

Absolute Rate Constants for Alkoxy-carbonyl Radical Reactions

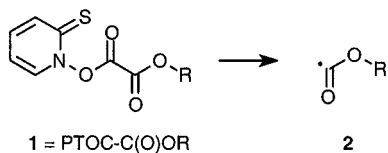
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PTOC oxalates (anhydrides of an oxalic acid monoester and *N*-hydroxypyridine-2-thione) were used in laser flash photolysis (LFP) kinetic studies. Irradiation of the PTOC oxalates gave the following alkoxy-carbonyl radicals $\text{ROC}(\cdot)=\text{O}$: **2a**, $\text{R} = \text{PhCH}_2$; **2b**, $\text{R} = (\textit{trans}\text{-}2\text{-phenylcyclopropyl})\text{methyl}$; **2c**, $\text{R} = (2,2\text{-diphenylcyclopropyl})\text{methyl}$. Rate constants for decarboxylation of radical **2a** measured by LFP were in agreement with those obtained previously by indirect kinetic methods. Rate constants for decarboxylation of radical **2c** were measured by LFP over the temperature range 3–48 °C; the reaction is described by $\log k = 12.2 - 9.6/2.3RT$ (kcal/mol). Reactions of Bu_3SnH with radical **2c** produced from the corresponding phenylseleno carbonate gave inconsistent kinetic results apparently due to the production of small amounts of PhSeH that reacted rapidly with **2c**. An approximate rate constant at 2 °C for reaction of Bu_3SnH with **2c** produced from the PTOC oxalate was obtained. Tin hydride reacts with the alkoxy-carbonyl radical approximately 1 order of magnitude less rapidly than it reacts with alkyl radicals. Rate constants for 5-*exo* cyclizations of simple alkoxy-carbonyl radicals were estimated from previous results and the approximate rate constant for tin hydride trapping; the cyclizations are slightly faster than 5-*exo* cyclizations of structurally related alkyl radicals.

Radical precursors that are cleaved efficiently by light are necessary for laser flash photolysis (LFP) kinetic measurements. Derivatives of peroxy-carboxylic acids are commonly employed for LFP studies of radicals because they contain weak heteroatom–heteroatom bonds, the acyloxyl radicals formed by homolysis decarboxylate very rapidly, and the requisite carboxylic acids are generally prepared relatively easily and are stable. Radical deoxygenation protocols employing precursors that are derivatives of alcohols are widely applied in synthesis but less commonly employed for LFP studies even though they are attractive in principle on the basis of the wide range of alcohols that are available. We report here an evaluation of PTOC¹ oxalate derivatives (**1**) as radical precursors for LFP studies. Derivatives **1** lead to alkoxy-carbonyl radicals (**2**), and LFP rate constants for decarboxylation of radicals **2** have been measured directly. A calibrated alkoxy-carbonyl radical clock was used in indirect kinetic studies to determine an approximate second-order rate constants for tin hydride trapping, and data from the literature was used to calculate rate constants for 5-*exo* cyclizations of *O*-alkenyl alkoxy-carbonyl radicals.

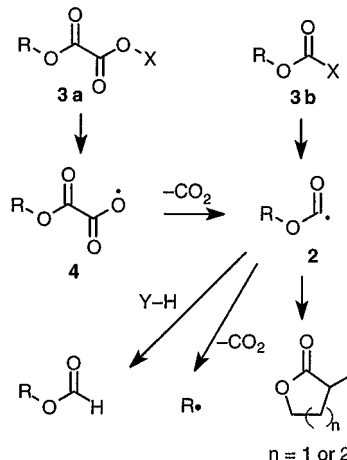


Results and Discussion

PTOC oxalates **1** were applied by the Barton, Crich, and Togo groups for alcohol deoxygenation and function-

(1) The acronym PTOC derives from (pyridine-2-thione)oxycarbonyl. The commonly used PTOC esters are anhydrides of a carboxylic acid and the thiohydroxamic acid *N*-hydroxypyridine-2-thione. In a similar manner, PTOC oxalates are anhydrides of an oxalic acid half ester and the thiohydroxamic acid.

Scheme 1



alization reactions^{2–4} and belong to the PTOC family of radical precursors developed by Barton and co-workers.⁵ These derivatives react upon photolysis or in radical chain reactions to give alkoxy-carbonyl radicals (**2**) by rapid decarboxylation of the first formed acyloxyl radicals **4** (Scheme 1). Other oxalate derivatives **3a** react in radical chain reactions to give, ultimately, radicals **2**, and carbonate derivatives **3b** react in chain reactions to produce radicals **2** directly. Alkoxy-carbonyl radicals **2** can react with a trapping agent to give formate derivatives or suffer a second decarboxylation to give an alkyl radical. Decarboxylations of radicals **2** to give aryloxy

(2) Barton, D. H. R.; Crich, D. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1603–1611.

(3) Crich, D.; Fortt, S. M. *Synthesis* **1987**, 35–37.

(4) Togo, H.; Fujii, M.; Yokoyama, M. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 57–67.

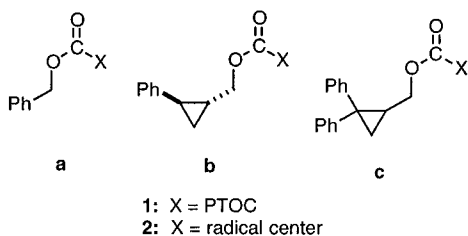
(5) Barton, D. H. R.; Crich, D.; Motherwell, W. B. *Tetrahedron* **1985**, *41*, 3901–3924.

(6) Pfenninger, J.; Heuberger, C.; Graf, W. *Helv. Chim. Acta* **1980**, *63*, 2328–2337.

or even alkoxy radicals also have been reported.⁶ When appropriate unsaturation is present, radicals **2** can cyclize to give the immediate precursors to γ - and δ -lactones.^{7,8} The rate of decarboxylation of radicals **2** is a function of the stability of the product radical, and this reaction can be beneficial as one of the steps in a reaction sequence that ultimately results in deoxygenation of alcohols (especially tertiary alcohols) or a nuisance when one is attempting to effect a cyclization reaction.

PTOC Oxalates for LFP Studies. Although invented for synthetic applications,⁵ the family of PTOC radical precursors has proven to be quite useful in LFP studies due to the presence of a long-wavelength chromophore centered at ca. 360 nm and the efficient homolytic cleavage of the weak N–O bond upon 355 nm irradiation from a Nd:YAG laser.^{9–11} As with other members of the PTOC family, PTOC oxalates were excellent precursors for LFP kinetic studies when they had adequate stability to permit handling. However, difficulties in isolation, purification, and handling of these activated acyl derivatives limited their utility considerably.

In synthetic applications previously reported, PTOC oxalates were prepared *in situ* and immediately used.^{2,3} We employed the same synthetic sequence for preparation of the PTOC oxalate precursors for radicals **2a–c**, but isolation of the compounds was necessary for LFP studies. Unlike PTOC esters that typically can be purified by chromatography with some loss of material, the PTOC oxalates decomposed completely upon attempted chromatography. Therefore, crude samples with purities of 50% or greater (as determined by NMR spectroscopy) were employed for LFP studies. The sample impurities did not have an effect on the LFP kinetics measured in this work because low concentrations of precursors (ca. 1×10^{-5} M) were employed and relatively fast unimolecular kinetics were observed.



The utility of PTOC oxalates for LFP studies is clearly limited. PTOC oxalate precursors have been prepared from tertiary alcohols for radical deoxygenation reactions,^{2,3} but we were unable to isolate the derivatives **1** from secondary and tertiary cyclopropylcarbinols. In the attempted preparative reactions of these precursors, extensive decomposition was apparent as evidenced by formation of alkene-containing products and loss of cyclopropyl proton signals in the NMR spectra of the crude products. In addition, the benzylic radical precursor **1a** rapidly decomposed upon handling, resulting in difficulties in LFP studies (see below).

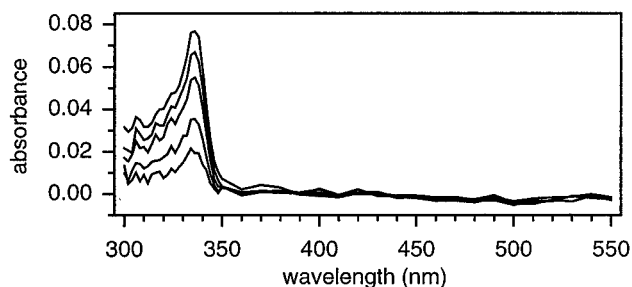
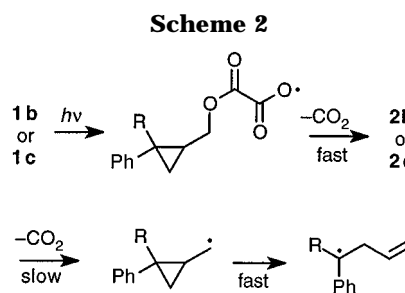


Figure 1. Time-resolved spectrum following laser irradiation of precursor **1c**. The signals are growing in over 20 μ s.



LFP Kinetic Studies. The kinetics of decarboxylation of the alkoxy carbonyl radicals **2a–c** were obtained by conventional LFP methods. Dilute solutions of the PTOC oxalate precursors **1a–c** in THF flowed through a flow-cell in the LFP unit. Irradiation by a 355 nm laser pulse produced initially the pyridyl-2-thiyl radical and [(alkoxy carbonyl)acyl]oxy radicals that decarboxylate rapidly to the alkoxy carbonyl radicals **2**. That radicals **2** are intermediates is known from the results of Bu₃SnH trapping experiments with PTOC oxalates that gave formate esters.² Decarboxylation of radical **2a** gave the UV-detectable benzyl radical as the product, whereas decarboxylation of radicals **2b** and **2c** gave aryl-substituted cyclopropylcarbinyl radicals that ring open very rapidly¹² to UV-detectable benzylic and diphenylalkyl radicals, respectively (Scheme 2). The “reporter group” concept employed in the latter two systems was discussed previously.¹³ The ultimate product radicals were identified from time-resolved UV spectra (e.g., Figure 1) that had long-wavelength absorbances centered at ca. 315 nm (benzylic radicals from **2a** and **2b**) and 336 nm (diphenylalkyl radical from **2c**).¹⁴

The kinetics of decarboxylations of radicals **2a** and **2c** were measured by LFP at various temperatures. That for decarboxylation of radical **2b**, which was expected to react with rate constants nearly equal to those of **2c**, was measured at one temperature (Table 1).

LFP kinetics for unimolecular reactions can be precise with errors at the 95% confidence interval as small as a few percent, often smaller than the error introduced in the temperature measurement. For rate constants in the 10^5 – 10^7 s⁻¹ range, the kinetics are usually also quite accurate measurements of the first-order reaction rate. The measured values (k_{obs}) are the sums of the rate constants for all processes that consume the initial

(7) Bachi, M. D.; Bosch, E. *Tetrahedron Lett.* **1986**, 27, 641–644.

(8) Bachi, M. D.; Bosch, E. *J. Org. Chem.* **1992**, 57, 4696–4705.

(9) Bohne, C.; Boch, R.; Scaiano, J. C. *J. Org. Chem.* **1990**, 55, 5414–5418.

(10) Ha, C.; Horner, J. H.; Newcomb, M.; Varick, T. R.; Arnold, B. R.; Luszyk, J. *J. Org. Chem.* **1993**, 58, 1194–1198.

(11) Aveline, B. M.; Kochevar, I. E.; Redmond, R. W. *J. Am. Chem. Soc.* **1995**, 117, 9699–9708.

(12) Newcomb, M.; Johnson, C. C.; Manek, M. B.; Varick, T. R. *J. Am. Chem. Soc.* **1992**, 114, 10915–10921.

(13) Newcomb, M.; Tanaka, N.; Bouvier, A.; Tronche, C.; Horner, J. H.; Musa, O. M.; Martinez, F. N. *J. Am. Chem. Soc.* **1996**, 118, 8505–8506.

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

Table 1. LFP Kinetics of Decarboxylations of Radicals 2 in THF

radical	T^a (°C)	$10^{-5} \times k$ (s ⁻¹)
2a	1.0	330
	15.6	470
	19.4	630
	21.0	770
	30.7	1240
2b	25.0	1.64 ± 0.12
2c	2.8	0.370 ± 0.006
	7.5	0.518 ± 0.005
	12.8	0.72 ± 0.01
	16.8	0.84 ± 0.01
	20.1	0.95 ± 0.05
	21.0	1.07 ± 0.01
	24.4	1.27 ± 0.01
	29.7	1.66 ± 0.09
	38.8	3.03 ± 0.11
	46.0	4.22 ± 0.14
	47.8	4.16 ± 0.15

^a ±0.2 °C.

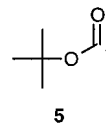
radical, but second-order reactions (radical–radical reactions and reactions of radicals with residual oxygen) have pseudo-first-order rate constants that are typically less than 10^4 s⁻¹.

Despite the precision in the rate measurements, the kinetic data for decarboxylation of **2a** was not very accurate.¹⁵ The lack of accuracy is apparent from the rate constants at 19.4 and 21.0 °C, which differ by an impossible 20%. Only a limited data set was obtained for decarboxylation of radical **2a** due to the instability of precursor **1a**, which required that the precursor was prepared immediately before an LFP study was conducted and prevented lengthy temperature equilibrations. From the kinetic values in Table 1, the Arrhenius function for decarboxylation of **2a** was calculated (eq 1 where errors are at 2σ and $\theta = 2.3RT$ in kcal/mol). The large uncertainty in eq 1 results both from the limited number of studies and the limited temperature range, and the equation is useful only for predicting rate constants, not for considerations of energy and entropy of activation terms. Nevertheless, the parameters in eq 1 are in good agreement with those for other alkoxy-carbonyl radical decarboxylations (see below).

$$\log(k \times s) = (13 \pm 2) - (7 \pm 2)/\theta \quad (1)$$

Despite our difficulties in measuring the rate constants for decarboxylation of **2a**, the approximate values we obtained serve a useful purpose. Decarboxylations of alkoxy-carbonyl radicals have been studied for years, but most of the kinetic studies of these species involved competition kinetic methods.¹⁶ Thus, determinations of the absolute kinetics of these reactions require knowledge of the kinetics of diffusional processes (for steady-state kinetic ESR methods) or of trapping reactions (for competitive trapping methods). An exception is the *tert*-butoxycarbonyl radical (**5**) for which the kinetics were

determined by Rügge and Fischer¹⁷ by a time-resolved kinetic ESR method that provided absolute rate constants directly and demonstrated that an earlier study of decarboxylation of **5** by Griller and Roberts¹⁸ using steady-state kinetic ESR required an adjustment in the diffusional rate constants. The kinetic values for decarboxylation of **5** comprise the foundation for an absolute kinetic scale for decarboxylation of other alkoxy-carbonyl radicals, and the LFP rate constants for decarboxylation of **2a** measured here provide a verification of that kinetic scale.



Recently, Beckwith and Bowry reported rate constants for decarboxylation of alkoxy-carbonyl radicals determined by competitive trapping with a nitroxyl radical.¹⁹ The nitroxyl radical-trapping rate constants were determined earlier²⁰ by competition against the fragmentation of radical **5** using the time-resolved kinetic ESR data of Rügge and Fischer.¹⁷ One of the alkoxy-carbonyl radicals studied indirectly by Beckwith and Bowry was radical **2a**. They determined rate constants for decarboxylation of **2a** between 49 and 79 °C and report rate constants for decarboxylation of, for example, 0.7×10^8 s⁻¹ at 42 °C and 2.2×10^8 s⁻¹ at 79 °C.¹⁹ From eq 1, one calculates rate constants for decarboxylation of **2a** of 1.4×10^8 s⁻¹ at 42 °C and 4.5×10^8 s⁻¹ at 79 °C.

The factor of 2 difference in the rate constants from the two works is in reasonably good agreement and verifies the kinetic scale for alkoxy-carbonyl radical decarboxylations. The kinetic data for decarboxylation of radical **5** was measured at low temperatures (–48 to –20 °C) in the Fischer laboratory and extrapolated to higher temperatures for use in the nitroxyl radical trapping studies in the Beckwith laboratory, and the indirect kinetic method requires multiple competition studies that compound errors and also an assumption that the measured rate constants for reactions of one radical are equal to those for a related radical of interest.¹⁶ For the direct study of **2a** in this work, the errors in eq 1 suggest that kinetic values calculated by extrapolation to temperatures outside the measured range should be considered approximate. Further, the Beckwith and Bowry study of **2a** was performed in cyclohexane, whereas our study of **2a** was conducted in THF, and there is no assurance that alkoxy-carbonyl radical decarboxylation reactions are completely insensitive to solvent identity. We conclude that a rate constant for decarboxylation of **2a** based on the direct study (eq 1) is likely to be more accurate than that from the Beckwith and Bowry study due to the multiple measurements and assumptions of the indirect approach but that either set of results will provide reasonable rate constants for most purposes.

(15) For fast reactions, convolution of the instrument response time with the rate of the reaction becomes a concern. Our unit has a measured response time for an “instantaneous” reaction (k_{inst}) of 2.5×10^8 s⁻¹, and measured rate constants with $k_{\text{obs}} > 5 \times 10^7$ s⁻¹ will have convolution errors exceeding a few percent. The rate constants listed in Table 1 for radical **2a** have been deconvoluted using an “error-free” exponential rate of 2.5×10^8 s⁻¹ for the instrument response. We note that the random errors in deconvoluted rate constants increase exponentially as the rate approaches the instrumental response limit.

(16) Newcomb, M. *Tetrahedron* **1993**, *49*, 1151–1176.

(17) Rügge, D.; Fischer, H. *Int. J. Chem. Kinet.* **1986**, *18*, 145–158.

(18) Griller, D.; Roberts, B. P. *J. Chem. Soc., Perkin Trans. 2* **1972**, 747–751.

(19) Beckwith, A. L. J.; Bowry, V. W. *J. Am. Chem. Soc.* **1994**, *116*, 2710–2716.

(20) Beckwith, A. L. J.; Bowry, V. W.; Moad, G. *J. Org. Chem.* **1988**, *53*, 1632–1641.

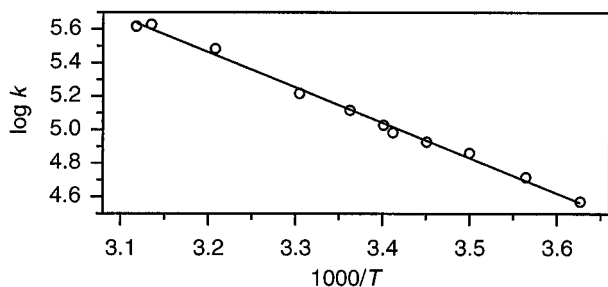


Figure 2. Observed rate constants for decarboxylation of radical **2c**.

Table 2. Rate Constants for Alkoxy-carbonyl Radical Decarboxylations at 20 °C^a

radical type	X = alkyl	X = cyclopropyl
XCH ₂ OC(•)=O	0.002 × 10 ⁵ ^b	1.1 × 10 ⁵ ^c
XR'CHO(•)=O	0.005 × 10 ⁵ ^b	7 × 10 ⁵ ^d
XR' ₂ CO(•)=O	1.1 × 10 ⁵ ^e	120 × 10 ⁵ ^d

^a Rate constants in units of s⁻¹. ^b Calculated from the product ratios in ref 6 using a rate constant for Bu₃SnH calculated from eq 3. Note that decarboxylations to give alkoxy radicals also occur for these radicals; see ref 6. ^c This work. ^d Reference 19. ^e Reference 17.

Radical precursors **1b** and **1c** were more stable and easier to handle than **1a**, and the kinetics of decarboxylation of radicals **2b** and **2c** should be accurate. These reactions are fast enough that second-order processes could only contribute a few percent to the observed rate constants, but slow enough such that instrument response time is not an issue. As expected, the rate of decarboxylation of radical **2b** was nearly the same as that for **2c** at 25 °C. Because the molar extinction coefficient for the ultimate diphenylalkyl radical product from **2c** is greater than that of the ultimate benzylic radical product from **2b**, the kinetics of decarboxylation of **2c** were more precise, and this radical was studied over a reasonably wide temperature range.

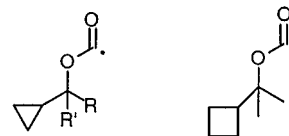
From the data in Table 1, the rate constants for decarboxylation of **2c** are described by eq 2 where errors are 2σ and θ = 2.3RT in kcal/mol and are shown graphically in Figure 2. Fragmentation reactions typi-

$$\log(k \times s) = (12.2 \pm 0.3) - (9.6 \pm 0.4)/\theta \quad (2)$$

cally have positive entropies of activation giving log A terms in the range of 15,²¹ but the decarboxylation of **2c** has ΔS[‡] = -4 cal (mol K)⁻¹, indicating that considerable reorganization is necessary to achieve the transition state. The log A term for **2c** is consistent with values in the range of 12–13 found by Beckwith and Bowry for decarboxylations of other alkoxy-carbonyl radicals,¹⁹ whereas the value for radical **5** was about 14.¹⁷

There now exists a reasonably complete set of rate constants for decarboxylation of alkoxy-carbonyl radicals (Table 2). The rate constants for the cyclopropyl-substituted systems are from the direct measurements of radical **2c** and nitroxyl radical trapping results of Beckwith and Bowry for radicals **6** and **7**.^{19,22} The rate constant for the tertiary alkyl system is from the results

for radical **5** measured by Rügge and Fischer.¹⁷ For the primary and secondary alkyl systems, we estimated the rate constants from product ratios reported for tin hydride trapping studies⁶ using the rate constant for tin hydride trapping estimated below, but these values should be considered lower limits because it is possible that some trapping by adventitious PhSeH occurred in the original studies (see below).



6: R = CH₃, R' = H
7: R = R' = CH₃

8

For both series of radicals in Table 2, a strong kinetic effect is apparent as one proceeds from a primary to a secondary to a tertiary radical product. This effect undoubtedly is related to the stabilities of the radical products, but it is also possible that there is a steric component at play. The large kinetic acceleration of the cyclopropyl group on alkoxy-carbonyl radical decarboxylations has been noted previously.¹⁹ The cyclobutyl ring in radical **8** also accelerates the decarboxylation reaction; specifically, the decarboxylation of **8** at 20 °C is approximately 4 × 10⁶ s⁻¹, nearly 40 times faster than that of tertiary radical **5**.^{23,24} The kinetic accelerations for the small-ring compounds might seem surprisingly large, but the cyclopropyl group stabilizes a radical center by about 2.5 kcal/mol as judged from low-temperature ESR measurements of the rotational barrier in cyclopropylcarbonyl radical.²⁵ Thus, the observed equality in the rate constants for decarboxylation of the tertiary alkyl system (radical **5**) and the primary cyclopropylcarbonyl system (radical **2c**) appears to be reasonable.

Tin Hydride Trapping Reactions. With the temperature-dependent function for decarboxylation available, radical **2c** is a "radical clock"²⁶ that, in principle, can be used to time bimolecular reactions of alkoxy-carbonyl radicals. For synthetic applications, radicals **2** have often been produced from selenocarbonates in tin hydride mediated radical-chain reactions, and we attempted to calibrate tin hydride trapping kinetics of radical **2c**. These studies proved to be quite complicated, and we obtained only an approximate rate constant for reaction of **2c** with Bu₃SnH at low temperature. We detail the studies here because we believe that the problems that arose in our work are likely to have introduced errors in previous competition kinetic studies and should be a continuing concern for those who plan to use alkoxy-carbonyl radicals in synthesis.

Because of the instability of PTOC oxalates in general and the fact that a pure sample of **1c** could not be obtained, our initial attempts to determine tin hydride trapping kinetics focused on the selenocarbonate derivative **9** as a precursor for radical **2c**. Precursor **9** was readily prepared by a literature route. Reactions of **9** in

(21) Benson, S. W. *Thermochemical Kinetics*, 2nd ed.; Wiley: New York, 1976.

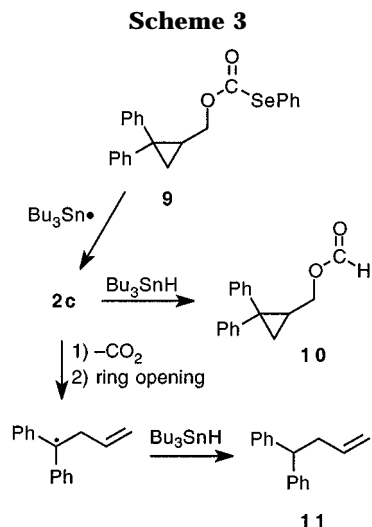
(22) The rate constant for radical **6** was determined at only one temperature.¹⁹ We have estimated the rate constant at 20 °C from this kinetic determination and the log A value for other alkoxy-carbonyl decarboxylation reactions.

(23) Ingold, K. U.; Maillard, B.; Walton, J. C. *J. Chem. Soc., Perkin Trans. 2* **1981**, 970–974.

(24) The rate constant for fragmentation calculated from the results in ref 23 has been multiplied by 5 in order to correct the diffusional rate constants.

(25) Walton, J. C. *Magn. Reson. Chem.* **1987**, 25, 998–1000.

(26) Griller, D.; Ingold, K. U. *Acc. Chem. Res.* **1980**, 13, 317–323.



benzene or toluene in the presence of Bu_3SnH with catalytic AIBN gave formate ester **10** and hydrocarbon **11**, which resulted from decarboxylation of **2c** followed by ring opening and trapping (Scheme 3).

One obvious problem with the use of precursor **9** was that the combined yields of **10** and **11** were only in the range of 45–75% and formate **10** was found to be unstable toward the reaction conditions. More problematic was the fact that, even with corrections for the loss of formate, the apparent kinetics for Bu_3SnH trapping of **2c** were absurd. Specifically, the apparent rate constant for tin hydride trapping decreased with increasing temperature in thermally initiated reactions conducted between 60 and 93 °C, and virtually no decarboxylation occurred in photochemically initiated reactions conducted in the 15–40 °C range.

The failure of the attempted kinetic study with selenocarbonate **9** is important for previously reported competition kinetic studies because essentially the same scheme was employed in this work as was used previously.⁶ It is quite likely that our poor results were due to production of small amounts of the highly reactive hydrogen atom transfer trapping agent PhSeH. Crich has demonstrated that diphenyl diselenide reacts with Bu_3SnH to form PhSeH and that the PhSe• radical rapidly reacts with tin hydride to regenerate PhSeH.²⁷ Further, benzeneselenol reacts with alkyl radicals about 3 orders of magnitude faster than does Bu_3SnH ,²⁸ and the difference in reactivity of the two reagents toward the alkoxy carbonyl radical **2c** is likely to be even greater (see below). A minor contamination of Ph_2Se_2 in the samples of selenocarbonate **9** could be the source of enough PhSeH to vitiate the kinetic results in the thermally initiated reactions with Bu_3SnH . For the photochemically initiated reactions at lower temperatures, the PhSe• radical is an expected product and PhSeH must be formed.

In retrospect, our problems with selenocarbonate **9**, especially in photochemically initiated reactions, were predictable in that reliable kinetics should not have been expected. One notes that the most complete study of the relative rates of decarboxylation of alkoxy carbonyl radicals in competition with Bu_3SnH trapping of which we

are aware also employed selenocarbonates.⁶ It seems apparent from the reported product ratios in that study that PhSeH was produced in photochemically initiated reactions, and it is possible that PhSeH interfered in thermally initiated reactions.

A series of reactions of PTOC oxalate **1c** in the presence of Bu_3SnH in THF at 2 °C was conducted. The total yields of **10** and **11** were in the 50–75% range, and the kinetic results were somewhat scattered. For four reactions, the values of k_{T} for reaction of Bu_3SnH with radical **2c** ranged from 1.1×10^5 to $2.5 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$ and averaged $1.7 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$. The amount of scatter was greater than one typically observes in competition kinetic studies, and poorer results might be expected at higher temperatures due to the instability of the precursor. The reaction of tin hydride with the alkoxy carbonyl radical **2c** at 2 °C is 1 order of magnitude less rapid than reactions with simple alkyl radicals,¹⁶ and this should serve as a guide for synthetic applications involving alkoxy carbonyl radicals.

Because the formyl C–H bond dissociation energy (BDE) of methyl formate is nearly identical to the secondary C–H BDE of propane,²⁹ one concludes that the slower reaction of Bu_3SnH with **2c** results from a more unfavorable polarization in the transition state of the reaction. In other words, an alkoxy carbonyl radical is more “nucleophilic” than an alkyl radical and reacts less rapidly with the electron-rich tin hydride even though the enthalpies of the two reactions are the same. This fact further compounds the problems that might arise when selenocarbonates are employed as precursors to alkoxy carbonyl radicals because the more nucleophilic radical will almost certainly react faster with the electron-deficient reagent PhSeH than does an alkyl radical. We estimate, therefore, that PhSeH reacts with alkoxy carbonyl radicals more than 4 orders of magnitude faster than does Bu_3SnH .

Typically, reactions of Bu_3SnH with alkyl radicals have log *A* terms of about 9,¹⁶ a value expected for a second-order reaction, and it is reasonable to assume that the log *A* values for reactions of Bu_3SnH with alkoxy carbonyl radicals will be similar. With this assumption and the determined rate constant for reaction of Bu_3SnH with radical **2c** at 2 °C of $1.7 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$, one calculates the Arrhenius function in eq 3 for reactions of alkoxy carbonyl radicals with tin hydride. This procedure might seem

$$\log(k \times \text{Ms}) = 9 - 4.8/\theta \quad (3)$$

somewhat arbitrary, but it is noteworthy that the rate constant calculated from eq 3 for reaction of tin hydride with alkoxy carbonyl radicals at 80 °C ($k_{\text{T}} = 1.1 \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$) is equal to the rate constant at 80 °C for reaction of tin hydride with acyl radicals, $\text{RC}(\cdot)=\text{O}$, recently determined by Chatgililoglu and co-workers.^{30,31} We believe that rate constants calculated from eq 3 in the vicinity of ambient temperature are likely to be accurate to within a factor of 2.

Kinetics of Alkoxy carbonyl Radical Cyclizations. One can use the approximate rate constants available

(29) Griller, D.; Kanabus-Kaminska, J. M.; Maccoll, A. *THEOCHEM* **1988**, *40*, 125–131.

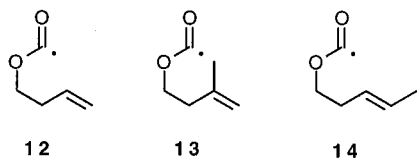
(30) Chatgililoglu, C.; Ferreri, C.; Lucarini, M.; Pedrielli, P.; Pedulli, G. F. *Organometallics* **1995**, *14*, 2672–2676.

(31) Chatgililoglu, C.; Lucarini, M. *Tetrahedron Lett.* **1995**, *36*, 1299–1302.

(27) Crich, D.; Yao, Q. W. *J. Org. Chem.* **1995**, *60*, 84–88.

(28) Newcomb, M.; Varick, T. R.; Ha, C.; Manek, M. B.; Yue, X. *J. Am. Chem. Soc.* **1992**, *114*, 8158–8163.

from eq 3 and previous results from Bachi's group to estimate the rate constants for cyclizations of alkoxy-carbonyl radicals. Bachi and Bosch reported the production of lactones from reactions of *O*-alkenyl and *O*-alkynyl phenyl selenocarbonates in the presence of tin hydride at 80 °C.⁸ Radicals **12** and **13** gave mixtures of lactones and formate esters when the tin hydride concentration was high. From the reported product ratios and tin hydride concentrations and using a rate constant for tin hydride trapping at 80 °C of $1.1 \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$ (from eq 3), the rate constants at 80 °C for cyclization are $4 \times 10^6 \text{ s}^{-1}$ (**12**) and $4 \times 10^5 \text{ s}^{-1}$ (**13**). At 80 °C, the 5-*exo* cyclizations of radicals **12** and **13** apparently are about 2–3 times faster than cyclizations of their respective carbon analogues, the 5-hexenyl and 5-methyl-5-hexenyl radicals.^{16,32}



A caution for the rate constants for cyclization of **12** and **13** is necessary. There is a possibility that reactive PhSeH was produced in the reactions that would vitiate the kinetic calculation (see above). However, the reasonable order of magnitude reduction in the rate constant for cyclization of **13** relative to that for cyclization of **12** is consistent with the steric effect expected on the basis of the reactivities of substituted 5-hexenyl radical analogues,³² and the concentrations of tin hydride were quite high (1–3.5 M) in these two reactions. In the case of radical **14**, however, PhSeH apparently was produced in significant amounts relative to the tin hydride. Bachi and Bosch⁸ report a mixture of cyclic and acyclic products from reaction of radical **14** in the presence of 0.02 M Bu₃SnH. From their results, one would calculate a rate constant for cyclization of **14** that is more than 1 order of magnitude smaller than that for radical **12**; this seems to be unreasonable because the rate constants for cyclization of **12** and **14** should be nearly equal on the basis of alkyl substituent effects in 5-hexenyl radicals.³²

Conclusion

The PTOC oxalates are of limited utility for LFP kinetics studies due to their high reactivity, which precludes purification and handling in most cases. The directly measured rate constants for alkoxy-carbonyl radical decarboxylations that could be obtained from PTOC oxalates are consistent with previous results and serve to verify a kinetic scale for these decarboxylation reactions that was based on kinetic studies of one radical. From limited data, approximate rate constants for reactions of alkoxy-carbonyl radicals with Bu₃SnH were determined, and these were used to calculate approximate rate constants for 5-*exo* cyclizations of alkoxy-carbonyl radicals from previously reported results. Alkoxy-carbonyl radicals cyclize slightly faster than analogous alkyl radicals but react 1 order of magnitude less rapidly with Bu₃SnH than do alkyl radicals, an ideal combination for synthetic applications. For alkoxy-carbonyl radicals

derived from primary and secondary alcohols, decarboxylation is too slow to compete efficiently with either cyclization or tin hydride trapping, but for radicals derived from tertiary alcohols the decarboxylation reaction can be competitive with the other reactions. When selenocarbonate precursors to alkoxy-carbonyl radicals are employed, one must be aware of the fact that generation of PhSeH from small impurities of PhSeSePh or from photolysis of the precursor can be problematical.

Experimental Section

General Methods. NMR spectra were recorded at 300 MHz (¹H) or 75 MHz (¹³C). GC analyses were performed on a Varian 3300 gas chromatograph (thermoconductivity detector) on a 15 m × 0.53 mm wide-bore capillary column. Reagents were purchased from Aldrich Chemical Co. unless noted. The sodium salt of *N*-hydroxypyridine-2-thione (Olin) was isolated as previously described.³³ Bu₃SnH was prepared by the method of Hayashi *et al.*³⁴

Preparation of PTOC Oxalates. The following general procedure was employed. A solution of alcohol (2 mmol) in 2 mL of CH₂Cl₂ was added to a solution of oxalyl chloride (4 mmol) in 10 mL of CH₂Cl₂ at room temperature. The mixture was stirred at room temperature for 24 h, and solvent and excess oxalyl chloride were removed by distillation under a water aspirator vacuum. The acid chlorides obtained by this procedure were stored under nitrogen.

A reaction vessel was protected from light by means of aluminum foil and charged with 1 mmol of the acid chloride. The vessel was cooled in an ice–water bath, and the sodium salt of *N*-hydroxypyridine-2-thione (1.1 mmol) in 15 mL of benzene was added. A catalytic amount of DMAP was added to the mixture, and the reaction was stirred for 1.5 h at room temperature. The crude mixture was filtered through an oven-dried porous glass filter in the dark. The solvent was removed in the dark on a rotary evaporator with a bath temperature of 20 °C. Crude PTOC oxalates were obtained in ca. 90% yield. Attempted chromatography on silica gel, alumina, or reversed-phase (C-18) columns resulted in decomposition. The crude PTOC oxalates, which were ≥50% pure as judged by NMR spectroscopy, were used in LFP studies.

***N*-[[[(Benzoyloxy)oxalyl]oxy]pyridine-2-thione (1a).** Following the general procedure, the acid chloride prepared from benzyl alcohol (0.18 g, 0.91 mmol) was allowed to react with the sodium salt of *N*-hydroxypyridine-2-thione (0.15 g, 1.0 mmol) to give **1a** (0.24 g, 75% pure). ¹H NMR (CDCl₃): δ 5.38 (s, 2H), 7.15–7.50 (m, 7H), 7.81 (dd, *J* = 2.1, 8.1 Hz, 1H), 8.30 (dd, *J* = 1.2, 6.3 Hz, 1H). ¹³C NMR (CDCl₃): δ 69.71, 124.08, 128.30, 128.79, 128.88, 129.13, 132.60, 139.61, 157.19.

***N*-[[[(*trans*-2-Phenylcyclopropyl)methoxy]oxalyl]oxy]pyridine-2-thione (1b).** Following the general procedure, the acid chloride prepared from (*trans*-2-phenylcyclopropyl)methanol³⁵ (0.15 g, 0.63 mmol) was allowed to react with the sodium salt of *N*-hydroxypyridine-2-thione (0.10 g, 0.69 mmol) to give **1b** (0.10 g, 50% pure). ¹H NMR (CDCl₃): δ 1.00–1.20 (m, 2H), 1.50–1.70 (m, 1H), 1.90–2.10 (m, 1H), 4.15–4.45 (m, 2H), 6.77 (dt, *J* = 1.5, 6.9 Hz, 1H), 7.00–7.60 (m, 8H), 7.91 (dd, *J* = 1.5, 9.2 Hz, 1H), 8.48 (dd, *J* = 1.5, 9.2 Hz, 1H).

***N*-[[[(2,2-Diphenylcyclopropyl)methoxy]oxalyl]oxy]pyridine-2-thione (1c).** Following the general procedure, the acid chloride from (2,2-diphenylcyclopropyl)methanol³⁶ (0.15 g, 0.48 mmol) was allowed to react with the sodium salt of *N*-hydroxypyridine-2-thione (0.078 g, 0.52 mmol) to give **1c** in 88% yield. ¹H NMR (CDCl₃): δ 1.42 (dd, *J* = 5.5, 9.3 Hz,

(33) Esker, J. L.; Newcomb, M. *J. Org. Chem.* **1993**, *58*, 4933–4940.

(34) Hayashi, K.; Iyoda, J.; Shiihara, I. *J. Organomet. Chem.* **1967**, *10*, 81–94.

(35) Gajewski, J. K.; Squicciarini, M. P. *J. Am. Chem. Soc.* **1989**, *111*, 6717–6728.

(36) Biro, V.; Voegtli, W.; Lauger, P. *Helv. Chim. Acta* **1954**, *37*, 2230–2247.

(32) Beckwith, A. L. J.; Blair, I. A.; Phillipou, G. *Tetrahedron Lett.* **1974**, 2251–2254.

1H), 1.52 (t, $J = 5.5$ Hz, 1H), 2.05–2.21 (m, 1H), 4.05 (dd, $J = 8.1, 11.1$ Hz, 1H), 4.25 (dd, $J = 6.6, 11.1$ Hz, 2H), 7.10–7.50 (m, 12H), 7.86 (dd, $J = 2.1, 8.4$ Hz, 1H), 8.33 (dd, $J = 1.5, 6.9$ Hz, 1H). ^{13}C NMR (CDCl_3): δ 18.22, 23.15, 36.53, 69.61, 126.30, 127.80, 128.41, 128.66, 130.23, 132.70, 139.56.

Selenocarbonic Acid *O*-(2,2-Diphenylcyclopropyl)methyl Ester *Se*-Phenyl Ester (9). To a solution of (2,2-diphenylcyclopropyl)methanol³⁶ (0.52 g, 2.3 mmol) in 10 mL of CH_2Cl_2 was added a 1.92 M solution of phosgene in toluene (1.8 mL, 3.5 mmol) at room temperature. The mixture was stirred at room temperature for 48 h, and solvent and excess phosgene and toluene were removed by distillation under a water aspirator vacuum followed by high vacuum to yield 0.67 g (2.3 mmol, 101%) of (2,2-diphenylcyclopropyl)methoxy chloroformate. ^1H NMR (CDCl_3): δ 1.44 (dd, $J = 5.4, 9.0$ Hz, 1H), 1.50 (t, $J = 5.4$ Hz, 1H), 2.05–2.20 (m, 1H), 4.02 (dd, $J = 8.4, 11.4$ Hz, 1H), 4.18 (dd, $J = 6.6, 11.1$ Hz, 1H), 7.15–7.45 (m, 10 H). ^{13}C NMR (CDCl_3): δ 18.19, 23.15, 36.43, 73.49, 126.39, 127.20, 127.75, 128.45, 128.69, 130.19, 139.85, 145.20.

Under a nitrogen atmosphere, to a solution of diphenyl diselenide (0.39 g, 0.125 mmol) in 10 mL of THF and absolute ethanol (10:1, v:v) was added NaBH_4 (0.17 g, 0.45 mmol), and the mixture was stirred for 30 min at room temperature. During the reaction time a complete disappearance of the bright yellow color attributed to PhSeSePh was observed. Excess sodium borohydride was quenched by careful addition of 0.2 mL of water. The reaction mixture was stirred for 5 min. To the colorless solution thus obtained was added a solution of (2,2-diphenylcyclopropyl)methoxy chloroformate (0.67 g, 2.3 mmol) in 5 mL of THF via cannula. The mixture was stirred for 24 h at room temperature. The reaction mixture was worked up with saturated aqueous NH_4Cl solution and dried over anhydrous MgSO_4 . Purification by column chromatography (silica gel, hexanes–ethyl acetate, 10:1) allowed isolation of 0.82 g (2.0 mmol, 87%) of the selenocarbonate **9**. ^1H NMR (CDCl_3): δ 1.38 (dd, $J = 5.1, 9.0$ Hz, 1H), 1.43 (t, $J = 5.4$ Hz, 1H), 2.06 (m, 1H), 3.87 (dd, $J = 8.4, 11.4$ Hz, 1H), 4.24 (dd, $J = 6.3, 11.1$ Hz, 1H), 7.10–7.50 (m, 13 H), 7.65–7.75 (m, 2H). ^{13}C NMR (CDCl_3): δ 18.03, 23.74, 36.30, 69.57, 126.20, 126.95, 127.86, 128.35, 128.51, 129.11, 129.30, 130.33, 135.88, 140.23, 145.67. MS (70 eV): m/z (relative intensity) 408 (1.4, M^+), 314 (0.9), 207 (26), 165 (17), 129 (100), 91 (83), 77 (14). HRMS: calcd for $\text{C}_{23}\text{H}_{20}\text{O}_2^{80}\text{Se}$ 408.0629, found 408.0633.

Formic acid (*trans*-2,2-diphenylcyclopropyl)methyl ester (10) was prepared by DCC esterification of the alcohol (83% yield). ^1H NMR (CDCl_3): δ 1.38 (dd, $J = 5.1, 8.7$ Hz, 1H), 1.44 (t, $J = 5.1$ Hz, 1H), 2.00–2.15 (m, 1H), 3.86 (ddd, $J = 1.0$ Hz, 7.8 Hz, 11.7 Hz, 1H), 4.06 (ddd, $J = 1.0, 6.6$ Hz, 11.7 Hz, 1H), 7.10–7.40 (m, 10 H), 8.06 (t, $J = 1.0$ Hz, 1H). ^{13}C NMR

(CDCl_3): δ 18.13, 23.71, 26.24, 32.84, 65.26, 126.17, 127.76, 128.35, 128.53, 130.29, 140.32, 160.95. MS (70 eV): m/z (relative intensity) 252 (M^+ , 1), 207 (17), 206 (100), 205 (29), 191 (27), 178 (21), 165 (26), 129 (21), 128 (21), 115 (939), 91 (65). HRMS: calcd for $\text{C}_{17}\text{H}_{16}\text{O}_2$ 252.1150, found 252.1148.

4,4-Diphenyl-1-butene (11) was prepared as previously reported.¹²

Laser flash photolysis kinetic studies were performed on an Applied Photophysics LK-50 kinetic spectrophotometer employing a Spectron Nd:YAG laser.¹⁰ Solutions of the PTOC esters **1** in spectral-grade THF were prepared such that the total absorbance at 355 nm was ca. 0.5. The solutions were purged with helium and thermally equilibrated at the desired temperature in a jacketed addition funnel. The solutions were allowed to flow through a flow cell for the LFP studies. Temperatures were measured with a thermocouple placed directly in the flowing solution stream ca. 1 cm above the irradiation zone. Time-resolved spectra were determined for **2a** and **2c**. Kinetic measurements were obtained in the region 315 nm for **2a** and 336 nm for **2c**. Each kinetic value reported is an average of 5–15 independent runs.

Indirect Kinetic Studies of PTOC Oxalate 2c. All handling, preparation of solutions, and thermal equilibration of **2c** solutions prior to actual trapping reaction were conducted under red light. Solvents were degassed under high vacuum by three freeze–thaw cycles. PTOC oxalate **2c** (ca. 0.1 mmol), tin hydride (0.15–0.22 mmol), and an internal standard hexadecane (1 μL) were dissolved in 1 mL of benzene in a volumetric flask. The reaction mixture was placed in an ice–water bath and equilibrated for 10 min. The reaction mixture was irradiated at the distance ca. 0.3 m with a 150 W tungsten-filament lamp for 1 h. The average temperature of the bath during the reaction was 2 °C. The crude reaction mixture was analyzed by GC. Molar amounts of products **10** and **11** were calculated from the chromatogram peak areas using predetermined response factors.

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Supporting Information Available: ^1H and ^{13}C NMR spectra of the acid chlorides used for preparation of PTOC oxalates **1** and compounds **1** and **9** (18 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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