Chemistry of Amidyl Radicals Produced from *N*-Hydroxypyridine-2-thione Imidate Esters[1]

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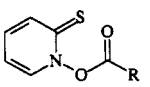
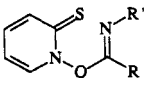
The title radical precursors were prepared from secondary amides by reaction of the amide with phosgene to give an imidoyl chloride followed by reaction with the sodium salt of *N*-hydroxypyridine-2-thione. Visible light initiated reactions of these precursors gave amidyl radicals **2** which could react with their precursors to give *N*-(2-pyridylthio) amides or with *t*-BuSH to give the parent amide. Radicals **2** containing δ,ϵ-unsaturation on the acyl or alkyl chain cyclized in a 5-*exo* fashion to give ultimately γ-lactams and *N*-acylpyrrolidines, respectively. Tandem 5-*exo* cyclizations of the *N*-allyl-4-pentenamidyl radical gave pyrrolizidinone products, and a tandem 5-*exo*/6-*endo* reaction sequence of the *N*-(4-pentenyl)benzamidyl radical gave, ultimately, 3,4-benzoindolizidinone. Several relative rate constants for cyclization and trapping of the amidyl radicals and for intramolecular reactions and trapping of the carbon-centered radicals formed by amidyl radical cyclizations were determined, and these values can be employed in synthetic planning.

Interest in radical-based methods for organic synthesis continues to increase.[2] Most attention has been directed toward reactions of carbon-centered radicals, but reactions of heteroatom-centered radicals also have been studied. In this work, we describe the reactions of amidyl radicals produced from *N*-hydroxypyridine-2-thione imidate esters (**1**). These radical precursors are related structurally and in their reactions to Barton's PTOC esters which are among the more important entries to carbon-centered radicals;[3-5] although technically a misnomer, we refer to precursors **1** as PTOC imidate esters. The PTOC esters react in radical chain reactions to give acyloxyl radicals, most of which decarboxylate readily. In contrast, PTOC imidate esters give amidyl radicals directly.



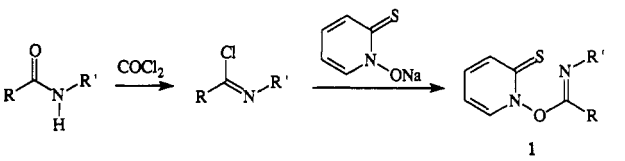
PTOC ester



PTOC imidate ester (**1**)

Amidyl radicals have been produced by UV-photolysis of *N*-halo amides and *N*-nitroso amides.[17,18] Saturated amidyl radicals can react by γ-hydrogen abstraction in a process similar to the Hofmann–Löffler–Freytag reaction of aminium cation radicals, and unsaturated systems undergo 4-*exo*, 5-*exo* and 6-*exo* cyclizations. These species are more reactive than aminyl radicals and offer an advantage over the reactive aminium cation radicals (and related metal-complexed aminyl radicals) in that completely neutral reaction conditions can be maintained.[18,19] Limitations in reactions of *N*-halo and *N*-nitroso amides are that only products of halogen atom transfer or nitroso group transfer are obtained after a radical addition step and that halogen atoms formed in homolytic processes can give undesired side reactions.

Scheme I



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a: R = R' = Bu; **b**: R = *c*-C_6H_{11}, R' = Bu; **c**: R = $CH_2CH_2CH{=}CH_2$, R' = Bu

d: R = $CH_2CH_2CH{=}CH_2$, R' = $CH_2CH{=}CH_2$; **e**: R = *c*-C_6H_{11}, R' = $(CH_2)_3CH{=}CH_2$

f: R = Pr, R' = $(CH_2)_3CH{=}CH_2$; **g**: R = Ph, R' = $(CH_2)_3CH{=}CH_2$; **h**: R = Ph, R' = CH_3

Results and Discussion

PTOC imidate esters were prepared as shown in Scheme I. Reactions of secondary amides with phosgene gave

(1) (a) Taken from the Ph.D. Thesis of J.L.E., Texas A&M University, 1992; this work was performed at Texas A&M University and Wayne State University. (b) A preliminary account of a portion of this work has appeared; see Newcomb, M.; Esker, J. L. *Tetrahedron Lett.* **1991**, *32*, 1035.

(2) Giese, B. *Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds*; Pergamon: 1986. Curran, D. P. *Synthesis* **1988**, 417, 489.

(3) Barton, D. H. R.; Crich, D.; Motherwell, W. B. *Tetrahedron* **1985**, *41*, 3901. Crich, D.; Quintero, L. *Chem. Rev.* **1989**, *89*, 1413.

(4) The PTOC acronym is derived from pyridine-2-thioneoxycarbonyl.

(5) Other members of the PTOC class of radical precursors provide entries to aminyl radicals,[6] aminium cation radicals,[7] iminyl radicals,[8] the phenoxyl radical[9] and amidyl radicals[10] by fragmentation of an acyloxyl precursor radical and direct entries to alkoxyl radicals,[11] the hydroxyl radical,[12,13] aroyloxyl and vinylacyloxyl radicals,[13,14] silyloxyl radicals,[13] alkoxycarbonyloxyl radicals[15] and phosphonyl radicals.[16]

(6) Newcomb, M.; Park, S.-U.; Kaplan, J.; Marquardt, D. J. *Tetrahedron Lett.* **1985**, *26*, 5651.

(7) (a) Newcomb, M.; Deeb, T. M. *J. Am. Chem. Soc.* **1987**, *109*, 3163. (b) Newcomb, M.; Deeb, T. M.; Marquardt, D. J. *J. Am. Chem. Soc.* **1990**, *46*, 2317.

(8) Boivin, J.; Fouquet, E.; Zard, S. Z. *Tetrahedron Lett.* **1991**, *32*, 4299.

(9) Togo, Y.; Nakamura, N.; Iwamura, H. *Chem. Lett.* **1991**, 1201.

(10) Esker, J. L.; Newcomb, M. *Tetrahedron Lett.* **1992**, *33*, 5913.

(11) Beckwith, A. L. J.; Hay, B. P. *J. Am. Chem. Soc.* **1988**, *110*, 4415. Hay, B. P.; Beckwith, A. L. J. *J. Org. Chem.* **1989**, *54*, 4330.

(12) Boivin, J.; Crépon, E.; Zard, S. Z. *Tetrahedron Lett.* **1990**, *31*, 6869.

(13) Barton, D. H. R.; Jaszberenyi, J. Cs.; Morrell, A. I. *Tetrahedron Lett.* **1991**, *32*, 311.

(14) Barton, D. H. R.; Lacher, B.; Zard, S. Z. *Tetrahedron Lett.* **1985**, *26*, 5939. Barton, D. H. R.; Ramesh, M. *Tetrahedron Lett.* **1990**, *31*, 949.

(15) Newcomb, M.; Kumar, M. U.; Boivin, J.; Crépon, E.; Zard, S. Z. *Tetrahedron Lett.* **1991**, *32*, 45. Beckwith, A. L. J.; Davison, I. G. E. *Tetrahedron Lett.* **1991**, *32*, 49.

(16) Avila, L. Z.; Frost, J. W. *J. Am. Chem. Soc.* **1988**, *110*, 7904.

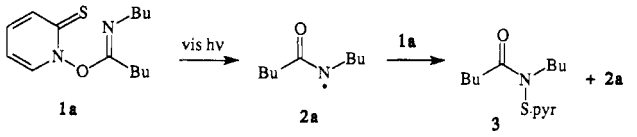
(17) Neale, R. S. *Synthesis* **1971**, 1. Mackiewicz, R.; Furstoss, R. *Tetrahedron* **1978**, *34*, 3241.

(18) Newcomb, M.; Esker, J. L. in *Advances in Heterocyclic Chemistry, Vol. 58*; Katritzky, A. R., Ed.; Academic: New York; in press.

(19) Stella, L. *Angew. Chem., Int. Ed. Eng.* **1983**, *22*, 337.

0022-3263/93/1958-4933$04.00/0

Scheme II



imidoyl chlorides which were allowed to react with the sodium salt of *N*-hydroxypyridine-2-thione. Imidate esters **1** were obtained in 52–96% yield from the amide. Isolated PTOC imidate esters were low-melting solids or oils. The isolated PTOC imidate esters were less stable toward hydrolysis than the related PTOC esters, and care was taken to assure that moisture was excluded during the preparations. In addition, as with other PTOC derivatives, imidate esters **1** were decomposed by light. In early studies, the imidate esters were isolated and characterized by ^1H and ^{13}C NMR spectroscopy. However, in many subsequent reactions, these precursors were prepared *in situ* and employed in radical reactions without isolation.

The water content of the *N*-hydroxypyridine-2-thione sodium salt used in the preparation of precursors **1** deserves special comment. Attempts to prepare imidate esters **1** gave only limited success unless the reagent was carefully isolated from a commercially available aqueous solution. The reagent we used had a water content of only 1–5 mol% as determined by ^1H NMR spectroscopy of the reagent in D_2O solutions.

Radical Chain Reactions of PTOC Imidate Esters. Reactions of the simple PTOC imidate esters **1a** and **1b** containing saturated alkyl groups established that these radical precursors react in much the same manner as the PTOC esters. Visible light irradiation of **1a** in benzene led to discharge of the yellow color of the precursor. From the reaction mixture, the *N*-(2-pyridylthio)amide **3** was isolated in 77% yield. The reaction sequence involves cleavage of **1a** by visible light in an initiation step that gives amidyl radical **2a**. Radical **2a** then reacts with precursor **1a** in a propagation step that gives **3** and another radical **2a** (Scheme II). In this reaction and all others studied, the amidyl radicals reacted exclusively at nitrogen; although the first formed radical from precursor **1** is most likely a Σ oxygen-centered radical, virtually instantaneous electronic and nuclear reorganization would give either a Π or Σ nitrogen-centered amidyl radical **2**.[20] We refer to the reaction of a radical with a PTOC class precursor as "self-trapping"; the reaction of amidyl radical **2** with precursor **1** is similar to the "self-trapping" reaction of carbon-centered radicals observed with PTOC esters.[3] This efficient reaction prevents the γ-hydrogen abstraction in radicals **2** observed when halo and nitroso amide precursors are employed.[17,18]

N-(2-Pyridylthio) amides (e.g. **3**) also were isolated as minor products in a number of cyclization reactions of amidyl radicals produced from precursors **1** that contained unsaturation. These *N*-thio-substituted amides might appear to be labile, but they actually were quite stable. They could be purified by chromatography on silica gel and analyzed by GC with no apparent decomposition. They were stable toward dilute acid or base solutions, but they were readily decomposed by reducing agents such as $NaBH_4$ to give the parent amide.

(20) Chow, Y. L.; Joseph, T. C. *J. Chem. Soc., Chem. Commun.* **1969**, 490. ESR results indicate that amidyl radical ground states are Π type radicals; see Sutcliffe, R.; Anpo, M.; Stolow, A.; Ingold, K. U. *J. Am. Chem. Soc.* **1982**, *104*, 6064 and references therein.

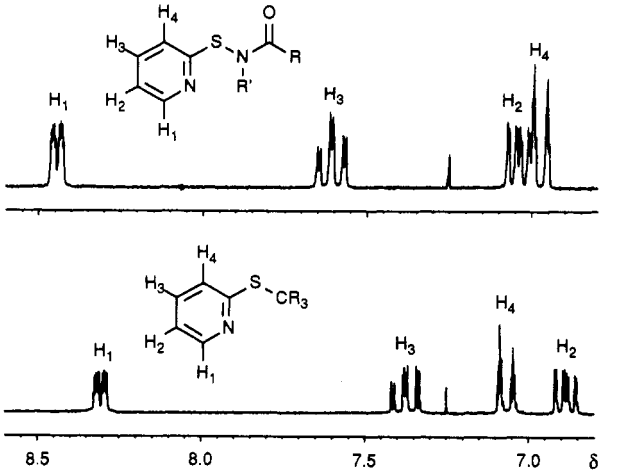
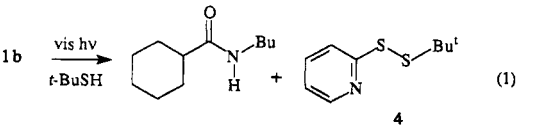


Figure 1. Downfield portion (δ 6.8–8.7) of the ^1H NMR spectra of an *N*-(2-pyridylthio) amide and an alkyl 2-pyridyl sulfide. The small singlets at δ 7.25 in each spectrum are from $CHCl_3$.

In several reactions discussed below, products from precursor **1** trapping of carbon-centered radicals were obtained. The *N*-(2-pyridylthio) products such as **3** were readily distinguished from these *C*-(2-pyridylthio) products by the pyridine patterns in the ^1H NMR spectra (Figure 1).

When PTOC imidate ester **1b** was allowed to react in benzene in the presence of 2-methylpropane-2-thiol (0.15 M), the starting amide and disulfide **4** were obtained (eq 1). In this reaction, the thiol reacted with amidyl radical



(1)

2b by hydrogen atom transfer faster than did precursor **1b**. The *t*-BuS· radical thus formed reacted with precursor **1b** to give **4** in a radical chain propagation step typical of the PTOC class of precursors.[3,5]

Radical Cyclizations Producing γ-Lactams. 5-*Exo* cyclizations of amidyl radicals containing δ,ε-unsaturation were expected on the basis of studies of amidyl radicals produced by reactions of *N*-halo and *N*-nitroso amides[17,18] and also from reactions of aminium cation radicals.[18,19] When PTOC imidate ester **1c** was allowed to react, lactam products **6** were obtained in good to excellent yields (Scheme III). In the absence of any radical trapping agent, radical **2c** cyclized to lactam radical **5** which subsequently reacted with precursor **1c** to give the 2-pyridylthio-substituted product **6b** (72% isolated). When similar reactions were run in the presence of the radical trapping agents *t*-BuSH and PhSeSePh, the self-trapping product **6b** was not observed; lactams **6a** (95% by GC) and **6c** (76% isolated) were formed by trapping of the cyclic radical by H-atom and SePh group transfer, respectively.

Reactions of PTOC **1c** conducted in the presence of high concentrations of *t*-BuSH (up to 0.7 M) gave no evidence of trapping of amidyl radical **2c** in competition with the cyclization reaction. However, both acyclic amide (**7a**) and lactam **6a** were produced when reactions were conducted in the presence of Bu_3SnH. For the electrophilic amidyl radical, this behavior was expected; *t*-BuSH reacts with nucleophilic carbon-centered radicals more rapidly

Scheme III

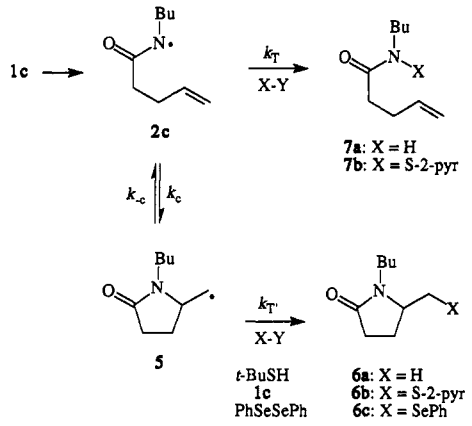


Table I. Products from Reactions of PTOC Imidate Ester 1c in the Presence of Bu_3SnH[a]

[Bu_3SnH] (M)	(6a/7a)[b]	% yield[c]
0.10	8.38	93
0.30	2.75	88
0.50	1.82	87
1.00	0.92	92

[a] Reactions run in benzene at 20 °C. [b] Ratio of products determined by GC. [c] Yield of **6a** plus **7a** determined by GC against an internal standard.

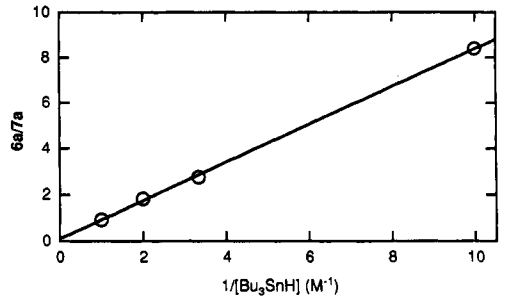


Figure 2. Product ratios from reactions of **1c** in the presence of Bu_3SnH; see Scheme III.

than does Bu_3SnH,[21,22] but the "hydridic" tin reagent is known to react with electrophilic aminium cation radicals more rapidly than does the thiol.[7b]

A series of reactions of **1c** were conducted at 20 °C with concentrations of Bu_3SnH ranging from 0.1 M to 1.0 M. The results are listed in Table I, and a plot of the ratio of lactam **6a** to acyclic amide **7a** versus the inverse of the concentration of Bu_3SnH is shown in Figure 2. For the sequence of reactions shown in Scheme III, this ratio is described by eq 2 when the concentration of Bu_3SnH is

$$\mathbf{6a/7a} = (k_{-c}k_{SnH}/k_c k_{SnH'}) + (k_c/k_{SnH})[Bu_3SnH]^{-1} \quad (2)$$

essentially unchanging over the course of the reaction. The intercept of the function shown in Figure 1 was (0.09 ± 0.12) at 2σ showing that the cyclization reaction was essentially irreversible under the conditions of the experiments (i.e. $k_{-c} << k_{SnH'}[Bu_3SnH]$). Because Bu_3SnH reacts with carbon-centered radicals[22b] with a rate constant at 20 °C of about 2×10^6 M^{-1} s^{-1}, we conclude that the first order rate constant for the ring opening of **5** was $k_{-c} < 1 \times 10^4$ s^{-1}. The slope in Figure 2 was (k_c/k_{SnH}) = (0.83 ± 0.02) M at 2σ. Absolute rate constants for the two competing steps cannot be evaluated, but this ratio can be employed in synthetic planning.

The self-trapping reaction of amidyl radical **2c** by the PTOC imidate ester **1c** also competed with the cyclization of **2c** to **5** although only to a minor extent. In a reaction of **1c** with an initial concentration of 0.044 M, the ratio of *N*-(2-pyridylthio) amide **7b** to self-trapped lactam **6b** was 1:11.4. If we assume that ring opening of radical **5** was unimportant in this reaction, then the approximate ratio of rate constants for cyclization (k_c) to self-trapping on nitrogen (k_{ST}) was (k_c/k_{ST}) = 0.25 M; thus, the rate constant for the self-trapping reaction of radical **2c** was about three times greater than that for the Bu_3SnH trapping reaction. A significant amount of self-trapping might be observed if cyclization reactions of PTOC imidate esters were conducted at high concentrations, but, because concentrations of the radical precursors are typically low, this reaction usually can be ignored. However, intermolecular additions of amidyl radicals to alkenes will be significantly slower than their intramolecular counterparts. Therefore, in an attempted intermolecular addition, self-trapping is expected to predominate unless the alkene is a highly activated, electron-rich species.[23]

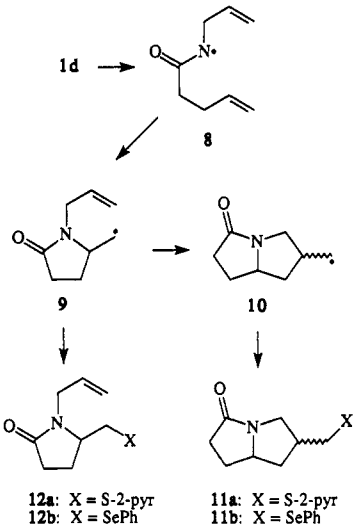
Tandem cyclization of an amidyl radical to construct a pyrrolizidinone ring system also was accomplished efficiently (Scheme IV). Reaction of the PTOC imidate ester **1d**, prepared *in situ* from *N*-allyl-4-pentenamide, under self-trapping conditions gave pyrrozidinone **11a** in 64% isolated yield as a 6:1 mixture of diastereomers.[24] The stereochemistry of the major isomer was not determined, but a *trans* orientation of the substituents on the pyrrolidine ring is expected.[26] It was possible that the carbon radical **9** initially formed in the cyclization of amidyl radical **8** could have been trapped to give the monocyclic lactam **12a** (Scheme IV), but, under the reaction conditions employed, the isolated yield of **12a** was <2%.

When precursor **1d** was allowed to react in the presence of PhSeSePh, an excellent carbon radical trapping agent, the monocyclic lactam radical **9** was intercepted in competition with the cyclization to **10**. A reaction of 0.05 M **1d** and 0.10 M PhSeSePh gave the pyrrolizidinone **11b** and the pyrrolidinone **12b** in 22% and 52% isolated yields, respectively. As expected, when the reaction was run at higher dilution (0.016 M **1d** and 0.028 M PhSeSePh), the ratio of **11b/12b** was increased to essentially 1:1 (96% combined yield). As with **11a**, the (phenylseleno)methyl-substituted pyrrolizidinone **11b** consisted of a 6:1 mixture of diastereomers.

The results of the PhSeSePh trapping experiments with **1d** were anticipated from known rate constants. Diphenyl diselenide reacts with primary carbon radicals at 25 °C with a rate constant of 2.6×10^7 M^{-1} s^{-1},[27] and the rate

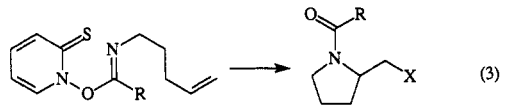
(21) Review of carbon radical kinetics: Newcomb, M. *Tetrahedron* **1993**, *49*, 1151.
(22) (a) Newcomb, M.; Glenn, A. G.; Manek, M. B. *J. Org. Chem.* **1989**, *54*, 4603. (b) Chatgilialoglu, C.; Ingold, K. U.; Scaiano, J. C. *J. Am. Chem. Soc.* **1981**, *103*, 7739.
(23) Low yields of an adduct from reaction of radical **2a** with the enamine 1-(dimethylamino)cyclohexene could be obtained; Esker, J. L., Ph.D. Thesis, Texas A&M University, 1992.
(24) Similar tandem radical cyclizations of the corresponding aminium cation radical have been reported.[25]
(25) Surzur, J.-M.; Stella, L. *Tetrahedron Lett.* **1974**, 2191. Newcomb, M.; Marquardt, D. J.; Deeb, T. M. *Tetrahedron* **1990**, *46*, 2329.
(26) Beckwith, A. L. J.; Schiesser, C. H. *Tetrahedron Lett.* **1985**, *26*, 373. Beckwith, A. L. J.; Schiesser, C. H. *Tetrahedron* **1985**, *41*, 3925. Spellmeyer, D. C.; Houk, K. N. *J. Org. Chem.* **1987**, *52*, 959.
(27) The rate constant for reaction of PhSeSePh with a primary alkyl radical originally reported[28] must be corrected.[21]

Scheme IV



constant for cyclization of the 5-hexenyl radical is 2.2×10^5 s^{-1} at 25 °C.[21,22b] If one assumes that the β-nitrogen substitution in radical **9** does not influence the rate constant for reaction with PhSeSePh, then the rate constant for cyclization of **9** can be calculated as 5×10^5 s^{-1} at 25 °C from our data. A slight increase in the rate constant for cyclization of **9** over that of the 5-hexenyl radical is expected due to the reduced conformational freedom in **9**.

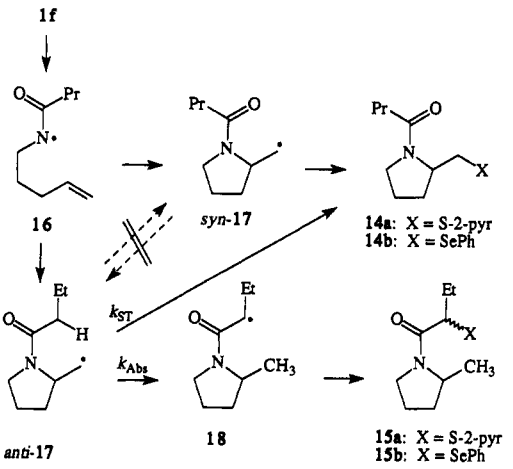
Radical Cyclizations Producing *N*-Acylpyrrolidines. It was also possible to effect 5-*exo* cyclizations of amidyl radicals onto δ,ε-unsaturated positions on the *N*-alkyl group to give, ultimately, *N*-acylpyrrolidine products. Reaction of PTOC imidate ester **1e**, prepared from *N*-(4-pentenyl)cyclohexanecarboxamide, in the presence of PhSeSePh gave the *N*-acylpyrrolidine **13a** in 61% isolated yield (eq 3). Interestingly, when a similar reaction



of **1e** was conducted without an additional radical trapping agent, the self-trapped pyrrolidine product **13b** was not formed in appreciable yield (< 1% yield as determined by GC–mass spectral analysis of the reaction mixture), but a complex mixture of partially characterized products was obtained. Taken together, these results suggest that the amidyl radical formed from **1e** cyclized efficiently but that some other reaction(s) of the intermediate pyrrolidinyl radical competed with the self-trapping reaction of the cyclic radical. We speculate that an intramolecular hydrogen abstraction sequence similar to that deduced for reactions of **1f** (see below) resulted in the complex mixture of products from **1e**.

Studies with the PTOC imidate ester **1f**, which has the less sterically demanding propyl group, revealed a new reaction (Scheme V). When **1f**, prepared *in situ* from *N*-(4-pentenyl)butanamide, was allowed to react under self-trapping conditions, the expected *N*-acylpyrrolidine **14a** was obtained in 35% yield. In addition, the *N*-acylpyrrolidines **15a** were obtained in 24% yield as an inseparable mixture of diastereomers. The cyclization of

Scheme V



amidyl radical **16** to radical **17** was efficient, but when the velocity of the subsequent trapping reaction of carbon-centered radical **17** was slow, 1,5-hydrogen atom transfer (a radical translocation)[29] occurred to give radical **18**, the immediate precursor to products **15a**. When **1f** was allowed to react in the presence of PhSeSePh, pyrrolidine **14b** was isolated in 66% yield, and translocation products **15b** were not detected; the lifetime of radical **17** in the presence of the diselenide was too short to permit the translocation.[30]

As shown in Scheme V, the cyclization of amidyl radical **16** can produce either *syn*-**17** or *anti*-**17** radicals, and, given the relatively slow rate of rotation of C–N bonds in amides,[32] it is unlikely that radicals **17** can interconvert by rotation in competition with the radical reactions of these species. Whereas *anti*-**17** can give either **14a** or **15a** (via radical **18**), *syn*-**17** can only lead to **14a**. Therefore, the ratio of products **14a** to **15a** was a function both of the initial partitioning of radical **16** upon cyclization and of the rates of the competing reactions of *anti*-**17**. Specifically, the ratio is described approximately by eq 4 where

$$\mathbf{14a}/\mathbf{15a} = (S/A) + ((S/A) + 1)(k_{ST}/k_{Abs}) \times [\text{PTOC } \mathbf{1f}]_m \quad (4)$$

(S/A) is the ratio of *syn*-**17** to *anti*-**17** formed in the partitioning of **16**, k_{ST} is the rate constant for self-trapping of *anti*-**17**, k_{Abs} is the rate constant for translocation in radical *anti*-**17**, and $[\text{PTOC } \mathbf{1f}]_m$ is the average concentration of the precursor PTOC imidate ester over the course of the reaction.

Reactions of **1f** at initial concentrations of 0.05, 0.10, and 0.17 M were run at 20 °C. The ratios of **14a** to **15a** were 1.4, 2.1, and 3.2, respectively. A plot of these ratios versus the average concentration of PTOC **1f** is shown in

(28) Russell, G. A.; Tashtoush, H. *J. Am. Chem. Soc.* **1983**, *105*, 1398.
(29) For examples of other intramolecular 1,5-hydrogen atom abstractions from an α-amide position, see: Curran, D. P.; Abraham, A. C.; Liu, H. T. *J. Org. Chem.* **1991**, *56*, 4335. Esker, J. L.; Newcomb, M. *Tetrahedron Lett.* **1992**, *33*, 5913.
(30) This was expected on the basis of the known rate constants for reactions of primary alkyl radicals with PTOC esters[31] and PhSeSePh;[27] the selenyl group transfer is about 100 times faster than self-trapping.
(31) Newcomb, M.; Kaplan, J. *Tetrahedron Lett.* **1987**, *28*, 1615. Curran, D. P.; Bosch, E.; Kaplan, J.; Newcomb, M. *J. Org. Chem.* **1989**, *54*, 1826.
(32) The slow C–N bond rotation in amides, often resulting in the observation of distinct rotamers in NMR spectra, is orders of magnitude less rapid than amidyl radical reactions studied here; *cf.* Neuman, R. C., Jr.; Jonas, V. *J. Org. Chem.* **1974**, *39*, 929.

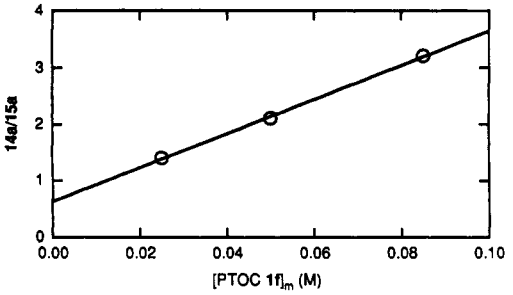


Figure 3. Product ratios from reactions of **1f**; see Scheme V.

Scheme VI

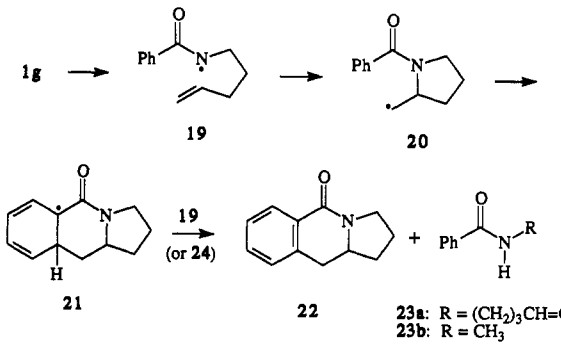
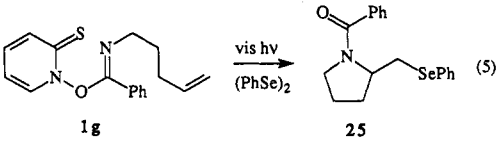


Figure 3. The intercept of the plot in this figure (0.63 ± 0.06), shows that the translocation product cannot exceed 60–65% yield even at diminishingly small concentrations of precursor **1f**; this confirms the expectation that *syn*-**17** and *anti*-**17** did not equilibrate on the time scale of our studies. The slope of the plot in Figure 3 was (30.1 ± 1.0) M^{-1}. From this slope and eq 4, the ratio of rate constants (k_{ST}/k_{Abs}) was calculated to be 18 M^{-1}. Assuming that the rate constant for the self-trapping reaction of *anti*-**17** by PTOC imidate ester **1f** is approximately equal to the rate constant for trapping of a primary alkyl radical by a PTOC ester,[31] the value of the rate constant for translocation (k_{Abs}) is about 5 × 10^4 s^{-1} at 20 °C.

Cyclizations of the benzamidyl radical **19**, produced from PTOC imidate ester **1g** also were studied. When reactions were conducted in the absence of an added trapping agent or in the presence of *t*-BuSH, the only products obtained were 3,4-benzoindolizidinone (**22**) and the original benzamide **23a**, and these products were consistently obtained in a 1:1 ratio (isolated yields up to 93%). Apparently, the sequence of reactions in Scheme VI was involved. Benzamidyl radical **19** cyclized to pyrrolidinyl radical **20**, but **20** was not trapped either by the starting PTOC imidate ester **1g** or by *t*-BuSH. Rather, a second cyclization of **20** gave the polycyclic radical **21**. The highly delocalized radical **21** apparently was persistent (i.e. reacted with neither trapping agent nor itself) and accumulated in solution such that it became an efficient trap for acyclic benzamidyl radical **19**. Radical–radical disproportionation of **21** and **19**, probably occurring with a rate constant at the spin statistically corrected diffusion control value of ca. 5 × 10^9 M^{-1} s^{-1}, would give the observed 1:1 mixture of products by "persistent radical steering".[33]

To provide evidence for or against the mechanism in Scheme VI, we conducted a reaction with an equimolar mixture of PTOC imidate esters **1g** and **1h**. These two structurally similar radical precursors were expected to react by photochemical cleavage with comparable velocities providing amidyl radicals **19** and PhC(=O)N(·)CH_3 (**24**) at about the same rate. However, whereas **19** can cyclize, **24** was expected to accumulate and become the primary oxidant of polycyclic radical **21**. As expected, the ratio of benzoindolizidinone **22** to benzamide **23a** was increased from 50:50 in the absence of **1h** to 78:22 when the sacrificial oxidant **24** was available. The simple benzamide **23b** was also formed in the latter case.

Further support for the mechanistic pathway in Scheme VI was provided when PTOC imidate ester **1g** was allowed to react in the presence of 0.1 M PhSeSePh. In this case, a conventional radical chain reaction sequence involving cyclization of **19** to **20** and trapping of **20** by the diselenide predominated, and the phenylseleno-substituted product **25** (eq 5) was obtained in 70% isolated yield along with



13% of **22**. It is noteworthy that **22** was produced even when the PTOC imidate ester **1g** was prepared in the presence of the diselenide, a procedure that ensures that radical chain initiation did not precede addition of the diselenide trapping agent. The cyclization of **20** is marginally competitive with diselenide trapping; an approximate rate constant for the cyclization of **20** to **21** at 20 °C of ca. 1 × 10^6 s^{-1} was calculated. This large value for the rate constant for cyclization of **20** and the high yields of benzoindolizidinone **22** obtained (considering the 50% maximum yield possible due to the disproportionation reaction) indicate that radical **20** was produced exclusively in the *anti* conformation drawn in Scheme VI.

Conclusion. Amidyl radicals can be generated efficiently from PTOC imidate ester precursors prepared from secondary amides via their imidoyl chlorides. The amidyl radicals produced by this method underwent 5-*exo* cyclizations with unsaturated positions on either the acyl or alkyl side chain to produce γ-lactams and *N*-acylpyrrolidines in good to excellent yields. For cases where competing 5-*exo* cyclizations at nitrogen or oxygen were possible, no evidence of formation of imidate esters via oxygen attack was found. An advantage of the PTOC imidate esters over *N*-chloro amides or *N*-nitroso amides as amidyl radical precursors is that the radical chain reactions are not limited to atom or group transfers from the precursors; the carbon-centered radicals from cyclizations of the amidyl radicals could be trapped efficiently by *t*-BuSH or PhSeSePh as well as by the PTOC precursors. In the case of intermolecular additions, however, the fast self-trapping reaction of amidyl radicals by the PTOC imidate ester precursors will require that low concentrations of precursors or highly reactive, electron-rich alkenes be employed.

Experimental Section

General. Reagents were purchased from Aldrich Chemical Co. unless noted. Solvents were dried by common methods and distilled under N_2 before use. For reactions conducted under inert atmosphere, flasks were flame dried and purged with dry

(33) Fischer has presented a quantitative evaluation of the effects of persistent radicals which can result in high yields of cross-termination products; see: Fischer, H. *J. Am. Chem. Soc.* **1986**, *108*, 3925.

N_2 until cool. 2-Methylpropane-2-thiol was dried over calcium oxide, distilled and stored over activated molecular sieves. Tributyltin hydride was distilled under N_2 and analyzed by GC before use. *N*-Hydroxypyridine-2-thione sodium salt was obtained from an aqueous solution (Olin Chemical); the method of isolation of the salt is described in the supplementary material.

Radial chromatography was performed on a Chromatotron Model 7924T (Harrison Research); rotors were coated with a 2 mm film of TLC grade silica gel (Merck). Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. NMR spectra were obtained from $CDCl_3$ solutions at 200 or 300 MHz (^1H) and at 50 or 75 MHz (^{13}C); chemical shifts are reported relative to TMS (^1H δ 0.00) or the center line of $CDCl_3$ (^{13}C δ 77.00). GC analyses were performed on Varian model 3400 chromatographs equipped with flame ionization detectors using 15 m wide bore capillary columns (SE-54 or Carbowax). GC-MS analyses were accomplished on a Hewlett-Packard Model 5890 chromatograph interfaced to an HP Model 5791 mass selective detector; a 15 m × 0.25 mm capillary column (DB-5) was used. High resolution mass analyses were performed by the departmental facilities at Texas A&M University and at Wayne State University.

Secondary amides were prepared by general methods. The synthetic reactions and NMR spectra are reported in the supplementary material.

PTOC Imidate Esters 1 were prepared by one of two protocols. In method C the PTOC imidate ester was isolated and characterized by NMR spectroscopy, whereas in method D the crude PTOC imidate ester was allowed to react in radical chain reactions without isolation. These radical precursors decomposed upon storage or exposure to moisture or to visible light, and they were not characterized by analysis.

Method C. To a 0.1 M solution of a secondary amide in benzene containing a catalytic amount of DMF at ca. 5 °C was transferred 1.5 equiv. of phosgene (1.9 M solution of phosgene in toluene). The solution was allowed to warm slowly to ambient temperature with stirring. The slow evolution of CO_2 was monitored via a mineral oil bubbler. After ca. 12 h, the evolution of CO_2 was complete. Excess phosgene and solvent were removed by distillation at room temperature and reduced pressure to give the imidoyl chloride as a clear liquid. Dry ether was added to give a 0.1 M solution of imidoyl chloride. The flask was wrapped in aluminum foil, and anhydrous 2-mercaptopyridine *N*-oxide sodium salt (1.2 equiv) was added via a solid addition tube under nitrogen. The mixture was stirred for 4–8 h. The residual salts were removed by filtration under nitrogen and were washed with dry ether. Concentration of the filtrate *in vacuo* gave the PTOC imidate esters 1 as yellow oils.

Method D. The preparations of the imidoyl chlorides and the PTOC imidate esters were similar to the procedures described in method A with the exceptions that the imidoyl chloride solution was concentrated to ca. one-half of the original volume and ether was not employed in the imidate ester preparation. Salts were filtered from the PTOC imidate ester solution and washed with dry benzene, and the resulting filtrate was diluted with dry benzene to give the desired concentration of PTOC imidate ester for subsequent reactions.

1-[(*N*-Butylcyclohexanecarboximidyl)oxy]-2(1*H*)-pyridinethione (1b) was prepared by Method C from 0.50 g (2.70 mmol) of *N*-butylcyclohexanecarboxamide. The imidoyl chloride had the following NMR spectra: ^1H NMR δ 3.57 (t, 2 H, J = 6.9 Hz), 2.62–2.44 (m, 1 H), 2.20–1.20 (m, 14 H), 0.92 (t, 3 H, J = 7.0 Hz); ^{13}C NMR δ 137.80, 51.81, 49.55, 31.37, 30.38, 25.40, 25.12, 20.22, 13.62. Radical precursor **1b** was obtained in quantitative yield as a viscous yellow oil from which removal of the final traces of solvent was difficult. Conformational isomers were observed in the NMR spectra: ^1H NMR δ 8.35–8.25 (m, 0.7 H), 7.70–7.10 (m, 3 H), 6.95 (dt, 0.3 H, J = 0.8, 5.0 Hz), 5.90–5.65 (m, 1 H), 3.55 (t, 1.33 H, J = 7.0 Hz), 3.27 (t, 0.66 H, J = 7.0 Hz), 2.45–2.25 (m, 1 H), 2.20–1.10 (m, 14 H), 0.92 (t, 3 H, J = 7.0 Hz); ^{13}C NMR δ 159.47, 148.28, 139.45, 125.65, 125.30, 122.32, 54.92, 50.88, 32.44, 30.96, 29.48, 25.97, 20.46, 13.90.

1-[(*N*-Butyl-4′-pentenimidoyl)oxy]-2(1*H*)-pyridinethione (1c) was prepared by method C from *N*-butyl-4-pentenamide (1.20 g, 7.74 mmol). The imidoyl chloride had the following NMR spectra: ^1H NMR δ 5.93–5.70 (m, 1 H), 5.15–4.95 (m, 2 H), 3.49 (t, 2H, J = 6.9 Hz), 2.70 (t, 2 H, J = 7.1 Hz), 2.50–2.35 (m, 2 H), 1.70–1.50 (m, 2 H), 1.50–1.30 (m, 2 H), 0.93 (t, 3 H, J = 7.2 Hz); ^{13}C NMR δ 145.25, 136.15, 115.96, 52.97, 41.69, 31.52, 30.68, 20.46, 13.78. The residue was carried on to give **1c** as a yellow oil (2.00 g, 7.58 mmol, 98%). Crystallization from dry ether/hexanes gave 1.07 g (4.05 mmol, 52%) of **1c**, mp 46.0–47.5 °C. Conformational isomers were observed in the NMR spectra: ^1H NMR δ 8.35–8.25 (m, 0.7 H), 7.70–7.10 (m, 3 H), 6.59 (dt, 0.3 H, J = 0.8, 5.0 Hz), 6.00–5.65 (m, 1 H), 5.20–4.90 (m, 2 H), 3.59 (t, 1.4 H, J = 7.0 Hz), 3.24 (t, 0.6 H, J = 7.0 Hz), 2.70–2.30 (m, 4 H), 1.80–1.20 (m, 4 H), 1.0–0.82 (m, 3 H); ^{13}C NMR δ (major) 155.37, 146.30, 139.83, 136.96, 129.00, 125.24, 124.12, 115.45, 54.54, 40.08, 32.38, 31.06, 20.53, 13.89; (minor) 139.80, 137.20, 136.63, 133.21, 115.99, 48.20, 32.88, 29.81, 20.22, 13.81.

1-[(*N*-(4′-Pentenyl)cyclohexanecarboximidoyl)oxy]-2(1*H*)-pyridinethione (1e) was prepared by method C from *N*-(4-pentenyl)cyclohexanecarboxamide (402 mg, 2.15 mmol). The imidoyl chloride had the following NMR spectra: ^1H NMR δ 5.95–5.70 (m, 1 H), 5.10–4.90 (m, 2 H), 3.48 (t, 2 H, J = 7.0 Hz), 2.62–2.44 (m, 1 H), 2.20–1.20 (m, 14 H); ^{13}C NMR δ 137.95, 114.83, 52.33, 50.42, 31.30, 30.58, 28.62, 25.75, 25.51. The residue was carried on to give **1e** as a yellow oil which was used directly in the photolysis reaction containing diphenyl diselenide: ^1H NMR δ 8.32–8.22 (m, 1 H), 7.30–7.05 (m, 3 H), 5.90–5.65 (m, 1 H), 5.10–4.85 (m, 2 H), 3.55 (t, 2 H, J = 6.0 Hz), 2.45–2.25 (m, 1 H), 2.20–1.10 (m, 14 H); ^{13}C NMR δ 159.85, 148.01, 139.44, 138.11, 125.77, 125.35, 122.47, 114.88, 54.38, 50.76, 31.38, 30.93, 29.47, 25.94, 25.78.

1-[(*N*-(4′-Pentenyl)benzimidoyl)oxy]-2(1*H*)-pyridinethione (1g) was prepared by method C from *N*-(4-pentenyl)benzamide (209 mg, 1.10 mmol). The imidoyl chloride had the following NMR spectra: ^1H NMR δ 8.05–7.95 (m, 2 H), 7.50–7.35 (m, 3 H), 6.00–5.70 (m, 1 H), 5.13–4.95 (m, 2 H), 3.72 (t, 2 H, J = 7.0 Hz), 2.25–2.10 (m, 2 H), 1.90–1.70 (m, 2 H); ^{13}C NMR δ 141.72, 138.06, 135.92, 131.12, 128.90, 128.22, 114.98, 53.46, 31.57, 28.22. The residue was carried on to give 315 mg (1.06 mmol, 96%) of **1g** as a yellow oil: ^1H NMR δ 8.25–8.17 (m, 2 H), 7.95–7.85 (m, 2 H), 7.40–7.25 (m, 3 H), 7.05–6.85 (m, 3 H), 5.95–5.73 (m, 1 H), 5.10–4.90 (m, 2 H), 3.87 (t, 2 H, J = 7.0 Hz), 2.30–2.10 (m, 2 H), 1.95–1.80 (m, 2 H); ^{13}C NMR δ 154.60, 148.90, 139.05, 138.07, 137.86, 130.78, 128.62, 128.49, 125.88, 125.29, 122.27, 115.03, 55.67, 31.59, 29.66. Crystallization from ether and hexanes gave material with mp 36–39 °C.

1-[(*N*-Methylbenzimidoyl)oxy]-2(1*H*)-pyridinethione (1h) was prepared by method C from *N*-methylbenzamide (1.00 g, 7.40 mmol). The imidoyl chloride had the following NMR spectra: ^1H NMR δ 8.05–7.95 (m, 2 H), 7.50–7.35 (m, 3 H), 3.48 (s, 3 H); ^{13}C NMR δ 143.80, 135.68, 131.26, 128.74, 128.27, 40.72. The residue was carried on to give 1.74 g (7.13 mmol, 96.4%) of **1h** as a yellow oil: ^1H NMR δ 8.25–8.15 (m, 1 H), 7.95–7.85 (m, 2 H), 7.40–7.25 (m, 3 H), 7.05–6.85 (m, 3 H), 3.68 (s, 3 H); ^{13}C NMR δ 156.30, 147.51, 139.08, 137.97, 130.80, 128.52, 128.28, 125.72, 125.34, 122.36, 43.29.

Reactions of PTOC Imidate Esters. Solutions of the PTOC imidate esters (0.05–0.10 M) in benzene or benzene/toluene were prepared under nitrogen in vessels shielded from light. Radical trapping agents, if desired, were added. The shield was removed, and the reaction mixtures were irradiated with a 150-W tungsten filament flood lamp at a distance of ca. 0.7 m until the bright yellow color of the PTOC precursor discharged (0.1–5 h) unless noted otherwise. The solvent was removed under reduced pressure, and products were purified by radial chromatography.

***N*-Butyl-*N*-(2-pyridylthio)pentanamide (3).** The PTOC imidate ester **1a** was prepared by method D from *N*-butylpentanamide (387 mg, 2.46 mmol). Irradiation of a 0.1 M solution, solvent removal, and radial chromatography of the residue (hexanes/ethyl acetate, 7:1) gave 506 mg of **3** (1.90 mmol, 77%) as a clear colorless oil: ^1H NMR δ 8.50–8.45 (m, 1 H), 7.72–7.60 (m, 1 H), 7.15–7.05 (m, 1 H), 7.02 (app d, 1 H, J = 8.0 Hz), 4.10–3.30 (bs, 2 H), 2.65 (bt, 2 H, J = 7.0 Hz), 1.72–1.50 (m, 4 H), 1.45–1.20 (m, 4 H), 0.92 (t, 3 H, J = 7.0 Hz), 0.87 (t, 3 H, J = 7.2 Hz); ^{13}C NMR δ 178.44, 160.96, 149.78, 137.01, 120.22, 116.50, 51.25, 32.68, 30.31, 27.36, 22.10, 19.69, 13.64, 13.62; MS m/z (rel inten), 267 ($(M + 1)^+$ from self CI, 4), 182 (3), 156 (14), 139 (25), 111 (100), 72 (60); HRMS calcd for $C_{14}H_{23}N_2OS$ $(M + 1)^+$ 267.1530, found 267.1535.

Irradiation of PTOC Imidate Ester 1b in the Presence of 2-Methylpropane-2-thiol. To a solution of PTOC imidate ester **1b** (100 mg, 0.30 mmol) in benzene (6 mL) was added 0.17 mL of 2-methylpropane-2-thiol (1 mmol). Irradiation of this solution for 6 h resulted in a colorless solution. GC analysis indicated only two products, *N*-butylcyclohexanecarboxamide and *tert*-butyl 2-pyridyl disulfide (**4**) in 80% yield. The known[3] disulfide **4** was isolated by radial chromatography (hexanes/ethyl acetate). The ^1H and ^{13}C NMR and mass spectrum of **4** were identical to those previously reported.[3]

***N*-Butyl-5-[(2′-pyridylthio)methyl]-2-pyrrolidinone (6b) and *N*-Butyl-*N*-(2′-pyridylthio)-4-pentenamide (7b).** Irradiation of a 0.044 M benzene solution of imidate ester **1c** (300 mg, 1.10 mmol), solvent removal, and radial chromatography (hexanes/ethyl acetate, 3:1) gave 18.5 mg (6.3%) of **7b** followed by 210 mg (72%) of **6b** as colorless oils.

Compound **6b** had the following properties: ^1H NMR δ 8.41 (dd, 1 H, J = 5.1, 1.5 Hz), 7.41 (dt, 1 H, J = 7.8, 1.5 Hz), 7.19 (dd, 1 H, J = 7.8, 1.1 Hz), 7.00 (dt, 1 H, J = 5.1, 1.1 Hz), 4.00–3.60 (m, 3 H), 3.15–2.90 (m, 2 H), 2.60–2.04 (m, 3 H), 1.95–1.75 (m, 1 H), 1.75–1.45 (m, 2 H), 1.45–1.20 (m, 2 H), 0.95 (t, 3 H, J = 7.0 Hz); ^{13}C NMR δ 174.90, 157.47, 149.33, 136.10, 122.59, 119.81, 57.02, 40.26, 32.21, 29.95, 29.46, 23.69, 20.15, 13.84; MS m/z (rel inten), 264 (M^+, 0.5), 154 (10), 140 (84), 111 (45), 84 (100); HRMS calcd for $C_{14}H_{20}N_2OS$ 264.1296, found 264.1298.

Compound **7b** had the following properties: ^1H NMR δ 8.48 (app d, 1 H, J = 5.0 Hz), 7.63 (ddd, 1 H, J = 2.0, 7.5, 8.0 Hz), 7.05–7.12 (m, 1 H), 7.02 (app d, 1 H, J = 8.0 Hz), 5.92–5.80 (m, 1 H), 5.10–4.90 (m, 2 H), 4.00–3.40 (bm, 2 H), 2.83–2.65 (bm, 2 H), 2.45–2.30 (m, 2 H), 1.75–1.55 (m, 2 H), 1.40–1.20 (m, 2 H), 0.92 (t, 3 H, J = 7.3 Hz); MS m/z (rel inten), 264 (M^+, 0.5), 182 (1.5), 154 (3), 139 (17), 111 (100), 72 (58), 55 (61). Due to the small amount of material, compound **7b** was not further analyzed.

***N*-Butyl-5-[(phenylseleno)methyl]-2-pyrrolidinone (6c).** Irradiation of a 0.05 M benzene solution of imidate ester **1c** (228 mg, 1.10 mmol) in the presence of 0.095 M diphenyl diselenide (650 mg, 2.08 mmol), solvent removal, and radial chromatography (hexanes/ethyl acetate, 3:1) of the residue gave 160 mg (0.604 mmol, 70%) of the known[34] (2-pyridylthio)phenyl selenide followed by 194 mg (0.626 mmol, 73%) of **6c** as a colorless oil: ^1H NMR δ 7.60–7.45 (m, 2 H), 7.35–7.20 (m, 3 H), 3.90–3.75 (m, 1 H), 3.65–3.45 (m, 1 H), 3.17 (dd, 1 H, J = 13.0, 2.8 Hz), 2.88 (dd, 1 H, J = 13.0, 8.0 Hz), 2.83–2.65 (m, 1 H), 2.60–2.03 (m, 3 H), 1.95–1.75 (m, 1 H), 1.45–1.13 (m, 4 H), 0.86 (t, 3 H, J = 7.0 Hz); ^{13}C-NMR δ 174.73, 133.33, 129.27, 127.55, 57.20, 39.96, 31.88, 30.02, 29.40, 24.37, 20.07, 13.72; MS m/z (rel inten), 311 (^{80}Se M^+, 4), 309 (^{78}Se M^+, 2), 157 (2), 140 (100), 98 (7), 84 (25); HRMS calcd for $C_{15}H_{21}N_2OSe$ 311.0788, found 311.0786.

Reactions of 1c in the Presence of Hydrogen Atom Donors. Solutions of **1c** and *t*-BuSH or Bu_3SnH in benzene were irradiated, and the products were analyzed by GC and GC-MS comparisons to authentic materials. Reactions in the presence of *t*-BuSH gave *N*-butyl-5-methyl-2-pyrrolidinone (**6a**). Reactions in the presence of Bu_3SnH gave **6a** and *N*-butyl-4-pentenamide (**7a**) in ratios dependent on the concentration of the tin hydride (see text).

The authentic sample of **6a** was prepared by deprotonation of 5-methyl-2-pyrrolidinone with NaH in THF and subsequent alkylation with iodobutane. Amide **6a** was isolated after aqueous workup and distillation (100 °C, 0.2 Torr) as a colorless liquid in 44% yield with the following properties: ^1H NMR δ 3.80–3.50 (m, 1 H), 2.45–2.30 (m, 2 H), 1.70–1.20 (m, 6 H), 1.21 (d, 3 H, J = 6.3 Hz), 0.92 (t, 3 H, J = 7.0 Hz); ^{13}C NMR δ 174.73, 53.34, 39.79, 30.36, 29.56, 26.80, 20.20, 19.80, 13.80; MS m/z (rel inten), 155 (M^+, 19), 140 (19), 112 (100), 98 (20), 84 (50).

***N*-Allyl-5-[(2′-pyridylthio)methyl]-2-pyrrolidinone (12a) and 7-[(2′-Pyridylthio)methyl]-2-pyrrolizidinone (11a).** The PTOC imidate ester **1d** was prepared by method D from *N*-allyl-4-pentenamide (330 mg, 2.37 mmol). The solution was diluted with benzene so that the theoretical concentration of imidate upon irradiation was 0.075 M. Following irradiation, products were separated by radial chromatography (gradient of hexanes/ethyl acetate to ethyl acetate/ethanol elution) to give 7.0 mg (0.028 mmol, 1.2%) of **12a** followed by 378 mg of **11a** (1.52 mmol, 64%) as colorless oils.

Compound **12a** had the following properties: ^1H NMR δ 8.40 (app d, 1 H, J = 5.0 Hz), 7.48 (ddd, 1 H, J = 2.0, 7.5, 8.0 Hz), 7.19 (app d, 1 H, J = 8.0 Hz), 7.02 (ddd, 1 H, J = 1.0, 5.0, 7.5 Hz), 5.90–5.65 (m, 1 H), 5.35–5.10 (m, 2 H), 4.34 (dd, 1 H, J = 4.9, 15.0 Hz), 4.00–3.52 (m, 1 H), 3.80–3.55 (m, 2 H), 3.08 (dd, 1 H, J = 8.5, 15.0 Hz), 2.60–1.70 (m, 4 H). Due to the small amount of compound, **12a** was not further characterized. Compounds **11a** consisted of an inseparable mixture of diastereomers (5:1); the stereochemistry of the major isomer was not determined.

Compounds **11a** had the following properties: ^1H NMR δ 8.45–8.35 (m, 1 H), 7.54–7.43 (m, 1 H), 7.20–7.13 (m, 1 H), 7.04–6.95 (m, 1 H), 4.18–3.85 (m, 2 H), 3.40–3.20 (m, 2 H), 2.90–2.20 (m, 5 H), 2.10–1.90 (m, 1 H), 1.80–1.55 (m, 2 H); ^{13}C NMR δ (major isomer), 174.90, 157.79, 149.12, 135.73, 122.15, 119.36, 59.82, 46.74, 39.95, 37.17, 34.47, 33.11, 27.91, (minor isomer) 61.76, 45.92, 41.62, 38.69, 34.69, 33.88, 26.88; MS m/z (rel inten), 248 (M^+, 12), 215 (45), 201 (100), 152 (47), 137 (48); HRMS calcd for $C_{13}H_{16}N_2OS$ 248.0983; found 248.0990.

***N*-Allyl-5-[(phenylseleno)methyl]-2-pyrrolidinone (12b) and 7-[(Phenylseleno)methyl]-2-pyrrolizidinone (11b).** A 0.05 M solution of the PTOC imidate ester **1d** was prepared by method D from *N*-allyl-4-pentenamide (327 mg, 2.35 mmol). Diphenyl diselenide was added to give a solution 0.10 M in the diselenide. Following irradiation, solvent removal and radial chromatography (gradient of hexanes/ethyl acetate to ethyl acetate/ethanol elution) gave 366 mg of **12b** (1.24 mmol, 52%) followed by 153 mg of **11b** (0.52 mmol, 22%) as colorless oils. The ratio of **12b** to **11b** was increased to 1.02 in 96% combined yield in a similar reaction that was 0.028 M in Ph_2Se_2 and 0.016 M in **1d**.

Compound **12b** had the following properties: ^1H NMR δ 7.56–7.45 (m, 2 H), 7.33–7.20 (m, 3 H), 5.78–5.53 (m, 1 H), 5.15–4.95 (m, 2 H), 4.91 (app. dd, 1 H, J = 5.2, 16.7 Hz), 3.90–3.73 (m, 1 H), 3.36 (app dd, 1 H, J = 7.4, 16.2 Hz), 3.17 (dd, 1 H, J = 2.9, 12.6 Hz), 2.87 (dd, 1 H, J = 8.2, 12.6 Hz), 2.60–2.10 (m, 3 H), 1.95–1.75 (m, 1 H); ^{13}C NMR δ 174.67, 133.25, 132.61, 129.21, 128.32, 127.48, 117.48, 57.12, 43.18, 31.74, 29.87, 24.24; MS m/z (rel inten), 295 (^{80}Se M^+, 10), 293 (^{78}Se M^+, 5), 124 (100), 41(77); HRMS calcd for $C_{14}H_{17}NO^{80}Se$ 295.0475, found 295.0481.

Compounds **11b** consisted of a 6:1 ratio of inseparable diastereomers; the stereochemistry of the isomers was not determined. Compounds **11b** had the following properties: ^1H NMR δ 7.53–7.43 (m, 2 H), 7.32–7.20 (m, 3 H), 4.08–3.80 (m, 1.7 H), 3.33–3.22 (m, 0.3 H, minor diastereomer), 3.05–2.85 (m, 2 H), 2.80–2.15 (m, 5 H), 2.00–1.85 (m, 1 H), 1.75–1.50 (m, 2 H); ^{13}C NMR δ (major) 174.95, 132.88, 129.00, 128.14, 127.07, 59.78, 47.51, 40.23, 38.10, 34.36, 32.00, 27.94, (minor), 61.84, 46.84, 42.08, 39.69, 34.56, 31.57, 26.84; MS m/z (rel inten), 295 (^{80}Se M^+, 25), 293 (^{78}Se M^+, 11), 162 (37), 151 (41), 138 (100), 113 (37), 55(48); HRMS calcd for $C_{14}H_{17}NO^{80}Se$ 295.0475, found 295.0477.

***N*-(Cyclohexylcarbonyl)-2-[(phenylseleno)methyl]pyrrolidine (13a).** To a benzene solution of **1e** (0.05 M) prepared by method C from the corresponding amide (402 mg, 2.15 mmol) under N_2 was added diphenyl diselenide (1.2 g, 3.8 mmol). The solution was irradiated for 10 h. Solvent removal and radial chromatography (hexanes/ethyl acetate, 4:1) gave 456 mg of **13a** (1.30 mmol, 61%). Recrystallization from hexanes gave material with mp 81–83 °C. Rotamers were observed in the NMR spectra (minor rotamer signals are indicated by *): ^1H NMR δ 7.76–7.50 (m, 2 H), 7.35–7.10 (m, 3 H), 4.40–3.85 (m, 1 H), 3.60–2.70 (m, 4 H), 2.40–2.10 (m, 1 H), 2.00–1.10 (m, 14 H); ^{13}C NMR δ 175.01, 174.95*, 135.35*, 134.40, 131.29, 130.26*, 129.42, 129.10*, 127.94*, 126.28, 57.35*, 56.83, 47.20, 45.68*, 43.03, 42.47* , 32.66, 30.23, 29.71, 29.64, 29.47, 29.28, 29.17, 28.48, 25.94, 25.80, 25.74, 25.57, 25.54, 24.01, 22.64, 21.53; rotamer signals could not be distinguished in the cyclohexyl region. MS m/z (rel inten), 351 (^{80}Se M^+, 11), 349 (^{78}Se M^+, 6), 194 (95), 180 (37), 83 (66), 70 (100). HRMS calcd for $C_{18}H_{25}NO^{80}Se$ 351.1101, found 351.1098.

***N*-Butanoyl-2-[(2′-pyridylthio)methyl]pyrrolidine (14a) and *N*-[2-(2′-Pyridylthio)butanoyl]-2-methylpyrrolidine (15a).** The PTOC imidate ester **1f**, prepared by method D from 183 mg (1.18 mmol) of *N*-(4-pentenyl)butanamide in ca. 20 mL of benzene/toluene, was irradiated for 6 h. Solvent removal and

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radial chromatography (hexanes/ethyl acetate, 3:1) gave 109 mg of **14a** (35%) followed by 74 mg of **15a** (24%).

Amide rotamers were resolved in the NMR spectra of **14a**. Compound **14a** had the following properties: ^{1}H NMR δ 8.40–8.20 (m, 1 H), 7.60–7.40 (m, 1.6 H), 7.13* (app d, 0.4 H, J = 7.5 Hz), 7.05–6.85 (m, 1 H), 4.40–4.1 (m, 1 H), 3.70–3.34 (m, 3 H), 3.10–2.50 (m, 2 H), 2.15–1.80 (m, 5 H), 1.70–1.50 (m, 2 H), 1.00–0.80 (m, 3 H); ^{13}C NMR δ 173.00, 172.17*, 159.18, 157.35*, 149.31*, 149.28, 136.51, 136.20*, 122.46*, 121.61, 119.88*, 119.49, 57.18*, 56.74, 47.56, 45.78*, 37.01, 36.23*, 32.76*, 31.74, 29.89, 29.76*, 28.70*, 23.98, 21.58*, 18.30, 14.23, 14.05*; MS m/z (rel inten), 264 (M^+, 8), 231 (3), 154 (11), 140 (19), 70 (100); HRMS calcd for $C_{14}H_{20}N_2OS$ 264.1296, found 264.1299.

Compounds **15a** consisted of an inseparable mixture of diastereomers (3:1). Amide rotamers were observed in the NMR spectra. Compounds **15a** had the following properties: ^{1}H NMR δ 8.42–8.30 (m, 1 H), 7.50–7.40 (m, 1 H), 7.23–7.15 (m, 1 H), 7.00–6.90 (m, 1 H), 5.00–4.70 (m, 1 H), 4.50–4.20 (m, 1 H), 3.80–3.45 (m, 2 H), 2.22–1.50 (m, 7 H), 1.25 (d, 1 H, J = 6.6 Hz), 1.19 (d, 0.8 H, J = 6.3 Hz), 1.10 (d, 1.2 H, J = 6.3 Hz), 1.02–0.95 (m, 3 H); ^{13}C NMR δ 170.35, 169.70, 157.84, 149.05, 135.99, 135.91, 122.41, 122.28, 119.61, 119.49, 53.81, 53.23, 53.04, 52.78, 46.87, 46.71, 46.56, 46.42, 45.87, 45.75, 33.00, 31.90, 31.82, 27.60, 26.48, 25.94, 24.02, 23.77, 22.05, 21.87, 19.57, 18.71, 12.13, 11.96, 11.79 (some of the expected signals for the minor diastereomer and rotamers were not observed); MS m/z (rel inten), 264 (M^+, 23), 180 (43), 153 (100), 125 (50), 112 (63), 84 (77), 69 (95); HRMS calcd for $C_{14}H_{20}N_2OS$ 264.1296, found 264.1300.

***N*-Butanoyl-2-[(phenylseleno)methyl]pyrrolidine (14b).** The PTOC imidate ester **1f**, prepared by method D from 172 mg (1.10 mmol) of *N*-(4-pentenyl)butanamide, was irradiated in the presence of diphenyl diselenide (0.83 g, 2.66 mmol, 0.15 M) for 6 h. Solvent removal and radial chromatography (hexanes/ethyl acetate, 4:1) gave 231 mg of **14b** (66%). Amide rotamers were observed in the NMR spectra: ^{1}H NMR δ 7.65–7.53 (m, 2 H), 7.35–7.05 (m, 3 H), 4.40–4.25 (m, 0.8 H), 3.97–3.83 (m, 0.2 H), 3.30–3.52 (m, 3 H), 3.05–2.70 (m, 1 H), 2.30–1.45 (m, 8 H), 0.94 (t, 2.4 H, J = 7.3 Hz), 0.80 (t, 0.6 H, J = 7.3 Hz); ^{13}C NMR δ 171.94, 134.27, 131.27, 130.16*, 129.29*, 129.07, 127.92*, 126.35, 56.93, 47.53, 45.74*, 36.92, 36.01*, 32.18*, 29.66, 29.56, 23.99, 21.65*, 18.76*, 18.16, 13.96. MS m/z (rel inten), 311 (^{80}Se M^+, 6), 309 (^{78}Se M^+, 3), 222 (8), 154 (41), 140 (18), 84 (18), 70 (100); HRMS calcd for $C_{15}H_{21}N_2O^{80}Se$ 311.0788, found 311.0786.

3,4-Benzoindolizidinone (22). A solution containing **1g** (170 mg, 0.57 mmol) in benzene (12 mL) was irradiated for 6 h. Solvent removal and radial chromatography (hexanes/ethyl acetate, 3:1) gave 50 mg of *N*-(4-pentenyl)benzamide (0.27 mmol, 46%) followed by 50 mg of the known[35] compound **22** (0.27 mmol, 47%). Recrystallization of **22** from CH_2Cl_2/hexanes gave a white solid: mp 108.0–108.5 °C (lit.[35] mp 98 °C); ^{1}H NMR δ 8.05 (d, 1 H, J = 7.5 Hz), 7.45–7.25 (m, 2 H), 7.17 (d, 1 H, J = 7.5 Hz), 3.90 3.57 (m, 3 H), 3.02 (dd, 1 H, J = 3.9, 14.8 Hz), 2.82 (dd, 1 H, J = 13.8, 14.8 Hz), 2.35–2.20 (m, 1 H), 2.18–2.00 (m, 1 H), 2.00–1.60 (m, 2 H); ^{13}C NMR δ 163.20, 137.54, 131.54, 130.24, 127.60, 127.05, 127.00, 56.86, 44.70, 35.01, 33.64, 23.01; MS 187 (M^+, 56), 132 (11), 118 (100), 90 (30). HRMS calcd for $C_{12}H_{13}NO$ 187.0997, found 187.0990.

***N*-Benzoyl-2-[(phenylseleno)methyl]pyrrolidine (25).** The PTOC imidate ester **1g** was generated by method D from *N*-(4-pentenyl)benzamide (270 mg, 1.43 mmol) in the presence of diphenyl diselenide (1.16 g, 3.7 mmol). Irradiation of this mixture in benzene (28 mL) for 10 h, solvent removal, and radial chromatography (hexanes/ethyl acetate, 3:1) of the residue gave 345 mg of the known[36] compound **25** (70%) followed by 34 mg of **22** (13%). Compound **25** had the following properties: ^{1}H NMR δ 7.59 (d, 2 H, J = 7.2 Hz), 7.45–7.13 (m, 8 H), 4.65–4.45 (m, 1 H), 3.80–3.20 (m, 4 H), 2.25–1.60 (m, 4 H); ^{13}C NMR δ 169.93, 137.24, 131.23, 129.83, 129.01, 127.95, 127.13, 126.30, 57.12, 50.80, 30.42, 24.93; MS m/z (rel inten), 345 (^{80}Se M^+, 5), 343 (^{78}Se M^+, 3), 188 (27), 174 (28), 105 (100), 77 (29); HRMS calcd for $C_{18}H_{19}NO^{80}Se$ 345.0631, found 345.0636.

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Supplementary Material Available: Experimental procedures and ^{1}H NMR spectra of secondary amides, the procedure for isolating the sodium salt of *N*-hydroxypyridine-2-thione, and ^{1}H NMR spectra of all new compounds (29 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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