Kinetics of the Oxiranylcarbinyl Radical Rearrangement

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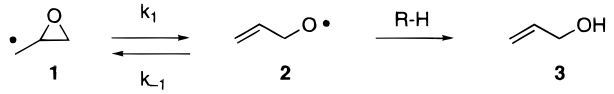
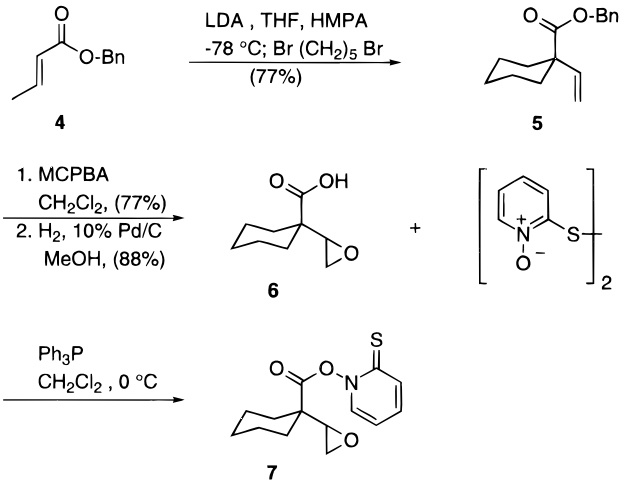
How fast is the oxiranylcarbinyl radical rearrangement (**1** → **2**, Scheme 1)? All indications to date are that it is very fast. The first hint of this was the report that reduction of epibromohydrin with tin hydride afforded only allyl alcohol and none of the direct reduction product, propene oxide.[2,3] A competition experiment showed the hexenyl radical cyclization ($k = 2.3 \times 10^5$ s^{-1} at 25 °C)[4] to be no match for the radical-induced epoxide fragmentation.[5,6] Attempted observation of the oxiranylcarbinyl radical by ESR proved unsuccessful, as its rearrangement to the allyloxy radical (e.g., **2**) was rapid, even at 128 K.[7−10] On the basis of these observations, the rate of the fragmentation was estimated to be $>4 \times 10^8$ s^{-1}.[10] In systems where the oxiranylcarbinyl radical is allowed to compete directly with the well-studied cyclopropylcarbinyl radical rearrangement ($k = 1.0 \times 10^8$ at 25 °C),[11,12] only products from epoxide fragmentation are observed.[13−15] By assuming the reverse reaction (**2** → **1**) to be relatively slow, an assumption that turns out to be not quite correct,[16] a lower limit for the forward rearrangement was set at 1×10^{10} s^{-1} at 70 °C.[14] Our long-standing interest in the synthetic potential of radical-induced epoxide fragmentations[17−21] prompted us to examine the rate of this rearrangement more precisely. We describe here the results of our investigations, which allowed the direct determination of this rate.[22]

Scheme 1



We took advantage of Newcomb's competition method to determine the rate of the oxiranylcarbinyl radical rearrangement,[11,23] which involves the use of Barton's PTOC esters [((pyridine-2-thione)oxy)carbonyl] as radical precursors[24] and hydrogen atom transfer from thiophenol or benzeneselenol as the basis reaction. The rates for trapping of alkyl radicals by PhSH and PhSeH are $\sim 10^8$ M^{-1} s^{-1} and $\sim 10^9$ M^{-1} s^{-1}, respectively, and are known to be relatively insensitive to radical structure.[11,23,25,26]

Scheme 2



A cyclohexyl-substituted oxiranylcarbinyl radical precursor was selected, since the products from its reduction or rearrangement would be less volatile than those from the parent system. The necessary PTOC ester was prepared in four steps as shown in Scheme 2. The enolate of benzylcrotonate [2.0 equiv, LDA (2.0 equiv), HMPA 3.0 equiv, in THF, −78 °C] was treated slowly with a THF solution of 1,5-dibromopentane to afford the spiro-bisalkylation product **5** in 77% yield.[27] Epoxidation of the alkene with *m*-CPBA followed by hydrogenolysis of the benzyl group gave epoxycyclohexanecarboxylic acid **6**. Treatment of the acid with triphenylphosphine and 2,2′-dithiobis(pyridine *N*-oxide) in CH_2Cl_2 at −5 °C gave a bright yellow solution containing PTOC ester **7**.[24] Removal of the solvent in vacuo, with the bath temperature maintained below 35 °C, gave the crude PTOC ester in quantitative yield. Ester **7** is photolabile, although it can be purified by column chromatography in subdued lighting, but with considerable loss of the product (32% yield). In practice, the crude PTOC ester was found to

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(27) The modified procedure described here allows the dialkylation to be carried out in one step and in good yield. See: Brocksom, T. J.; Constantino, M. G.; Ferraz, H. M. C. *Synth. Commun.* **1977**, *7*, 483−493.

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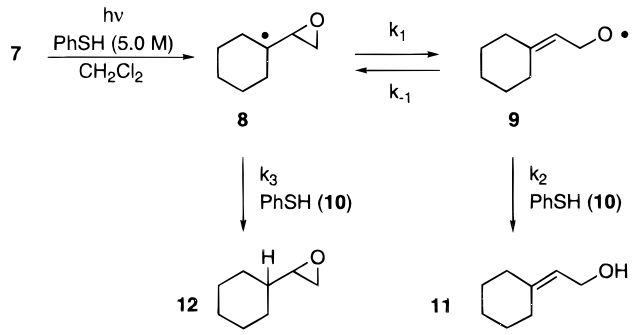
Scheme 3



be suitable for these studies, since it was identical by ^{1}H NMR with the purified sample and, more importantly, the two samples gave identical results in the competition experiments.

The kinetic studies were carried out using Newcomb's general protocol for the "PTOC/thiol method."[11,23] The expected outcome of the photolysis is shown in Scheme 3. The equation used to analyze the rate of the fragmentation reaction (k_1) was derived as shown in eqs 1−4. A steady-state analysis for intermediate **9** (eq 2) gave the relationship shown in eq 3. This equation can be simplified further by making the reasonable assumptions that k_{-1} is smaller than k_1 and that k_3 is smaller than k_2. Under these conditions the second term drops out and gives the simplified relationship shown in eq 4.

$$[\mathbf{11}]/[\mathbf{12}] = k_3[\mathbf{8}]/k_2[\mathbf{9}] \quad (1)$$

$$[\mathbf{9}] = k_1[\mathbf{8}]/(k_{-1} + k_2[\mathbf{10}]) \quad (2)$$

$$[\mathbf{11}]/[\mathbf{12}] = (k_3[\mathbf{10}]/k_1) + (k_{-1}k_3/k_1k_2) \quad (3)$$

$$[\mathbf{11}]/[\mathbf{12}] = k_3[\mathbf{10}]/k_1 \quad (4)$$

In the event, a solution of unpurified PTOC ester **7** in a pressure tube was treated with a measured amount of PhSH and irradiated with a sunlamp for 10 min. The temperature of the reaction was maintained between 25 and 30 °C using a water bath. The ^{1}H NMR of the crude product showed only peaks corresponding to the allylic alcohol **11** and not the direct reduction product **12**. So as to maximize the amount epoxide **12**, a high concentration of PhSH was used. Even at 5 M PhSH concentration, the amount of **12** was too small to be determined by NMR. However, analysis of the reaction mixture by GC, using authentic samples of **11** and **12** for comparison, indicated **11** and **12** to be present reproducibly in a 57.5:1 ratio.[28−30] It is noteworthy that this result represents the first time that the oxiranylcarbinyl radical has been trapped in the unrearranged form. Using the reported rate constant of 1.1×10^8 s^{-1} at 25 °C for the hydrogen abstraction from thiophenol by a tertiary alkyl radicals,[25] the approximate rate for the rearrangement of **8** to **9** at 25−30 °C is 3.2×10^{10} s^{-1}.

Our results show the oxiranylcarbinyl radical rearrangement to be quite fast, about 2 orders of magnitude faster than the cyclopropylcarbinyl radical rearrangement. The observed high rate for the rearrangement is consistent with the results of high level computational studies of Jackson and Lee, which predicted a low barrier (<4.8 kcal/mol) for the C−O bond cleavage.[31] More recent calculations by Pasto suggest an even lower barrier for this rearrangement.[32]

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Supporting Information Available: Experimental procedures and spectral data of all new compounds employed in this study (15 pages).

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(28) Complex reaction products were obtained using selenophenol as the hydrogen donor. One problem appears to be the instability of the reduced epoxide (**12**) to benzeneselenol.

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