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Competition Methods and Scales for Alkyl Radical Reaction Kinetics

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Contents

Interest in organic radical reactions has rapidly increased over the past several years as radical-based methods for organic synthesis have evolved[1] and as it has become increasingly apparent that radical intermediates might be formed in a number of biologically important reactions. For both mechanistic studies and synthetic applications, knowledge of the rate constants of radical reactions is important. This is apparent in mechanistic studies in which an investigator wishes to test for a possible radical intermediate in a reaction pathway or measure the rate of reaction of a known radical intermediate. Upon first consideration, the importance of kinetic information might be less apparent in a synthetic application. However, successful radical-based synthetic procedures usually involve chain reactions wherein a series of propagation steps must be appropriately timed; at least a qualitative understanding of radical kinetics is required for the selection of reagents and concentrations.

The determination of radical kinetics, especially for fast radical reactions, has progressed rapidly in the past several years. Early kinetic studies employed ESR techniques, the importance of which cannot be overstated, but kinetic ESR studies are somewhat limited in precision. More recently, the temperature and dynamic limits of radical kinetic studies were expanded by laser flash photochemical or pulse radiolytic generation of radical intermediates coupled with a rapid time-resolved analysis usually by UV-visible spectroscopy. This permits direct determinations at room temperature of rate constants that approach the diffusion control limit in solution.

Although direct methods are ultimately required for any kinetic scale, indirect competition methods have been developed that span literally the entire range of radical kinetics in solution and can now exceed the limits of picosecond laser flash methods. Competition methods involve *post facto* analyses of product mixtures, often by chromatography, and typically require neither special functional groups in the substrate nor highly specialized instrumentation in the laboratory. Therefore, they have been the workhorse of radical kinetic determinations and increasingly are being employed by other than kineticists.

The purpose of this report is to provide an overview of indirect methods that are commonly applied in alkyl radical kinetic studies. Popular indirect methods are briefly described followed by collections of rate constants that can be used as basis reactions in indirect studies. This is not an exhaustive review of radical kinetics about which volumes have been compiled,[2] nor is it a complete survey of reactions that can be employed in competition kinetic measurements. Rather, the report focuses on unimolecular radical rearrangements that can be employed as radical clocks and simple bimolecular radical reactions, mainly hydrogen atom transfer reactions, that provide readily analyzed products. It is to be hoped that those studying radical kinetics will find the collection of information useful, but the report is more directed to organic chemists who wish to optimize the yield or test the feasibility of a radical-based conversion; perhaps the collection of methods and rate constants will encourage non-kineticists to measure rate constants necessary for their studies.

COMPETITION KINETICS

Competition kinetic methods require partitioning of a radical intermediate between two reaction channels, the reaction of interest with an unknown rate constant and the basis reaction with a known rate constant. In principle, any competing reactions can be employed, but in practice one usually prefers a situation where one reaction is unimolecular and the other is bimolecular. The analysis is simplified when the partitioning reactions are irreversible under the experimental conditions. However, reversible reactions can be treated with steady state approximations; most commonly the reversible reactions are unimolecular processes. For further simplification, the reactions often can be designed such that a reagent involved in a bimolecular reaction is present in a large excess and experiences essentially no concentration change over the course of the reaction. Kinetic expressions that encompass the most commonly encountered situations are collected in Table 1 on the next page.

Most often, irreversible first and second order processes compete (Figure 1). When the trapping agent involved in the second order process is in large excess (greater than five-fold excess with respect to radical precursor), the second order reaction should be treated as a pseudo-first order process. Under these constraints and provided that the products are stable to the reaction conditions, a ratio of rate constants can be obtained directly from the product distribution via equation 1 where k_1 and k_2 are the rate constants of the unimolecular and bimolecular reaction, [R'X] and [RX] are, respectively, the final products from the rearrangement reaction and the trapping reaction, and $[XY]_m$ is the average concentration of the trapping reagent involved in the bimolecular reaction over the course of the reaction.

In cases where the reagent in the bimolecular process is present in slight excess and its concentration changes appreciably during the course of the reaction, second order kinetics can be applied for the trapping reaction. Integration of the expression obtained by dividing the rate law for the unimolecular process (using a

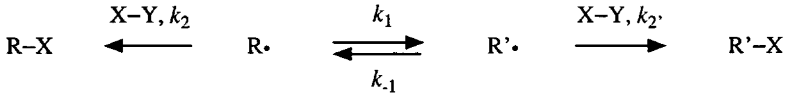


Figure 1. A competition kinetics experiment involving a unimolecular and bimolecular reaction. Radical R• rearranges (rate constant k_1) to give radical R'• in competition with trapping by reagent X-Y (rate constant k_2) which gives product R-X. Rearranged radical R'• is trapped by X-Y in a step which is kinetically unimportant when the rearrangement of R• is effectively irreversible.

Table 1. Kinetic Expressions for Common Competition Experiments

Rxn 1 (k_1)	Rxn 2 (k_2)	Kinetic Expression	eq
$R\bullet \rightarrow R'\bullet$	$R\bullet + XY \rightarrow RX$	$k_1/k_2 = ([R'X]/[RX])\,[XY]_m$	1
$R\bullet \rightarrow R'\bullet$	$R\bullet + XY \rightarrow RX$	$k_1/k_2\,\{\ln([XY]_i+k_1/k_2)-\ln([XY]_f+k_1/k_2)\} =$ $[Sub]_i([R'X]/[RX])(1+([R'X]/[RX]))^{-1}$	2
$R\bullet + XY \rightarrow RX$	$R\bullet + X'Y \rightarrow RX'$	$k_1/k_2 = ([RX]/[RX'])([X'Y]_m/[XY]_m)$	3
$R\bullet + XY \rightarrow RX$	$R\bullet + X'Y \rightarrow RX'$	$k_1/k_2 = (\ln([XY]_i/([XY]_i-[RX])))/(\ln([X'Y]_i/([X'Y]_i-[RX'])))$	4
$R\bullet \leftrightarrow R'\bullet$	$R\bullet + XY \rightarrow RX$	$(k_1/k_2)(k_{2'}/(k_{-1}+k_{2'}[XY]_m)) = [R'X]/[RX]$	5

Eq 1 and 2 are for competitions between a unimolecular and a bimolecular process under pseudo-first order and second order conditions, respectively. Eq 3 and 4 are for competing bimolecular process under pseudo-first order and second order conditions. Rate constants k_1 and k_2 are for reactions 1 and 2; [RX] and [R'X] are the observed yields of unrearranged and rearranged products from reactions of radicals with reagent X-Y in an experiment involving a unimolecular process; [RX'] is the yield of product from reaction of the radical with reagent X'-Y; subscripts m, i and f refer to mean, initial and final concentrations of reagents, respectively. In eq 2, $[Subs]_i$ is the initial concentration of radical precursor. Eq 5 is for a reversible unimolecular process competing with a second order process under pseudo-first order conditions; k_{-1} is the rate constant for the reverse of reaction 1, and $k_{2'}$ is the second order rate constant for trapping rearranged radical.

steady state approximation for the radical) by the rate law for the bimolecular process gives the solution in equation 2 for competition between irreversible first and second order reactions. When eq 2 is applied, it is useful to estimate k_1/k_2 from eq 1 and then solve for a more accurate value of this ratio by trial.

For competing irreversible second order reactions, equation 3 applies when the concentrations of reagents do not vary appreciably. Equation 4 results when the concentrations are not constant.

For many applications, especially in synthesis, a single kinetic determination may be adequate. When more precise kinetic values are desired, a series of competition reactions can be run in which the concentration of the bimolecular trapping agent is varied. For the case of a unimolecular reaction competing with a bimolecular process under pseudo first order conditions, the ratio of rate constants is found as the slope of a plot of [RX]/[R'X] as a function of the trapping agent concentration, the graphical form of equation 1.

The practice of varying the concentration of the trapping reagent in a series of reactions also provides a test of irreversibility for the partitioning reactions and permits the method to be used when a reaction is reversible. A reversible first order reaction would most often complicate a kinetic analysis. For such a case and when the bimolecular trapping agent is present in large excess, the product distribution is described by equation 5 which can be rearranged to give equation 5b. When the reverse reaction is significant, a plot of [RX]/[R'X] versus [XY] will have a non-zero intercept, but the slope of the plot will still yield the desired ratio of rate constants. An example is shown in Figure 2. However, when the forward and reverse reactions are too fast and the radical and its rearranged product effectively equilibrate before trapping, the slope of the plot will approach zero. One should note that the intercept of the plot contains the rate constant of the reverse reaction (k_{-1}) and the rate constant for trapping the rearranged radical ($k_{2'}$) as well as the rate terms in the slope. In favorable cases when the data is adequately precise, division of the intercept by the slope gives a reasonably accurate ratio of the reverse unimolecular rate constant to the rate constant for the trapping reaction of the rearranged radical.

$$[RX]/[R'X] = (k_2k_{-1})/(k_{2'}k_1) + (k_2/k_1)\,[XY]_m \qquad (5b)$$

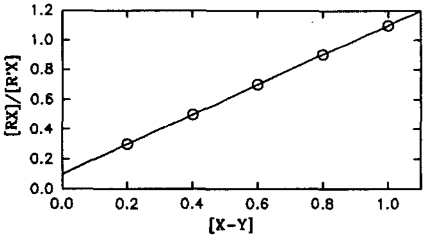


Figure 2. Results of a hypothetical competition reaction between a reversible unimolecular process and an irreversible bimolecular process with $k_1 = 10 \times k_{-1}$ and $k_2 = k_{2'}$. The slope of the function is the ratio k_2/k_1. Because of the equality in the trapping rate constants in this example, the intercept is equal to the inverse of the unimolecular equilibrium constant.

INDIRECT METHODS

In principle, competition kinetic measurements of radical reactions can be accomplished by a wide variety of techniques. In order to simplify product analyses, all radicals should be either reduced or oxidized in a formal sense. The competition method must involve a partitioning of a radical between two processes, and both processes should be competent steps in a radical chain sequence that permits high conversions of the radical precursors. A notable exception to the requirement of a chain reaction sequence is the use of nitroxyl radical couplings (see below). In practice, most competition kinetic measurements have been based on one of three methods, the tin hydride method, the PTOC-thiol method, or the nitroxyl radical coupling method.

The Tin Hydride Method

The most commonly employed indirect technique is the tin hydride method which is based on trialkyltin hydride reduction of an alkyl halide.[3] In this technique, an alkyl halide or pseudohalide (thio or seleno ether) serves as the radical precursor, and a metal hydride (most commonly Bu_3SnH) provides the basis reaction by hydrogen atom transfer trapping of the radical. The method involves the series of reactions shown in Figure 3

$$\text{In–In} \rightarrow 2\,\text{In}\bullet \tag{6}$$

$$\text{In}\bullet + Bu_3Sn\text{–H} \rightarrow \text{In–H} + Bu_3Sn\bullet \tag{7}$$

$$Bu_3Sn\bullet + \text{R–X} \rightarrow Bu_3Sn\text{–X} + \text{R}\bullet \tag{8}$$

$$\text{R}\bullet + Bu_3Sn\text{–H} \rightarrow \text{R–H} + Bu_3Sn\bullet \tag{9}$$

$$\text{R}\bullet \rightarrow \text{R}'\bullet \tag{10}$$

$$\text{R}'\bullet + Bu_3Sn\text{–H} \rightarrow \text{R}'\text{–H} + Bu_3Sn\bullet \tag{11}$$

Figure 3. Important reactions in the tin hydride method. Reactions 6 and 7 comprise the initiation steps. Reactions 8 and 9 are the propagation steps in a conventional tin hydride reduction. Reaction 10, which can be a unimolecular rearrangement or a bimolecular process such as an addition, competes with reaction 9 for alkyl radical, and reaction 11 is another propagation step. Chain termination processes (radical couplings and disproportionations) are not shown.

for Bu_3SnH. Radical chain initiation, usually accomplished by thermolysis of azobisisobutyrylnitrile (AIBN) or a peroxy compound, gives initiator radicals that react with the metal hydride. The metal-centered radical thus formed abstracts halogen or pseudo-halogen from the radical precursor to give the desired radical, R•. The competition reactions are metal hydride trapping of R• to give product R–H and the rearrangement of R• or bimolecular reaction of R•, either of which gives a new radical R'•. Radical R'• also reacts with the metal hydride giving product R'–H.

Rate constants and Arrhenius functions for reactions of Bu_3SnH with a number of radicals have been measured directly by laser flash methods,[4,5] and these values comprise one of the important sets of primary kinetic data for radical kinetic scales. At room temperature, simple alkyl radicals react with Bu_3SnH with rate constants on the order of 2×10^6 M^{-1} s^{-1}. Therefore, Bu_3SnH has been employed extensively for studies of reactions with first order or pseudo first order rate constants in the range of 1×10^4 to 1×10^8 s^{-1} at room temperature. At the upper limit, the competition reaction will greatly predominate over hydrogen atom transfer from Bu_3SnH, and the accuracy of the analytical technique employed to determine the product distribution is an important factor for setting the practical limit of a given study.

The lower limits of utility of Bu_3SnH trapping result from two requirements. On the one hand, one must have enough reagent present to trap all of the radicals formed during the reaction. Usually, tin hydride concentrations not less than 0.01 M are used. Low concentrations can be achieved by employing a small initial concentration of tin hydride and continually regenerating R_3SnH *in situ* from product R_3SnX by reaction with a borohydride reducing agent such as $NaBH_4$ or $NaBH_3(CN)$.[6] It must be assumed that excess borohydride reagent will convert R_3SnX to R_3SnH in an effectively instantaneous reaction, and there is evidence that this assumption is valid.[7] It is also assumed that the radicals will not react rapidly with the borohydride reducing agent; Russell has demonstrated that $NaBH_4$ does not react with alkyl radicals with a measurable rate constant.[8]

The second requirement in regard to lower kinetic limits in metal hydride trapping studies is that the radical chain propagation steps remain fast relative to chain termination steps. As the velocities of the radical reactions are slowed either by reduced concentrations of tin hydride or by the use of a low reactivity metal hydride, the concentration of radical R• will increase. This results in the increasing intrusion of radical-radical reactions that are chain termination steps because radical-molecule reaction velocities increase directly with the radical concentrations whereas radical-radical reaction velocities increase with the square of the radical concentrations.

Most radical-radical reactions will occur with diffusion limited rate constants that are spin statistically limited to 25% efficiency (i.e. only one out of four encounters involves a singlet radical pair that can produce ground state products).[9a] At room temperature in typical organic solvents, the rate constant for radical-radical reactions will be about 5×10^9 M^{-1} s^{-1}.[9] With a Bu_3SnH concentration of 1×10^{-2} M, the velocities of alkyl radical trapping by tin hydride and chain termination will become equal when the radical concentration reaches 4×10^{-6} M. Because the total rate of chain termination reactions must equal the total rate of chain initiation reactions, one can calculate crudely the velocity of chain termination (and, therefore, the total radical concentration) with some knowledge of the rate constants of the initiation reaction.[10] In studies performed at the lower limit of the tin hydride method, one can control the rate of initiation (i.e. maintain low initiator concentrations or low temperatures) in order to extend the total time period of the reaction and prevent high concentrations of radicals.

Other metal hydrides can be substituted for Bu_3SnH to increase the dynamic range of the method or to avoid the difficulties associated with maintaining low concentrations of the tin hydride. The only requirement is that both the hydrogen atom transfer reactions and the halogen atom abstraction reactions must be fast enough to propagate the chain reaction sequence. Trialkylgermanium hydrides react with radicals less rapidly than do tin hydrides,[5,11,12] and, like the R_3Sn• radical, the R_3Ge• radical readily abstracts halogens from alkyl halides.[13] However, Bu_3GeH has never gained popularity most likely because the metal hydride must be prepared from the commercial metal halide and the metal halide is expensive.

Recently, the metal hydride tris(trimethylsilyl)silane, $(Me_3Si)_3SiH$, was reported to be a practical substitute for tin hydride in alkyl halide reductions,[14] and it can be used in the tin hydride method. The compound is commercially available. The rate constants for hydrogen atom transfer from $(Me_3Si)_3SiH$ to alkyl halides are about an order of magnitude smaller than those of Bu_3SnH.[15] In addition to $(Me_3Si)_3SiH$, other silylsilanes[14,16] and phenylsilanes[17] can be used in metal hydride reductions of alkyl halides.

Simple trialkylsilanes such as Et_3SiH are not useful substitutes for tin hydride because the rate constants for hydrogen atom transfer from the metal hydride to the radical are too small.[18,19] Simple thiols, which react rapidly with alkyl radicals,[20] also cannot be used, in this case because the thiyl radical will not abstract halogen from an alkyl halide rapidly enough to maintain a chain reaction. However, a cleverly conceived modification of the tin hydride method involves the use of a mixture of a silane and a thiol.[21] The thiol reacts readily with the alkyl radical (eq 12) to give a thiyl radical which will abstract hydrogen from the silane (eq 13). The silyl radical thus formed continues the chain reaction by abstracting halogen from an alkyl halide (eq 14) or by reaction with another radical precursor. Unfortunately in regard to kinetic studies with unsaturated species, the thiol is partially consumed during the reaction sequence by addition to an isolated double bond, and it appears to be unlikely that this modification of the tin hydride method can be used for accurate kinetic determinations of radical rearrangements.

$$R\bullet + \text{alkyl-S-H} \rightarrow R\text{-}H + \text{alkyl-S}\bullet \qquad (12)$$

$$\text{alkyl-S}\bullet + Et_3Si\text{-}H \rightarrow \text{alkyl-S-H} + Et_3Si\bullet \qquad (13)$$

$$Et_3Si\bullet + R\text{-}X \rightarrow Et_3Si\text{-}X + R\bullet \qquad (14)$$

The silanethiol $(Me_3Si)_3SiSH$ accomplishes the same effect as the hybrid silane/thiol reduction.[22] Reaction of this agent with a radical (eq 15) gives a thiyl radical. A 1,2-shift (eq 16) then produces a silyl radical that can propagate a chain reaction with an alkyl halide or other radical precursor (eq 17). The silanethiol reacts rapidly with a primary radical,[22] but its use in kinetic studies is likely to be complicated by the fact that it can isomerize (via eq 16 followed by hydrogen atom transfer) to $(Me_3Si)_2Si(H)SSiMe_3$, a less active reducing agent, under the reaction conditions.

$$R\bullet + (Me_3Si)_3SiS\text{-}H \rightarrow R\text{-}H + (Me_3Si)_3SiS\bullet \qquad (15)$$

$$(Me_3Si)_3SiS\bullet \rightarrow (Me_3Si)_2Si(\bullet)SSiMe_3 \qquad (16)$$

$$(Me_3Si)_2Si(\bullet)SSiMe_3 + R\text{-}X \rightarrow (Me_3Si)_2Si(X)SSiMe_3 + R\bullet \qquad (17)$$

In its various modifications, the tin hydride method can, in principle, be employed in studies of first order reactions at room temperature ranging from the lower kinetic limit to about $10^8\ s^{-1}$. However, there are caveats. If a silane is employed in a study of a rearrangement, hydrosilylation of the double bonds in the reagents and/or products can occur under free radical conditions due to the rapid rate of addition of silyl radicals to alkenes.[23,24] Further, in attempts to apply the method for the study of fast radical rearrangements, one must be concerned about the stability of the radical precursors in regard to polar reactions. Fast radical rearrangements result from strained radicals, and the alkyl halide precursors for these radicals may not be stable towards ionic dissociation and ensuing cationic rearrangements. Because a cationic rearrangement will often result in the same skeletal reorganization as the radical rearrangement, contamination of the precursor alkyl halide with rearranged alkyl halide (which will be reduced to rearranged hydrocarbon) will complicate, if not vitiate, a kinetic analysis. The problem of precursor instability can be alleviated somewhat by working with alkyl chlorides rather than bromides or, in extreme cases, by employing alkyl phenyl selenides as radical precursors.

The PTOC-Thiol Method

The PTOC-thiol method was developed as a technique that can avoid the inherent kinetic boundary and precursor instability problems at the upper limit of the tin hydride method.[18,25] The key feature of the method is the use of Barton's PTOC esters[26] rather than alkyl halides as radical precursors. (The acronym derives from pyridine-2-thione-*N*-oxycarbonyl.) The chain reaction sequence involved is shown in Figure 4 for the case where a unimolecular rearrangement competes with bimolecular trapping. Addition of any of a number of types of radicals (see below) to the thione group of the PTOC ester results in production of an acyloxyl radical that gives an alkyl radical by rapid decarboxylation. The alkyl radical R• partitions between reaction with an appropriate trapping agent (X–H in Figure 4) and the competing reaction of interest which gives R'•. Radicals X• produced by reactions of X–H with both R• and R'• propagate the chain reaction by addition to the PTOC ester.

The PTOC esters (actually mixed anhydrides of a carboxylic acid and the thiohydroxamic acid) were originally invented as convenient sources of radicals for synthetic applications,[26] and they are one of the more important entries to radicals for a number of conversions. They contain a strong, long wavelength chromophore at ca. 350 nm which extends into the visible giving the compounds a characteristic light yellow color. They are useful radical precursors for ESR studies[27] and for direct kinetic studies employing a laser pulse for radical synthesis.[28] In the case of competition kinetic studies, the PTOC esters are superior to alkyl halides as radical precursors for a number of reasons. They are readily produced from the corresponding carboxylic acid or acid chloride, and many PTOC esters are solids that are easy to purify by recrystallization or chromatography. They are stable when stored at room temperature or below and shielded from light, and they can be employed in kinetic studies up to about 60-80 °C with no special precautions. The pyridine-thione chromophore extending into the visible permits radical chain initiation with visible light from a simple tungsten filament bulb. Therefore, one does not employ an additional initiator in the reactions. In an indirect kinetic study, one first equilibrates a PTOC ester solution in a light-shielded reaction vessel placed in a temperature controlled bath and then initiates the reaction simply by removing the shielding and turning on a lamp. Because all of the radical initiator is depleted at the end of the PTOC conversion, undesired radical reactions such as hydrosilylation are avoided.

The features enumerated above make the PTOC esters convenient radical sources, but two additional properties are vital for the study of fast radical reactions. First, because the radical is produced in a decarboxylation step, highly strained but stable carboxylic acids can be used; this in turn permits the produc-

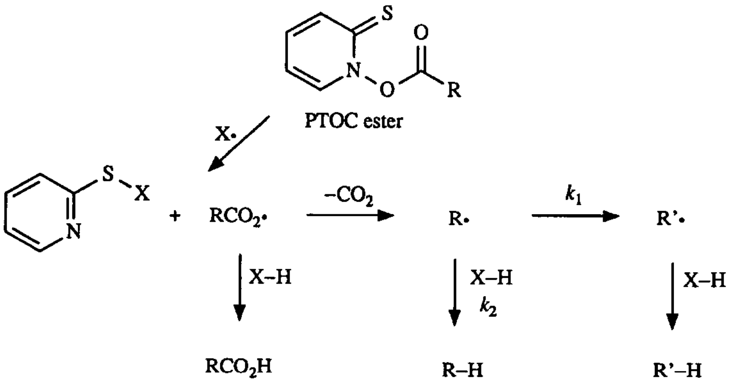


Figure 4. Reactions in the PTOC-thiol method applied to a competing rearrangement and bimolecular hydrogen atom transfer trapping.

tion of highly reactive radicals. Second, the high reactivity of the thione group permits radical chain reactions with a wide variety of radical types including carbon-, silicon-, germanium-, tin-, sulfur- and selenium-centered radicals. The latter feature allows one to employ very reactive hydrogen atom transfer agents such as PhSH and PhSeH in the competing basis reaction and permits kinetic measurements of rearrangements that proceed with rate constants that exceed 1×10^{11} s^{-1} at room temperature.

The highly reactive thione group also provides the lower practical limit for the PTOC-thiol method. Alkyl radicals add to the thione moiety of a PTOC ester in a "self-trapping" reaction with a rate constant at room temperature of about 1×10^6 M^{-1} s^{-1}.[12,29,30] Therefore, if one wished to employ a low reactivity trapping agent such as Et_3SiH in a kinetic study with a PTOC ester precursor, experimental modifications would be required to maintain very low concentrations of the PTOC ester. Because the PTOC esters are radical chain initiators as well as chain propagation agents, low concentrations of PTOC do not result in the degree of problems associated with chain collapse in the tin hydride method. In principle, complete chain collapse resulting from highly dilute solutions of PTOC ester could be accommodated by extended photolysis. In practice, radical entry from a PTOC precursor probably would not be the optimum method of study for reactions with first-order or pseudo-first-order rate constants of less than 1×10^5 s^{-1} at room temperature.

Self-trapping by the PTOC ester creates a limitation for the PTOC-thiol method, but this addition reaction actually can be used in kinetic studies. For example, hydrogen atom transfer reactions from "slow" H-atom donors were measured against the self-trapping reaction,[18] and Curran, Newcomb, *et al.* employed self-trapping by PTOC precursors as the competing basis reaction for measuring the kinetics of halogen atom transfer from reactive halides.[30] Figure 5 shows the propagation steps in the latter study for ethyl iodoacetate. In this type of study, the product ratio can be determined both as the ratio of alkyl pyridyl sulfide to alkyl iodide and as the ratio of the two pyridyl sulfide products; therefore, the method contains an internal check of product distributions. A minor disadvantage in using the PTOC self-trapping reaction as a basis reaction is that pseudo-first-order conditions in PTOC cannot be maintained.

The PTOC-thiol method has some other limitations. Oxygen centered radicals also can react with the thione moiety of the PTOC ester, and this limits the types of radicals that can be produced from these precursors. Aryl and vinyl radicals generally are not available from these precursors because the acyloxyl radical intermediates to these radicals decarboxylate too slowly to avoid reaction with the PTOC precursor.[31] In fact, cyclopropylacyloxyl radicals also can be trapped by PTOC precursors at high concentrations[31] although decarboxylations of these intermediates apparently are rapid enough to compete effectively when the PTOC concentrations are low.[32]

Highly reactive hydrogen atom transfer agents such as PhSeH and PhSH apparently trap acyloxyl radicals in competition with decarboxylation as shown in Figure 4.[33] This reaction is not of kinetic significance, but it can limit the precision of the method by reducing the amount of radical R• produced. In addition, both PhSH and PhSeH have been reported to react with PTOC precursors in polar transacylation reactions.[34] These potential difficulties have not been a serious problem in kinetic studies conducted in the temperature range of about –40 to 50 °C. However, one should be aware of the possibilities that extensive acyloxyl radical trapping might occur at lower temperatures because the bimolecular trapping reaction has a lower energy of activation than the unimolecular decarboxylation reaction, and that extensive transacylation could occur in reactions that are equilibrated for long periods at high (>60 °C) temperatures or that involve sterically congested PTOC esters that have enhanced polar reactivity.

$$RCO_2\bullet \rightarrow R\bullet + CO_2 \tag{18}$$

$$R\bullet + EtO_2CCH_2\text{–}I \rightarrow R\text{–}I + EtO_2CCH_2\bullet \tag{19}$$

$$R\bullet + \text{PTOC–R} \rightarrow \text{R-S-2-pyridyl} + RCO_2\bullet \tag{20}$$

$$EtO_2CCH_2\bullet + \text{PTOC–R} \rightarrow EtO_2CCH_2\text{-S-2-pyridyl} + RCO_2\bullet \tag{21}$$

Figure 5. Propagation reactions in a bimolecular competition kinetic study of halogen atom transfer employing PTOC ester trapping as the basis reaction.

Nitroxyl Radical Couplings

Nitroxyl radicals of the general formula $R_2NO\bullet$ that contain either no hydrogen atoms beta to the nitrogen atom or only bridgehead β-hydrogen atoms are relatively stable. The more hindered members of this class such as 2,2,6,6-tetramethylpiperidine-*N*-oxyl (TEMPO) are dissociated in solution, and TEMPO itself is commercially available. Whereas self-coupling of somewhat hindered nitroxyl radicals does not occur or is reversible, nitroxyl radicals will couple with carbon-centered radicals. Therefore, one can employ nitroxyl radicals at high concentrations as trapping agents in competition kinetic studies, and this is another important indirect method for the study of very fast radical reactions.

Unlike most competition methods, nitroxyl radical couplings do not involve chain reactions (Figure 6). Radicals are produced by hydrogen atom abstraction by the *tert*-butoxy radical (*t*-BuO•), generated from di-*tert*-butyl peroxide or from di-*tert*-butylhyponitrite, by photolysis of a symmetrical diketone, or by photolysis of a diacyl peroxide or a peroxy ester. In order to prevent the formation of numerous radicals in the hydrogen atom abstraction step, H-atom abstraction is limited to cases of highly symmetrical hydrocarbon precursors or species that contain only one reactive hydrogen atom. As was the case with the PTOC-thiol method, the use of carboxylic acid derivatives as the radical precursors permits one to generate highly strained and reactive radicals that would not be accessible from an alkyl halide.

Rate constants for nitroxyl radical couplings with carbon radicals have been determined by laser flash methods and by competition against radical clocks.[35-40] These reactions are very fast and have only slight activation energies. However, even when one corrects for the expected spin statistical factor in radical-radical couplings, it is apparent that nitroxyl-alkyl radical couplings do not proceed at diffusion controlled rates. The coupling reactions of a given nitroxyl radical show little sensitivity to the stability of the carbon radical which is a positive feature in that one can estimate rate constants for coupling of a calibrated nitroxyl with good confidence. On the negative side, nitroxyl radical coupling rates are sensitive to the sterics of the two participants[39] which means that one cannot use a rate constant for reaction of one nitroxyl radical to estimate that for another, and they are subject to solvent polarity and hydrogen bonding effects that can be substantial.[38]

Due to the methods employed for radical generation, nitroxyl radical kinetics have been most often conducted at temperatures above 25 °C. The trialkylhydroxylamine products are unstable with respect to dissociation at high temperatures which would have disastrous consequences in the study of a radical rearrangement reaction; therefore, the reactions are seldom run at >125 °C, and the stability of the products under the reaction conditions should be demonstrated. The thermal instability of the products often precludes GC analyses, and HPLC product analyses typically are required. For adducts with TEMPO, which does not have a UV-chromophore, HPLC/MS analyses have been employed.

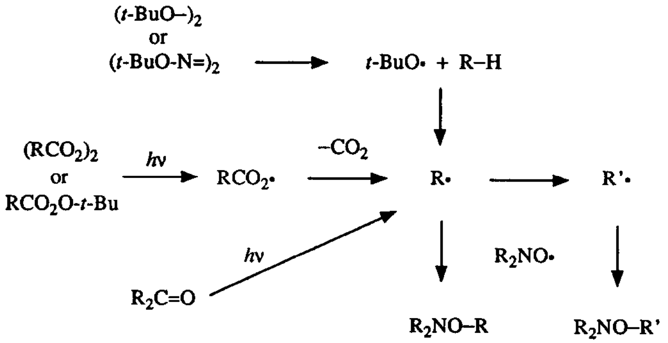
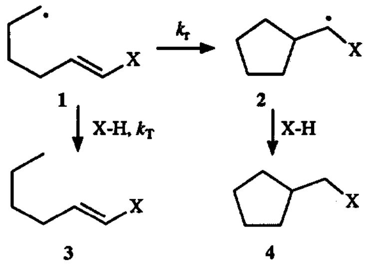


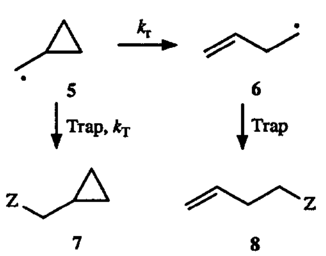
Figure 6. Reactions in competition kinetic studies based on nitroxyl radical couplings.

Approximations in Indirect Kinetic Studies

By their design, indirect kinetic studies often contain two important assumptions. First, in many cases one must assume that the rate constant for reaction of a given radical can be approximated accurately by that for another, structurally related radical. In addition, one often must assume that a particular radical reaction rate constant will not be subject to significant solvent effects. Evidence supporting these two assumptions is relatively strong.

Consider the case where an investigator wishes to determine the rate constant for cyclization of a 6-substituted-5-hexenyl radical **1** by the tin hydride method. The ratio of rate constants k_r/k_T can be obtained from the ratio of products **3** and **4** and the concentration of Bu_3SnH. Next, the assumption is made that k_T for radical **1** is equal to that for reaction of other primary alkyl radicals with Bu_3SnH, specifically the ethyl and butyl radicals, for which rate constants for reaction with Bu_3SnH are known.[4] Multiplication of the experimentally determined rate ratio by k_T gives k_r. In this case, the assumption concerning the value of k_T appears to be quite safe because the radical center is well insulated from the functionality in radical **1**.





However, in order to measure the rate constants for ring opening of the cyclopropylcarbinyl radical (**5**) from the distributions of products **7** and **8**, the same kinetic assumption was necessary. Specifically, the rate constants for reactions of **5** with PhSH and with nitroxyl radicals were assumed to be equal to those for reactions of primary alkyl radicals with these agents.[25,38] Here, the assumption appears to be less sound, especially in light of ESR results that suggest that the spin density in radical **5** is delocalized into the cyclopropyl ring.[41] Whereas an increase in the stability of radical **5** relative to a primary alkyl radical should have little effect on the rate constants for nitroxyl radical couplings (which are quite insensitive to radical stability), such a change in radical stability could have a noticeable effect on the PhSH trapping rate constants.

In practice, the Arrhenius function for ring opening of radical **5** determined against PhSH trapping in the temperature range –37 to 50 °C had the expected activation parameters.[25] In fact, this Arrhenius function was equal within experimental error to that obtained when the PhSH data was combined with kinetic ESR data[42] in the –145 to –120 °C range and nitroxyl radical trapping data[37,40,43] in the 40 to 125 °C range. In addition, the same cyclopropylcarbinyl radical ring opening rate constants are calculated from product distributions with the hydrogen atom transfer trapping agents *t*-BuSH and Bu_3SnH with the assumption that the rate constants for trapping primary and cyclopropylcarbinyl radicals are equal.[20,44] Thus, all evidence available to date suggests that the rate constants for bimolecular reactions of cyclopropylcarbinyl radicals are approximately equal to those for reactions of primary alkyl radicals.

The second assumption commonly made in indirect kinetic studies of radical reactions, that the rate constants are relatively insensitive to solvent effects, appears unusual to one more familiar with polar reaction rate constants. However, the heats of solvation of radicals are essentially equal to those of hydrocarbons,[45] and little charge development is expected in the transition states for many reactions of alkyl radicals. Therefore, the assumption appears to be reasonable for hydrogen atom transfer reactions and radical rearrangements and has been made routinely. Recently, Ingold's group provided evidence that the rate constants of several radical rearrangements were not influenced by solvent change.[38] In cases where the radical is polarized or a polar group is transferred, however, the kinetics should be subject to solvent effects. Solvent effects on the rate constants of nitroxyl radical couplings were noted above.

CALIBRATED RADICAL REACTIONS

Bimolecular Reactions

Hydrogen atom transfer trapping reactions have been most commonly employed as basis reactions in the tin hydride method and in the PTOC-thiol method. The products thus formed are generally stable and usually can be analyzed by GC. In addition, the rate constants for reactions of Bu_3SnH and PhSH with alkyl radicals have been measured directly, and a number of other H-atom donors have been calibrated carefully. The result is that a wide kinetic range of H-atom trapping agents is now available for studies of alkyl radical rates. This is especially the case for primary alkyl radicals as shown in Figure 8 at the end of the text.

Table 2 contains a list of some hydrogen atom transfer agents and their rate constants for reactions with alkyl radicals. A few other trapping agents are also included in this table. In most cases, Arrhenius functions for the reactions are available, and these have been listed. The log A and E_a terms in the Arrhenius functions have been rounded off to leave only the significant figures. Stated errors for the Arrhenius functions have been omitted, and the reader is referred to the original works for these values. Whereas the standard errors reported for Bu_3SnH and PhSH trappings are experimental errors, those reported for a number of trapping agents measured by indirect methods against radical rearrangements are actually errors for the relative Arrhenius function, i.e. for log (k_r/k_T), and do not incorporate estimated errors in the basis rate constants while some results from indirect studies do incorporate estimated errors for the basis reaction kinetics. Some of the kinetic values in Table 2 and Chart 1 (see below) were adjusted by the author to correct for changes in the accepted values of the rate constants of the basis reactions used in the original studies.

In applications based on the tin hydride method, the silylsilanes, the germanium hydride, the silanethiol and, of course, tin hydride can be employed. Et_3SiH reacts with radicals so slowly that chain propagation will be inefficient, and the thiols and selenide also cannot be employed in the tin hydride method because halogen atom abstractions are not efficient for the radicals from these agents. In principle, any hydride donor listed in Table 2 can be used in the PTOC-thiol method with the possible exception of dicyclohexylphosphine (DCPH).[18] However, in practice, alkyl radical addition to the PTOC ester will compete with the slower hydride donors requiring highly dilute solutions of the precursors.

Simple group transfer reactions such as halogen atom transfers and chalcogen transfers are also compatible with the PTOC-thiol method due to the wide range of radicals that will propagate chain reactions by addition to the PTOC esters. Again, one must be concerned with the PTOC self-trapping reaction when a slow group transfer agent is employed.

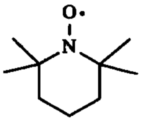
For the reactive H-atom donor PhSH, it is instructive to note that the rate constants and Arrhenius functions for trapping 1°, 2° and 3° radicals are quite similar. This is also seen in the values for Bu_3SnH trappings of the series of alkyl radicals. These trapping reactions are highly exergonic, and it is perhaps not surprizing that changes in the final product stabilities (i.e. formation of a tertiary C-H bond as opposed to a primary C-H bond) have little effect on the energetics of the early transition states. It is almost certain that even smaller changes in $\Delta G°$ of H-atom transfer reactions that will arise from remote substitution differences in a series of, for example, primary radicals will have no measurable effect on the kinetics of trapping reactions, and the important kinetic approximation discussed above is justified. The small difference in rate constants of reactions of PhSH with alkyl radicals of different substitution also suggests that the rate constant given for reactions of primary radicals with the more reactive donor PhSeH will be a good approximation for the rate constants for reactions of simple 2° and 3° radicals with this agent.

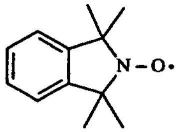
As noted, rate constants for alkyl radical couplings with nitroxyl radicals are relatively insensitive to the radical stability as can be seen for the rate constants listed for reactions of the nitroxyl radicals 2,2,6,6-tetramethylpiperidine-*N*-oxyl (TEMPO) and 2,2,5,5-tetramethylisoindole-*N*-oxyl (TMIO) in non-polar solvents.[35-39] For comparison, rate constants for reactions of the H-atom donor PhSH with the series of radicals shown for TEMPO span four orders of magnitude. Because of the high reactivity of nitroxyl radicals, they are most useful for studies of fast radical reactions. The reader is referred to a recent publication for more detailed kinetic listings.[39]

Table 2. Calibrated Bimolecular Radical Reactions.

Donor	Radical	Rate Constant ($M^{-1}s^{-1}$)[a]	log(k·Ms)[b]	Ref
Et_3Si–H	$RCH_2\bullet$	$k_{25} = 7 \times 10^2$	$8.7 - 8.0/\theta$	19
	$R_3C\bullet$	$k_{50} = 3 \times 10^3$		18
Ph_3Si–H	$RCH_2\bullet$	$k_{50} = 3 \times 10^4$		18
$(Me_3Si)_2Si(Me)$–H	$RCH_2\bullet$	$k_{25} = 3.2 \times 10^4$	$8.9 - 6.0/\theta$	46
Bu_3Ge–H	$CH_3\bullet$	$k_{27} = 5 \times 10^5$		5
	$RCH_2\bullet$	$k_{25} = 1 \times 10^5$	$8.4 - 4.7/\theta$	11
	$R_2CH\bullet$	$k_{25} = 1.8 \times 10^4$	$8.3 - 5.5/\theta$	12
	$R_3C\bullet$	$k_{25} = 2 \times 10^4$		12
1,4-CHD[c]	$RCH_2\bullet$	$k_{50} = 2 \times 10^5$		18
	$R_3CCH_2\bullet$	$k_{50} = 5 \times 10^5$		18
$(Me_3Si)_3Si$–H	$RCH_2\bullet$	$k_{25} = 3.8 \times 10^5$	$8.9 - 4.5/\theta$	15
	$R_2CH\bullet$	$k_{25} = 1.4 \times 10^5$	$8.3 - 4.3/\theta$	15
	$R_3C\bullet$	$k_{25} = 2.5 \times 10^5$	$7.9 - 3.4/\theta$	15
DCP–H[d]	$RCH_2\bullet$	$k_{50} = 7 \times 10^5$		18
	$R_3CCH_2\bullet$	$k_{27} = 1.0 \times 10^6$		18
	$PhCH_2\bullet$	$k_{25} = 2.4 \times 10^3$	$8.0 - 6.3/\theta$	47
Bu_3Sn–H	$c\text{-}C_3H_5\bullet$	$k_{25} = 8.5 \times 10^7$	$9.3 - 1.9/\theta$	5
	$CH_3\bullet$	$k_{25} = 1.1 \times 10^7$	$9.4 - 3.2/\theta$	4
	$RCH_2\bullet$	$k_{25} = 2.4 \times 10^6$	$9.1 - 3.7/\theta$	4
	$Me_3CCH_2\bullet$	$k_{25} = 3.3 \times 10^6$	$8.5 - 2.7/\theta$	5
	$Me_2CH\bullet$	$k_{25} = 1.4 \times 10^6$	$8.7 - 3.5/\theta$	4
	$c\text{-}C_6H_{11}\bullet$	$k_{25} = 1.8 \times 10^6$	$9.2 - 4.0/\theta$	4
	$Me_3C\bullet$	$k_{25} = 1.6 \times 10^6$	$8.4 - 3.0/\theta$	4
	$PhCH_2\bullet$	$k_{25} = 3.6 \times 10^4$	$8.6 - 5.6/\theta$	47
Ph_3Sn–H	$RCH_2\bullet$	$k_{25} =$ ca. 5×10^6, $k_{70} = 1.5 \times 10^7$		48
t-BuS–H	$RCH_2\bullet$	$k_{25} = 8.0 \times 10^6$	$8.4 - 2.0/\theta$	20
	$R_3CCH_2\bullet$	$k_{32} = 1.1 \times 10^7$		18
$(Me_3Si)_3SiS$–H	$RCH_2\bullet$	$k_{85} = 4 \times 10^7$		22
PhS–H	$c\text{-}C_3H_5\bullet$	$k_{20} = 4.1 \times 10^9$		35
	"$c\text{-}C_4H_7\bullet$"	$k_0 = 5 \times 10^8$		33
	$RCH_2\bullet$	$k_{25} = 1.4 \times 10^8$	$9.4 - 1.7/\theta$	49
	$Me_2CH\bullet$	$k_{25} = 1.0 \times 10^8$	$9.3 - 1.7/\theta$	49
	$Me_3C\bullet$	$k_{25} = 1.1 \times 10^8$	$9.2 - 1.6/\theta$	49
	$PhCH_2\bullet$	$k_{25} = 3.1 \times 10^5$	$8.3 - 3.8/\theta$	47
PhSe–H	$RCH_2\bullet$	$k_{25} = 2.1 \times 10^9$	$10.9 - 2.1/\theta$	50
Cl_3C–Cl	$RCH_2\bullet$	$k_{25} = 1.2 \times 10^4$	$8.1 - 5.5/\theta$	51a
	$RCH_2\bullet$	$k_{25} = 6 \times 10^4$		51b
Cl_3C–Br	$RCH_2\bullet$	$k_{25} = 1.6 \times 10^8$	$9.6 - 1.9/\theta$	52
EtO_2CCH_2–Br	$RCH_2\bullet$	$k_{50} = 7 \times 10^4$		30
EtO_2CCH_2–I	$RCH_2\bullet$	$k_{50} = 2.6 \times 10^7$		30
$NCCH_2$–I	$RCH_2\bullet$	$k_{50} = 1.7 \times 10^9$		30
PhS–SPh	$RCH_2\bullet$	$k_{25} = 1.7 \times 10^5$		53
PhSe–SePh	$RCH_2\bullet$	$k_{25} = 2.6 \times 10^7$		53
PhTe–TePh	$RCH_2\bullet$	$k_{25} = 1.1 \times 10^8$		53
Addition to PTOC	$RCH_2\bullet$	$k_{25} = 7 \times 10^5$	$9.8 - 5.4/\theta$	30

[a] Reaction temp. (°C) as subscript. [b] $\theta = 2.3RT$ in kcal/mol. [c] 1,4-Cyclohexadiene. [d] Dicyclohexylphosphine





Radical	TEMPO	TMIO
cyclopropyl	$k_{25} = 1.2 \times 10^9\ M^{-1}\ s^{-1}$	
cyclobutyl	$k_{18} = 1.4 \times 10^9\ M^{-1}\ s^{-1}$	
primary	$k_{20} = 1.2 \times 10^9\ M^{-1}\ s^{-1}$	$k_{18} = 1.3 \times 10^9\ M^{-1}\ s^{-1}$
secondary	$k_{18} = 1.0 \times 10^9\ M^{-1}\ s^{-1}$	$k_{18} = 1.1 \times 10^9\ M^{-1}\ s^{-1}$
tertiary	$k_{20} = 0.8 \times 10^9\ M^{-1}\ s^{-1}$	$k_{20} = 0.9 \times 10^9\ M^{-1}\ s^{-1}$
benzyl	$k_{20} = 0.5 \times 10^9\ M^{-1}\ s^{-1}$	$k_{20} = 0.6 \times 10^9\ M^{-1}\ s^{-1}$

Unimolecular Rearrangements; Radical Clocks

As suggested earlier, one often wishes to incorporate a unimolecular radical reaction, a rearrangement, into a competition study in order to minimize difficulties. Calibrated radical rearrangements employed as basis reactions are usually referred to as "radical clocks", an appellation used by Griller and Ingold in a seminal review of the subject in 1980.[54]

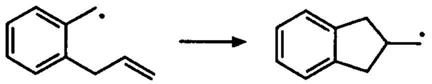
At the time of the Griller and Ingold review, radical clocks were available with rate constants at room temperature that ranged from about $1 \times 10^3\ s^{-1}$ (the practical lower limit of useful radical reactions) to $1 \times 10^8\ s^{-1}$. Since then, the rate constants of most of the clocks have been determined more precisely and more accurately, and new clock reactions have been developed. The top end of the radical clock scale moved up consistently throughout the last several years and recently jumped to greater than $1 \times 10^{11}\ s^{-1}$ at room temperature.[55,56] This means that radical clocks now exist for the entire range of radical kinetics that might be of interest; diffusion controlled bimolecular reactions have rate constants on the order of $2 \times 10^{10}\ M^{-1}\ s^{-1}$ at room temperature, and the fastest possible unimolecular reaction, the decay of a transition state, has a rate constant of about $6 \times 10^{12}\ s^{-1}$ at room temperature.

Any unimolecular radical reaction qualifies as a radical clock once the rate constant for the reaction is known. This includes fragmentation reactions as well as the more commonly employed rearrangements. Most clock applications for alkyl radicals have involved *exo* cyclizations (such as cyclization of the 5-hexenyl radical), ring openings of small ring "carbinyl" radicals (the reverse of an *exo* cyclization), and 1,2-migrations that proceed by an *exo* cyclization followed by a ring opening. Some of the features of these three types of clock reactions are discussed below.

Reviews of radical rearrangements have appeared over the past several years,[57] but many of the rate constants given in earlier reviews, when available, have been revised recently. A number of calibrated alkyl radical clocks are collected in Chart 1 which is not all inclusive but which contains many of the more reliably calibrated clock reactions. Typically, radicals that rearrange to give predominantly one product were selected for the chart. The clocks are listed approximately in increasing rates of reaction, and rate constants and Arrhenius functions, when available, are given. Again, the log A and E_a terms in the Arrhenius functions have been rounded off to the significant figures, and the error limits in the original works are not included. For some cyclopropylcarbinyl radicals, the Arrhenius functions are predicted (see discussion below); in these cases, the temperature dependent functions are given in brackets.

There are a number of primary alkyl radical clocks available, especially if a neopentyl-type radical is considered to be a primary radical and primary radical clocks with a kinetic range exceeding eight powers of ten are known (see Figure 8 at end of text). Fewer secondary and tertiary alkyl radical clocks have been calibrated. Benzylic radical clocks are almost non-existent, and the recent measurement by Ingold's group of a rate constant for rearrangement of **CL-30** is important. A cyclobutyl radical clock (**CL-31**) is also available.

Chart 1. Calibrated Radical Clocks[a]

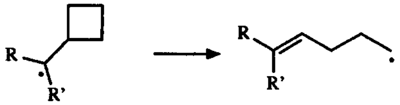


CL-1

$k_{25} = 0.14\ s^{-1}$, log (k·s) = 11.1 − 16.3/θ, ref 58

CL-2

$k_{25} = 4 \times 10^3\ s^{-1}$, log ($k$·s) = 11.8 − 11.1/θ, ref 59



CL-3: R = R' = H

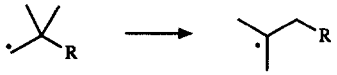
$k_{25} = 5 \times 10^3\ s^{-1}$, log ($k$·s) = 12.6 − 12.2/θ, ref 60, 61, 62

CL-4: R = Me, R' = H

$k_{60} = 6 \times 10^3\ s^{-1}$, ref 61

CL-5: R = R' = Me

$k_{60} = 4 \times 10^3\ s^{-1}$, ref 61



CL-6: R = Ph

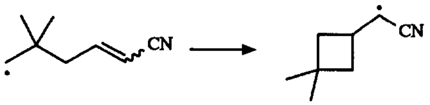
$k_{25} = 9 \times 10^2\ s^{-1}$, log ($k$·s) = 11.6 − 11.8/θ, ref 58

CL-7: R = C(=O)CMe$_3$

$k_{25} = 2 \times 10^5\ s^{-1}$, log ($k$·s) = 10.9 − 7.8/θ, ref 51

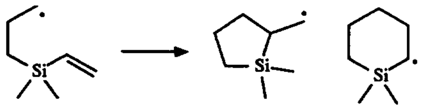
CL-8: R = CH=CH$_2$

$k_{25} = 5 \times 10^6\ s^{-1}$, log ($k$·s) = 11.0 − 5.9/θ, ref 63



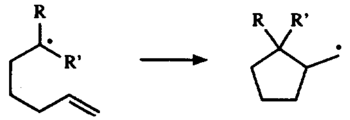
CL-9

$k_{50} = 1.9 \times 10^4\ s^{-1}$, ref 64



CL-10

5-*exo*: $k_{25} = 6 \times 10^4\ s^{-1}$,
6-*endo*: $k_{25} = 4 \times 10^3\ s^{-1}$, ref 65



CL-11: R = R' = H

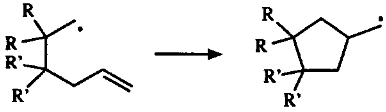
$k_{25} = 2.3 \times 10^5\ s^{-1}$, log ($k$·s) = 10.4 − 6.85/θ, ref 4

CL-12: R = Me, R' = H

cis: $k_{25} = 3 \times 10^4\ s^{-1}$, log ($k$·s) = 9.9 − 7.4/θ
trans: $k_{25} = 1.0 \times 10^5\ s^{-1}$, log ($k$·s) = 9.8 − 6.5/θ, ref 12, 66

CL-13: R = R' = Me

$k_{25} = 3 \times 10^5\ s^{-1}$, log ($k$·s) = 9.9 − 6.0/θ, ref 15

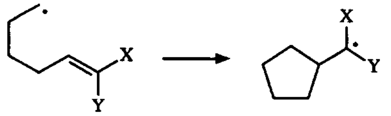


CL-14: R = Me, R' = H

$k_{25} = 5 \times 10^6\ s^{-1}$, log ($k$·s) = 9.9 − 4.4/θ, ref 5, 66

CL-15: R = H, R' = Me

$k_{25} = 5 \times 10^6\ s^{-1}$, log ($k$·s) = 10.5 − 5.1/θ, ref 66



CL-16: X = Y = Ph

$k_{25} = 5 \times 10^7\ s^{-1}$, log ($k$·s) = 10.4 − 3.7/θ, ref 67

CL-17: X, Y = OMe, H

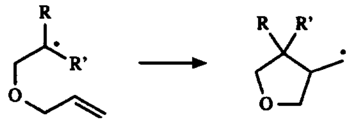
$k_{50} = 1.4 \times 10^6\ s^{-1}$, ref 68

CL-18: X, Y = CN, H

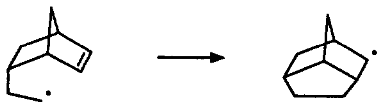
$k_{25} = 1.6 \times 10^8\ s^{-1}$, log ($k$·s) = 11.0 − 3.8/θ, ref 50, 68

CL-19: X, Y = OMe, CN

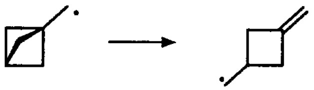
$k_{50} = 2.5 \times 10^8\ s^{-1}$, ref 68



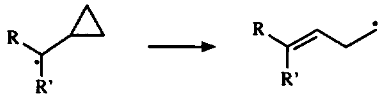
CL-20: R = R' = H
$k_{25} = 9 \times 10^{6}\ \mathrm{s}^{-1}$, $\log(k\cdot\mathrm{s}) = 9.9 - 4.0/\theta$, ref 69
CL-21: R = Me, R' = H
$k_{25} = 4 \times 10^{6}\ \mathrm{s}^{-1}$, $\log(k\cdot\mathrm{s}) = 9.6 - 4.1/\theta$, ref 70
CL-22: R = R' = Me
$k_{25} = 1.4 \times 10^{7}\ \mathrm{s}^{-1}$, $\log(k\cdot\mathrm{s}) = 9.7 - 3.5/\theta$, ref 37



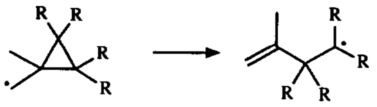
CL-23
$k_{65} = 1.1 \times 10^{7}\ \mathrm{s}^{-1}$, ref 71



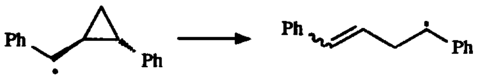
CL-24
$k_{25} = 1.2 \times 10^{7}\ \mathrm{s}^{-1}$, $\log(k\cdot\mathrm{s}) = 12.8 - 7.8/\theta$, ref 72, 73



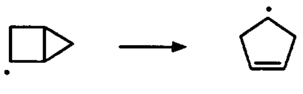
CL-25: R = R' = H
$k_{25} = 9.4 \times 10^{7}\ \mathrm{s}^{-1}$, $\log(k\cdot\mathrm{s}) = 13.15 - 7.05/\theta$, ref 25
CL-26: R = Me, R' = H
$k_{25} = 4 \times 10^{7}\ \mathrm{s}^{-1}$, $[\log(k\cdot\mathrm{s}) = 13.15 - 7.5/\theta]$, ref 74
CL-27: R = R' = Me
$k_{25} = 5 \times 10^{7}\ \mathrm{s}^{-1}$, $[\log(k\cdot\mathrm{s}) = 13.15 - 7.4/\theta]$, ref 74



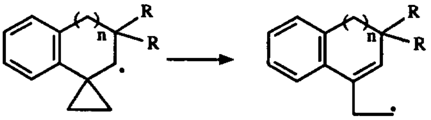
CL-28: R = H
$k_{25} = 5 \times 10^{7}\ \mathrm{s}^{-1}$, $[\log(k\cdot\mathrm{s}) = 13.15 - 7.4/\theta]$, ref 74
CL-29: R = Me
$k_{25} = 4 \times 10^{9}\ \mathrm{s}^{-1}$, $[\log(k\cdot\mathrm{s}) = 13.15 - 4.9/\theta]$, ref 74



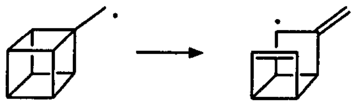
CL-30
$k_{40} = 3 \times 10^{8}\ \mathrm{s}^{-1}$, $[\log(k\cdot\mathrm{s}) = 12.8 - 6.3/\theta]$, ref 75



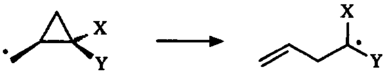
CL-31
$k_{25} = 1.5 \times 10^{9}\ \mathrm{s}^{-1}$, $\log(k\cdot\mathrm{s}) = 13.0 - 5.2/\theta$, ref 33, 74



n = 0, R = H, Me, Et; n = 1, R = H, Me
$k_{75} = 2\text{-}9 \times 10^{9}\ \mathrm{s}^{-1}$, ref 76
CL-32: n = 0, R = H
$k_{75} = 2 \times 10^{9}\ \mathrm{s}^{-1}$, $[\log(k\cdot\mathrm{s}) = 12.85 - 5.6/\theta]$, ref 76



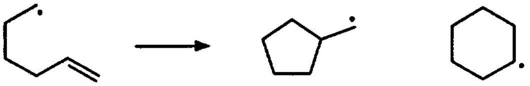
CL-33
$k_{25} = 3 \times 10^{10}\ \mathrm{s}^{-1}$, $\log(k\cdot\mathrm{s}) = 13.2 - 3.7/\theta$, ref 77



CL-34: X = Ph, Y = H
$k_{25} = 3 \times 10^{11}\ \mathrm{s}^{-1}$, $\log(k\cdot\mathrm{s}) = 13.8 - 3.2/\theta$, ref 56
CL-35: X = H, Y = Ph
$k_{25} = 4 \times 10^{11}\ \mathrm{s}^{-1}$, $\log(k\cdot\mathrm{s}) = 13.9 - 3.1/\theta$, ref 56
CL-36: X = Y = Ph
$k_{25} = 5 \times 10^{11}\ \mathrm{s}^{-1}$, $\log(k\cdot\mathrm{s}) = 13.1 - 2.0/\theta$, ref 56

[a] Temperature of reaction in °C given as subscript; $\theta = 2.3RT$ in kcal/mol.

Radical cyclizations. Rate constants for many 5-*exo* radical cyclizations are given in Chart 1. Cyclization of the 5-hexenyl radical (**CL-11**) to the cyclopentylmethyl radical is perhaps the best known reaction in this class proceeding with a rate constant of 2.3×10^5 s^{-1} at 25 °C. The thermodynamically favored product from cyclization of the 5-hexenyl radical, the cyclohexyl radical, is formed by a 6-*endo* process in about 2% yield.[57a,78] In general, similarly high regioselectivity is seen in related systems with 5-*exo* radical cyclizations greatly favored over 6-*endo* processes. The exceptions are cases with alkyl substitution at C(5) of the chain or the sila analogues such as **CL-10**, and the exceptions usually arise because the 5-*exo* process is slowed whereas the 6-*endo* cyclization is relatively unaffected.[57a]

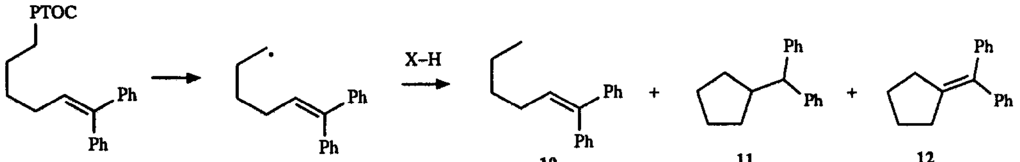


CL-11 5-*exo* cyclization 6-*endo* cyclization
50 : 1

Most of the measured log A terms for 5-*exo* radical cyclizations are close to 10.4, the value for the parent 5-hexenyl radical. It is to be expected that the entropic requirements of the transition states for these cyclizations should be similar. Therefore, to a first approximation, one should expect that a single reliable rate constant at one temperature for a 5-*exo* cyclization of a 5-hexenyl radical that does not contain a substituent at C(5) could be used with a log A value of 10.4 to calculate a reasonable rate constant at another temperature.

The 5-hexenyl type cyclizations are generally useful at the low and middle regions of the kinetic scale. However, incorporation of a radical stabilizing group or groups onto the alkene terminus can significantly increase the rate constant for cyclization. The 6-cyano-5-hexenyl radical (**CL-18**) and the 6-cyano-6-methoxy-5-hexenyl radical (**CL-19**) rearrange faster than the cyclopropylcarbinyl radical (**CL-25**) and can be used as clocks for quite fast bimolecular reactions. The 6,6-diphenyl-5-hexenyl radical (**CL-16**) also cyclizes quite rapidly with a rate constant of about one-half that of the cyclopropylcarbinyl ring opening.

There is a caution, however, in the use of clocks such as **CL-16** that give a stabilized radical product upon rearrangement. The cyclic diphenyl-substituted radical apparently reacts somewhat slowly with *t*-BuSH, and when PTOC ester **9** was allowed to react in the presence of low concentrations of *t*-BuSH, accumulation of radicals resulted in disproportionation reactions as evidenced by the formation of **12**. In this case, the ratio of reduced products **10** and **11** would have led to an inaccurate ratio of rate constants because the cyclic radical was selectively depleted. However, PhSH and Bu_3SnH (and *t*-BuSH at high concentrations) reacted fast enough such that high yields of the two reduction products **10** and **11** were observed.[67]



9 **CL-16** **10** **11** **12**

		% Yields	
t-BuSH, 0.1 M	2	80	11
t-BuSH, 5.1 M	44	51	2
PhSH, 1.4 M	75	20	0
Bu_3SnH, 1.8 M	8	88	0

Radical ring openings. A number of radical ring opening clocks are listed in Chart 1. These reactions are the reverse of *exo* cyclizations, and they are driven by the strain energy of a small ring that is ruptured in the rearrangement. The cyclopropylcarbinyl radical ring openings are perhaps the best known of this group, and the ring opening of the parent radical, cyclopropylcarbinyl (**CL-25**), is the archetypal fast radical rearrangement with a rate constant for ring opening at 25 °C of nearly 1 × 10^8 s^{-1}. Several alkyl substituted cyclopropylcarbinyl rearrangements were recently calibrated by Ingold's group;[74] the fastest clock of this series is **CL-29** which opens about 40 times faster at room temperature than the parent. Rate constants for ring openings of cyclobutylcarbinyl radicals[61] are less well characterized than those for reactions of their three-membered ring analogs, but they provide a useful set of relatively slow radical rearrangements.

The incorporation of radical stabilizing groups onto the cyclopropyl ring results in extremely fast ring openings. The phenyl-substituted cyclopropylcarbinyl radicals **CL-34**, **CL-35** and **CL-36** have rate constants for ring opening that are accelerated over that of the parent, cyclopropylcarbinyl radical, by more than three orders of magnitude,[55,56] and these clocks can be used in competition with the fastest possible reaction. The carboethoxy group apparently leads to a similar rate acceleration. A mixture of *cis*- and *trans*-2-(carboethoxy)cyclopropylcarbinyl radicals gave only ring opened products in an attempt to measure the kinetics of ring opening by nitroxyl radical trapping; the rate constants for ring opening were estimated to be $>5 \times 10^{10}$ s^{-1} at 60 °C.[40]

The cyclopropylcarbinyl radical (**CL-25**) ring opening is an important linchpin reaction for the entire set of indirect kinetic studies. The Arrhenius function for this reaction results from a combination of the kinetic data acquired with three independent techniques (kinetic ESR spectroscopy, PhSH trapping, and nitroxyl radical coupling) over a temperature range of >250 °C.[25,37,42,43] In addition, many other trapping agents included Bu_3SnH,[44] Ph_3SnH,[79] *t*-BuSH[20] and PhSeH[50,55] have been employed in reactions with this radical. The result is that the kinetic scale of bimolecular trapping reactions is highly interrelated via this radical rearrangement. One sees, for example, that the independent direct kinetic measurements of Bu_3SnH, PhSH and nitroxyl trappings are positioned equivalently with regard to kinetics of reactions with primary alkyl radicals.

The Arrhenius function measured for cyclopropylcarbinyl radical ring opening, $\log (k{\cdot}s) = 13.15 - 7.05/\theta$, is important for another reason. In a rigid species such as cyclopropylcarbinyl, one can anticipate with confidence that the transition state for ring opening will require the isolation of only one molecular rotor, the rotation of the methylene group.[42] Accordingly, the entropy of activation for the ring opening reaction can be predicted. The isolated methylene rotation in the transition state, leading to an entropic penalty, is essentially completely compensated by the fact that two modes of ring opening for the radical exist, cleavage of either cyclopropyl bond containing C(1) of the ring. The predicted entropy of activation is $\Delta S^{\ddagger} = 0$ which leads to $\log A = 13.1$ at room temperature.[80] The experimental log *A* term is in excellent agreement with the anticipated value.

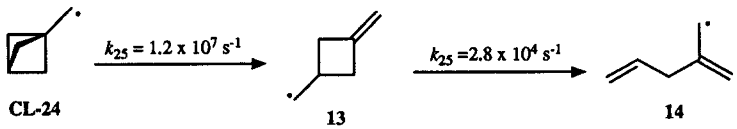
For cleavage of one of the bonds in cyclopropylcarbinyl, the log *A* term is 12.85 (subtraction of $\log 2 = 0.3$), and one should expect that this value will also be the log *A* term for cleavage of a single bond in any cyclopropylcarbinyl radical or similarly rigid radical. Therefore, one can calculate an Arrhenius function for ring opening of a rigid radical from one rate constant and $\log A = 12.85$ per bond. In fact, Ingold *et al.* have claimed that this approach and a single accurate kinetic value will lead to a more accurate Arrhenius function for rearrangement than can be measured by any single technique, and they used this expediency to calculate temperature dependent functions for a number of substituted cyclopropylcarbinyl ring openings.[74] The Arrhenius functions thus calculated, either by the Ingold group or by this author, are given in Chart 1 in brackets.

The linear free energy relationship in cyclopropylcarbinyl radical ring openings manifested above in terms of similar entropic demands for the transition states, also leads to an interesting semi-quantitative prediction of rate constants via Marcus theory. In addition to the rate constant for ring opening of the cyclopropylcarbinyl radical to the 3-butenyl radical, the rate constant for cyclization of the 3-butenyl radical is known;[59] therefore, one can calculate the equilibrium constant and ΔG° for the reaction. Employing this ΔG°

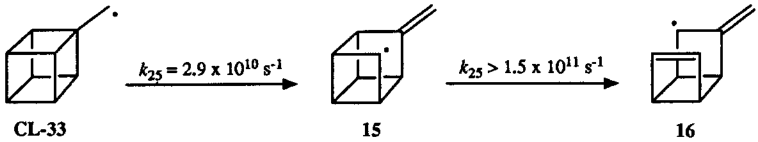
and the $\Delta G^\ddagger$ value from the rate constant for ring opening in the Marcus equation (eq 22),[81] Newcomb *et al.*[56] calculated an intrinsic free energy of activation ($\Delta G^\ddagger_i$) of 9.32 kcal/mol for the reaction; this is the expected activation energy for a thermoneutral cyclopropylcarbinyl ring opening. Then, employing estimates of ΔG° derived from hydrocarbon bond dissociation energies, they used the Marcus relationship to calculate $\Delta G^\ddagger$ values for more highly exergonic reactions. Extrapolation to the highly reactive radicals **CL-34**, **CL-35** and **CL-36** led to predicted rate constants at 25 °C of 1×10^{11} s^{-1} for the first two and 4×10^{11} s^{-1} for the latter, in quite good agreement with the experimental values.[56]

$$\Delta G^\ddagger = \Delta G^\ddagger_i + \Delta G^\circ/2 + (\Delta G^\circ)^2/(16\Delta G^\ddagger_i) \tag{22}$$

The bicyclo[1.1.1]pentylcarbinyl radical (**CL-24**) and the cubylcarbinyl radical (**CL-33**) rearrangements also involve openings of rigid species. In these cases, three equivalent bonds can break. Therefore, the expected log A values are 12.85 plus log 3 (0.48) or 13.3. The experimental value of log A = 13.2 for cleavage of radical **CL-33** is quite close to the expected value.



CL-24 **13** **14**

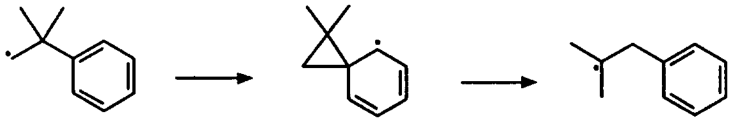


CL-33 **15** **16**

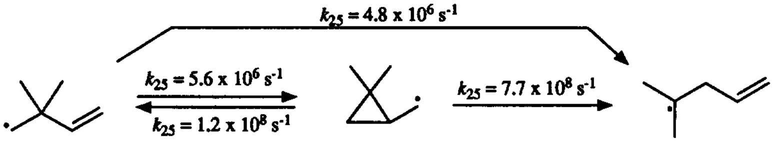
The ring opening rearrangements of **CL-24**[72,73] and **CL-33**[77,82] are noteworthy for another reason. In both cases, the initial ring opening reaction is followed by a second bond cleavage reaction that gives a radical with spin density at the original radical site. In the former system, the second radical rearrangement, a cyclobutylcarbinyl ring opening, is slower than the first bond cleavage.[83] For the cubylcarbinyl radical, however, the second bond cleavage is faster than the first, and, indeed, the two bonds might be broken in a synchronous process.[77] The fact that spin density resides at the original radical site after the second rearrangement might prove to be an important point in mechanistic studies of enzyme oxidations where free molecular rotation of a radical intermediate could be prevented by steric constraints in the enzyme's active site. To this author's knowledge, this potentially important facet of the reactions was first pointed out by Branchaud *et al.* who coined the term "round trip radical probe" for this class of radicals.[72]

1,2-Migrations. Several of the clocks in Chart 1 rearrange by 1,2-migrations. The archetypal reaction of this class is the neophyl radical (**CL-6**) rearrangement that was first reported half a century ago by Kharasch.[84] Although the mechanism of 1,2-migrations was in dispute for some time, it is now clear that many of these reactions proceed by an initial 3-*exo* radical cyclization followed by a ring opening step as shown for the neophyl rearrangement.

Consistent with the cyclization-ring opening pathway for 1,2-migrations is the fact that the log A terms for radical rearrangements of this type are about 11.[51] An alternative mechanism, involving a dissociation followed by a radical addition, would be expected to have a larger log A term. In addition, the 2,2-dimethyl-3-butenyl radical (**CL-8**) system is very well characterized with rate constants for ring opening of the intermediate 2,2-dimethylcyclopropylcarbinyl radical (**19**) to both the 2,2-dimethyl-3-butenyl radical and the 1,1-



CL-6 **17** **18**

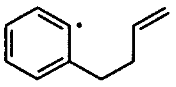


CL-8 **19** **20**

dimethyl-3-butenyl radical (**20**) known.[63] When 2,2-dimethyl-3-butenyl radical was generated in the presence of PhSH, a small amount of 1,1,2-trimethylcyclopropane was formed by trapping cyclic radical **19**; this amount was the same as that predicted from the Arrhenius functions for the various conversions shown in the drawing.[63]

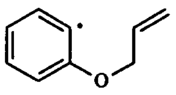
VINYL AND ARYL RADICAL REACTIONS

Competition kinetic studies also have been reported for vinyl and aryl radical reactions. For example, for the radicals **21-23**, the ratios of rate constants for cyclization and trapping by Bu_3SnH are shown below.[5,85,86] The ratios would give absolute kinetic values for cyclization if the trapping rate constants were known.



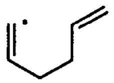
21

k_c/k_T = 0.6 M at 25 °C



22

k_c/k_T = 1.0 M at 25 °C



23

k_c/k_T = 0.9 M at 80 °C

In fact, rate constants for reactions of Bu_3SnH with the phenyl radical and a vinyl radical were reported by Ingold *et al.*[5] In this study,[5] radicals were produced by decarboxylation of acyloxyl and aroyloxyl radical precursors, and the rate constants for growth of the $Bu_3Sn•$ radical were measured. However, it was later found that the decarboxylation reaction of $ArCO_2•$ was slower than originally expected.[87] Therefore, the reactions producing the $Bu_3Sn•$ radical included reaction of the aroyloxyl radical with the tin hydride. In a subsequent publication, Beckwith *et al.* stated that the rate constants for reactions of Bu_3SnH with aryl radicals are described by $\log (k \cdot \mathrm{Ms}) = 9.6 - 1.7/\theta$ based on unpublished work.[88] These kinetic values are close to those originally reported,[5] but, because experimental details and the identities of the aryl radicals were not provided in the latter work,[88] it is difficult to anticipate the accuracy of the values.

The rate constants for reaction of vinyl radical with Bu_3SnH are also vitiated for the same reason. Vinyl acyloxyl radicals react with PTOC ester precursors before decarboxylation as was noted earlier,[31] and recent measurements found that the rate constants for decarboxylations of these vinyl radical precursors are small.[89] As a final caveat for rate constants for radicals produced by acyloxyl decarboxylations, we note that it is possible that some cyclopropyl radical rate constants are inaccurate for the same reasons; cyclopropylacyloxyl radicals also can react with PTOC ester precursors before decarboxylation,[31] and preliminary results indicate that a cyclopropylacyloxyl radical was trapped by PhSH in competition with decarboxylation.[32]

EXAMPLES

The three indirect kinetic methods discussed in this report are demonstrated in this section in a few examples. As noted earlier, the tin hydride method has been most commonly employed, and numerous examples of applications of this method have been reported. There are a limited number of examples of the more recently developed PTOC-thiol method, but this method has a much wider kinetic range than the tin hydride method and should see increased use. Nitroxyl radical trappings are quite fast, and this method is best suited for studies of very fast radical reactions.

The classic example of the tin hydride method is the calibration of the 5-hexenyl radical (**CL-11**) cyclization. Studies of the product distributions from reactions of 6-bromo-1-hexene in the presence of R_3SnH date from the original demonstration of the kinetic method by Walling.[3b] In the first report of the direct measurement of absolute rate constants for reactions of various alkyl radicals with Bu_3SnH,[4] the average value for reaction of Bu_3SnH with primary alkyl radicals was used to calculate the rate constants for cyclization of **CL-11**. Thus, the relative Arrhenius function for cyclization to trapping was known to be that given in eq 23;[4] this is the experimental value for the ratio of rate constants from product distribution studies. The Arrhenius function for trapping was that given in eq 24. Addition of the eq 23 to eq 24 gave the now accepted Arrhenius function for cyclization of **CL-11**.[4]

$$\log (k_r/k_T) = 1.30(8) - 3.16(10)/\theta \qquad (23)$$

$$\log (k_T) = 9.07(24) - 3.69(32)/\theta \qquad (24)$$

In a recent example of the tin hydride method, Curran and Palovich determined approximate rate constants for 5-*exo* and 6-*exo* cyclizations of acyl(triphenyl)germane radicals **25**.[90a] Curran and Liu had reported that acylgermane **24a** was converted to cyclopentanone in 92-95% yield under free radical conditions (10% AIBN and 10% Ph_3GeH at 80 °C or UV photolysis) but not when a radical inhibitor was present.[90b] The radical chain reaction for **24a** is shown in the Figure 7. The acylgermane is seen to be the equivalent of a carbonyl radical acceptor in radical synthon terminology.[91]

In the kinetic study, iodides **24** were allowed to react at 80 °C in the presence of Ph_3SnH to give a mixture of cyclic ketone and reduced acyclic acylgermane. The product ratios found with 0.2 M **24** and 1.3 equivalents of Ph_3SnH are shown in Figure 7. A precise rate constant for reaction of Ph_3SnH with a primary alkyl radical is not available, but Curran and Palovich estimated the rate constant at 80 °C for this reaction to

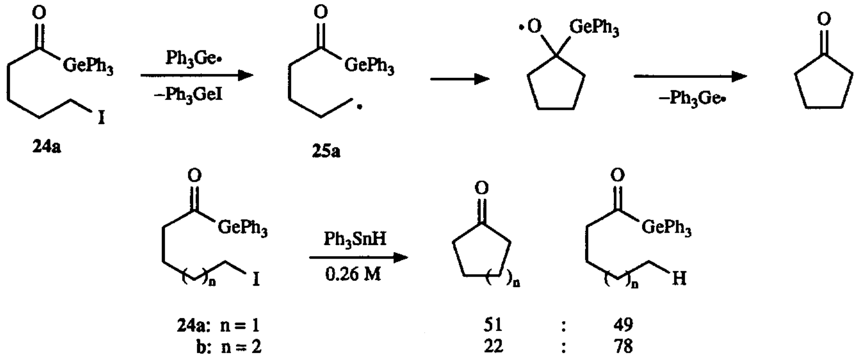
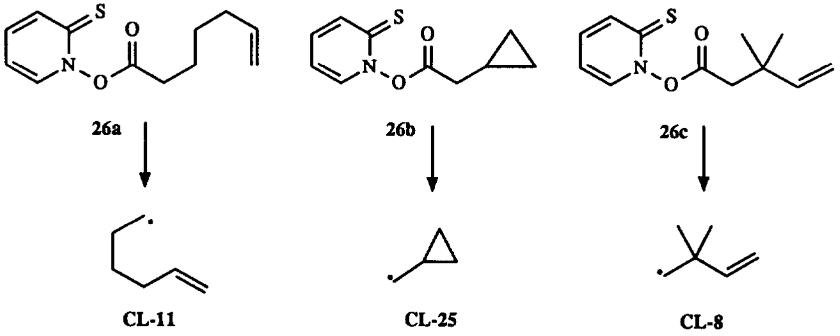


Figure 7. Reaction scheme and product distributions for radical chain reactions of acyl(triphenyl)germanes.

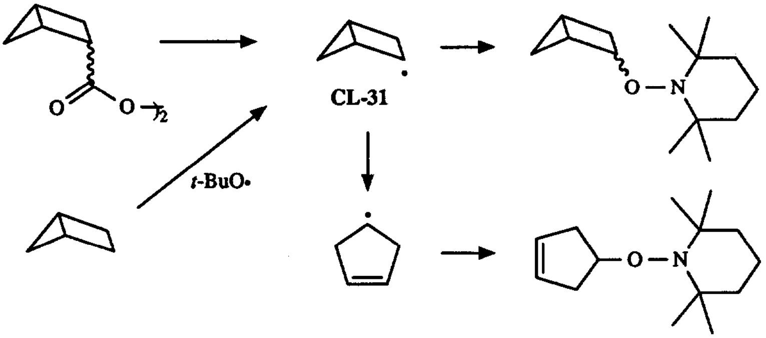
be 2 × 10^7 M^{-1} s^{-1}. Trapping of radical **25** consumed Ph_3SnH, and, if one assumes that the $Ph_3Ge\bullet$ radical formed by cyclization of **25** reacted with precursor **24** faster than it abstracted a hydrogen atom from Ph_3SnH, the cyclization reaction did not consume the stannane. Using an average concentration of Ph_3SnH of 0.22 M in the reaction of **24a** and kinetic equation 1 from Table 1, one calculates a rate constant for 5-*exo* cyclization of **25a** of $k_{80} = 6 \times 10^6$ s^{-1}. For **24b**, the average concentration of Ph_3SnH was 0.18 M, and an approximate rate constant for 6-*exo* cyclization of **25b** is $k_{80} = 1 \times 10^6$ s^{-1}. These values are adequately precise for synthetic feasibility considerations.

An example of the PTOC-thiol method is the measurement of the rate constants for reactions of *tert*-butylthiol with primary alkyl radicals which employed a series of radical clocks.[20] Previously, a wide range of rate constants for reactions of thiols with radicals had been reported from studies employing various techniques. The PTOC esters **26** were prepared from the corresponding carboxylic acids; each is a precursor to a calibrated radical clock. The PTOC esters **26** were allowed to react in the presence of excess *t*-BuSH at temperatures ranging from -45 to 50 °C. The concentrations of PTOC **26** were ca. 0.04 M, and the concentrations of *t*-BuSH were 0.07 to 2.8 M. Each reaction was conducted in a small sealed tube containing a stir bar and one mL of solution. The reaction vessels were wrapped in aluminum foil and equilibrated at the desired temperature for several minutes, and then the shield was removed and the vessels were irradiated with a 150 W tungsten-filament bulb. Reaction mixtures were analyzed by GC.



Each temperature dependent function for *t*-BuSH trapping was determined from nine to eleven runs. From the ratios of rearranged and unrearranged products, the concentrations of *t*-BuSH, and the known values for the rate constants for rearrangement, rate constants for trapping were calculated via kinetic equation 1 in Table 1. The Arrhenius function for k_T from the results with radical **CL-11** in THF solvent was log (k_T·Ms) = 8.38(11) - 2.02(13)/θ and that from the results with **CL-25** in THF was log (k_T·Ms) = 8.34(9) - 1.96(11)/θ where the errors in parentheses are 2σ for the final figure and do not include the uncertainty in the radical clock kinetics. This study[20] not only established rate constants for *t*-BuSH trapping but also demonstrated that the clocks **CL-11** and **CL-25** were equivalently calibrated even though their calibrations were based on different sets of direct kinetic measurements.

The nitroxyl radical coupling method is best suited for studies of fast radical reactions because most of the nitroxyl radical couplings are quite fast. In a recent extensive study of the kinetics of ring openings of cyclopropylcarbinyl and related radicals, Bowry, Lusztyk and Ingold employed TEMPO trapping to calibrate 16 radical ring opening reactions at 37 °C.[74] Radicals were generated by TEMPO-induced decay of a diacyl peroxide precursor or by hydrogen atom abstraction from a hydrocarbon by the *t*-BuO• radical produced by thermolysis of di-*tert*-butylhyponitrite. Both methods were employed for production of the bicyclo[2.1.0]pent-2-yl radical (**CL-31**). The TEMPO trapped products, trialkylhydroxyamines, were analyzed by HPLC/MS. From the ratios of products, the concentrations of TEMPO, and the known rate constant for TEMPO trapping, the rate constants for rearrangements of the radicals at 37 °C were calculated via kinetic equation 1 in Table 1. Then, the assumption was made that all ring openings had log $A = 12.85$ per reactive bond, and the E_a term in the Arrhenius function was calculated from the kinetic result. Because the kinetic determination was made at a temperature likely to be near that employed in subsequent clock applications, the assumption is reasonable. This work[74] provided a new "horologery" of fast radical clocks.



CONCLUSION

Indirect kinetic studies of alkyl radical reactions are now relatively mature. Bimolecular trapping reactions of alkyl radicals span a wide kinetic range, and the trapping agents have been demonstrated to be equivalently placed on the kinetic scale, at least for reactions with primary alkyl radicals. At the extreme limit, indirect kinetic measurements can exceed the capabilities of picosecond spectrometers, and primary alkyl radical clocks are available for timing radical reactions with essentially any rate including the fastest possible reactions. The development of a larger repertoire of secondary, tertiary and benzylic radical clocks is to be expected in the near future, and one should expect that uncertainties regarding kinetics of vinyl and aryl radical reactions will soon be resolved.

Unfortunately, despite the progress in studies of simply alkyl radicals, the application of indirect kinetic methods for studies of reactions of heteroatom-centered radicals and stabilized carbon-centered radicals is poorly developed. In concluding their review on radical clocks in 1980,[54] Griller and Ingold looked forward to an increase in the number of heteroatom-centered radical clocks over the decade of the 1980s. Although this did not come to pass, this author believes that it is now likely that indirect kinetic methods will soon be extended to reactions of heteroatom-centered radicals and carbon-centered radicals stabilized by both electron withdrawing and electron donating groups.

ACKNOWLEDGEMENTS

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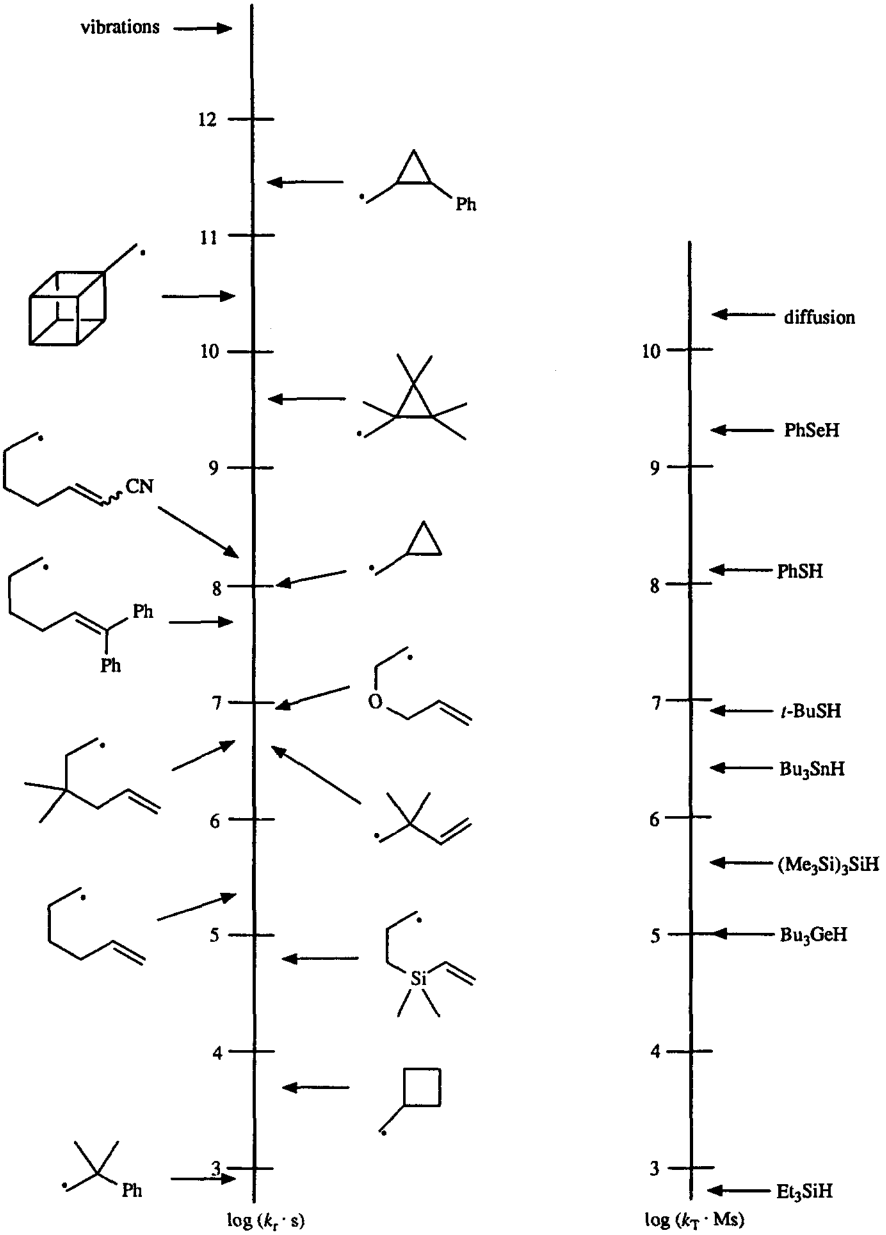

Figure 8. Kinetic scales for carbon radical reactions. The rate constants for unimolecular rearrangements at 25 °C of primary alkyl radical clocks are shown on the left. Rate constants for bimolecular hydrogen atom transfer at 25 °C from trapping agents to primary alkyl radicals are shown on the right. Approximate rate constants for vibrations and for diffusion indicate the maximum attainable rates.

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