Selenium Stabilized Carbanions. Preparation of α-Lithio Selenides and Applications to the Synthesis of Olefins by Reductive Elimination of β-Hydroxy Selenides and Selenoxide Syn Elimination[1]

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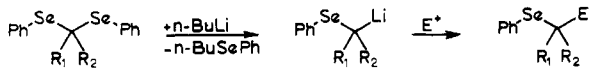
Abstract: The deprotonation of several alkyl aryl selenides with lithium amide bases has been studied. The kinetic acidity of methyl *m*-trifluoromethylphenyl selenide was found to be 1/3.8 that of the sulfur analogue. The introduction of a *m*-trifluoromethyl substituent into methyl phenyl sulfide increased the kinetic acidity by a factor of 22.4. A variety of β-hydroxy selenides have been prepared by the reduction of α-phenylseleno ketones and the addition of α-lithio selenides (prepared by deprotonation of benzyl phenyl selenide, bis(phenylseleno)methane, methoxymethyl *m*-trifluoromethylphenyl selenide, and phenylselenoacetic acid, and by *n*-butyllithium cleavage of bis(phenylseleno)methane) to carbonyl compounds. These β-hydroxy selenides are converted to olefins on treatment with methanesulfonyl chloride and triethylamine. This reductive elimination proceeds exclusively or predominantly with anti stereochemistry. Simple olefins, styrenes, cinnamic acids, vinyl ethers, and vinyl selenides have been prepared using this technique. Attempts to carry out the syn reductive elimination of β-hydroxy selenoxides or related compounds have not been successful. α-Lithio selenides can also be alkylated, and the derived selenides converted to olefins by selenoxide syn elimination.

The unique chemical properties of organoselenium compounds have been successfully exploited for a variety of olefin-forming processes.[3] The synthetic utility of these reactions is amplified by the capacity of the selenium function to serve as an activating group for carbon–carbon bond formation, in addition to its role in the introduction of the double bond. The preparation, properties, and reactions of α-lithio selenides will be the subject of this paper. The following paper[4] describes our work on the chemistry of α-lithio selenoxides.

All of the standard procedures for the preparation of alkyllithium reagents are, in principle, applicable to the preparation of α-lithio selenides. In practice, only two methods have been used widely: the *n*-butyllithium cleavage of selenoacetals and -ketals[5,6] and the deprotonation of selenides using strong bases.[1a,5,7] The former procedure developed by Seebach and co-workers[5,6a,b] is generally applicable to systems **1** where R_1 and R_2 can be hydrogen or an alkyl or aryl group. The resulting lithium reagents **2** have high nucleophilicity; they react with



1 2 3

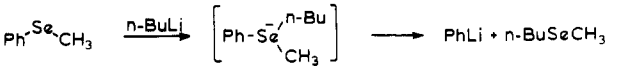
a variety of electrophiles including alkyl halides, epoxides, ketones, aldehydes, esters, amides, silyl halides, and disulfides. The products (**3**) themselves are useful starting materials for the preparation of a variety of selenium-free compounds.

Two major disadvantages of the selenoketal cleavage are apparent: (1) The precursor bis(phenylseleno) compounds **1** (except where $R_1 = R_2 = H$) are usually prepared by the reaction of ketones and aldehydes with malodorous and air-sensitive benzeneselenol under strongly acidic conditions.[8] This requires that any functional groups in R_1 and R_2 be stable in *both* strongly acidic and strongly basic media. (2) The process uses up an expensive phenylseleno group, which then contaminates the product as butyl phenyl selenide. It would clearly be more advantageous to deprotonate the appropriate selenides, a procedure which avoids the necessity of handling benzeneselenol, the harsh conditions for selenoketal formation, and contamination by BuSePh. The great nucleophilicity of $PhSe^-$ assures that alkyl selenides can be prepared not only from traditional substrates for S_N2 displacements such as halides and sulfonates, but also from lactones,[9] esters,[10] monoactivated cyclopropanes,[11] quaternary ammonium salts,[12] and amines.[13] Furthermore, selenides are available by routes not involving S_N2 displacements at carbon, such as the reaction of organometallic reagents with benzeneselenenyl chloride, or the acid-catalyzed or free-radical addition of benzeneselenol to certain olefins.

Prior to our research in this area, only a few selenium stabilized carbanions had been prepared by deprotonation: the metalation of *tert*-butoxyselenophene (to give **4**) and benzoselenophene (to give **5**) with *n*-BuLi[7a] and the deprotonation

4 5

of $(PhSe)_2CH_2$ and $(PhSe)_3CH$ with lithium diisobutylamide.[5] Although alkyllithium reagents are frequently and routinely used for the deprotonation of sulfides, their application to the deprotonation of selenides is rarely successful, an observation made in early work by Gilman[14] and Seebach,[5] and confirmed repeatedly in subsequent work in our laboratory and elsewhere. In fact, the deprotonation of phenylselenotrimethylsilylmethane with *sec*-butyllithium[7d] is the only successful reaction of this type in addition to the selenophene derivatives mentioned above. The major process is usually attack of the lithium reagent at selenium, presumably giving an ate complex **6** fol-



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lowed by Se–C bond cleavage.[6b,d] As a result it becomes necessary to use lithium dialkylamides or similar bases for deprotonation of selenium compounds.

Results and Discussion

Preparation of Selenides. The selenides used in this work were prepared by standard procedures involving nucleophilic displacements by PhSeNa in ethanol. For small-scale reactions the reduction of diphenyl diselenide using sodium borohydride presents a convenient source of ethanolic PhSeNa.[15] We have frequently used sodium hydroxymethyl sulfoxylate (Rongalite, $Na^+{}^-OSOCH_2OH$)[16] in alkaline ethanol as a reducing agent. This procedure has several features which make it particularly

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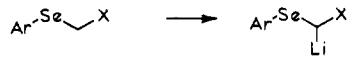
Table I. Substituted Arylselenomethyllithium Reagents Prepared by Deprotonation



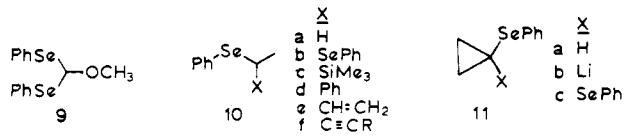
7a Ar = Ph
b Ar = m-CF_3-C_6H_4 **8**

X	base[a]	conditions	ref
	Ar = Phenyl		
PhSe-	$LiNR_2$[b]	−78 °C, 60 min	5
	LDA[d]	−78 °C, <15 min	*c*
$SiMe_3$	*sec*-BuLi/TMEDA[e]	25 °C, 90 min	1a
	LDA/TMEDA	−78 °C, 45 min	18
Ph	LDA	−78 °C, 5 min	*c*, 7c
vinyl	LDA, LiTMP	*f*	7e
ethynyl	LDA	*f*	7f
CO_2Li	LDA	−78 °C, <10 min	*c*
CO_2Et	$LiNR_2$[g]	−78 °C <5 min	7b
COPh	LDA	−78 °C, <5 min	7h
	$CH_3S(O)CH_2Na$[h]		20a
	Ar = *m*-Trifluoromethylphenyl		
H	LiTMP	−55 °C, 120 min	*c*
OCH_3	LiTMP	−78 °C, 5 min	*c*
$SiMe_3$	LiTMP	−40 °C, 40 min	7d

[a] In THF unless otherwise noted. [b] Lithium diisobutylamide. [c] Present work. [d] Ether can also be used. [e] In hexane. [f] Variable, depending on substitution. [g] Lithium *N*-isopropylcyclohexylamide. [h] In Me_2SO.

attractive for large-scale reactions: it is inexpensive and, unlike the borohydride reduction, there is no hydrogen evolution. PhSeH and PhSeNa have also been prepared by reduction of diphenyl diselenide with hypophosphorous acid.[17] PhSeNa in DMF[9a] and HMPA[10,9b] and PhSeLi with 12-crown-4 in benzene[11] show superior reactivity over that observed in protic solvents.

Deprotonation of Selenides. We have routinely used lithium diisopropylamide (LDA) and lithium 2,2,6,6-tetramethylpiperidide (LiTMP) for the deprotonation of selenides. The latter appears to be at least a power of ten more reactive, although steric effects are important. Our survey of a number of selenides had shown that any phenylselenomethane with one additional anion stabilizing group (**7**) can be deprotonated with LDA (Table I). However, even LiTMP does not give complete anion formation for the methoxy-substituted compound $PhSeCH_2OCH_3$. It is, therefore, necessary to use the methoxy selenide **7b** with the *m*-trifluoromethyl group, a technique which enhances the kinetic acidity of the methylene group by approximately a factor of 20 (see below). An alternative route to phenylselenomethoxymethyllithium (**8a**, X = OCH_3) is available upon BuLi cleavage of bis(phenylseleno)methoxymethane (**9**). Treatment of **9** with LDA at −78 °C gave



9 **10** **11**

products tentatively identified as *cis*- and *trans*-1,2-bis(phenylseleno)-1,2-methoxyethene, a product derived from phenylselenomethoxycarbene.

Neither phenylselenoethane (**10a**) nor the activated systems **10b–f** are satisfactorily deprotonated with LDA in THF.[19] α-Methyl substitution has been repeatedly shown to result in pronounced decreases in the kinetic and thermodynamic acidity of C–H bonds.[20] Cyclopropyl phenyl selenide (**11a**) is not deprotonated by LDA, LiTMP, or $LiNEt_2$ in THF. The anion **11b** can, however, be prepared by cleavage of 1,1-bis(phenylseleno)cyclopropane.[4,7i]

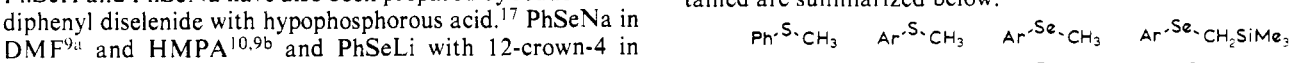
Table II. Substituent Effects for Reactions Involving Carbanion Intermediates

compd	quantity measured	base/solvent	$k_{m\text{-}CF_3}/k_H$	ρ	ref
$ArSCH_3$	k[a]	LiTMP/THF-hexane	22.4	3.14[b]	*c*
$ArC{\equiv}CCH_3$	k[a]			1.3	25
$ArPh_2CH$	k[a]	PhLi		2.2	26
$ArCH_2T$	k[d]	LiNH-c-Hex/H_2N-c-Hex	68	4.0	27
$ArCH_3$	pK_a	$NaCH_2SOCH_3$/Me_2SO		12[e]	28

[a] Rate of deprotonation. [b] Two points only. [c] This work. [d] Isotopic exchange rate. [e] Based on strongly electron-withdrawing substituents only.

Vinyl[21] and allenyl phenyl selenides[21a] can also be deprotonated with LDA.

Kinetic Acidity of Simple Selenides and Sulfides. Our observation that *m*-trifluoromethylphenyl (henceforth, Ar) selenides are substantially more acidic than the phenyl analogues prompted a brief study of some relative kinetic acidities, measured under typical synthetic conditions. Competitive deprotonations of two-component mixtures were carried out. Each sample was treated with an amount of LiTMP in hexane/THF at −56 °C such that only partial deprotonation of the most acidic compound occurred. This mixture of anions was either methylated (CH_3I) or silylated ($(CH_3)_3SiCl$), and the product mixture analyzed by GLC. Control experiments showed that proton transfer between the lithiated and protonated compounds was not occurring. The relative rates obtained are summarized below.



k_{rel} 1.0 22.4 5.9 2.1

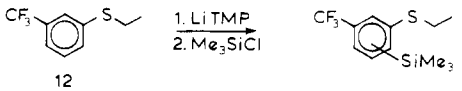
These results show that ArSMe is kinetically about four times as acidic as ArSeMe. This is compatible with published results: (1) The kinetic acidity of PhSMe exceeds that of PhSeMe by a factor of 10 using KNH_2/NH_3.[22] (2) The acidity of $(PhS)_2CH_2$ exceeds that of $(PhSe)_2CH_2$ by about two orders of magnitude.[5] (3) The pK_as (in Me_2SO) of phenylthio- and phenylselenoacetophenones are 17.1 and 18.6, respectively.[20a] The results are not, however, compatible with a theoretical prediction of greater stability for α-seleno carbanions than α-thio carbanions.[23]

The magnitude of the *m*-trifluoromethyl substitution effect was not measured in the selenium compounds because of the slow rate of deprotonation of $PhSeCH_3$. It was found to be 22.4 in the sulfur compounds. This data translates into a Hammett ρ of 3.14 if a σ of 0.43 is used for the *m*-CF_3 group.[24] This value is compared in Table II with several other metalations, isotopic exchange rates, and pK_a studies. According to the results of the kinetic experiments, the phenylthio group appears to transmit charge in the transition state almost as efficiently as the π-conjugated groups. Two opposing factors are operative. The deprotonation of ArSMe with LiTMP is exothermic, hence likely to develop little charge at the transition state; this would lead to a small value for ρ. On the other hand, the lithium reagent formed is almost certainly pyramidal, which would lead to the prediction that the Brønsted α would be close to unity, and hence ρ would be larger here than for the more planar conjugated carbanions, for which α is small.[29] It would clearly be desirable to have thermodynamic pK_as for these or related compounds.

It is unexpected that the trimethylsilyl substituent *reduces* the kinetic acidity of $ArSeCH_2SiMe_3$ toward LiTMP by a factor of 2.8. With LDA as base, however, the silyl substituent has the opposite effect; $ArSeCH_2SiMe_3$ is deprotonated at

least 25 times as fast as is $ArSeCH_3$. Presumably steric effects cancel the normally acidifying effect of trimethylsilyl when a hindered base such as LiTMP is used.

The *m*-CF_3 substituent effect is not sufficiently large to negate the huge deactivating effect of a methyl substituent. Thus the ethyl sulfide **12** is deprotonated on the ring, and not α to sulfur.[30]



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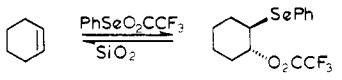
The extraordinary kinetic basicity of amide bases is shown by the behavior of methyl phenyl sulfide. It is normally deprotonated with BuLi/Dabco at 0 °C,[20c] but can be deprotonated with LiTMP in THF at −56 °C.

"Reductive Elimination" of β-Hydroxy Selenides. The three most important reactions of α-lithio selenides as synthetic reagents are those with carbonyl compounds, alkyl halides, and acylating agents. The first provides a route to β-hydroxy selenides, which can be easily converted to olefins by elimination of the elements of PhSeOH. The reaction was first observed by the discovery that $PhSeO_2CCF_3$ adducts (**13**)[31] of



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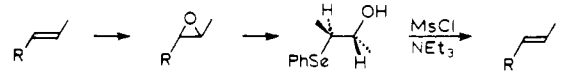
olefins spontaneously reverted to the olefins under a variety of conditions (for example, attempted chromatography on silica gel). The reaction is apparently a reversal of the electrophilic addition of PhSeOR.

A number of reagents are suitable for the conversion of β-hydroxy selenides to olefins; all have in common the ability to convert the hydroxy group into a better leaving group. The most successful reagent we found was methanesulfonyl chloride-triethylamine ($MsCl/NEt_3$) in dichloromethane at 0–25 °C.[1b] Krief and co-workers[32] have since reported additional reagents to effect the same transformation ($SOCl_2/NEt_3$, TsOH/pentane, $HClO_4$/ether, $(CF_3CO)_2O/NEt_3$, $C_6H_4O_2PCl/NaH$).

Stereochemistry. The PhSeOH reductive elimination is highly stereospecific, proceeding with anti stereochemistry. This was demonstrated by elimination of the threo and erythro β-hydroxy selenides (**14,** mixture of regioisomers) obtained from pure *cis*- and *trans*-2,3-epoxydecane, respectively, as shown below. In this way >99% *trans*-2-decene was converted



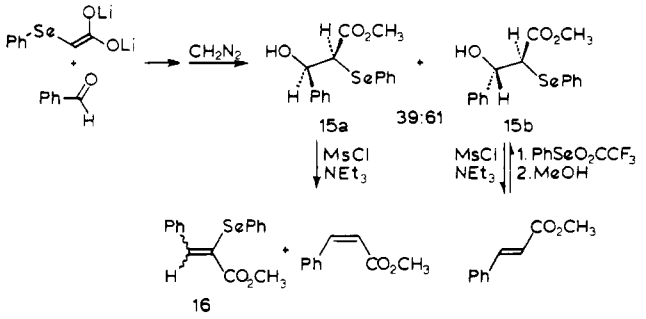
R = C_7H_{15} 14

via epoxide and **14** to >99% *trans*-2-decene, and 97% *cis*-2-decene was similarly converted to 95% *cis*-2-decene. Since the epoxidation and nucleophilic opening proceed with defined stereochemistry, the reductive elimination must proceed anti. Rémion and Krief[32a] have also shown that other conditions for elimination of PhSeOH proceed with anti stereochemistry.

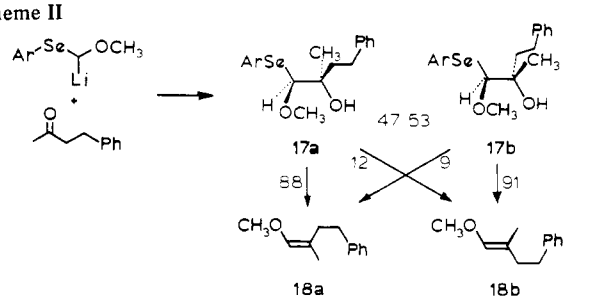
Similar conclusions can be drawn from the experiments outlined in Scheme I. Addition of phenylselenoacetic acid dianion to benzaldehyde gave stereoisomeric adducts, whose esters (**15**) could be chromatographically separated. Isomer **15b** was cleanly converted to methyl *trans*-cinnamate, whereas **15a** was converted to methyl *cis*-cinnamate and the dihydration product **16.** Addition of $PhSeO_2CCF_3$ to methyl *trans*-cinnamate gave only isomer **15b.** This agrees with published results which show that addition of selenenic[31,33] and sulfenic[34] acid derivatives to olefins invariably proceeds with anti stereochemistry.

We have also shown that the diastereomeric selenides **17** (Scheme II) formed as shown give ~90% stereospecific elim-

Scheme I

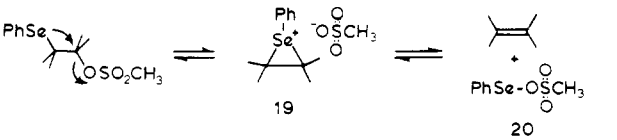


Scheme II

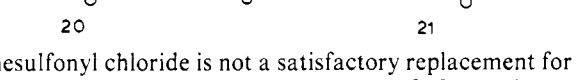


ination, although no independent proof of the stereochemistry of the hydroxy selenides **17** was obtained. The geometry of the vinyl ethers **18a** and **18b** was assigned on the basis of their NMR Eu(fod)$_3$ shifts.

The stereochemical evidence and other mechanistic considerations suggest a pathway involving an episelenonium ion. Since the crucial olefin-forming step is reversible, some method for disposal of the active electrophile **20** must be available. We



suggest that for the $MsCl/NEt_3$ reagent sulfene may play this role; the reaction appears to be clean and complete only when an excess of the reagent was used. This mechanism is supported by other observations: only about 30% of the selenium appears as diphenyl diselenide after the reaction, the remainder being lost as water-soluble material, presumably **21,** X = OH; *p*-



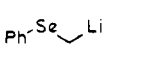
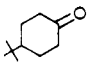
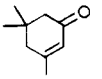
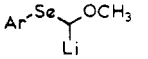
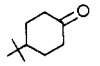
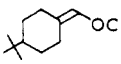
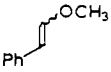
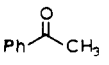
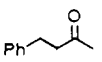
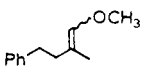
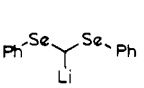
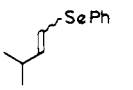
20 21

toluenesulfonyl chloride is not a satisfactory replacement for methanesulfonyl chloride. The involvement of **19** as an intermediate is also supported by the observation[21b] that when phenyl is replaced by *m*-trifluoromethylphenyl more vigorous reaction conditions are sometimes needed to achieve "reductive elimination". Additional evidence pertaining to the mechanism has been presented by Rémion and Krief.[32a]

Olefins from α-Lithio Selenides and Carbonyl Compounds. Table III summarizes the olefins prepared by addition of α-lithio selenides to aldehydes and ketones, followed by "reductive elimination". In addition to simple olefins, a vinyl selenide and several vinyl ethers have been prepared. Two attempts at preparing dienes by addition of phenylselenomethyllithium to enones failed at the reductive elimination stage. Dienes with other substitution patterns have, however, been prepared successfully by this technique.[4,32a]

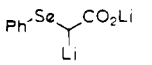
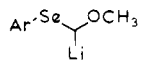
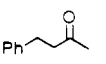
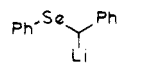
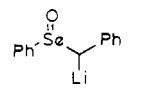
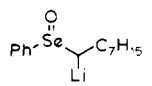
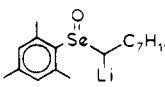
As illustrated in Schemes I and II and Table IV, the addition of chiral lithium reagents (those bearing three different substituents at the anionic carbon) leads to diastereomeric hydroxy selenides upon reaction with an aldehyde or unsymmetrical ketone. These diastereomers in turn give isomeric *E* or *Z* olefin in a largely stereospecific reaction. Some of the cases we have

Table III. Hydroxy Selenides and Olefins Prepared from α-Lithio Selenides and Carbonyl Compounds

RUN NO	LITHIUM REAGENT	KETONE ALDEHYDE	YIELD[a] %	OLEFIN	YIELD %
1			71		91[b]
2			66		<10
3			55		<10
4[c]			83		62
5			76		72
6			70		73
7[d]			77		85
8			77		81[b]

[a] Yield of β-hydroxy selenide. [b] NMR yield. [c] Ar = *m*-CF_3-C_6H_4. [d] See Scheme II.

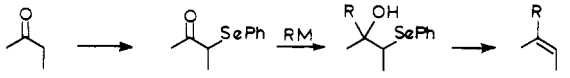
Table IV. Diastereomer Ratios of β-Hydroxy Selenides from Addition of α-Lithio Selenides and Selenoxides[a] to Ketones and Aldehydes

RUN NO	LITHIUM REAGENT	CARBONYL COMPOUND	RS-SR[b] RR-SS
1			39/61
2			47/53
3			46/54
4			54/46
5			59/41
6			44/56
7			52/48

[a] See ref 4 for experimental details on α-lithio selenoxide reactions. [b] Determined by analysis of the olefins obtained by reductive elimination. The *RS, SR* diastereomer leads to *Z* olefin, the *RR, SS* diastereomer to *E* olefin.

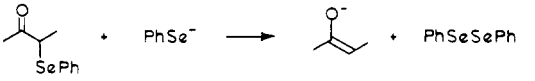
studied are summarized in Table IV. The selectivity is low, ranging from 39/61 to 59/41. These ratios were measured under normal synthetic conditions, and no efforts were made to improve selectivity by carrying out reactions at very low temperature or in less strongly coordinating solvents. A comparison of an α-lithio selenide with the analogous α-lithio selenoxide is presented in runs 4 and 5. Almost identical ratios are observed. The more sterically demanding mesityl selenoxide in run 7 gave no pronounced stereochemical control. Previous studies of the reaction of chiral α-lithio selenides,[32a,c,35a] α-lithio sulfoxides,[35b] or α-lithio sulfides[30] either have reported reactions only with symmetrical carbonyl compounds or have not determined the stereochemistry of the product alcohols.

Olefins from α-Phenylseleno Carbonyl Compounds. The addition of organometallic or hydride reagents to the readily available α-phenylselenocarbonyl compounds[36,7b] provides an alternative route to β-hydroxy selenides. "Reductive elimination" of these β-hydroxy selenides leads to an overall process in which a ketone is converted to an olefin with control of regiochemistry.



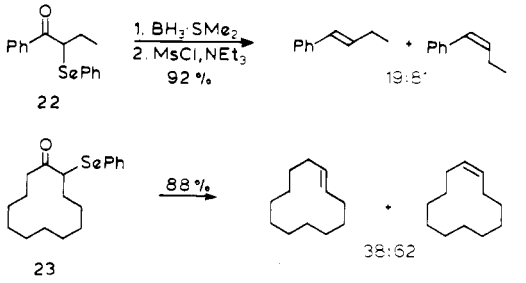
A significant obstacle to the general applicability of this scheme (which resembles the Cornforth olefin synthesis[37]) is that α-phenylseleno carbonyl compounds are easily deselenated by nucleophiles.[32b,36c]

Exploratory experiments with the model α-phenylseleno ketones **22** and **23** have shown that the former is reduced cleanly without Se-C bond cleavage by $LiAlH_4$/ether, BH_3/THF, BH_3·SMe_2/THF, and DIBALH/benzene, but is largely deselenated with $NaBH_4$/EtOH. The dialkyl ketone **23**, on the other hand, is partially or completely deselenated by $LiAlH_4$/ether, $NaBH_4$/EtOH, and commercial BH_3/THF, which contains 5% $NaBH_4$ as stabilizer. Clean reduction of **23** was observed with BH_3·SMe_2, and this is the reagent we recommend for reduction of α-seleno carbonyl compounds. The mechanism of the deselenation is not clear at this point, but may involve cleavage by attack of benzeneselenolate anion



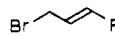
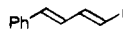
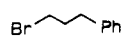
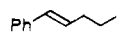
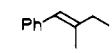
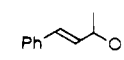
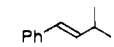
at selenium.[38] The reducing agent would rapidly convert the diphenyl diselenide back to selenolate.

The conversion of α-phenylseleno carbonyl compounds to olefins is illustrated in the reactions below.



The addition of Grignard and lithium reagents to α-phenylseleno ketones also results in varying amounts of deselenation; e.g., methyllithium added quantitatively to the carbonyl group of **22**, but gave complete deselenation with **23**. Apparently α-phenylseleno aldehydes react predominantly at the carbonyl group.[32b] Trimethylaluminum will react cleanly with **22** to form the tertiary alcohol, but again **23** is more sensitive and suffers primarily deselenation with this reagent.

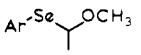
Table V. Formation of Olefins by Reaction of Deprotonated Benzyl Phenyl Selenide with Electrophiles

RUN	ELECTROPHILE	OXIDANT	OLEFIN	YIELD %[a]
1		$NaIO_4$[b]		55
2		H_2O_2		81
3		O_3		78[c]
4		H_2O_2		66
5		H_2O_2		66

[a] Overall yield based on selenide is reported. [b] The oxidation-elimination was carried out according to the procedure given in ref 36c and 40. [c] A mixture of *E* and *Z* isomers was isolated.

Alkylation of α-Lithio Selenides. All of the lithium reagents in Table I can be alkylated with primary iodides or bromides, and some with secondary halides. The derived selenides can then be converted oxidatively or otherwise to selenium-free materials. Table V presents olefins prepared by alkylation of phenyl benzyl selenide followed by selenoxide syn elimination.

The methoxy selenide **24,** prepared by methylation of **8b** (X

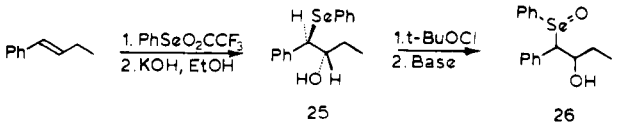


24

= OCH_3), does not give methyl vinyl ether when the derived selenoxide is warmed in the presence of dimethylamine.[39] Presumably radical or carbonium ion processes occur in preference to the syn elimination. A related sulfoxide is reported to decompose by a free-radical process.[41]

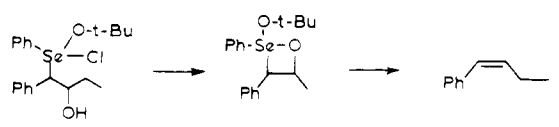
Attempted Syn Reductive Elimination of β-Hydroxy Selenides. Because of the ease with which β-hydroxyl selenides can be prepared in stereospecific or stereoselective fashion (by opening of epoxides with PhSeNa,[42,32c] addition of PhSeOR to olefins,[31,43] addition of organometallics to α-phenylseleno carbonyl compounds,[32b] and addition of α-lithio selenides and selenoxides[1,4,6a,d,32a] to aldehydes and ketones), it would be highly desirable to have available a procedure for syn elimination of PhSeOH or the equivalent to complement the anti elimination outlined above. In particular, the sequence of anti addition of PhSeOH followed by syn reductive elimination could provide a procedure for the inversion of olefins which does not involve opening of an epoxide, a reaction which fails for highly substituted olefins.[44]

Most of the exploratory experiments were carried out using the diastereomerically pure hydroxy selenide **25,** prepared as



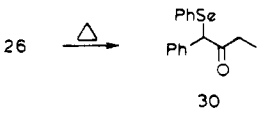
25 26

shown. A number of experiments involved treatment of **25** with oxidants such as *tert*-butyl hypochlorite followed by base, a sequence which we hoped would lead to syn elimination as shown below. However, no olefin **27** was formed in these experiments, only the stable selenoxide **26.** This selenoxide was



28 29 27

also not converted to **27** on treatment with acid, base, or silylating reagents. Thermolysis of **26** (CCl_4, 80 °C) led cleanly to an internal redox reaction (**30**).[45]



30

Apparently the activation energy for formation of crucial intermediates such as **29** is too high. Adequate precedent exists for transformations such as **28** to **29** to **27** in sulfur[46] and phosphorus chemistry.

Comparison of the PhSeOH Reductive Elimination with Related X–Y Eliminations. The three most desirable features of olefin synthesis by PhSeOH reductive elimination are as follows:

(1) The PhSeOH elimination occurs under extraordinarily mild conditions compatible with virtually all functionalities; the major exception is an unprotected alcohol, which would, of course, be converted to mesylate. These conditions contrast with powerful reductive conditions employed for PhS–OH ($TiCl_4/Zn$[47]), PhS–O_2CPh (Li/NH_3[48]), and sulfoximide–OR (Al/Hg[49]) eliminations. Temperatures of 80 °C are required for the thermolytic syn elimination of β-hydroxy sulfinamides.[46]

(2) The PhSe–OH elimination proceeds with high anti stereospecificity. The reductive eliminations of sulfoximide–OR groups under dissolving metal conditions proceed with loss of stereochemistry.[49a]

(3) Hydroxy selenides are easily available from a variety of starting materials. Even tetrasubstituted olefins[4,32a] can be prepared in a connective fashion, a situation where Wittig and related reactions normally fail as a consequence of carbonyl compound enolization.

Summary

A variety of alkyl aryl selenides can be deprotonated with lithium diisopropylamide or lithium tetramethylpiperidide. The α-lithio selenides prepared in this way react with aldehydes or ketones to give β-hydroxy selenides, which are readily converted to olefins by an anti reductive elimination of PhSe and OH. α-Lithio selenides can also be alkylated. Oxidation of the selenides formed in this way leads to olefins by selenoxide syn elimination.

Experimental Section

General. Nuclear magnetic resonance (NMR) spectra were obtained on JEOL MH-100, FX-60, or Bruker WH-270 spectrometers. Infrared (IR) spectra were obtained on a Perkin-Elmer IR-267 spectrophotometer and mass spectra (MS) on an AEI MS-902 spectrometer. Unless specified otherwise NMR spectra were measured in CCl_4 solution and IR spectra of neat liquid between salt plates were recorded. Elemental analyses were performed by either Spang Microanalytical Laboratories or Galbraith Laboratories. Melting and boiling points are uncorrected.

Starting materials were commercially available except for diphenyl diselenide, 3,3′-bis(trifluoromethyl)diphenyl diselenide, and 2,4,6,2′,4′,6′-hexamethyldiphenyl diselenide, which were prepared according to procedures in ref 36c. Tetrahydrofuran (THF) was freshly distilled from lithium aluminum hydride or sodium benzophenone ketyl. Diisopropylamine and 2,2,6,6-tetramethylpiperidine were distilled from potassium hydroxide and stored over 4A molecular sieves. Pyridine was stored over potassium hydroxide. All reactions involving organolithium reagents, selenols, or selenolate anions were run under an atmosphere of dry nitrogen. Apparatus for anhydrous reactions was dried in a 110 °C oven for at least 3 h.

Lithium diisopropylamide (LDA) solutions (1 M) were prepared as in ref 36c and titrated with diphenylacetic acid.[50] **Lithium tetramethylpiperidide (LiTMP)** in THF was freshly prepared prior to use. To 2,2,6,6-tetramethylpiperidine (0.169 g, 0.203 mL, 1.2 mmol) in 1 mL of THF at 0 °C was added 0.714 mL of 1.4 M BuLi. After stirring for 5 min, the solution of LiTMP was ready for use.

Normal workup consisted of adding the reaction mixture to 1:1 ether-pentane (50 mL) and saturated $NaHCO_3$ solution, washing the organic layer with saturated NaCl solution, drying the solution by filtering through a cone of anhydrous Na_2SO_4, and evaporating solvent on a rotary evaporator. Preparative thin layer chromatography (TLC) was carried out using Merck PF-254 silica gel.

Caution. Organoselenium compounds are toxic and should be handled with care.

Preparation of Selenides. Alkyl aryl selenides were synthesized according to literature methods[7d] from the appropriate halide or mesylate using $ArSe^-$ in ethanol, prepared by reduction of the diselenides with either $NaBH_4$ or Rongalite (sodium formaldehyde sulfoxylate). Several model procedures are presented below. α-Phenylselenocarbonyl compounds were prepared by literature procedures.[36c]

Phenylselenoacetic Acid. In a 100-mL three-neck flask equipped with a reflux condenser were placed diphenyl diselenide (3.12 g, 10 mmol) and 50 mL of absolute ethanol. The mixture was stirred rapidly under nitrogen while $NaBH_4$ (0.85 g, 22.4 mmol) was added in portions. Hydrogen was evolved and the reaction mixture turned colorless and homogeneous upon complete reduction of the selenide. Chloroacetic acid (1.89 g, 20 mmol) in 7 mL of ethanol was added to the reaction mixture. After stirring at room temperature for 7.5 h, 10 mL of saturated $NaHCO_3$ solution was added. The entire product mixture was poured into 30 mL of H_2O and 30 mL of 2:1 ether/hexane. The organic layer, which contained diphenyl diselenide, was removed. The aqueous phase was acidified and extracted with 3 × 30 mL of 2:1 ether/hexane. The combined organic phases were dried. Concentration and crystallization from 5% ether/hexane afforded 2.98 g (69% yield) of the phenylselenoacetic acid as white prisms: mp 35.5–36.5 °C (lit.[51] 36–37 °C); NMR 3.48 (s, 2 H), 7.25 (m, 3 H), 7.55 (m, 2 H), 11.1 (s, 1 H); IR ($CHCl_3$) 3000, 1705 cm^{-1}.

Bis(phenylseleno)methane (7a, X = PhSe). Diphenyl diselenide (17.15 g, 0.055 mol) in 120 mL of ethanol was stirred rapidly in a 250-mL three-neck flask equipped with a reflux condenser and thermometer. The system was purged with N_2 while sodium formaldehyde sulfoxylate (9.06 g, 0.058 mol) and a solution of NaOH (6 g, 0.15 mol) in 50 mL of water was added. The mixture was warmed to 50 °C under N_2; after 15 min, the reaction mixture decolorized, but still contained white sodium salts. Neat dichloromethane (5.04 g, 3.8 mL, 0.059 mol) was quickly added by syringe. (We found $PhSeCH_2Cl$ to be more reactive toward substitution than CH_2Cl_2 itself.) After 20 h, the crude product mixture was poured into 200 mL of H_2O and 100 mL of 50% ether/hexane. The aqueous phase was extracted with 3 × 75 mL of 50% ether/hexane. The combined organic phases were washed with $NaHCO_3$ and NaCl solutions and dried. Concentration of the solvent yielded 18.17 g of the crude selenide as an oil. Crystallization from 5% ether/hexane produced 16.47 g (92% yield) of $(PhSe)_2CH_2$ as brittle, white crystals: mp 30.0–30.6 °C (previously obtained as an oil, bp 138 °C (0.1 mm[5])); NMR δ 4.12 (s, 2 H), 7.10–7.30 (m, 6 H), 7.30–7.72 (m, 4 H).

Methoxymethyl Phenyl Selenide (7a, X = OCH_3). This selenide was prepared according to the procedure outlined for phenylselenoacetic acid. Diphenyl diselenide (6.24 g, 20 mmol) was reduced and treated with neat chloromethyl methyl ether (3.06 g, 2.88 mL, 38 mmol). (All equipment that came in contact with the latter reagent was immediately immersed in a 3 N NH_4OH bath.) After stirring at 20 °C for 16 h, chloroacetic acid (0.378 g, 4 mmol) in 2 mL of ethanol was added to the reaction. This method of using a base-extractable halide to trap unreacted PhSeNa minimized the diselenide contaminant in the product mixture. The reaction was quenched with 3 N NH_4OH after 1 h and worked up. Kugelrohr distillation (34–45 °C (0.06 mm)) yielded 7.15 g (94% yield) of $PhSeCH_2OCH_3$[6b] as a clear oil; NMR δ 3.31 (s, 3 H), 5.10 (s, 2 H), 7.1 (m, 3 H), 7.45 (m, 2 H); MS M^+ 201.9895 (calcd, 201.9897).

Methoxymethyl *m*-Trifluoromethylphenyl Selenide (7b, X = OCH_3). This compound was prepared using the same procedure as above. Kugelrohr distillation (bath temperature 35–43 °C (0.018 mm)) gave a 73% yield: NMR δ 3.41 (s, 3 H), 5.23 (s, 2 H), 7.15–7.9 (m, 4 H); MS M^+ 269.9780 (calcd, 269.9770).

Anal. Calcd for $C_9H_9F_3OSe$: C, 40.17; H, 3.37. Found: C, 40.20; H, 3.33.

Methoxybis(phenylseleno)methane (9). Compound **9** was prepared from diphenyl diselenide (12.5 g, 40 mmol) and dichloromethyl methyl ether (4.37 g, 3.33 mL, 38 mmol) according to procedures described for methoxymethyl phenyl selenide. Low-boiling impurities were removed by distillation. A yield of 11.01 g (82%) of **9** was obtained as a yellow oil (NMR pure): NMR δ 2.45 (s, 3 H), 6.66 (s, 1 H), 6.99–7.43 (m, 3 H), 7.43–7.87 (m, 2 H); MS M^+ 357.9373 (calcd, 357.9375).

Octyl Phenyl Selenide. Octyl phenyl selenide was prepared from diphenyl diselenide (9.36 g, 0.030 mol) and octyl bromide (11.0 g, 9.32 mL, 0.057 mol) according to the general procedure using a sodium borohydride reduction. The crude selenide was purified by Kugelrohr distillation (bath 88–93 °C (0.02 mm)) to yield 14.55 g (95%) of the selenide as a clear oil: NMR δ 0.88 (broad t, 3 H), 1.1–1.9 (m, 12 H), 2.83 (t, J = 7 Hz, 2 H), 7.20 (m, 3 H), 7.45 (m, 2 H); MS M^+ 270.0878 (calcd, 270.0887).

Octyl Mesityl Selenide. Octyl mesityl selenide was prepared from dimesityl diselenide (1.06 g, 3.0 mmol) and octyl bromide (1.10 g, 0.93 mL, 5.7 mmol) using standard methods involving a sodium borohydride reduction. The crude product was purified by Kugelrohr distillation to give 1.58 g (89% yield) of the selenide as a clear oil; NMR δ 0.88 (broad t, 3 H), 1.06–1.78 (m, 12 H), 2.22 (s, 3 H), 2.40–2.80 (m, 8 H, including a singlet at 2.50), 6.83 (s, 2 H).

Anal. Calcd for $C_{17}H_{28}Se$: C, 65.56; H, 9.07. Found: C, 65.58; H, 9.21.

Procedure for Competitive Deprotonations. A typical procedure for competitive deprotonation is given here for PhSMe and $ArSeCH_2SiMe_3$.

A solution of 1 mL of dry 2,2,6,6-tetramethylpiperidine in 23 mL of anhydrous THF was prepared. Each competition experiment was run using 2 mL of this solution. Ether used for workup in competition experiments was anhydrous and free of peroxides; olefin-free pentane was distilled from CaH_2 and stored over 4A molecular sieves.

n-BuLi (0.1 mL, 1.57 M) was added to 2 mL of the THF solution of 2,2,6,6-tetramethylpiperidine at 0 °C. After 5 min the flask was transferred to a −56 °C bath and stirred for 5 min. PhSMe (30 mg, 0.25 mmol) and $ArSeCH_2SiMe_3$ (76.9 mg, 0.25 mmol) were simultaneously added in less than 2 s to this solution. After 20 min 0.05 mL of methyl iodide (Me_3SiCl was used for the ArSMe/ArSeMe pair) was rapidly added to the reaction mixture. After 10 s 0.2 mL of 25% HOAc/THF solution was added and the solution was allowed to warm up. The reaction mixture was poured into saturated $NaHCO_3$ solution and extracted with ether/pentane. The combined organic extracts were washed with 1.2 N HCl solution and saturated NaCl solution, dried, and concentrated on a rotary evaporator (bath temperature <25 °C). CCl_4 (0.5 mL) was added to the concentrated filtrate and the relative amounts of starting materials and products were determined by GC. The GC response on a molar basis for starting material and the methylation product was identical within the accuracy of determination. It was determined that $k(ArSeCH_2SiMe_3)/k(PhSMe)$ = 2.12. Results are summarized in Table VI.

Gas chromatographic analysis was performed on a Varian 1700 gas chromatograph with a flame ionization detector. A ⅛ in. × 12 ft long column packed with 3% SE-30 on Chromosorb W was used. The oven temperature was programmed to rise from 50 to 120 °C at a rate of 4 °C/min. The GC retention times for the various compounds analyzed under these conditions are given in Table VII.

Reductive Elimination of β-Hydroxy Selenides by Methanesulfonyl Chloride and Triethylamine. A General Procedure. To a solution of selenide (1 mmol) in 1.5 mL of CH_2Cl_2 was added NEt_3 (0.70 mL, 5 mmol). The reaction flask was cooled to 0 °C and $MeSO_2Cl$ (0.345 g, 0.23 mL, 3 mmol) in 1 mL of CH_2Cl_2 was added slowly by syringe over a 5–10-min period. The reaction mixture darkened with the formation of diphenyl diselenide. It was warmed to room temperature and quenched by the addition of water; the product mixture was poured into 10 mL of 50% ether/hexane and 5 mL of water. The organic phase was washed successively with 10% HCl, 3 N NH_4OH, and aqueous NaCl, filtered through anhydrous sodium sulfate, and concentrated at reduced pressure.

Stereochemistry of PhSeOH Reductive Elimination, *cis*- and *trans*-2-Decene. To a stirred solution of *cis*-2-decene (97% pure, 0.140 g, 1.0 mmol) in 1.5 mL of CH_2Cl_2 was added in portions *m*-chloroperbenzoic acid (85% pure, 0.204 g, 1.0 mmol) at room temperature. After the addition was completed the mixture was stirred for 14 h and filtered through Celite, and filtrate was washed twice with 5% Na_2CO_3 solution and saturated NaCl and dried. The crude epoxide (quantitative) was used without further purification: NMR δ 0.90 (broad t, 3 H), 1.1–1.6 (m, including d at 1.2, 15 H), 2.6–3.0 (m, 2 H).

cis-2,3-Epoxydecane was converted to the hydroxy selenide by reaction with PhSeNa generated from a sodium borohydride reduction

Table VI. Relative Rates of Deprotonation of Sulfides and Selenides

no.	pair of compds[a] (A/B)	mmol of base used	extent of reaction A/B	rel rate of deprotonation
1	$ArSeCH_2SiMe_3$/PhSMe	0.157	27.7/14.2	2.12
2	$ArSeCH_2SiMe_3$/PhSMe	0.204	43.9/24.3	2.07
3	$ArSeCH_2SiMe_3$/ArSeMe	0.204	12/29.7	0.36
4	$ArSeCH_2SiMe_3$/ArSeMe	0.157	5/13.8	0.33
5	ArSMe/$ArSeCH_2SiMe_3$	0.102	47/5.4	10.6
6	ArSMe/$ArSeCH_2SiMe_3$	0.094	20.2/2.1	10.8
7	ArSMe/ArSeMe[c]	0.204	45.9/16.5	3.42
8	$ArSeCH_2SiMe_3$/ArSeMe[d]	0.204	33.4/<1.5	>25.4
9	$ArSeCH_2SiMe_3$/ArSeMe[d]	0.204	36.2/<1.6	>25.8

[a] Ar = *m*-CF_3-C_6H_4. [b] Unless noted otherwise relative rate of deprotonation is measured in THF/hexane at −56 °C using lithium 2,2,6,6-tetramethylpiperidide as base and methyl iodide for quenching anion. [c] Me_3SiCl was used for quenching anions. [d] LDA was used as a base.

Table VII. GC Retention Times (s) for Starting Materials and Products

	compd	methylation product	silylation product
PhSMe	510	630	
ArSMe	540	645	1185
ArSeMe	615	720	1305
$ArSeCH_2SiMe_3$	1305	1425	

of diphenyl diselenide (0.156 g, 0.5 mmol).[42] *cis*-2,3-Epoxydecane in 2 mL of ethanol was added. The mixture was stirred at 25 °C for 15 h. After a normal workup, the hydroxy selenides were obtained as a mixture of regioisomers of erythro configuration (**14**). They were purified by preparative TLC with 10% ether/pentane to give 0.222 g (71% yield) of **14**: R_f 0.2; NMR δ 0.80 (broad t, 3 H), 1.1–1.8 (m, 15 H), 2.26 (broad s, 1 H), 2.79–3.79 (m, 2 H), 7.02–7.31 (m, 3 H), 7.31–7.62 (m, 2 H); MS M^+ 314.1150 (calcd, 314.1149).

The erythro β-hydroxy selenide (0.222 g, 0.708 mmol) in CH_2Cl_2 was converted to *cis*-2-decene by general procedures for reductive elimination using NEt_3 (0.358 g, 0.50 mL, 3.54 mmol) and $MeSO_2Cl$ (0.244 g, 0.17 mL, 2.12 mmol).

***trans*-2-Decene.** *trans*-2-Decene was converted to the threo β-hydroxy selenides in the same manner as for the erythro isomer (**14**): NMR δ 0.88 (broad t, 3 H), 1.0–1.9 (m, 15 H), 2.26 (broad s, 1 H), 2.79–3.79 (m, 2 H), 7.02–7.31 (m, 3 H), 7.31–7.62 (m, 2 H); MS M^+ 314.1158 (calcd, 314.1149). Spectral data for the *trans*-2,3-epoxydecane: NMR δ 0.89 (broad t, 3 H), 1.1–1.6 (m, including d at 1.28, 15 H), 2.33–2.69 (m, 2 H).

In the same manner as before, the threo β-hydroxy selenide (0.323 g, 1.03 mmol) was converted to *trans*-2-decene using NEt_3 (0.520 g, 0.72 mL, 5.15 mmol) and $MeSO_2Cl$ (0.355 g, 0.24 mL, 3.09 mmol).

Analyses of Stereochemistry. The GC analysis of the decenes was carried out on a Varian Aerograph 1700 instrument, using a 61.6-m capillary column coated with SE-30. The crude olefins were treated with 2 equiv of 30% H_2O_2 in 2 mL of CH_2Cl_2 to oxidize selenium contaminants. Following a typical workup, the decenes (approximately 1% in CH_2Cl_2) were analyzed. Retention times follow: *trans*-2-decene, 581 s; *cis*-2-decene, 613 s. Starting with 99 + % pure *trans*-2-decene, the PhSeOH reductive eliminations gave 99 + % pure *trans*-2-decene. Starting with 97% *cis*-2-decene, the sequence gave 95% pure *cis*-2-decene.

1-Methylene-4-*tert*-butylcyclohexane (Table III, Run 1). To bis(phenylseleno)methane (0.783 g, 2.40 mmol) dissolved in 5 mL of THF at −78 °C under N_2 was added 2.4 mmol of *n*-BuLi. After 10 min, 4-*tert*-butylcyclohexanone (0.309 g, 2 mmol) in 1 mL of THF was added to the phenylselenomethyllithium solution and allowed to react for 5 min. The reaction mixture was transferred by cannula into 10 mL of water and 15 mL of 50% ether/hexane and worked up. Contaminants such as methyl phenyl selenide, butyl phenyl selenide, and ketone starting material were removed by short-path distillation at reduced pressure. The NMR of the crude product shows a 20:80 mixture of diastereomers. Crystallization of the oil from 5% ether/hexane yielded 0.144 g of one of the hydroxy selenides as white plates: mp 68.5–70.0 °C, as a first crop; NMR (one diastereomer) δ 0.95–1.96 (m, 10 H), 0.86 (s, 9 H), 3.04 (s, 2 H), 7.20 (m, 3 H), 7.50 (m, 2 H). A second crop of 0.145 g and a third crop of 0.142 g, both as brittle, white crystals, mp 60–61.5 °C, were obtained: NMR (mixture of diastereomers) δ 0.95–1.96 (m, 10 H), 0.83, 0.86 (s, 9 H), 3.20, 3.04 (s, 2 H), 7.20 (m, 3 H), 7.50 (m, 2 H); IR (CCl_4) 3500 cm^{-1}. The total yield of β-hydroxy selenides was 0.459 g (71%).

Anal. Calcd for $C_{17}H_{26}OSe$: C, 62.76; H, 8.06. Found: C, 62.86; H, 8.04.

1-Phenylselenomethyl-4-*tert*-butylcyclohexanol (0.309 g, 0.951 mmol) in CH_2Cl_2 was treated with NEt_3 (0.480 g, 0.67 mL, 4.76 mmol) and $MeSO_2Cl$ (0.326 g, 0.221 mL, 2.85 mmol) according to the general procedure. An NMR yield of 91% of 1-methylene-4-*tert*-butylcyclohexane[52] was determined by a comparison with an internal standard: NMR δ 0.88 (s, 9 H), 1.00–1.20 (m, 3 H), 1.68–2.00 (m, 4 H), 2.12–2.44 (m, 2 H), 4.52 (s, 2 H); IR (CCl_4) 1650, 880 cm^{-1}.

1-(Phenylselenomethyl)-2-cyclopenten-1-ol (Table III, Run 2). Bis(phenylseleno)methane (0.326 g, 1 mmol) was dissolved in 3 mL of THF and cooled to −78 °C under N_2. One equivalent of *n*-BuLi was added to the stirred solution to form phenylselenomethyllithium. After 20 min cyclopentenone (0.084 mL, 1 mmol) in 0.5 mL of THF was added and stirred for 5 min. The reaction mixture was worked up and purified by preparative TLC with 20/79/1 ether/pentane/NEt_3 (load sample with Et_3N) to give 0.161 g (66% yield) of the β-hydroxy selenide: NMR δ 1.9 (m, 2 H), 2.3 (m, 2 H), 2.7 (s, 1 H), 3.15 (s, 2 H), 5.5–5.85 (m, 2 H), 7.2 (m, 3 H), 7.4 (m, 2 H).

1-(Phenylselenomethyl)-3-methyl-5,5-dimethyl-2-cyclohexen-1-ol (Table III, Run 3). Phenylselenomethyllithium (1 mmol) was treated with isophorone (0.138 g, 0.150 mL, 1 mmol) according to the procedure for 1-(phenylselenomethyl)-2-cyclopenten-1-ol. The product was purified by preparative TLC with 10/90/1 ether/hexane/Et_3N, R_f 0.2, to give 0.169 g (55% yield) of the β-hydroxy selenide: NMR δ 0.96 (s, 3 H), 1.02 (s, 3 H), 1.10–2.14 (m, including s at 1.67, 7 H), 3.02 (s, 2 H), 5.28 (broad s, 1 H), 7.18 (m, 3 H), 7.50 (m, 2 H); MS M^+ 310.0838 (calcd, 310.0836).

2-Phenyl-1-methoxyethene (Table III, Run 5). LiTMP (1.2 mmol) was prepared at 0 °C under N_2 and cooled to −78 °C. To the stirred solution was added methoxymethyl *m*-trifluoromethylphenyl selenide (0.269 g, 0.165 mL, 1 mmol). After 5 min, benzaldehyde (0.136 g, 1.30 mL, 1.28 mmol) was added by syringe. After 10 min the reaction was quenched and worked up. Purification by preparative TLC using 10% ether/pentane gave 0.286 g (76% yield) of 1-phenyl-2-methoxy-2-phenylselenoethanol as an oil: R_f 0.1; NMR (mixture of diastereomers) δ 3.07 (broad s, 1 H), 3.35, 3.48 (s, 3 H), 4.76 (m, 2 H), 7.05–7.71 (m, 9 H); MS M^+ 376.0192 (calcd, 376.0189).

The selenide (0.76 mmol) was dissolved in CH_2Cl_2 and treated with NEt_3 and $MeSO_2Cl$ using the general procedure to give the methyl enol ether. Purification by short-path distillation (28–38 °C (38 mm)) afforded 0.073 g (72% yield) of the pure ether;[53] NMR (46:54 mixture of *Z* and *E*) δ 3.60, 3.71 (s, 3 H), 5.14, 5.72 (d, J = 7 Hz, d, J = 12 Hz, 1 H), 6.03, 6.96 (d, J = 7 Hz, d, J = 12 Hz, 1 H), 6.80–7.61 (m, 5 H); MS M^+ 134.0732 (calcd, 134.0732).

4-*tert*-Butyl-1-methoxymethylenecyclohexane (Table III, Run 4). Methoxy-*m*-trifluoromethylphenylselenomethyllithium (**8b**, X = OCH_3, 1.0 mmol) was treated with 4-*tert*-butylcyclohexanone (0.154 g, 1.0 mmol) according to procedures previously described. The unreacted ketone was removed from the crude product mixture by sublimation. Purification by preparative TLC using 10/89/1 ether/pentane/Et_3N afforded 0.217 g of one diastereomer [R_f 0.2; NMR

δ 0.68–1.88 (m, 7 H), 0.85 (s, 9 H), 1.88–2.58 (m, 3 H), 3.39 (s, 3 H), 5.09 (s, 1 H), 7.42 (m, 2 H), 7.78 (m, 2 H)] and 0.140 g of the other diastereomer (total yield 83%) [R_f 0.3; NMR δ 0.70–1.78 (m, 8 H), 0.88 (s, 9 H), 1.78–2.34 (m, 2 H), 3.40 (s, 3 H), 4.64 (s, 1 H), 7.43 (m, 2 H), 7.77 (m, 2 H)].

Anal. Calcd for $C_{19}H_{27}F_3O_2Se$: C, 53.88; H, 6.43. Found: C, 54.02; H, 6.55.

A mixture of the diastereomers (0.284 g, 0.672 mmol) was converted to olefin according to the general procedure. The methyl enol ether was purified by short-path distillation (bp 40–50 °C (0.072 mm); lit.[54] bp 79–84 °C (0.55 mm)): NMR δ 0.69–2.24 (m, 8 H), 0.82 (s, 9 H), 2.82 (dm, J = 14 Hz, 1 H), 3.48 (s, 3 H), 5.66 (broad s, 1 H); MS M^+ 182.1674 (calcd, 182.1671).

1-Methoxy-2-phenyl-1-propene (Table III, Run 6). Methoxy-*m*-trifluoromethylphenylselenomethyllithium prepared from methoxymethyl *m*-trifluoromethylphenyl selenide (0.269 g, 0.165 mL, 1.0 mmol) and LiTMP (1.2 mmol) was treated with acetophenone (0.120 g, 0.118 mL, 1.0 mmol) according to procedures previously described. The crude product was purified by preparative TLC, eluting three times with 10% ether/pentane to give 0.269 g (69% yield) of the β-hydroxy selenide as an oil: R_f 0.1; NMR (mixture of diastereomers) δ 1.57, 1.61 (s, 3 H), 2.75 (broad s, 1 H), 3.32, 3.39 (s, 3 H), 4.76 4.79 (s, 1 H), 6.94–7.60 (m, 9 H); MS M^+ 390.0344 (calcd, 390.0345).

The β-hydroxy selenides (0.69 mmol) were converted to the olefin according to the general procedure. The crude product was purified by short-path distillation (30–40 °C (30 mm)) to give 0.075 g (73% yield) of the enol ether: NMR (*E,Z* mixture) δ 1.87, 1.92 (s, 3 H), 3.58, 3.60 (s, 3 H), 6.01–6.30 (q, J = 1.5 Hz, 1 H), 6.91–7.63 (m, 5 H); MS M^+ 148.0888 (calcd, 148.0888).

1-Phenylseleno-3-methyl-1-butene (Table III, Run 8). To a stirred solution of bis(phenylseleno)methane (0.326 g, 1 mmol) in 2 mL of THF cooled to −78 °C was added 1.1 mL of 1 M LDA under N_2. After 30 min isobutyraldehyde (0.078 g, 0.098 mL, 1.08 mmol) was added by syringe and stirred for 5 min. The reaction mixture was transferred by cannula into 5 mL of water and 10 mL of 50% ether/hexane and worked up. The crude product was purified by preparative TLC with 20% ether/pentane to give 0.306 g (77% yield) of β-hydroxy selenide, R_f 0.2, as an oil: NMR δ 0.78 (d, J = 7 Hz, 3 H), 0.95 (d, J = 7 Hz, 3 H), 1.95–2.35 (septet, J = 7 Hz, 1 H), 2.75 (broad s, 1 H), 3.14–3.45 (m, 1 H), 4.56, 4.59 (d, J = 3 Hz, 1 H), 7.10–7.30 (m, 6 H), 7.30–7.50 (m, 2 H), 7.50–7.70 (m, 2 H); MS M^+ 399.9848 (calcd, 399.9844).

1-Bis(phenylseleno)-3-methyl-2-butanol (0.306 g, 0.769 mmol) in CH_2Cl_2 was treated with NEt_3 (0.388 g, 0.54 mL, 3.85 mmol) and $MeSO_2Cl$ (0.265 g, 0.18 mL, 2.31 mmol) according to the general procedure. An NMR yield of 81% olefin was determined by comparison with an internal standard: NMR (mixture of *E,Z* isomers) δ 1.05 (d, J = 7 Hz, 6 H), 2.47, 2.74 (d septet, J = 7 Hz, 1 H), 5.86, 6.04 (t, J = 9 Hz, dd, J = 9, 15 Hz, 1 H), 6.31, 6.37 (d, J = 9 Hz, d, J = 15 Hz, 1 H), 7.24 (m, 3 H), 7.45 (m, 2 H); MS M^+ 226.0267 (calcd, 226.0261).

Anal. Calcd for $C_{11}H_{14}Se$: C, 58.67; H, 6.27. Found: C, 58.56; H, 6.27.

In a separate synthesis, an overall yield of 65% (1.45 g) was obtained from a 10-mmol reaction. The vinyl selenide product was purified by distillation (63 °C (0.028 mm)).

Stereochemistry of Reductive Elimination to a Methyl Enol Ether. 1-Methoxy-2-methyl-4-phenyl-1-butene (Scheme II). The β-hydroxy selenide **17** was prepared from methoxymethyl *m*-trifluoromethylphenyl selenide (0.188 g, 0.115 mL, 0.70 mmol) and benzylacetone (0.104 g, 0.105 mL, 0.70 mmol). Unreacted ketone was removed from the crude product mixture by sublimation. Purification by preparative TLC, eluting six times with 99/1 pentane/NEt_3, afforded 0.105 g of diastereomer **17b** [R_f 0.15; NMR (C_6D_6) δ 1.32 (s, 3 H), 1.90 (m, 1 H), 2.05 (m, 1 H), 2.27 (s, 1 H), 2.70 (m, 2 H), 3.01 (s, 3 H), 4.64 (s, 1 H), 6.75 (t, J = 8 Hz, 1 H), 7.16 (m, 6 H), 7.47 (d, J = 8 Hz, 1 H), 7.94 (s, 1 H)] and 0.119 g of the other diastereomer **17a** (total yield 77%) [R_f 0.3; NMR (C_6D_6) δ 1.26 (s, 3 H), 1.98 (m, 2 H), 2.29 (s, 1 H), 2.75 (m, 2 H), 2.96 (s, 3 H), 4.71 (s, 1 H), 6.77 (t, J = 8 Hz, 1 H), 7.11 (m, 6 H), 7.51 (d, J = 8 Hz, 1 H), 7.97 (s, 1 H)].

Each of the two diastereomers was converted to the corresponding enol ether by treatment with $NEt_3/MeSO_2Cl$. In this manner, the former isomer **17b** gave 80% yield of olefin **18b** while the latter **17a** gave 90% yield of olefin **18a.** Both were isolated from the crude product mixture by short-path distillation (34 °C (0.034 mm)). NMR (C_6D_6) *E* isomer **18b:** δ 1.75 (d, J = 1.3 Hz, 3 H), 2.15 (m, 2 H), 2.58 (m, 2 H), 3.13 (s, 3 H), 5.57 (q, J < 1 Hz, 1 H), 7.16 (m, 5 H). MS: M^+ 176.1201 (calcd, 176.1201). NMR (C_6D_6) *Z* isomer **18a:** δ 1.47 (d, J = 1.5 Hz, 3 H), 2.53 (m, 2 H), 2.70 (m, 2 H), 3.09 (s, 3 H), 5.56 (s, 1 H), 7.16 (m, 5 H). MS: M^+ 176.1201 (calcd, 176.1201). The allylic CH_3 group of **18b** showed a 0.3-ppm shift on addition of 1.0 equiv of Eu(fod)$_3$; **18a** showed a 0.1-ppm shift.

Analyses of Stereochemistry by NMR. Identification of olefins **18** and the hydroxy selenide precursors **17** was performed on the Brucker WH-270 spectrometer.

Isomeric purity of the two selenides **17b** and **17a** was determined by expanding the region corresponding to the methoxy protons, δ 3.01 (**17b**) and 2.96 (**17a**), cutting out the traces, and taking an average weight (N = 4) of the peak areas. Selenide **17b** was determined to be 94.8% pure and selenide **17a** 95.1% pure.

The corresponding enol ethers were similarly treated. Isomeric purities were determined from the weighted averages (N = 4) of both the methoxy protons (δ 3.13 for **18b** and 3.09 for **18a**) and methyl protons (δ 1.75 for **18b** and 1.47 for **18a**). By this method, selenide **17b** was converted to 86.1% **18b** and 13.9% **18a,** a 91% retention of stereochemistry. Likewise, selenide **17a** was converted to 16.0% **18b** and 84.0% **18a,** an 88% retention of stereochemistry.

1-Phenyl-1-phenylseleno-2-butanol (25, Table IV, Run 4). Benzyl phenyl selenide (2.47 g, 10 mmol) was dissolved in 50 mL of THF under N_2 and cooled to −78 °C. LDA (1 M, 10.5 mL) was added to the stirred solution; it immediately took on a yellow color which was indicative of the formation of the benzyl anion. After 5 min propionaldehyde (0.64 g, 0.79 mL, 11 mmol) was added to the reaction mixture; after 5 min the entire mixture was quenched by transferring it by cannula into water. Workup and purification by dry column chromatography, R_f 0.1, with 10% ether/pentane gave 2.13 g (70% yield) of a diastereomeric mixture (54:46 *RS, SR:RR, SS*) of the selenides as a viscous oil. Crystallization from pentane afforded white crystals of the *RS, SR* isomer: mp 63.5 °C; NMR δ 0.9 (t, J = 8 Hz, 3 H), 1.4 (m, 2 H), 2.60 (s, 1 H), 3.80 (m, 1 H), 4.09 (d, J = 9 Hz, 1 H), 7.18 (m, 5 H); IR (CCl_4) 3500 cm^{-1}; MS M^+ 306.0516 (calcd, 306.0523).

Anal. Calcd for $C_{16}H_{18}OSe$: C, 62.93; H, 5.95. Found: C, 63.04; H, 5.92.

The pure *RR, SS* diastereomer can be prepared by treating *trans*-1-phenyl-1-butene with silver trifluoroacetate and benzeneselenenyl chloride.

***trans*-1-Phenyl-1-butene.** To a stirred solution of lithium aluminum hydride (0.963 g, 25.3 mmol) in 30 mL of ether was added, dropwise to maintain a gentle reflux, butyrophenone (7.40 g, 50 mmol) in 10 mL of ether. The reaction mixture was refluxed for 45 min and cooled in an ice bath. Excess lithium aluminum hydride was destroyed by slow addition of 20 mL of wet ether, 5 mL of water, and 5 mL of 0.5 N HCl. The entire mixture was then poured into a separatory funnel with about 200 mL of 2 N HCl to dissolve the lithium alkoxides and worked up. To the crude alcohol was added sodium bisulfate (0.483 g, 4.0 mmol). Nitrogen was bubbled into the mixture and it was distilled at 205–210 °C (bath temperature) over a period of 1 h using a Woods metal bath. The distillate was dried and distilled under reduced pressure (76–81 °C, 10 mm) to yield 4.5 g (68%) of *trans*-1-phenyl-1-butene[55] (<5% cis); NMR δ 1.07 (t, J = 7 Hz, 3 H), 2.18 (td, J = 7, 5.5 Hz, 2 H), 5.95–6.5 (m, 2 H), 7.16 (m, 5 H); IR (CCl_4) 965, 694 cm^{-1}.

Conversion of *trans*-1-Phenyl-1-butene to the (*RR, SS*) Diastereomer 25. To a stirred solution of *trans*-1-phenyl-1-butene (0.264 g, 2 mmol) and silver trifluoroacetate (0.464 g, 2.1 mmol) in 6 mL of benzene was added benzeneselenenyl chloride (0.421 g, 2.2 mmol) in 2 mL of benzene. The reaction mixture turned yellow and silver chloride precipitated. After 5 min excess silver trifluoroacetate was destroyed by adding a drop of aqueous NaCl and aqueous $NaHCO_3$ to the reaction mixture. The entire mixture was filtered through a cake of Celite and sodium sulfate. The resultant trifluoroacetoxy selenide in benzene was hydrolyzed by treatment with potassium hydroxide (0.168 g, 3.0 mmol) in 10 mL of ethanol for a few minutes. The reaction mixture was worked up and the crude β-hydroxy selenide was purified by preparative TLC with 10% ether/pentane to give 0.478 g (78% yield) of product (R_f 0.1): NMR δ 0.90 (t, J = 8 Hz, 3 H), 1.4 (m, J = 8 Hz, 2 H), 2.39 (s, 1 H), 3.82 (m, 1 H), 4.19 (d, J = 6 Hz, 1 H), 7.18 (m, 5 H); IR (CCl_4) 3500 cm^{-1}.

Stereochemistry of α-Lithio Selenoxide Addition. 3-Phenylseleno-2-decanol (Table IV, Run 6). The β-hydroxy selenide was prepared from octyl phenyl selenide (0.269 g, 0.222 mL, 1.0 mmol) and freshly

distilled acetaldehyde (0.051 g, 0.065 mL, 1.2 mmol) in 0.5 mL of THF according to the literature procedure,[4] using MCPBA to oxidize the selenide, LDA for deprotonation, and an acetic acid/sodium iodide/sodium bisulfite reduction. The crude product was purified by preparative TLC using 10% ether/pentane to give 0.235 g (75% yield) of the selenide as an oil: R_f 0.15; NMR (mixture of diastereomers) δ 0.90 (broad t, 3 H), 1.04–1.91 (m, 15 H), 2.15 (broad s, 1 H), 2.97, 3.18 (m, 1 H), 3.57–3.91 (m, 1 H), 7.06 (m, 3 H), 7.37 (m, 2H); MS M^+ 314.1126 (calcd, 314.1149).

3-(2,4,6-Trimethylphenylseleno)-2-decanol (Table IV, Run 7). The β-hydroxy selenide was prepared from octyl mesityl selenide (0.311g, 0.269 mL, 1.0 mmol) via the corresponding selenoxide and freshly distilled acetaldehyde (0.110 g, 0.14 mL, 2.5 mmol) according to the standard procedure[4] using an acetic acid/sodium iodide/sodium bisulfite reduction. The crude product was purified by preparative TLC using 10% ether/pentane to give 0.218 g (61% yield) of the β-hydroxy selenide as an oil: R_f 0.2; NMR (mixture of diastereomers) δ 0.88 (broad t, 3 H), 1.01–1.70 (m, 15 H, including two d at 1.10 and 1.14), 1.70–2.14 (broad s, 1 H), 2.22 (s, 3 H), 2.50 (s, 6 H), 2.92 (m, 1 H), 3.46–3.84 (m, 1 H), 6.82 (s, 2 H); MS M^+ 356.1608 (calcd, 356.1618).

2-Decenes. The selenides prepared above were converted to the *cis*- and *trans*-2-decenes by reductive elimination. The olefin was isolated by short-path distillation and the *E*/*Z* ratio analyzed by GC. *E*/*Z* ratios of 56:46 and 48:52 were obtained for the olefin from the phenylseleno and mesitylseleno reagents, respectively.

Methyl 2-Phenylseleno-3-hydroxy-3-phenylpropionate (15, Scheme I). To a flask conatining phenylselenoacetic acid (1.075 g, 5.0 mmol) in 20 mL of THF cooled to −78 °C was added 11 mL of 1 M LDA. The dianion was treated with neat benzaldehyde (0.530 g, 0.60 mL, 5.0 mmol). After 5 min the reaction was quenched. An acidic workup afforded crude β-hydroxy selenide which was used without further purification. The selenide was dissolved in 20 mL of ether, cooled to 0 °C, and treated with diazomethane generated from bis(*N*-methyl-*N*-nitroso)terephthalamide.[56] The system was purged by bubbling N_2 through the product mixture. A basic workup and purification by preparative TLC separated the two diastereomers (61:39 mixture, 76% yield). Isomer **15b,** R_f 0.05, was obtained in a 0.778-g yield: NMR δ 3.52 (s, 3 H), 3.76 (d, J = 8 Hz, 1 H), 4.96 (d, J = 8 Hz, 1 H), 7.00–7.35 (m, 10 H). Isomer **15a,** R_f 0.15, was obtained in a 0.50-g yield: NMR δ 3.46 (s, 3 H), 3.73 (d, J = 6.5 Hz, 1 H), 5.00 (d, J = 6.5 Hz, 1 H), 7.00–7.50 (m, 10 H). Crystallization from 20% ether/hexane afforded fluffy, white crystals, 0.506 g, mp 47.5–48.5 °C, white needles, 0.486 g, mp 38.5–39.5 °C, of **15b** and **15a,** respectively.

Anal. Calcd for $C_{16}H_{16}O_3Se$ (**15b**): C, 57.32; H, 4.81. Found: C, 57.35; H, 4.77.

Isomer **15b** can also be prepared from methyl *trans*-cinnamate by treatment with silver trifluoroacetate and benzeneselenenyl chloride using the same procedure as for addition to 1-phenylbutene. The trifluoroacetoxy derivative was hydrolyzed by stirring it with 4 equiv of pyridine and methanol (1:10 v/v) for 2 min. The crude product was purified by preparative TLC with 20% ether/pentane; the NMR spectrum was identical with that for **15b.**

***trans*- and *cis*-Methyl Cinnamate by Reductive Elimination.** Isomer **15b** (0.073 g, 0.218 mmol) in CH_2Cl_2 was treated with NEt_3 (0.110 g, 0.15 mL, 1.09 mmol) and $MeSO_2Cl$ (0.075 g, 0.05 mL, 0.654 mmol) to give methyl *trans*-cinnamate. Similarly isomer **15a** (0.064 g, 0.190 mmol) was treated with NEt_3 (0.096 g, 0.13 mL, 0.950 mmol) and $MeSO_2Cl$ (0.656 g, 0.044 mL, 0.570 mmol) to give a 12:88 mixture of methyl *cis*-cinnamate and dehydrated selenide **16.** NMR spectra for the cinnamates were identical with values reported by Brockhurst et al.[57] The dehydration product was separated by preparative TLC using 10% ether/pentane: NMR δ 3.55 (s, 3 H), 7.19 (m, 3 H), 7.32 (m, 5 H), 7.59 (m, 2 H), 8.04 (s, 1 H); MS M^+ 318.0154 (calcd, 318.0159).

Cyclododecene from 2-Phenylselenocyclododecanone (23). Cyclododecanone was converted to 2-phenylselenocyclododecanone (**23**).[36c] Crystallization from 10% ether/pentane gave needles, mp 49.5–52.0 °C (previously obtained as an oil[36c]). The keto selenide (3.37 g, 10 mmol) was dissolved in 20 mL of benzene in a 50-mL flask equipped with a reflux condenser under N_2. Neat borane–methyl sulfide complex (0.828 g, 1.09 mL, 10.9 mmol) was introduced into the reaction flask by syringe. The reaction mixture was refluxed for 2 h, cooled, poured into 50 mL of H_2O and 50 mL of 50% ether/hexane, and worked up.The solvent was concentrated to give the β-hydroxy selenide: NMR δ 0.98–2.20 (m, 20 H), 2.48 (broad s, 1 H), 3.34 (m, 1 H), 3.65 (m, 1 H), 7.23 (m, 3 H), 7.51 (m, 2 H).

The crude selenide was dissolved in 15 mL of CH_2Cl_2 and converted to olefin according to the general procedure. Kugelrohr distillation (36 °C, 0.37 mm) yielded 1.47 g (88% yield) of cyclododecene as a clear oil: NMR δ 1.00–1.88 (m, 16 H), 1.88–2.36 (m, 4 H), 5.39 (m, 2 H). The ratio of cis/trans isomers was determined to be 62/38 from the relative intensities of the allylic carbons at δ 27.16 (cis) and 32.30 (trans)[58] in the ^{13}C NMR spectrum.

1-Phenylbutene from 2-Phenylseleno-1-phenyl-1-butanone (22). A solution of 2-phenylseleno-1-phenyl-1-butanone[36c] (4.55 g, 15 mmol) in 30 mL of benzene was treated with neat borane–methyl sulfide complex (1.25 g, 1.65 mL, 16.5 mmol) according to the procedure described for reduction of 2-phenylselenocyclododecanone. The crude β-hydroxy senenide was pure by NMR: δ 1.03 (t, J = 7 Hz, 3 H), 1.19–1.82 (m, J = 7 Hz, 2 H), 2.90–3.28 (m, 2 H), 4.46 (d, J = 8 Hz, 1 H), 7.30 (m, 3 H), 7.58 (m, 2 H). It was then treated with NEt_3–$MeSO_2Cl$ to give 1.82 g (92% yield) of an 81:19 *Z*:*E* mixture of 1-phenyl-1-butenes,[55] distilled by Kugelrohr: bp 53 °C (0.37 mm); NMR (*cis*-1-phenylbutene) δ 1.03 (t, J = 7 Hz, 3 H), 2.00–2.57 (m, J = 7 Hz, 2 H), 5.51 (dt, J = 13, 7 Hz, 1 H), 6.28 (broad d, J = 13 Hz, 1 H), 7.13 (s, 5 H).

(*E*)-1,4-Diphenyl-1-butene (Table V, Run 2). The anion of benzyl phenyl selenide (0.495 g, 2 mmol), prepared by addition of 2.1 mmol of LDA solution in THF, was treated with 0.32 mL (2.1 mmol) of 1-bromo-3-phenylpropane at −78 °C. After 15 min, the reaction mixture was poured into 10% HCl and worked up as usual to give 0.63 g of crude 1,4-diphenyl-1-phenylselenobutane.

Pyridine (0.2 mL) was added to a CH_2Cl_2 (5 mL) solution of alkylated selenide obtained above. Water (0.5 mL) and 0.5 mL of 30% H_2O_2 were added to this solution and stirred for 0.5 h. The reaction mixture was poured into saturated $NaHCO_3$ solution, and the combined organic extracts were washed with 10% HCl and saturated NaCl solution, dried, and concentrated. (*E*)-1,4-Diphenyl-1-butene[59] (0.334 g, 81% yield) was isolated by preparative TLC using 10% ether/pentane as eluent: NMR δ 2.49 (m, 2 H), 2.73 (m, 2 H), 6.08 (dt, J = 15 and 5.5 Hz, 1 H), 6.31 (d, J = 15 Hz, 1 H), 7.1 (m, 5 H); IR 3020, 2920, 1595, 1490, 1450, 690 cm^{-1}.

2-Methyl-1-phenyl-1-butene (Table V, Run 3). The anion of benzyl phenyl selenide (0.246 g, 1 mmol), prepared as usual, was treated with 0.11 mL (1.0 mmol) of 2-bromobutane at −78 °C in THF. After 1 h the reaction mixture was quenched with 1.2 N HCl solution and worked up as usual to isolate crude 2-methyl-1-phenyl-1-phenylselenobutane: NMR δ 0.86 (d, J = 7 Hz, 3 H), 0.94 (t, J = 7 Hz, 3 H), 1.19 (m, 2 H), 1.95 (m, 1 H), 4.15 (d, J = 8 Hz, 1 H), 7.1–7.5 (m, 10 H).

Ozone gas was bubbled into a CH_2Cl_2 (3 mL) solution of the alkylated product obtained above at −78 °C until the solution was pale blue. Excess ozone was removed by purging the reaction mixture with N_2 and the cold solution was added to refluxing CCl_4 (10 mL) containing 0.15 mL (1.07 mmol) of *i*-Pr_2NH. The yellow solution was poured into 7% $NaHCO_3$ solution and worked up as usual. Diphenyl diselenide was removed from the concentrated filtrate by treatment with 0.25 mL of H_2O_2, 0.25 mL of water, and 0.1 mL of pyridine in CH_2Cl_2 at room temperature. Preparative TLC of the product obtained after normal workup resulted in isolation of 0.114 g (78% yield) of 2-methyl-1-phenyl-1-butene[60] as a mixture of *E* and *Z* isomers; NMR δ 1.11 (t, J = 7 Hz, 3 H), 1.82 (broad s, 3 H), 4.15 (q, J = 7 Hz, 2 H), 6.21 (s, 1 H), 7–7.4 (m, 5 H); IR 3020, 2960, 1596, 1492, 1440, 695 cm^{-1}.

4-Phenyl-3-buten-2-ol (Table V, Run 4). To a cooled (−78 °C) solution of 2.46 g (10 mmol) of benzyl phenyl selenide in 25 mL of THF was added 10.0 mL of 1 M LDA solution. After 5 min 0.66 mL (10.2 mmol) of propylene oxide was added and stirred for 0.5 h. The reaction mixture was poured into 1.2 N HCl. After normal workup, crude 4-phenyl-4-phenylseleno-2-butanol was dissolved in 30 mL of dichloromethane in a flask equipped with a reflux condenser. To this solution were added 2.5 mL of water, 1 mL of pyridine, and 0.5 mL of 30% H_2O_2. After 5 min of vigorous stirring, when dichloromethane had started to condense on the sides of the flask, it was immersed in a cold water bath and three portions of 0.5 mL each of 30% H_2O_2 were added within 15 min. The reaction mixture was stirred for 15 min, then poured into saturated $NaHCO_3$ solution and extracted with 2 × 70 mL of ether/pentane. The combined organic extracts were washed with 1.2 N HCl solution and saturated NaCl solution, dried, and concentrated. The concentrate upon Kugelrohr distillation gave 0.973

g (66% yield) of 4-phenyl-3-buten-2-ol[61] (bp 42–45 °C, 0.05 mm): NMR δ 1.28 (d, J = 6.5 Hz, 3 H), 3.51 (broad s, 1 H), 4.34 (q, J = 6.5 Hz, 1 H), 6.1 (dd, J = 15, 6 Hz, 1 H), 6.42 (d, J = 15 Hz, 1 H), 7.17 (m, 5 H); IR 3360, 3020, 2970, 1596, 1490, 1450, 745, 690 cm^{-1}.

(*E*)-3-Methyl-1-phenyl-1-butene (Table V, Run 5). Following the procedure given for the preparation of 1,4-diphenyl-1-phenylselenobutane, 0.246 g (1 mmol) of benzyl phenyl selenide and 0.114 mL (1.05 mmol) of isobutyl bromide gave 0.251 g of alkylated product.

The product selenide was oxidized and eliminated, following the procedure given for the preparation of (*E*)-1,4-diphenyl-1-butene, to yield 0.104 g (66%) of (*E*)-3-methyl-1-phenyl-1-butene[62] isolated by preparative TLC: NMR δ 1.05 (d, J = 7 Hz, 6 H), 2.44 (octet, J = 7 Hz, 1 H), 5.05 (dd, J = 16 and 7 Hz, 1 H), 6.06 (d, J = 16 Hz, 1 H), 7.2 (m, 5 H); IR 3040, 2979, 1600, 1497, 1468, 1452, 750, 695 cm^{-1}; MS M^+ 146.1094 (calcd, 146.1096).

1-Phenyl-1-phenylselenino-2-butanol (26). A solution of **25** (0.232 g, 0.761 mmol) in 10 mL of CH_2Cl_2 was treated with ozone until the blue color of excess ozone appeared. The reaction mixture was purged with nitrogen and the solvent concentrated at reduced pressure. The resultant pale yellow powder was washed three times with CCl_4 to yield white, powdery crystals of the selenoxide. Recrystallization of 16 mg from 40 mL of CCl_4 produced fine, white needles: mp 110–112 °C dec; NMR ($CDCl_3$) δ 0.90 (t, J = 7 Hz, 3 H), 1.34 (m, J = 7 Hz, 3 H), 3.80 (d, J = 4 Hz, 1 H), 4.64 (m, 1 H), 7.33 (s, 10 H); IR ($CHCl_3$) 3200 cm^{-1}.

Anal. Calcd: C, 59.79; H, 5.65. Found: C, 59.64; H, 5.47.

The selenoxide **26** can be prepared by a second route. Benzyl phenyl selenoxide was prepared by ozonolysis of benzyl phenyl selenide. To the selenoxide (0.056 g, 0.213 mmol) in 2 mL of THF at 0 °C was added 0.25 mL of 1 M LDA. The reaction mixture was cooled to −78 °C and neat propionaldehyde (0.023 g, 0.03 mL, 0.40 mmol) was added by syringe. After 10 min, the mixture was transferred into 5 mL of water and 10 mL of ether. The organic phase was washed with aqueous NaCl, dried, and concentrated. The selenoxide fell out as a white powder; the NMR spectrum showed a mixture of diastereomers in a 49:51 ratio.

Warming a solution of **26** in CCl_4 to 80 °C produced 1-phenyl-1-phenylseleno-2-butanone (**30**): NMR δ 0.92 (t, J = 7 Hz, 3 H), 2.38 (q, J = 7 Hz, 2 H), 4.80 (s, 1 H), 7.12 (m, 10 H); MS M^+ 304.0380 (calcd, 304.0366).

Acknowledgment. We gratefully acknowledge support of this work by the National Science Foundation (Grant CHE 77-15988) and the Wisconsin Alumni Research Foundation. The National Science Foundation also provided funds for the purchase of a mass spectrometer data system (Grant CHE 77-08961). H.J.R. expresses his appreciation to the Du Pont Co. for a Young Faculty Grant and the A. P. Sloan Foundation for a Fellowship. Mr. David Ting assisted in the preparation of a number of selenides.

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Selenium Stabilized Carbanions. α-Lithio Selenoxides as Reagents for the Synthesis of Olefins, Allyl Alcohols, and Dienes[1]

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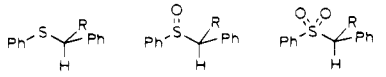
Abstract: Techniques for the preparation of α-lithio selenoxides have been developed. These reagents react cleanly with most aldehydes and ketones to give β-hydroxy selenoxides, which can be thermolyzed to allyl alcohols or reduced to β-hydroxy selenides. The β-hydroxy selenides are further transformed to olefins by reductive elimination. α-Lithio selenoxides can also be alkylated and acylated, although these reactions are of lesser scope and usefulness than the reaction with aldehydes and ketones. A synthesis of 1,1-bis(phenylseleno)cyclopropane was developed based on an intramolecular alkylation of an α-lithio selenoxide. The compound is a suitable precursor for the preparation of 1-phenylselenocyclopropyllithium, which was used to prepare cyclopropyl phenyl selenide and 1-phenylselenocyclopropanecarboxylic acid.

Heteroatom stabilized organometallic reagents are powerful tools for the formation of functionalized carbon–carbon bonds. The most widely used reagents of this type are the phosphonium ylides (Wittig reagents), although sulfonium ylides and phosphorus, sulfur, and to a lesser extent silicon stabilized anions have become increasingly important. Developments in the preparation and reactions of selenium stabilized lithium and other organometallic reagents have been fostered by the interesting and useful chemistry available to selenides and selenoxides.[3] In the preceding paper[4] the chemistry of α-lithio selenides was presented. We report here the results of our study of the preparation and reactions of α-lithio selenoxides.

The incentive for the study of α-lithio *selenoxides* is provided by the lack of satisfactory procedures for the general preparation of α-lithio *selenides* by deprotonation of selenides, a result of the limited acidifying power of the phenylseleno group, and the propensity of selenides to be fragmented upon treatment with powerful metalating agents. The substantially greater acidity expected for selenoxides, however, should allow their deprotonation in cases where the corresponding selenides are insufficiently acidic. The greater acidity of selenoxide vs. selenide can be inferred from comparisons with kinetic and thermodynamic acidity data available for sulfides, sulfoxides, and sulfones. Bordwell and co-workers[5] have reported the following pK_a data (Me_2SO solvent and references).

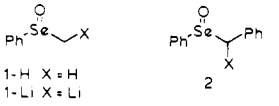


R = Ph	26.7	24.5	22.3
R = H	30.8		23.4

Since most alkyl selenoxides are at best only marginally stable at room temperature,[6] it is not surprising that deprotonations and pK_a studies of selenoxides had not been attempted. In addition to their thermal instability, selenoxides have physical properties which present difficulties in manipulation. They are extremely polar. Many are hygroscopic and tenaciously retain water of hydration.[7] As a result, the lower alkyl selenoxides are sufficiently water soluble that significant losses can accompany an aqueous workup.

Results and Discussion

Preparation of α-Lithio Selenoxides. To assess the viability of these reagents as synthetic intermediates, exploratory work was carried out with the relatively stable selenoxides, **1**-H and **2**-H, and the derived lithium reagents, **1**-Li and **2**-Li. Methyl



1-H X = H
1-Li X = Li

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phenyl selenoxide (**1**-H) could be prepared by ozonization of methyl phenyl selenide in dichloromethane. Purification of the selenoxide beyond simple removal of solvent led to decomposition or the essentially irreversible absorption of water of hydration. For this reason, an in situ generation of the lithio compound is preferable for **1**-Li; the procedure is described below.

In contrast benzyl phenyl selenoxide (**2**-H) is more tractable: it can easily be obtained anhydrous and crystalline.[8] Deprotonation of **2**-H with lithium diisopropylamide (LDA) in THF at −78 °C appears to lead smoothly to the α-lithio selenoxide **2**-Li as indicated by the formation of olefins upon alkylation and selenoxide syn elimination (see Table II). The more easily prepared α-lithio selenide[4,9] analogous to **2**-Li would seem to be preferable for most applications since it is a better nucleophile. The only exception might be in a situation where an easily oxidized function was present in the electrophile.

Our approach to the preparation of lithium reagents from thermally labile selenoxides involves the low-temperature oxidation of selenides and in situ deprotonation of the resultant selenoxides. The oxidant for this purpose must be reactive at low temperatures under anhydrous conditions, must not leave byproducts which interfere with subsequent organometallic reactions, and must be compatible with ether solvents. Of many reagents available for the conversion of selenides to selenoxides (O_3, RCO_3H, H_2O_2, $NaIO_4$, $PhICl_2/H_2O$, Cl_2, Br_2/H_2O, N_2O_4, $Tl(NO_3)_3$, *t*-BuOOH),[3a] only two, ozone and *m*-chloroperbenzoic acid, met these requirements.

Ozone has a long history as a convenient oxidant for the preparation of selenoxides.[10] Further oxidation to selenone can

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