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Syn Elimination of Alkyl Selenoxides. Side Reactions Involving Selenenic Acids. Structural and Solvent Effects on Rates[1]

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The olefin-forming syn elimination of alkyl aryl selenoxides was examined. The formation of β-hydroxy selenides by addition of the elements of benzeneselenenic acid (PhSeOH) to olefin product was found to be a persistent side reaction unless an alkylamine was present during syn elimination. The selenium(II) electrophile is provided by a comproportionation (reverse disproportionation) of Ph_2Se_2 and $PhSeO_2H$. If an intramolecular reaction is possible (as for the decomposition of **1**) only an unhindered secondary amine will prevent the electrophilic addition to the double bond. The selenoxide syn elimination was shown to be irreversible for compound **1**. Alkyl aryl selenoxides react with dimethyl acetylenedicarboxylate to form ylides (e.g. **8**). Solvent and substitutent effects on the rates of selenoxide syn eliminations were measured. Protic solvents reduce the rate of syn elimination. Chloro and phenyl substituents at either the α or β position or alkyl at the α position accelerate the syn elimination, whereas β-alkyl and methoxy substituents retard it. Methyl aryl selenoxides were shown to catalytically decompose hydrogen peroxide, a widely used oxidant for selenides. Reaction conditions for optimizing rates and yields for selenoxide syn eliminations are proposed.

The selenoxide syn elimination has been shown to be a mild and selective procedure for olefin formation.[3,4] The reaction frequently provides high yields of clean products, but side reactions have been identified in certain cases. For example, some α-phenylselenino ketones in acidic media undergo seleno-Pummerer reactions leading to α-dicarbonyl compounds.[3a] Reactions of enols, enolates, and enamines with active selenium(II) electrophiles formed during syn eliminations have also given unwanted products in some systems.[3a,5] Alkyl selenoxide eliminations, however, have generally been assumed to be free of byproducts, although low yields particularly for primary alkyl selenoxides have occasionally been reported in the published literature[4c,6] as well as in private communications to the authors. Modifications of the selenide reagent[6a] and elimination reaction conditions[3b] have been proposed to improve yields for such compounds.

The scattered results available suggested that selenoxide decompositions were complex. It is clear in retrospect that the long delay in recognition of the selenoxide syn elimination was a consequence of alternate reaction pathways available during the thermolysis.[7] The work described here was initiated to identify side reactions which may be occurring, and to gather product and kinetic data which will serve as a guide to optimizing reaction conditions for synthetic applications of the syn elimination.

Thermolysis of 2,2-Dimethyl-2,3-dihydrobenzo[*b*]-selenophene Oxide (1). The selenoxide is obtained by ozonization of 2,2-dimethyl-2,3-dihydrobenzo[*b*]selenophene in CH_2Cl_2, $CHCl_3$, or CF_2HCl at −78 to −60 °C. NMR spectra of the selenoxide can be obtained if taken rapidly at ambient probe temperature or more leisurely at sub-zero probe temperatures. Complete decomposition takes a few hours in organic solvents at room temperature. In the ^1H NMR spectrum of the ozonization solutions are observed two methyl singlets assigned to the diastereotopic *gem*-dimethyl group and an AB quartet corresponding to the benzylic hydrogens. An IR absorption assigned to the seleninyl $\nu_{Se=O}$ stretch[8] can be observed. Undecomposed solutions of **1** when treated with aqueous potassium iodide are reduced to the starting selenide. Although **1** does not lend itself to mass analysis, the above physical and spectral parameters satisfactorily characterize the compound.

If **1** is allowed to decompose completely, preparative TLC affords an ~4:1 mixture of isomeric alcohols in 77% combined yield which were assigned structures **2** (major) and **3** (minor) (Scheme I) on the basis of their NMR spectra and mass spectral analysis. The *p*-nitrobenzoate of **2** was isolated and successfully analyzed for C and H. The ^1H NMR spectrum of **2** in benzene-d_6 shows two AB quartets corresponding to the benzylic (δ 2.70, 2.96; J_{AB} = 15.2 Hz) and hydroxymethyl protons (δ 3.29, 3.25; J_{AB} = 11.0 Hz). Assignments are based on the magnitude of the benzylic coupling constant typical of indane structures[9] and the ~1 ppm downfield shift of the hydroxymethyl protons in going to the *p*-nitrobenzoate of **2**.

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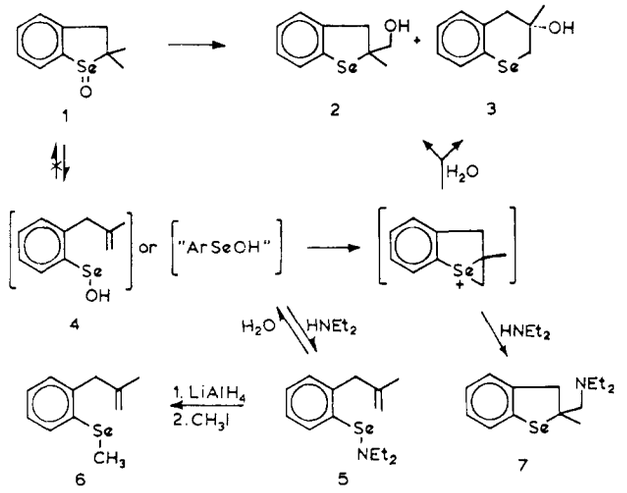
Scheme I



Spectral assignments for **3** are less secure, though they are tentatively assigned on the basis of the magnitude of J_{gem} characteristic of chroman compounds:[10] benzylic protons (δ 2.16 and 2.36; J_{AB} = 15.5 Hz) and methylene protons α to selenium (δ 2.47 and 2.65; J_{AB} = 11.0 Hz) in benzene-d_6. In $CDCl_3$ the hydroxymethyl protons of **2** and benzylic protons of **3** appear as apparent singlets. Selenium-77 (7.6% abundance) satellites (J_{SeCCH} = 12 Hz) observed for the methyl singlet of **2** and absent from that of the minor isomer serve to further differentiate the isomers and establish the structure of **2**.

Decomposing the selenoxide in the presence of triethylamine or acetic acid in methylene chloride or hydrochloric acid or sodium carbonate in aqueous solution does not significantly alter the product ratio; the major isomer always dominates in the range of 80–90%.

The thermal transformations of **1** are probably initiated by selenoxide syn elimination to selenenic acid **4**. To confirm the existence of ring-opened species along the reaction pathway to the alcohols, the selenoxide was decomposed in the presence of dialkylamines. Previous work has shown that selenenamides are isolable, though easily hydrolyzable compounds, and that they are formed when selenoxide syn eliminations are buffered with dialkylamines (eq 1).[5,11]

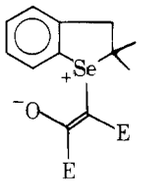
$$R'SeOH + HNR_2 \rightleftharpoons R'SeNR_2 + H_2O \qquad (1)$$

When **1** is decomposed in the presence of excess diethylamine, proton and carbon NMR resonances assignable to selenenamide **5** are observed. Little of the alcohols **2** and **3** is formed. Particularly informative are the ^{13}C resonances for a terminal vinyl carbon and a CH_2N carbon 10 ppm downfield from that of diethylamine having selenium satellites (J_{SeNC} = ~10 Hz). Attempts to isolate **5** by evaporation of solvent and excess diethylamine resulted in the formation of alcohols **2** and **3** apparently by forcing the equilibrium in eq 1 to revert in favor of selenenic acid leading to the alcohols **2** and **3**. Other results[5] had suggested that the diisopropylselenenamide might not be so labile; however, when a large excess of diisopropylamine is present during the decomposition of **1** only the alcohols can be observed, suggesting that the forward reaction in eq 1 does not successfully compete with the rearrangement of **4** to the alcohols when sterically bulky amines are used.

To obtain more concrete evidence for the selenenamide, a solution of **5** in diethylamine–ether was cleaved with excess lithium aluminum hydride at 0 °C and then treated with iodomethane. On workup a compound was isolated by TLC in 60% yield. Vinyl resonances (δ 4.60, 4.86) and a methyl singlet (δ 2.28) with selenium satellites (J_{SeCH} = 12.0 Hz) are observed in the ^1H NMR spectrum. The ^1H NMR and analytic data required the aryl methyl selenide **6**.

If a solution of **5** in diethylamine stands for a day at room temperature, the vinyl resonances in the ^1H NMR spectrum disappear and a complex mixture of products is formed from which can be isolated in 17% yield a compound with ^1H NMR and mass spectra consistent with structure **7**. Observable quantities of the ring-expanded diethylamino adduct corresponding to **3** are not formed, but the alcohols **2** and **3** are isolated in 18% yield in a 4:1 ratio.

The chemistry described above provided an opportunity to test the reversibility of the selenoxide syn elimination. It is reasonable to anticipate that selenenic acids react with olefins, since sulfoxide syn eliminations have been shown to be highly reversible both intra- and intermolecularly.[12] When selenoxide **1** was decomposed under different conditions in the presence of excess D_2O, *no* deuterium incorporation in either of the products **2** and **3** could be detected. Attempts to trap the selenenic acid **4** in an intermolecular reaction by thermolysis of **1** in the presence of dimethyl acetylene dicarboxylate (a process with much precedent in sulfur chemistry[12a,b,c]) led instead to the formation of the ylide **8** by direct



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reaction of **1** with the acetylene. Methyl phenyl selenoxide forms the analogous ylide. Similar reactions have been observed under more vigorous conditions for sulfoxides[13] and phosphine imides.[14]

The evidence presented points out several departures of the behavior of selenoxide syn elimination products from that of sulfoxide. In contrast with the observed behavior of sulfenic acid intermediates, the selenenic acid does not revert to selenoixde but instead is attacked by olefin without activation by external electrophilic agents such as acetic anhydride or protic acid necessary for similar reactions of sulfur compounds. Olefin may attack the selenenic acid directly to give an episelenonium ion. An alternative electrophilic selenium species is the selenenic acid anhydride (or protonated form thereof), a proposed intermediate along the disproportionation pathway of selenenic acids.[15] The anhydride may take either of the forms pictured (the selenolseleninate is precedented by the known thiolsulfinate, an established intermediate along the disproportionation pathway of sulfenic acids[12a,f,18]) as either provides the identical suitable leaving group, the selenenate anion $RSeO^-$, for displacement by olefin. For simplicity, the active electrophile will hereafter be referred to as "ArSeOH".

RSe(=O)SeR or RSeOSeR

Sulfenic acid anhydrides, thiolsulfinates, though they do not undergo direct nucleophilic attack by π systems are attacked at sulfenyl sulfur by alkyl mercaptide ions.[19]

Scheme I is a representation and interpretation of the observed results. Apparently the selenenic acid reacts further more rapidly than it can revert to selenoxide; "ArSeOH" is intramolecularly attacked by olefin to form the episelenonium ion more rapidly than it can continue along the disproportionation pathway to diselenide and seleninic acid.[15] Diethylamine reacts with "ArSeOH" faster than olefin capture. In either case the selenenamide must be in equilibrium with the active species in order to gain access to the episelenonium ion. Water can attack the episelenonium ion at the secondary (to

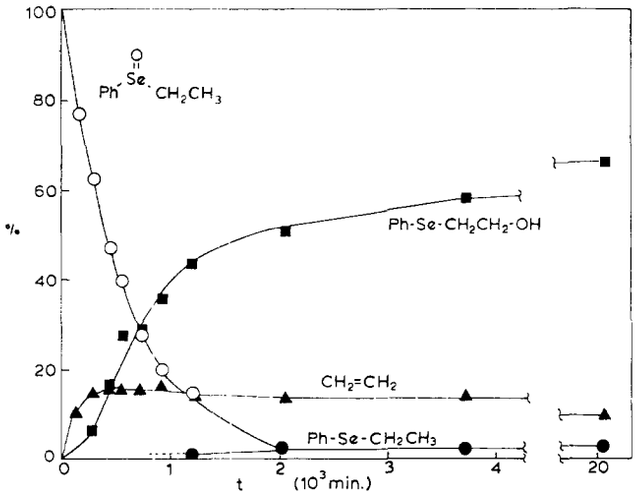


Figure 1. Decomposition of ethyl phenyl selenoxide (0.4 M) in $CDCl_3$ at 38 °C: ○ ethyl phenyl selenoxide; ● ethyl phenyl selenide; ■ β-hydroxyethyl phenyl selenide; ▲ ethylene *in solution* (a large fraction of the ethylene is in the gas phase).

give **2**) or quaternary carbon (**3**). When present, diethylamine competes with water by attack at the less hindered secondary site to give **7**.

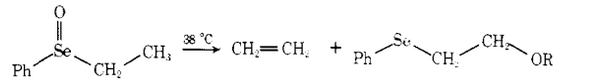
Thermolysis of Alkyl Phenyl Selenoxides. The facile intramolecular selenenic acid olefin addition described above raised the question whether such reactions also occur intermolecularly. When a solution of ethyl phenyl selenoxide in $CDCl_3$ was heated at 38 °C, slow decomposition ($t_{1/2}$ = 360 min) occurred to give ethylene and a second product which was identified as β-hydroxyethyl phenyl selenide (Table I).[20] Depending on reaction conditions, the latter product amounts to 50–85% of the product.[19] Figure 1 shows product composition as a function of time for this reaction. Note that the formation of the β-hydroxy selenide does not proceed to completion even after long reaction times. Other alkyl selenoxides behave in a similar fashion. The formation of β-hydroxyethyl phenyl selenide is completely suppressed by the addition of alkyl amines, but is only slightly affected by pyridine. The intermolecular electrophilic addition is thus more easily prevented than the intramolecular case, since the latter is unaffected by either tertiary or hindered secondary amines.

Additional experiments with 2-phenylpropyl phenyl selenoxide (**9**) led to the results reported in Table II. As observed for the ethyl selenoxide, most or all of the olefin presumably formed by syn elimination reacts with a selenium(II) electrophile to give β-hydroxy selenide **10** *unless base is present.*[22]

Solvent Effects. Protic solvents exert a profound effect on both product composition and rate of the syn elimination. For example, ethyl phenyl selenoxide gives 2-acetoxyethyl phenyl selenide as essentially the only product when as little as 1.5 equiv of acetic acid is added to the $CDCl_3$ solution, and the rate of elimination slows down by approximately a factor of 5! In pure methanol, selenoxide **9** eliminates only one-tenth as rapidly as in $CDCl_3$ solution, and no olefin (**11**) is formed, only the addition product **10** (R = CH_3). In acetic acid the rate is <1% that in $CDCl_3$. The solvent effect on rate is probably a consequence of the powerful hydrogen-bonding properties of selenoxides. Some disruption of the solvation may be necessary to achieve the syn elimination transition state.

Redox Equilibria Involving Selenenic Acids. The selenium species that reacts with olefin is probably selenenic acid or some derivative ("PhSeOH").[15] An important observation was that the normal disproportionation products of benzeneselenenic acid (eq 2)[23] react with olefins to give β-hydroxy selenides (eq 3) at rates comparable to syn elimination rates. The reaction does not go to completion when olefin, $PhSeO_2H$, and Ph_2Se_2 are used in a stoichiometric ratio (3:1:1). A portion of the Ph_2Se_2 remains, suggesting that some process is causing reduction of $PhSeO_2H$.[24,25] This was also observed during syn elimination experiments (Figure 1).

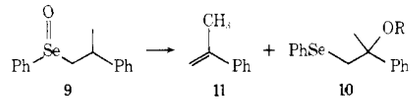
Table I. Product Data for Syn Elimination of Ethyl Phenyl Selenoxide



Solvent	Product ratio[a]
$CDCl_3$	53:47 (R = H)[b]
$CDCl_3$ + 1.5 equiv of pyridine	70:30
$CDCl_3$ + 1.5 equiv of NMe_3 or $HNMe_2$	100:0
$CDCl_3$ + 1.5 equiv of CH_3CO_2H	0:100 (R = CH_3CO_2)

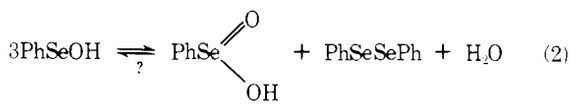
[a] At 80% reaction. [b] Approximately 5% of ethyl phenyl selenide was formed in this run only.

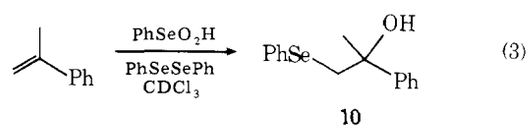
Table II. Rate and Product Data for Syn Elimination of 2-Phenylpropyl Phenyl Selenoxide (9)



Solvent	k_{rel} ($t_{1/2}$, min)	Product ratio (11/10)[a]
$CDCl_3$	1.0[b]	40:60[d]
$CDCl_3$ + 1.5 equiv of $HNMe_2$	1.0[c]	100:0
CD_3OD	0.13[b]	0:100[e]
CD_3OD + 1.5 equiv of $HNMe_2$	0.1	100:0
CD_3CO_2D	<0.01	0:100[f]

[a] At 80% reaction. [b] The reaction did not follow good first-order kinetics (inhibition by products). [c] First-order rate constant: $k = 4.0 \times 10^{-4}$ s^{-1} at 38 °C. [d] Approximately 5% of selenide was formed. [e] R = CD_3O. [f] R = CD_3CO_2.





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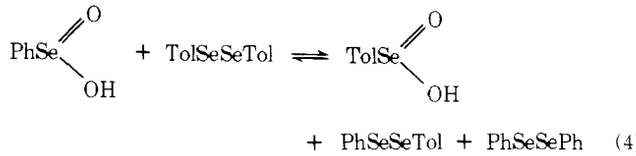
Since neither $PhSeO_2H$ nor PhSeSePh alone in $CDCl_3$ give β-hydroxy selenides rapidly in the presence of olefins,[28] this observation strongly suggests that the disproportionation of eq 2 is reversible, and that the reverse process provides the active electrophile. The occurrence of such a comproportionation[29] is experimentally supported: diselenide and seleninic acid in $CDCl_3$ exchange oxidation states (eq 4) in an acid-catalyzed process more rapidly than the addition of eq 3. This redox reaction can be most reasonably interpreted as proceeding through PhSeOH or a related symmetric species such as PhSeOSePh.



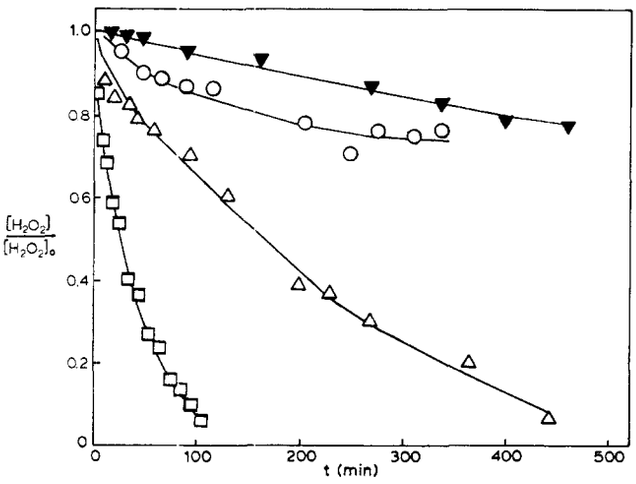
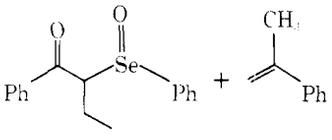


Figure 2. Decomposition of hydrogen peroxide (0.18 M) at 38 °C catalyzed by methyl aryl selenoxides (0.018 M): ▼ phenyl methyl selenoxide in 90% THF/10% H_2O–H_2O_2; ○ methyl 2-nitrophenyl selenoxide in 90% CH_3OH/10% H_2O–H_2O_2; ▽ methyl 3-trifluoromethylphenyl selenoxide in 90% CH_3OH; □ methyl phenyl selenoxide in 90% CH_3OH. Benzeneseleninic acid ($PhSeO_2H$) caused <5% decomposition after 400 min in 90% methanol.

That a comproportionation (eq 2) is the source of most of the selenium electrophile, rather than PhSeOH adding directly to the olefin as it is formed, is demonstrated by the following experiment: syn elimination of selenoxide **12** in $CDCl_3$ (complete in seconds at 38 °C) in the presence of 2-phenylpropene leads to enone, the normal disproportionation products, and only 10% of the hydroxy selenide **10.**



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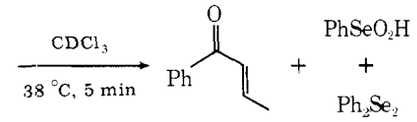
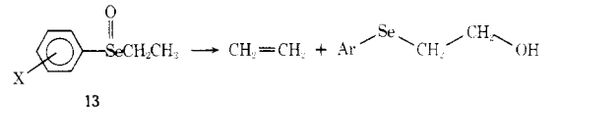


Hori and Sharpless[30] have developed a synthetically viable procedure using the acid-catalyzed comproportionation of $PhSeO_2H/Ph_2Se_2$ for the conversion of olefins to β-hydroxy selenides and hence to allyl alcohols by selenoxide syn elimination. High regioselectivity in favor of the tertiary alcohol is observed when a trisubstituted olefin is used.

Side Reactions during Selenoxide Syn Eliminations. The above observations clearly show that "PhSeOH"–olefin reactions are likely to occur during selenoxide syn eliminations if the olefin formed is not deactivated toward electrophilic addition. We feel that low or erratic yields sometimes observed are a consequence of such reactions, and that high yields can routinely be achieved by thermolysis of the selenoxide in the presence of an amine. Side reactions involving "PhSeOH" have been detected during syn elimination of some α-phenylseleno ketones.[3a] These are also prevented by the presence of an unhindered secondary amine which converts "PhSeOH" to $PhSeNR_2$.

Hydrogen peroxide has frequently been used for the conversion of selenides to selenoxides and hence to olefins by syn elimination.[3-6] Excess H_2O_2 is usually used, resulting in a convenient workup procedure since Ph_2Se_2 is rapidly oxidized to $PhSeO_2H$, which is easily removed. This should also, in principle, prevent the formation of β-hydroxy selenides. We were thus quite surprised to find that treatment of 2-phenylpropyl phenyl selenide under typical synthetic oxidation conditions (10 equiv of H_2O_2) led to the formation of mixtures of products containing a large amount of the β-hydroxy selenide **10.** A control experiment showed that $PhSeO_2H$ in the presence of 2-phenylpropene gave only 8% of **10.** The explanation for these observations is that hydrogen peroxide is catalytically decomposed to oxygen by selenoxides.[31] Figure 2 illustrates that H_2O_2 is rapidly destroyed in aqueous methanol in the presence of a catalytic amount (10%) of methyl phenyl selenoxide ($PhSeO_2H$ does not destroy H_2O_2). The decomposition is much slower in tetrahydrofuran. Primary selenoxides thus may cause destruction of even a large excess of H_2O_2 before syn elimination is complete, and "PhSeOH" readdition can occur. To achieve optimum yields by selenoxide syn elimination it is thus desirable to either ensure the presence of excess oxidant throughout the elimination, or to form selenoxide at low temperature and carry out the elimination with amine present as a separate step. These precautions are less important when selenoxide elimination leads to olefins inductively or conjugatively deactivated toward electrophilic attack by the presence of electron-withdrawing substituent (i.e., α,β-unsaturated carbonyl compounds and nitriles, vinyl halides), or when syn elimination is very rapid. The rate data reported below allow estimation of syn elimination rates for typical selenoxides so that experimental conditions can be properly chosen.

Table III. Products and Rate Data for Selenoxide Syn Elimination of Ethyl Aryl Selenoxides (38 °C in $CDCl_3$)



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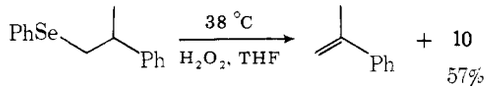
	X	Registry no.	k_{rel} ($t_{1/2}$, min)[a]	Product ratio[b]
13a	H	65275-41-4	1.0 (360)	53:47
b	4-CH_3	65275-42-5	0.63 (550)	
c	3-CF_3	65275-43-6	1.7 (217)	75:25
d	2-NO_2-4-CH_3	65275-44-7	24 (18)	97:3
e	4-NO_2	65275-45-8	4.4 (80)	*c*
f	4-OCH_3	65275-46-9	0.40 (890)	

[a] Rates were measured at 38 °C in $CDCl_3$ in the presence of 1.5 equiv of dimethylamine. [b] At 80% reaction in $CDCl_3$, no amine added, ethylene/β-hydroxyethyl selenide. [c] After 73% of selenoxide had disappeared, 50% of product appeared as ethyl 4-nitrophenyl selenide (reduction).



Effects of Substituents on the Aryl Ring. Improved yields of olefins have been reported by Sharpless and Young for aryl alkyl selenoxides bearing electron-withdrawing substituents on the aromatic ring[6a] and considerable use has been made of this effect by Grieco in several natural products syntheses.[6b,c] In principle this could be a consequence of faster elimination rates, less tendency toward "ArSeOH" addition to olefin products, reduced rates of comproportionation, reduced rates of H_2O_2 destruction, or some combination of these. All of these factors have been briefly studied, and results for several systems are presented in Table III.

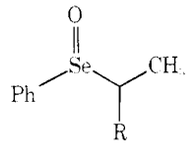
The rate constants in Table III were measured in the presence of a small amount of amine, since otherwise the elimination does not always follow good first-order kinetics because protic materials generated during the reaction ($ArSeO_2H$, β-hydroxy selenide) slow it down. The substituent effects for elimination of ethyl aryl selenoxides ($\rho = 0.8$) are

quite similar to those observed for elimination of propyl aryl sulfoxides (ρ = 0.5 at 180 °C in diphenyl ether).[32]

The *o*-nitro substitution in the aryl selenide provides a dramatic increase in the elimination rate, as well as a minimum (although not complete absence) of "ArSeOH" addition products. The use of *o*-nitrophenyl selenides is clearly justified, particularly for difficult systems of the isobutyl type (primary selenide, tertiary hydrogen) where syn elimination is very slow.

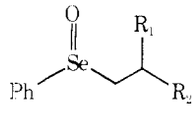
The destruction of hydrogen peroxide by methyl *o*-nitrophenyl selenoxide also appears to be less efficient than in the unsubstituted system (Figure 2).

Selenoxide Syn Elimination Rates. The rates of elimination of a series of alkyl phenyl selenoxides were measured in $CDCl_3$ at 38 °C under conditions such that β-hydroxy selenide formation is suppressed (1.5 equiv of $(CH_3)_2NH$ added). As expected from behavior of sulfoxides,[32b] α-alkyl substituents accelerate elimination, whereas β-alkyl groups retard the rate. Phenyl and chloro substitution causes an acceleration of the elimination, particularly in the α position.



14

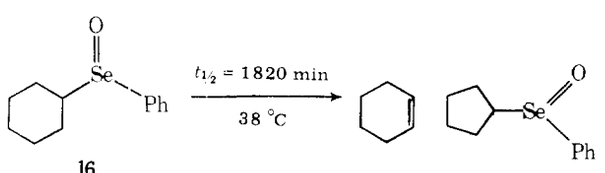
	R	k_{rel} ($t_{1/2}$, min)
13a	H	1.0 (360)
14a	CH_3	9.5 (38)
b	CH_2OCH_3	10 (35)
c	Ph	>360 (<1)
d	Cl	12 (31)



15

	R_1	R_2	k_{rel} ($t_{1/2}$, min)
13a	H	H	1.0 (360)
15a	H	CH_3	0.5 (675)
b	CH_3	CH_3	0.18 (1800)
c	H	Ph	37 (9)
d (9)	CH_3	Ph	4.4 (72)
e	H	Cl	1.4 (280)
f	H	OCH_3	~0.07 (~70 h)

Cyclohexyl (**16**) and cyclopentyl (**17**) phenyl selenoxides are the only cyclic systems we have examined. As expected from the qualitative results in the published literature, the rate of elimination of **16** is unusually slow compared to isopropyl phenyl selenoxide (k_{16}/k_{14a} = 1/48). This means that cyclohexyl eliminations will be very prone to side reactions, an observation already made in connection with the formation of cyclohexenones by oxidation of 2-phenylselenocyclohexanones.[3a] Special care must be taken to use proper reaction conditions for elimination of cyclohexyl selenoxides. The more favorable dihedral angles in the cyclopentyl compound **17** results in an unusually fast syn elimination rate.



16 17, $t_{1/2}$ <5 min

β-Heteroatom substituents are of great interest since the high regioselectivity of elimination for β-hydroxy (as well as β-OCH_3 and β-OAc) selenides to give allyl alcohols rather than enols, first reported by Sharpless and co-workers,[16,33] has resulted in several important applications of selenium reagents.[33,3b,34] β-Methoxyethyl selenoxide (**15f**), as expected, eliminates extremely slowly. When, as in **14b** the selenoxide can eliminate toward or away from an oxygen function, only the allyl ether is formed at a rate similar to the elimination of **14a.** This demonstrates that the directive effect of hydroxy, alkoxy, and acetoxy groups is *not* a consequence of accelerated elimination away from the substituent, but rather a result of retarded elimination toward the substituent. We found also that elimination toward chlorine is slightly accelerated, a result consistent with the observation that a β-chloro selenoxide eliminates to give comparable amounts of vinyl and allyl chlorides.[16]

Conclusions

The following factors should be considered when performing selenoxide syn eliminations.

1. Areneselenenic acids generated during selenoxide syn elimination are in equilibrium with diaryl diselenide and areneseleninic acid. Under neutral or acidic conditions they react with olefins to yield β-hydroxy selenides. This readdition is inhibited in a basic medium.

2. Protic solvents such as water, methanol, and acetic acid should be avoided for the following reasons: they greatly slow down syn elimination rates, and they promote both solvolytic heterolysis of the C–Se bond (particularly when unusually stable carbonium ions can be formed)[35] and "PhSeOH" addition to olefins (Table II).

3. Hydrogen peroxide is destroyed catalytically by selenoxides under some conditions. When used as an oxidant for syn elimination care must be taken to ensure that excess oxidant is present until syn elimination is complete. Otherwise "PhSeOH" readdition may occur.

4. The use of *o*-nitrophenyl alkyl selenoxides results in a faster rate of elimination as well as reduced tendency for ArSeOH addition to olefinic products.

5. When tetra-, tri-, and even some disubstituted olefins are being formed, hydrogen peroxide together with seleninic acids can lead to epoxide formation, presumably via areneperseleninic acid.[29,36] The epoxidation is particularly rapid when the aryl group bears electron-withdrawing substituents.

6. When peracids are used to oxidize selenoxides, the presence of amine during the syn elimination step is obligatory since carboxylic acids greatly retard syn elimination and promote electrophilic olefin addition (Table I).

7. Most of the difficulties mentioned above are not encountered when the following procedure is used: (1) oxidation to selenoxide at low temperature (*m*-CPBA in CH_2Cl_2 or THF, ozone in CH_2Cl_2, or even H_2O_2 for slow to eliminate selenoxides); (2) addition of 2 equiv of amine ($HNiPr_2$, NEt_3, $HNEt_2$, etc.); and (3) thermolysis of the basic selenoxide solution by addition to refluxing hexane or carbon tetrachloride. Under these conditions no selenenic acid additions, epoxidations, or selenoxide reductions occur. The nonpolar medium also suppresses formation of carbonium ions by C–Se bond solvolysis. Even β,β-disubstituted alkyl phenyl selenoxides usually give good yields of olefins under these conditions, and use of the *o*-nitrophenyl selenides (which are more expensive, less easily prepared, and less easily oxidized to selenoxides) is not necessary. It should be emphasized that side reactions do not occur in all systems and simple oxidation procedures frequently give good yields of olefins. When problems are encountered, however, the above procedure will frequently solve them.

Table IV. Rate Constants for Selenoxide Syn Eliminations and NMR Spectral Data for Selenides and Selenoxides

Compd	$k \times 10^4$[a]	Registry no. of selenide	NMR chemical shifts[b] Selenide α-H	Selenide β-H	Selenide Other	Selenoxide α-H	Selenoxide β-H	Selenoxide Other
13a	0.32	17774-38-8	2.93 (q)*	1.39 (t)*		2.89 (m)	1.28 (t)	
b	0.20	37773-43-6	2.88 (q)	1.40 (t)		2.85 (m)	1.25 (t)	
c	0.54	37773-36-7	2.94 (q)*	1.45 (t)*		2.90 (dq), 3.03 (dq)	1.30 (t)	
d	7.7	65275-57-2	2.95 (q)	1.48 (t)		3.00 (m)	1.27 (t)	
e	1.4	65275-58-3	3.00 (q)	1.43 (t)		2.92 (m)	1.27 (t)	
f	0.12	37773-41-4	3.12 (q)	1.36 (t)		2.84 (m)	1.25 (t)	
14a	3.0	22233-89-2	3.45 (sept)	1.43 (d)		3.08 (sept)	1.30 (dd)	
b	3.3	65275-34-5	3.5 (m)	3.5 (m), 1.42 (d)	3.35 (s)	3.0–4.0 (m)	3.0–4.0 (m), 1.14 (dd)	3.44 (s)
c	>150	39192-26-2	4.44 (q)	1.73 (d)			1.75 (d) 1.55 (d)	
d	3.7	63017-68-5	5.48 (q)	1.97 (d)		4.85 (q), 4.66 (q)	1.89 (d), 1.52 (d)	
16[d]	0.062	22233-91-6	3.30 (m)	1.5–2.1 (m)	1.3–1.8 (m)	2.9 (m)	1.3–1.9 (m)	1.3–1.9 (m)
17[d]	~20	65275-35-6	3.60 (m)	1.6–2.2 (m)				
15a	0.17	22351-63-9	2.90 (t)	1.72 (hex)	1.00 (t)	2.84 (t)	1.67 (m)	1.04 (t)
b	0.064	22233-92-7	2.92 (d)	1.87 (m)	1.04 (d)	2.88 (dd)	2.24 (m)	1.10 (dd)
c	~13	65275-36-7	2.95 (m)	2.95 (m)		3.11 (m)	3.11 (m)	
d ($CDCl_3$)	1.3	65275-37-8	3.0 (m)*	3.0 (m)*	1.35 (d)	3.0 (m)	3.49 (m)	1.43 (t)
(CD_3OD)	0.21					3.25 (m)	3.25 (m)	1.43 (dd)
(CD_3CO_2D)[c]	~0.02					3.5 (m)	3.5 (m)	1.43 (d)
e	0.41	50630-24-5	3.10 (AA'BB')*	3.65 (AA'BB')*		3.28 (dt)	3.60 (dt), 4.08 (dt)	
f	~0.03	65275-38-9	3.00 (t)*	3.55 (t)*	3.28 (s)*	3.08 (t)	3.62 (dt), 3.90 (dt)	3.40 (s)

[a] Measured in $CDCl_3$ at 38 °C (unless noted otherwise), 0.2 M selenoxide, 0.3 M Me_2NH. Error limits for the rate constants are ±5 to ±15% unless they are indicated as approximate values, in which case they are ±50%. [b] Measured in $CDCl_3$ in ppm (δ) from Me_4Si except for selenide chemical shifts identified by an asterisk, which were measured in CCl_4. [c] No Me_2NH was added in this run. [d] Registry no.: **16**, 65275-39-0; **17**, 65275-40-3.

Experimental Section

Nuclear magnetic resonance spectra were obtained on a JEOL MH-100 and Varian XL-100 spectrometers and mass spectra were obtained on an AEIMS-902 spectrometer at an ionizing voltage of 70 eV. Ozonizations were carried out using a Welsbach ozonator. Preparative thin layer chromatography was carried out using Merck PF-254 silica gel. Elemental analyses were performed by Spang Microanalytical Laboratories or by Galbraith Laboratories, Inc.

Diphenyl diselenide,[3a] 3,3′-bis(trifluoromethyl)diphenyl diselenide,[3a] benzeneselenenyl chloride,[3a] 4-methyl-2-nitrophenyl selenocyanate,[37] and 4-nitrophenyl selenocyanate[6a] were prepared by literature procedures. Alkyl aryl selenides (except for selenide precursors for **14d** and **15e**) were prepared by reaction of $ArSe^-$ with the appropriate methanesulfonate (for **14b** and **15f**) or halide according to the model procedures below. NMR spectra of selenides and selenoxides are reported in Table IV.

CAUTION. Selenium compounds are toxic and should be handled with due care.

2-Phenylpropyl Phenyl Selenide. To a 250-mL three-neck round-bottom flask fitted with a reflux condenser, addition funnel, and a thermometer were added diphenyl diselenide (8.58 g, 22.5 mmol) in 60 mL of ethanol, sodium formaldehyde sulfoxylate (4.53 g, 24.1 mmol), and sodium hydroxide (3 g, 75 mmol) in 25 mL of water. The system was purged with nitrogen and warmed to 50 °C under N_2 for a 30-min period. 1-Bromo-2-phenylpropane (10.45 g, 7.94 mL, 55 mmol) was added to the reaction mixture. After stirring for 16.5 h, 100 mL of 10% HCl was added and the mixture was extracted with hexane (3 × 60 mL). The combined organic extracts were washed with 40 mL of saturated $NaHCO_3$ and 40 mL of NaCl solution. The crude product was distilled [Kugelrohr, 97 °C (0.032 mm)] to give 14.85 g (98.2%) of the selenide as a clear oil.

Anal. Calcd for $C_{15}H_{16}Se$: C, 65.45; H, 5.86. Found: C, 65.68; H, 5.94.

Ethyl 4-Methyl-2-nitrophenyl Selenide. 4-Methyl-2-nitrophenyl selenocyanate (1.69 g, 7.0 mmol) and 30 mL of absolute EtOH were placed in a flask equipped with a condenser and flushed with nitrogen. $NaBH_4$ (0.348 g, 9.0 mmol) was added slowly through the top of the condenser. The solution became deep red. After an additional 15 min, ethyl bromide (0.530 mL, 7.1 mmol) was added and the solution was stirred at room temperature for 5 h and poured into 30 mL of 1.2 N HCl and 40 mL of 1:1 ether–hexane. The organic layer was washed with dilute HCl, 7% $NaHCO_3$ solution, and saturated NaCl solution and filtered through Na_2SO_4, and the solvent was removed to give a yellow solid. Recrystallization from ether–hexane gave fine gold needles (1.18 g, 69%): mp 49.5–50 °C; MS *m/e* 244.9955 (M^+) (calcd for $C_9H_{11}NO_2Se$: 244.9950).

Anal. Calcd: C, 44.27; H, 4.54. Found: C, 44.05; H, 4.64.

1-Methoxy-2-phenylselenopropane. 1-Methoxy-2-propanol was converted to the mesylate according to the procedure of Crossland and Servis:[38] NMR ($CDCl_3$) δ 1.28 (d, J = 6 Hz, 3 H), 3.08 (s, 3 H), 3.44 (s, 3 H), 3.50 (d, J = 6 Hz, 2 H), 4.85 (m, 1 H).

$NaBH_4$ (~0.6 g) was added slowly to a suspension of 1.35 g (4.33 mmol) of diphenyl diselenide in 20 mL of absolute EtOH under nitrogen until the solution became colorless. After cooling to 25 °C, the mesylate from 0.895 g (9.94 mmol) of 1-methoxy-2-propanol in 5 mL of EtOH was added dropwise. After stirring overnight at 25 °C the suspension was poured into 50 mL of 1.2 N HCl and 50 mL of 1:1 ether–pentane. Workup and distillation gave 1.26 g (63%) of selenide: MS *m/e* 230.0210 (M^+) (calcd for $C_{10}H_{14}OSe$: 230.0217).

Anal. Calcd: C, 52.41; H, 6.16. Found: C, 52.59; H, 6.24.

2-Chloroethyl Phenyl Selenide.[39] Ethylene was passed into 75 mL of CH_2Cl_2 in a flask fitted with a dry ice–EtOH condenser. A solution of 2.03 g of benzeneselenenyl chloride (10.6 mmol) in 60 mL of CH_2Cl_2 was added slowly by cannula with the cannula tip in the ethylene solution. Ethylene was slowly added for 1 h after addition was complete and then the solvent was removed to give an oil (2.31 g) 92% pure by NMR. Distillation [60 °C (0.05 mm)] gave 1.80 g of product: MS *m/e* 219.9558 (M^+) (calcd for C_8H_9ClSe: 219.9555).

1-Chloroethyl Phenyl Selenide. Diphenyl diselenide (3.12 g, 10.0 mmol) was stirred in 40 mL of CH_2Cl_2 and 50 mL of concentrated HCl under N_2. Zn dust (5.1 g, 78 mmol) was added slowly until the solution became colorless. The two layers were separated and the organic layer was washed with 10 mL of concentrated HCl under N_2, after which it was added slowly to distilled acetaldehyde (1.8 mL, 41 mmol) in 40 mL of CH_2Cl_2 and 40 mL of concentrated HCl at 50 °C under N_2. The mixture was stirred for 8 h and the layers were then separated. The CH_2Cl_2 solution was washed twice with 40 mL of 7% $NaHCO_3$ and then saturated NaCl and filtered through anhydrous Na_2SO_4, and the solvent was removed. Distillation [56 °C (0.1 mm)] gave 2.96 g (67%) of product: MS *m/e* 219.9558 (M^+) (calcd for C_8H_9ClSe: 219.9555).

2,3-Dihydro-2,2-dimethylbenzo[*b*]selenophene. The compound was prepared by an extension of the literature procedure for 2-methyldihydrobenzo[*b*]selenophene[40] from methallyl phenyl selenide. Diphenyl diselenide (31.2 g, 0.1 mol) was slurried under N_2 at 55 °C in 300 mL of EtOH with 15.4 g (0.1 mol) of Rongalite ($CH_2OHOSONa{\cdot}2H_2O$, sodium formaldehyde sulfoxylate). A solution of 12 g of NaOH in 200 mL of absolute ethanol was added with an addition funnel and the resulting mixture was stirred until the yellow color of diphenyl diselenide had disappeared. Methallyl chloride (19.9 g, 0.22 mol) was added and the mixture was refluxed for 2 h. The reaction was diluted with 200 mL of water and extracted with four portions of 75 mL of pentane. The pentane layer was washed with 150 mL of 7% $NaHCO_3$ and 150 mL of saturated NaCl. After drying over Na_2SO_4 the product was fractionally distilled under vacuum to give 38.57 g (91%) of methallyl phenyl selenide, bp 80 °C (0.5 mm).

The methallyl phenyl selenide (29.0 g) was mixed with 70 g of freshly distilled quinoline and refluxed under an air-cooled condenser for 45 min while N_2 was bubbled through the mixture. (The mixture was purged with N_2 for 15 min prior to heating.) The cooled mixture was poured in 400 mL of ether and washed three times with 500 mL of 0.5 N HCl, 200 mL of 5 N HCl, and finally with water. The organic layer was filtered through a pad of Celite, washed with saturated NaCl, and dried over Na_2SO_4. Fractional distillation under vacuum gave 6.54 g (22.6%) of selenide: bp 64 °C (0.8 mm); NMR ($CDCl_3$) δ 1.67 (s, J_{SeH} = 11 Hz, 3 H), 3.12 (s, 2 H), 7.04 (m, 3 H), 7.24 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 30.6 (q, J_{SeC} = 13.7 Hz), 44.7 (s, J_{SeC} = 44.7 Hz), 54.0 (t, J_{SeC} = 3.1 Hz), 124.4 (d), 125.0 (d, J_{SeC} = 2.9 Hz), 125.9 (d, J_{SeC} = 12.3 Hz), 126.9 (d, J_{SeC} = 3.8 Hz), 142.2 (s), 138.0 (s, J_{SeC} = 100.0 Hz); MS *m/e* 212.0106 (calcd for $C_{10}H_{12}Se$: 212.0104). An analytical sample was prepared by GC with a 2.5-ft SE-30 column at 110 °C.

Anal. Calcd for $C_{10}H_{12}Se$: C, 56.88; H, 5.73. Found: C, 56.84; H, 5.69.

2,3-Dihydro-2,2-dimethylbenzo[*b*]selenophene 1-Oxide (1). Samples of this compound were prepared by ozonization of the selenide in various solvents at −60 to −78 °C. To prepare an IR sample, 211 mg (1 mmol) of selenide in 5 mL of $CHCl_3$ was ozonized at −60 °C to a blue color. Excess ozone was purged with a stream of N_2 and the sample was kept at 0 °C to avoid decomposition until the IR scan could be made: IR ($\nu_{Se=O}$) 810 cm^{-1}. After the sample was stored at room temperature overnight this IR absorption disappeared. NMR samples were prepared similarly using $CDCl_3$ or $CHClF_2$.

Decomposition of 1 in Organic Solvent under Neutral Conditions. Preparation of 2,3-Dihydro-2-(hydroxymethyl)-2-methylbenzo[*b*]selenophene (2) and 3-Hydroxy-3-methylselenochroman (3). When a CH_2Cl_2 solution of **1** (1 mmol in 5 mL) was allowed to completely decompose over several hours at room temperature and the resulting solution was evaporated to dryness and chromatographed by preparative TLC (silica gel, buffered with triethylamine; 50% ether–pentane), 174 mg of an 85:15 mixture (by NMR integration) of **2** and **3** was obtained (77% combined yield). By more careful chromatography (TLC on silica gel, 20% ether–pentane) using multiple elutions and by taking only part of the TLC band, relatively pure samples of **2** were obtained for derivatization (see below). Compound **2**: NMR (C_6D_6) δ 1.44 (s, J_{SeH} = 12.0 Hz, 3 H), 1.64 (br s, 1 H), 2.70, 2.96 (ABq, J = 15.2 Hz, 2 H), 3.29, 3.35 (ABq, J = 11.0 Hz, 2 H), 6.64 (m, 3 H), 6.83 (m, 1 H); MS *m/e* 228.0048 (calcd for $C_{10}H_{12}OSe$: 228.0053). Compound **3**: NMR (C_6D_6) δ 1.18 (s, 3 H), 1.2 (br, s, 1 H), 2.16, 2.32 (ABq, J = 15.5 Hz, 2 H), 2.47, 2.65 (ABq, J = 11.0 Hz, 2 H), 6.80 (m, 3 H), 7.15 (m, 1 H); MS *m/e* 228.0050 (calcd for $C_{10}H_{12}OSe$: 228.0053).

Derivatization of 2 *p*-Nitrobenzoate. A 170-mg sample of alcohol **2** was dissolved in 0.6 mL of pyridine and 100 mg of *p*-nitrobenzoyl chloride and the mixture was heated briefly to boiling. Water (2 mL) was added and the aqueous layer was decanted, leaving behind a yellow oil which was dissolved in 10 mL of ether. The ethereal solution was washed with 1 mL of saturated Na_2CO_3 and dried over Na_2SO_4. Evaporation of the solvents gave an oily residue which was recrystallized from 95% ethanol to give 138 mg (50%) of light yellow prisms: mp 80–81 °C; IR 1760 cm^{-1}; NMR ($CDCl_3$) δ 1.83 (s, 3 H), 3.26, 3.42 (ABq, J = 16 Hz, 2 H), 4.56 (s, 2 H), 7.1–7.4 (m, 4 H), 8.03, 8.25 (AA'BB', J = 8 Hz, 4 H).

Anal. Calcd for $C_{17}H_{15}NO_4Se$: C, 54.27; H, 4.02. Found: C, 54.26; H, 4.05.

Decomposition of 1 in Organic Solvent with Acid or Base Present. Fresh solutions of 0.25 mmol of **1** were prepared as above in 1 mL of chloroform or methylene chloride and acid or base was added to the solutions prior to decomposition. **Acid.** When 0.01 mL of acetic acid was added, a 63% combined yield of alcohols **2** and **3** was obtained in a ratio of 90:10 (NMR integration) on decomposition and isolation by TLC. **Base.** When 0.01 mL of triethylamine was added, an 80:20 ratio of **2** and **3** in 78% combined yield was obtained. Product ratios were determined by NMR integration.

Decomposition of 1 in Deuterium Oxide Solution with Acid or Base Present. Two solvent-free samples of **1** were prepared by ozonization of 0.25 mmol of the selenide in $CHClF_2$ and flash evaporation of the solvent (bp −40 °C) at 0 °C, and 0.01 N DCl or D_2O containing dissolved anhydrous Na_2CO_3 (10 mg in 1 mL) was added to each sample. Initially, colorless homogeneous solutions were obtained; however, on standing over several days light yellow droplets of product formed. After a week of standing the product alcohols were extracted into ether and the alcohols were purified by TLC. Analysis of the two samples for deuterium incorporation (any alcoholic deuterium was washed out in workup) by low electron volt and expanded-intensified mass spectra showed <5% deuterium incorporation for both the acid and base samples.

Formation of *N,N*-Diethyl-2-(2-methyl-2-propenyl)benzeneselenamide (5). A solution of 0.5 mmol of **1** in 0.5 mL of $CDCl_3$ was prepared by ozonization at −65 °C. After the excess ozone was removed in a stream of N_2, excess diethylamine (0.1 mL) was added and the solution was warmed to room temperature for a few hours. The progress of the reaction was monitored by ^1H NMR spectroscopy. When all the selenoxide **1** had decomposed as indicated by the disappearance of the *gem*-dimethyl resonances at δ 1.26 and 1.65 in the ^1H NMR spectrum, the spectrum showed **5** (vinyl resonances) and very little of alcohols **2** and **3** to be present: NMR ($CDCl_3$/$HNEt_2$, ~6:1) δ 1.13 (t, J = 7 Hz, 6 H), 1.69 (s, 3 H), 3.08 (q, J = 7 Hz, 4 H), 3.28 (s, 2 H), 4.59 (s, 1 H), 4.80 (s, 1 H), 7.1 (m, 3 H), 7.75 (m, 1 H). A carbon NMR spectrum of **5** was obtained on the same solution at −15 °C: δ 14.6 (q), 22.5 (q), 43.1 (t), 54.1 (t, J_{SeC} = 10 Hz), 112.7 (t), 125.8, 126.6, 128.1, 129.7 (doublets), 137.0, 137.2, 143.6 (singlets). When the excess diethylamine was removed by evacuation of a similarly prepared solution under oil pump vacuum, the vinyl resonances of **5** vanished and only resonances corresponding to alcohols **2** and **3** were observed.

Formation and Isolation of 2,3-Dihydro-2-(*N,N*-diethylaminomethyl)-2-methylbenzo[*b*]selenophene (7). A solution of selenenamide **5** prepared from 0.25 mmol of selenoxide **1** (from ozonization of 52 mg of selenide in $CHClF_2$ at −78 °C) and a fourfold excess of diethylamine was kept at room temperature for 1 day. The solution was chromatographed on silica gel (TLC) with 20% ether–pentane to give 12 mg (17%) of **7**, identified by ^1H NMR spectroscopy, along with 10 mg (18%) of alcohols **2** and **3**: NMR (C_6D_6) δ 0.88 (t, J = 7 Hz, 6 H), 1.61 (s, 3 H, J_{SeH} = 12.0 Hz), 2.47 (q, J = 7 Hz, 4 H), 2.68, 2.77 (ABq, J = 11.0 Hz, 2 H), 2.83, 3.24 (ABq, J = 15.5 Hz, 2 H), 7.0 (m, 3 H), 7.2 (m, 1 H). A sample of **7** suitable for mass spectral analysis was obtained by GC on a 20% SE-30 column: MS *m/e* 283.0846 (calcd for $C_{14}H_{21}NSe$: 283.0839).

Preparation of Methyl 2-(2′-Methylpropenyl)phenyl Selenide (6) from Selenenamide 5. Selenenamide **5**, prepared by ozonization of 211 mg (1 mmol) of selenide in 3 mL of ether followed by addition of 4 mL of diethylamine to the solution of **1** and 45 min of standing at room temperature, was added to a slurry of 100 mg of $LiAlH_4$ in 20 mL of ether at 0 °C. The mixture was stirred 10 min and 5 mL of methyl iodide was added. After 30 min the reaction was quenched with saturated NH_4Cl. The ether layer was decanted, washed with water, and dried over Na_2SO_4. Evaporation of the solvent and preparative TLC (silica gel, pentane) gave 135 mg (60%) of the aryl methyl selenide: NMR ($CDCl_3$) δ 1.76 (s, 3 H), 2.28 (s, 3 H, J_{SeH} = 12.0 Hz), 3.44 (s, 3 H), 7.16 (m, 3 H), 7.40 (m, 1 H); MS *m/e* 226.0258 (calcd for $C_{11}H_{14}Se$: 226.0261). An analytical sample was prepared by GC on a 20% SE-30 column.

Anal. Calcd for $C_{11}H_{14}Se$: C, 58.67; H, 6.27. Found: C, 58.68; H, 6.23.

Formation of a Selenonium Ylide from 1 and Dimethyl Acetylenedicarboxylate, Compound 8. To a solution of 1 mmol of **1** in 0.5 mL of $CDCl_3$ at 0 °C was added 0.123 mL (1 mmol) of dimethyl acetylenedicarboxylate. An immediate exothermic reaction ensued. After 15 min a ^1H NMR spectrum of the reaction showed that the selenoxide **1** had completely reacted and a single product had been formed. Preparative TLC (silica gel–methyl acetate or acetone) afforded a gummy yellow product (286 mg, 78%) identified as the selenonium ylide **8** on the basis of its NMR properties and IR data: NMR ($CDCl_3$) δ 1.62 (s, 3 H, J_{SeH} = 12.0 Hz), 1.71 (s, 3 H, J_{SeH} = 24.0 Hz), 3.55 (s, 3 H), 3.66 (s, 3 H), 3.17, 4.04 (ABq, J = 15.5 Hz, 2 H), 7.0 (m, 3 H), 7.25 (m, 1 H); IR ($CHCl_3$) 1745, 1680, 1570 cm^{-1}. Attempts to crystallize the product were unsuccessful. An analytical sample was prepared by careful preparative TLC (silica gel–acetone).

Anal. Calcd for $C_{16}H_{18}O_5Se$: C, 52.04; H, 4.91. Found: C, 52.13; H, 4.93.

Preparation of an Analogous Selenonium Ylide from Methyl Phenyl Selenoxide. Methyl phenyl selenoxide was prepared by

ozonization of 171 mg (1 mmol) of methyl phenyl selenide in 5 mL of CH_2Cl_2 at −78 °C. The excess ozone was removed in a stream of N_2. Dimethyl acetylenedicarboxylate (0.125 mL, 1 mmol) was added and the mixture was warmed to room temperature. Some exothermicity was observed as the temperature of the solution neared 0 °C. The solvent was evaporated and the residue was chromatographed, TLC on silica with 10% methanol–ether, to give 180 mg (55%) of the yellow, gummy ylide: NMR ($CDCl_3$) δ 3.21 (s, 3 H, J_{SeH} = 30.0 Hz), 3.68 (s, 3 H), 3.87 (s, 3 H), 7.5 (m, 3 H), 7.7 (m, 2 H); IR ($CHCl_3$) 1735, 1670, 1560 cm^{-1}. An analytical sample was prepared by careful TLC (silica gel–acetone): MS *m/e* 330.0000 (calcd for $C_{13}H_{14}O_5Se$: 330.0006).

Isolation of 2-Hydroxyethyl Phenyl Selenide from the Elimination of Ethyl Phenyl Selenoxide (13a). Ethyl phenyl selenide (0.287 g, 1.55 mmol) was ozonized in 4.5 mL of $CHCl_3$ at −60 °C. The selenoxide was warmed to 38 °C for 70 h in a sealed tube, after which it was poured into 10 mL of 7% $NaHCO_3$ solution and 10 mL of ether. The organic layer was washed with saturated NaCl solution and filtered through anhydrous Na_2SO_4 and the solvent was removed. Preparative TLC (1% NEt_3–10% ether–89% pentane), R_f 0.06, gave 1.57 g (50%) of 2-hydroxyethyl phenyl selenide: NMR (CCl_4) δ 7.4 (m, 2 H), 7.15 (m, 3 H), 3.65 (t, *J* = 7 Hz, 2 H), 3.32 (bs), 2.95 (t, *J* = 7 Hz, 2 H); MS *m/e* 201.9897 (M^+) (calcd for $C_8H_{10}OSe$: 201.9897). The dibromide was prepared by slow addition of bromine in CCl_4 to a solution of the selenide in CCl_4. The solvent was removed from the pale yellow precipitate. Recrystallization in EtOH gave a fine yellow crystalline solid, mp 117–119 °C (lit. mp[44] 113 °C).

2-Phenyl-1-phenylseleno-2-propanol (10). Diphenyl diselenide (0.219 g, 0.702 mmol) was stirred in 9 mL of absolute EtOH under nitrogen. $NaBH_4$ (0.067 g, 1.7 mmol) was added until the solution became colorless, after which α-methylstyrene oxide (0.190 g, 1.42 mmol) was added. The solution was stirred at room temperature for 0.5 h, refluxed for 1.5 h, and poured into 10 mL of 1.2 N HCl and 10 mL of ether. The ether layer was washed with 7% $NaHCO_3$ and saturated NaCl and filtered through anhydrous Na_2SO_4, and the solvent was removed. Preparative TLC (1% NEt_3–10% ether–89% pentane), R_f 0.2, gave 0.313 g (76%) of **10**: NMR ($CDCl_3$) δ 7.5–7.1 (m, 10 H), 3.56 (d, *J* = 12 Hz, 1 H), 3.30 (d, *J* = 12 Hz, 1 H), 2.8 (bs, 1 H), 1.60 (s, 3 H); IR (neat) 3460, 3060, 2980, 1580, 1480, 1440, 1062, 1022, 765, 738, 698 cm^{-1}; MS *m/e* 292.0366 (M^+) (calcd for $C_{15}H_{16}OSe$: 292.0361). The selenide **10** was converted to the corresponding selenoxide (2-phenyl-1-phenylselenino-2-propanol) by ozonization and crystallization from pentane–ethyl acetate. A single diastereomer crystallized: mp 125–125.5 °C; NMR ($CDCl_3$) δ 7.6–7.3 (m, 10 H), 3.55 (d, *J* = 12 Hz, 1 H), 3.35 (d, *J* = 12 Hz, 1 H), 1.65 (s, 3 H).

Anal. calcd for $C_{15}H_{16}O_2Se$: C, 58.64; H, 5.25. Found: C, 58.21; H, 5.48.

Equilibration of Ditolyl Diselenide and Benzeneseleninic Acid. Solutions of benzeneseleninic acid in $CDCl_3$ (0.30 mL, 0.037 M, 0.011 mmol) and ditolyl diselenide in $CDCl_3$ (0.15 mL, 0.073 M, 0.011 mmol) were combined in a NMR tube and immediately inserted in the NMR probe (38 °C). Equilibration as demonstrated by the appearance of a new $ArCH_3$ resonance occurred within 15 min, at which time the methyl peak due to ditolyl diselenide (δ 2.35) and that due to tolueneseleninic acid (δ 2.45) were in a 2:1 ratio. In the presence of 1 drop of pyridine, the equilibration took 1.5–2 h, while the equilibration was complete within 1 min when 1 drop of trifluoroacetic acid was added instead.

Elimination of 12 in the Presence of 2-Phenylpropene. 1-Phenyl-2-phenylseleno-1-butanone (33.9 mg, 0.112 mmol) was ozonized in 0.55 mL of $CHCl_3$ at −60 °C. 2-Phenylpropene (0.012 mL, 0.112 mmol) was added and the solution was warmed to 38 °C for 5 min. Triethylamine (0.03 mL, 0.21 mmol) was then added to inhibit further readdition. The solution was poured into 5 mL of ether and 5 mL of 7% $NaHCO_3$ solution. The ethereal layer was rinsed with a saturated NaCl solution and filtered through anhydrous Na_2SO_4 and the solvent was removed. The product mixture contained 1-phenylpropenone, 2-phenylpropene, $(PhSe)_2$, and **10**. The NMR of the mixture indicated that 12% of the 2-phenylpropene had reacted to form **10**.

Reaction of 2-Phenylpropene with $PhSeO_2H$ and Ph_2Se_2. Diphenyl diselenide (12.8 mg, 0.041 mmol) and benzeneseleninic acid (7.8 mg, 0.041 mmol) were placed in an NMR tube with 0.3 mL of $CDCl_3$ at 0 °C. 2-Phenylpropene (0.016 mL, 0.125 mmol) was added and the tube was warmed to 38 °C. The readdition was followed by NMR. After 4 h, 50% of the 2-phenylpropene was converted to 2-phenyl-1-phenylseleno-2-propanol (**10**). Only 66% conversion occurred after 66 h.

Oxidation of 1-Phenylseleno-2-phenylpropane. To a stirred solution of 1-phenylseleno-2-phenylpropane (0.550 g, 0.413 mL, 2 mmol) in 2.4 mL of THF was added 2.3 mL of 30% H_2O_2 (20 mmol), 1.1 mL initially and the rest 10 min later. After stirring for 5 h at 38 °C, the reaction was cooled and extracted with 3 × 60 mL of CH_2Cl_2. Purification by preparative TLC (10% ether–pentane) gave 0.333 g (57.2%) of hydroxy selenide **10**.

Catalytic Decomposition of H_2O_2 by Methyl Phenyl Selenoxide. A 1.83 M aqueous H_2O_2 solution was prepared by dilution of 4.50 mL of commercial 30% H_2O_2 (found to be 10.15 M by iodometric titration) to 25.00 mL. Methyl phenyl selenide (0.0604 mL, 0.500 mmol) was diluted to 25.00 mL with anhydrous methanol (0.0200 M) and 18.00 mL of selenide solution plus 2.00 mL of the H_2O_2 solution were combined at 38 °C. Aliquots of the solution were titrated iodometrically[42] at intervals. A similar procedure was followed for the other H_2O_2 decomposition runs.

Elimination Rates of Selenoxides. All selenoxides were prepared by ozonization (−60 °C) of solutions of the selenides in $CDCl_3$ or CD_3OD. Phenyltrimethylsilane was added as a standard. The cold solutions were transferred to NMR tubes, 1.3–1.5 equiv of Me_2NH was added, and enough solvent was added to dilute to 0.2 M. The tubes were sealed and warmed to 38 °C. The reactions were followed by NMR integration (probe temperature 38 °C). Between 8 and 15 points were recorded during the first 3 half-lives for each selenoxide. The chemical shifts of the selenides and selenoxides as well as the rate constants are reported in Table IV.

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Registry No.—**1**, 60096-30-2; **2**, 60430-44-6; **2**,*p*-nitrobenzoate derivative, 65275-30-1; **3**, 60430-45-7; **5**, 60430-46-8; **6**, 60430-47-9; **7**, 60430-48-0; **8**, 60096-31-3; **10** (R = H), 53188-76-4; **14a**, 65275-47-0; **14b**, 65275-48-1; **14c**, 65275-49-2; **14d**, 65275-50-5; **15a**, 65275-51-6; **15b**, 65275-52-7; **15c**, 65275-53-8; **15d**, 65275-54-9; **15e**, 65275-55-0; **15f**, 65275-56-1; diphenyl diselenide, 1666-13-3; 1-bromo-2-phenylpropane, 1459-00-3; 4-methyl-2-nitrophenyl selenocyanate, 65275-29-8; 1-methoxy-2-propanolmesylate, 24590-51-0; benzeneselenyl chloride, 5707-04-0; 2,3-dihydro-2,2-dimethylbenzo[*b*]selenophene, 60096-27-7; methallyl chloride, 563-47-3; methallyl phenyl selenide, 59085-70-0; *p*-nitrobenzoyl chloride, 122-04-3; diethylamine, 109-89-7; dimethyl acetylenedicarboxylate, 762-42-5; methyl phenyl selenoxide, 25862-09-3; methyl phenyl selenide, 4346-64-9; methylphenylselenonium ylide, 65275-31-2; 2-hydroxyethyl phenyl selenide, 65275-32-3; α-methylstyrene oxide, 2085-88-3; 2-phenyl-1-phenylselenino-2-propanol, 65275-33-4; 1-phenyl-2-phenylseleno-1-butanone, 57204-89-4; 2-phenylpropene, 98-83-9; benzeneseleninic acid, 6996-92-5.

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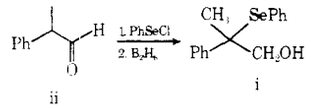

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Secondary Isotope Effects in Intramolecular Catalysis. Mono-*p*-bromophenyl Succinate Hydrolysis[1]

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Kinetic isotope effects have been measured for the intramolecular nucleophilic carboxylate-catalyzed hydrolysis, k_s, of mono-*p*-bromophenyl succinate and mono-*p*-bromophenyl succinate-d_4. The resulting isotope effect, $k_s^{H_4}/k_s^{D_4}$, equals 1.035, a *normal* effect. This is contrary to what is expected for acyl transfer reactions where the transition-state structure resembles a tetrahedral intermediate. However, the direction of the isotope effect is in agreement with a transition-state structure resembling succinic anhydride. Combining this result with previous kinetic and structural studies, a detailed transition-state structure for the hydrolysis reaction is proposed.

Intramolecularly catalyzed reactions have been studied as chemical models for reactions of an enzyme–substrate complex.[3] An additional reason to study this class of reactions is that it represents the simplest reactions in which detailed pictures of transition-state structures can be developed. Transition-state structure elucidation is facilitated in these reactions since the "diffusion complex" is already formed and thus its structure is defined.

To resolve in great detail the transition-state structure for succinate half-ester hydrolysis is an important goal for a variety of biochemical reasons. Succinates are a major tool for the reversible derivitization of bioactive agents for the purpose of improving their chemical and physical properties as drugs (thus for the design of prodrugs[4]). Hydrolytic rate studies of half-esters of succinate and of various succinate derivatives have been essential in developing theories of catalytic power.[3,5]

Half-esters of succinic acid exhibit large rate accelerations in the comparison of their intramolecularly catalyzed hydrolysis to biomolecular carboxylate-catalyzed ester hydrolysis.[6] Additional rate enhancements are observed when alkyl groups are substituted in the succinyl backbone.[7,8] Rate increases brought about by alkyl substitution are well-known phenomena in other intramolecular reactions.[9,10]

A further essential contribution to the study of these rate effects would be to examine the transition state. The kinetic isotope effects method offers a distinct advantage over alkyl substitution in that substitution of one isotope for another

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