(w) cm^{-1}; ^1H NMR δ 0.80 (t, 3, J = 7 Hz, Me), 1.2-2.0 (m, 8, methylenes), 2.5-3.1 (m, 2, benzyl H_2), 3.2-3.4 (m, 2, NCH_2), 3.94 (s, 1, NCH), 6.9-7.9 (m, 4, aromatic Hs); MS, m/e (relative intensity) 254 (M^+, 12), 253 (12), 185 (40), 59 (base).

Dehydroaspidospermidine (18). A mixture of 100 mg (0.39 mmol) of amine **16b** and 200 mg of solid, anhydrous potassium carbonate in 3 mL of redistilled 1,2-dibromoethane was heated at 140 °C for 20 min and then poured onto ice and 1 mL of concentrated hydrochloric acid. The mixture was neutralized with 10% sodium bicarbonate solution and extracted with methylene chloride. Evaporation of the extract and thick-layer chromatography of the residue on alumina (development with chloroform) led to the recovery of 60 mg of unchanged starting amine and the isolation of 35 mg (32%; 80%, based on consumed starting amine) of viscous oily (±)-dehydroaspidospermidine (**18**): UV λ_{max} 222 nm (ϵ 22 000), 264 (9000); IR [CH, Wenkert-Bohlmann bands] 2780 (m), 2720 (m), [C=N] 1590 (m) cm^{-1}; MS, m/e (relative intensity) 280 (M^+, 44), 251 (33), 210 (base), 125 (84), 124 (56); spectrally identical with a sample of natural base derived from decarboxylative hydrolysis of vincadifformine.

Aspidospermidine (19). A mixture of 30 mg (0.11 mmol) of imine **18** and 1.00 g of lithium aluminum hydride in 25 mL of dry ether was stirred at room temperature for 2 h and then poured into a 10% sodium hydroxide solution. It was extracted with methylene chloride and the extract evaporated. Thick-layer chromatography of the residue on alumina (development with chloroform) yielded 21 mg (70%) of crystalline (±)-aspidospermidine (**19**): mp 104-106 °C (lit.[19b] mp 108-110 °C; lit.[19c] mp 106-110°C, lit.[19d] mp 99-103 °C); MS, m/e (relative intensity) 282 (M^+, 5), 254 (15), 124 (base); spectrally identical with a sample of the natural base.

Acknowledgment. We are indebted to the Public Health Service for financial support of this work.

Thermal and Trimethylsilyl Triflate Catalyzed Additions of Allylsilanes to Nitrones

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A new methodology is described for the coupling of allylsilanes and nitrones with trimethylsilyl triflate as a catalyst to afford homoallylhydroxylamines in yields ranging from 70% to 95%. Lower yields were obtained with shorter reaction times. The reaction also proceeds intramolecularly, giving mixtures of cis and trans tetrahydropyridines in excellent yield. The TMSOTf-catalyzed process is compared and contrasted with the thermally induced intramolecular nitrone cycloaddition.

Cycloaddition reactions of nitrones have been extensively studied and have recently been reviewed.[2] The reaction generally proceeds thermally to efficiently give cycloadducts and represents an excellent method for stereoselective carbon-carbon bond formation with concomitant introduction of additional functionality.

Recently Sakurai,[3] Kakisawa,[4] and DeShong[5] have examined the cycloaddition of nitrones with allylsilanes which proceed to give the expected isoxazolidines. We now report that the addition of allylsilanes to nitrones may be catalyzed with trimethylsilyl triflate (TMSOTf). We have found that treating a mixture of nitrone **1** and allyltrimethylsilane in methylene chloride at room temperature in the presence of TMSOTf gives a diastereomeric mixture[6] of cycloadducts **4** and homoallylhydroxylamine **6b**. The reaction is clearly catalyzed by trimethylsilyl triflate because without it temperatures >100 °C are required to achieve the usual (3 + 2) cycloaddition. Moreover,

Table I. Trimethylsilyl Triflate Catalyzed Additions of Allylsilanes to Nitrones

entry	nitrone (1)	catalyst amount, equiv	reactn time (h)	% yield[b]	ratio **6b**/**4**
1	Ph	1[a]	12	32	>50:1[c]
2	Ph	1	36	90	>50:1
3	Ph	0.1	36	86	>50:1
4	EtO_2C	0.1	1	76	1:4.5
5	EtO_2C	0.1	50	71	>50:1
6	3-pyridyl	1	6	86	9:1
7	3-pyridyl	1	63	94	>50:1
8	3-pyridyl	0.1	9	79	1:1.4

[a] $TiCl_4$ was used as catalyst. [b] Yields are for chromatographically isolated material. [c] A ratio of >50:1 indicates that the cyclic material was not detected.

TMSOTf appears to be unique in its effect on the reaction since early attempts to carry out the reaction with Lewis acids such as $SnCl_4$ and $BF_3{\cdot}Et_2O$ were generally unsuccessful, with $TiCl_4$, as the only exception, producing a 32% yield of the homoallylhydroxylamine **6b** (entry 1). An examination of Table I reveals our results to date. The reaction may be run catalytically or stoichiometrically in TMSOTf. In either case the yields are excellent (>70%). The use of 1 equiv is preferred since this leads to a single product in less time with better overall yield than the catalytic process.

A useful heuristic explaining the results involves initial silylation of nitrone **1** to form the transient electrophilic *N*-siloxyimminium ion **2** which reacts with allylsilane to give **3** (Scheme I). The fate of carbenium ion **3** may be

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(2) For reviews of nitrone chemistry, see: (a) Padwa, A. *1,3-Dipolar Cycloaddition Chemistry*; Wiley: New York, 1984. (b) Tufariello, J. J. *Acc. Chem. Res.* **1979**, *12*, 396. (c) Hamer, J.; Macaluso, A. *Chem. Rev.* **1964**, *64*, 473. (d) Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 10. (e) Black, D. S. C.; Crozier, R. F.; Davis, V. C. *Synthesis*, **1975**, 205. (f) Padwa, A. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 123.

(3) Hosomi, A.; Shoji, H.; Sakurai, H. *Chem. Lett.* **1985**, 1049.

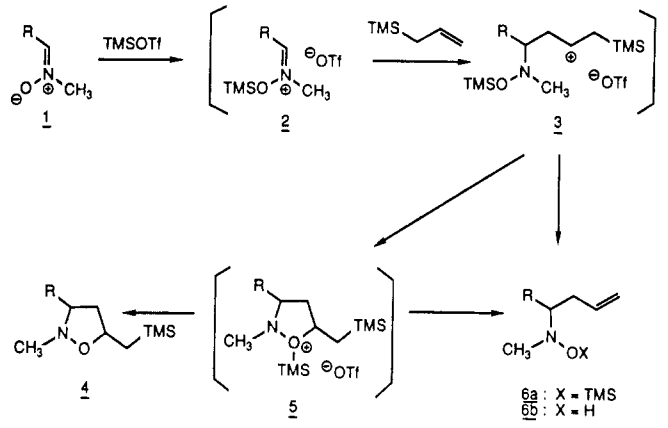
(4) Niwayama, S.; Dan, S.; Inouye, Y.; Kakisawa, H. *Chem. Lett.* **1985**, 957.

(5) DeShong, P.; Leginus, J. M.; Lander, S. W., Jr. *J. Org. Chem.* **1986**, *51*, 574.

(6) The ratio of diastereomers is generally ≈1:1 for the cases examined to date.

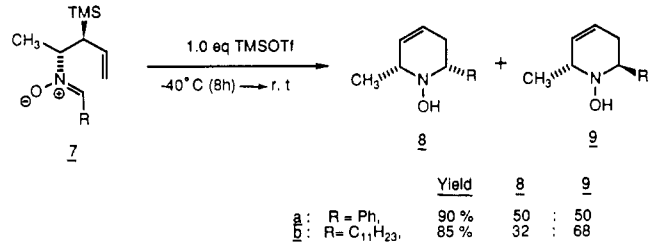
0022-3263/88/1953-1957$01.50/0

Scheme I



twofold. It may close to give **5** which goes to **4** or eliminate the silyl group to give **6a**. Our observations that the treatment of isolated **4** with TMSOTf leads to the formation of **6a** and that this transformation is much slower implies that the cycloadduct **4** is formed initially, followed by TMSOTf-catalyzed Peterson olefination[7] to afford **6a**. Although a concerted mechanism which involves the interaction of **2** with allyltrimethylsilane to form **5** directly may be postulated, we feel this to be much less likely based on the usual reactions of allylsilanes with other electrophilic species.[8,9]

We have also examined the intramolecular version of the reaction and are pleased to report that ring closure of nitrones **7a** and **7b**[10] proceeds smoothly to give the tetrahydropyridines **8** and **9** in high yield. The reaction is



considerably more facile than the intermolecular case since cyclization is achieved in 8 h at −40 °C. Also there was no evidence for the formation of bicyclic products, which is probably due to steric strain. When R = Ph we obtained a 1:1 ratio of cis and trans isomers in 90% yield, while when R = $C_{11}H_{23}$ a cis/trans ratio of 32:68 is obtained in

(7) (a) Peterson, D. J. *J. Org. Chem.* **1968**, *33*, 780. (b) Hudrlik, P. F.; Peterson, D. J.; Rona, R. J. *Ibid.* **1975**, *40*, 2263.

(8) For reviews, see: (a) Weber, W. P. *Silicon Reagents for Organic Synthesis*; Springer-Verlag: New York, 1983; pp 173–205. (b) Colvin, E. W. *Silicon in Organic Synthesis*; Butterworths: London, 1981; pp 97–124. (c) Chan, T. H.; Fleming, I. *Synthesis* **1979**, 761. (d) Sukurai, H. *Pure Appl. Chem.* **1982**, *54*, 1.

(9) For the reactions of *N*-acyliminium ions with allylsilanes, see: (a) Hiemstra, H.; Speckamp, W. N. *Tetrahedron Lett.* **1983**, *24*, 1407. (b) Hiemstra, H.; Fortgens, H. P.; Speckamp, W. N. *Ibid.* **1985**, *25*, 3155. (c) Aratani, M.; Sawada, K.; Hashimoto, M. *Ibid.* **1982**, *23*, 3921. (d) Kraus, G. A.; Neuenschwander, K. *J. Chem. Soc., Chem. Commun.* **1982**, 134.

(10) The precursor hydroxylamines were prepared by the condensation of acetaldehyde oxime i with with boronate ii in 73% yield to form a 3.8:1 mixture of the anti and syn hydroxylamines iii and iv. For an earlier example of the reaction of oximes with boronates, see: Hoffmann, R. W.; Eichler, G.; Endesfelder, A. *Liebigs Ann. Chem.* **1983**, 2000.

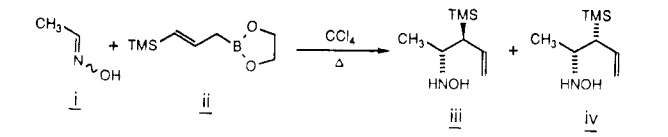
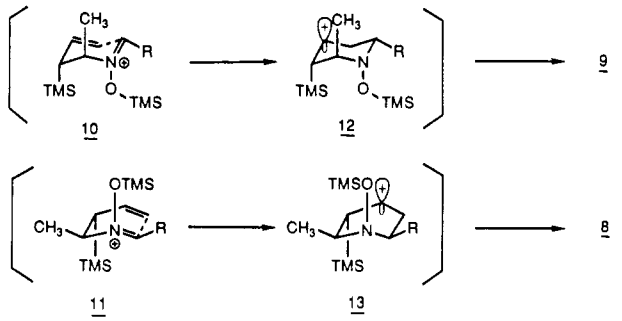


Table II. Intramolecular [3 + 2] Cycloaddition of Nitrones 7

R	solvent	reactn time, h	yield[a] (%)	ratio of isomer[b] **18:19:20:15**
C_6H_5	toluene	2	87	79:17:4:0
C_6H_5	benzene	22	82	69:7:24:0
$C_{11}H_{23}$	toluene	2	78	79:16:0:5
$C_{11}H_{23}$	benzene	6	86	78:10:0:12

[a] Isolated yield. [b] Ratio of **18** to **19** was determined by ^1H NMR, and the quantity of **20** or **15** was determined by isolation.

85% yield. The cis/trans isomers may be envisioned to arise from the chair and boat transition states **10** and **11**, respectively, which have the silyl group in an axial position, thus achieving $\sigma-\pi$ stabilization of the developing silyl cation in intermediates **12** and **13**. Isomerization of the nitrone was ruled out as a reason for the formation of cis and trans isomers when NMR studies showed complete configurational stability at −40 °C and at room temperature.



The reaction may, alternatively, proceed through transition states in which an aza-Cope rearrangement precedes the cyclization. Overman has demonstrated that cationic aza-Cope rearrangements are fast relative to ring closure in simple iminium ions.[11] Corroboration for the aza-Cope rearrangement is demonstrated with the cyclization of **14** in which the cis and trans piperidines **8a** and **9a** are isolated along with the product of aza-Cope rearrangement **15a** in a ratio of 34:52:14 in 62% yield. *trans*-Vinylsilane **15a** fails to cyclize due to the inability to achieve $\sigma-\pi$ stabilization in the transition state in either a chair or boat conformation.[12]

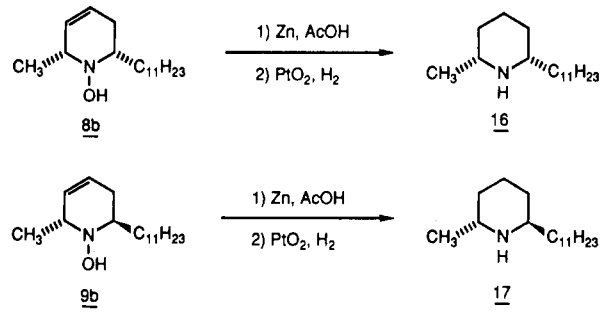
The stereochemistries of the undecyl derivatives **8b** and **9b** were correlated with the naturally occurring *trans*-2-undecyl-6-methylpiperidine (**17**), a component in the venom of the fire ant *Solenopsis saevissima*, and its cis isomer **16**.[13] Both the cis and trans isomers were independently reduced with zinc/acetic acid to give the corresponding amines which were then hydrogenated with

(11) Overman, L. E.; Malone, T. C.; Meier, G. P. *J. Am. Chem. Soc.* **1983**, *105*, 6993. For a similar situation in *N*-acyliminium ions, see: (a) Hart, D. M.; Tsai, Y.-M. *Tetrahedron Lett.* **1981**, *22*, 1567. (b) Nossin, P. M. M.; Speckamp, W. N.; *Ibid.* **1981**, 3289. (c) Ent, H.; Konig, H.; Speckamp, W. N. *Ibid.* **1985**, 5105.

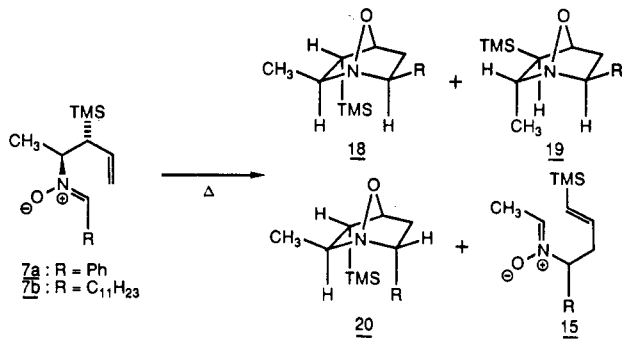
(12) Overman, L. E.; Burk, R. M. *Tetrahedron Lett.* **1984**, *25*, 5739.

(13) For previous syntheses of this substance, see: Takahashi, K.; Kurita, H.; Ogura, K.; Iida, H. *J. Org. Chem.* **1985**, *50*, 4368 and references cited therein.

PtO_2 to give the respective cis and trans piperidines **16** and **17**.

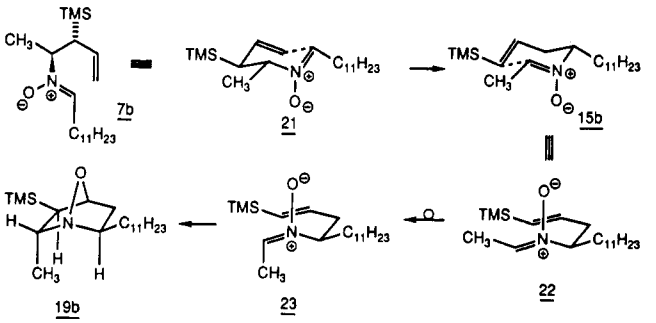


In contrast to the above TMSOTf-catalyzed intramolecular additions, the thermal reactions proceed in the usual direction to give the 1-aza-7-oxobicyclo[2.2.1]heptanes.[14] Thus the cycloaddition of **7a** proceeded smoothly by heating in a benzene or toluene solution, giving three isomeric bicyclic isoxazolidines, **18a**, **19a**, and **20a**, in high yield (82–87%). In the case of **7b** (R = $C_{11}H_{23}$), only two

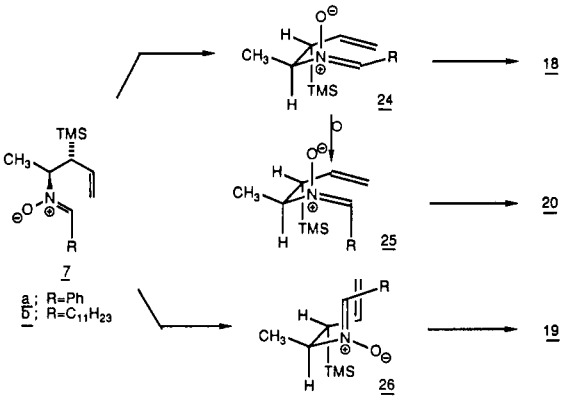


bicyclic adducts **18b** and **19b** were obtained along with nitrone **15b** derived from a Cope rearrangement. In both the phenyl and undecyl series the isomers **18** and **19** could not be separated by chromatography but could readily be separated from the third isomer **20** or **15**. The product distributions for each case are summarized in Table II.

As shown in Table II, the isomer distribution and the proportion of Cope rearrangement product **15** was found to be temperature-dependant. A mixture of cycloadducts **18b** and **19b** was heated to reflux in toluene for 12 h to help clarify some of the mechanistic details. The mixture was recovered unchanged, which suggests that cycloreversion followed by recyclization is not a participating factor in determining the product distribution. Also, when the isolated nitrone **15b** was heated to reflux in benzene for 48 h, a 17.5:1 mixture of **19b** and **18b** was isolated in 30% yield which indicates that the products are not formed by initial Cope rearrangement to **15b** followed by cyclization. In this case the bicyclic isoxazolidine **19b** is formed from conformer **23** after isomerization of the Cope rearrangement product **15b**. Nitrone **15b** probably does not cyclize directly through conformer **22** because of the severe steric congestion between the silyl and methyl groups in the transition state raises the barrier for cyclization relative to isomerization.[15] The fact that no evidence for the formation of the Cope product **15a** was found would indicate that resonance stabilization achieved



through conjugation with the aromatic ring prevents this rearrangement from occurring. On the other hand, conjugation facilitates nitrone isomerization from **7a** to **25a** which accounts for the formation of isomer **20a**. The

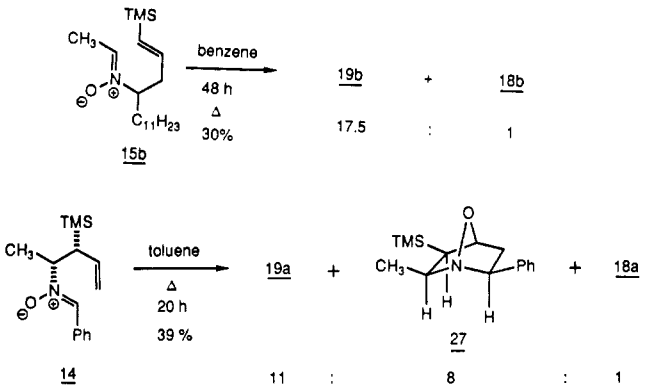


absence of the analogous isomerization in the undecyl series is probably due to the fact that the energy barrier for cyclization is much lower than that for isomerization. The predominance of **18** over **19** may be rationalized as follows: In the transition state **21** leading to **18** the TMS group which has a larger *A* value then the methyl group[16] occupies the sterically more demanding endo position which would predict that **19** should be favored over **18** and thus clearly steric effects are being overridden by a favorable electronic stabilization. We believe that in cyclization through transistion state **24** the carbon of the incipient C–O bond must have some partial positive charge associated with it which is stabilized by the antiperiplaner TMS group, thus overcoming the steric effect of the endo TMS group in **24**. Such stabilization is geometrically not possible for transition state **26** and therefore **18** is favored over **19**. These results would suggest that cyclization of the syn nitrone **14** would prove to be difficult due to the steric conjestion imposed by the vicinal relationship between the methyl and silyl groups in the transition states for cyclization. The prediction was confirmed when we found that 20 h in refluxing toluene were required to consume the starting nitrone and that only a 39% yield of isoxazolidines **19a**, **27**, and **18a** was produced in a 11:8:1 ratio. Of the two possible conformers for cyclization, **28** is the most sterically encumbered due to the endo and vicinal nature of the methyl and silyl groups and thus undergoes a Cope rearrangement through a boat transition state followed by an isomerization before cyclizing to **18a**. On the other hand the exo nature of the substituents in conformer **33** lowers the transition-state energy enough relative to Cope rearrangement that now cyclization occurs without prior rearrangement. The major product **19a** is formed via initial Cope rearrangement through a favorable

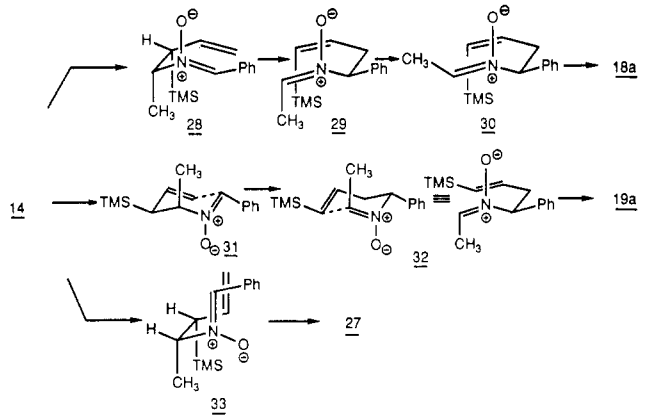
(14) (a) Lumma, W. C., Jr. *J. Am. Chem. Soc.* **1969**, *91*, 2820. (b) Lau, H. H.; Schollkopf, U. *Liebigs Ann. Chem.* **1981**, 1378. (c) Oppolzer, W.; Siles, S.; Snowden, R. L.; Bakker, B. H.; Peirzilka, M. *Tetrahedron Lett.* **1979**, 4391. (d) Hoffmann, R. W.; Endesfelder, A. *Liebigs Ann. Chem.* **1986**, 1823.

(15) Bjoge, J.; Boyd, D. R.; Neill, D. C. *J. Chem. Soc., Chem. Commun.* **1974**, 478. Boyle, L. W.; Peagram, M. J.; Whithan, G. H. *J. Chem. Soc. B* **1971**, 1728.

(16) The *A* value for TMS is 2.5 and that for methyl is 1.7. Kitching, W.; Olszowy, H. A.; Drew, G. M.; Adcock, W. *J. Org. Chem.* **1982**, *47*, 5153.



chair transition state **31** to nitrone **32** followed by cycloaddition.



The stereochemical assignments for the bicyclic isoxazolidines were derived from their ^1H NMR spectral data and and a series of decoupling experiments. Tables III and IV summarized the chemical shifts and the coupling constants. Typical values of the chemical shift of the bridgehead protons at C-4 range from 4.60 and 4.98 ppm, and their spin multiplicities are diagnostic of the relative stereochemistry of the silyl substituent at C-3. In the case of isomers **18** having an endo silyl group, a triplet (J = 4.9 Hz) at low field (δ 4.90 for R = C_6H_5, δ 4.78 for R = $C_{11}H_{23}$) is assigned to the bridgehead proton at C-4, coupled nearly equally to the exo protons at C-3 and C-5 and negligibly to the endo proton at C-5 due to a dihedral angle of approximately 90°. The exo proton at C-3 is coupled to the exo proton at C-5, with a small coupling constant (J = 2.4 Hz) to give an eight-line multiplet. A 12-line multiplet centered at δ 1.90 (R = C_6H_5) is assigned to the exo proton at C-5, since this is coupled to the 3-exo, 5-endo, 6-endo, and C-4-bridgehead protons. In the case of isomers **19** having an exo silyl group, the doublet (J = 4.5 Hz) for the bridgehead proton at C-4 is observed at low field (δ 4.77 for R = C_6H_5, δ 4.60 for R = $C_{11}H_{23}$) since this is not coupled to the exo protons at the C-3 and C-5 positions.

The relative stereochemistry at the C-2 and C-6 positions was assigned on the basis of the magnitude of the coupling constants. It is generally accepted that bicyclo[2.2.1]-heptane systems present differences in the coupling constants of the syn (endo–endo or exo–exo) and the anti (endo–exo) vicinal protons. This difference is rationalized in terms of the different dihedral angles. Inspection of the published coupling constants for these systems reveals a potentially useful trend in which the anti vicinal coupling constants are generally smaller than their syn counterpart.[14a,17] For isomer **27**, a large coupling constant ($J_{2,3}$ = 9.5 Hz) is observed for the syn (exo–exo) vicinal protons whereas compounds **18**, **19**, and **20** show small coupling constants ($J_{2,3}$ = 6.2–7.6 Hz) for the anti (endo–exo) vicinal protons. The stereochemistry at C-6 was also assigned in the same manner. The H_6/H_5 anti vicinal protons present small coupling constants ($J_{5\beta,6}$ = 4.8–5.6 Hz) and the syn vicinal protons give larger coupling constants ($J_{5\alpha,6}$ = 7.6–8.3 Hz). Although the stereochemistry of the isomers was well established by their ^1H NMR spectra, final conformation was secured by preparation of the piperidine ring, via a reductive cleavage of the nitrogen–oxygen bond in the bicyclic oxazolidines.

The nitrogen–oxygen bond of the bicyclic isoxazolidines was cleaved by treatment of the 4.6:1 mixture of cycloadducts (**18a** and **19a**) with excess zinc (20 equiv) in acetic acid/H_2O at 60 °C for 4 h, giving a mixture of piperidinol derivatives **34** and **35** in quantitative yield, inseparable by chromatography. It is noteworthy that the dehydroxysilylation (Peterson olefination)[7] did not occur under the acidic reaction conditions. The ^1H NMR spectrum indicates that the major product **34** exists in chair conformation **36** in solution ($CDCl_3$) and all the substituents occupy

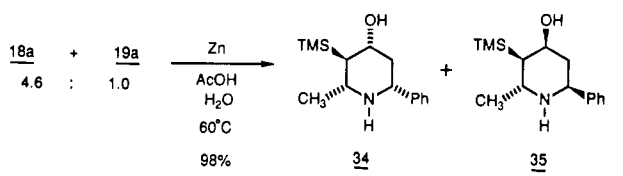
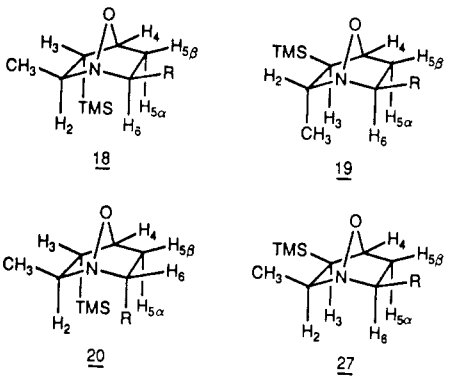


Table III. Summary of Chemical Shift (ppm) in 1-Aza-7-oxabicyclo[2.2.1]heptanes



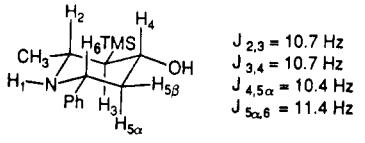
	chemical shift, R =					
	18		19		20	27
	C_6H_5	$C_{11}H_{23}$	C_6H_5	$C_{11}H_{23}$	C_6H_5	C_6H_5
H_2	2.93	2.72	3.45	3.32	2.95	3.37
H_3	1.12	1.01	0.47	0.30	1.10	1.19
H_4	4.90	4.78	4.77	4.60	4.98	4.84
$H_{5\alpha}$	2.22	1.39	2.15	1.51	1.78	2.02
$H_{5\beta}$	1.90	1.77	2.02	1.68	2.33	2.18
H_6	3.74	2.57	4.36	3.16	4.64	3.92

Table IV. Summary of Coupling Constant (Hz) in 1-Aza-7-oxabicyclo[2.2.1]heptanes

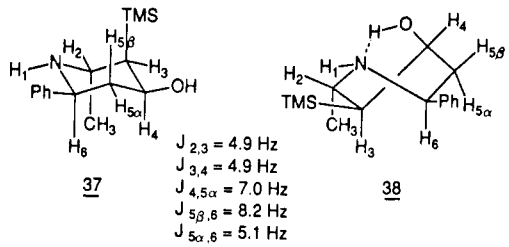
	coupling constant, R =					
	18		19		20	27
	C_6H_5	$C_{11}H_{23}$	C_6H_5	$C_{11}H_{23}$	C_6H_5	C_6H_5
$J_{2,3}$	6.2	6.4	7.6	7.4	6.5	9.5
$J_{3,4}$	4.9	4.8	0	0	4.3	0
$J_{3,5\beta}$	2.4	2.4	0	0	2.3	0
$J_{4,5\beta}$	4.9	4.8	4.5	4.5	5.7	4.3
$J_{4,5\alpha}$	0	0	0	0	0	0
$J_{5\alpha,5\beta}$	11.9	11.6	10.8	10.9	11.4	11.2
$J_{5\alpha,6}$	8.2	7.6	8.2	7.7	6.6	8.3
$J_{5\beta,6}$	5.2	4.8	5.3	5.0	10.1	5.6

(17) Anet, F. A. L. *Can. J. Chem.* **1961**, *39*, 789.

equatorial positions. However, the ^1H NMR spectrum of the minor product **35** shows a triplet (J = 4.9 Hz) for H_3, a doublet of doublets (J = 8.2, 5.1 Hz) for H_6, and a doublet of triplets (J = 7.0, 4.9 Hz) for H_4. If chair conformation **37** is assumed for **35**, the values 4.9 Hz for $J_{2,3}$ and $J_{3,4}$ and 5.1 Hz for $J_{5\beta,6}$ fall in the range of J_{ax-eq} and J_{eq-eq} coupling. However, the higher coupling values, 8.2 Hz for $J_{5\alpha,6}$ and 7.0 Hz for $J_{4,5\alpha}$, are not typical for J_{ax-ax} coupling. This indicates that **35** prefers a boat conformation, which may be stabilized by an intramolecular hydrogen bond and an increase in the number of equatorial substituents, as shown in **38**. The NMR data are in accord with a boat conformation, in which the 3-silyl group is pseudoequatorial. Similar observations[18] have been reported for other 4-hydroxypiperidines.

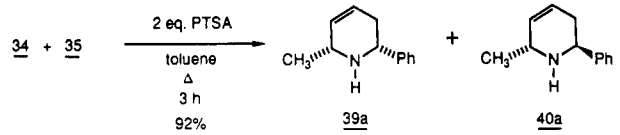


36



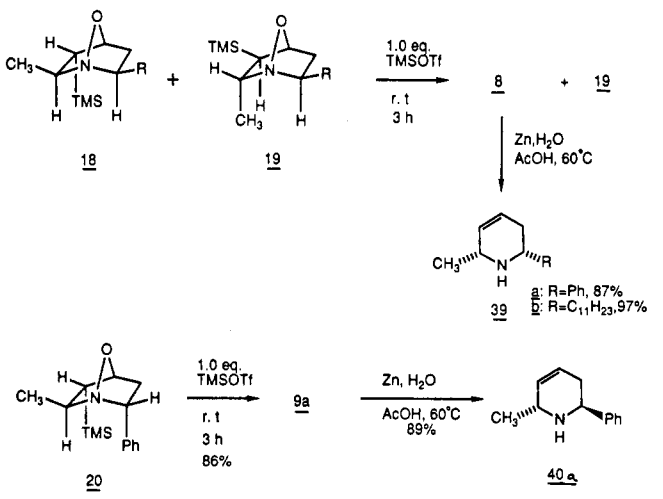
37 **38**

These compounds were further characterized by dehydroxysilylation to their respective tetrahydropyridines. Thus treatment of the 4.6:1 mixture of **34** and **35** with *p*-toluenesulfonic acid (2 equiv) in refluxing toluene for 3 h gives a mixture of cis and trans isomers **39a** and **40a** in 92% yield and a 5.4:1 ratio also inseparable by chromatography. It should be noted that the major compound **34** reacts much faster than the minor isomer **35**. The ^1H NMR spectrum of the refuxing reaction mixture in toluene showed that approximately 70% of **35** remained unreacted after 0.5 h, whereas **34** was completely consummed. An



39a **40a**

alternative route for the conversion of the bicyclic isoxazolidines to their respective tetrahydropyridines was examined which utilizes TMSOTf-induced cleavage previously discussed. When a mixture of **18** and **19** is treated with trimethylsilyl triflate at room temperature for 3 h, only the endo bicyclic isoxazolidine **18** reacts to afford *cis*-*N*-hydroxytetrahydropyridine **8** in high yield (91–94%). The exo silyl adduct **19** does not react and is recovered. Application of the same procedure to **20** affords *trans*-*N*-hydroxytetrahydropyridine **9a** in 86% yield. Therefore, such TMSOTf-mediated dehydroxysilylation reactions proceed only in bicyclic isoxazolidines where the relationship between the trimethylsilyl group and oxygen atom is antiperiplanar in geometry. It should be noted that these *cis*- and *trans*-*N*-hydroxytetrahydropyridines **8** and **9a** all give broad peaks in their NMR spectra, a result of



nitrogen inversion. Compounds **8** and **9a** were independently reduced with zinc (20 equiv) in acetic acid/H_2O at 60 °C for 4 h to give the respective cis and trans disubstituted tetrahydropyridines **39** and **40a**.[19,20]

In conclusion we have demonstrated the possibility of catalyzing the nitrone cycloaddition reaction and have developed a facile one-step procedure for addition of the allyl unit to a nitrone in high yield. The intramolecular version is a particularly powerful reaction and has considerable promise in the construction of a variety of alkaloids. Also, our comparison studies on the thermal reaction would indicate that the prefered stereochemistry in this case is opposite to the TMSOTf-catalyzed reactions, although further experimental work is required to establish this unambiguously.

Experimental Section

The nitrones **1a**, **1b**, and **1c** were prepared following the literature procedures.[21-23]

General Procedure for the Synthesis of *N*-(1-Substituted-3-butenyl)-*N*-hydroxylamines 6 from Allyltrimethylsilane and Nitrones 1. In a 25-mL two-necked round-bottom flask equipped with a magnetic stirrer, an argon inlet, and a rubber septum were placed α-3-pyridylnitrone **1c** (0.68 g, 5.0 mmol) and allyltrimethylsilane (0.69 g, 6.0 mmol) in 5 mL of dry methylene chloride. Trimethylsilyl triflate (1.11 g, 5.0 mmol) was added via syringe at room temperature under argon. While the resulting solution was stirred, the reaction progress was monitored by TLC. As the reaction proceeded, two new spots appeared on TLC. After the α-3-pyridylnitrone was completely consumed, the reaction mixture was kept stirring until the lower R_f spot (isoxazolidine) was completely converted to the higher R_f spot (*O*-(trimethylsilyl)-*N*-homoallylhydroxylamine). The reaction was quenched with 3.0 N aqueous HCl (5.0 mL), stirred for an additional 1 h, neutralized with 3.0 N NaOH, and extracted with diethyl ether (2 × 25 mL). The combined ether layer was washed with water and brine, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel with 5% ethanol in ethyl acetate containing

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(19) For recent syntheses, see: (a) Ogawa, M.; Nakajima, J.; Natsume, M. *Heterocycles* **1982**, *19*, 1247. (b) Bonin, M.; Romero, J. R.; Grierson, D. S.; Husson, H. P. *J. Org. Chem.* **1984**, *49*, 2392. (c) Nader, B.; Bailey, T. R.; Franck, R. W.; Weinreb, S. M. *J. Am. Chem. Soc.* **1981**, *103*, 7593.

(20) Some natural products having the cis or trans 2,6-disubstituted tetrahydropyridine moiety are found. For examples, see: (a) Lotter, H.; Abraham, D. J.; Turner, C. E.; Knapp, J. E.; Schiff, P. L., Jr.; Slatkin, D. J. *Tetrahedron Lett.* **1975**, 2815. (b) Wasserman, H. H.; Leadbetter, M. R.; Kopka, I. E. *Ibid.* **1984**, 2391. (c) Weinreb, S. M.; Bailey, T. R.; Garipipati, R. S.; Morton, J. A. *J. Am. Chem. Soc.* **1984**, *106*, 3240. (d) Colau, B.; Hootele, C. *Can. J. Chem.* **1983**, *61*, 470.

(21) Deshong, P.; Dicken, C. M. *J. Org. Chem.* **1982**, *47*, 2047.

(22) Inouye, Y.; Watanabe, Y.; Takahashi, S.; Kahisawa, H. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 3762.

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1% triethylamine as an eluent to afford 0.65 g (94%) of pyridylhydroxylamine **6c**.

***N*-Methyl-*N*-(1-phenyl-3-butenyl)hydroxylamine 6a.** To a solution of α-phenyl-*N*-methylnitrone (**1a**) (0.68 g, 5.0 mmol) and allylsilane (0.69 g, 6.0 mmol) in 5 mL of dry methylene chloride was added trimethylsilyl triflate (0.11 g, 0.5 mmol). The resulting solution was stirred for 36 h at room temperature. Workup proceded as described in the general procedure. Purification by flash chromatography (silica gel, 30% ethyl acetate in hexane containing 1% Et_3N) afforded 763 mg (86%) of **6a** as a white solid, mp 93–95 °C (recrystallized from hexane). ^1H NMR (300 MHz, $CDCl_3$): 7.36–7.24 (m, 5 H), 6.92 (br, 1 H), 5.57 (ddt, J = 17.1, 10.0, 7.0 Hz, 1 H), 5.02–4.89 (m, 2 H), 3.54 (dd, J = 9.5, 4.8 Hz, 1 H), 2.92 (m, 1 H), 2.57 (m, 1 H), 2.51 (s, 3 H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): 140.16, 135.57, 129.08, 128.58, 127.84, 116.92, 74.48, 46.17, 38.12 ppm. IR (KBr): 3500–3120 (br), 3078, 3063, 3033, 3005, 2973, 1638, 1600, 1453, 1356, 1111, 1089, 1018 cm^{-1}. Anal. Calcd for $C_{11}H_{15}NO$: C, 74.54, H, 8.53, N, 7.90. Found: C, 74.49, H, 8.48, N, 7.88.

***N*-(1-Carbethoxy-3-butenyl)-*N*-methylhydroxylamine (6b) and Ethyl 2-Methyl-5-[(trimethylsilyl)methyl]isoxazolidine-3-carboxylate (4b and 4b′).** To a solution of α-carbethoxy-*N*-methylnitrone (**1b**) (0.66 g, 5.0 mmol, *E*:*Z* = 3.5:1) and allylsilane (0.69 g, 6.0 mmol) was added trimethylsilyl triflate (0.11 g, 0.5 mmol) under argon. After the resulting solution was stirred for 1 h at room temperature, the starting material was completely consumed. The reaction was quenched with 3 N aqueous HCl and workup proceded as described in the general procedure. The three compounds were separated by flash chromatography (silica gel, eluted with 70:30:1–50:50:1 ethyl acetate/hexane/Et_3N), resulting in the cycloadduct stereoisomers **4b** (325 mg, 26%, R_f 0.54) and **4b′** (416 mg, 33%, R_f 0.44), along with the more polar products of homoallylhydroxylamine **6b** (116 mg, 13%, R_f 0.31). The relative configuration of stereoisomers **4b** and **4b′** was not determined. For compound **4b**, R_f 0.54 (50:50:1 ethyl acetate/hexane/Et_3N). ^1H NMR (300 MHz, $CDCl_3$): 4.25–4.14 (m, 3 H), 3.27 (dd, J = 10.0, 6.1 Hz, 1 H), 2.79 (s, 3 H), 2.55 (ddd, J = 12.2, 6.1, 6.1 Hz, 1 H), 2.03 (ddd, J = 12.2, 10.0, 8.5 Hz, 1 H), 1.30 (t, J = 7.1 Hz, 3 H), 1.07 (dd, J = 14.0, 5.6 Hz, 1 H), 0.83 (dd, J = 14.0, 8.9 Hz, 1 H), 0.45 (s, 9 H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): 170.90, 75.56, 70.18, 61.09, 45.27, 41.73, 22.75, 14.18, –0.93 ppm. IR (neat): 2940, 2880, 1730, 1450, 1360, 1250, 1200, 1050 cm^{-1}. Anal. Calcd for $C_{11}H_{23}NO_3Si$: C, 53.84; H, 9.45; N, 5.71; Si, 11.45. Found: C, 53.99; H, 9.49; N, 5.77; Si, 11.48. For compound **4b′**, R_f 0.44 (50:50:1 ethyl acetate/hexane/Et_3N). ^1H NMR (300 MHz, $CDCl_3$): 4.39–4.30 (m, 1 H), 4.21 (q, J = 7.1 Hz, 2 H), 3.52 (dd, J = 8.4, 6.7 Hz, 1 H), 2.76 (s, 3 H), 2.64 (ddd, J = 12.3, 8.4, 6.7 Hz, 1 H), 2.14 (ddd, J = 12.3, 7.8, 6.5 Hz, 1 H), 1.29 (t, J = 7.1 Hz, 3 H), 1.10 (dd, J = 14.1, 5.8 Hz, 1 H), 0.93 (dd, J = 14.1, 8.7 Hz, 1 H), 0.49 (s, 9 H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): 171.44, 74.69, 70.03, 61.19, 45.28, 41.06, 22.87, 14.23, –0.90 ppm. IR (neat): 2940, 2890, 1730, 1450, 1380, 1360, 1250, 1200, 1050 cm^{-1}. Anal. Calcd for $C_{11}H_{23}NO_3Si$: C, 53.84; H, 9.45; N, 5.71; Si, 11.45. Found: C, 53.72; H, 9.53; N, 5.79; Si, 11.42. For compound **6b**, R_f 0.31 (50:50:1 ethyl acetate/hexane/Et_3N). ^1H NMR (300 MHz, $CDCl_3$): 6.25 (br, 1 H, N–OH), 5.90 (ddt, J = 17.1, 10.0, 7.1 Hz, 1 H), 5.16–5.06 (m, 2 H), 4.21 (q, J = 7.1 Hz, 2 H), 3.40 (dd, J = 7.6, 5.8 Hz, 1 H), 2.73 (s, 3 H), 2.57–2.43 (m, 2 H), 1.29 (t, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): 171.93, 133.97, 117.79, 71.61, 60.80, 45.21, 34.30, 14.31 ppm. IR (neat): 3500–3100 (br), 3080, 2980, 1725, 1650, 1450, 1380, 1200 cm^{-1}. Anal. Calcd for $C_8H_{15}NO_3$: C, 55.47; H, 8.73; N, 8.09. Found: C, 55.45; H, 8.88; N, 8.05.

***N*-Methyl-*N*-[1-(3-pyridyl)-3-butenyl]hydroxylamine (6c) and 2-Methyl-3-(3-pyridyl)-5-[(trimethylsilyl)methyl]isoxazolidine (4c).** To a solution of α-3-pyridyl-*N*-methylnitrone (**1c**) (0.68 g, 5.0 mmol) and allylsilane (0.69 g, 6.0 mmol) in 5 mL of methylene chloride was added trimethylsilyl triflate (1.11 g, 5.0 mmol) at room temperature. The resulting solution was stirred for 6 h and workup proceded as described in the general procedure. The two compounds were separated by flash chromatography (silica gel, eluted by 100:1 ethyl acetate/Et_3N), resulting in the cycloadduct **4c** (89 mg, 9%, R_f 0.44), along with the hydroxylamine **6c** (802 mg, 77%, R_f 0.32). For compound **4c**, R_f 0.44 (100:1 ethyl acetate/Et_3N). ^1H NMR (300 MHz, $CDCl_3$): 8.57 (d, J = 2.0 Hz, 1 H), 8.53 (dd, J = 4.8, 1.7 Hz, 1 H), 7.75 (dt, J = 7.9, 2.0 Hz, 1 H), 7.29 (m, 1 H), 4.35 (m, 1 H), 3.55 (t, J = 8.4 Hz, 1 H), 2.59 (s, 3 H), 2.59–2.19 (m, 2 H), 1.15 (dd, J = 14.0, 5.3 Hz, 1 H), 0.90 (dd, J = 14.0, 9.3 Hz, 1 H), 0.06 (s, 9 H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): 149.86, 149.49, 136.38, 135.27, 123.80, 75.44, 71.09, 47.97, 43.32, 23.64, –0.85 ppm. IR (neat): 3020, 2940, 1575, 1425, 1360, 1250, 1190, 1120, 1090 cm^{-1}. Anal. Calcd for $C_{13}H_{22}N_2OSi$: C, 62.35; H, 8.85; N, 11.19; Si, 11.22. Found: C, 62.37; H, 8.98; N, 11.26; Si, 11.08. For **6c**, R_f 0.32 (100:1 ethyl acetate/Et_3N). ^1H NMR (300 MHz, $CDCl_3$): 8.48 (dd, J = 4.9, 1.7 Hz, 2 H), 8.02 (br, 1 H, N–OH), 7.67 (dt, J = 7.8, 1.8 Hz, 1 H), 7.26 (dd, J = 7.8, 4.9 Hz, 1 H), 5.57 (ddt, J = 17.1, 10.1, 7.1 Hz, 1 H), 4.99–4.92 (m, 2 H), 3.61 (dd, J = 9.4, 5.0 Hz, 1 H), 2.89 (m, 1 H), 2.61–2.51 (m, 4 H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): 150.73, 149.07, 136.71, 135.80, 134.81, 123.48, 117.66, 71.59, 46.17, 37.90 ppm. IR (neat): 3600–3000 (br, vs), 2840 (vs), 1645, 1585, 1430 (s), 1320, 1190, 1110 cm^{-1}. Anal. Calcd for $C_{10}H_{14}N_2O$: C, 67.39; H, 7.92; N, 15.72. Found: C, 67.26; H, 8.02; N, 15.61.

(1*R,2*S**)- and (1*R**,2*R**)-*N*-Hydroxy-3-(trimethylsilyl)-4-penten-2-amine (*anti*-iii and *syn*-iv).** A 100-mL two-necked round-bottom flask equipped with a magnetic stirrer, a rubber septum, and a reflux condenser under an argon atmosphere was charged with a solution of acetaldoxime (i) (1.47 g, 25.0 mmol, *Z*:*E* = 1.7:1.0) in 25 mL of dry carbon tetrachloride. The solution was warmed up to 70 °C and treated with ethylene glycol *trans*-1-(trimethylsilyl)-1-propene-3-boronate[24] (ii) (6.86 g, 37.5 mmol) by dropwise addition via syringe under argon. The reaction mixture was heated to reflux for 3 h, cooled to room temperature, and concentrated under reduced pressure. The residue was dissolved in 70 mL of anhydrous diethyl ether. The addition of triethanolamine (5.59 g, 37.5 mmol) produced a fine white precipitate. After an additional 2 h of stirring, the solid was removed by filtering and washed with diethyl ether. The filtrate was poured into 15 mL of 2.0 N aqueous NaOH solution and extracted three times with 20-mL portions of diethyl ether. The combined extracts were washed with water and brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give 3.13 g (73%) of a yellow liquid, which crystallized upon standing (mp 48 °C). ^1H NMR analysis (360 MHz) of crude product showed a 3.8:1.0 mixture of diastereomers. The diastereomers were separated by column chromatography on silica gel (70–230-mesh), eluting with 60:40:2 hexane/ethyl acetate/NH_4OH. For anti isomer iii as the major product, R_f 0.30 (60:40:2 hexane/ethyl acetate/Et_3N). ^1H NMR (360 MHz, $CDCl_3$): 6.55 (br, NOH), 5.65 (br, NH), 5.65 (dt, J = 17.1, 10.4 Hz, 1 H), 5.01 (dd, J = 10.3, 1.9 Hz, 1 H), 4.93 (ddd, J = 17.1, 1.9, 0.7 Hz, 1 H), 3.09 (dq, J = 10.0, 6.3 Hz, 1 H), 1.61 (t, J = 10.0 Hz, 1 H), 1.20 (d, J = 6.3 Hz, 3 H), 0.05 (s, 9 H) ppm. IR (neat): 3600–3050 (br), 3075 (sh), 2960, 2900, 1630, 1415, 1375, 1260, 1130 cm^{-1}. Anal. Calcd for $C_8H_{19}NOSi$: C, 55.44; H, 11.05; N, 8.08. Found: C, 55.14; H, 11.24; N, 8.14. For syn isomer iv as the minor product, R_f 0.26 (60:40:2 hexane/ethyl acetate/Et_3N). ^1H NMR (360 MHz, $CDCl_3$): 6.55 (br, NH and OH), 5.73 (dt, J = 17.6, 10.9 Hz, 1 H), 5.04–4.90 (m, 2 H), 3.20 (qd, J = 6.7, 3.6 Hz, 1 H), 2.07 (dd, J = 10.9, 3.6 Hz, 1 H), 1.10 (d, J = 6.7 Hz, 3 H), 0.04 (s, 9 H) ppm. IR (neat): 3600–3050 (br), 3073 (sh), 2960, 2900, 1630, 1415, 1250, 1130 cm^{-1}.

(1*R,2*S**)-(*Z*)-*N*-Benzylidene-3-(trimethylsilyl)-4-penten-2-amine *N*-Oxide (7a).** To a cooled (0 °C) suspension of anti hydroxylamine iii (471 mg, 272 mmol) and finely ground anhydrous calcium chloride (1.51 g, 13.6 mmol) in 10 mL of anhydrous diethyl ether in a 25-mL round-bottom flask was added freshly distilled benzaldehyde (1.44 g, 13.6 mmol) via syringe under argon. After being stirred for 1 h at 0 °C, the reaction mixture was allowed to warm up to room temperature and kept stirring at that temperature for an additional 26-h period. Filtration through a Celite pad followed by concentration gave the crude product. Flash chromatography on 53 g of silica gel, eluting with 27% ethyl acetate in hexane, afforded 609 mg (86%) of the *Z* nitrone **7a**, mp 64 °C. ^1H NMR (360 MHz, $CDCl_3$): 8.24–8.19 (m, 2 H), 7.42–7.26 (m, 4 H), 5.67 (dt, J = 17.0, 10.3 Hz, 1 H), 4.93 (dd, J = 17.0, 1.6 Hz, 1 H), 4.89 (dd, J = 10.1, 1.6 Hz, 1 H), 4.10 (dq, J = 10.4, 6.6 Hz, 1 H), 2.33 (t, J = 10.4 Hz, 1 H), 1.55 (d, J = 6.6 Hz, 3 H), 0.11 (s, 9 H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): 135.89, 131.68, 129.74, 128.54, 128.41, 126.82, 115.20, 74.20,

(24) Tsai, D. J. S.; Matteson, D. S. *Tetrahedron Lett.* **1981**, *22*, 2751.

40.21, 20.10, -1.42 ppm. IR (neat): 3070, 2950, 2900, 1630, 1580, 1565, 1250, 1220, 1005 cm^{-1}. Anal. Calcd for $C_{15}H_{23}NOSi$: C, 68.91; H, 8.87; N, 5.36. Found: C, 68.65; H, 8.76; N, 5.28.

(1*R,2*R**)-(*Z*)-*N*-Benzylidene-3-(trimethylsilyl)-4-penten-2-amine *N*-Oxide (14).** Compound 14 was prepared as described in the above procedure. To a cooled (0 °C) suspension of syn hydroxylamine iv (134 mg, 0.77 mmol) and finely ground anhydrous calcium chloride (429 mg, 3.9 mmol) was added freshly distilled benzaldehyde (410 mg, 3.87 mmol) in 3 mL of anhydrous diethyl ether. The mixture was stirred at room temperature for 23 h. After filtration and removal of solvent in vacuo, the residue was purified by silica gel flash chromatography (75:25 hexane/ethyl acetate), affording 165 mg (82%) of the *Z* nitrone **14**. ^1H NMR (360 MHz, $CDCl_3$): 8.24–8.21 (m, 2 H), 7.46–7.26 (m, 4 H), 5.71 (dt, J = 16.9, 10.5 Hz, 1 H), 5.03 (dd, J = 10.2, 1.7 Hz, 1 H), 4.98 (dd, J = 16.9, 1.7 Hz, 1 H), 4.19 (p, J = 6.9 Hz, 1 H), 2.39 (dd, J = 10.7, 7.5 Hz, 1 H), 1.54 (d, J = 6.6 Hz, 3 H), 0.04 (s, 9 H) ppm. ^{13}C NMR (90.56 MHz, $CDCl_3$): 134.88, 131.90, 130.84, 129.93, 128.49, 128.41, 115.71, 73.06, 40.24, 19.04, -2.85 ppm.

(1*R,2*S**)-(*Z*)-*N*-Undecylidene-3-(trimethylsilyl)-4-penten-2-amine *N*-Oxide (7b).** A suspension of anti hydroxylamine iii (340 mg, 1.96 mmol) and finely ground anhydrous calcium chloride (1.09 g, 9.81 mmol) in 8 mL of anhydrous diethyl ether was prepared in a 25-mL round-bottom flask that was fitted with an argon system, a rubber septum, and a magnetic stirrer. The suspension was cooled to -20 °C, and dodecyl aldehyde (1.81 g, 9.81 mmol) was added dropwise via syringe. The reaction mixture was stirred at -20 °C for 12 h. Suction filtration through a Celite pad followed by removal of solvent at 5 °C under reduced pressure produced a viscous oil. Flash chromatography on 85 g of silica gel, eluting with diethyl ether, afforded 666 mg (100%) of the *Z* nitrone **7b**, which was used immediately in the next step because the intramolecular cyclization occurs slowly at room temperature. ^1H NMR (300 MHz, $CDCl_3$): 6.56 (t, J = 5.8 Hz, 1 H), 5.58 (dt, J = 16.4, 10.7 Hz, 1 H), 4.92 (dd, J = 10.7, 1.7 Hz, 1 H), 4.91 (dd, J = 16.4, 1.7 Hz, 1 H), 3.87 (dt, J = 10.6, 6.6 Hz, 1 H), 2.47–2.33 (m, 2 H), 2.24 (t, J = 10.5 Hz, 1 H), 1.46 (d, J = 6.6 Hz, 3 H), 1.47–1.14 (m, 18 H), 0.88 (t, J = 6.7 Hz, 3 H), ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): 136.67, 136.35, 115.13, 72.40, 39.62, 32.02, 29.71, 29.63, 29.42, 26.23, 25.93, 22.74, 19.90, 14.08, -1.4 ppm. IR (neat): 3060, 2880, 1630, 1585, 1450, 1380, 1300, 1250, 1160, 1120, 1030 cm^{-1}.

1-Hydroxy-*cis*-2-methyl-6-phenyl-1,2,5,6-tetrahydropyridine (8a) and Trans Isomer 9a from Nitrone 7a and TMSOTf. A solution of the α-phenyl-*anti*-nitrone **7a** (130 mg, 0.50 mmol) in 1 mL of dry methylene chloride was stirred at -40 °C in a 10-mL round-bottom flask equipped with a magnetic stirrer and a rubber septum. Trimethylsilyl triflate (110 g, 0.50 mmol) was added via syringe under argon. After being stirred for 8 h at -40 °C, the reaction mixture was allowed to warm up slowly to room temperature, quenched with 3.0 N aqueous HCl (2 mL), and stirred for an additional 1 h. After addition of diethyl ether (5 mL), the solution was neutralized with 3.0 N aqueous NaOH and extracted with diethyl ether (2 × 5 mL). The combined ether layer was washed with brine, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure to provide the crude product. The stereoisomers were separated by flash chromatography (silica gel 80:20:1 hexane/ethyl acetate/Et_3N). The isomer with the higher R_f value was the cis isomer **8a** (R_f 0.31, 43 mg, 46%, mp 78–79 °C) while the isomer with the lower R_f value was the trans isomer **9a** (R_f 0.13, 42 mg, 45%, mp 119 °C) (91% overall yield, a 1:1 cis/trans ratio). For the cis isomer **8a**, R_f 0.31 (80:20:1 hexane/ethyl acetate/Et_3N). ^1H NMR (300 MHz, $CDCl_3$): 7.48–7.23 (m, 5 H), 5.67 (br, 1 H), 5.50 (br, m, 1 H), 4.61 (br, N–OH), 3.80 (dd, J = 10.1, 3.4 Hz, 1 H), 3.47 (br, 1 H), 2.40 (br, 1 H), 2.28 (br, 1 H), 1.31 (d, J = 6.7 Hz, 3 H) ppm. IR (KBr): 3490–3110 (br), 3057, 3034, 2990, 2964, 1735, 1662, 1602, 1496, 1450, 1390, 1303, 1131 cm^{-1}. MS (EI, 70 eV): m/z (relative intensity) 189 (M^+, 96.8), 174 (100), 156 (22.5), 143 (2.7), 129 (11.2), 122 (40.1), 115 (8.3), 104 (11.4), 94 (4.7), 91 (25.3), 80 (17.4), 77 (9.6). Anal. Calcd for $C_{12}H_{15}NO$: C, 76.16; H, 7.99; N, 7.40. Found: C, 75.97; H, 8.06; N, 7.30. For the trans isomer **9a**, R_f 0.13 (80:19:1 hexane/ethyl acetate/triethylamine). ^1H NMR (300 MHz, $CDCl_3$): 7.42–7.25 (m, 5 H), 7.0 (br, N–OH), 5.85 (br, 1 H), 5.60 (m, 1 H), 3.97 (dd, J = 8.0, 5.5 Hz, 1 H), 3.28 (br, 1 H), 2.66 (br, 1 H), 2.29 (br, 1 H), 1.19 (d, J = 7.0 Hz, 3 H) ppm. IR (KBr): 3549–3117 (br), 3064, 3023, 2964, 2904, 1656, 1603, 1487, 1450, 1370, 1138, 1065 cm^{-1}. Anal. Calcd for $C_{12}H_{15}NO$: C, 76.16; H, 7.99; N, 7.40. Found: C, 76.00; H, 8.05; N, 7.27.

1-Hydroxy-*trans*-2-methyl-6-undecyl-1,2,5,6-tetrahydropyridine (9b) and Its Cis Isomer (8b) from Nitrone 7b and TMSOTf. The same procedure as outlined in the above reaction was applied to the α-undecyl-*anti*-nitrone **7b**. The nitrone (340 mg, 1.0 mmol) was dissolved in 2 mL of methylene chloride and treated at -40 °C with trimethylsilyl triflate (222 mg, 1.0 mmol). The reaction was stirred at that temperature for 8 h and warmed slowly to room temperature. Subsequent quenching and workup afforded the mixture of isomers, which was separated by flash chromatography (silica gel, 75:25:1 hexane/ethyl acetate/Et_3N). The isomer with the higher R_f was the cis isomer **8b** (R_f 0.31, 73 mg, 27%, mp 41 °C), while the isomer with the lower R_f was the trans isomer **9b** (R_f 0.24, 153 mg, 58%, mp 43 °C) (85% overall yield, 1:2.1 cis/trans ratio). For the cis isomer **8b**, R_f 0.31 (75:25:1 hexane/ethyl acetate/Et_3N). ^1H NMR (300 MHz, $CDCl_3$): 5.63 (br, 1 H), 5.39 (m, 1 H), 4.74 (br, N–OH), 3.29 (br, 1 H), 2.73 (br, 1 H), 2.30–1.89 (br, 2 H), 1.51–1.13 (m, 23 H), 0.88 (t, J = 6.7 Hz, 3 H) ppm. IR (KBr): 3600–3083 (br), 3083 (w), 3037, 2990–2832, 1736, 1662, 1636, 1470, 1370, 1211, 1105, 1073, 1050, 1032 cm^{-1}. MS (EI, 70 eV): m/z (relative intensity) 268 ($[M + 1]^+$, 3.3), 252 (7.8), 236 (0.5), 224 (0.2), 200 (4.8), 112 (100.0), 68 (17.6). Anal. Calcd for $C_{17}H_{33}NO$: C, 76.35; H, 12.44; N, 5.24. Found: C, 76.43; H, 12.38; N, 5.25. For the trans isomer **9b**, R_f 0.24 (75:25:1 hexane/ethyl acetate/Et_3N). ^1H NMR (300 MHz, $CDCl_3$): 6.38 (br, 1 H, N–OH), 5.71 (br, 1 H), 5.55 (m, 1 H), 3.57 (br, 1 H), 2.98 (br, 1 H), 2.07 (br, 1 H), 1.72 (br, 1 H), 1.32–1.22 (m, 20 H), 1.19 (d, J = 7.1, 3 H), 0.88 (t, J = 6.7, 3 H) ppm. Anal. Calcd for $C_{17}H_{33}NO$: C, 76.35; H, 12.44; N, 5.24. Found: C, 76.39; H, 12.20; N, 5.25.

1-Hydroxy-*cis*-2-methyl-6-phenyl-1,2,5,6-tetrahydropyridine (8a) and Its Trans Isomer (9a) from Nitrone 14 and TMSOTf. The same procedure as described in the above reaction was used. To a solution of α-phenyl-*syn*-nitrone **14** (43.0 mg, 0.16 mmol) in 0.5 mL of dry methylene chloride at -40 °C was added trimethylsilyl triflate. The resulting solution was stirred for 8 h and warmed slowly to room temperature. After workup as above and removal of the volatile compounds in vacuo, the three compounds were separated by flash chromatography (silica gel, 80:20:1 hexane/ethyl acetate/Et_3N), affording the cis isomer **8a** (R_f 0.31, 6.0 mg, 21%) and the trans isomer **9a** (R_f 0.13, 9.2 mg, 32%), along with aza-Cope rearranged product **15a** (R_f 0.09, 3.8 mg, 9%). For the cis and trans isomers (**8a** and **9a**). The spectra of **8a** and **9a** were the same as those obtained from the above reaction. For **15a**, R_f 0.09 (80:20:1 hexane/ethyl acetate/Et_3N). ^1H NMR (300 MHz, $CDCl_3$): 7.18–7.52 (m, 5 H), 6.73 (qd, J = 7.2, 2.2 Hz, 1 H), 5.92 (dt, J = 18.0, 6.2 Hz, 1 H), 5.79 (d, J = 18.5 Hz, 1 H), 4.72 (dd, J = 8.0, 5.8 Hz, 1 H), 3.29 (ddd, J = 14.4, 8.0, 6.2 Hz, 1 H), 2.70 (ddd, J = 14.4, 6.2, 5.8 Hz, 1 H), 1.85 (dd, J = 7.2, 2.2 Hz, 3 H) ppm.

***cis*-2-Methyl-6-undecyl-1,2,5,6-tetrahydropyridine (39b).** A suspension of *cis*-6-undecylhydroxylamine **8b** (76 mg, 0.28 mmol), zinc dust (371 mg, 5.68 mmol) in glacial acetic acid (2.0 mL), and water (0.8 mL) was heated at 60 °C for 4 h. The reaction mixture was then worked up as described in the procedure for **39a** (see below). Purification by short column chromatography on alumina (95:5 hexane/ethyl acetate) afforded 68 mg (97%) of the cis tetrahydropyridine **39b** as a yellow liquid. ^1H NMR (360 MHz, $CDCl_3$): 5.72 (dddd, J = 10.0, 4.8, 2.4, 1.4 Hz, 1 H), 5.54 (ddt, J = 10.0, 2.7, 1.4, 1.4 Hz, 1 H), 3.49 (m, 1 H), 2.75 (dtd, J = 10.4, 6.3, 4.0 Hz, 1 H), 2.00 (dddd, J = 17.2, 4.8, 4.0, 2.4 Hz, 1 H), 1.77 (ddq, J = 17.2, 10.4, 2.7, 2.4, 2.4 Hz, 1 H), 1.61 (br, N–H), 1.43–1.16 (m, 20 H), 1.13 (d, J = 6.8 Hz, 3 H), 0.88 (t, J = 6.8 Hz, 3 H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): 132.15, 125.04, 53.46, 50.63, 37.06, 32.15, 31.95, 29.83, 29.65, 29.38, 25.89, 22.71, 22.19, 14.11 ppm. IR (neat): 3275 (w), 3024, 2957, 2923, 2870, 1654 (w), 1591 (w), 1579 (w), 1485, 1437, 1368, 1354, 1298, 1125 cm^{-1}. MS (EI, 70 eV): m/e (relative intensity) 252 ($[M + 1]^+$, 7.7), 236 (9.8), 196 (0.4), 184 (6.5), 120 (0.8), 107 (4.3), 96 (100.0), 94 (9.8). Anal. Calcd for $C_{17}H_{33}N$: C, 81.20; H, 13.23; N, 5.57. Found: C, 81.70; H, 12.82; N, 5.50.

***cis*-2-Methyl-6-undecylpiperidine (16).** The cis-unsaturated piperidine **39b** (30.0 mg, 0.12 mmol) was dissolved in 10 mL of ethanol and 5% PtO_2/carbon was added. The mixture was stirred

and exposed to hydrogen at atmospheric pressure until H_2 up-take ceased and then filtered through Celite. The solvent was removed under reduced pressure and bulb-to-bulb distillation (112–125 °C/0.01 mmHg) gave 30 mg (100%) of cis piperidine **16** as a pale yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$): 2.69–2.58 (m, 1 H), 2.54–2.44 (m, 1 H), 1.81–1.23 (m, 26 H), 1.07 (d, J = 6.4 Hz, 3 H), 0.88 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): 57.45, 52.73, 37.67, 34.78, 32.56, 32.00, 29.97, 29.70, 29.40, 26.10, 25.14, 23.14, 22.71, 14.02 ppm. IR (neat): 3280 (w), 2954–2710, 1465, 1440, 1376, 1330, 1322, 1308, 1128, 1113 cm^{-1}. MS (EI, 70 eV): m/z (relative intensity) 254 ([M + 1]$^+$, 0.7), 238 (3.5), 210 (0.7), 184 (0.5), 98 (100.0). Anal. Calcd for $C_{17}H_{35}N$: C, 80.56; H, 13.92; N, 5.53. Found: C, 80.67; H, 14.05; N, 5.58.

***trans*-2-Methyl-6-undecyl-1,2,5,6-tetrahydropyridine.** A suspension of *trans*-6-undecylhydroxylamine **9b** (106 mg, 0.40 mmol), zinc dust (517 mg, 7.9 mmol) in glacial acetic acid (3.0 mL), and water (1.0 mL) was heated at 60 °C for 4 h. After cooling and filtering zinc dust, the filtrate was concentrated under reduced pressure. The resulting residue was diluted with water, made alkaline with aqueous 3.0 N NaOH solution, and extracted ether (3 × 15 mL). The combined extracts were washed with brine, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. Purification of a short column chromatography on alumina (95:5 hexane/ethyl acetate) afforded 93.2 mg (97%) of the trans tetrahydropyridine. ^{1}H NMR (360 MHz, $CDCl_3$): 5.71 (ddt, J = 10.1, 4.4, 2.2, 2.2 Hz, 1 H), 5.63 (dddd, J = 10.1, 3.2, 2.3, 1.5 Hz, 1 H), 3.53 (m, 1 H), 2.88 (m, 1 H), 2.06 (dtd, J = 17.4, 4.4, 4.3, 1.5 Hz, 1 H), 1.74 (ddq, J = 17.4, 8.3, 2.3, 2.3, 2.2 Hz, 1 H), 1.43–1.18 (m, 21 H), 1.16 (d, J = 6.8 Hz, 3 H), 0.88 (t, J = 6.8 Hz, 3 H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): 131.78, 124.24, 47.77, 47.58, 36.15, 31.97, 31.81, 29.87, 29.68, 29.37, 26.17, 22.67, 21.73, 14.01 ppm. IR (neat): 3280 (w), 3022, 2957–2853, 1651 (w), 1592 (w), 1579 (w), 1465, 1429, 1388, 1376, 1123, 1062 cm^{-1}. MS (EI, 70 eV): m/z (relative intensity) 252 ([M + 1]$^+$, 13.2), 236 (24.8), 210 (0.4), 196 (0.5), 184 (6.8), 120 (1.2), 107 (6.2), 96 (100.0), 94 (10.0). Anal. Calcd for $C_{17}H_{33}N$: C, 81.20; H, 13.23; N, 5.57. Found: C, 81.27; H, 13.34; N, 5.65.

***trans*-2-Methyl-6-undecylpiperidine (17).** The tetrahydropyridine from **9b** was subjected to the same procedure as described in the above reaction. A mixture of **9b** (42.1 mg, 0.17 mmol) and a catalytic amount of PtO_2 in 10 mL of ethanol was exposed to hydrogen at atmospheric pressure. After filtration, bulb-to-bulb distillation (112–125 °C/0.01 mmHg) afforded 42 mg (100%) of trans piperidine **17** as a pale yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$): 3.11–3.01 (m, 1 H), 2.92–2.83 (m, 1 H), 1.83–1.16 (m, 26 H), 1.08 (d, J = 6.4 Hz, 3 H), 0.88 (t, J = 7.0 Hz, 3 H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): 50.05, 46.11, 34.38, 33.26, 32.00, 31.13, 29.89, 29.71, 29.39, 26.59, 22.71, 21.22, 19.81, 14.01 ppm. IR (neat): 3287 (w), 2953–2834, 1465, 1442, 1375, 1341, 1330, 1297, 1140, 1097, 1088 cm^{-1}. MS (CI, 70 eV): m/z (relative intensity) 254 ([M + 1]$^+$, 5.2), 238 (2.1), 210 (0.3), 184 (0.3), 168 (0.1), 120 (0.5), 107 (3.16), 98 (100.0). Anal. Calcd for $C_{17}H_{35}N$: C, 80.56; H, 13.92; N, 5.53. Found: C, 80.37; H, 14.00; N, 5.57.

***exo*-2-Methyl-*exo*-6-phenyl-*endo*-3-(trimethylsilyl)-1-aza-7-oxabicyclo[2.2.1]heptane (18a) and Isomers 19a and 20.** A 10-mL round-bottom flask equipped with a magnetic stirrer and a reflux condenser was charged with a solution of the α-phenyl-*anti*-nitrone **7a** (131 mg, 0.50 mmol) in 3 mL of dry toluene. The solution was heated to reflux for 2 h under argon. The reaction mixture was allowed to cool to room temperature and concentrated in vacuo. The residue was purified by flash chromatography (silica gel, eluting with 15% ethyl acetate in hexane) to provide 109 mg (83%) of an inseparable mixture of **18a** and **19a** and 5 mg (4%) of **20**. ^{1}H NMR analysis (360-MHz) for the mixture showed a 4.6:1 ratio of isomers. For compound **18a** (in a mixture), R_f 0.44 (85:15 hexane/ethyl acetate). ^{1}H NMR (360 MHz, $CDCl_3$): 7.42–7.17 (m, 5 H), 4.96 (t, J = 4.9 Hz, 1 H), 3.74 (dd, J = 8.2, 5.2 Hz, 1 H), 2.93 (td, J = 6.4, 6.2 Hz, 1 H), 2.22 (dd, J = 11.9, 8.2 Hz, 1 H), 1.90 (dddd, J = 11.9, 5.2, 4.9, 2.4 Hz, 1 H), 1.12 (ddd, J = 6.2, 4.9, 2.4 Hz, 1 H), 1.21 (d, J = 6.4 Hz, 3 H), 0.14 (s, 9 H) ppm. ^{13}C NMR (90.56 MHz, $CDCl_3$): 144.78, 128.62, 127.03, 126.95, 83.34, 70.65, 66.53, 43.52, 40.67, 24.29, −1.14 ppm. For compound **19a** (in a mixture), R_f 0.44 (85:15 hexane-/ethyl acetate). ^{1}H NMR (360 MHz, $CDCl_3$): 7.42–7.18 (m, 5 H), 4.77 (d, J = 4.5 Hz, 1 H), 4.36 (dd, J = 8.1, 5.3 Hz, 1 H), 3.45 (dt, J = 7.6, 6.9 Hz, 1 H), 2.15 (dd, J = 10.8, 8.3 Hz, 1 H), 2.02 (ddd, J = 10.8, 5.3, 4.5 Hz, 1 H), 1.33 (d, J = 6.9 Hz, 3 H), 0.47 (dd, J = 7.6, 0.6 Hz, 1 H), 0.06 (s, 9 H) ppm. ^{13}C NMR (90.56 MHz, $CDCl_3$): 144.90, 128.68, 127.10, 126.90, 83.44, 64.52, 61.43, 47.55, 41.80, 16.90, −2.77 ppm. IR (neat, as a mixture of **18a** and **19a**): 3060, 3020, 2960, 1600, 1250, 1180, cm^{-1}. MS (EI, 70 eV, as a mixture): m/z (relative intensity) 261 (M$^+$, 0.5), 246 (9.7), 230 (0.1), 218 (0.1), 202 (0.2), 193 (6.3), 184 (1.5), 178 (12.13), 156 (6.6), 142 (6.81), 132 (17.3), 116 (6.6), 104 (9.8), 73 (100.0). Anal. Calcd for $C_{15}H_{23}NOSi$: C, 68.91; H, 8.87; N, 5.36. Found (as a mixture): C, 68.71; H, 8.69; N, 5.37. For compound **20**, R_f 0.25 (85:15 hexane/ethyl acetate). ^{1}H NMR (360 MHz, $CDCl_3$): 7.38–7.24 (m, 5 H), 4.98 (dd, J = 5.7, 4.3 Hz, 1 H), 4.64 (dd, J = 10.1, 6.6 Hz, 1 H), 2.95 (dt, J = 6.5, 6.5 Hz, 1 H), 2.33 (dddd, J = 11.4, 10.1, 5.7, 2.3 Hz, 1 H), 1.78 (dd, J = 11.4, 6.6 Hz, 1 H), 1.14 (d, J = 6.5 Hz, 3 H), 1.10 (m, 1 H), −0.37 (s, 9 H) ppm. ^{13}C NMR (90.56 MHz, $CDCl_3$): 137.85, 128.65, 128.52, 127.37, 85.84, 70.67, 58.31, 46.17, 33.20, 23.55, −0.63 ppm.

***exo*-2-Methyl-*exo*-6-phenyl-*endo*-3-(trimethylsilyl)-1-aza-7-oxabicyclo[2.2.1]heptane (18a) and Isomers 19a and 20.** The same procedure as described in the above reaction was used. A solution of α-phenyl-*anti*-nitrone **7a** (169 mg, 0.65 mmol) in dry benzene (3 mL) was refluxed for 22 h under argon. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (silica gel, eluting with 15% ethyl acetate in hexane) to provide 106 mg (62%) of a inseparable mixture of **18a** and **19a** and 33 mg (20%) of **20**. ^{1}H NMR analysis (360-MHz) of the mixture showed a 10:1 ratio of isomers.

***exo*-2-Methyl-*endo*-3-(trimethylsilyl)-*exo*-6-undecyl-1-aza-7-oxabicyclo[2.2.1]heptane (18b), Isomer 19b, and (*Z*)-*N*-Ethylidene-1-(trimethylsilyl)-1(*E*)-pentadecen-4-amine *N*-Oxide (15b).** A 10-mL round-bottom flask equipped with a magnetic stirrer and a reflux condenser was charged with a solution of the α-undecyl-*anti*-nitrone **7b** (101 mg, 0.30 mmol) in 2 mL of dry toluene. The solution was refluxed for 2 h under argon. After cooling the reaction mixture, the solvent was removed under reduced pressure. The residue was purified by flash chromatography (silica gel, eluting with 10% ethyl acetate in hexane) to afford 74 mg (74%) of an inseparable mixture of **18b** and **19b**, along with 4 mg (4%) of aza-Cope rearrangement product **15**. ^{1}H NMR analysis (360-MHz) for the mixture showed a 5.0:1 ratio of isomers. For compound **18b** (in a mixture), R_f 0.33 (90:10 hexane/ethyl acetate). ^{1}H NMR (360 MHz, $CDCl_3$): 4.78 (t, J = 4.8 Hz, 1 H), 2.72 (td, J = 6.4, 6.4 Hz, 1 H), 2.57 (dtd, J = 7.6, 7.1, 4.8 Hz, 1 H), 1.77 (dd, J = 11.6, 7.6 Hz, 1 H), 1.36 (dddd, J = 11.6, 4.8, 4.8, 2.4 Hz, 1 H), 1.32–1.22 (m, 20 H), 1.14 (d, J = 6.4 Hz, 3 H), 1.01 (ddd, J = 6.3, 4.8, 2.4 Hz, 1 H), 0.88 (t, J = 6.7 Hz, 3 H), 0.07 (s, 9 H) ppm. ^{13}C NMR (90.56 MHz, $CDCl_3$): 83.26, 68.04, 65.91, 43.03, 37.48, 37.11, 32.02, 29.71, 29.44, 26.80, 24.14, 22.75, 14.14, −1.18 ppm. For compound **19b** (in a mixture), R_f 0.33 (90:10 hexane/ethyl acetate). ^{1}H NMR (360 MHz, $CDCl_3$): 4.60 (d, J = 4.5 Hz, 1 H), 3.32 (td, J = 7.8, 7.4 Hz, 1 H), 3.16 (dtd, J = 7.7, 7.2, 5.0 Hz, 1 H), 1.68 (dd, J = 10.9, 7.7 Hz, 1 H), 1.51 (ddd, J = 10.9, 5.0, 4.5 Hz, 1 H), 1.32–1.22 (m, 20 H), 1.19 (d, J = 7.8 Hz, 3 H), 0.88 (t, J = 6.9 Hz, 3 H), 0.30 (d, J = 7.4 Hz, 1 H), 0.02 (s, 9 H) ppm. ^{13}C NMR (90.56 MHz, $CDCl_3$): 83.20, 63.92, 58.55, 44.42, 41.40, 36.85, 32.04, 29.74, 29.46, 27.05, 22.77, 16.87, 14.14, −2.86 ppm. IR (neat, as a mixture): 2920–2840, 1445, 1370, 1250, 1180, 1050 cm^{-1}. MS (EI, 70 eV, as a mixture): m/z (relative intensity) 340 ([M + 1]$^+$, 0.3), 324 (4.5), 272 (0.3), 266 (0.4), 234 (1.1), 226 (0.9), 210 (6.8), 198 (0.3), 184 (100.0), 168 (1.0), 156 (0.8), 142 (0.6), 112 (1.6). Anal. Calcd for $C_{20}H_{41}NOSi$: C, 70.73; H, 12.17; N, 4.12; Si, 8.27. Found (as a mixture): C, 70.90; H, 12.18; N, 4.17; Si, 8.33. For compound **15**, R_f 0.14 (90:10 hexane/ethyl acetate). ^{1}H NMR (360 MHz, $CDCl_3$): 6.67 (q, J = 5.8 Hz, 1 H), 5.88 (dt, J = 18.5, 6.3 Hz, 1 H), 5.75 (d, J = 18.5 Hz, 1 H), 3.60 (ddt, J = 8.8, 8.8, 4.4 Hz, 1 H), 2.73 (ddd, J = 14.4, 8.8, 6.3 Hz, 1 H), 2.30 (m, 1 H), 1.99 (d, J = 5.8 Hz, 3 H), 1.50–1.16 (m, 20 H), 0.88 (t, J = 6.9 Hz, 3 H), 0.04 (s, 9 H) ppm. ^{13}C NMR (90.56 MHz, $CDCl_3$): 141.93, 134.61, 133.46, 75.77, 39.78, 32.10, 32.02, 29.70, 29.43, 29.37, 26.29, 22.76, 14.13, 12.16, −1.27 ppm.

***endo*-2-Methyl-*exo*-6-phenyl-*exo*-3-(trimethylsilyl)-1-aza-7-oxabicyclo[2.2.1]heptane (19a) and Isomers 18a and 27 from (1*R**,2*R**)-(*Z*)-*N*-Benzylidene-3-(trimethylsilyl)-4-penten-4-amine *N*-Oxide (14).** α-Phenyl-*syn*-nitrone **14** (53 mg, 0.20 mmol) was dissolved in 2 mL of dry toluene. The solution was heated to reflux for 20 h, concentrated in vacuo, and then

flash chromatographed to afforded 21 mg (39%) of an inseparable mixture of **19a**, **27**, and **18a**. ^{1}H NMR analysis (360-MHz) showed a 11:8:1 ratio. The ^{1}H NMR spectra of **19a** and **18a** were the same as those obtained from the previous reaction. For compound **27** (in a mixture). ^{1}H NMR (360 MHz, $CDCl_3$): 7.42–7.17 (m, 5 H), 4.84 (d, J = 4.3 Hz, 1 H), 3.92 (dd, J = 8.3, 5.6 Hz, 1 H), 3.37 (m, 1 H), 2.18 (dd, J = 11.2, 5.6 Hz, 1 H), 2.02 (m, 1 H), 1.29 (d, J = 6.6 Hz, 3 H), 1.19 (d, J = 9.3, 1 H), 0.14 (s, 9 H) ppm.

(2*R,3*R**,4*R**,6*R**)-2-Methyl-6-phenyl-3-(trimethylsilyl)-4-piperidinol (34) and 2*R**,3*R**,4*S**,6*S** Isomer (35).** To a solution of the 4.6:1 mixture of bicyclic isoxazolidine (65 mg, 0.25 mmol, **18a**:**19a** = 4.6:1) in glacial acetic acid (2 mL) and H_2O (2 mL) which was prepared in a 25-mL round-bottom flask equipped with a magnetic stirrer and a reflux condenser was added zinc dust (327 mg, 5.0 mmol), and the suspension was stirred for 4 h at 60 °C. The cooled solution mixture was filtered in order to remove the zinc, which was washed thoroughly with ethyl acetate. The combined filterate and washing were concentrated under reduced pressure. The residue was diluted with water, then made basic with 2 N NaOH solution, and extracted with diethyl ether. The ethereal extract was subsequently washed with water and brine, dried over anhydrous sodium sulfate, and evaporated in vacuo. Flash chromatography (silica gel, eluting with 70:30:2 hexane/ethyl acetate/Et_3N), yielded in 65 mg (100%) of a mixture of the piperidinols **34** and **35**. The isomers were inseparable by chromatography. For compound **34** (in a mixture). ^{1}H NMR (300 MHz, $CDCl_3$): 7.45–7.20 (m, 5 H), 3.79 (ddd, J = 10.7, 10.4, 4.6 Hz, 1 H), 3.66 (dd, J = 11.4, 2.6 Hz, 1 H), 2.84 (dq, J = 10.7, 6.2 Hz, 1 H), 2.16 (ddd, J = 12.0, 4.6, 2.6 Hz, 1 H), 1.72 (br, 2 H, NH and OH), 1.48 (ddd, J = 12.0, 11.4, 10.4 Hz, 1 H), 1.22 (d, J = 6.2 Hz, 3 H), 0.69 (t, J = 10.7 Hz, 1 H), 0.16 (s, 9 H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): 144.34, 128.74, 126.93, 71.21, 59.39, 53.01, 44.88, 41.64, 23.44, 0.35 ppm. For compound **35** (in a mixture). ^{1}H NMR (300 MHz, $CDCl_3$): 7.45–7.20 (m, 5 H), 4.31 (ddd, J = 7.0, 4.6, 4.9 Hz, 1 H), 4.14 (dd, J = 8.2, 5.1 Hz, 1 H), 3.54 (td, J = 6.6, 6.3 Hz, 1 H), 2.06–1.88 (m, 2 H), 1.72 (br, 2 H, NH and OH), 1.28 (d, J = 6.6 Hz, 3 H), 1.00 (t, J = 4.9 Hz, 1 H), 0.14 (s, 9 H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): 145.06, 127.49, 127.19, 68.75, 52.61, 47.54, 41.64, 37.35, 22.04, 0.15 ppm. IR (neat, as a mixture): 3600–3100, 3070, 3020, 1600, 1420, 1350, 1245, 1150, 1050 cm^{-1}. MS (EI, 70 eV): m/z (relative intensity) 264 ([M + 1]$^+$, 18.5), 248 (100.0), 230 (3.4), 218 (1.6), 204 (2.0), 190 (8.3), 180 (24.0), 178 (10.9), 172 (18.3), 162 (6.3), 158 (54.4), 146 (25.1), 144 (20.5), 132 (58.4), 119 (14.3), 104 (67.6), 91 (16.1). Anal. Calcd for $C_{15}H_{25}NOSi$: C, 68.39; H, 9.56; N, 5.32; Si, 10.70. Found (as a mixture): C, 68.27; H, 9.62; N, 5.42; Si, 10.62.

***cis*-2-Methyl-6-phenyl-1,2,5,6-tetrahydropyridine (39a) and Trans Isomer 40a.** To a solution of a 4.6:1 mixture of piperidinol **34** and **35** (60 mg, 0.23 mmol) in dry toluene (2 mL) in a 10-mL round-bottom flask was added p-toluenesulfonic acid·H_2O (987 mg, 0.46 mmol). The resulting solution was heated to reflux for 3 h. The cooled mixture was treated with saturated sodium bicarbonate (5 mL) and extracted with diethyl ether (2 × 10 mL). The extracts were washed with brine, dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was purified by a short column chromatography on alumina (95:5 hexane/ethyl acetate) to afford 36 mg (92%) of a 5.4:1 mixture of cis/trans tetrahydropyridines **39a** and **40a**. The spectral data of **41a** and **42a** were described. Anal. Calcd for $C_{12}H_{15}N$: C, 83.19; H, 8.73; N, 8.08. Found (as a mixture): C, 83.14; H, 8.70; N, 8.10.

1-Hydroxy-*cis*-2-methyl-6-phenyl-1,2,5,6-tetrahydropyridine (8a) from Compound 18a and TMSOTf. A 4.6:1.0 mixture of *exo*-6-phenyl bicyclic isoxazolidines **18a** and **19a** (112 mg, 0.43 mmol) was dissolved in dry methylene chloride (1 mL) in a 10-mL round-bottom flask equipped with a magnetic stirrer and a rubber septum. Trimethylsilyl triflate (95 mg, 0.43 mmol) was added via syringe under argon. The resulting solution was stirred for 2.5 h at room temperature, quenched with 3.0 N aqueous HCl (1 mL), and stirred for an additional 1 h. After addition of diethyl ether (5 mL), the solution was neutralized with 3.0 N aqueous NaOH and extracted with diethyl ether (3 × 5 mL). The combined ether layer was washed with brine, dried over anhydrous sodium sulfate, and evaporated under reduced pressure. The residue was purified by flash chromatography (silica gel, eluting with 90:10:1 hexane/ethyl acetate/Et_3N) to afford 64 mg (94%, based on the recovered starting material) of *cis*-6-phenyl-*N*-hydroxytetrahydropyridine (**8a**) and 18 mg of the exo silyl starting material **19a** (mp 78–79 °C). The spectral data were identical with those previously described.

1-Hydroxy-*cis*-2-methyl-6-undecyl-1,2,5,6-tetrahydropyridine (8b) from Compound 18b and TMSOTf. The same procedure as described in the above reaction was used. To a solution of 6-undecyl bicyclic isoxazolidines **18b** and **19b** (132 mg, 0.39 mmol, **18b**:**19b** = 7.8:1) in 2 mL of dry methylene chloride was added trimethylsilyl triflate (86 mg, 0.39 mmol) at room temperature under argon. The resulting solution was stirred for 3 h. After workup as above and removal of the volatiles in vacuo, the residue was purified by flash chromatography (silica gel, eluting with 90:10:1 hexane/ethyl acetate/Et_3N) to afford 87 mg (91%) of *cis*-6-undecyl-*N*-hydroxytetrahydropyridine (**8b**) and 11 mg of the exo silyl starting material **19b**. The spectral data were identical with those previously described.

1-Hydroxy-*trans*-2-methyl-6-phenyl-1,2,5,6-tetrahydropyridine (9a). The same procedure as described in the above reaction was used. To a solution of *endo*-6-phenyl bicyclic isoxazolidine **20** (26 mg, 0.10 mmol) in 0.5 mL of dry methylene chloride was added trimethylsilyl triflate (22 mg, 0.10 mmol) at room temperature under argon. The resulting solution was stirred for 3 h. After workup as above and removal of the volatiles in vacuo, the residue was purified by flash chromatography (silica gel, eluting with 80:20:1 hexane/ethyl acetate/Et_3N) to afford 16 mg (85%) of *trans*-6-phenyl-*N*-hydroxytetrahydropyridine (**9a**) (mp 19 °C).

***cis*-2-Methyl-6-phenyl-1,2,5,6-tetrahydropyridine (39a).** A 25-mL round-bottom flask equipped with a reflux condenser and a magnetic stirrer was charged with a solution of *cis*-6-phenylhydroxylamine **8a** (76 mg, 0.40 mmol) in glacial acetic acid (3.0 mL) and water (1.0 mL). The solution was treated with zinc dust (524 mg, 8.03 mmol) with vigorous stirring. The mixture was heated at 60 °C for 4 h, and cooled to room temperature. Zinc dust was filtered off and washed with glacial acetic acid (2 mL) and ethyl acetate (3 mL). After the filtrate was concentrated under reduced pressure, the residue was diluted with water, made alkaline with aqueous 3.0 N NaOH, and extracted three times with 10 mL portions of ether. The ether extracts were washed with brine, dried over anhydrous Na_2SO_4 and evaporated in vacuo. The residue was purified by short column chromatography on alumina (95:5 hexane/ethyl acetate) to afford 60.7 mg (87%) of the amine product **39a** as a pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): 7.41–7.22 (m, 5 H), 5.81 (ddt, J = 10.0, 4.6, 2.3, 2.3 Hz, 1 H), 5.63 (ddt, J = 10, 2.3, 1.7, 1.6 Hz, 1 H), 3.91 (dd, J = 9.1, 5.4 Hz, 1 H), 3.69 (m, 1 H), 2.28–2.14 (m, 2 H), 1.69 (br, N–H), 1.20 (d, J = 6.8 Hz, 3 H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): 145.07, 132.28, 128.46, 127.18, 126.61, 125.08, 58.58, 51.55, 34.39, 22.26 ppm. IR (neat): 3300 (br, w), 3083, 3061, 3028, 2963, 2822, 1658, 1600, 1582, 1452, 1301, 1200, 1110 cm^{-1}. MS (EI, 70 eV): m/z (relative intensity) 173 (M$^+$, 74.7), 158 (68.5), 141 (5.6), 128 (6.5), 115 (11.0), 106 (100.0), 96 (6.6), 91 (21.2). Anal. Calcd for $C_{12}H_{15}N$: C, 83.19; H, 8.73; N, 8.08. Found: C, 83.22; H, 8.82; N, 8.05.

***trans*-2-Methyl-6-phenyl-1,2,5,6-tetrahydropyridine (40a).** A suspension of *trans*-6-phenylhydroxylamine **9a** (59.0 mg, 0.31 mmol), zinc dust (407 mg, 6.24 mmol) in glacial acetic acid (2.0 mL), and water (0.8 mL) was heated at 60 °C for 4 h. The reaction mixture was then worked up as described in the above procedure followed by chromatographic purification (alumina, 95:5 hexane/ethyl acetate) to afford 48.1 mg (89%) of the trans amine **40a**. ^{1}H NMR (300 MHz, $CDCl_3$): 7.38–7.22 (m, 5 H), 5.84 (dddd, J = 10.1, 4.7, 2.9, 1.8 Hz, 1 H), 5.73 (ddt, J = 10.1, 3.6, 1.8, 1.8 Hz, 1 H), 4.05 (dd, J = 8.0, 5.4 Hz, 1 H), 3.64 (m, 1 H), 2.24 (m, 2 H), 1.65 (s, N–H), 1.25 (d, J = 6.8 Hz, 3 H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): 144.87, 131.68, 128.41, 127.04, 126.84, 124.67, 52.10, 48.74, 33.29, 21.68 ppm. IR (neat): 3270 (br), 3040, 3020, 2960–2800, 1650, 1600, 1580, 1430, 1320, 1300, 1200, 1110 cm^{-1}. Anal. Calcd for $C_{12}H_{15}N$: C, 83.19; H, 8.73; N, 8.08. Found: C, 83.22; H, 8.82; N, 8.05.

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