Cyclization of *N*-Butyl-4-pentenylaminyl: Implications for the Cyclization of Alkenylaminyl Radicals

Brendan J. Maxwell and John Tsanaktsidis*,†

Contribution from the School of Chemistry, The University of Melbourne, Parkville, Victoria 3052, Australia

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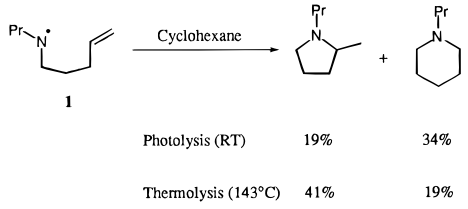
Abstract: The utility of arenesulfenamides as aminyl radical precursors has been clearly demonstrated. The cyclization of *N*-butyl-4-pentenylaminyl is shown to be a slow and irreversible process that is accelerated significantly by small amounts of bis(tributyltin) oxide.

Introduction

The practice of chemical synthesis has benefited enormously, in recent times, from the maturation of the discipline of free radical chemistry.[1] In particular, the development of several reliable, highly chemoselective, techniques for generating carbon-centered radicals, along with the deeper understanding of the factors that govern the regio- and diasteroselectivity of their inter- and intramolecular addition reactions to carbon−carbon and carbon−heteroatom (N, O, S) multiple bonds, has been critical.[2] The analogous reactions of heteroatom-centered radicals, however, have not found similar favor in modern chemical synthesis despite their potential for the construction of heterocyclic ring systems of various sizes. Indeed, recent contributions from the laboratories of Newcomb,[3] Suginome,[4] Kim,[5] and Bowman[6] on the cyclization reactions of alkenylaminyl radicals have served to focus considerable attention on the mechanistic features of these processes.

Scheme 1



Careful scrutiny of the available literature on the cyclization reactions of aminyl radicals reveals an uncertain situation. Pioneering studies by Michejda and co-workers[7] on the cyclization reactions of *N*-propyl-4-pentenylaminyl (**1**), generated by photolysis of the corresponding symmetric tetrazene in cyclohexane at room temperature, indicate formation of *N*-propyl-2-methylpyrrolidine and *N*-propylpiperidine[8] in 19% and 34% yields, respectively, whereas thermolysis (143 °C) of the tetrazene precursor in the same solvent produced the same products in 41% and 19% yields, respectively (Scheme 1). Subsequent efforts by Maeda and Ingold to measure the rate of cyclization of **1** and other representative alkenylaminyl radicals using kinetic EPR spectroscopy, however, were unsuccessful and led to the conclusion that cyclization of **1** at 25 °C is immeasurably slow ($k_c \leq 5\ s^{-1}$).[9,10] More recently, Newcomb and co-workers[3d−f] studied the cyclization of the alkenylaminyl **9**, generated by photolysis of **2**, in the presence of tributyltin hydride (Bu_3SnH) and concluded that **9** undergoes *reversible* cyclization ($k_c = 3.5 \times 10^3\ s^{-1}$, $k_{-c} = 1.0 \times 10^4\ s^{-1}$; $K = 0.35$ at 50 °C)[11] (Scheme 2), whereas Bowman and co-workers failed to observe cyclization of **9** in the presence of low concentrations of Bu_3SnH in boiling cyclohexane.[6] Against this uncertain background of conflicting reports we describe herein our results on this topic. Specifically, we demonstrate the utility of arenesulfenamides as aminyl radical precursors and we show that the cyclization of **9** is an irreversible process (*i.e.*, $k_c \gg k_{-c}$) and that the rate of cyclization in benzene is enhanced

† Current address: Division of Chemicals and Polymers, CSIRO, Private Bag 10, Rosebank MDC, Clayton, Victoria 3169, Australia. E-mail: j.tsanaktsidis@chem.csiro.au.

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(4) (a) Tokuda, M.; Fujita, H.; Suginome, H. *J. Chem. Soc., Perkin Trans. 1* **1994**, 777. (b) Tokuda, M.; Miyamoto, T.; Fujita, H.; Suginome, H. *Tetrahedron* **1991**, *47*, 747. (c) Tokuda, M.; Yamada, Y.; Takagi, T.; Suginome, H. *Tetrahedron* **1987**, *43*, 281.

(5) (a) Kim, S.; Yoon, K. S.; Kim, S. S.; Seo, H. S. *Tetrahedron* **1995**, *51*, 8437. (b) Kim, S.; Joe, G. H.; Do, J. Y. *J. Am. Chem. Soc.* **1994**, *116*, 5521. (c) Kim, S.; Joe, G. H.; Do, J. Y. *J. Am. Chem. Soc.* **1993**, *115*, 3328.

(6) (a) Bowman, W. R.; Clark, D. N.; Marmon, R. J. *Tetrahedron* **1994**, *50*, 1275. (b) Bowman, W. R.; Clark, D. N.; Marmon, R. J. *Tetrahedron* **1994**, *50*, 1295. (c) Bowman, W. R.; Clark, D. N.; Marmon, R. J. *Tetrahedron Lett.* **1991**, *32*, 6441.

(7) Michejda, C. J.; Campbell, D. H.; Sieh, D. H.; Koepke, S. R. In, *Organic Free Radicals*; Pryor, W. A., Ed.; ACS Symposium Series 69; American Chemical Society: Washington, DC, 1978; p 292.

(8) This result is belived to be in error; see ref 3d.

(9) Maeda, Y.; Ingold, K. U. *J. Am. Chem. Soc.* **1980**, *102*, 328.

(10) This value is believed to be underestimated by about a factor of 5; see: Nazran, A. S.; Griller, D. *J. Am. Chem. Soc.* **1983**, *105*, 1970.

(11) This value has been recently revised to 1; see ref 3b.

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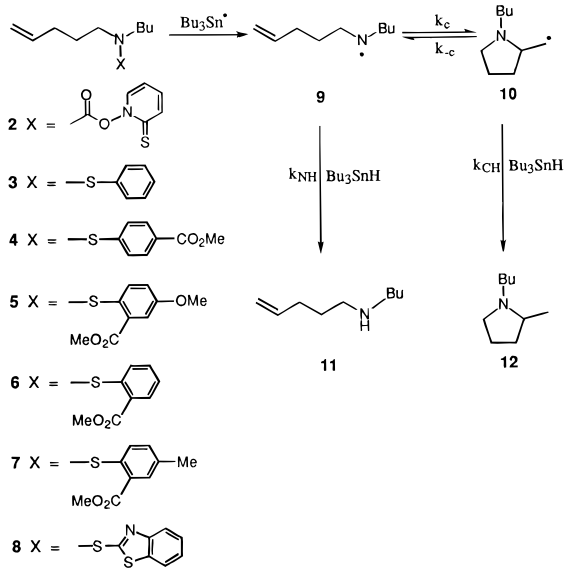
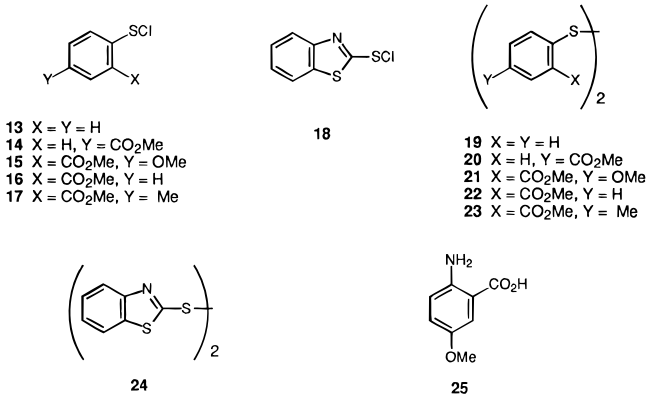
Scheme 2



significantly by the presence of small quantities of bis(tributyltin) oxide ($(Bu_3Sn)_2O$).[12]

Results and Discussion

Studies in these[12b] and other[6] laboratories have shown that benzenesulfenamides, $PhSNR^1R^2$, derived from dialkylamines undergo smooth homolytic substitution at sulfur by tributyltin radicals ($Bu_3Sn^•$), under standard reaction conditions (benzene, catatytic AIBN, 80 °C), thus producing the corresponding dialkylaminyl radical, $R^1R^2N^•$. In our hands, however, purification of the benzenesulfenamide **3** by chromatography on either silica or neutral alumina was complicated by competitive hydrolysis.[13] A search for more robust precursor substrates led to the investigation of several other arenesulfenamides, **4**−**8** (Scheme 2). The sulfenamides **3**−**8** were prepared from **11** upon treatment with the appropriate arenesulfenyl chloride (**13**−**18**) in dry diethyl ether under nitrogen in the presence of triethylamine.[14] The sulfenyl chlorides **13**−**18** were prepared from the corresponding disulfides **19**−**24**, respectively, upon treatment with sulfuryl chloride in dichloromethane. **20**, **21**, and **23** were synthesized from *p*-aminobenzoic acid, 2-amino-5-methoxybenzoic acid (**25**), and 2-amino-5-methylbenzoic acid,



respectively, using standard literature methodology.[15] Sulfenamides **4** and **5**, like **3**, were prone to hydrolysis upon exposure to silica, whereas **6**, **7**, and **8** could be chromatographed without incident on both silica gel and alumina. Exploratory experiments of **4**, **6**, **7**, and **8** with 1 equiv of Bu_3SnH in boiling benzene, in the presence of catalytic AIBN, resulted in the formation of **11** and **12**, thus implicating the intermediacy of the aminyl **9** in these reactions, and at the same time demonstrated the superior reactivity of **8** ($t_{1/2}$ = ∼15 min at 80 °C) relative to **6** and **7** ($t_{1/2}$ = ∼5 h at 80 °C) toward $Bu_3Sn^•$. A disturbing feature of these experiments, however, was the lack of consistency in the observed ratio of **11** to **12** (*i.e.*, ∼2 to >200), irrespective of the sulfenamide precursor used (*vide infra*).

In order to assess properly the effectiveness of arenesulfenamides as precursors for dialkylaminyl radicals, the radical chain reactions of the sulfenamide **8** and Bu_3SnH[16] in benzene (80 °C, catalytic AIBN) were performed under pseudo-first-order conditions at several Bu_3SnH concentrations. The resultant solutions were analyzed by gas chromatography and products identified by comparison with authentic materials. Response factors for **11** and **12**, relative to an internal standard (nonane), were determined independently using authentic samples. The free radical nature of these reactions was demonstrated by a series of control experiments. For example, in the absence of Bu_3SnH and AIBN, **8** was recovered unchanged; however, upon addition of Bu_3SnH a slow reaction ensued, leading to a mixture of the amines **11** and **12**. This process was interrupted completely upon addition of a radical inhibitor (2,4,6-tri-*tert*-butylphenol).[17]

Application of the steady state assumption to the kinetic analysis consistent with the mechanism depicted in Scheme 2 leads to the approximate rate equation (eq 1) where $[Bu_3SnH]_m$ represents the mean Bu_3SnH concentration during the reaction.[3d,18] The results from these experiments are depicted graphically in

$$\mathbf{11}/\mathbf{12} = (k_{NH}k_{-c})/(k_{CH}k_c) + (k_{NH}/k_c)[Bu_3SnH]_m \quad (1)$$

Figure 1. Consideration of the data revealed a variation in the ratio **11**/**12** which is inconsistent with eq 1. These observations prompted a thorough examination of our experimental technique, and ultimately led to the realization that small amounts of $(Bu_3Sn)_2O$,[19,20] present in the Bu_3SnH employed, may have been responsible for the observed variation in the ratio **11**/**12**. The importance of $(Bu_3Sn)_2O$ in these reactions was demonstrated beyond doubt through reaction of **8** with 1 equiv of Bu_3SnH (0.05 M) in benzene (catalytic AIBN) in the presence of differing amounts of $(Bu_3Sn)_2O$. As illustrated by Figure 2, *the presence of* $(Bu_3Sn)_2O$, *even at very low concentrations*, *leads to significantly more cyclization*. This previously unrecognized influence of $(Bu_3Sn)_2O$ is suggestive of a Lewis acid-type interaction with the aminyl **9**[21,22] and is reminiscent of the

(12) Part of this work has appeared in preliminary form: (a) Maxwell, B. J.; Tsanaktsidis, J. *J. Chem. Soc., Chem. Commun.* **1994**, 533. (b) Beckwith, A. L. J.; Maxwell, B. J.; Tsanaktsidis, J. *Aust. J. Chem.* **1991**, *44*, 1809.

(13) Cf. ref 6c.

(14) (a) Craine, L.; Rabin, M. *Chem. Rev.* **1989**, *89*, 589. (b) Davis, F. A. *Int. J. Sulfur Chem.* **1973**, *8*, 71.

(15) Allen, C. F. H.; MacKay, D. D. *Organic Syntheses*; Wiley: New York, 1943; Collective Vol. 2, p 580.

(16) Bu_3SnH was prepared by $NaBH_4$ reduction of $(Bu_3Sn)_2O$; see: Szammer, J.; Ötvös, L. *Chem. Ind.* **1988**, 754.

(17) A reviewer pointed out that 2,4,6-tri-*tert*-butylphenol does not trap carbon- or tin-centered radicals at significant rates and suggested that our observations may imply the generation of nitrogen-centered radicals in the control experiments.

(18) Newcomb, M. *Tetrahedron* **1993**, *49*, 1151.

(19) $(Bu_3Sn)_2O$ is only one of several possible oxides of tin resulting from the aerobic oxidation of Bu_3SnH[20] potentially capable of influencing these reactions; every effort was made to minimize such impurities in these reactions.

(20) Omae, I. *Journal of Organometallic Chemistry Library*; Organotin Chemistry. Elsevier: Amsterdam, 1989; Vol. 21, p 66.

(21) ^{119}Sn NMR experiments failed to identify a significant interaction between $(Bu_3Sn)_2O$ and **8**.

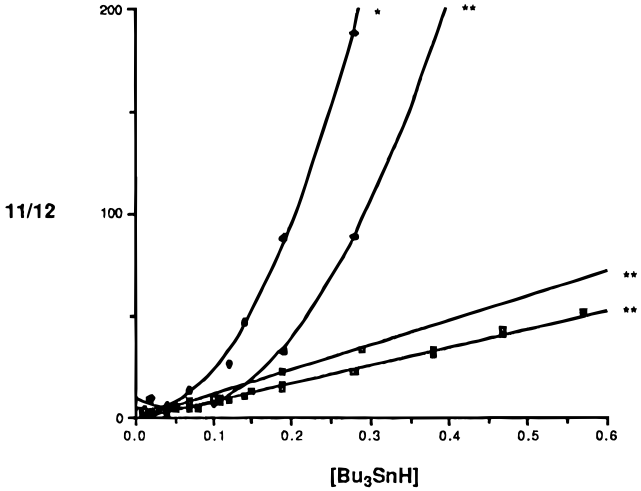


Figure 1. Results from the reactions of **8** with Bu_3SnH (10 equiv) in benzene at 75 (*) and 80 (**) °C.

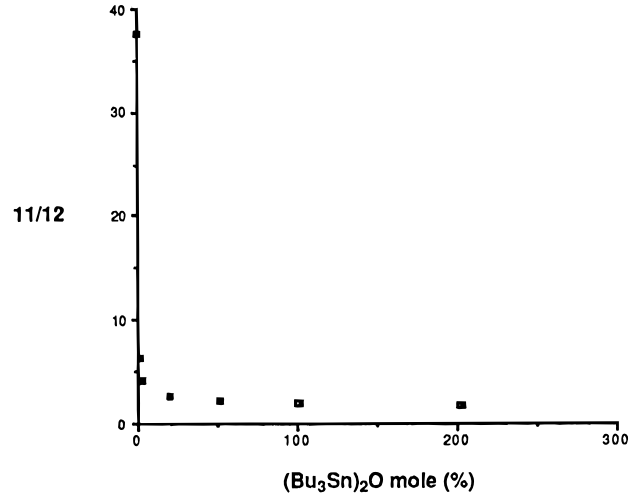


Figure 2. Results from the reactions of **8** with Bu_3SnH (10 equiv) in benzene at 75 °C in the presence of $(Bu_3Sn)_2O$.

acceleration afforded to alkenylaminyl radical cyclizations by protonation or complexation with a metal center.[3c,23] The generality of this influence was investigated through the reactions of carbamate **2** with freshly distilled Bu_3SnH (10 equiv) under pseudo-first-order conditions in boiling benzene both in the absence (data set 1) and in the presence (data set 2) of added $(Bu_3Sn)_2O$ (1 equiv) (Figure 3). The significantly higher levels of cyclization of **9** in the latter case (data set 2) are suggestive of a specific interaction between **9** and $(Bu_3Sn)_2O$ and not the precursor substrate.

In order to shed more light on this influence, the reaction of **8** with 1 equiv of Bu_3SnH (0.05 M) in benzene (catalytic AIBN) in the presence of several tin-containing Lewis acids was investigated (Table 1). Although consideration of these data provides little insight as to the nature of the putative interaction between **9** and the more active tin-based additives (entries 2−5), two points can be made. Firstly, there does not appear to be

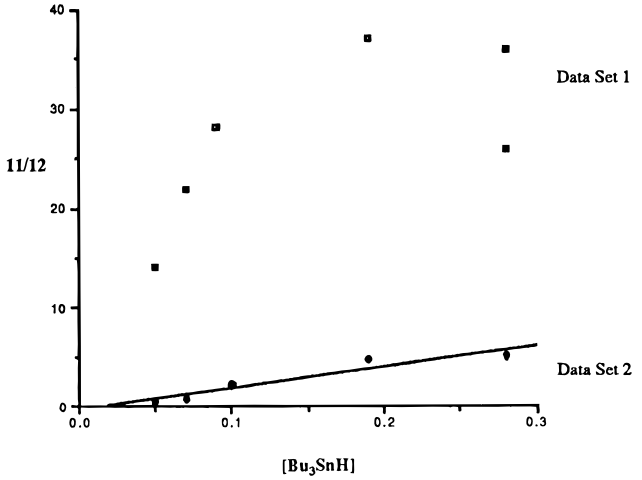


Figure 3. Results from the reactions of **2** with Bu_3SnH (10 equiv) in benzene at 80 °C in the absence (data set 1) and the presence (data set 2) of $(Bu_3Sn)_2O$ (1 equiv).

Table 1. Reaction of **8** with Bu_3SnH (1 equiv, 0.05 M) in Benzene (80 °C, AIBN) in the Presence of a Lewis Acid

entry	additive	[additive] (mol %)	**11**/**12**
1	none		>200
2	$(Bu_3Sn)_2O$	7	2.6
3	$(Ph_3Sn)_2O$	6	4.7
4	Sn ladder[a]	5	17.4
5	$Bu_2Sn(Cl)OSn(Cl)^tBu_2$	18	21.4
6	Bu_3SnCl	20	>200
7	Bu_2SnCl_2	23	>200

[a] 1-Hydroxy-3-(isothiocyanato)tetrabutyldistannoxane.

an obvious correlation between Lewis acid strength and activity, and secondly, the presence of the Sn−O−Sn linkage seems to be significant.[24] Indeed, these observations led to the speculation that the interaction between $(Bu_3Sn)_2O$ and **9** may be chelative in nature.[25]

These observations made it clear that a meaningful kinetic investigation of the cyclization of **9** using the Bu_3SnH method was likely to be problematic. Accordingly, a full kinetic analysis of the cyclization of **9** in the presence of added $(Bu_3Sn)_2O$ was undertaken. Treatment of **8** with excess Bu_3SnH (benzene, catalytic AIBN) in the presence of 1 equiv of $(Bu_3Sn)_2O$, under pseudo-first-order conditions, produced the data represented graphically in Figure 4. The excellent fit of these data to eq 1 along with the effectively zero intercept vindicated this approach. This result is consistent with an irreversible cyclization of the $(Bu_3Sn)_2O$-complexed aminyl **9**. In the light of these findings and the clear incompatability of the kinetic data depicted in Figure 1 with eq 1, the proposed equilibrium[3d] between **9** and **10** in the absence of $(Bu_3Sn)_2O$ was questioned. Accordingly, the reaction of the selenide **26** and Bu_3SnH was reinvestigated (Scheme 3). **26** was prepared according to the procedure of Newcomb and co-workers[26] and treated with *freshly distilled* (0.01 and 0.005 M) Bu_3SnH (10 equiv) in benzene (catalytic AIBN) at both 50 and 80 °C. GC analysis of the reaction mixtures failed to reveal the presence (<0.5%) of the acyclic amine **11**. If this process were reversible, ∼5−

(22) For other Lewis acid influenced radical reactions, see: (a) Nishida, M.; Hayashi, H.; Yamaura, Y.; Nishida, A.; Kawahara, N. *Tetrahedron Lett.* **1995**, *36*, 269. (b) Renaud, P.; Moufid, N.; Kuo, L. H.; Curran, D. P. *J. Org. Chem.* **1994**, *59*, 3547. (c) Renaud, P.; Bourquard, T.; Gerster, M.; Moufid, N. *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1601. (d) Yamamoto, Y.; Onuki, S.; Yumoto, M.; Asao, N. *J. Am. Chem. Soc.* **1994**, *116*, 421. (e) Nagano, H.; Kuno, Y. *J. Chem. Soc., Chem. Commun.* **1994**, 987. (f) Feldman, K. S.; Romanelli, A. L.; Ruckle, R. E.; Miller, R. F. *J. Am. Chem. Soc.* **1988**, *110*, 3300. (g) Clark, T. *J. Chem. Soc. Chem. Commun.* **1986**, 1774.

(23) Stella, L. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 337.

(24) The coproduct 2-benzothiazolyltributyltin sulfide, produced *in situ* from the reaction of **8** with Bu_3SnH, is unlikely to be important in these reactions due to the absence of cyclization under "$(Bu_3Sn)_2O$-free" conditions (see Table 1, entry 1).

(25) This assertion assumes that the key interaction between alkenylaminyls of the type **9** and $(Bu_3Sn)_2O$ is with the nitrogen center. Although this is reasonable, a discrete interaction between $(Bu_3Sn)_2O$ and the olefinic center bond cannot be excluded; see ref 22g.

(26) Newcomb, M.; Marquardt, D. J.; Kumar, M. U. *Tetrahedron* **1990**, *46*, 2345.

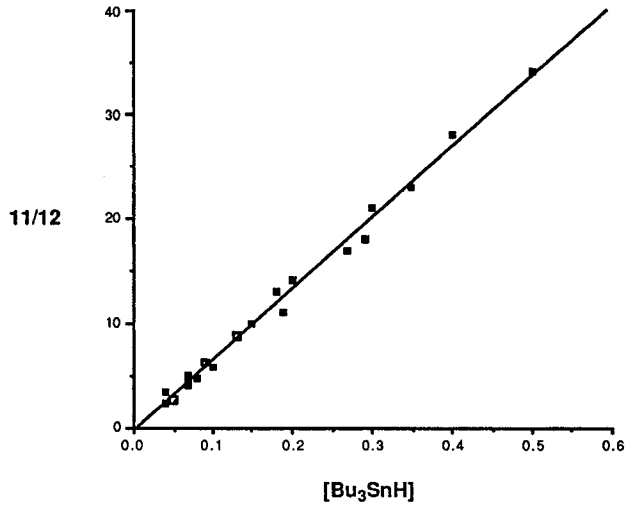


Figure 4. Results from the reactions of **8** with Bu_3SnH (1 equiv) in benzene at 80 °C in the presence of $(Bu_3Sn)_2O$ (1 equiv).

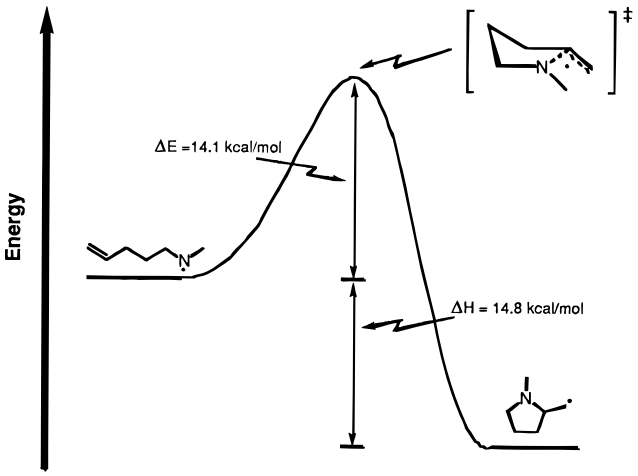
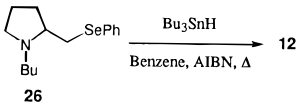


Figure 5. *Ab initio* calculated energy profile for the 5-*exo*-trig ring closure of **27**.

Scheme 3

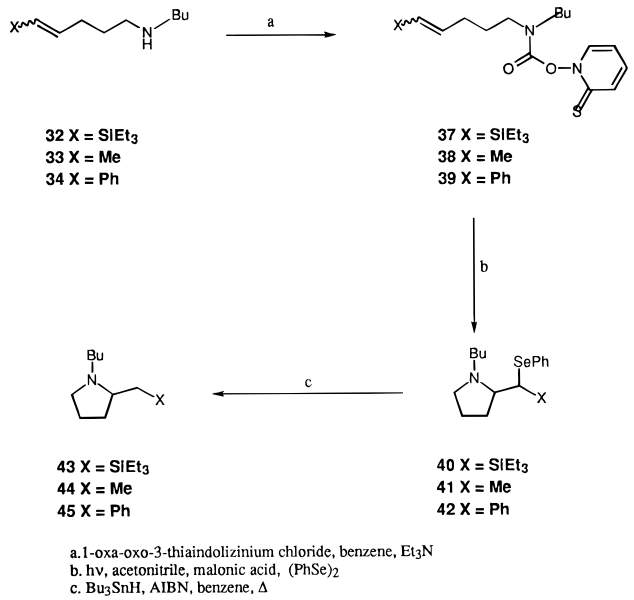


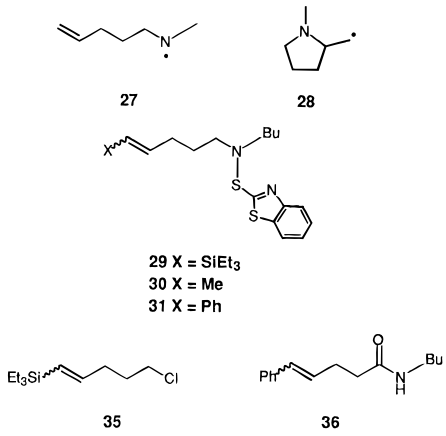
6% of **11** would be expected under these reaction conditions.[3d] It should be stressed at this point that the potential of $(Bu_3Sn)_2O$ to alter the ring opening process (**10** → **9**) was fully appreciated, and therefore, every effort was made to exclude its presence.

As further Bu_3SnH-mediated experimental investigations were likely to be ambiguous in view of the difficulty of consistently excluding the presence of $(Bu_3Sn)_2O$ from such reactions, high-level *ab initio* molecular orbital calculations on the cyclization of *N*-methyl-*N*-4-pentenylaminyl (**27**) through both the *exo* and *endo* modes of ring closure were performed.[27] Three important findings stemmed from this study: (i) the *exo* mode of cyclization is preferred at the MP2/6-31G*//UHF/6-31G* level of theory by 6.6 kcal/mol, (ii) there is a significant barrier to cyclization *via* the *exo* mode (14.1 kcal/mol), and (iii) conversion of **27** to the corresponding pyrrolidinomethyl radical **28** is significantly exothermic (14.8 kcal/mol) (Figure 5). These findings, along with the experimental results of this study, are consistent with a *slow*,[9] *irreversible* cyclization of **9** *via* the *exo* mode.

(27) Maxwell, B. J.; Schiesser, C. H.; Smart, B. A.; Tsanaktsidis, J. *J. Chem. Soc., Perkin Trans. 2* **1994**, 2385.

Scheme 4





The influence of substituents on the cyclization of **9** was then investigated through the reactions of the sulfenamides **29**, **30**, and **31** with Bu_3SnH in the presence of added $(Bu_3Sn)_2O$. **29**, **30**, and **31** were prepared from the corresponding amines **32**, **33**, and **34** and 2-benzothiazolesulfenyl chloride (**18**) as described above. The amines **32** and **34** were prepared from **35** and **36**, respectively, which in turn were sysnthesized from 5-chloro-1-pentyne and 5-phenyl-4-pentenoic acid, respectively, whereas **33** was available from (*E*)-4-hexen-1-ol by an adaptation of a literature procedure.[3e] Authentic samples of the pyrrolidines **43**, **44**, and **45** were prepared from the corresponding phenyl selenides **40**, **41**, and **42**,[26] which were in turn obtained from the carbamates **37**, **38**, and **39**[3h] (Scheme 4).

Treatment of **29**, **30**, and **31** with Bu_3SnH in benzene at 80 °C in the presence of 1 equiv of $(Bu_3Sn)_2O$ under pseudo-first-order conditions as described above produced the results displayed graphically in Figure 6. These data display a modest acceleration in the rate of conversion of **29** and **30** to **43** and **44**, respectively, relative to the parent cyclization (**8** → **12**), whereas **31** was converted to **45** at a rate significantly greater than that of the parent process (**8** → **12**). Although the interpretation of these results is open to discussion, useful insight is gained if they are related to the well-defined pattern of

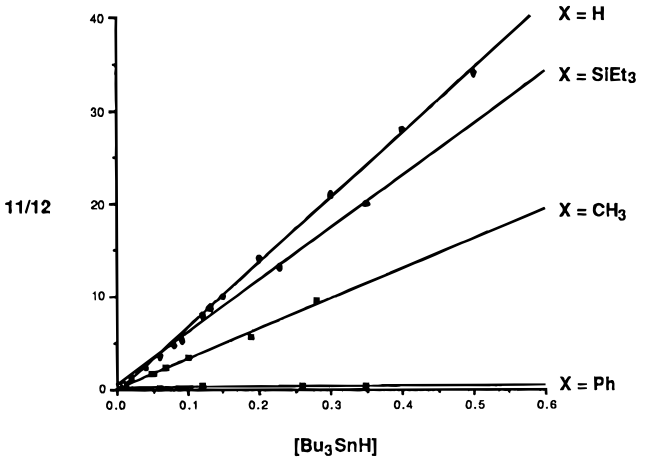


Figure 6. Results from the reactions of **8** (X = H), **29** (X = $SiEt_3$), **30** (X = CH_3) and **31** (X = Ph) with Bu_3SnH (10 equiv) in benzene at 80 °C in the presence of $(Bu_3Sn)_2O$ (1 equiv).

behavior encountered in the addition of carbon−centered radicals to alkenes.[28] For example, the modest acceleration afforded by the electron-releasing triethylsilyl and methyl substituents is notionally consistent with resonance stabilization of a "product-like" (*i.e.*, late) transition state, whereas the electron-withdrawing phenyl substituent is found to have the greatest influence presumably through a combination of cooperative electronic and resonance effects.[28] Indeed, these results are consistent with the view that alkenylaminyl radical cyclizations in the presence of $(Bu_3Sn)_2O$ are slow, irreversible reactions which are accelerated by both electron-donating and electron-withdrawing olefinic substituents through resonance stabilization of the product-like transition state. This description is in qualitative agreement with our theoretical calculations which predict a considerable barrier to cyclization (14.1 kcal/mol) and a significantly exothermic process (14.8 kcal/mol) for the conversion of **27** to **28** in the absence of Lewis acid catalysis and lead to the suggestion that the $(Bu_3Sn)_2O$-modified aminyls are more akin to nucleophilic[29] aminyl radicals, rather than electrophilic[23] aminium cation radicals, in their cyclization reactions.

Experimental Section

General Procedures. Where necessary, reactions were conducted in flame-dried glassware under an atmosphere of nitrogen, purified by passage over activated 4Å molecular sieves and BASF R3-11 copper catalyst. Melting points were determined using a Gallenkamp melting point apparatus and are uncorrected. Boiling points are uncorrected and correspond to the oven temperature of a GKR-51 Kugelrohr apparatus. ^1H and ^{13}C NMR spectra were recorded as $CDCl_3$ solutions on a Varian Unity 300 spectrometer at 300 and 75 MHz, respectively. Unless otherwise stated low- and high-resolution mass spectra were recorded on a Joel JMS-AX505H spectrometer and a V.G. Micromass 7070F spectrometer, respectively, in electron impact mode at 70 eV. Microanalyses were performed by either the Australian Microanalytical Service, Melbourne, or Chemical and Micro Analytical Services Pty. Ltd., Melbourne. Gas chromatography was conducted using either a 15 m DB-1301 or AT-1301 capillary column (i.d. 0.25 mm) on a Hewlett-Packard 5890 gas chromatograph equipped with a flame ionization detector. Peak areas were determined using a HP3394A intergrator, and identification of products was made by comparison of retention times with authentic samples. Product yields were determined with correction for detector response by reference to an internal standard (nonane). The lowest limit of detection of amine products was conservatively estimated to be ~0.5%. Benzene was purified by stirring with concentrated sulfuric acid for 15 h followed by desiccation ($MgSO_4$) and distillation from CaH_2 under nitrogen.[30] Bu_3SnH was prepared by reduction of $(Bu_3Sn)_2O$ with sodium borohydride,[16] distilled at reduced pressure and stored under nitrogen at 4 °C. *N*-Butyl-4-pentenylamine (**11**)[3d], *N*-butyl-2-methylpyrrolidine (**12**),[3d] and *N*-butyl-2-[(phenylseleno)methyl]pyrrolidine (**26**)[26] were prepared using literature procedures, whereas *p*-aminobenzoic acid, 2-amino-5-methylbenzoic acid, 5-methoxy-2-nitrobenzoic acid, and the disulfides **19**, **22**, and **24** were purchased from the Aldrich Chemical Co.

Dimethyl 4,4′-Dithiobisbenzoate (20). 4,4′-Dithiobisbenzoic acid, prepared from *para*-aminobenzoic acid (31.5 g),[15] was heated under reflux in methanol (400 mL) containing concentrated sulfuric acid (10 mL) for 24 h. Removal of the methanol afforded a residue which was dissolved in dichloromethane and washed with aqueous $NaHCO_3$ and water. Desiccation ($MgSO_4$) followed by concentration (*in vacuo*) afforded a brown solid which after sublimation and recrystallization (methanol) delivered the title disulfide **20** as a colorless solid (5.9 g, 43%), mp 127−8 °C (lit.[31] mp 124 °C).

Dimethyl 2,2′-Dithiobis(5-methoxybenzoate) (21). **21** was prepared from 2-amino-5-methoxybenzoic acid (**25**), in 44% crude yield using literature methodology:[15] ^1H NMR δ 3.81 (s, 3H), 3.98 (s, 3H), 6.99 (dd, J = 8.9, 2.8 Hz, 1H), 7.56 (d, J = 2.8 Hz, 1H), 7.65 (d, J = 8.9 Hz, 1H); ^{13}C NMR δ 52.39, 55.56, 115.75, 119.86, 127.47, 128.05, 131.18, 157.63, 166.63; MS *m*/*z* 394 ($M^{\bullet+}$, 46), 362 (23), 197 (100), 167 (31); HRMS for $C_{18}H_{18}O_6S_2$, *m*/*z* calcd 394.0545, found 394.0551.

2-Amino-5-methoxybenzoic Acid (25). 5-Methoxy-2-nitrobenzoic acid (2.0 g, 0.01 mol) was dissolved in absolute ethanol (50 mL) and hydrogenated over Pd on C at atmospheric pressure. Filtration, concentration (*in vacuo*), and recrystallization (water) gave the title acid **25** (1.26 g, 74%), mp 150−152 °C (lit.[32] mp 149−151 °C).

Dimethyl 2,2′-Dithiobis(5-methylbenzoate) (23). Application of literature methodology[15] to 2-amino-5-methylbenzoic acid gave a 6:1 mixture of disulfide **23** and the corresponding trisulfide [dimethyl 2,2′-trithiobis(5-methylbenzoate)], in 53% yield after esterification. Purification through a combination of radial chromatography and recrystallization (methanol) delivered the disulfide **23** as a pale yellow solid in 40% yield: mp 126−128 °C; ^1H NMR δ 2.33 (s, 3H), 3.98 (s, 3H), 7.21 (dd, J = 8.2, 1.8 Hz, 1H), 7.62 (d, J = 8.2 Hz, 1H), 7.86 (d, J = 1.8 Hz, 1H); ^{13}C NMR δ 20.46, 52.23, 125.81, 126.92, 131.82, 133.91, 135.28, 136.94, 166.90; MS *m*/*z* 362 ($M^{\bullet+}$, 22), 181 (100), 166 (20), 151 (18), 121 (21); HRMS for $C_{18}H_{18}O_4S_2$, *m*/*z* calcd 362.0646, found 362.0643. Dimethyl 2,2′-trithiobis(5-methylbenzoate) was isolated as a colorless solid in 5% yield: mp 168−170 °C; ^1H NMR δ 2.38 (s, 3H), 3.88 (s, 3H), 7.39 (d, J = 8.2 Hz, 1H), 7.79 (s, 1H), 8.09 (d, J = 8.2 Hz, 1H); ^{13}C NMR δ 20.63, 52.23, 127.50, 127.62, 131.64, 133.82, 136.09, 136.33, 166.78; MS *m*/*z* 394 ($M^{\bullet+}$, 6), 362 (8), 181 (100), 166 (16), 151 (15), 121 (18); HRMS for $C_{18}H_{18}O_4S_3$, *m*/*z* calcd 394.0367, found 394.0382.

5-Chloro-1-(triethylsilyl)-1-pentene (35). 5-Chloropentyne (10.0 g, 0.1 mol), triethylsilane (11.3g, 0.1 mol), and chloroplatinic acid (~10 mg) were stirred under nitrogen at *ca.* −5 to 0°C for 12 days. The mixture was then filtered through silica gel, aided by a small portion of diethyl ether, concentrated, and distilled (Kugelrohr, 92−94 °C, 2 mmHg) to give a clear liquid (17.7 g, 83%) which was shown to be a 85:15 mixture of **35** and the regioisomer 5-chloro-2-(triethylsilyl)-1-pentene: ^1H NMR (major isomer) δ 0.55 (q, J = 7.9 Hz, 6H), 0.93 (t, J = 7.9 Hz, 9H), 1.88 (qn, J = 6.9 Hz, 2H), 2.20−2.32 (m, 2H), 3.53 (t, J = 6.7 Hz, 2H), 5.62 (d, 18.8 Hz, 1H), 5.99 (dt, J = 18.8, 6.4 Hz, 1H); ^{13}C NMR (major isomer) δ 3.47, 7.33, 31.62, 33.95, 44.35, 127.64, 146.13; MS *m*/*z* 189 ($M^{\bullet+} - C_2H_5$, 7), 123 (33), 121 (100), 95 (22), 93 (61), 58 (37). Anal. Calcd for $C_{11}H_{23}ClSi$: C, 60.37; H, 10.59. Found: C, 60.39; H, 10.77.

(*E*)-*N*-Butyl-5-(triethylsilyl)-4-pentenamine (32). The silane **35** (3.9 g, 0.018 mol) (85:15 mixture of terminal and internal isomers) in butylamine (20 mL) was heated under reflux for ~18 h, under nitrogen, then cooled to room temperature (RT), and concentrated under reduced

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pressure. The residue was taken up into diethyl ether (50 mL) and washed with water (50 mL × 3) and brine (50 mL). Desiccation ($MgSO_4$) followed by removal of solvent (*in vacuo*) furnished a yellow oil which upon distillation (Kugelrohr, 120 °C, 0.3 mmHg) yielded **32** as a colorless oil (4.1 g, 90%) as a 85:15 mixture of regioisomers: ^{1}H NMR (major isomer) δ 0.54 (q, J = 8.1 Hz, 6H), 0.86−1.00 (m, 12 H), 1.25−1.39 (m, 2H), 1.39−1.53 (m, 2H), 1.54−1.67 (m, 2H), 2.03−2.21 (m, 2H), 2.52−2.66 (m, 4H), 5.56 (dt, J = 18.2, 1.4 Hz, 1H), 6.03 (dt, J = 18.2, 6.3 Hz, 1H); ^{13}C NMR (major isomer) δ 3.49, 7.35, 14.01, 20.52, 29.19, 32.35, 34.78, 49.50, 49.76, 126.10, 147.95; MS *m*/*z* 255 ($M^{\bullet+}$, 1), 115 (21), 87 (30), 86 (100), 70 (29), 58 (27); HRMS for $C_{15}H_{33}NSi$, *m*/*z* calcd 255.2382, found 255.2384.

(*E*)-*N*-Butyl-4-hexenamine (33). *p*-Toluenesulfonyl chloride (36.0 g, 0.19mol) was added to a solution of (*E*)-4-hexenol (16.0 g, 0.16 mol) in pyridine (120 mL) at 0 °C, and then allowed to stir at room temperature for 1.5 h. The mixture was poured onto crushed ice (300 g) and extracted with diethyl ether (3 × 200 mL). The ether portions were combined and washed with 10% HCl solution (2 × 100 mL) and brine (1 × 100 mL). Desiccation ($MgSO_4$), followed by concentration (*in vacuo*), gave the corresponding tosylate, which was treated with butylamine (200 mL) and heated to reflux for *ca.* 2 days. The excess butylamine was removed by rotary evaporation and the residue diluted with 10% NaOH (400 mL) and extracted with diethyl ether (3 × 200 mL). The combined ethereal portions were then washed with brine (2 × 200 mL), dried ($MgSO_4$), and concentrated (*in vacuo*) to yield a yellow oil. Distillation (Kugelrohr, 81−84°C, 10 mmHg) afforded **33** as a colorless liquid (19.0 g, 77%): ^{1}H NMR δ 0.70−1.0 (br s, 1H), 0.92 (t, J = 7.4 Hz, 3H), 1.26−1.61 (m, 6H), 1.64 (d, J = 4.0 Hz, 3H), 1.96−2.06 (m, 2H), 2.59 (t, J = 7.4 Hz, 4H) 5.30−5.55 (m, 2H); ^{13}C NMR δ 14.03, 17.89, 20.53, 30.01, 30.44, 32.39, 49.65, 49.79, 124.97, 131.01; MS *m*/*z* 155 ($M^{\bullet+}$, 2%), 112 (43), 86 (100), 70 (28), 56 (22), 54 (50); HRMS for $C_{10}H_{21}N$, *m*/*z* calcd 155.1674, found 155.1675.

***N*-Butyl-(*E*)-5-Phenyl-4-pentenamide (36).** Oxalyl chloride (3.6 g, 0.029 mol) was added to a dichloromethane (25 mL) solution of (*E*)-5-phenyl-4-pentenoic acid[4b] (4.6 g, 0.026 mol) containing a few drops of DMF. This was allowed to stir at room temperature for ∼30 min before being added dropwise to a stirred mixture of butylamine (1.9 g, 0.032 mol) in aqueous sodium hydroxide (0.9 M, 30 mL). After stirring for ∼15 min, the layers were separated, and the aqueous layer was extracted with a portion of dichloromethane (30 mL). The organics were combined, washed with water (50 mL) and brine (50 mL), dried ($MgSO_4$), and concentrated (*in vacuo*) to give a yellow solid which, after purification by radial chromatography (40% EtOAc in hexanes) and recrystallization from hexanes/diethyl ether, yielded the required amide **36** as white needles (5.1 g, 61%): mp 77−78 °C; ^{1}H NMR δ 0.89 (t, J = 7.3 Hz, 3H), 1.24−139 (m, 2H), 1.40−1.52 (m, 2H), 2.32 (t, J = 7.4 Hz, 2H), 2.55 (q, J = 7.2 Hz, 2H), 3.25 (q, J = 6.7 Hz, 2H), 5.55 (br s, 1H), 6.20 (dt, J = 15.7, 6.9 Hz, 1H), 6.43 (d, J = 15.7 Hz, 1H), 7.16−7.36 (m, 5H); ^{13}C NMR δ 13.68, 20.03, 29.03, 31.71, 36.43, 39.22, 125.98, 127.09, 128.45, 128.78, 130.95, 137.31, 171.97; MS *m*/*z* 231 ($M^{\bullet+}$, 100), 140 (27), 131 (23), 130 (36), 129 (21), 117 (90), 115 (37), 104 (21), 91 (52), 56 (80). Anal. Calcd for $C_{15}H_{21}NO$: C, 77.88; H, 9.15; N, 6.05. Found: C, 77.86; H, 8.92; N, 5.92.

***N*-Butyl-5-phenyl-4-pentenamine (34).** A solution of $LiAlH_4$ in THF (1.0M, 3.5 mL) was added slowly to a solution of **36** (0.82 g, 3.6 mmol) in THF (5 mL) under an atmosphere of nitrogen and then heated under reflux for 2 h. The cooled reaction mixture was treated with a minimum amount of saturated aqueous Na_2SO_4 and then filtered through a pad of Celite and the filtrate concentrated under reduced pressure. Distillation (Kugelrohr, 121°C, 0.1 mmHg) of the resulting residue afforded **34** as a colorless liquid (0.52 g, 68%) which was shown to be a ∼3:1 mixture of *E*/*Z* isomers: ^{1}H NMR δ 0.91 (t, J = 7.3 Hz, 3H), 1.20−1.58 (m, 5H), 1.58−1.72 (m, 2H), 2.26 (q, J = 7.2 Hz, 2H), 2.56−2.70 (m, 4H), 6.18−6.28 (m, 1H), 6.40 (d, J = 16.0 Hz, 1H), 7.14−7.37 (m, 5H); ^{13}C NMR (major isomer) δ 13.93, 20.42, 29.63, 30.78, 32.17, 49.44, 49.63, 125.81, 126.74, 128.35, 129.97, 130.31, 137.62; MS *m*/*z* 217 ($M^{\bullet+}$, 43), 174 (25), 129 (28), 117 (40), 115 (40), 112 (52), 91 (67), 86 (100), 70 (23), 56 (30), 55 (22); HRMS for $C_{15}H_{23}N$, *m*/*z* calcd 217.1830, found 217.1822.

General Procedure for the Preparation of Arenesulfenamides 3−8 and 29−31. A solution of the appropriate disulfide (6.3 mmol) in dichloromethane (15 mL) (at reflux for 2,2′-dithiobis(benzothiazole)) containing a drop of pyridine was treated with sulfuryl chloride (6.4 mmol) and allowed to stir for *ca.* 10 min. The resultant sulfenyl chloride solution was added dropwise by syringe to the corresponding secondary amine (12.9 mmol) and triethylamine (∼5 equiv) in diethyl ether (40 mL) maintained at 0 °C. The mixture was allowed to warm to room temperature and left to stir for an additional 1−2 h, at which time the mixture was diluted with diethyl ether (50 mL) and the layers were separated. The aqueous layer was extracted with additional diethyl ether, and the organics were combined and washed with brine (50 mL). Desiccation ($MgSO_4$) and concentration (*in vacuo*) gave oils which could be purified by either flash[33] or radial chromatography or distillation.

***N*-Butyl-*N*-4-pentenyl-4-carbomethoxybenzenesulfenamide (4)** was obtained as a pale yellow oil in 57% yield after flash chromatography on neutral alumina (1.5% EtOAc/hexanes): ^{1}H NMR (400 MHz) δ 0.90 (t, J = 7.3 Hz, 3H), 1.20−1.40 (m, 2H), 1.52−1.64 (m, 2H), 1.64−1.76 (m, 2H), 2.00−2.10 (m, 2H), 3.00−3.04 (m, 4H), 3.89 (s, 3H), 4.90−5.05 (m, 2H), 5.72−5.84 (m, 1H), 7.28 (d, J = 8.8 Hz, 2H), 7.93 (d, J = 8.8 Hz, 2H); ^{13}C NMR (100 MHz) δ 13.95, 20.15, 27.67, 30.65, 31.10, 51.91, 57.97, 58.52, 114.84, 121.88, 126.23, 129.75, 138.14, 150.18, 166.95; MS *m*/*z* 307 ($M^{\bullet+}$, 17), 264 (50), 252 (66), 210 (100), 167 (26), 139 (22), 137 (22), 126 (37), 86 (45), 69 (22), 57 (26), 44 (20), 42 (26), 41 (55), 29 (25); HRMS for $C_{17}H_{25}NO_2S$, *m*/*z* calcd 307.1606, found 307.1606.

***N*-Butyl-*N*-4-pentenyl-2-carbomethoxy-4-methoxybenzenesulfenamide (5)** was obtained as a pale yellow oil in 57% yield after distillation (Kugelrohr, 172°C, 0.02 mmHg): ^{1}H NMR δ 0.88 (t, J = 7.3 Hz, 3H), 1.20−1.40 (m, 2H), 1.50−1.80 (m, 4H), 1.95−2.15 (m, 2H), 2.90−3.10 (m, 4H), 3.83 (s, 3H), 3.91 (s, 3H), 4.85−5.10 (m, 2H), 5.65−5.90 (m, 1H), 7.11 (dd, J = 8.8, 2.7 Hz, 1H), 7.53 (d, J = 2.7 Hz, 1H), 7.71 (d, J = 8.8 Hz, 1H); ^{13}C NMR δ 13.96, 20.33, 27.81, 30.76, 31.35, 52.04, 55.61, 57.74, 58.23, 114.63, 115.09, 120.06, 123.85, 124.74, 138.37, 141.03, 156.30, 166.64; MS *m*/*z* 337 ($M^{\bullet+}$, 9), 197 (100), 167 (28), 126 (39), 98 (22), 86 (43); HRMS for $C_{18}H_{27}NO_3S$, *m*/*z* calcd 337.1712, found 337.1719.

***N*-Butyl-4-pentenyl-2-carbomethoxybenzenesulfenamide (6)** was obtained as a pale yellow oil in 52% yield after radial chromatography on silica (10% EtOAc/hexanes): ^{1}H NMR δ 0.88 (t, J = 7.3 Hz, 3H), 1.20−1.40 (m, 2H), 1.50−1.80 (m, 4H), 2.00−2.10 (m, 2H), 2.95−3.10 (m, 4H), 3.90 (s, 3H), 4.90−5.03 (m, 2H), 5.65−5.90 (m, 1H), 7.11 (t, J = 7.4 Hz, 1H), 7.44−7.52 (m, 1H), 7.83 (d, J = 8.3 Hz, 1H), 8.00 (dd, J = 7.9, 1.4 Hz, 1H); ^{13}C NMR (benzene-d_6) δ 14.10, 20.61, 28.12, 31.04, 31.63, 51.49, 57.84, 58.31, 114.85, 123.44, 123.67, 124.20, 131.63, 132.27, 138.48, 150.72, 166.42; MS *m*/*z* 307 ($M^{\bullet+}$, 11), 167 (100), 152 (12), 86 (11); HRMS for $C_{17}H_{25}NO_2S$, *m*/*z* calcd 307.1606, found 307.1603.

***N*-Butyl-*N*-4-pentenyl-2-carbomethoxy-4-methylbenzenesulfenamide (7)** was obtained as a pale yellow oil in 74% yield after radial chromatography on silica (10−30% EtOAc/hexanes): ^{1}H NMR δ 0.89 (t, J = 7.1 Hz, 3H), 1.20−1.40 (m, 2H), 1.50−1.80 (m, 4H), 1.95−2.15 (m, 2H), 2.35 (s, 3H), 2.95−3.10 (m, 4H), 3.90 (s, 3H), 4.85−5.10 (m, 2H), 5.65−5.90 (m, 1H), 7.31 (d, J = 8.6 Hz, 1H), 7.70 (d, J = 8.6 Hz, 1H), 7.82 (s, 1H); ^{13}C NMR δ 13.95, 20.30, 20.43, 27.77, 30.72, 31.32, 51.89, 57.63, 58.13, 114.60, 123.02, 123.36, 131.58, 132.89, 133.39, 138.34, 146.61, 166.92; MS *m*/*z* 321 ($M^{\bullet+}$, 9), 181 (100), 166 (15), 151 (15), 121 (13); HRMS for $C_{18}H_{27}NO_2S$, *m*/*z* calcd 321.1762, found 321.1754.

***N*-Butyl-*N*-4-pentenyl-2-benzothiazolesulfenamide (8)** was obtained as a pale yellow oil in 62% yield after flash chromatography on silica (10−30% EtOAc/hexanes): ^{1}H NMR δ 0.93 (t, J = 7.4 Hz, 3H), 1.24−1.44 (m, 2H), 1.60−1.73 (m, 2H), 1.73−1.85 (m, 2H), 2.04−2.16 (m, 2H), 3.06−3.16 (m, 4H), 4.93−5.08 (m, 2H), 5.72−5.88 (m, 1H), 7.25 (t, J = 7.6 Hz, 1H), 7.38 (t, J = 7.6 Hz, 1H), 7.78 (d, J = 8.0 Hz, 1H), 7.81 (d, J = 8.0 Hz, 1H); ^{13}C NMR δ 13.90, 20.13, 27.54, 30.50, 31.04, 57.98, 58.52, 115.01, 120.89, 121.55, 123.52, 125.75, 135.00, 137.90, 154.93, 177.89; MS *m*/*z* 306 ($M^{\bullet+}$, 0.2), 167 (44), 140 (62), 85 (65), 83 (100); HRMS for $C_{16}H_{22}N_2S_2$, *m*/*z* calcd 306.1224, found 306.1230.

***N*-Butyl-*N*-[5-(triethylsilyl)-4-pentenyl]-2-benzothiazolesulfenamide (29)** was obtained as a pale yellow oil in 66% yield after radial

(33) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

chromatography on silica (10−30% EtOAc/hexanes): ^{1}H NMR (major isomer) δ 0.53 (q, J = 7.9 Hz, 6H), 0.91 (t, J = 7.9 Hz, 9H), 0.92 (t, J = 7.3 Hz, 3H), 1.26−1.44 (m, 2H), 1.58−1.73 (m, 2H), 1.73−1.90 (m, 2H), 2.08−2.26 (m, 2H), 3.00−3.22 (m, 4H), 5.58 (d, J = 18.5 Hz, 1H), 6.01 (dt, J = 18.5, 6.2 Hz, 1H), 7.24 (t, 7.6 Hz, 1H), 7.38 (t, J = 7.6 Hz, 1H), 7.77 (d, J = 7.6 Hz, 1H), 7.82 (d, J = 7.6 Hz, 1H); ^{13}C NMR (major isomer) δ 3.51, 7.33, 13.91, 20.15, 27.38, 30.53, 34.18, 57.83, 58.55, 120.89, 121.56, 123.51, 125.75, 126.79, 135.04, 147.29, 154.95, 177.92; MS *m*/*z* 420 ($M^{\bullet+}$, 1), 255 (24), 254 (100), 167 (53), 126 (28), 115 (48), 87 (48), 86 (26), 58 (30). Anal. Calcd for $C_{22}H_{36}N_2S_2Si$: C, 62.8; H, 8.6. Found: C, 62.7; H, 8.8.

***N*-Butyl-*N*-4-hexenyl-2-benzothiazolesulfenamide (30)** was obtained as a pale yellow oil in 57% yield after radial chromatography on silica (35% CH_2Cl_2/hexanes): ^{1}H NMR δ 0.92 (t, J = 7.1 Hz, 3H), 1.28−1.44 (m, 2H), 1.56−1.80 (m, 7H), 1.96−2.12 (m, 2H), 3.04−3.15 (m, 4H), 5.28−5.52 (m, 2H), 7.25 (t, J = 7.8 Hz, 1H), 7.38 (t, J = 7.8 Hz, 1H), 7.74−7.84 (m, 2H); ^{13}C NMR δ 13.93, 17.86, 20.16, 28.20, 29.91, 30.50, 58.12, 58.51, 120.90, 121.53, 123.48, 125.52, 125.75, 130.42, 135.01, 154.98, 178.32; MS *m*/*z* 320 ($M^{\bullet+}$, 1), 167 (52), 166 (23), 154 (100), 54 (23); HRMS for $C_{17}H_{24}N_2S_2$, *m*/*z* calcd 320.1381, found 320.1387.

***N*-Butyl-*N*-(5-phenyl-4-pentenyl)-2-benzothiazolesulfenamide (31)** was obtained as a pale yellow oil in 44% yield after radial chromatography on silica (35% CH_2Cl_2/hexanes): ^{1}H NMR δ 0.92 (t, J = 7.3 Hz, 3H), 1.25−1.45 (m, 2H), 1.56−1.76 (m, 2H), 1.80−1.94 (m, 2H), 2.27 (q, J = 7.2 Hz, 2H), 3.04−3.22 (m, 4H), 6.20 (dt, J = 15.8, 6.8 Hz, 1H), 6.40 (d, J = 15.8 Hz, 1H), 7.10−7.44 (m, 7H), 7.78 (d, J = 7.9 Hz, 1H), 7.82 (d, J = 7.9 Hz, 1H); ^{13}C NMR (major isomer) δ 13.96, 20.15, 28.00, 30.38, 30.49, 57.99, 58.64, 120.91, 121.53, 123.53, 125.78, 125.91, 126.92, 128.45, 129.77, 130.46, 134.95, 137.51, 154.90, 177.99; MS *m*/*z* 382 ($M^{\bullet+}$, 0.3), 218 (34), 216 (56), 167 (70), 166 (34), 126 (76), 124 (23), 117 (44), 91 (49), 86 (100), 56 (27); HRMS for $C_{22}H_{26}N_2S_2$, *m*/*z* calcd 382.1537, found 382.1529.

General Procedure[3h] for the preparation of *N*-Hydroxypyridine-2-thione Carbamates 37−39. Phosgene (3.4 mL, 20% solution in toluene) was added to a suspension of the sodium salt of *N*-hydroxypyridine-2-thione (6.4 mmol) in benzene at 0 °C. The resultant solution was maintained at 0 °C for a further 45 min and then allowed to warm to room temperature and stirred for ∼1 h. The flask was then shielded from light and a solution of triethylamine (6.4 mmol) and the appropriate secondary amine (6.4 mmol) in benzene (5 mL) added while the temperature was maintained below 25 °C. This was then allowed to stir at room temperature for ∼4 h. After this time the reaction was diluted with water (30 mL), and the phases separated. The organic portion was washed with brine (30 mL), dried ($MgSO_4$), and concentrated (*in vacuo*) to provide the crude carbamates which were purified by radical chromatography on silica (EtOAc/hexanes).

1-[[*N*-Butyl-*N*-[5-(triethylsilyl)-4-pentenyl]carbamoyl)oxy]-2(1*H*)-pyridinethione (37) was obtained as a yellow oil in 74% yield: ^{1}H NMR δ 0.48−0.68 (m, 6H), 0.88−1.00 (m, 12H), 1.30−1.46 (m, 2H), 1.50−2.00 (m, 4H), 2.10−2.30 (m, 2H), 3.26−3.40 (m, 2H), 3.45−3.60 (m, 2H), 5.54−5.72 (m, 1H), 5.96−6.12 (m, 1H), 6.61 (t, J = 6.9 Hz, 1H), 7.17 (t, J = 7.8 Hz, 1H), 7.58−7.68 (m, 2H); ^{13}C NMR δ 3.23, 7.10, 13.50, 13.56, 19.64, 19.79, 26.22, 27.29, 29.31, 30.46, 33.64, 33.69, 46.90, 47.52, 48.42, 48.64, 111.93, 126.57, 126.82, 133.18, 136.74, 138.50, 138.53, 146.60, 146.73, 151.33, 176.07; MS *m*/*z* 408 ($M^{\bullet+}$, 2), 282 (81), 252 (28), 126 (100), 115 (33), 111 (26), 87 (76), 86 (28), 83 (20), 58 (62), 56 (25); HRMS for $C_{21}H_{36}N_2O_2SSi$, *m*/*z* calcd 408.2267, found 408.2272.

1-[(*N*-Butyl-*N*-4-hexenylcarbamoyl)oxy]-2(1*H*)-pyridinethione (38)was obtained as a yellow oil in 34% yield: ^{1}H NMR δ 0.88−1.02 (m, 3H), 1.25−1.48 (m, 2H), 1.54−1.88 (m, 7H), 1.96−2.16 (m, 2H), 3.27-3.39 (m, 2H), 3.45−3.57 (m, 2H), 5.35−5.55 (m, 2H), 6.56−6.63 (m, 1H), 7.14−7.21 (m, 1H), 7.60−7.69 (m, 2H); ^{13}C NMR δ 13.71, 13.77, 17.83, 19.86, 20.00, 27.21, 28.39, 29.52, 29.62, 29.78, 30.70, 47.35, 47.64, 48.67, 48.86, 112.09, 121.61, 125.68, 125.82, 129.91, 129.99, 133.33, 137.06, 138.70, 151.58, 176.32; MS *m*/*z* 308 ($M^{\bullet+}$, 1), 182 (30), 126 (45), 78 (25), 56 (37), 54 (100); HRMS for $C_{16}H_{24}N_2O_2S$, *m*/*z* calcd 308.1558, found 308.1555.

1-[[*N*-Butyl-*N*-(5-phenyl-4-pentenyl)carbamoyl]oxy]-2(1*H*)-pyridinethione (39) was obtained as a yellow oil in 74% yield: ^{1}H NMR δ 0.88−1.02 (m, 3H), 1.28−1.46 (m, 2H), 1.54−2.04 (m, 4H), 2.30 (q, J = 6.6 Hz, 2H), 2.62 (q, J = 6.6 Hz, 0.25H), 3.25−3.64 (m, 4H), 6.14−6.29 (m, 1H), 6.36−6.49 (m, 1H), 6.54−6.64 (m, 1H), 7.12−7.40 (m, 6H), 7.56−7.72 (m, 2H); ^{13}C NMR δ 13.68, 13.75, 19.80, 19.95, 27.01, 28.14, 29.48, 30.06, 30.18, 30.64, 47.29, 47.62, 48.58, 48.86, 112.12, 125.86, 126.83, 126.94, 128.28, 128.35, 128.40, 129.20, 129.40, 130.48, 130.61, 133.37, 136.97, 138.62, 151.51, 151.57, 176.21; MS *m*/*z* 370 ($M^{\bullet+}$, 11), 246 (20), 244 (92), 243 (27), 126 (36), 117 (33), 111 (24), 91 (100), 86 (30), 78 (22), 56 (29); HRMS for $C_{21}H_{26}N_2O_2S$, *m*/*z* calcd 370.1715, found 370.1702.

General Procedure[30] for the Preparation of the Phenylseleno Pyrrolidines 40−42. *N*-Hydroxypyridine-2-thione carbamate (1.0 mmol), malonic acid (3.0 mmol), diphenyl diselenide (2.0 mmol), and acetonitrile (10 mL) were placed in a two necked round bottom flask under a nitrogen atmosphere. The flask was then irradiated with a 100 W tungsten lamp for 3 h at 20−30 °C. The solvent was removed under reduced pressure and the residue taken up into ether and extracted twice with 10% HCl solution. The combined aqueous portions were basified with 10% NaOH solution, extracted (twice) into ether, and concentrated under vacuum. The residue was dissolved in ∼5 mL of ethanol and $NaBH_4$ added until the solution became nearly colorless. Ether and 10% NaOH were added, and the organic layer was dried ($MgSO_4$) and concentrated to yield the crude phenylseleno pyrrolidines which were further purified by radial chromatography on silica (EtOAc/hexanes).

***N*-Butyl-2-[(1-phenylseleno)(triethylsilyl)methyl]pyrrolidine (40)** was obtained as a yellow oil in 57% yield: ^{1}H NMR δ 0.50−1.20 (m, 19H), 1.20−2.30 (m, 9H), 2.30−3.20 (m, 4H), 7.10−7.35 (m, 3H), 7.45−7.54 (m, 1H), 7.62−7.72 (m, 1H); ^{13}C NMR δ 3.36, 3.79, 4.75, 7.77, 7.91, 8.25, 14.14, 20.79, 20.85, 20.94, 22.41, 22.82, 30.32, 30.79, 32.76, 35.02, 53.16, 54.20, 54.27, 54.71, 58.82, 65.75, 68.36, 126.36, 126.42, 128.22, 128.31, 128.79, 132.12, 133.91, 138.52; MS *m*/*z* 411 ($M^{\bullet+}$ 1), 126 (72), 70 (44), 58 (100); HRMS for $C_{21}H_{37}NSeSi$, *m*/*z* calcd 411.1860, found 411.1847.

***N*-Butyl-2-[1-(phenylseleno)ethyl]pyrrolidine (41)** was obtained as a yellow oil in 50% yield: ^{1}H NMR δ 0.80−1.00 (m, 3H), 1.20−1.56 (m, 7H), 1.60−1.94 (m, 4H), 2.05−2.22 (m, 2H), 2.38−2.50 (m, 0.5H), 2.58−2.76 (m, 1H), 2.76−2.88 (m, 0.5H), 3.10−3.26 (m, 1H), 3.42−3.56 (m, 0.5H), 3.60−3.73 (m, 0.5H), 7.18−7.32 (m, 3H), 7.51−7.64 (m, 2H); ^{13}C NMR δ 14.06, 14.14, 15.56, 19.65, 20.65, 20.80, 22.59, 23.36, 26.50, 27.45, 30.76, 31.00, 42.49, 43.54, 54.15, 54.55, 54.74, 67.56, 69.12, 127.02, 128.59, 128.86, 134.07, 135.50, 160.47; MS (CI) *m*/*z* 314 (4), 312 (22), 310 (19), 308 (8), 154 (57), 126 (100); HRMS (CI) for $C_{16}H_{26}SeN$ *m*/*z* calcd (M + H), 312.1230, found 312.1243.

***N*-Butyl-2-[phenyl(phenylseleno)methyl]pyrrolidine (42)** was obtained as a yellow oil in 51% yield: ^{1}H NMR δ 0.84 (t, J = 7.2 Hz, 1.8H), 0.92 (t, J = 7.2 Hz, 1.2 H), 1.10−1.92 (m, 7H), 1.94−2.38 (m, 3H), 2.54−2.90 (m, 2H), 3.04−3.32 (m, 1H), 4.41 (d, J = 6.5 Hz, 0.4 H), 4.51 (d, J = 5.2 Hz, 0.6H), 7.00−7.36 (m, 10H); ^{13}C NMR δ 14.05, 14.14, 20.57, 22.84, 23.76, 29.47, 29.50, 30.70, 31.22, 53.97, 54.36, 55.00, 55.04, 55.88, 56.83, 69.10, 69.24, 126.42, 126.48, 126.73, 126.77, 127.64, 127.80, 128.36, 128.38, 129.17, 129.27, 130.38, 130.60, 134.20, 134.26, 140.79, 141.40; MS *m*/*z* 216 ($M^{\bullet+}$ − SeC_6H_5, 4), 126 (100), 70 (13); HRMS for $C_{15}H_{22}N$, *m*/*z* calcd 216.1752, found 216.1742.

General Procedure for the Preparation of the Pyrrolidines 43−45. Seleno pyrrolidine **40**, **41**, or **42** and AIBN (catalytic amount) were dissolved in benzene and heated to reflux under a nitrogen atmosphere for ∼5 min, and then Bu_3SnH (1.1 equiv, 0.06−0.15 M) was added by syringe. After ∼2 h at reflux the mixture was allowed to cool and extracted with 10% HCl solution (10% H_2SO_4 used for **43**). The aqueous layer was then basified with 10% NaOH and extracted into diethyl ether. Desiccation ($MgSO_4$) and removal of solvent (*in vacuo*) gave a crude product which was distilled (Kugelrohr) to yield the pyrrolidines as colorless oils.

***N*-Butyl-2-[(triethylsilyl)methyl]pyrrolidine (43)** was obtained as a colorless oil in 81% yield after distillation (82 °C, 0.1 mmHg): ^{1}H NMR δ 0.40−0.65 (m, 8H), 0.85−1.00 (m, 12H), 1.20−2.40 (m, 11H), 2.80−3.00 (m, 1H), 3.10−3.22 (m, 1H); ^{13}C NMR δ 3.87, 7.37, 14.03, 16.09, 21.02, 21.55, 30.92, 32.63, 53.22, 53.66, 62.16; MS *m*/*z* 255 ($M^{\bullet+}$, 3), 126 (100), 115 (30), 87 (19), 69 (22), 58 (20), 57 (26), 56 (25), 54 (29); HRMS for $C_{15}H_{33}NSi$, *m*/*z* calcd 255.2382, found 255.2372.

***N*-Butyl-2-ethylpyrrolidine (44)** was obtained as a colorless oil in 61% yield after distillation (80 °C, 10 mmHg): ^{1}H NMR δ 0.88 (t, J

= 7.5 Hz, 3H), 0.92 (t, J = 7.2 Hz, 3H), 1.10−1.60 (m, 6H), 1.60−1.82 (m, 3H), 1.82−2.18 (m, 4H), 2.72−2.86 (m, 1H), 3.12−3.23 (m, 1H); ^{13}C NMR δ 10.81, 14.05, 20.97, 21.91, 26.76, 29.93, 30.89, 54.30, 54.51, 66.73; MS *m*/*z* 155 ($M^{\bullet+}$, 5), 126 (100), 112 (28), 70 (31); HRMS for $C_{10}H_{21}N$, *m*/*z* calcd 155.1674, found 155.1675.

***N*-Butyl-2-benzylpyrrolidine (45)** was obtained as a colorless oil in 86% yield after distillation (93 °C, 0.05 mmHg): ^{1}H NMR δ 0.94 (t, J = 7.3 Hz, 3H), 1.25−1.85 (m, 8H), 2.05−2.20 (m, 2H), 2.36−2.54 (m, 2H), 2.82−2.95 (m, 1H), 2.98−3.11 (m, 1H), 3.14−3.24 (m, 1H), 7.14−7.32 (m, 5H); ^{13}C NMR δ 14.06, 20.91, 21.87, 30.36, 31.01, 40.96, 54.14, 54.56, 66.43, 125.78, 128.12, 129.11, 140.20; MS *m*/*z* 174 ($M^{\bullet+}$ − C_3H_7, 5), 126 (85), 91 (100), 84 (29), 70 (68), 65 (34), 54 (36); HRMS for $C_{12}H_{16}N$, *m*/*z* calcd 174.1283, found 174.1283.

General Procedure for the Reaction of Sulfenamides 3, 4, 6, 7, and 8 with 1 equiv of Bu_3SnH. The appropriate sulfenamide, 2,2′-azoisobutyronitrile (AIBN), and nonane (GC standard) were added to a dry 10 mL two-necked round bottom flask, equipped with a magnetic stir bar, reflux condenser, nitrogen inlet, and rubber septum. Benzene was then added by syringe and the mixture heated to reflux for *ca.* 5 min to remove any oxygen from the system, whereupon tributyltin hydride (1.1 equiv) was added by syringe. After designated intervals aliquots were removed, diluted with diethyl ether, and analyzed by gas chromatography.

Kinetic Methods. The appropriate sulfenamide, AIBN, and nonane were weighed into a 10 mL volumetric flask which was then capped with a rubber septum and flushed with nitrogen. Bu_3SnH (10 equiv) was added by syringe and the flask made up to the mark with benzene. A portion of this standard solution (between 0.05 and 2 mL) was then added by syringe to a Pyrex tube under nitrogen. This was then followed by addition of the appropriate amount of benzene to dilute the sample up to 2 mL. The sample was then degassed by the freeze−pump−thaw method and sealed under vacuum. Using this technique, up to 10 samples of different concentrations were prepared from a single standard solution in a couple of hours. These reaction vessels were then placed in a thermostated oil bath and heated for 3 h (>99% conversion), after which they were opened, diluted with diethyl ether, and analyzed by gas chromatography. The results from four such reaction sets with sulfenamide **8** are displayed in Figure 1. For reactions conducted in the presence of $(Bu_3Sn)_2O$, 1 equiv of this material was added to the initial standard solution. Figure 4 shows the combined results for three data sets for reactions of sulfenamide **8**, and Figure 6 contains the results from one reaction set for each of the sulfenamides **29**−**31**.

Reaction of Sulfenamide 8 with Bu_3SnH in the Presence of Varying Amounts of $(Bu_3Sn)_2O$. Sulfenamide **8** (296 mg), AIBN (3 mg), and nonane (136 mg) were weighed into a 10 mL volumetric flask and sealed with a rubber septum. The flask was flushed with nitrogen and then freshly distilled Bu_3SnH (282 mg, 1 equiv) added by syringe. Addition of benzene diluted the sample up to 10 mL. A 1 mL portion of this solution was added to each of seven pyrex tubes under nitrogen and diluted with 0, 0.1, or 0.5 mL of a 0.0055 M solution of $(Bu_3Sn)_2O$ in benzene or 0.01, 0.025, 0.05, or 0.1 mL neat $(Bu_3Sn)_2O$. Additional benzene was added to make up the samples to 2 mL. Degassing (freeze−pump−thaw) and sealing provide seven samples containing sulfenamide (0.05 M), Bu_3SnH (0.05 M), and 0, 0.5, 2.8, 20, 51, 101, or 203 mol % $(Bu_3Sn)_2O$. These reaction vessels were then heated in a thermostated oil bath at 75 °C for 3 h, after which they were opened and analyzed by gas chromatography. The measured ratio **11**/**12** is shown graphically in Figure 2.

Reaction of Selenide 26 with Bu_3SnH. Selenide **26** (9.4 mg), AIBN (∼1 mg) and nonane were weighed into a 25 mL volumetric flask and sealed with a rubber septum. After purging with nitrogen, Bu_3SnH (73 mg, 10 equiv) was added and benzene added to the mark. Two 2 mL samples (0.01 M Bu_3SnH) were prepared in sealed tubes by the method described above and heated at either 50 or 80°C. Two samples containing 0.005 M Bu_3SnH were also prepared as above by diluting 1 mL of the standard solution with 1 mL of benzene and heated at either 50 or 80 °C. After ∼3 h (at 80 °C) or ∼7 h (at 50 °C), analysis by GC indicated the presence of only cyclic amine **12** and no evidence of the acyclic amine **11**.

Reaction of Sulfenamide 8 with Bu_3SnH in the Presence of Various Tin-Containing Lewis Acid Additives. A standard solution (**A**) containing sulfenamide **8** (0.3 g), Bu_3SnH (0.27 mL; 1 equiv), nonane (151 mg), and benzene was prepared in a 10 mL volumetric flask. Three additional standard solutions were prepared containing Bu_2SnCl_2 (34 mg) (**B**), $^tBu_2SnClOSnCl^nBu_2$ (48 mg) (**C**), or Bu_3SnCl (32 mg) (**D**), in 5 mL of benzene. Three samples were then prepared in glass ampules under scrupulously oxygen free conditions containing 1 mL mL of **A** plus 1 mL of **B**, **C**, or **D**, and sealed under vacuum. Two control samples were prepared, both before and after preparing the other samples, containing **A** plus 1 mL of benzene. After heating for 2 h at 80 °C, the ampules were opened and analyzed by GC. The above procedure was repeated for addition of $(Bu_3Sn)_2O$ (21 mg), $(Ph_3Sn)_2O$ (21 mg) and 1-hydroxy-3-(isothiocyanato)tetrabutyldistannoxane[34] (25 mg) in 5 mL of benzene. All four of the control reactions showed no cyclized amine **12**. The measured ratio **11**/**12** is displayed in Table 1.

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