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Tandem Inter [4+2]/Intra [3+2] Cycloadditions. 8.[‡] Cycloadditions with Unactivated Dipolarophiles

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Abstract: The tandem intermolecular [4+2/intramolecular [3+2] cycloaddition of nitroalkenes bearing a pendant olefin is presented. The success of the tandem process is remarkable in view of the potential for intramolecular reaction with the tethered alkene. Cycloadditions of di- and trisubstituted nitroalkenes bearing two- and three-methylene tethers which contain mono-, di- and trisubstituted olefins are described. In all cases the tandem process is high yielding (with *n*-butyl vinyl ether as the dienophile) and highly stereoselective. Hydrogenolysis of the resulting nitroso acetals leads cleanly to fused pyrrolidines in high yields. Copyright © 1996 Elsevier Science Ltd

Introduction

In recent years we have demonstrated the synthetic potential of tandem cycloadditions reactions of nitroalkenes.[1] Of the four possible permutations, the most abundantly documented and synthetically useful variant is the tandem intermolecular [4+2]/intramolecular [3+2] cycloaddition, Figure 1. Within this variant there exists four subfamilies of tandem cycloadditions which arise from the four different points of attachment of the dipolarophilic tether. Of these subfamilies, the most well studied example is the so-called fused mode cycloaddition in which the tether extends from the β-position of the nitroalkene, and ultimately from C(4) of the nitronate, Scheme 1. As illustrated in Scheme 1, the success of this concept rests in the electronic complementarity of the [4+2] and [3+2] processes. Since the heterodiene [4+2] cycloaddition is governed by inverse electron demand,[2] an electron rich (D = electron donor substituent) dienophile is preferred. In contrast the [3+2] cycloaddition process is regarded as a $\mathrm{HOMO}_{\mathrm{dipole}}$ - $\mathrm{LUMO}_{\mathrm{dipolarophile}}$ reaction suggesting that electron poor (A = electron acceptor substituent) dipolarophile is preferred. This situation is ideal since, despite the intramolecularity, electron poor tethers cannot effectively compete with the external dienophile in the [4+2] process. We thus became intrigued by the possibility of employing simple olefins as dipolarophiles in conjunction with vinyl ethers as dienophiles. This report discloses the successful participation of many substitution patterns of simple alkyl substituted olefins in this tandem process.

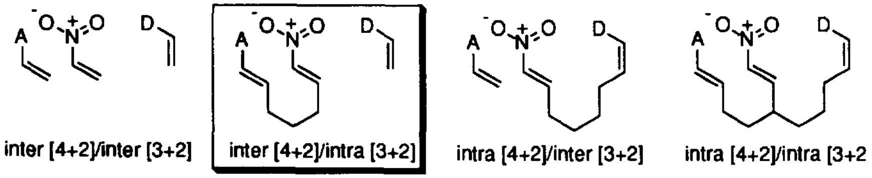
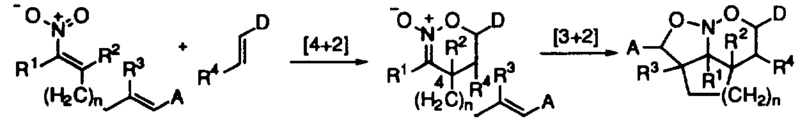


Figure 1. Families of tandem [4+2]/[3+2] cycloadditions of nitroalkenes.

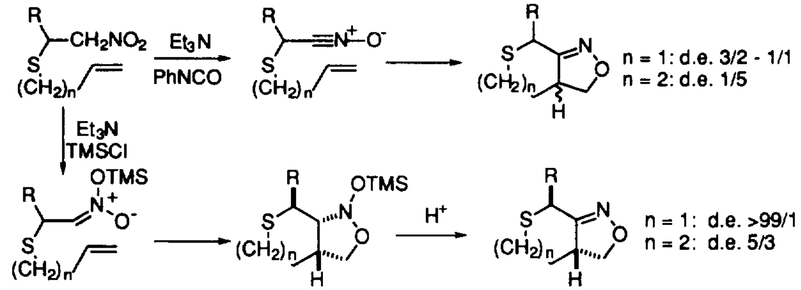
Scheme 1



Background

The [3+2] cycloadditions of nitronates has been well studied and in most cases electron deficient dipolarophiles have been employed.[3] In some cases, enol ethers have been used, but these are generally much slower reactions.[4] An interesting comparison of intramolecular cycloaddition of nitrile oxides and silyl nitronates with simple olefins has been reported by Hassner.[5] The cycloaddition of silyl nitronates with simple olefins is significantly more stereoselective and initial cycloadduct can be easily converted to the product derived from nitrile oxide cycloaddition, Scheme 2. This study also shows that the silyl nitronate-olefin cycloaddition selectivity is dependent on the tether length; increasing length by one methylene unit, lowered the diastereoselectivity from 99/1 to 5:3. For the nitrile oxide diastereoselectivity decreased from 3/2 - 1/1 to 1/5.

Scheme 2



In our study four variables were considered namely, nitroalkene substitution, dipolarophile substitution and geometry and tether length. For this study, eight different nitroalkenes were examined, Scheme 3 and Table 1. For the construction of 5-6-6 (n=6) ring systems, both di- and trisubstituted nitroalkenes tethered by three methylene units to a disubstituted dipolarophile with both *Z*- and *E*- geometry were considered. For the construction of 5-5-6 ring systems (n=5), only trisubstituted nitroalkenes tethered by two methylene units to mono-, di-(both *Z*- and *E*-) and trisubstituted dipolarophiles were considered. *n*-Butyl vinyl ether was used as the dienophile.

Scheme 3

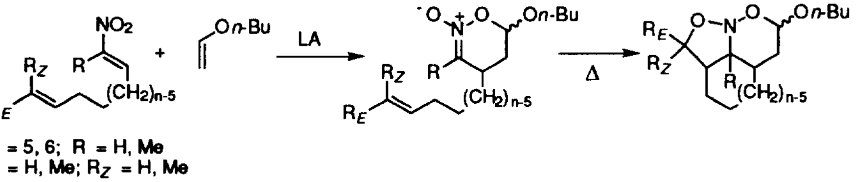


Table 1. Nitroalkenes Employed in Cycloaddition Studies

n	R	R_E	R_Z	nitroalkene[a]
5	Me	H	H	**1**
5	Me	Me	H	(*E*)-**2**
5	Me	H	Me	(*Z*)-**2**
5	Me	Me	Me	**3**
6	H	Me	H	(*E*)-**4**
6	H	H	Me	(*Z*)-**4**
6	Me	Me	H	(*E*)-**5**
6	Me	H	Me	(*Z*)-**5**

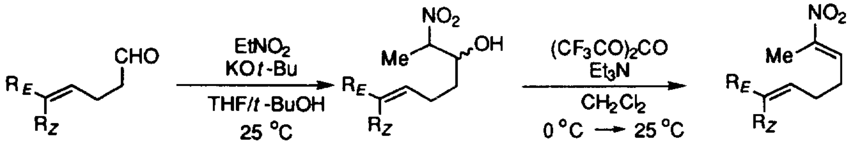
[a] The configurational descriptors designate the dipolarophile geometry.

Results and Discussion

Preparation of Nitroalkenes.

The preparation of nitroalkenes tethered to olefins by two methylene units utilized a single, general strategy starting from four different aldehydes **6**, (*E*)-**8**, (*Z*)-**8** and **10** as shown in Scheme 4. All of these aldehydes were prepared from known alcohols 4-pentenol[6a] and (*E*) and (*Z*)-4-hexenol[6b] and 5-methyl-4-hexenol[6c] by pyridinium chlorochromate oxidation. The crude aldehydes were converted to nitro alcohols **7**, (*E*)-**9**, (*Z*)-**9** and **11** by Henry reaction (nitro aldol) with nitroethane and potassium *tert*-butoxide. The target nitroalkenes **1**, (*E*)-**2**, (*Z*)-**2** and **3** were obtained by dehydration of the nitro alcohols with trifluoroacetic anhydride and triethylamine in 80-82% yield. This method is highly selective for the formation of *E* nitroalkenes, none of the *Z* isomer was detected by GC.

Scheme 4



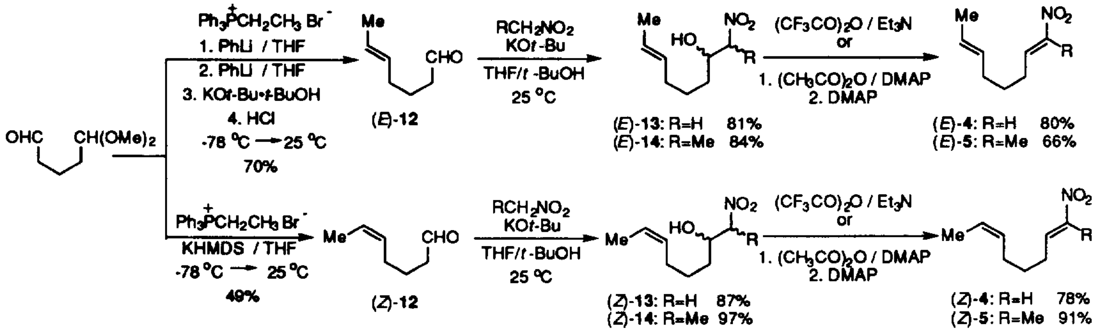
6: $R_E = R_Z = H$
(*E*)-**8**: $R_E = Me, R_Z = H$
(*Z*)-**8**: $R_E = H, R_Z = Me$
10: $R_E = R_Z = Me$

7: $R_E = R_Z = H$ (48%)
(*E*)-**9**: $R_E = Me, R_Z = H$ (54%)
(*Z*)-**9**: $R_E = H, R_Z = Me$ (78%)
11: $R_E = R_Z = Me$ (80%)

1: $R_E = R_Z = H$ (80%)
(*E*)-**2**: $R_E = Me, R_Z = H$ (82%)
(*Z*)-**2**: $R_E = H, R_Z = Me$ (80%)
3: $R_E = R_Z = Me$ (81%)

The preparation of nitroalkenes **4** and **5** bearing a three-methylene tether are outlined in Scheme 5. Aldehydes (*E*)-**12** and (*Z*)-**12** (prepared by Wittig olefination and hydrolysis of 5,5-dimethoxypentanal) were treated with nitromethane or nitroethane in the Henry reaction as described above to produce nitro alcohols (*E*)- and (*Z*)-**13** and (*E*)- and (*Z*)-**14**. Two different dehydration protocols were employed. For **13**, the trifluoroacetic anhydride method described above afforded the nitroalkenes (*E*)-**4** and (*Z*)-**4** in good yield. For **14** an older two-step method involving the formation of the nitro acetate in a discrete step followed by DMAP-induced elimination let to (*E*)-**5** and (*Z*)-**5** in high yield and with complete (GC) *E* selectivity for the nitroalkene double bond.

Scheme 5



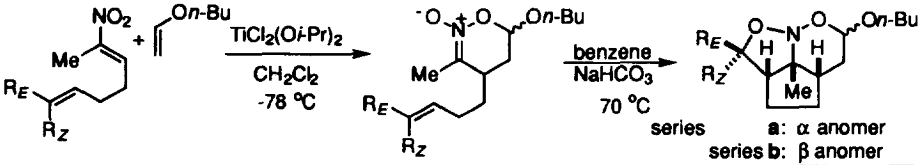
Cycloadditions.

General. All cycloadditions were performed in the presence of $TiCl_2(Oi\text{-}Pr)_2$ as the Lewis acid and *n*-butyl vinyl ether as the dienophile in dichloromethane at -78 °C. The isolated nitronates were heated (benzene or toluene and $NaHCO_3$) to effect the [3 + 2] cycloaddition. The mixtures of crude nitroso acetals were analyzed by GC using cyclododecane as the internal standard. In the cycloaddition of nitroalkenes tethered by three methylene units, the Lewis acid was added slowly at -78 °C to a mixture of nitroalkene and *n*-butyl vinyl ether to minimize intramolecular cycloaddition.

Cycloaddition of Nitroalkenes Tethered by Two Methylene Units. Treatment of nitroalkene **1** with $TiCl_2(Oi\text{-}Pr)_2$ followed by addition of *n*-butyl vinyl ether at -78 °C gave a mixture of two compounds in 88% yield. Analysis of the ^1H NMR spectrum indicated that they were nitronate anomers **15a** and **15b** from the initial [4+2] cycloaddition. These nitronates are stable and they do not undergo spontaneous [3+2] cycloaddition in contrast to the same nitronate with an ester-activated dipolarophile.[7] The mixture was heated to 70 °C in benzene to effect the [3+2] cycloaddition. The crude mixture was shown to comprise only two anomers of nitroso acetals as determined by ^1H NMR and GC analysis. Column chromatographic purification gave nitroso acetals **16a** and **16b** in 80% yield. Similarly nitroalkenes (*E*)-**2**, (*E*)-**2**, and **3** were allowed to react with *n*-butyl vinyl ether in the presence of $TiCl_2(Oi\text{-}Pr)_2$. The isolated mixtures of nitronates were subjected to thermal cycloaddition at 70 °C in benzene and the crude nitroso acetal mixtures were analyzed by GC and ^1H NMR spectroscopy. The major anomers of nitroso acetals were isolated by column chromatography. The results for these cycloadditions are summarized in Table 2.

In our previous studies with activated (ester) dipolarophiles the ring fusion stereochemistry was established by X-ray crystallography since ^1H NMR analysis was not informative. Therefore, in these cycloadditions, it is assumed that the ring fusion stereochemistry is the same as that established with activated dipolarophiles, i.e. all cis.[7] The isolated compounds then represented mixtures of anomers. The assignment of stereostructure for each anomer was based on the NMR analysis of HC(5) and C(5). Selected ^1H and ^{13}C NMR data for these compounds are summarized in Table 3. In previous studies with an *E*-dipolarophile, it was found that in the α anomer, HC(5) appeared as a doublets of doublets whereas for the β anomer, the same proton appeared as a triplet. In addition, a clear trend is seen in the ^{13}C NMR shifts of C(5) which reveal a downfield shift for the α-anomers as compared to the β-anomers as expected.[8]

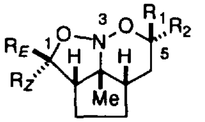
Table 2. Results for Cycloaddition of Nitroalkenes Tethered with Two Methylene Units



nitroalkene			nitronate[a]		nitroso acetal[b]			
	R_E	R_Z	product	yield, %	product	time, h	ratio[c] a / b	yield, %[d] (ratio, α/β)[e]
1	H	H	**15**	85	**16**	13	1/2.8	83 (1/3.2)
(*E*)-2	Me	H	**17**	86	**18**	12	1/5.3	80 (1/5.8)
(*Z*)-2	H	Me	**19**	88	**20**	33	24/11/1[f]	80 (1/3)
3	Me	Me	**21**	-[g]	**22**	18	1/6	70 (1/7)

[a] At -78 °C, CH_2Cl_2 (0.2 M). [b] 70 °C in benzene. [c] By GC analysis. [d] Overall by column chromatography. [e] Isolated major anomers. [f] Third component not identified. [g] Not isolated.

Table 3. Diagnostic NMR Data for Nitroso Acetals **16**, **18**, **20**, **22**.



nitroso acetal	R_1	R_2	R_E	R_Z	HC(5), ppm (*J*, Hz)	C(5), ppm
16a	H	O*n*-Bu	H	H	5.09 (dd, 6.5, 3.6)	99.64
16b	O*n*-Bu	H	H	H	5.00 (t, 7.5)	98.70
18a	H	O*n*-Bu	Me	H	5.06 (dd, 6.7, 3.7)	99.56
18b	O*n*-Bu	H	Me	H	4.98 (t, 7.5)	98.48
20a	H	O*n*-Bu	H	Me	5.00 (t, 5.2)	100.13
20b	O*n*-Bu	H	H	Me	4.98 (dd, 8.0, 6.6)	97.75
22a	H	O*n*-Bu	Me	Me	4.98 (dd, 5.9, 3.8)	99.84
22b	O*n*-Bu	H	Me	Me	4.91 (t, 7.3)	98.04

The cycloaddition of nitroalkene **1** with a monosubstituted dipolarophile afforded a mixture of nitroso acetals in a 2.8/1 ratio. The ^1H NMR analysis of the isolated anomers showed peaks at 5.09 ppm (dd, $J = 6.5$, 3.6) for the minor (α) anomer **16a** whereas for the major (β) anomer **16b** this proton appeared as a triplet at 5.00 ppm ($J = 7.5$ Hz).

The nitroalkene (*E*)-**2** provided a 5.3/1 mixture (GC) of the tandem cycloadducts. The column chromatographic separation allowed the isolation of two anomers in a 5.8/1 ratio. The ^1H NMR spectrum of the α anomer **18a** displayed a doublet of doublets for HC(5) and for the β anomer **18b** HC(5) appeared a triplet. The formation of only two anomers indicated that [3+2] cycloadditions with the *E*-dipolarophile proceeded with extremely high diastereoselectivity.

The nitroalkene (*Z*)-**2** intially afforded a mixture of three isomers in a 24/11/1 ratio (GC). However, only two isomers in a 3/1 ratio were isolated by column chromatography. The ^{1}H NMR analysis of the minor (α) anomer **20a** revealed a triplet for HC(5) and for the major (β) anomer **20b**, HC(5) appeared as a doublet of doublets. This runs counter to the usual trend for these anomer, therefore we made recourse to the ^{13}C NMR chemical shifts of C(5) to make an assignment. The third isomer must belong to a trans ring fusion family. Therefore, the endo/exo selectivity in the [3+2] cycloaddition for the Z-dipolarophile is 35/1.

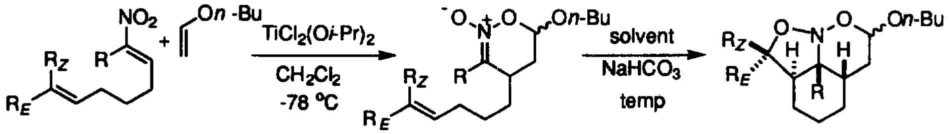
The tandem cycloaddition of nitroalkene **3** tethered to a trisubstituted dipolarophile afforded two anomers in a 6/1 ratio as judged by GC. Column chromatography afforded nitroso acetal anomers (7/1 ratio) which were analyzed by ^{1}H NMR. The minor (α) anomer **22a** showed a doublet of doublets for HC(5) and for major (β) anomer **27b** same proton appeared as a triplet.

In this phase of the study, significant effects of dipolarophile geometry and substitution on the rate of the [3+2] cycloaddition were observed. The rate of the cycloaddition with unactivated dipolarophiles is considerably slower than with activated dipolarophiles. The order of the cycloaddition rates was found to be trans > monosubstituted > trisubstituted > cis. This trend is the same as that observed with activated dipolarophiles in which an *E*-enoate cyclizes faster than a Z-enoate. On the basis of the firmly established endo preference of the side chain with ester dipolarophiles in the [3+2] cycloaddition, we assume that these reactions proceed in a similar fashion. The large difference in cyclization times between **17** and **19** can be explained by the overriding preference for an endo transition structure which, in **19**, necessitates placing the methyl group under the nitronate ring. In addition, the difference in cycloaddition rates between the *E*- and the monosubstituted dipolarophiles and between the tri- and Z-substituted dipolarophiles imply that addition of a methyl group (electron donating group) accelerates the cycloaddition. Therefore, the cycloaddition of a simple olefin to a nitronate is believed to be $\text{HOMO}_{\text{dipolarophile}}$-$\text{LUMO}_{\text{dipole}}$ controlled. The [3 + 2] cycloaddition of a nitrone to a simple olefin is $\text{HOMO}_{\text{dipolarophile}}$ - $\text{LUMO}_{\text{dipole}}$ controlled according to FMO calculations.[9]

The [3+2] cycloadditions to form five-membered rings proceeded with extremely high selectivity. In the case of monosubstituted, *E*-disubstituted and trisubstituted dipolarophiles only two anomers were obtained and no other isomers were detected by GC. However, in the cycloaddition with (*Z*)-**2** a minor isomer was detected by GC presumably arising from an exo fold of the tether. The higher selectivity for an *E*-dipolarophile was also observed with an ester activated dipolarophile. These selectivities also imply that there are no secondary orbital interactions for the [3+2] cycloadditions of nitronates with simple olefins.

Cycloaddition of Nitroalkenes Tethered by Three Methylene Units. To maximize the probability of intermolecular cycloaddition, the Lewis acid ($\text{TiCl}_2(\text{O}i\text{-Pr})_2$) was added to a cold (-78 °C) solution of the nitroalkene and *n*-butyl vinyl ether. In all cases, the nitronates arose from an intermolecular cycloaddition; none of the nitronates from intramolecular cycloaddition with the tethered olefin were observed. The nitronates **23** and **25** from disubstituted nitroalkenes, (*E*)-**4** and (*Z*)-**4**, underwent slow [3+2] cycloaddition already at RT as judged by ^{1}H NMR analysis. The crude mixtures of nitronates were heated to 80 °C in benzene in the presence of NaHCO_3. e diastereomeric ratios of crude nitroso acetals were determined by GC and ^{1}H NMR spectroscopy and the major anomers were separated by column chromatography, Table 4. The [3+2] cycloaddition of nitronates **27** and **29** from trisubstituted nitroalkenes (*E*)-**5** and (*Z*)-**5**, was very slow at 80 °C but could be effected at 110 °C in toluene in the presence of $NaHCO_3$. The diastereomeric ratios of the crude nitroso acetals were determined by GC and ^1H NMR spectroscopy and the major anomers were separated by column chromatography, Table 4.

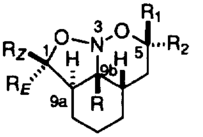
Table 4. Results from the Tandem Cycloaddition of Nitroalkene **4** and **5**.



nitroalkene				nitronate	nitroso acetal				
	R	R_E	R_Z	product	solvent, (temp, °C)	time, h	product	ratio[a] a / b	yield[b], % (ratio, α/β)[c]
(*E*)-**4**	H	Me	H	**23**	benzene (80)	32	**24**	2.8/1	72 (4.5/1)
(*Z*)-**4**	H	H	Me	**25**	benzene (80)	18	**26**	1/0	76 (9.9/1)
(*E*)-**5**	Me	Me	H	**27**	toluene (110)	14	**28**	22/2/1	81 (15.2/1)
(*Z*)-**5**	Me	H	Me	**29**	toluene (110)	9	**30**	22/5.2/1	80 (1/4.5)

[a] By GC analysis. [b] Yield of isolated anomers. [c] Two major anomers isolated.

Table 5. Selected NMR Data for Nitroso Acetals **24**, **26**, **28**, and **30**.



nitroso acetal	R_1	R_2	R	R_E	R_Z	HC(5), ppm (*J*, Hz)	C(5), ppm
24a	H	O*n*-Bu	H	Me	H	4.76 (dd, 9.2, 2.5)	100.07
24b	O*n*-Bu	H	H	Me	H	4.95 (t, 7.1)	99.96
26a	H	O*n*-Bu	H	H	Me	4.66 (dd, 9.6, 2.1)	100.46
26b	O*n*-Bu	H	H	H	Me	4.93 (d, 3.6)	100.10
28a	H	O*n*-Bu	Me	Me	H	4.94 (t, 7.2)	99.67
28b	O*n*-Bu	H	Me	Me	H	4.90 (d, 3.1)	99.47
30a	H	O*n*-Bu	Me	H	Me	4.87 (t, 7.0)	99.79
30b	O*n*-Bu	H	Me	H	Me	4.89 (d, 3.6)	99.25

The nitroso acetals were analyzed by ^1H and ^{13}C NMR spectroscopy, Table 5. The assignments of the acetal proton were based on the previous cycloadditions with an activated dipolarophile.[7] The X-ray crystallographic analysis from earlier studies revealed that the 1,2-dihydrooxazine exists in a chair conformation. The axially-oriented acetal proton resonates at higher field suggesting an equatorially oriented OR group (α anomer). However in the R=Me series, this is not diagnostic, perhaps due to other conformations. The ^{13}C NMR shift for C(5) provides a more consistent trend for assignment.

The GC analysis of the crude mixture of nitroso acetals from disubstituted nitroalkene (*E*)-**4** revealed that it consisted of a 2.8/1 ratio of isomers. The ^{1}H NMR resonance for HC(5) in the major (α) anomer **24a** appeared at 4.76 ppm and the same proton for the minor (β) isomer **24b** appeared as a triplet at 4.98 ppm. Since only two anomers were formed in this cycloaddition the diastereoselectivity for the disubstituted nitroalkene is extremely high. The ^{1}H NMR analysis of **24a** revealed that hydrogen HC(9b) appeared at 3.00 ppm as a doublet of doublets (J_d =12.0, 4.7 Hz) and hydrogen HC(9a) appeared at 2.75 ppm as a triplet of doublet of doublets (J_t = 12.0, J_d = 8.9, J_d = 3.2 Hz). The large coupling constant (12.0 Hz) indicated the diaxial relationship between hydrogens HC(9a) and HC(9b). Similarly, **24b**, showed a large coupling (12.0 Hz) between hydrogens HC(9a) and HC(9b) indicating diaxial relationship between them.

Although the tandem cycloaddition products from the disubstituted nitroalkene (*Z*)-**4** was shown to consist of a single isomer as judged by GC analysis, column chromatographic purification provided a mixture of two anomers in a 9.9/1 ratio. The ^{1}H NMR analysis of HC(5) in the major (α) anomer **26a** indicated a doublet of doublets at 4.76 ppm and the minor (β) anomer **26b** showed a triplet at 4.93 ppm. Since no other isomers detected by GC, the exo / endo diastereoselectivity for the cycloaddition must have been extremely high.

Trisubstituted nitroalkene (*E*)-**5** afforded a mixture of nitroso acetals in a 22/2/1 ratio (GC). By column chromatography two anomers were isolated in a 15/1 ratio. The ^{1}H NMR analysis of the major anomer, **28a** showed a triplet at 4.94 (J = 7.2) and the same proton for the minor anomer, **28b** appeared as a doublet at 4.90 (J = 3.1). Neither the chemical shifts nor the coupling patterns allow an unambiguous assignment of configuration. We therefore relied on the ^{13}C NMR shifts to make a tentative assignment, i.e. that the lower field signal for C(5) corresponds to the α anomer. The third isomer (detected by GC) was not isolated however, it can be assumed to belong to the cis fused series (endo fold of the tether). Therefore, the exo/endo diastereoselectivity for the *E*-dipolarophile is 24/1.

Cycloaddition of trisubstituted nitroalkene (*Z*)-**5** provided nitroso acetals as a mixture in a ratio of 22/5.2/1 as judged by GC. Two anomers in a 4.5/1 ratio were isolated by column chromatography. The ^{1}H NMR analysis of HC(5) again failed to allow an assignment. Therefore we tentatively assign the major isomer **30b** to be an the β anomer and the minor isomer **30a** to be the α anomer on the basis of the trends in ^{13}C NMR chemical shifts. The change in relative abundance of these isomers clearly makes these assignments tenuous. The third isomer can be assumed to belong to the cis family (endo fold). Therefore the exo/endo diastereoselectivity of the Z-dipolarophile is 27/1.

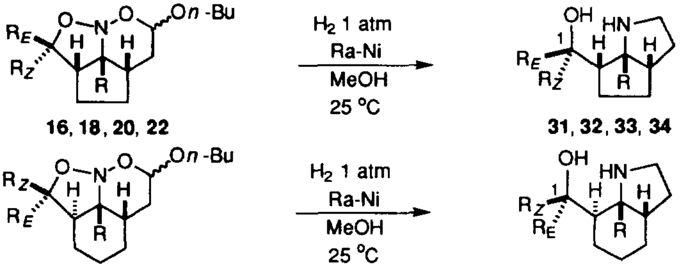
The effect of substituents on the rates of [3+2] cycloaddition can be easily understood in terms of simple steric effects. A disubstituted nitronate cyclized at a faster rate than a trisubstituted nitronate and also a *Z*-dipolarophile cyclized at a faster rate than an *E*-dipolarophile. These cycloaddition rates are in agreement with the previous trends with activated dipolarophiles.[7] Therefore, it is reasonable to assume that the cycloaddition of an unactivated dipolarophile also proceeded via an exo (tether) transition structure. This was further confirmed by the

^{1}H NMR analysis of **24a** and **24b** in which the trans ring fusion between the five- and six-membered rings is established by a large vicinal coupling constant between hydrogens HC(9a) and HC(9b). The stereoselectivity for the cycloadditions was extremely high; for C(3) unsubstituted nitronates the selectivity was greater than for C(3) unsubstituted nitronates. Thus, a nitroalkene tethered by three methylene units to an unactivated dipolarophile reacted with *n*-butyl vinyl ether to produce nitroso acetals in high selectivity.

N-O Bond Cleavage.

The synthetic utility of the tandem process is revealed by the facile transformation of the nitroso acetals by hydrogenolytic N-O bond cleavage and pyrrolidine formation.[10] The major anomer of each nitroso acetal from the tandem cycloaddition was subjected to the hydrogenolysis with a catalytic amount of Raney nickel in methanol at atmospheric pressure of hydrogen, Scheme 6. This process is analogous to that observed previously except that this transformations sequence terminates after the imine hydrogenation step due to the absence of an ester group to form a lactam.[10]

Scheme 6



16, 18, 20, 22 → **31, 32, 33, 34**

24, 26, 28, 30 → **35, 36, 37, 38**

Table 6. Results and Characteristic ^{1}H NMR Data for 1,3-Amino Alcohols

amino alcohol	R	R_E	R_Z	yield, %	HC(1), ppm (*J*, Hz)
31	Me	H	H	87	4.04 (d, 4.3)
32	Me	Me	H	84	3.77 (quintet, 6.5)
33	Me	H	Me	81	4.15 (quintet, 6.2)
34	Me	Me	Me	76	-
35	H	Me	H	76	3.48 (quintet, 6.1)
36	H	H	Me	76	3.67 (quintet, 6.3)
37	Me	Me	H	82	3.96 (quintet, 6.5)
38	Me	H	Me	80	4.32 (quintet, 5.6)

The ^{1}H NMR analysis of each amino alcohol showed characteristic chemical shifts for a proton attached to a hydroxyl bearing carbon and this proton showed a quintet when it is attached to a methyl bearing carbon atom. The appearance of a broad IR absorption in the region of ~ 3200 cm^{-1} for each of these compounds further indicated the presence of hydroxyl and amine groups. The mass spectroscopic data for all of these compounds confirmed their molecular ion. The ring fusion of the amino alcohol is assumed to be the same as in the corresponding cycloadduct.

Summary

In order to test the complementary electronic properties of dipoles and dipolarophiles, tandem cycloaddition involving nitroalkenes tethered to an simple olefinic dipolarophile were studied. In every case, the external butyl vinyl ether served as the dienophile and no product arising from intramolecular cycloaddition were observed. These nitronates were stable enough to be isolated and upon heating in benzene or toluene, nitroso acetals were isolated as a mixture of butyloxy anomers. The tandem cycloadditions of nitroalkenes tethered to an unactivated dipolarophile are also highly stereoselective. The transition states for both [4+2] and [3+2] cycloadditions are in agreement with the results previously disclosed for cycloadditions with activated dipolarophiles. The mode of the [3+2] cycloaddition is dependent upon the tether length and not on the geometry of the dipolarophile. This is reflected in the rate of the cycloaddition; the *E*-dipolarophile cyclized faster than the *Z*-dipolarophile for the nitroalkene tethered with two methylene units, whereas the *Z*-dipolarophile cyclized faster than the *E*-dipolarophile in the case of nitroalkenes tethered with three methylene units. As expected the rate of the cycloaddition of a nitroalkene tethered with two methylene units is faster than that of the nitroalkene tethered with three methylene units.

The synthetic utility of these cycloadducts was demonstrated by hydrogenolysis of the nitroso acetals to 1,3-amino alcohols. These fused pyrrolidines with both five- and six-membered rings are useful intermediates and can be generated in high yield and with high and predictable stereoselectivity. The employment of chiral dienophiles to generate the 1,3-amino alcohols in optically active form and the application of this process in the total synthesis of pyrrolidine-containing natural products will be the subject of future reports.

EXPERIMENTAL

General Information. Boiling points (bp) from bulb-to-bulb distillations refer to air bath temperature and are uncorrected. Melting points (mp) were determined in sealed capillaries and are corrected. Analytical TLC was performed on Merck silica gel plates with QF-254 indicator. Visualization was accomplished with UV light, iodine and/or sulfuric acid-vanillin-ethanol solution. Solvents for extraction and chromatography were technical grade and distilled from the indicated drying agents; hexane, dichloromethane ($CaCl_2$), ether ($CaSO_4$/ $FeSO_4$), ethyl acetate (K_2CO_3). Column chromatography was performed using 32-63 mm silica gel (Woelm). Optical rotations are reported as follows: $[\alpha]^{\text{temperature}}_{\text{wavelength}}$ concentration (c = g/100 mL), and solvent. Analytical gas chromatography were performed with a flame ionization detector, N_2 carrier gas 30 mL/min, silicone OV-17 on 60-80 chromosorb column or HP-5. Retention times (t_R) and integrals were obtained from a Hewlett Packard 3390 reporting integrator. Brine refers to a sat. aq. solution of sodium chloride. All reactions were performed in oven dried and/or flame dried glassware under an inert atmosphere of dry N_2.

^1H NMR and ^{13}C NMR spectra were obtained at either 200 MHz ^1H (50.4 MHz ^{13}C), 300 MHz ^1H (75.5 MHz ^{13}C) or 500 MHz ^1H (125.8 MHz ^{13}C) in $CDCl_3$ with $CHCl_3$ as an internal standard (^1H δ=7.26 ppm ^{13}C δ=77.07 ppm). Chemical shifts are given in ppm (δ); multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), and br (broad). Coupling constants (*J*) are reported in Hz. Infrared spectra (IR) were obtained in CCl_4 solution unless otherwise noted. Peaks are reported in cm^{-1} with the following relative intensities; s (strong, 67-100%), m (medium, 34-66%), w (weak, 0-33%). Electron impact (EI) mass spectra were obtained with ionization voltages of 70 or 10 eV. Data are reported in the form m/e (intensity relative to base = 100). Elemental analyses were performed by the University of Illinois Microanalytical Service Laboratory.

Starting Materials. The following compounds were prepared by literature methods; 5,5-dimethoxypentanal, 6,6-dimethoxyhexanal, 7,7-dimethoxyheptanal,[11] and *t*-butanol·potassium *t*-butoxide complex.[12]

Preparation of Aldehydes

(*E*)-5-Heptenal ((*E*)-12). To a suspension of ethyltriphenylphosphonium bromide (2.59 g, 6.81 mmol) in THF (15 mL)/Et_2O (8 mL) was added PhLi (3.35 mL, 2 M in hexane/ Et_2O, 6.70 mmol). The resulting dark orange mixture was allowed to stir at RT for 30 min, cooled to -78 °C and aldehyde 5,5-dimethoxypentanal (0.978 g, 6.70 mmol) was added dropwise. The color changed to light orange and after 30 min PhLi (3.35 mL, 2 M in hexane/Et_2O, 6.70 mmol, 1.0 equiv) was added. The dark brown mixture was allowed to stir at -29 °C. After 30 min *t*-BuOH·KO*t*-Bu complex (1.74 g, 10.26 mmol, 1.5 equiv) was added. The light brown mixture stirred at -29 °C for 1 h and allowed to warm to RT. The mixture was centrifuged and the supernatant washed with H_2O until neutral. The organic layer was dried ($MgSO_4$), filtered and concentrated. The residue was purified by column chromatography on silica gel (hexane/ EtOAc (8/1)).

The crude acetal was dissolved in THF (50 mL) and 1 N HCl (25 mL) and was stirred at RT for 90 min. The mixture was partitioned between H_2O and petroleum ether. The organic layer was washed with H_2O, sat. aq. $NaHCO_3$ solution and brine and the aqueous layers were back extracted with petroleum ether. The organic extracts were dried (Na_2SO_4), filtered and concentrated. The residue was distilled to give 0.484 g (70%) of (*E*)-**12** as a clear liquid: bp 35 °C (1 Torr, air bath); ^1H NMR (300 MHz) 9.76 (t, *J* = 1.5, 1 H, HC(1)), 5.43-5.29 (m, 2 H, HC(5), HC(6)), 2.41 (td, *J* = 7.2, 1.4, 2 H, $H_2C(2)$), 2.01 (q, *J* = 6.7, 2 H, $H_2(C4)$), 1.73-1.68 (m, 2 H, $H_2C(3)$), 1.64 (d, *J* = 5.7, 3 H, $H_3C(7)$); ^{13}C NMR: (75.5 MHz) 202.73 (C(1)), 130.03 (C(5)), 126.12 (C(6)), 43.15 (C(2)), 31.82 (C(4)), 21.84 (C(4)), 17.86 (C(7)); IR (CCl_4) 1730 (s); MS (70 eV) 112 (M^+, 3); TLC R_f 0.50 (hexane /EtOAc (4/1)); GC t_R 6.11 min (OV-17, 50 °C(2 min), 10 °C/min, 230 °C). Anal. Calcd for $C_7H_{12}O$ (112.71): C, 74.95; H, 10.78. Found: C, 75.04; H, 10.81.

(*Z*)-5-Heptenal ((*Z*)-12). To a magnetically-stirred suspension of ethyltriphenylphosphonium bromide (15.65 g, 42.2 mmol, 1.4 equiv) in dry THF (140 mL) and HMPA (16 mL) in a 250-mL, 3-necked flask fitted with a N_2 inlet, rubber septum and glass stopper was added potassium hexamethyldisilazide (61 mL, 0.45 M in toluene, 39 mmol, 1.3 equiv). The bright red mixture was stirred at RT for 30 min. The mixture was cooled to -78 °C and the chilled mixture was treated with 5,5-dimethoxypentanal (4.40 g, 30 mmol) maintaining -78 °C. The mixture was allowed to warm to RT over one h, and the resulting yellowish brown solution was partitioned between petroleum ether and H_2O. The organic layer was washed with H_2O, and the aqueous layers were extracted with petroleum ether. The combined organic layers were dried ($MgSO_4$), filtered, and concentrated to give an oil. The crude product was purified by column chromatography using silica gel (hexane/EtOAc (8/1)). The desired fraction was concentrated and the residue was dissolved in 0.1 N HCl/THF (50 mL/50 mL) mixture and stirred at RT for 2 h. The reaction mixture was partition between Et_2O and H_2O. The organic layer was washed with sat. aq. $NaHCO_3$ solution and brine. The aqueous layers were back extracted with Et_2O. The combined organic extracts were dried ($MgSO_4$), filtered and concentrated, then distilled to give 1.19 g (49%) of (*Z*)-**12** as a colorless liquid: bp 92 °C (87 Torr, air bath); ^1H NMR (300 MHz) 9.76 (d, *J* = 1.4, 1 H, HC(1)), 5.48 (dt, *J* = 10.8, 6.6, 1 H, HC(6)), 5.35 (dt, *J* = 10.8, 6.4, 1 H, HC(5)), 2.43 (dt, *J* = 7.3, 1.6, 2 H, $H_2C(4)$), 2.07 (m, 2 H, $H_2C(2)$), 1.70 (m, 2 H, $H_2C(3)$), 1.59 (d, *J* = 6.6, 3 H, $H_3C(7)$); ^{13}C NMR (75.5 MHz) 202.47 (C(1)), 129.11 (C(5)), 125.00 (C(6)), 43.14 (C(2)), 25.26 (C(4)), 21.78 (C(3)), 12.63 (C(7)); IR (CCl_4) 1730 (s); MS (70 eV) 112 (M^+, 10); TLC R_f 0.51 (hexane/ EtOAc (4/1)); GC t_R 5.96 min (OV-17, 50 m, 50 °C(2 min), 10 °C/ min, 200 °C). Anal. Calcd for $C_7H_{12}O$ (112.71): C, 74.95; H, 10.78. Found: C, 74.98; H, 10.76.

General Procedure for the Preparation of Nitro Alcohols. To a magnetically-stirred solution of the aldehyde in THF/*t*-BuOH (1 / 1) (0.5 M) was added nitromethane (3.0 equiv) and a catalytic amount of KO*t*-Bu. The resulting faint yellow solution allowed to stir at RT. After the indicated reaction time, the reaction mixture was diluted with CH_2Cl_2 and washed with H_2O and brine. The aqueous layers were back extracted with CH_2Cl_2. The combined organic extracts were dried ($MgSO_4$), filtered and concentrated. The residue was purified by column chromatography on silica gel to afford the nitro alcohol as a clear oil.

General Procedures for the Preparation of Nitroalkenes. Method A. To a solution of the nitro alcohol in dry Et_2O (0.8 M) was added dry acetic anhydride (1.2 equiv) and a catalytic amount of 4-(*N,N*-dimethylamino)pyridine and the mixture was stirred at RT and was monitored by TLC analysis. After 1 h the reaction mixture was diluted with CH_2Cl_2 and washed with H_2O, sat. aq. $NaHCO_3$ solution and brine. The aqueous layers were back extracted with CH_2Cl_2. The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated to give nitro acetate as a colorless liquid.

To a stirred solution of nitro acetate in CH_2Cl_2 (0.5 M) was added 4-(*N,N*-dimethylamino)pyridine (1.1 equiv). The resulting solution was stirred at RT. After 3 h the reaction mixture was diluted with CH_2Cl_2 and washed with H_2O, 0.1 N HCl, and brine. The aqueous layers were back extracted with CH_2Cl_2. The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated. The crude product was purified by column chromatography on silica gel (hexane/ EtOAc (2/1)) followed by bulb-to-bulb distillation to give the nitroalkene as a pale brown oil.

Method B. To a magnetically-stirred solution of the nitro alcohol CH_2Cl_2 (0.5 M) was added was added dropwise, at 0 °C, trifluoroacetic anhydride (1.05 equiv) followed by Et_3N (2.1 equiv). After the indicated reaction time, the resulting pale brown solution was diluted with CH_2Cl_2 and washed sequentially with H_2O, sat. aq. NH_4Cl solution and brine. The aqueous layers were back extracted with CH_2Cl_2 and the combined organic extracts were dried ($MgSO_4$), filtered and concentrated. The residue was purified by silica gel column chromatography and then distillation to afford the nitroalkene as a light brown oil.

(*E*)-2-Nitro-6-heptene-3-ol (7). To a magnetically stirred suspension of pyridinium chlorochromate (10.00 g, 46.44 mmol, 2 equiv) and 4 Å molecular sieves in CH_2Cl_2 (46 mL) was added 4-pentenol[6a] (2.00 g, 23.22 mmol). The orange solution turned dark and was allowed to stir at room temperature. After 1 h the mixture was diluted with Et_2O and filtered through a celite pad. The filtrate was concentrated to give crude aldehyde **6** which was directly used in the next reaction without further purification.

From aldehyde **6** (1.95 g, 23.22 mmol), nitroethane (4.14 mL, 69.66 mmol, 3 equiv) and a catalytic amount of KO*t*-Bu in THF (23 mL)/*t*-BuOH (23 mL). Reaction time 30 min. Purification (silica gel (hexane/EtOAc, 8/1)) afforded 1.78 g (48% from the alcohol) of nitro alcohol **7** as a clear oil: ^1H NMR (300 MHz) 5.85-5.74 (m, 1 H, HC(6)), 5.11-5.02 (m, 2 H, $H_2C(7)$), 4.57-4.49 (m, 1 H, HC(2)), 4.23-4.18 (m, 0.5 H, HC(3)), 3.96-3.91 (m, 0.5 H, HC(3)), 2.37-2.15 (m, 3 H), 1.65-1.49 (m, 2 H), 1.56 (d, J = 6.8, 3 H, $H_3C(1)$); ^{13}C NMR (75.5 MHz) 137.29 and 137.18 (C(6)), 115.80 (C(7)), 87.75 and 86.33 (C(2)), 72.26 and 71.41 (C(3)), 31.03 and 31.95, 29.83 and 29.34, 12.37; TLC R_f 0.45 (hexane /EtOAc, 4/1).

(*E*)-2-Nitro-2,6-heptadiene (1). Method B. From nitro alcohol **7** (1.60 g, 10.05 mmol), trifluoroacetic anhydride (1.5 mL, 10.55 mmol, 1.05 equiv) and a catalytic amount of DMAP in Et_2O (20 mL). Reaction time: 30 min. The residue was dissolved in CH_2Cl_2 (20 mL) and Et_3N (0.729 mL, 11.05 mmol, 1.1 equiv) was added dropwise at 0 °C. Reaction time: 1 h. Purification (silica gel, hexane/EtOAc (10/1)) and distillation afforded 1.14 g (80%) of **1** as a clear oil: bp 85-87 °C (4 Torr, air bath); ^1H NMR (300 MHz) 7.12 (t, J = 7.3, 1 H, HC(3)), 5.79 (ddt, J_d = 16.9, J_d = 10.4, J_t = 6.1, 1 H, HC(6)), 5.11-5.03 (m, 2 H, $H_2C(7)$), 2.37-2.22 (m, 4 H), 2.16 (s, 3 H, $H_3C(1)$); ^{13}C NMR (75.5 MHz) 147.86 (C(2)), 136.41 (C(6)), 135.42 (C(3)), 116.27 (C(7)), 32.19 (C(4)), 27.45 (C(5)), 12.60 (1)); IR (CCl_4) 1641 (w), 1526 (s); TLC R_f 0.63 (hexane /EtOAc (10/1)); GC t_R 6.61 min (HP-5, 150 °C(4 min), 10 °C/min, 250 °C). Anal. Calcd for $C_7H_{11}NO_2$ (141.17): C, 59.56; H, 7.85; N, 9.92. Found: C, 59.43; H, 7.82; N, 9.88.

(*E*)-2-Nitro-6-octene-3-ol ((*E*)-9). To a magnetically stirred suspension of pyridinium chlorochromate (4.31 g, 19.97 mmol, 2 equiv) and 4 Å molecular sieves (2 g) in CH_2Cl_2 (20 mL) was added (*E*)-4-hexenol[6b] (1.00 g, 9.99 mmol). The orange solution turned dark and was allowed to stir at room temperature. After 1 h the mixture was diluted with Et_2O and filtered through a celite pad. The filtrate was concentrated to give crude aldehyde (*E*)-**7** which was used directly in the next reaction without further purification.

From (*E*)-**7** (0.98 g, 10.00 mmol) nitroethane (2.15 mL, 29.95 mmol, 3 equiv) and a catalytic amount of KO*t*-Bu in THF (10 mL)/*t*-BuOH (10 mL). Reaction time: 15 min. Purification (silica gel (hexane/EtOAc, 8/1)) afforded 0.927 g (54% from the alcohol) of nitro alcohol (*E*)-**9**: ^1H NMR (300 MHz) 5.55-5.35 (m, 2 H, HC(6), HC(7)), 4.56-4.48 (m, 1 H, HC(2)), 4.21-4.17 (m, 0.5 H, HC(3)), 3.96-3.90 (m, 0.5 H, HC(3)), 2.34 (d, J =

4.7, 0.5 H, OH), 2.27 (d, J = 6.7, 0.5 H, OH), 2.22-2.04 (m, 2 H), 1.66 (d, J = 5.9, 3 H, $H_3C(8)$), 1.55 (d, J = 6.9, 3 H, $H_3C(1)$), 1.62-1.42 (m, 2 H); ^{13}C NMR (75.5 MHz) 129.72 and 129.62 (C(6)), 126.56 (C(7)), 87.78 and 86.35 (C(2)), 72.37 and 71.49 (C(3)), 32.69 and 32.62, 28.72 and 28.24, 17.93 and 16.17 (C(8)), 12.39 (C(1)); IR (CCl_4) 3574 (br, m), 2942 (m), 2855 (m), 1551 (s), 1452 (m), 1391 (m), 1358 (m), 1263 (m), 1072 (m), 1036 (m), 968 (s) cm^{-1}; TLC R_f 0.48 (hexane /EtOAc, 4/1).

(2*E*,6*E*)-2-Nitro-2,6-octadiene ((*E*)-2). Method B. From nitro alcohol (*E*)-**9** (0.90 g, 5.16 mmol), trifluoroacetic anhydride (0.779 mL, 5.455 mmol, 1.05 equiv) and Et_3N (1.52 mL, 10.91 mmol, 2.1 equiv) in CH_2Cl_2 (10 mL). Reaction time: 45 min. Purification (silica gel, hexane/EtOAc (8/1)) and distillation afforded 0.662 g (82%) of (*E*)-**2** as a clear oil: bp 85-87 °C (0.8 Torr, air bath); ^1H NMR (300 MHz) 7.12 (t, J = 7.5, 1 H, HC(3)), 5.54-5.36 (m, 2 H, HC(6), HC(7)), 2.28 (q, J = 7.2, 2 H, CH_2), 2.19 (q, J = 7.0, 2 H, CH_2), 2.15 (s, 3 H, $H_3C(1)$), 1.66 (d, J = 5.6, 3 H, $H_3C(8)$); ^{13}C NMR (75.5 MHz) 147.71 (C(2)), 135.80 (C(3)), 128 .95 (C(6)) 126.93 (C(7)), 31.13 (CH_2), 28.16 (CH_2), 17.90(C(8)), 12.57(C(1)); IR (CCl_4) 1674 (w), 1524 (s), 1334 (s); TLC R_f 0.71 (hexane /EtOAc (4/1)); GC t_R 8.25 min (150 °C(4 min), 10 °C/min, 250 °C). Anal. Calcd for $C_8H_{13}NO_2$ (155.20): C, 61.91; H, 8.44; N, 9.03. Found: C, 61.95; H, 8.33; N, 9.10.

(*Z*)-2-Nitro-6-octene-3-ol ((*Z*)-9). To a magnetically stirred suspension of pyridinium chlorochromate (3.23 g, 14.98 mmol, 2 equiv) and 4 Å molecular sieves (2 g) in CH_2Cl_2 (15 mL) was added alcohol (Z)-4-hexenol (0.75 g, 7.49 mmol). The orange solution turned dark and was allowed to stir at room temperature. After 1 h the mixture was diluted with Et_2O and filtered through a celite pad. The filtrate was concentrated to give crude aldehyde (Z)-**7** which was directly used in the next reaction without further purification.

From aldehyde (Z)-**7** (0.735 g, 7.46 mmol), nitroethane (1.614 mL, 22.46 mmol, 3 equiv) and a catalytic amount of KO*t*-Bu in THF (7.5 mL)/*t*-BuOH (7.5 mL). Reaction time 30 min. Purification (silica gel (hexane/EtOAc, 8/1)) afforded 1.03 g (78%) of (Z)-**9** as a clear oil: ^1H NMR (300 MHz) 5.56-5.32 (m, 2 H, HC(6), HC(7)), 4.56-4.49 (m, 1 H, HC(2)), 4.21-4.17 (m, 0.5 H, HC(3)), 3.95-3.90 (m, 0.5 H, HC(3)), 2.42 (d, J = 4.7, 0.5 H, OH), 2.35 (d, J = 6.8, 0.5 H, OH), 2.24 (q, J = 7.4, 2 H, $H_2C(5)$), 1.63 (d, J = 6.7, 3 H, $H_3C(8)$), 1.55 (d, J = 6.8, 3 H, $H_3C(1)$), 1.54-1.40 (m, 2 H, $H_2C(4)$); ^{13}C NMR (75.5 MHz) 128.81 and 128.73 (C(6)), 125.56 (C(7)), 87.80 and 86.34 (C(2)), 72.49 and 71.62 (C(3)), 32.64 and 32.56, 23.03 and 22.59, 16.18 (C(8)), 12.79 and 12.38 (C(1)); IR (CCl_4) 3576 (br, m), 2941 (m), 1551 (s), 1453 (m), 1391 (m), 1358 (m) cm^{-1}; TLC R_f 0.47 (hexane /EtOAc, 4/1).

(2*E*,6*Z*)-2-Nitro-2,6-octadiene ((Z)-2). Method B: From nitro alcohol (Z)-**9** (1.00 g, 5.77 mmol), trifluoroacetic anhydride (0.856 mL, 6.06 mmol, 1.05 equiv) and Et_3N (1.69 mL, 12.12 mmol, 2.1 equiv) in CH_2Cl_2 (15 mL). Reaction time: 45 min. Purification (silica gel, hexane/EtOAc (8/1)) and distillation afforded 0.717 g (80%) of (Z)-**2** as a clear oil.: bp 88-90 °C (0.8 Torr, air bath); ^1H NMR (300 MHz) 7.12 (t, J = 7.1, 1 H, HC(3)), 5.55 (dq, J_d = 10.8, J_q = 6.7, 1 H, HC(7)), 5.37 (m, 1 H, HC(6)), 2.27 (m, 4 H, $H_2C(4)$, $H_2C(5)$), 2.16 (s, 3 H, $H_3C(1)$), 1.62 (d, J = 6.6, 3 H, $H_3C(8)$); ^{13}C NMR (75.5 MHz) 147.82 (C(2)), 135.72 (C(3)), 127.99 (C(6)) 126.00 (C(7)), 28.08 (CH_2), 25.50 (CH_2),12.82 (C(8)), 12.59(C(1)); IR (CCl_4) 1676 (w), 1526 (s), 1335 (s); TLC R_f 0.71 (hexane/EtOAc (4/1)); GC t_R 8.44 min (HP-5, 150 °C(4 min), 10 °C/min, 250 °C). Anal. Calcd for $C_8H_{13}NO_2$ (155.20): C, 61.91; H, 8.44; N, 9.03. Found: C, 62.04; H, 8.32; N, 9.05.

7-Methyl-2-nitro-6-octene-3-ol (11). To a magnetically stirred suspension of pyridinium chlorochromate (3.78 g, 17.52 mmol, 2 equiv) and 4 Å molecular sieves (2 g) in CH_2Cl_2 (17.5 mL) was added alcohol 5-methyl-4-hexenol (1.00 g, 8.76 mmol). The orange solution turned dark and was allowed to stir at room temperature. After 1 h the mixture was diluted with Et_2O and filtered through a celite pad. The filtrate was concentrated to give crude aldehyde **10** which was directly used in the next reaction without further purification.

From aldehyde (0.98 g, 8.76 mmol) was added nitroethane (1.89 mL, 26.27 mmol, 3 equiv) and a catalytic amount of KO*t*-Bu in THF (8 mL)/*t*-BuOH (8 mL), reaction time: 15 min. Purification (silica gel (hexane/EtOAc, 8/1)) afforded 1.39 g (80%) of nitro alcohol **11** as a clear liquid: ^1H NMR (300 MHz) 5.10 (t, J = 7.1, 1 H, HC(6)), 4.56-4.48 (m, 1 H, HC(2)), 4.21-4.16 (m, 0.5 H, HC(3)), 3.93-3.89 (m, 0.5 H, HC(3)), 2.35 (d, J = 4.7, 0.5 H, OH), 2.28 (d, J = 6.7, 0.5 H, OH), 2.18 (q, J = 7.8, 2 H, $H_2C(5)$), 1.69 (s, 3 H, $H_3C(8)$), 1.63 (s, 3,H, $H_3C(9)$), 1.55 (d, J = 7.1, 3 H, $H_3C(1)$), 1.60-1.42 (m, 2 H, $H_2C(4)$); ^{13}C NMR (75.5 MHz) 133.31 (C(7)), 122.85 and 122.78 (C(6)), 87.80 and 86.41 (C(2)), 72.58 and 71.67 (C(3)), 32.95 and 32.87 (C(4)), 25.73 (C(5)), 24.20 and 23.73 (C(8)), 17.71 and 16.18 (C(9)), 12.38 (C(1)); IR (CCl_4) 3576 (br, m), 2971 (m), 2916 (m), 1551 (s), 1452 (m), 1390 (m), 1358 (m), 1263 (m), 1109 (w), 1070 (w) cm^{-1}; TLC R_f 0.49 (hexane/EtOAc, 4/1).

(*E*)-7-Methyl-2-Nitro-2,6-octadiene (3). Method B: From nitro alcohol **11** (1.00 g, 5.34 mmol), trifluoroacetic anhydride (0.79 mL, 5.81 mmol, 1.05 equiv) and Et_3N (1.56 mL, 11.21 mmol, 2.1 equiv) in CH_2Cl_2 (20 mL). Reaction time: 30 min. Purification (silica gel, hexane/EtOAc (5/1)) and distillation afforded 0.772 g (85%) of **3** as a clear oil, bp 80° C (0.2 Torr, air bath).

(*E*)-1-Nitro-6-octene-2-ol ((*E*)-13). From aldehyde (*E*)-**12** (0.80 g, 7.13 mmol), nitromethane (1.3 mL, 21.4 mmol, 3 equiv) and a catalytic amount of KO*t*-Bu in THF (7 mL)/*t*-BuOH (7 mL). Reaction time: 30 min. Purification (silica gel, hexane/EtOAc (8/1)) afforded 1.0 g (81%) of (*E*)-**13**: ^1H NMR (300 MHz) 5.47-5.36 (m, 2 H, HC(7), HC(6)), 4.45-4.31 (m, 3 H, $H_2C(1)$, HC(2)), 2.49 (d, J = 4.4, 1 H, OH), 2.01 (m, 2 H, $H_2C(5)$), 1.65 (d, J = 5.0, 3 H, $H_3C(8)$), 1.60-1.42 (m, 4 H); ^{13}C NMR (75.5 MHz) 130.39 (C(6)), 125.78 (C(7)), 80.66 (C(1)), 68.61 (C(2)), 33.07, 32.07, 25.01, 17.91 (C(8)); IR (CCl_4) 3594 (w, br), 1557 (s), 1379 (m); TLC R_f 0.38 (hexane/EtOAc (5/1)).

(1*E*,6*E*-)-1-Nitro-1,6-octadiene ((*E*)-4). Method B. From nitro alcohol (*E*)-**13** (1.0 g, 5.77 mmol), trifluoroacetic anhydride (0.856 mL, 6.06 mmol, 1.05 equiv) and Et_3N (1.7 mL, 12.12 mmol, 2.1 equiv) in CH_2Cl_2 (11.5 mL). Reaction time: 45 min. Purification (silica gel, hexane/EtOAc (10/1)) and distillation afforded 0.710 g (80%) of (*E*)-**4** as a clear oil: bp 59-60 °C (0.05 Torr, air bath); ^1H NMR (300 MHz) 7.27 (dt, J_d = 13.5, J_t = 7.3, 1 H, HC(2)), 6.97 (d, J = 13.4, 1 H, HC(1)), 5.52-5.32 (m, 2 H, HC(6), HC(7)), 2.26 (q, J = 7.5, 2 H, $H_2C(5)$), 2.04 (q, J = 6.9, 2 H, $H_2C(3)$), 1.65 (d, J = 6.4, 3 H, $H_3C(8)$), 1.62-1.52 (m, 2 H, $H_2C(4)$); ^{13}C NMR (75.5 MHz) 142.66 (C(2)), 139.59 (C(1)), 129.75 (C(6)), 126.31 (C(7)), 31.79 (C(5)), 27.74, 27.43, 17.87(C(8)); IR (CCl_4) 1653 (w), 1532 (s), 1352 (s); TLC R_f 0.69 (hexane/EtOAc (4/1)); GC t_R 8.53 min (150 °C(4 min), 10 °C/min, 250 °C). Anal. Calcd for $C_8H_{13}NO_2$ (155.20): C, 61.91; H, 8.44; N, 9.03. Found: C, 61.87; H, 8.49; N, 8.99.

(*Z*)-1-Nitro-6-octene-2-ol ((*Z*)-13). From aldehyde (*Z*)-**12** (0.78 g, 6.95 mmol), nitromethane (1.24 mL, 20.86 mmol, 3 equiv) and a catalytic amount of KO*t*-Bu in THF (7 mL)/*t*-BuOH (7 mL). Reaction time: 15 min. Purification (silica gel, hexane/EtOAc, 8/1) afforded 1.04 g (87%) of (*Z*)-**13** as a clear oil: ^1H NMR (300 MHz) 5.52-5.46 (m, 1 H, HC(7)), 5.40-5.33 (m, 1 H, HC(6)), 4.47-4.30 (m, 3 H, $H_2C(1)$, HC(2)), 2.53(1 H, OH), 2.11-2.05 (m, 2 H, $H_2C(5)$), 1.61 (d, J = 6.7, 3 H, $H_3C(8)$), 1.58-1.26 (m, 4 H); ^{13}C NMR (75.5 MHz) 129.55 (C(6)), 124.80 (C(7)), 80.66 (C(1)), 68.62 (C(2)), 33.17, 26.33, 25.06, 12.83 (C(8)); IR (CCl_4) 3584 (m, br), 1555 (s), 1379 (m); TLC R_f 0.38 (hexane/EtOAc (5/1)).

(1*E*,6*Z*)-1-Nitro-1,6-octadiene ((*Z*)-4). Method B. From nitro alcohol (*Z*)-**13** (1.04 g, 6.0 mmol), trifluoroacetic anhydride (0.89 mL, 6.30 mmol, 1.05 equiv) and Et_3N (1.76 mL, 12.61 mmol, 2.1 equiv) in CH_2Cl_2 (12 mL). Reaction time: 30 min. Purification (silica gel, hexane/EtOAc (8/1)) and distillation afforded 0.741 g (78%) of (*Z*)-**4** as a pale brown oil: bp 59-60 °C (0.05 Torr, air bath); ^1H NMR: (300 MHz) 7.28 (td, J = 13.5, 7.2, 1 H, HC(2)), 6.98 (dd, J = 13.4, 1.3, 1 H, HC(1)), 5.55-5.46 (dt, J = 10.8, 6.4, 1 H, HC(6)), 5.39-5.30 (dt, J_d = 10.8, J_t = 6.6, 1 H, HC(7)), 2.28 (qd, J_q = 7.3, J_d = 1.1, 2 H, $H_2C(3)$), 2.11 (q, J = 7.2, 2 H, $H_2C(5)$), 1.60 (d, J = 7.1, 3 H, $H_3C(8)$), 1.64-1.54 (m, 2 H, $H_2C(4)$); ^{13}C NMR (75.5 MHz) 142.59 (C(2)), 139.62 (C(1)), 128.91 (C(6)), 125.19 (C(7)), 27.84, 27.46, 26.05, 12.80 (C(8)); IR (CCl_4) 1655 (w), 1532 (s), 1352 (s); TLC R_f 0.69 (hexane/EtOAc (4/1)); GC t_R 8.71 min (150 °C(4 min), 10 °C/min, 250 °C). Anal. Calcd for $C_8H_{13}NO_2$ (155.20): C, 61.91; H, 8.44; N, 9.03. Found: C, 62.08; H, 8.46; N, 9.00.

Preparation of (*E*)-2-Nitro-7-nonene-3-ol ((*E*)-14). From (*E*)-**12** (0.80 g, 7.13 mmol), nitroethane (1.54 mL, 21.40 mmol, 3 equiv) and a catalytic amount of KO*t*-Bu in THF (7 mL)/*t*-BuOH (7 mL). Reaction time: 15 min. Purification (silica gel, hexane/EtOAc (8/1)) afforded 1.12 g (84%) of nitro alcohol (*E*)-**14**: ^1H NMR (300 MHz) 5.48-5.35 (m, 2 H, HC(8), HC(7)), 4.55-4.48 (m, 1 H, HC(2)), 4.20-4.16 (m, 0.5 H, HC(3)), 3.91-3.88 (m, 0.5 H, HC(3)), 2.32 (d, J = 4.9, 0.5 H, OH), 2.23 (d, J = 6.9, 0.5 H, OH), 2.01 (m, 2 H, $H_2C(6)$), 1.64 (d, J = 5.00, 3 H, $H_3C(1)$), 1.55 (d, J = 6.6, 3 H, $H_3C(9)$), 1.51-1.36 (m, 4 H); ^{13}C NMR: (75.5 MHz) 130.47 and 130.45 (C(7)), 125.68 (C(8)), 87.80 and 86.35 (C(2)), 72.77 and 72.00 (C(3)), 32.41

and 32.26, 32.10, 25.58, and 24.92, 17.90, and 16.19 (C(9)), 12.29 (C(1)); IR (CCl$_4$) 3577 (br, w), 2986 (m), 2940 (m), 1551 (s), 1453 (m), 1393 (m), 1360 (m), 1264 (s); TLC R_f 0.43 (hexane /EtOAc (5/1)).

Preparation of (2*E*,7*E*)-2-Nitro-2,7-nonadiene ((*E*)-5). Method A. From 0.56 g (3.00 mmol) of nitro alcohol (*E*)-**14** was obtained 0.61 g (87%) of nitro acetate and 0.34 g (76%) of nitroalkene (*E*)-**5**: bp 70 °C (0.2 Torr, air bath); ^{1}H NMR (300 MHz) 7.12 (t, J = 8.1, 1 H, HC(3)), 5.40 (m, 2 H, HC(7), HC(8)), 2.21 (m, 2 H, H$_2$C(2)), 2.14 (s, 3 H, H$_3$C(1)), 2.02 (m, 2 H, H$_2$C(6)), 1.65 (d, J = 5.2, 3 H, H$_3$C(9)), 1.55(m, 2 H, H$_2$C(5)); ^{13}C NMR (75.5 MHz) 147.54 (C(2)), 136.19 (C(3)), 129.45 (C(7)), 126.00 (C(8)), 31.91 (C(6)), 27.97 (C(5)), 27.35 (C(4)), 17.81 (C(9)), 12.38 (C(1)); IR (CCl$_4$) 1676 (w), 1526 (s), 1333 (m); TLC R_f 0.72 (hexane/EtOAc (3/1)); GC t_R 13.61 min (OV-17, 50 °C (2 min), 10 °C/ min, 230 °C). Anal. Calcd for C$_9$H$_{15}$NO$_2$ (169.22): C, 63.88; H, 8.93; N, 8.28. Found: C, 63.93; H, 8.64; N, 8.25.

Preparation of (*Z*)-2-Nitro-7-nonene-3-ol ((*Z*)-14). From aldehyde (*Z*)-**12** (0.78 g, 6.95 mmol), nitroethane (1.5 mL, 20.86 mmol, 3 equiv) and a catalytic amount of KO*t*-Bu in THF (7 mL)/*t*-BuOH (7 mL). Reaction time: 15 min. Purification (silica gel, hexane/EtOAc, 8/1) afforded 1.02 g (77%) of (*Z*)-**14** as a clear oil: ^{1}H NMR (300 MHz) 5.51-5.43 (m, 1 H, HC(7)), 5.39-5.30 (m, 1 H, HC(8)), 4.52 (m, 1 H, HC(2)), 4.18 (m, 0.5 H, HC(3)), 3.91 (m, 0.5 H, HC(3)), 2.30 (d, J = 4.8, 0.5 H, OH), 2.21 (d, J = 6.9, 0.5 H, OH), 2.07 (m, 2 H, H$_2$C(6)), 1.46 (m, 4 H); ^{13}C NMR (75.5 MHz) 129.65 (C(8)), 124.71 (C(7)), 87.79 and 86.37 (C(2)), 72.82 and 72.02 (C(3)), 32.49, 32.40, 26.35, 25.62, 24.98, 16.24 (C(1)), 12.84 and 12.32 (C(9)); IR (CCl$_4$) 3573 (br, w), 1551 (s), 1360 (m); TLC R_f 0.43 (hexane/EtOAc (5/1)).

(2*E*,7*Z*)-2-Nitro-2,7-nonadiene ((*Z*)-5). Method A. From 2.33 g (12.5 mmol) of alcohol (*Z*)-**14** was obtained 2.77 g (96%) of nitro acetate and 1.89 g (95%) of nitroalkene (*Z*)-**5**: bp: 85 °C (0.15 Torr, air bath); ^{1}H NMR (300 MHz) 7.12 (t, J = 8.0, 1 H, HC(3)), 5.49 (m, 1 H, HC(7)), 5.34 (m, 1 H, HC(8)), 2.22 (m, 2 H, H$_2$C(4)), 2.14 (s, 3 H, H$_3$C(1)), 2.08 (m, 2 H, H$_2$C(6)), 1.55 (m, 5 H, H$_3$C(9), H$_2$C(5)); ^{13}C NMR (75.5 MHz) 147.64 (C(2), 136.13 (C(3)), 129.14 (C(7)), 125.00 (C(8)), 28.02 (C(6)), 27.47 (C(4)), 26.22 (C(5)), 12.73 (C(1)), 12.40 (C(9)); IR (CCl$_4$) 1674 (w), 1526 (s), 1333 (s); TLC R_f 0.56 (hexane/EtOAc (4/1)); GC t_R 8.32 min (OV-17, 50 m, 130 °C, isothermal). Anal. Calcd for C$_9$H$_{15}$NO$_2$ (169.22): C, 63.88; H, 8.93; N, 8.28. Found: C, 63.64; H, 8.92; N, 8.40.

General Procedure for the Tandem Cycloadditions. Preparation of Nitronates. To a cold (-78 °C), magnetically-stirred solution of the nitroalkene in CH$_2$Cl$_2$ (0.25 M) was added a solution of freshly prepared TiCl$_2$(O*i* -Pr)$_2$ (2.4 equiv) in CH$_2$Cl$_2$ (3 mL). The resulting pale yellow solution was stirred at -78 °C for 10 min and *n*-butyl vinyl ether (1.5 equiv) was added and allowed to stir at -78 °C. After the indicated time, the mixture was quenched with 1 N NaOH in methanol (1 mL/mL CH$_2$Cl$_2$) at -78 °C and was allowed to warm to RT. The mixture was poured into CH$_2$Cl$_2$ and washed with H$_2$O and brine. The aqueous layers were back extracted with CH$_2$Cl$_2$ and the combined organic extracts were dried (MgSO$_4$/NaHCO$_3$ (1/1)), filtered and concentrated. The residue was purified by column chromatography on silica gel to afford a mixture of the nitronate anomers as a clear oil.

Preparation of Nitroso Acetals. A magnetically-stirred solution of the nitronates in benzene (0.05 M) was treated with NaHCO$_3$ (~50 mg) and was heated to 70 °C. After the indicated time, the mixture was filtered and the filtrate was concentrated to give a pale yellow oil. The residue was purified by column chromatography on silica gel to provide the separated nitroso acetal anomers which could be distilled to afford clear oils.

***rel*-(4*R*,6(*R*,*S*))-4-(3-Butenyl)-6-butoxy-3-methyl-5,6-dihydro-4H-[1,2]-oxazine-*N*-oxide (15a/b).** From nitroalkene **1** (400 mg, 2.832 mmol), TiCl$_2$(O*i* -Pr)$_2$ (7.364 mmol, 2.4 equiv) and *n*-butyl vinyl ether (0.55 mL, 4.248 mmol, 1.5 equiv) in CH$_2$Cl$_2$ (14 mL). Reaction time: 30 min. Purification (silica gel, hexane/EtOAc (3/1-1/1)) afforded 578 mg (85%) of nitronates **15a/b** as a clear oil. Data for **15b**: ^{1}H NMR (300 MHz) 5.77 (m, 1 H, HC(10)), 5.28 (m, 1 H, HC(6)), 5.08-5.00 (m, 2 H, H$_2$C(11)), 3.93 (dt, J_d = 9.6, J_t = 6.7, 1H, HC(12)), 3.60 (dt, J = 9.6, 6.5, 1 H, HC(12)), 2.65 (q, J = 6.3, 1 H, HC(4)), 2.06 (s, 3 H, H$_3$C(7)), 1.86-1.30 (m, H), 0.90 (t, J = 7.3, 3 H, H$_3$C(15)); ^{13}C NMR (75.5 MHz) 136.85 (C(10)), 124.49 (C(3)), 115.57 (C(11)), 100.90 (C(6)), 68.79 (C(12)), 32.65 (C(4)), 31.38 (C(13)), 31.22 (CH$_2$), 30.29 (CH$_2$), 30.17 (CH$_2$), 18.95 (C(14)), 16.51 (C(7)), 13.62 (C(15)); TLC R_f 0.34 and 0.29 (hexane/EtOAc (1/1)).

rel **(3*R*,5*S*,6a*S*,8a*S*,8b*R*)-5-Butoxy-8b-methyl-6a,7,8,8a-tetrahydrocyclopenta [1,2,3-*hj*]isooxazolo[2,3-*b*][1,2]oxazine (16a)** and ***rel*** **(3*R*,5*R*,6a*S*,8a*S*,8b*R*)-5-Butoxy-8b-methyl-6a,7,8,8a-tetrahydrocyclopenta[1,2,3-*hj*]isooxazolo[2,3*b*][1,2]oxazine (16a).** From, nitronates **20** (540 mg, 2.38 mmol) and $NaHCO_3$ (~50 mg) in benzene (40 mL). Reaction time: 13 h. Purification (silica gel, hexane/EtOAc (10/1)) and bulb-to-bulb distillation afforded 107 mg (20%) of **16a** and 340 mg (63%) of **16b** as clear oils. Data for **16a**: bp 78-80 °C (0.08 Torr, air bath); ^1H NMR (300 MHz) 5.09 (dd, *J* = 6.5, 3.6, 1 H, HC(5)), 4.38 (t, *J* = 8.7, 1 H, HC(1)), 4.08 (t, *J* = 8.4, 1 H, HC(1)), 3.87 (td, J_t = 9.7, J_d = 6.8, 1 H, HC(10)), 3.51 (dt, J_d = 9.7, J_t = 6.8, 1 H, HC(10)), 2.63 (q, *J* = 8.6, 1 H, HC(8a)), 2.11-1.29 (m, 11 H), 1.26 (s, 3 H, $H_3C(9)$), 0.90 (t, *J* = 7.3, 3 H, $H_3C(13)$); ^{13}C NMR (75.5 MHz) 99.64 (C(5)), 82.32 (C(8b)), 77.67 (C(1)), 69.59 (C(10)), 52.98 (C(8a)), 43.45 (C(6a)), 34.59 (CH_2), 31.86 (C(11)), 28.88 (CH_2), 27.76 (CH_2), 25.00 (C(9)), 19.16 (C(12)), 13.83 (C(13)); TLC R_f 0.46 (hexane/EtOAc (10/1)); GC t_R 12.22 min (HP - 5, 200 °C, isothermal). Anal. Calcd for $C_{13}H_{23}NO_3$ (241.33): C, 64.70; H, 9.61; N, 5.80. Found: C, 64.79; H, 9.63; N, 5.79. Data for **16b**: bp 135-138 °C (0.5 Torr, air bath); ^1H NMR (300 MHz) 5.00 (t, *J* = 7.5, 1 H, HC(5)), 4.41 (t, *J* = 8.7, 1 H, HC(1)), 4.03 (t, *J* = 8.3, 1 H, HC(1)), 3.90 (dt, J_d = 9.8, J_t = 6.9, 1 H, HC(10)), 3.43 (dt, J_d = 9.7, J_t = 7.2, 1 H, HC(10)), 2.65 (q, *J* = 8.6, 1 H, HC(8a)), 1.29 (s, 3 H, $H_3C(9)$), 0.90 (t, *J* = 7.3, 3 H, $H_3C(13)$); ^{13}C NMR (75.5 MHz) 98.70 (C(5)), 84.74 (C(8b)), 78.09 (C(1)), 67.93 (C(10)), 52.16 (C(8a)), 43.12 (C(6a)), 31.57 (C(11)), 31.51 (CH_2), 28.38 (CH_2), 26.84 (CH_2), 23.96 (C(9)), 19.20 (C(12)), 13.87 (C(13)); TLC R_f 0.33 (hexane/EtOAc (10/1)); GC t_R 13.15 min (HP-5, 200 °C, isothermal). Anal. Calcd for $C_{13}H_{23}NO_3$ (241.33):C, 64.70; H, 9.61; N, 5.80. Found: C, 64.87; H, 9.61; N, 5.81.

rel**-(4*R*,6(*R*,*S*))-6-Butoxy-3-methyl-2-oxido-4-(3*E*-pentenyl)-5,6-dihydro-4H-[1,2]-oxazine (17a/b).** From nitroalkene (*E*)-2 (400 mg, 2.58 mmol), $TiCl_2(O\textit{i}\text{-}Pr)_2$ (6.70 mmol, 2.6 equiv), and *n*-butyl vinyl ether (0.5 mL, 3.865 mmol, 1.5 equiv) in CH_2Cl_2 (14 mL). Reaction time: 75 min. Purification (silica gel, hexane/EtOAc (3/1-1/1)) afforded 566 mg (86%) of **17a/b** as a clear oil. Data for **17b**: ^1H NMR (300 MHz) 5.50-5.33 (m, 2 H, HC(11), HC(10)), 5.29-5.26 (m, 1 H, HC(6)), 3.95 (dt, J_d = 9.6, J_t = 6.7, 1 H, HC(13)), 3.59 (dt, J_d = 9.6, J_t = 6.5, 1 H, HC(13)), 2.62 (q, *J* = 6.5, 1 H, HC(4)), 2.05 (s, 3 H, $H_3C(7)$), 2.04-1.30 (m, 10 H), 1.65 (d, *J* = 5.8, 3 H, $H_3C(12)$), 0.90 (t, *J* = 7.3, 3 H, $H_3C(16)$); ^{13}C NMR (75.5 MHz) 129.25 (C(10)), 126.15 (C(11)), 124.68 (C(3)), 100.93 (C(6)), 68.81 (C(13)), 32.65 (C(4)), 32.07 (CH_2), 31.24 (C(14)), 30.29 (CH_2), 29.07 (CH_2), 18.97 (C(15)), 17.77 (C(12)), 16.53 (C(7)), 13.64 (C(16)); TLC R_f 0.45 and 0.32 (hexane/EtOAc (1/1)).

rel **(1*S*,3*R*,5*S*,6a*S*,8a*S*,8b*R*)-5-Butoxy-1,8b-dimethyl-6a,7,8,8a-tetrahydrocyclo penta-[1,2,3-*hj*]isooxazolo[2,3-*b*][1,2]oxazine (18a)** and **(1*S*,3*R*,5*R*,6a*S*,8a*S*,8b*R*)-5-Butoxy-1,8b-dimethyl-6a,7,8,8a-tetrahydrocyclopenta[1,2,3-*hj*]isooxazolo[2,3-*b*] [1,2]oxazine (18b).** From a mixture of nitronates **22a/b** (550 mg, 2.15 mmol) and $NaHCO_3$ (~50 mg) in benzene (40 mL). Reaction time: 12 h. Purification (silica gel, hexane/EtOAc (10/1)) and bulb-to-bulb distillation afforded 64 mg (12%) of **18a** and 374 mg (68%) of **18b** as clear oils. Data for **18a**: bp 83-85 °C (0.08 Torr, air bath); ^1H NMR (300 MHz) 5.06 (dd, *J* = 6.7, 3.7, 1 H, HC(5)), 4.50 (dq, J_d = 8.1, J_q = 6.3, 1 H, HC(1)), 3.87 (dt, J_d = 9.7, J_t = 6.7, 1H, HC(11)), 3.50 (dt, J_d = 9.7, J_t = 6.8, 1H, HC(11)), 2.12 (q, *J* = 8.2, 1 H, HC(8a)), 2.05-1.30 (m, 11 H), 1.35 (d, *J* = 6.2, 3 H, $H_3C(10)$), 1.26 (s, 3 H, $H_3C(9)$), 0.89 (t, *J* = 7.3, 3 H, $H_3C(14)$); ^{13}C NMR (75.5 MHz) 99.56 (C(5)), 86.18 (C(1)), 83.06 (C(8b)), 69.61 (C(11), 60.59 (C(8a)), 43.94 (C(6a)), 34.88 (CH_2), 31.88 (C(12)), 28.73 (CH_2), 27.12 (CH_2), 25.36(C(9)), 19.17(C(13)), 18.14 (C(10)), 13.85 (C(14)); TLC R_f 0.51 (hexane/EtOAc, 10/1); GC t_R 11.99 min (HP-5, 200 °C, isothermal). Anal. Calcd for $C_{14}H_{25}NO_3$ (255.36): C, 65.85; H, 9.87; N, 5.49. Found: C, 66.09; H, 9.89; N, 5.55. Data for **18b**: bp 85-87 °C (0.08 Torr, air bath); ^1H NMR (300 MHz) 4.98 (t, *J* = 7.5, 1 H, HC(5))), 4.47 (dq, *J* = 7.9, 6.2, 1 H, HC(1)), 3.88 (dt, J_d = 9.7, J_t = 6.9, 1 H, HC(11)), 3.39 (dt, J_d = 9.7, J_t = 7.1, 1 H, HC(11)), 2.09 (q, *J* = 8.5, 1 H, HC(8a)), 2.08-1.53 (m, 11 H), 1.33 (d, *J* = 6.2. 3 H, $H_3C(10)$), 1.28 (s, 3 H, $H_3C(9)$), 0.88 (t, *J* = 7.3, 3 H, $H_3C(14)$); ^{13}C NMR (75.5 MHz) 98.48 (C(5)), 86.27 (C(1)), 85.02 (C(8b)), 67.62 (C(11)), 59.65 (C(8a)), 43.41 (C(6a)), 31.52 (C(12)), 31.41 (CH_2), 27.53 (CH_2), 26.33 (CH_2), 24.25 (C(9)), 19.08 (C(13)), 18.15 (C(10)), 13.74 (C(14)); TLC R_f 0.40 (hexane/EtOAc (10/1)); GC t_R 12.85 min (HP-5, 200 °C, isothermal). Anal. Calcd for $C_{14}H_{25}NO_3$ (255.36): C, 65.85; H, 9.87; N, 5.49. Found: C, 65.80; H, 9.90; N, 5.48.

***rel*-(4*R*,6(*R*,*S*))-6-Butoxy-3-methyl-4-(3*Z*-pentenyl)-5,6-dihydro-4H-[1,2]oxazine-*N*-oxide (19a/b).** From nitroalkene (*Z*)-**2** (400 mg, 2.577 mmol), $TiCl_2(Oi\text{-}Pr)_2$ (6.70 mmol, 2.6 equiv) and *n*-butyl vinyl ether (0.50 mL, 3.87 mmol, 1.5 equiv) in CH_2Cl_2 (13 mL). Reaction time: 2 h. Purification (silica gel, hexane/EtOAc (3/1-1/1)) afforded 580 mg (88%) of a mixture of nitronates **19a/b** as a clear oil. Data for **19b**: ^{1}H NMR (300 MHz) 5.54-5.43 (m, 1 H, HC(11)), 5.35-5.24 (m, 2 H, HC(6), HC(10)), 3.94 (dt, J_d = 9.6, J_t = 6.7, 1 H, HC(13)), 3.58 (dt, J_d = 9.6, J_t = 6.5, 1 H, HC(13)), 2.65 (q, J = 8.0, 1 H, HC(4)), 2.04 (s, 3 H, $H_3C(7)$), 2.04-1.30 (m, 10 H), 1.58 (d, J = 6.6, 3 H, $H_3C(12)$), 0.88 (t, J = 7.3, 3 H, $H_3C(16)$); ^{13}C NMR (75.5 MHz) 128.53 (C(10)), 125.19 (C(11)), 124.66 (3)), 100.96 (C(6)), 68.86 (C(13)), 32.80 (C(4)), 31.94 (CH_2), 31.28 (C(14)), 30.35 (CH_2), 23.39 (CH_2), 19.01 (C(15)), 16.56 (C(7)),13.67 (C(16)), 12.70 (C(12)); TLC R_f 0.45 and 0.31 (hexane/EtOAc (1/1)).

***rel*-(1*R*,3*S*,5*R*,6a*R*,8a*R*,8b*S*)-5-Butoxy-1,8b-dimethyl-6a,7,8,8a-tetrahydrocyclopenta[1,2,3-*hj*]isooxazolo[2,3-*b*][1,2]oxazine (20a) and *rel*-(1*R*,3*S*,5*S*,6a*R*,8a*R*, 8b*S*)-5-Butoxy-1,8b-dimethyl-6a,7,8,8a-tetrahydrocyclopenta [1,2,3-*hj*]isooxazolo [2,3-*b*][1,2]oxazine (20b).** From a mixture of nitronates **19a/b** (570 mg, 2.23 mmol) and $NaHCO_3$ (~50 mg) in benzene (45 mL). Reaction time: 33 h. Purification (silica gel, hexane/EtOAc (10/1)) and bulb-to-bulb distillation afforded 98 mg (17%) of **20a** and 305 mg (54%) of **20b** along with 52 mg (9%) of mixture of **20a** and **20b** as clear oils. Data for **20a**: bp 85-87°C (0.08 Torr, air bath); ^{1}H NMR (300 MHz) 5.00 (t, J = 5.2, 1 H, HC(5)), 4.47 (quintet, J = 7.2, 1 H, HC(1)), 3.85 (dt, J_d = 9.7, J_t = 6.7, 1H, HC(11)), 3.49 (dt, J_d = 9.7, J_t = 6.6, 1H, HC(11)), 2.55 (q, J = 7.3, 1 H, HC(8a)), 1.98-1.50 (m, 11 H), 1.35 (d, J = 6.8, 3 H, $H_3C(10)$), 1.26 (s, 3 H, $H_3C(9)$), 0.89 (t, J = 7.3, 3 H, $H_3C(14)$); ^{13}C NMR (75.5 MHz) 100.13 (C(5)), 81.15 (C(8b)), 80.40 (C(1)), 69.01 (C(11)), 55.39 (C(8a)), 41.95 (C(6a)), 33.94 (CH_2), 31.87 (C(12)), 29.18 (CH_2), 25.38 (CH_2), 24.50 (C(9)), 19.17 (C(13)), 16.87 (C(10)), 13.79 (C(14)); TLC R_f 0.38 (hexane/EtOAc (10/1); GC t_R 13.85 min (HP-5, 200 °C, isothermal). Anal. Calcd for $C_{14}H_{25}NO_3$ (255.36): C, 65.85; H, 9.87; N, 5.49. Found: C, 65.91; H, 9.88; N, 5.48. Data for **20b**: bp 85-87 °C (0.08 Torr, air bath); ^{1}H NMR (300 MHz) 4.98 (dd, J = 8.0, 6.6, 1 H, HC(5)), 4.62 (dq, J = 7.4, 6.7, 1 H, HC(1)), 3.89 (dt, J_d = 9.7, J_t = 6.7, 1H, HC(11)), 3.41 (dt, J_d = 9.7, J_t = 7.1, 1 H, HC(11)), 2.61 (q, J = 8.6, 1 H, HC(8a)), 2.18-1.53 (m, 11 H), 1.37 (d, J = 6.7.,3 H, $H_3C(10)$), 1.29 (s, 3 H, $H_3C(9)$), 0.89 (t, J = 7.3, 3 H, $H_3C(14)$); ^{13}C NMR (75.5 MHz) 97.75 (C(5)), 83.33 (C(8b)), 82.84 (C(1)), 68.09 (C(11), 54.89 (C(8a)), 42.46 (C(6a)), 32.46 (CH_2), 31.60 (C(12)), 28.70 (CH_2), 26.08 (CH_2), 23.02 (C(9)), 19.16 (C(13)), 17.43 (C(10)), 13.84 (C(14)); TLC R_f 0.29 (hexane/EtOAc (10/1)); GC t_R 14.72 min (HP - 5, 200 °C, isothermal). Anal. Calcd for $C_{14}H_{25}NO_3$ (255.36): C, 65.85; H, 9.87; N, 5.49. Found: C, 66.02; H, 9.88; N, 5.66.

***rel*-(4*R*,6(*R*,*S*))-6-Butoxy-3-methyl-4-[(4-methyl)-3-pentenyl]-5,6-dihydro-4H-[1,2]-oxazine-*N*-oxide (21a/b).** From nitroalkene **3** (300 mg, 1.77 mmol), $TiCl_2(Oi\text{-}Pr)_2$ (4.61 mmol, 2.6 equiv) and *n*-butyl vinyl ether (0.34 mL, 2.69 mmol, 1.5 equiv) in CH_2Cl_2 (9 mL) . Reaction time: 2.5 h. Purification (silica gel, hexane/EtOAc (3/1-2/1)) afforded a mixture of nitronates **21a/b** which although still impure was taken on to th next step. Data for **21b**: ^{1}H NMR (300 MHz) 5.28 (d, J = 2.3, 1 H, HC(6)), 5.06 (t, J = 6.9, 1 H, HC(10)), 3.95 (dt, J_d = 9.6, J_t = 6.8, 1 H, HC(14)), 3.58 (dt, J_d = 9.6, J_t = 6.5, 1 H, HC(14)), 2.05 (s, 3 H, $H_3C(7)$), 2.04-1.30 (m , 11 H), 1.69 (s, 3 H, $H_3C(13)$), 1.60 (s, 3 H, $H_3C(12)$), 0.90 (t, J = 7.3, 3 H, $H_3C(17)$); ^{13}C NMR (75.5 MHz) 132.57 (C(11)), 124.61 (C(3)), 122.51 (C(10)), 100.81 (C(6)), 68.64 (C(14)), 32.63 (C(4)), 32.07 (CH_2), 31.12 (CH_2), 30.17 (CH_2), 25.43 (C(15)), 19.25 (C(12)), 17.42 (CH_2), 16.36 (C(13)), 13.74 (C(17)),13.51 (C(7)); TLC R_f 0.21 and 0.33 (hexane/EtOAc (1/1)).

***rel*-(3*R*,5*S*,6a*S*,8a*S*,8b*R*)-5-Butoxy-1,1,8b-trimethyl-6a,7,8,8a-tetrahydrocyclopenta [1,2,3-*hj*]isooxazolo[2,3-*b*][1,2]oxazine (22a) and (3*R*,5*R*,6a*S*,8a*S*,8b*R*)-5-Butoxy-1,1,8b-trimethyl-6a,7,8,8a-tetrahydrocyclopenta[1,2,3-*hj*]isooxazolo[2,3-*b*][1,2] oxazine (22b).** From a mixture of nitronates **26a/b** and $NaHCO_3$ (~50 mg) in benzene (40 mL). Reaction time: 18 h. Purification (silica gel, hexane/EtOAc (10/1)) and bulb-to-bulb distillation afforded 41 mg (9%) of **22a** and 291 mg (61%) of **22b**, as clear oils. Data for **22a**: bp 118-120 °C (0.01 Torr, air bath);.^{1}H NMR (300 MHz) 4.98 (dd, J = 5.9 3.8, 1 H, HC(5)), 3.83 (dt, J_d = 9.8, J_t = 6.7, 1H, HC(12)), 3.49 (dt, J_d = 9.8, J_t = 6.6, 1H, HC(12)), 2.36 (dd, J = 9.4, 3.8, 1 H, HC(8a)), 2.05-1.48(m, 11 H), 1.47 (s, 3 H, H_3C), 1.36 (s, 3 H, H_3C), 1.30 (s, 3 H, H_3C), 0.89

(t, *J* = 7.3, 3 H, H$_3$C(15)); ^{13}C NMR (75.5 MHz) 99.84 (C(5)), 92.27 (C(1)), 84.38 (C(8b)), 69.33 (C(12), 61.78 (C(8a)), 43.52 (C(6a)), 35.29 (CH$_2$), 31.98 (CH$_2$), 30.89 (CH$_3$), 29.63 (CH$_2$), 26.60 (CH$_2$), 25,74 (CH$_3$), 19.23 (CH$_2$), 13.79 (C(15)); TLC *R$_f$* 0.32 (hexane/EtOAc, 8/1); GC *t*$_R$ 13.571 min (HP-5, 200 °C, isothermal). Anal. Calcd for $C_{15}H_{27}NO_3$ (269.38): C, 66.88; H, 10.10; N, 5.20. Found: C, 66.81; H, 10.09; N, 5.20. Data for **22b**: bp 118-120 °C (0.01 Torr, air bath); ^{1}H NMR (300 MHz) 4.91 (t, *J* = 7.3, 1 H, HC(5)), 3.86 (dt, *J*$_d$ = 9.7, *J*$_t$ = 6.9, 1H, HC(12)), 3.37 (dt, *J*$_d$ = 9.7, *J*$_t$ = 7.1, 1H, HC(12)), 2.35 (dd, *J* = 9.5, 3.7, 1 H, HC(8a)), 2.03-1.50 (m, 11 H), 1.42 (s, 3 H, H$_3$C), 1.34 (s, 3 H, H$_3$C), 1.31 (s, 3 H, H$_3$C), 0.87 (t, *J* = 7.3, 3 H, H$_3$C(15)); ^{13}C NMR (75.5 MHz) 98.04 (C(5)), 92.77 (C(1)), 85.82 (C(8b)), 67.84 (C(12), 61.06 (C(8a)), 43.46 (C(6a)), 32.66 (CH$_2$), 31.64 (CH$_2$), 30.94 (CH$_3$), 27.76 (CH$_2$), 27.22 (CH$_2$), 25.98 (CH$_3$), 24.59 (CH$_3$), 19.26 (C(14), 13.97 (C(15)); TLC *R$_f$* 0.27 (hexane/EtOAc (8/1)); GC *t*$_R$ 14.04 min (HP-5, 200 °C). Anal. Calcd for $C_{15}H_{27}NO_3$ (269.38): C, 66.88; H, 10.10; N, 5.20. Found: C, 66.78; H, 10.10; N, 5.21.

***rel*-(1*S*,3*R*,5*S*,6a*S*,9a*R*,9b*R*)-5-Butoxy-1-methylhexahydro-1H-isooxazolo[2,3,4-*h*][2,1]benzoxazine (24a) and (1*S*,3*R*,5*R*,6a*S*,9a*R*,9b*R*)-5-Butoxy-1-methylhexahydro-1H-isooxazolo[2,3,4-*h*][2,1]benzoxazine (24b).** From nitroalkene (*E*)-**4** (300 mg, 1.937 mmol), TiCl$_2$(O*i*-Pr)$_2$ (5.026 mmol, 2.6 equiv) and *n*-butyl vinyl ether (0.375 mL, 2.90 mmol, 1.5 equiv) in CH$_2$Cl$_2$ (10 mL). Reaction time: 45 min. A solution of the crude nitronates **23a/b** and NaHCO$_3$ (~50 mg) in benzene (25 mL) was heated to 80 °C. Reaction time: 32 h. Purification (silica gel, hexane/EtOAc (10/1)) and bulb-to-bulb distillation afforded 281 mg (59%) of **24a** and 63 mg (13%) of **24b** (72%) as clear oils. Data for **24a**: bp 120-123 °C (0.1 Torr, air bath); ^{1}H NMR (300 MHz) 4.76 (dd, *J* = 9.2, 2.5, 1 H, HC(5)), 4.43 (quintet, *J* = 6.2, 1 H, HC(1)), 3.92 (dt, *J*$_d$ = 9.5, *J*$_t$ = 7.0, 1 H, HC(11)), 3.52 (dt, *J*$_d$ = 9.5, *J*$_t$ = 7.1, 1 H, HC(11)), 3.52 (d, *J* = 9.5, 1 H, HC(9b)), 2.44 (m, 1 H, HC(6a)), 1.91-1.82 (m, 1 H, HC(9a)), 1.77-1.32 (m, 12 H), 1.33 (d, *J* = 6.4. 3 H, H$_3$C(10)), 0.86 (t, *J* = 7.3, 3 H, H$_3$C(14)); ^{13}C NMR (75.5 MHz) 100.07 (C(5)), 85.30 (C(1)), 69.31 (C(11)), 68.29 (C(9b)), 43.62 (C(9a)), 32.62 (CH$_2$), 31.62 (CH$_2$), 27.97 (C(6a)), 24.22 (CH$_2$), 23.43 (CH$_2$), 19.06 (CH$_2$), 18.46 (C(10)), 16.56 (C(13)), 13.80 (C(14)); TLC *R$_f$* 0.22 (hexane/EtOAc (10/1)); GC *t*$_R$ 8.78 min (HP-5, 200 °C, isothermal). Anal. Calcd for $C_{14}H_{25}NO_3$ (255.40): C, 65.85; H, 9.87; N, 5.49. Found: C, 65.66; H, 9.91; N, 5.46. Analytical data for **24b**: bp 120 -123 °C (0.1 Torr, air bath);.^{1}H NMR (300 MHz) 4.95 (t, *J* = 7.1, 1 H, HC(5)), 4.40 (quintet, *J* = 5.8, 1 H, HC(1)), 3.88 (dt, *J*$_d$ = 9.4, *J*$_t$ = 6.9, 1H, HC(11)), 3.66 (t, *J* = 9.5, 1 H, HC(9b)), 3.40 (dt, *J*$_d$ = 9.5, *J*$_t$ = 7.0, 1 H, HC(11)), 2.34-2.26 (m, 1 H, HC(6a)), 2.07-1.82 (m, 3 H, H$_2$C(6), HC(9a)), 1.73-1.10 (m, 10 H), 1.33 (d, *J* = 6.3, 3 H, H$_3$C(10)), 0.90 (t, *J* = 7.3, 3 H, H$_3$C(14)); ^{13}C NMR (75.5 MHz) 99.96 (C(5)), 87.97 (C(1)), 67.74 (C(11)), 67.52 (C(9b)), 44.78 (C(9a)), 31.69 (CH$_2$), 31.11 (CH$_2$), 29.49 (C(6a)), 29.33 (CH$_2$), 28.77 (CH$_2$), 22.46 (CH$_2$), 19.60 (C(10)), 19.34 (CH$_2$), 13.98 (C(14)); TLC *R$_f$* 0.17 (hexane/EtOAc (10/1)); GC *t*$_R$ 8.96 min (HP-5, 200 °C, isothermal). Anal. Calcd for $C_{14}H_{25}NO_3$ (255.40): C, 65.85; H, 9.87; N, 5.49. Found: C, 65.73; H, 9.89; N, 5.48.

***rel*-(1*R*,3*R*,5*S*,6a*S*,9a*R*,9b*R*)-5-Butoxy-1-methylhexahydro-1H-isooxazolo[2,3,4-*h*]-[2,1]-benzoxazine (26a) and (1*R*,3*R*,5*R*,6a*S*,9a*R*,9b*R*)-5-Butoxy-1-methylhexahydro-1H-isooxazolo[2,3,4-*h*][2,1]benzoxazine (26b).** To nitroalkene (*E*)-**4** (300 mg, 1.937 mmol) and *n*-butyl vinyl ether (0.375 mL, 2.90 mmol, 1.5 equiv) in CH$_2$Cl$_2$ (6.7 mL) was added TiCl$_2$(O*i* -Pr)$_2$ (5.026 mmol, 2.6 equiv) in CH$_2$Cl$_2$ (3 mL). Reaction time: 45 min. A solution of the crude nitronates **25a/b** and NaHCO$_3$ (~50 mg in benzene (25 mL) was heated to 80 °C. Reaction time: 18 h. Purification (silica gel, hexane/EtOAc (10/1)) and bulb-to-bulb distillation afforded 337 mg (69%) of **26a** and 32 mg (7%) of **26b** as clear oils. Data for **26a**: bp 120 -23 °C (0.1 Torr, air bath);.^{1}H NMR (300 MHz) 4.68 (quintet, *J* = 6.8, 1 H, HC(1)), 4.66 (t, *J* = 9.6, 1 H, HC(5)), 3.95 (dt, *J*$_d$ = 9.4, *J*$_t$ = 6.7, 1H, HC(11)), 3.50 (dt, *J*$_d$ = 9.4, *J*$_t$ = 7.1, 1 H, HC(11)), 2.92 (dd, *J* = 12.2, 4.7, 1 H, HC(9b)), 2.79 (tdd, *J*$_t$ = 12.0, *J*$_d$ = 8.4, *J*$_d$ = 3.1, 1 H, HC(9a)), 2.58 (m, 1 H, HC(6a)), 1.86 (td, *J*$_t$ = 12.4, *J*$_d$ = 2.2, 1 H, HC(9)), 1.72-1.12 (m, 11 H), 1.08(d, *J* = 6.6. 3 H, H$_3$C(10)), 0.89 (t, *J* = 7.3, 3 H, H$_3$C(14)); ^{13}C NMR (75.5 MHz) 100.46 (C(5)), 80.67 (C(1)), 70.79 (C(9b)), 69.52 (C(11)), 36.79 (C(9a)), 31.63 (CH$_2$), 29.57 (CH$_2$), 29.53 (C(6a)), 28.09 (CH$_2$), 24.64 (CH$_2$), 21.34 (CH$_2$), 19.10 (CH$_2$), 15.91 (C(10), 13.86 (C(14)); TLC *R$_f$* 0.16 (hexane/EtOAc (10/1)); GC *t*$_R$ 10.48 min (HP-5, 200 °C, isothermal). Anal. Calcd for $C_{14}H_{25}NO_3$ (255.40): C, 65.85; H, 9.87; N, 5.49. Found: C, 65.79; H, 9.89; N, 5.53. Data for **26b**: bp 120-123 °C (0.1 Torr, air bath); ^{1}H NMR (300 MHz) 4.93 (d, *J* = 3.6, 1 H, HC(5)), 4.66 (dq, *J* = 8.7, 6.7, 1 H, HC(1)), 3.92 (dt, $J_d = 9.6$, $J_t = 6.9$, 1H, HC(11)), 3.43 (dt, $J_d = 9.6$, $J_t = 6.8$, 1 H, HC(11)), 3.00 (dd, $J = 12.0$, 4.7, 1 H, HC(9b)), 2.92 (m, 1 H, HC(6a)), 2.75 (tdd, $J_t = 12.0$, $J_d = 8.9$, $J_d = 3.2$, 1 H, HC(9a)), 1.87 (td, $J_t = 13.2$, $J_d = 3.6$, 1 H, HC(6)), 1.71-1.11 (m, 11 H), 1.08 (d, $J = 6.6$. 3 H, H_3C(10)), 0.91 (t, $J = 7.3$, 3 H, H_3C(14)); ^{13}C NMR (75.5 MHz) 100.10 (C(5)), 80.79 (C(1)), 71.09 (C(9b)), 67.04 (C(11)), 36.80 (C(9a)), 31.51(CH_2), 28.53 (CH_2), 26.77 (CH_2), 26.53 (C(6a)), 24.87 (CH_2), 21.08 (CH_2), 19.42 (CH_2), 16.12 (C(10), 14.03 (C(14)); TLC R_f 0.19 (hexane /EtOAc (10/1)); GC t_R 10.041 min (HP-5, 200 °C, isothermal). Anal. Calcd for $C_{14}H_{25}NO_3$ (255.40): C, 65.85; H, 9.87; N, 5.49. Found: C, 65.92; H, 9.89; N, 5.49.

***rel*-(4*R*,6(*R*,*S*))-6-Butoxy-4-(4*E*-hexenyl)-3-methyl-5,6-dihydro-4H-[1,2]-oxazine-*N*-oxide (27a/b).** To a solution of nitroalkene (*E*)-**5** (400 mg, 2.363 mmol) and *n*-butyl vinyl ether (0.5 mL, 3.54 mmol, 1.5 equiv) in CH_2Cl_2 (8.8 mL) was added $TiCl_2$(O*i* -Pr)$_2$ (6.14 mmol, 2.6 equiv) in CH_2Cl_2 (3 mL). Reaction time: 45 min. Purification (silica gel, hexane/EtOAc (3/1-1:2)) to afford 601 mg (94%) of a mixture of nitronates **27a/b** as a clear oil. Data foir **27a**: ^{1}H NMR (300 MHz) 5.47-5.29 (m, 2 H, HC(11), HC(12)), 5.28-5.22 (m, 1 H, HC(6)), 3.92 (dt, $J_d = 9.6$, $J_t = 6.8$, 1 H, HC(14)), 3.56 (dt, $J_d = 9.6$, $J_t = 6.5$, 1 H, HC(14)), 2.60 (q, $J = 8.1$, 1 H, HC(4)), 2.03 (s, 3 H, H_3C(7)), 1.63 (d, $J = 5.2$, 3 H, H_3C(13)), 1.38-1.28(m,11 H), 0.88 (t, $J = 7.3$, 3 H, H_3C(17)); ^{13}C NMR (75.5 MHz) 130.18 (C(11)), 125.52 (C(12)), 124.79 (C(3)), 100.91 (C(6)), 68.76 (C(14)), 32.92 (C(4)), 32.11 (CH_2), 31.44 (CH_2), 31.21 (CH_2), 30.28 (CH_2), 25.84 (CH_2), 18.95 (C(16)), 17.74 (C(13)), 16.44 (C(7)),13.62 (C(17)); TLC R_f 0.44 and 0.25 (hexane/EtOAc (1/1)).

***rel*-(1*S*,3*R*,5*S*,6a*S*,9a*R*,9b*R*)-5-Butoxy-1-9b-dimethylhexahydro-1H-isooxazolo[2,3,4*h*]-[2,1]benzoxazine (28a) and (1*S*,3*R*,5*R*,6a*S*,9a*R*,9b*R*)-5-Butoxy-1-9b-dimethylhexahydro-1H-isooxazolo[2,3,4-*h*][2,1]benzoxazine (28b).** From nitronates **27a/b** (590 mg, 2.19 mmol) and $NaHCO_3$ (~50 mg in toluene (30 mL) at 110 °C. Reaction time: 14 h. Purification (silica gel, hexane/EtOAc (10/1)) and bulb-to-bulb distillation afforded 452 mg (76%) of **28a** and 29 mg (5%) of **28b** as clear oils. Data for **28a**: bp 120-122 °C (0.05 Torr, air bath); ^{1}H NMR (300 MHz) 4.94 (t, $J = 7.2$, 1 H, HC(5)), 4.40 (quintet, $J = 6.2$, 1 H, HC(1)), 3.87 (dt, $J_d = 9.6$, $J_t = 6.8$, 1H, HC(12)), 3.40 (dt, $J_d = 9.5$, $J_t = 7.1$, 1 H, HC(12)), 2.03-1.55 (m, 12 H), 1.37 (d, $J = 6.3$, 3 H, H_3C(11)), 1.17 (m, 2 H), 1.15 (s, 3 H, H_3C(10)), 0.89 (t, $J = 7.3$, 3 H, H_3C(15)); ^{13}C NMR (75.5 MHz) 99.67 (C(5)), 88.86 (C(1)), 72.03 (C(9b)), 67.80 (C(12), 51.65 (C(9a)), 38.57 (C(6a)), 31.54 (CH_2), 30.57 (CH_2), 30.20 (CH_2), 29.79 (C(10)), 29.50, 22.29, 19.80 (C(11)), 19.19 (C(14)), 13.87 (C(15)); TLC R_f 0.28 (hexane/EtOAc (10/1)); GC t_R 18.079 min (HP-5, 200 °C, isothermal). Anal. Calcd for $C_{15}H_{27}NO_3$ (269.36): C, 66.88; H, 10.10; N, 5.20. Found: C, 66.89; H, 10.10; N, 5.15. Data for **28b**: bp 120-122 °C (0.05 Torr, air bath); ^{1}H NMR (300 MHz) 4.90 (d, $J = 3.1$, 1 H, HC(5)), 4.40 (m, 2 H, HC(1), HC(12)), 3.43 (dt, $J_d = 9.5$, $J_t = 6.7$, 1 H, HC(12)), 2.51-2.38 (m, 2 H), 1.96 (td, $J_t = 13.3$, $J_d = 3.5$, 1 H), 1.82-1.44 (m, 11 H), 1.41 (d, $J = 6.0$, 3 H, H_3C(11)),1.16 (s, 3 H, H_3C(10)), 0.91 (t, $J = 7.3$, 3 H, H_3C(15)); ^{13}C NMR (75.5 MHz) 99.47 (C(5)), 81.93 (C(1)), 71.84 (C(9b)), 66.85 (C(12)), 44.04 (C(9a)), 33.05 (C(6a)), 31.52 (CH_2), 27.47 (CH_2), 25.90 (CH_2), 22.81 (CH_2), 21.28 (CH_2), 20.50 (C(10)), 19.34 (C(14)), 18.39 (C(11)), 13.99 (C(15)); TLC R_f 0.25 (hexane/EtOAc (10/1)); GCt_R 17.64 min (HP-5, 200 °C, isothermal). Anal. Calcd for $C_{15}H_{27}NO_3$ (269.36): C, 66.88; H, 10.10; N, 5.20. Found: C, 66.91; H, 10.11; N, 5.19.

rel-(4*R*,6(*R*,*S*))-6-Butoxy-4-(4*Z*-hexenyl)-3-methyl-5,6-dihydro-4H-[1,2]-oxazine-*N*-oxide (29a/b). To a cold (-78 °C), magnetically-stirred solution of nitroalkene (*E*)-**5** (400 mg, 2.363 mmol) and *n*-butyl vinyl ether (0.48 mL, 3.54 mmol, 1.5 equiv) in CH_2Cl_2 (8.8 mL) was added $TiCl_2$(O*i* -Pr)$_2$ (6.14 mmol, 2.6 equiv) in CH_2Cl_2 (3 mL). Reaction time: 60 min. Purification (silica gel, hexane/EtOAc (3/1-1/2)) afforded 597 mg (94%) of a mixture of nitronates **29a/b** as a clear oil. Data for **29a**: ^{1}H NMR (300 MHz) 5.51-5.41 (dq, $J = 10.8$, 6.6, 1 H, HC(12)), 5.39-5.28 (m, 2 H, HC(6), HC(11)), 3.93 (dt, $J = 9.6$, 6.8, 1 H, HC(14)), 3.57 (dt, $J_d = 9.6$, $J_t = 6.5$, 1 H, HC(14)), 2.61 (q, $J = 8.3$, 1 H, HC(4)), 2.04 (s, 3 H, H_3C(7)), 1.58 (d, $J = 6.4$, 3 H, H_3C(13)), 1.39-1.29 (m , 12 H), 0.89 (t, $J = 7.3$, 3 H, H_3C(17)); ^{13}C NMR (75.5 MHz) 129.32 (C(11)), 124.73 (C(3)), 124.27 (C(12)), 100.89 (C(6)), 68.73 (C(14)), 32.94 (C(14)), 31.49 (CH_2), 31.19 (CH_2), 30.26 (CH_2), 26.32 (CH_2), 25.82 (CH_2), 18.93 (C(16)), 16.40 (C(7)), 13.59 (C(13)),12.63 (C(17)); TLC R_f 0.41 and 0.24 (hexane/EtOAc (1/1)).

***rel*-(1*R*,3*R*,5*S*,6a*S*,9a*R*,9b*R*)-5-Butoxy-1-9b-dimethylhexahydro-1H-isooxazolo[2,3,4*h*]-[2,1]benzoxazine (30a) and (1*R*,3*R*,5*R*,6a*S*,9a*R*,9b*R*)-5-Butoxy-1-9b-dimethylhexahydro-1H-isooxazolo[2,3,4-*h*][2,1]benzoxazine (30b).** From nitronates **29a/b** (580 mg, 2.15 mmol) and $NaHCO_3$ (~50 mg) in toluene (30 mL) at 110 °C. Reaction time: 9 h. Purification (silica gel, hexane/EtOAc (10/1)) and bulb-to-bulb distillation afforded 74 mg of **30a** (13%) and 334 mg (58%) of **30b** as clear oils. Data for **30a**: bp 120-122 °C (0.05 Torr, air bath); ^1H NMR (300 MHz) 4.87 (t, J = 7.0, 1 H, HC(5)), 4.63 (quintet, J = 6.8, 1 H, HC(1)), 3.87 (dt, J_d = 9.6,J_t = 6.9, 1H, HC(12)), 3.39 (dt, J_d = 9.5, J_t = 7.4, 1 H, HC(12)), 2.06 (td, J_t = 13.3, J_d = 6.7, 1 H, HC(9a)), 1.92-1.36 (m, 13 H), 1.32(d, J = 6.4, 3 H, H_3C(11)), 1.15 (s, 3 H, H_3C(10)), 0.87 (t, J = 7.3, 3 H, H_3C(15)); ^{13}C NMR (75.5 Hz) 99.79 (C(5)), 83.17 (C(1)), 72.17 (C(9b)), 68.03 (C(12), 48.05 (C(9a)), 38.08 (C(6a)), 31.61 (CH_2), 30.51 (CH_2), 29.23 (CH_2), 26.32 (C(10)), 24.18 (CH_2), 23.23 (CH_2), 19.25 (C(14)), 16.34 (C(11)), 13.95 (C(15)); TLC R_f 0.17 (hexane/EtOAc (10/1)); GC t_R 20.50 min (HP-5, 200 °C, isothermal). Anal.Calcd for $C_{15}H_{27}NO_3$ (269.36): C, 66.88; H, 10.10; N, 5.20. Found: C, 67.04; H, 10.07; N,.5.19. Data for **30b**: bp 120-122 °C (0.05 Torr, air bath); ^1H NMR (300 MHz) 4.89 (d, J = 3.6, 1 H, HC(5))), 4.56 (dq, J = 9.8, 6.9, 1 H, HC(1)), 3.92 (dt, J_d = 9.5, J_t = 6.9, 1H, HC(12)), 3.41 (dt, J_d = 9.5, J_t = 6.5, 1 H, HC(12)), 2.90 (td, J_t = 9.8, J_d = 2.8, 1 H, HC(9a)), 2.48-2.42 (m, 1 H, HC(6a)), 1.95 (td, J_t = 13.2, J_d = 3.7, 1 H, HC(6)), 1.81-1.26 (m, 11 H), 1.24 (s, 3 H, H_3C(10)), 1.18 (d, J = 6.9, 3 H, H_3C(11)), 0.90 (t, J = 7.3, 3 H, H_3C(15)); ^{13}C NMR (75.5 MHz) 99.25 (C(5)), 79.68 (C(1)), 71.74 (C(9b)), 66.52 (C(12)), 38.57 (C(9a)), 34.28 (C(6a)), 31.32 (CH_2), 27.35 (CH_2), 25.76 (CH_2), 21.71 (CH_2), 20.45 (C(10)), 19.21 (C(14)), 16.39 (C(11)), 13.81 (C(15)); TLC R_f 0.27 (hexane/EtOAc, 10/1); GC t_R 25.71 min (HP-5, 200 °C, isothermal). Anal. Calcd for $C_{15}H_{27}NO_3$ (269.36): C, 66.88; H, 10.10; N, 5.20. Found: C, 66.92; H, 10.14; N, 5.17.

General Procedure for the Hydrogenation of Nitroso Acetals. To a solution of the nitroso acetal (ca. 1.0 mmol) in methanol (10 mL) was added a catalytic amount of W-2 Raney nickel. The suspension was allowed to stir at RT under an atmosphere of hydrogen. After 24 h, the mixture was filtered through a celite pad and concentrated to afford the crude amino alcohol as a white solid, which was purified by distillation or recrystallization.

Preparation of rel (2*S*,2a*R*,5a*S*)-[2a-methylperhydro[*b*]pyrrolo]]cyclopentanemethanol (31). From nitroso acetal **16** (235 mg, 0.986 mmol) was obtained 133 mg (87%) of **31** as a white solid which was recrystallized from CH_2Cl_2 /hexane: mp 164 °C (CH_2Cl_2 /hexane); ^1H NMR (300 MHz) 7.00 (br, 2 H, NH, OH), 4.04 (d, J = 4.3, 2 H, H_2C(1)), 3.50 (ddd, J = 11.2, 6.6, 4.9, 1 H, HC(4)), 3.27 (ddd, J = 11.1, 9.0, 6.9, 1 H, HC(4)), 2.42 (dt, J_d = 7.9, J_t = 6.6, 1 H), 2.30 (m, 1 H, HC(5)), 2.00-1.53(m, 6 H), 1.65 (s, 3 H, H_3C(8)); ^{13}C NMR (75.5 MHz) 76.42 (C(2a)), 59.71 (C(1)), 50.41 (C(2)), C(5a)), 45.73 (C(4)), 31.37(CH_2), 30.22 (CH_2), 27.03 (CH_2), 24.72 (C(8)). HRMS calcd for $C_9H_{17}NO$ 155.13101, found 155.13075; TLC R_f 0.08 (EtOAc).

Preparation of rel-(1*R*,2*S*,2a*R*,5a*S*)-1-Methyl-[2a-methylperhydro[*b*]pyrrolo]]cyclopentanemethanol (32). From nitroso acetal **18** (200 mg, 0.783 mmol) was obtained 111 mg (84%) of **32** as a colorless oil: bp 75-76 °C (0.1 Torr, air bath); ^1H NMR (300 MHz) 5.50 (br, 2 H, NH, OH), 3.77 (quintet, J = 6.5, 1 H, HC(1)), 2.99 (ddd, J = 11.2, 7.2, 5.1, 1 H, HC(4)), 2.85 (dt, J_d = 11.1, J_t = 7.2, 1 H, HC(4)), 2.10 (m, 1 H), 1.87 (m, 1 H), 1.74-1.40 (m, 6 H), 1.34 (s, 3 H, H_3C(9)), 1.21 (d, J = 6.2, 3 H, H_3C(8)); ^{13}C NMR (75.5 MHz) 72.49 (C(2a)), 69.26 (C(1)), 55.60 (C(2)), 51.91 (C(5a)), 47.81 (C(4)), 34.14 (CH_2), 30.82 (C(9)), 30.50 (CH_2), 29.67 (CH_2), 22.95 (C(8)); TLC R_f 0.11 (EtOAc). Anal. Calcd for $C_{10}H_{19}NO$ (169.27): C, 70.96; H, 11.31; N, 8.28. Found: C, 70.80; H, 11.33; N, 8.37.

Preparation of rel-(1*S*,2*S*,2a*R*,5a*S*)-1-Methyl-[2a-methylperhydro[*b*]pyrrolo]] cyclopentanemethanol (33). From nitroso acetal **20** (195 mg, 0.768 mmol) was obtained 105 mg (81%) of **33** as a clear oil: bp 59-60 °C (0.02 Torr, air bath); ^1H NMR (300 MHz) 4.71 (br, 2 H, NH, OH), 4.15 (quintet, J = 6.2, 1 H, HC(1)), 2.91 (m, 1 H, HC(4)), 2.80 (m, 1 H, HC(4)), 2.20 (m 1 H), 1.87-1.37 (m, 6 H), 1.24 (s, 3 H, H_3C(8)), 1.18 (d, J = 6.5, 3 H, H_3C(9)); ^{13}C NMR (75.5 MHz) 71.60 (C(2a)), 65.11 (C(1)), 54.68 (C(2)), 50.24 (C(5a)), 47.38 (C(4)), 34.75 (CH_2), 29.95 (CH_2), 27.30 (C(9)), 23.07 (CH_2), 22.40 (C(8)); TLC R_f 0.09 (EtOAc). Anal. Calcd for $C_{10}H_{19}NO$ (169.27): C, 70.96; H, 11.31; N, 8.28. Found: C, 70.68; H, 11.37; N, 8.30.

Preparation of rel-(2*S*,2a*R*,5a*S*)-1,1-Dimethyl-[2a-methylperhydro[*b*]pyrrolo]]cyclopentanemethanol (34). From nitroso acetal **22** (195 mg, 0.724 mmol) was obtained 101 mg (76%) of **34** as a white solid, which was recrystallized with EtOAc/hexane: mp 160-161 °C (EtOAc/hexane); ^{1}H NMR (300 MHz) 9.50 (br, 1 H, NH), 5.79 (br, 1 H, OH), 3.37 (m, 1 H, HC(4)), 3.20 (m, 1 H, HC(4)), 2.40 (t, J = 5.8, 1 H, HC(2)), 2.14 (m, 2 H), 1.85 (m, 1 H), 1.70 (m, 3 H), 1.68 (s, 3 H, H$_3$C(10), 1.58 (s, 3 H, H$_3$C(9)), 1.35 (s, 3 H, H$_3$C(9)); ^{13}C NMR: (75.5 MHz) 75.70 (C(1)), 72.76 (C(2a)), 56.88 (C(2)), 53.38 (C(5a)), 45.66 (C(4)), 31.38 (C(9), or (C(8)), 30.98 (CH$_2$), 29.90 (C(8), or (C(9)), 27.88 (CH$_2$), 27.66 (C(10)), 26.59 (CH$_2$); HRMS calcd for C$_{11}$H$_{21}$NO 183.16231, found 183.16197; TLC R_f0.09 (EtOAc).

Preparation of rel-(1*S*,2*R*,2a*R*,5a*S*)-1-Methyl-[perhydro[*b*]pyrrolo]]cyclohexanemethanol (36). From nitroso acetal **26** (200 mg, 0.785 mmol) was obtained white solid which was recrystallized with EtOAc/hexane to afford 101 mg (76%) of **36** mp: 105-106 °C (hexane/EtOAc); ^{1}H NMR (300 MHz) 3.67 (quintet, J = 6.3, 1 H, HC(1)), 3.18 (t, J = 4.4, 1 H, HC(2a)), 3.09 (dt, J_d = 11.4, J_t = 7.8, 1 H, HC(4)), 2.86 (td, J_t = 11.0, J_d = 4.1, 1 H, HC(4)), 2.70 (br, 2 H, HO, NH, D$_2$O exch), 2.00-1.91 (m, 1 H, HC(2)), 1.84-1.19 (m, 8 H), 1.23 (d, J = 6.3, 3 H, H$_3$C(9)), 1.01 (m, 1 H, HC(5a)); ^{13}C NMR (75.5 MHz) 70.47 (C(1)), 58.07 (C(2a)), 44.67 (C(2)), 44.36 (C(4)), 38.77 (C(5a)), 31.64 (CH$_2$), 27.80 (CH$_2$), 25.15 (CH$_2$), 24.34 (CH$_2$), 22.05 (C(9));.TLC R_f 0.10 (EtOAc). Anal. Calcd for C$_{10}$H$_{19}$NO (169.27): C, 70.96; H, 11.31; N, 8.28. Found: C, 70.83; H, 11.27; N, 8.28.

Preparation of rel-(1*S*,2*R*,2a*R*,5a*S*)-1-Methyl-[7a-methylperhydro[*b*]pyrrolo]]cyclohexanemethanol (37). From nitroso acetal **28** (290 mg, 1.077 mmol) was obtained 161 mg (82%) of **37** as a white solid which was recrystallized with CH$_2$Cl$_2$ /hexane: mp: 134-136 °C (CH$_2$Cl$_2$ /hexane); ^{1}H NMR (300 MHz) 3.96 (quintet, J = 6.5, 1 H, HC(1)), 2.98 (m, 2 H, H$_2$C(4)), 1.91-1.83 (m, 1 H, HC(5)), 1.80-1.62 (m, 2 H), 1.59-1.30 (m, H), 1.22 (s, 3 H, H$_3$C(10)), 1.14 (d, J = 6.2, 3 H, H$_3$C(9)); ^{13}C NMR (75.5 MHz) 69.38 (C(1)), 62.66 (C(2a)), 50.75 (C(2)), 47.57 (C(5a), 43.72 (C(4)), 31.69 (CH$_2$), 29.16 (C(10)), 27.48 (CH$_2$), 25.33 (CH2), 22.10 (CH$_2$), 19.66 (C(9)); MS (70 eV) 183 (8), 168 (12), 124 911), 96 (100), 83 (160, 82 (14), 41 (12); HRMS calcd for C$_{11}$H$_{21}$NO 183.16231, found 183.16120; TLC R_f 0.08 (EtOAc).

Preparation of rel-(1*R*,2*R*,2a*R*,5a*S*)-1-Methyl-[7a-methylperhydro[*b*]pyrrolo]]cyclohexanemethanol (38). From nitroso acetal **30** (180 mg, 0.706 mmol) was obtained 143 mg (80%) of **38** as a white solid, which was recrystallized with CH$_2$Cl$_2$ /hexane: mp 242-246 °C (CH$_2$Cl$_2$ /hexane); ^{1}H NMR (300 MHz) 8.00 (br, 2 H, NH, OH), 4.32 (quintet, J = 5.6, 1 H, HC(1)), 3.46 (m, 2 H, H$_2$C(4)), 2.20 - 1.91 (m, 4 H), 1.72 (s, 3 H, H$_3$C(10), 1.66 - 1.19 (m, 6 H), 1.31 (d, J = 6.6, 3 H, H$_3$C(9)); ^{13}C NMR (75.5 MHz) 71.37 (C(1)), 64.47 (C(2a)), 50.12 (C(2)), 42.40 (C(4)), 39.89 (C(5a)), 29.45 (CH$_2$), 25.72 (CH$_2$), 24.60 (CH$_2$), 22.19 (C(10)), 21.40 (CH$_2$), 20.76 (C(9)); HRMS calcd for C$_{11}$H$_{21}$NO 183.16231, found 183.16215; TLC R_f 0.09 (EtOAc).

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