

Halogenation of Aldehydes and Ketones by Selenium (IV) Oxyhalides Generated *in-situ* from Selenium Dioxide and Halotrimethylsilanes

Jong Gun Lee*, In Soo Park, and Jong Wha Seo

Department of Chemistry, College of Natural Sciences, Pusan National University, Pusan 609-735, Korea

Received January 23, 1995

Bromo- and chlorotrimethylsilane react with selenium dioxide in halocarbon solvents and generate selenium oxybromide and oxychloride, respectively. These *in-situ* generated oxyhalides turned out to be very efficient for selective bromination and chlorination of aldehydes and ketones. Under carefully controlled reaction conditions, second and third introduction of halogens into carbonyl compounds can be greatly suppressed, and high yields of monohalo compounds were obtained. The product ratios of this halogenation reactions can be best explained if the reactions are assumed to involve intermediate β -ketoselenenyl chlorides.

Introduction

The reactions of selenium oxyhalides with inorganic compounds have been relatively thoroughly investigated.¹ When the structural similarity to thionyl halides is considered, selenium oxyhalides are expected to find useful applications in the halogenation of certain organic compounds. However, reports on the applications of these reagents in the oxidation and halogenation of organic compounds are rare, because of the limited availability and a lack of convenient methods of preparation. Selenium oxychloride and oxybromide are known to be prepared by the reaction of selenium dioxide with appropriate selenium tetrahalides.¹ Selenium oxybromide can be prepared by distilling the selenium oxychloride over excess sodium bromide.¹

Earlier we reported that selenium dioxide reacts with chlorotrimethylsilane either in the presence or in the absence of a solvent to produce selenium oxychloride.² This method of preparing selenium oxychloride is much more efficient and convenient than those already reported.³ Selenium oxychloride generated from the reaction of selenium dioxide and chlorotrimethylsilane, proved to be a good chlorinating reagent for the conversion of alcohols to the corresponding alkyl chlorides.³ The most striking advantage of this chlorination reaction is that selenium oxychloride can be regenerated from selenium dioxide after the reaction with an alcohol, and only a catalytic amount of selenium dioxide is needed.

Unlike thionyl halides which have been used only for non-oxidative halogenation and dehydration reactions,⁴ selenium oxychloride and oxybromide might have some interesting oxidative halogenation properties for various functionalities. Chlorination of carbonyl compounds by selenium oxychloride was briefly investigated.⁵ Now that both selenium oxychloride and oxybromide can be easily generated by simply mixing selenium dioxide and halotrimethylsilanes, it is worth the effort to investigate their oxidative halogenation properties toward aldehydes, ketones, esters, and other active methylene compounds as well as olefinic hydrocarbons. In this report, the results of our investigation on α -halogenation of carbonyl compounds by these *in-situ* generated selenium oxyhalides are described.

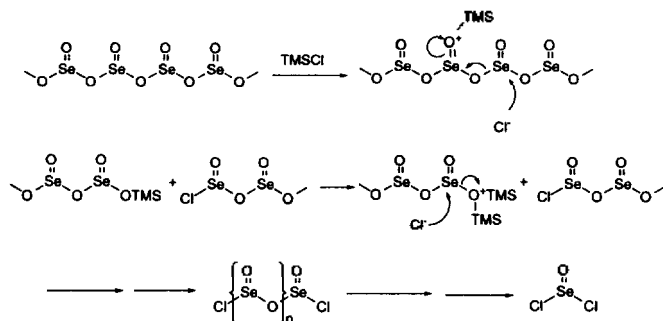
Results and Discussion

Reactions of Selenium Dioxide with Halotrimethylsilanes. Some gaseous or monomeric inorganic oxides are known to be inserted into reactive silicon-hetero atom bonds. Sulfur trioxide is known to be inserted into silicon-oxygen as well as silicon-halogen bonds including even more stronger silicon-fluorine bond.⁶ We attempted a similar insertion of selenium dioxide into the silicon-chlorine bond of chlorotrimethylsilane to understand the dissolution process. When stirred in chlorotrimethylsilane, powdered selenium dioxide dissolved completely with the evolution of heat. On standing, the mixture was separated into two layers. The upper layer was exclusively composed of hexamethyldisiloxane, and the lower layer was mainly selenium oxychloride with traces of dissolved hexamethyldisiloxane. The reaction can also be performed in dichloromethane, chloroform and carbon tetrachloride solvent. Since both reaction products are soluble in these solvents a homogeneous solution was obtained. When exactly two equivalents of chlorotrimethylsilane were employed, selenium dioxide was almost quantitatively converted into selenium oxychloride. On distillation of hexamethyldisiloxane, slightly colored but practically pure selenium oxychloride were obtained. It can be further purified by slow distillation under reduced pressure.



The mechanism of selenium oxychloride formation is believed to closely resemble that of chromyl chloride formation from the reaction of chromium trioxide with chlorotrimethylsilane.⁷ Both selenium dioxide and chromium trioxide are known to exist as a linear polymer.⁸ The dissolution of selenium dioxide in chlorotrimethylsilane could be understood as a depolymerization of this linear polymer.

The initial reaction of chlorotrimethylsilane somewhere along the linear polymeric chain of selenium dioxide fragments the polymer resulting in the formation of a selenium-chlorine bond at the end of one unit and trimethylsilyloxy-selenium bond on the other. The trimethylsilyloxy group is replaced with chloro in a further reaction with chlorotrimethylsilane. The displacement of initially formed trimethylsilyl-



Scheme 1. Degradation of selenium dioxide polymer chain by chlorotrimethylsilane.

oxy group with chloro was also found in the reaction of chlorotrimethylsilane with chromium trioxide to form chromyl chloride,⁷ with sodium nitrate to form nitryl chloride,⁹ and with alkyl nitrite to form nitrosyl chloride.¹⁰ Repeated chain cleavage and chlorine displacement shorten the selenium dioxide polymer chain with both ends carrying chloro groups. This process continues until the chain is completely fragmented and all selenium oxide moieties are converted to selenium oxychloride. This sequential reactions are depicted in Scheme 1. In agreement with this scheme, NMR spectra of the reaction mixture after appropriate time intervals showed that trimethylsilyl groups only from chlorotrimethylsilane and hexamethyldisiloxane are present. Trimethylsilyl group of trimethylsilyl chloroselenite was not apparent anytime during the course of the reaction.

Bromotrimethylsilane also reacted with selenium dioxide. The reaction is highly exothermic, and the reactions were carried out always in carbon tetrachloride. As in the reaction with chlorotrimethylsilane, hexamethyl disiloxane was the only detected and isolated trimethylsilyl compound detected by NMR and GC. Selenium oxybromide was the inorganic product. Due to the thermal instability, the isolation of selenium oxybromide was not attempted.

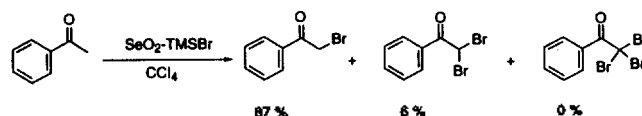


Similar degradation of selenium dioxide polymer by other trimethylsilyl halides, pseudohalides, and esters failed. Hexamethyldisiloxane, trimethylsilyl acetate and trimethylsilyl trifluoroacetate did neither produce bis(trimethylsilyl) selenite, selenium oxyacetate nor oxytrifluoroacetate. Selenium dioxide remained undissolved and the reactant silanes were recovered totally unchanged even after prolonged heating. The only exception was the trimethylsilyl polyphosphate (PPSE), and selenium dioxide-PPSE were used for the high yield aromatization of cyclohexenes.¹¹

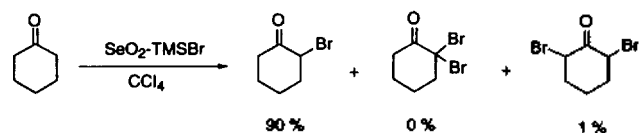
Bromination of Aldehydes and Ketones with Selenium Dioxide-Bromo trimethyl silane. Displacement of hydrogen atoms adjacent to a carbonyl or other activating groups has been one of the most frequently encountered fundamental synthetic procedures. Concerning the preparation and reactions of α -halocarbonyl compounds, a comprehensive review was published lately.¹² Molecular bromine has been the most frequently used for brominating ketones.^{12,13} The reagent, however, has some drawbacks. The bromination is partially reversible and precautions have to be taken

to drive the reaction far to the product. The product α -bromoketones sometimes disproportionate and some α -bromoketones rearrange under the influence of hydrogen bromide.^{12,13} The reaction is also dependent upon the nature of the solvent employed. Not only mono-bromination of unsymmetrical ketones is rarely regiospecific, but di-bromination is hard to suppress. Pyridinium and other ammonium as well as phosphonium bromide perbromides were introduced for selective bromination.¹⁴ 5,5-Dibromo-2,2-dimethyl-4,6-dioxo-1,3-dioxane and other dibromosuccinic acid derivatives were claimed to mono-brominate saturated aldehydes and ketones.¹⁵ A selective α -bromination of unsymmetrical aliphatic ketones using *t*-butyl bromide/DMSO¹⁶ was also reported.

The bromination of various ketones was attempted using selenium oxybromide generated *in-situ* from the reaction of selenium dioxide with bromotrimethylsilane in carbon tetrachloride. Carbon tetrachloride is one of the better and often employed nonpolar solvent and used throughout this study. As can be seen in Table 1, most ketones underwent mono-bromination in satisfactory yields. Pinacolone and acetophenone produced mono-brominated ketones in about 85% yields. Regiocontrol is unnecessary for these ketones, because bromination can occur only at one carbon. Bicyclo[2,2,1]heptan-2-one was brominated mainly on *exo* position.



Acetone produced 1-bromoacetone in 85% yield along with di- and tribromoacetones. This is far better than the reported yield of 50% in bromination using molecular bromine. 3-Pentanone, and cyclohexanone produced α -mono-brominated ketones in greater than 85% yield. The optimum mono-bromination for some symmetrical ketones such as acetone and cyclohexanone was obtained when the reactions were carried out by slowly adding a mixture of the ketone and bromotrimethylsilane into the stirring suspension of selenium dioxide in carbon tetrachloride. This method gave better results than the method of adding a ketone slowly into the pre-stirred solution of bromotrimethylsilane and selenium dioxide in carbon tetrachloride. The yield of 2-bromocyclohexanone reached to 90% following this method.



It is also evident that the second introduction of bromine onto the same carbon of a ketones was greatly suppressed as was shown by the ratio of 2,2-dibromo-3-pentanone and 2,4-dibromo-3-pentanone of 1 : 5. Formation of more 2,6-dibromocyclohexanone than 2,2-dibromocyclohexanone was observed in the bromination of cyclohexanone. In a reaction of cyclohexanone using two equivalents of reagents produced 2,6- and 2,2-dibromocyclohexanone in a 10 : 1 ratio.

The regiocontrol of the bromination for aliphatic ketones having two kinds of α -protons failed in general. Benzyl ketones such as 1-phenylpropanone, however, were more regio-

Table 1. Product Distribution in Bromination of Carbonyl Compounds by SeO₂-TMSBr^a

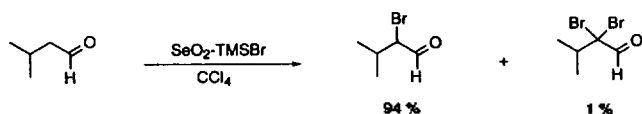
Carbonyl compound	Temp.	Time (hr)	Product Distribution ^b				
acetone	r.t.	10 ^c	unbromo 5	1-bromo- 85	1,3-dibromo- 5	1,1-dibromo- 4	
3-pentanone	r.t.	10 ^c	unbromo 7	2-bromo 84	2,4-dibromo 5	2,2-dibromo 1	poly 3
cyclopentanone	r.t.	10	unbromo 10	2-bromo 63	2,5-dibromo 12	2,2-dibromo 7	poly 8
cyclohexanone	r.t.	18 ^c	unbromo 0	2-bromo 90	2,6-dibromo 1	2,2-dibromo 0	poly 9
	r.t.	18	unbromo 3	2-bromo 71	2,6-dibromo 10	2,2-dibromo 1	poly 15
4- <i>t</i> -butylcyclohexanone	r.t.	18 ^c	unbromo 1	2-bromo 35	2,6-dibromo 14	2,2-dibromo 0	poly 50
1-phenylpropanone	r.t.	20	unbromo 1	1-bromo 84	3-bromo 12	1,3-dibromo 0	poly 3
acetophenone	r.t.	15	unbromo 7	α -bromo 87	α,α -dibromo 6		
propiophenone	r.t.	18 ^d	unbromo 9	α -bromo 90	α,α -dibromo 1		
3-methyl-2-butanone	r.t.	20	unbromo 0	3-bromo 37	1-bromo 42		poly 21
2-methylcyclohexanone	r.t.	18	unbromo 3	1-bromo 60	6-bromo 8		poly 30
3,3-dimethyl-2-butanone	r.t.	22	unbromo 8	1-bromo 88	1,1-dibromo 4	1,1,1-tribromo 0	
camphor	reflux	20	unbromo 72	3-bromo 28			
2-methylpentanal	r.t.	17	unbromo 2	2-bromo 97	2,2-dibromo 1		
2-phenylpropanal	r.t.	13	unbromo 3	2-bromo 94			unknown ^f 3
propanal	r.t.	19	unbromo 0	2-bromo 94	2,2-dibromo 6		
butanal	r.t.	19	unbromo 0	2-bromo 94	2,4-dibromo 3		unknown ^f 3
3-methylbutanal	r.t.	20	unbromo 5	2-bromo 94	2,2-dibromo 1		
2-butenal	r.t.	10	unbromo 5	2,3-bromo 93			unknown ^f 2
<i>trans</i> -3-phenylpropenal	r.t.	20	unbromo 20	2,3-dibromo 80			
2-cyclohexenone	r.t.	0.5	unbromo 1		2,3-dibromo ^g 94		unknown ^f 5
2,4-pentandione	r.t.	0.3 ^e	unbromo 4	3-bromo 83	3,3-dibromo 11		unknown ^f 2
	r.t.	20	unbromo 0	2-bromo 6	3,3-dibromo 84		10
ethyl acetoacetate	r.t.	20 ^c	unbromo 2	2-bromo 87	2,2-dibromo 11		
ethyl cyanoacetate	r.t.	70	unbromo 30	2-bromo 56	2,2-dibromo 10		unknown ^f 4
ethyl acetate	reflux	30	unbromo 100				
acetyl chloride	r.t.	20	unbromo 0				acid bromide 100

^aReaction at room temperature. To a stirred mixture of 2.0-2.2 eq. of TMSBr and 1.0 eq. of SeO₂ was added the ketone, unless otherwise mentioned. All reactions were carried out in CCl₄ as a solvent. ^bBased on GC analysis. The products were identified by NMR. Unidentified poly-brominated compounds are noted as poly. ^cA mixture of a ketone and TMSBr was added over a 1-2 hour period to the stirring mixture of SeO₂ in CCl₄. ^dTo a stirring mixture of a ketone and SeO₂ was added TMSBr at 0 °C for 1 hr and further stirred for mentioned time at room temperature. ^eUnknown or unidentified product. Poly-brominated compounds which were not identified. ^fThe reaction produced mainly 2,3-dibromocyclohexanone along with a small amount of 2-bromo-2-cyclohexenone.

selectively mono-brominated at the benzylic position. Unsymmetrical ketones, such as 2-methylcyclohexanone, 3-methylbutanone gave a regioisomeric mixture of mono-brominated products with less than satisfactory selectivity. When 3-methylbutanone reacted with selenium oxybromide, the bromination was slightly favored at less substituted carbon atom. Hydrogen bromide, a by-product, may catalyze the rearrangement of initially formed 3-bromo-3-methylbutanone into 1-bromo-3-methyl-2-butanone. When an α,β -unsaturated carbonyl compound was allowed to react with selenium dioxide-bromotrimethylsilane, an addition of bromine across the carbon-carbon double bond became a major reaction pathway. α' -Brominated products were barely detected in the reaction mixture.

Owing to the higher reactivity of carbonyl function in aldehydes compared with that in ketones, the direct bromination of aldehydes with molecular bromine often results in poor yield of α -bromoaldehydes. Low temperature (-10°C or below), the presence of dioxane, high dilution of the reaction mixture using dry CH_2Cl_2 and other solvents were reported to improve the yields but not satisfactorily.¹² In addition, more activation of α -proton by the aldehyde group make it difficult to suppress the introduction of second bromine alpha to the carbonyl. The bromination of aldehydes were done in many cases in the form of dimethylacetals. The Amberlyst A26 in the form of perbromide,^{14d} 5,5-dibromobarbituric acid,¹⁵ bromotrimethylsilane-DMSO¹⁷ were the reagents developed for the aldehyde bromination.

Despite of the strong oxidizing power of selenium(IV) oxybromide, an aldehyde group was not oxidized under our reaction conditions. In a control experiment, benzaldehyde was recovered unchanged after a long period of reflux. All aldehydes with at least one enolizable proton reacted with selenium oxybromide to afford the corresponding α -halogenated aldehydes in high yields (Table 1). Having only one α -hydrogen, 2-methylpentanal and 2-phenylpropanal and cyclohexane carboxaldehyde produced the corresponding α -bromoaldehyde in excellent yields. Aldehydes with two enolizable protons were also successfully brominated. The formation of dibromo products can be successfully suppressed. Propanal, butanal and octanal produced the corresponding α -bromo aldehydes in greater than 90% yields. If necessary, aldehydes having two enolizable protons could be dibrominated using excess reagents at higher temperature.



Mono-bromination of methylene groups doubly activated by either carbonyl, carboalkoxy, or nitrile function could also be selectively mono-brominated. 2,4-Pentanedione and ethyl acetoacetate produced the corresponding mono-brominated product in satisfactory yields. When necessary, di-bromination can also be easily achieved by excess reagents. At 70°C , 3,3-dibromo-2,4-pentanedione was obtained in 84% yield. Reactions of simple esters failed to produce α -bromoesters. Attempted bromination of more reactive acid chlorides was not successful either. Acid bromides were obtained instead.

Chlorination of Aldehydes and Ketones with Selenium Dioxide-Chlorotrimethylsilane. Chlorination of

ketones by molecular chlorine usually requires higher temperature and tends to produce a complex mixture of products. Synthetically useful procedures are hard to find except for some poly-chlorinated compounds. But, even under a carefully controlled reaction conditions, mono-selectivity and regiocontrol are hard to achieve.^{12,13} Sulfuryl chloride has been used more often than molecular chlorine. Chlorination of aldehydes and ketones with sulfuryl chloride generally produce complicated mixtures of not only chloro products but cyclic ether trimers and linear polyethers.¹⁸ For example, 2-butanone produces 3,3-dichloro-, 1,3-dichloro-, 3-chloro-, 1-chloro-2-butanones in 48 : 27 : 19 : 3 ratio in a reaction with an equivalent of sulfuryl chloride.¹⁹ Sulfuryl chloride in sulfur dioxide solution containing methanol is still a poor mono-chlorinating reagent for symmetrical ketones.²⁰ Chlorination reactions using selenium oxychloride was reported by Schaefer and Sonnenberg.⁵ The study was not extensive and the chlorination examples of only 5 different ketones in very modest yields were listed in the report.

We have examined the chlorination of ketones with selenium oxychloride generated *in-situ* from selenium dioxide and chlorotrimethylsilane. The results are listed in Table 2. Cyclohexanone produced a mere 57% yield of 2-chlorocyclohexanone along with 26% of 2,2- and 2,6-dichlorocyclohexanone. Fair amounts of poly chlorinated products were also formed. Acetophenone, however, could be chlorinated to get mono-, di- and trichloroacetophenone satisfactorily by adjusting the amount of chlorinating agent. Although selenium oxychloride used in this procedure can be prepared conveniently by mixing common laboratory chemicals, the yields of the mono-chlorinated ketones were not greatly improved compared with the earlier report⁵ using isolated selenium(IV) oxychloride.

The poorer mono-selectivity and regiocontrol in chlorination reactions compared with the bromination by selenium dioxide-bromotrimethylsilane, may ascribe to the slower decomposition of the selenium intermediate. To get better % conversion, the reaction mixture had to be allowed to react for a longer period of time, or at elevated temperature or using a larger excess of the halogenating agents.

Aldehydes, on the other hand, gave an excellent yield of α -chloroaldehydes. Having only one enolizable proton, 2-methylbutanal, and 2-phenylpropanal produced the corresponding α -chloroaldehydes in high yields. Aldehydes with two enolizable protons also produced satisfactory yield of mono-chlorinated products. The synthetic utility of selenium dioxide-chlorotrimethylsilane in the chlorination of aldehydes is particularly noteworthy, since the reaction of aldehydes with inorganic chlorinating agents leads in general to either formation of acids or extensive degradation products in addition to α -chloroaldehydes. In a control experiment, benzaldehyde was quantitatively recovered after prolonged period of refluxing with selenium dioxide and chlorotrimethylsilane in carbon tetrachloride.

A reaction with 2-cyclohexenone, 2-chloro-2-cyclohexenone was produced in 75% yield along with 10% of 2,3-dichlorocyclohexanone. This can be compared with the bromine addition to the olefinic double bond in the bromination reaction of 2-cyclohexenone. Doubly activated 2,4-pentanedione and ethyl acetoacetate were hardly mono-chlorinated but gave almost quantitative yields of dichlorinated products. As with

Table 2. Product Distribution in Chlorination of Carbonyl Compounds by $\text{SeO}_2\text{-TMSCl}^a$

Carbonyl compound	Temp.	Time (hr)	Product Distribution ^b				
3-pentanone	r.t.	24	unchloro	2-chloro	2,4-dichloro	2,2-dichloro	poly
			5	40	9	29	17
cyclohexane	r.t.	15	unchloro	2-chloro	2,6-dichloro	2,2-dichloro	poly
		1	1	57	12	14	18
	reflux	1	0	39	10	13	36
acetophenone	r.t.	20	unchloro	α -chloro	α,α -dichloro	α,α,α -trichloro	
		5	4	22	36	20	
	reflux	5	1	4	5	85	
2-methylcyclohexanone	r.t.	14	unchloro	1-chloro	6-chloro	1,6-dichloro	poly
			0	23	4	22	51
2-methylpentanal	40 °C	17	unchloro	2-chloro	2,2-dichloro		
			3	95	2		
2-phenylpropanal	r.t.	15	unchloro	2-chloro			
			3	97			
octanal	40 °C	20	unchloro	2-chloro	2,2-dichloro		
			9	71	19		
2-cyclohexenone ^c	reflux	1	unchloro	2-chloro	2,3-dichloro		poly
			2	74	10		14
2,4-pentandione	reflux	4	unchloro	3-chloro	3,3-dichloro		poly
			0	2	96		2
ethyl 3-ketobutanoate	reflux	5	unchloro	2-chloro	2,2-dichloro		
			1	1	98		
ethyl acetate	reflux	40	unchloro				
			100				

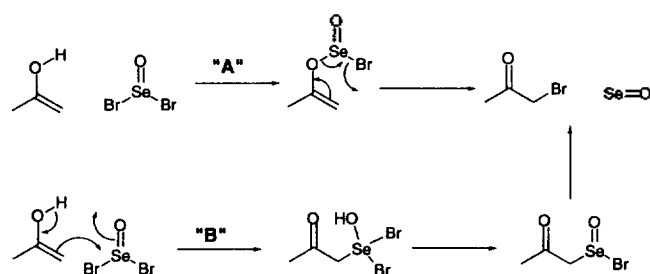
^aThe substrate was added to a pre-stirred mixture of 2-2.2 eq. of TMSCl and 1 eq. of SeO_2 . All reactions were carried out in CCl_4 as a solvent. ^bBased on the NMR and GC analysis. Products were identified by NMR. The structure of poly-chlorinated compounds were not identified. ^cThe reaction produced a mixture of 2-chloro-2-cyclohexenone and 2,3-dichlorocyclohexanone.

selenium oxybromide, the chlorination of simple esters and other acid derivatives was not successful.

The Mechanism of Halogenation by Selenium Oxyhalides. Like the sulfur analogs, the molecular structure of the selenium oxyhalides is believed to be pyramidal with the selenium atom at apex as evidenced by the electron diffraction study of selenium oxychloride.¹ It is known that selenium oxychloride is very polar and partially ionized according to the following equation.¹ This high polarity of the reagent greatly facilitates the ionic halogenation of carbonyl much easier.



Two distinct mechanisms were claimed for the selenium dioxide oxidation of carbonyls to α -dicarbonyl compounds. One mechanism involves a selenate ester of the enol.²¹ In the other mechanism,²² α,β -ketoselenenyl derivative may be the principle intermediate, through which a ketone was claimed to be oxidized by seleninic acid. The bromination of carbonyl compounds is believed to proceed through enol formation. The mechanism of bromination can be deduced from that of oxidation of a methylene adjacent to carbonyl function by selenous acid. When the enol selenate ester mechanism is extended to the bromination by selenium oxybromide, mechanism A in Scheme 2 can be postulated. The other mechanism involving a β -ketoselenenyl derivative is depicted in Mechanism B.



Scheme 2. Two possible reaction mechanisms for bromination of carbonyls by $\text{SeO}_2\text{-TMSBr}$.

Of these two possible reaction mechanisms, A and B, the one proceeding through a β -ketoselenenyl derivative seems to better explain the bromination properties of the selenium oxybromide. If mechanism A is operating, the distribution of brominated products should reflect the relative stability of the possible enols. The mono-bromination for 3-methyl-2-butanone does not reflect the stabilities of the two possible enols. The less stable 1-bromo-3-methyl-2-butanone was produced in greater yields than the more stable enol-derived 3-bromo-3-methyl-2-butanone. Bromination on a sterically less hindered position should be favored if the steric factor of the β -ketoselenenyl intermediate in mechanism B is taken into account. The formation of a fair amount of 3-bromo-1-

phenylpropanone from phenylpropanone can also be explained. This steric hindrance may be a crucial factor for the tedious reaction rate of bromination of camphor. Sterically hindered 4,4-dimethyl-2-pentanone produced more 1-bromo- than 3-bromopentanone. The retarded second bromination on the same carbon in the bromination of symmetrical ketones such as acetone, 3-pentanone, cyclohexanone can also be explained by the steric requirement of the intermediate.

The chlorination by *in situ* generated selenium oxychloride is also believed to follow mechanism B. The reaction rate of chlorination was observed noticeably slower than that of bromination. This difference in reactivity can be understood if the carbon-halogen bond formation by the degradation of β -ketoselenium intermediate is assumed to be rate-determining. A similar decomposition of β -haloselenium trichloride was reported to be the slower step in the chlorination of olefinic double bonds by selenium tetrachloride.²³ The β -ketoselenium intermediates in chlorination may be sterically less requiring than in the bromination. This favorably explains the less regioselectivity, and more dichloro substitution on the same carbon. Slower formation of carbon-chlorine bond compared with carbon-bromine bond during the decomposition of the intermediate results in more selenoxide type elimination resulting in the formation of unsaturated carbonyls which leads to more unidentifiable polychlorination.

Conclusion

Selenium dioxides reacts with halotrimethylsilanes to produce selenium oxyhalides which can be utilized for carbonyl halogenation reactions. The bromination and chlorination of carbonyl compounds by selenium oxyhalides have the following distinct features. Most ketones can be successfully mono-brominated by selenium oxybromide with the exception of very hindered ketones. Chlorination of ketones with selenium oxychloride *in situ* generated gave mixture of mono-, di- and poly-chlorinated products making the procedure synthetically less attractive. Selective mono-halogenation of ketones with two different kinds of enolizable protons are difficult to achieve and produces mixtures of regioisomers. However, both reagents are exceptionally good for bromination and chlorination of aldehydes. The halogenation properties of the present reagents can best be explained, when it is assumed that these halogenation reactions proceed through the formation of β -ketoselenenyl halides.

Experimental

Selenium dioxide and chlorotrimethylsilane and all aldehydes and ketones were purchased from Aldrich Chem. Co. and used without further purification. Bromotrimethylsilane was prepared by refluxing a mixture of phosphorous tribromide and hexamethyldisiloxane and slow distillation of the mixture according to the known procedure.²⁴ Dichloromethane and carbon tetrachloride were purchased from Dongyang Chem. Co. and were purified by distilling over phosphorous pentoxide. Column chromatography was performed by Merck Kieselgel 60 (70-230 mesh ASTM).

Proton NMR spectra were recorded with Varian EM-360A (60 MHz) and with Varian Gemini-200 (200 MHz). Gas chro-

matographic analyses were done on a Hewlett Packard 5880A with a flame ionization detector. Coiled fused silica capillary columns (HP-5 and HP-20M) of 10, 20, or 50 m in length, 0.53 mm in inner diameter, and 2.65 or 1.33 micrometer in film thickness were used.

Selenium Oxychloride. In a 100 mL round-bottom flask was placed 15 g (0.136 mol) of selenium dioxide. Chlorotrimethylsilane (37 g, 0.34 mmol) was then added with stirring at room temperature. After 2 hour stirring, all solid selenium dioxide dissolved. On standing, the mixture was separated into two layers. ¹H NMR spectra showed that the upper layer was composed exclusively of hexamethyldisiloxane containing only a trace of residual chlorotrimethylsilane. The lower layer was mainly composed of selenium oxychloride which showed no NMR signals. Evaporation of lower boiling material gave crude selenium oxychloride. It was purified by distillation under reduced pressure without decomposition. When the same reaction was performed using either dichloromethane or carbon tetrachloride as a solvent, the mixture was homogeneous without separation of layers even after standing for a long period. For our chlorination reactions, the reagents were allowed to react either before the addition of a substrate or in the presence of the substrates.

Selenium Oxybromide. The reaction was carried out in a similar manner at room temperature by adding bromotrimethylsilane (1.4 g, 9 mmol) to a heterogeneous mixture of selenium dioxide (0.5 g, 45 mmol) and carbon tetrachloride (5 mL). Evolution of heat was observed during the reaction and a formation of red-yellow solid was observed. The reaction mixture was further stirred at room temperature for about 10 minutes. At this stage, a proton NMR of the reaction mixture showed that bromotrimethylsilane virtually disappeared and hexamethyldisiloxane was the exclusive trimethylsilyl product. Due to the thermal instability of selenium oxybromide, further purification of selenium oxybromide was not attempted.

Bromination of Acetophenone (Bromination of Ketone, Method 1). In a 30 mL round-bottom flask equipped with an oil bubbler were placed selenium dioxide (1.1 g, 10 mmol) and 3 mL of CCl₄. A solution of bromotrimethylsilane (3.4 g, 22 mmol) in 3 mL of CCl₄ was slowly added over a period of several minutes. The mixture was stirred until the evolution of heat ceased. After 10 minutes at room temperature, acetophenone (1.2 g, 10 mmol) diluted in 3 mL of CCl₄ was slowly added. The reaction mixture was stirred for 15 hours. The proton NMR spectrum of the crude reaction mixture showed complete conversion of acetophenone to α -bromoacetophenone and a small amount of α,α -dibromoacetophenone. By GC analysis, overall products conversion was 94% and the yields of α -bromoacetophenone and α,α -dibromoacetophenone was 87% and 7%, respectively. These are consistent with that obtained from NMR integration. The reaction mixture was then poured into an aqueous solution of 5% sodium bicarbonate and extracted with ether. Most of the elemental selenium formed was removed by filtration. The combined ether extracts was dried over MgSO₄. Evaporation of ether, carbon tetrachloride and hexamethyldisiloxane gave the crude product. Silica gel chromatography gave 1.61 g of α -bromoacetophenone (81%), mp 47.5-50.5 °C; ¹H NMR (CCl₄), δ =4.3 (s, 2H), 7.1-8.1 (m, 5H).

Bromination of Cyclohexanone (Bromination of

Ketone, Method 2). To a stirred heterogeneous solution of selenium dioxide (1.1 g, 10 mmol) in 3 mL of CCl_4 were slowly added bromotrimethylsilane (3.4 g, 22 mmol) and cyclohexanone (0.1 g, 10 mmol) diluted in 3 mL of CCl_4 at room temperature and the resulting mixture was stirred for 18 hours at room temperature. After the similar work-up, a crude product containing 90% of 2-bromocyclohexanone and 9.9% of di- or poly-brominated ketones was obtained. Pure 2-bromocyclohexanone (1.55 g, 88%) was obtained by chromatography on silica gel. Ketones having two different α -protons gave better yields of the mono-brominated product following this procedure.

2-Bromobutanal (Bromination of Aldehydes). In a 30 mL of round-bottom flask equipped with an oil-bubbler, were placed selenium dioxide (1.1 g, 10 mmol) and bromotrimethylsilane (3.4 g, 22 mmol) and 3 mL of CCl_4 . After several minutes stirring at room temperature, butanal (0.72 g, 10 mmol) was added to the mixture. The resulting mixture was stirred for 19 hours at room temperature. ^1H NMR spectrum of the crude reaction mixture showed a 94% conversion of octanal to 2-bromooctanal at this point. The yield of 2-bromo octanal after aqueous workup and chromatography was 1.24 g (94%). ^1H NMR (CCl_4) δ =0.7-2.2 (m, 5H), 4.0-4.3 (m, 1H), 9.40 (d, 1H).

Bromination of Ethyl Acetoacetate. To a stirred solution of bromotrimethylsilane (3.4 g, 22 mmol) and selenium dioxide (1.1 g, 10 mmol) in 3 mL of CCl_4 was added ethyl acetoacetate (1.3 g, 10 mmol) diluted in 2 mL of CCl_4 at room temperature and resulting mixture was stirred for 21 hr. After the similar work-up, the organic layer was evaporated and analyzed by GC and NMR. Mono-brominated compound was produced in 77% yield along with 22% of di-brominated compound. The bromination occurred only on the doubly activated methylene group. ^1H NMR (CCl_4): δ =1.33 (t, 3H), 2.35 (s, 3H), 4.23 (q, 2H), 4.55 (s, 1H).

Chlorination of 2-Phenylpropanal. The α -chlorination of 2-phenylpropanal was carried out in a similar manner. Chlorotrimethylsilane (2.4 g, 22 mmol) and selenium dioxide (1.1 g, 10 mmol) were mixed in 3 mL of CCl_4 and stirred for several minutes, before 2-phenylpropanal (1.34 g, 10 mmol) was added to the mixture. The resulting mixture was stirred for 15 hours at room temperature. At this point, the crude reaction mixture was analyzed by GC and NMR. The yield of 2-chloro-2-phenylpropanal was 97% by GC. Washing with 2% oxalic acid followed by the purification using a silica gel column gave 1.53 g of 2-phenyl-2-propanal (91%). ^1H NMR (CCl_4), δ =1.9 (s, 3H), 7.0-7.45 (m, 5H), 9.25 (s, 1H).

Acknowledgment. The authors appreciate the financial support from Korea Science and Engineering Foundation through Organic Chemistry Research Center (1992-1994).

References

- (a) Bagnol, K. W. In *Comprehensive Inorganic Chemistry*; Bailar, J. C.; Emeleus, H. J.; Niholm, R.; Dickenson, A. F. T. Eds.; Pergamon Press: Oxford, 1976, Vol. 2, pp 935-1007. (b) Bagnall, K. W. *The Chemistry of Selenium, Tellurium and Polonium*; Elsevier: Amsterdam, 1966; p 14. (c) Claude, P. *Selenium Reagents and Intermediates in Organic Synthesis*; Pergamon Press: 1986; p 13.
- Lee, J. G.; Kang, K. K. *J. Org. Chem.* 1988, 53, 3634.
- (a) Lenher, V. *J. Am. Chem. Soc.* 1921, 43, 29. (b) Haynes, R. K.; Indorato, C. *Aust. J. Chem.* 1984, 37, 1183.
- Thionyl chloride and bromide has never been for halogenation of aldehydes and ketones. Pizey, J. S. *Synthetic Reagents*; Ellis Horwood: Chichester, 1974; Vol. 1. p 321.
- Schaefer, J. P.; Sonnenberg, F. *J. Org. Chem.* 1963, 28, 1128.
- (a) Bott, R. N.; Eaborn, C.; Rushton, B. M. *J. Organomet. Chem.* 1965, 3, 448. (b) Schmidbauer, H. *Chem. Ber.* 1961, 94, 2137. (c) Schmidt, M.; Schmidbauer, H. *Angew. Chem.* 1958, 70, 657.
- (a) Lee, J. G.; Ha, D. S. *Bull. Korean Chem. Soc.* 1988, 9, 407. (b) Lee, J. G.; Ha, D. S. *Bull. Korean Chem. Soc.* 1987, 8, 117. (c) Lee, J. G.; Ha, D. S. *Bull. Korean Chem. Soc.* 1987, 8, 435.
- Bisrom, A.; Wilhelmi, A. K. *Acta Chem. Scand.* 1950, 411, 319. (b) Hanic, F.; Stempelova, D. *Chem. Zvesti*, 1960, 14, 165.
- Lee, J. G.; Hwang, J. P. *Tetrahedron Lett.* 1990, 31, 6677.
- Lee, J. G.; Cha, H. T. *Tetrahedron Lett.* 1992, 33, 3167.
- Lee, J. G.; Kim, K. K. *Tetrahedron Lett.* 1992, 33, 6363.
- Kimpe, N. D.; Verhe, R. *The Chemistry of α -Haloketones, α -Haloaldehydes and α -Haloimines*; John Wiley and Sons: New York, 1988.
- House, H. O. *Modern Synthetic Reactions*; Benzamin: Menlo Park, 1972; pp 459-478.
- Djerassi, C.; Scholz, C. R. *Am. Chem. Soc.* 1948, 70, 417. (b) Forlani, L. *Synthesis* 1980, 487. (c) Armstrong, V. W.; Chishti, N. H.; Ramage, R. *Tetrahedron Lett.* 1975, 373. (d) Cacchi, S.; Caglioti, L. *Synthesis* 1978, 64. (e) Bongini, A.; Cainelli, G.; Contento, M.; Manescalchi, F. *Synthesis* 1980, 143.
- Bloch, R. *Synthesis* 1978, 140. (b) Calo, V.; Lopez, L.; Pesce, G.; Todesco, P. E. *Tetrahedron* 1973, 29, 1625. (c) Sekiya, M.; Ito, K.; Suzuki, K. *Tetrahedron* 1975, 31, 231.
- Armani, E.; Dossena, R.; Marchelli, R.; Casnati, G. *Tetrahedron* 1964, 40, 2035.
- Bellesia, F.; Ghelfi, F.; Grndi, R.; Pagnoni, U. M. *J. Chem. Res. (S)* 1986, 428.
- Pizey, J. S. *Synthetic Reagents*; Ellis Horwood: Chichester, 1981, Vol. 5, pp 336-396.
- (a) Wyman, D. P.; Kaufman, R. J. *J. Org. Chem.* 1964, 29, 1956. (b) Wyman, D. P.; Kaufman, R. J.; Freeman, W. R. *J. Org. Chem.* 1964, 29, 2706.
- Masilamani, D.; Rogic, M. M. *J. Org. Chem.* 1981, 46, 4486.
- Corey, E. J.; Schafer, J. P. *J. Am. Chem. Soc.* 1960, 82, 918.
- Sharpless, K. B.; Gordon, K. M. *J. Am. Chem. Soc.* 1976, 98, 300.
- Uemura, S.; Onoe, A.; Okano, M. *Bull. Chem. Soc. Jpn.* 1975, 48, 3702; 1977, 50, 1078.
- Gilliam, W. G.; Meals, R. N.; Sauer, R. D. *J. Am. Chem. Soc.* 1946, 68, 1161.