Organic Chemistry Cume

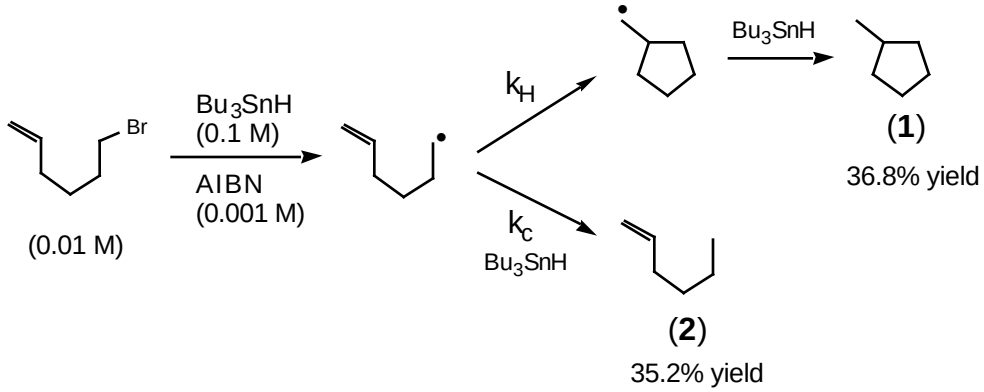
February 6, 1999

Competition Methods for the Determination of Radical Reaction Rates

(M. Newcomb Tetrahedron 1993, 49(6), 1151)

Introduction: Most kinetic methods rely upon either direct or indirect measurements of the rate of appearance of a product or disappearance of a reactant during the course of a reaction. Competition methods are quite different in that they depend on analysis of product distribution *after the reaction is over* to estimate reaction rate constants. This means by using simple methods like column chromatography, HPLC or GC to measure the relative amounts of products that are formed in a reaction, one may be able to calculate reaction rates. If the reaction system that you are interested in is appropriate, this can be a very-easy-to-use, powerful technique. We'll look at some examples below.

1. **Determination of a Cyclization Rate Constant.** Competition kinetics was used to determine the rate for the ring closure (k_c) the hexenyl radical. This reaction has potential synthetic uses and knowledge of the cyclization rate is important for knowing how to best utilize this reaction. (Beckwith and Roberts *JACS* **1986**, *108*, 5893)



(a) To get warmed up... Show a complete arrow-pushing mechanism for this radical chain reaction. Show initiation, propagation and possible termination steps. (10 pts)

(b) In the reaction above, **1** and **2** are the only major products (yield here does not total 100%; reactions need not be run to completion in competition experiments). Given the reaction conditions, the product yields, and the values given in the table at the end of the cume, estimate the value of k_c.

- Show how you derived the kinetic expression(s) that you used to estimate k_c.
- Clearly state any estimations or assumptions that you are making. (20 pts)

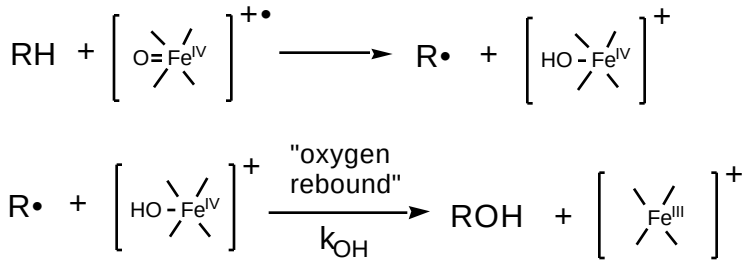
(c) Would your analysis change if the concentration of Bu_3SnH was 0.01 M? Explain your answer. (5 pts)

(d) Above, you calculated k_c based upon a single data point (**1**:**2** ratio). More accurate values can be obtained by determining product ratios [1:2] at differing Bu_3SnH concentrations. Write your kinetic expression in the form m=y/x (slope=rise/run) and show how you would plot data to obtain kinetic data from this system. Explain how you would obtain k_c from your plot. (5 pts)

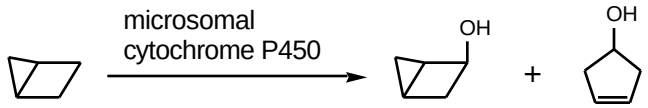
(e) These researchers took some pains to remove molecular oxygen before starting their reactions. Please explain why. (5 pts)

2. **Using a "Radical Clock" to Determine a Reaction Rate.** Kinetically well characterized unimolecular rearrangements can be used as probes to estimate unknown rate constants for reactions of interest. The kinetically well characterized rearrangement reactions used for such experiments are called "radical clocks".

Use of a radical clock reaction to determine the rate of oxygen rebound in the cytochrome P450 reaction. The mechanism of oxygen atom insertion into the C-H bond of alkanes is proposed to follow the mechanism shown below:



Given the information in the attached tables and given the data for the reaction shown below, estimate the rate of the oxygen rebound reaction for P450. (Ortiz de Montellano and Stearns *JACS* **1987**, *109*, 3415) Please show all your work. (15 pts)



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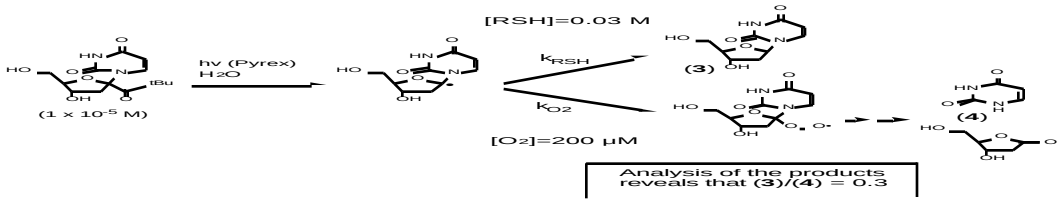
3. **Competition Methods In Systems That Are (Slightly) More Complex.** Although he did not discuss this work in detail during his talk yesterday, Friday's colloquium speaker Professor Greenberg has used competition kinetic methods to estimate biologically important rate constants for DNA radical intermediates (Goodman and Greenberg *JOC* **1996**, *61*, 2-3). For example, his group performed the following reaction to study the biological chemistry of the C1' radical of deoxyuridine:



(a) What type of reaction is used to generate the radical? Show the other products generated in this photochemical reaction. (5 pts)

(b) Why does molecular oxygen react readily with radicals? (5 pts)

(b) Set up a competition kinetic expression that allows you estimate the ratio of rate constants k_{RSH}:k_{O2}. Show how you arrived at your kinetic expression (10 pts)

(c) In order to estimate the rate constant for k_{RSH}, you must make an assumption about the value of the rate constant for k_{O2} (see attached tables). Once you assume a value for k_{O2}, you have one equation with one variable (so you can solve it!). Using the data in the Scheme above, estimate the value of k_{RSH}. In these experiments RSH=2-mercaptoethanol. Does the value that you calculated for k_{RSH} seem reasonable? Explain how you decided whether the value is reasonable. (10 pts)