Multiple Reaction Channels of (*N*-Acyl-*N*-alkylcarbamoyl)oxyl Radicals from *N*-Acyl PTOC Carbamates[1]

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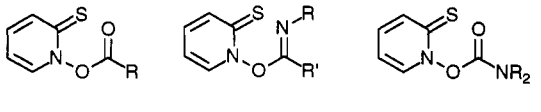
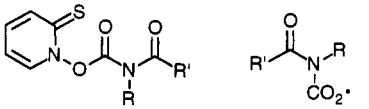
N-Acyl-*N*-alkyl-*N'*-hydroxypyridine-2-thione carbamates (*N*-acyl PTOC carbamates) **1** are prepared in good to excellent yield by reactions of *N*-acylcarbamoyl chlorides with *N*-hydroxypyridine-2-thione sodium salt. Methods for production of the requisite carbamoyl chlorides by reaction of a secondary amide with trimethylsilyl triflate followed by treatment with phosgene were optimized. Precursors **1** react in radical chain reactions to give the title radicals (**2**) that can further react by several pathways. Decarboxylations of radicals **2** give amidyl radicals, and this method is excellent for production of acetamidyl radicals and in particular the *N*-methylacetamidyl radical which is difficult to prepare by other routes. 5-*Exo* cyclizations of amidyl radicals produced by decarboxylation of **2** give, ultimately, lactams and *N*-acylpyrrolidines. 1,5-Hydrogen transfer reactions of **2** to give α-amide radicals compete with decarboxylation; cyclization of an α-amide radical thus formed also is reported. The Lewis acid $MgBr_2$ can reduce the 1,5-hydrogen atom transfer reaction apparently by a chelation effect on the precursor that leads to production of radical **2** in a conformation unfavorable for hydrogen atom transfer. By appropriate experimental design, radicals **2** often can be directed toward one desired reaction, and several relative rate constants for reactions of **2** necessary for such design were determined in this work.

Applications of radical-based methods in synthesis continue to increase as new entries to radical intermediates emerge and a better understanding of radical kinetics evolves. One of the most important families of the radical precursors is comprised of the derivatives of *N*-hydroxypyridine-2-thione, the socalled PTOC[2] precursors. The parent class of this family, the PTOC esters, was introduced



PTOC ester PTOC imidate ester PTOC carbamate

by Barton as sources of alkyl radicals,[3] but during the past several years, the family has grown to include precursors to a wide range of heteroatom-centered radicals.[4] In this work, we report the preparation and reactions of *N*-acyl-*N*-alkyl-*N'*-hydroxypyridine-2-thione carbamates (*N*-acyl PTOC carbamates) **1**.[1] These precursors react in radical chain reactions to give initially (*N*-acyl-*N*-alkylcarbamoyl)-oxyl radicals **2** that can react by decarboxylation to give amidyl radicals and by 1,5-hydrogen abstraction resulting in α-amide radicals.



1 **2**

The initial interest in precursors **1** involved a search for convenient precursors to amidyl radicals. Entries to several types of nitrogen-centered radicals are known,[16] but the utility of many of these radicals is limited. Neutral aminyl radicals are relatively stable species that react sluggishly in, for example, simple 5-*exo* cyclizations, producing the pyrrolidine nucleus. Protonation of an aminyl radical to give an aminium cation radical or complexation of an aminyl radical with a Lewis acid results in a much more reactive species, but the required acid negates the inherent advantage of neutral reaction conditions enjoyed in most radical-based conversions. Amidyl radicals, however, are reactive species that can be produced under completely neutral conditions. Early studies of amidyl radicals employed *N*-halo- and *N*-nitrosoamides

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(1) A portion of this work has been communicated, see: Esker, J. L.; Newcomb, M. *Tetrahedron Lett.* **1992**, *33*, 5913.

(2) The acyronym PTOC derives from pyridine-2-thione-*N*-oxycarbonyl.

(3) Barton, D. H. R.; Crich, D.; Motherwell, W. B. *Tetrahedron* **1985**, *41*, 3901.

(4) In a radical chain reaction, a radical adds to the thione group of the PTOC precursor with subsequent or concomitant cleavage of the weak N–O bond giving, initially, an oxygen-centered radical. The PTOC family can be broadly divided into two groups of precursors, one which gives acyloxyl radicals that decarboxylate to give the desired radical and the other which produces the desired radicals directly. The former group includes precursors to aminyl,[5] aminium cation,[6] iminyl,[7] and phenoxyl[8] radicals in addition to alkyl radicals.[3] The latter includes precursors to alkoxyl,[9] hydroxyl,[10,11] aroyloxyl and vinylacyloxyl,[11,12] silyloxyl,[11] alkoxycarbonyloxyl,[13] phosphonyl,[14] and amidyl[15] radicals.

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

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

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

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

(9) 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.

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

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

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

(13) 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.

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

(15) Esker, J. L.; Newcomb, M. *J. Org. Chem.* **1993**, *58*, 4933.

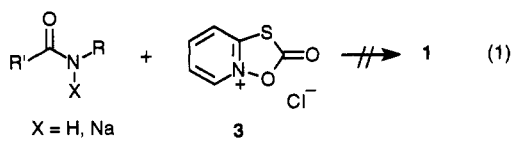
(16) For reviews of nitrogen-centered radicals, see: Neale, R. S. *Synthesis* **1971**, *1*, 1. Mackiewicz, P.; Furstoss, R. *Tetrahedron* **1978**, *34*, 3241. Stella, L. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 337. Esker, J. L.; Newcomb, M. in *Advances in Heterocyclic Chemistry*, Vol. 58; Katritsky, A. A., Ed.; Academic: New York, 1993; pp 1–45.

0022-3263/94/1959-2779$04.50/0

as radical precursors, and the products formed in reactions of these species were limited to chlorides and oximes produced in chain reactions.[16,17] Recently, *N*-(phenylthio)-amides have been shown to be useful amidyl radical precursors,[18] but reactions of these species are mediated by tin hydride and ultimate radical reduction is a necessary consequence of the reaction conditions. PTOC imidate esters give amidyl radicals under conditions that permit radical trapping by a variety of agents,[15] but these precursors are especially sensitive to hydrolysis and the precursors to low molecular weight amidyl radicals, such as the simple *N*-methylacetamidyl radical, cannot be prepared. The observed hydrolytic stability of PTOC carbamates[5,6] in comparison to PTOC imidate esters[15] suggested that *N*-acyl PTOC carbamates might be relatively stable precursors that permitted amidyl radical reactions under a variety of trapping conditions.

Preparation of *N*-Acyl-*N*-alkyl-*N*-hydroxypyridine-2-thione Carbamates

Initial attempts to prepare *N*-acyl PTOC carbamates focused on formation of the N–C(O) bond of the carbamate group by reaction of an amide with the pyridinium salt **3** in the presence of triethylamine (eq 1).



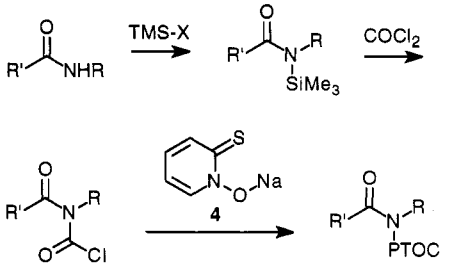
X = H, Na 3 (1)

This route is similar to one employed successfully for production of PTOC esters, i.e., reaction of carboxylic acids with **3**.[3] However, the reaction was unsuccessful for preparing *N*-acyl PTOC carbamates. In addition, deprotonation of an amide to give the sodium salt followed by treatment with pyridinium salt **3** also failed to give *N*-acyl PTOC carbamates.

An *N*-acylcarbamate is not a commonly encountered functional group in organic chemistry, and there appear to be no direct methods for the conversion of an amide to an *N*-acylcarbamate suitable for the preparation of *N*-hydroxypyridine-2-thione carbamates. However, the conversion of an *N*-silylamide to an *N*-acylcarbamoyl chloride, while not commonly employed, has been reported.[19] The combination of this reaction for the preparation of carbamoyl chlorides with subsequent treatment with 2-mercaptopyridine *N*-oxide sodium salt (**4**) gave the desired *N*-acyl PTOC carbamates (Scheme 1).

An efficient conversion of amides to *N*-silylamides was the final step required. The simple *N*-silylation of amides with trimethylchlorosilane (TMS-Cl) and triethylamine (TEA) gave only modest conversions even when the mixture was heated to 60 °C for several hours, but this procedure was satisfactory when *N*-silylamides were prepared on a large scale and could be separated from the unreacted amide by distillation.

Scheme 1



a: R = CH_3, R' = Ph
b: R = CH_3, R' = CH_3
c: R = Bu, R' = Bu
d: R = Bu, R' = $CH(CH_3)_2$
e: R = Bu, R' = CH_2Ph
f: R = Bu, R' = $(CH_2)_2CH{=}CH_2$
g: R = $(CH_2)_3CH{=}CH_2$, R' = CH_3
h: R = Bu, R' = $(CH_2)_4CH{=}CH_2$

Quantitative *N*-silylation was achieved by treatment of a secondary amide with the very reactive silylating agent trimethylsilyl trifluoromethanesulfonate (TMS-OTf) and TEA, and this reaction was incorporated into a one-pot, multistep sequence. Amide *N*-silylation was achieved by reaction with TMS-OTf and TEA. Removal of the ammonium salt and subsequent treatment of the reaction mixture with phosgene at −78 °C gave the appropriate carbamoyl chloride and TMS-Cl. The reaction mixture was warmed to ambient temperature, and the byproduct TMS-Cl was removed under reduced pressure. Treatment of the resulting mixture with 1 equiv of sodium salt **4** gave the *N*-acyl PTOC carbamates. Typically, an 80–90% yield of the radical precursor was obtained on the basis of the initial amount of secondary amide employed.

An alternative sequence is possible for a carbamoyl chloride that is unstable at room temperature. The reaction mixture containing the carbamoyl chloride can be maintained at −78 °C as an excess of sodium salt **4** is added. In this procedure, 2 equiv of **4** are required because the TMS-Cl byproduct also reacts with salt **4**, giving *O*-(trimethylsilyl)-*N*-hydroxypyridine-2-thione, which is rapidly decomposed in an aqueous workup.[11,20] Yields of *N*-acyl PTOC carbamates prepared by the alternate method were comparable to those achieved in the general method described in the Experimental Section.

The *N*-acyl PTOC carbamates **1** were stable to aqueous washes with 1 M HCl and 1 M NaOH and could be purified by chromatography on silica gel with only partial decomposition. This behavior was similar to that of the analogous PTOC esters and *N*,*N*-dialkyl PTOC carbamates. The *N*-acyl PTOC carbamates **1a** and **1b** were crystalline compounds with sharp melting points, and compound **1b** gave a consistent elemental analysis. Other isolated radical precursors **1** were oils that were characterized by NMR spectroscopy. Precursor **1c** was prepared *in situ* for subsequent reactions.

The ^1H NMR spectra of compounds **1** at 22 °C were clearly resolved, showing only one set of signals suggesting either that one conformation highly predominated or that rotation about the acyl C–N bond was rapid on the NMR time scale. Low-temperature ^1H NMR spectra also were similarly simple. However, in the ^{13}C NMR spectra, some

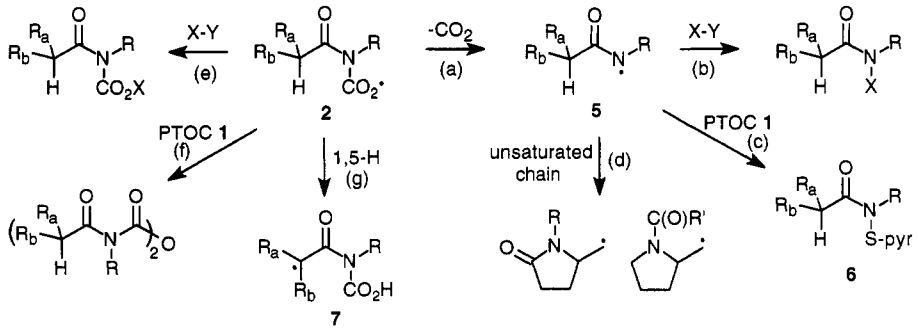
(17) For examples of amidyl radical cyclizations followed by chlorine atom or nitroso group transfers, see the following. Kuehne, M. E.; Horne, D. A. *J. Org. Chem.* **1975**, *40*, 1287. Mackiewicz, P.; Furstoss, R.; Waegell, B.; Cote, R.; Lessard, J. *J. Org. Chem.* **1978**, *43*, 3746. Chow, Y. L.; Perry, R. A. *Can. J. Chem.* **1985**, *63*, 2203.

(18) Esker, J. L.; Newcomb, M. *Tetrahedron Lett.* **1993**, *34*, 6877.

(19) Mironov, V. F.; Sheludyakov, V. D.; Kozyukov, V. P. *Zh. Obshch. Khim.* **1969**, *39*, 220.

(20) In a control reaction, TMS-Cl was found to react with sodium salt **4** to give the adduct[11] in 81% isolated yield as a waxy yellow solid, characterized by ^1H and ^{13}C NMR spectroscopy.

Scheme 2



signals for carbons close to the carbamate group were obscured apparently due to near coalescence. This NMR spectral behavior is similar to that previously observed in the NMR spectra of *N*-hydroxypyridine-2-thione carbonates.[13]

An unambiguous proof of the structure of an *N*-acyl PTOC carbamate was achieved by solution of the X-ray crystal structure of the *N*-methyl-*N*-benzoyl derivative **1a**.[21] To the best of our knowledge, X-ray crystal structures of PTOC radical precursors have not been reported previously. The isolation of the PTOC derivatives discussed here, the melting behavior of **1a** and **1b**, and the crystal structure determination of **1a** demonstrate that crystalline PTOC derivatives can be relatively stable despite their facile reactivity in radical chain reactions and their sensitivity to visible light.

The crystal structure of **1a** provided an important piece of information for understanding the reactions of (*N*-acyl-*N*-alkylcarbamoyl)oxyl radicals **2**. Specifically, it showed an *anti*-coplanar orientation of the acyl oxygen and the PTOC moiety. This arrangement also was expected in solution in low dielectric solvents on the basis of both minimization of the molecular dipole and steric considerations. From this reasoning, the results of NMR spectra, the X-ray crystal structure of **1a**, and the products observed in reactions of radicals **2**, we deduced that *N*-acyl PTOC carbamates **1** exist in solution predominantly in the *anti* conformation.

Reactions of (*N*-Acyl-*N*-alkylcarbamoyl)oxyl Radicals

As with other members of the PTOC family of radical precursors, carbamates **1** were sensitive to visible light and reacted in radical chain reactions. The (*N*-acyl-*N*-alkylcarbamoyl)oxyl radicals **2** produced from precursors **1** could react by several pathways as shown in Scheme 2. The most obvious reaction is decarboxylation (path a), giving an amidyl radical (**5**). The majority of acyloxyl radical intermediates formed from the PTOC class of precursors decarboxylate rapidly.[4] For example, simple alkyl acyloxyl radicals decarboxylate with rate constants in the range of 1×10^9 to 1×10^{10} s^{-1} at room temperature,[22] and there is no evidence that carbamoyloxyl radicals, produced from PTOC carbamates[5,6] and related precursors,[23] are involved in any reaction except decarboxylation to give the corresponding aminyl radicals. Following decarboxylation, amidyl radical **5** can be trapped by an added trapping agent (path b), react with the PTOC precursor to give an *N*-(2-pyridylthio)amide (**6**) (a "self-trapping" reaction, path c), or cyclize onto a δ,ϵ-unsaturated position (path d). Each of reactions b–d has been reported for amidyl radicals produced from PTOC imidate esters.[15]

However, radicals **2** decarboxylate to give highly reactive amidyl radicals, and when an incipient radical is relatively unstable, decarboxylation of the corresponding acyloxyl radical is slowed. Several competing reaction channels for radicals **2** were thus possible. In the presence of an active trapping agent, atom or group transfer trapping (path e) could occur. In the absence of an added trapping agent, a "self-trapping" of the acyloxyl radical by the precursor also could occur (path f); the acyloxyl self-trapping products for the PTOC family of radical precursors are known to rearrange to give, ultimately, anhydride products.[24] The α-hydrogen atoms of the amide moiety in radicals **2** are optimally positioned for abstraction (path g), which can result in a relatively stable α-amide radical (**7**).

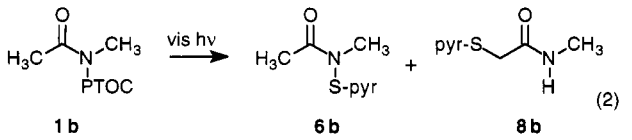
It is likely that each of the reaction channels for the acyloxyl radicals **2** and the amidyl radicals produced in their decarboxylations might be realized with appropriate control of reaction conditions. In practice, all but paths b and f were demonstrated in this work.

Decarboxylations vs 1,5-hydrogen Abstractions. The simplest amidyl radical produced from precursors **1** is the *N*-methylacetamidyl radical (**5b**). The availability of radical **5b** is noteworthy because the PTOC imidate ester precursor to this radical cannot be prepared due to the volatility of the requisite intermediate imidoyl chloride.[15] Reactions of precursor **1b** permitted an evaluation of the relative rate constants for decarboxylation, α-hydrogen atom abstraction, and reactions with the trapping agent *t*-BuSH.

When **1b** (initial concentration 0.15 M) was allowed to react in benzene in the absence of added trapping agents, the *N*-pyridylthio-substituted amide **6b** and the α-pyridylthio-substituted product **8b** (from initial 1,5-hydrogen transfer giving α-amide radical **7b** followed by reaction with precursor **1b**) were produced in a 70:1 ratio as determined by NMR analysis of the crude reaction mixture (eq 2). The *N*-(pyridylthio)amide **6b** was isolated in 75% yield.

In the presence of 0.15 M *t*-BuSH in benzene with an initial precursor concentration of 0.05 M, **1b** reacted to give *N*-pyridylthio-substituted acetamide **6b** and *N*-methylacetamide in nearly equal amounts. Two routes to

(21) Horner, J. H.; Heeg, M. J.; Esker, J. L.; Shahin, H.; Newcomb, M. In preparation.
(22) Falvey, D. E.; Schuster, G. B. *J. Am. Chem. Soc.* **1986**, *108*, 7419. DeCosta, D. P.; Pincock, J. A. *J. Am. Chem. Soc.* **1989**, *111*, 8948.
(23) Newcomb, M.; Weber, K. A. *J. Org. Chem.* **1991**, *56*, 1309.
(24) The initially formed *O*-(2-pyridylthio)acyl product rearranges in a polar reaction; see ref 12b.



the simple amide were possible: (1) decarboxylation of radical **2b** to give amidyl radical **5b** followed by hydrogen atom transfer trapping of **5b** by the thiol or (2) reaction of radical **2b** with the thiol to give a carbamic acid that decarboxylated (Scheme 3). However, in the study of the reactions of PTOC imidate esters, which react in chain reactions to give amidyl radicals directly, *t*-BuSH trapping of amidyl radicals was found to be quite inefficient.[15] A conservative estimate of the relative rate constants for amidyl radical self-trapping (k_{ST}) by a PTOC imidate ester and *t*-BuSH trapping of an amidyl radical ($k_{C(O)N-H}$) from that work[15] is $k_{ST}/k_{C(O)N-H} > 100$. If we make the reasonable assumption that the rate constant for self-trapping of an amidyl radical with an *N*-acyl PTOC carbamate is approximately equal to that for reaction of an amidyl radical with a PTOC imidate ester, then it follows that virtually all of amidyl radical **5b** reacted with precursor **1b** and that essentially all of the *N*-methylacetamide must have arisen from reaction of the acyloxyl radical **2b** with the thiol in competition with decarboxylation. That is, the relative rate constants for decarboxylation (k_{Dec}) and thiol trapping of the acyloxyl radical **2b** ($k_{C(O)O-H}$) are $(k_{Dec}/k_{C(O)O-H}) \approx 0.15$ M. An important consequence of this result for synthetic applications is that the efficient reaction of *t*-BuSH with acyloxyl radicals **2** precludes the use of thiol as a radical trapping–chain transfer agent in reactions of the *N*-acyl PTOC carbamates.

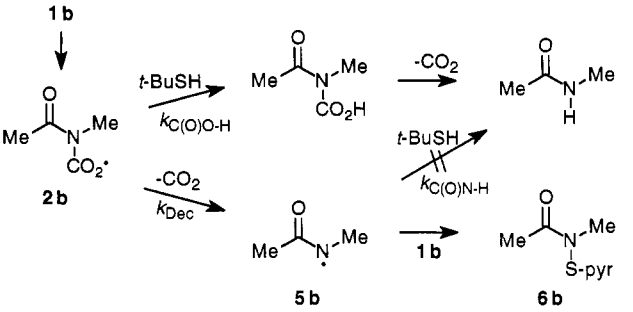
A 1,5-hydrogen transfer in the acyloxyl radical intermediates **2**, a radical translocation reaction producing an α-amide radical (**7**), competes with the decarboxylation reaction of these intermediates that gives amidyl radicals. These competing reaction pathways could complicate synthetic applications of the *N*-acyl PTOC carbamates, but one's ability to direct the course of reaction of the acyloxyl radical would be a significant advantage in that, in principle, two different radicals could be produced from the same precursor. The translocation reaction is especially attractive because it results in a highly regioselective C–H bond homolysis.

One important point to consider at the outset is that bond rotation about the N–C(O) bond in acyloxyl radicals **2** is likely to be slow in comparison to the decarboxylation and hydrogen abstraction reactions.[25] If this is the case, then the conformation of radical **2** at the instant of formation is critically important because the *syn* conformer would only lead to amidyl radical formation by decarboxylation, whereas the *anti* conformer could partition between the two possible products (Scheme 4). Accordingly, the conformational population of the reacting *N*-acyl PTOC carbamate precursors would be an important feature that might be subject to control by manipulation of the reaction conditions. Our conclusion from the X-ray crystal structure of **1a** and the typically observed absence of distinct signals for minor conformations in the NMR spectra of precursors **1** was that the *anti* conformers of these precursors predominate in solution.

The series of radical precursors **1b–e** was allowed to react in chain reactions in benzene. Reactions were

(25) Bond rotations in amides are quite slow in comparison to radical reactions. *Cf.* Neuman, R. C., Jr.; Jonas, V. *J. Org. Chem.* **1974**, *39*, 929.

Scheme 3



Scheme 4

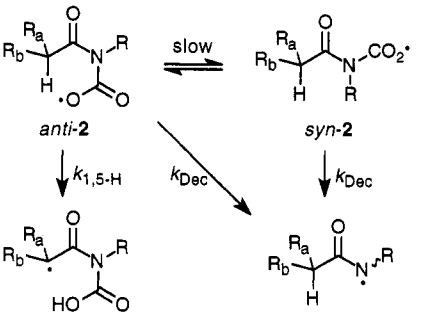


Table 1. Products from Reactions of 1b–e

				relative % yield[b]	
precursor	R	R′	% yield[a]	6	8
1b	Me	Me	75	98.5[c]	1.5
1c	Bu	Bu	84	56	44
1d	Bu	*i*-Pr	83	27	73
			60[d]		
1e	Bu	CH_2Ph	74[e]	40	60
			30[d]		

[a] Isolated yield. [b] Relative yield of isolated products unless noted. [c] Ratio determined from NMR spectrum of crude product mixture. [d] Yield of α-(phenylselenyl)amide **9** from reactions conducted in the presence of Ph_2Se_2. [e] Includes α-dimer product **10**.

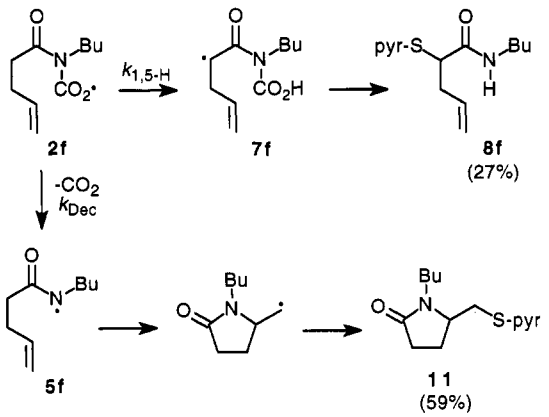
conducted in the absence of an added radicophile and, for two precursors, in the presence of the reactive radical trapping agent diphenyl diselenide. In the absence of a trapping agent, *N*-(2-pyridylthio)amides **6** and α-(2-pyridylthio)amides **8** were produced. From similar reactions of **1d** and **1e** conducted in the presence of PhSeSePh, α-(phenylselenyl)amides **9** were obtained. The α-substituted products **8** and **9** resulted from radical translocations followed by trapping, and the *N*-substituted thiopyridyl products **6** were formed by decarboxylation followed by trapping. In the case of the two reactions conducted with Ph_2Se_2, we presume that amidyl radicals reacted to give *N*-(phenylselenyl)amides that subsequently decomposed; similar *N*-seleno compounds are known to be unstable.[26]

Table 1 contains the results. The ratios of products are in general agreement with expectations based on the assumption that the *anti* conformers of **2** largely predominate. The rate constants for the decarboxylations should be essentially constant for this series, but the rate constants for hydrogen abstraction should be accelerated as the substitution on the α-carbon is increased to give more stable incipient α-amide radicals.

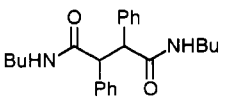
Upon first consideration, the results with the phenyl-substituted precursor **1e** appear to be inconsistent with

(26) Kirsch, G.; Christiaens, L. *The Chemistry of Organic Selenium and Tellurium Compounds*; Patai, S., Ed.; Wiley: Chichester, U.K., 1987; pp 424–426.

Scheme 5



the trend found with the precursors **1b–d** because the highly stabilized, benzylic α-amide radical **7e** should have been produced in high yield. However, this system clearly reacted in a complex sequence. From the reaction in the absence of an additional trapping agent, a complex product mixture was obtained containing, in addition to products **6e** and **8e**, substantial amounts of *N*-butylphenylacetamide (23%) and the succinic diamide **10** (11%).



10

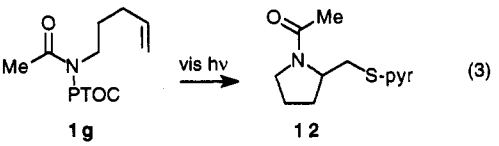
Formation of diamide **10**, which arises from coupling of α-amide radicals **7e** and is expected to be produced with a diffusionally controlled rate, indicates that the concentration of the benzylic α-amide radical was relatively high. Apparently, the stability of this radical resulted in a relatively slow reaction with the PTOC precursor. The high concentration of α-amide radical **7e** would provide alternate radical–radical reaction pathways for all radicals present,[27] and it is possible that the unsubstituted *N*-butylphenylacetamide arose from such a reaction although a route to its formation is elusive. In any event, any mechanistic conclusion based upon the product mixtures formed in reactions of PTOC precursor **1e** must be viewed with caution.

The relative rate constants for decarboxylation and 1,5-hydrogen abstraction in an *N*-acyloxyl radical were also evaluated by a second approach. Precursor **1f** gives acyloxyl radical **2f**, which will partition between α-amide radical **7f** and amidyl radical **5f**. The α-amide radical can react with precursor to give an α-(2-pyridylthio)amide (**8f**) as observed in reactions of **1b–e**, but the amidyl radical **5f** will cylcize to a lactam radical that subsequently reacts with the PTOC precursor to give the ((2-pyridylthio)-methyl)-substituted lactam product **11** (Scheme 5). Reaction of precursor **1f** gave **8f** and **11** in 27% and 59% isolated yields, a 1:2 ratio of products consistent with that obtained in reactions of the saturated analog (i.e., PTOC precursor **1c**).

The results with precursors **1b–f** are consistent with our assumption that the acyloxyl radicals **2** are produced predominantly in the *anti* conformation. As such, the ratio of products from the radical translocation reaction and the decarboxylation reaction represents the inherent reactivity of the *anti* conformers in the two competing unimolecular reaction channels, and it is unlikely that the translocation reactions can be promoted at the expense of the decarboxylations except by increased substitution at the α-carbon. However, the converse is not true because the *syn* conformer of **2** cannot react by 1,5-hydrogen abstraction.

A variety of experimental modifications were employed in reactions of precursor **1f**, and the product distributions were determined. Changes in reaction temperature and in the dielectric constant of the medium had little effect on the product ratio. Similarly, reactions conducted in the presence of the Lewis acids $BF_3{\cdot}OEt_2$ and $Ti(O\text{-}i\text{-}Pr)_4$ did not lead to different product ratios. However, when **1f** was allowed to react in the presence of $MgBr_2$ in acetonitrile solvent, lactam **11** and amide **8f** were obtained in a 22:1 ratio. The reduction in the relative yield of amide **8f** from 35% to 4% upon addition of $MgBr_2$ suggests that the relative population of the *anti* conformation of **2f** was only ca. 10% in the latter case. However, as a caveat to our conclusions regarding conformations of the PTOC precursors and acyloxyl radicals, we note that there was no obvious difference in the ^1H NMR spectra of PTOC carbamate **1f** in acetonitrile in the presence and absence of $MgBr_2$.

5-*Exo* Radical Cyclizations. Studies with **1f** showed that decarboxylation to give the amidyl radical could be enhanced by controlling the conformation of the precursor with a resulting high conversion to the lactam product **11** produced by a 5-*exo* amidyl radical cyclization. In the case of acetamidyl radical precursors, conformational population control is unnecessary due to the low reactivity of the methyl group toward translocation (see Table 1). Consistent with this observation, PTOC precursor **1g** reacted in benzene under standard conditions to give the *N*-acetylpyrrolidine product **12** in 69% isolated yield (eq 3); the *N*-(pyridylthio)amide **8g** was a minor product (2%). Successful 5-*exo* cyclizations onto both the alkyl and acyl chains of amidyl radicals produced from PTOC imidate esters have been observed previously.[15,18,28]



1g **12** (3)

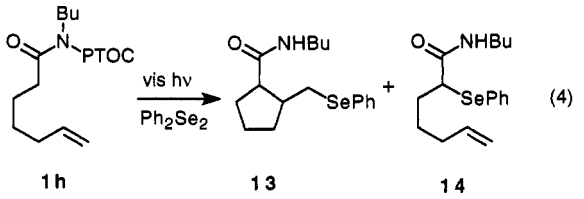
A 5-*exo* cyclization of an α-amide radical formed by 1,5-hydrogen translocation also was possible. Precursor **1h** reacted in the presence of Ph_2Se_2 to give the cyclopentanecarboxamide **13** in 37% isolated yield (eq 4). The α-substituted amide product **14** was detected in low yield (at most 8% yield) by NMR spectroscopy but was not isolated. A complete product analysis for this reaction was not obtained, but when one considers that only about 50% translocation should have occurred (*cf.* Table 1), then the cyclization reaction of the α-amide radical is seen to be relatively efficient.

The cyclization of the α-amide radical to give product **13** is noteworthy in that the olefin moiety in the inter-

(27) For a quantitative treatment of the effects of persistent radicals that can result in high yields of radical cross-termination products, see: Fischer, H. *J. Am. Chem. Soc.* **1986**, *108*, 3925.

(28) A previous report based on ESR studies that 5-*exo* amidyl radical cyclizations onto the acyl chain are greater than 100 times faster than 5-*exo* cyclizations onto the alkyl chain[29] has been shown to be incorrect.[18]

(29) Sutcliffe, R.; Ingold, K. U. *J. Am. Chem. Soc.* **1982**, *104*, 6071.



mediate contained no activating group. Curran *et al.* have reported that when α-amide radicals were produced by translocation to *N*-aryl radicals in the presence of the requisite tributyltin hydride, tin hydride trapping of the α-amide radical was fast relative to 5-*exo* cyclization unless the olefin contained an activating group.[30]

Conclusion

The *N*-acyl PTOC carbamates are relatively stable radical precursors that are readily accessible in high yield from a wide range of secondary amides. In the special case of the acetamides, these precursors appear to be superior sources of amidyl radicals, especially for the simple *N*-methylacetamidyl radical. For the more general case, a variety of radical reactions are possible from the acyloxyl radicals formed when these precursors react in chain-transfer sequences, but as demonstrated in this work, appropriate control of reaction conditions and design of experiments often can direct the intermediates toward one predominant product.

For synthetic applications of radical reactions, knowledge of the relative kinetics of competing reactions (in lieu of the absolute kinetics) is critically important for planning. A number of relative rate constants for reactions of radicals **2** were established in this work (*cf.* Table 1); the more important ones are summarized in Figure 1.

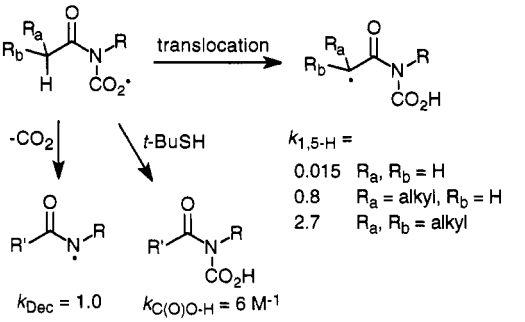


Figure 1. Relative rate constants at room temperature for reactions of (*N*-acyl-*N*-alkylcarbamoyl)oxyl radicals.

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 N_2 until cool. *tert*-Butyl mercaptan was dried over CaO, distilled, and stored over activated molecular sieves. *N*-Hydroxypyridine-2-thione sodium salt (**4**) was obtained from an aqueous solution (Olin Chemical) as previously described.[15]

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 are uncorrected. NMR spectra were obtained from $CDCl_3$ solutions at 200 or 300 MHz (^1H) or 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 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 by 0.25 mm capillary column (DB-5) was used. High resolution mass spectral analyses were performed by the Central Instrument Facility at Wayne State University.

Secondary amides were commercially available or known[15] or the preparations and NMR spectra are given in the supplementary material.

1-[(*N*-Acetyl-*N*-methylcarbamoyl)oxy]-2(1*H*)-pyridinethione (1b). *N*-Methylacetamide (5.00 g, 68.4 mmol) was added to 100 mL of Et_2O and 8.30 g (82.1 mmol) of triethylamine (TEA). Trimethylchlorosilane (TMS-Cl) (9.55 g, 75.2 mmol) was added dropwise, and the mixture was stirred for 12 h. The TEA HCl salt precipitated. Filtration of the salts, concentration under reduced pressure, and distillation at 82–86 °C (50 mmHg) gave 5.75 g (39.6 mmol, 58% yield) of *N*-methyl-*N*-(trimethylsilyl)-acetamide. ^1H NMR: δ 2.75 (s, 3H), 2.01 (s, 3H), 0.19 (s, 9H). ^{13}C NMR: δ 177.98, 32.16, 22.02, –0.42.

N-Acetyl-*N*-methylcarbamoyl chloride was prepared by a reported procedure.[19] The above silylated acetamide (4.58 g, 31.5 mmol) was added to 12 mL of Et_2O, and the resulting solution was cooled to –78 °C. Phosgene (3 mL, 41.9 mmol) in 5 mL of Et_2O at –78 °C was added. The mixture was stirred for 1 h while being warmed to ambient temperature. Et_2O and TMS-Cl were removed under reduced pressure. Distillation at 60 °C (11 mmHg) gave 3.30 g (24.4 mmol, 77% yield) of the desired carbamoyl chloride. ^1H NMR: δ 3.38 (s, 3H), 2.50 (s, 3H). ^{13}C NMR: δ 171.28, 150.91, 34.31, 26.36.

To a mixture of the above carbamoyl chloride (0.47 g, 3.5 mmol) and 12 mL of CH_2Cl_2 in a vessel shielded from light was added salt **4** (0.73 g, 3.9 mmol). The mixture was stirred for 4 h. Filtration of the salts and crystallization by addition of ether gave PTOC **1b** (0.70 g, 3.1 mmol, 89%) as a yellow solid, mp 112–113 °C. ^1H NMR: δ 7.78 (app bd, 1H, J = 5.0 Hz), 7.71 (app dd, 1H, J = 1.5, 8.0 Hz), 7.32–7.20 (m, 1H), 6.72 (app bt, 1H, J = 5.0 Hz), 3.48 (s, 3H), 2.57 (s, 3H). ^{13}C NMR: δ 172.83, 151.50, 137.81, 136.84, 133.58 (br), 112.87 (br), 30.93, 25.94; some signals were broad due to coalescence in $CDCl_3$. Anal. Calcd for $C_9H_{10}N_2O_3S$: C, 47.78; H, 4.46. Found: C, 47.93; H, 4.53.

General Procedure for the Preparation of *N*-Acyl PTOC Carbamates. To a secondary amide (1.30 mmol) in Et_2O (17 mL) were added TEA (0.220 mL, 1.58 mmol) and TMS-OTf (0.290 mL, 1.50 mmol). The solution was stirred for 12 h, after which the separated ammonium triflate oil was removed via syringe. The solution was cooled to –78 °C, and phosgene (0.15 mL, 2.0 mmol) in 5 mL of Et_2O was added. The mixture was stirred for 1 h as it warmed to ambient temperature. Benzene (15 mL) was added, and the solution was concentrated to ca. 10 mL under reduced pressure to remove excess phosgene and TMS-Cl. The reaction vessel was shielded from light, and salt **4** (0.21 g, 1.4 mmol) was added. The mixture was stirred for 3 h, resulting in a yellow solution. Benzene (10 mL) was added, and the solution was washed sequentially with 10 mL each of H_2O, a 5% $NaHCO_3$ solution, and a saturated aqueous NaCl solution and dried over $MgSO_4$. Filtration and concentration under reduced pressure gave the *N*-acyl PTOC carbamate in 90 to >95% purity as determined by ^1H NMR spectroscopy; the major contaminant was the starting amide.

1-[(*N*-Methyl-*N*-benzoylcarbamoyl)oxy]-2(1*H*)-pyridinethione (1a) was prepared from *N*-methylbenzamide (509 mg, 3.77 mmol) by the general method. Recrystallization from CH_2Cl_2 and hexanes gave 790 mg of **1a** (2.74 mmol, 73% yield), mp 125.0–125.5 °C. ^1H NMR: δ 7.80–7.32 (m, 8H), 7.12 (app t, 1H, J = 7.0 Hz), 3.55 (s, 3H). ^{13}C NMR: δ 172.12, 138.07, 137.78, 133.96, 132.25, 128.60, 128.12, 33.24. Some signals were obscured due to coalescence.

1-[(*N*-Butyl-*N*-(2-methylpropanoyl)carbamoyl)oxy]-2(1*H*)-pyridinethione (1d) was prepared from *N*-butyl-2-methylpropanamide (289 mg, 2.02 mmol) by the general method to give 557 mg of **1d** (1.88 mmol, 93%) as a yellow oil. ^1H NMR (300 MHz): δ 7.68 (app d, 2H, J = 8.0 Hz), 7.36–7.20 (app t, 1H, J = 7.0 Hz), 6.72 (app bt, 1H, J = 5.0 Hz), 4.00 (bt, 2H, J = 7.5 Hz), 3.65 (bm,

(30) Curran, D. P.; Abraham, A. C.; Liu, H. *J. Org. Chem.* **1991**, *56*, 4335.

1H), 1.78–1.65 (m, 2H), 1.47–1.30 (m, 2H), 1.19 (d, 6H, J = 6.9 Hz), 0.93 (t, 3H, J = 7.3 Hz). ^{13}C NMR (75 MHz): δ 174.64, 137.74, 137.42, 133.58, 112.43, 44.89, 34.89, 30.86, 20.03, 19.41, 13.74. Some signals were obscured due to coalescence.

1-[(*N*-Butyl-*N*-(phenylacetyl)carbamoyl)oxy]-2(1*H*)-pyridinethione (1e) was prepared from *N*-butylphenylacetamide (316 mg, 1.65 mmol) by the general method to give 516 mg of **1e** (1.50 mmol, 91%) as a yellow oil. ^{1}H NMR (300 MHz): δ 7.68 (app d, 1H, J = 8.0 Hz), 7.60 (bm, 1H), 7.40–7.18 (m, 6H), 6.65 (bm, 1H), 4.28 (s, 2H), 4.03 (bt, 2H, J = 7.5 Hz), 1.78–1.65 (m, 2H), 1.47–1.30 (m, 2H), 0.95 (t, 3H, J = 7.3 Hz). ^{13}C NMR (75 MHz): δ 173.20, 137.89, 137.48, 133.95, 129.77, 129.64, 128.43, 127.30, 112.69, 45.38, 44.31, 30.75, 20.15, 13.84.

1-[(*N*-Butyl-*N*-(4-pentenoyl)carbamoyl)oxy]-2(1*H*)-pyridinethione (1f) was prepared by the general method from *N*-butyl-4-pentenamide[15] (1.00 g, 6.44 mmol) to give 1.78 g of **1f** (5.78 mmol, 90% yield) as a yellow oil. ^{1}H NMR: δ 7.74 (app bd, 1H, J = 5.0 Hz), 7.68 (app dd, 1H, J = 1.5, 8.0 Hz), 7.26–7.18 (m, 1H), 6.69 (app bt, 1H, J = 5.0 Hz), 5.93–5.71 (m, 1H), 5.13–4.94 (m, 2H), 4.07–3.93 (m, 2H), 3.03 (t, 2H, J = 6.9 Hz), 2.50–2.34 (m, 2H), 1.72–1.60 (m, 2H), 1.48–1.25 (m, 2H), 0.95 (t, 3H, J = 7.2 Hz). ^{13}C NMR: δ 173.94, 136.42, 115.35, 44.51, 37.03, 30.48, 28.37, 19.79, 13.49. Some signals were obscured due to coalesence.

1-[(*N*-(4-Pentenyl)-*N*-acetylcarbamoyl)oxy]-2(1*H*)-pyridinethione (1g) was prepared by the general method from *N*-(4-pentenyl)acetamide (301 mg, 2.37 mmol) to give 505 mg of **1g** (1.80, 76% yield) as a yellow oil. ^{1}H NMR: δ 7.70 (bm, 1H), 7.62 (app d, 1H, J = 8.0 Hz), 7.25–7.15 (m, 1H), 6.63 (bm, 1H), 5.86–5.70 (m, 1H), 5.08–4.90 (m, 2H), 3.96 (bt, 2H, J = 7.5 Hz), 2.52 (s, 3H), 2.18–1.76 (m, 4H). ^{13}C NMR: δ 171.85, 137.87, 137.29, 137.19, 133.91, 115.23, 112.74, 44.43, 30.86, 27.53, 26.40, 26.26.

1-[(*N*-Butyl-*N*-(6-heptenoyl)carbamoyl)oxy]-2(1*H*)-pyridinethione (1h) was prepared from *N*-butyl-6-heptenamide (313 mg, 1.71 mmol) by the general method to give 542 mg of **1h** (1.61 mmol, 94% yield) as a yellow oil. ^{1}H NMR: δ 7.72 (app d, 2H), 7.30–7.20 (m 1H), 7.15 (bm, 1H), 5.90–5.72 (m, 1H), 5.07–4.93 (m, 2H), 4.01 (bt, 2H, J = 6.5 Hz), 2.94 (bt, 2H), 2.16–2.04 (m, 2H), 1.83–1.57 (m, 4H), 1.50–1.37 (m, 4H), 0.97 (t, 3H, J = 7.2 Hz). ^{13}C NMR: δ 174.73, 138.28, 137.75, 137.17, 133.58, 114.50, 112.44, 44.57, 37.70, 33.25, 30.62, 28.05, 24.00, 19.88, 13.55. Some signals were obscured by coalesence.

General Method for Reactions of Precursors 1. A solution of the radical precursor (typically 0.05 M) in benzene was prepared under nitrogen in a flask sealed with a septum stopper. Trapping agents were added as desired. The solution was irradiated with a 250-W tungsten filament lamp at a distance of 0.5 m until the yellow color of the precursor dissipated (typically 0.5 h) or for several hours. Solvent was removed at reduced pressure, and the residual crude mixture of products was purified by radial chromatography.

***N*-Methyl-*N*-(2-pyridylthio)acetamide (6b)** was obtained from photolysis of **1b** (203 mg, 0.899 mmol) in benzene (6 mL). Chromatography (hexanes–ethyl acetate, 2:1) gave 123 mg of **6b** (0.675 mmol, 75% yield). ^{1}H NMR: δ 8.50 (app d, 1H, J = 5.0 Hz), 7.65 (ddd, 1H, J = 2.0, 7.5, 8.0 Hz), 7.08 (ddd, 1H, J = 1.5, 5.0, 7.5 Hz), 7.02 (app d, 1H, 8.0 Hz), 3.35 (s, 3H), 2.32 (s, 3H). ^{13}C NMR: δ 176.77, 160.35, 150.14, 137.27, 120.51, 116.73, 40.16, 21.48. MS: m/z (rel intensity) 182 (M^+, 3), 140 (15), 111 (100), 78 (35), 67(87), 43(79). HRMS: calcd for $C_8H_{10}N_2OS$ 182.0514, found 182.0520.

α-(2-Pyridylthio)acetamide (**8b**) was not isolated from the reaction of **1b** but was identified in the ^{1}H NMR spectrum of the crude reaction mixture by signals at δ 3.81 (s) and at δ 2.90 (d, J = 6.0 Hz) in the expected 2:3 ratio. The signals at δ 2.32 (from **6b**) and at δ 2.90 (from **8b**) integrated in a 70:1 ratio.

***N*-Butyl-*N*-(2-pyridylthio)pentanamide (6c) and *N*-Butyl-2-(2-pyridylthio)pentanamide (8c).** A sample of **1c** prepared *in situ* from 90 mg (0.57 mmol) of *N*-butylpentanamide[15] in 6 mL of benzene was photolyzed. Chromatography (hexanes–ethyl acetate, 3:1) gave 71 mg of **6c** (47% yield) which was identical to an authentic sample[15] by NMR and GC analyses and 56 mg of **8c** (37% yield) which was partially characterized by NMR spectroscopy and GC–mass spectrometry: ^{1}H NMR: δ 8.41 (app d, 1H, J = 5.0 Hz), 7.52 (ddd, 1H, J = 2.0, 7.5, 8.0 Hz), 7.22 (app d, 1H, J = 8.0 Hz), 7.04 (ddd, 1J, J = 1.5, 5.0, 7.5 Hz), 4.28 (t, 1H, J = 7.4 Hz), 3.21 (q, 2H, J = 6.8 Hz), 2.20–1.10 (m, 8H), 0.94 (t, 3H, J = 7.2 Hz), 0.82 (t, 3H, J = 7.2 Hz). ^{13}C NMR: δ 172.07, 158.40, 148.97, 136.30, 122.54, 119.88, 46.24, 39.04, 32.49, 31.32, 20.68, 19.82, 13.74, 13.60. MS: m/z (rel intensity) 266 (M^+, 4), 164 (19), 138 (89), 125 (100), 111 (85), 78 (60), 57 (68).

***N*-Butyl-*N*-(2-pyridylthio)-2-methylpropanamide (6d) and *N*-Butyl-2-(2-pyridylthio)-2-methylpropanamide (8d).** A solution of 253 mg (0.855 mmol) of **1d** in 18 mL of degassed benzene was photolyzed until the solution became colorless (ca. 3 h). Chromatography (hexanes–ethyl acetate) gave 49 mg (0.19 mmol, 23%) of product **6d** and 129 mg (0.512 mmol, 60%) of product **8d**.

Compound **6d** had the following properties. ^{1}H NMR: δ 8.48 (d, 1H, J = 4.8 Hz), 7.70–7.60 (m, 1H), 7.12–7.05 (m, 1H), 7.00 (d, 1H, J = 8.4 Hz), 4.20–3.20 (br m, 2H), 3.50–3.40 (m, 1H), 1.70–1.55 (m, 2H), 1.40–1.25 (m, 2H), 1.11 (d, 6H, J = 6.9 Hz), 0.92 (t, 3H, J = 7.3 Hz). ^{13}C NMR: δ 182.68, 161.53, 149.95, 137.16, 120.35, 116.68, 51.37, 30.42, 19.89, 19.81, 13.79. MS: m/z (rel intensity) 253 ($(M + H)^+$, 0.8), 142 (13), 139 (18), 111 (100), 72 (53). HRMS: calcd for $C_{13}H_{21}N_2OS$ $(M + H)^+$ 253.1374, found, 253.1368.

Compound **8d** had the following properties. ^{1}H NMR: δ 8.43 (d, 1H, J = 4.2 Hz), 8.12 (bs, 1H), 7.60–7.50 (m, 1H), 7.26 (d, 1H, J = 6.1 Hz), 7.15–7.05 (m, 1H), 3.22 (app q, 2H, J = 6.0 Hz), 1.64 (s, 6H), 1.50–1.40 (m, 2H), 1.35–1.20 (m, 2H), 0.86 (t, 3H, J = 7.2 Hz). ^{13}C NMR: δ 174.61, 157.26, 149.13, 136.62, 124.90, 120.84, 52.59, 39.71, 31.42, 26.94, 20.10, 13.84. MS: m/z (rel intensity) 252 (5), 180 (9), 153 (83), 138 (29), 120 (100). HRMS: calcd for $C_{13}H_{20}N_2OS$, 252.1296, found, 252.1300.

***N*-Butyl-2-methyl-2-(phenylselenyl)propanamide (9d).** A mixture of **1d** (253 mg, 0.85 mmol) and diphenyl diselenide (560 mg, 1.8 mmol) in 12 mL of benzene was irradiated. Chromatography (hexanes–ethyl acetate, 3:1) gave 180 mg (0.514 mmol, 60%) of **9d**. ^{1}H NMR: δ 7.60–7.50 (m, 2H), 7.40–7.25 (m, 3H), 6.45 (s, 1H), 3.21 (q, 2H, J = 6.9 Hz), 1.60 (s, 6H), 1.50–1.20 (m, 4H), 0.92 (t, 3H, J = 7.2 Hz). ^{13}C NMR: δ 174.11, 136.35, 128.86, 128.71, 127.66, 48.37, 39.67, 31.45, 27.39, 19.98, 13.69. MS: m/z (rel intensity) 299 (^{80}Se M^+, 20), 297 (^{78}Se M^+, 9), 199 (11), 142 (76), 114 (100). HRMS: calcd for $C_{14}H_{21}NO^{80}Se$ 299.0788, found 299.0786.

***N*-Butyl-*N*-(2-pyridylthio)phenylacetamide (6e), *N*-Butyl-α-(2-pyridylthio)phenylacetamide (8e), and *N,N'*-Dibutyl-2,3-diphenylsuccinamide (10).** Irradiation of a solution of **1e** (258 mg, 0.75 mmol) in 11.5 mL of benzene, solvent removal, and ^{1}H NMR analysis of the crude product mixture showed the presence of **6e** (30%), **8e** (33%), **10** (11%), and *N*-butylphenylacetamide (23%). Chromatography (hexanes–ethyl acetate, gradient from 7:1 to 1:100) gave pure samples of **6e**, **8e**, and **10**.

Compound **6e** had the following properties. ^{1}H NMR: δ 8.45 (app d, 1H, J = 5.0 Hz), 7.55 (m, 1H), 7.30–7.15 (m, 5H), 7.10–7.00 (m, 1H), 6.85 (app d, 1H, J = 8.0 Hz), 4.00 (s, 3H), 2.64–2.54 (m, 2H), 2.35–2.20 (m, 2H), 0.92 (t, 3H, J = 7.3 Hz). ^{13}C NMR: δ 176.47, 160.57, 149.75, 136.90, 134.66, 129.28, 128.18, 126.52, 120.26, 116.73, 51.63, 40.24, 30.21, 19.72, 13.65. MS: m/z (rel intensity) 300 (M^+, 3), 190 (15), 139 (20), 111 (100), 91 (60), 72 (54). HRMS: calcd for $C_{17}H_{20}N_2OS$ 300.1296, found 300.1294.

Compound **8e**, recrystallized from CH_2Cl_2 and hexanes, had the following properties. Mp: 77.0–78 °C. ^{1}H NMR: δ 8.45 (app d, 1H, J = 5.0 Hz), 7.60–6.95 (m, 9H), 5.58 (s, 1H), 3.25 (q, 2H, J = 6.8 Hz), 1.50–1.20 (m, 4H), 0.92 (t, 3H, J = 7.2 Hz). ^{13}C NMR: δ 169.63, 157.34, 149.20, 136.21, 136.15, 128.54, 128.16, 127.83, 122.04, 120.09, 51.96, 39.36, 31.23, 19.74, 13.56. MS: m/z (rel intensity) 300 (M^+, 13), 226 (33), 201 (100), 168 (83), 121 (23). HRMS: calcd for $C_{17}H_{20}N_2OS$ 300.1296, found 300.1290.

Compound **10** had the following properties. Mp: 216–217 °C. ^{1}H NMR: δ 7.20–7.00 (m, 10H), 5.66 (bs, 2H), 4.10 (s, 2H), 3.30–3.15 (m, 4H), 1.477–1.18 (m, 8H), 0.85 (t, 6H, J = 7.3 Hz). ^{13}C NMR: δ 172.59, 137.64, 128.55, 128.33, 127.11, 56.22, 39.59, 31.60, 20.00, 13.81. MS: m/z (rel intensity) 380 (M^+, 4), 307 (11), 281 (100), 182 (39), 91 (76), 57 (79). HRMS: calcd for $C_{24}H_{32}N_2O_2$ 380.2463, found 380.2466.

***N*-Butyl-α-(phenylselenyl)phenylacetamide (9e).** Irradiation of **1e** (419 mg, 1.22 mmol) and diphenyl diselenide (560 mg, 1.8 mmol) in benzene (20 mL), solvent removal, and radial chromatography gave 127 mg of **9e** (0.366 mmol, 30% yield), which was recrystallized from hot hexanes. Mp: 97–97.5 °C. ^{1}H NMR: δ 7.60–7.10 (m, 10H), 6.45 (s,1H), 4.96 (s, 1H), 3.25 (q, 2H,

J = 6.9 Hz), 1.50–1.20 (m, 4H), 0.86 (t, 3H, J = 7.2 Hz). ^{13}C NMR: δ 169.25, 137.12, 133.91, 129.55, 129.18, 128.74, 128.40, 128.06, 127.89, 52.09, 39.83, 31.44, 19.96, 13.72. MS: m/z (rel intensity) 347 (^{80}Se M$^+$, 15), 345 (^{78}Se M$^+$, 7), 190 (24), 162 (100), 91 (54). HRMS: calcd for $C_{18}H_{21}NO^{80}Se$ 347.0788, found 347.0792.

***N*-Butyl-2-(2-pyridylthio)-4-pentenamide (8f) and *N*-Butyl-5-((2-pyridylthio)methyl)-2-pyrrolidinone (11).** Photolysis of **1f** (156 mg, 0.508 mmol) in benzene (5 mL) until the solution was colorless (0.5 h), solvent removal under reduced pressure, and chromatography (hexanes–ethyl acetate, gradient from 2:1 to 4:1) gave lactam **11** (79.5 mg, 59.2% yield) and amide **8f** (43.8 mg, 27.5% yield).

Lactam **11** was identical to an authentic sample[15] by NMR and GC analyses.

Compound **8f** had the following properties. ^{1}H NMR: δ 8.42–8.38 (m, 1H), 7.58–7.47 (m, 1H), 7.45–7.30 (bs, 1H), 7.24–7.18 (m, 1H), 6.00–5.75 (m, 1H), 5.21–5.05 (m, 2H), 4.37 (t, 1H, J = 6.9 Hz), 3.30–3.15 (m, 2H), 2.93–2.75 (m, 1H), 2.67–2.49 (m, 1H), 1.50–1.10 (m, 4H), 0.84 (t, 3H, J = 7.2 Hz). ^{13}C NMR: δ 171.47, 158.10, 148.98, 136.38, 134.74, 122.63, 120.02, 117.57, 45.85, 39.10, 34.62, 31.31, 19.83, 13.61. HRMS: calcd for $C_{14}H_{20}N_2OS$ 264.1296, found 264.1299.

***N*-Acetyl-2-((2-pyridylthio)methyl)pyrrolidine (12).** Photolysis of **1g** (479 mg, 1.71 mmol) in benzene (36 mL), solvent removal under reduced pressure, and chromatography (hexanes–ethyl acetate, gradient from 2:1 to 100% ethyl acetate) gave 277 mg of **12** (1.17 mmol, 69% yield). Amide rotamers were observed in the NMR spectra of **12**. ^{1}H NMR: δ 8.37 (app d, 1H, J = 5.0 Hz), 7.60–40 (m, 1.6H), 7.15 (app d, 0.4 H, J = 8.0 Hz), 7.05–6.88 (m, 1H), 4.35–4.05 (m, 1H), 3.65–2.72 (m, 4H), 2.30 (s, 1.2H), 2.15–1.80 (m, 4H), 2.02 (s, 1.8H). ^{13}C NMR: δ 170.04, 169.70, 159.24, 157.44, 149.19, 136.35, 136.15, 122.35, 121.54, 119.80, 119.40, 114093, 57.84, 56.68, 48.19, 45.72, 32.55, 31.50, 29.84, 28.70, 23.85, 22.87, 22.16, 21.67. MS: m/z (rel intensity) 236 (M$^+$, 8), 203 (3), 164 (4), 112 (58), 70 (100). HRMS: calcd for $C_{11}H_{16}N_2OS$ 236.0983, found 236.0981.

The chromatography also gave 7.8 mg (0.033 mmol, 1.9% yield) of *N*-(4-pentenyl)-2-(2-pyridylthio)acetamide (**8g**), which was not fully characterized. ^{1}H NMR: δ 8.45 (app d, 1H, J = 5.0 Hz), 7.55 (m, 1H), 7.45 (bs, 1H), 7.28 (app d, 1H, J = 8.0 Hz), 7.07 (m, 1H), 5.85–5.70 (m, 1H), 4.98–4.90 (m, 2H), 3.80 (s, 2H), 3.28 (q, 2H, J = 6.9 Hz), 2.04–1.95 (m, 2H), 1.65–1.50 (m, 2H).

***N*-Butyl-2-((phenylselenyl)methyl)cyclopentanecarboxamide (13).** A solution of **1h** (289 mg, 0.86 mmol) and diphenyl diselenide (536 mg, 1.72 mmol) in benzene (20 mL) was irradiated for 6 h. Solvent removal and NMR analysis of the crude product mixture indicated that **13** was present along with a minor component tentatively identified as *N*-butyl-2-(phenylselenyl)-6-heptenamide (**14**). Chromatography (hexanes–ethyl acetate, 4:1) gave 108 mg of **13** (0.32 mmol, 37% yield), apparently as a single diastereomer. Amide **14** was not isolated.

Compound **13** had the following properties. ^{1}H NMR: δ 7.55–7.45 (m, 2H), 7.30–7.20 (m, 3H), 5.47 (bs, 1H), 3.33–3.20 (m, 2H), 3.20–2.92 (m, 2H), 2.60–2.50 (m, 1H), 2.33 (q, 1H, J = 7.3 Hz), 2.10–1.55 (m, 6H), 1.50–1.25 (m, 4H), 0.92 (t, 3H, J = 7.2 Hz). ^{13}C NMR: δ 134.46, 132.25, 129.10, 126.75, 51.74, 44.25, 39.19, 33.65, 32.93, 31.68, 30.50, 24.75, 20.01, 13.69. MS: m/z (rel intensity) 339 (^{80}Se M$^+$, 8), 337 (^{78}Se M$^+$, 4), 182 (100), 157 (7), 83 (31), 57 (54). HRMS: calcd for $C_{19}H_{25}NO^{80}Se$ 339.1101, found 339.1106.

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Supplementary Material Available: Experimental procedures and NMR spectra for the secondary amide precursors to **1d**, **1e**, **1g**, and **1h**, ^{1}H NMR spectra for all precursors **1** except **1c**, and ^{1}H NMR spectra of new products from reactions of **1** (25 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.