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NUCLEOPHILIC DISPLACEMENT REACTIONS AT Se(II). REACTION OF ARENESELENENYL CHLORIDES AND 2-CHLOROALKYL PHENYL SELENIDES[1]

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ABSTRACT: *The products of the title reaction depend upon the relative concentrations of reactants. With equimolar concentrations or an excess of 2-chloroalkyl phenyl selenide, the products are 1,2-dichloroethane and a diaryldiselenide. When excess areneselenenyl chloride is used, the products are a diaryl diselenide and 2-chloroalkyl phenyl selenide dichloride. A mechanism involving nucleophilic displacement at selenenyl selenium is proposed to account for the observed products. Structural changes in the selenide or varying substituents in the 4-position of areneselenenyl chloride has little effect on the rate of the reaction. In the proposed continuum of mechanisms of nucleophilic displacement reactions at Se(II), an* S_N2*-like transition state best accounts for the data.*

One of the fundamental reactions of Se(II) containing compounds is the displacement of a group or atom bonded to selenium by a nucleophile. The general equation for such a reaction can be written as follows:

$$\mathrm{Nu}^{n} + \mathrm{RSeL} \longrightarrow \mathrm{RSeNu}^{n+1} + \mathrm{L}^{-}$$

where Nu is the nucleophile, L is the leaving group and R is an alkyl or aryl group. While many examples of such nucleophilic displacement reactions are known,[3] little is known about their mechanism(s).

Austad[4] reported the reaction of thiourea and benzenethiolsulfonate with 4-substituted-2-nitrobenzeneselenenyl bromides in methanol at 25°C. All substitutents increased the rate compared to the unsubstituent compound. However, electron releasing substituents have a large rate enhancing effect and consequently values of $\rho = -1.2$ (for thiourea) and -0.34 (for benzenethiolsulfonate) were calculated from rather poor Hammett plots. Austad concluded that his data are compatible with a transition state in which the bonding is of the three-center four-electron type. Gancarz and Kice[5] studied the rate of the raction of benzeneselenosulfonates $[C_6H_5SeS(O_2)Ar]$ with cyanide ion in a Tris buffer in 90% acetonitrile at 25°C. A value of $\rho = +0.6$ was obtained from the Hammett plot of three compounds (H, 4-Cl, 4-CH_3).

We have recently pointed out that the addition of areneselenenyl chlorides to (E)- and (Z)-1-phenylpropenes can be regarded equally well as a nucleophilic displacement at Se(II).[1] Electron donating groups in the phenyl rings of both the areneselenenyl chloride and alkene enhance the rate of reaction. From these data it is concluded that C–Se bond making lags behind Se–Cl bond breaking in the rate determining transition state.

Several mechanisms can be envisioned for nucleophilic displacement reactions at Se(II). A simple way of viewing these various mechanisms is by means of the reaction coordinate contour diagram shown in Figure 1.[6] At corner

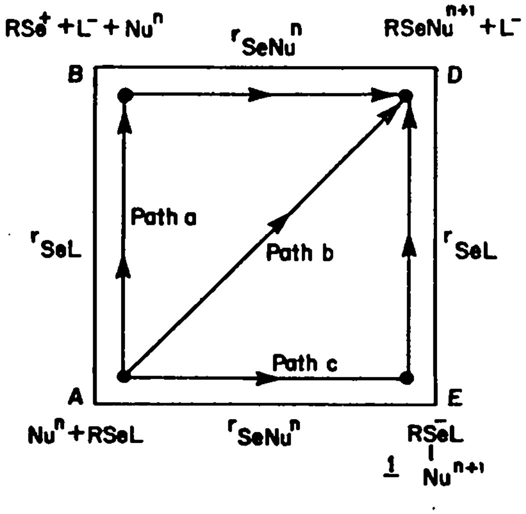


Figure 1. Reaction coordinate contour diagram for nucleophilic displacement reactions at Se(II).

A of the diagram is located the reactants (RSeL) and Nu^n). The products, RSe Nu^{n+1} and L^-, are found at corner D. Approaching Nu^n to ArSeL without breaking the Se-L bond corresponds to movement along the edge AE to form the intermediate 1 at corner E. Breaking the Se-L bond of ArSeL corresponds to movement along the edge AB to form the selenium ion ($ArSe^+$) and L^-. On this diagram, an S_N1-like mechanism is represented by path a. Path b represents an S_N2-like mechanism and path c represents an addition-elimination mechanism. Viewing nucleophilic displacement reactions in this way suggests a continuum of mechanism between one extreme, the S_N1-like mechanism (path a) and the other, the addition-elimination mechanism (path c). The nature of R,L,Nu^n, and solvent will determine the relative energies of corners A,B,D, and E and consequently the mechanistic path of the reaction.

Nucleophilic displacement reactions at S(II) can be viewed in a similar way.[7] From the available data, it is concluded that these reactions at S(II) occur by at least two mechanisms. The data support an S_N2-like mechanism for the addition of arenesulfenyl halides to alkenes[7], the reaction of hydroxide ion with $ArSOC_2H_5$,[8] and the reaction of cyanide ion with $ArSSO_3^-$.[9] An addition-elimination mechanism explains the effect of changing the leaving group on the rate of the reaction of $(C_6H_5)_3CSX$ with a number of nucleophiles[10] as well as the reaction of amines with arenesulfenyl chlorides.[11] An S_N1-like mechanism for reactions of S(II) seems unlikely since claims for the formation of sulfenium ions (RS^+) have been shown to be unfounded.[12] Thus the continuum of mechanisms for nucleophilic displacement reactions at S(II) spans the region between an S_N2-like mechanism as one extreme to an addition-elimination mechanism at the other extreme.

Only limited data are available to analyze the reaction of nucleophiles with Se(II) in this way and reach mechanistic conclusions. The object of this publication is to provide additional kinetic and product data for this type of reaction. Specifically the rates and products of the reactions of a selenium containing nucleophile with areneselenenyl chlorides are reported and their mechanistic implications are discussed.

RESULTS AND DISCUSSION

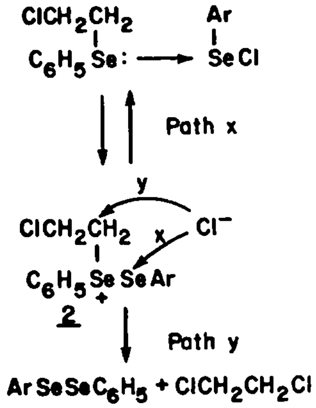
Products

When equimolar quantities of benzeneselenenyl chloride and 2-chloroethyl phenyl selenide are mixed, 1,2-dichloroethane and diphenyldiselenide are formed as products (equation 1).

$$\begin{array}{c} C_6H_5SeCl + C_6H_5SeCH_2CH_2Cl \\ \downarrow \\ C_6H_5SeSeC_6H_5 + ClCH_2CH_2Cl \end{array} \qquad (1)$$

The same reaction occurs when an excess of 2-chloroethyl phenyl selenide is used. When equimolar quantities of 4-chlorobenzeneselenenyl chloride and 2-chloroethyl phenyl selenide are reacted, 1,2-dichloroethane and the mixed diselenide $4\text{-}ClC_6H_4SeSeC_6H_5$ are formed.

These results can be explained by a mechanism involving nucleophilic displacement at selenenyl selenium by the selenium of 2-chloroethyl phenyl selenide to form the selenonium ion intermediate 2 as shown in equation 2.



(2)

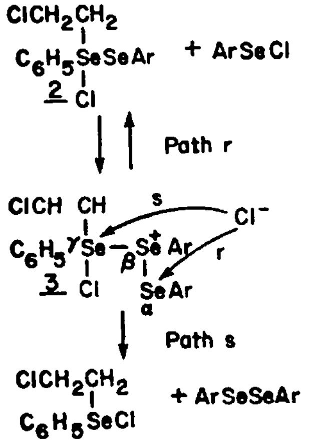
Intermediate 2 can undergo nucleophilic attack by chloride ion at two locations. Attack at Se(II) (path x) regenerates the reactants while attack at carbon (path y) forms the observed products.

According to the mechanism in equation 2, attack by chloride ion at carbon of intermediate 2 should occur by an S_N2 mechanism leading to inversion at carbon.

This may be tested by using the diastereomeric 3-chlorobutyl-2 phenyl selenides. The reaction of equimolar quantities of benzeneselenenyl chloride and 2-RS, 3-RS-3-chlorobutyl-2 phenyl selenide forms only 2-SR, 3-RS- 2,3-dichlorobutane and diphenyldiselenide. Similarly reaction of benzeneselenenyl chloride and 2-SR, 3-RS-3-chlorobutyl-2 phenyl selenide forms only 2-RS, 3-RS-2,3-dichlorobutane and diphenyldiselenide. These results confirm the inversion in configuration at carbon required by the proposed mechanism.

Different products are formed when a large excess of areneselenenyl chloride is used in the reaction. Thus the reaction of at least a five-fold excess of either benzene- or 4-chlorobenzeneselenenyl chloride with 2-chloroethyl phenyl selenide forms the symmetrical diselenide as well as 2-chloroethyl phenyl selenide dichloride [$C_6H_5Se(Cl)_2CH_2CH_2Cl$] . No apparent reaction occurs between either areneselenenyl chloride and an equimolar mixture of 1,2-dichloroethane and the corresponding symmetrical diselenide. If less than a five-fold excess of 4-chlorobenzene selenenyl chloride is present during the reaction , a mixture of all four possible products is formed. This is evidence that the rate of the first reaction (equation 1) is faster than the second.

The different products formed in the presence of excess areneselenenyl chloride can be explained if it is assumed that intermediate 2 is sufficiently stable and long lived to react with the excess areneselenenyl chloride as shown in equation 3 to form another intermediate 3.



(3)

Intermediate 3 can again undergo reaction at two sites. Attack at selenium α (path r) regenerates 2 while attack at selenium γ (path s) forms the observed products.

The formation of the products of the reaction of either equimolar or excess benzeneselenenyl chloride and 2-chloroethyl phenyl selenide can be explained by means of a mechanism involving nucleophilic displacement at Se(II). The chloride ion of benzeneselenenyl chloride is the leaving group and the Se(II) of 2-chloroethyl phenyl selenide and intermediate 2 are the nucleophilic atoms.

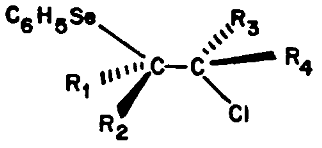
Kinetics

The rates of reaction of benzene-, 4-toluene-, and 4-chlorobenzeneselenenyl chloride with 2-chloroalkyl phenyl selenides 4-10 were determined by measuring the decrease in absorption of the areneselenenyl chlorides at 433 nm in anhydrous methylene chloride at 25°C using a Durrum-Gibson stopped-flow spectrophotometer. The kinetics were carried out under pseudo first order conditions to insure that the rate of the reaction in equation 1 was the one actually measured. All reactions were found to exhibit second order kinetics, first order in areneselenenyl chloride and first order in 2-chloroalkyl phenyl selenide to at least 80% completion of the reaction. The rate constants are reported in Table 1.

The rates of these reactions are almost too slow to follow by stopped flow technique. This is in contrast to the rates of reaction of benzeneselenenyl chloride and alkenes under identical conditions which are near the upper limit of the stopped flow technique.[13] Representative data are given in Table 2. From these data we can conclude that a carbon-carbon double bond is a better nucleophile towards Se(II) of benzeneselenenyl chloride than the bivalent selenium in a 2-chloralkyl phenyl selenide. This is understandable in terms of hard and soft acid and base theory as applied to nucleophilic substitution reactions.[14] A carbon-carbon double bond is a softer base than the selenium atom of a selenide. Consequently it would react faster with the relatively soft Se(II) electrophilic center of the areneselenenyl chloride.

Varying the substituents in the 4-position of the phenyl ring of the

Table 1. Specific Second Order Rate Constants for the Reaction of Benzene, 4-Touluene-, and 4-Chlorobenzeneselenenyl Chloride with 2-Chloroalkyl phenyl selenides in Methylene Chloride at 25°C.



					$k_2^*(M^{-2}s^{-1})$ $4\text{-}XC_6H_4SeCl$ X		
R_1	R_2	R_3	R_4		CH_3	H	Cl
H	H	H	H	4	0.092	0.089	0.061
H	H	H	CH_3	5	---	0.095	---
H	H	CH_3	CH_3	6	0.35	1.48	0.13
CH_3	H	CH_3	H	7	0.32	1.23	0.50
CH_3	H	H	CH_3	8	0.28	0.55	0.62
CH_3	H	CH_3	CH_3	9	---	0.21	---
CH_3	CH_3	CH_3	CH_3	10	---	1.92	---

*Rates reproducible to $\pm 5\%$.

Table 2. Comparison of Rate Constants for Reaction of Benzeneselenenyl Chloride with Alkenes and 2-Chloroalkyl Phenyl Selenides in Methylene Chloride at 25°C.

Adduct	$k_2 M^{-1} s^{-1}$	Alkene	$k_2^* M^{-1} s^{-1}$
4	.089	$CH_2{=}CH_2$	498
5	.095	$CH_3CH{=}CH_2$	4360
6	1.48	$(CH_3)_2C{=}CH_2$	3370
7	1.23	Z-$CH_3CH{=}CHCH_3$	1870
8	0.55	E-$CH_3CH{=}CHCH_3$	1040
9	0.21	$(CH_3)_2C{=}CHCH_3$	1880
10	1.92	$(CH_3)_2C{=}C(CH_3)_2$	1230

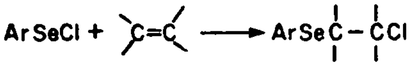
*ref. 13.

areneselenenyl chloride has little effect on the rate. In contrast, such substitution has a large effect on the reaction of areneselenenyl chlorides and alkenes.[7] Replacing any two hydrogens on the methylene carbons of 2-chloroethyl phenyl sulfide by methyl groups does have a slight rate enhancing effect. Replacing more than two hydrogens by methyl groups does not affect the rate appreciably.

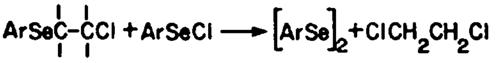
Conclusions

The lack of a large substituent effect in this reaction means that there is little or no charge on the selenenyl selenium in the rate-determining transition state. This suggests an S_N2-like mechanism in which bond-breaking and bond-making to selenenyl selenium are nearly equivalent. This corresponds to a transition state near the diagonal AD in Figure 1. This is in contrast to the mechanism of the reaction of alkenes and areneselenenyl chlorides where bond-making to Se(II) lags behind Se-Cl bond-breaking in the transition state. Consequently the structure of the transition state is located in the region between an S_N2-like mechanism and an addition-elimination. Thus the structure of the rate-determining transition states for these two reactions differ. This is the first evidence that nucleophilic displacement reactions at Se(II) may indeed occur by a continuum of mechanisms.

Our data clearly establish that a carbon-carbon double bond is a better nucleophile toward Se(II) than the selenium atom of 2-chloroalkyl phenyl selenide. In addition to mechanistic implications, this observation has practical significance for synthesis of organoselenium compounds. In general, the products of the reactions of arene- or alkaneselenenyl chlorides with a variety of compounds are themselves Se nucleophiles. As a result, they can react further with areneselenenyl chlorides. For example, 2-chloroalkyl phenyl selenides are the adducts formed by the reaction of areneselenenyl with alkenes (equation 4).



$$\mathrm{ArSeCl} + \mathrm{{>}C{=}C{<}} \longrightarrow \mathrm{ArSe}\overset{|}{\underset{|}{\mathrm{C}}}-\overset{|}{\underset{|}{\mathrm{C}}}\mathrm{Cl} \quad (4)$$



$$\mathrm{ArSe}\overset{|}{\underset{|}{\mathrm{C}}}-\overset{|}{\underset{|}{\mathrm{C}}}\mathrm{Cl} + \mathrm{ArSeCl} \longrightarrow [\mathrm{ArSe}]_2 + \mathrm{ClCH_2CH_2Cl} \quad (5)$$

These same adducts react as Se(II) nucleophiles with areneselenenyl chlorides as we have shown in this work (equation 5). We know that in this case the rate constants for equation 4 are generally about 10^3 greater than those for equation 5 (Table 2). Consequently under the usual conditions, either excess alkene or equimolar amounts of alkene and areneselenenyl chloride, the rate of reaction 5 is negligible compared to 4. Therefore reaction 5 will not interfere with either the determination of the kinetics or the formation of a high yield of the adduct in reaction 4. But this may not always be the case. If the first formed product is the better Se(II) nucleophile, it will never be observed since as soon as it is formed it will react with the original Se(II) center. The more interesting case is when the Se(II) nucleophility of the original reactant and the first formed product are about the same. A complicated rate law and a product composition that varies with changes in relative concentrations of the original reactants might be expected. Such a complication should be kept in mind when attempting the synthesis of selenium containing compounds by nucleophilic displacement reactions at Se(II).

EXPERIMENTAL

All melting points are uncorrected. Microanalyses were carried out by A.G. Gygli Microanalysis Laboratory, Toronto. GLC analysis was carried out by using a Varian Aerograph Series 2740 analytical instrument equipped with an FID and a 2m x 6mm 30% Carbowax 20M on Chromosorb P (60/80 mesh) column. All magnetic resonance spectra were recorded in $CDCl_3$ containing $(CH_3)_4Se$ as internal standard. Methylene chloride was purified as previously reported.[15] Benzeneselenenyl chloride was obtained from Aldrich Chemical Company and recrystallized from methylene chloride, m.p. 63·7-64·5°C (lit.[16] 64°C). Bis-(4-chlorobenzene) diselenide was prepared as previously reported,[1] m.p. 85-87°C (lit.[17] 87-88°C). Diphenyl diselenide was prepared from benzeneselenol as previously reported,[13] m.p. 62.7-63°C (lit.[18] m.p. 63°C). 2-Chloroethyl phenyl selenide was prepared by the addition of equimolar amounts of ethylene and benzeneselenenyl chloride in methylene chloride as previously reported.[19] 2-Chloroethyl phenyl selenide dichloride was prepared by the reaction of Cl_2 to 2-chloroethyl phenyl selenide by the procedure previously reported.[20] The two diastereomers of 2,3-dichlorobutane were prepared by adding Cl_2 gas to E- and Z-2-butene according to the method of Poutsma.[21]

Reaction of areneselenenyl chloride and 2-chloroethyl phenyl selenide.

(a) Equimolar concentration of benzeneselenenyl chloride. To 0·225 g. (1.02mmol) of 2-chloroethyl phenyl selenide in 10mL CH_2Cl_2 was slowly added with stirring 10mL of an equimolar CH_2Cl_2 solution of benzeneselenenyl chloride at room temperature. After standing for 30 minutes, the reaction mixture was analyzed by glc. The dichloride peak was identified as 1,2-dichloroethane by spiking the reaction mixture with an authentic sample. The solvent was removed from the remainder of the reaction mixture under reduced pressure. The residue had ^{13}C spectrum and m.p. identical to that of an authentic sample of diphenyl diselenide. (b) excess benzeneselenenyl chloride. A procedure similar to

(a) was followed except that a solution of 1·05 g (5·5 mmol) of benzeneselenenyl chloride in 20 mL CH_2Cl_2 was used. The solid obtained after removal of solvent was separated by tlc into two components. The ^{13}C, ^1H spectra and melting points of the two products were identical to those of authentic samples of diphenyl diselenide and 2-chloroethyl phenyl selenide dichloride.

(c) equimolar concentration of 4-chlorobenzeneselenenyl chloride.

The same procedure as in (a) was used except that a solution of 0·240 g (1.07 mmol) of 4-chlorobenzeneselenenyl chloride in 10mL CH_2Cl_2 was used. After removal of the solvent, an oil remained. [Found C,41·5; H, 2·6; Cl, 10·1. $C_{12}H_9Se_2Cl$ requires C, 41·6; H, 2·6; Cl, 10·2].

(d) excess 4-chlorobenzeneselenenyl chloride. A procedure similar to (a) was used except that a solution of 1·32 g (5·9mmol) of 4-chlorobenzeneselenenyl chloride in 20mL CH_2Cl_2. The solid obtained after removal of the solvent was identified by the method in procedure (b) to be a mixture of bis-(4-chlorobenzene) diselenide and 2-chlorethyl phenyl selenide dichloride.

Reaction of benzeneselenenyl chloride and 3-chlorobutyl-2 phenyl selenide.

To 0·250 g (1·01mmol) of 3-chlorobutyl-2 phenyl selenide in 10mL CH_2Cl_2 was slowly added with stirring at room temperature a solution of 0·200 g (1·05mmol) of benzeneselenenyl chloride. After standing at room temperature for approximately 30 min., the reaction mixture was analyzed by glc. Spiking with authentic samples identified the product of the reaction of 2-RS, 3-RS-3-chlorobutyl-2 phenyl selenide as 2-SR, 3-RS-2,3-dichlorobutane. The product of reaction of 2-SR, 3-RS-3-chlorobutyl-2 phenyl selenide formed 2-RS, 3-RS-2,3-dichlorobutane as product.

Kinetics.

The rate data were obtained by the method previously reported[19] except that 2-chloroalkyl phenyl selenide was used instead of an alkene.

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