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PAPER

Rate constants for cyclizations of α-hydroxy radical clocks†‡

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The 1-hydroxy-1-methyl-6,6-diphenyl-5-hexenyl radical (**4a**) and the 1-hydroxy-1-methyl-7,7-diphenyl-6-heptenyl radical (**4b**) were prepared from the corresponding PTOC esters (anhydrides of a carboxylic acid and *N*-hydroxypyridine-2-thione). The key step in the synthetic method for the precursors was a coupling reaction of the respective carboxylic acids with the thiohydroxamic acid, which was conducted for *ca.* 5 min and followed rapidly by chromatography. Rate constants for cyclizations of radicals **4a** and **4b** in acetonitrile and in THF were measured directly between –30 and 60 °C by laser flash photolysis methods. The Arrhenius functions in acetonitrile are $\log k = 9.9–2.6/2.303RT$ and $\log k = 8.9–4.4/2.303RT$ (kcal mol^{-1}) for **4a** and **4b**, respectively. Rate constants for cyclizations at room temperature of 9×10^7 s^{-1} and 4×10^5 s^{-1} are somewhat larger than the rate constants for cyclizations of analogous alkyl radicals. Crude rate constants at room temperature for H-atom trapping of **4a** by thiophenol and **4b** by *t*-butylthiol were $k_T = 1.2 \times 10^9$ M^{-1} s^{-1} and $k_T = 2 \times 10^7$ M^{-1} s^{-1}, respectively, which are modestly larger than rate constants for reactions of alkyl radicals with the same trapping agents.

Introduction

In the past few decades, a rapidly increasing knowledge of radical kinetics has been linked to fundamental advances in applications of radicals in organic synthesis and in understanding radical reactions in biology. Many of the practical applications of radical kinetics have relied on indirect kinetic studies using radical clock methodology,[1,2] where a reaction of interest competes with a calibrated (typically first-order) radical clock reaction, and the rate constant of interest is calculated from product ratios determined after the reaction and the known rate constant for the clock reaction. Often, radical clocks involve intramolecular rearrangement reactions such as radical cyclizations, and early radical clock calibrations were reported by pioneers in organic radical chemistry such as Walling[3] and Beckwith.[4,5]

A wide range of radical clocks exists, but the number of calibrated clocks for substituted carbon-centered radicals is somewhat limited. In this work, we report absolute kinetic studies of cyclizations of two α-hydroxy-substituted radicals that can serve as clocks. α-Hydroxy radicals are produced in a number of contexts, and perhaps the two most important are in biology and in commercial radical polymerization chemistry. In biology, α-hydroxy radicals are present in the form of DNA and RNA radicals, in both productive and destructive reactions, and in enzyme-catalyzed reactions of alcohols, polyols, and sugars.[6–9] In radical polymerizations, α-hydroxy radicals are produced in efficient photochemical cleavages of α-hydroxyketone photo-initiators, and these nucleophilic radicals rapidly react with acrylates.[10–12] In synthetic applications of radicals, unprotected alcohol groups are acceptable because the hydroxy group is effectively inert to radicals due to the high bond energy of the O–H bond, but synthetic applications of α-hydroxy radicals are uncommon due to difficulties in preparation of precursors for these species.

Results and Discussion

The kinetics method used in this work is similar to that previously reported by our group for a number of direct kinetic studies using laser flash photolysis (LFP) methods,[13] and the technique was previously applied for kinetic studies of related α- and β-methoxy-substituted radicals.[14,15] The radical precursors were Barton PTOC esters **1**.[16,17] These precursors contain a long wavelength chromophore centered at about 360 nm, and they are readily cleaved by photolysis with 355 nm light from a Nd-YAG laser (Scheme 1). The initial photochemical reaction cleaves the N–O bond of the precursor to give the pyridine-2-thiyl radical (**2**) and acyloxyl radicals **3**. The acyloxyl radicals decarboxylate rapidly to give α-hydroxy radicals **4**. Cyclizations of radicals **4** give diphenylalkyl radicals **5**, which have a strong long wavelength chromophore centered at *ca.* 335 nm. In LFP applications with Nd-YAG lasers and fast photomultiplier tubes, first-order rate constants in excess of 1×10^8 s^{-1} can be measured.

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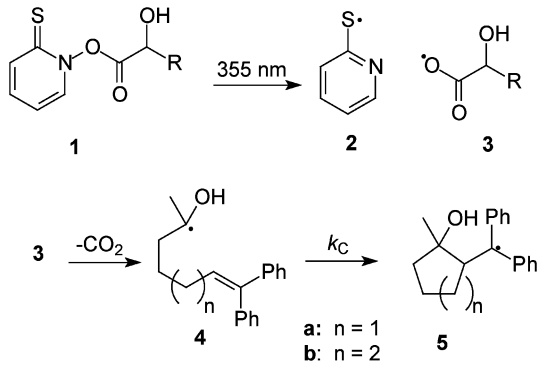
† This work is dedicated to the memory of Athel Beckwith, a teacher and scientist from whom we learned how to study chemistry by example. His pioneering advances in radical chemistry laid the foundation for much of the current radical clock methodology.

‡ Electronic supplementary information (ESI) available: Kinetic results and NMR spectra. See DOI: 10.1039/c0ob00588f



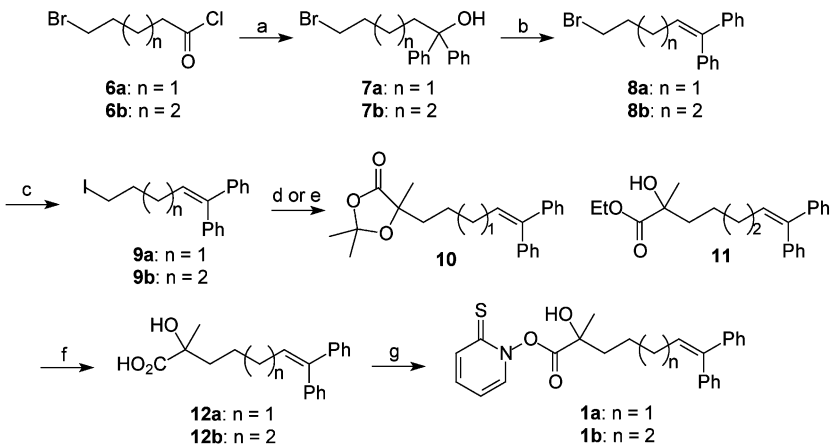
Scheme 1

Barton PTOC esters[17] were originally designed for synthetic applications of radicals and are seldom isolated when applied in synthesis.[16] The preparative methods we used were generally routine, but isolation of the precursors was necessary, and PTOC esters from α-hydroxy acids have not been reported previously to our knowledge. Precursors **1** proved to be unstable when stored for short periods at room temperature, as one might expect for compounds containing the reactive PTOC moiety, a mixed anhydride of the thiohydroxamic acid and a carboxylic acid, and an unprotected hydroxy group. Nonetheless, they could be isolated in acceptably pure form when they were prepared in short duration reactions and purified quickly. We note that the PTOC ester entry for unprotected tertiary α-hydroxy radicals such as those prepared here might have synthetic utility.

The preparative route for radical precursors **1** is shown in Scheme 2. 5-Bromopentanoyl chloride (**6a**) and 6-bromohexanoyl chloride (**6b**), prepared from reaction of the acids with oxalyl chloride, were treated with excess phenylmagnesium bromide to give the diphenyl-substituted alcohols **7** that were dehydrated to give the known bromoalkenes **8**.[18–20] The bromides were converted to iodides **9**; **9a** is a known and characterized compound.[21] Iodides **9** were used in enolate alkylation reactions that gave derivatives of the desired α-hydroxy acids (**12**) in the form of the ketal (**10**) and ester (**11**). The ketal enolate alkylation reaction giving **10** was attempted first. Due to the modest yield of that reaction, we conducted the second alkylation with the enolate from ethyl lactate,[22] but the yield of **11** was similar to the yield of **10**. Hydrolyses of **10** and **11** gave acids **12** that were converted to the PTOC esters. Acids **12** were characterized by NMR spectroscopy and high resolution mass spectrometry.

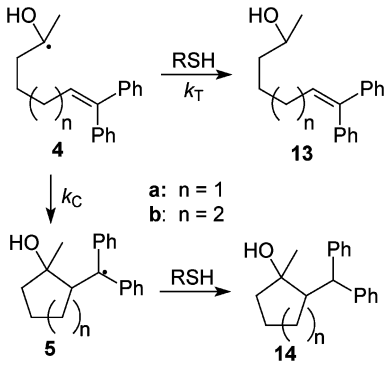
As noted, we are unaware of previous preparations of PTOC esters from α-hydroxy acids. In our initial attempts to couple acids **12** with *N*-hydroxypyridine-2-thione, unidentified products were obtained when the reactions were conducted under typical reactions conditions of room temperature and reaction times of *ca.* 30 min to 3 h. Acceptable yields of **1** were obtained when the reaction time was reduced to 5 min, the reaction mixture was poured directly onto a chromatography column, and the product was rapidly eluted from the column. We used 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide as the coupling agent to avoid precipitation of the urea by-product, which would complicate the rapid chromatography step. The PTOC esters were obtained in 45–50% yields in about 95% purity as judged from NMR spectroscopy, which was acceptable for our studies. In our hands, these compounds decomposed on standing at room temperature or when stored at *ca.* 0 °C for more than a day. The samples used in the kinetic studies were stored at −78 °C and used within a few days of preparation.

The conception of our kinetic studies was that radicals **4** would cyclize rapidly to give product radicals that are readily detected by fast UV-visible spectroscopy. We conducted preparative reactions with PTOC esters **1** to ensure that the overall reaction sequence was as expected. Thus, PTOC esters **1** were allowed to react in radical chain reactions in the presence of thiols. The thiols can trap the initially formed α-hydroxy radicals **4** by H-atom transfer in competition with the cyclization reactions to give acyclic alcohols **13**, and they also will react with cyclic radicals **5** to give hydrocarbon products **14** (Scheme 3). We used thiophenol as the trapping agent for the reaction of radical **4a** because the cyclization reaction is fast enough to compete with this trapping agent. For



Key: (a) PhMgBr, THF; (b) *p*-TsOH, benzene; (c) NaI, acetone; (d) 2,2-5-trimethyl-1,3-dioxolane-4-one, LDA, THF; (e) ethyl lactate, 2 equiv LDA, THF; (f) LiOH, THF, H_2O; (g) 1-hydroxy-1*H*-pyridine-2-thione, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide, CH_2Cl_2.

Scheme 2



Scheme 3

the 6-*exo* cyclization of radical **4b**, we used *tert*-butylthiol as the trapping agent.

In practice, radical chain reactions of PTOC esters **1** gave mixtures of **13** and both diastereomers of **14**. For the reaction of radical **4a** in the presence of thiophenol, we obtained **13a** and a *ca.* 2 : 1 mixture of diastereomers of **14a** that were partially purified by chromatography. From ^{1}H 1-D NOE experiments, the major diastereomer in the mixture was assigned as the (1*R*,2*R*) and (1*S*,2*S*) mixture. Specifically, irradiation of the protons of the methyl groups in the diastereomers of **14a** resulted in enhanced absorptions from the benzhydryl C–H for the (1*S*,2*R*) diastereomer and from the C2-H for the (1*R*,2*R*) diastereomer.

For the reaction of radical **4b** in the presence of *t*-butylthiol, a mixture of **13b** and diatereromers **14b** was obtained. Products **14b** were again approximately a 2 : 1 mixture as determined from NMR spectroscopy, but the diastereomers were not separated. The reaction of **4b** with *t*-butylthiol also gave some 8,8-diphenyl-7-octen-2-one from disproportionation of radical **4b**. This type of behavior was seen previously in kinetic studies of alkyl radical cyclizations in the presence of *t*-butylthiol,[13] which does not react fast enough in chain reactions to prevent accumulation of relatively high radical concentrations.

Rate constants for cyclizations of radicals **4** were measured directly in laser flash photolysis (LFP) studies.[13] Dilute solutions of PTOC ester precursors **1** were sparged with helium in a temperature controlled addition funnel and allowed to flow through the reaction cell. Fresh samples were irradiated with 355 nm light from a Nd-YAG laser, and signal growth or decay was monitored over the range 300–560 nm.

Fig. 1 shows a time-resolved spectrum observed from reaction of radical **4a**. A strong signal with $\lambda_{max} \approx 335$ nm growing in with time is attributed to the diphenylalkyl radical **5a** formed by cyclization of **4a**.[13] A broad signal with $\lambda_{max} \approx 490$ nm is decaying with time; this signal is due to the pyridine-2-thiyl radical (**2**), for which the UV-visible spectrum has been reported.[23] On the time scale of this kinetic measurement, only a small amount of decay of **2** was observed. The inset in Fig. 1 shows the kinetic trace recorded at 335 nm, which was solved for first-order exponential growth.

Kinetic studies for radicals **4** were performed in acetonitrile and in THF over the temperature range –30 to 60 °C. Each rate constant was determined from the average of ten independent kinetic measurements. The 5-*exo* cyclizations of radical **4a** were so fast that essentially no competing reaction occurred. The 6-*exo* cyclization of **4b** was fast enough such that reaction with residual oxygen would not be appreciable. Reactions of radicals with the PTOC precursors have second-order rate constants on the order of 10^6 M^{-1} s^{-1},[24] and these reactions cannot compete with the cyclizations given the low concentrations of precursors used in LFP studies. Therefore, the measured rate constants for cyclizations of radicals **4** were not corrected, and these values are listed in Tables S1 and S2 in the ESI.‡ The results are shown in the form of Arrhenius functions in Fig. 2, and the Arrhenius parameters are collected in Table 1. Within experimental limits, the cyclization reactions displayed no solvent effects.

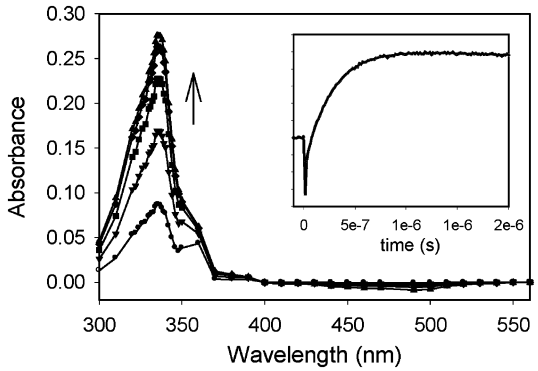


Fig. 1 Time-resolved spectrum from reaction of radical **4a** at room temperature. The traces show absorbances at 24, 36, 56, 89, and 223 ns after the laser pulse. The inset shows the kinetic trace recorded at 335 nm and solved for a single exponential growth function.

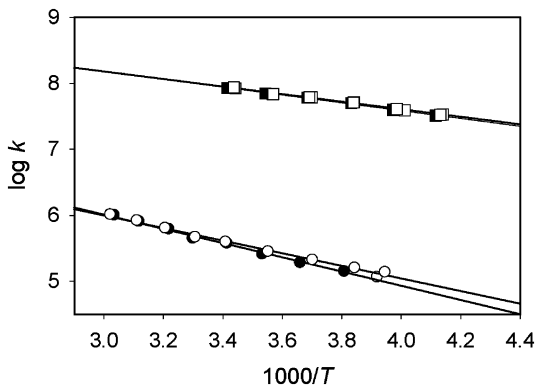


Fig. 2 Temperature-dependent kinetics of cyclizations of radicals **4**. Rate constants for the 5-*exo* cyclizations of **4a** are squares, and those for 6-*exo* cyclizations of **4b** are circles. Reactions in acetonitrile are filled symbols, and reactions in THF are unfilled symbols. The lines are regression fits.

Table 1 Arrhenius parameters for cyclizations of radicals **4**[a]

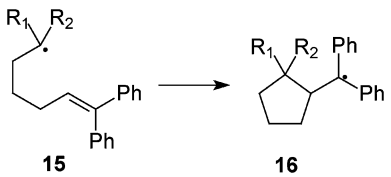
Radical	Solvent	log A[b]	E_A[c]/kcal mol^{-1}	$k_{20\,°C}$/s^{-1}[d]
4a	CH_3CN	9.9 ± 0.1	2.6 ± 0.1	9.1×10^7
	THF	10.0 ± 0.1	2.7 ± 0.2	9.7×10^7
4b	CH_3CN	8.9 ± 0.2	4.4 ± 0.3	4.1×10^5
	THF	9.2 ± 0.2	4.9 ± 0.3	3.5×10^5

[a] From analysis of the rate constants in ESI;‡ errors are 2σ. [b] Pre-exponential factor. [c] Activation energy. [d] Rate constant at 20 °C calculated from the Arrhenius function.

Table 2 Rate constants for 5-*exo* cyclizations of radicals **4a** and **15** in acetonitrile at 20 °C

Radical	R_1	R_2	k/s^{-1}	Ref
4a	OH	CH_3	9.2×10^7	this work
15a	H	H	4×10^7	13
15b	H	CH_3	2×10^7	19
15c	CH_3	CH_3	1×10^7	19
15d	OCH_3	H	3.6×10^7	14
15e	OCH_3	CH_3	6.1×10^7	25
15f	CN	CH_3	2×10^5	19
15g	CO_2Et	CH_3	4×10^5	19

Rate constants for 5-*exo* and 6-*exo* cyclizations of several terminal diphenylethene radicals with various substituents at the radical center have been measured directly.[13,14,19,25] Table 2 lists the rate constants at 20 °C for 5-*exo* cyclizations for radical **4a** and radicals **15** (Scheme 4). Radical stabilizing groups typically have small effects on rate constants for cyclizations because the substituent group has counterbalancing effects on both the reactant and product radical. Thus, the rate constants for cyclizations of the hydroxy-substituted radical (**4a**) and the methoxy-substituted radicals (**15d**, **15e**) are similar to those for the primary (**15a**), secondary (**15b**), and tertiary (**15c**) radicals. Note that a substituent can have a major effect on the rate of cyclization when it is conjugated with the radical center (giving a planar structure) such that increased steric compression is present in the transition state for the cyclizations, and this effect is seen in radicals **15f** and **15g**.[19] The hydroxy radical substituent in radical **4a** does not give a planar radical center, and the cyclization reaction is faster than that of the unsubstituted parent radical (**15a**).



Scheme 4

Although the data set is not as complete, similar conclusions can be made for the 6-*exo* cyclization of radical **4b**. The rate constant for cyclization of this radical at room temperature is 4×10^5 s^{-1}. The important comparisons are for the 6-*exo* cyclizations of the 7,7-diphenyl-6-heptenyl radical ($k = 5 \times 10^5$ s^{-1}),[19] the 1-methyl-7,7-diphenyl-6-heptenyl radical ($k = 2 \times 10^5$ s^{-1}),[19] the 1-methoxy-7,7-diphenyl-6-heptenyl radical ($k = 1.4 \times 10^5$ s^{-1}),[14] and the 1-methyl-1-methoxy-7,7-diphenyl-6-heptenyl radical ($k = 1 \times 10^5$ s^{-1}).[25] The α-hydroxy-substituted radical **4b** cyclizes somewhat faster than most of its analogs.

We did not study cyclizations of α-hydroxy radicals with unsubstituted alkene moieties at the terminus, but it is noteworthy that the 5-*exo* cyclization of the 1-methoxy-5-hexenyl radical was determined to be equal to that of the unsubstituted 5-hexenyl radical.[26] From that observation and the fact that radical **4a** cyclizes about 1.5 times as fast as radical **15e**, one should expect that the 1-hydroxy-5-hexenyl radical will cyclize with rate constants similar to or somewhat larger than those of the 5-hexenyl radical.[27] At room temperature, the predicted rate constant for cyclization of the 1-hydroxy-5-hexenyl radical is $2–3 \times 10^5$ s^{-1}.

The results of the trapping reactions we conducted provide approximate second-order rate constants for reactions of the thiols with radicals **4**. As indicated in Scheme 3, the cyclization rate constant and ratio of products can be used to calculate a trapping rate constant by indirect competition kinetics methods.[2] This method does not give highly precise rate constants when only one competition reaction is studied, but a single competition study does give approximate kinetic values. For reaction of radical **4a** in the presence of thiophenol at room temperature, we calculate an approximate rate constant for trapping of $k_T = 1.2 \times 10^9$ M^{-1} s^{-1}. For reaction of **4b** with *t*-butylthiol, we calculate a rate constant of $k_T = 2 \times 10^7$ M^{-1} s^{-1}. We estimate that the errors in these values are on the order of ± 20%.

Although admittedly low precision, the second-order rate constants for reactions of the thiols with radicals **4** are larger than those for reactions of the same thiols with unsubstituted primary alkyl radicals. Thiophenol reacts with a primary alkyl radical at 25 °C with a rate constant $k_T = 1.4 \times 10^8$ M^{-1} s^{-1},[28,29] and *t*-butylthiol reacts with a primary alkyl radical at 25 °C with a rate constant of 8×10^6 M^{-1} s^{-1}.[30] That is, the thiophenol reaction with **4a** is nearly an order of magnitude faster than with an alkyl radical, and the *t*-butylthiol reaction with **4b** is about a factor of 2.5 times faster than reaction with an alkyl radical. The increased reactivity of the hydroxy-substituted radicals presumably reflects favorable polarization in the transition state for the H-atom transfer reaction where the H-atom of the thiol has relatively positive charge and the hydroxy-substituted radicals have nucleophilic character even greater than that of simple alkyl radicals. Such nucleophilic behavior for an α-hydroxy radical was observed by Fischer and co-workers for addition reactions of hydroxy-substituted radicals to alkenes.[10] Previously, the rate constants for reactions of an alkanethiol with a methoxy-substituted radical and an unsubstituted analog were found to be approximately equal,[15] and the assumption was made then that rate constants for hydroxy-substituted radicals with thiols would be similar to those of alkyl radicals, but we now suggest that the reactions of the thiols with α-hydroxy radicals are faster than those with alkyl radicals.

Conclusions

The PTOC ester method was shown in this work to be viable for the production of tertiary α-hydroxy radicals, and this method might have synthetic utility. Rate constants for 5-*exo* and 6-*exo* cyclizations of the α-hydroxy radicals **4a** and **4b** were measured by laser flash photolysis methods. At room temperature, these reactions have rate constants of $k = 9 \times 10^7$ s^{-1} and $k = 4 \times 10^5$ s^{-1}, respectively, which are somewhat faster than cyclizations of analogous alkyl radicals. Reactions of these radicals with thiophenol and *t*-butylthiol are efficient, and the rate constants for H-atom trapping from the thiols are somewhat larger than those for H-atom trapping of alkyl radicals.

Experimental

General

Nuclear magnetic resonance (NMR) spectra were recorded in deuterated solvents on 300 or 500 MHz instruments. Chemical shifts in ^{1}H NMR spectra are reported in parts per million (ppm) relative to tetramethylsilane (TMS) ($\delta = 0$ ppm). Chemical shifts of ^{13}C NMR spectra are reported in ppm using TMS (δ = 0 ppm) or the central peak of $CDCl_3$ (δ = 77.23 ppm) for calibration. High resolution mass spectra were acquired by the Mass Spectrometry Laboratory (MSL) of the University of Illinois at Urbana/Champaign. All reagents were purchased from Sigma–Aldrich Co. or Thermo–Fisher Scientific Inc. and were used as received unless noted. THF, Et_2O, and CH_2Cl_2 were purified and dried in a commercial solvent system. Air- or moisture-sensitive reactions were performed under nitrogen or argon. Reaction products were purified by column chromatography on silica gel unless noted.

5-Bromo-1,1-diphenylpent-1-ene (8a) and 6-bromo-1,1-diphenylhex-1-ene (8b)

were prepared as previously reported and had ^{1}H and ^{13}C NMR that matched those previously reported.[18–20]

5-Iodo-1,1-diphenylpent-1-ene (9a)

was prepared from bromide **8a** by reaction with NaI in acetone (similar to the reaction described below) and had NMR spectra that matched those previously reported.[21]

6-Iodo-1,1-diphenylhex-1-ene (9b)

Bromide **8b** (20.74 g, 65.8 mmol) was dissolved in 250 mL of acetone, and NaI (30 g, 195 mmol) was added. The reaction was stirred at room temperature overnight and diluted with 200 mL of Et_2O and 200 mL of water. The aqueous layer was extracted three times with 100 mL of Et_2O. The organic layers were combined and washed sequentially with an aqueous 10% sodium bisulfate solution and brine. The ethereal solution was dried over $MgSO_4$, and the solvent was removed *via* a rotary evaporator. Column chromatography on silica gel (5% ethyl acetate in hexanes) gave 22.6 g, (95%) of the title compound as a colorless oil. ^{1}H NMR: δ 1.97 (m, 2H), 2.21 (m, 2H), 3.14 (t, J = 7.5 Hz, 2H), 6.02 (t, J = 7.5 Hz, 1H), 7.15-7.36 (overlapping signals, 10H). ^{13}C NMR: δ 6.2, 30.9, 34.1, 127.3, 127.4, 127.5, 127.7, 128.3, 128.5, 130.0, 140.0, 142.6, 143.2.

5-(5,5-Diphenylpent-4-enyl)-2,2,5-trimethyl-1,3-dioxolan-4-one (10)

A 500 mL round-bottomed flask was equipped with a stir bar and placed under nitrogen. Diisopropylamine (1.47 mL, 10.4 mmol) in 100 mL of THF was added. The flask was cooled to −78 °C and *n*-BuLi (6.50 mL, 1.6 M in hexanes, 10.4 mmol) was added dropwise. The mixture was stirred for 45 min, and 2,2,5-trimethyl-1,3-dioxolan-4-one[31] (1.35 g, 10.4 mmol) in 25 mL of THF was added dropwise. The mixture was placed in a 0 °C bath, stirred for 45 min, and cooled to −78 °C. Iodide **9a** (3.28 g, 9.43 mmol) dissolved in 15 mL of THF was added dropwise. The mixture was warmed to −20 °C, stirred for 6 h, and allowed to warm to room temperature over 2 h. The reaction was quenched with aqueous HCl (10%) and diluted with 100 mL of Et_2O. The layers were partitioned, and the aqueous layer was extracted three times with 50 mL of Et_2O. The organic phases were combined, and the mixture was washed sequentially with aqueous $Na_2S_2O_3$ (10%) and brine and dried over $MgSO_4$. Rotary evaporation followed by chromatography over silica gel (5–15% ethyl acetate in hexanes) gave 1.44 g (44%) of the desired compound as a colorless oil. ^{1}H NMR: δ 1.42 (m, 2H), 1.46 (s, 3H), 1.57, (s, 3H), 1.58 (s, 3H), 1.71 (m, 2H), 2.15 (m, 2H), 6.05 (t, J = 7.0 Hz, 1H), 7.15–7.34 (overlapping signals, 10H). ^{13}C NMR: δ 24.3, 25.0, 28.1, 28.8, 29.5, 38.4, 80.3, 109.38, 126.96, 126.98, 127.2, 128.1, 128.2, 128.9, 129.9, 140.1, 142.3, 142.6, 175.4.

Ethyl 2-hydroxy-2-methyl-8,8-diphenyloct-7-enoate (11)

was prepared by a method similar to that reported for alkylation of ethyl lactate.[22] A 500 mL round-bottomed flask was equipped with a stir bar and placed under N_2 gas. Diisopropylamine (7.8 mL, 55.0 mmol) in 100 mL of THF was added. The mixture was cooled to −78 °C, and *n*-BuLi (32.8 mL, 1.6 M in hexanes, 52.5 mmol) was added dropwise. The reaction mixture was stirred for 45 min, and ethyl lactate (2.95 g, 25.0 mmol) in 10 mL of THF was added. The flask was placed in a 0 °C bath, stirred for 45 min, and cooled to −78 °C. Iodide **9b** (22.6 g, 62.4 mmol) in 50 mL of THF was added dropwise. The flask was warmed to −10 °C, stirred for 4h, and allowed to warm to room temperature over 1 h. Aqueous HCl (100 mL, 10%) was added, followed by 100 mL of Et_2O. The layers were partitioned, and the aqueous layer was extracted three times with 50 mL of Et_2O. The organic layers were combined, washed sequentially with aqueous $Na_2S_2O_3$ (10%) and brine, and dried over $MgSO_4$. Rotary evaporation followed by chromatography over silica gel (5–15% ethyl acetate in hexanes) gave 4.8 g (55%) of the desired compound as a colorless oil. ^{1}H NMR: δ 1.25 (t, J = 7 Hz, 3H), 1.37 (s, 3H), 1.42 (m, 4H), 1.59 (m, 1H), 1.69 (m, 1H), 2.10 (q, J = 7.5 Hz, 2H), 3.19 (s, 1H), 4.19, (q, J = 7 Hz, 2H), 6.05 (t, J = 7.5 Hz), 7.15–7.36 (overlapping signals, 10H). ^{13}C NMR: δ 14.3, 23.4, 26.1, 29.6, 30.1, 40.0, 61.8, 74.4, 126.8, 126.9, 127.2, 128.1, 128.2, 129.8, 130.0, 140.3, 141.8, 142.8, 177.3. HRMS (EI+): Calcd for $C_{23}H_{28}O_3$ 352.2038; found, 352.2031.

2-Hydroxy-2-methyl-7,7-diphenylhept-6-enoic acid (12a)

Dioxolanone **10** (0.655 g, 1.87 mmol) was dissolved in THF (6 mL), 6 mL of 1.0 M LiOH in H_2O was added, and the mixture was heated at reflux. The mixture was stirred vigorously until the reaction appeared to be complete by TLC (*ca.* 6 h). The mixture was cooled in an ice water bath, and 1 M $NaHSO_4$ solution was added dropwise to bring the pH to 4. The reaction mixture was poured into a separatory funnel and extracted three times with 15 mL of ethyl acetate. The organic phases were combined, washed with brine, and dried over $MgSO_4$. Rotary evaporation followed by high vacuum left 511 mg (88%) of the title compound as a white foam. ^{1}H NMR: δ 1.40 (m, 1H), 1.46, (s, 3H), 1.68, (m, 2H), 1.79 (m, 1H), 2.15, (q, J = 7.5 Hz, 2H), 6.06 (t, J = 7.5 Hz, 1H), 7.15–7.38 (overlapping signals, 10H). ^{13}C NMR: δ 24.0, 26.0, 29.6, 39.5, 74.6, 126.9, 127.0, 127.2, 128.1, 128.2, 129.1, 129.9, 140.12,

142.2, 142.6, 181.9. HRMS (EI+): Calcd for $C_{20}H_{22}O_3$ 310.1569; found, 310.1582.

2-Hydroxy-2-methyl-8,8-diphenyloct-7-enoic acid (12b)

was prepared as above from ester **11** (4.43 g, 12.56 mmol). The title compound was isolated as a white foam (3.71 g, 91%). ^{1}H NMR: δ 1.23 (m, 2H), 1.41 (s, 3H), 1.45 (m, 2H), 1.60 (m, 1H), 1.72 (m, 1H), 2.10 (q, J = 7.5 Hz, 2H), 6.04 (t, J = 7.5 Hz, 1H), 7.15–7.36 (overlapping signals, 10H). ^{13}C NMR: δ 23.3, 25.9, 29.6, 29.8, 30.0, 39.8, 74.7, 126.8, 126.9, 127.2, 128.1, 128.2, 129.6, 130.0, 140.2, 141.9, 142.8, 181.9. HRMS (EI+): Calcd for $C_{21}H_{24}O_3$, 324.1725; found, 324.1712.

1-(2-Hydroxy-2-methyl-6,6-diphenylhex-5-enoyloxy)pyridine-2(1*H*)-thione (1a)

1-Hydroxy-1*H*-pyridine-2-thione (0.127 g, 1.0 mmol) and 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (0.192 g, 1.0 mmol) were dissolved in 2 mL of CH_2Cl_2 in a 25 mL round-bottomed flask. The flask was shielded from light, and acid **12a** (0.311 g, 1.0 mmol) dissolved in 3 mL of CH_2Cl_2 was added. The mixture was stirred for 5 min and poured onto a silica gel (35 g) column. The column was eluted with 60% ethyl acetate in hexanes. After rotary evaporation and high vacuum (< 1 Torr), the desired product remained as a yellow oil (0.212 g, 50%). ^{1}H NMR: δ 1.61 (m, 1H), 1.64 (s, 3H), 1.72 (m, 1H), 1.87 (m, 1H), 1.97 (m, 1H), 2.18 (q, J = 7.5 Hz, 2H), 3.62 (bs, 1H), 6.08 (t, J = 7.5 Hz, 1H), 6.70 (td, J = 7, 1.5 Hz, 1H), 7.17–7.26 (overlapping signals, 8H), 7.29, (d, J = 7.5 Hz, 1H), 7.37 (t, J = 7.5 Hz, 2H), 7.60, (d, J = 7 Hz, 1H), 7.68 (dd, J = 7.5, 1.5 Hz, 1H). ^{13}C NMR: δ 23.9, 26.0, 29.7, 39.6, 76.2, 114.4, 126.9, 127.0, 127.2, 128.1, 128.3, 129.1, 129.9, 132.4, 132.8, 136.8, 140.1, 142.3, 142.6, 167.1, 175.4.

1-(2-Hydroxy-2-methyl-8,8-diphenyloct-7-enoyloxy)pyridine-2(1*H*)-thione (1b)

was prepared as above from acid **12b** (1.55 g, 4.80 mmol). The title compound was isolated as a yellow oil (0.914 g, 50%). ^{1}H NMR: δ 1.40 (m, 1H), 1.50 (m, 2H), 1.57 (m, 1H), 1,83 (m, 1H), 1.92 (m, 1H), 2.15 (q, J = 7.5 Hz, 2H), 3.50 (bs, 1H), 6.08 (t, J = 7.5 Hz, 1H), 6.61 (td, J = 7, 1.5 Hz, 1H),7.15–7.26 (overlapping signals, 8H), 7.30 (d, J = 7.5 Hz, 1H), 7.36 (t, J = 7.5 Hz, 2H), 7.56 (d, J = 6 Hz, 1H), 7.66 (dd, J = 6.5, 1.5 Hz, 1H). ^{13}C NMR: δ 23.4, 26.2, 29.7, 30.3, 40.0, 76.4, 114.3, 126.8, 126.9, 127.2, 128.1, 128.2, 129.6, 129.9, 132.9, 136.9, 137.9, 140.2, 141.9, 142.7, 168.3, 175.5

Thiophenol trapping reaction

PTOC ester **1a** (0.105 g, 0.25 mmol) and thiophenol (77 μL, 0.75 mmol) were dissolved in 25 mL of THF in a flask shielded from light. Argon gas was bubbled through the solution with a syringe needle for 5 min. The flask was kept under argon pressure and irradiated with a 250 W tungsten filament lamp until TLC showed no trace of the PTOC ester. The solution was washed with 1 M aqueous NaOH to remove the thiol and extracted three times with 25 mL of Et_2O. The combined organics were dried over $MgSO_4$, and the solvent was removed *via* rotary evaporator. The remaining residue was chromatographed on silica gel to give compound **13a** (14 mg, 21%) and a mixture of diastereomers **14a** (combined 41 mg, 61%).

7,7-Diphenylhept-6-en-2-ol (13)

^{1}H NMR: δ 1.24 (d, J = 7 Hz, 3H), 1.46 (m, 2H), 1.55 (m, 2H), 2.15 (m, 2H), 3.75 (m, 1H), 6.08 (t, J = 7.5 Hz, 1H), 7.16–7.35 (overlapping signals, 10H). ^{13}C NMR: δ 23.5, 26.1, 29.6, 38.8, 68.0, 126.0, 126.8, 127.0, 128.1, 128.2, 129.6, 129.9, 140.1, 141.9, 143.0. HRMS (EI+): Calcd for $C_{19}H_{23}O$ 266.1671, found, 266.1661.

(1*R*, 2*R*)- and (1*S*, 2*S*)-2-Benzhydryl-1-methylcyclopentanol (14a, major isomer)

^{1}H NMR: δ 0.82 (s, 3H), 1.46 (m, 2H), 1.57 (bs, 1H), 1.70 (m, 4H), 2.61 (m, 1H), 4.03 (d, J = 11.5 Hz, 1H), 7.14 (m, 2H), 7.26 (m, 4H), 7.35 (m, 2H), 7.41 (m, 2H). ^{13}C NMR: δ 19.8, 22.3, 24.9, 43.8, 55.4, 57.1, 82.1, 126.1, 126.3, 128.4, 128.5, 129.3, 129.5, 143.0, 143.1.

(1*S*, 2*R*)- and (1*R*, 2*S*)-2-Benzhydryl-1-methylcyclopentanol (14a, minor isomer)

^{1}H NMR: δ 1.23 (s, 3H), 1.48 (m, 2H), 1.56 (bs, 1H), 1.71 (m, 4H), 2.93 (m, 1H), 3.72 (d, J = 11.5 Hz, 1H), 7.17 (m, 2H), 7.25, (m 4H), 7.30 (m, 2H), 7.43 (m, 2H). ^{13}C NMR: δ 20.1, 24.8, 27.8, 40.1, 43.6, 55.6, 82.4, 126.2, 126.3, 128.5, 128.7, 129.6, 129.9, 143.0, 143.2.

HRMS (ES+) of a mixture of **14a** isomers: Calcd for $C_{19}H_{23}O$ 266.1671; found, 266.1657.

***t*-Butylthiol trapping reaction**

PTOC ester **1b** (0.195 g, 0.45 mmol) and $(CH_3)_3CSH$ (0.25 mL, 2.25 mmol) were dissolved in 45 mL of THF in a flask shielded from light. Argon gas was bubbled through the solution with a syringe needle for five minutes with stirring. The flask was maintained under argon while being irradiated with a 250 W tungsten filament lamp until TLC showed no trace of the PTOC ester. The solvent was removed *via* rotary evaporator, and the residue was chromatographed on silica gel to give the compounds **13b** (47 mg, 38%), 8,8-diphenyloct-7-en-2-one (32 mg, 26%), and both diastereomers of **14b** (combined 18 mg, 15%).

8,8-Diphenyloct-7-en-2-ol (13b)

^{1}H NMR: δ 1.17 (d, J = 7 Hz, 3H), 1.31–1.48 (overlapping signals, 6H), 1.61 (bs, 1H), 2.12 (q, J = 7.5 Hz, 2H), 3.75 (m, 1H), 6.08 (t, J = 7.5 Hz, 1H), 7.16–7.38 (overlapping signals, 10H). ^{13}C NMR: δ 23.5, 25.4, 29.7, 30.0, 39.2, 68.1, 126.8, 126.9, 127.2, 128.1, 128.2, 129.8, 130.0, 140.2, 141.7, 142.8. HRMS (EI+): Calcd for $C_{20}H_{24}O$ 280.1827; found, 280.1834

8,8-Diphenyloct-7-en-2-one

^{1}H NMR: δ 1.44 (qu, J = 7.5 Hz, 2H), 1.58 (m, 2H), 2.10 (s, 3H), 2.12 (m, 2H), 2.36 (t, J = 7.5 Hz, 2H), 6.07 (t, J = 7.5 Hz, 1H), 7.15–7.39 (overlapping signals, 10H). ^{13}C NMR: δ 23.3, 29.4, 29.9, 43.5, 126.8, 126.9, 127.2, 128.1, 128.2, 129.4, 129.9, 140.2, 142.0, 142.7, 209.0. HRMS (EI+): Calcd for $C_{20}H_{22}O$ 278.1671; found, 278.1664.

2-Benzhydryl-1-methylcyclohexanol (14b)

was produced as a 3.3 : 1 mixture of diastereomers. In the proton NMR spectrum, signals for the major isomer at δ 4.34, 2.28, and 1.04 did not overlap with the corresponding signals from the

minor isomer at δ = 3.79, 2.54 and 1.56; other signals for the diastereomers overlapped. Except as noted, signals reported are for the mixture. ^{1}H NMR: δ 1.04 (s, 2.3H, major isomer), 1.2–1.65 (overlapping m, 8H overlapped with s, 0.7H, minor isomer), 2.29 (m, 0.8 H, major isomer), 2.57 (dt, J = 3.4, 11.8 Hz, 0.25 H, minor isomer), 3.78 (d, J = 11.1 Hz, 0.2 H, minor isomer), 4.35 (d, J = 7.3 Hz, 0.7 H, major isomer), 7.13–7.40 (m, 10H). ^{13}C NMR: (major isomer) δ 21.9, 26.2, 26.9, 30.61, 41.6, 49.0, 50.6, 72.5, 125.9, 126.1, 128.2, 128.3, 128.5, 129.5144.0, 144.7, 146.1; (minor isomer) δ 22.1, 23.8, 29.7, 29.9, 42.2, 55.6, 74.4, 126.1, 126.7, 128.0, 128.7, 129.0. HRMS (EI+): calc for $C_{20}H_{24}O$ 280.1827, found 280.1838.

Laser flash photolysis (LFP) experiments

were performed on LK-50 and LK-60 laser kinetic spectrometers (Applied Photophysics) using Nd-YAG lasers irradiating at 355 nm (third harmonic; 40 mJ/pulse; 7 ns pulse). The direction of the laser beam was adjusted using a prism so that the largest signal was achieved when photolyzing a PTOC solution. The detection beam was adjusted by the position of several convex lenses so that the greatest light level going through the cell was reached. Concentrations of radical precursors in solution were adjusted so that the absorbance of the solutions at 355 nm was *ca.* 0.3 AU. Solutions of precursors were placed in a thermally jacketed funnel and degassed by helium sparging. After thermal equilibration at the desired temperatures, the solutions were allowed to flow through a quartz cell for the LFP studies such that fresh solution was used for each experiment. Temperatures of reaction mixtures were measured with a thermocouple placed in the flowing solution above the irradiation zone. Data was collected and analyzed with the Applied Photophysics LFP software. Kinetic traces were generally collected with *ca.* 500 data points and were fit to single or double exponential equations using nonlinear least-squares methods. The time scale of the acquisition was adjusted to fit the formation of signals. To improve signal to noise ratios, a 64 : 1 over-sampling method was used. Kinetic results for a given temperature are from traces that are the average of ten independent kinetic measurements.

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