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Free radical S_H2' reaction mechanism study by comparing free radical S_H2' reaction with free radical addition reaction

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Abstract—It is not clear whether the mechanism of the S_H2' reaction of allyl chloride is concerted or stepwise. The relative rates of the competitive free radical addition to two different double bonds in (2-chloroallyl)-(2-choromethylallyl) ether have been determined. There are two competitive free radical addition reactions, one is free radical S_H2' reaction and the other is free radical addition reaction. The mechanism of the S_H2' reaction is discussed by comparing free radical S_H2' reaction with free radical addition reaction.
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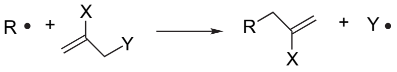
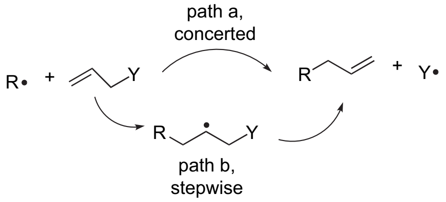
1. Introduction

The addition reactions of alkyl radicals to alkenes have been intensively investigated from both the theoretical and the experimental points of view[1] in the last two decades. The formation of a new carbon–carbon single bond by an S_H2' reaction involving the attack of a carbon radical onto a double bond by displacement of a radical from the allylic position is a useful synthetic process (Eq. 1).



(1)

Barton and Crich indicated[2] that there are two possible mechanisms for the S_H2' process: first, one in which the addition of the radical is concerted with the loss of the leaving radical (Scheme 1, path a); second, a stepwise mechanism in which the adduct radical has a definite existence (Scheme 1, path b). The Migita et al.[3] reported that the reactions of phenyl radical with allylic sulfides and halides yielded allyl benzene as a major product, and the stepwise mechanism was proposed to explain the reactions. Russell et al.[4] indicated that the *t*-butyl radical addition to allyl derivatives proceeded with the stepwise S_H2' reaction mechanism as shown in Scheme 2.



Scheme 1.

$$CH_2{=}CHCH_2Y \quad + \quad R\bullet \longrightarrow R\dot{C}HCH_2Y \qquad (2)$$

$$R\dot{C}HCH_2Y \longrightarrow RCH_2CH{=}CH_2 \quad + \quad Y\bullet \qquad (3)$$

$$Y\bullet \quad + \quad RHgCl \longrightarrow YHgCl \quad + \quad R\bullet \qquad (4)$$

Scheme 2.

The alkyl radical adds to the terminal carbon of the double bond to form an intermediate radical, which undergoes fast β-elimination of the leaving group Y• in a chain process, and the radical addition to double bond is a rate determining step (Scheme 2). However, a concerted S_H2' mechanism was suggested by Barton and Crich[2] for the reaction of alkyl radical with allylic derivatives. In our previous work,[5] the mechanism of free radical S_H2' reaction was investigated by the leaving group effect and the secondary α-deuterium kinetic isotope effect. The free radical S_H2' reactions of allyl halides seem to favor the concerted mechanism. Therefore, the controversy that exists in the mechanism of radical S_H2' reaction still remains to be elucidated. The free radical addition reactions, for example: $AX{+}CH_2{=}CHE \rightarrow ACH_2CHEX$, have been studied comprehensively. The general mechanism[6] of free radical addition reaction is shown in

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Keywords: Free radical S_H2' reaction; *t*-Butyl radical; Radical addition reaction; Concerted mechanism; Stepwise mechanism.

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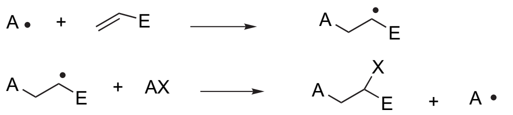
Scheme 3. The mechanism is stepwise and free radical addition to double bond is a rate determining step.



(5)

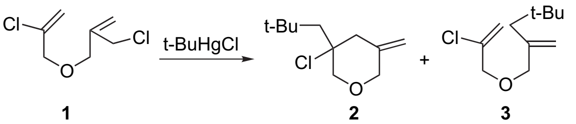
(6)

Scheme 3.

In this article, we try to clarify the mechanism of free radical S_H2' reaction by comparing free radical S_H2' reaction with free radical addition reaction.

2. Results and discussion

The reactions of *t*-BuHgCl with (2-chloroallyl)-(2-choromethylallyl) ether (**1**), under photolytic condition, gave the corresponding product (**2**), 3-chloro-3-(2-trimethylpropyl)-5-methylene tetrahydro pyran, the product (**3**), (2-chloroallyl)-(2-trimethylpropyl allyl) ether and a trace amount of unknown (Eq. 7).



1 **2** **3** (7)

Compound **1** was synthesized by reported method. Compound **1**, *t*-BuHgCl, and internal standard (0.05 mmol of biphenyl) were dissolved in 1 mL of nitrogen-purged dry dimethylsulfoxide and the reaction conditions were shown in Table 1. The solution was added to dry and nitrogen-purged quartz tubes equipped with a rubber septum. The tubes were irradiated at 37±2 °C with a 100 W UV lamp placed about 20 cm from the reaction tubes. Reaction tubes were removed at various times and the yields of the products were determined by gas chromatography. GLC yields were determined by using an internal standard (biphenyl) and were corrected with predetermined response factors. The yields of the products were shown in Table 1. The products were isolated after reaction by flash column chromatography and identified by mass spectroscopy and NMR spectrum.

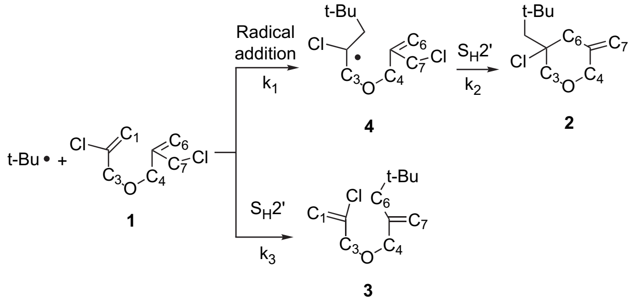
The possible mechanism of the reaction (Eq. 7) is illustrated as in Scheme 4. The *t*-butyl radical is generated by photolysis of *t*-BuHgCl. The *t*-butyl radical has two possible ways to add to compound **1**, one is the alkyl radical adds to the C_1 carbon of compound **1** to produce the intermediate radical **4** which, then, proceeds the free radical S_H2' reaction to form cyclization product **2**, the other is the alkyl radical adds to the C_6 carbon of compound **1** to progress the S_H2' reaction to generate product **3**. The k_1 and k_3 are the rate constants of *t*-butyl radical addition to the C_1 carbon and C_6 carbon of compound **1**, respectively, and the k_2 is the rate constant of radical **4** addition to C_6 carbon of compound **1**.

Table 1. Reactions of *t*-butyl radical with (2-chloroallyl)-(2-choromethylallyl) ether

Compound **1** (mmol)	*t*-BuHgCl (mmol)	Conditions[a] *hν* (h)	Compound **2**[b] (%)	Compound **3**[b] (%)	k_1/k_3
0.1	0.1	2	19	39	0.49
0.1	0.1	3	21	42	0.50
0.1	0.1	4	23	44	0.52
0.1	0.1	5	21	45	0.47
0.1	0.1	6	21	44	0.48
0.1	0.1	10	21	44	0.48

[a] The mixture in a 5 mm quartz tube was irradiated at 37±2 °C with a 100 W UV lamp ca. 20 cm from the tube. Each reaction was run at least three times. Error is ±4%.

[b] The yield was determined by gas chromatography.

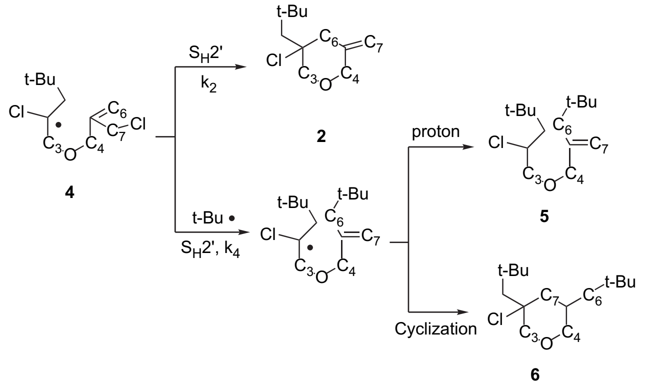


Scheme 4.

The steric effect should be negligible in compound **1** because the positions of these two double bonds attacked by the radical are unsubstituted. Giese[7] has reported that the rate of addition of alkyl radicals to alkenes is controlled mainly by the polar effects of the substituents. Therefore, the substituent effects of the free radical addition reactions must be same for these two double bonds in compound **1**, if the addition reaction rates of these two double bonds would be compared correctly. It should be evident that a number of criteria are important in choosing a model system for evaluating the reaction rates on the radical addition reactions: (1) the steric effect should be negligible, (2) the substituent effect in these two double bonds should be same, (3) the side reaction should be minimized; and the model compound **1** should be readily accessible for these criteria except the substituent effect should be same. Two substituents are on each double bond of compound **1**, one of substituents on each double bond is same and the other is different, therefore, the substituent effects of two double bonds in compound **1** are different. The substituent effects have been studied exclusively on the radical addition reaction and the S_H2' reaction. Wu indicated[8] that the ρ value of free radical S_H2' reaction of *t*-butyl radical addition to 2-substituted allyl chloride is 3.39 in DMSO and the ρ values (3.1–3.8) have been reported by Giese for the addition of cyclohexyl radical to substituted alkene.[9] The ρ values of substituent effects of free radical addition reactions and free radical S_H2' reactions are not exactly same, but they are pretty close. This implies that the substituent effect for both reactions would locate within the same order. We choose the S_H2' reaction of *t*-BuHgCl with compound **1** (Eq. 7) as fulfilling these criteria without excessive experimental difficulty.

The relative rates of free radical addition reaction and free radical S_H2' reaction as given in Table 1, were measured by the relative yields of the two products, compound **2** and compound **3** if the radical addition to C_1C_2 double bond was a rate determining step for the formation of the cyclization product **2**.

From Table 1, it is obvious that k_3 is greater than k_1 or k_2 if either k_1 or k_2 is the rate determining step for the formation of product **2**. If k_2 is the rate determining step for formation of product **2**, then, $k_3 > k_2$, it means the rate of *t*-butyl radical addition to C_6 carbon of the intermediate **4**, would be faster than the cyclization rate of the intermediate **4**. The value of k_4 should be close to the value of k_3, therefore, the di-*t*-butyl addition products such as the product **5** or **6**, which are shown in Scheme 5, might be observed in the reaction. However, these products were not found in the photolytic reaction of compound **1** with *t*-BuHgCl. We might guess that k_2 is not the rate determining step for the formation of product **2** and the cyclization rate of the intermediate **4** should be much faster than the addition rate of *t*-butyl radical addition to C_5C_6 double bond, therefore, it seems plausible to assume that k_1 is the rate determining step for the formation of product **2**. It is likely that the relative rates of free radical addition reaction and free radical S_H2' reaction as given in Table 1, were measured by the relative yields of the products **2** and **3**.



Scheme 5.

From Table 1, it is obvious that the rate of free radical addition to C_5C_6 double bond of compound **1** is faster than that to C_1C_2 double bond of compound **1**. It is unlikely that free radical addition rate on C_1C_2 double bond of compound **1** is slower than that on C_5C_6 double bond of compound **1** if it is rational then the assumption of the ρ values of the substituent effect for the radical addition reaction and the radical S_H2' reaction are close. There are two substituents on the C_2 carbon of compound **1**, one is the chloro substituent and the other is the CH_2OR group. However, the C_5 carbon of compound **1** also has two substituents, one is the CH_2Cl group and the other is the CH_2OR' group. The inductive effect of the substituent plays an important role in both the radical addition reaction and the free radical S_H2' reaction.[7,8] The Hammett σ_m constant is an index of the inductive effect of the substituent,[10] then, the Hammett σ_m constant could be used to represent the degree of the inductive effect of the substituent. The Hammett σ_m constants of chloro, CH_2Cl, and CH_2OR are 0.37, 0.11, and 0.06–0.08 (R=Ph, 0.06; R=Me, 0.08), respectively.[11] The σ_m constants of CH_2OR and CH_2OR' should be close because the structure of R and R′ are related. It is likely that the summation of the σ_m constants of two substituents represents the inductive effect of the substituents on the 1,1-dibustituted alkene. It is apparent that the summation of the σ_m constants of the substituents on C_1C_2 double bond is greater than that on C_5C_6 double bond. The inductive effect of the substituents on C_1C_2 double bond would be greater than that on C_5C_6 double bond, thus, we would expect the rate of alkyl radical addition to C_1C_2 double bond should be faster than that to C_5C_6 double bond. It means the yield of product **2** should be larger than that of product **3**. However, this is controversy to the experimental data in Table 1. It is interesting to clarify this controversy. If alkyl radical addition reaction and free radical S_H2' reaction obey the mechanisms, which are stepwise, shown in Scheme 3 and Scheme 2, respectively, the rate of alkyl radical addition to C_1C_2 double bond (k_1) should be faster than that to C_5C_6 double bond (k_3), that means $k_1 > k_3$, because of the inductive effect of substituents. It is unlikely that k_1 is greater than k_3, therefore, we might guess that it is not true that the assumption of both of free radical addition reaction and free radical S_H2' reaction might proceed the stepwise mechanisms.

There is no literature to question the mechanism of free radical addition reaction as shown in Scheme 3. Therefore, there is only one possible way left to resolve this controversy, that is, free radical S_H2' reaction might not process the stepwise mechanism. The other possible mechanism for free radical S_H2' reaction is to process the concerted mechanism as shown in Scheme 1 (path a) if free radical S_H2' reaction does not obey the stepwise mechanism.

The controversy described above might be resolved if free radical S_H2' reaction proceed the concerted mechanism. The larger the inductive effect of the substituent is, the faster the radical addition to double bond is. This is not observed for two different double bonds of compound **1**, owing to one of two double bonds (C_5C_6) proceeds free radical S_H2' reaction, which follows the concerted mechanism, thus, the reaction rate not only depends upon the inductive effect of substituents but also depends upon the leaving group effect.[5,12] The activation energy of alkyl radical addition to C_1C_2 double bond of compound **1** might depend upon the energy of breaking π bond of C_1C_2 double bond. However, the activation energy of free radical S_H2' reaction for alkyl radical addition to C_5C_6 double bond of compound **1** might depend upon the energy of breaking π bond of C_5C_6 double bond and forming π bond of C_5C_7 double bond simultaneously. We might guess that the activation energy of free radical S_H2' reaction would diminish, if the S_H2' reaction proceed the concerted mechanism, because the activation energy might compensate from the formation of π bond between the C_5 and C_7 of compound **1** in the transition state. The above discussion might be the reason for the reaction rate of free radical S_H2' reaction is faster than that of free radical addition reaction in compound **1**. Therefore, we might conclude that the S_H2' reaction of allyl chloride would rather proceed the concerted mechanism than the stepwise mechanism.

3. Experimental

3.1. General

Analytical gas chromatography was performed using Perkin–Elmer Autosystem with a DB-5 column (0.25 μM, 60 M) and a flame ionization detector. ^1H NMR spectra were recorded on a 300 MHz VXR FT-NMR spectrometer with tetramethylsilane as the internal standard. GC–MS were recorded on a Quattro GCMS 5022 spectrometer or HP 5890 Series II Gas Chromatograph with HP 5972A MSD. Melting points were determined on a Thomas–Hoover capillary melting point apparatus and were uncorrected.

3.2. Materials

Solvents were purchased from Riedel-de Haen and Mallinckrodt. Dimethylsulfoxide (DMSO) was distilled from calcium hydride and stored over 4 Å molecular sieves under nitrogen; diethyl ether, and tetrahydrofuran were distilled from sodium metal. Other solvents were purchased and used without purification. 3-Chloro-1-methyl-1-propene, 2-chloro-2-propen-1-ol, *t*-butyl chloride, 3-chloro-2-chloromethyl-1-propene, NaH, and biphenyl were purchased from Aldrich Chemical Company. In most cases, the reagents were used without further purification. Organomercurials were synthesized by the standard Grignard procedure.[4]

3.2.1. The preparation of (2-chloroallyl)-(2-choromethylallyl) ether (1). Compound **1** was prepared by dropwise addition of 2-chloro-2-propen-1-ol (8 mL) into NaH (4.8 g, 50%) in dry THF (200 mL) at 0 °C under nitrogen. The solution was refluxed for 2 h after addition was complete. Then, the reaction was cooled to room temperature, 3-chloro-2-chloromethyl-1-propene (11.5 mL) was added to the solution slowly. The reaction was refluxed for 3 h after addition was complete. The saturated NH_4Cl aqueous solution (100 mL) was added to the reaction after the solution was cooled to room temperature. The filtrate was concentrated in vacuum after the solution was filtrated by suction. Ether was added to the concentrated filtrate, then anhydrous $MgSO_4$ was added to remove water. After removal of the ether in vacuo, the product was purified by distillation to give material with bp 52–53 °C/10 mmHg; MS (EI) *m*/*z* (relative intensity) 184 ($M+4^+$, 0.01), 182 ($M+2^+$, 0.04), 180 (M^+, 0.06), 147 (10), 145 (30), 92 (22), 75 (76), 50 (100); ^1H NMR (300 MHz, $CDCl_3$): δ 4.03 (s, 2H), 4.10 (s, 4H), 5.26 (s, 1H), 5.33 (s, 1H), 5.36 (s, 1H), 5.48 (s, 1H).

3.2.2. General procedure for competitive photostimulated reactions of compound 1 with *t*-butylmercury chloride.[8] Compound **1**, *t*-BuHgCl, and internal standard (0.05 mmol of biphenyl) were dissolved in 1 mL of nitrogen-purged dry dimethylsulfoxide and the reaction conditions were shown in Table 1. The solution was added to dry and nitrogen-purged quartz tubes equipped with a rubber septum. The tubes were irradiated at 37±2 °C with a 100 W UV lamp placed about 20 cm from the reaction tubes. Reaction tubes were removed at various times and the yields of the products were determined by gas chromatography. GLC yields were determined by using an internal standard (biphenyl) and were corrected with predetermined response factors. The yields of the products were shown in Table 1. The products were isolated after reaction by flash column chromatography and identified by mass spectroscopy and NMR spectrum. The mass spectroscopy and NMR spectrum of 3-chloro-3-(2-trimethylpropyl)-5-methylene tetrahydro pyran (product **2**) were shown as following: MS (EI) *m*/*z* (relative intensity) 202 (M^+, 0.5), 167 (13), 116 (11), 79 (14), 57 (100); ^1H NMR (300 MHz, $CDCl_3$): δ 1.06 (s, 9H), 1.81 (d, 1H), 1.83 (d, 1H), 2.70 (s, 2H), 3.75 (s, 2H), 4.04 (d, 1H), 4.11 (d, 1H), 4.87 (d, J=0.6 Hz, 1H), 4.96 (d, J=0.6 Hz, 1H); ^{13}C NMR (75 MHz,$CDCl_3$) δ 29.69, 31.62, 32.19, 47.96, 50.90, 71.93, 76.53, 112.56, 139.94. The mass spectroscopy and NMR spectrum of (2-chloroallyl)-(2-trimethylpropyl allyl) ether (product **3**) were shown as following: MS (EI) *m*/*z* (relative intensity) 202 (M^+, 1.5), 167 (6), 110 (10), 57 (100); ^1H NMR (300 MHz, $CDCl_3$): 0.92 (s, 9H), 1.96 (s, 2H), 3.96 (s, 2H), 4.02 (s, 2H), 4.93 (s, 1H), 5.18 (s, 1H), 5.36 (s, 1H), 5.48 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 29.84, 31.36, 46.25, 72.16, 74.29, 113.16, 115.27, 138.28, 143.27.

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