Absolute Rate Constants for α-Amide Radical Reactions

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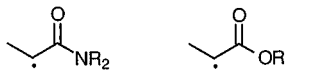
The 1-(diethylcarbamoyl)-6,6-diphenyl-5-hexenyl radical (**4a**), the 1-(diethylcarbamoyl)-7,7-diphenyl-6-heptenyl radical (**4b**), and the 1-(diethylcarbamoyl)-1-methyl-6,6-diphenyl-5-hexenyl radical (**4c**) were produced from the corresponding PTOC esters (anhydrides of the carboxylic acid and *N*-hydroxypyridine-2-thione) by laser flash photolysis methods. The kinetics of cyclizations of radicals **4a** and **4b** were measured at various temperatures, and that of cyclization of **4c** was measured at ambient temperature. Radicals **4a** and **4b** were employed as radical clocks in indirect kinetic studies to determine rate constants for reaction of secondary α-amide radicals with Bu_3-SnH. The calibrated tin hydride trapping reaction was then employed to determine rate constants for cyclization of the 1-(diethylcarbamoyl)-5-hexenyl radical (**12**). The rate constants for 5-*exo* cyclizations of secondary α-amide radicals are similar to those of their isostructural alkyl radical analogues. The rate constants for the 5-*exo* cyclization of tertiary α-amide radical **4c** and the 6-*exo* cyclization of the secondary α-amide radical **4b** are smaller than those of the analogous alkyl radicals and α-ester substituted radicals, apparently due to steric effects. The rate constants for tin hydride trapping of secondary α-amide radicals are similar to those for reactions with secondary α-ester radicals.

α-Amide radicals, usually produced by radical additions to acrylamides, but also available from atom abstraction reactions, are common intermediates in synthetic and polymer chemistry. In syntheses, the use of these radicals obviously provides a functional group for further synthetic conversions, but α-amide radicals also are playing a prominent role in the rapidly evolving area of acyclic stereoselection via radicals, especially in asymmetric induction reactions employing chiral auxiliaries.[1] The utility of α-amide radicals for accomplishing and understanding stereoselectivity derives in part from predictable conformational preferences in both the radicals and their acrylamide precursors and the fact that conformational equilibrations of these radicals are relatively slow processes in comparison to most useful elementary radical reactions. Rotation about the bond between the α-carbon and carbonyl carbon in a simple α-amide radical occurs with a rate constant of about 2×10^4 s^{-1} at ambient temperature,[2] and rotation about the carbonyl carbon to nitrogen bond in these radicals also appears to be slow[3] as one might expect on the basis of the slow C−N bond rotations of amides.



α-amide radical α-ester radical

Few absolute rate constants for reactions of α-amide radicals are available although one might expect that these species will react with rate constants similar to those of the structurally and electronically similar α-ester radicals which are better studied. In this work, we report the calibration of α-amide "radical clocks"[4] that can be used for measuring absolute rate constants and rate constants for reaction of tin hydride with secondary α-amide radicals. The tin hydride trapping kinetics are similar to those of secondary α-ester radicals, but the rates of some α-amide radical cyclizations are slightly to modestly reduced in comparison to the those of isostructural α-ester radicals. The kinetic information should provide synthetic chemists with increased predictive power for applications of α-amide radicals in chain processes.

Results

The general approach used was similar to that employed in developing kinetic scales for substituted carbon radicals and heteroatom-centered radicals. Rate constants for unimolecular reactions of selected α-amide radicals were measured directly by laser flash photolysis (LFP) methods. These calibrated reactions serve as radical clocks for indirect kinetic studies of second-order rate constants. Rate constants for reactions of tin hydride with two of these clocks were measured by indirect methods, and the tin hydride trapping reaction was used to calibrate a simple α-amide radical clock.

Direct Kinetic Studies. For direct LFP studies, we employed PTOC ester[5] radical precursors (**1**) derived from malonic acid monoamides. PTOC esters have a long wavelength absorbance centered at about 360 nm and

(1) Curran, D. P.; Porter, N. A.; Giese, B. *Stereochemistry of Radical Reactions: Concepts, Guidelines, and Synthetic Applications*; VCH: Weinheim, 1995.
(2) Strub, W.; Roduner, E.; Fischer, H. *J. Phys. Chem.* **1987**, *91*, 4379−4383.
(3) Curran, D. P.; Tamine, J. *J. Org. Chem.* **1991**, *56*, 2746−2750.
(4) Griller, D.; Ingold, K. U. *Acc. Chem. Res* **1980**, *13*, 317−323.
(5) The acronym PTOC results from pyridine-2-thioneoxycarbonyl. PTOC esters were initially developed by Barton for synthetic applications; see: Barton, D. H. R.; Crich, D.; Motherwell, W. B. *Tetrahedron* **1985**, *41*, 3901−3924. For early applications of PTOC esters in LFP studies, see: Bohne, C.; Boch, R.; Scaiano, J. C. *J. Org. Chem.* **1990**, *55*, 5414−5418. Ha, C.; Horner, J. H.; Newcomb, M.; Varick, T. R.; Arnold, B. R.; Lusztyk, J. *J. Org. Chem.* **1993**, *58*, 1194−1198.

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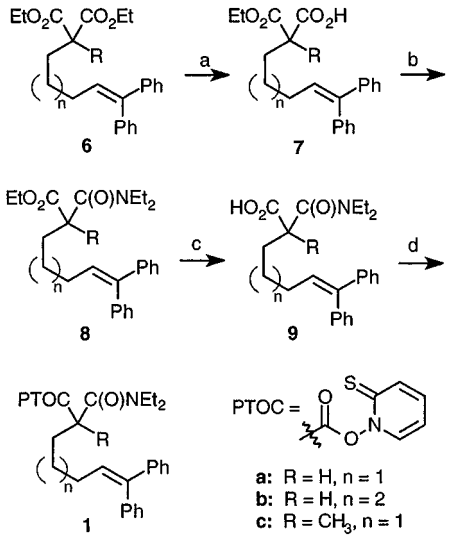
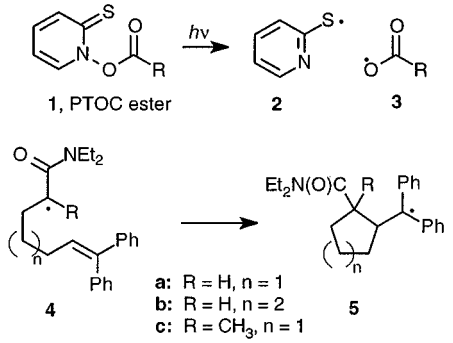
Scheme 1



(a) LiOH; (b) $(COCl)_2$, Et_2NH; (c) LiOH; (d) $(COCl)_2$, *N*-hydroxypyridine-2-thione sodium salt.

are cleaved efficiently by 355 nm light from a Nd:YAG laser. The initial photochemical cleavage reaction produces the (2-pyridine)thiyl radical (**2**) and acyloxyl radicals **3** that rapidly decarboxylate to give the desired radicals for kinetic studies. The α-amide radicals **4** were produced in LFP studies, and the rate constants for cyclization of these radicals to the diphenylalkyl radicals **5** were measured. The diphenylalkyl radical moieties in **5** absorb strongly in the 330−340 nm region and are detected readily by UV-spectroscopy.



The LFP apparatus and the design of the kinetic studies were conventional. In brief, the unit employs a Nd:YAG laser for production of 355 nm light with an 8 ns duration. Due to the strong absorbance of the PTOC esters at 355 nm, dilute flowing solutions of samples are employed. Temperature control is achieved by circulating a solution from a constant temperature bath through a jacket around the sample reservoir that contains a gas dispersion tube through which helium is passed. Temperatures are measured with a thermocouple inserted in the flow cell and held about 1 cm above the irradiation zone.

The radical precursors for LFP studies were prepared by the sequence in Scheme 1. Alkylation of diethyl malonate and diethyl methylmalonate with 5-bromo-1,1-diphenyl-1-pentene and of diethyl malonate with 6-bromo-1,1-diphenyl-1-hexene gave malonate esters **6** which were partially hydrolyzed with LiOH to give the malonate monoesters **7**; compounds **6** and **7** were reported previously.[6] Compounds **7** were converted to the α-ethoxycarbonyl amides **8** via the acid chlorides. Hydrolysis of the ester groups in **8** gave malonic acid monoamides **9** that were converted to the PTOC esters **1** by a conventional reaction sequence. All of the synthetic intermediates were characterized by NMR spectroscopy, and the α-ethoxycarbonyl amides **8** were also characterized by high-resolution mass spectrometry.

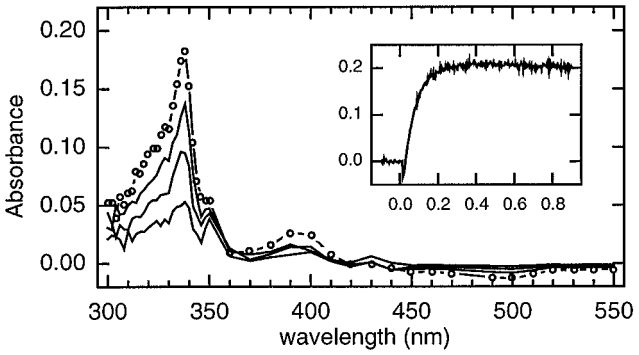


Figure 1. Time-resolved spectrum observed following laser irradiation of PTOC ester **1a** in THF. The traces are for 51, 71, 101, and 161 ns after irradiation with the signals obtained 31 ns after irradiation subtracted to give a base line. The 161 ns trace contains symbols that show the wavelengths at which measurements were made. The peaks at 340 and 390 nm are growing with time. The decaying peak at 490 nm is from radical **2**, the byproduct of the photolysis. The inset shows a kinetic trace at 338 nm where the *X* axis is time in μs.

The stability of α-amide PTOC esters **1** is noteworthy for those who employ the PTOC protocol in synthesis. Some PTOC esters are quite labile, and we previously found that PTOC ester precursors to α-ester and α-nitrile radicals were difficult to handle and that some decomposed or hydrolyzed upon attempted chromatography.[6] The α-amide PTOC derivatives **1** prepared in the this work, although still quite reactive, appeared to be more stable than their α-ester analogues and could be purified by silica gel chromatography. The samples of **1** were judged to be >95% pure by NMR spectroscopy.

Kinetic studies of radical **4a** were routine. Following the laser pulse, a transient grew in smoothly with first-order kinetics. The time-resolved spectrum shown in Figure 1 has been "background-adjusted" by subtraction of the signals measured 31 ns after the laser pulse from those obtained at later times. This procedure corrects for the initial photochemical bleaching caused by destruction of the precursor which has a long wavelength λ_{max} at about 360 nm, and the spectrum at 31 ns (not shown in Figure 1) would be a null spectrum with an absorbance of zero at all wavelengths. All signals appearing above zero are growing in with time, and the negative signal centered at 490 nm, from the instantaneously formed (2-pyridine)thiyl radical (**2**), is decaying with time.

The growing spectrum in Figure 1, with a strong absorbance centered at λ = 338 nm, is typical for diphenylalkyl radicals,[7] and we assign it to radical **5a**. The rate constants for formation of **5a** were similar to those for 5-*exo* cyclizations of other diphenylethene-

(6) Newcomb, M.; Horner, J. H.; Filipkowski, M. A.; Ha, C.; Park, S. U. *J. Am. Chem. Soc.* **1995**, *117*, 3674−3684.

(7) Chatgilialoglu, C. In *Handbook of Organic Photochemistry*; J. C. Scaiano, J. C., Ed.; CRC Press: Boca Raton, FL, 1989; Vol. 2; pp 3−11.

Table 1. Observed Rate Constants for Cyclizations of Radicals 4

			k_{obs} (s^{-1})	
radical	solvent	temp (°C)[a]	set 1	set 2
4a	THF	−0.2	1.00 E7	1.02 E7
		9.4	1.28 E7	1.29 E7
		19.2	1.60 E7	1.59 E7
		29.0	1.94 E7	1.93 E7
		40.7	2.39 E7	2.37 E7
		49.6	2.76 E7	2.79 E7
	CH_3CN	−0.8	0.948 E7	0.951 E7
		9.1	1.22 E7	1.21 E7
		19.1	1.47 E7	1.47 E7
		28.2	1.86 E7	1.83 E7
		40.3	2.37 E7	2.32 E7
		49.0	2.65 E7	2.63 E7
4b	THF	1.7	0.78 E4	
		18.7	1.58 E4	
		27.8	2.02 E4	
		37.3	3.12 E4	
4c	THF	29.5	1.4 E4	

[a] ±0.2 °C.

containing radicals that are isostructural with radical **4a**.[6,8] Further confirmation of the course of the reaction was obtained from preparative scale studies with the PTOC precursor to **4a** that gave the expected products (see below).

The rate constants for the 5-*exo* cyclization of radical **4a** are in the range of 10^7 s^{-1} which is where the LFP results are most accurate. The dynamic limit of the unit is about 2.5×10^8 s^{-1}, so the reactions were slow enough that deconvolution of the kinetics from the instrument response times was not necessary. On the other hand, the cyclizations of **4a** were fast enough such that radical−radical and radical-oxygen reactions could not compete with the cyclizations. The latter point is important because the measured rate constants for formation of **5a** are actually the sum of the rate constants for all reactions that consume **4a**.

Rate constants for cyclization of **4a** were determined over a 50 °C temperature range in both THF and acetonitrile (Table 1). The observed kinetics have standard errors of only a few percent of the measured value, and the major errors in the measurements result from temperature fluctuations of ±0.2 °C which occur during the course of a measurement that typically involves a summation of 12−15 independent runs. From the rate constants in Table 1, the Arrhenius functions in eqs 1 and 2 were calculated where errors are 2σ and $\theta = 2.3RT$ in kcal/mol. Cyclizations of **4a** (both cis and trans products are formed, see below) are insensitive to the solvent, showing that little if any polarization occurs in the transition states.

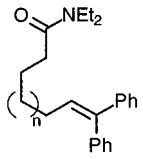
$$\log(k_C \times s)_{THF} = (9.84 \pm 0.05) - (3.53 \pm 0.07)/\theta \quad (1)$$

$$\log(k_C \times s)_{ACN} = (9.90 \pm 0.08) - (3.63 \pm 0.11)/\theta \quad (2)$$

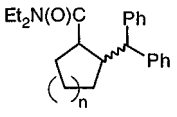
Radicals **4b** and **4c** also cyclized to give diphenylalkyl radical products, but these reactions were appreciably slower than the cyclization of radical **4a** with observed rate constants in the 10^4 s^{-1} range (Table 1). The observed rate constants for formation of the cyclic radicals are actually the sums of the rate constants for all reactions that deplete the precursor, and we have shown previously that in our experimental design radicals react with residual oxygen and other radicals with pseudo-first-order rate constants of about 5×10^3 s^{-1} at ambient temperatures.[9] Thus, an observed rate constant of 1×10^4 s^{-1} will not be an accurate measure of the rate of cyclization. Accordingly, the measured rate constants for the 6-*exo* cyclization of the secondary α-amide radical **4b** are only limiting values, and the actual rate constants for cyclization are smaller than the measured values. We would have estimated errors of about 25% in the measured rate constants for cyclization of **4b**, but competition studies involving tin hydride trapping (see below) suggest that the error is smaller and a reasonable Arrhenius function could be calculated from the observed kinetic data (eq 3). The measured rate constant for 5-*exo* cyclization of the tertiary α-amide radical **4c** at 30 °C was small enough such that it should contain about a 50% error, and we did not attempt variable temperature studies of this cyclization reaction.

$$\log(k_C \times s)_{THF} = (9.0 \pm 0.5) - (6.4 \pm 0.7)/\theta \quad (3)$$

Indirect Kinetic Studies. Radicals **4a** and **4b** were used to calibrate the trapping reaction with Bu_3SnH by a conventional indirect kinetic method.[10] The PTOC esters **1a** and **1b** reacted in the presence of tin hydride to give a mixture of acyclic amide products **10** and cyclic amide products **11**. The 5-*exo* cyclization of **4a** gave a 1:1 mixture of *cis*-**11a** and *trans*-**11a**. The 6-*exo* cyclization of **4b** displayed reasonably high diastereoselectivity giving *cis*-**11b** and *trans*-**11b** in a 1:6 ratio. Authentic samples of acyclic amides **10** were prepared by decarboxylation of the corresponding acids **9**. Both diastereomers of cyclopentanecarboxamide **11a** were isolated from a preparative scale reaction of PTOC ester **1a**. Authentic samples of both diastereomers of cyclohexanecarboxamide **11b** were prepared from a mixture of diastereomers of the (known) corresponding acid.



10a: n = 1
b: n = 2



11a: n = 1
b: n = 2

The results of the indirect kinetic studies of Bu_3SnH reactions are given in Table 2. The rate constants for tin hydride trapping were calculated from the observed product ratios, the mean concentration of tin hydride, and the rate constants for the cyclization reactions of radicals **4a** and **4b**.[10] The ratios of rate constants (k_C/k_H) for reaction of tin hydride with radical **4a** give the relative Arrhenius function in eq 4. Subtraction of eq 4 from eq 1 gives the Arrhenius function for H-atom trapping in eq 5. The rate constants for α-amide radical trapping by Bu_3SnH are slightly larger than those for reaction of tin hydride with a secondary alkyl radical[11] and similar

(8) Johnson, C. C.; Horner, J. H.; Tronche, C.; Newcomb, M. *J. Am. Chem. Soc.* **1995**, *117*, 1684−1687.

(9) Musa, O. M.; Horner, J. H.; Shahin, H.; Newcomb, M. *J. Am. Chem. Soc.* **1996**, *118*, 3862−3868.

(10) Newcomb, M. *Tetrahedron* **1993**, *49*, 1151−1176.

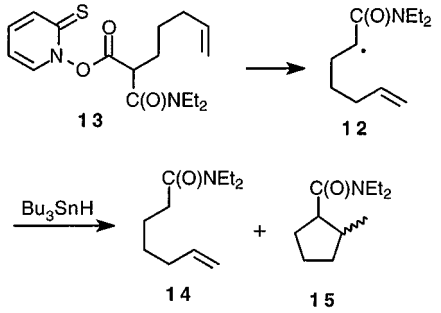
(11) Chatgilialoglu, C.; Ingold, K. U.; Scaiano, J. C. *J. Am. Chem. Soc.* **1981**, *103*, 7739−7742.

Table 2. Results of Bu_3SnH Trapping of Radicals 4a and 4b in THF

radical	temp (°C)[a]	[Bu_3SnH] (M)[b]	[**11**]/[**10**]	% yield[c]	(k_C/k_H)[d] (M)	k_H[e] $(Ms)^{-1}$
4a	32	0.64	8.9	73	5.7	3.6 E6
	20	0.29	20.3	71	5.9	2.7 E6
	20	0.65	8.4	62	5.4	2.9 E6
	1	0.38	10.9	68	4.1	2.6 E6
	1	0.32	12.2	66	4.0	2.6 E6
	−20	0.29	10.5	59	3.0	2.0 E6
	−20	0.36	8.8	81	3.2	1.9 E6
4b	20	0.070	0.080	98	0.0055	2.9 E6
	20	0.126	0.050	109	0.0063	2.5 E6

[a] ±1 °C. [b] Average concentration of Bu_3SnH. [c] Combined yield of **11** and **10** determined by GC employing an internal standard. [d] Ratio of rate constants for cyclization versus trapping. [e] Rate constant for hydrogen atom transfer.

Scheme 2



to those found for reaction of a secondary α-ester radical with tin hydride.[6]

$$\log((k_C/k_H)/\mathrm{M})_{THF} = (2.2 \pm 0.3) - (2.0 \pm 0.4)/\theta \quad (4)$$

$$\log(k_H \times \mathrm{Ms})_{THF} = (7.6 \pm 0.3) - (1.5 \pm 0.4)/\theta \quad (5)$$

It is possible that the activation parameters in eq 5 are not useful for calculating the entropy and enthalpy of activation of the H-atom transfer reaction. This caution results from the fact that the value of the log *A* is smaller than that found for tin hydride trapping of a secondary alkyl radical (log $A = 8.7$),[11] but we note that the log *A* term for reaction of a secondary α-ester radical with tin hydride also is somewhat small (log $A = 8.1$).[6] In any event, eq 5 accurately predicts the trapping rate constants for the temperature range studied (−20 to 32 °C) and should be useful for calculating values at temperatures up to 80 °C.

The tin hydride trapping reaction was used to calibrate the 5-*exo* cyclization of the simple secondary α-amide radical **12** (Scheme 2) which is more representative of the α-amide radicals that one would envision in synthetic applications. PTOC ester **13** was prepared by a sequence of reactions similar to those used to prepare PTOC esters **1**. Reaction of **13** in the presence of tin hydride gave the acyclic amide **14** and cyclopentanecarboxamides **15** (Scheme 2) which were identified by comparison to authentic samples prepared independently. As observed for the 5-*exo* cyclization of radical **4a**, the diastereoselectivity in the cyclization reaction of **12** was low with *cis*-**15** to *trans*-**15** ratios of about 1:2.

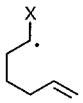
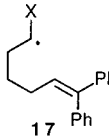
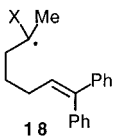
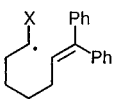
The results of a series of competition kinetic studies with radical **12** are given in Table 3. The relative rate constants for cyclization versus trapping of **12** give the function in eq 6. Addition of eq 6 to eq 5 gives the

Table 3. Results of Bu_3SnH Trapping of Radical 12 in THF

temp[a] (°C)	[Bu_3SnH][b] (M)	[**15**]/[**14**]	% yield[c]	(k_C/k_H)[d] (M)
25	0.298	0.155	87	0.046
	0.138	0.263	69	0.036
22	0.109	0.321	75	0.035
	0.188	0.197	80	0.037
0	0.117	0.178	86	0.0209
	0.201	0.096	93	0.0193
	0.419	0.047	96	0.0197
−21	0.179	0.048	91	0.0087
	0.296	0.033	87	0.0099
	0.452	0.023	107	0.0106
−40	0.220	0.026	78	0.0057
	0.389	0.0112	94	0.0044
	0.390	0.0165	92	0.0064

[a] ±1 °C. [b] Mean concentration of Bu_3SnH. [c] Combined yield of **15** and **14** determined by GC employing an internal standard. [d] Ratio of rate constants for cyclization versus trapping.

Table 4. Rate Constants for Radical Cyclizations at 20 °C[a]

X	 **16**	 **17**	 **18**	 **19**
CH_3[b]	1 E5	2 E7	1 E7	1 E5
$C(O)NEt_2$[c]	1 E5	2 E7	1 E4	2 E4
CO_2Et[d]	2 E5	4 E7	3 E5	7 E5
CN[e]			2 E5	
OCH_3[f]	2 E5	4 E7	6 E7	1 E5

[a] Approximate rate constants in units of s^{-1}. [b] Data from refs 6, 12, 15. [c] This work. [d] Data from refs 6, 14. [f] Data from refs 8, 14, 16.

Arrhenius function for cyclization of **12** in eq 7. The rate constant for cyclization of **12** at 20 °C is 9×10^4 s^{-1}.

$$\log((k_C/k_H)/\mathrm{M}) = (1.73 \pm 0.32) - (4.28 \pm 0.38)/\theta \quad (6)$$

$$\log(k_C \times \mathrm{s}) = (9.3 \pm 0.4) - (5.8 \pm 0.6)/\theta \quad (7)$$

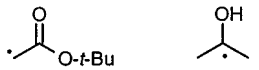
Discussion

The kinetic studies in this work add to the growing number of rate constants that are useful for predicting the outcome of synthetic reactions employing radicals. Kinetic values are important because most radical-based synthetic sequences involve chain reactions in which competitions between a desired reaction and an undesired one are inevitable. We have collected some rate constants for radical cyclizations and tin hydride trapping reactions that can be compared to the values obtained here for α-amide radicals.

Rate constants for cyclization of four series of isostructural radicals at 20 °C are listed in Table 4.[6,8,10,12−16] Despite intuitive notions one might have regarding the

(12) Beckwith, A. L. J.; Easton, C. J.; Lawrence, T.; Serelis, A. K. *Aust. J. Chem.* **1983**, *36*, 545−556.
(13) Lusztyk, J.; Maillard, B.; Deycard, S.; Lindsay, D. A.; Ingold, K. U. *J. Org. Chem.* **1987**, *52*, 3509−3514.
(14) Newcomb, M.; Filipkowski, M. A.; Johnson, C. C. *Tetrahedron Lett.* **1995**, *36*, 3643−3646.
(15) Belcher, T. A.; Horner, J. H.; Newcomb, M. Unpublished results.

effects of radical stability on the kinetics of cyclizations, it is clear that electronic factors are much less important than steric effects in these reactions. The only influence of the radical stabilizing groups in the 5-*exo* cyclizations of the simple secondary radicals **16** and the diphenylethene-substituted radicals **17** is to lead to an *increased* rate of cyclization for the ester- and methoxy-substituted systems. The reactivity in these cyclizations is similar to the intermolecular reactivity observed in additions of radicals to simple alkenes where the α-ester radical **20**[17] adds to simple alkenes faster than does the methyl radical,[18] and the 1-methyl-1-hydroxyethyl radical (**21**) adds somewhat less rapidly.[19]



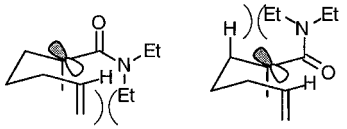
20 **21**

The close similarity of the rate constants for 5-*exo* cyclizations in the series of radicals **16** and in the series of radicals **17** also suggests that the transition states for these reactions are at most only slightly polarized. That fact was demonstrated directly in this work for cyclization of radical **4a** (**17**, X = $C(O)NEt_2$) in that the rate constants in THF and acetonitrile were indistinguishable. In a similar manner, the rate constants for cyclization of the methoxy-substituted radicals **17** and **18** (X = OCH_3) were the same in THF and acetonitrile.[8,16]

Unlike the case with the secondary radicals, the kinetics of 5-*exo* cyclizations of the tertiary radicals **18** display strong substituent effects. On the basis of the absence of significant electronic effects in the cyclizations of the secondary radicals **16** and **17**, one assumes that electronic effects are also minor in the case of the tertiary radicals **18**. Accordingly, the observed rate reductions for radicals **18** containing electron-withdrawing groups appear to reflect sterics. We have noted this phenomenon for 5-*exo* cyclizations of tertiary radicals previously and suggested that it results from an enforced planarity at the radical center.[6,14] Thus, the tertiary alkyl radical **18** (X = CH_3) can deform from planarity with little or no energy penalty, but an energy penalty would result from deformation of the planar radical center in the conjugated tertiary radicals **18** (X = $C(O)NEt_2$, CO_2Et, CN). In any transition state for a 5-*exo* radical cyclization of a tertiary radical, one group at the radical center will interact with the vinyl group if the planar radical does not deform (arrows in **22** and **23**). The enforced planarity argument explains how the relatively small electron-withdrawing group in the tertiary α-nitrile radical **18** (X = CN) can lead to a reduction in the rate of cyclization comparable to that observed for the ester group in **18** (X = CO_2Et).

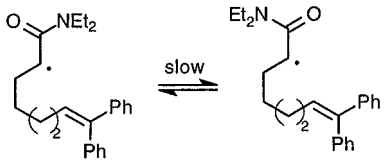
22 **23**

An additional steric effect apparently is present in the cyclization of the tertiary α-amide radical **4c** (**18**, X = $C(O)NEt_2$) which is more than order of magnitude less rapid than cyclization of the α-ester and α-nitrile analogues (**18**, X = CO_2Et, CN). We assume that this effect results from the bulk of the amide group (but see below). For example, **24** and **25** show two of the possible conformations for cyclization of **4c**. The indicated steric interactions could be avoided for an α-ester radical and would not exist for an α-nitrile radical. For the 6-*exo* cyclizations of the secondary radicals **19**, the α-amide radical **4b** again appears to suffer an order of magnitude kinetic retardation due to a steric effect that is not present in the α-ester radical, and we again assume this results from the two substituents on the nitrogen of the amide.



24 **25**

It is noteworthy that the rate constants for cyclization of radicals **4b** and **4c** are quite similar to the rate constant Fischer reported for rotation about the C−C bond between the carbonyl carbon and the radical center in a simple α-amide radical.[2] This raises the interesting possibility that the measured kinetics for **4b** and **4c** might actually be those for a slow conformational interconversion (shown below for (*Z*)-**4b** and (*E*)-**4b**) that is followed by a faster radical cyclization. We do not have adequate kinetic data to exclude this possibility for **4c**, but the activation parameters obtained for **4b** are not consistent with this hypothesis. Specifically, the conformational interconversion of **4b** via rotation should have only a slightly negative entropy of activation leading to a log *A* term of 12−13.[20] The observed log *A* = 9 for **4b** is consistent with the well-organized transition state of a 6-*exo* cyclization reaction; for example, log *A* = 9 for cyclization of radical **19** (X = CH_3) in which conformational equilibrations are not an issue.[14]



Z-**4b** *E*-**4b**

The slow interconversion of rotamers in the α-amide radicals might be important in regard to the observed low diastereoselectivity in the 5-*exo* cyclizations of radicals **4a** and **12**. One does not know the rotamer populations of these radicals, and the rate constants for their cyclizations are greater than or of the same order of magnitude as those for rotamer interconversion. Therefore, the observed low diastereoselection in the 5-*exo* cyclization reactions does not necessarily require that the diastereoselectivity is low for the cyclization of each particular rotamer. Synthetic chemists should not dismiss the possibility that good diastereoselectivity in 5-*exo* cyclizations of secondary α-amide radicals might be possible if the radical rotamer population can be con-

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Table 5. Rate Constants for Reaction of Bu_3SnH with RCH(•)X

X	Arrhenius function[a]	k_{20} °C (M^{-1} s^{-1})
CH_3[b]	$\log k = 8.7 - 3.5/\theta$	1.2 E6
$C(O)NEt_2$[c]	$\log k = 7.6 - 1.5/\theta$	3.0 E6
CO_2Et[d]	$\log k = 8.1 - 2.2/\theta$	3.2 E6
OMe[e]	$\log k = 8.4 - 3.8/\theta$	3.6 E5

[a] $\theta = 2.3RT$ in kcal/mol. [b] Reference 11. [c] This work. [d] Reference 6. [e] Reference 8.

trolled; such control might be achieved by Lewis acid complexation by an appropriately functionalized radical precursor.

Rate constants for reactions of tin hydride with secondary radicals are collected in Table 5.[6,8,10,11] For the hydrogen atom transfer reaction from Bu_3SnH to a radical, the C−H bond dissociation energies will reflect the thermodynamics of the reactions, and the tin hydride reaction with a secondary alkyl radical is more exothermic than reactions with the substituted radicals. The fact that the rate constants for reaction of tin hydride with the α-amide and α-ester radicals are slightly greater than that for reaction with the alkyl radical apparently reflects a favorable polarity match between the electron deficient radicals and the electron rich tin hydride that results in a polarization in the transition states for reactions of the electron deficient radicals. For the electron rich methoxy-substituted radical, the rate constant for reaction of tin hydride is smaller than that for reaction of the alkyl radical as one would expect.[8]

In summary, the rate constants for cyclizations of and hydrogen atom transfer to α-amide radicals are subject to the same minor electronic effects one observes in related α-ester radicals. Steric effects, however, can lead to reductions in the rate constants of α-amide radical cyclization reactions greater than those observed with other electron deficient radicals. The bulk of the amide group and the relatively slow rates of conformational interconversion about the C−C (carbonyl to radical center)[2] and C−N (carbonyl to nitrogen) bonds should be considered in attempts to incorporate α-amide radical cyclizations into synthetic schemes. That the rate constant for 5-*exo* cyclization of the prototypical α-amide radical **12** is faster than conformational equilibration might be important for achieving high diastereoselectivities in cyclization reactions.

Experimental Section

General. NMR spectra of $CDCl_3$ solutions were obtained at 300 or 500 MHz (^1H) and 75 or 125 MHz (^{13}C). Radial chromatography was performed on a model 7924T Chromatotron (Harrison Research). Melting points were obtained on a Thomas-Hoover capillary melting point apparatus. Diethyl malonates **6** and the malonate monoesters **7** were prepared by the methods previously reported.[6] *N*-Hydroxypyridine-2-thione sodium salt was prepared as described previously.[21]

Synthesis of α-Ethoxycarbonyl Amides 8 (Method A). Carboxylic acid chlorides were prepared by reaction of the corresponding acids **7** (1 equiv) in benzene cooled at 5 °C under nitrogen with a catalytic amount of DMF and oxalyl chloride (1.5 equiv) added dropwise. The mixture was stirred until gas evolution ceased, and the excess oxalyl chloride was removed by distillation under reduced pressure. Diethylamine (2 equiv) and triethylamine (1 equiv) were added dropwise to the crude residue of acid chloride in diethyl ether at 0 °C. The solution was stirred for 12 h. After filtration of the ammonium salts, the filtrate was washed with water, 1 M NaOH, 1 M HCl, saturated aqueous $NaHCO_3$, and saturated aqueous NaCl. The organic phase was combined and dried over $MgSO_4$, filtered, and concentrated at reduced pressure to yield crude α-ethoxycarbonyl amides **8** which were purified by column chromatography on silica gel.

Synthesis of α-Carboxy Amides 9. Method B. α-Ethoxycarbonyl amides **8** (1 equiv) and LiOH (1.1 equiv) in 95% EtOH were heated at reflux for 5 h. The mixture was cooled and concentrated. The residue was dissolved in water, and the resulting solution was acidified with HCl. The mixture was extracted three times with ether, and the combined ethereal extracts were washed with saturated NaCl solution and dried over $MgSO_4$. Concentration under reduced pressure gave crude **9** which was purified by column chromatography on silica gel.

Preparation of PTOC Esters 1. Method C. To a solution of α-carboxy amide **9** (1 equiv) in dry benzene were added oxalyl chloride (1.5 equiv) and two drops of DMF. The mixture was stirred until gas evolution ceased, and excess oxalyl chloride was removed by distillation under reduced pressure. The residue was dissolved in dry benzene, and the resulting solution was transferred via cannula into a light-shielded vessel containing a suspension of *N*-hydroxypyridine-2-thione sodium salt (1.1 equiv) and a catalytic amount of DMAP in dry benzene. The mixture was stirred for 2 h. The reaction mixture was washed with saturated $NaHCO_3$ solution and saturated aqueous NaCl solution. After drying over $MgSO_4$, the solution was concentrated to give the crude PTOC esters **1** which were purified by column chromatography on silica gel.

***N,N*-Diethyl-2-(ethoxycarbonyl)-7,7-diphenyl-6-heptenamide (8a)** was prepared by method A from **7a** (0.50 g, 1.81 mmol). Column chromatography (hexanes−EtOAc, 3:1) gave 0.50 g of **8a** (1.23 mmol, 68%). ^1H NMR: δ 7.37−7.15 (m, 10H), 6.07 (t, 1H, J = 7.2 Hz), 4.15 (q, 2H, J = 7.2 Hz), 3.45−3.20 (m, 5H), 2.16 (q, 2H, J = 7.5 Hz), 1.96 (q, 2H, J = 6.9 Hz), 1.50−1.43 (m, 2H), 1.22 (t, 3H, J = 7.2 Hz), 1.15−1.09 (m, 6H). ^{13}C NMR: δ 170.09, 167.79, 142.63, 142.09, 140.11, 129.86, 129.16, 128.30, 128.17, 128.04, 127.20, 126.91, 126.85, 61.06, 48.53, 42.53, 42.14, 40.59, 29.47, 28.87, 27.71, 14.49, 14.09, 12.80. MS: *m*/*z* (rel intens) 407 (100.0), 261 (23.4), 260 (23.5), 206 (41.6), 205 (18.4), 191 (14.1), 187 (40.8), 178 (12.5), 167 (13.0), 165 (15.8), 129 (13.3), 128 (25.3), 115 (26.7), 100 (28.9), 91 (35.4), 74.1 (27.0), 73 (15.5), 72 (58.9), 58 (21.0). HRMS: calcd for $C_{26}H_{33}NO_3$, 407.2460; found, 407.2463.

***N,N*-Diethyl-2-(ethoxycarbonyl)-8,8-diphenyl-7-octenamide (8b)** was prepared by method A from **7b** (2.23 g, 6.09 mmol). Column chromatography (hexanes−EtOAc, 3:1) gave 1.67 g of **8b** (1.23 mmol, 65%). ^1H NMR: δ 7.38−7.14 (m, 10H), 6.05 (t, 1H, J = 7.5 Hz), 4.15 (q, 2H, J = 6.9 Hz), 3.49−3.22 (m, 5H), 2.12 (q, 2H, J = 7.5 Hz), 1.90 (q, 2H, J = 7.5 Hz), 1.53−1.43 (m, 2H), 1.32−1.27 (m, 2H), 1.25−1.16 (m, 6H), 1.11 (t, 3H, J = 7.2 Hz). ^{13}C NMR: δ 170.15, 167.88, 142.75, 141.70, 140.19, 129.85, 129.70, 128.11, 128.01, 127.16, 126.82, 126.76, 61.06, 48.87, 42.12, 40.61, 29.86, 29.55, 29.25, 27.28, 14.50, 14.08, 12.77. MS: *m*/*z* (rel intens) 421 (100.0), 246 (14.4), 205 (10.6), 200 (10.5), 193 (14.1), 192 (10.3), 191 (14.4), 187 (37.0), 180 (14.5), 178 (15.8), 167 (17.6), 165 (13.7), 128 (26.6), 115 (36.7), 100 (34.4), 91 (31.5), 74 (38.7), 73 (14.2), 72 (61.2), 58 (25.7). HRMS: calcd for $C_{27}H_{35}NO_3$, 421.2617; found, 421.2626.

***N,N*-Diethyl-2-(ethoxycarbonyl)-2-methyl-7,7-diphenyl-6-heptenamide (8c)** was prepared by method A from **7c** (2.13 g, 5.82 mmol). Column chromatography (hexanes−EtOAc, 3:1) gave 1.54 g of **8c** (3.66 mmol, 63%). ^1H NMR: δ 7.37−7.14 (m, 10H), 6.07 (t, 1H, J = 7.2 Hz), 4.15 (q, 2H, J = 6.9 Hz), 3.35 (q, 2H, J = 6.6 Hz), 3.11 (q, 2H, J = 6.6 Hz), 2.13 (q, 2H, J = 7.2 Hz), 1.94−1.75 (m, 2H), 1.48−1.30 (m, 2H), 1.39 (s, 3H), 1.23 (t, 3H, J = 7.5 Hz), 1.11−1.04 (m, 6H). ^{13}C NMR: δ 174.63, 170.03, 142.59, 142.04, 140.10, 129.83, 129.17, 128.13, 128.03, 127.14, 126.85, 126.80, 61.05, 52.43, 41.02, 39.96, 36.23, 30.00, 24.49, 21.84, 14.09, 13.41, 12.29. MS: *m*/*z* (rel intens) 421 (87.4), 348 (11.2), 276 (11.3), 275 (50.7), 274 (47.6), 228 (10.3), 207 (17.7), 206 (100.0), 205 (22.0), 201 (20.2), 193 (18.1), 192 (10.3), 191 (20.7), 183 (15.4), 178 (18.1), 167

(11.3), 165 (15.3), 142.1 (11.9), 141 (10.0), 129 (16.0), 128 (17.5), 115 (35.6), 105 (13.2), 100 (41.2), 91 (46.9), 73 (21.5), 72 (43.7), 69 (12.7), 58 (17.4). HRMS: calcd for $C_{27}H_{35}NO_3$, 421.2617; found, 421.2625.

***N,N*-Diethyl-2-carboxy-7,7-diphenyl-6-heptenamide (9a)** was prepared by method B from **8a** (1.5 g, 3.69 mmol). Column chromatography (hexanes−EtOAc, 1:1) gave 1.3 g of **9a** (3.43 mmol, 93%). ^{1}H NMR: δ 11.83 (bs, 1H), 7.39−7.13 (m, 10H), 6.02 (t, 1H, J = 7.2 Hz), 3.62−3.50 (m, 1H), 3.47 (t, 1H, J = 6.9 Hz), 3.39−3.17 (m, 3H), 2.14 (q, 2H, J = 7.2 Hz), 1.87 (q, 2H, J = 7.5 Hz), 1.60−1.50 (m, 2H), 1.18 (t, 3H, J = 6.9 Hz), 1.14 (t, 3H, J = 7.2 Hz). ^{13}C NMR: δ 172.13, 171.44, 142.53, 142.42, 139.94, 129.81, 128.38, 128.20, 128.08, 127.19, 126.10, 46.43, 42.45, 41.20, 32.20, 29.27, 27.05, 14.41, 12.74.

***N,N*-Diethyl-2-carboxy-8,8-diphenyl-7-octenamide (9b)** was prepared by method B from **8b** (2.0 g, 4.75 mmol). Column chromatography (hexanes−EtOAc, 1:1) gave 1.78 g of **9b** (4.53 mmol, 95%). ^{1}H NMR: δ 12.00 (bs, 1H), 7.39−7.13 (m, 10H), 6.03 (t, 1H, J = 7.5 Hz), 3.56−3.44 (m, 2H), 3.34−3.21 (m, 3H), 2.15 (q, 2H, J = 7.2 Hz), 1.83 (q, 2H, J = 6.6 Hz), 1.47−1.38 (m, 4H), 1.21 (t, 3H, J = 6.9 Hz), 1.13 (t, 3H, J = 6.9 Hz). ^{13}C NMR: δ 172.34, 171.23, 142.60, 142.03, 140.06, 129.82, 129.16, 128.16, 128.04, 127.16, 126.91, 126.85, 46.48, 42.43, 41.20, 32.67, 29.49, 29.34, 26.44, 14.43, 12.72.

***N,N*-Diethyl-2-carboxy-2-methyl-7,7-diphenyl-6-heptenamide (9c)** was prepared by method B from **8c** (0.89 g, 2.11 mmol). Column chromatography (hexanes−EtOAc, 1:1) gave 0.74 g of **9c** (1.88 mmol, 89%). ^{1}H NMR: δ 11.20 (bs, 1H), 7.38−7.13 (m, 10H), 6.04 (t, 1H, J = 7.5 Hz), 3.34 (bs, 2H), 3.21 (bs, 2H), 2.12 (q, 2H, J = 7.2 Hz), 1.85 (t, 2H, J = 8.7 Hz), 1.44 (s, 3H), 1.40−1.30 (m, 2H), 1.09 (t, 6H, J = 6.6 Hz). ^{13}C NMR: δ 179.50, 170.11, 142.54, 142.13, 140.06, 129.88, 129.00, 128.14, 128.05, 127.16, 126.89, 126.86, 52.39, 41.55, 40.56, 36.12, 29.93, 24.56, 22.06, 13.08, 12.34.

1-[[(1-(*N,N*-Diethylcarbamoyl)-6,6-diphenyl-5-hexenyl)carbonyl]oxy]-2(1*H*)-pyridinethione (1a) was prepared by method C from **9a** (0.26 g, 0.69 mmol). Column chromatography (hexanes−EtOAc, 1:1) gave 0.27 g of **1a** (0.51 mmol, 73%). ^{1}H NMR: δ 7.67 (dd, 1H, J = 8.7, 1.5 Hz), 7.60 (dd, 1H, J = 7.2, 1.5 Hz), 7.38−7.16 (m, 11H), 6.60 (dt, 1H, J = 6.9, 1.8 Hz), 6.07 (t, 1H, J = 7.2 Hz), 4.01 (t, 1H, J = 6.9 Hz), 3.56−3.27 (m, 4H), 2.24−2.12 (m, 2H), 2.02−1.96 (m, 2H), 1.66−1.57 (m, 2H), 1.25 (t, 3H J = 6.9 Hz), 1.16 (t, 3H, J = 7.2 Hz). ^{13}C NMR: δ 175.68, 166.79, 165.84, 142.51, 142.38, 140.03, 137.84, 137.11, 133.73, 129.86, 128.70, 128.32, 128.23, 128.07,127.22, 127.00, 126.91, 112.63, 46.95, 42.95, 40.89, 29.45, 28.74, 27.46, 14.71, 12.84.

1-[[(1-(*N,N*-Diethylcarbamoyl)-7,7-diphenyl-6-heptenyl)carbonyl]oxy]-2(1*H*)-pyridinethione (1b) was prepared by method C from **9b** (0.27 g, 0.69 mmol). Column chromatography (hexanes−EtOAc, 1:1) gave 0.26 g of **1b** (0.48 mmol, 68%). ^{1}H NMR: δ 7.67 (dd, 1H, J = 9.0, 1.5 Hz), 7.61 (dd, 1H, J = 7.5, 1.5 Hz), 7.37−7.14 (m, 11H), 6.60 (dt, 1H, J = 6.9, 1.8 Hz), 6.05 (t, 1H, J = 7.5 Hz), 4.00 (t, 1H, J = 7.2 Hz), 3.58−3.26 (m, 4H), 2.22−2.10 (m, 2H), 2.02−1.92 (m, 2H), 1.47−1.42 (m, 4H), 1.27 (t, 3H, J = 6.0 Hz), 1.14 (t, 3H, J = 7.2 Hz). ^{13}C NMR: δ 175.54, 166.83, 165.85, 142.66, 141.89, 140.1, 137.85, 136.95, 133.89, 129.83, 129.44, 128.32, 128.20, 128.07, 127.12, 126.92, 126.83, 112.76, 46.98, 42.96, 40.92, 29.68, 29.43, 29.06, 26.87, 14.75, 12.87.

1-[[(1-(*N,N*-Diethylcarbamoyl)-1-methyl-6,6-diphenyl-5-hexenyl)carbonyl]oxy]-2(1*H*)-pyridinethione (1c) was prepared by method C from **9c** (0.17 g, 0.43 mmol). Column chromatography (hexanes−EtOAc, 1:1) gave 0.14 g of **1c** (0.26 mmol, 60%). ^{1}H NMR: δ 7.66 (dd, 1H, J = 9.0, 1.8 Hz), 7.47 (d, 1H, J = 6.6 Hz), 7.37−7.14 (m, 11H), 6.58 (t, 1H, J = 7.2 Hz), 6.09 (t, 1H, J = 7.2 Hz), 3.48−3.31 (m, 4H), 2.17 (q, 2H, J = 7.2 Hz), 2.08 (t, 2H, J = 7.8 Hz), 1.74 (s, 3H), 1.39−1.51 (m, 2H), 1.13 (t, 6H, J = 6.9 Hz). ^{13}C NMR: δ 180.86, 168.33, 145.09, 142.48, 142.33, 140.05, 137.53, 133.34, 129.84, 128.78, 128.20, 128.06, 127.17, 126.92, 112.55, 53.43, 42.53, 40.76, 35.89, 29.81, 24.91, 22.33, 13.55, 12.32.

***N,N*-Diethyl-7,7-diphenyl-6-heptenamide (10a)** was obtained by thermal decarboxylation of acid **7a** (30 mg, 0.079 mmol) at 170−175 °C for 30 min. The acyclic amide **10a** was isolated by silica gel chromatography (hexanes−acetone, 8:2) as a yellow oil (20.5 mg, 0.061 mmol, 77%). ^{1}H NMR: δ 7.39−7.14 (m, 10H), 6.08 (t, 1H, J = 7.2 Hz), 3.35 (q, 2H, J = 6.9 Hz), 3.24 (q, 2H, J = 7.2 Hz), 2.25−2.10 (m, 4H), 1.71−1.61 (m, 2H), 1.54−1.46 (m, 2H), 1.15−1.07 (dt, 6H, J = 9.6, 6.9 Hz). ^{13}C NMR: δ 171.9, 142.7, 141.7, 140.2, 129.9, 129.7, 128.1, 128.0, 127.2, 126.8, 126.7, 41.9, 40.0, 32.8, 29.7, 29.5, 24.9, 14.4, 13.1. MS: *m*/*z* (rel intens) 335 (100.0), 262 (10), 206 (23), 168 (45), 128 (78), 115 (70), 100 (41), 91 (34), 72 (40), 58 (23). HRMS: calcd for $C_{23}H_{29}NO$, 335.2249; found, 335.2248.

***N,N*-Diethyl-8,8-diphenyl-7-heptenamide** (**10b**) was obtained by thermal decarboxylation of acid **7b** (32 mg, 0.081 mmol) at 170−175 °C for 30 min. The acyclic amide **10b** was isolated by silica gel chromatography (hexanes−acetone, 8:2) as a yellow oil (22 mg, 0.063 mmol, 78%). ^{1}H NMR: δ 7.40−7.15 (m, 10H), 6.07 (t, 1H, J = 7.5 Hz), 3.35 (q, 2H, J = 6.9 Hz), 3.27 (q, 2H, J = 7.2 Hz), 2.25 (t, 2H, J = 7.2 Hz), 2.11 (m, 2H), 1.62 (m, 2H), 1.47 (m, 2H), 1.34 (m, 2H), 1.19−1.05 (dt, 6H, J = 9.6 Hz, J = 6.9 Hz). ^{13}C NMR: δ 172.1, 142.8, 141.5, 140.3, 130.0, 129.9, 128.1, 128.0, 127.2, 126.8, 126.7, 41.9, 40.0, 33.0, 29.8, 29.7, 29.2, 25.4, 14.4, 13.1. MS: *m*/*z* (rel intens) 349 (95.0), 276 (3), 156 (24.0), 148 (38.0), 115 (100.0), 91 (28.0), 72 (32.0), 58 (28.0). HRMS: calcd for $C_{24}H_{31}NO$, 349.2406; found, 349.2405.

***cis*- and *trans*-*N,N*-Diethyl-2-(diphenylmethyl)cyclopentanecarboxamide (11a)** were isolated from the reaction of the corresponding PTOC ester **1a** (60 mg, 0.123 mmol) and 5 equiv of Bu_3SnH (0.178 g, 0.614 mmol) in 10 mL of dry THF. The reaction mixture was sealed with a septum, flushed with nitrogen, and photolyzed with visible light for 3 h at room temperature. GC and GC−mass spectral analyses showed that a 1:1 mixture of diastereomeric cyclization products was formed in addition to the acyclic product. Both diastereomers (*cis*-**11a**: 12 mg, 29%, mp 100−101 °C, *trans*-**11a**: 10 mg, 22%, mp 98−99 °C) were isolated by radial chromatography on silica gel (hexanes−acetone, 8:2).

cis-**11a** was characterized as follows: ^{1}H NMR: δ 7.37−7.03 (m, 10H), 4.24 (d, 1H, J = 11.1 Hz), 3.35 (sextet, 1H, J = 7.5 Hz), 3.05 (sextet, 1H, J = 7.0 Hz), 2.90 (m, 2H), 2.51 (m, 2H), 2.00−1.84 (m, 3H), 1.80−1.70 (m, 1H), 1.68−1.46 (m, 2H), 1.03 (t, 3H, J = 7.2 Hz), 0.69 (t, 3H, J = 6.9 Hz). ^{13}C NMR: δ 174.8, 145.4, 145.1, 128.4, 128.3, 128.1, 127.7, 126.1, 125.9, 53.0, 49.5, 41.6, 41.3, 40.4, 31.8, 31.2, 24.4, 14.3, 13.1. MS: *m*/*z* (rel intens) 335 (100.0), 262 (9.5), 206 (19.3), 168 (43.4), 128 (73.3), 115 (59.9), 100 (36.2), 72 (36.6), 58 (17.3). HRMS: calcd for $C_{23}H_{29}NO$, 335.2249; found, 335.2253.

trans-**11a** was characterized as follows: ^{1}H NMR: δ 7.20−7.05 (m, 10H), 3.66−3.51 (m, 2H), 3.25 (sextet, 1H, J = 7.5 Hz), 3.08 (sextet, 1H, J = 7.2 Hz), 2.75 (m, 2H), 2.55 (m, 1H), 1.95−1.50 (m, 5H), 1.35−1.24 (m, 1H), 0.96 (t, 3H, J = 7.9 Hz), 0.65 (t, 3H, J = 8.1 Hz), 1.95−1.72 (m, 3H), 1.72−1.60 (m, 2H). ^{13}C NMR: δ 175.9, 145.0, 144.6, 128.5, 128.4, 128.3, 127.8, 126.2, 126.0, 59.1, 46.7, 46.0, 41.5, 40.6, 33.5, 33.3, 26.1, 14.1, 13.0. MS: *m*/*z* (rel intens) 335 (100.0), 262 (8.0), 206 (11.0), 168 (78.8), 167 (61.1), 115 (36.4), 72 (27.3), 41 (10.5). HRMS: calcd for $C_{23}H_{29}NO$, 335.2249; found, 335.2255.

***cis*- and *trans*-*N,N*-Diethyl-2-(diphenylmethyl)cyclohexancarboxamide (11b)** were prepared by method A from 2-(diphenylmethyl)cyclohexanecarboxylic acid[22] (0.07 g, 0.24 mmol). Column chromatography (hexanes−EtOAc, 3:1) gave 0.04 g of *trans*-**11b** (0.115 mmol, 48%) and 0.02 g of *cis*-**11b** (0.057 mmol, 24%).

cis-**11b** was characterized as follows: ^{1}H NMR: δ 7.34−7.07 (m, 10H), 4.04 (d, 1H, J = 11.7 Hz), 3.36−3.24 (m, 1H), 3.23−3.12 (m, 1H), 2.73−2.64 (m, 2H), 2.47−2.29 (m, 2H), 2.25−2.13 (m, 1H), 1.78−1.45 (m, 5H), 1.30−1.15 (m, 2H), 1.09 (t, 3H, J = 7.2 Hz), 0.50 (t, 3H, J = 7.2 Hz). ^{13}C NMR: δ 173.40, 144.76, 144.14, 128.58, 128.36, 128.33, 127.95, 126.08, 125.85, 55.68, 43.33, 41.48, 39.90, 36.31, 30.21, 26.34, 26.27,

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21.33, 13.53, 12.99. MS: *m*/*z* (rel intens) 349 (100.0), 182 (31.1), 167 (30.4), 165 (15.4), 128 (23.1), 115 (27.9), 100 (23.4), 91 (10.0), 72 (16.2). HRMS: calcd for $C_{24}H_{31}NO$, 349.2406; found, 349.2406.

trans-**11b** was characterized as follows: ^{1}H NMR: δ 7.31−7.11 (m, 10H), 4.23 (d, 1H, J = 6.0 Hz), 3.43−3.29 (m, 1H), 3.22−3.11 (m, 1H), 2.84 (q, 2H, J = 7.5 Hz), 2.78−2.65 (m, 1H), 2.21 (t, 1H, J = 10.2 Hz), 1.79−1.50 (m, 5H), 1.30−1.14 (m, 3H), 1.08 (t, 3H, J = 6.9 Hz), 0.87 (t, 3H, J = 7.2 Hz). ^{13}C NMR: 174.69, 143.53, 142.00, 130.42, 128.48, 128.13, 127.88, 126.32, 125.61, 53.40, 43.81, 43.73, 41.56, 40.09, 31.33, 27.49, 25.92, 25.75, 14.21, 12.99. MS: *m*/*z* (rel intens) 349 (100.0), 182 (52.3), 167 (30.1), 165 (15.8), 128 (20.2), 115 (25.6), 100 (39.1), 72 (19.2). HRMS: calcd for $C_{24}H_{31}NO$, 349.2406; found, 349.2403.

1-[[(1-(*N*,*N*-Diethylcarbamoyl)-5-hexenyl)carbonyl]oxy]-2(1*H*)-pyridinethione (13). *N*,*N*-Diethyl-2-(ethoxycarbonyl)-6-heptenecarboxamide was prepared by method A from ethyl 2-carboxy-6-heptenoate (0.89 g, 4.43 mmol). Column chromatography (hexanes−EtOAc, 3:1) gave 0.80 g of the desired amide (3.14 mmol, 71%). ^{1}H NMR: δ 5.80−5.65 (m, 1H), 4.97−4.87 (m, 2H), 4.14−4.06 (m, 2H), 3.47−3.21 (m, 5H), 2.09−1.98 (m, 2H), 1.91−1.84 (m, 2H), 1.39−1.28 (m, 2H), 1.16 (dt, 6H, J = 6.9, 3.3 Hz), 1.06 (dt, 3H, J = 6.9, 3.3 Hz). ^{13}C NMR: δ 170.08, 167.84, 138.11, 128.22, 114.73, 61.02, 48.73, 42.03, 40.55, 33.50, 28.73, 26.78, 14.41, 13.99, 12.68. MS: *m*/*z* (rel intens) 255 (12.1), 210 (14.9), 187 (31.2), 182 (16.5), 100 (47.1), 74 (10.4), 73 (19.5), 72 (100.0), 58 (59.3), 55 (17.4). HRMS: calcd for $C_{14}H_{25}NO_3$, 255.1834, found 255.1839. Some of the NMR signals were obscured due to coalescence.

N,*N*-Diethyl-2-carboxy-6-heptenecarboxamide was prepared by method B from the above amide (0.49 g, 1.92 mmol). Column chromatography (hexanes−EtOAc, 1:1) gave 0.41 g of the desired amide (1.81 mmol, 94%). ^{1}H NMR: δ 8.90 (bs, 1H), 5.78−5.64 (m, 1H), 5.00−4.91 (m, 1H), 3.56−3.41 (m, 2H), 3.40−322 (m, 3H), 2.08−2.00 (m, 2H), 1.89−1.81 (m, 2H), 1.50−1.39 (m, 2H), 1.20 (t, 3H, J = 6.9 Hz), 1.11 (t, 3H, J = 7.5 Hz). ^{13}C NMR: δ 171.79, 171.60, 137.60, 115.25, 46.59, 42.42, 41.12, 33.09, 31.55, 25.93, 14.36, 12.66.

PTOC ester **13** was prepared by method C from the above amide (0.46 g, 2.03 mmol). Column chromatography (hexanes−EtOAc, 1:1) gave 0.51 g of **13** (1.52 mmol, 75%). ^{1}H NMR: δ 7.64 (dd, 1H, J = 8.7, 1.5 Hz), 7.60 (dd, 1H, J = 6.9, 1.2 Hz), 7.18 (dt, 1H, J = 7.2, 1.8 Hz), 6.59 (dt, 1H, J = 6.9, 1.5 Hz), 5.84−5.71 (m, 1H), 5.05−4.94 (m, 2H), 4.02 (t, 1H, J = 7.2 Hz), 3.61−3.30 (m, 4H), 2.18−2.08 (m, 3H), 2.00−1.91 (m, 1H), 1.60−1.48 (m, 2H), 1.27 (t, 3H, J = 7.2 Hz), 1.14 (t, 3H, J = 6.9 Hz). ^{13}C NMR: δ 175.62, 166.85, 165.79, 137.81, 137.03, 133.78, 115.19, 112.66, 46.96, 42.89, 40.81, 33.31, 28.50, 26.36, 14.68, 12.77.

***N*,*N*-Diethyl-6-heptenamide (14)** was prepared by method A from commercially available 6-heptenoic acid (0.50 g, 3.9 mmol). Column chromatography (hexanes−EtOAc, 3:1) gave 0.57 g of **14** (3.11 mmol, 80%). ^{1}H NMR: δ 5.77−5.64 (m, 1H), 4.94−4.81 (m, 2H), 3.26 (q, 2H, J = 6.9 Hz), 3.20 (q, 2H, J = 4.8 Hz), 2.20 (t, 2H, J = 7.2 Hz), 2.01−2.01−1.97 (m, 2H), 1.61−1.51 (m, 2H), 1.39−1.31 (m, 2H), 1.07 (t, 3H, J = 6.9 Hz), 1.00 (t, 3H, J = 6.9 Hz). ^{13}C NMR: δ 171.91, 138.53, 114.36, 41.83, 39.90, 33.50, 32.81, 28.63, 24.84, 14.28, 13.00. MS: *m*/*z* (rel intens) 183 (30.9), 142 (20.4), 128 (47.3), 115 (87.1), 100 (68.3), 87 (12.8), 86 (14.2), 74 (11.0), 58 (59.3), 72 (49.8), 58 (100.0), 55 (31.7), 44 (20.2), 41 (20.5), 28 (26.6). HRMS: calcd for $C_{11}H_{21}NO$, 183.1623, found 183.1620.

***N*,*N*-Diethyl 2-methylcyclopentanecarboxamides (15)** were prepared by method A from 2-methylcyclopentanecarboxylic acid[23] (0.87 g, 6.80 mmol). Column chromatography (hexanes−EtOAc, 3:1) gave 0.98 g of **15** (5.36 mmol, 79%). GC analysis showed that a 3.6:1 mixture of diastereomers was formed. ^{1}H NMR: δ 3.66−2.81 (m, 4H), 2.38−2.02 (m, 2H), 1.92−1.77 (m, 2H), 1.75−1.31 (m, 8H), 1.15 (t, 3H, J = 6.9 Hz), 1.06 (t, 3H, J = 7.2 Hz), 0.93 (d, 2.3H, J = 6.6 Hz), 0.80 (d, 0.7H, J = 6.9 Hz). ^{13}C NMR: δ 174.90, 173.18, 49.15, 44.73, 41.68, 41.39, 40.18, 39.77, 39.14, 36.17, 34.67, 34.47, 30.93, 28.50, 24.30, 24.12, 19.00, 16.59, 14.90, 14.47, 13.11, 12.96. MS: *m*/*z* (rel intens) 183 (52.5), 168 (36.1), 142 (35.0), 140 (10.8), 128 (91.6), 111 (11.5), 100 (44.7), 83 (100.0), 74 (12.1), 67 (11.7), 58 (68.0, 55 (69.4). HRMS: calcd for $C_{11}H_{21}NO$, 183.1623, found 183.1619.

Laser flash photolysis kinetic studies[5,6,8] were performed on an Applied Photophysics LK-50 kinetic spectrometer employing a Spectron Nd:YAG laser. Solutions of the PTOC esters in spectral grade THF or acetonitrile were prepared such that the total absorbance at 355 nm was ca. 0.4. The solutions were sparged with helium and thermally equilibrated in a jacketed addition funnel; a solution of methanol−water from a temperature-regulated bath was pumped through the jacket. The solutions were allowed to flow through a flow cell for the LFP studies. Temperatures were measured with a thermocouple placed in the flowing stream approximately 1 cm above the irradiation zone. Time-resolved spectra were determined for each radical **4**. Kinetic measurements were obtained in the region 330−335 nm. Each kinetic value reported is an average of 12−15 independent runs.

Indirect Kinetic Studies.[10] In flame-dried tubes containing a small stir bar, mixtures of radical precursors **1a**, **1b**, or **13** (ca. 0.04 M), Bu_3SnH, and a hydrocarbon standard (eicosane for **1** or dodecane for **13**) in freshly dried THF were sparged with nitrogen. The tubes were placed in a constant temperature bath while being shielded from light. After thermal equilibration, the solutions were irradiated with a 150 W tungsten-filament lamp at a distance of ca. 0.4 m for 40 min. The reaction mixtures were analyzed by GC with thermal conductivity detectors employing 15 m × 0.53 mm columns (SE-30 for analysis of products from precursors **1** or Carbowax for analysis of products from precursor **13**). Yields reported for indirect kinetic experiments were calculated from response factors determined with authentic samples.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra of new compounds (36 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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