Communication

The Leaving Group Effect in Free Radical S$_H$2′ Reactions

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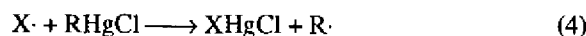
The relative rates of the leaving groups in free radical S$_H$2′ reactions have been determined. The order of the relative elimination rates of the leaving group is: I > Br (14) > SPh (2) > Cl (1) >> OPh, SiMe$_3$. This is consistent with the bond dissociation energy of the C-X bond. The less the bond dissociation energy value is, the better the leaving group is.

The leaving group effect is fully studied in aliphatic nucleophilic substitution reactions, including S$_N$1 and S$_N$2.[1] It is rare to find depicted in the literature the leaving group ability in radical substitution reactions because the following reaction (eq. 1) seldom occurs in free radical chemistry.

$$A\cdot + -\overset{|}{\underset{|}{C}}\text{-LG} \longrightarrow A\text{-}\overset{|}{\underset{|}{C}}- + \text{LG}\cdot \tag{1}$$
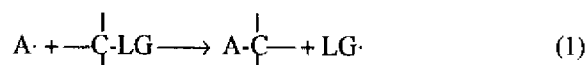
Russell et al.[2] indicated that the *tert*-butyl radical addition to allyl derivatives proceeded with the S$_H$2′ reaction mechanism as shown in Scheme I.

Scheme I

$$CH_2=CHCH_2X + R\cdot \longrightarrow RCH_2\overset{\cdot}{C}HCH_2X \tag{2}$$

$$RCH_2\overset{\cdot}{C}HCH_2X \longrightarrow RCH_2CH=CH_2 + X\cdot \tag{3}$$

$$X\cdot + RHgCl \longrightarrow XHgCl + R\cdot \tag{4}$$

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 X· in a chain process. It looks like the X· acts as a leaving group in S$_H$2′ reaction. The S$_H$2′ reaction may be a good candidate for studying the leaving group effect in free radical addition-elimination reactions. Russell et al.[2] also indicated that the rate of *tert*-butyl radical addition to allyl derivatives obeyed the following order: H$_2$C=CHCH$_2$Cl > H$_2$C=CHCH$_2$Br > H$_2$C=CHCH$_2$I. This does not mean that the Cl radical is a better leaving group than the others in the S$_H$2′ reaction because the halogen in the allylic derivatives might play a role in the substituent effect as well as in the leaving group effect in the S$_H$2′ reaction. Giese[3] 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 the

same for different leaving groups, if the leaving group effects could be determined correctly. It should be evident that a number of criteria are important in choosing a model system for evaluating the leaving group effect on radical addition reactions: (1) the substituent effect in the system should not be changed as the leaving group is altered (2) the side reactions should be minimized (3) the steric effect should be negligible; and the model compound 1 should be readily accessible. Compound 1 includes two different leaving groups, X^1 and X^2; the substituent effect would be identical for these two leaving groups in an S$_H$2′ reaction. The reactions of 2-substituted allyl derivatives with *tert*-BuHgCl, under photolytic condition, gave the substituted products in good yields and there was no steric effect observed.[4] We chose the S$_H$2′ reaction of *tert*-BuHgCl with compound 1 (eq. 5) as fulfilling these criteria without excessive experimental difficulty.

$$\tag{5}$$
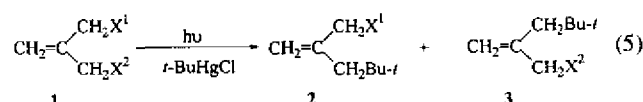
	1a	1b	1c	1d	1e
X^1=	Cl	Cl	Cl	Cl	Cl
X^2=	I	Br	SPh	OPh	SiMe$_3$

In the present report, we investigated the leaving group effect of compound 1 with *tert*-BuHgCl in a photostimulated S$_H$2′ reaction. Compounds 1a-1d were synthesized by reported methods.[5] The competitive kinetic experiments were carried out by compound 1 (at least 10 times with respect to *tert*-BuHgCl in CH$_3$CN or Me$_2$SO) and after at least 3 half-lives determining the relative amounts of two adducts by GC. Identification of substitution products was confirmed by comparison of their GCMS data with those of the

Table 1. The Reaction of Compound 1 with *tert*-BuHgCl at 35-45 °C in CH₃CN or Me₂SO[a]

Substrate	conditions	% product 2[b]	% product 3	k_X^2/k_X^1
1a	3h, CH₃CN	43	0	-
1b	3h, CH₃CN	57	4	14.3
1c	3h, CH₃CN	55	26	2.1
1d	3h, CH₃CN	0	70	-
1e	3h, Me₂SO	0	6	-

[a] Substrate (1 M) and mercurial (0.01 M) in nitrogen-purged dry Me₂SO or CH₃CN were irradiated with a 100 W UV lamp ca. 20 cm from the reaction quartz tube. Each reaction was run at least three times. Error ±4 %.

[b] The yield was determined by GC.

authentic compounds synthesized by methods reported in the literature.[4,6,7] The relative elimination rates of the leaving groups as given in Table 1, were measured by the relative yields of the two substitution products, compound 2 and compound 3.

From Table 1, the relative elimination rate of the leaving group follows the order: I > Br > SPh > Cl >> OPh, SiMe₃. This is consistent with bond dissociation energy of the C-X bond (Table 2). The less the bond dissociation energy value is, the better the leaving group is. The photolytic reaction of compound 1b with *tert*-BuHgCl in CH₃CN gave only compound 2b and 3b as the substitution products and a similar result was found in the photolytic reaction of compound 1c. The yields of substitution products and relative elimination rates are shown on Table 1. The relative ratio of k_{Br}/k_{Cl} is 14 and k_{SPh}/k_{Cl} is 2.1 in CH₃CN. This suggests that the Br and SPh radicals are better leaving groups than the Cl radical in S_H2' reactions. The bond dissociation energy of the C-X bond follows the order: C-Cl > C-S > C-Br. It seems reasonable that the elimination rate of the leaving group is k_{Br} > k_{SPh} > k_{Cl}.

The photolytic reaction of compound 1a with *tert*-BuHgCl gave more complicated results. The products included compound 2a, 2-methylallyl chloride, and *tert*-butyl iodide, but compound 3a was not observed. This indicated the iodo radical might be a better leaving group than the

chloro radical; moreover, the yields of these products were low. Owing to the small bond dissociation energy of the C-I bond, the abstraction of iodo by *tert*-butyl radical is competitive with the addition of *tert*-butyl radical in a photolytic reaction of compound 1a. The iodo abstraction by *tert*-butyl radical caused a low yield of substitution product and resulted in the formation of *tert*-butyl iodide and 2-chloromethyl-2-propenyl radical which formed 2-methylallyl chloride by abstraction of hydrogen. Similar results were also observed by Russell et al.[2] in the photolytic reaction of propargyl iodide with *tert*-BuHgCl. It is recognized that oxygen-centered radicals are not readily eliminated in reaction 3. That's why only the 70% yield of compound 3d was observed and none of compound 2d was detected in the photolytic reaction of compound 1d. The photolytic reaction of compound 1e with *tert*-BuHgCl in Me₂SO solution gave low yields of substitution products which included a small amount of compound 2e, 2,4,4-trimethyl-1-pentene, hexamethylsiloxane; none of 3e was observed. There was none of compound 2e and 3e detected and hexamethylsiloxane, 2-methylallyl chloride, 2,4,4-trimethyl-1-pentene formed in CH₃CN solution. The allyltrimethylsilane was unreactive with isopropylmercury chloride under photolytic condition as previously reported by Hershberger et al.[8] This is consistent with our result. It seemed unlikely that this reaction proceeded via the S_H2' mechanism. The electron transfer might be involved in this reaction;[9] this part will be discussed in another place.

ACKNOWLEDGMENT

Table 2. Bond Dissociation Energy of C-X bond (kcal/mol)

C-X	Cl[a]	Br[a]	I[a]	S[b]	O[c]	Si[b]
	71	57	44	65	84	77

[a] Cited from Wentrup, C. "*Reactive Molecules*" John Wiley & Sons, New York **1984**, pp 29.

[b] Cited from reference 8.

[c] Cited from reference 1, pp 147.

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5. Compound **1c** was prepared by treatment of 2-chloromethyl-3-chloro-1-propene with thiophenolate which was produced by the reaction of NaH and thiophenol in dry ether. ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.4-7.1 (m, 5H), 5.18 (s, 1H), 5.12 (s, 1H), 4.21 (s, 2H), 3.69 (s, 2H); MS (EI) *m/z* 200 (M+2$^+$, 20), 199 (M+1$^+$, 6.6), 198 (M$^+$, 55), 163 (80), 135 (50), 129 (45), 109 (61), 89 (75), 77 (30), 53 (100). Compound **1d** was prepared by the reaction of 2-chloromethyl-3-chloro-1-propene with phenolate which was produced by the reaction of potassium *t*-butoxide and phenol in *t*-butanol. b.p. 84-86 °C/0.1 mmHg; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.28 (m, 2H), 6.95 (m, 3H), 5.37 (m, 2H), 4.62 (s, 2H), 4.18 (s, 2H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 158, 141, 130, 121, 117, 115, 68, 45; MS (EI) *m/z* 184 (M+2$^+$, 6), 182 (M$^+$, 17), 147 (100), 77 (30), 53 (80).

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7. Authentic **3b** was prepared by the reaction of 3-chloromethyl-4,4-dimethyl-1-pentene with NaBr in DMF solution. ^{1}H NMR (300 MHz, CDCl$_3$) δ 5.32 (s, 1H), 4.94 (s, 1H), 4.02 (s, 2H), 2.17 (s, 2H), 0.93 (s, 9H); MS (EI) *m/z* 192 (M+2$^+$, 0.08), 190 (M+, 0.08), 175 (0.32), 95 (10), 57 (100). Authentic **3c** was prepared by the reaction of 3-chloromethyl-4,4-dimethyl-1-pentene with thiophenoate in THF solution. ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.38 (m, 2H), 7.36 (m, 2H), 7.29 (m, 1H), 5.05 (s, 1H), 4.84 (s, 1H), 3.6 (s, 2H), 2.15 (s, 2H), 0.98 (s, 9H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 143, 137, 130, 129, 126, 117, 48, 43, 30. MS (EI) *m/z* 222 (M+2$^+$, 1.6), 221 (M+1$^+$, 4.7), 220 (M$^+$, 29), 205 (3), 164 (15), 149 (26), 131 (21), 111 (14), 110 (24), 109 (15), 95 (22), 77 (11), 69 (33), 57 (100). Authentic **3d** was prepared by the reaction of compound **1d** with *tert*-butyl magnesium chloride in THF solution. ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.29-7.26 (m, 2H), 6.93-6.90 (m, 3H), 5.29 (d, *J* = 1.8 Hz, 1H), 4.98 (d, *J* = 1.8 Hz, 1H), 4.45 (s, 2H), 2.06 (s, 2H), 0.96 (s, 9H), ^{13}C NMR (75 MHz, CDCl$_3$) δ 159, 143, 129, 120, 115, 114, 72, 47, 31, 30; GCMS (EI) *m/z* 205 (M+1$^+$, 1.3), 204 (M$^+$, 10.6), 133 (50), 94 (50), 57 (100).

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