Tandem Cycloaddition Chemistry of Nitroalkenes: Preparative and Theoretical Studies on the Stereochemical Course of [3 + 2] Cycloaddition of Cyclic Nitronates

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Intermolecular [3 + 2] cycloadditions between two cyclic nitronates and a series of dipolarophiles are examined. High facial selectivity is observed in all cases and is analyzed with the aid of ab initio transition structure calculations. Monosubstituted dipolarophiles reacted with exclusive regiocontrol. Disubstituted dipolarophiles reacted with varying degrees of regiocontrol, which was dependent on the substituent. A theoretical approach for predicting regioselectivity is discussed. Exo selectivity was generally favored due to steric effects, and was especially high with cis-disubstituted dipolarophiles.

Introduction

The tandem [4 + 2]/[3 + 2] cycloaddition of nitroalkenes has emerged as a powerful method for the rapid and stereoselective construction of complex polyheterocyclic systems.[1] A critical strategic feature that imparts great versatility and stereocontrol to this sequence is the [3 + 2] cycloaddition of the first-formed nitronate (Figure 1). Of the four fundamental permutations of this tandem sequence, the two most studied are those which terminate in an intramolecular [3 + 2] process.[2−5] In these cases, the regio- and stereochemical outcome of the cycloaddition is primarily determined by the constraints imposed by the tether.

Of equal synthetic interest are those tandem processes that terminate in an intermolecular [3 + 2] cycloaddition.[6−9] In these cases the stereochemical course of the reaction is less predictable. Thus, to expatiate our knowledge of the factors controlling selectivity in these cycloadditions, we set out to systematically explore [3 + 2] cycloadditions of representative cyclic nitronates formed from a nitroalkene [4 + 2] cycloaddition with a variety of dipolarophiles, to examine the effects of dipolarophile substitution on regio-, stereo-, and facial selectivity.

Background

Regioselectivity. The regiochemical issues in cycloadditions of the structurally similar nitrones[10,11] and nitrile oxides[12] have been extensively studied. In addition to compilations of experimental results, rationalizations from theoretical studies have also been forwarded.[13] Both nitrones and nitrile oxides display very similar behavior, so only the case of nitrones will be discussed here.

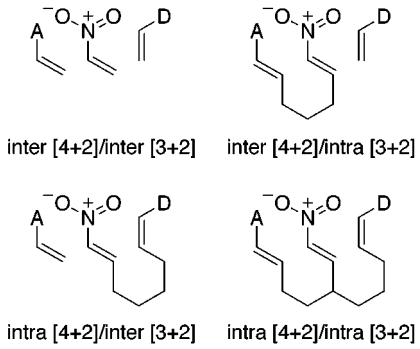

Figure 1. Family of tandem [4 + 2]/[3 + 2] cycloadditions (A = electron acceptor, D = electron donor).

The most common method of rationalizing regioselectivity is frontier molecular orbital (FMO) theory.[14] The frontier molecular orbitals of a simple nitrone are shown below (Figure 2).[15] The largest coefficient of the nitrone HOMO is on the oxygen, while the largest coefficient of the nitrone LUMO is at the carbon. Comparison of these frontier orbitals with those of common monosubstituted alkenes shows that the interaction with the smaller energy gap is $HOMO_{dipolarophile}-LUMO_{nitrone}$, which leads to 5-substituted isoxazolidines (**a**).[16] In the case of alkenes with strongly electron-withdrawing groups, the $LUMO_{dipolarophile}-HOMO_{nitrone}$ interaction becomes more significant, and one would expect to see the other regioisomer (**b**).

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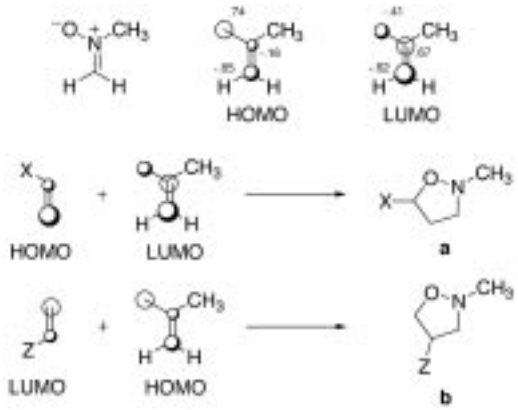


Figure 2. Matching coefficients of nitrones and dipolarophiles.

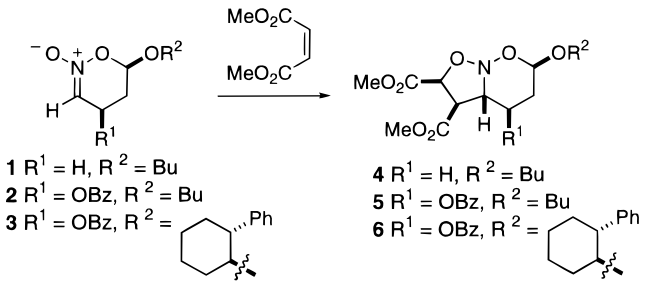
In general, cycloadditions of nitrones with monosubstituted alkenes are consistent with this analysis.[13] Highly electron-deficient dipolarophiles are more likely to produce 4-substituted isoxazolidines (**a**). Nitrones substituted at carbon have a higher energy HOMO than those without. With these nitrones, the $LUMO_{dipolarophile}$—$HOMO_{nitrone}$ interaction becomes even more significant, and an increase in the amount of isomer **b** is generally observed. Examinations of disubstituted alkenes have shown that the addition of alkyl groups can markedly alter the regiochemical outcome.[17]

The frontier orbitals of nitronates with electron-withdrawing groups attached to carbon have been calculated and show the same pattern of coefficients as nitrones and nitrile oxides.[18−20] A different sort of arrangement is observed with calculations on simple alkyl-substituted nitronates.[21] With these dipoles, the larger coefficient is on carbon in both the HOMO and the LUMO. When matched with electron-deficient dipolarophiles, the smaller energy gap is the $LUMO_{dipolarophile}$—$HOMO_{nitronate}$. FMO theory predicts 5-isoxazolidines would always predominate; this has been the case with both electron-deficient[22−25] and electron-rich[6] monosubstituted dipolarophiles. With the exception of several intramolecular cycloadditions[1] and cycloadditions with symmetrical olefins,[8,26] [3+2] cycloadditions between cyclic nitronates and 1,2-disubstituted alkenes are rare.[27,28]

Stereoselectivity. The stereochemical course of cycloadditions of acyclic nitronates to mono-[20] and di-activated[26,29] alkenes has been extensively studied by Carrié. In most cases, exclusive exo (with respect to the electron-withdrawing group) selectivity was seen; exceptions were acrylonitrile, which gave an equal mixture of stereoisomers, and dimethyl maleate, which formed only the endo adduct. In all cases, the authors explained the stereoselectivity as the effect of secondary orbital interactions; INDO calculations of the frontier orbitals have been used to support the rationale.

Studies from our laboratories have shown that an exo orientation is generally preferred.[1] In a complete reversal of the precedent with acyclic nitronates, dimethyl maleate gave a single product resulting from exo approach to nitronates **1**,[30] **2**,[31] and **3**[8] (Scheme 1). A fundamental difference in these systems (compared to those of Carrié) is that there is no electron-withdrawing group on the nitronate carbon, which affects the relative size of the coefficients in the frontier orbitals, but not their signs; any secondary orbital effect in the Carrié acyclic system should therefore also be present in these cyclic systems.

Scheme 1

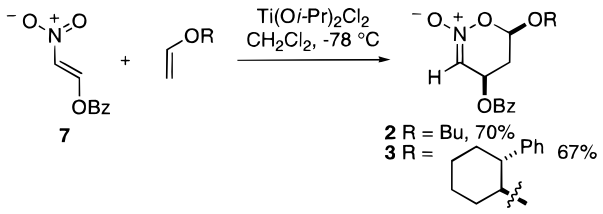


To better understand the nature of [3 + 2] cycloadditions of cyclic nitronates, a systematic study of dipolarophile structure was undertaken. Nitronates **2** and **3** were chosen for their ease of preparation and use; it was also expected that the cycloadditions would be highly facially selective, which would halve the number of possible cycloadducts and ease identification.

Experimental Results

Preparation of 1,3-Dipoles. Nitronate **2** was prepared in good yield and as a single diastereomer (d.r. > 25/1) by $Ti(O\text{-}i\text{-}Pr)_2Cl_2$-promoted cycloaddition of nitroalkene **7**[8] with *n*-butyl vinyl ether (Scheme 2). This Lewis acid generally promotes highly endo selective cycloadditions.[1] The crystalline nitronate **2** was easily handled and stable indefinitely, but only when stored rigorously free from air. Nitronate **3** was prepared as previously reported from these laboratories.[8]

Scheme 2



Preparation of Monosubstituted Dipolarophiles. The aldehyde precursors for several vinyl ketones were prepared as outlined in Scheme 3. Aldehydes **11** and **12** were prepared in 2 steps from 1,4-butenediol **8** by hydroxyl protection and ozonolysis of the alkene. The addition of vinylmagnesium bromide to aldehyde **11**

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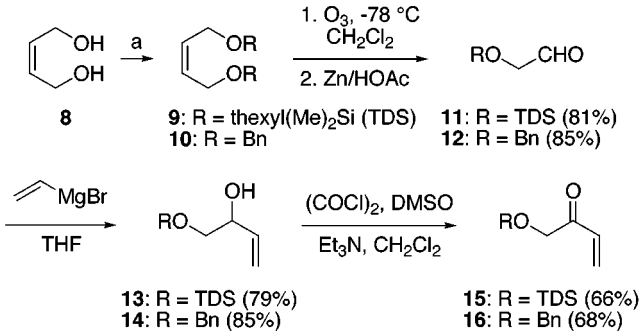
provided the allyl alcohol **13** in 79% yield. Oxidation of the alcohol using the Swern procedure[32] resulted in the clean conversion of the alcohol into the ketone. The yields of the process were widely variable due to the tendency of the product to polymerize during distillation, even at 10^{-5} mmHg. We found no deleterious effect on the subsequent [3 + 2] cycloaddition by using the ketone immediately after initial chromatographic purification and found the yields to fall within the 66−75% range. (Benzyloxy)methyl vinyl ketone (**16**) was prepared by Swern oxidation of the known alcohol **14**[33] in 68% yield or by using the Dess−Martin reagent[34,35] (87%).

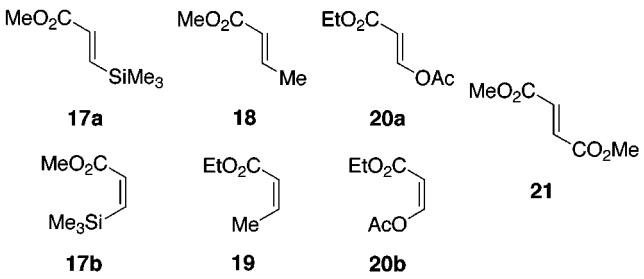
Scheme 3[a]



[a] Key: (a) R = TDS: TDSCl imidazole, DMF (97%); R = Bn: NaH, $Bu_4N^+I^-$, BnCl, THF, 66 °C, (99%).

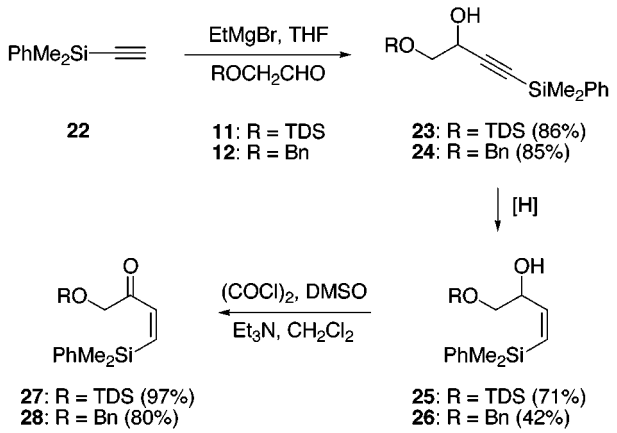
Preparation of Disubstituted Dipolarophiles. A series of disubstituted acrylate derivatives was chosen for study (Chart 1). (*E*)-2-Trimethylsilylpropenoate **17a**[36] was prepared from oxidation and esterification of the known allyl alcohol.[37] (*Z*)-2-Substituted propenoates **17b**[36] and **19**[38] were synthesized by Lindlar[39] hydrogenation of the corresponding alkynes. A separable mixture of **20a** and **20b** was prepared from O-acetylation of sodium ethyl formyl acetate.[40] The analogous methyl esters could be synthesized by a similar procedure, but in much lower yields.

Chart 1



Two (*Z*)-2-disubstituted enones were also examined. The *β*-silylvinyl ketone **28** was prepared from (benzyloxy)acetaldehyde (**12**) by the sequence depicted in Scheme 4. Metalation of silyl acetylene **22**[41] followed by the addition of aldehyde **12** provided the propargyl alcohol **24** in 85% yield. Catayltic reduction of the alkynes **23** and **24**[42,43] was plagued with variability and lack of reproducibility. For example, hydrogenation of alkyne **24** over 5% palladium on calcium carbonate in the presence of quinoline (6 mol %) provided the allylic alcohols (*Z*)-**26** (42%) and (*E*)-**26** (7%) in addition to the saturated product (18%). The use of 1 molar equivalent of quinoline (relative to substrate) failed to suppress over-reduction. The use of either 5% palladium on calcium carbonate poisoned with lead (Lindlar catalyst)[39] or palladium on barium sulfate[44] offered no advantages; the reduction times were significantly extended (11 h vs 3 h) and resulted in lower (2−4/1) *Z*/*E* selectivities. Fortunately, the components were separable by MPLC but were routinely carried into the next reaction as a mixture. Ultimately, we found that the propargyl alcohol **23** could be selectively reduced with dicyclohexylborane (followed by protonolysis with acetic acid) to afford (*Z*)-**25** in 71% yield as a single isomer. Conversion of **25** and **26** to **27** and **28** proceeded in high yield and without isomerization under the Swern oxidation conditions.

Scheme 4



[3 + 2] Cycloadditions with Monosubstituted Dipolarophiles. The results of the thermal cycloaddition reaction between nitronates **2** or **3** and monosubstituted dipolarophiles are collected in Table 1. The reactions were facile; in general, the nitronates were converted into the corresponding nitroso acetals in the presence of 5−6 equiv of the dipolarophile in benzene at room temperature. The cycloaddition was performed with 1.1−1.3 equivalents of the dipolarophile at a higher substrate concentration (0.1 M vs 0.03 M) when **15** and **16** were used in order to conserve material. The [3 + 2] cycloadditions occurred at ambient temperature within a reasonable time span (1.5−12 h). Elevated reaction temperatures were required for the rapid and complete consumption of nitronate **3** in the [3 + 2] cycloaddition with allyl alcohol.

Each of the nitroso acetals **29**−**36** were formed in high yield (79−91%) as a pair of diastereomers. The effect of

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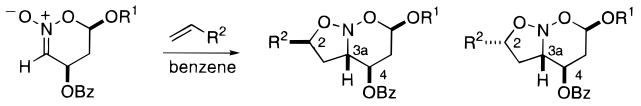
Table 1. [3 + 2] Cycloadditions with Monosubstituted Dipolarophiles



2 R^1 = Bu
3 R^1 = (1*S*,2*R*)-2-phenylcyclohexyl

						HC(2) ppm		C(2) ppm		
nitronate	R^2	temp, °C	time, h	yield, %	nitroso acetal	**a**	**b**	**a**	**b**	d.r.[a], **a**/**b**
2	CO_2Me	rt	6	79	**29**	5.09	4.84	80.5	80.8	7.6/1
3	CO_2Me	rt	6	86	**30**	5.02	4.78	80.6	80.8	6.5/1
3	CO_2−*t*-Bu	rt	2.5	91	**31**	4.88	4.66	81.4	81.8	11.4/1
3	COMe	rt	1.5	88	**32**	4.92	4.61	87.1	88.0	6.2/1[b]
3	$COCH_2OTDS$	rt	4	90	**33**	5.15	4.76	85.1	86.5	5/1[b]
3	$COCH_2OBn$	rt	12	89	**34**	5.06	4.74	85.5	86.6	5.7/1
3	CHO	rt	3.5	*c*	**35**	4.88	4.62	*c*		1/2
3	CH_2OH	80	1.5	81	**36**	4.74	4.66	84.1	86.8	1.3/1

[a] Product ratios determined by isolation. [b] Determined by ^{1}H NMR analysis of the mixture. [c] Converted to **36** by reduction with $NaBH_4$ in 62% overall yield. Nitroso acetals **35** characterized only by ^{1}H NMR analysis.

the vinyl ether substituent (OR^1) on the diastereoselectivity was minimal (cf., Table 1, entries 1 and 2). Separation of the diastereomers was made easier using the chiral auxiliary; therefore, the cycloaddition study with monosubstituted dipolarophiles was conducted with nitronate **3**. The cycloadditions were found to be under kinetic control. Nitroso acetal **30b** was quantitatively recovered after being stirred with *tert*-butyl acrylate in benzene; no trace of **31a** or **31b** was detected. The rate and selectivity of the cycloaddition were not subject to significant solvent effects. Comparable yields for the formation of nitroso acetals **29** were found in benzene and acetonitrile, but the diastereomeric ratio was slightly lower (5.5/1) in the latter. In all cases, the products were assigned a configuration reflecting approach of the dipolarophile to the face opposite the C(4) benzoate. This assignment was proven unambiguously in the case of **30** (vide infra) and is consistent with previous studies[8] and X-ray crystal structure determinations.[45]

In accord with previous trends in the intermolecular [3 + 2] cycloaddition of nitronates,[8,18−20,46,47] the major nitroso acetals (**29a**−**36a**) arose from an exo orientation of the dipolarophile controlling group (R^2). The sole exception was seen with acrolein; endo approach to provide nitroso acetal **35b** was slightly favored (an X-ray crystal structure of **36b**[45] confirmed the assignment). A noticeable correlation between the size of the dipolarophile substituent and the diastereomeric ratio of nitroso acetals was found. For example, the cycloaddition of nitronate **3** with *tert*-butyl acrylate resulted in an 11.4/1 ratio of diastereomeric products. With methyl acrylate, methyl vinyl ketone, allyl alcohol, and acrolein, the diastereomeric ratios gradually decreased from 7/1 to 1/2.

A compilation of diagnostic NMR data for each of the diastereomeric pairs of nitroso acetals is listed in Table 1. In all cases, the 2-D NMR analyses were consistent with the attachment of the dipolarophile controlling group (R^2) at C(2). The ^{1}H NMR resonance for HC(2) for each of the exo-derived nitroso acetals was downfield by 0.12 ppm to 0.39 ppm relative to the endo-derived isomer. Examination of the ^{13}C NMR data revealed that the C(2) resonance for **29b**−**36b** was downfield relative to the other isomer (0.2 ppm to 2.7 ppm).

Proof of Facial Selectivity. In the [3 + 2] cycloaddition there is an issue of regioselectivity in which the carbon bearing the activating group of the dipolarophile is attached to either the oxygen atom (head-to-head) or to the carbon atom (head-to-tail) of the dipole. There are also two issues of stereoselectivity. The first involves the approach of the dipolarophile to either face of the dipole; the second is the orientation of the activating group of the dipolarophile (endo or exo) with respect to the dipole. Overall this creates a set of eight possible isomers from each nitronate. 2-D NMR analysis was consistent with the head-to-head connectivity for all isomers, thereby reducing the number of possible isomers to four. To identify the origin of stereoisomerism, we sought a simple method that would enable us to distinguish among the four possibilities. That two diastereomers were formed in the cycloaddition of both nitronates **2** and **3** indicated that the stereochemical complexity was due to either endo/exo isomerism or to facial indiscrimination. Since two new stereocenters are created in the cycloaddition, removal of one would result in the retention of sufficient stereochemical information to eliminate one of the possible pathways. Independent hydrogenolysis of the nitroso acetals followed by removal of the hydroxy group would provide a pair of deoxylactams. If the stereochemical duplicity were due to facial indiscrimination, the remaining stereogenic center would reflect that and the lactams **38a** and **38b** would differ in the configuration at the ring junction. The deoxylactams would be identical if the dipolarophile approached from the same face; the stereoisomerism would then arise from endo/exo pathways.

Deoxygenation of the lactam was accomplished using the two-step procedure reported previously[8] (Scheme 5). The alcohol **37a**[45] was first acylated with phenoxy chlorothionocarbonate. Tributyltin hydride and AIBN were then slowly added to a benzene solution of the thionocarbonate at 80 °C to furnish the deoxygenated lactam **38a** in 58% yield. In a similar manner, the minor nitroso acetal **37b** was transformed to the deoxygenated lactam

(45) The authors have deposited atomic coordinates for the X-ray crystal structures of **36b** (no. 113363), **37a** (no. 113364), **40b$_i$** (no. 113365), **42a$_{ii}$** (no. 113366), and **44b$_i$** (no. 113367) with the Cambridge Crystallographic Data Centre. The data can be obtained, upon request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, U.K.

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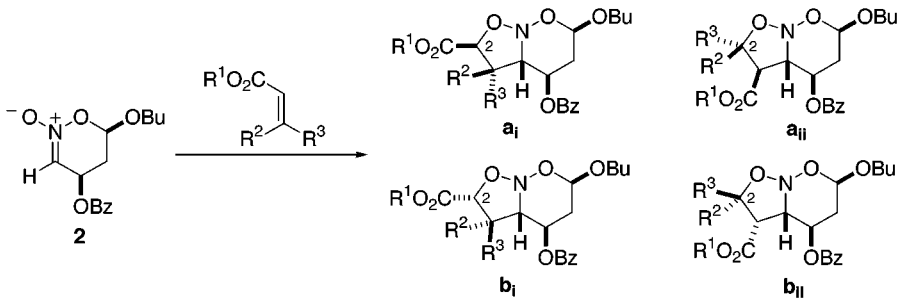
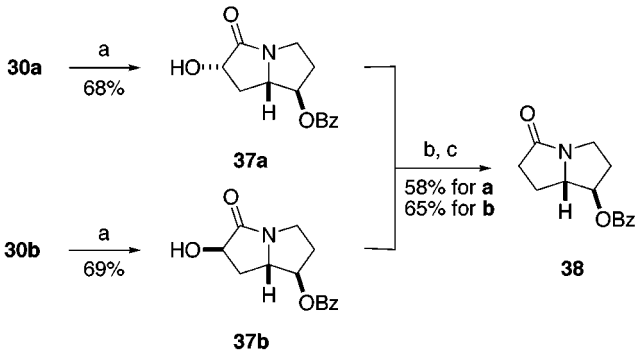
Table 2. [3+2] Cycloadditions with Disubstituted Acrylates



									HC(2) ppm		
no.	R^1	R^2	R^3	solvent	temp, °C	time, h	yield, %	nitroso acetal	**i**	**ii**	d.r.[a], $\mathbf{a_i/a_{ii}/b_i/b_{ii}}$
	Me	H	H	benzene	rt	6	79	**29**			7.6/*c*/1/*c*
17b	Me	$SiMe_3$	H	CH_3CN	65	38	72	**39**	5.13	4.50	2.4/1/*c*/*c*
17a	Me	H	$SiMe_3$	CH_3CN	65	22	77	**40**	4.64, 4.60	4.16	1/1.5/2.1/*c*
19	Et	Me	H	CH_3CN	65	22	75	**41**	5.07	5.07	1/1.6/*c*/*c*
20b	Et	OAc	H	CH_2Cl_2	70[b]	3	54	**42**		6.89	*c*/1/*c*/*c*
20a	Et	H	OAc	CH_3CN	65	24	78	**43**	4.94, 4.80	6.99, 6.79	*d*
21	Me	H	CO_2Me	benzene	rt	23	82	**44**			1/−/1/−

[a] Product ratios determined by isolation or ^1H NMR analysis of mixtures. [b] Concentration ~6 M in **20b**; solution did not reflux. [c] Not observed. [d] Regioselectivity 1/2.7 **i**/**ii** by ^1H NMR analysis of reaction mixture; stereoselectivity could not be determined.

Scheme 5[a]



[a] Reagents: (a) H_2 (160 psi), Ra-Ni, MeOH; (b) PhOCSCl, pyridine, THF; (c) Bu_3SnH, AIBN, C_6H_6, 80 °C.

38b. Comparison of the melting points and ^1H and ^{13}C NMR spectra revealed that lactams **38a** and **38b** were identical.

Hydrogenolysis of nitroso acetals **29a**−**31a** provided the same α-hydroxy lactam (**37a**). This outcome is consistent with a similar stereostructure of the cycloadducts, arising from the approach of the dipolarophile to the same face of the nitronate with the same orientation. The ^1H and ^{13}C NMR data for C(2) also support the assignment of **29a**−**36a** as arising from the same facial approach and orientation. A similar analysis of the NMR data for the nitroso acetals **29b**−**36b** suggests that all of these isomers are of the same stereochemical sense. We therefore conclude that in all cases, the diastereomers from the [3 + 2] cycloaddition with monosubstituted dipolarophiles with nitronates **2** and **3** are the result of endo/exo isomerism with complete facial control.

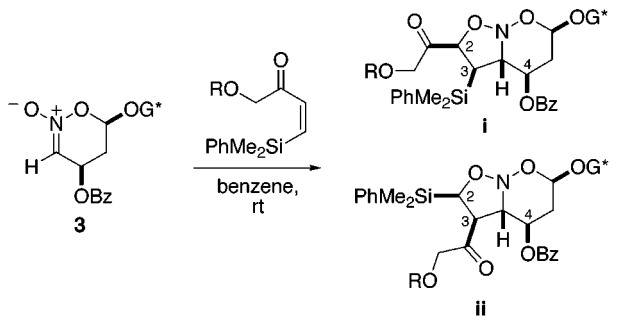
[3 + 2] Cycloadditions with Disubstituted Dipolarophiles. With the exception of methyl crotonate (**18**), all of the acrylate derivatives reacted smoothly with nitronate **2** (Table 2). All attempts with **18** resulted only in decomposition of the nitronate and no product formation. Unlike the monosubstituted dipolarophiles (vide supra), disubstituted acrylates were unreactive at room temperature; CH_3CN and CH_2Cl_2 proved better solvents than benzene for cycloadditions that required heating. These reactions usually gave lower yields of nitroso acetals and a small amount of several decomposition products, owing to the thermal instability of the nitronate. Dimethyl fumarate (**21**) reacted rapidly at room temperature. In contrast to nitroso acetals **29**−**36**, cycloadducts derived from disubstituted acrylates were more easily separated when nitronate **2** was used.

In cycloadditions with nitronate **2**, disubstituted dipolarophiles showed the high degree of diastereofacial selectivity previously seen with monosubstituted dipolarophiles. The structure of three of these nitroso acetals ($\mathbf{40b_i}$, $\mathbf{42a_{ii}}$, and $\mathbf{44b_i}$) was secured by X-ray crystallography.[45] In all cases, the structures revealed that the dipolarophile had approached exclusively to the β-face of the nitronate; the only relevant issues are regio- and stereocontrol. Nitroso acetals **i** arise from approach of the acrylate ester proximal to the nitronate oxygen (head-to-head); nitroso acetals **ii** are the opposite regioisomers. As before, nitroso acetals **a** and **b** derive from an exo and endo (respectively) approach of the ester to the nitronate.

In contrast to the earlier examples, disubstituted acrylates reacted with poorer regiocontrol. With a silicon-based β-substituent (nitroso acetals **39** and **40**) the major products still were those with the ester on C(2) of the isoxazoline, but with one-third of the product being the other regioisomer. Replacing a silicon-based substituent with carbon-based substituent (nitroso acetals **41**) resulted in a reversal in regiocontrol, now favoring isomer **ii**. The acetoxy acrylates were even more selective for the head-to-tail pathway, with cis-acrylate **20b** providing nitroso acetal $\mathbf{42a_{ii}}$ as a single cycloadduct.

The cis-disubstituted dipolarophiles exhibited greatly enhanced exo selectivity compared to the monosubstituted dipolarophiles. In all cases, only products arising from exo approach could be detected. The trans-dipolarophiles were much less selective. The major product from the cycloaddition of silane **17a** was $\mathbf{40b_i}$ (45% of product), the structure of which was determined by X-ray crystallography,[45] and which resulted from endo approach of the ester (hence exo approach of the bulky silane). The other

Table 3. [3+2] Cycloadditions with Alkoxymethyl Vinyl Ketones



no.	R	time, h	yield, %	nitroso acetal	HC(3) ppm i	HC(3) ppm ii	C(3) ppm i	C(3) ppm ii	d.r., i/ii
27	TDS	12	97	**45**[a]	2.30		32.0		26/1[b]
28	Bn	5	98	**46**	2.31	3.81	32.1	52.8	32/1[c]

[a] Nitronate (+)-**3** used in this case. [b] Determined by ^{1}H NMR analysis of the mixture. [c] Determined by ^{1}H NMR analysis and isolation.

head-to-head product, **40a$_i$** (22%), arose from a less favorable endo approach of the silane. The sole head-to-tail product isolated was determined by NOE analysis (see Supporting Information) to be **40a$_{ii}$**, which came from endo approach of the TMS group. The stereoselectivity in the cycloaddition of acetoxy acrylate **20a** could not be determined, owing to the inseparability of the four products. Dimethyl fumarate **21** displayed no stereoselectivity.

The results of the thermal cycloaddition between nitronate **3** and β-silylvinyl ketones **27** and **28** are listed in Table 3. To conserve material, only 1.2 equiv of the dipolarophile were used at higher substrate concentration (0.1 M). The [3 + 2] cycloadditions occurred at ambient temperature within five to 12 h. The reactions were typically performed immediately following the Swern oxidation of the precursor alcohols **25** and **26** and were allowed to proceed overnight for convenience. Both nitroso acetals **45** and **46** were formed in high yield as a pair of regioisomers.

The cycloaddition between nitronate **3** and ketone **28** provided the corresponding nitroso acetal **46** in 98% yield as a 32/1 ratio of regioisomers; cycloaddition with **27** was only slightly less selective. The ^{1}H NMR resonance of C(2) of **46$_{ii}$** was shifted upfield by 0.36 ppm relative to **46$_i$**. That difference was consistent with the range seen in nitroso acetals **39** and **40**, but was also within the range noted in the cycloaddition studies on simple, monosubstituted dipolarophiles where it was determined that the minor isomers arose from an endo orientation of the dipolarophile. Comparison of the ^{1}H and ^{13}C NMR shifts at C(3) was instrumental in deciphering the identity of the isomers. The ^{1}H NMR resonance of C(3) in the major isomer was found *1.5 ppm upfield* from that of the minor suggesting that the silicon atom was directly attached there. In the ^{13}C NMR spectrum, C(3) of the major nitroso acetal was located at 32.1 ppm while that of the minor isomer was located at 52.8 ppm. The positional differences clearly indicate that an electron-withdrawing group (carbonyl) was attached at C(3) of the minor isomer. Comparison with data for similar (*Z*)-β-silyl-substituted dipolarophile cycloadditions was also consistent with the identity of the minor isomer as a regioisomer.

Scheme 6

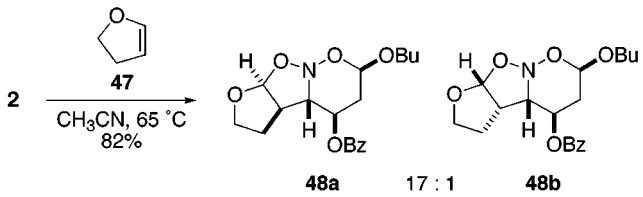
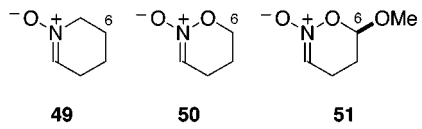


Chart 2



To devise a basis for predicting the regiochemical outcome of cycloadditions of nitronates of type **2** and **3** with disubstituted dipolarophiles (vide infra), we examined the dipolar cycloaddition of nitronate **2** with 2,3-dihydrofuran (**47**, Scheme 6).

Nitronate **2** and **47** underwent ready cycloaddition to provide two products (**48a** and **48b**) in a ratio of 17/1 (as determined by ^{1}H NMR analysis of the mixture). Surprisingly, the minor isomer was not the head-to-tail regioisomer, but rather derived from endo approach of the dipolarophile, as assigned by NOE studies on both diastereomers (see Supporting Information).

Theoretical Results

Although different dipolarophiles combine with nitronates **2** and **3** with varying levels of regio- and stereoselectivity, one constant factor is the high degree of facial selectivity. This has previously been attributed to steric repulsion from the C(4) benzoyloxy substituent.[8] However, even nitronates with no substituent at that atom (such as **1**) have shown significant facial selectivity (6/1 to 8/1) in cycloadditions with various dipolarophiles.[30] A theoretical study using three model 1,3-dipoles (Chart 2) was undertaken to help understand the origin of facial bias. Both nitrone **49**[48] and nitronate **50**[49] are known compounds. Because they are achiral, experiments cannot be used to test facial biases; theoretical studies can, however, examine individual chiral conformations. Nitronate **51** is a simplified model for nitronate **1**.

Transition structures for cycloadditions of half-chair conformations of **49**−**51** with ethylene were fully optimized at the RHF and B3LYP levels (Figures 3−6). In all cases, approach of ethylene distal to the C(6) axial group (which is proximal to the C(6) methoxy group in Figure 6) produced a transition structure wherein the six-membered ring adopted a chairlike conformation. Approach from the opposite face forced the six-membered ring to twist into a boatlike arrangement. Other boatlike transition structures (which originated from approach of ethylene to a half-boat conformation of the 1,3-dipole) were observed but not studied systematically.

Absolute and relative energies for the calculated transition structures are listed in Table 4. There was little difference in geometry or energy between the HF/6-31G* and HF/6-31+G* optimized structures; however,

(48) Tufariello, J. J.; Gatrone, R. C. *Tetrahedron Lett.* **1978**, 2753.
(49) Chlenov, I. E.; Morozova, N. S.; Khudak, V. I.; Tartakovskii, V. A. *Bull. Acad. Sci. USSR, Div. Chem. Sci.* (*Engl. Trans.*) **1970**, 2492; *Izv. Akad. Nauk. SSSR, Ser. Khim.* **1970**, 2641.

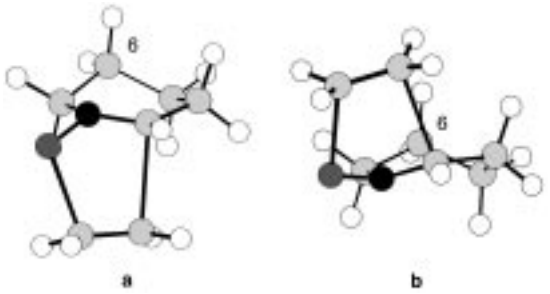


Figure 3. Chairlike (a) and boatlike (b) transition structures of nitrone **49** with ethylene.

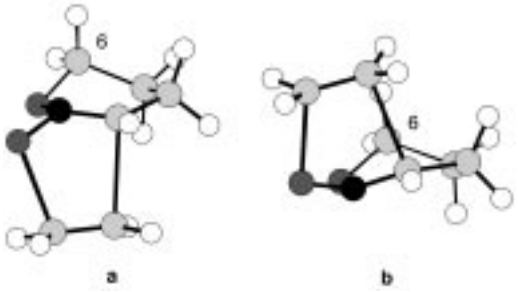


Figure 4. Chairlike (a) and boatlike (b) transition structures of nitronate **50** with ethylene.

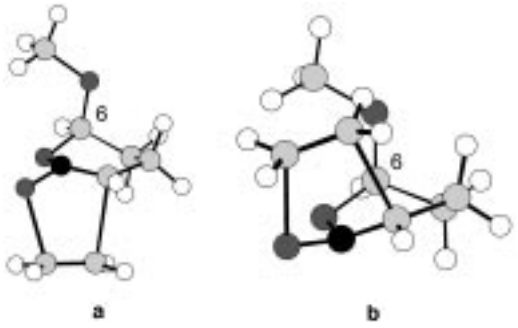


Figure 5. Chairlike (a) and boatlike (b) transition structures of nitronate **51** with ethylene (axial MeO−).

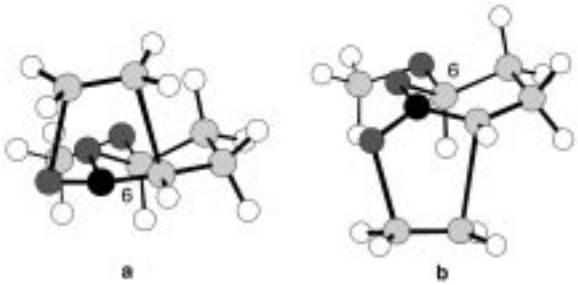


Figure 6. Chairlike (a) and boatlike (b) transition structures of nitronate **51** with ethylene (equatorial MeO−).

the HF/3-21G optimized structures displayed a facial preference significantly lower in magnitude.

For any given conformation of 1,3-dipole, approach to afford a boatlike transition structure was about 3−5 kcal/mol higher in energy than the corresponding chairlike arrangement. The only exception was the B3LYP/3-21G calculated structures with **51**. The conformer in which the C(6) methoxy group is axial favors distal approach by only 0.9 kcal/mol. Although singular among the calculated transition structures, this result best matches the experimentally determined facial bias of nitronate **1**.[30] For nitronate **51**, approach distal to the C(6) methoxy group is preferred when the methoxy group is in an axial orientation (Figure 5), while proximal approach is preferred when the methoxy group is equatorially disposed (Figure 6).

Table 5 contains selected bond lengths in the calculated transition structures of ethylene and the axial methoxy conformation of nitronate **51**. The structures denoting chairlike and boatlike arrangements are very similar; one important difference is that a boatlike arrangement brings about slightly shorter (0.02−0.07 Å) atom distances representing the forming bonds.

Discussion

As with other cycloadditions, the key stereochemical issues are facial selectivity (with respect to the axial C(6) substituent), regioselectivity (head-to-head vs head-to-tail approach), and stereoselectivity (exo vs endo orientation) (Figure 7).

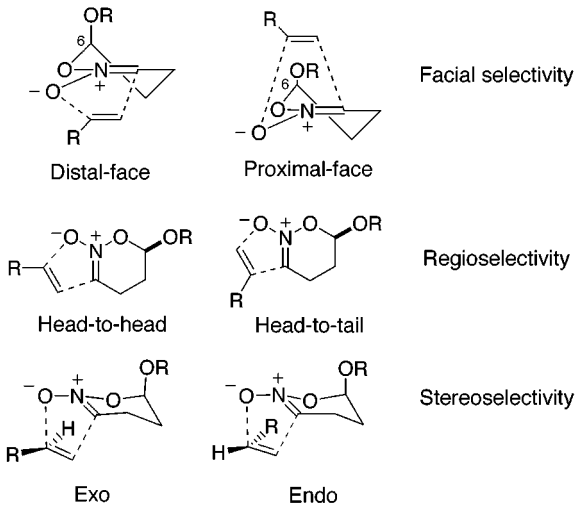


Figure 7. Selectivity issues for [3 + 2] cycloadditions of cyclic nitronates.

Facial Selectivity. The enhanced facial selectivity exhibited in nitronates **2** and **3** compared to nitronate **1** is a consequence of the C(4) benzoyloxy substituent. Because nitronate **1** does react with modest selectivity,[30] it is clear that the benzoyloxy group is not solely responsible for the facial bias, but that it does augment it.

The theoretical studies show that the conformation of the nitronate is an important determinant for facial selectivity. When ethylene approaches from the face distal to the axial C(6) substituent (which is the only facial approach observed in experiments with **2** and **3**), the six-membered ring may fold directly into a chair as the reaction progresses from transition state to product. Proximal approach would require the six-membered ring to either flip to the other chair conformation, or fold directly into a boat. The result is that proximal approach is disfavored.

A possible electronic source of facial bias is the kinetic anomeric effect (KAE), a stereoelectronic stabilization well-documented in cycloadditions[50] and nucleophilic

(50) Vasella, A. *Helv. Chim. Acta* **1977**, *60*, 1273.

Table 4. Calculated Energies (au), Relative Energies (kcal/mol, in Parentheses) for Transition Structures of Cycloadditions of Ethylene and 1,3-Dipoles

	RHF			B3LYP	
structure	3-21G	6-31G*	6-31+G*	3-21G	6-31G*
49 chairlike	−399.56896 (0.0)	−401.78868 (0.0)	−401.79864 (0.0)	−402.22103 (0.0)	−404.42659 (0.0)
boatlike	−399.56333 (3.5)	−401.78184 (4.3)	−401.79166 (4.4)	−402.21623 (3.0)	−404.42064 (3.7)
50 chairlike	−435.12446 (0.0)	−437.55037 (0.0)	−437.56281 (0.0)	−437.86951 (0.0)	−440.28109 (0.0)
boatlike	−435.11876 (3.6)	−437.54222 (5.1)	−437.55432 (5.3)	−437.86493 (2.9)	−440.27460 (4.1)
51 (ax. MeO−) chairlike	−548.39020 (0.0)	−551.44195 (0.0)	−551.45681 (0.0)	−551.77298 (0.0)	−554.81020 (0.0)
boatlike	−548.38522 (3.1)	−551.43454 (4.6)	−551.44910 (4.8)	−551.77153 (0.9)	−554.80574 (2.8)
51 (eq. MeO−) chairlike	−548.38306 (0.0)	−551.43861 (0.0)	−551.45442 (0.0)	−551.76618 (0.0)	−554.80653 (0.0)
boatlike	−548.37722 (3.7)	−551.43008 (5.4)	*a*	−551.76155 (2.9)	*a*

[a] This structure would not optimize with this model.

Table 5. Calculated Atom Distances (Å) for Transition Structures of Cycloadditions of Ethylene and Nitronate 51 (Axial Methoxy)

	RHF			B3LYP	
bond	3-21G	6-31G*	6-31+G*	3-21G	6-31G*
		Chairlike			
ethylene C=C	1.36	1.37	1.38	1.36	1.38
forming C−O	2.10	2.07	2.07	2.22	2.21
forming C−C	2.31	2.18	2.17	2.34	2.17
N−O	1.34	1.26	1.26	1.30	1.25
N−C	1.30	1.32	1.32	1.33	1.35
		Boatlike			
ethylene C=C	1.36	1.38	1.38	1.37	1.38
forming C−O	2.06	2.04	2.04	2.20	2.18
forming C−C	2.28	2.16	2.15	2.27	2.13
N−O	1.34	1.26	1.26	1.30	1.25
N−C	1.31	1.32	1.32	1.33	1.35

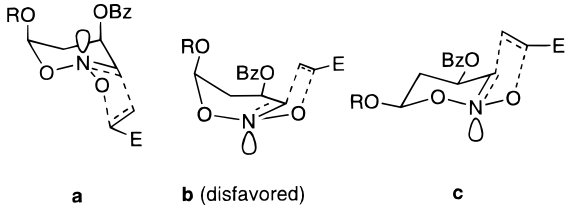


Figure 8. Dipolarophile approach to various nitronate conformations.

additions[51] to nitrones. The KAE is defined in these cases as an interaction in the transition state between the incipient sp^3 orbital on nitrogen and an adjacent electron-deficient bond. Vasella[50] has used this effect to rationalize the high stereoselectivity in the cycloadditions of nitrones with olefins; the favored transition structure displays an anti-periplanar orientation of the forming lone pair on nitrogen and the C−O bond of a sugar auxiliary.

A similar effect has been used to explain high stereoselectivity in [3 + 2] cycloadditions of certain nitronates with activated dipolarophiles.[26a,52,53] In these cases, the favorable interaction in the transition structure is between the forming sp^3 orbital on nitrogen and one (or both) of the newly formed anti-periplanar bonds to ethylene (Figure 8). The calculated transition structures show that a nearly anti-periplanar orientation is possible regardless of the face of approach (Figure 8 a,b); again, however, this orientation is much more easily satisfied with a chairlike conformation, wherein the nitrogen lone-pair inhabits a pseudoaxial position (this is analogous to the conformational constraints imposed on tetrahydopyrans by the "classic" anomeric effect).

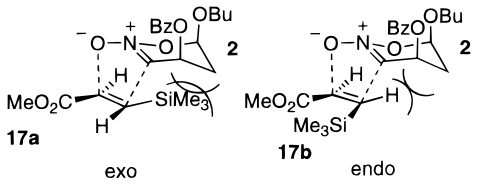


Figure 9. Approach of **17a** and **17b** to **2**.

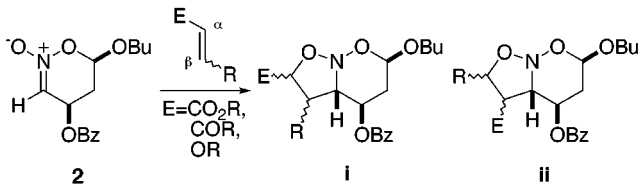
Regioselectivity. With both cis- and trans-dipolarophiles, a general qualitative pattern of regioselectivity is apparent. With regard to the β-substituent, head-to-tail regioselectivity is favored by O > C > Si > H. This pattern must, of course, be the result of a combination of steric and electronic effects. Because both the HOMO and the LUMO of nitronates such as **2** have the highest coefficient on carbon, a switch in regioselectivity cannot properly be explained by FMO theory; as a result, any electronic contribution needs another rationale.

The replacement of hydrogen (methyl acrylate) with silicon (**17a**,**b**) is accompanied by a modest amount of head-to-tail product (about 30% with each, see Table 2). In the case of **17a**, this can easily be explained with a steric argument (Figure 9). Exo, head-to-head approach of the dipolarophile to **2** places the TMS group in close contact with the cyclic core, which destabilizes the transition state relative to methyl acrylate. If a steric effect were the dominant regiochemical controller, one would expect the head-to-head approach of **17b** to be less destabilized relative to that of **17a**; in fact, both dipolarophiles display similar regioselectivity. Enones **27** and **28**, which contain a bulkier β-silicon group, are actually much more head-to-head selective than the β-silyl acrylates (Table 3). The dominance of steric effects would require the enones to be at least as head-to-tail selective as **17a**,**b**. The regiochemical preference of isocrotonate **19** is also not as easily explained by steric effects. By any metric a methyl group is smaller than a trimethylsilyl group, so a steric rationale would predict less head-to-tail product; this is not the case, as the major product in the [3 + 2] cycloaddition with **19** is the head-to-tail adduct (**41a**$_{ii}$, see Table 2). Overall, a rationale of overriding steric effects is inconsistent with the regiochemical trends.

The regioselectivities seen with disubstituted dipolarophiles must be due more to an electronic perturbation. Because FMO theory failed as a general predictive tool, another method was sought that could also be easily applied, but which was consistent with experiment. The

(51) Petrzilka, M.; Felix, D.; Eschenmoser, A. *Helv. Chim. Acta* **1973**, *56*, 2950.
(52) Denmark, S. E.; Dappen, M. S.; Cramer, C. J. *J. Am. Chem. Soc.* **1986**, *108*, 1306.
(53) Denmark, S. E.; Cramer, C. J.; Sternberg, J. A. *Helv. Chim. Acta* **1986**, *69*, 1971.

Table 6. HF/6-31G* Atomic Charge Calculations



dipolarophile	nitroso acetal	electrostatic atomic charge, $C(\alpha)$	electrostatic atomic charge, $C(\beta)$	**i**/**ii**	log(**i**/**ii**)	$(C(\alpha)+1)/(C(\beta)+1)$, P
47	**48**	0.08	−0.38	**i** only		1.74
28[a]	**46**	−0.22	−0.42	32	1.51	1.34
17b	**39**	−0.42	−0.33	2.4	0.38	0.87
17a	**40**	−0.51	−0.28	2.1	0.32	0.68
19	**41**	−0.64	0.12	0.59	−0.23	0.32
20a	**42**	−0.68	0.31	0.37	−0.43	0.24
20b	**43**	−0.76	0.36	**ii** only		0.18

[a] A smaller version of this dipolarophile was used. See Supporting Information for details.

standard arsenal of substituent parameters calculated by Taft[54−56] and others[57] did not lend itself to a simple application in this case.

In an effort to formulate a general and quantifiable theory to explain regioselectivity with ambident anions (e.g., enolates and allyl anions), Gompper[58] has introduced the concept of allopolarization. For a given ambident anion, the relative charge density at each end is calculated. From this is derived the "polarity index" (P) which is the ratio of the relative charge densities; this is then related linearly to the log of the product ratio. The foundation of the allopolarization principle is that a change in polarity of the ambident anion will affect a change in its reactivity with an electrophile.

A similar analysis was made with the present system. Table 6 lists the electrostatic atomic charges calculated (with the HF/6-31G* model) for several of the disubstituted dipolarophiles; C(α) is the carbon adjacent to the electronic "controlling" group (i.e., carboalkoxy, ketone, or ether group). As before, nitroso acetal **i** arises from head-to-head approach of the electronic controlling group, while nitroso acetal **ii** derives from a head-to-tail approach.

It was found that the calculated atomic charges at C(α) were an excellent qualitative predictor of regioselectivity; they assign all of the disubstituted dipolarophiles into the correct order, from most head-to-head selective to most head-to-tail selective. Atomic charges at C(β) were also mostly consistent with this ordering. What is most relevant, of course, is the relationship between the charge at both ends of the dipolarophile. The allopolarization principle applied to ambident anions takes this into account by dividing the atomic charges; the sign of the charge at either end is always the same. With these dipolarophiles, the sign of the atomic charge can change as the substituents change. This is one of the strengths of dipolar cycloadditions with nitronates (and also many other 1,3-dipoles); either electron-rich or electron-deficient dipolarophiles can be used with equal efficiency. However, to fully apply this modified allopolarization principle would require dividing the list of charges as they pass through zero; this would provide a list of quotients which was unnaturally parabolic. To remedy this, all of the charges were increased by 1 before division. Although this is an arbitrary transformation, there is in fact good agreement with this "polarity index" and the log of the product ratio (Figure 10); the plot is linear with $r^2 = 0.97$.

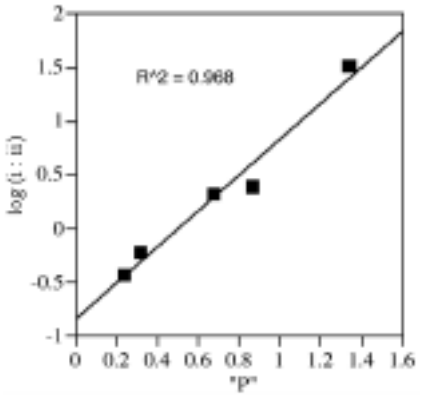


Figure 10. Relationship of product ratio to polarity index.

To test the ability of this method to predict the regiochemical outcome of cycloadditions with nitronates of type **2**, 2,3-dihydrofuran (**47**) was chosen as a test substrate. In the acrylate series, replacing a β-hydrogen with a methyl group dramatically altered the regioselectivity (see **41**, Table 2). It was known[6] that monosubstituted vinyl ethers react with high head-to-head selectivity; the analysis presented in Table 6 predicts that replacing a β-hydrogen with a methylene would not alter the regioselectivity. The experiment was consistent with this prediction; nitroso acetals **48** were formed in good yield, and no trace of the head-to-tail regioisomer could be detected.

This method is not too far removed from the theory underlying standard electronic substituent parameters.[55,57] The primary difference here is that the effects of the individual substituents are calculated not separately, but taken together as a collection of field and resonance effects within an entire molecule.

Stereoselectivity. Exo approach of monosubstituted dipolarophiles is generally favored and is correlated to the size of the substituent (Table 1). The modest endo preference observed in the case of acrolein (the smallest of the carbonyl substituted alkenes) suggests that there is a stabilizing electronic interaction associated with an endo approach. However, this stabilizing interaction is easily overpowered by the steric bulk of the dipolarophile.

The stereoselectivity observed in cycloadditions of cis-1,2-disubstituted acrylate and enone derivatives to cyclic nitronates is very high and is always exo. This is in contrast to the report of Carrié[26a] that dimethyl maleate adds to acyclic nitronates with exclusive endo orientation. Carrié ascribes his results to secondary orbital interactions that are favorable in some cases, and unfavorable in others; the results with cyclic nitronates cannot be explained in a similar fashion. Because of the failure of FMO theory to explain the regiochemical results in these systems, it is difficult to justify an FMO approach to

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describing the stereochemical results. The outcome with cis-dipolarophiles can, however, easily be explained using steric arguments. Since methyl acrylate is moderately exo selective, replacing the cis-β-hydrogen with a larger group should enhance exo selectivity; this is exactly what is observed.

Replacing the trans-β-hydrogen with a larger substituent tends to decrease the exo selectivity, which again suggests that electronic effects alone do not determine stereoselectivity. In fact, when the trans-β-substituent is sterically demanding and has little electronic significance (silane **17a**) the major approach is with the ester group endo. When the β-substituent is approximately the same size as the ester (acrylate **20a** and fumarate **21**), essentially no stereoselectivity is observed.

There does appear to be an electronic contributor to stereoselectivity in the case of 2,3-dihydrofuran (**47**). Unlike the cis-disubstituted enones and acrylates, **47** reacted with nitronate **2** to give **48b** as a minor (6%) product, which arises from endo approach of the dipolarophile. There apparently exists a small stabilizing effect when an electron-rich dipolarophile is oriented endo.

Conclusions

Intermolecular [3 + 2] cycloadditions between two disubstituted cyclic nitronates (**2** and **3**) and several dipolarophiles were studied. Remarkably high facial selectivity was observed; this was attributed to a combination of steric shielding from the nitronate C(4) substituent and an inherent facial bias from the chiral conformation of the nitronate. Monosubstituted dipolarophiles provided cycloadducts with exclusive head-to-head regioselectivity. Regioselectivity with disubstituted dipolarophiles varied from low to excellent (>25/1). With regard to the β-substituent, head-to-tail regioselectivity was favored by O > C > Si > H and was qualitatively consistent with an analysis based on electrostatic atomic charge calculations. Stereoselectivity was found to be mostly dependent on the steric nature of the dipolarophile; an electronic contribution weakly favored an endo approach, but was generally overruled by a more favorable exo approach of dipolarophiles bearing bulky substituents.

Experimental Section

General Experimental. See Supporting Information.

General Computational. Ground-state atomic charge calculations were performed on an Apple Power Macintosh 9500 with MacSpartan.[59] Transition structure calculations were performed on a Silicon Graphics Origin200 with Gaussian94.[60] See Supporting Information for coordinates. All transition structures were fully optimized with the indicated model and were characterized by harmonic frequency calculations and had one negative vibrational frequency.

***rel*-(4*R*,6*R*)-4-(Benzoyloxy)-6-(butyloxy)-5,6-dihydro-4*H*-[1,2]oxazine *N*-Oxide (2).** To a solution of $TiCl_4$ (510 μL, 4.65 mmol, 3.0 equiv) in CH_2Cl_2 (16 mL) was added Ti(O-*i*-Pr)$_4$ (1.38 mL, 4.68 mmol, 3.0 equiv). The clear solution was stirred at room temperature for 30 min. To a solution of **7** (304.9 mg, 1.58 mmol) in CH_2Cl_2 (4 mL) was added butyl vinyl ether (415 μL, 3.21 mmol, 2.0 equiv). The solution was cooled to −82 °C, and the solution of "Ti(O-*i*-Pr)$_2$Cl$_2$" (6.0 equiv) was added to it over 10 min. The resulting solution was allowed to warm over 20 min to −76 °C and then was stirred for an additional 3 h and 15 min. The reaction was quenched at −76 °C with 1 M NaOH in methanol (15 mL) and then was poured into CH_2Cl_2 (200 mL), washed with water (3 × 75 mL), and back extracted with CH_2Cl_2 (2 × 50 mL). The organic layer was dried (Na_2SO_4), filtered through a pad of Celite, and concentrated in vacuo. The residue was purified by silica gel chromatography (hexane/EtOAc, 85/15, 80/20, 65/35, 50/50) and recrystallized (EtOAc/hexane) to afford 323.6 mg (70%) of **2** as a crystalline white solid. Data for **2**: mp 74−75 °C (EtOAc/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (dd, J = 8.4, 1.3, 2H), 7.60 (tt, J = 7.4, 1.5, 1H), 7.46 (tt, J = 8.1, 7.2, 2H), 6.62 (d, J = 4.1, 1H), 5.71 (ddd, J = 6.3, 4.1, 2.1, 1H), 5.49 (t, J = 2.3, 1H), 4.02 (dt, J = 9.4, 6.5, 1H), 3.63 (dt, J = 9.2, 6.3, 1H), 2.44 (ddd, J = 15.3, 6.4, 3.2, 1H), 2.35 (dt, J = 15.3, 2.1, 1H), 1.69−1.62 (m, 2H), 1.48−1.39 (m, 2H), 0.93 (t, J = 7.3, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 133.4, 129.6, 129.2, 128.3, 109.5, 101.2, 69.5, 61.3, 31.4, 29.5, 19.0, 13.7; IR ($CHCl_3$) 3018 (m), 1719 (s), 1625 (s) cm^{-1}; MS (CI, CH_4) m/z 294 (M^+ + 1, 9), 57 (100); TLC R_f 0.20 (hexane/EtOAc, 65/35). Anal. Calcd for $C_{15}H_{19}NO_5$ (293.32): C, 61.42; H, 6.53; N, 4.78. Found: C, 61.50; H, 6.56; N, 4.57.

***(Z)*-1,4-Bis-(dimethyl(1,1,2-trimethylpropyl)silyloxy)-2-butene (9).** Diol **8** (3.52 g, 40.0 mmol) and imidazole (12.25 g, 180 mmol, 4.5 equiv) were dissolved in DMF (20 mL), and the mixture was cooled to 5 °C, whereupon thexyldimethylsilyl chloride (16.52 mL, 84 mmol, 2.1 equiv) was added. The mixture was allowed to warm to room temperature and stir for 18 h. The reaction mixture was diluted with *tert*-butyl methyl ether (TBME) (200 mL) and was washed with sat. aq NH_4Cl solution (3 × 50 mL) and brine (25 mL). The aqueous layers were back extracted with TBME (50 mL). The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. The crude product was purified by silica gel chromatography (hexane/EtOAc, 97.5/2.5) and distillation to afford 14.43 g (97%) of **9** as a clear liquid. Data for **9**: bp 180 °C (0.1 mmHg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.53 (t, J = 4.0, 2H), 4.20 (d, J = 4.2, 4H), 1.62 (septet, J = 7.0, 2H), 0.88 (d, J = 6.8, 12H), 0.84 (s, 12H), 0.10 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 130.1, 59.3, 34.1, 25.1, 20.3, 18.5, −3.3; IR (CCl_4) 2950 (s), 2872 (s) cm^{-1}; MS (CI, CH_4) m/z 373 (M^+ + 1, 26), 129 (100); TLC R_f 0.74 (hexane/EtOAc, 97/3). Anal. Calcd for $C_{20}H_{44}O_2Si_2$ (372.74): C, 64.45; H, 11.90. Found: C, 64.42; H, 11.95.

2-[(Dimethyl(1,1,2-trimethylpropyl)silyl)oxy]ethanal (11). To a 250 mL, three-necked round-bottom flask equipped with a thermometer and gas inlet were added **9** (5.0 g, 13.41 mmol) and CH_2Cl_2 (75 mL). After the solution was cooled to −78 °C, ozone was bubbled through the solution until a blue coloration appeared. The solution was then purged with oxygen. Zinc (1.32 g, 20.12 mmol, 1.5 equiv) was added followed by 50% aq acetic acid solution (35 mL). The mixture was allowed to slowly warm to 0 °C. After 30 min the mixture was allowed to warm to room temperature and then was stirred for 1 h. The mixture was diluted with CH_2Cl_2 (200 mL) and was washed with water (3 × 50 mL). The aq layers were back extracted with CH_2Cl_2 (50 mL). The combined organic layers were washed with sat. aq $NaHCO_3$ solution (50 mL) and brine (50 mL), dried (Na_2SO_4), and concentrated in vacuo. The crude product was purified by silica gel chromatography (hexane/EtOAc, 91/9) and distillation to afford 4.40 g (81%) of **11** as a colorless oil. Data for **11**: bp 100 °C (0.2 mmHg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.70 (t, J = 1.0, 1H), 4.19 (d, J = 0.7, 2H), 1.65 (septet, J = 6.8, 1H), 0.89 (d, J = 6.8, 6H), 0.88 (s, 6H), 0.13 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.2, 69.3, 34.0, 25.2, 20.1, 18.4, −3.6; IR (CCl_4) 2900 (s), 1742 (s) cm^{-1}; MS (CI, CH_4) m/z 203 (M^+ + 1, 6), 117 (100); TLC R_f 0.56

(59) MacSpartan Version 1.1. Wavefunction, Inc. 18401 Von Karman Avenue, Suite 370. Irvine, CA 92612.

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(hexane/EtOAc,91/9). Anal. Calcd for $C_{10}H_{22}O_2Si$ (202.37): C, 59.35; H, 10.96. Found: C, 59.34; H, 10.94.

1-[(Dimethyl-1-(1,1,2-trimethylpropyl)silyl)oxy]-3-butene-2-ol (13). A solution of aldehyde **11** (5.01 g, 24.8 mmol) in THF (25 mL) was added dropwise over 15 min to the THF solution of vinylmagnesium bromide (1.0 M, 32 mL, 32 mmol, 1.3 equiv) at 0 °C. Upon complete addition, the reaction mixture was heated at reflux for 1 h and then cooled to 0 °C, and the reaction was quenched with sat. aq NH_4Cl solution (10 mL). The contents of the reaction were poured into water (70 mL) and extracted with Et_2O (2 × 50 mL). The combined organic phases were washed with water (50 mL) and brine (50 mL) and dried ($MgSO_4$). The crude material was purified by chromatography on silica (hexane/EtOAc, 91/9) and distilled (bulb-to-bulb) to provide 4.53 g (79%) of **13** as a colorless liquid. Data for **13**: bp 150 °C (0.2 mmHg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.81 (ddd, J = 17.3, 10.5, 5.6, 1H), 5.34 (dt, J = 17.1, 1.7, 1H), 5.18 (dt, J = 10.5, 1.7, 1H), 4.19−4.13 (m, 1H), 3.64 (dd, J = 10, 3.7, 1H), 3.43 (dd, J = 9.8, 7.6, 1H), 2.55 (bs, 1H), 1.62 (septet, J = 6.8, 1H), 0.88 (d, J = 6.8, 6H), 0.85 (s, 6H), 0.11 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.7, 116.3, 72.9, 66.7, 34.1, 25.1, 20.2, 18.4, −3.6; IR (neat) 2959 (s) cm^{-1}; MS (CI, CH_4) m/z 231 (M^+ + 1, 4), 129 (100); TLC R_f 0.46 (hexane/EtOAc, 80/20). Anal. Calcd for $C_{12}H_{26}O_2Si$ (230.43): C, 62.55; H, 11.37. Found: C, 62.28; H, 11.48.

1-[(Dimethyl(1,1,2-trimethylpropyl)silyl)oxy]-3-buten-2-one (15). A solution of dimethyl sulfoxide (350 μL, 4.93 mmol, 2.3 equiv) in CH_2Cl_2 (17 mL) was cooled to −74 °C and then treated with oxalyl chloride (210 μL, 2.41 mmol, 1.1 equiv) in one portion. After 45 min, a solution of alcohol **13** (500 mg, 2.17 mmol) in CH_2Cl_2 (5 mL) was added dropwise via cannula. The resultant cloudy mixture was maintained for 1 h before triethylamine (1.5 mL, 11 mmol, 5 equiv) was introduced dropwise. The reaction mixture was maintained at −74 °C for 10 min and then allowed to warm to room temperature over 15 min. The reaction mixture was diluted with Et_2O (100 mL) and washed with 0.1 M hydrochloric acid (35 mL), water (35 mL), and brine (35 mL). The combined aq layers were back extracted with Et_2O (50 mL), and the organic layers were dried (Na_2SO_4). The residue was purified by rapid chromatography on neutral alumina (III) (hexane/EtOAc, 91/9) to provide the ketone **15** as a faint gold liquid. The ketone was further purified by distillation (bulb-to-bulb) to provide 325 mg (66%) of **15** as a colorless liquid that rapidly polymerized. Data for **15**: bp 165 °C (0.15 mmHg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.67 (dd, J = 17.6, 10.8, 1H), 6.35 (dd, J = 17.6, 1.6, 1H), 5.78 (dd, J = 10.6, 1.5, 1H), 4.34 (s, 2H), 1.65 (septet, J = 6.8, 1H), 0.90 (d, J = 7.0, 6H), 0.88 (s, 6H), 0.13 (s, 6H); TLC R_f 0.37 (hexane/EtOAc, 80/20).

1-(Phenylmethoxy)-3-buten-2-one (16). A solution of dimethyl sulfoxide (440 μL, 6.20 mmol, 2.2 equiv) in CH_2Cl_2 (22 mL) was cooled to −74 °C and then treated with oxalyl chloride (270 μL, 3.10 mmol, 1.1 equiv) in one portion. After 45 min, a solution of alcohol **14** (506 mg, 2.84 mmol) in CH_2Cl_2 (6 mL) was added dropwise via cannula. The resultant cloudy mixture was maintained for 1 h before triethylamine (2.0 mL, 14 mmol, 5 equiv) was introduced dropwise. The reaction mixture was maintained at −74 °C for 10 min and then allowed to warm to room temperature over 15 min. The reaction mixture was diluted with CH_2Cl_2 (60 mL) and washed with 0.1 M hydrochloric acid (40 mL), water (40 mL), and brine (40 mL). The combined aq layers were back extracted with CH_2Cl_2 (40 mL), and the organic layers were dried (Na_2SO_4). The residue was purified by rapid chromatography on neutral alumina (III) (hexane/EtOAc, 86/14) to provide 355 mg (68%) of ketone **16** as a light gold liquid. The ketone was further purified by distillation (bulb-to-bulb) to provide 144 mg (29%) as a colorless liquid that rapidly polymerized. Data for **16**: bp 140 °C (1.2 × 10^{-5} mmHg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.31 (m, 5H), 6.55 (dd, J = 17.6, 10.5, 1H), 6.34 (dd, J = 17.6, 1.5, 1H), 5.83 (dd, J = 10.7, 1.5, 1H), 4.62 (s, 2H), 4.28 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.0, 137.1, 132.3, 129.2, 128.4, 127.9, 127.9, 73.7, 73.2; IR (neat) 1714 (s), 1698 (s) cm^{-1}; TLC R_f 0.30 (hexane/EtOAc, 80/20).

1-[(Dimethyl(1,1,2-trimethylpropyl)silyl)oxy]-4-(dimethylphenylsilyl)-3-butyn-2-ol (23). A solution of ethyl bromide (2.30 mL, 30.8 mmol, 1.25 equiv) in Et_2O (12 mL) was added dropwise to a suspension of magnesium turnings (737 mg, 30.3 mmol, 1.23 equiv) in Et_2O (13 mL) at a rate such as to maintain a gentle reflux. Upon complete addition, the reaction mixture was heated at reflux for 1.5 h and then was allowed to cool to room temperature. A solution of alkyne **22** (4.95 g, 30.9 mmol, 1.25 equiv) in THF (13 mL) was added dropwise over 15 min, and the reaction mixture was heated at reflux for 1 h. Upon cooling to room temperature, a solution of the aldehyde **11** (5.00 g, 24.7 mmol) in THF (13 mL) was added dropwise over 15 min. The reaction mixture was then heated at reflux for 1 h and allowed to cool to room temperature, and the reaction was quenched with sat. aq NH_4Cl solution. The reaction mixture was poured into water (300 mL) and extracted with pentane (3 × 100 mL). The organic phase was washed with water (100 mL) and brine (100 mL) and dried (Na_2SO_4). The crude material was purified by chromatography on silica (hexane/EtOAc, 94/6) and distilled (bulb-to-bulb) to provide 7.71 g (86%) of **23** as a colorless liquid. Data for **23**: bp 175 °C (8.5 × 10^{-5} mmHg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63−7.35 (m, 5H), 4.42 (ddd, J = 6.2, 5.5, 3.8, 1H), 3.77 (dd, J = 10.1, 3.8, 1H), 3.66 (dd, J = 10.1, 6.4, 1H), 2.60 (d, J = 5.5, 1H), 1.61 (septet, J = 6.8, 1H), 0.88 (d, J = 6.8, 6H), 0.86 (s, 6H), 0.42 (s, 6H), 0.13 (s, 3H), 0.13 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.5, 133.7, 129.4, 127.8, 105.4, 88.0, 66.5, 63.5, 34.1, 25.1, 20.3, 18.5, −1.0, −3.5; IR (neat) 3479 (bw), 2959 (s) cm^{-1}; MS (CI, CH_4) m/z 364 (M^+ + 1, 1), 261 (100); TLC R_f 0.28 (hexane/EtOAc, 90/10). Anal. Calcd for $C_{20}H_{34}O_2Si_2$ (362.66): C, 66.24; H, 9.45; Si, 15.49. Found: C, 66.07; H, 9.41; Si, 15.74.

4-(Dimethylphenylsilyl)-1-(phenylmethoxy)-3-butyn-2-ol (24). A solution of ethyl bromide (1.85 mL, 24.8 mmol, 1.24 equiv) in Et_2O (12 mL) was added dropwise to a suspension of magnesium turnings (598 mg, 24.6 mmol, 1.23 equiv) in Et_2O (12 mL) at a rate such as to maintain a gentle reflux. Upon complete addition, the reaction mixture was heated at reflux for 1.5 h and then allowed to cool to room temperature. A solution of alkyne **22** (4.00 g, 25.0 mmol, 1.25 equiv) in THF (12 mL) was added dropwise over 15 min, and the reaction mixture heated at reflux for 1 h. Upon cooling to room temperature, a solution of aldehyde **12** (3.00 g, 20.0 mmol) in THF (12 mL) was added dropwise over 15 min, and the reaction mixture was heated at reflux for 1 h and then was cooled to 0 °C. The reaction was then quenched with saturated aq NH_4Cl solution. The reaction mixture was poured into sat. aq NH_4Cl solution and extracted with Et_2O (2 × 100 mL). The organic phase was washed with water (100 mL) and brine (100 mL). The aq phase was back extracted with Et_2O (50 mL), and the combined organic layers were dried (Na_2SO_4). The crude material was purified by chromatography on silica (hexane/EtOAc, 89/11) and distilled (bulb-to-bulb) to provide 5.26 g (85%) of **24** as a colorless liquid. Data for **24**: bp 250 °C (3.4 × 10^{-5} mmHg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62−7.29 (m, 10H), 4.63 (d, J = 12, 1H), 4.61 (d, J = 12, 1H), 4.62−4.59 (m, 1H), 3.68 (dd, J = 9.9, 3.7, 1H), 3.60 (dd, J = 9.7, 7.3, 1H), 2.47 (d, J = 4.9, 1H), 0.42 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.6, 136.5, 133.7, 129.5, 128.5, 127.9, 127.7, 104.8, 88.6, 73.5, 73.4, 62.2, −1.1; IR (neat) 2959 (m) cm^{-1}; MS (CI, CH_4) m/z 311 (M^+ + 1, weak), 91 (100); TLC R_f 0.44 (hexane/EtOAc, 67/33). Anal. Calcd for $C_{19}H_{22}O_2Si$ (310.47): C, 73.50; H, 7.14; Si, 9.05. Found: C, 73.47; H, 7.19; Si, 9.23.

(*Z*)-1-[(Dimethyl(1,1,2-trimethylpropyl)silyl)oxy]-4-(dimethylphenylsilyl)-3-buten-2-ol (25). Freshly distilled cyclohexene (3.4 mL, 34 mmol, 4 equiv) was added dropwise over 5 min to a solution of BH_3·THF (1.0 M, 16.5 mL, 16.5 mmol, 2 equiv) maintained at 0 °C. The reaction mixture was maintained for 1 h during which it gradually thickened. A solution of alkyne **23** (3.00 g, 8.27 mmol) in THF (8 mL) was added dropwise to the white suspension over 15 min. The reaction mixture was maintained at 0 °C for 1 h (reaction mixture clarified) and then allowed to warm to room temperature. After 1 h, acetic acid (950 μL, 16.6 mmol, 2 equiv) was added dropwise over 5 min, and the reaction mixture was

maintained overnight (12 h). The contents of the reaction were diluted with Et_2O (100 mL) and washed with water (50 mL) and brine (50 mL). The combined aq layers were back extracted with Et_2O (50 mL), and the organic layers were dried (Na_2SO_4). The crude material was purified by chromatography on silica (hexane/EtOAc, 96/4) to give a colorless oil which was distilled (bulb-to-bulb) to provide 2.14 g (71%) of cis-alkene **25** as a colorless liquid. Data for **25**: bp 165 °C (7.0×10^{-5} mmHg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55−7.34 (m, 5H), 6.32 (dd, J = 14.5, 8.2, 1H), 5.91 (d, J = 14.3, 1H), 4.19−4.16 (m, 1H), 3.43 (dd, J = 10.1, 3.8, 1H), 3.33 (dd, J = 9.7, 7.9, 1H), 2.48 (d, J = 2.2, 1H), 1.59 (septet, J = 6.8, 1H), 0.85 (d, J = 6.8, 6H), 0.82 (s, 6H), 0.42 (s, 3H), 0.40 (s, 3H), 0.05 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.4, 139.2, 133.6, 131.5, 129.0, 127.9, 72.3, 66.2, 34.1, 25.1, 20.2, 18.5, −0.6, −0.9, −3.5, −3.6; IR (neat) 3486 (bw), 2958 (s) cm^{-1}; MS (CI, CH_4) m/z 365 ($M^+ + 1$, weak), 147 (100); TLC R_f 0.35 (hexane/EtOAc, 90/10). Anal. Calcd for $C_{20}H_{36}O_2Si_2$ (364.68): C, 65.87; H, 9.95; Si, 15.40. Found: C, 65.90; H, 10.28; Si, 15.59.

***(Z)*-4-(Dimethylphenylsilyl)-1-(phenylmethoxy)-3-buten-2-ol (26).** Palladium on calcium carbonate (102 mg, 5% (no lead content)) was suspended in benzene (1 mL) and prehydrogenated for 20 min. Quinoline (23 μL, 0.19 mmol, 0.06 equiv) was added followed by a solution of alkyne **24** (1.02 g, 3.29 mmol) in benzene (2.3 mL). The progress of the reaction was monitored by HPLC, and after 2 h and 40 min, the starting material had been consumed. The catalyst was removed by filtration (SiO_2/EtOAc), and the crude material was prepurified by chromatography on silica (hexane/EtOAc, 80/20). The three components were separated by MPLC (hexane/EtOAc, 90/10) and individually distilled (bulb-to-bulb) to provide 429 mg (42%) of the cis-alkene (*Z*)-**26**, 76.1 mg (7%) of the trans-alkene (*E*)-**26**, and 183 mg (18%) of the saturated alkane **26b** as colorless liquids. Data for (*Z*)-**26**: bp 170 °C (3.2×10^{-5} mmHg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55−7.25 (m, 10H), 6.32 (dd, J = 14.3, 8.2, 1H), 5.91 (dd, J = 14.3, 0.9, 1H), 4.44 (d, J = 13.0, 1H), 4.41 (d, J = 13.0, 1H), 4.39−4.34 (m, 1H), 3.30 (d, J = 5.3, 2H), 2.29 (d, J = 2.7, 1H), 0.41 (s, 3H), 0.38 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.0, 139.1, 137.8, 133.6, 131.7, 129.0, 128.4, 127.9, 127.8, 127.7, 73.5, 73.1, 70.9, −0.8, −1.0; IR (neat) 3448 (bs), 2954 (s) cm^{-1}; MS (CI, CH_4) m/z 330 ([M + CH_5]$^+$, 49), 219 (100); TLC R_f 0.44 (hexane/EtOAc, 67/33). Anal. Calcd for $C_{19}H_{24}O_2Si$ (312.49): C, 73.03; H, 7.74; Si, 8.99. Found: C, 72.92; H, 7.83; Si, 8.74. Data for (*E*)-**26**: bp 190 °C (6.0×10^{-5} mmHg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52−7.28 (m, 10H), 6.15 (dd, J = 18.8, 1.3, 1H), 5.91 (ddd, J = 18.8, 4.4, 2.0, 1H), 4.56 (s, 2H), 4.39−4.37 (m, 1H), 3.56 (dd, J = 9.5, 3.3, 1H), 3.36 (ddd, J = 9.5, 7.9, 1.6, 1H), 2.52−2.50 (m, 1H), 0.34 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.5, 138.3, 137.8, 133.8, 129.3, 129.0, 128.5, 127.8, 127.8, 127.7, 73.8, 73.3, 72.9, −2.7, −2.7; IR (neat) 3434 (bs), 2954 (s) cm^{-1}; MS (CI, CH_4) m/z 330 ([M + CH_5]$^+$, 6.4), 91 (100); TLC R_f 0.43 (hexane/EtOAc, 67/33). Anal. Calcd for $C_{19}H_{24}O_2Si$ (312.49): C, 73.03; H, 7.74; Si, 8.99. Found: C, 72.76; H, 7.76; Si, 9.04. Data for **26b**: bp 190 °C (6.5×10^{-5} mmHg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56−7.32 (m, 10H), 4.58 (d, J = 19.4, 1H), 4.54 (d, J = 19.4, 1H), 3.78−3.74 (m, 1H), 3.53 (dd, J = 9.3, 2.7, 1H), 3.37−3.33 (m, 1H), 2.51 (m, 1H), 1.55−1.47 (m, 2H), 0.98−0.91 (m, 1H), 0.79−0.69 (m, 1H), 0.41 (s, 3H), 0.38 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.9, 137.9, 133.5, 128.8, 128.4, 127.7, 127.7, 127.7, 74.0, 73.2, 72.5, 27.3, 11.1, −3.3; IR (neat) 3435 (bs) cm^{-1}; MS (CI, CH_4) m/z 332 ([M + CH_4]$^+$, 2.0), 91 (100); TLC R_f 0.40 (hexane/EtOAc, 67/33). Anal. Calcd for $C_{19}H_{26}O_2Si$ (314.50): C, 72.56; H, 8.33; Si, 8.93. Found: C, 72.45; H, 8.14; Si, 9.22.

***(Z)*-1-[(Dimethyl(1,1,2-trimethylpropyl)silyl)oxy]-4-(dimethylphenylsilyl)-3-buten-2-one (27).** A solution of dimethyl sulfoxide (1.55 mL, 21.5 mmol, 2.2 equiv) in CH_2Cl_2 (80 mL) was cooled to −74 °C and treated with oxalyl chloride (955 μL, 10.9 mmol, 1.1 equiv) in one portion. After 45 min, a solution of alcohol **25** (3.63 g, 9.95 mmol) in CH_2Cl_2 (18 mL) was added dropwise via cannula. The resultant cloudy mixture was maintained for 1 h before triethylamine (7.0 mL, 50 mmol, 5 equiv) was introduced dropwise. The reaction mixture was maintained at −74 °C for 5 min and then allowed to warm over 15 min. The reaction mixture was diluted with pentane (300 mL) and washed with 0.1 M hydrochloric acid (100 mL), water (100 mL), and brine (100 mL). The combined aq layers were back extracted with pentane (100 mL), and the organic layers were dried (Na_2SO_4). The residue was purified by chromatography on silica (pentane, then pentane/Et_2O, 97.5/2.5) to provide 3.51 g (97%) of ketone **27** as a light gold oil. Data for **27**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60−7.34 (m, 5H), 7.22 (d, J = 14.3, 1H), 6.66 (d, J = 14.3, 1H), 4.24 (s, 2H), 1.66 (septet, J = 6.8, 1H), 0.91 (d, J = 7.0, 6H), 0.89 (s, 6H), 0.47 (s, 6H), 0.12 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.5, 150.2, 139.5, 138.3, 133.7, 128.7, 127.6, 69.3, 34.1, 25.2, 20.2, 18.5, −2.6, −3.5; IR (neat) 1715 (w), 1694 (m) cm^{-1}; MS (CI, CH_4) m/z 364 ($M^+ + 1$, 4), 201 (100); TLC R_f 0.57 (hexane/EtOAc, 94/6). Anal. Calcd for $C_{20}H_{34}O_2Si_2$ (362.66): C, 66.24; H, 9.45; Si, 15.49. Found: C, 66.40; H, 9.36; Si, 15.32.

***(Z)*-4-(Dimethylphenylsilyl)-1-(phenylmethoxy)-3-buten-2-one (28).** A solution of dimethyl sulfoxide (170 μL, 2.40 mmol, 2.2 equiv) in CH_2Cl_2 (6 mL) was cooled to −74 °C and treated with oxalyl chloride (100 μL, 1.15 mmol, 1.1 equiv) in one portion. After 30 min, a solution of alcohol (*Z*)-**26** (341 mg, 1.09 mmol) in CH_2Cl_2 (5 mL) was added dropwise via cannula. The resultant cloudy mixture was maintained for 1 h before triethylamine (760 μL, 5.45 mmol, 5 equiv) was introduced dropwise. The reaction mixture was maintained at −74 °C for 5 min and then allowed to warm over 15 min. The reaction mixture was diluted with CH_2Cl_2 (50 mL) and washed with 0.1 M hydrochloric acid (20 mL), water (20 mL), and brine (20 mL). The combined aq layers were back extracted with CH_2Cl_2 (20 mL), and the organic layers were dried (Na_2SO_4). The residue was purified by rapid chromatography on neutral alumina (III) (hexane/EtOAc, 92/8) to provide 270 mg (80%) of ketone **28** as a light gold oil. Data for **28**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59−7.28 (m, 10H), 7.06 (d, J = 14.3, 1H), 6.65 (d, J = 14.1, 1H), 4.55 (s, 2H), 4.14 (s, 2H), 0.46 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.3, 151.0, 139.2, 138.3, 137.0, 133.7, 128.5, 128.0, 128.0, 127.6, 75.0, 73.2, −2.6; IR (neat) 1709 (s), 1694 (s) cm^{-1}; MS (CI, CH_4) m/z 311 ($M^+ + 1$, 13), 233 (100); TLC R_f 0.25 (hexane/EtOAc, 94/6). Anal. Calcd for $C_{19}H_{22}O_2Si$ (310.47): C, 73.50; H, 7.14; Si, 9.05: Found: C, 73.79; H, 7.25; Si, 9.22.

***rel*-(2*S*,3a*S*,4*R*,6*R*)-4-(Benzoyloxy)-6-(butyloxy)hexahydroisoxazolo[2,3-*b*][1,2]oxazine-2-carboxylic Acid Methyl Ester (29a) and *rel*-(2*R*,3a*S*,4*R*,6*R*)-4-(Benzoyloxy)-6-(butyloxy)hexahydroisoxazolo[2,3-*b*][1,2]oxazine-2-carboxylic Acid Methyl Ester (29b).** Methyl acrylate (1.2 mL, 13 mmol, 6 equiv) was added to a solution of nitronate **2** (666 mg, 2.27 mmol) and several crystals of 1,4-di-*tert*-butylhydroquinone in benzene (75 mL), and the reaction mixture was maintained at room temperature for 6 h. Upon concentration of the solution in vacuo, the residue (931 mg) was purified by radial chromatography (hexane/TBME, 60/40, 4 mm SiO_2 plate). The major nitroso acetal was recrystallized from TBME/pentane to provide 599 mg (70%) of **29a** as colorless, spiny needles. The minor nitroso acetal was recrystallized from TBME/pentane to provide 78.5 mg (9%) of **29b** as colorless, spiny needles. Data for **29a**: mp 61−62 °C (TBME/pentane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 7.1, 2H), 7.59 (t, J = 7.6, 1H), 7.46 (t, J = 7.8, 2H), 5.27 (ddd, J = 8.3, 4.6, 3.7, 1H), 5.09 (dd, J = 9.0, 5.0, 1H), 4.97 (t, J = 5.1, 1H), 3.97 (dt, J = 9.3, 6.6, 1H), 3.85−3.80 (m, 1H), 3.77 (s, 3H), 3.46 (dt, J = 9.3, 6.6, 1H), 2.69−2.63 (m, 2H), 2.30 (ddd, J = 14, 5.6, 5.1, 1H), 2.16 (ddd, J = 14, 8.1, 4.9, 1H), 1.67−1.60 (m, 2H), 1.46−1.37 (m, 2H), 0.93 (t, J = 7.6, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 165.7, 133.2, 129.7, 129.4, 128.3, 98.2, 80.5, 72.0, 68.9, 67.5, 52.4, 32.9, 31.5, 29.5, 19.2, 13.8; IR (CCl_4) 1725 (s) cm^{-1}; MS (CI, CH_4) m/z 380 ($M^+ + 1$, 11), 105 (100); TLC R_f 0.32 (hexane/EtOAc, 67/33). Anal. Calcd for $C_{19}H_{25}NO_7$ (379.41): C, 60.15; H, 6.64; N, 3.69. Found: C, 60.33; H, 6.60; N, 3.71. Data for **29b**: mp 79−80 °C (TBME/pentane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 8.3, 2H), 7.58 (t, J = 7.3, 1H), 7.45 (t, J = 8.1, 2H), 5.34 (ddd, J = 8.1, 4.6, 3.2, 1H), 4.95 (t, J = 4.6, 1H), 4.84 (t, J = 8.1, 1H), 4.00 (dt, J = 9.5, 6.6, 1H), 3.82 (s, 3H), 3.74 (td, J = 9.3, 2.9, 1H), 3.44 (dt, J = 9.3, 6.6, 1H), 2.72 (t, J = 8.3, 2H), 2.28 (dt, J = 14.4, 5.4, 1H), 2.09 (ddd, J =

14.4, 6.8, 4.2, 1H), 1.66−1.59 (m, 2H), 1.46−1.37 (m, 2H), 0.92 (t, J = 7.3, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 165.8, 133.2, 129.8, 129.6, 128.3, 98.4, 80.8, 72.3, 68.6, 67.7, 52.6, 31.6, 31.0, 29.1, 19.2, 13.9; IR (CCl_4) 1722 (s) cm^{-1}; MS (CI, CH_4) m/z 380 (M^+ + 1, 13), 105 (100); TLC R_f 0.28 (hexane/EtOAc, 67/33). Anal. Calcd for $C_{19}H_{25}NO_7$ (379.41): C, 60.15; H, 6.64; N, 3.69. Found: C, 60.18; H, 6.65; N, 3.61.

***rel*-(2*S*,3a*S*,4*R*,6*R*)-4-(Benzoyloxy)-6-[(1*S*,2*R*)-(2-phenylcyclohexyl)oxy]hexahydroisoxazolo[2,3-*b*][1,2]-oxazine-2-carboxylic Acid Methyl Ester (30a) and *rel*-(2*R*,3a*S*,4*R*,6*R*)4-(Benzoyloxy)-6-[(1*S*,2*R*)(2-phenylcyclohexyl)oxy]hexahydroisoxazolo[2,3-*b*][1,2]oxazine-2-carboxylic Acid Methyl Ester (30b).** Methyl acrylate (1.6 mL, 18 mmol, 5 equiv) was added to a solution of nitronate **3** (1.42 g, 3.59 mmol) and several crystals of 1,4-di-*tert*-butylhydroquinone in benzene (118 mL), and the reaction mixture was maintained at room temperature for 6 h. Upon concentration of the solution in vacuo, the residue was purified by chromatography on silica (hexane/EtOAc/, 80/20). The major nitroso acetal (1.43 g) was recrystallized from CH_2Cl_2/hexane to provide 1.29 g (75%) of **30a** as colorless, spiny needles. The minor nitroso acetal was recrystallized from CH_2Cl_2/hexane to provide 197 mg (11%) of **30b** as colorless, spiny needles. Data for **30a**: mp 125−126 °C (CH_2Cl_2/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (dd, J = 8.3, 1.2, 2H), 7.59 (tt, J = 7.5, 1.5, 1H), 7.46 (t, J = 7.8, 2H), 7.27−7.15 (m, 5H), 5.02 (dd, J = 9.8, 3.7, 1H), 4.95 (dt, J = 9.3, 4.9, 1H), 4.12 (t, J = 5.9, 1H), 3.74 (s, 3H), 3.71 (ddd, J = 11.5, 7.8, 3.9, 1H), 3.63 (dd, J = 10.5, 4.4, 1H), 2.62 (ddd, J = 12.2, 7.8, 3.9, 1H), 2.56−2.48 (m, 2H), 2.42−2.38 (m, 1H), 1.90−1.83 (m, 3H), 1.78−1.71 (m, 2H), 1.67−1.27 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 165.6, 144.1, 133.3, 129.7, 129.4, 128.3, 128.0, 127.8, 126.2, 98.7, 81.9, 80.6, 72.6, 69.5, 52.4, 51.2, 34.5, 33.5, 32.4, 29.8, 25.7, 25.2; IR (CCl_4) 1726 (s) cm^{-1}; MS (CI, CH_4) m/z 482 (M^+ + 1, 7.8), 159 (100); TLC R_f 0.41 (hexane/EtOAc, 67/33). Anal. Calcd for $C_{27}H_{31}NO_7$ (481.55): C, 67.35; H, 6.49; N, 2.91. Found: C, 67.49; H, 6.62; N, 2.94. Data for **30b**: mp 107−108 °C (CH_2Cl_2/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (dd, J = 8.1, 1.2, 2H), 7.59 (tt, J = 7.3, 1.2, 1H), 7.46 (t, J = 7.8, 2H), 7.26−7.14 (m, 5H), 5.05 (ddd, J = 7.1, 5.9, 3.7, 1H), 4.78 (dd, J = 9.0, 7.3, 1H), 4.17 (t, J = 5.4, 1H), 3.80 (s, 3H), 3.66−3.60 (m, 2H), 2.71−2.44 (m, 4H), 1.88−1.85 (m, 2H), 1.79−1.71 (m, 3H), 1.67−1.27 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 165.6, 144.1, 133.2, 129.7, 129.6, 128.3, 127.9, 127.7, 126.1, 99.0, 82.1, 80.8, 72.7, 69.0, 52.4, 51.2, 34.4, 32.5, 31.5, 29.2, 25.8, 25.1; IR (CCl_4) 1724 (s) cm^{-1}; MS (CI, CH_4) m/z 483 (M^+ + 1, 4), 159 (100); TLC R_f 0.31 (hexane/EtOAc, 67/33). Anal. Calcd for $C_{27}H_{31}NO_7$ (481.55): C, 67.35; H, 6.49; N, 2.91. Found: C, 67.21; H, 6.53; N, 2.90.

***rel*-(2*S*,3a*S*,4*R*,6*R*)-4-(Benzoyloxy)-6-[(1*S*,2*R*)-(2-phenylcyclohexyl)oxy]hexahydroisoxazolo[2,3-*b*][1,2]oxazine-2-carboxylic Acid 1,1-Dimethylethyl Ester (31a) and *rel*-(2*R*,3a*S*,4*R*,6*R*)-4-(Benzoyloxy)-6-[(1*S*,2*R*)-(2-phenylcyclohexyl)oxy]hexahydroisoxazolo[2,3-*b*][1,2]oxazine-2-carboxylic Acid 1,1-Dimethylethyl Ester (31b).** *tert*-Butyl acrylate (1.6 mL, 11 mmol, 5 equiv) was added to a solution of nitronate **3** (803 mg, 2.03 mmol) and several crystals of 1,4-di-*tert*-butylhydroquinone in benzene (64 mL), and the reaction mixture was maintained at room temperature for 2.5 h. Upon concentration of the solution in vacuo, the residue (1.23 g) was purified by chromatography on silica (hexane/EtOAc, 91/9, 89/11, 86/14). The major nitroso acetal (960 mg) was recrystallized from TBME/pentane to provide 891 mg (84%) of **31a** as colorless, spiny needles. The minor nitroso acetal was recrystallized from Et_2O/pentane to provide 78.0 mg (7%) of **31b** as colorless, spiny needles. Data for **31a**: mp 138−139 °C (TBME/pentane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (dd, J = 8.3, 1.2, 2H), 7.59 (tt, J = 7.6, 1.2, 1H), 7.46 (t, J = 7.8, 2H), 7.29−7.15 (m, 5H), 4.95 (dt, J = 9.0, 4.6, 1H), 4.88 (dd, J = 9.8, 4.2, 1H), 4.12 (t, J = 5.9, 1H), 3.70 (ddd, J = 10.3, 8.1, 3.9, 1H), 3.63 (td, J = 10.3, 4.2, 1H), 2.57−2.39 (m, 4H), 1.89−1.82 (m, 3H), 1.77−1.70 (m, 2H), 1.63−1.26 (m, 4H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.9, 165.6, 144.1, 133.2, 129.7, 129.5, 128.3, 127.9, 127.8, 126.2, 98.6, 82.2, 81.9, 81.4, 72.6, 69.6, 51.2, 34.5, 33.4, 32.4, 29.8, 27.8, 25.7, 25.1; IR (CCl_4) 1726 (s) cm^{-1}; MS (CI, CH_4) m/z 525 (M^+ + 1, 39), 159 (100); TLC R_f 0.34 (hexane/EtOAc, 80/20). Anal. Calcd for $C_{30}H_{37}NO_7$ (523.63): C, 68.81; H, 7.12; N, 2.67. Found: C, 68.92; H, 7.16; N, 2.61. Data for **31b**: mp 143−144 °C (Et_2O/pentane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (dd, J = 8.2, 1.1, 2H), 7.58 (t, J = 7.5, 1H), 7.45 (t, J = 7.7, 2H), 7.25−7.14 (m, 5H), 4.98 (ddd, J = 9.3, 4.8, 4.6, 1H), 4.66 (dd, J = 9.0, 7.0, 1H), 4.19 (t, J = 6.0, 1H), 3.63−3.56 (m, 2H), 2.68−2.46 (m, 4H), 1.89−1.74 (m, 5H), 1.64−1.29 (m, 4H), 1.50 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.9, 165.8, 144.3, 133.3, 129.7, 129.7, 128.4, 128.0, 127.8, 126.2, 98.7, 82.2, 81.8, 80.8, 73.5, 70.0, 51.2, 34.5, 32.7, 32.2, 30.1, 27.9, 25.8, 25.3; IR (KBr) 1739 (s), 1719 (s), 1713 (s) cm^{-1}; MS (CI, CH_4) m/z 524 (M^+, 7), 292 (100); TLC R_f 0.28 (hexane/EtOAc, 80/20). Anal. Calcd for $C_{30}H_{37}NO_7$ (523.63): C, 68.81; H, 7.12; N, 2.67. Found: C, 68.93; H, 7.30; N, 2.71.

***rel*-(2*S*,3a*S*,4*R*,6*R*)-4-(Benzoyloxy)-6-[(1*S*,2*R*)-(2-phenylcyclohexyl)oxy]-2-(1-oxoethyl)hexahydroisoxazolo-[2,3-*b*][1,2]oxazine (32a) and *rel*-(2*R*,3a*S*, 4*R*,6*R*)-4-(Benzoyloxy)-6-[(1*S*,2*R*)-(2-phenylcyclohexyl)oxy]-2-(1-oxoethyl)hexahydroisoxazolo[2,3-*b*][1,2]oxazine (32b).** Methyl vinyl ketone (0.5 mL, 6.0 mmol, 8 equiv) was added to a solution of nitronate **3** (302 mg, 0.764 mmol) and several crystals of 1,4-di-*tert*-butylhydroquinone in benzene (25 mL), and the reaction mixture was maintained at room temperature for 1.5 h. Upon concentration of the solution in vacuo, the residue was purified by chromatography on silica (hexane/EtOAc, 86/14). The inseparable mixture of diastereomers (345 mg) was recrystallized from CH_2Cl_2/hexane to provide 306 mg (88%) of a 6.2/1 mixture of ketones **32a** and **32b** as colorless, spiny needles. Data for 6.2/1 mixture of **32a** and **32b**: mp 165−166 °C (dec); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, J = 7.1, 2H), 7.59 (t, J = 7.3, 1H), 7.46 (t, J = 7.9, 2H), 7.27−7.15 (m, 5H), 4.95 (dt, J = 9.0, 4.6, 1H), 4.92 (dd, J = 10.2, 4.2, 1H), 4.61 (dd, J = 9.5, 6.2, 1H), 4.16 (t, J = 6, 1H), 3.64 (td, J = 10.4, 4.4, 1H), 3.57 (ddd, J = 10.4, 8.4, 4.2, 1H), 2.58 (ddd, J = 12.4, 8.2, 4.2, 1H), 2.57−2.51 (m, 1H), 2.43−2.39 (m, 1H), 2.42 (dt, J = 12.6, 10.2, 1H), 2.36 (s, 3H), 2.22 (s, 3H), 1.90−1.71 (m, 6H), 1.67−1.54 (m, 2H), 1.52−1.43 (m, 1H), 1.38 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.9, 200.7, 165.6, 144.0, 133.3, 129.7, 129.5, 128.3, 128.3, 128.0, 128.0, 127.8, 127.7, 126.3, 99.0, 98.9, 88.0, 87.1, 82.3, 72.5, 69.5, 51.3, 34.6, 32.4, 31.9, 29.7, 26.6, 25.7, 25.2; IR (KBr) 1721 (s) cm^{-1}; MS (CI, CH_4) m/z 466 (M^+ + 1, 3), 159 (100); TLC R_f 0.15 (hexane/EtOAc, 80/20). Anal. Calcd for $C_{27}H_{31}NO_6$ (465.55): C, 69.66; H, 6.71; N, 3.01. Found: C, 69.36; H, 6.66; N, 3.05.

***rel*-(2*S*,3a*S*,4*R*,6*R*)-4-(Benzoyloxy)-2-{2-[(dimethyl(1,1,2-trimethylpropyl)silyl)oxy]-1-oxoethyl}-6-[(1*S*,2*R*)-(2-phenylcyclohexyl)oxy]hexahydroisoxazolo[2,3-*b*][1,2]oxazine (33a) and *rel*-(2*R*,3a*S*,4*R*,6*R*)-4-(Benzoyloxy)-2-{2-[(dimethyl(1,1,2-trimethylpropyl)silyl)oxy]-1-oxoethyl}-6-[(1*S*,2*R*)-(2-phenylcyclohexyl)oxy]hexahydroisoxazolo-[2,3-*b*][1,2]oxazine (33b).** A solution of dimethyl sulfoxide (340 μL, 4.79 mmol, 2.2 equiv) in CH_2Cl_2 (20 mL) was cooled to −74 °C and treated with oxalyl chloride (210 μL, 2.41 mmol, 1.1 equiv) in one portion. After 30 min, a solution of alcohol **13** (501 mg, 2.17 mmol) in CH_2Cl_2 (2 mL) was added dropwise via cannula. The resultant cloudy mixture was maintained for 1 h before triethylamine (1.5 mL, 11 mmol, 5 equiv) was introduced dropwise. The reaction mixture was maintained at −74 °C for 10 min and then allowed to warm over 15 min. The reaction mixture was diluted with Et_2O (120 mL) and washed with 0.1 M hydrochloric acid (30 mL), water (30 mL), and brine (30 mL). The aq layers were back extracted with Et_2O (50 mL), and the combined organic layers were dried (Na_2SO_4). The residue was purified by rapid chromatography on silica (pentane/Et_2O, 91/9) and dried at 0.1 mmHg to provide 374 mg (75%) of ketone **15** as a golden oil. The ketone was not purified further but was used directly in the next reaction. Nitronate **3** (490 mg, 1.24 mmol) was added to a solution of ketone **15** (369 mg, 1.62 mmol, 1.3 equiv) and several crystals of 1,4-di-*tert*-butylhydroquinone in benzene (12 mL), and the reaction mixture was maintained at room temperature for 4 h. Upon concentration of the solution in vacuo, the residue was prepurified by gradient chromatogra-

phy on silica (pentane/Et_2O, 91/9, then Et_2O) to provide 770 mg of ketones **33a** and **33b** in a 5/1 ratio. The diastereoisomers were separated by radial chromatography (hexane/EtOAc, 89/11, 4 mm SiO_2 plate) to give 607 mg (79%) of nitroso acetal **33a** and 87.2 mg (11%) of nitroso acetal **33b** as foams after drying at 7.5×10^{-5} mmHg. Data for **33a**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (dd, J = 8.2, 1.1, 2H), 7.58 (tt, J = 7.5, 1.3, 1H), 7.45 (t, J = 8.2, 2H), 5.15 (dd, J = 10.2, 4.0, 1H), 4.95 (ddd, J = 9.2, 4.9, 4.8, 1H), 4.43 (s, 2H), 4.16 (t, J = 5.9, 1H), 3.63 (td, J = 10.4, 4.4, 1H), 3.55 (ddd, J = 10.6, 8.2, 4.2, 1H), 2.61 (ddd, J = 12.4, 8.1, 4.2, 1H), 2.53 (ddd, J = 13.0, 10.4, 3.7, 1H), 2.45 (dt, J = 12.6, 10.6, 1H), 2.41−2.38 (m, 1H), 1.89−1.72 (m, 6H), 1.66−1.53 (m, 2H), 1.51−1.42 (m, 1H), 1.37−1.29 (m, 1H), 0.88 (d, J = 7.0, 6H), 0.85 (s, 6H), 0.10 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.6, 165.6, 144.1, 133.3, 129.7, 128.4, 128.1, 127.8, 126.3, 98.9, 85.1, 82.3, 72.3, 69.5, 67.4, 51.3, 34.6, 34.0, 32.5, 32.1, 29.8, 25.8, 25.2, 25.2, 20.1, 18.4, −3.6; IR (CCl_4) 1726 (s) cm^{-1}; MS (CI, CH_4) m/z 624 (M^+, 2.5), 159 (100); TLC R_f 0.41 (hexane/EtOAc, 80/20). Anal. Calcd for $C_{35}H_{49}NO_7Si$ (623.87): C, 67.38; H, 7.92; N, 2.25. Found: C, 67.22; H, 7.97; N, 2.34. Data for **33b**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (dd, J = 8.1, 1.1, 2H), 7.58 (tt, J = 7.5, 1.3, 1H), 7.46 (t, J = 8.1, 2H), 7.24−7.14 (m, 5H), 4.96 (ddd, J = 8.6, 4.9, 3.8, 1H), 4.87 (d, J = 18.8, 1H), 4.76 (dd, J = 9.5, 6.2, 1H), 4.57 (d, J = 18.7, 1H), 4.10 (t, J = 5.7, 1H), 3.59 (m, 1H), 3.54 (td, J = 10.6, 4.6, 1H), 2.62 (ddd, J = 12.6, 9.5, 8.6, 1H), 2.55−2.47 (m, 2H), 2.41−2.38 (m, 1H), 1.91−1.87 (m, 2H), 1.79−1.55 (m, 6H), 1.47−1.27 (m, 2H), 0.93 (d, J = 7.0, 6H), 0.91 (s, 6H), 0.16 (s, 3H), 0.14 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.2, 165.7, 144.0, 133.3, 129.8, 129.7, 128.4, 128.1, 127.8, 126.4, 99.2, 86.5, 82.7, 73.1, 69.5, 67.6, 51.2, 34.6, 34.1, 32.6, 30.6, 29.5, 25.8, 25.4, 25.3, 20.4, 20.3, 18.5, 18.5, −3.4, −3.6; IR (CCl_4) 2931 (s), 1720 (s), 1716 (s) cm^{-1}; MS (CI, CH_4) m/z 624 (M^+, 1), 159 (100); TLC R_f 0.31 (hexane/EtOAc, 80/20). Anal. Calcd for $C_{35}H_{49}NO_7Si$ (623.87): C, 67.38; H, 7.92; N, 2.25. Found: C, 67.10; H, 7.97; N, 2.19.

***rel*-(2*S*,3a*S*,4*R*,6*R*)-4-(Benzoyloxy)-6-[(1*S*,2*R*)-(2-phenylcyclohexyl)oxy]-2-[2-(phenylmethoxy)-1-oxoethyl]hexahydroisoxazolo[2,3-*b*][1,2]oxazine (34a) and *rel*-(2*R*,3a*S*,4*R*,6*R*)-4-(Benzoyloxy)-6-[(1*S*,2*R*)-(2-phenylcyclohexyl)oxy]-2-[2-(phenylmethoxy)-1-oxoethyl]hexahydroisoxazolo[2,3-*b*][1,2]oxazine (34b).** A solution of water (56 μL, 3.1 mmol, 1.1 equiv) in CH_2Cl_2 was added dropwise over 70 min to a solution of the Dess−Martin periodinane (1.40 g, 3.30 mmol, 1.2 equiv) and the allyl alcohol **14** (503 mg, 2.82 mmol) in CH_2Cl_2 (14 mL). After an additional 20 min, the cloudy reaction mixture was diluted with Et_2O (100 mL) and filtered (Watman 1). The organic phase was washed with 1/1 (v/v) saturated aq $NaHCO_3$/0.1 N aq sodium thiosulfate solution (50 mL), water (50 mL), and brine (50 mL). The aq layers were back extracted with Et_2O (25 mL), and the combined organic layers were dried (Na_2SO_4). The residue was purified by rapid chromatography on silica (pentane/Et_2O, 67/33) and dried at 0.1 mmHg to provide 430 mg (87%) of ketone **16** as an oil. The ketone was not purified further but was used directly in the next reaction. Nitronate **3** (720 mg, 1.82 mmol) was added to a solution of ketone **16** (424 mg, 2.41 mmol, 1.3 equiv) and several crystals of 1,4-di-*tert*-butylhydroquinone in benzene (19 mL), and the reaction mixture was maintained at room temperature for 12 h. Upon concentration of the solution in vacuo, the residue was prepurified by gradient chromatography on silica (hexane/EtOAc, 86/14, 80/20, 67/33). The diastereoisomers were separated by radial chromatography (hexane/EtOAc, 87/13, 4 mm SiO_2 plate) to give 795 mg (76%) of the major nitroso acetal **34a** as a foam. The minor nitroso acetal was recrystallized from TBME/hexane to provide 140 mg (13%) of **34b** as colorless, spiny needles. Data for **16**: bp 140 °C (1.2×10^{-5} mmHg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.31 (m, 5H), 6.55 (dd, J = 17.6, 10.5, 1H), 6.34 (dd, J = 17.6, 1.5, 1H), 5.83 (dd, J = 10.7, 1.5, 1H), 4.62 (s, 2H), 4.28 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.0, 137.1, 132.3, 129.2, 128.4, 127.9, 127.9, 73.7, 73.2; IR (neat) 1721 (s) cm^{-1}; TLC R_f 0.30 (hexane/EtOAc, 80/20). Data for **34a**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (dd, J = 8.2, 1.3, 2H), 7.59 (tt, J = 7.3, 1.5, 1H), 7.46 (t, J = 7.7, 2H), 7.33−7.16 (m, 10H), 5.06 (dd, J = 10.4, 4.2, 1H), 4.93 (ddd, J = 9.1, 4.8, 4.2, 1H), 4.59 (d, J = 11.9, 1H), 4.56 (d, J = 11.9, 1H), 4.31 (s, 2H), 4.15 (t, J = 5.9, 1H), 3.61 (td, J = 10.4, 4.4, 1H), 3.51 (ddd, J = 10.2, 8.2, 3.8, 1H), 2.61 (ddd, J = 12.4, 8.2, 4.2, 1H), 2.55−2.50 (m, 1H), 2.46 (dt, J = 12.8, 10.4, 1H), 2.38−2.35 (m, 1H), 1.89−1.70 (m, 5H), 1.66−1.42 (m, 3H), 1.37−1.28 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 204.3, 165.6, 144.0, 136.8, 133.3, 129.7, 129.5, 128.4, 128.3, 128.1, 128.0, 128.0, 127.8, 126.3, 98.9, 85.5, 82.3, 73.3, 72.7, 72.3, 69.4, 51.3, 34.5, 32.5, 32.2, 29.7, 25.7, 25.1; IR (CCl_4) 1726 (s) cm^{-1}; MS (CI, CH_4) m/z 572 (M^+, 1), 91 (100); TLC R_f 0.51 (hexane/EtOAc, 67/33). Anal. Calcd for $C_{34}H_{37}NO_7$ (571.68): C, 71.44; H, 6.52; N, 2.45. Found: C, 71.31; H, 6.57; N, 2.52. Data for **34b**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, J = 7.1, 2H), 7.59 (t, J = 7.3, 1H), 7.46 (t, J = 7.9, 2H), 7.41−7.12 (m, 10H), 4.97 (ddd, J = 8.8, 5.3, 3.8, 1H), 4.76 (d, J = 18.1, 1H), 4.74 (dd, J = 9.5, 6.2, 1H), 4.63 (s, 2H), 4.43 (d, J = 18.1, 1H), 4.09 (t, J = 5.7, 1H), 3.59 (ddd, J = 10.1, 8.6, 3.5, 1H), 3.45 (td, J = 10.4, 4.4, 1H), 2.61 (dt, J = 12.6, 9.3, 1H), 2.53−2.47 (m, 2H), 2.34−2.31 (m, 1H), 1.88−1.86 (m, 2H), 1.78−1.67 (m, 3H), 1.62−1.51 (m, 2H), 1.41−1.28 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.2, 165.6, 143.9, 137.4, 133.3, 129.7, 129.6, 128.5, 128.3, 128.0, 128.0, 127.9, 127.9, 127.7, 126.3, 99.2, 86.6, 82.7, 73.2, 72.9, 72.9, 69.3, 51.1, 34.5, 32.5, 30.5, 29.2, 25.7, 25.2; IR (CCl_4) 1727 (s), 1719 (s) cm^{-1}; MS (CI, CH_4) m/z 572 (M^+, 2), 91 (100); TLC R_f 0.31 (hexane/EtOAc, 67/33). Anal. Calcd for $C_{34}H_{37}NO_7$ (571.68): C, 71.44; H, 6.52; N, 2.45. Found: C, 71.51; H, 6.53; N, 2.52.

***rel*-(2*R*,3a*S*,4*R*,6*R*)-4-(Benzoyloxy)-2-(hydroxymethyl)-6-[(1*S*,2*R*)-(2-phenylcyclohexyl)oxy]hexahydroisoxazolo[2,3-*b*][1,2]oxazine (36b) and *rel*-(2*S*,3a*S*,4*R*,6*R*)-4-(Benzoyl-oxy)-2-(hydroxymethyl)-6-[(1*S*,2*R*)-(2-phenyl-cyclohexyl)oxy-]hexahydroisoxazolo[2,3-*b*][1,2]oxazine (36a). [3 + 2] Cycloaddition with Acrolein.** Acrolein (440 μL, 6.59 mmol, 6.5 equiv) was added to a solution of nitronate **3** (401 mg, 1.01 mmol) and several crystals of 1,4-di-*tert*-butylhydroquinone in benzene (30 mL), and the reaction mixture was maintained at room temperature for 3.5 h. Upon concentration of the solution in vacuo, the residue was purified by chromatography on silica (hexane/EtOAc, 80/20, 67/33, 50/50). The major nitroso acetal **35b** (296 mg) and minor nitroso acetal **35a** (158 mg) were repurified by chromatography two additional times and dried azeotropically with benzene to afford 251 and 97.3 mg, respectively. The hydrated aldehyde pair were combined, dissolved in EtOH (2 mL), and treated with $NaBH_4$ (61.3 mg, 1.62 mmol, 2.1 equiv) in portions at 0 °C. After 1 h, the reaction mixture was poured into water (25 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The extracts were washed with water (10 mL) and brine (10 mL) and dried (Na_2SO_4). The residue was purified by radial chromatography (CH_2Cl_2/methanol, 99/1, 4 mm SiO_2 plate). The major nitroso acetal was recrystallized from TBME/pentane to provide 193 mg (42%) of **36b** as colorless, spiny needles. The minor nitroso acetal was recrystallized from TBME/pentane to provide 93.6 mg (20%) of **36a** as colorless, spiny needles. Data for 1/2 mixture of **35a** and **35b**:^{1}H NMR (500 MHz, $CDCl_3$) δ 9.76 (d, J = 1.1, 1H), 9.65 (d, J = 1.8, 1H), 8.06 (dd, J = 8.2, 1.1, 2H), 8.02 (dd, J = 8.2, 1.1, 2H), 7.61−7.57 (m, 1H), 7.48−7.44 (m, 2H), 7.27−7.15 (m, 5H), 5.00 (ddd, J = 8.4, 4.9, 3.8, 1H), 4.93 (dt, J = 9.0, 4.9, 1H), 4.88 (ddd, J = 10.2, 4.0, 1.8, 1H), 4.62 (ddd, J = 9.7, 5.9, 1.1, 1H), 4.17 (t, J = 6.0, 1H), 4.14 (t, J = 5.5, 1H), 3.68−3.53 (m, 2H), 2.65−2.30 (m, 4H), 1.90−1.29 (m, 9H). Data for **36b**: mp 138−139 °C (TBME/pentane);^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (dd, J = 8.3, 1.2, 2H), 7.59 (tt, J = 7.6, 1.2, 1H), 7.46 (t, J = 8.1, 2H), 7.26−7.15 (m, 5H), 5.01 (ddd, J = 8.8, 4.9, 3.9, 1H), 4.66 (tt, J = 8.5, 2.4, 1H), 4.20 (t, J = 5.6, 1H), 3.89 (dt, J = 12.7, 2.2, 1H), 3.65 (ddd, J = 11.5, 7.6, 3.7, 1H), 3.61 (td, J = 10.7, 4.4, 1H), 3.57 (ddd, J = 12.7, 10.0, 2.9, 1H), 2.66 (dd, J = 10.0, 2.4, 1H), 2.52 (ddd, J = 12.9, 10.3, 3.4, 1H), 2.39 (dt, J = 12.0, 7.8, 2H), 2.30 (td, J = 12.0, 8.8, 1H), 1.89−1.74 (m, 5H), 1.66−1.28 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.8, 144.1, 133.3, 129.8, 129.7, 128.4, 128.1, 127.9, 126.3, 99.1, 87.0, 82.4, 73.9, 69.4, 61.9, 51.3, 34.6, 32.6, 29.9, 28.8, 25.8, 25.2; IR (KBr) 1721 (s) cm^{-1}; MS (CI, CH_4) m/z 454 (M^+ + 1, 8), 159 (100); TLC R_f 0.35 (EtOAc/hexane, 50/50). Anal. Calcd for $C_{26}H_{31}NO_6$ (453.54): C, 68.86; H, 6.89; N, 3.09.

Found: C, 68.88; H, 6.90; N, 3.11. Data for **36a**: mp 140−141 °C (TBME/pentane);^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (dd, J = 8.3, 1.2, 2H), 7.58 (tt, J = 7.6, 1.2, 1H), 7.45 (t, J = 8.1, 2H), 7.26−7.16 (m, 5H), 4.97 (dt, J = 8.8, 4.9, 1H), 4.76−4.72 (m, 1H), 4.15 (t, J = 5.9, 1H), 3.84 (ddd, J = 12.5, 4.9, 2.7, 1H), 3.66 (ddd, J = 9.3, 8.3, 4.4, 1H), 3.64 (td, J = 11.0, 4.4, 1H), 3.60 (ddd, J = 12.5, 8.8, 3.9, 1H), 2.52 (ddd, J = 12.9, 10.3, 3.4, 1H), 2.40−2.36 (m, 1H), 2.36 (ddd, J = 12.7, 8.3, 4.2, 2H), 2.26 (dt, J = 12.0, 9.8, 1H), 1.89−1.28 (m, 10H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.8, 144.2, 133.3, 129.8, 129.7, 128.4, 128.1, 127.9, 126.3, 98.8, 84.1, 82.1, 73.7, 70.1, 63.1, 51.4, 34.7, 32.6, 31.1, 29.9, 25.8, 25.3; IR (KBr) 3488 (s), 2927 (s), 1727 (s) cm^{-1}; MS (CI, CH_4) m/z 454 (M^+ + 1, 14), 278 (100); TLC R_f 0.33 (EtOAc/hexane, 50/50). Anal. Calcd for $C_{26}H_{31}NO_6$ (453.54): C, 68.86; H, 6.89; N, 3.09. Found: C, 69.05; H, 6.98; N, 3.08.

***rel*-(2*R*,3a*S*,4*R*,6*R*)-4-(Benzoyloxy)-2-(hydroxymethyl)-6-[(1*S*,-2*R*)-(2-phenylcyclohexyl)oxy]hexahydroisoxazolo[2,3-*b*][1,2]-oxazine (36b) and *rel*-(2*S*,3a*S*,4*R*,6*R*)-4-(Benzoyloxy)-2-(hydroxymethyl)-6-[(1*S*,2*R*)-(2-phenylcyclohexyl)oxy]-hexahydroisoxazolo[2,3*b*][1,2]oxazine (36a).** Allyl alcohol (0.5 mL, 7.4 mmol, 6 equiv) was added to a solution of nitronate **3** (485 mg, 1.23 mmol) and several crystals of 1,4-di-*tert*-butylhydroquinone in benzene (40 mL), and the reaction mixture was maintained at 80 °C for 1.5 h. Upon concentration of the solution in vacuo, the residue was purified by radial chromatography (CH_2Cl_2/methanol, 99/1, 4 mm SiO_2 plate). The minor nitroso acetal (235 mg) was recrystallized from TBME/pentane to provide 199 mg (36%) of **36b** as colorless, spiny needles. The major nitroso acetal (280 mg) was recrystallized from TBME/pentane to provide 253 mg (45%) of **36a** as colorless, spiny needles. Data for **36b**: mp 137−138 °C (TBME/pentane);^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (dd, J = 8.4, 1.3, 2H), 7.59 (tt, J = 7.5, 1.3, 1H), 7.46 (t, J = 7.5, 2H), 7.26−7.16 (m, 5H), 5.01 (ddd, J = 8.6, 4.8, 3.8, 1H), 4.66 (tt, J = 8.2, 2.2, 1H), 4.20 (t, J = 5.5, 1H), 3.89 (dt, J = 12.6, 2.2, 1H), 3.65 (ddd, J = 11.2, 7.3, 3.5, 1H), 3.65−3.55 (m, 2H), 2.65 (dd, J = 10.1, 2.2, 1H), 2.55−2.50 (m, 1H), 2.42−2.36 (m, 2H), 2.30 (td, J = 11.5, 9.0, 1H), 1.89−1.74 (m, 5H), 1.66−1.28 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.7, 144.0, 133.2, 129.7, 129.6, 128.3, 128.0, 127.8, 126.2, 99.1, 86.8, 82.3, 73.8, 69.3, 62.0, 51.2, 34.5, 32.5, 29.8, 28.8, 25.7, 25.1; IR (CCl_4) 1724 (s) cm^{-1}; MS (CI, CH_4) m/z 454 (M^+ + 1, 1), 123 (100); TLC R_f 0.35 (EtOAc/hexane, 50/50). Anal. Calcd for $C_{26}H_{31}NO_6$ (453.54): C, 68.86; H, 6.89; N, 3.09. Found: C, 68.98; H, 6.89; N, 3.27. Data for **36a**: mp 128−129 °C (TBME/pentane);^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 8, 2H), 7.58 (t, J = 8, 1H), 7.45 (t, J = 8, 2H), 7.25−7.15 (m, 5H), 4.97 (ddd, J = 9.0, 8.6, 4.9, 1H), 4.74 (dtd, J = 7.1, 4.5, 3.9, 1H), 4.16 (t, J = 5.6, 1H), 3.84 (ddd, J = 12.5, 4.9, 2.7, 1H), 3.68−3.52 (m, 3H), 2.52 (ddd, J = 12.9, 9.5, 3.4, 1H), 2.41−2.36 (m, 1H), 2.36 (ddd, J = 11.7, 8.5, 4.6, 1H), 2.26 (dt, J = 12.0, 9.8, 1H), 1.89−1.30 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 144.1, 133.1, 129.7, 129.6, 128.2, 128.0, 127.8, 126.2, 98.7, 84.1, 81.9, 73.4, 70.0, 62.8, 51.2, 34.5, 32.4, 30.8, 29.7, 25.7, 25.1; IR (CCl_4) 2932 (s), 1725 (s) cm^{-1}; MS (CI, CH_4) m/z 454 (M^+ + 1, 17), 160 (100); TLC R_f 0.33 (EtOAc/hexane, 50/50). Anal. Calcd for $C_{26}H_{31}NO_6$ (453.54): C, 68.86; H, 6.89; N, 3.09. Found: C, 68.97; H, 6.89; N, 3.17.

***rel*-(2*S*,7*R*,7a*S*)-7-(Benzoyloxy)-2-hydroxyhexahydro-1*H*-pyrrolizidin-3-one (37a).** To a suspension of W-2 Raney nickel (1.88 g) [washed with water (6 × 10 mL) and methanol (3 × 15 mL)] in methanol (90 mL) was added nitroso acetal **30a** (1.20 g, 2.49 mmol). The suspension was maintained under an atmosphere of H_2 (160 psi) with vigorous stirring for 48 h, filtered through Celite (methanol, CH_2Cl_2), and concentrated in vacuo. The crude material was purified by chromatography on silica (EtOAc) to provide 437 mg (100%) of the chiral auxiliary and 517 mg of lactam **37a**. Recrystallization from EtOAc/hexane provided 441 mg (68%) of lactam **37a** as fine, colorless needles. Data for **37a**: mp 111−112 °C (EtOAc/hexane);^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 7.1, 2H), 7.60 (t, J = 7.3, 1H), 7.47 (t, J = 8.1, 2H), 5.12 (dt, J = 6.8, 3.9, 1H), 4.60 (t, J = 8.1, 1H), 3.97 (ddd, J = 11.7, 8.1, 3.9, 1H), 3.81 (ddd, J = 9.8, 5.6, 4.2, 1H), 3.77−3.52 (bs, 1H), 3.24 (dt, J = 11.7, 7.8, 1H), 2.99 (ddd, J = 12.5, 7.3, 6.1, 1H), 2.32 (ddd, J = 15.1, 13.9, 8.1, 1H), 2.23 (dddd, J = 15.4, 7.6, 3.9, 1.7, 1H), 1.87 (dt, J = 11.5, 10.7, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.7, 165.9, 133.2, 129.4, 129.2, 128.3, 77.9, 71.9, 61.6, 40.8, 36.6, 31.6; IR (CCl_4) 1723 (s) cm^{-1}; MS (CI, CH_4) m/z 262 (M^+ + 1, 100); TLC R_f 0.17 (EtOAc). Anal. Calcd for $C_{14}H_{15}NO_4$ (261.28): C, 64.36; H, 5.79; N, 5.36. Found: C, 64.35; H, 5.96; N, 5.34.

***rel*-(2*R*,7*R*,7a*S*)-7-(Benzoyloxy)-2-hydroxyhexahydro-1*H*-pyrrolizidin-3-one (37b).** To a suspension of W-2 Raney nickel (680 mg) [washed with water (3 × 10 mL) and methanol (2 × 20 mL)] in methanol (90 mL) was added nitroso acetal **30b** (425 mg, 0.883 mmol). The suspension was maintained under an atmosphere of H_2 (160 psi) with vigorous stirring for 48 h, filtered through Celite (methanol, CH_2Cl_2), and concentrated in vacuo. The crude material was purified by chromatography on silica (EtOAc) to provide 131 mg (84%) of the chiral auxiliary and 185 mg of lactam **37b**. Recrystallization from CH_2Cl_2/hexane provided 159 mg (69%) of lactam **37b** as fine, colorless needles. Data for **37b**: mp 198−199 °C (CH_2Cl_2/hexane);^{1}H NMR (400 MHz, Me_2SO-d_6) δ 7.98 (d, J = 7.1, 2H), 7.67 (t, J = 7.6, 1H), 7.53 (t, J = 7.6, 2H), 5.74 (d, J = 5.1, 1H), 4.98 (dt, J = 7.3, 5.1, 1H), 4.08 (m, 1H), 4.01 (q, J = 6.3 1H), 3.60 (ddd, J = 11.7, 8.5, 4.9, 1H), 3.14 (dt, J = 11.5, 7.6, 1H), 2.34 (ddd, J = 15.6, 7.6, 7.3, 1H), 2.21−2.05 (m, 3H); ^{13}C NMR (100 MHz, Me_2SO-d_6) δ 174.7, 165.6, 133.6, 129.4, 129.3, 128.8, 77.6, 73.0, 63.9, 40.2, 34.8, 32.2; IR (CCl_4) 1703 (s), 1699 (s) cm^{-1}; MS (CI, CH_4) m/z 262 (M^+ + 1, 100); TLC R_f 0.45 (CH_2Cl_2/methanol, 90/10). Anal. Calcd for $C_{14}H_{15}NO_4$ (261.28): C, 64.36; H, 5.79; N, 5.36. Found: C, 64.41; H, 5.82; N, 5.39.

***rel*-(7*R*,7a*S*)-7-(Benzoyloxy)hexahydro-1*H*-pyrrolizidin-3-one (38a).** Phenoxy chlorothionocarbonate (160 μL, 1.16 mmol, 2 equiv), pyridine (93 μL, 1.15 mmol, 2 equiv), and 4-(*N*,*N*-dimethylamino)pyridine (35.5 mg, 0.291 mmol, 0.5 equiv) were added to a solution of lactam **37a** (150 mg, 0.574 mmol) in CH_2Cl_2 (7.5 mL), and the reaction mixture was maintained at room temperature for 5.5 h. Upon concentration in vacuo, the residue was purified by chromatography on silica (hexane/EtOAc, 67/33) to give the solid thionocarbonate (226 mg) which was recrystallized from EtOAc/hexane. The thionocarbonate [162 mg, 71% (mp 151−152 °C)] was dissolved in benzene (43 mL) and heated at reflux. A solution of tributyltin hydride (143 μL, 0.532 mmol, 1.3 equiv) and azobisisobutyronitrile (13 mg, 0.079 mmol, 0.2 equiv) in benzene (5 mL) was added dropwise to the reaction mixture over 45 min via syringe pump. After an additional 2.5 h at reflux, the reaction mixture was allowed to cool to room temperature and concentrated in vacuo in the presence of 100 mg of 1/1 SiO_2−KF. Chromatographic purification on silica (EtOAc/hexane, 90/10) provided an oil (85.8 mg) which was triturated with hexanes and recrystallized (TBME/hexane) to give 81.6 mg (58%) of lactam **38a** as a white solid. Data for **38a**: mp 82−83 °C (TBME/hexane);^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (dd, J = 8.4, 1.3, 2H), 7.60 (tt, J = 7.3, 1.3, 1H), 7.47 (t, J = 7.7, 2H), 5.06 (dt, J = 7.3, 4.6, 1H), 4.00 (ddd, J = 8.2, 7.1, 4.6, 1H), 3.90 (ddd, J = 12.3, 8.4, 4.4, 1H), 3.22 (dtd, J = 11.9, 7.9, 1.1, 1H), 2.68 (dtd, J = 16.5, 10.4, 1.1, 1H), 2.50 (dddd, J = 13.0, 8.8, 7.1, 1.6, 1H), 2.42 (ddd, J = 16.7, 9.3, 1.8, 1H), 2.38 (m, 1H), 2.21 (ddt, J = 13.7, 8.1, 4.6, 1H), 1.99 (ddt, J = 13.0, 11.5, 9.0, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.6, 166.2, 133.3, 129.6, 129.5, 128.4, 78.1, 66.5, 40.5, 33.9, 32.6, 26.2; IR (KBr) 1703 (s) cm^{-1}; MS (CI, CH_4) m/z 246 (M^+ + 1, 100); TLC R_f 0.15 (EtOAc/hexane, 90/10). Anal. Calcd for $C_{14}H_{15}NO_3$ (245.28): C, 68.56; H, 6.16; N, 5.71. Found: C, 68.38; H, 5.87; N, 5.85.

***rel*-(7*R*,7a*S*)-7-(Benzoyloxy)hexahydro-1*H*-pyrrolizidin-3-one (38b).** Phenoxy chlorothionocarbonate (105 μL, 0.759 mmol, 2 equiv), pyridine (62 μL, 0.77 mmol, 2 equiv), and 4-(*N*,*N*-dimethylamino)pyridine (23.5 mg, 0.192 mmol, 0.5 equiv) were added to a solution of lactam **37b** (99.1 mg, 0.379 mmol) in CH_2Cl_2 (5 mL) and the reaction mixture maintained at room temperature for 5 h. Upon concentration in vacuo, the residue was purified by chromatography on silica (hexane/EtOAc, 67/33) to give the thionocarbonate as an oil (147 mg). The thionocarbonate was dissolved in benzene (37 mL) and heated at reflux. A solution of tributyltin hydride (197 μL,

0.732 mmol, 1.9 equiv) and azobisisobutyronitrile (12 mg, 0.073 mmol, 0.2 equiv) in benzene (5 mL) was added dropwise to the reaction mixture over 35 min via syringe pump. After an additional 2.5 h at reflux, the reaction mixture was allowed to cool to room temperature and concentrated in vacuo in the presence of 100 mg of 1/1 SiO_2−KF. Chromatographic purification on silica (EtOAc) provided an oil (86.8 mg) which was triturated with hexanes and recrystallized (TBME/hexane) to give 60.7 mg (65%) of lactam **38b** as a white solid. Data for **38b**: mp 82−83 °C (TBME/hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (dd, J = 8.4, 1.3, 2H), 7.60 (tt, J = 7.3, 1.3, 1H), 7.47 (t, J = 7.7, 2H), 5.06 (dt, J = 7.3, 4.6, 1H), 4.00 (ddd, J = 8.2, 7.1, 4.6, 1H), 3.90 (ddd, J = 12.1, 8.4, 4.4, 1H), 3.22 (dtd, J = 11.7, 7.7, 1.1, 1H), 2.68 (dtd, J = 16.5, 10.4, 1.1, 1H), 2.50 (dddd, J = 13.0, 8.8, 7.1, 1.6, 1H), 2.42 (ddd, J = 16.7, 9.3, 1.8, 1H), 2.38 (m, 1H), 2.21 (ddt, J = 13.7, 8.1, 4.6, 1H), 1.99 (ddt, J = 13.0, 11.5, 9.0, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.6, 166.2, 133.6, 129.6, 129.5, 128.4, 78.1, 66.5, 40.6, 33.9, 32.6, 26.2; IR (KBr) 1703 (s), 1698 (s), 1693 (s) cm^{-1}; MS (CI, CH_4) m/z 246 (M^+ + 1, 100); TLC R_f 0.15 (EtOAc/hexane, 90/10). Anal. Calcd for $C_{14}H_{15}NO_3$ (245.28): C, 68.56; H, 6.16; N, 5.71. Found: C, 68.56; H, 6.15; N, 5.74.

***rel*-(2*S*,3*R*,3a*R*,4*R*,6*R*)-4-(Benzoyloxy)-6-(butyloxy)-3-(trimethylsilyl)hexahydroisoxazolo[2,3-*b*][1,2]oxazine-2-carboxylic Acid Methyl Ester (39a$_i$) and *rel*-(2*R*,3*R*,-3a*S*,4*R*,6*R*)-4-(Benzoyloxy)-6-(butyloxy)-2-(trimethylsilyl)hexahydroisoxazolo[2,3-*b*][1,2]oxazine-3-carboxylic Acid Methyl Ester (39a$_{ii}$).** To a solution of **2** (303.0 mg, 1.03 mmol) in CH_3CN (4.5 mL) was added **17b** (340 mg, 2.15 mmol, 2.1 equiv). The solution was degassed, heated at 65 °C (ext) for 38 h, and then concentrated and chromatographed on silica (hexane/EtOAc, 95/5) to afford 337 mg of a 2.4/1 mixture of **39a$_i$** (51%) and **39a$_{ii}$** (21%) as a colorless, viscous oil. Data for 2.4/1 mixture of **39a$_i$** and **39a$_{ii}$**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10−8.07 (m, 2H), 8.09 (dd, J = 7.3, 0.6, 2H), 7.62−7.58 (m, 1H), 7.60 (t, J = 7.4, 1H), 7.49−7.45 (m, 2H), 7.47 (t, J = 7.9, 2H), 5.28 (dt, J = 9.1, 4.6, 1H), 5.19 (dt, J = 8.7, 4.3, 1H), 5.13 (d, J = 9.5, 1H), 5.01 (t, J = 5.8, 1H), 4.94 (t, J = 5.8, 1H), 4.50 (d, J = 10.9, 1H), 4.10 (dd, J = 8.3, 4.7, 1H), 3.99 (dd, J = 13.1, 4.3, 1H), 3.99−3.94 (m, 1H), 3.96 (dt, J = 9.5, 6.6, 1H), 3.75 (s, 3H), 3.68 (s, 3H), 3.63 (dd, J = 10.8, 8.1, 1H), 3.50−3.44 (m, 1H), 3.47 (dt, J = 9.4, 6.8, 1H), 2.41 (dt, J = 13.5, 5.3, 1H), 2.34−2.14 (m, 2H), 2.25 (dd, J = 12.7, 9.8, 1H), 2.10−2.04 (m, 1H), 1.68−1.60 (m, 2H), 1.46−1.36 (m, 2H), 0.93 (t, J = 7.2, 3H), 0.11 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.3, 170.5, 165.7, 165.4, 133.2, 133.1, 129.6, 129.5, 129.4, 128.4, 128.3, 128.2, 98.1, 98.0, 85.2, 77.8, 77.4, 73.9, 69.4, 69.1, 67.7, 67.6, 52.0, 50.4, 32.8, 31.4, 31.4, 30.2, 30.1, 19.1, 19.1, 13.7, −1.9, −3.1; IR ($CHCl_3$) 2958 (s), 1743 (s), 1722 (s) cm^{-1}; MS (CI, CH_4) m/z 452 (M^+ + 1, 33), 378 (100); TLC R_f 0.23 (hexane/EtOAc, 85/15). Anal. Calcd for $C_{22}H_{33}NO_7Si$ (451.59); C, 58.51; H, 7.37; N, 3.10; Si, 6.22. Found: C, 58.48; H, 7.29; N, 3.24; Si, 6.01.

***rel*-(2*R*,3*R*,3a*R*,4*R*,6*R*)-4-(Benzoyloxy)-6-(butyloxy)-3-(trimethylsilyl)hexahydroisoxazolo[2,3-*b*][1,2]oxazine-2-carboxylic Acid Methyl Ester (40b$_i$), *rel*-(2*S*,3*S*,-3a*R*,4*R*,6*R*)-4-(Benzoyloxy)-6-(butyloxy)-3-(trimethylsilyl)-hexahydroisoxazolo[2,3-*b*][1,2]oxazine-2-carboxylic Acid Methyl Ester (40a$_i$), and *rel*-(2*S*,3*R*,3a*S*,4*R*,6*R*)-4-(Benzoyloxy)-6-(butyloxy)-2-(trimethylsilyl)hexahydroisoxazolo[2,3-*b*][1,2]oxazine-3-carboxylic Acid Methyl Ester (40a$_{ii}$).** To a solution of **2** (306.1 mg, 1.04 mmol) in CH_3CN (4.5 mL) was added **17a** (264.0 mg, 1.67 mmol, 1.6 equiv). The solution was degassed, heated at 65 °C (ext) for 21.5 h, and then concentrated and chromatographed on silica MPLC (hexane/EtOAc, 95/5) to afford 197.0 mg of a 1.5/1 mixture of **40a$_{ii}$** (25%) and **40a$_i$** (17%) as a colorless oil, and 166 mg (35%) of **40b$_i$** as a white solid. Approximately 10 mg of **40a$_{ii}$** was separated as the less polar component from approximately 20 mg of the mixture via preparative HPLC (hexane/EtOAc, 95/5). A single crystal of **40b$_i$** was grown from Et_2O/pentane. Data for 1.5/1 mixture of **40a$_{ii}$** and **40a$_i$**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07−8.04 (m, 2H), 7.61−7.56 (m, 1H), 7.48−7.43 (m, 2H), 5.38−5.32 (m, 1H), 5.02 (t, J = 6.5, 1H), 4.90 (t, J = 5.9, 1H), 4.64 (d, J = 10.5, 1H), 4.16 (d, J = 11.2, 1H), 3.97−3.89 (m, 2H), 3.65 (s, 3H), 3.62 (s, 3H), 3.50−3.31 (m, 2H), 2.35−2.28 (m, 1H), 2.18 (ddd, J = 13.7, 9.3, 5.9, 1H), 2.04 (ddd, J = 13.4, 10.4, 6.4, 1H), 1.65−1.59 (m, 2H), 1.44−1.38 (m, 2H), 0.93 (t, J = 7.4, 3H), 0.13 (s, 9H), 0.11 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.8, 171.2, 165.7, 133.3, 129.7, 129.7, 129.6, 128.4, 128.4, 97.8, 97.6, 81.9, 77.5, 75.6, 69.0, 68.0, 67.7, 67.0, 52.4, 50.1, 48.9, 31.7, 31.6, 31.4, 30.7, 19.2, 13.9, 10.6, −3.6, −4.0; IR (CCl_4) 2957 (s), 1738 (s), 1725 (s) cm^{-1}; MS (CI, CH_4) m/z 452 (M^+ + 1, 2), 105 (100); TLC R_f 0.27 (hexane/EtOAc, 85/15). Anal. Calcd for $C_{22}H_{33}NO_7Si$ (451.59): C, 58.51; H, 7.37; N, 3.10; Si, 6.22. Found: C, 58.74; H, 7.46; N, 3.00; Si, 6.02. Data for **40a$_{ii}$**: ^{1}H NMR (500 MHz, C_6D_6) δ 8.11 (dd, J = 8.4, 1.3, 2H), 7.11 (tt, J = 7.3, 1.2, 1H), 7.04 (t, J = 7.5, 2H), 5.45 (dt, J = 8.9, 4.6, 1H), 4.51 (t, J = 5.9, 1H), 4.28 (d, J = 11.3, 1H), 4.06 (dd, J = 10.3, 3.8, 1H), 3.94 (dt, J = 9.3, 6.6, 1H), 3.45 (t, J = 10.8, 1H), 3.29 (s, 3H), 3.27 (dt, J = 9.3, 6.5, 1H), 2.23 (ddd, J = 13.5, 9.3, 5.8, 1H), 2.00 (dt, J = 13.5, 5.5, 1H), 1.57−1.51 (m, 2H), 1.42−1.30 (m, 2H), 0.84 (t, J = 7.3, 3H), 0.14 (s, 9H). Data for **40b$_i$**: mp 150−151 °C (Et_2O/pentane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11−8.09 (m, 2H), 7.60−7.56 (m, 1H), 7.46−7.42 (m, 2H), 5.37 (td, J = 5.1, 3.0, 1H), 4.96 (t, J = 4.0, 1H), 4.60 (d, J = 8.5, 1H), 4.01 (dt, J = 9.2, 6.6, 1H), 3.81 (s, 3H), 3.64 (dd, J = 12.4, 2.7, 1H), 3.43 (dt, J = 9.5, 6.7, 1H), 2.33−2.27 (m, 1H), 2.30 (dd, J = 12.2, 8.4, 1H), 1.98 (ddd, J = 14.5, 5.4, 3.3, 1H), 1.67−1.60 (m, 2H), 1.48−1.38 (m, 2H), 0.93 (t, J = 7.5, 3H), 0.15 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.3, 165.8, 133.2, 129.9, 129.8, 128.3, 98.5, 85.0, 74.6, 68.7, 67.7, 52.6, 31.7, 30.1, 28.9, 19.3, 13.9, −2.6; IR (CCl_4) 2956 (s), 1737 (s) cm^{-1}; MS (CI, CH_4) m/z 452 (M^+ + 1, 11), 105 (100); TLC R_f 0.20 (hexane/EtOAc, 85/15). Anal. Calcd for $C_{22}H_{33}NO_7Si$ (451.59): C, 58.51; H, 7.37; N, 3.10; Si, 6.22. Found: C, 58.37; H, 7.55; N, 2.95; Si, 6.41.

***rel*-(2*R*,3*R*,3a*S*,4*R*,6*R*)-4-(Benzoyloxy)-6-(butyloxy)-2-methylhexahydroisoxazolo[2,3-*b*][1,2]oxazine-3-carboxylic Acid Ethyl Ester (41a$_{ii}$) and *rel*-(2*S*,3*R*,3a*S*,*R*,6*R*)-4-(Benzoyloxy)-6-(butyloxy)-3-methylhexahydroisoxazolo[2,3-*b*][1,2]oxazine-2-carboxylic Acid Ethyl Ester (41a$_i$).** To a solution of **2** (273.7 mg, 0.933 mmol) in CH_3CN (5.0 mL) was added **19** (212.7 mg, 1.86 mmol, 2.0 equiv). The solution was degassed, heated at 65 °C (ext) for 22 h, and then concentrated and chromatographed on silica MPLC (hexane/EtOAc, 95/5) to afford 175.4 mg (46%) of **41a$_{ii}$** as a white crystalline solid (recrystallized from Et_2O/hexane), and 111.0 mg (29%) of **41a$_i$** as a white crystalline solid (recrystallized from Et_2O/hexane). Data for **41a$_{ii}$**: mp 83−84 °C (Et_2O/hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (d, J = 7.9, 2H), 7.55 (t, J = 7.2, 1H), 7.42 (d, J = 7.9, 2H), 5.19 (dt, J = 9.3, 4.7, 1H), 5.07 (dq, J = 9.7, 6.5, 1H), 4.96 (t, J = 5.9, 1H), 4.21 (dd, J = 8.6, 4.6, 1H), 4.17 (q, J = 7.1, 2H), 3.93 (dt, J = 9.3, 6.7, 1H), 3.57 (t, J = 9.3, 1H), 3.44 (dt, J = 9.4, 6.8, 1H), 2.28 (dt, J = 14.0, 5.4, 1H), 2.21 (ddd, J = 14.0, 9.0, 5.6, 1H), 1.64−1.58 (m, 2H), 1.43−1.35 (m, 2H), 1.26 (d, J = 6.5, 3H), 1.23 (t, J = 7.2, 3H), 0.90 (t, J = 7.4, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.3, 165.9, 133.3, 129.8, 129.6, 128.4, 98.0, 80.8, 76.3, 69.8, 67.8, 61.3, 51.9, 31.6, 30.3, 19.3, 15.2, 14.2, 13.9; IR ($CHCl_3$) 1724 (s) cm^{-1}; MS (CI, CH_4) m/z 408 (M^+ + 1, 3), 184 (100); TLC R_f 0.23 (hexane/EtOAc, 85/15). Anal. Calcd for $C_{21}H_{29}NO_7$ (407.46): C, 61.90; H, 7.17; N, 3.44. Found: C, 61.92; H, 7.30; N, 3.40. Data for **41a$_i$**: mp 75.5−76.5 °C (Et_2O/hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (d, J = 7.6, 2H), 7.59 (t, J = 7.4, 1H), 7.45 (d, J = 7.8, 2H), 5.35 (dt, J = 6.8, 4.1, 1H), 5.07 (d, J = 9.6, 1H), 4.98 (t, J = 4.8, 1H), 4.24 (q, J = 7.1, 2H), 3.96 (dt, J = 9.3, 6.7, 1H), 3.52 (dd, J = 10.2, 3.5, 1H), 3.45 (dt, J = 9.4, 6.7, 1H), 3.04 (tq, J = 9.9, 7.0, 1H), 2.27 (dt, J = 14.2, 5.3, 1H), 2.08 (ddd, J = 14.2, 7.0, 4.3, 1H), 1.66−1.60 (m, 2H), 1.45−1.37 (m, 2H), 1.29 (t, J = 7.1, 3H), 1.15 (d, J = 7.0, 3H), 0.92 (t, J = 7.4, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.9, 165.8, 133.3, 129.8, 129.7, 128.4, 98.4, 83.8, 76.8, 68.1, 67.6, 61.3, 39.0, 31.6, 29.8, 19.3, 14.2, 13.8, 12.2; IR ($CHCl_3$) 1747 (s), 1719 (s) cm^{-1}; MS (CI, CH_4) m/z 408 (M^+ + 1, 17), 184 (100); TLC R_f 0.14 (hexane/EtOAc, 85/15). Anal. Calcd for $C_{21}H_{29}NO_7$ (407.46): C, 61.90; H, 7.17; N, 3.44. Found: C, 61.83; H, 7.25; N, 3.38.

***rel*-(2*S*,3*R*,3a*S*,4*R*,6*R*)-2-(Acetyloxy)-4-(benzoyloxy)-6-(butyloxy)hexahydroisoxazolo[2,3-*b*][1,2]oxazine-3-car-**

boxylic Acid Ethyl Ester (42a$_{ii}$). To a solution of nitronate **2** (78.8 mg, 0.269 mmol) in CH_2Cl_2 (450 μL) was added **20b** (437.9 mg, 2.77 mmol, 10.3 equiv). This solution was heated at 69−70 °C (internal) for 3 h, and then concentrated. The residue was chromatographed on silica (hexane/EtOAc, 80/20) and crystallized from EtOAc/hexane. The solid was recrystallized (EtOAc/hexane) to afford 65.1 mg (54%) of **42a$_{ii}$** as white crystals. Data for **42a$_{ii}$:** mp 96.5−97.5 °C (hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 8.2, 2H), 7.58 (t, J = 7.5, 1H), 7.45 (t, J = 7.7, 2H), 6.89 (d, J = 6.3, 1H), 5.38 (dt, J = 9.5, 4.7, 1H), 4.92 (t, J = 6.1, 1H), 4.26 (dd, J = 10.9, 4.5, 1H), 4.13 (q, J = 7.1, 2H), 3.92 (dt, J = 9.4, 6.7, 1H), 3.85 (dd, J = 11.1, 6.3, 1H), 3.45 (dt, J = 9.4, 6.7, 1H), 2.31 (ddd, J = 14.0, 6.1, 4.9, 1H), 2.19 (ddd, J = 13.8, 9.6, 6.0, 1H), 2.01 (s, 3H), 1.64−1.57 (m, 2H), 1.43−1.33 (m, 2H), 1.17 (t, J = 7.0, 3H), 0.90 (t, J = 7.2, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7, 166.2, 165.7, 133.3, 129.8, 129.5, 128.4, 98.2, 98.2, 70.9, 68.1, 68.0, 61.7, 51.1, 31.5, 30.5, 20.6, 19.2, 14.0, 13.8; IR ($CHCl_3$) 1721 (m) cm^{-1}; MS (CI, CH_4) m/z 452 (M^+ + 1, 3), 270 (100); TLC R_f 0.16 (hexane/EtOAc, 80/20). Anal. Calcd for $C_{22}H_{29}NO_9$ (451.47): C, 58.53; H, 6.47; N, 3.10. Found: C, 58.52; H, 6.58; N, 3.07.

Isomers of *rel*-(3a*S*,4*R*,6*R*)-2-(Acetyloxy)-4-(benzoyloxy)-6-(butyloxy)hexahydroisoxazolo[2,3-*b*][1,2]oxazine-3-carboxylic Acid Ethyl Ester and *rel*-(3a*S*,4*R*,6*R*)-3-(Acyloxy)-4-(benzoyloxy)-6-(butyloxy)hexahydroisoxazolo[2,3-*b*][1,2]oxazine-2-carboxylic Acid Ethyl Ester (43a$_i$, a$_{ii}$, b$_i$, b$_{ii}$). To a solution of nitronate **2** (305.7 mg, 1.04 mmol) in CH_3CN (4.5 mL) was added **20a** (344.8 mg, 2.18 mmol, 2.1 equiv). This solution was degassed, then heated at 65 °C (ext) for 24 h, and then concentrated and chromatographed on silica (hexane/EtOAc, 85/15) to afford 365 mg (78%) of a mixture **43a$_i$, a$_{ii}$, b$_i$, b$_{ii}$** as a light brown oil. Data for **43a$_i$, a$_{ii}$, b$_i$, b$_{ii}$**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11−8.04 (m, 2H), 7.62−7.58 (m, 1H), 7.49−7.44 (m, 2H), 6.99 (d, J = 2.3, 0.36H), 6.79 (d, J = 4.5, 0.17H), 5.79 and 5.76 (dt, J = 10.7, 5.4 and dd, J = 7.2, 3.4, 0.66H), 5.48−5.45 (m, 0.42H), 5.41 (dd, J = 8.5, 2.6, 0.11H), 5.06−5.01 (m, 0.81H), 4.94 (d, J = 3.6, 0.17H), 4.80 (d, J = 3.3, 0.03H), 4.30−4.07 (m, 2.47H), 4.04−3.90 (m, 1.76H), 3.73−3.67 (m, 0.43H), 3.59 (dd, J = 7.5, 2.1, 0.43H), 3.52−3.45 (m, 0.96H), 2.97 (dd, J = 15.9, 8.3, 0.13H), 2.91 (d, J = 3.2, 0.11H), 2.49 (dt, J = 13.4, 6.6, 0.49H), 2.43−2.35 (m, 0.57H), 2.19 (s, 0.63H), 2.17 (s, 0.72H), 2.11 (s, 0.32H), 2.09 (s, 1.15H), 2.06−2.00 (m, 0.68H), 1.66−1.58 (m, 2.27H), 1.45−1.37 (m, 2.00H), 0.96−0.91 (m, 2.63H); IR (CCl_4) 2961 (s), 1741 (s), 1737 (s), 1727 (s) cm^{-1}; MS (CI, CH_4) m/z 452 (M^+ + 1, 3), 270 (100); TLC R_f 0.08 (hexane/EtOAc, 85/15). Anal. Calcd for $C_{22}H_{29}NO_9$ (451.47): C, 58.53; H, 6.47; N, 3.10. Found: C, 58.29; H, 6.61; N, 3.06.

***rel*-(2*S*,3*S*,3a*S*,4*R*,6*R*)-4-(Benzoyloxy)-6-(butyloxy)-hexahydroisoxazolo[2,3-*b*][1,2]oxazine-2,3-dicarboxylic Acid Dimethyl Ester (44a$_i$) and *rel*-(2*R*,3*R*,3a*S*,4*R*,6*R*)-4-(Benzoyloxy)-6-(butyloxy)hexahydroisoxazolo[2,3-*b*][1,2]oxazine-2,3-dicarboxylic Acid Dimethyl Ester (44b$_i$).** To a solution of **2** (266.3 mg, 0.908 mmol) in benzene (20 mL) was added dimethyl fumarate (520.8 mg, 3.613 mmol, 4.0 equiv). This clear solution was degassed, stirred at room temperature for 23 h, and then concentrated and separated on silica MPLC (hexane/EtOAc, 85/15) to afford 162.1 mg (41%) of **44a$_i$** as a light yellow oil and 163.1 mg (41%) of **44b$_i$** as a white crystalline solid. A single crystal of **44b$_i$** was grown from Et_2O/hexane. Data for **44a$_i$**: ^{1}H NMR: (400 MHz, $CDCl_3$) δ 8.04 (dd, J = 8.4, 1.3, 2H), 7.58 (tt, J = 7.5, 1,4, 1H), 7.44 (t, J = 7.5, 2H), 5.62 (d, J = 6.8, 1H), 5.47 (dt, J = 9.7, 5.0, 1H), 4.96 (t, J = 6.0, 1H), 4.15 (dd, J = 10.3, 5.3, 1H), 3.91 (dt, J = 9.5, 6.8, 1H), 3.78 (s, 3H), 3.78 (dd, J = 10.2, 7.0, 1H), 3.69 (s, 3H), 3.45 (dt, J = 9.5, 6.6, 1H), 2.22 (ddd, J = 13.7, 6.0, 5.1, 1H), 2.01 (ddd, J = 13.7, 9.1, 5.9, 1H), 1.63−1.56 (m, 2H), 1.43−1.33 (m, 2H), 0.90 (t, J = 7.4, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.6, 168.7, 165.4, 133.3, 129.6, 129.3, 128.4, 97.8, 82.7, 73.9, 67.9, 66.3, 52.8, 52.8, 48.8, 31.4, 30.5, 19.2, 13.8; IR ($CHCl_3$) 1743 (s) cm^{-1}; MS (CI, CH_4) m/z 438 (M^+ + 1, 8), 145 (100); TLC R_f 0.15 (hexane/EtOAc, 80/20). Anal. Calcd for $C_{21}H_{27}NO_9$ (437.45): C, 57.66; H, 6.22; N, 3.20. Found: C, 57.71; H, 6.41; N, 2.92. Data for **44b$_i$:** mp 91−92 °C (Et_2O/hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (d, J = 7.3, 2H), 7.55 (t, J = 7.4, 1H), 7.42 (t, J = 7.8, 2H), 5.54 (ddd, J = 5.9, 4.9, 3.1, 1H), 5.20 (d, J = 5.6, 1H), 4.94 (t, J = 4.3, 1H), 4.00 (dd, J = 10.2, 5.7, 1H), 3.94 (dt, J = 9.5, 6.5, 1H), 3.91 (dd, J = 10.0, 3.0, 1H), 3.81 (s, 3H), 3.74 (s, 3H), 3.39 (dt, J = 9.2, 6.6, 1H), 2.26 (dt, J = 14.5, 5.0, 1H), 2.08 (ddd, J = 14.6, 5.8, 3.5, 1H), 1.61−1.55 (m, 2H), 1.41−1.34 (m, 2H), 0.88 (t, J = 7.3, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.6, 170.2, 165.6, 133.2, 129.7, 129.6, 128.2, 98.7, 83.4, 75.1, 67.8, 67.7, 52.9, 52.8, 49.1, 31.5, 28.6, 19.1, 13.8; IR ($CHCl_3$) 1744 (s), 1724 (s) cm^{-1}; MS (CI, CH_4) m/z 438 (M^+ + 1, 4), 214 (100); TLC R_f 0.13 (hexane/EtOAc, 80/20). Anal. Calcd for $C_{21}H_{27}NO_9$ (437.45): C, 57.66; H, 6.22; N, 3.20. Found: C, 57.76; H, 6.28; N, 3.35.

(2*S*,3*R*,3a*R*,4*R*,6*R*)-4-(Benzoyloxy)-2-{2-[dimethyl-(1,1,2-trimethylpropyl)silyloxy]-1-oxoethyl}-3-(dimethylphenylsilyl)-6-[(1*S*,2*R*)-(2-phenylcyclohexyl)oxy]hexahydroisoxazolo[2,3-*b*][1,2]oxazine (45a$_i$) and (2*R*,3*R*,3a*S*-,4*R*,6*R*)-4-(Benzoyloxy)-3-{2-[dimethyl-(1,1,2-trimethylpropyl)silyloxy]-1-oxoethyl}-2-(dimethylphenylsilyl)-6-[(1*S*,2*R*)-(2-phenylcyclohexyl)oxy]hexahydroisoxazolo[2,3-*b*][1,2]oxazine (45a$_{ii}$). Nitronate (+)-**3** (1.06 g, 2.68 mmol) was added to a solution of ketone **27** (1.17 g, 3.21 mmol, 1.2 equiv) in benzene (25 mL), and the reaction mixture was maintained at room temperature for 12 h. Upon concentration of the solution in vacuo, the residue was purified by chromatography on silica (pentane/Et_2O, 90/10, 70/30) to provide 1.96 g (97%) of a 26/1 mixture of (−)-**45a$_i$** and **45a$_{ii}$** as a colorless foam. Data for 26/1 mixture of (−)-**45a$_i$** and **45a$_{ii}$**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (dd, J = 8.4, 1.3, 2H), 7.59 (tt, J = 7.5, 1.3, 1H), 7.47 (t, J = 7.9, 2H), 7.36 (dd, J = 8.1, 1.3, 2H), 7.30 (tt, J = 7.5, 1.3, 1H), 7.21 (t, J = 7.5, 4H), 7.15 (td, J = 7.9, 1.3, 3H), 5.11 (d, J = 9.5, 1H), 4.68 (d, J = 11.0, 1H), 4.62 (ddd, J = 8.8, 4.6, 4.2, 1H), 4.16 (t, J = 5.7, 1H), 4.13 (d, J = 18.8, 1H), 4.08 (d, J = 18.8, 1H), 3.73 (dd, J = 12.4, 4.0, 1H), 3.59 (td, J = 10.4, 4.2, 1H), 2.51 (ddd, J = 13.0, 10.2, 3.5, 1H), 2.42−2.38 (bm, 1H), 2.30 (dd, J = 12.6, 9.9, 1H), 1.86 (bd, J = 12.4, 2H), 1.75 (bd, J = 13.0, 1H), 1.68−1.40 (m, 6H), 1.31 (tt, J = 12.8, 3.5, 1H), 0.88 (d, J = 6.8, 6H), 0.84 (s, 6H), 0.39 (s, 3H), 0.37 (s, 3H), 0.05 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.9, 165.0, 144.1, 137.3, 133.7, 133.2, 129.8, 129.7, 129.4, 129.4, 128.1, 128.0, 127.7, 126.3, 99.2, 88.2, 82.5, 74.6, 69.3, 68.2, 51.2, 34.7, 34.0, 32.8, 32.0, 29.7, 25.8, 25.2, 20.2, 20.2, 18.5, 18.4, −2.5, −3.4, −3.5, −3.6; IR (CCl_4) 1720 (m) cm^{-1}; MS (FAB) m/z 759 (M^+ + 1, 1), 105 (100); $[\alpha]_D^{23}$ −32.3° ($CHCl_3$, c = 1.07); TLC R_f 0.49 (hexane/EtOAc, 80/20). Anal. Calcd for $C_{43}H_{59}NO_7Si_2$ (758.12): C, 68.13; H, 7.84; N, 1.85; Si, 7.41. Found: C, 68.02; H, 7.87; N, 1.90; Si, 7.27.

***rel*-(2*S*,3*R*,3a*R*,4*R*,6*R*)-4-(Benzoyloxy)-3-(dimethylphenylsilyl)-6-[(1*S*,2*R*)-(2-phenylcyclohexyl)oxy]-2-[2-(phenylmethoxy)-1-oxoethyl]hexahydroisoxazolo[2,3-*b*][1,2]oxazine (46a$_i$) and *rel*-(2*R*,3*R*,3a*S*,4*R*,6*R*)-4-(Benzoyloxy)-2-(dimethylphenylsilyl)-6-[(1*S*,2*R*)-(2-phenylcyclohexyl)oxy]-3-[2-(phenylmethoxy)-1-oxoethyl]hexahydroisoxazolo[2,3-*b*][1,2]oxazine (46a$_{ii}$).** Nitronate **3** (469 mg, 1.19 mmol) was added to a solution of ketone **28** (443 mg, 1.43 mmol, 1.2 equiv) in benzene (12 mL) and the reaction mixture was maintained at room temperature for 5 h. Upon concentration of the solution in vacuo, the residue was purified by chromatography on silica (pentane/Et_2O, 80/20) to provide 806 mg (96%) of **46a$_i$** as a colorless foam and 14.5 mg, (1.7%) of the sensitive minor nitroso acetal **46a$_{ii}$**. Data for **46a$_{ii}$**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, J = 8.3, 2H), 7.55 (t, J = 7.6, 1H), 7.47 (d, J = 7.8, 2H), 7.40 (t, J = 8.1, 2H), 7.37−7.15 (m, 14H), 4.83 (dt, J = 10.5, 4.6, 1H), 4.70 (d, J = 10.7, 1H), 4.18 (d, J = 12.0, 1H), 4.16 (t, J = 6.6, 1H), 4.12 (d, J = 12.0, 1H), 3.87 (dd, J = 8.3, 4.6, 1H), 3.81 (dd, J = 10.7, 8.5, 1H), 3.60 (td, J = 10.3, 4.2, 1H), 3.44 (d, J = 17, 1H), 3.40 (d, J = 17, 1H), 2.52 (ddd, J = 12.9, 10.3, 3.4, 1H), 2.37 (dd, J = 12.7, 3.4, 1H), 1.92−1.86 (m, 3H), 1.77 (bd, J = 12.9, 1H), 1.68−1.42 (m, 6H), 1.37−1.28 (m, 1H), 0.38 (s, 3H), 0.36 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 98.4, 82.1, 78.8, 78.6, 75.7, 72.4, 69.5, 52.8, 51.1. Data for **46a$_i$**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (d, J = 7.6, 2H), 7.59

(t, J = 7.3, 1H), 7.47 (t, J = 7.6, 2H), 7.39−7.13 (m, 15H), 5.06 (d, J = 9.8, 1H), 4.69 (ddd, J = 8.5, 4.4, 4.2, 1H), 4.40 (s, 2H), 4.15 (t, J = 5.6, 1H), 3.94 (d, J = 18.6, 1H), 3.89 (d, J = 18.6, 1H), 3.71 (dd, J = 12.7, 3.9, 1H), 3.59 (td, J = 10.5, 4.4, 1H), 2.53−2.48 (m, 1H), 2.39−2.36 (m, 1H), 2.31 (dd, J = 12.7, 9.8, 1H), 1.87−1.84 (m, 2H), 1.76−1.73 (m, 1H), 1.66 (ddd, J = 13.9, 5.6, 5.4, 1H), 1.63−1.23 (m, 5H), 0.41 (s, 3H), 0.37 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.0, 165.0, 144.1, 137.1, 137.0, 133.7, 133.3, 129.8, 129.7, 129.4, 128.4, 128.4, 128.1, 128.0, 128.0, 127.9, 127.7, 126.3, 99.2, 88.6, 82.5, 74.6, 73.8, 73.1, 69.2, 51.2, 34.7, 32.7, 32.1, 29.6, 25.8, 25.2, −2.7, −3.2; IR (CCl_4) 1725 (m) cm^{-1}; MS (FAB) m/z 706 (M^+ + 1, 6), 104 (100); TLC R_f 0.30 (hexane/EtOAc, 80/20). Anal. Calcd for $C_{42}H_{47}NO_7Si$ (705.93): C, 71.46; H, 6.71; N, 1.98; Si, 3.98. Found: C, 71.19; H, 6.70; N, 1.93; Si, 4.27.

***rel*-(3a*S*,3b*S*,4*R*,6*R*,9a*R*)-4-(Benzoyloxy)-6-(butyloxy)-octahydro(furo[1,2-*d*]isoxazolo)[4,5-*b*][1,2]oxazine (48b) and *rel*-(3a*R*,3b*S*,4*R*,6*R*,9a*S*)-4-(Benzoyloxy)-6-(butyloxy)-octahydro(furo[1,2-*d*]isoxazolo)[4,5-*b*][1,2]oxazine (48a).** To a solution of nitronate **2** (297.0 mg, 1.0 mmol) in CH_3CN (5.0 mL) was added 2,3-dihydrofuran (750 μL, 695 mg, 10.0 mmol, 10.0 equiv). This was heated at 65 °C (ext) for 9 h and then concentrated and chromatographed on silica (hexane/EtOAc, 80/20) to afford 302.8 mg (82%) of a 17/1 mixture of **48a** and **48b** as a pale yellow oil. A portion of the mixture was separated by preparative HPLC (hexane/EtOAc, 90/10) to afford 7.0 mg of **48b** and 203.8 mg of **48a**. Data for 17/1 mixture of **48a** and **48b**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (d, J = 7.7, 2H), 8.04 (d, J = 7.5, 2H), 7.60 (t, J = 7.5, 1H), 7.47 (t, J = 7.7, 2H), 6.31 (d, J = 5.4, 1H), 6.15 (d, J = 5.5, 1H), 5.36 (dt, J = 8.1, 4.2, 1H), 4.98 (t, J = 5.2, 1H), 4.92 (t, J = 7.0, 1H), 4.09 (t, J = 8.4, 1H), 3.96 (dt, J = 9.4, 6.7, 1H), 3.88 (ddd, J = 12.3, 8.9, 4.9, 1H), 3.50 (dd, J = 8.0, 4.2, 1H), 3.47 (dt, J = 9.4, 6.7, 1H), 3.17 (td, J = 7.9, 5.5, 1H), 2.30 (dt, J = 14.2, 5.2, 1H), 2.18−2.08 (m, 2H), 1.87 (dd, J = 12.8, 4.7, 1H), 1.67−1.61 (m, 2H), 1.46−1.39 (m, 2H), 0.93 (t, J = 7.5, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.0, 133.4, 129.8, 128.4, 114.5, 98.2, 76.4, 69.6, 67.8, 67.3, 46.8, 31.6, 30.9, 29.8, 19.3, 13.9; IR ($CHCl_3$) 1720 (m) cm^{-1}; MS (CI, CH_4) m/z 364 (M^+ + 1, 7), 168 (100); TLC R_f 0.49 (hexane/EtOAc, 65/35). Anal. Calcd for $C_{19}H_{25}NO_6$ (363.41): C, 62.80; H, 6.93; N, 3.85. Found: C, 62.91; H, 6.86; N, 3.93. Data for **48b**: ^{1}H NMR (500 MHz, C_6D_6) δ 8.06 (d, J = 7.5, 2H), 7.13 (t, J = 7.5, 1H), 7.05 (t, J = 7.5, 2H), 5.90 (d, J = 5.8, 1H), 5.04 (dt, J = 12.4, 5.2, 1H), 4.41 (t, J = 7.2, 1H), 4.24 (dt, J = 10.8, 7.3, 1H), 3.90 (dt, J = 9.4, 6.7, 1H), 3.78 (t, J = 8.3, 1H), 3.27 (dt, J = 9.3, 6.6, 1H), 3.18 (dd, J = 8.4, 5.3, 1H), 2.57 (dddd, J = 11.0, 8.3, 5.8, 2.5, 1H), 2.43 (td, J = 12.6, 7.8, 1H), 2.09 (ddd, J = 12.5, 6.7, 5.5, 1H), 1.92 (dd, J = 13.4, 6.7, 1H), 1.65 (dtd, J = 13.2, 11.0, 9.0, 1H), 1.57−1.51 (m, 2H), 1.39−1.30 (m, 2H), 0.84 (t, J = 7.3, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 165.5, 133.2, 130.1, 129.9, 128.5, 115.7, 97.6, 74.4, 67.8, 67.4, 67.3, 45.2, 31.7, 31.6, 27.2, 19.3, 13.8; TLC R_f 0.51 (hexane/EtOAc, 65/35). Data for **48a**: ^{1}H NMR (500 MHz, C_6D_6) δ 8.22 (d, J = 8.3, 2H), 7.13−7.07 (m, 3H), 6.31 (d, J = 5.5, 1H), 5.13 (dt, J = 7.8, 4.0, 1H), 4.62 (t, J = 5.0, 1H), 4.03 (dt, J = 9.3, 6.6, 1H), 3.57 (t, J = 8.4, 1H), 3.46 (ddd, J = 12.6, 8.7, 4.4, 1H), 3.31 (dt, J = 9.4, 6.5, 1H), 3.27 (dd, J = 8.1, 3.8, 1H), 2.59 (td, J = 8.0, 5.7, 1H), 2.06 (ddd, J = 13.8, 7.6, 4.8, 1H), 1.80 (dt, J = 14.0, 5.2, 1H), 1.60−1.54 (m, 2H), 1.46 (tt, J = 12.6, 8.1, 1H), 1.43−1.33 (m, 2H), 1.15 (dd, J = 12.7, 4.7, 1H), 0.86 (t, J = 7.3, 3H); ^{13}C NMR: (125 MHz, C_6D_6) δ 165.8, 133.1, 130.5, 130.1, 128.4, 114.5, 97.9, 76.4, 70.0, 67.8, 67.0, 46.4, 31.6, 30.5, 29.5, 19.5, 13.8; TLC R_f 0.47 (hexane/EtOAc, 65/35).

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Supporting Information Available: General experimental, a full list of ^{1}H NMR and ^{13}C NMR listings with assignments, IR absorbances, and MS fragments for all new compounds, as well as coordinates for all calculated structures. This material is available free of charge via the Internet at http://pubs.acs.org.

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