Tandem Inter [4 + 2]/Intra [3 + 2] Nitroalkene Cycloadditions. 5. Origin of the Lewis Acid Dependent Reversal of Stereoselectivity

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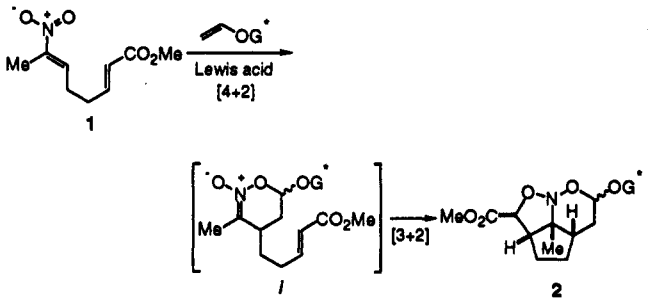
The stereochemical course of the tandem [4 + 2]/[3 + 2] nitroalkene cycloaddition with chiral enol ethers has been shown to exhibit remarkable sensitivity to the nature of the Lewis acid promoter. Cycloadditions using (+)-camphor-derived vinyl ether **3** or (−)-*trans*-2-phenylcyclohexanol-derived vinyl ether **6** gave a predominance of the 1*S* hydroxy lactam **4** when promoted by $Ti(O\text{-}i\text{-}Pr)_2Cl_2$. The same vinyl ethers selectively produced the 1*R* hydroxy lactam **4** when promoted by MAPh. The (*E*)- and (*Z*)-1-propenyl ethers of (−)-*trans*-2-phenylcyclohexanol have been used to investigate the reversal of selectivity. Cycloadditions promoted by $Ti(O\text{-}i\text{-}Pr)_2Cl_2$ were found to be endo selective (12:1), while MAD and MAPh favored exo approach of the dienophile. High levels of asymmetric induction were observed in the endo mode of the cycloaddition for propenyl ethers (*E*)-**13** and (*Z*)-**13**, 97.9% ee and 82.2% ee, respectively, but an erosion of selectivity occurred in the exo mode (72.2% ee) presumably through an s-cis enol ether conformation.

Introduction and Background

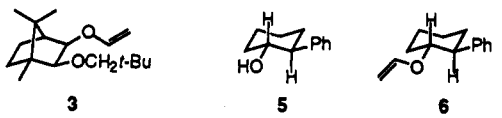
The stereoselective construction of heterocyclic, six-membered ring systems is clearly the domain of the hetero [4 + 2] cycloaddition reaction. Whether through the use of chiral dienes,[1] chiral dienophiles,[2] or chiral Lewis acid catalysts[3] many factors play crucial roles in obtaining high selectivity. Recent disclosures from these laboratories have established the Lewis acid promoted heterodiene cycloaddition between a chiral enol ether and a nitroalkene as a powerful method for the construction of tricyclic lactams in optically active form.[4] The salient features of this transformation are illustrated in Scheme I. The [4 + 2] cycloaddition of nitroalkene **1** with a chiral vinyl ether promoted by a Lewis acid, $Ti(O\text{-}i\text{-}Pr)_2Cl_2$, followed in tandem by a [3 + 2] cycloaddition of the intermediate cyclic nitronate, **i**, with a tethered electron-deficient olefin leads to the construction of nitroso acetal **2**. Overall, the tandem intermolecular [4 + 2]/intramolecular [3 + 2] cycloaddition allows for the construction of five stereogenic centers, two of which are controlled by the outcome of the initial [4 + 2] cycloaddition. Therefore, good asymmetric induction is dependent upon obtaining high π-facial selectivity in this step. In our previously reported studies, this has been accomplished by the use of vinyl ether **3** derived from (+)-camphor. For example, in the cycloaddition with nitroalkene **1**, the α-hydroxy lactam **4** was

Scheme I



produced with extremely high levels of asymmetric induction (>98% ee). Furthermore, the auxiliary alcohol was recovered in 92% yield, Scheme II.[4b,c]

The extreme selectivity observed with **3** demonstrated the feasibility of the chiral auxiliary approach for the asymmetric synthesis of complex heterocycles. At the same time, important practical and conceptual issues were immediately apparent. First the preparation of auxiliary **3**, though well described, required six steps from (+)-camphor.[5] Thus, the search for other, more readily



available chiral alcohols capable of similar levels of asymmetric induction became an important goal. Moreover, both antipodes of these alcohols should be equally available since (−)-camphor is very expensive. On the basis of these considerations *trans*-2-phenylcyclohexanol (**5**) was chosen as a logical first choice.[6] The racemate is easily prepared in two steps from cyclohexene, and the enzymatic resolution is well described and efficient.[7] Second, the utilization of β-substituted enol ethers could in principle

† Taken in part from Senanayake, C. B. W. Ph.D. Thesis, University of Illinois, Urbana, IL, 1991.

(1) (a) Lyssikatos, J. P.; Bednarski, M. D. *Synlett* **1990**, 230. (b) Tripathy, R.; Carroll, P. J.; Thornton, E. R. *J. Am. Chem. Soc.* **1990**, *112*, 6743. (c) Bednarski, M.; Danishefsky, S. *J. Am. Chem. Soc.* **1986**, *108*, 7060. (d) Schmidt, R.; Maier, M. *Tetrahedron Lett.* **1985**, *26*, 2065. (e) Tietze, L. F.; Glüsenkamp, K. H. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 887.

(2) (a) Schreiber, S. L.; Meyers, H. V. *J. Am. Chem. Soc.* **1988**, *110*, 5198. (b) Posner, G. H.; Wettlaufer, D. G. *Tetrahedron Lett.* **1986**, *27*, 667. (c) Fuji, K.; Tanaka, K.; Abe, H.; Itoh, A.; Node, M.; Taga, T.; Miwa, Y.; Shiro, M. *Tetrahedron: Asymmetry* **1991**, *2*, 179. (d) Broek, L.; Porskamp, P.; Haltiwanger, R. C.; Zwanenburg, B. *J. Org. Chem.* **1984**, *49*, 1691.

(3) (a) Seebach, D.; Beck, A. K.; Imwinkelried, R.; Roggo, S.; Wonnacott, A. *Helv. Chim. Acta* **1987**, *70*, 954. For reviews see: (b) Narasaka, K. *Synthesis* **1991**, 1. (c) Tomioka, K. *Synthesis* **1990**, 541.

(4) (a) Denmark, S. E.; Moon, Y. C.; Senanayake, C. B. W. *J. Am. Chem. Soc.* **1990**, *112*, 311. (b) Denmark, S. E.; Senanayake, C. B. W.; Ho, G. D. *Tetrahedron* **1990**, *46*, 4857. (c) Denmark, S. E.; Schnute, M. E. *J. Org. Chem.* **1991**, *56*, 6738.

(5) Oppolzer, W.; Chapuis, C.; Dupuis, D.; Guo, M. *Helv. Chim. Acta* **1985**, *68*, 2100.

(6) (a) Whitesell, J. K.; Chen, H. H.; Lawrence, R. M. *J. Org. Chem.* **1985**, *50*, 4663. (b) Castro, J.; Sörensen, H.; Riera, A.; Morin, C.; Mayano, A.; Pericàs, M. A.; Greene, A. E. *J. Am. Chem. Soc.* **1990**, *112*, 9388. (c) Choudhury, A.; Franck, R. W.; Gupta, R. B. *Tetrahedron Lett.* **1989**, *30*, 4921. (d) Prapansiri, V.; Thornton, E. R. *Tetrahedron Lett.* **1991**, *32*, 3147.

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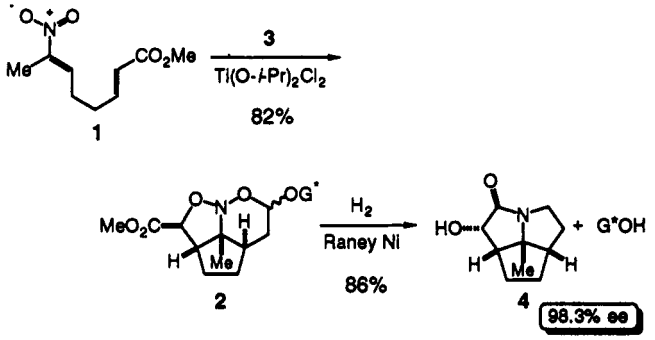
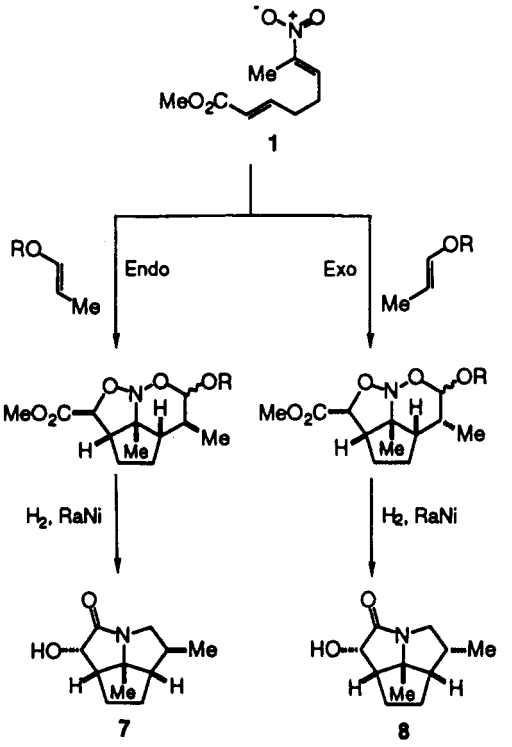
Scheme II



Scheme III



allow for the creation of six contiguous stereogenic centers in the cycloaddition. Studies with achiral propenyl ethers have shown that such cycloadditions are feasible and highly diastereoselective.[8] Toward this end, the synthesis and evaluation of both (*E*)- and (*Z*)-1-propenyl ethers derived from both of the auxiliaries were planned. Third, a detailed investigation into the stereochemical variables that govern selectivity, including the conformation of the enol ether, the dienophile face selectivity, and the endo/exo folding selectivity was in order. The study of propenyl ether cycloadditions not only allows for the incorporation of a methyl substituent in the cycloadduct but also allows for the precise determination of the endo/exo selectivity in the reaction since different diastereomeric α-hydroxy lactams, **7** and **8**, are produced after subsequent hydrogenolytic cleavage of the nitroso acetal cycloadducts, Scheme III.

During the development of these auxiliary-based cycloadditions we discovered a remarkable Lewis acid dependence on the stereochemical outcome of the reaction. This unexpected behavior allowed for a unified understanding of the factors that control the overall stereochemical course of the reaction. The influence of an achiral Lewis acid on the stereochemical outcome of an asymmetric Diels–Alder reaction has been observed by others including Helmchen[9] and Waldmann.[10] In these cases the reversal of selectivity is believed to result from changes in the mode of Lewis acid complexation.[11] Also, Ghosez[12] has reported a pronounced Lewis acid dependence on the endo/exo selectivity in Diels–Alder reactions involving chiral acylamides and has interpreted the change in reaction mode on the basis of Lewis acid bulk.

The following paper is a full account of our studies on the origin of stereocontrol in the tandem cycloaddition reaction with chiral enol ethers. A preliminary report on the Lewis acid phenomenon has appeared.[4c]

Results

Preparation of Nitroalkene 1 and Vinyl Ethers 3 and 6. The preparation of nitroalkene **1** has been described in full in the preceding paper.[8] Racemic *trans*-2-phenylcyclohexanol was prepared by the CuI-catalyzed ring opening of cyclohexene oxide with phenylmagnesium bromide. The alcohol was resolved by a lipase-catalyzed, selective hydrolysis of the enantiomeric chloroacetates.[7] The resulting (−)-(1*R*,2*S*)-*trans*-2-phenylcyclohexanol (**5**) (98.9% ee by chiral HPLC analysis[13] of the corresponding 3,5-dinitrophenyl carbamate derivative) was transformed to the vinyl ether by a mercuric acetate catalyzed transetherification reaction with ethyl vinyl ether.[14] Camphor derived vinyl ether **3** was prepared from the corresponding alcohol[5] in analogy to a two-step method described by Greene[15] involving dichloroenol ether formation, in situ dechlorination with *n*-BuLi, and semihydrogenation with Pd/$BaSO_4$ in the presence of quinoline.[4b]

Preparation of Propenyl Ethers. Chiral propenyl ethers of the camphor-based auxiliary and (1*R*,2*S*)-*trans*-2-phenylcyclohexanol were prepared by a divergent route analogous to the method employed to synthesize vinyl ether **3**, Scheme IV. The corresponding lithium acetylide was quenched with iodomethane to yield the propynyl ethers **10** and **12** in 83% and 61% yield, respectively. The (*E*)-1-propenyl ethers (*E*)-**11** and (*E*)-**13** were prepared by lithium aluminum hydride reduction of the corresponding propynyl ethers in 89% and 66% yield (>99/1 *E*/*Z*), respectively. Semihydrogenation in the presence of Pd/$BaSO_4$ employing a mixture of hexane and methanol (1:1) as solvent afforded the (*Z*)-1-propenyl ethers (*Z*)-**11** and (*Z*)-**13** in 88% and 71% yield (>99/1 *Z*/*E*), respectively.

Cycloadditions with Vinyl Ether 6. The Lewis acid $Ti(O\text{-}i\text{-}Pr)_2Cl_2$ had previously been found to be an effective promoter for nitroalkene cycloadditions involving both butyl vinyl ether and vinyl ether **3**. The [4 + 2]

(7) Schwartz, A.; Madan, P.; Whitesell, J. K.; Lawrence, R. M. *Org. Synth.* **1990**, *69*, 1.
(8) Denmark, S. E.; Senanayake, C. B. W. Previous paper in this issue.
(9) Poll, T.; Helmchen, G.; Bauer, B. *Tetrahedron Lett.* **1984**, *25*, 2191.
(10) (a) Waldmann, H. *J. Org. Chem.* **1988**, *53*, 6133. (b) Suzuki, H.; Mochizuki, K.; Hattori, T.; Takahashi, N.; Tajima, O.; Takiguchi, T. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 1999–2005.
(11) Poll, T.; Metter, J. O.; Helmchem, G. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 112–114.
(12) (a) Lamy-Schelkens, H.; Giomi, D.; Ghosez, L. *Tetrahedron Lett.* **1989**, *30*, 5887. (b) Lamy-Schelkens, H.; Ghosez, L. *Tetrahedron Lett.* **1989**, *30*, 5891.
(13) (a) Pirkle, W. H.; Mahler, G.; Hyun, M. H. *J. Liq. Chromatogr.* **1986**, *9*, 443. (b) Pirkle, W. H.; Pochapsky, T. C.; Burke, J. A.; Deming, K. C. In *Chiral Separations*; Stevenson, D., Wilson, I. D., Eds.; Plenum: New York, 1988; p 23.
(14) Watanabe, W. H.; Conlon, L. E. *J. Am. Chem. Soc.* **1957**, *79*, 2828.
(15) Moyano, A.; Charbonnier, F.; Greene, A. E. *J. Org. Chem.* **1987**, *52*, 2919.

Scheme IV

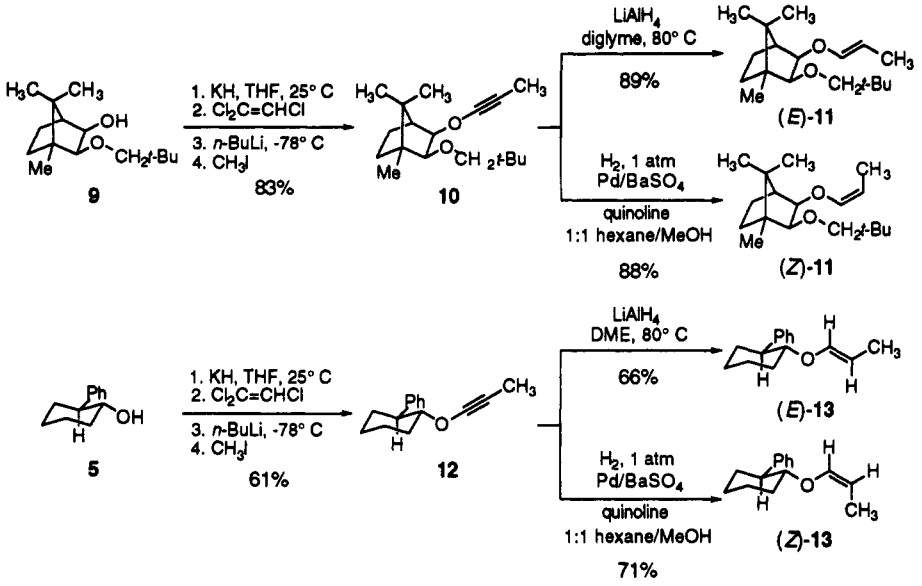
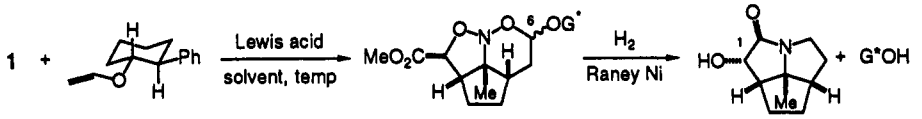


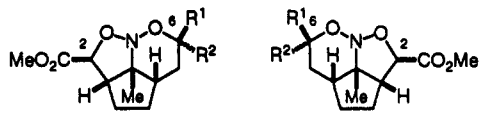
Table I. Influence of the Lewis Acid on Cycloadditions with Vinyl Ether 6



Lewis acid	equiv	6, equiv	14,[a] yield, %	ratio 14,[b] α:β:α':β'	yield, % 4	yield, % G*OH	% ee 4[c] (config)
$Ti(O\text{-}i\text{-}Pr)_2Cl_2$	3.0	1.5	73	81.0:1.0:0.0:0.0	76	92	97.7 (1*S*)
MAD	3.0	1.5	88	3.5:1.5:0.0:1.0	73	78	72.4 (1*S*)
MAPh	3.0	3.0	85	1.0:2.0:0.0:0.0:38.7	76	97	79.2 (1*R*)

[a] Isolated as a mixture of diastereomers. [b] Determined by ^1H NMR; α/β refers to configuration of alkoxy at C(6). [c] Determined by chiral HPLC.

Table II. Selected NMR Data for Nitroso Acetals 14α, -β, and -β' Derived from Vinyl Ether 6



14α, 14β 14α', 14β'

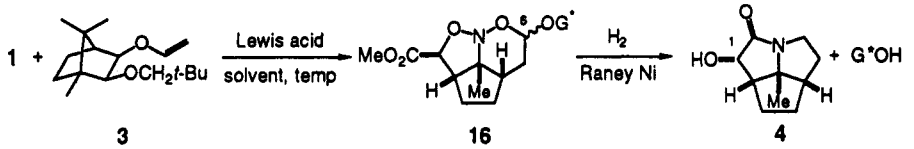
nitroso acetal	R^1	R^2	HC(6), ppm (*J*, Hz)	HC(2), ppm (*J*, Hz)	$H_3C(10)$, ppm	C(6), ppm
14α	H	OG*	4.42 (dd, 6.2, 3.6)	4.82 (d, 8.3)	3.78	100.77
14β	OG*	H	5.26 (t, 7.2)	4.79 (d, 8.2)	3.79	92.85
14β'	OG*	H	4.24 (t, 7.5)	4.75 (d, 7.8)	3.77	99.50

cycloaddition of nitroalkene substrate 1 with (−)-6, promoted by $Ti(O\text{-}i\text{-}Pr)_2Cl_2$ at −90 °C followed by the [3 + 2] cycloaddition after workup at room temperature, resulted in a 73% yield of the nitroso acetal 14 as an 81:1 mixture of α and β anomers, Table I. Assignment of the configuration at the anomeric center, either α or β with respect to the alkoxy group, was made by comparison of the coupling pattern observed for the anomeric proton (HC(6)) in the ^1H NMR spectrum, Table II. The anomeric proton of the major component was observed as a doublet of doublets at 4.42 ppm (J = 6.2, 3.6 Hz) while the minor component exhibited a triplet at 5.26 ppm (J = 7.2 Hz). This can be rationalized in terms of a twist-boat conformation of the six-membered N–O heterocyclic ring, therefore placing the alkoxy group in a pseudoequatorial and pseudoaxial orientation for the α and β anomers, respectively.[4b] On the basis of this argument, the major diastereomer is an α anomer (14α) which, if produced kinetically, is derived from an endo approach of the dienophile in the [4 + 2] cycloaddition. On the other hand, an exo approach would produce the β anomer. In order to determine the extent of asymmetric induction, the mixture of nitroso acetals was cleaved to the tricyclic α-hydroxy lactam 4 in 76% yield by hydrogenation at atmospheric pressure over Raney nickel. The chiral auxiliary was recovery in 92% yield. Analysis of the corresponding 3,5-dinitrophenyl carbamate derivative 15 by chiral HPLC showed the lactam to be significantly enantiomerically enriched (97.7% ee). The major enantiomer possessed the 1*S* configuration as previously determined by comparison of the *O*-methyl mandelate esters.[4b] Though high selectivity was obtained, isolated yields of the nitroso acetal cycloadduct were not as high as previously seen with vinyl ether 3.

A survey of numerous bulky monomeric aluminum reagents[16] revealed that methyl aluminum bis(2,6-di-*tert*-4-methylphenoxide) (**MAD**) and methyl aluminum bis-(2,6-diphenylphenoxide) (**MAPh**) were capable of inducing the nitroalkene cycloaddition in high yields. When MAD was employed as the Lewis acid, the cycloaddition

(16) These reagents have recently found uses as Lewis acids in carbonyl activation, Claisen rearrangements, intramolecular ene reactions, and Diels–Alder reactions: (a) Maruoka, K.; Itoh, T.; Yamamoto, H. *J. Am. Chem. Soc.* **1985**, *107*, 4573. (b) Nonoshita, K.; Banno, H.; Maruoka, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1990**, *112*, 316. (c) Maruoka, K.; Ooi, T.; Yamamoto, H. *J. Am. Chem. Soc.* **1990**, *112*, 9011. (d) Maruoka, K.; Itoh, T.; Shirasaka, T.; Yamamoto, H. *J. Am. Chem. Soc.* **1988**, *110*, 310. (e) Posner, G. H.; Kinter, C. M. *J. Org. Chem.* **1990**, *55*, 3967.

Table III. Influence of the Lewis Acid on Cycloadditions with Vinyl Ether 3

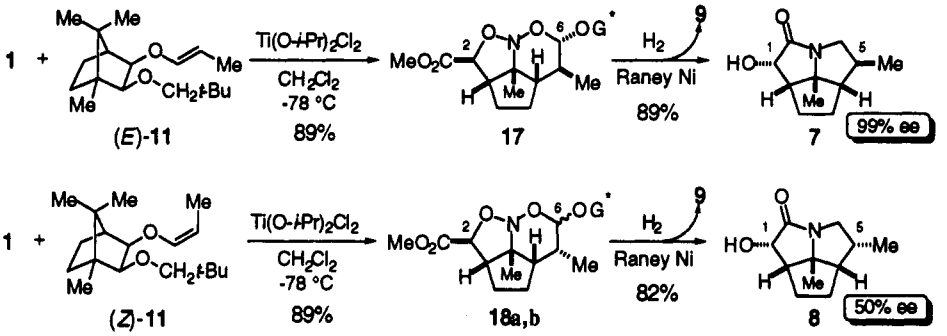


3 16 4

Lewis acid	equiv	3, equiv	16, yield, %	ratio 16,[c] α:β:α′:β′	yield, % 4	yield, % G*OH	% ee 4[d] (config)
Ti(O-*i*-Pr)$_2$Cl$_2$[a]	2.4	1.2	82	4.1:1.0:0.0:0.0	86	92	98.3 (1*S*)
MAD	3.0	1.2	86[b]	1.0:0.0:0.0:1.1	67	81	2.3 (1*S*)
MAPh	6.0	1.2	83	0.0:0.0:0.0:1.0	88	86	98.9 (1*R*)

[a] From ref 4b. [b] Isolated as a mixture of diastereomers. [c] Determined by ^{1}H NMR. [d] Determined by chiral HPLC.

Scheme V



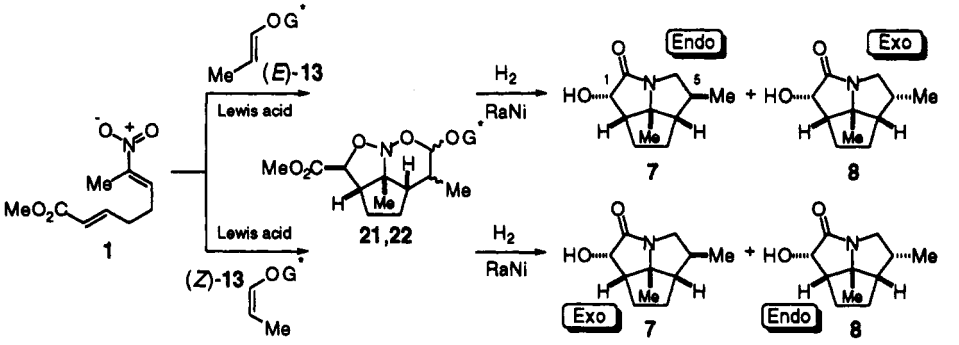
between nitroalkene 1 and vinyl ether (−)-6 yielded an inseparable mixture of nitroso acetal diastereomers in 88% yield, Table I. On the basis of ^{1}H NMR analysis, three diastereomers were present, one α anomer and two β anomers in the ratio of 3.5:1.5:1.0 (14α:14β:14β′). Because of the high stereoselectivity (>100:1) in the [3 + 2] cycloaddition, only four possible diastereomers can be produced in the reaction; the result of endo/exo and α/β face approach. Therefore, the other β anomer (designated as 14β′) must be derived from the opposite enantiomeric series. This was confirmed by subsequent cleavage to a single α-hydroxy lactam to show the major enantiomer was still of the 1*S* configuration, however, not enriched to as high an extent (72% ee), Table I.

An interesting observation was made when MAPh was used as the Lewis acid promoter. Optimized cycloaddition conditions required 3 equiv each of vinyl ether (−)-6 and MAPh at −78 °C to yield a mixture of nitroso acetal diastereomers in 86% yield. Three diastereomers were again present as determined by ^{1}H NMR; however, in this case a β anomer predominated in a ratio of 1.0:2.0:38.7 (14α:14β:14β′). *The corresponding lactam 4 was found to be enriched in the opposite enantiomeric series, 79.2% ee (R), to that observed with Ti(O-i-Pr)$_2$Cl$_2$ or MAD.*

Cycloadditions with Vinyl Ether 3. To further explore this remarkable Lewis acid dependent reversal of selectivity in the tandem inter [4 + 2]/intra [3 + 2] cycloaddition and determine its generality, cycloadditions were performed using the enol ether 3 derived from (+)-camphor. Cycloaddition of nitroalkene 1 with chiral vinyl ether 3 in the presence of MAD (3.0 equiv) at −78 °C resulted in a 1.1:1.0 mixture of nitroso acetal diastereomers (86% yield) after subsequent [3 + 2] cycloaddition, Table III. One diastereomer corresponded to the α anomer obtained previously from Ti(O-*i*-Pr)$_2$Cl$_2$-promoted cycloadditions.[4b] The other component, however, exhibited a triplet at 4.98 ppm (J = 7.3 Hz) indicating this was a previously unseen β anomer. Subsequent cleavage of the nitroso acetal mixture and derivatization showed that the α-hydroxy lactam was produced in essentially racemic form (2.3% ee, 1*S* configuration). This result is consistent in that the α and β anomers produced are of opposite enantiomeric series. In contrast, when the cycloaddition was carried out with MAPh (6.0 equiv) as the Lewis acid promoter, a single nitroso acetal was isolated in 83% yield and identified as 16β′. Hydrogenolytic cleavage of the nitroso acetal resulted in an 88% yield of the α-hydroxy lactam 4 with an 86% recovery of the auxiliary. The resulting α-hydroxy lactam was found to be enriched in the 1*R* configuration to the extent of 98.9% ee as opposed to 98.3% ee of the 1*S* configuration obtained with Ti(O-*i*-Pr)$_2$Cl$_2$. *Therefore, the cycloaddition promoted by MAPh afforded the same magnitude of asymmetric induction as previously seen with Ti(O-i-Pr)$_2$Cl$_2$ but now in the opposite sense.*

Cycloadditions with Propenyl Ethers (*E*)-11 and (*Z*)-11. One explanation for the observed reversal in the sense of asymmetric induction is that a corresponding reversal in the endo/exo preference of the [4 + 2] cycloaddition had occurred. While it is possible to determine endo or exo orientation from the configuration of the anomeric center (such evidence supports this hypothesis), this argument relies on complete kinetic control in the reaction and the absence of epimerization. As mentioned above, chiral propenyl ethers allow for the unambiguous determination of the endo/exo selectivity in the cycloaddition. Chiral (*E*)-1-propenyl ether (*E*)-11 was subjected to the cycloaddition with nitroalkene 1 in the presence of Ti(O-*i*-Pr)$_2$Cl$_2$ at −78 °C, Scheme V. A single nitroso acetal 17 was isolated in 89% yield. The ^{1}H NMR spectrum of 17 showed a doublet at 4.68 ppm (J = 4.7 Hz) for HC(6) and a doublet at 4.85 ppm (J = 8.2 Hz) for HC(2). The formation of a single anomer in the cycloaddition is in agreement with previous studies with ethyl (*E*)-1-propenyl ether. Reaction of chiral (*Z*)-1-propenyl ether (*Z*)-11 with nitroalkene 1 in the presence of Ti(O-*i*-Pr)$_2$Cl$_2$ produced a mixture of nitroso acetal anomers 18a and 18b in 89% yield. The ^{1}H NMR

Scheme VI



spectrum showed two sets of doublets. Nitroso acetal **18a** showed a doublet at 5.16 ppm (J = 6.8 Hz) for HC(6) and a doublet at 4.87 ppm (J = 8.0 Hz) for HC(2), while **18b** showed a doublet at 5.26 ppm (J = 7.2 Hz) for HC(6) and a doublet at 4.85 ppm (J = 10 Hz) for HC(2).

To determine the degree of asymmetric induction for the chiral 1-propenyl ether cycloadditions, nitroso acetals **17** and **18a,b** were subjected to hydrogenolytic cleavage catalyzed by Raney nickel. Nitroso acetal **17** provided an 89% yield of a single α-hydroxy lactam (−)-**7** and a 91% yield of chiral alcohol **9**. Similarly, the mixture of nitroso acetals **18a,b** gave an 82% yield of a single α-hydroxy lactam (−)-**8** and an 87% yield of chiral alcohol **9**. Stereochemical assignments for the lactams were made by ^{1}H NMR comparisons to the racemic α-hydroxy lactams derived from (*E*)- and (*Z*)-ethyl 1-propenyl ethers.[8] The crucial orientation of the methyl substituent at C(5) had been established in the achiral series by NOE difference studies. The ^{1}H NMR spectrum for (−)-**8** showed a doublet at 3.21 ppm (J = 8.7 Hz) for $H_2C(4)$ while lactam (−)-**7** showed a doublet of doublets at 4.04 ppm (J = 7.3, 11.8 Hz) for HC(4). The ^{1}H NMR data satisfactorily correspond to those obtained for the lactam alcohols isolated from the corresponding ethyl 1-propenyl ethers. The optical purity of the α-hydroxy lactams was determined by HPLC analysis of the corresponding 3,5-dinitrophenyl carbamates (**19, 20**). Racemic lactams **7** and **8** derived from ethyl (*E*)-1-propenyl ether were employed for calibration. Lactam (−)-**7** derived from chiral (*E*)-1-propenyl ether **11** was found to be highly enantiomerically enriched (99% ee). The α-hydroxy lactam (−)-**8** from chiral (*Z*)-1-propenyl ether **11** showed only moderate asymmetric induction to the extent of 50% ee. In both cases the 1*S* enantiomer predominated. The determination of absolute configuration was based on HPLC elution order in analogy to the previous chiral vinyl ether series.

An important consideration in employing chiral propenyl ethers as dienophiles is the irreversibility of the initial bond formation step during the [4 + 2] cycloaddition. If the initial bond formation step was indeed reversible, a mixture of products would be formed due to enol ether isomerization. This question, however, is easily addressed by isolation of the unreacted propenyl ether from the cycloaddition. Analogous cycloadditions with both (*E*)- and (*Z*)-propenyl ethers were conducted but in these cases quenching the reaction mixtures after 5 min to isolate unreacted enol ethers. The recovered propenyl ethers (*E*)-**11** and (*Z*)-**11** were found to be unchanged by ^{1}H NMR and GC analysis. The other isomer was not detected. Therefore, in both cases no isomerization had occurred under the reaction conditions.

Table IV. Propenyl Ether Cycloadditions Promoted by $Ti(O\text{-}i\text{-}Pr)_2Cl_2$

enol ether	21, 22, yield, %	7, 8, yield, %	ratio[a] endo/exo	% ee (config) endo	% ee (config) exo
(*E*)-**13**	86	77	11.9:1.0	97.9 (*S*)	64.8 (*S*)
(*Z*)-**13**	83	71	10.7:1.0	82.2 (*S*)	64.4 (*S*)

[a] Determined by chiral HPLC.

Table V. Propenyl Ether Cycloadditions Promoted by MAD

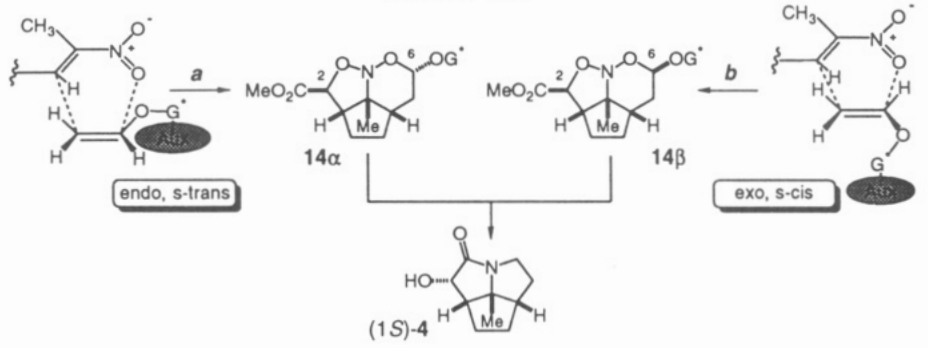
enol ether	21, 22, yield, %	7, 8, yield, %	ratio[a] endo/exo	% ee (config) endo	% ee (config) exo
(*E*)-**13**	86	81	1.0:2.6	99.8 (*S*)	72.2 (*S*)
(*Z*)-**13**	72	83	8.7:1.0	100.0 (*S*)	16.9 (*R*)

[a] Determined by chiral HPLC.

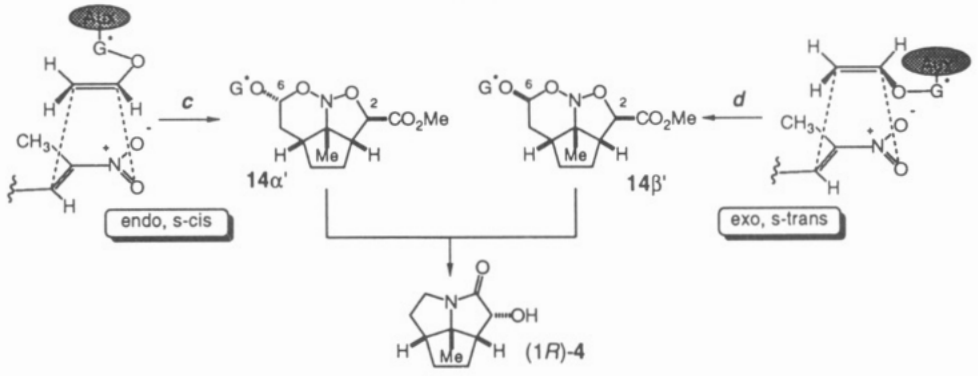
Cycloadditions with Propenyl Ethers (*E*)-13 and (*Z*)-13. Cycloadditions with both the (*E*)- and (*Z*)-1-propenyl ethers of phenylcyclohexanol were also promoted by $Ti(O\text{-}i\text{-}Pr)_2Cl_2$ using the optimized conditions obtained from the vinyl ether studies. For the propenyl ether (*E*)-**13** three diastereomeric nitroso acetals were formed in the combined yield of 86% and in the approximate ratio of 1:2:24 based on ^{1}H NMR analysis. To determine the endo/exo selectivity of the reaction and subsequent asymmetric induction, the mixture of nitroso acetals was cleaved to the α-hydroxy lactam in 77% yield with 86% recovery of the auxiliary, Scheme VI. Contrary to the previous studies with the camphor-derived propenyl ethers giving a single α-hydroxy lactam diastereomer, a mixture of methyl epimers was observed in a ratio of 12:1 (**7**:**8**). This result correlates to an endo/exo selectivity of 12:1. Since the two methyl epimers were not separable by column chromatography, the mixture was converted to the corresponding 3,5-dinitrophenyl carbamate methyl epimers (**19, 20**). Enantiomeric excess was determined by chiral HPLC using a solvent system capable of separating the methyl epimers as well as their corresponding enantiomers. The resulting analysis showed an endo/exo ratio of 11.9:1.0 which was in close agreement to the evidence from NMR. The endo mode cycloaddition was observed to be highly enantioselective (97.9% ee) with the major enantiomer possessing the 1*S* configuration. An erosion of selectivity occurred in the exo mode cycloaddition, however, where the lactam was found to be enriched only to the extent of 64.8% ee and also possessing the 1*S* configuration, Table IV. *It is important to note that both the endo and exo modes favored the same enantiomeric series.*

Likewise, propenyl ether (*Z*)-**13** underwent cycloaddition with nitroalkene **1** promoted by $Ti(O\text{-}i\text{-}Pr)_2Cl_2$ to yield in 83% a mixture of four nitroso acetal diastereomers in the

Scheme VII



Scheme VIII



approximate ratio of 4:1:21:2 by ^{1}H NMR. Subsequent cleavage to the corresponding α-hydroxy lactam methyl epimers, derivatization, and analysis by chiral HPLC indicated that once again there was a significant contribution by the exo orientation of the [4 + 2] cycloaddition. The endo/exo selectivity was calculated to be 10.7:1.0. The α-hydroxy lactam derived from endo approach, **8**, was found to be enriched in the 1*S* configuration to the extent of 82.2% ee while in the exo mode the lactam showed the same sense of induction but to a lesser extent (64.4% ee).

Cycloaddition of (*E*)-1-propenyl ether **13** with nitroalkene **1** promoted by MAD followed the conditions established for vinyl ether cycloadditions to afford a mixture of nitroso acetal diastereomers in 86% yield, Table V. Analysis of the mixture by ^{1}H NMR revealed three diastereomers in a ratio of 4:6:1. Endo/exo selectivity was determined to be 1.0:2.6 by cleavage to the α-hydroxy lactam methyl epimers. In this case the exo approach of the dienophile dominated. Asymmetric induction from the endo approach of the enol ether was found to be extremely high (>99.5% ee); however, the lactam derived from exo approach was only enriched to the extent of 72.2% ee. Once again in both cases the 1*S* configuration predominated. The (*Z*)-1-propenyl ether exhibited low reactivity under promotion by MAD; however, after subsequent [3 + 2] cycloaddition, a mixture of nitroso acetal diastereomers was isolated in 72% yield. Analysis of the mixture by ^{1}H NMR revealed three diastereomers in a ratio of 1:2:29 where the major diastereomer corresponded to that observed in the $Ti(O\text{-}i\text{-}Pr)_2Cl_2$-promoted example. Cleavage to the mixture of α-hydroxy lactam methyl epimers showed the surprising preference for the endo orientation of the dienophile in the order of 8.7:1.0. Endo orientation in the presence of the exceedingly bulky Lewis acid MAD could explain the significantly slower rate. Chiral HPLC analysis of the 3,5-dinitrophenyl carbamates (**19**, **20**) showed essentially complete stereocontrol in the endo cycloaddition mode (>99.5% ee) as the 1*S* configuration. The minor exo component showed enantiomeric enrichment in the 1*R* series to the extent of only 16.9% ee.

Discussion

A combination of three stereocontrolling elements dictates the overall stereochemical outcome of the [4 + 2] cycloaddition. First, the approach of the enol ether dienophile to the nitroalkene may be either in an endo or an exo orientation with respect to the alkoxy group. Secondly, the conformation of the enol ether, either s-cis or s-trans, will define which face of the dienophile π-system will be accessible. Thirdly, the extent of dienophile face selectivity toward the *si* or the *re* face of the nitroalkene will determine the level of asymmetric induction. Because there are three variables in the [4 + 2] cycloaddition, there are eight possible combinations of diene and dienophile that can lead to products. If perfect shielding were provided by the auxiliary, four such combinations would not be allowed since the neopentyl ether in **3** or the phenyl ring in **6** would be placed between the dienophile and diene. This simplifies the analysis to four combinations, two leading to the 1*S*-configured α-hydroxy lactam, Scheme VII, and two leading to the 1*R*-configured lactam, Scheme VIII. The cycloadditions of vinyl ethers and propenyl ethers have allowed each of the three controlling elements to be studied, and their role in the origin of stereocontrol in the [4 + 2] cycloaddition can now be analyzed.

Endo/Exo Preference. The preference for the endo orientation of a vinyl ether in an inverse electron demand Diels–Alder reaction has been documented both in general[17] and in our own studies as well.[4] However, the

(17) (a) Posner, G. H.; Haces, A.; Harrison, W.; Kinter, C. M. *J. Org. Chem.* **1987**, *52*, 4836. (b) Boger, D. L.; Curran, T. T. *J. Org. Chem.* **1990**, *55*, 5439. (c) Desimoni, G.; Cellerino, G.; Minoli, G.; Tacconi, G. *Tetrahedron* **1972**, *28*, 4003. (d) Desimoni, G.; Colombo, G.; Righetti, P. P.; Tacconi, G. *Tetrahedron* **1973**, *29*, 2635.

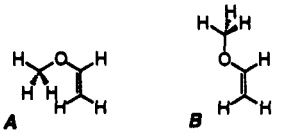


Figure 1. Possible conformation of methyl vinyl ethers.

employment of an extremely bulky Lewis acid such as MAD or MAPh coordinated to the substrate could significantly alter the selectivity. Cycloadditions of both the (*E*)- and (*Z*)-1-propenyl ethers (11) promoted by Ti(O-*i*-Pr)$_2$Cl$_2$ formed a single α-hydroxy lactam after hydrogenolytic cleavage. The resulting configuration at C(5) proved that the products were the result of an endo approach of the dienophile in the [4 + 2] cycloaddition. One would expect the endo approach of propenyl ether (*Z*)-11 would be less favored due to nonbonded interaction between the methyl substituent and the nitroalkene. However, the formation of a single α-hydroxy lactam methyl epimer (8) was conclusive proof that only the endo mode was operative. Though the 2-phenylcyclohexyl auxiliary appeared to be inherently less selective, the major α-hydroxy lactam once again corresponded to the product derived from endo approach for both the (*E*)- and (*Z*)-1-propenyl ethers (13) to the extent of 11.9:1 and 10.7:1, respectively. On the other hand, essentially a 1:1 mixture of α and β anomers was produced in the cycloaddition of vinyl ether 3 when promoted by MAD indicating an equal likelihood of exo approach as endo approach of the dienophile. This result was also supported from the cycloaddition of propenyl ether (*E*)-13 affording a 2.6:1 mixture of α-hydroxy lactams favoring the product derived from exo approach. Cycloadditions of vinyl ether 3 promoted by MAPh, however, produced a single nitroso acetal corresponding to a β-anomer which indicated an exclusive exo approach. Similarly, a β-anomer predominated from the cycloaddition with vinyl ether 6. The combination of results obtained from the three Lewis acids Ti(O-*i*-Pr)$_2$Cl$_2$, MAD, and MAPh demonstrated a shift in endo/exo selectivity from Ti(O-*i*-Pr)$_2$Cl$_2$ which promoted a very highly endo selective cycloaddition, to MAD which was unselective, and finally MAPh which promoted a highly exo selective cycloaddition.

Enol Ether Conformation. An enol ether can exist in two limiting conformations, s-cis (**A**) and s-trans (**B**), Figure 1. Extensive studies into the conformation of enol ethers have been conducted using spectroscopic and computational methods.[18] For methyl vinyl ether, spectroscopic evidence indicates that the s-cis conformation dominates while a minor component, less stable by 1.15 kcal/mol experimentally,[19] is believed to be the s-trans staggered conformation.[20] Evidence suggests, however, that sterically larger alkoxy groups (i.e., *tert*-butyl vinyl ether) favor the s-trans conformation.[21] Studies of propenyl ethers indicate that the s-trans conformation is favored for (*Z*)-1-propenyl ethers, while the conformer population is dependent on the size of the alkyl group in (*E*)-1-propenyl ethers.[22]

Table VI. Calculated MM2 Relative Ground-State Energy for Enol Ethers

	relative MM2 energy (kcal/mol)			
	camphor		phenylcyclohexyl	
enol ether	s-cis	s-trans	s-cis	s-trans
vinyl ether	0.00	1.30	0.00	0.01
(*Z*)-propenyl	3.40	0.00	5.71	0.00
(*E*)-propenyl	0.00	1.30	0.64	0.00

To obtain high asymmetric induction in the [4 + 2] cycloaddition only one enol ether conformation should be amenable to the reaction. Molecular mechanics (MM2) calculations were performed on vinyl ethers 3 and 6 as well as their corresponding propenyl ethers in attempts to establish the ground-state conformer population, Table VI. The minimized ground-state energy for both the s-cis and s-trans conformations of phenylcyclohexyl vinyl ether 6 were found to be essentially identical, therefore inferring little selectivity between the two conformations. This is in contrast to the camphor-derived vinyl ether 3 where the s-cis conformation was calculated to be favored by 1.3 kcal/mol. For the propenyl ethers of 2-phenylcyclohexanol, the s-trans (*E*)-1-propenyl ether ground-state conformation was found to be more stable than the s-cis by 0.64 kcal/mol, and likewise as expected on the basis of steric effects, the (*Z*)-1-propenyl s-trans conformation was found to be significantly more favored than the s-cis conformation. Similar calculations for the camphor-derived propenyl ethers predicted the s-cis conformation to be favored by 1.3 kcal/mol in (*E*)-1-propenyl ether 11 but disfavored by 3.4 kcal/mol in the (*Z*)-1-propenyl ether.

For both endo and exo approaches, s-cis and s-trans enol ether conformations afford enantiomeric α-hydroxy lactams after cleavage of the nitroso acetal. Since the orientation of the approach can be determined on the basis of the propenyl ether study as demonstrated above, the reactive conformation of the enol ether in the cycloaddition can be inferred from the configuration of the resulting α-hydroxy lactam. The exclusive formation of 7 from (*E*)-11 and 8 from (*Z*)-11 demonstrates that the cycloadditions with these camphor-based propenyl ethers were exclusively endo selective when promoted by Ti(O-*i*-Pr)$_2$Cl$_2$. This is the expected behavior on the basis of previous cycloadditions in the achiral series. In addition, very high asymmetric induction (99% ee, 1*S*) was observed with (*E*)-1-propenyl ether 11. On the basis of a product analysis, the observed 1*S*-configured lactam must arise from cycloaddition through the endo mode and an s-trans enol ether conformation (pathway a, Scheme VII). In the case of MAPh, the cycloaddition was found to be highly exo selective and likewise highly enantioselective affording the 1*R*-configured lactam 4 (98% ee). By a similar analysis the cycloaddition must proceed through the exo approach and again an s-trans enol ether conformation (pathway d, Scheme VIII). Therefore, in cycloadditions promoted by Ti(O-*i*-Pr)$_2$Cl$_2$ and MAPh the reactive conformation of the enol ether is the same (s-trans), but the dienophile approach changes from endo in the case of Ti(O-*i*-Pr)$_2$Cl$_2$ to exo in the case of MAPh. This analysis is also consistent with the low selectivity obtained from the MAD-promoted cycloaddition. Given that s-trans is the reactive confor-

(18) (a) Bond, D.; Schleyer, P. v. R. *J. Org. Chem.* **1990**, *55*, 1003. (b) For a review see: Fischer, P. Enol Ethers–Structure, Synthesis, and Reaction. In *The Chemistry of Ethers, Crown Ethers, Hydroxyl Groups, and their Sulphur Analogs*; Patai, S., Ed.; Wiley: New York, 1980; Part 2, p 761.

(19) Owen, N. L.; Sheppard, N. *Trans. Faraday Soc.* **1964**, *60*, 634.

(20) (a) Gallinella, E.; Cadioli, B. *J. Mol. Struct.* **1991**, *249*, 343. (b) Bernardi, F.; Epiotis, N. D.; Yates, R. L.; Schlegel, H. B. *J. Am. Chem. Soc.* **1976**, *98*, 2385.

(21) Kalabin, G. A.; Krivdin, L. B.; Shcherbakov, V. V.; Trofimov, B. A. *J. Mol. Struct.* **1986**, *143*, 569.

(22) Taskinen, E. *Tetrahedron* **1978**, *34*, 353.

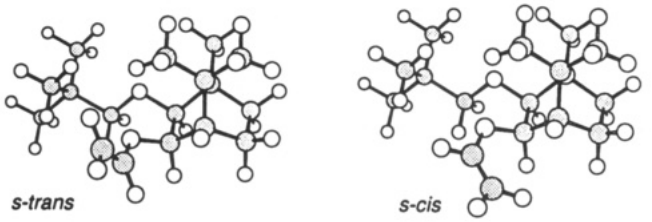


Figure 2. Calculated ground-state conformations of **3**.

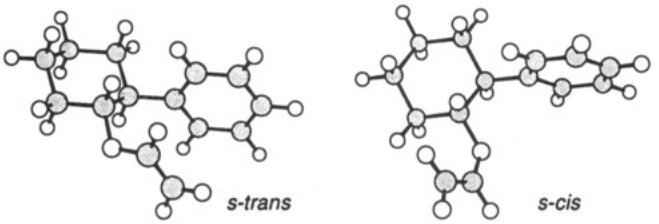


Figure 3. Calculated ground-state conformations of **6**.

mation in both the endo and exo modes, the endo *re* face approach afforded the 1*S* enantiomer while exo *si* face attack produced the 1*R* enantiomer. Since endo/exo selectivity in the reaction was essentially 1:1, the product was racemic.

Unlike the studies conducted with camphor-based propenyl ethers, a significant contribution of exo folding of the dienophile was observed for the 2-phenylcyclohexyl auxiliary. While preparatively disadvantageous this allows for additional mechanistic insight into the reversal of selectivity observed with the vinyl ethers. When promoted by $Ti(O\text{-}i\text{-}Pr)_2Cl_2$, endo approach of the (*E*)-1-propenyl ether was found to be highly selective leading to the 1*S* configuration of **7** (97.9% ee). On the basis of the preceding analysis, this product can only arise from endo, *re* face approach of the dienophile in an s-trans conformation (pathway a, Scheme VII). In the exo-derived product low selectivity was observed (64.8% ee) but interestingly still the 1*S* configuration predominated. If the s-trans conformation was operative, the opposite enantiomer would be expected. Rather the dominant approach appears to be of the s-cis conformer toward the *re* face of the nitroalkene (pathway b, Scheme VII). The similar finding for the (*Z*)-1-propenyl ether in the exo mode was unexpected since molecular mechanics calculations predicted a large ground-state energy difference between the s-cis and s-trans conformations. However, nearly identical results suggest the same possibility of s-cis participation in the exo addition mode. *From these results it can be concluded that in cycloadditions of enol ethers* **6**, (*E*)-**13**, *and* (*Z*)-**13** *promoted by* $Ti(O\text{-}i\text{-}Pr)_2Cl_2$, *attack of the enol ether in an endo approach favors the s-trans conformation while the exo approach favors the s-cis conformation.*

When promoted by MAD, the endo cycloaddition mode of both the (*E*)- and (*Z*)-1-propenyl ethers was very highly selective (>99% ee) in the 1*S* configuration. The increased steric size of the Lewis acid now effectively only allows the s-trans conformer to react in the endo mode. Exo approach of the (*E*)-1-propenyl ether follows the same arguments as discussed for the $Ti(O\text{-}i\text{-}Pr)_2Cl_2$-promoted cycloaddition with the s-cis conformer now believed to be the reactive conformation. This phenomenon allows for an explanation for the higher enantioselectivity observed with vinyl ether **6** (72% ee) than vinyl ether **3** (2% ee) when promoted by MAD. As indicated by the appearance of both α and β anomers in the cycloaddition with vinyl ether **6**, products

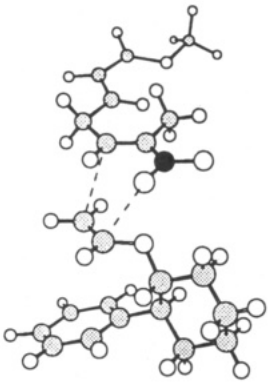


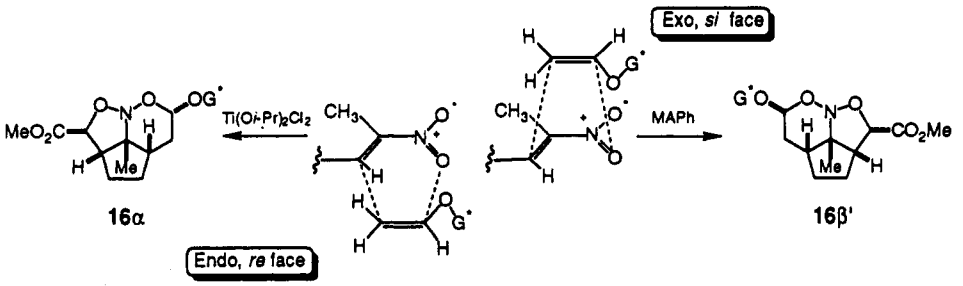
Figure 4. Endo approach of s-trans enol ether to *re* face of nitroalkene.

of both endo and exo approach of the dienophile are present. However, since the s-trans conformation is the reactive conformation in the endo mode while the s-cis conformation is reactive in the exo mode, the 1*S* enantiomer still predominates.

Dienophile π-Facial Selectivity. The dienophile face selectivity is dictated by stereodifferentiation provided by the auxiliary to the two diastereotopic π faces of the olefin. In the case of the camphor auxiliary, this is accomplished through steric blocking of one face by the neopentyl ether as shown in Figure 2 by the representations of the MM2 ground-state structures for the s-cis and s-trans conformations. It should be noted that a different face of the olefin is shielded in the two conformations. A similar effect occurs with *trans*-2-phenylcyclohexanol where the auxiliary is designed so that the phenyl ring shields one face of the olefin. As shown in Figure 3, this is indeed the case for the s-trans staggered conformation. In the s-cis conformation, however, two local minima were located by molecular mechanics calculations separated by 1.3 kcal/mol. The ground-state conformation as shown staggers the olefin away from the phenyl ring by 46°. It can be seen that this conformation would leave the theoretically shielded face of the olefin considerably open to attack. The higher local minimum corresponds to the conformer staggering the olefin toward the phenyl ring as desired. This observation would tend to suggest high stereocontrol would only be obtained from the s-trans conformer. A study of the predicted ground-state conformations of the (*E*)-1-propenyl ether **13** once again showed efficient shielding by the phenyl ring in the s-trans staggered conformation; however, significant erosion was predicted in the s-cis conformation. Likewise for the (*Z*)-1-propenyl ether **13** the s-trans conformation exhibited the desired staggering towards the phenyl ring.

The high enantioselectivities obtained in cycloadditions promoted by $Ti(O\text{-}i\text{-}Pr)_2Cl_2$ with vinyl ethers **3** (98.3% ee) and **6** (97.7% ee) are clear evidence of effective shielding by either the neopentyl ether in **3** or the phenyl ring in **6**. Endo approach of the reactive s-trans conformer to the *re* face of the nitroalkene, Figure 4, is substantially more favored than approach to the *si* face. When promoted by $Ti(O\text{-}i\text{-}Pr)_2Cl_2$ and MAD, however, exo approach of the enol ether showed only moderate selectivity (65% ee) but of the same absolute configuration as the endo mode. This was rationalized in terms of participation of the enol ether s-cis conformation in the exo mode. The low enantioselectivity is consistent with the predictions made by modeling suggesting poor facial shielding in the s-cis

Scheme IX



conformation of the phenylcyclohexanol-derived enol ethers. Stereochemical leakage presumably occurs through attack to the *si* face of the nitroalkene involving the "inner" face of the enol ether. These experiments, however, cannot unambiguously rule out leakage through an s-trans conformer.

Although camphor-derived propenyl ether (*E*)-11 showed very high asymmetric induction (99% ee), propenyl ether (*Z*)-11 only exhibited low selectivity (50% ee). Since in both cases cleavage of the nitroso acetal resulted in the formation of a single α-hydroxy lactam corresponding to the endo-derived product, the erosion of enantioselectivity cannot be related to the endo/exo selectivity. Two possible pathways can explain the lower selectivity. First, the presence of the s-cis conformation of (*Z*)-11, though unlikely based on MM2 calculations, would lead to the opposite enantiomer of 8. Second, the enol ether could react via the s-trans conformation but the neopentyl ether fails to afford adequate π-facial differentiation possibly due to steric interactions with the enol ether methyl substituent. The latter is believed to be the more plausible explanation.

Summary of Transition Structure Analysis. The interdependency of the endo/exo folding selectivity, the reactive conformation of the enol ether, and the auxiliary facial selectivity on the stereochemical outcome of the [4 + 2] cycloaddition manifests itself for both the camphor-derived auxiliary as well as for enols ethers derived from 2-phenylcyclohexanol (5). Several generalizations, however, can be made. In cycloadditions of camphor-derived enol ethers 3, (*E*)-11, and (*Z*)-11 the s-trans conformation is always the reactive conformation. The Lewis acid Ti(O-*i*-Pr)$_2$Cl$_2$ promotes a highly endo selective cycloaddition with these enol ethers favoring approach to the *re* face of the nitroalkene (pathway a, Scheme VII) as governed by the auxiliary design. On the other hand, MAPh promotes a highly exo selective cycloaddition with approach to the *si* face of the nitroalkene (pathway d, Scheme VIII). The defining factors that govern the endo/exo selectivity of the cycloaddition are a coupling of both the steric nature of the Lewis acid as well as a stereoelectronic stabilization of an attractive interaction between the nitro functionality of the diene and the alkoxy of the enol ether in the transition state. Reduced stabilization and the introduction of the steric demand afforded by the extremely bulky aluminum reagents overrides the inherent endo selectivity of the reaction. This phenomenon manifests itself as the high exo selectivity observed with MAPh.

In the case of the 2-phenylcyclohexyl-derived enol ethers 6, (*E*)-13, and (*Z*)-13 the reactive conformation of the enol ether is dependent on the nature of the Lewis acid and the orientation of the dienophile approach, endo or exo. Endo approach with the Lewis acids Ti(O-*i*-Pr)$_2$Cl$_2$, MAD, and MAPh proceeds through the s-trans conformation which minimizes nonbonded steric interactions with the nitroalkene. With Ti(O-*i*-Pr)$_2$Cl$_2$ and MAD, however, the s-cis conformation is the reactive conformation in the exo mode, while s-trans is the reactive conformation when promoted by MAPh. The switch in the enol ether reactive conformation stems from the minimization of steric strain in the transition structure which is also the basis for the observed switch in the absolute configuration in the products.

Conclusion

The Lewis acid dependent reversal of stereoselectivity in the tandem [4 + 2]/[3 + 2] nitroalkene cycloaddition arises from a switch between the endo and exo approach of the dienophile while the enol ether still presents the same diastereomeric face toward the nitroalkene. Therefore, with the (+)-camphor-derived vinyl ether 3 it is possible to obtain both enantiomeric series of cycloadducts in high selectivity by simply changing the Lewis acid since excellent π face selectivity is observed in both the endo and the exo modes of approach, Scheme IX. The 2-phenylcyclohexyl auxiliary has demonstrated its ability to provide high asymmetric induction with vinyl ethers and propenyl ethers from an endo cycloaddition mode; however, it suffers limitations in the exo mode due to the participation of a poorly shielded s-cis conformation. The Lewis acids MAD and MAPh, though superficially similar, impart very different steric environments to the nitroalkene/Lewis acid complex which not only influence the endo/exo selectivity but also the reactive conformation of the enol ether dienophile. The application of this chemistry in the total synthesis of natural products as well as the development of a readily available and highly selective auxiliary for exo mode and propenyl ether cycloadditions is currently being explored.

Experimental Section

General. For general procedures see the preceding paper in this issue.[8] Analytical high-pressure liquid chromatography was performed on a Hewlett-Packard 1090 liquid chromatograph with a Perkin-Elmer LC-75 spectrophotometric detector (λ = 254 nm) and a Pirkle Covalent L-naphthylalanine column (250 × 4.5 mm, 5 μm (Regis)). Solvent systems include method A (hexane/EtOAc, 7/3, 1.5 mL/min), method B (hexane/EtOAc, 75/25, 1.5 mL/min), or method C (hexane/EtOAc, 85/15, 2.0 mL/min, 25 min, ramp for 2 min to hexane/EtOAc, 75/25, 2.0 mL/min). Analytical capillary gas chromatography was performed using an HP5 column (50 m). Optical rotations are reported as follows: $[\alpha]^{\text{temperature}}_{\text{wavelength}}$, concentration (*c* = g/100 mL), and solvent. ^{1}H NMR and ^{13}C NMR spectra were recorded at 400 MHz ^{1}H (100 MHz ^{13}C) or at 300 MHz ^{1}H (75.5 MHz ^{13}C) in $CDCl_3$ with $CHCl_3$ (^{1}H δ = 7.26 ppm, ^{13}C δ = 77.0 ppm) or tetramethylsilane (TMS) as an internal standard. Electron impact (EI) mass spectra were

obtained at an ionization voltage of 70 eV. Low- and high-resolution fast atom bombardment (FAB) spectra were obtained on a VG ZAB-SE spectrometer in magic bullet. Data are reported in the form *m/z* (intensity relative to base = 100). Elemental analyses were performed by the University of Illinois Microanalytical Service Laboratory. Molecular modeling was performed using MM2 force field parameters as applied in the program MacroModel (version 3.0)[23] running on a Silicon Graphics 4D/25G or microVAX 2000.

(1*R*,2*S*)-*trans*-[(2-Phenylcyclohexyl)oxy]ethene (6). (−)-*trans*-2-Phenylcyclohexanol (5) (2.00 g, 11.35 mmol, 1.0 equiv) was dissolved in 50 mL of ethyl vinyl ether (0.523 mol, 46.0 equiv), and a catalytic amount of $Hg(OAc)_2$ (900 mg, 2.83 mmol, 0.25 equiv) was added. After the mixture was heated at reflux for 24 h, an additional 900 mg of $Hg(OAc)_2$ (2.83 mmol, 0.25 equiv) was added and the mixture was heated at reflux for an additional 12 h. The solution was allowed to cool to rt and was quenched with 25 mL of saturated aqueous K_2CO_3 solution. The reaction mixture was diluted with 200 mL of MTBE and was washed with saturated aqueous K_2CO_3 (3 × 25 mL). The aqueous layers were back-extracted with MTBE (2 × 25 mL). Combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified by column chromatography on basic alumina (pentane, MTBE) to yield 1.52 g of vinyl ether (−)-6 as a colorless liquid after distillation (68%) along with 590 mg of unreacted starting material 5: bp 75 °C (0.1 Torr); ^{1}H NMR (300 MHz) 7.16–7.31 (m, 5 H, HC(8–10)), 6.05 (dd, J = 14.1, 6.5, 1 H, HC(1')), 4.11 (dd, J = 14.0, 1.1, 1 H, $H_aC(2')$), 3.84 (dt, J_d = 10.3, J_t = 4.5, 1 H, HC(1)), 3.77 (dd, J = 6.6, 1.11, 1 H, $H_bC(2')$), 2.65 (dt, J_d = 11.8, J_t = 3.5, 1 H, HC(6)), 2.20–2.25 (m, 1 H), 1.86–1.94 (m, 2 H), 1.74–1.78 (m, 1 H), 1.34–1.58 (m, 4 H); ^{13}C NMR (75.5 MHz) 151.07 (C(1')), 143.66 (C(7)), 128.24 (C(9)), 127.58 (C(8)), 126.23 (C(10)), 87.37 (C(2')), 81.77 (C(1)), 50.32 (C(2)), 34.08 (C(6)), 32.14 (C(3)), 25.88 (C(4)), 24.81 (C(5)); IR (CCl_4) 3030.5 (w), 2936.0 (s), 2858.9 (m), 1632.0 (s), 1558.7 (w), 1495.0 (w), 1448.7 (m), 1356.1 (w), 1182.5 (s), 1118.9 (m), 1076.4 (s), 817.9 (s); MS (70 eV) 202.1 (M^+, 1.1), 160.1 (3.0), 159.1 (27.6), 158.1 (10.6), 91.1 (100), 81.0 (17), 67.1 (7.5), 55.1 (6.1); $[\alpha]^{25}_D$ = −42.6° (CH_2Cl_2, c = 1.15); TLC R_f 0.71 (hexane/EtOAc (2/1)). Anal. Calcd for $C_{14}H_{18}O$ (202.30): C, 83.12; H, 8.97. Found: C, 83.14; H. 8,98.

(1*R*,2*S*)-*trans*-2-Phenyl-1-(1-propynyloxy)cyclohexane (12). To a suspension of KH (1.60 g, 40 mmol, 2.0 equiv) in THF (40 mL) was added dropwise a solution of alcohol 5 (3.52 g, 20 mmol, 1.0 equiv) in THF (30 mL). The suspension was stirred at room temperature for 3 h and at 35–40 °C for 1 before being cooled to −70 °C. A solution of trichloroethylene (1.77 mL, 20 mmol, 1.0 equiv) in THF (30 mL) was added dropwise. The reaction mixture was allowed to warm to rt, and the dark brown mixture was stirred for 1 h. The solution was cooled to −70 °C, and *n*-BuLi (32.7 mL, 1.53 M in hexane, 50.0 mmol, 2.5 equiv) was added dropwise. The reaction mixture was stirred for an additional 1 h at −70 °C and then allowed to warmed to −50 °C. Iodomethane (6.23 mL, 100 mmol, 5.0 equiv) was added dropwise, and the solution was allowed to warm to rt. After 1 h, the reaction mixture was cooled to 0 °C and poured into 400 mL of a cold, saturated aqueous NH_4Cl solution. The mixture was extracted with pentane (4 × 100 mL), and the combined organic layers were washed with brine (75 mL), dried over Na_2SO_4, and concentrated in vacuo to a brown oil. The residue was purified by column chromatography (basic alumina, pentane) to yield 2.6 g of 12 (61%) as a clear liquid: mp 25 °C (hexane); bp 120 °C (0.1 Torr); ^{1}H NMR (400 MHz) 7.20–7.34 (m, 5 H, phenyl), 3.99 (dt, J_d = 4.4, J_t = 11.0, 1 H, HC(1)), 2.71 (ddd, J = 3.7, 10.7, 12.1, 1 H, HC(6)), 2.39–2.43 (m, 1 H, $H_{eq}C(2)$), 1.90–1.95 (m, 2 H), 1.74–1.78 (m, 1 H), 1.67 (s, 3 H, $H_3C(3')$), 1.39–1.66 (m, 5 H); ^{13}C NMR (100 MHz) 142.72 (C(7)), 128.28 (C(9)), 127.44 (C(8)), 126.46 (C(10)), 88.24 (C(1)), 86.16 (C(1')), 48.95 (C(6)), 33.84 (C(2')), 33.79 (C(5)), 30.95 (C(2)), 25.52 (CH_2), 24.63 (CH_2), 1.73 (C(3')); IR (CCl_4) 3065 (w), 3030 (m), 2938 (s), 2274 (s), 1495 (m), 1450 (m), 1250 (s), 1217 (m), 999 (s), 939 (s); MS (70 ev) 214 (M^+, 1), 159 (33), 145 (9), 129 (4), 117 (11), 91 (100), 81 (15), 67 (7), 55 (5), 41 (3), 39 (3); $[\alpha]^{25}_D$ = −74.7° (CH_2Cl_2, c = 1.8); TLC R_f 0.57 (hexane/EtOAc (20/1)). Anal. Calcd for $C_{15}H_{18}O$ (214.31): C, 84.07; H, 8.47. Found: C, 84.08; H, 8.47.

(1*R*,2*S*)-*trans*-2-Phenyl-1-(1(*Z*)-propenyloxy)cyclohexane ((*Z*)-13). To a mixture of 10 mL of hexane and 10 mL of methanol was added $Pd/BaSO_4$ (660 mg), and the resulting mixture was allowed to stir under 1 atm of H_2 for 15 min. A solution of propynyl ether 12 (1.00 g, 4.67 mmol, 1.0 equiv) and quinoline (606 μL, 5.13 mmol, 1.1 equiv) in 2.5 mL of methanol was added to the catalyst. The suspension was allowed to stir under 1 atm of H_2 until uptake stopped (1.5 h). The reaction mixture was filtered through Celite, washed with hexane (20 mL) and CH_2Cl_2 (20 mL), and concentrated in vacuo. The crude product was purified by column chromatography (basic alumina, pentane) and distilled to afford 710 mg (71%) of (*Z*)-13 as a clear liquid: bp 90 °C (0.05 Torr); ^{1}H NMR (400 MHz), 7.16–7.29 (m, 5 H, phenyl), 5.73 (dq, J_d = 6.1, J_q = 1.7, 1 H, HC(1')), 4.12 (dq, J_d = 6.8, J_q = 7.0, 1 H, HC(2')), 3.59 (dt, J_d = 4.2, J_t = 10.3, 1 H, HC(1)), 2.65 (ddd, J = 11.8, 3.7, 1.2, 1 H, HC(6)), 2.13–2.18 (m, 1 H, HC(2)), 1.85–1.93 (m, 2 H), 1.74–1.78 (m, 1 H), 1.35–1.59 (m, 4 H), 1.33 (dd, J = 6.6, 1.7, 3 H, $H_3C(3')$); ^{13}C NMR (100 MHz) 144.44 (C(1')), 143.92 (C(7)), 128.06 (C(8)), 127.76 (C(9)), 126.10 (C(10)), 100.64 (C(2')), 83.73 (C(1)), 50.50 (C(6)), 33.57 (CH_2), 32.88 (CH_2), 25.86 (CH_2), 24.94 (CH_2), 9.07 (C(3')); IR (CCl_4) 3032 (m), 2934 (s), 2858 (s), 1667 (s), 1495 (m), 1448 (m), 1352 (m), 1342 (m), 1259 (s), 1113 (s), 1091 (s); MS (70 ev) 216 (M^+, 1.8), 159 (15.2), 129 (4.0), 117 (10.3), 104 (3.7), 91 (100), 81 (16.2), 67 (10.0), 55 (7.7), 41 (8.5), 39 (7.2); $[\alpha]^{25}_D$ = −116.4° (CH_2Cl_2, c = 1.4); TLC R_f 0.58 (hexane/EtOAc (20/1)). Anal. Calcd for $C_{15}H_{20}O$ (216.32): C, 83.29; H, 9.32. Found: C, 83.13; H, 9.32.

(1*R*,2*S*)-*trans*-2-Phenyl-1-(1(*E*)-propenyloxy)cyclohexane ((*E*)-13). To a suspension of $LiAlH_4$ (263 mg, 6.59 mmol, 1.5 equiv) in DME (12 mL) was added a solution of propynyl ether 12 (0.950 g, 4.39 mmol, 1.0 equiv) in DME (5 mL). The mixture was heated at 80 °C for 1.5 h and then cooled to 0 °C. The reaction mixture was carefully quenched with 750 μL of water. The suspension was diluted with 20 mL of pentane and allowed to stir over Na_2SO_4 at rt for 1 h. The suspension was filtered through a plug of basic alumina and concentrated in vacuo. The crude product was purified by column chromatography (basic alumina, pentane) and distilled to afford 630 mg (66%) of (*E*)-13 as a clear liquid: bp 90 °C (0.05 Torr); ^{1}H NMR (400 MHz) 7.15–7.31 (m, 5 H, phenyl), 5.83 (dd, J = 12.3, 1.5, 1 H, HC(1')), 4.69 (dq, J_d = 13.4, J_q = 6.6, 1 H, HC(2')), 3.69 (dt, J_d = 5.0, J_t = 10.2, 1 H, HC(1)), 2.61 (ddd, J = 10.1, 3.8, 1.2, 1 H, HC(6)), 2.18–2.22 (m, 1 H, HC(2)), 1.84–1.91 (m, 2 H, HC(4)), 1.72–1.76 (m, 1 H), 1.42–1.54 (m, 1 H, HC(5)), 1.38 (dd, J = 6.6, 1.7, 3 H, $H_3C(3')$), 1.29–1.35 (m, 3 H); ^{13}C NMR (100 MHz) 145.41 (C(1')), 143.79 (C(7)), 128.03 (C(8)), 127.43 (C(9)), 125.98 (C(10)), 100.07 (C(2')), 81.90 (C(1)), 50.17 (C(6)), 34.03 (CH_2), 32.21 (CH_2), 25.77 (CH_2), 24.69 (CH_2), 12.24 (C(3')); IR (CCl_4) 3030 (m), 2934 (s), 2888 (m), 2859 (s), 1674 (s), 1655 (m), 1495 (m), 1449 (m), 1250 (w), 1169 (s), 1120 (s), 1035 (m); MS (70 eV) 216 (M^+, 2.6), 159 (20.3), 129 (2.6), 117 (7.4), 91 (100), 81 (17.0), 67 (9.0), 55 (6.4), 41 (6.1), 39 (4.6); $[\alpha]^{25}_D$ = −10.4° (CH_2Cl_2, c = 1.38); TLC R_f 0.31 (hexane). Anal. Calcd for $C_{15}H_{20}O$ (216.32): C, 83.29; H. 9.32. Found: C, 83.28; H, 9.31.

(1*S*,2*R*,3*S*,4*R*)-3-(2,2-Dimethylpropoxy)-2-(1-propynyloxy)-4,7,7-trimethylbicyclo[2.2.1]heptane (10). To a suspension of oil-free potassium hydride (626 mg, 15.61 mmol, 2.7 equiv) in THF (15 mL) was added dropwise with stirring a solution of alcohol 9 (1.40 g, 5.82 mmol) in THF (10 mL). The mixture was stirred at rt for 4 h, and the resulting pale brown mixture was treated with a solution of trichloroethylene (0.52 mL, 5.82 mmol, 1 equiv) in THF (15 mL) at −50 °C and was allowed to warm to rt. The resulting dark mixture was cooled to −78 °C and treated with *n*-BuLi (11 mL, 1.6 M in hexane, 17.47 mmol, 3 equiv) dropwise. The mixture was allowed to warm to −40 °C and was treated with iodomethane (1.82 mL, 29.12 mmol, 5 equiv). The mixture was warmed to rt and stirred for 75 min. The mixture was then cooled to 0 °C and poured into an ice-cooled saturated aqueous NH_4Cl solution. The mixture was extracted with pentane and washed with water and brine. The aqueous layers were back-extracted with pentane. The combined organic layers were dried (Na_2SO_4), filtered, and concentrated to give a brown oil. The crude product was purified by column chromatography

(23) Mohamadi, F.; Richards, N. G. J.; Guida, W. C.; Liskamp, R.; Lipton, M.; Caufield, C.; Chang, G.; Hendrickson, T.; Still, W. C. *J. Comput. Chem.* **1990**, *11*, 440.

on basic alumina (pentane) to give 1.345 g (83%) of **10** as a colorless oil: bp 75–77 °C (0.05 Torr); ^{1}H NMR (300 MHz) 4.06 (d, J = 6.4, 1 H, HC(2)), 3.40, 2.92 (ABq, J = 7.8, 2 H, $H_2C(1'')$), 3.23 (d, J = 6.4, 1 H, HC(3)), 2.10 (d, J = 5.0, 1 H, HC(1)), 1.74 (s, 3 H, $H_3C(3')$), 1.72–1.44 (m, 2 H), 1.10 (s, 3 H, CH_3), 1.01–0.91 (m, 2 H), 0.91 (s, 9 H, 3 × $H_3C(3'')$), 0.88 (s, 3 H, CH_3), 0.78 (s, 3 H, CH_3); ^{13}C NMR (75.5 MHz) 92.14 (C(2)), 88.88 (C(1')), 87.62 (C(3)), 83.02 (C(1'')), 49.90 (C), 48.94 (C(1)), 46.57 (C), 33.44 (CH_2), 32.53 (C), 32.45 (C), 26.82 (CH_3), 23.53 (CH_2), 20.93 (CH_3), 20.43 (CH_3), 11.42 (CH_3), 1.92 (C(3')); IR (CCl_4) 2955 (s), 2880 (m), 2276 (s), 1475 (m), 1458 (m), 1393 (m), 1362 (m), 1289 (w), 1252 (s), 1190 (w), 1142 (m), 1117 (m), 1086 (m), 1034 (m), 1018 (m), 999 (m); MS (70 eV) 153 (48), 135 (14), 109 (16), 95 (12), 93 (10), 71 (100), 55 (15), 43 (74), 41 (22); TLC R_f 0.45 (pentane); GC t_R 14.50 min (HP-5, 150 °C (4 min), 10 °C/min, 250 °C). Anal. Calcd for $C_{18}H_{30}O_2$ (278.43): C, 77.65; H, 10.86. Found: C, 77.66; H, 10.87.

(1*S*,2*R*,3*S*,4*R*)-3-(2,2-Dimethylpropoxy)-2-(1(*E*)-propenyloxy)-4,7,7-trimethylbicyclo[2.2.1]heptane ((*E*)-11). To a suspension of lithium aluminum hydride (0.138 g, 3.636 mmol, 1.5 equiv) in diglyme (5 mL) was added a solution of **10** (0.683 g, 2.453 mmol) in diglyme (2 mL) and the resulting mixture allowed to stir at 80 °C. After 1 h, the reaction mixture was cooled to 0 °C and quenched with water (256 μL, 14.2 mmol, 6 equiv). The mixture was diluted with pentane, and Na_2SO_4 was added. After being stirred at rt for 1 h, the mixture was filtered through a basic alumina plug and concentrated. The residue was purified by column chromatography on basic alumina (pentane) to give 0.611 g (89%) of (*E*)-**11** as a colorless oil: bp 67–69 °C (0.05 Torr); ^{1}H NMR (300 MHz) 6.15 (d, J = 12.5, 1 H, HC(1')), 4.69 (dq, J_d = 12.6, J_q = 6.4, 1 H, HC(2')), 3.75 (d, J = 6.7, 1 H, HC(2)), 3.24, 2.91 (ABq, J = 7.9, 2 H, $H_2C(1'')$), 3.19 (d, J = 6.6, 1 H, HC(3)), 1.80 (d, J = 4.7, 1 H, HC(1)), 1.68–1.42 (m, 2 H), 1.54 (d, J = 6.4, 3 H, $H_3C(3')$), 1.12 (s, 3 H, CH_3), 1.10–0.92 (m, 2 H), 0.89 (s, 12 H, 3 × $H_3C(3'')$, CH_3), 0.76 (s, 3 H, CH_3); ^{13}C NMR (75.5 MHz) 145.99 (C(1')), 99.74 (C(2')), 88.45 (C(2)), 87.20 (C(3)), 82.82 (C(1'')), 49.94 (C(1)), 49.67 (C), 46.59 (C), 33.76 (CH_2), 32.52 (C), 26.94 (CH_3), 23.99 (CH_2), 21.11 (CH_3), 20.69 (CH_3), 11.67 (CH_3), 9.60 (CH_3); IR (CCl_4) 2955 (s), 2884 (m), 1674 (w), 1653 (w), 1476 (w), 1458 (w), 1391 (w), 1372 (w), 1362 (w), 1175 (m), 1134 (m), 1119 (m), 1067 (w), 922 (w); MS (70 eV) 280 (M^+, 3), 153 (38), 135 (21), 109 (22), 95 (13), 93 (12), 83 (12), 71 (100), 57 (12), 55 (15), 43 (73), 41 (27); TLC R_f 0.62 (pentane); GC t_R 13.561 min (HP-5, 150 °C (4 min), 10 °C/min, 250 °C). Anal. Calcd for $C_{18}H_{32}O_2$ (280.45): C, 77.09; H, 11.50. Found: C, 77.20; H, 11.47.

(1*S*,2*R*,3*S*,4*R*)-3-(2,2-Dimethylpropoxy)-2-(1(*Z*)-propenyloxy)-4,7,7-trimethylbicyclo[2.2.1]heptane ((*Z*)-11). A solution of **10** (0.825 g, 2.96 mmol) and quinoline (0.20 mL) in methanol (15 mL) was added to a suspension of preactivated 5% palladium on barium sulfate (0.421 g) in hexane (15 mL). The mixture was allowed to stir under H_2 (1 atm) at rt. After 1 h the catalyst was filtered off and the filtrate was concentrated. The residue was purified by column chromatography on basic alumina (pentane) to give 0.728 g (88%) of (*Z*)-**11** as a colorless oil: bp 65–67 °C (0.05 Torr); ^{1}H NMR (300 MHz) 5.95 (dd, J = 5.9, 1.2, 1 H, HC(1')), 4.31 (quintet, J = 6.6, 1 H, HC(2')), 3.74 (d, J = 6.6, 1 H, HC(2)), 3.35, 2.87 (d, J = 7.9, 2 H, $H_2C(1'')$), 3.21 (d, J = 6.6, 1 H, HC(3)), 1.77 (d, J = 4.8, 1 H, HC((4)), 1.65–1.41 (m, 2 H), 1.56 (dd, J = 6.8, 1.2, 3 H, $H_3C(3')$), 1.18 (s, 3 H, CH_3), 1.13–0.94 (m, 2 H), 0.90 (s, 12 H, 3 × $H_3C(3'')$, CH_3), 0.77 (s, 3 H, CH_3); ^{13}C NMR (75.5 MHz) 149.78 (C(1')), 98.49 (C(2')), 88.11 (C(2)), 84.35 (C(3)), 82.71 (C(1'')), 49.59 (C), 49.23 (C(1)), 46.67 (C), 33.62 (CH_2), 32.54 (CH), 26.89 (CH_3), 24.04 (CH_2), 21.13 (CH_3), 20.64 (CH_3), 12.76 (CH_3), 11.62 (CH_3); IR (CCl_4) 3040 (w), 2653 (s), 2880 (m), 1667 (m), 1476 (m), 1458 (w), 1408 (w), 1391 (w), 1372 (w), 1358 (m), 1256 (m), 1152 (m), 1119 (m), 1103 (m), 1080 (m), 1061 (w); MS (70 eV) 280 (M^+, 3), 153 (39), 135 (19), 109 (21), 95 (13), 93 (12), 83 (11), 81 (11), 71 (100), 57 (12), 55 (15), 43 (73), 41 (27); TLC R_f 0.55 (pentane); GC t_R 13.63 min (HP-5, 150 °C (4 min), 10 °C/min, 250 °C). Anal. Calcd for $C_{18}H_{32}O_2$ (280.45): C, 77.09; H, 11.50. Found: C, 77.04; H, 11.44.

Cycloadditions Promoted by Ti(O-*i*-Pr)$_2$Cl$_2$. General Procedure. To a cold (–90 or –78 °C) solution of nitroalkene **1** (199 mg, 1.00 mmol, 1.0 equiv) in CH_2Cl_2 (5.0 mL) was added a solution of chiral enol ether (1.50 mmol, 1.5 equiv) in CH_2Cl_2 (1.0 mL). A freshly prepared solution of dichlorotitanium diisopropoxide (3.00 mmol, 3.0 equiv) in CH_2Cl_2 (1.6 mL) was added dropwise over 10 min. The resulting pale yellow solution was stirred at –90 or –78 °C for a specified length of time. The reaction mixture was quenched with a 1 N solution of NaOH in methanol (6.0 mL) and allowed to warm for 5 min. The mixture was diluted with 200 mL of CH_2Cl_2 and was washed with water (2 × 50 mL) and brine (50 mL). The aqueous layers were back-extracted with CH_2Cl_2 (2 × 100 mL). The combined organic layers were dried over $MgSO_4$/$NaHCO_3$ (1:1) and concentrated in vacuo. The crude concentrate was allowed to stand at rt for a specified length of time to allow for the [3 + 2] cycloaddition to occur. The crude products were then purified by column chromatography to afford the corresponding nitroso acetal.

Cycloadditions Promoted by MAPh. General Procedure. To a solution of 2,6-diphenylphenol in CH_2Cl_2 was added dropwise Me_3Al (2.0 M in toluene). The solution was allowed to stir at rt for 30 min and then was cooled to 0 °C. A solution of nitroalkene **1** (199 mg, 1.00 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) was added dropwise resulting in a deep, red colored solution. The mixture was cooled to –78 °C, and then a solution of chiral enol ether in CH_2Cl_2 (1.0 mL) was added dropwise. The reaction mixture was allowed to stir at –78 °C for a specified length of time and then was quenched with 2.0 mL of water. The reaction mixture was diluted with 200 mL of CH_2Cl_2 and was washed with water (2 × 75 mL) and brine (50 mL). The aqueous layers were back-extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried over $MgSO_4$/$NaHCO_3$ (1:1) and concentrated in vacuo. The crude concentrate was allowed to stand at rt for a specific length of time to allow for the [3 + 2] cycloaddition to occur and then was purified by column chromatography to afford the corresponding nitroso acetal.

Cycloadditions Promoted by MAD. General Procedure. To a solution of 2,6-di-*tert*-butyl-4-methylphenol (1.32 g, 6.00 mmol, 6.0 equiv) in toluene (6.0 mL) was added dropwise Me_3Al (2.0 M in toluene, 1.50 mL, 3.0 mmol, 3.0 equiv). The clear solution was allowed to stir at rt for 1 h before being cooled to –78 °C. A solution of nitroalkene **1** (199 mg, 1.00 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) was added dropwise resulting in a deep, red colored solution. The mixture was allowed to stir for 10 min, and a solution of chiral enol ether in CH_2Cl_2 (1.0 mL) was added dropwise over 10 min. The reaction mixture was allowed to stir at –78 °C for a specified amount of time as the red color gradually faded to yellow. The reaction mixture was quenched with 2.5 mL of water and was allowed to warm until the yellow color disappeared. The reaction mixture was diluted with 100 mL of CH_2Cl_2 and washed with water (3 × 50 mL), and the aqueous layers were back-extracted with CH_2Cl_2 (3 × 25 mL). The combined organic layers were dried over $MgSO_4$/$NaHCO_3$ (1:1) and concentrated in vacuo. The crude concentrate was allowed to stand at rt for a specified length of time to allow for the [3 + 2] cycloaddition to occur and then was purified by column chromatography to afford the corresponding nitroso acetal.

Hydrogenolysis. General Procedure. To a solution of the nitroso acetal (0.623 mmol) in methanol (35 mL) was added a catalytic amount of Raney nickel. The suspension was stirred for 24 h under 1 atm of H_2 at rt, filtered through Celite, and concentrated in vacuo. The residue was purified by column chromatography (hexane/EtOAc (1/1, 1/3)) to afford the corresponding α-hydroxy lactam as a white solid.

Derivatization. General Procedure. A solution of 3,5-dinitrobenzoyl azide (29 mg, 0.121 mmol, 1.1 equiv) in toluene (5 mL) was heated at reflux for 15 min. A solution of the α-hydroxy lactam (0.110 mmol, 1.0 equiv) in toluene (1.0 mL) was then added. The solution was heated at reflux for 1 h and then was allowed to cool to rt. The reaction mixture was concentrated in vacuo, and the crude product was purified by column chromatography (hexane/EtOAc (3/1, 1/1)) to afford the corresponding 3,5-dinitrophenyl carbamate as a white solid.

***rel*-(1*S*,3*R*,5*S*,5a*S*,7a*S*,7b*R*)-Octahydro-1-[*N*-(3,5-dinitrophenyl)carbamoxy]-5,7b-dimethyl-2*H*-cyclopenta[*gh*]pyrrolizin-2-one ((±)-19).** A solution of 3,5-dinitrobenzoyl azide (11 mg, 0.046 mmol, 1.1 equiv) in toluene (5 mL) was heated to reflux for 10 min, and a solution of (±)-7 from ethyl (*E*)-1-propenyl ether[8] (8 mg, 0.041 mmol) in toluene (1 mL) was added. The mixture was heated to reflux for 10 min, cooled to rt, and

concentrated. The off-white solid was purified by column chromatography on silica gel (hexane/EtOAc (3/1, 1/1)) to afford 14 mg (82%) of (±)-19 as a white solid: ^{1}H NMR (300 MHz) 9.60 (br, 1 H, NH), 8.63 (d, J = 2.0, 1 H, HC(6′)), 8.58 (d, J = 1.9, 2 H, 2 × HC(4′)), 5.86 (d, J = 6.7, 1 H, HC(1)), 4.12 (dd, J = 11.9, 7.3, 1 H, HC(4)), 2.76–2.63 (m, 2 H), 1.98 (m, 2 H), 1.64–1.49 (m, 4 H), 1.46 (s, 3 H, H_3C(8)), 1.13 (d, J = 6.7, 3 H, H_3C(9)); ^{13}C NMR (75.5 MHz) 171.58 (C(2)), 152.57 (C(1′)), 148.65 (C(5′)), 141.10 (C(3′)), 118.12 (C(4′)), 112.48 (C(6′)), 75.85 (C(1)), 74.85 (7b)), 58.11, 50.82, 50.21, 42.55, 31.18, 26.18, 24.13, 17.54; TLC R_f 0.47 (hexane/EtOAc (1/1)); HPLC (method A) t_R (1*R*)-19, 5.72 min (49.53%) and t_R (1*S*)-19, 17.44 min (50.49%).

***rel*-(1*S*,3*R*,5*R*,5a*S*,7a*S*,7b*R*)-Octahydro-1-[*N*-(3,5-dinitrophenyl)carbamoxy]-5,7b-dimethyl-2*H*-cyclopenta[*gh*]pyrrolizin-2-one ((±)-20).** A solution of 3,5-dinitrobenzoyl azide (13 mg, 0.056 mmol, 1.1 equiv) in toluene (5 mL) was heated to reflux for 10 min, and a solution of (±)-8 from ethyl (*Z*)-1-propenyl ether[8] (10 mg, 0.051 mmol) in toluene (1 mL) was added. The mixture was heated to reflux for 10 min, cooled to rt, and concentrated. The off-white solid was purified by column chromatography on silica gel (hexane/EtOAc (3/1, 1/1)) to afford 18 mg of (86%) of (±)-20 as a white solid: ^{1}H NMR (300 MHz) 10.30 (br, 1 H, NH), 8.61 (t, J = 1.8, 1 H, HC(5′)), 8.55 (d, J = 1.8, 2 H, 2 × HC(3′)), 5.94 (d, J = 7.9, 1 H, HC(1)), 3.36 (t, J = 9.6, 1 H, HC(4)), 3.24 (dd, J = 11.8, 8.6, 1 H, HC(4)), 2.92 (t, J = 8.3, 1 H), 2.77 (quintet, J = 6.7, 1 H), 2.23–1.65 (m, 4 H), 1.48 (s, 3 H, H_3C(8)), 1.25–1.10 (m, 1 H), 1.07 (d, J = 6.9, 3 H, H_3C(9)); ^{13}C NMR (75.5 MHz) 172.97 (C(2)), 152.44 (C(1′)), 148.67 (C(4′)), 141.21 (C(3′)), 118.16 (C(4′)), 112.53 (C(6″)), 77.92 (C(1)), 73.95 (C(7b)), 54.23, 48.83, 47.75, 34.05, 25.99, 25.70, 21.79 (C(8)), 15.13 (C(9)); TLC R_f 0.46 (hexane/EtOAc (1/1)); HPLC (method A) t_R (1*R*)-20, 6.41 min (48.86%) and t_R (1*S*)-20, 22.05 min (51.14%).

Inter [4 + 2]/Intra [3 + 2] Tandem Cycloadditions with Vinyl Ether 6. Promoted by Ti(O-*i*-Pr)$_2$Cl$_2$: (2*S*,2a*S*,4a*S*,6*S*,7a*R*,7b*R*)-6-[(1*R*,2*S*)-2-(Phenylcyclohexyl)oxy]octahydro-7b-methyl-1,7-dioxa-7a-azacyclopent[*cd*]indene-2-carboxylic Acid Methyl Ester (14α). To a cold (−90 °C) solution of nitroalkene 1 (199 mg, 1.00 mmol, 1.0 equiv) in CH_2Cl_2 (5.0 mL) was added a solution of vinyl ether 6 (303 mg, 1.50 mmol, 1.5 equiv) in CH_2Cl_2 (1.0 mL) and a solution of dichlorotitanium diisopropoxide (3.00 mmol, 3.0 equiv) in CH_2Cl_2 (1.6 mL). The solution was stirred at −90 °C for 30 min and then at −78 °C for an additional 3 h. After standing for 6 h at rt, the crude products were then purified by column chromatography (hexane/MTBE (6/1,4/1)) to afford 295 mg (74%) of nitroso acetals 14α, 14β (ratio 81:1 by ^{1}H NMR) and 26 mg of recovered nitroalkene 1. An analytical sample of 14α was obtained by recrystallization from hexane/EtOAc. Data for 14α: mp 86–88 °C; ^{1}H NMR (300 MHz) 7.15–7.30 (m, 5 H, HC(phenyl)), 4.82 (d, J = 8.3, 1 H, HC(2)), 4.42 (dd, J = 6.2, 3.6, 1 H, HC(6)), 3.78 (s, 3 H, HC(10)), 3.68 (dt, J_d = 10.2, J_t = 4.8, 1 H, HC(1′)), 2.65 (dt, J_d = 8.4, J_t = 3.0, 1 H, HC(2a)), 2.51 (ddd, J = 10.3, 13.1, 3.5, 1 H, HC(6′)), 2.15–2.20 (m, 1 H), 1.97–2.06 (m, 1 H), 1.71–1.89 (m, 7 H), 1.57 (dd, J = 12.8, 3.2, 2 H, H_2C(5′)), 1.21–1.45 (m, 5 H), 1.17 (s, 3 H, H_3C(8)); ^{13}C NMR (75.5 MHz) 170.21 (C(9)), 143.98 (C(7′)), 128.02 (C(9′)), 127.97 (C(8′)), 126.12 (C(10′)), 100.77 (C(6)), 86.54 (C(2)), 83.93 (C(1′)), 82.91 (C(7b)), 57.17 (C(2a)), 52.30 (C(10)), 51.39 (C(4a)), 43.34 (C(6′)), 35.11 (CH_2), 34.06 (CH_2), 32.74 (CH_2), 28.09 (CH_2), 25.74 (CH_2), 25.16 (CH_2), 24.47 (C(8)); IR (CCl_4) 2934 (s), 2858 (m), 1744 (m), 1716 (m), 1558 (m), 1448 (w), 1253 (w), 1205 (w), 1097 (w), 1018 (w); MS (70 eV) 213 (3.1), 195 (11.2), 159 (55.4), 117 (10.1), 91 (100), 81 (29.6), 67 (9.6), 55 (8.7); TLC R_f 0.45 (hexane/EtOAc (2/1)). Anal. Calcd for $C_{23}H_{31}NO_5$ (401.50): C, 68.81; H, 7.78; N, 3.49. Found: C, 68.83; H, 7.79; N, 3.39.

(1*S*,3*R*,5a*S*,7a*S*,7b*R*)-Octahydro-1-hydroxy-7b-methyl-2*H*-cyclopenta[*gh*]pyrrolizin-2-one (4). Hydrogenolysis of the mixture of nitroso acetals 14α and 14β (250 mg, 0.623 mmol) afforded 85 mg (76%) of 4 as a white solid and 101 mg (82%) of recovered alcohol 5. Data for 4: ^{1}H NMR (300 MHz) 4.68 (d, J = 7.2, 1 H, HC(1)), 3.89 (ddd, J = 12.0, 8.5, 3.6, 1 H, HC(4)), 2.93 (dt, J_d = 11.8, J_t = 8.0, 1 H, HC(4)), 2.79 (br, 1 H, HOC(1)), 2.65 (q, J = 7.4, 1 H, HC(7a)), 2.25 (m, 1 H), 1.76 (m, 3 H), 1.47 (m, 1 H), 1.31 (s, 3 H, H_3C(8)), 1.26 (m, 1 H); IR (CCl_4) 3390 (m), 2961 (s), 2869 (m), 1732 (s), 1345 (m); $[\alpha]^{25}_D$ = −36.9° (CH_2Cl_2, c = 0.98); TLC R_f 0.10 (hexane/EtOAc (1/1)).

(1*S*,3*R*,5a*S*,7a*S*,7b*R*)-Octahydro-1-[*N*-(3,5-dinitrophenyl)carbamoxy]-7b-methyl-2*H*-cyclopenta[*gh*]pyrrolizin-2-one (15). Derivatization of 4 (20.0 mg, 0.110 mmol, 1.0 equiv) afforded 36 mg (84%) of 15 as a white solid: ^{1}H NMR (300 MHz) 9.96 (bs, 1 H, NH), 8.63 (d, J = 1.9, 1 H, HC(6′)), 8.58 (d, J = 1.9, 2 H, HC(4′)), 5.92 (d, J = 7.2, 1 H, HC(1)), 3.96 (ddd, J = 12.3, 8.6, 3.8, 1 H, HC(4)), 3.08 (dt, J_d = 11.9, J_t = 3.4, 1 H, HC(4)), 2.82 (q, J = 7.3, 1 H, HC(7a)), 2.40 (m, 1 H), 2.21–2.29 (m, 1 H, HC(5a)), 1.46–1.90 (m, 3 H), 1.44 (s, 3 H, H_3C(8)), 1.25–1.30 (m, 1 H); IR ($CDCl_3$) 2965 (w), 1690 (m), 1547 (m), 1346 (m), 1246 (m), 1223 (m); TLC R_f 0.38 (hexane/EtOAc (1/1)); HPLC (method B) t_R (1*R*)-15 9.8 min (1.1%), t_R (1*S*)-15 29.7 min (98.9%).

Promoted by MAPh: (2*R*,2a*R*,4a*R*,6*R*,7a*R*,7b*S*)-6-[(1*R*,2*S*)-2-(Phenylcyclohexyl)oxy]octahydro-7b-methyl-1,7-dioxa-7a-azacyclopent[*cd*]indene-2-carboxylic Acid Methyl Ester (14β′), (2*S*,2a*S*,4a*S*,6*R*,7a*R*,7b*R*)-6-[(1*R*,2*S*)-2-(Phenylcyclohexyl)oxy]octahydro-7b-methyl-1,7-dioxa-7a-azacyclopent-[*cd*]indene-2-carboxylic Acid Methyl Ester (14β), and (2*S*,2a*S*,4a*S*,6*S*,7a*R*,7b*R*)-6-[(1*R*,2*S*)-2-(Phenylcyclohexyl)oxy]octahydro-7b-methyl-1,7-dioxa-7a-azacyclopent[*cd*]indene-2-carboxylic Acid Methyl Ester (14α). To a solution of 2,6-diphenylphenol (1.48 g, 6.00 mmol, 6.0 equiv) in CH_2Cl_2 (15 mL) was added Me_3Al (2.0 M in toluene, 1.50 mL, 3.0 mmol, 3.0 equiv). After 30 min, a solution of nitroalkene 1 (199 mg, 1.00 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) was added at 0 °C, and then a solution of vinyl ether 6 (607 mg, 3.0 mmol, 3.0 equiv) in CH_2Cl_2 (1.0 mL) was added at −78 °C. The reaction mixture was allowed to stir at −78 °C for 3 h. After standing for 10 h at rt, the crude products were purified by column chromatography (hexane/EtOAc (20/1, 10/1, 4/1)) to afford 344 mg (86%) of a mixture of nitroso acetals (14α:14β:14β′ = 1.0:2.0:38.7 by ^{1}H NMR) and 1.4 g of recovered 2,6-diphenylphenol. An analytical sample of 14β′ was obtained by recrystallization from hexane/EtOAc. Data of 14β′: mp 152–153 °C (EtOAc/hexane); ^{1}H NMR (300 MHz) 7.18–7.29 (m, 5 H, HC(8′–10′)), 4.75 (d, J = 6.8, 1 H, HC(2)), 4.24 (t, J = 7.5, 1 H, HC(6)), 3.57 (dt, J = 10.2, 4.5, 1 H, HC(1′)), 3.77 (s, 3 H, H_3C(10)), 2.64 (m, 1 H, HC(2a)), 2.54 (ddd, J = 3.7, 10.4, 10.2, HC(6′)), 2.32–2.36 (m, 1 H), 1.74–1.85 (m, 8 H), 1.43–1.65 (m, 7 H), 1.27 (s, 3 H, H_3C(8)); ^{13}C NMR (75.5 MHz) 170.3 (C(10)), 144.3 (C(7′)), 127.9 (C(8′),C(9′)), 126.0 (C(10′)), 99.5 (C(6)), 87.1 (C(2)), 84.9 (C(1′)), 82.0 (C(7b)), 56.7 (C(2a)), 52.3 (C(10)), 51.2 (C(4a)), 42.9 (C(6′)), 34.5 (CH_2), 32.6 (CH_2), 31.3 (CH_2), 28.7 (CH_2), 26.5 (CH_2), 25.8 (CH_2), 25.2 (CH_2), 23.6 (C(8)); IR (CCl_4) 3030 (m), 2934 (s), 2859 (m), 1743 (s), 1653 (w), 1558 (m), 1449 (m), 1115 (m), 1072 (s), 1005 (m); MS (70 eV) 213 (2.5), 195 (8.6), 159 (48.6), 117 (8.8), 91 (100), 81 (26.8), 67 (8.5), 55 (8.4), 41 (10.4); TLC R_f 0.45 (hexane/EtOAc (2/1)). Anal. Calcd for $C_{23}H_{31}NO_5$ (401.50): C, 68.81; H, 7.78; N, 3.49. Found: C, 68.81; H, 7.81; N, 3.46.

(1*R*,3*S*,5a*R*,7a*R*,7b*S*)-Octahydro-1-hydroxy-7b-methyl-2*H*-cyclopenta[*gh*]pyrrolizin-2-one (4). Hydrogenolysis of the mixture of nitroso acetals 14β′, 14α, and 14β (300 mg, 0.747 mmol) afforded 102 mg (76%) of 4 as a white solid and 128 mg (97%) of recovered alcohol 5. Data for 4: ^{1}H NMR (300 MHz) 4.69 (d, J = 7.2, 1 H, HC(1)), 3.91 (ddd, J = 12.0, 8.5, 3.6, 1 H, HC(4)), 2.93 (dt, J_d = 11.8, J_t = 8.0, 1 H, HC(4)), 2.84 (br, 1 H, HOC(1)), 2.65 (q, J = 7.4, 1 H, HC(7a)), 2.27 (m, 1 H), 1.62–1.84 (m, 3 H), 1.42–1.55 (m, 1 H), 1.31 (s, 3 H, H_3C(8)), 1.26 (m, 1 H); IR (CCl_4) 3360 (b, m), 2961 (s), 2850 (m), 1703 (s), 1390 (m), 1310 (m); $[\alpha]^{25}_D$ = +28.9° (CH_2Cl_2, c = 1.35); TLC R_f 0.10 (hexane/EtOAc (1/1)).

(1*R*,3*S*,5a*R*,7a*R*,7b*S*)-Octahydro-1-[*N*-(3,5-dinitrophenyl)carbamoxy]-7b-methyl-2*H*-cyclopenta[*gh*]pyrrolizin-2-one (15). Derivatization of 4 (20.0 mg, 0.110 mmol, 1.0 equiv) afforded 32 mg (76%) of 15 as a white solid: ^{1}H NMR (300 MHz, $CDCl_3$) 9.99 (bs, 1 H, NH), 8.63 (d, J = 2.0, 1 H, HC(6′)), 8.57 (d, J = 1.7, 2 H, HC(4′)), 5.93 (d, J = 7.1, 1 H, HC(1)), 3.95 (ddd, J = 10.3, 8.4, 4.6, 1 H, HC(4)), 3.08 (dt, J_d = 12.1, J_t = 4.3, 1 H, HC(4)), 2.83 (q, J = 7.3, 1 H, HC(7a)), 2.37–2.42 (m, 1 H), 2.18–2.27 (m, 1 H, HC(5a)), 1.46–1.90 (m, 3 H), 1.45 (s, 3 H, H_3C(8)), 1.25–1.31 (m, 1 H); IR ($CDCl_3$) 2966 (w), 1693 (m), 1549 (m), 1346 (m), 1223 (m); TLC R_f 0.35 (hexane/EtOAc (1/1)); HPLC (method A) t_R (1*R*)-15 6.7 min (89.6%), t_R (1*S*)-15 19.7 min (10.4%).

Promoted by MAD: (2*S*,2a*S*,4a*S*,6*S*,7a*R*,7b*R*)-6-[(1*R*,2*S*)-2-(Phenylcyclohexyl)oxy]octahydro-7b-methyl-1,7-dioxa-7a-azacyclopent[*cd*]indene-2-carboxylic Acid Methyl Ester

(14α), (2*S*,2a*S*,4a*S*,6*R*,7a*R*,7b*R*)-6-[(1*R*,2*S*)-2-(Phenylcyclohexyl)oxy]octahydro-7b-methyl-1,7-dioxa-7a-azacyclopent[*cd*]indene-2-carboxylic Acid Methyl Ester (14β), and (2*R*,2a*R*,4a*R*,6*R*,7a*R*,7b*S*)-6-[(1*R*,2*S*)-2-(Phenylcyclohexyl)oxy]octahydro-7b-methyl-1,7-dioxa-7a-azacyclopent[*cd*]indene-2-carboxylic Acid Methyl Ester (14β′). To a solution of 2,6-di-*tert*-butyl-4-methylphenol (1.32 g, 6.00 mmol, 6.0 equiv) in toluene (6.0 mL) was added Me_3Al (2.0 M in toluene, 1.50 mL, 3.0 mmol, 3.0 equiv). To the cold (−78 °C) solution of MAD was added a solution of nitroalkene **1** (199 mg, 1.00 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) and then a solution of vinyl ether **6** (303 mg, 1.5 mmol, 1.5 equiv) in CH_2Cl_2 (1.0 mL). The reaction mixture was allowed to stir at −78 °C for 1 h. After standing for 8 h at rt the crude products were purified by column chromatography (hexane/MTBE (6/1, 4/1)) to afford 351 mg (87%) of a mixture of nitroso acetals (14α:14β:14β′ = 3.5:1.5:1.0 by ^1H NMR). Data for **14β**, **14α**, and **14β′**: ^1H NMR (300 MHz) 7.14–7.36 (m, 5 H, HC(phenyl)), 5.28 (t, J = 7.2, 0.3 H, HC(6)), 4.83 (d, J = 8.2, 0.5 H, HC(2)), 4.81 (d, J = 8.2, 0.4 H, HC(2)), 4.76 (d, J = 8.2, 0.1 H, HC(2)), 4.43 (dd, J = 6.3, 4.6, 0.5 H, HC(6)), 4.19–4.25 (m, 0.5 H, HC(6)), 3.80 (s, 1.2 H, H_3C(10)), 3.78 (s, 1.4 H, H_3C(10)), 3.77 (s, 0.4 H, H_3C(10)), 3.59–3.64 (m, 1 H, HC(1′)), 1.20–2.68 (m, 11 H), 1.18 (s, 1.8 H, H_3C(8)), 1.14 (s, 1.2 H, H_3C(8)).

(1*S*,3*R*,5a*S*,7a*S*,7b*R*)-Octahydro-1-hydroxy-7b-methyl-2*H*-cyclopenta[*gh*]pyrrolizin-2-one (4). Hydrogenolysis of the mixture of nitroso acetals 14α, 14β, and 14β′ (350 mg, 0.872 mmol) afforded 115 mg (73%) of **4** as a white solid and 119 mg (78%) of recovered alcohol **5**. Data for **4**: ^1H NMR (300 MHz), 4.68 (d, J = 7.2, 1 H, HC(1)), 3.91 (ddd, J = 12.0, 8.5, 3.6, 1 H, HC(4)), 2.93 (dt, J_d = 11.8, J_t = 8.0, 1 H, HC(4)), 2.78 (br, 1 H, HOC(1)), 2.62 (q, J = 7.4, 1 H, HC(7a)), 2.28 (m, 1 H), 1.70–1.85 (m, 3 H), 1.43–1.55 (m, 1 H), 1.32 (s, 3 H, H_3C(8)), 1.26 (m, 1 H); IR (CCl_4) 3470 (b,m), 2961 (s), 2860 (m), 1705 (s), 1390 (m), 1395 (m), 1320 (m); $[\alpha]^{25}_D$ = −28.3° (CH_2Cl_2, c = 1.07); TLC R_f 0.19 (hexane/EtOAc (1/1)).

(1*S*,3*R*,5a*S*,7a*S*,7b*R*)-Octahydro-1-[*N*-(3,5-dinitrophenyl)carbamoxy]-7b-methyl-2*H*-cyclopenta[*gh*]pyrrolizin-2-one (15). Derivatization of **4** (20.0 mg, 0.110 mmol, 1.0 equiv) afforded 32 mg (74%) of **15** as a white solid: ^1H NMR (300 MHz) 10.12 (bs, 1 H, NH), 8.62 (d, J = 2.0, 1. H, HC(6′)), 8.56 (d, J = 1.9, 2 H, HC(4′)), 5.94 (d, J = 7.2, 1 H, HC(1)), 3.95 (ddd, J = 12.1, 8.3, 3.7, 1 H, HC(4)), 3.08 (dt, J_d = 11.9, J_t = 3.4, 1 H, HC(4)), 2.82 (q, J = 7.1, 1 H, HC(7a)), 2.37–2.41 (m, 1 H), 2.21–2.27 (m, 1 H, HC(5a)), 1.48–1.91 (m, 3 H), 1.44 (s, 3 H, H_3C(8)), 1.25–1.30 (m, 1 H); IR ($CDCl_3$) 2966 (w), 1741 (w), 1691 (m), 1547 (m), 1427 (w), 1346 (m), 1223 (m); TLC R_f 0.35 (hexane/EtOAc (1/1)); HPLC (method B) t_R (1*R*)-**15** 9.9 min (13.8%), t_R (1*S*)-**15** 31.1 min (86.2%).

Inter [4 + 2]/Intra [3 + 2] Tandem Cycloadditions with Vinyl Ether 3. Promoted by MAPh: (2*R*,2a*R*,4a*R*,6*R*,7a*R*,7b*S*)-6-[(1*S*,2*R*,3*S*,4*R*)-3-(2,2-Dimethylpropoxy)-4,7,7-trimethylbicyclo[2.2.1]hept-2-oxy]octahydro-7b-methyl-1,7-dioxa-7a-azacyclopent[*cd*]indene-2-carboxylic Acid Methyl Ester (16β′). To a solution of 2,6-diphenylphenol (2.96 g, 12.0 mmol, 12.0 equiv) in CH_2Cl_2 (18 mL) was added Me_3Al (2.0 M in toluene, 3.00 mL, 6.0 mmol, 6.0 equiv). After 30 min, a solution of nitroalkene **1** (199 mg, 1.00 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) was added at 0 °C, and then a solution of vinyl ether **3** (319 mg, 1.2 mmol, 1.2 equiv) in CH_2Cl_2 (1.0 mL) was added at −78 °C. The reaction mixture was allowed to stir at −78 °C for 3 h. After standing for 10 h at rt, the crude products were purified by column chromatography (hexane/EtOAc (20/1, 10/1, 4/1)) to afford 388 mg (83%) of nitroso acetal **16β′**, 13 mg of recovered nitroalkene **1**, and 2.70 g of recovered 2,6-diphenylphenol. Data for **16β′**: mp 75–77 °C; ^1H NMR (300 MHz) 4.98 (t, J = 7.2, 1 H, HC(6)), 4.84 (d, J = 7.9, 1 H, HC(2)), 3.81 (d, J = 6.3, 1 H, HC(2′)), 3.79 (s, 3 H, H_3C(10)), 3.16 (d, 1 H, J = 6.7, HC(3′)), 3.08, 3.01 (ABq, J = 7.8, 2 H, H_2C(1″)), 2.72 (dt, J_d = 7.9, J_t = 2.4, 1 H, HC(2a)), 2.05–1.60 (m, 8 H), 1.91–1.82 (m, 2 H), 1.44–1.26 (m, 2 H), 1.34 (s, 3 H, H_3C(8)), 1.13 (s, 3 H, CH_3)), 0.89 (s, 9 H, H_3C(3″)), 0.88 (s, 3 H, CH_3), 0.75 (s, 3 H, CH_3); ^{13}C NMR (75.5 MHz) 170.48 (C(9)), 99.09 (C(6)), 88.58 (CH), 87.13 (CH), 84.96 (C(7b)), 82.79 (C(1″)), 82.02 (CH), 57.08 (C(2a)), 52.32 (C(10)), 50.54 (C(2′)), 49.67 (C), 46.60 (C), 43.23 (C(4a)), 33.77 (CH_2), 32.37 (C(2″)), 31.73 (CH_2), 28.81 (CH_2)), 27.13 (CH_2), 26.96 (C(3″)), 24.21 (CH_2), 23.80 (C(8)), 20.95 (CH_3), 20.59 (CH_3), 11.70 (CH_3); IR (CCl_4) 2953 (s), 2874 (m), 1743 (m), 1475 (w), 1458 (w), 1361 (w), 1145 (m), 1116 (m), 1091 (w); MS (LRFAB) 466 (M^+ + H, 30), 244 (22), 228 (52), 226 (100), 210 (18), 198 (25), 169 (15), 153 (75), 135 (22), 123 (16), 119 (15), 109 (24); $[\alpha]^{25}_D$ = +13.4° (CH_2Cl_2, c = 1.0); TLC R_f 0.59 (hexane/EtOAc (2/1)). Anal. Calcd for $C_{26}H_{43}NO_6$ (465.63): C, 67.07; H, 9.31; N, 3.01. Found: C, 67.08; H, 9.33; N, 2.96.

(1*R*,3*S*,5a*R*,7a*R*,7b*S*)-Octahydro-1-hydroxy-7b-methyl-2*H*-cyclopenta[*gh*]pyrrolizin-2-one (4). Hydrogenolysis of nitroso acetal **16β′** (250 mg, 0.537 mmol) afforded 86 mg (88%) of **4** as a white solid and 111 mg (86%) of recovered alcohol **9**. Data for **4**: ^1H NMR (300 MHz) 4.68 (d, J = 7.2, 1 H, HC(1)), 3.91 (ddd, J = 12.0, 8.5, 3.6, 1 H, HC(4)), 2.93 (dt, J_d = 11.8, J_t = 8.0, 1 H, HC(4)), 2.78 (d, J = 2.5, 1 H, HOC(1)), 2.62 (q, J = 7.4, 1 H, HC(7a)), 2.28 (m, 1 H), 1.68–1.85 (m, 3 H), 1.43–1.55 (m, 1 H), 1.32 (s, 3 H, H_3C(8)), 1.26 (m, 1 H); IR (CCl_4) 3390 (b, s), 2961 (s), 2860 (m), 1705 (s), 1325 (s); $[\alpha]^{25}_D$ = +36.5° (CH_2Cl_2, c = 0.98); TLC R_f 0.19 (hexane/EtOAc (1/1)).

(1*R*,3*S*,5a*R*,7a*R*,7b*S*)-Octahydro-1-[*N*-(3,5-dinitrophenyl)carbamoxy]-7b-methyl-2*H*-cyclopenta[*gh*]pyrrolizin-2-one (15). Derivatization of **4** (20.0 mg, 0.110 mmol) afforded 33 mg (77%) of **15** as a white solid: ^1H NMR (300 MHz) 10.16 (bs, 1 H, NH), 8.63 (t, J = 2.0, 1 H, HC(6′)), 8.56 (d, J = 1.8, 2 H, HC(4′)), 5.95 (d, J = 7.1, 1 H, HC(1)), 3.95 (ddd, J = 12.3, 9.6, 3.8, 1 H, HC(4)), 3.08 (dt, J_d = 11.9, J_t = 3.4, 1 H, HC(4)), 2.82 (q, J = 7.3, 1 H, HC(7a)), 2.38–2.42 (m, 1 H), 2.22–2.26 (m, 1 H, HC(5a)), 1.46–1.90 (m, 3 H), 1.45 (s, 3 H, H_3C(8)), 1.26–1.30 (m, 1 H); IR ($CDCl_3$) 2965 (w), 1742 (w), 1691 (m), 1606 (w), 1547 (m), 1425 (w), 1346 (m), 1265 (m), 1223 (m); TLC R_f 0.35 (hexane/EtOAc (1:1)); HPLC (method A) t_R (1*R*)-**15** 6.8 min (99.4%), t_R (1*S*)-**15** 20.8 min (0.6%).

Promoted by MAD: (2*R*,2a*R*,4a*R*,6*R*,7a*R*,7b*S*)-6-[(1*S*,2*R*,3*S*,4*R*)-3-(2,2-Dimethylpropoxy)-4,7,7-trimethylbicyclo[2.2.1]hept-2-oxy]octahydro-7b-methyl-1,7-dioxa-7a-azacyclopent[*cd*]indene-2-carboxylic Acid Methyl Ester (16β′) and (2*S*,2a*S*,4a*S*,6*R*,7a*R*,7b*R*)-6-[(1*S*,2*R*,3*S*,4*R*)-3-(2,2-Dimethylpropoxy)-4,7,7-trimethylbicyclo[2.2.1]hept-2-oxy]octahydro-7b-methyl-1,7-dioxa-7a-azacyclopent[*cd*]indene-2-carboxylic Acid Methyl Ester (16α). To a solution of 2,6-di-*tert*-butyl-4-methylphenol (1.10 g, 5.00 mmol, 6.0 equiv) in toluene (5.0 mL) was added Me_3Al (2.0 M in toluene, 1.25 mL, 2.5 mmol, 3.0 equiv). To the cold (−78 °C) solution of MAD was added a solution of nitroalkene **1** (166 mg, 0.833 mmol, 1.0 equiv), in CH_2Cl_2 (1.0 mL) and then a solution of vinyl ether **3** (266 mg, 1.0 mmol, 1.2 equiv) in CH_2Cl_2 (1.0 mL). The reaction mixture was allowed to stir at −78 °C for 1 h. After standing for 8 h at rt the crude products were purified by column chromatography (hexane/EtOAc (20/1, 10/1, 4/1)) to afford 336 mg (87%) of a mixture of nitroso acetals in a ratio of 1.0:1.1 (16α:16β′) by ^1H NMR and 8 mg of recovered nitroalkene **1**. Data of **16β′** and **16α**: ^1H NMR (300 MHz) 5.10 (dd, J = 6.3, 2.6, 0.5 H, HC(6)), 4.98 (t, J = 7.3, 0.5 H, HC(6)), 4.88 (d, J = 8.2, 0.5 H, HC(2)), 4.84 (d, J = 7.9, 0.5 H, HC(2)), 3.81 (d, J = 6.3, 0.5 H, HC(2′)), 3.79 (s, 1.5 H, H_3C(10)), 3.78 (s, 1.5 H, H_3C(10)), 3.76 (d, J = 6.7, 0.5 H, HC(2′)), 3.18, 2.94 (ABq, J = 7.9, 1 H, H_2C(1″)), 3.08, 3.01 (ABq, J = 7.8, 1 H, H_2C(1″)), 3.15 (d, J = 6.7, 1 H, HC(3′)), 2.72 (m, 1 H, HC(2a)), 2.23–1.30 (m, 12 H), 1.33 (s, 1.5 H, H_3C(8)), 1.30 (s, 1.5 H, CH_3), 1.16 (s, 1.5 H, CH_3)), 1.09 (s, 1.5 H, CH_3), 0.90 (s, 9 H, H_3C(3″)), 0.88 (s, 1.5 H, CH_3), 0.87 (s, 3 H, CH_3), 0.74 (s, 3 H, CH_3).

(1*S*,3*R*,5a*S*,7a*S*,7b*R*)-Octahydro-1-hydroxy-7b-methyl-2*H*-cyclopenta[*gh*]pyrrolizin-2-one (4). Hydrogenolysis of the mixture of nitroso acetals **16β′** and **16α** (275 mg, 0.591 mmol) afforded 72 mg (67%) of **4** as a white solid and 115 mg (81%) of recovered alcohol **9**. Data for **4**: ^1H NMR (300 MHz) 4.68 (d, J = 7.2, 1 H, HC(1)), 3.90 (ddd, J = 12.0, 8.5, 3.6, 1 H, HC(4)), 2.88–2.99 (m, 2 H, HOC(1), HC(4)), 2.62 (q, J = 7.4, 1 H, HC(7a)), 2.25 (m, 1 H), 1.68–1.85 (m, 3 H), 1.47 (m, 1 H), 1.33 (s, 3 H, H_3C(8)), 1.26 (m, 1 H); IR (CCl_4) 3380 (b,s), 2982 (s), 2860 (m), 1734 (s), 1346 (m); TLC R_f 0.15 (hexane/EtOAc (1/1)).

(1*S*,3*R*,5a*S*,7a*S*,7b*R*)-Octahydro-1-[*N*-(3,5-dinitrophenyl)carbamoxy]-7b-methyl-2*H*-cyclopenta[*gh*]pyrrolizin-2-one (15). Derivatization of **4** (20.0 mg, 0.110 mmol, 1.0 equiv) afforded 35 mg (81%) of **15** as a white solid: ^1H NMR (300 MHz) 9.90 (bs, 1 H, NH), 8.63 (t, J = 1.9, 1 H, HC(6′)), 8.58 (d, J = 1.9, 2 H, HC(4′)), 5.92 (d, J = 7.1, 1 H, HC(1)), 3.95 (ddd, J = 12.3,

8.4, 4.7, 1 H, HC(4)), 3.07 (dt, J_d = 12.1, J_t = 3.4, 1 H, HC(4)), 2.82 (q, J = 7.2, 1 H, HC(7a)), 2.37–2.41 (m, 1 H), 2.21–2.29 (m, 1 H, HC(5a)), 1.50–1.89 (m, 3 H), 1.44 (s, 3 H, H_3C(8)), 1.24–1.32 (m, 1 H); IR ($CDCl_3$) 2967 (w), 1691 (m), 1547 (m), 1425 (w), 1346 (m), 1246 (m), 1223 (w); TLC R_f 0.35 (hexane/EtOAc (1/1)); HPLC (method A) t_R (1*R*)-**15** 6.8 min (48.9%), t_R (1*S*)-**15** 20.5 min (51.1%).

Inter [4 + 2]/Intra [3 + 2] Tandem Cycloadditions with Propenyl Ether (*Z*)-11. (2*S*,2a*S*,4a*S*,5*R*,6*S*,7a*R*,7b*R*)-6-[(1*S*,2*R*,3*S*,4*R*)-3-(2,2-Dimethylpropoxy)-4,7,7-trimethylbicyclo[2.2.1]hept-2-oxy]octahydro-5,7b-dimethyl-1,7-dioxa-7a-azacyclopent[*cd*]indene-2-carboxylic Acid Methyl Ester (18a) and (2*S*,2a*S*,4a*S*,5*R*,6*R*,7a*R*,7b*R*)-6-[(1*S*,2*R*,3*S*,4*R*)-3-(2,2-Dimethylpropoxy)-4,7,7-trimethylbicyclo[2.2.1]hept-2-oxy]octahydro-5,7b-dimethyl-1,7-dioxa-7a-azacyclopent[*cd*]indene-2-carboxylic Acid Methyl Ester (18b). To a cold (−78 °C) solution of nitroalkene **1** (150 mg, 0.753 mmol) in CH_2Cl_2 (2 mL) was added Ti(O-*i*-Pr)$_2$Cl$_2$ (1.808 mmol, 2.4 equiv) in CH_2Cl_2 (1 mL) and a solution of chiral propenyl ether (*Z*)-**11** (253 mg, 0.904 mmol, 1.2 equiv) in CH_2Cl_2 (0.7 mL). The solution was stirred at −78 °C for 1 h. After standing for 8 h at rt the crude products were purified by column chromatography on silica gel (hexane/EtOAc (10/1)) to afford 321 mg (89%) of a mixture of **18a** and **18b** as a white solid. Data for **18a** and **18b**: ^{1}H NMR (300 MHz) 5.16 (d, J = 6.8, 1 H, HC(5)), 4.87 (d, J = 8.0, 1 H, HC(1)), 3.79 (s, 3 H, H_3C(11)), 3.80 (d, J = 6.7, 1 H, HC(2′)), 3.30 and 2.97 (ABq, J = 8.3, 2 H, H_2C(1″)), 3.17 (d, J = 6.7, 1 H, HC(3′)), 2.75 (m, 1 H, HC(8a)), 2.20 (m, 1 H), 2.00–1.40 (m, 13 H), 1.30 (s, 3 H, H_3C(9)), 1.09 (d, J = 7.5, 3 H, H_3C(12)), 1.08 (s, 3 H, CH_3), 0.90 (s, 9 H, 3 × H_3C-(3″)), 0.88 (s, 3 H, CH_3), 0.74 (s, 3 H, CH_3); ^{13}C NMR (75.5 MHz) 170.22 (C(10)), 101.81 (C(5)), 89.31 (CH), 87.10 (CH), 85.26 (C(8b)), 83.92 (CH), 83.30 (C(1″)), 56.87 (C(8a)), 52.16 (C(2″)), 51.46 (CH), 50.57 (CH), 49.77 (C), 46.31 (C), 33.65 (C(6a)), 32.43 (CH_2), 31.34 (CH), 29.58 (CH_2), 28.28 (CH_2), 26.83 (CH_3, CH_2), 24.00 (CH_2), 23.96 (CH_3), 20.86 (CH_3), 14.04 (CH_3), 11.81 (CH_3); IR (CCl_4) 2955 (s), 2874 (s), 1744 (m), 1478 (w), 1458 (w), 1439 (m), 1390 (w), 1201 (m), 1134 (m), 1101 (m), 1018 (m), 908 (w), 841 (w); MS (LRFAB) 480 (M^+ + 1, 38), 464 (12), 299 (10), 258 (55), 242 (84), 224 (21), 223 (22), 212 (23), 182 (12), 169 (10), 155 (25), 154 (16), 153 (100), 152 (10), 149 (17), 137 (10), 135 (29), 123 (17), 121 (14), 119 (38), 109 (29), 103 (18); HRMS calcd for $C_{27}H_{46}NO_6$, M + H 480.3325, found 480.3316; TLC R_f 0.52 (hexane/EtOAc (5/1)).

(1*S*,3*R*,5*R*,5a*S*,7a*S*,7b*R*)-Octahydro-1-hydroxy-5,7b-dimethyl-2*H*-cyclopenta[*gh*]pyrrolizin-2-one (8). Hydrogenolysis of the mixture of nitroso acetals **18a** and **b** (220 mg, 0.459 mmol) afforded 96 mg (87%) of chiral alcohol **9** and 73 mg (82%) of (−)-**8** as a white solid. Data for **8**: ^{1}H NMR (300 MHz) 4.66 (d, J = 7.8, 1 H, HC(1)), 3.19 (d, J = 8.9, 2 H, H_2C(4)), 2.76–2.62 (m, 2 H), 1.69–1.53 (m, 4 H), 1.34 (s, 3 H, H_3C(8)), 1.02 (d, J = 6.9, 3 H, H_3C(9)); ^{13}C NMR (75.5 MHz) 177.37 (C(2)), 77.49 (C(7b)), 71.89 (C(1)), 54.26 (C(5a)), 50.24 (C(7a)), 47.34 (C4)), 33.97 (C(5)), 25.45 (C(7)), 24.82 (C(6)), 21.95 (C(8)), 14.90 (C(9)); TLC R_f 0.16 (hexane/EtOAc (1/1)).

(1*S*,3*R*,5*R*,5a*S*,7a*S*,7b*R*)-Octahydro-1-[*N*-(3,5-dinitrophenyl)carbamoxy]-5,7b-dimethyl-2*H*-cyclopenta[*gh*]pyrrolizin-2-one (20). Derivatization of **8** (10 mg, 0.051 mmol) from (*Z*)-**14** afforded 14 mg (82%) of (1*S*)-**20**: ^{1}H NMR (300 MHz) 10.37 (br, s, 1 H, NH), 8.63 (d, J = 2.1, 1 H, HC(6′)), 8.58 (d, J = 1.7, 2 H, HC(4′)), 5.95 (d, J = 7.8, 1 H, HC(1)), 3.36 (t, J = 11.0, 1 H, HC(4)), 3.24 (t, J = 10.0, 1 H, HC(4)), 2.92 (t, J = 7.9, 1 H), 2.77 (quintet, J = 6.6, 1 H, HC(7a)), 2.24–1.61 (m, 4 H), 1.48 (s, 3 H, H_3C(8)), 1.25 (m, 1 H), 1.07 (d, J = 6.8, H_3C(9)); ^{13}C NMR (75.5 MHz) 172.29 (C(2)), 152.42 (C(1′)), 148.62 (C(5′)), 141.20 (C(3′)), 118.11 (C(4′)), 112.53 (C(6′)), 77.90 (C(1)), 73.95 (C(7b)), 54.18 (C(5a)), 48.18 (C(7a)), 47.70 (C(4)), 34.00 (C(5)), 25.93 (CH_2), 25.65 (CH_2), 21.77 (C(8)); TLC R_f 0.54 (hexane/EtOAc (1/1)); HPLC (method A) t_R (1*R*)-**20**, 6.21 min (25.90%) and t_R (1*S*)-**20**, 21.07 min (74.11%).

Inter [4 + 2]/Intra [3 + 2] Tandem Cycloadditions with Propenyl Ether (*E*)-11. (2*S*,2a*S*,4a*S*,5*S*,6*S*,7a*R*,7b*R*)-6-[(1*S*,2*R*,3*S*,4*R*)-3-(2,2-Dimethylpropoxy)-4,7,7-trimethylbicyclo[2.2.1]hept-2-oxy]octahydro-5,7b-dimethyl-1,7-dioxa-7a-azacyclopent[*cd*]indene-2-carboxylic Acid Methyl Ester (17). To a cold (−78 °C) solution of nitroalkene **1** (150 mg, 0.753 mmol) in CH_2Cl_2 (2 mL) was added Ti(O-*i*-Pr)$_2$Cl$_2$ (1.808 mmol, 2.4 equiv) in CH_2Cl_2 (1 mL) and a solution of chiral propenyl ether (*E*)-**11** (253 mg, 0.904 mmol, 1.2 equiv) in CH_2Cl_2 (0.7 mL). The solution was stirred at −78 °C for 1 h. The crude products were purified by column chromatography on silica gel (hexane/EtOAc (10/1)) to afford 318 mg (89%) of **17** as a white solid: ^{1}H NMR (300 MHz) 4.85 (d, J = 8.2, 1 H, HC(1)), 4.68 (d, J = 4.7, 1 H, HC(5)), 3.79 (s, 3 H, H_3C(11)), 3.70 (d, J = 6.7, 1 H, HC(2′)), 3.28 and 2.85 (ABq, J = 8.0, 2 H, H_2C-(1″), 3.16 (d, J = 6.7, 1 H, HC(3′)), 2.66 (dt, J_d = 8.2, J_t = 5.8, 1 H, HC(8a)), 2.05–1.72 (m, 8 H), 1.63–1.39 (m, 2 H), 1.38 (s, 3 H, H_3C(9)), 1.09 (d, J = 7.5, 3 H, H_3C(12)), 1.08 (s, 3 H, CH_3), 0.99–0.89 (m, 1 H), 0.89 (s, 9 H, 3 × H_3C(3″)), 0.87 (s, 3 H, CH_3), 0.74 (s, 3 H, CH_3); ^{13}C NMR (75.5 MHz) 170.29 (C(10)), 107.29 (C(5)), 88.49 (CH), 86.33 (CH), 86.02 (CH), 82.68 (C(8b), 82.49 (C(1″)), 59.19 (C(8a)), 52.20 (C(2″)), 51.70 (CH), 50.67 (CH), 49.28 (C), 46.27 (C), 37.11 (C(6a)), 35.74 (CH_2), 33.73 (CH_2), 32.35 (C), 28.13 (CH_2), 27.18 (CH_3), 26.85 (CH_3), 23.92 (CH_2), 20.92 (CH_3), 20.87 (CH_3), 18.79 (CH_3), 11.56 (CH_3); IR (CCl_4) 2953 (s), 2872 (s), 1744 (s), 1549 (s), 1476 (m), 1458 (m), 1439 (m), 1381 (m), 1372 (m), 1362 (m), 1285 (m), 1248 (m), 1202 (s), 1148 (s), 1121 (s), 1101 (m), 997 (s); MS (LRFAB) 480 (M^+ + 1, 17), 464 (11), 308 (28), 306 (20), 305 (17), 274 (12), 258 (29), 242 (21), 154 (90), 153 (25), 152 (39), 151 (41), 149 (10), 136 (16), 134 (73), 120 (20), 118 (100); HRMS calcd for $C_{27}H_{46}NO_6$, M + H 480.3325, found 480.3312; TLC R_f 0.15 (hexane).

(1*S*,3*R*,5*S*,5a*S*,7a*S*,7b*R*)-Octahydro-1-hydroxy-5,7b-dimethyl-2*H*-cyclopenta[*gh*]pyrrolizin-2-one (7). Hydrogenolysis of nitroso acetal **17** (220 mg, 0.459 mmol) afforded 100 mg (91%) of chiral alcohol **9** and 79 mg (89%) of (−)-**7** as a white solid. Data for **7**: ^{1}H NMR (300 MHz) 4.65 (d, J = 6.6, 1 H, HC(1)), 4.00 (dd, J = 11.9, 7.3, 1 H, HC(4)), 3.71 (br, 1 H, OH), 2.48 (m, 2 H, HC(4), HC(7a)), 1.80–1.38 (m, 6 H), 1.29 (s, 3 H, H_3C(8)), 1.03 (d, J = 6.7, 3 H, H_3C(9)); ^{13}C NMR (75.5 MHz) 176.15 (C(2)), 75.34 (C(7b)), 72.44 (C(1)), 57.09 (C(5a)), 51.87 (C(7a)), 50.45 (C(4)), 42.09 (C(5)), 30.86 (CH_2), 25.29 (CH_2), 24.14 (C(8)), 17.50 (C(9)); IR (CCl_4) 3370 (br, w), 2957 (s), 2876 (m), 1710 (s), 1460 (w), 1453 (w), 1402 (m), 1395 (m), 1335 (m), 1286 (w), 1265 (w), 1209 (m), 1097 (w), 1042 (w); TLC R_f 0.20 (hexane/EtOAc (1/1)); $[\alpha]^{25}_D$ = −11.42 (*c* 1.17, CH_2Cl_2).

(1*S*,3*R*,5*S*,5a*S*,7a*S*,7b*R*)-Octahydro-1-[*N*-(3,5-dinitrophenyl)carbamoxy]-5,7b-dimethyl-2*H*-cyclopenta[*gh*]pyrrolizin-2-one (19). Derivatization of **7** (8 mg, 0.041 mmol) from (*E*)-**11** afforded 14 mg (82%) of **19** as a white solid: ^{1}H NMR (300 MHz) 10.24 (br, s, 1 H, NH), 8.58 (d, J = 1.9, 1 H, HC(6′)), 8.52 (d, J = 1.7, 2 H, HC(4′)), 5.90 (d, J = 6.8, 1 H, HC(1)), 4.10 (dd, J = 11.9, 7.3, 1 H HC(4), 2.68 (m, 2 H, HC(4), HC(7a)), 1.96–1.46 (m, 6 H), 1.46 (s, 3 H, H_3C(8)), 1.14 (d, J = 6.6, H_3C(9)); ^{13}C NMR (75.5 MHz) 171.75 (C(2)), 152.61 (C(1′)), 148.58 (C(5′)), 141.18 (C(3′)), 118.04 (C(4′)), 112.40 (C(6′)), 75.84 (C(1)), 74.66 (C(7b)), 58.05 (C(5a)), 50.81 (C(7a)), 50.14 (C(4)), 42.66 (C(5)), 31.19 (CH_2), 26.23 (CH_2), 24.11 (C(8)), 17.53 (C(9)); TLC R_f 0.47 (hexane/EtOAc (1/1)); HPLC (method A) t_R (1*R*)-**19**, 5.91 min (0.47%) and t_R (1*S*)-**19**, 18.22 min (99.57%).

Inter [4 + 2]/Intra [3 + 2] Tandem Cycloadditions with Propenyl Ether (*Z*)-13. Promoted by Ti(O-*i*-Pr)$_2$Cl$_2$: (2*S*,2a*S*,4a*S*,5*R*,6*S*,7a*R*,7b*R*)-6-[(1*R*,2*S*)-2-(Phenylcyclohexyl)-oxy]octahydro-5,7b-dimethyl-1,7-dioxa-7a-azacyclopent[*cd*]-indene-2-carboxylic Acid Methyl Ester (22) and (2*S*,2a*S*,4a*S*,5*S*,6*S*,7a*R*,7b*R*)-6-[(1*R*,2*S*)-2-(Phenylcyclohexyl)-oxy]octahydro-5,7b-dimethyl-1,7-dioxa-7a-azacyclopent[*cd*]-indene-2-carboxylic Acid Methyl Ester (21). To a cold (−90 °C) solution of nitroalkene **1** (199 mg, 1.00 mmol, 1.0 equiv) in CH_2Cl_2 (5.0 mL) was added a solution of propenyl ether (*Z*)-**13** (324 mg, 1.50 mmol, 1.5 equiv) in CH_2Cl_2 (0.5 mL), and then a solution of dichlorotitanium diisopropoxide (3.00 mmol, 3.0 equiv) in CH_2Cl_2 (1.5 mL) was added. The solution was stirred at −90 °C for 30 min and then at −78 °C for an additional 2 h. After standing for 10 h at rt, the crude products were then purified by column chromatography (hexane/EtOAc (8/1, 4/1)) to afford 345 mg (83%) of a mixture of nitroso acetals **21** and **22** as a white solid. An analytical sample was purified by recrystallization from EtOAc/hexane. Data for **22**: mp 102–104 °C (EtOAc/hexane); ^{1}H NMR (400 MHz) 7.15–7.28 (m, 5 H, phenyl), 4.85 (d, J = 7.7, 1 H, HC(2)), 4.72 (d, J = 6.6, 1 H, HC(6)), 3.78 (s, 3 H, H_3C(10)), 3.61 (dt, J_d = 4.4, J_t = 9.9, 1 H, HC(1′)), 2.66 (dt, J_d = 2.2, J_t =

8.1, 1 H, HC(2a)), 2.51 (dt, J_d = 4.0, J_t = 10.7, 1 H, HC(6')), 2.19–2.22 (m, 1 H), 2.03–2.11 (m, 1 H), 1.68–1.91 (m, 8 H), 1.22–1.61 (m, 6 H), 1.20 (s, 3 H, H_3C(8)), 0.40 (d, J = 7.0, 3 H, H_3C(11)); ^{13}C NMR (100 MHz) 170.45 (C(9)), 144.56 (C(7')), 128.04 (C(9')), 127.99 (C(8')), 126.06 (C(10')), 103.18 (C(6)), 86.99 (C(2)), 85.39 (C(7b)), 84.21 (C(1')), 56.68 (C(2a)), 52.29 (C(10)), 51.65 (C(6')), 50.15 (C(4a)), 35.34 (CH_2), 33.87 (CH_2), 31.08 (C(5)), 29.43 (CH_2), 28.50 (CH_2), 25.82 (CH_2), 25.15 (CH_2), 24.02 (C(8)), 12.77 (C(11)); IR (CCl_4) 2932 (s), 1744 (m), 1449 (m), 1375 (w), 1201 (m), 1120 (w), 1018 (m); MS (LRFAB) 416 (M^+ + H, 23), 400 (7), 385 (11), 309 (15), 279 (10), 258 (100), 240 (32), 212 (17), 159 (64), 155 (41), 135 (27), 119 (57); TLC R_f 0.61 (hexane/EtOAc (2/1)). Anal. Calcd for $C_{23}H_{31}NO_5$ (415.53): C, 69.37; H, 8.00; N, 3.37. Found: C, 69.41; H, 8.03; N, 3.41.

(1*S*,3*R*,5*R*,5a*S*,7a*S*,7b*R*)-Octahydro-1-hydroxy-5,7b-dimethyl-2*H*-cyclopenta[*gh*]pyrrolizin-2-one (8) and (1*S*,3*R*,5*S*,5a*S*,7a*S*,7b*R*)-Octahydro-1-hydroxy-5,7b-dimethyl-2*H*-cyclopenta[*gh*]pyrrolidin-2-one (7). Hydrogenolysis of the nitroso acetal mixture of **22** and **21** (250 mg, 0.606 mmol) obtained from (*Z*)-**13** afforded 83 mg of a mixture of **7** and **8** (71%) in a ratio of 10:1 (**8**:**7**) as a white solid and 87 mg (82%) of recovered alcohol **5**. Data for **7** and **8**: ^1H NMR (300 MHz) 4.65 (d, J = 7.6, 0.9 H, HC(1)), 4.04 (dd, J = 7.4, 4.3, 0.1 H, HC(4)), 3.21 (d, J = 8.7, 1.8 H, H_2C(4)), 2.64–2.77 (m, 3 H), 2.08–2.18 (m, 2 H), 1.57–1.71 (m, 3 H), 1.36 (s, 3 H, H_3C(8)), 1.07 (d, J = 7.0, 0.3 H, H_3C(9)), 1.03 (d, J = 6.9, 2.7 H, H_3C(9)); IR (CCl_4) 3335 (b,w), 2965 (s), 2876 (m), 1707 (s), 1547 (m), 1327 (m), 1381 (w); TLC R_f 0.17 (hexane/EtOAc (1/1)).

(1*S*,3*R*,5*R*,5a*S*,7a*S*,7b*R*)-Octahydro-1-[*N*-(3,5-dinitrophenyl)carbamoxy]-5,7b-dimethyl-2*H*-cyclopenta[*gh*]pyrrolizin-2-one (20) and (1*S*,3*R*,5*S*,5a*S*,7a*S*,7b*R*)-Octahydro-1-[*N*-(3,5-dinitrophenyl)carbamoxy]-5,7b-dimethyl-2*H*-cyclopenta[*gh*]pyrrolizin-2-one (19). Derivatization of a mixture of **7** and **8** (19.5 mg, 0.100 mmol, 1.0 equiv) afforded 34 mg (85%) of a mixture of **19** and **20** as a white solid: ^1H NMR (300 MHz) 10.19 (br, 1 H, NH), 8.63 (t, J = 1.7, 1 H, HC(6')), 8.56 (d, J = 2.0, 2 H, HC(4')), 5.94 (d, J = 7.9, 0.85 H, HC(1)), 5.88 (d, J = 7.0, 0.15 H, HC(1)), 4.12 (dd, J = 12.0, 7.3, 0.1 H, HC(4)), 3.21–3.36 (m, 2 H), 2.92 (t, J = 8.7, 0.9 H), 2.75–2.79 (m, 1 H), 2.22 (dt, J_d = 10.2, J_t = 6.4, 1 H, HC(7a)), 1.65–2.18 (m, 4 H), 1.47 (s, 3 H, H_3C(8)), 1.07 (d, J = 6.9, 3 H, H_3C(9)); IR (CH_2Cl_2) 3055 (m), 2967 (m), 1740 (w), 1689 (s), 1610 (w), 1547 (s), 1424 (m), 1347 (m), 1136 (w), 1095 (w), 897 (w); TLC R_f 0.35 (hexane/EtOAc (1/1)); HPLC (method C) t_R (1*R*)-**19** 15.1 min (1.5%), t_R (1*R*)-**20** 17.6 min (8.1%), t_R (1*S*)-**19** 37.2 min (7.0%), t_R (1*S*)-**20** 41.9 min (83.3%).

Promoted by MAD: (2*S*,2a*S*,4a*S*,5*S*,6*S*,7a*R*,7b*R*)-6-[(1*R*,2*S*)-2-(Phenylcyclohexyl)oxy]octahydro-5,7b-dimethyl-1,7-dioxa-7a-azacyclopent[*cd*]indene-2-carboxylic Acid Methyl Ester (21) and (2*S*,2a*S*,4a*S*,5*R*,6*S*,7a*R*,7b*R*)-6-[(1*R*,2*S*)-2-(Phenylcyclohexyl)oxy]octahydro-5,7b-dimethyl-1,7-dioxa-7a-azacyclopent[*cd*]indene-2-carboxylic Acid Methyl Ester (22). To a degassed solution of 2,6-di-*tert*-butyl-4-methylphenol (1.32 g, 6.00 mmol, 6.0 equiv) in toluene (6.0 mL) was added Me_3Al (2.0 M in toluene, 1.50 mL, 3.0 mmol, 3.0 equiv). To the cold (−78 °C) solution of MAD was added a degassed solution of propenyl ether (*Z*)-**13** (324 mg, 1.50 mmol, 1.5 equiv) in toluene (0.5 mL), and then a degassed solution of nitroalkene **1** (199 mg, 1.00 mmol, 1.0 equiv) in toluene (0.5 mL) was added. The reaction mixture was allowed to stir at −78 °C in the dark for 1.5 h. After standing for 6 h at rt, the crude products were purified by column chromatography (hexane/EtOAc (10/1, 4/1)) to afford 298 mg (72%) of a diastereomeric mixture of nitroso acetals in a ratio of 1:2:29 (**21**:**21'**:**22**) by ^1H NMR. Data for **22**, **21'**, and **21**: ^1H NMR (400 MHz) 7.12–7.28 (m, 5 H, phenyl), 5.13 (d, J = 4.4, 0.05 H), 4.84 (d, J = 7.8, 0.95 H, HC(2)), 4.71 (d, J = 6.8, 0.95 H), 4.31–4.36 (m, 0.25 H, HC(2)), 3.78 (s, 2.7 H, H_3C_a(10)), 3.75 (s, 0.2 H, H_3C_b(10)), 3.75 (s, 0.1 H, H_3C_c(10)), 3.61 (dt, J_d = 4.6, J_t = 10.0, 1 H, HC(1')), 2.64 (dt, J_d = 2.0, J_t = 8.1, 1 H, HC(2a)), 3.51 (dt, J_d = 12.5, J_t = 3.7, 1 H, HC(6')), 2.19–2.22 (m, 1 H), 2.03–2.11 (m, 1 H), 1.69–1.90 (m, 7 H), 1.25–1.61 (m, 6 H), 1.20 (s, 3 H, H_3C(8)), 0.81 (d, J = 6.8, 0.1 H, H_3C_c(11)), 0.55 (d, J = 6.6, 0.2 H, H_3C_b(11)), 0.40 (d, J = 7.3, 2.7 H, H_3C_a(11)); ^{13}C NMR (100 MHz) 170.44 (C(9)), 144.56 (C(7')), 128.04 (C(8')), 127.99 (C(9')), 127.89 (C_b(8')), 126.10 (C_b(9')), 126.06 (C(10')), 125.70 (C_b(10')), 103.17 (C(6)), 100.75 (C_b(6)), 86.99 (C(2)), 85.39 (C(7b)), 84.20 (C(1')), 82.51, 81.79, 75.87, 57.95, 56.68 (C(2a)), 52.35, 52.29 (C(10)), 51.75, 51.66 (C(6')), 50.15 (C(5)), 45.73, 35.33, 34.44, 33.87, 33.63, 33.53, 33.50, 33.48, 31.08, 29.42, 29.23, 28.50, 26.11, 26.04, 25.81, 25.14, 25.18, 24.60, 24.01 (C(8)), 15.16 (C_b(11)), 12.76 (C(11)); IR (CCl_4) 3028 (w), 2932 (s), 1744 (m), 1493 (w), 1448 (m), 1437 (w), 1377 (w), 1340 (w), 1282 (w), 1203 (m), 1120 (w); MS (LRFAB) 417 (M^+ + H + 1, 22), 416 (M^+ + H, 81), 400 (10), 385 (11), 258 (67), 240 (18), 212 (16), 159 (100), 155 (20), 135 (25), 119 (42), 103 (24).

(1*S*,3*R*,5*R*,5a*S*,7a*S*,7b*R*)-Octahydro-1-hydroxy-5,7b-dimethyl-2*H*-cyclopenta[*gh*]pyrrolizin-2-one (8) and (1*S*,3*R*,5*S*,5a*S*,7a*S*,7b*R*)-Octahydro-1-hydroxy-5,7b-dimethyl-2*H*-cyclopenta[*gh*]pyrrolizin-2-one (7). Hydrogenolysis of the nitroso acetal mixture of **21** and **22** (160 mg, 0.385 mmol) obtained from (*Z*)-**13** afforded 62 mg of a mixture of **8** and **7** (83%) as a white solid (^1H NMR ratio = 7.4:1.0) and 58 mg (87%) of recovered alcohol **5**. Data for **7** and **8**: ^1H NMR (300 MHz) 4.65 (d, J = 7.5, 1 H, HC(1)), 4.04 (dd, J = 11.8, 7.4, 0.1 H, HC_b(4)), 3.19 (d, J = 8.5, 1.8 H, H_2C_a(4)), 2.94 (br, 1 H, HOC(1)), 2.53–2.77 (m, 2.5 H), 2.04–2.18 (m, 2 H), 1.47–1.83 (m, 3 H), 1.36 (s, 3 H, H_3C(8)), 1.05 (d, J = 6.9, 1 H, H_3C(9)); ^{13}C NMR (100 MHz) 177.04 (C(2)), 77.64 (C(7b)), 54.25 (C(5a)), 50.31 (C(7a)), 47.37 (C(4)), 34.08 (C(5)), 25.49 (C(7)), 24.79 (C(6)), 22.06 (C(8)), 14.91 (C(9)); 72.44 (C(1)), 58.11 (C(5a)), 51.93 (C(7a)), 50.49 (C(4)), 42.10 (C(5)), 30.82, 26.09, 25.25, 24.19 (C(8)), 17.50 (C(9)); IR (CCl_4) 3373 (w, br), 2963 (m), 2874 (m), 1703 (s), 1558 (w), 1454 (w), 1381 (m), 1325 (m), 1184 (w), 1147 (w), 1086 (w); TLC R_f 0.19 (hexane/EtOAc (1/1)).

(1*S*,3*R*,5*R*,5a*S*,7a*S*,7b*R*)-Octahydro-1-[*N*-(3,5-dinitrophenyl)carbamoxy]-5,7b-dimethyl-2*H*-cyclopenta[*gh*]pyrrolizin-2-one (20) and (1*S*,3*R*,5*S*,5a*S*,7a*S*,7b*R*)-Octahydro-1-[*N*-(3,5-dinitrophenyl)carbamoxy]-5,7b-dimethyl-2*H*-cyclopenta[*gh*]pyrrolizin-2-one (19). Derivatization of a mixture of **7** and **8** (19.5 mg, 0.100 mmol, 1.0 equiv) afforded 33 mg (83%) of a mixture of **19** and **20** as a white solid: ^1H NMR (400 MHz) 10.31 (br s, 1 H, NH), 8.63 (t, J = 2.2, 1 H, HC(6')), 8.56 (d, J = 2.0, 2 H, HC(4')), 5.94 (d, J = 8.1, 1 H, HC(1)), 4.04–4.15 (m, 0.2 H, HC_b(4)), 3.36 (t, J = 10.6, 1 H, HC_a(4)), 3.24 (dd, J = 8.5, 11.9, 1 H, HC_a(4)), 2.92 (t, J = 8.3, 1 H), 2.75–2.79 (m, 1 H, HC(7a)), 2.22 (dt, J_d = 10.5, J_t = 6.3, 1 H), 2.02–2.05 (m, 1 H), 1.79–1.87 (m, 1 H), 1.65–1.70 (m, 1 H), 1.48 (s, 3 H, H_3C(8)), 1.10–1.15 (m, 1 H), 1.07 (d, J = 6.8, 3 H, H_3C(9)); ^{13}C NMR (100 MHz) 172.45 (C(2)), 152.38 (C(1')), 148.65 (C(5')), 141.15 (C(3')), 118.10 (C(4')), 112.53 (C(6')), 77.85 (C(1)), 73.85 (C(7b)), 54.20 (C(5a)), 48.78 (C(7a)), 47.70 (C(4)), 34.00 (C(5)), 25.94, 25.64, 21.77 (C(8)), 15.09 (C(9)); IR (CH_2Cl_2) 3056 (m), 2966 (w), 1740 (w), 1686 (m), 1549 (s), 1423 (m), 1347 (m), 1254 (m), 1225 (w), 1136 (w); TLC R_f 0.35 (hexane/EtOAc (1/1)); HPLC (method C) t_R (1*R*)-**19** 14.9 min (6.0%), t_R (1*S*)-**19** 37.2 min (4.3%), t_R (1*S*)-**20** 42.1 min (89.7%).

Inter [4 + 2]/Intra [3 + 2] Tandem Cycloadditions with Propenyl Ether (*E*)-13. Promoted by $Ti(O\text{-}i\text{-}Pr)_2Cl_2$: (2*S*,2a*S*,4a*S*,5*S*,6*S*,7a*R*,7b*R*)-6-[(1*R*,2*S*)-2-(Phenylcyclohexyl)oxy]octahydro-5,7b-dimethyl-1,7-dioxa-7a-azacyclopent[*cd*]indene-2-carboxylic Acid Methyl Ester (21) and (2*S*,2a*S*,4a*S*,5*R*,6*S*,7a*R*,7b*R*)-6-[(1*R*,2*S*)-2-(Phenylcyclohexyl)oxy]octahydro-5,7b-dimethyl-1,7-dioxa-7a-azacyclopent[*cd*]indene-2-carboxylic Acid Methyl Ester (22). To a cold (−90 °C) solution of nitroalkene **1** (199 mg, 1.00 mmol, 1.0 equiv) in CH_2Cl_2 (5.0 mL) was added a solution of propenyl ether (*E*)-**13** (324 mg, 1.50 mmol, 1.5 equiv) in CH_2Cl_2 (0.5 mL), and then a solution of dichlorotitanium diisopropoxide (3.00 mmol, 3.0 equiv) in CH_2Cl_2 (1.5 mL) was added. The solution was stirred at −90 °C for 30 min and then at −78 °C for an additional 2 h. After standing for 10 h at rt, the crude products were then purified by column chromatography (hexane/EtOAc (8/1, 4/1)) to afford 355 mg (86%) of a mixture of nitroso acetals **21** and **22** as a white solid. An analytical sample was purified by recrystallization from EtOAc/hexane. Data for **21**: mp 130–131 °C (EtOAc/hexane); ^1H NMR (300 MHz) 7.15–7.29 (m, 5 H, phenyl), 4.79 (d, J = 8.4, 1 H, HC(2)), 4.08 (d, J = 6.8, 1 H, HC(6)), 3.77 (s, 3 H, H_3C(10)), 3.69 (dt, J_d = 4.0, J_t = 12.8, 1 H, HC(1')), 2.50–2.61 (m, 2 H, HC(6'), HC(2a)), 2.29–2.32 (m, 1 H, HC(2')), 1.70–1.88 (m, 7 H), 1.28–1.59 (m, 6 H), 1.26 (s, 3 H, H_3C(8)), 0.28 (d, J = 7.2, 3 H, H_3C(11)); ^{13}C NMR (75.5 MHz) 170.35 (C(9)), 144.30 (C(7')), 128.13 (C(8')), 128.00 (C(9')), 126.12 (C(10')), 106.68 (C(6)), 85.24

(C(2)), 84.18 (C(1')), 82.40 (C(7b)), 58.68 (C(2a)), 52.31 (C(10)), 51.54 (C(6')), 50.75 (C(5)), 36.84 (C(4a), 36.01 (CH_2), 35.06 (C(2')), 33.76 (C(5')), 28.28 (CH_2), 27.37 (C(8)), 25.80 (CH_2), 25.18 (CH_2), 17.03 (C(11)); IR (CCl_4) 2932 (s), 2859 (w), 1744 (s), 1449 (m), 1199 (w), 1169 (m), 1146 (m), 1030 (m); MS (LRFAB) 417 (M^+ + H + 1, 22), 416 (M^+ + H, 85), 400 (6), 385 (10), 258 (100), 242 (30), 240 (18), 212 (8), 159 (40), 135 (12), 119 (24); TLC R_f 0.60 (hexane/EtOAc (2/1)). Anal. Calcd for $C_{23}H_{31}NO_5$ (415.53): C, 69.37; H, 8.00; N, 3.37. Found: C, 69.42; H, 8.05; N, 3.43.

(1*S*,3*R*,5*S*,5a*S*,7a*S*,7b*R*)-Octahydro-1-hydroxy-5,7b-dimethyl-2*H*-cyclopenta[*gh*]pyrrolizin-2-one (7) and (1*S*,3*R*,5*R*,5a*S*,7a*S*,7b*R*)-Octahydro-1-hydroxy-5,7b-dimethyl-2*H*-cyclopenta[*gh*]pyrrolizin-2-one (8). Hydrogenolysis of the nitroso acetal mixture of **21** and **22** (250 mg, 0.606 mmol) obtained from (*E*)-**13** afforded 90 mg of a mixture of **7** and **8** (77%) as a white solid (^1H NMR ratio = 12:1) and 91 mg (86%) of recovered alcohol **5**. Data for **7** and **8**: ^1H NMR (300 MHz) 4.64 (d, J = 7.4, 0.9 H, HC(1)), 4.04 (dd, J = 7.3, 11.8, 0.9 H, HC(4)), 3.21 (d, J = 8.5, 0.15 H, $H_2C(4)$), 2.89 (br, 1 H, OH), 2.64–2.77 (m, 3 H), 2.49 (m, 2 H), 1.35–1.83 (m, 6 H), 1.33 (s, 3 H, $H_3C(8)$), 1.06 (d, J = 6.7, 3 H, $H_3C(9)$), 1.03 (d, J = 6.9, 0.3 H, $H_3C(9)$); IR (CCl_4) 3385 (b, w), 2959 (m), 2870 (m), 1709 (s), 1541 (w), 1404 (w), 1335 (w), 1209 (w), 1140 (w); TLC R_f 0.19(hexane/EtOAc (1/1)).

(1*S*,3*R*,5*S*,5a*S*,7a*S*,7b*R*)-Octahydro-1-[*N*-(3,5-dinitrophenyl)carbamoxy]-5,7b-dimethyl-2*H*-cyclopenta[*gh*]pyrrolizin-2-one (19) and (1*S*,3*R*,5*R*,5a*S*,7a*S*,7b*R*)-Octahydro-1-[*N*-(3,5-dinitrophenyl)carbamoxy]-5,7b-dimethyl-2*H*-cyclopenta[*gh*]pyrrolizin-2-one (20). Derivatization of the mixture of **7** and **8** (19.5 mg, 0.100 mmol, 1.0 equiv) afforded 35 mg (88%) of a mixture of **19** and **20** as a white solid: ^1H NMR (300 MHz) 9.79 (br, 1 H, NH), 8.63 (t, J = 2.0, 1 H, HC(6')), 8.56 (d, J = 1.9, 2 H, HC(4')), 5.87 (d, J = 6.8, 1 H, HC(1)), 4.11 (dd, J = 11.9, 7.3, 1 H, HC(4)), 2.63–2.75 (m, 2 H), 1.82–1.98 (m, 3 H), 1.46 (s, 3 H, $H_3C(8)$), 1.13 (d, J = 6.7, 3 H, $H_3C(9)$); IR (CH_2Cl_2) 3055 (m), 2988 (w), 1742 (w), 1689 (s), 1547 (s), 1422 (m), 1346 (m), 1275 (m), 895 (m); TLC R_f 0.35 (hexane/EtOAc, 1/1); HPLC (method C) t_R (1*R*)-**19** 14.75 min (1.0%), t_R (1*R*)-**20** 17.6 min (1.4%), t_R (1*S*)-**19** 37.0 min (91.3%), t_R (1*S*)-**20** 41.2 min (6.4%).

Promoted by MAD: (2*S*,2a*S*,4a*S*,5*S*,6*S*,7a*R*,7b*R*)-6-[(1*R*,2*S*)-2-(Phenylcyclohexyl)oxy]octahydro-5,7b-dimethyl-1,7-dioxa-7a-azacyclopent[*cd*]indene-2-carboxylic Acid Methyl Ester (21) and (2*S*,2a*S*,4a*S*,5*R*,6*S*,7a*R*,7b*R*)-6-[(1*R*,2*S*)-2-(Phenylcyclohexyl)oxy]octahydro-5,7b-dimethyl-1,7-dioxa-7a-azacyclopent[*cd*]indene-2-carboxylic Acid Methyl Ester (22). To a solution of 2,6-di-*tert*-butyl-4-methylphenol (1.32 g, 6.00 mmol, 6.0 equiv) in toluene (6.0 mL) was added Me_3Al (2.0 M in toluene, 1.50 mL, 3.0 mmol, 3.0 equiv). To the cold (−78 °C) solution of MAD was added a solution of nitroalkene **1** (199 mg, 1.00 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL), and then a solution of propenyl ether (*E*)-**13** (324 mg, 1.50 mmol, 1.5 equiv) in CH_2Cl_2 (0.5 mL) was added. The reaction mixture was allowed to stir at −78 °C for 1 h. After standing for 8 h at rt, the crude products were purified by column chromatography (hexane/EtOAc (20/1, 4/1)) to afford 355 mg (85.5%) of a diastereomeric mixture of nitroso acetals in a ratio of 4:6:1 (**21**:**22**:**22'**) by ^1H NMR. Data for **22**, **22'**, and **21**: ^1H NMR (400 MHz) 7.11–7.34 (m, 5 H, phenyl), 4.80 (d, J = 8.3, 0.4 H), 4.79 (d, J = 8.1, 0.3 H, HC(2)), 4.77 (d, J = 7.3, 0.1 H), 4.73 (d, J = 6.8, 0.5 H), 4.07–4.18 (m, 0.6 H), 4.02 (d, J = 7.2, 0.2 H), 3.80 (s, 1.5 H, $H_3C(10)$), 3.77 (s, 1.5 H, $H_3C(10)$), 3.65–3.71 (m, 1 H), HC(1')), 2.64–2.67 (m, 1 H, HC(2a)), 2.50–2.59 (m, 1 H), 2.22–2.35 (m, 1 H), 1.20–1.98 (m, 11 H), 1.26 (s, 1.2 H, $H_3C(8)$), 1.23 (s, 0.4 H, $H_3C(8)$), 1.14 (s, 2.0 H, $H_3C(8)$), 0.83 (d, J = 6.8, 1.5 H, $H_3C(11)$), 0.27–0.31 (m, 1.5 H, $H_3C(11)$); ^{13}C NMR (100 MHz) 143.95 (C(7')), 127.97 (C(8')), 127.88 (C(9')), 125.53 (C(10')), 99.53 (C(6)), 87.14, 86.81, 75.04, 56.82 (C(2a)), 52.34 (C(10)), 49.81, 49.59, 35.73, 31.62, 31.05, 28.11, 28.00, 26.21, 24.88, 23.65, 16.71 (C(11)), 144.32 (C_b(7')), 128.14 (C_b(8')), 128.02 (C_b(9')), 126.13 (C_b(10')), 106.70 (C_b(6)), 85.25 (C_b(2)), 84.19 (C_b(1')), 82.40 (C_b(7b)), 58.70 (C_b(2a)), 52.32 (C_b-(10)), 51.57 (C_b(6')), 50.77 (C_b(5)), 36.86 (C_b(4a), 36.03 (CH_2), 35.08 (C_b(2')), 33.78 (C_b(5')), 28.30 (CH_2), 27.39 (C_b(8)), 25.81 (CH_2), 25.20 (CH_2), 17.05 (C_b(11)); IR (CCl_4) 3028 (w), 2932 (s), 2876 (m), 1744 (s), 1659 (w), 1603 (w), 1637 (w), 1449 (s), 1377 (m), 1282 (m), 1250 (m), 1201 (s), 1095 (s), 1014 (s), 956 (s); MS (LRFAB) 417 (M^+ + H + 1, 8), 416 (M^+ + H, 28), 400 (5), 385 (13), 258 (34), 242 (14), 240 (100), 212 (27), 159 (82).

(1*S*,3*R*,5*S*,5a*S*,7a*S*,7b*R*)-Octahydro-1-hydroxy-5,7b-dimethyl-2*H*-cyclopenta[*gh*]pyrrolizin-2-one (8) and (1*S*,3*R*,5*R*,5a*S*,7a*S*,7b*R*)-Octahydro-1-hydroxy-5,7b-dimethyl-2*H*-cyclopenta[*gh*]pyrrolizin-2-one (7). Hydrogenation of the nitroso acetal mixture of **21** and **22** (250 mg, 0.606 mmol) obtained from (*E*)-**13** afforded 95 mg of a mixture of **7** and **8** (81%) as a white solid (^1H NMR ratio = 1.9:1) and 85 mg (80%) of recovered alcohol **5**. Data for **7** and **8**: ^1H NMR (400 MHz) 4.63–4.67 (m, 1 H, HC(1)), 4.04 (dd, J = 7.3, 11.7, 0.4 H, HC_a(4)), 3.20 (d, J = 8.5, 1.5 H, H_2C_b(4)), 3.15 (br, 0.5 H, HOC_b(1)), 3.03 (br, 0.4 H, HOC_a(1)), 2.74 (t, J = 8.1, 0.7 H), 2.61–2.71 (m, 1 H), 2.50–2.55 (m, 0.7 H), 2.06–2.17 (m, 2 H), 1.45–1.82 (m, 4 H), 1.35 (s, 2 H, H_3C_b(8)), 1.33 (s, 1 H, H_3C_a(8)), 1.05 (d, J = 6.8, 1 H, H_3C_a(9)), 1.02 (d, J = 6.8, 2 H, H_3C_b(9)); ^{13}C NMR (100 MHz) 72.44 (C(1), 58.13 (C(5a)), 51.93 (C(7a)), 50.32 (C(4)), 42.11 (C(5)), 30.83, 25.26, 24.21 (C(8)), 17.50 (C(9)), 77.66 (C(7b)), 71.95 (C(1)), 54.27 (C(5a)), 50.50 (C(7a)), 47.39 (C(4)), 34.09 (C(5)), 25.50 (C(7)), 24.79 (C(6)), 22.08 (C(8)), 14.91 (C(9)); IR (CCl_4) 3383 (br,w), 2963 (m), 2874 (w), 1707 (s), 1553 (w), 1456 (w), 1404 (w), 1379 (w), 1327 (w), 1209 (w), 1148 (w), 1086 (w), 997 (w); TLC R_f 0.19 (hexane/EtOAc (1/1)).

(1*S*,3*R*,5*S*,5a*S*,7a*S*,7b*R*)-Octahydro-1-[*N*-(3,5-dinitrophenyl)carbamoxy]-5,7b-dimethyl-2*H*-cyclopenta[*gh*]pyrrolizin-2-one (20) and (1*R*,3*S*,5*S*,5a*R*,7a*R*,7b*S*)-Octahydro-1-[*N*-(3,5-dinitrophenyl)carbamoxy]-5,7b-dimethyl-2*H*-cyclopenta[*gh*]pyrrolizin-2-one (19). Derivatization of the mixture of **7** and **8** (19.5 mg, 0.100 mmol, 1.0 equiv) afforded 31 mg (78%) of a mixture of **19** and **20** as a white solid: ^1H NMR (300 MHz) 9.68 (br, 0.6 H, NH_a), 9.38 (br, 0.4 H, NH_b), 8.65 (d, J = 1.9, 1 H, HC(6')), 8.57 (d, J = 1.6, 2 H, HC(4')), 5.89 (d, J = 8.0, 0.7 H, HC_a(1)), 5.85 (d, J = 6.7, 0.3 H, HC_b(1)), 4.12 (dd, J = 12.0, 7.3, 0.4 H, HC_b(4)), 3.21–3.39 (m, 2 H), 2.94 (t, J = 8.5, 1 H), 2.62–2.78 (m, 2 H), 2.22 (dt, J_d = 10.3, J_t = 6.5, 1 H, HC-(7a)), 1.50–2.07 (m, 4 H), 1.47 (s, 2.4 H, H_3C_a(8), 1.45 (s, 0.6 H, H_3C_b(8), 1.13 (d, J = 6.6, 0.9 H, $H_3C(9)$), 1.06 (d, J = 6.9, 2.1 H, $H_3C(9)$); IR (CH_2Cl_2) 2980 (w), 1691 (w), 1605 (w), 1549 (m), 1468 (w), 1346 (w), 1219 (w), 1095 (w); TLC R_f 0.35 (hexane/EtOAc, 1/1); HPLC (method C) t_R (1*R*)-**19** 14.9 min (0.02%), t_R (1*R*)-**20** 17.7 min (10.0%), t_R (1*S*)-**19** 36.5 min (28.1%), t_R (1*S*)-**20** 41.2 min (61.9%).

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Supplementary Material Available: ^1H and ^{13}C NMR spectra for compounds 14β/14α/14β' (mixture, ^1H only), **17**, **18a**/**18b**, (±)-**19**, (−)-**19**, (±)-**20**, (−)-**20**, **22**/**21'**/**21** (mixture), and **21**/**22**/**22'** (mixture) (18 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.