26.92, 26.26, 26.17, 18.37; TLC R_f 0.57 ($CHCl_3$/CH_3OH/NH_4OH, 10/5/1); optical rotation $[\alpha]^{25}_D$ = −31.2° (c = 0.96, CH_3OH).

[(1*S*,3*R*,4*S*,5*R*)-4-Acetylamino-5-cyclohexyl-4-methyl]-1,3-cyclopentanedimethanol Diacetate ((−)-17). According to general procedure V, amino diol (−)-**16** (25 mg, 0.106 mmol) was dissolved in pyridine (1.5 mL) and acetic anhydride (1.5 mL) and was left to stir at room temperature for 1.5 h. Purification by silica gel column chromatography (Et_2O) provided 29 mg (77%) of analytically pure triacetate (−)-**17** as a clear oil. The enantiomeric excess was determined to be 95% by chiral HPLC. The analytical data for (−)-**17**, except for the sign of the rotation, were identical to the data obtained for triacetate (+)-**17** which was derived from a tandem sequence using $SnCl_4$ as the Lewis acid in the [4 + 2] cycloaddition. Data for (−)-**17**: ^{1}H NMR (499.7 MHz, $CDCl_3$) δ 5.64 (s, 1 H), 4.13 (dd, J = 10.1, 4.8, 1 H), 4.10 (dd, J = 11.3, 4.1, 1 H), 4.03 (dd, J = 11.3, 6.8, 1 H), 3.85 (dd, J = 10.6, 8.6,

1 H), 2.39−2.34 (m, 1 H), 2.25−2.19 (m, 1 H), 2.07 (s, 3 H), 2.05−2.00 (m, 4 H), 1.93 (s, 3 H), 1.81−1.78 (m, 1 H), 1.75−1.73 (m, 2 H), 1.66−1.54 (m, 4 H), 1.51−1.44 (m, 4 H), 1.34−1.20 (m, 2 H), 1.16−1.02 (m, 3 H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 171.18, 170.90, 169.43, 69.14, 65.06, 64.49, 54.08, 46.47, 37.89, 36.36, 33.90, 30.25, 30.05, 26.86, 26.43, 26.23, 24.49, 21.00, 20.96, 20.20; TLC R_f 0.36 (EtOAc/hexane, 2/1); optical rotation $[\alpha]^{22}_D = -23.7°$ ($c = 0.9$, $CHCl_3$); chiral HPLC (Chiralcel OJ, (hexane/*i*-PrOH, 95/5), 0.4 mL/min); t_R (−)-**17** 42.19 min (97.6%); t_R (+)-**17** 63.40 min (2.4%), 95% ee. Anal. Calcd for $C_{20}H_{33}NO_5$ (367.49): C, 65.37; H, 9.05; N, 3.81. Found: C, 65.68; H, 9.27; N, 3.86.

(4*S*,5*S*,6*S*)-4-Phenyl-5-(2-propenyl)-6-[(1*R*,2*S*)-(2-phenylcyclohexyl)oxy]-5,6-dihydro-4*H*-[1,2]-oxazine 2-Oxide (20a). According to general procedure II, a solution of MAPh (2.4 mmol, 2.0 equiv) was transferred, via cannula, to a second reaction vessel containing a −78 °C solution of nitroalkene **18** (179 mg, 1.2 mmol) and vinyl ether (−)-**6** (436 mg, 1.8 mmol, 1.5 equiv) in CH_2Cl_2 (3 mL). The resulting dark brown solution was allowed to warm slowly to −50 °C over 1 h and then was left to stir at −50 °C for 2 h (the color faded to a light brown), after which time the reaction was quenched with H_2O (6 mL). After an aqueous extraction, the crude material was purified by silica gel column chromatography (hexane/EtOAc, 7/1 (800 mL), 6/1) to afford 432 mg (92% yield) of a mixture of nitronates **20a** and **20b** and nitroso acetal **22**. Data for **20a**: ^{1}H NMR (499.7 MHz, C_6D_6) δ 7.11−6.99 (m, 6 H), 6.95−6.94 (m, 2 H), 6.63−6.61 (m, 2 H), 6.00−5.99 (m, 1 H), 4.90−4.82 (m, 1 H), 4.73−4.68 (m, 2 H), 4.60 (s, 1 H), 4.12 (dd, $J = 6.4$, 3.1, 1 H), 3.73−3.69 (m, 1 H) 2.72−2.69 (m, 1 H), 2.56−2.49 (m, 1 H), 1.72−0.84 (m, 10 H); TLC R_f 0.29 (hexane/EtOAc, 3/1)

(1*R*,6*S*,7*S*,8*S*,9*S*)-8-Phenyl-6-[(1*R*,2*S*)-(2-phenylcyclohexyl)oxy]-4-aza-3,5-dioxatricyclo[5.2.1.0^{4,9}]decane (22a). According to general procedure III, nitronate **20a** (403 mg, 1.10 mmol) was added to a suspension of sodium bicarbonate (277 mg, 3.3 mmol, 3 equiv) in benzene (60 mL) and the mixture was heated to reflux for 1 h. Purification by column chromatography on neutral alumina (III) (hexane/Et_2O 5/1) provided 373 mg (87%) of nitroso acetal **22a** as a 25:1 (**22a**/**22b**) mixture as determined by ^{1}H NMR integration. An analytical sample of **22a** was obtained by recrystallization (Et_2O): mp 112−115 °C (Et_2O); ^{1}H NMR (499.7 MHz, C_6D_6) δ 7.18−7.14 (m, 4 H), 7.09−7.00 (m, 4 H), 6.81−6.80 (m, 2 H) 5.00 (m, 0.02 H), 4.31 (s, 1 H), 4.29 (dd, $J = 2.6$, 1.8, 0.98 H), 3.98−3.92 (m, 2 H), 3.84 (d, $J = 6.0$, 1 H), 3.75 (td, $J = 10.4$, 4.4, 1 H), 2.73−2.69 (m, 1 H), 2.53 (ddd, $J = 12.8$, 10.4, 3.7, 1 H), 1.73−1.55 (m, 3 H), 1.50−1.48 (m, 1 H) 1.42−1.34 (m, 2 H), 1.29−1.20 (m, 1 H), 1.13−1.05 (m, 1 H), 0.76 (dd, $J = 3.7$, 2.2, 1 H); ^{13}C NMR (125.6 MHz, C_6D_6) δ 145.22, 140.53, 128.65, 128.34, 126.54, 126.47, 126.38, 106.08, 81.91, 81.39, 79.05, 51.89, 44.15, 40.50, 39.39, 35.11, 33.35, 32.91, 26.16, 25.40; IR ($CHCl_3$) 2936, 1093, 1083; MS (FAB) 392 ($M^+ + 1$, 29), 159 (100); TLC R_f 0.31 (hexane/EtOAc, 4/1); optical rotation $[\alpha]^{24}_D = -15.75°$ ($c = 1.3$, $CHCl_3$). Anal. Calcd for $C_{25}H_{29}NO_3$ (391.5): C, 76.70; H, 7.47; N, 3.58. Found: C, 76.64; H, 7.71; N, 3.41.

[(1*S*,3*R*,4*S*,5*S*)-4-(Acetylamino)-5-phenyl]-1,3-cyclopentanedimethanol Diacetate (24). According to general procedure IV, $NaBH_4$ (55 mg, 1.44 mmol, 2 equiv) was added to a solution of anhydrous nickel chloride (103 mg, 0.79 mmol, 1.1 equiv) in methanol (11 mL). A black precipitate formed almost immediately with the concomitant evolution of hydrogen. The nickel boride was then cooled to 0 °C, and $NaBH_4$ (55 mg, 1.44 mmol, 2 equiv) was added followed by the addition of a solution of nitroso acetals **22a/b** (282 mg, 0.72 mmol) in methanol (2 mL) and ethanol (1 mL). After approximately 10 min, $NaBH_4$ (55 mg, 1.44 mmol, 2 equiv) was added. After ca. 30 min, the methanol was removed in vacuo to provide a black solid. Purification by silica gel column chromatography ($CHCl_3$/MeOH, 10/1 (200 mL), then $CHCl_3$/MeOH/NH_4OH, 10/5/1) afforded 130 mg (82%) of amino diol **24** as a 2.8/1 ratio of **24a**/**24b** (determined by ^{1}NMR integration) and 120 mg (97% yield) of recovered (−)-(1*R*,2*S*)-phenylcyclohexanol ((−)-**4**).

According to general procedure V, amino diols **24a** and **24b** (221 mg, 0.0.565 mmol) were dissolved in pyridine (3 mL) and acetic anhydride (3 mL) and left to stir at room temperature for 1.5 h. Purification by silica gel column chromatography (EtOAc/hexanes, 2/1) provided 54 mg of analytically pure triacetate **26** as a 9.5/1 (**26a**/**26b**) mixture of epimers and 35 mg of a 1.4:1 (**26a**/**26b**) mixture of epimers for a combined yield of 59%. Data for **26b**: ^{1}H NMR (499.7 MHz, CD_3OD) δ 7.36−7.22 (m, 5 H), 3.76−3.69 (m, 1 H), 3.63−3.56 (m, 2 H), 3.49 (dd, $J = 10.8$, 3.5, 1 H), 3.38−3.10 (m, 1 H), 2.69−2.63 (m, 1 H), 2.51−2.46 (m, 1 H), 2.24−2.10 (m, 2 H), 1.55−1.49 (m, 0.74 H), 1.36−1.30 (m, 0.26 H). Data for (−)-**26a**: ^{1}H NMR (499.7 MHz, $CDCl_3$) δ 7.32−7.29 (m, 2 H), 7.25−7.22 (m, 1 H), 7.18−7.16 (m, 2 H), 5.47 (d, $J = 8.1$, 0.90 H), 4.88 (d, $J = 9.0$ 0.10 H), 4.58 (dt, $J = 11.0$, 8.5, 0.90 H), 4.38 (q, $J = 9.2$, 0.10 H), 4.16 (dd, $J = 11.2$, 5.6, 1 H), 4.06−4.02 (m, 2 H), 3.91 (dd, $J = 11.0$, 6.1, 1 H), 2.83−2.76 (m, 1 H), 2.61 (t, $J = 11.0$, 1 H), 2.38−2.30 (m, 1 H), 2.28−2.22 (m, 1 H), 2.11 (s, 3 H), 1.88 (s, 3 H), 1.85 (s, 3 H), 1.43 (ddd, $J = 13.4$, 9.5, 6.6, 1 H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 171.17, 171.00, 170.06, 139.59, 128.85), 127.58, 127.31, 65.85, 64.79, 57.69, 53.69, 43.11, 37.38, 30.21, 23.11, 21.09, 20.63; IR ($CHCl_3$) 1736, 1246; MS (FAB) 348 ($M^+ + 1$, 100); TLC R_f 0.22 (EtOAc/hexane, 2/1); optical rotation $[\alpha]^{21}_D = -28.7°$ ($c = 0.6$, $CHCl_3$); chiral HPLC (Chiralcel OJ, (hexane/EtOH, 78/22), 0.7 mL/min.); t_R (−)-**26a** 6.32 min (97.3%), t_R (+)-**26a** 8.71 min (2.7%), 94.6% ee. Anal. Calcd for $C_{19}H_{25}NO_5$ (347.42): C, 65.69; H, 7.25; N, 4.03. Found: C, 65.46; H, 7.25; N, 3.98.

(4*R*,5*R*,6*S*)-4-Benzoyloxy-5-(2-propenyl)-6-[(1*R*,2*S*)-(2-phenylcyclohexyl)oxy]-5,6-dihydro-4*H*-[1,2]-oxazine 2-Oxide (21). According to general procedure II, a solution of MAPh (2.6 mmol, 2.0 equiv) was transferred, via cannula, to a second reaction vessel containing a −78 °C solution of nitroalkene **19** (250 mg, 1.3 mmol) and vinyl ether (−)-**6** (469 mg, 1.9 mmol, 1.5 equiv) in toluene (6 mL). The resulting dark brown solution was left to stir at −78 °C for 2 h (the color faded to a light brown), after which time the reaction was quenched with H_2O (8 mL). After an aqueous extraction, the crude material was purified by silica gel column chromatography (hexane/EtOAc, 9/1 (1000 mL), 8/1) to afford 384 mg (68% yield) of a mixture of nitronates **21** and nitroso acetal **23**. Diasteremomeric ratios for the nitronates could not be determined for this reaction. Data for **21**: ^{1}H NMR (499.7 MHz, C_6D_6) δ 7.96−7.91 (m, 2 H), 7.14−6.88 (m, 2 H), 6.09 (d, $J = 3.8$, 1 H),5.47−5.45 (m, 1 H), 5.17−5.09 (m, 1 H), 4.76−4.69 (m, 2 H), 4.60 (d, $J = 4.8$, 1 H), 3.57 (td, $J = 11.8$, 4.6, 1 H), 2.46−2.44 (m, 1 H) 2.39−2.33 (m, 1 H), 1.83−1.75 (m, 2 H), 1.70−1.57 (m, 2 H), 1.48−1.41 (m, 2 H), 1.27−0.94 (m, 3 H); TLC R_f 0.29 (hexane/EtOAc, 3/1).

[(1*R*,3*R*,4*R*,5*R*)-4-Amino-5-benzoyloxy]-1,3-cyclopentanedimethanol ((+)-25a). According to general procedure III, to a solution of nitronates **21** (0.383 g, 0.88 mmol) in acetonitrile (50 mL) and benzene (40 mL) was added sodium bicarbonate (0.222 g, 2.64 mmol, 3 equiv). The suspension was heated to reflux for 30 min and was left to stir for 10 h at room temperature. Concentration afforded a yellow foam which was subjected to hydrogenolysis without purification.

According to general procedure IV, $NaBH_4$ (66 mg, 1.76 mmol, 2 equiv) was added to a solution of anhydrous nickel chloride (114 mg, 0.88 mmol, 1 equiv) in methanol (12 mL) at room temperature. A black precipitate formed almost immediately with the concomitant evolution of hydrogen. The nickel boride was then cooled to 0 °C, and another 2 equiv of $NaBH_4$ (66 mg, 1.76 mmol, 2 equiv) was added followed by the addition of a solution of nitroso acetals **23** (0.880 mmol) in methanol (6 mL). After ca. 10 min, the last 2 equiv of $NaBH_4$ (66 mg, 1.76 mmol, 2 equiv) was added. After approximately 30 min, the methanol was removed in vacuo to provide a black solid. The crude organic concentrate was purified by silica gel column chromatography ($CHCl_3$/MeOH, 10/1 (200 mL), then $CHCl_3$/MeOH/NH_4OH, 10/5/1) to afford 141 mg (61% yield over two steps) of amino diol (+)-**25a** as a clear oil and 113 mg (75% yield) of recovered (−)-(1*R*,2*S*)-phenylcyclohexanol ((−)-**4**). Data for (+)-**23a**: ^{1}H NMR (499.7 MHz, C_6D_6) δ 7.96−7.94 (m, 2 H), 7.19−7.01 (m, 5 H), 7.12−7.02 (m, 3 H), 6.28 (s, 1 H), 4.18 (dd, $J = 3.1$, 1.3, 1 H), 3.92−3.91 (m, 2 H), 3.75 (dd, $J = 6.0$, 1.3, 1 H), 3.63 (ddd, $J = 10.6$, 10.4, 4.4, 1 H), 2.60−2.57

(m, 1 H), 2.48−2.43 (m, 1 H), 2.14−2.13 (m, 2 H), 1.68−1.44 (m, 6 H), 1.39−1.30 (m, 1 H) 1.20−1.14 (m, 1 H), 1.20−1.02 (m, 1 H), 0.77 (dd, J = 13.5, 2.4, 1 H); ^{13}C NMR (125.7 MHz, C_6D_6) δ 164.86, 145.05, 133.03, 129.83, 128.86, 128.48, 128.41, 128.31, 126.37, 110.32, 104.97, 100.19, 81.71, 80.48, 78.97, 72.40, 51.41, 43.22, 39.19, 34.83, 32.90, 32.32, 25.99, 25.35. Data for (+)-**25a**: ^{1}H NMR (499.7 MHz, CD_3OD) δ 8.06−8.04 (m, 2 H), 7.65−7.61 (m, 1 H) 7.51−7.48 (m, 2 H), 5.16−5.13 (m, 1 H), 3.81−3.65 (m, 5 H), 2.61−2.53 (m, 1 H), 2.47−2.40 (m, 1 H), 210−2.04 (m, 1 H), 1.70−1.63 (m, 1 H, H); ^{13}C NMR (125.7 MHz, CD_3OD) δ 168.11, 134.63, 131.02, 130.74, 129.68, 82.56, 63.07, 61.82, 59.36, 46.74, 42.27, 28.12; MS (FAB) 266 (M^+ + 1, 100); TLC R_f 0.16 ($CHCl_3$/CH_3OH/NH_4-OH, 10/5/1); optical rotation $[\alpha]^{27}_D$ = 25.3° (c = 1.02, CH_3OH); HRMS (FAB) Calcd for $C_{14}H_{19}NO_4$, 266.139233; Found, 266.139200.

[(1*R*,3*R*,4*R*,5*R*)-4-(Acetylamino)-5-benzoyloxy]-1,3-cyclopentanedimethanol Diacetate ((−)-27a). According to the general procedure, the amino diol (+)-**25a** (118 mg, 0.44 mmol) was dissolved in pyridine (5 mL) and acetic anhydride (5 mL) and was left to stir at room temperature for 1 h. Purification by silica gel column chromatography (EtOAC/hexane 2/1) provided 118 mg (68%) of analytically pure triacetate (−)-**27a** as clear oil: ^{1}H NMR (499.7 MHz, CD_3OD) δ 7.99 (d, J = 7.1, 2 H), 7.56 (dd, J = 7.5, 7.3, 1H) 4.42 (dd, J = 7.9, 7.7, 2 H), 6.5 (d, J = 6.8, 1 H), 5.22 (dd, J = 9.0, 8.8, 1 H), 4.45 (q, J = 8.8, 1 H) 5.16 (*A*B*X*, J_{ab} = 11.1, J_{ax} = 5.9, 1 H), 5.13 (A*B*X, J_{bx} = 5.6, 1 H), 4.04 (*A*BX, J_{ab} = 12.5, J_{ax} = 6.9, 1 H), 4.02 (A*B*X, J_{bx} = 7.2, 1 H), 2.79−2.72 (m, 1 H), 2.56−2.48 (m, 1 H), 2.24−2.18 (m, 1 H), 2.10 (s, 3 H), 1.92 (s, 3 H), 1.90 (s, 3 H),1.45−1.39 (m, 1 H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 170.83, 170.71, 170.42, 167.08, 133.44, 129.68, 129.28, 128.43, 78.69, 64.99, 64.12, 56.87, 39.90, 35.79, 26.94, 23.04, 21.03, 20.65; IR ($CHCl_3$) 1737, 1733, 1276, 1245; MS (FAB) 392 (M^+ + 1, 100); TLC R_f 0.10 (EtOAc/hexane, 2/1); optical rotation $[\alpha]^{22}_D$ = −12.8° (c = 0.68, $CHCl_3$); chiral HPLC (Chiralcel OD, (hexane/EtOH, 97/3), 1 mL/min); t_R (−)-**27a** 34.29 min (99.3%), t_R (+)-**27a** 43.47 min (0.7%), >98% ee. Anal. Calcd for $C_{20}H_{25}NO_7$ (391.42): C, 61.37; H, 6.44; N, 3.58 Found: C, 61.41 H, 6.32; N, 3.61.

(4*R*,5*S*,6*R*)-3-Methyl-4-phenyl-5-(2-propenyl)-6-[(1*R*,2*S*)-(2-phenylcyclohexyl)oxy]-5,6-dihydro-4*H*-[1,2]-oxazine 2-Oxide (9d). According to general procedure I, tin tetrachloride (0.175 mL, 1.5 mmol, 1 equiv) was added to a −78 °C solution of nitroalkene **8** (245 mg, 1.5 mmol) in CH_2Cl_2 (28 mL), and the resulting bright yellow complex was left to stir for 15 min. A solution of vinyl ether (−)-**7** (485 mg, 2.00 mmol, 1.33 equiv) in CH_2Cl_2 (2 mL) was added rapidly to the cold reaction mixture via syringe. The reaction was left to stir at −78 °C for an additional 5 min and was then quenched with 1 N NaOH/MeOH (6 mL). After an aqueous extraction, the crude organic concentrate was purified by silica gel column chromatography (hexane/EtOAc, 7/1 (800 mL), 6/1 (700 mL), 4/1) to afford 519 mg of **9d** and 0.047 g of nitronate **9e**. The overall yield of the reaction was 0.566 g (93%) and diastereofacial selectivity 11/1 (**9d**/**9e**). An analytical sample of **9d** was obtained after recrystallization (hexane). Nitronate **9e** was found to be identical by ^{1}H NMR to the nitronate **9e** obtained from a MAPh-promoted [4 + 2] cycloaddition. Additionally, nitronate **9d** was found to be identical to **9d** derived from the $SnCl_4$-promoted [4 + 2] cycloaddition of **8** with trans vinyl ether (−)-**6**. Data for **9d**: 102−103 °C (hexane); ^{1}H NMR (499.7 MHz, C_6D_6) δ 7.34−7.29 (m, 4 H), 7.04−7.01 (m, 1 H), 6.95−6.94 (m, 3 H) 6.59−6.57 (m, 2 H), 5.33 (d, J = 1.5, 1 H), 5.29−5.21 (m, 1 H), 4.86 (dd, J = 19.2, 10.8, 2 H), 4.29 (td, J = 10.3, 3.9, 1 H), 2.76 (d, J = 9.0, 1 H), 2.52 (td, J = 13.1, 3.5, 1 H), 2.11−2.09 (m, 1 H), 1.92−1.81 (m, 3 H), 1.72−1.70 (m, 1 H), 1.55−1.54 (m, 1 H) 1.46−1.44 (m, 1 H), 1.36−1.28 (m, 4 H), 1.11−0.97 (m, 3 H); ^{13}C NMR (125.6 MHz, C_6D_6) δ 144.62, 140.21, 134.90, 129.00, 128.81, 128.62, 128.04, 127.49, 126.21, 118.79, 117.46, 96.08, 75.62, 51.38, 46.63, 42.13, 34.81, 33.38, 30.37, 26.28, 24.52, 17.46; TLC R_f 0.30 (hexane/EtOAc, 2/1); optical rotation $[\alpha]^{23}_D$ = −306.9° (c = 1.03, $CHCl_3$). Anal. Calcd for $C_{26}H_{31}NO_3$ (405.53): C, 77.01; H, 7.71; N, 3.45. Found: C, 77.04; H, 7.52; N, 3.56.

(4*S*,5*R*,6*S*)-3-Methyl-4-phenyl-5-(2-propenyl)-6-[(1*R*,2*S*)-(2-phenylcyclohexyl)oxy]-5,6-dihydro-4*H*-[1,2]-oxazine 2-Oxide (9e). According to general procedure II, a solution of MAPh (3.0 mmol, 2.0 equiv) was transferred, via cannula, to a second reaction vessel containing a −78 °C solution of nitroalkene **8** (0.245 g, 1.5 mmol) and vinyl ether (−)-**7** (545 mg, 2.25 mmol, 1.5 equiv) in CH_2Cl_2 (5 mL). The resulting dark, red-brown solution was allowed to warm slowly to −35 °C over 30 min and was then left to stir at −35 °C for 6 h (the color faded to a light brown), after which time the reaction was quenched with H_2O (8 mL). After an aqueous workup, the crude material was purified by silica gel column chromatography (hexane/EtOAc, 8/1 (900 mL), 5/1 (600 mL), 3/1) to afford 376 mg of nitronate **9e** and 47 mg of diastereomer **9d** for a combined yield of 423 mg (70%). The diastereofacial selectivity of the reaction was established to be 8/1 (**9e**/**9d**). An analytical sample of **9e** obtained after a second silica gel column chromatography (hexane/EtOAc, 4/1). Nitronate **9d** was found to be identical by ^{1}H NMR to the nitronate obtained from the $SnCl_4$-promoted [4 + 2] cycloaddition of **8** with vinyl ethers (−)-**6** and (−)-**7**. Data for **9e**: 127−128 °C (hexane); ^{1}H NMR (499.7 MHz, C_6D_6) δ 7.12−7.11 (m, 2 H), 7.06−7.01 (m, 3 H), 6.95−6.93 (m, 3 H), 6.69−6.67 (m, 2 H), 4.89 (d, J = 2.7, 1 H), 4.81−4.72 (m, 1 H), 4.60 (d, J = 10.0, 1 H), 4.42 (dd, J = 17.1, 1.0, 1 H), 3.78 (td, J = 10.6, 4.1, 1 H), 3.18 (d, J = 11.0, 1 H), 2.82−2.79 (m, 1 H), 2.54−2.49 (m, 1 H), 1.85−1.78 (m, 1 H), 1.71−1.38 (m, 9 H), 1.32−1.22 (m, 3 H) 1.09−1.00 (m, 1 H); ^{13}C NMR (125.6 MHz, C_6D_6) δ 144.95, 140.21, 135.16, 129.04, 128.86, 128.73, 128.13, 127.53, 126.62, 119.55, 116.40, 103.06, 82.67, 51.79, 47.20, 44.02, 34.63, 32.70, 26.01, 25.21, 17.51; IR ($CHCl_3$) 2938, 1619, 1232, 895; MS (FAB) 406 (M^+ + 1, 100); TLC R_f 0.39 (hexane/EtOAc, 2/1); optical rotation $[\alpha]^{23}_D$ = 90.09° (c = 1.05, $CHCl_3$). Anal. Calcd for $C_{26}H_{31}NO_3$ (405.53): C, 77.01; H, 7.71; N, 3.45. Found: C, 76.75; H, 7.74; N, 3.32.

(1*R*,6*R*,7*S*,8*R*,9*S*)-9-Methyl-8-phenyl-6-[(1*R*,2*S*)-(2-phenylcyclohexyl)oxy]-4-aza-3,5-dioxatricyclo[5.2.1.0^{4,9}]-decane (10d). According to general procedure III, nitronate **9d** (418 mg, 1.03 mmol) was added to a suspension of sodium bicarbonate (609 mg, 7.25 mmol, 7 equiv) in toluene (100 mL) and the mixture was heated to reflux for 9 h. Purification by column chromatography basic alumina (III) (hexane/Et_2O, 6/1) afforded 390 mg (93% yield) of analytically pure nitroso acetal **10d** as a white solid: 185 °C: ^{1}H NMR (499.7 MHz, C_6D_6) δ 7.67 (d, J = 7.3, 2 H), 7.31−7.25 (m, 4 H), 7.23−7.20 (m, 2 H), 7.15−7.07 (m, 2 H) 5.07 (d, J = 5.1, 1 H), 3.97 (td, J = 10.4, 4.0, 1 H), 3.69 (dd, J = 9.2, 7.9, 1 H), 2.81 (dd, J = 7.9, 4.6, 1 H), 2.70 (d, J = 4.6, 1 H), 2.46−2.41 (m, 1 H), 2.24 (q, J = 5.0, 1 H), 1.89 (td, J = 9.5, 4.6, 1 H), 1.76−1.64 (m, 3 H) 1.37−1.18 (m, 4 H), 1.15 (s, 3 H), 1.00−0.72 (m, 3 H); ^{13}C NMR (125.6 MHz, C_6D_6) δ 145.36, 137.11, 130.42, 128.54, 128.50, 128.48, 126.83, 126.22, 95.58, 79.96, 76.49, 76.15, 53.33, 51.48, 49.17, 45.89, 34.78, 30.46, 29.98, 26.23, 24.64, 21.97; IR ($CHCl_3$) 2934, 1079; MS (FAB) 406 (M^+ + 1, 100); TLC R_f 0.58 (hexane/EtOAc, 2/1); optical rotation $[\alpha]^{23}_D$ = −109.4° (c = 1.04, $CHCl_3$). Anal. Calcd for $C_{26}H_{31}NO_3$ (405.53): C, 77.01; H, 7.71; N, 3.45. Found: C, 77.24; H, 7.77; N, 3.26.

[(1*S*,3*R*,4*S*,5*R*)-4-Amino-4-methyl-5-phenyl]-1,3-cyclopentanedimethanol ((−)-11b). According to general procedure IV, nickel chloride (123 mg, 0.95 mmol, 1.1 equiv) was added to a solution of nitroso acetal **10e** (350 mg, 0.86 mmol) in ethanol (30 mL). $NaBH_4$ (100 mg, 2.66 mmol, 3.1 equiv) was added to the suspension, and after ca. 15 min, more $NaBH_4$ (70 mg, 1.72 mmol, 2 equiv) was added. $NaBH_4$ (149 g, 3.9 mmol, 7 equiv) was added at various intervals throughout the next 1.5 h. The ethanol was then removed in vacuo providing a black solid. The crude organic concentrate was purified by silica gel column chromatography ($CHCl_3$/MeOH, 10/1 (100 mL), then $CHCl_3$/MeOH/NH_4OH, 10/5/1) to afford 0.169 g (83% yield) of amino diol (−)-**11b** as a light brown solid and 0.136 g (92% yield) of recovered (−)-(1*R*,2*S*)-phenylcyclohexanol ((−)-**4**). The analytical data for (−)-**11b**, except for the sign of the rotation, were identical to the data obtained for amino diol (+)-**11b** which was derived from a tandem sequence using MAPh as the Lewis acid in the [4 + 2]

cycloaddition. Data for (−)-**11b**: ^{1}H NMR (499.7 MHz, CD_3OD) δ 7.37−7.33 (m, 4 H), 7.30−7.27 (m, 1 H), 3.78 (d, J = 5.7, 2 H), 3.52 (dd, J = 11.0, 2.4, 1 H), 3.39 (dd, J = 11.0, 3.7, 1 H), 3.16 (d, J = 9.9, 1 H), 2.49−2.43 (m, 1 H), 2.19 (dt, J = 13.3, 9.3, 1 H), 2.07−2.01 (m, 1 H), 1.86−1.78 (m, 1 H), 1.14 (s, 3 H); MS (FAB) 236 (M^+ + 1, 100); TLC R_f 0.66 ($CHCl_3$/CH_3OH/NH_4OH, 10/5/1); optical rotation $[\alpha]^{23}_D$ = −23.34° (c = 1.0, CH_3OH); HRMS (FAB) calcd for $C_{14}H_{22}NO_2$ 236.16505, found 236.16510.

[(1*S*,3*R*,4*S*,5*R*)-4-(Acetylamino)-4-methyl-5-phenyl]-1,3-cyclopentanedimethanol Diacetate ((−)-12b). According to general procedure V, the amino diol (−)-**11b** (13 mg, 0.057 mmol) was dissolved in pyridine (2 mL) and acetic anhydride (2 mL) and was left to stir at room temperature for 1.0 h. Purification by silica gel column chromatography (hexane/EtOAc, 1/1) followed by a second silica gel column chromatography (Et_2O) provided 15 mg (73%) of triacetate (−)-**12b** as slightly yellow oil. The analytical data for (−)-**12b**, except for the sign of the rotation, were identical to the data obtained for triacetate (+)-**12b** which was derived from a tandem sequence using MAPh as the Lewis acid in the [4 + 2] cycloaddition. Data for (−)-**12b**: ^{1}H NMR (499.7 MHz, $CDCl_3$) δ 7.33−7.30 (m, 2 H), 7.27−7.24 (m, 1 H), 7.20−7.19 (m, 2 H), 5.72 (s, 1 H), 4.40 (ddd, J = 11.3, 6.0, 1.6, 1 H), 4.23 (ddd, J = 11.3, 7.5, 1 H), 3.79 (d, J = 6.4, 2 H), 3.35 (d, J = 8.8, 1 H), 2.79−2.71 (m, 1 H), 2.48−2.42 (m, 1 H), 2.18−2.12 (m, 1 H), 2.10 (s, 3 H), 1.98 (s, 3 H), 1.79 (s, 3 H), 1.71 (s, 3 H) 1.70−1.63 (m, 1 H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 170.93, 170.46, 169.46, 136.83, 130.06, 128.52, 127.26, 65.21, 64.76, 63.84, 60.38, 49.22, 39.51, 31.11, 28.27, 24.30, 21.00, 20.88; TLC R_f 0.23 (EtOAc/hexane, 2/1); optical rotation $[\alpha]^{23}_D$ = −18.58° (c = 1.07, $CHCl_3$); chiral SFC (Chiralcel OJ, 150 bar, 40 °C, 3% CH_3OH in CO_2, 3.0 mL/min); t_R (+)-**12b** 2.42 min (2.5%), t_R (−)-**12b** 2.78 min (97.5%), 95% ee.

(1*S*,6*S*,7*R*,8*S*,9*R*)-9-Methyl-8-phenyl-6-[(1*R*,2*S*)-(2-phenylcyclohexyl)oxy]-4-aza-3,5-dioxatricyclo[5.2.1.0^{4,9}]-decane (10e). According to general procedure III, nitronate **9e** (290 mg, 0.715 mmol) was added to a suspension of sodium bicarbonate (420 mg, 5.0 mmol, 7 equiv) in toluene (70 mL) and the mixture was heated to reflux for 14 h. Purification by column chromatography using basic alumina (III) (hexane/Et_2O, 6/1) afforded 250 mg (86% yield) of analytically pure nitroso acetal **10e** as a white crystalline solid: 172 °C; ^{1}H NMR (499.7 MHz, C_6D_6) δ 7.51−7.49 (m, 2 H), 7.19−7.15 (m, 2 H), 7.08−7.05 (m, 1 H), 7.03−6.96 (m, 3 H), 6.84−6.82 (m, 2 H, 4.25 (d, J = 5.1, 1 H), 4.20 (dd, J = 7.3, 4.6, 1 H), 4.14 (dd, J = 9.0, 7.3, 1 H), 3.30 (td, J = 10.5, 4.3, 1 H), 2.59 (d, J = 4.4, 1 H), 2.53−2.49 (m, 1 H), 2.38−2.33 (m, 1 H), 2.03 (td, J = 9.4, 4.5, 1 H), 1.87−1.81 (m, 2 H) 1.62−1.55 (m, 2 H), 1.47−1.39 (m, 2 H), 1.24−0.97 (m, 7 H); ^{13}C NMR (125.6 MHz, C_6D_6) δ 145.60, 139.95, 130.19, 128.29, 128.11, 127.91, 126.58, 126.18, 102.54, 83.37, 79.76, 77.12, 53.01, 52.02, 49.91, 45.61, 35.00, 33.35, 30.20, 26.09, 25.26, 22.06; IR ($CHCl_3$) 2935, 1085; MS (FAB) 406 (M^+ + 1, 100); TLC R_f 0.60 (hexane/EtOAc, 2/1); optical rotation $[\alpha]^{23}_D$ = 25.33° (c = 1.07, $CHCl_3$). Anal. Calcd for $C_{26}H_{31}NO_3$ (405.53): C, 77.01; H, 7.71; N, 3.45. Found: C, 76.89; H, 7.73; N, 3.46.

[(1*R*,3*S*,4*R*,5*S*)-4-Amino-4-methyl-5-phenyl]-1,3-cyclopentanedimethanol ((+)-11b). According to general procedure IV, nickel chloride (76 mg, 0.583 mmol, 1.1 equiv) was added to a solution of nitroso acetal **10e** (215 mg, 0.53 mmol) in ethanol (10 mL). $NaBH_4$ (80 mg, 2.11 mmol, 4 equiv) was added to the suspension, and after 15 min, $NaBH_4$ (80 mg, 2.11 mmol, 4 equiv) was added. The remainder of the $NaBH_4$ (0.080 g, 2.11 mmol, 4 equiv) was added at various intervals throughout the next 1.5 h. The ethanol was removed in vacuo providing a black solid. Purification by silica gel column chromatography ($CHCl_3$/MeOH, 10/1 (100 mL), then $CHCl_3$/MeOH/NH_4OH, 10/5/1) afforded 100 mg (81% yield) of amino diol (+)-**11b** as a light brown solid and 86 mg (94% yield) of recovered (−)-(1*R*,2*S*)-phenylcyclohexanol ((−)-**4**). The ^{1}H NMR, ^{13}C NMR, and MS of amino diol (+)-**11b** were identical to the data obtained for amino diol (−)-**11b** which is derived from a tandem sequence using $SnCl_4$ as the Lewis acid in the [4 + 2] cycloaddition. However, the sign of the rotation of the two amino diols are opposite. Data for (+)-**11b**: ^{1}H NMR (499.7 MHz, CD_3OD) δ 7.37−7.27 (m, 5 H), 3.84−3.78 (m, 2 H), 3.53 (dd, J = 11.0, 2.4, 1 H), 3.41 (dd, J = 11.0, 3.7, 1 H), 3.20 (d, J = 9.9, 1 H), 2.52−2.46 (m, 1 H), 2.20 (dt, J = 13.2, 9.5, 1 H), 2.10−2.03 (m, 1 H), 1.91−1.84 (m, 1 H), 1.17 (s, 3 H); ^{13}C NMR (125.7 MHz, CD_3OD) δ 131.21, 130.92, 128.57, 127.18, 62.06, 61.59, 61.20, 60.75, 49.61, 41.93, 28.38, 25.96; IR (KBr) 3249, 2967, 2935; MS (FAB) 236 (M^+ + 1, 100); TLC R_f 0.66 ($CHCl_3$/CH_3OH/NH_4OH, 10/5/1); optical rotation $[\alpha]^{23}_D$ = 23.93° (c = 1.02, CH_3OH); HRMS (FAB) calcd for $C_{14}H_{22}NO_2$ 236.16505, found 236.16510.

[(1*R*,3*S*,4*R*,5*R*)-4-(Acetylamino)-4-methyl-5-phenyl]-1,3-cyclopentanedimethanol Diacetate ((+)-12b). According to general procedure V, the amino diol (+)-**11b** (67 mg, 0.285 mmol) was dissolved in pyridine (4 mL) and acetic anhydride (4 mL) and was left to stir at room temperature for 1 h. Purification by silica gel column chromatography (EtOAc/hexane 1/1) followed by a second silica gel column chromatography (Et_2O) provided 78 mg (76%) of triacetate (+)-**29** as a slightly yellow oil. The analytical data for (+)-**12b**, except for the sign of the rotation, was identical to the data obtained for triacetate (−)-**12b** which was derived from a tandem sequence using $SnCl_4$ as the Lewis acid in the [4 + 2] cycloaddition. Data for (+)-**12b**: ^{1}H NMR (499.7 MHz, $CDCl_3$) δ 7.33−7.30 (m, 2 H), 7.27−7.23 (m, 1 H), 7.21−7.19 (m, 2 H), 5.73 (s, 1 H), 4.40 (dd, J = 11.3, 6.0, 1 H), 4.23 (ddd, J = 11.3, 7.5, 1 H), 3.80 (d, J = 6.4, 2 H), 3.35 (d, J = 8.8, 1 H), 2.80−2.72 (m, 1 H), 2.48−2.42 (m, 1 H), 2.18−2.12 (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 (125.7 MHz, $CDCl_3$) δ 170.97, 170.50, 169.49, 136.84, 130.07, 128.54, 127.28, 65.23, 64.78, 63.86, 60.39, 49.23, 39.51, 31.13, 28.29, 24.33, 21.00, 20.91; IR (neat) 1738, 1687, 1682, 1368, 1238, 1033; MS (FAB) 362 (M^+ + 1, 65), 302 (100); TLC R_f 0.23 (EtOAc/hexane, 2/1); optical rotation $[\alpha]^{23}_D$ = 21.72° (c = 0.58, $CHCl_3$); chiral SFC (Chiralcel OJ, 150 bar, 40 °C, 3% CH_3OH in CO_2, 3.0 mL/min); t_R (+)-**12b**, 2.38 min (99.3%), t_R (−)-**12b**, 2.74 min (0.7%), >98% ee. Anal. Calcd for $C_{20}H_{27}NO_5$ (361.44): C, 66.46; H, 7.53; N, 3.88. Found: C, 66.50; H, 7.57; N, 3.89.

(4*R*,5*S*,6*S*)-4-Benzoyloxy-5-(2-propenyl)-6-[(1*R*,2*S*)-(2-phenylcyclohexyl)oxy]-5,6-dihydro-4*H*-[1,2]-oxazine 2-Oxide (21b). According to general procedure II, a solution of MAPh (2.0 mmol, 2.0 equiv.) was transferred, via cannula, to a second reaction vessel containing a −78 °C solution of nitroalkene **19** (194 mg, 1.0 mmol) and vinyl ether (−)-**7** (364 mg, 1.5 mmol, 1.5 equiv) in toluene (1 mL). The resulting dark brown solution was left to stir at −78 °C for 2 h and was allowed to warm slowly to 0 °C over a 4 h period. The reaction was left to stir at −10 to 0 °C for 64 h after which time it was quenched with H_2O (6 mL). After an aqueous workup, the crude material was purified by silica gel column chromatography (pretreated with Et_3N/hexane (1.5 mL/ 100 mL) (hexane/EtOAc, 9/1 (1000 mL), 8/1) to afford 260 mg (60% yield) of nitronates **28**. Diasteremomeric ratios for the nitronates could not be determined for this reaction due to small amounts of decomposed products. Data for **28**: ^{1}H NMR (499.7 MHz, C_6D_6) δ 7.95−7.93 (m, 2 H), 7.13−7.10 (m, 1 H), 7.07−7.01 (m, 4 H), 6.97−6.94 (m, 1 H), 6.92−6.91 (m, 2 H), 6.19 (d, J = 3.1, 1 H), 5.61 (dd, J = 8.9, 3.2, 1 H), 5.12−5.04 (m, 1 H), 4.68−4.66 (m, 2 H), 4.60 (dd, J = 17.1, 1.6, 1 H), 3.51 (td, J = 10.6, 4.4, 1 H), 2.51−2.48 (m, 1 H) 2.35−2.30 (m, 1 H), 1.93−1.88 (m, 1 H), 1.73−1.67 (m, 1 H), 1.61−1.58 (m, 2 H), 1.46−1.35 (m, 3 H), 1.25−1.11 (m, 2 H), 1.03−0.94 (m, 1 H); ^{13}C NMR (125.6 MHz, C_6D_6) δ 165.58, 144.41, 134.67, 133.36, 130.03, 128.62, 128.55, 128.29, 128.10, 126.64, 116.77, 107.99, 104.53, 84.16, 68.19, 51.28, 39.44, 34.37, 33.87, 31.95, 25.76, 25.05; TLC R_f 0.29 (hexane/EtOAc, 4/1).

[(1*S*,3*S*,4*S*,5*R*)-4-(Acetylamino)-5-benzoyloxy]-1,3-cyclopentanedimethanol Diacetate ((+)-31). To a solution of nitronate **28** (250 mg, 0.57 mmol) in benzene (58 mL) was added sodium bicarbonate (338 mg, 4.02 mmol, 7 equiv). The suspension was heated to reflux for 8 h. The majority of the sodium bicarbonate was removed by filtration through a pipet plug, washing with benzene (15 mL). Concentration of the

filtrate afforded a yellow foam which was directly subjected to hydrogenolysis without purification.

$NaBH_4$ (86 mg, 2.28 mmol, 4 equiv) was added to a solution of anhydrous nickel chloride (82 mg, 0.63 mmol, 1.1 equiv) in methanol (8 mL) at room temperature. A black precipitate formed almost immediately with the concomitant evolution of hydrogen. The nickel boride was then cooled to 0 °C, and $NaBH_4$ (86 mg, 2.28 mmol, 4 equiv) was added followed by the addition of a solution of nitroso acetal **29** (0.57 mmol) in methanol (4 mL). After ca. 10 min, $NaBH_4$ (86 mg, 2.28 mmol, 4 equiv) was added. After approximately 1 h, the methanol was removed in vacuo to provide a black solid. Purification by silica gel column chromatography ($CHCl_3$/MeOH, 10/1 (200 mL), then $CHCl_3$/MeOH/NH_4OH, 10/5/1) afforded amino diol **30** which was directly acetylated.

According to general procedure V, the amino diol **30** (0.57 mmol) was dissolved in pyridine (4 mL) and acetic anhydride (4 mL) and was left to stir at room temperature for 1 h. Purification by silica gel column chromatography (EtOAC/hexane 2/1) followed by an additional by silica gel column chromatography (Et_2O) provided 36 mg (16% yield over three steps) of analytically pure triacetate (+)-**31** as clear oil: ^{1}H NMR (499.7 MHz, $CDCl_3$ δ 7.73−7.71 (m, 2 H), 7.54−7.50 (m, 1 H), 7.47−7.43 (m, 2 H), 6.66 (d, J = 8.1, 2 H), 5.47 (t, J = 4.8, 1 H), 4.80−4.75 (m, 1 H), 4.20 (dd, J = 11.2, 7.0, 1 H), 4.15 (dd, J = 11.2, 8.2, 1 H), 4.05 (dd, J = 11.2, 6.4, 1 H), 4.01 (dd, J = 11.3, 5.9, 1 H), 2.88−2.80 (m, 1 H), 2.54−2.47 (m, 1 H), 2.18−2.14 (m, 4 H), 2.03 (s, 3 H), 1.96 (s, 3 H),1.44−1.38 (m, 1 H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 171.10, 170.87, 170.48, 167.32, 133.97, 129.68, 131.81, 128.73, 126.87, 75.74, 65.13, 62.66, 53.62, 39.96, 37.12, 29.02, 20.91, 20.90, 20.83; IR (neat) 1737, 1732, 1226; MS (FAB) 392 ($M^+ + 1$, 100); TLC R_f 0.28 (EtOAc/hexane, 2/1); optical rotation $[\alpha]^{22}_D = 32.11°$ (c = 1.09, $CHCl_3$); chiral HPLC (Chirapak AD, (hexane/*i*-PrOH, 85/15), 1.0 mL/min); t_R (−)-**31** 15.5 min (0.5%), t_R (+)-**31** 23.00 min (99.5%), 99% ee. Anal. Calcd for $C_{20}H_{25}NO_7$ (391.42): C, 61.37; H, 6.44; N, 3.58. Found: C, 61.57 H, 6.66; N, 3.34.

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Supporting Information Available: Experimental procedures along with complete ^{1}H NMR, ^{13}C NMR, IR, MS, and microanalytical data for all characterized compounds (41 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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