Free Radical Chemistry of β-Lactones. Arrhenius Parameters for the Decarboxylative Cleavage and Ring Expansion of 2-Oxetanon-4-ylcarbinyl Radicals. Facilitation of Chain Propagation by Catalytic Benzeneselenol

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Abstract: 2-Oxetanon-4-ylcarbinyl radicals undergo facile ring opening with cleavage of the C−O bond to give 3-butenoxyl radicals which in turn suffer loss of carbon dioxide to provide allyl radicals. When the initial radical is generated from a bromolactone with Bu_3SnH and AIBN, chain propagation is poor owing to the relatively slow abstraction of hydrogen from the stannane by the allyl radical. The inclusion of catalytic Ph_2Se_2, reduced in situ to PhSeH, provides for much smoother cleaner reactions because of the better hydrogen donating capacity of the selenol. The oxetanon-4-ylcarbinyl radical derived from 6-benzyl-1-(bromomethyl)-8-oxa-7-oxobicyclo[4.2.0]octane is anomalous and undergoes a radical ring expansion in competition with the fragmentation process. Possible reasons for this anomaly are presented as are Arrhenius functions for the fragmentation and rearrangement. The Arrhenius function for the fragmentation of a simple 2-oxetanon-4-yl radical is also presented. Conditions are described under which the fragmentation of 2-oxetanon-4-yl radicals may be suppressed.

Introduction

One of the most rapid radical rearrangements known is the reversible[1,2] cleavage of oxiranylcarbinyl radicals to allyloxy radicals,[3,4] for which the rate constant has been estimated, by competition kinetics, to be $\sim 10^{10}$ s^{-1}.[5] Thus, this rearrangement is approximately some 2 orders of magnitude more rapid than the prototypical simple cyclopropylcarbinyl to homoallyl[6] ring opening. A feature of the cleavage of oxiranylcarbinyl radicals,[7] is the usual kinetic preference for rupture of the C−O rather than the C−C bond. On the basis of ab initio MO calculations Pasto advanced 3.57 kcal·mol^{-1} as the activation energy for cleavage of the C−O bond in the oxiranylmethyl radical[8] and concluded that the inclusion of the oxygen atom in the three-membered ring not only facilitates cleavage of the ring by rupture of the C−O bond but also retards cleavage by C−C bond scission. Somewhere near the other end of the spectrum of radical rearrangments[9,10] is the cleavage of cyclobutylcarbinyl to 4-pentenyl radicals. In its simplest, unsubstituted form this rearrangement has a rate constant of 5×10^3 s^{-1} at 25 °C.[11−13] Our interest in the free radical rearrangements of esters and lactones[14−16] led us to consider the possible reactions of 2-oxetanon-4-ylcarbinyl radicals. These might be subject to ring expansion or fragmentation by cleavage of either the C−C or C−O bonds (Scheme 1). Cleavage of the C−C bond would lead to a resonance-stabilized α-carboxyl radical but in the higher energy anti conformer. Should cleavage of the C−O bond occur this would be followed by decarboxylation to give a resonance-stabilized allyl radical. The radical ionic pathways favored for cleavage of some β-(phosphatoxy)alkyl radicals[14] also dictated consideration of a heterolytic pathway for rupture of the C−O bond; however, we recognized that this would also be followed by rapid decarboxylation and so would be functionaly indistinguishable from the pure radical pathway. The fragmentation of β-(acyloxy)alkyl radicals to alkenes and carboxyl radicals is an extremely rare event and, with one apparent exception,[17] has only been reported when the newly formed multiple bond is part of an aromatic ring.[18]

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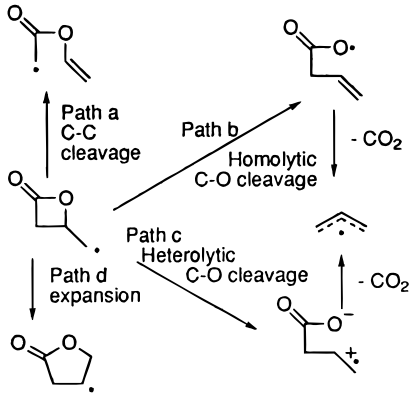
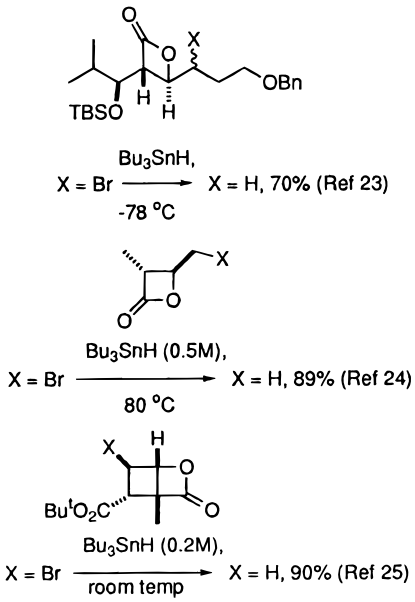
Scheme 1

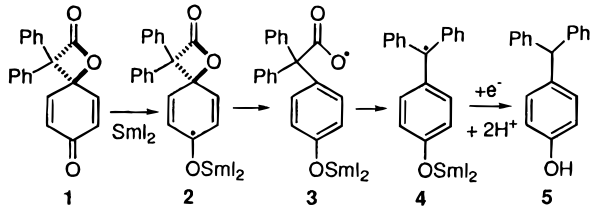


Scheme 2



Indirect evidence for the heterolytic cleavage of some α-oxygen-substituted β-(acyloxy)alkyl radicals in polar media has been advanced by the groups of Norman and Schulte-Frohlinde.[14,19−21] On the basis of the differing behavior of oxiranylcarbinyl and cyclopropylcarbinyl radicals, we reasoned that the most likely pathway would be b (Scheme 1). Moreover, we reasoned that any such cleavage would occur several orders of magnitude more rapidly than the cyclobutylcarbinyl rearrangement and so be observable under preparative conditions. The literature provided a single example of the ring opening of an oxetanylcarbinyl radical which, indeed, occurred with preferential cleavage of the C−O bond.[22] The literature also revealed three examples of the reduction of 4-bromoalkyl-β-lactones (Scheme 2) which were reported to proceed in good yield, with no mention of the type of fragmentation anticipated here.[23−25]

Scheme 3



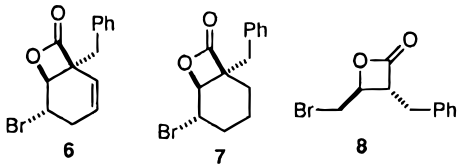
The pericyclic extrusion of CO_2 from β-lactones is a well-known reaction.[26] However, the rate constants (10^{-1}−10^{-4} s^{-1})[27−30] for this type of cleavage are typically several orders of magnitude slower than even the cyclobutylcarbinyl rearrangement and therefore such chemistry was not expected to be a serious complication in this study. Here, we report in full our study of the free radical chemistry of 4-oxetanonylcarbinyl radicals.[31]

Results and Discussion

Initially we prepared the known spirocyclic β-lactone **1**[32] and subjected it to reduction by 2 equiv of SmI_2[33] in THF at −78 °C, followed by warming to room temperature when the triarylmethane **5** was isolated in 76% yield. This result may be rationalized in terms of rapid fragmentation of the initial Sm(III) ketyl **2** to give carboxyl radical **3**, which then decarboxylates to provide **4**. A second electron transfer then gives the corresponding triarylmethyl anion which, on workup, provides **5** (Scheme 3). We cannot altogether rule out the possibility that the initial ketyl undergoes a second one-electron reduction to give a dianion, which is followed by a two-electron fragmenation and decarboxylation. However, given that the triphenylacetoxy anion does not undergo decarboxylation in alkaline aqueous solution at room temperature unless in a photoexcited state,[34] we consider this to be unlikely.

We then turned to the reaction of bromolactones with stannanes. Substrate **7** was prepared by hydrogenation of the β-lactone **6**,[35] which, in turn, like **8**[24] was obtained from the seco acid by bromolactonization. A further bromo-β-lactone **12** was obtained by Wittig olefination of **9**,[36] followed by saponification, and kinetic bromolactonization (Scheme 4).

Reaction of **6** with Bu_3SnH and AIBN at 30 °C, under irradiation from a sunlamp provided, after 38 h, the hydrocarbon



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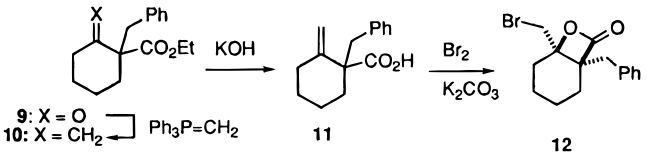
Scheme 4

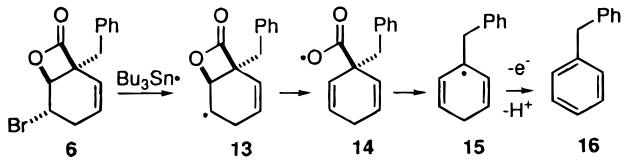


16 in 63% isolaed yield. We envisage **16** as having been formed by the anticipated radical fragmentation followed by oxidation of the resulting cyclohexadienyl radical **15** and loss of a proton (Scheme 5). The formal oxidation of cyclohexadienyl-type radicals to aromatic systems is a common occurrence in the chemistry of radical addition to arenes and is additionally characterized by poor chain propagation and the requirement for considerable amounts of radical initiator.[37] Indeed, to obtain the recorded result, it was necessary to work with 0.4 mol equiv of AIBN.

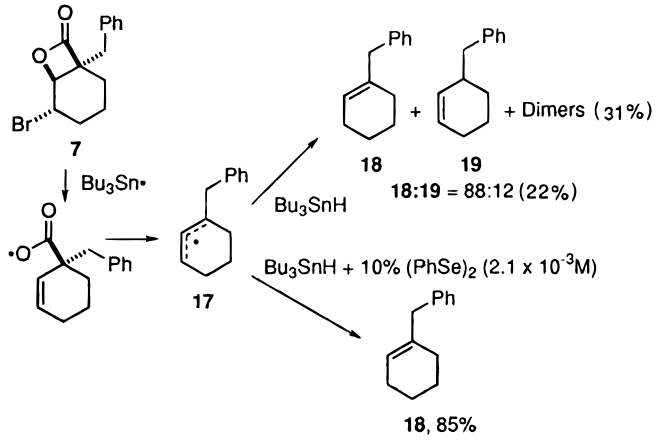
The saturated analogue (**7**) of **6** was irradiated with the sunlamp in benzene at 60 °C in the presence of Bu_3SnH and AIBN for 8 h, after which examination by ^{1}H NMR spectroscopy revealed a complex mixture devoid of substrate. Preparative TLC enabled isolation of an 88:12 mixture of isomeric olefins **18** and **19** in 22% yield and a complex mixture of dimeric products in 31% yield. Again these results were readily interpreted in terms of the anticipated radical fragmentation giving the allylic radical **17** followed either by quenching by the stannane to give the two olefins or by dimerization (Scheme 6). The isolation of the dimers in greater combined yield than the two olefins suggests that chain propagation was not efficient, and this was again reflected in the requirement for 0.4 mol equiv of AIBN as an initiator for the reaction to proceed to completion. We reasoned that the poor chain propagation might be overcome by the inclusion of a catalytic quantity of Ph_2Se_2, reduced in situ to PhSeH (and $PhSeSnBu_3$),[37−39] which, with its superior hydrogen donating capacity,[40] would overcome this problem. The benzeneselenol is constantly regenerated by reaction of the PhSe$^\bullet$ radical with stoichiometric Bu_3SnH. In the event, working at 40 °C in benzene, using only 10 mol % of di-*tert*-butyl peroxalate (DBPO) as an initiator and 10 mol % of Ph_2Se_2 (2.1×10^{-3} M) and 1.35 equiv of Bu_3SnH, the bromolactone was consumed in less than 3 h and the olefin **18** isolated in 85% yield. Similarly, in benzene reflux, the inclusion of 10 mol % of Ph_2Se_2 in the reaction mixture enabled the amount of AIBN to be reduced to 10 mol % when smooth conversion of the substrate to alkene **18**, isolated in 84% yield after only 1.5 h. Thus, the catalytic quantity of PhSeH resulted in dramatic reductions of the reaction times and in much cleaner, smoother reactions. No dimers were formed in these PhSeH-catalyzed reactions, indicating that the selenol operates by efficient quenching of the allyl radical **17**. Moreover, quenching of **17** was highly regioselective, providing only **18** (**18**:**19** > 95:5).

A further example was provided by the monocyclic β-lactone **8**, a simple model for the literature reactions presented in Scheme 2. In line with the above results, when the reaction was conducted with excess Bu_3SnH in the absence of catalytic PhSeH, it was slow and complex. However, operating in the presence of 5 mol % Ph_2Se_2 (2.6×10^{-3} M) and 10 mol %

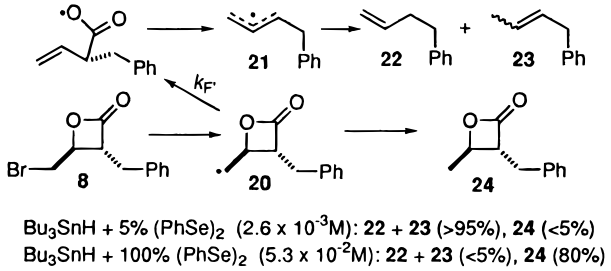
Scheme 5



Scheme 6



Scheme 7



AIBN in benzene at reflux provided a very clean reaction mixture consisting only of the isomeric olefins **22** and **23**. No evidence was found for the formation of the simple reduction product **24** under these conditions (Scheme 7). However, when a similar reaction was conducted at room temperature in the presence of DBPO (10 mol %) as initiator and using a full equivalent of Ph_2Se_2 (5.3×10^{-2} M), <5% of **22** and **23** was formed as judged by ^{1}H NMR spectroscopy but the reduction product **24** was isolated in 80% yield. A high concentration of PhSeH is therefore effective in preventing the radical fragmentation reaction.

Treatment of β-lactone **12** with Bu_3SnH and AIBN alone was again inefficient, owing to poor chain propagation by the intermediate allyl radical. However, exposure of **12** to Bu_3SnH and 5 mol % of Ph_2Se_2 (1.5×10^{-3} M), with initiation by only 5% of DBPO at room temperature, resulted in complete consumption of **12** after 3 h. ^{1}H NMR spectroscopy revealed a clean reaction mixture in which olefin **27**, isolated in 78% yield, was accompanied by two other minor products. The experiment was repeated with 30 mol % of Ph_2Se_2 (9.0×10^{-3} M) when **27** and the two, previously minor, products were formed in the ratio 1:1.8:0.4. Chromatographic separation enabled isolation of **27** in 25% yield and a 4:1 mixture of the two other products, which spectroscopic investigation revealed to be the reduction product **28** and the rearranged lactone **30**, respectively (Scheme 8). Enhancement of the benzylic methylene protons in the ^{1}H NMR spectrum on double irradiation of the bridgehead hydrogen led to the assignment of **30** as the cis-fused structure depicted. In a further experiment using a

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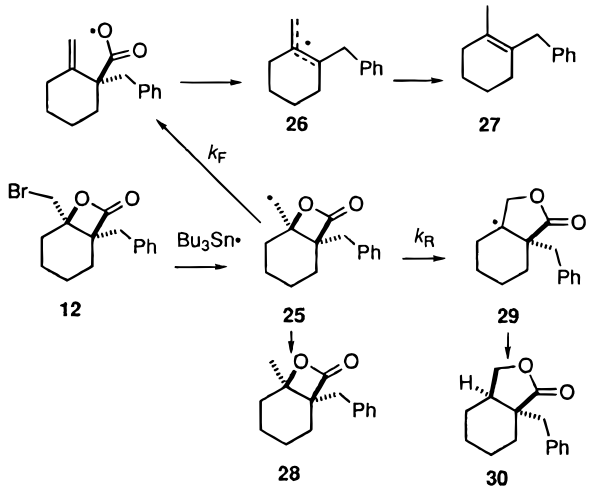
Scheme 8



full molar equivalent of Ph_2Se_2 (3.0×10^{-2} M), the reduced product **28** was formed in >95% yield as determined by ^{1}H NMR spectroscopy of the crude reaction mixture. Thus, in one or another of the various examples, all distinguishable processes in Scheme 1 with the exception of C−C bond cleavage have been observed.

We next turned to the full kinetic characterizaton of these new radical rearrangements. First, we decided to investigate the cleavage/fragmentation of **12** as this was the only example in which a rearrangement was observed, and second, we chose to study **8** as being more representative of the type of β-lactone most likely to be encountered in synthetic schemes. As usual we have made use of our catalytic adaptation[41] of Newcomb's PhSeH clock reaction.[40] In this method trapping by a catalytic quantity of PhSeH at a known concentration is used as the clock reaction. The PhSeH is constantly regenerated by reaction of the PhSe• radical with stoichiometric Bu_3SnH. As with any type of indirect radical clock method, the validity of the result depends on the applicability of the clock reaction employed. Here, the assumption is made that the clock reaction, quenching of primary alkyl radicals by PhSeH (and Bu_3SnH), is not affected by the β-acyloxy group. β-Oxygen effects in pure radical,[42−44] as opposed to radical cation,[45] reactions are typically small, and the assumption should be correct to a first approximation.

Initially, **12** was reacted at 40 °C with Bu_3SnH and DBPO as an initiator in the presence of a range of concentrations of PhSeH. This enabled plots to be made of the ratios of the reduction product (**28**) with both the fragmentation product (**27**) and the rearrangement product (**30**) against the concentration of PhSeH. In each case linear plots were obtained whose slopes are equal to k_H/k_F and k_H/k_R, respectively, wherein k_H is the rate constant for trapping of a primary alkyl radical by PhSeH at 40 °C, calculated from the known Arrhenius equation (eq 1)

$$\log(k_H) = 10.35 - 1.76/(2.3RT) \quad (1)$$

,[41] k_F is the rate constant for the fragmentation providing **27**, and k_R is that for the rearrangement leading ultimately to **30**. In this manner the rate constants k_F(**25** → **26**) and k_R(**25** → **29**) were determined to be 3.8×10^6 and 1.8×10^6 s^{-1}, respectively, at 40 °C.

Subsequently the reaction of **12** with Bu_3SnH was carried out in the presence of a fixed concentration of PhSeH over a 85° range of temperature enabling Arrhenius plots to be made for the fragmentation and rearrangement of radical **25**. Both were straight lines which enabled the extraction of the Arrhenius equations (eqs 2 and 3).

$$\log(k_F) = (8.3 \pm 0.3) - (2.5 \pm 0.4)/(2.3RT)^{46} \quad (2)$$

$$\log(k_R) = (8.2 \pm 0.2) - (2.7 \pm 0.2)/(2.3RT)^{46} \quad (3)$$

Next we turned to the fragmentation of β-lactone **8**. In this instance we directly studied the fragmentation at a range of different temperatures enabling determination of the Arrhenius equation (eq 4) in which $k_{F'}$ is the rate constant for this

$$\log(k_{F'}) = (13.3 \pm 0.2) - (8.7 \pm 1.0)/(2.3RT)^{46} \quad (4)$$

fragmentation. The Arrhenius parameters for the fragmentation of radical **20** (eq 4) appear perfectly straightforward for such a radical fragmentation reaction and invite no special comment. They lead to a rate constant of 8.2×10^6 s^{-1} for the opening of this radical at 25 °C. This is some 3 orders of magnitude greater than that of the cyclobutylmethyl radical,[11−13] as predicted in the initial analysis of the problem. With these measured values of the rate constants for fragmentation, we can now reconsider the previous literature reports of the reactions of oxetanoylcarbinyl radicals. The rate constant for the fragmentation of **8** at 80 °C is calculated to be 8.1×10^7 s^{-1}. From this rate constant and that calculated for trapping of the *n*-butyl radical by Bu_3SnH at 80 °C (6.3×10^6 s^{-1}),[47] we calculate that a Bu_3SnH concentration of 50 M would be necessary to obtain an 80% yield of the reduction product **24** and a 20% yield of the combined fragmentation products (**22** and **23**) in benzene at reflux, without catalysis by the selenol. This concentration of Bu_3SnH is significantly higher than that reported by Shibata (Scheme 2, 0.5 M)[24] and must cast some doubt on the reported yield. Similarly, we calculate that Mead operated with Bu_3SnH concentration of at least 9×10^{-2} M to obtain a 70% yield of reduction product at −78 °C (Scheme 2).[23] These yields, temperatures, and concentrations (Scheme 2) are to be contrasted with the 80% isolated yield of **24** isolated on reducing **8** in benzene at room temperature with 0.13 M Bu_3SnH, assisted by 0.05 M PhSeH (Scheme 7). The lack of fragmentation in the third example of Scheme 2[25] presumably derives from the fact that this would result in the formation of a cyclobutene whose strain would offset that lost on β-lactone opening.

In contrast to eq 4, the Arrhenius parameters for the fragmentation and rearrangement (eqs 2 and 3, respectively) of radical **25** are somewhat unusual. Indeed the comportment of radical **25** is unusual, at least among the examples studied here, insofar as it provided the only example in which a detectable amount of the ring expansion process was observed. The activation energies in eqs 2 and 3, while low, are reasonably consistent with those for other highly exothermic radical

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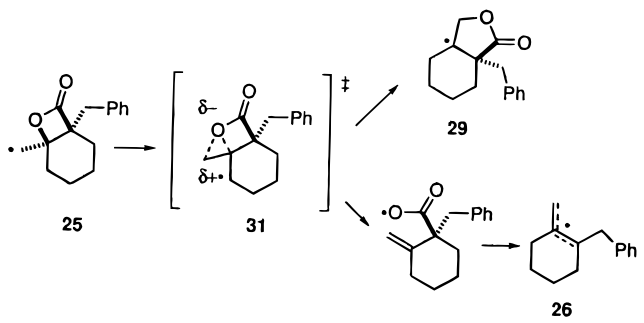
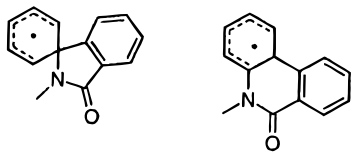
Scheme 9



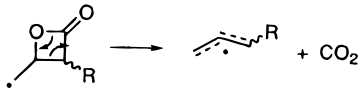
fragmentation reactions, e.g. the cubylcarbinyl radical (E_A = 3.7 kcal·mol^{-1}), the 2,2-diphenylcyclopropylcarbinyl radical (E_A = 2.0 kcal·mol^{-1}), and the bicyclo[2.1.0]pent-2-yl radical (E_A = 5.2 kcal·mol^{-1}).[48−51] The log *A* values are however unusually small, both for fragmentations[9,52] and for acyloxy migrations,[14,53] and suggest[52] tight transition states for these reactions. The close similarity between the two equations (eqs 2 and 3) and the log *A* values suggest to us that both reactions proceed along the same reaction coordinate to a bridged transition state (**31**) then diverge to the fragmentation and rearrangement products (Scheme 9). Transition state **31** is directly analogous to the three-electron, three-center cyclic transition state for the 1,2-migration of β-(acyloxy)alkyl radicals, for which there is ample literature precedent.[14] The alternative five-electron, five-center cyclic transition state, corresponding to that of a 2,3-migration of an acyloxyalkyl radical, would be highly strained and requires the unlikely closure of the initial radical **25** onto the β-lactone carbonyl oxygen. Moreover, the observed rate constant for the rearrangement of **25** to **29** is consistent with those previously determined for 1,2-acyloxy shifts but not with those for the corresponding 2,3-shifts.[14] An alternative pathway involving radical ionic fragmentation (Scheme 1, path c), followed by competing fragmentation and recombination, is considered to be highly unlikely on the grounds that extensive experimentation has so far failed to provide any evidence for such a mechanism in β-(acyloxy)alkyl radical rearrangements.[14] We also note that radical **25** has the potential to undergo cleavage of the exocyclic C−O, of an exocyclic C−C bond, or of the transannular C−C bond. In this it is not unlike numerous bicyclo[3.2.0]heptan-1-oxyl radicals which prefer cleavage of the transannular bond.[54] It seems likely, as Dowd and Zhang have suggested,[55] that in such 1-bicyclo[4.2.0]octylalkyl and oxyl radicals and their [3.2.1]heptyl congenors there is a better overlap of the singly occupied orbital with the transannular bond than with the exocyclic bonds, which leads to preferential cleavage of the former. In the context of radical **25** this would mean that cleavage of the C−O is retarded. The alternate formation of the strained transition state (**31**) for the acyloxy migration therefore becomes possible (Scheme 9).

Returning to the theme of catalysis of chain transfer by PhSeH, we note that this was very successful when the intermediate radical was an allyl radical, as in Schemes 6−8. However, PhSeH failed to catalyze the quenching of of the cyclohexadienyl **15**. Thus, even in the presence of a full 1 equiv of PhSeH, the cleavage of **6** was unchanged and provided the oxidative cleavage product **16** (Scheme 5). This causes us to draw attention to recent work from this laboratory[37] in which it was found that cyclohexadienyl **32** was readily quenched by PhSeH, in a catalytic system similar to the one used here, giving good isolated yields of cyclohexadienyls. In contrast it was found that the isomer **33** underwent "oxidation" even in the presence of PhSeH. As was noted,[37] the cyclohexadiene C−H and PhSeH Se−H bond energies are very similar and any additional stabilization of the cyclohexadienyl radical by the substituents will prevent effective reduction by the selenol.



Finally, we raise the possibility of an additional mechanism for the radical fragmentations presented here. We have considered the fragmentations in terms of stepwise processes involving expulsion of β-acyloxy radicals followed by rapid decarboxylation (Scheme 1). We have also noted the possibility of a radical ionic fragmentation followed by decarboxyation (Scheme 1). We ruled out the possibility of concerted loss of CO_2 either from the substrate followed by reduction of an allyl bromide or from the reduction products owing to the known kinetics of this type of concerted loss of CO_2 from β-lactones. Moreover, all experiments were conducted at temperatures at which blank experiments indicated the β-lactones to be stable, at least on the time scale of the reactions. However, and without being able to provide a solution at the present time, we feel justified in raising the possibility of a concerted loss of CO_2 from the first formed radical (Scheme 10). The suggestion is

Scheme 10



that the 4π-pericyclic fragmentation may be accelerated by several orders of magnitude by conjugation with the exocyclic radical. We are prompted to offer this suggestion by the enormous rate enhancements, of up to 10 orders of magnitude, seen when an exocyclic anion is conjugated with a pericyclic transition state, as in the oxyanion Cope rearrangment.[56−58] At the present time the prospects for distinguishing between the stepwise radical pathway and the concerted pathway do not appear good; the rate constant for the reactions measured here and the near diffusion controlled loss of CO_2 from carboxyl radicals conspire against the possibility of trapping any such intermediate species.

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Experimental Section

General Procedures. ^{1}H and ^{13}C NMR spectra were recorded as $CDCl_3$ solutions at 300 and 75 MHz, respectively, with chemical shifts (δ) in parts per million downfield from tetramethylsilane as an internal standard. All solvents were dried and distilled by standard methods. Extracts were dried over Na_2SO_4 and solvents removed in vacuo. Microanalyses were performed by Midwest Microlabs (Indianapolis, IN).

Reaction of 1 with SmI_2. To a stirred solution of **1**[32] (76 mg, 0.25 mmol) in THF/MeOH (3/1) (10 mL) was added dropwise SmI_2 (5 mL, 0.1 M in THF) by a syringe at −78 °C under Ar. The reaction was complete within 2 min. Saturated NH_4Cl was then added and the aqueous phase extracted with CH_2Cl_2. The organic layer was dried and concentrated. The residue was dissolved in a minimum of CH_2Cl_2 and treated with hexane to give a yellow solid **5**,[59,60] which was collected by filtration (49.5 mg, 76%): mp 107−109 °C (CH_2Cl_2/hexane); ^{1}H NMR δ 5.02 (br. s, 1H), 5.46 (s, 1H), 6.69 (d, J = 10.5 Hz, 2H), 6.92 (d, J = 10.5 Hz, 2H), 7.20 (m, 10H); IR (neat) ν (cm^{-1}) 3388.

Reaction of 6 with Bu_3SnH and AIBN. A solution of **6**[35] (70 mg, 0.24 mmol), Bu_3SnH (100 μL, 1.5 equiv), and AIBN (17 mg, 0.4 equiv) in benzene (3 mL) was irradiated at 30 °C with a sunlamp with monitoring by TLC. After 38 h at the same temperature, **6** was consumed. Removal of the volatiles afforded a residue, which was purified by preparative TLC on silica gel (eluent: hexane) to give **16**[61] as a colorless oil (25.4 mg, 63%): ^{1}H NMR δ 3.99 (s, 2H), 7.2 (m, 6H), 7.32 (m, 4H).

Reaction of 7 with Bu_3SnH and AIBN. A mixture of **7** (120.4 mg, 0.407 mmol), Bu_3SnH (178 μL, 1.5 equiv), and AIBN (29 mg, 0.4 equiv) in benzene (4 mL) was irradiated at 60 °C with a sunlamp for 8 h. After the solvent was removed in vacuo, examination of the reaction mixture by ^{1}H NMR spectroscopy showed a complex reaction mixture containing several olefins and the absence of starting material. Preparative TLC on silica gel (eluent: hexane/EtOAc = 16/1) enabled the separation of two closely migrating bands. One band contained the dimers, as a complex mixture of diastereomers (22 mg, 32%); HRMS: Calcd for $C_{26}H_{30}$ 342.2347 ($M^{+\bullet}$), found 342.2346), while the other was found to consist of **18** and its regioisomer **19** in the ratio 88:12 as determined by ^{1}H NMR spectral analysis (15.4 mg, 22%). **18**:[62] ^{1}H NMR δ 1.26−1.57 (m, 4H), 1.86 (m, 2H), 2.02 (m, 2H), 3.25 (s, 2H), 5.47 (s, 1H), 7.20−7.26 (m, 5H). Olefin **19**[63] was confirmed by the following diagnostic signals: ^{1}H NMR δ 2.38 (m, 1H), 2.55 (dd, J = 8.0, 13.1 Hz, 1H), 2.62 (dd, J = 7.0, 13.1 Hz, 1H), 5.59 (m, 1H), 5.68 (m, 1).

Reaction of 7 with Bu_3SnH, AIBN or DBPO, and PhSeH. To a solution of **7** (27.4 mg, 0.093 mmol), Ph_2Se_2 (2.9 mg, 0.1 equiv), and DBPO (2.2 mg, 0.1 equiv) in benzene (3 mL) under Ar was added dropwise Bu_3SnH (33 μL, 1.2 equiv) by syringe at 40 °C. After the mixture was stirred for 3 h at that temperature, the solvent was evaporated to give a residue. Inspection of this residue by ^{1}H NMR spectroscopy revealed **18** to be the exclusive product. Preparative TLC on silica gel (eluent: hexane/EtOAc = 16/1) gave pure **18** (13.6 mg, 85%), which was identical to that described above. A similar experiment was carried out with 10% of AIBN in place of DBPO in refluxing benzene for 1.5 h, when an 84% yield of **18** was isolated.

Reaction of 8 with Bu_3SnH, AIBN, and 5% PhSeH in Benzene at Reflux. To a solution of **8**[24] (132 mg, 0.52 mmol), Ph_2Se_2 (8 mg, 0.05 equiv), and AIBN (10 mg, 0.1 equiv) in benzene (10 mL) under Ar was added Bu_3SnH (188 μL, 1.35 equiv) by a syringe. The reaction mixture was brought to reflux with stirring for 3 h. The reaction mixture was then cooled to room temperature, and the solvent was removed to afford a residue of which inspection by ^{1}H NMR spectroscopy revealed only **22**[64] and (*E*)- and (*Z*)-**23**[62] in the ratio 1:2:4. No evidence was found, by ^{1}H NMR spectroscopy, for formation of reduction product **24**. When a similar reaction was conducted without Ph_2Se_2 a complex mixture was obtained. Pertinent spectral data for **22**, and (*E*)- and (*Z*)-**23** were in good agreement with the literature.[64,62] **22**: ^{1}H NMR δ 2.20 (td, J = 7.7, 6.6 Hz, 2H); 2.60 (t, J = 7.7 Hz, 2H), 4.85 (m, 2H), 5.70 (m, 1H), 7.1 (m, 5H). (*E*)-**23**: ^{1}H NMR δ 1.70 (d, J = 6.0 Hz, 3H), 3.30 (d, J = 6.3 Hz, 2H), 5.55 (m, 2H), 7.25 (m, 5H). (*Z*)-**23**: ^{1}H NMR δ 1.73 (d, J = 4.9 Hz, 3H), 3.40 (d, J = 5.1 Hz, 2H), 5.55 (m, 2H), 7.25 (m, 5H).

Reaction of 8 with Bu_3SnH, DBPO, and 100% PhSeH in Benzene at Room Temperature. To a solution of **8** (27 mg, 0.106 mmol), Ph_2Se_2 (33 mg, 1 equiv), and DBPO (2.5 mg, 0.1 equiv) in benzene (2 mL) under Ar at room temperature was added Bu_3SnH (66 μL, 2.3 equiv), followed by stirring at room temperature for 4 h. Removal of solvent and inspection of the reaction mixture by ^{1}H NMR spectroscopy revealed **24** (>95%) and **22** and **23** (<5%). The reaction mixture was dissolved in CH_2Cl_2 and MeOH and treated with $NaBH_4$ at 0 °C and quenched by the addition of water. The aqueous phase was extracted with CH_2Cl_2, and the combined organic solvents were dried (Na_2SO_4) and concentrated to give a residue, which after TLC on silica gel (eluent: hexane/EtOAc = 9/1) afforded **24**[24] (14.6 mg, 80%) as an oil: ^{1}H NMR δ 1.44 (d, J = 6.1 Hz, 3H), 3.02 (dd, J = 9.31, 14.5 Hz, 1H), 3.16 (dd, J = 5.7, 14.5 Hz, 1H), 3.46 (m, 1H), 4.45 (m, 1H), 7.27 (m, 5H); IR (neat) ν (cm^{-1}) 1810.

Reaction of 12 with Bu_3SnH, DBPO, and 5% of PhSeH. **12** (61.8 mg, 0.2 mmol), Ph_2Se_2 (3.1 mg, 0.05 equiv), and DBPO (2.4 mg, 0.05 equiv) were dissolved in benzene (6.5 mL) under Ar and treated with Bu_3SnH (66 μL, 1.2 equiv) at room temperature, followed by stirring for 3 h. The solvent was then removed in vacuo whereupon inspection of the reaction mixture by ^{1}H NMR spectroscopy indicated that only trace amounts of **28** and **30** were formed in addition to **27**. Column chromatography on silica gel (eluent: hexane/$CHCl_3$ = 3:1) gave pure **27**[65] (29 mg, 78%) as a colorless oil: ^{1}H NMR δ 1.59 (m, 4H), 1.74 (s, 3H), 1.88 (m, 2H), 2.03 (m, 2H), 3.37 (s, 2H), 7.17 (m, 3H), 7.27 (m, 2H).

Reaction of 12 with Bu_3SnH, DBPO, and 30% of PhSeH. The above experiment was repeated with 100 mg of **12** and 30% of PhSeH. Removal of solvent gave a mixture, inspection of which by ^{1}H NMR spectroscopy revealed that not only **27** but also **28** and **30** were generated in the ratio 1:1.8:0.4. The reaction mixture was again dissolved in CH_2Cl_2 (5 mL) and methanol (1 mL) and treated with $NaBH_4$ at 0 °C. After quenching with water and extraction of the aqueous phase with CH_2Cl_2, the combined organics were dried and concentrated to a residue. After preparative TLC on silica gel (eluent: $CHCl_3$), this afforded **27** (15 mg, 24.8%) and a mixture of **28** and **30** as a mixture in the ratio ~4:1 (41 mg, 55%). Anal. Calcd for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88. Found: C, 77.93; H, 7.74%. Pure **28** was obtained in the form of a white solid by triturating the mixture of **28** and **30** with hexane: mp 100−102 °C (dec); ^{1}H NMR δ 1.62 (m, 8H), 1.75 (m, 2H), 2.76 (d, J = 14.3 Hz, 1H), 3.28 (d, J = 14.3 Hz, 1H), 7.28 (m, 5H); ^{13}C NMR δ 16.0, 17.8, 23.2, 26.0, 31.1, 37.0, 58.7, 83.2, 127.0, 128.5, 130.3, 136.1, 174.6; IR (KBr) ν (cm^{-1}) 1810. **30**, which was not obtained pure, was identified by the following diagnostic signals: ^{1}H NMR δ 2.24 (m, 1H), 2.86 (d, J = 13.7 Hz, 1H), 3.07 (d, J = 13.7 Hz, 1H), 3.97 (dd, J = 7.8, 8.6 Hz, 1H), 4.06 (dd, J = 7.4, 8.6 Hz, 1H); ^{13}C NMR δ 21.7, 24.1, 30.3, 36.4, 40.0, 46.8, 69.0, 127.1, 128.7, 130.4, 137.0, 181.0; IR (KBr) ν (cm^{-1}) 1761.

Reaction of 12 with Bu_3SnH, DBPO, and 100% of PhSeH. A experiment similar to that described above was conducted in the presence of 100% of PhSeH by using 100 mg of **12**. Inspection of the reaction mixture by ^{1}H NMR spectroscopy revealed **28** (>95%), **30** (<2%), and **27** (<2%). **28** was isolated in 85% yield.

Determination of the Kinetics of Decarboxylation and Rearrangement of β-Lactone 12. Stock solutions of **12** (100 mg, 0.3234 mmol) in benzene (5 mL), Ph_2Se_2 (156 mg, 0.5 mmol) in benzene (5 mL), Bu_3SnH (291 mg, 1.0 mmol) in benzene (5 mL), and DBPO (23.4

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mg, 0.1 mmol) in benzene (1 mL) under Ar were prepared. The stock solution of **12** (800 μL, 0.0518 mmol) in benzene was transferred by a syringe to each of five 25-mL Pyrex test tubes equipped with septa and stir bars, which had been prepared by evacuation and flushing with Ar several times beforehand. Stock solutions of 130 μL (0.0130 mmol, 0.25 equiv), 156 μL (0.0155 mmol, 0.3 equiv), 182 μL (0.0181 mmol, 0.35 equiv), 208 μL (0.0207 mmol, 0.40 equiv), or 234 μL (0.0233 mmol, 0.45 equiv) of Ph_2Se_2 were added to these tubes, respectively, followed by an amount of Bu_3SnH in benzene (stock solution) corresponding to that of Ph_2Se_2. After decolorization, further Bu_3SnH stock solution (337 μL, 1.3 equiv) was then added to each tube followed by sufficient benzene (86−242 μL) to make the volume 1574 μL. Each tube was then immersed into a boiling CH_2Cl_2 bath maintained at 40 °C, followed by addition of the stock solution of DBPO in benzene (26 μL, 0.05 equiv), making the final volume in each tube 1.6 mL. After the reaction mixtures were stirred at 40 °C for 4 h, the solvent was removed in vacuo and the residues were examined by ^{1}H NMR spectoscopy. In each case the substrate was completely consumed. Integration of the benzydryl singals (PhC*HaHb*) of **28** at δ 3.28 (*Ha* or *Hb*), **30** at δ 3.07 (*Ha* or *Hb*), and **27** at 3.37 (*Ha* = *Hb*) gave the ratios of **28**/**30** and **28**/**27** recorded in Table 1 (Supporting Information).

Determination of the Arrhenius Parameters for Decarboxylation and Rearrangement of 12. Stock solutions of **12** (200 mg, 0.6468 mmol) in toluene (5 mL), Ph_2Se_2 (156 mg, 0.5 mmol) in toluene (5 mL), Bu_3SnH (291 mg, 1.0 mmol) in toluene (5 mL), and DBPO (23.4 mg, 0.1 mmol) in toluene (1 mL) under Ar were prepared. The stock solution of **12** (400 μL, 0.0518 mmol) was transferred by a syringe to each of four 25-mL Pyrex test tubes equipped with septa and stir bars, which were evacuated and flushed with Ar several times beforehand. A toluene solution of Ph_2Se_2 (208 μL, 0.0207 mmol, 0.4 equiv) was added to each of these tubes followed by an amount of Bu_3SnH in toluene (104 μL, stock solution) corresponding to that of Ph_2Se_2. Further stock solution of Bu_3SnH in toluene (337 μL, 1.3 equiv) was then added to each tube followed by 525 μL of toluene to make the volume 1574 μL. Each tube was then equilibrated at the required temperature and treated with the stock solution of DBPO in toluene (26 μL, 0.05 equiv). The total volume in each tube was finally made up to 1.6 mL. The reactions was stirred at the temperature indicated in Tables 2 and 3. Irradiation with a 140-W medium-pressure mercury lamp (Hanovia) was necessary when the reactions proceeded at −15 or −25 °C (entries 4 and 5 in Table 2). The solvent was removed in vacuo, and the residues were examined by ^{1}H NMR spectoscopy, which gave the ratios of **27**/**28** and **30**/**28** recorded in Tables 2 and 3, respectively (Supporting Information). The data for 40 °C were taken from the results of Table 1 (Supporting Information).

Determination of the Arrhenius Parameters for Decarboxylation of 8. Stock solutions of **8** (140 mg, 0.6486 mmol) in benzene (5 mL), Bu_3SnH (291 mg, 1.0 mmol) in benzene (5 mL), Ph_2Se_2 (156 mg, 0.5 mmol) in benzene (5 mL), and DBPO (23.4 mg, 0.1 mmol) in benzene (1 mL) under Ar were prepared. A stock solution of lactone **8** (450 μL, 0.0494 mmol), 250 μL of the solution of Ph_2Se_2 (0.025 mmol, 0.506 equiv), and 450 μL of the Bu_3SnH solution (0.089 mmol, 1.81 equiv) were transferred to each of five 25-mL Pyrex test tubes equipped with septa and stir bars, which were evacuated and flushed with Ar several times beforehand. Each tube was then equilibrated at the specific temperature shown in Table 4. To each reaction mixture was then added 50 μL of the benzene solution of DBPO (0.005 mmol, 0.1 equiv) followed by stirring under Ar for 4 h. Irriadiation with a 140-W medium-pressure mercury lamp (Hanovia) was necessary when the reaction proceeded at 11 °C (284 K). The solvents were removed in vacuo (cold water bath temperature), and the residues were examined by ^{1}H NMR spectroscopy. In each case the substrate was completely consumed. Integration of the benzyl signals of **24** at δ 3.16 (PhC*HaHb*, *Ha*, or *Hb*), **22** at δ 2.60 (PhCH_2CH$_2$), (*E*)-**23** at δ 3.30 (PhCH_2CH), and (*Z*)-**23** at δ 3.4 (PhCH_2CH) gave the ratios of (**22** + **23**)/**24** recorded in Table 4 (Supporting Information).

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Supporting Information Available: Details of the preparation of compounds **7** and **10**−**12** and Tables 1−4 of kinetic data (5 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

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