Tetrahedron. Vol. 34, pp. 1049 to 1132. Pergamon Press 1978. Printed in Great Britain

TETRAHEDRON REPORT NUMBER 50

MODERN ORGANOSELENIUM CHEMISTRY

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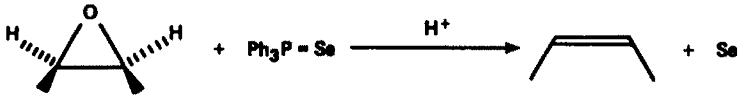
INTRODUCTION

Allylic hydroxylation by selenium dioxide and the use of elemental selenium for dehydrogenation and isomerisation of olefins have been known for many years.[1] Beginning in 1973 several new reagents, in which selenium is attached to an organic structure, have been introduced for synthesis, but before this date the *formal* use of selenium-containing species as reagents—other than the element and its dioxide—was sporadic and not properly appreciated. However, in the last four years the new reagents have been accepted avidly by synthetic chemists and this Report is an analysis of the role now played by selenium and its compounds in organic chemistry.[a]

SURVEY OF MODERN ORGANOSELENIUM CHEMISTRY

The first modern work in which a selenium-containing substance was introduced *explicitly* as a *general* reagent for use in synthesis is the discovery that epoxides are converted into olefins by treatment with triphenylphosphine selenide in the presence of an acid[3] (eqn 1).

Shortly afterwards three groups[4-6] recognised, independently, that selenoxide fragmentation—the *syn* elimination process summarised by eqn (2)—constitutes a very mild procedure for introducing unsaturation into a carbon sigma-bond system. Methods were found for attaching the phenylseleno-group (PhSe-) to organic molecules so that the gentle and efficient fragmentation of the derived selenoxide could be used to make carbon–carbon double bonds. The procedures have been developed to a high level of refinement and they now constitute a standard synthetic method for introducing unsaturation (eqns 3 and 4).



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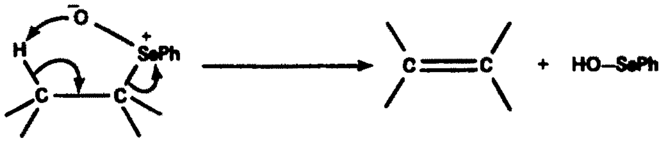

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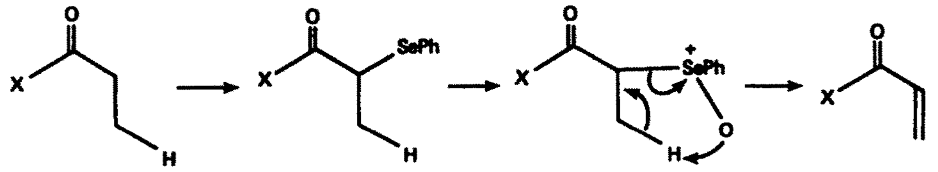
[a] The abstracted literature from Jan. 1967 to Oct. 1976 (*Chem. Abstr.* 85(14), 1976) was examined. Very thorough coverage of earlier research is already available.[2]



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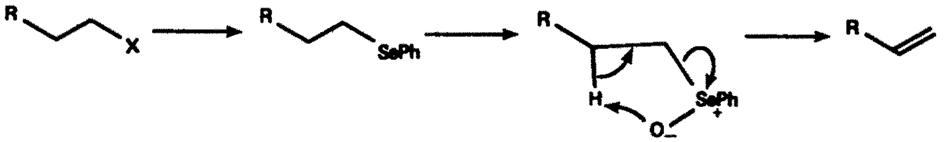


(4)

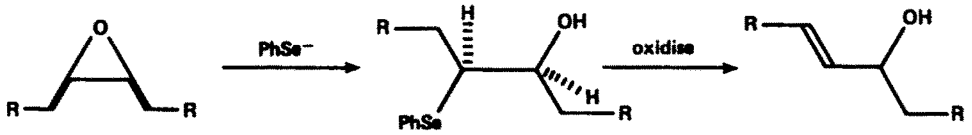
Epoxides can be converted into allylic alcohols by ring-opening with PhSe$^-$ followed by selenoxide fragmentation (eqn 5) and the intermediate β-hydroxyalkyl selenides can be converted into olefins in the sense of eqn (6). The latter is not a trivial process because β-hydroxyalkyl selenides are also available from ketones and aldehydes by treatment with selenium-stabilized carbanions (eqn 7). These anions, which are highly nucleophilic, are readily generated by the action of butyl lithium on selenoketals (eqn 8).

Important new experiments have also been done with the traditional reagents, selenium dioxide and selenium metal. The element can play a catalytic role in the reaction of amines and alcohols with carbon monoxide to produce, for example, ureas and carbonates (eqns 9 and 10).

Substantial insight into the mode of action of selenium dioxide on olefins has been obtained and the results, which are summarised by eqn (11) have led to the discovery of aza-analogues of the dioxide which have the ability to aminate olefins (eqn 12).

In addition, a new use has been discovered for selenium dioxide: it converts semicarbazones into 1,2,3-selenadiazoles which collapse at high temperatures to produce acetylenes (eqn 13).

Finally, the synthesis of selenium-containing fulvenes as components of organic metals has developed rapidly and has been reviewed.[7]



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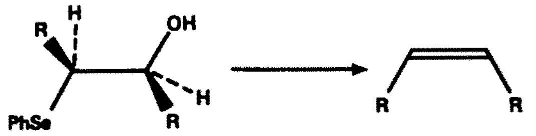

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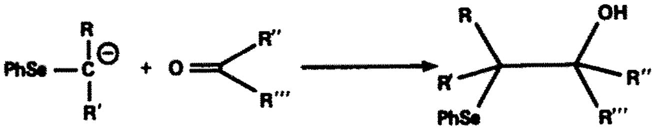

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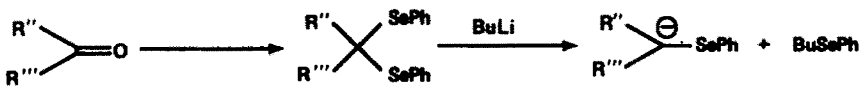

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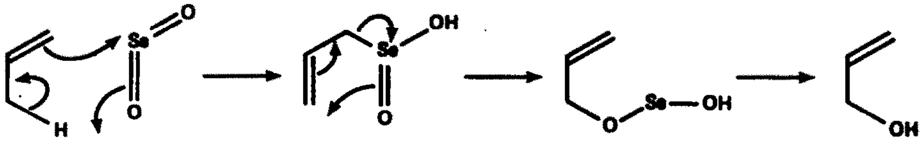
$$\mathrm{RNH_2 + CO + Se \xrightarrow{base} RNHCONHR} \qquad (9)$$

$$\mathrm{ROH + CO + Se \xrightarrow{base} ROCOOR} \qquad (10)$$



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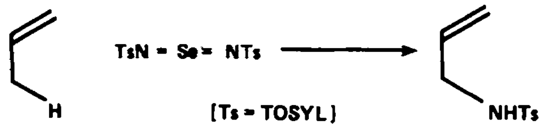

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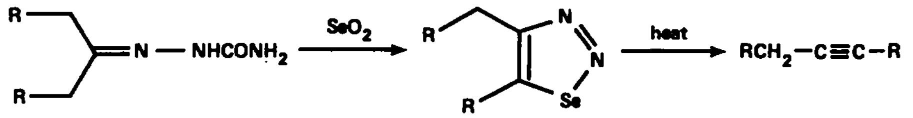
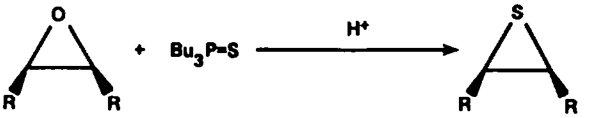


(13)

1. CONVERSION OF EPOXIDES INTO OLEFINS

The observation[8] that epoxides are convertible into episulphides (eqn 14) by treatment with a phosphine sulphide in the presence of acid suggested that a similar reaction might occur in the selenium series; although an episelenide was not expected to be the final reaction product. Previous attempts to make episelenides had, instead, afforded the derived olefin.[9] The generation of episelenides in the gas phase and their collapse into olefins had, however, been observed spectroscopically[10] and so the proposed reaction (eqn 15) would constitute a method for deoxygenating epoxides.[b] Phosphine selenides have been known for many years[12] but they had not been used before in synthesis. We examined triphenylphosphine selenide, choosing it for ease of preparation and handling, and found that it reacts with epoxides according to eqn (15).



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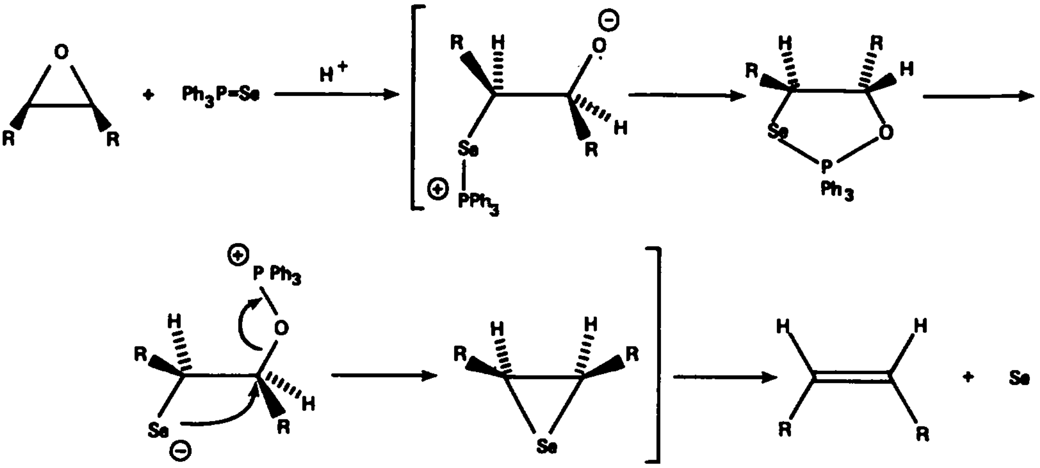


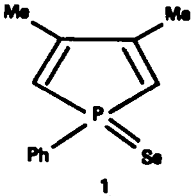
(15)

Experimentally, the process involves adding trifluoroacetic acid [1 equiv.] in dichloromethane to a solution, in the same solvent, of the epoxide and an excess of triphenylphosphine selenide. Metallic selenium is deposited and the olefin can be isolated after a suitable time which is usually less than 2.5 hr. Typical results[3] are shown in Table 1.

A strong acid is essential[13] and the reaction is similar to the corresponding[8] process for the sulphur series but is followed by loss of selenium from the episelenide with preservation of stereochemical integrity. Formal analogy for extrusion of a heavy atom (with a triplet ground state) is available in the stereospecific thermolysis of episulphides.[14]

Further studies[15] have provided support for the above mechanism (eqn 15),and formation of the intermediate episelenide, as well as its collapse, can be followed spectroscopically. It has also been possible to isolate an episelenide in solution but attempted concentration, even at −40°, led to deposition of Se and production of olefin. Possibly the collapse of episelenides is bimolecular.[15]

The deoxygenation is not limited to tributyl-[15] and triphenylphosphine selenides and, in fact, they are both much less reactive in this process than the heterocyclic selenide 1.[16] Incorporation of the phosphorus atom into a 5-membered ring should favour[17] production of the proposed intermediate phosphorane 2 and this factor may be responsible for the enhanced reactivity of 1.



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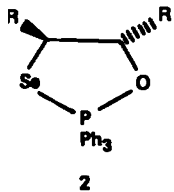

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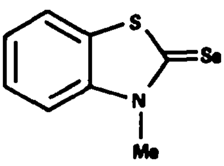
[b] It should be noted that epoxides of predictable stereochemistry are available by reaction of a Grignard reagent with an α-chloroaldehyde.[11]

Table 1.

Epoxide	Olefin Yield
1,2-epoxyoctane	71%
trans-2-epoxyoctane	68
cis-2-epoxyoctane	73
cis-stilbene	71
cyclohexene oxide	53[a]
cis-cyclooctene oxide	72[b]

[a] This yield refers to the crystalline derivative with 2,4-dinitrobenzene-sulphenyl chloride. [b] Refluxing CH_2Cl_2 (19 hr) was used.

Recently, a very promising modification of the phosphine selenide route has been discovered.[18] The selenoxobenzothiazole 3, in stoicheiometric proportions,



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reacts very rapidly with epoxides in dichloromethane in the presence of CF_3COOH [1 equiv.] (eqn 16). The reaction is fast even at −15°.

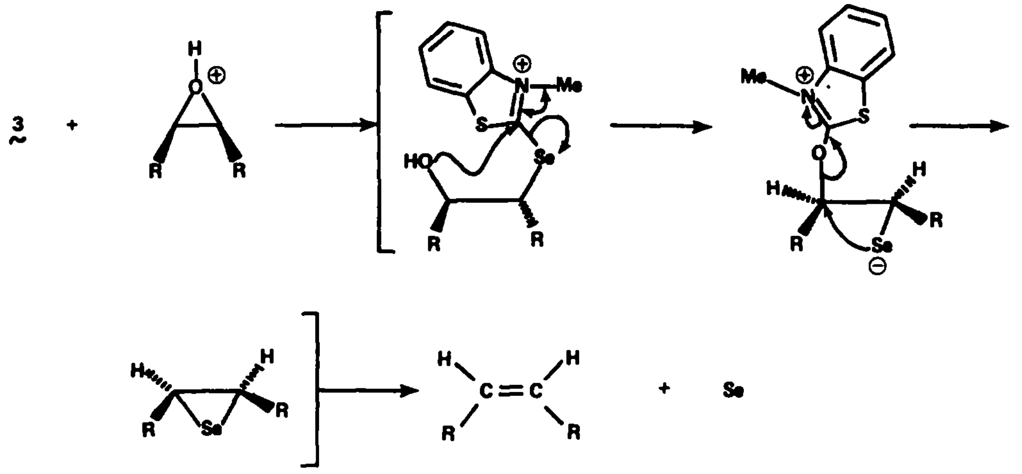
Cyclohexene, styrene, *cis*- and *trans*-stilbene and chloroethylene were made in better than 90% yield. The reagent 3 also converts[18] episulphides into olefins but this reaction is slower and a higher temperature (47°) is desirable.

This heterocyclic reagent as well as triphenylphosphine selenide and tributylphosphine selenide have been examined in sufficient detail to be able to predict that the relative geometry about the carbon–carbon bond of an epoxide is retained and that yields of olefin are usually high. Acidic media are necessary with all of these reagents but exposure to acid is not for prolonged periods because the deoxygenations are usually fast. Moreover, some protection from the acid may be afforded by the basic nature[19] of the phosphine oxide that is produced.

The purely inorganic reagent, potassium selenocyanate, also reacts with epoxides.[9a] The deoxygenation, which works best for terminal epoxides,[13,20] is generally slow and its effectiveness depends on the solvent.[21] It appears necessary to use a protic solvent because the reaction does not work in dimethylformamide or dimethyl sulphoxide,[21] but aqueous alcohols, in which KSeCN produces an alkaline solution,[21] are suitable. The reaction probably proceeds with a high (at least 90%) degree of retention of stereochemistry[22] by means of the mechanism shown (eqn 17).

The response of cyclic epoxides to KSeCN is variable:[21] cyclohexene epoxides are deoxygenated and so is cycloheptene epoxide (34% yield) but simple cyclic C_5, C_8 and C_{12} epoxides are inert.

Clearly, the use of KSeCN is indicated when acidic



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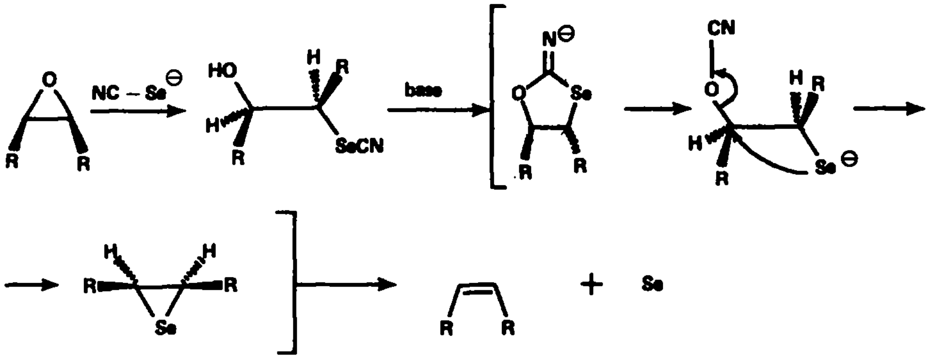
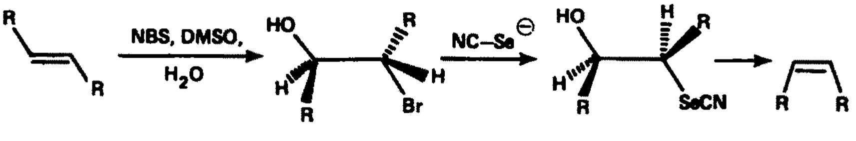


(17)

conditions must be avoided but the compound has utility in another context: that of inverting the geometry of an olefin[22] (Section 2).

2. INVERSION OF OLEFIN GEOMETRY

Bromohydrins (derived by *trans* addition of hypobromous acid to olefins) react with KSeCN in DMF.[22] Careful control of the reaction conditions [24–48 hr; 60°] produces the stereochemical results of the type shown (4→5) and treatment of the β-hydroxyalkyl selenide 5 with potassium carbonate yields an olefin whose geometry is opposite to that of the starting olefin (eqn 18).



4 5 (18)

Only a few simple acyclic olefins have been examined; yields, from bromohydrin are below 60% but the extent of inversion is high (at least 88%) and the conditions fairly mild.

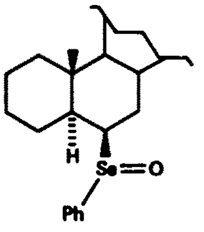
3. SELENOXIDE FRAGMENTATION

(A) *General considerations*

Early studies[23] of the oxidation of phenyl alkyl selenides and the decomposition of phenyl alkyl selenoxides did not reveal the potential applications of these compounds to synthesis and their utility was not appreciated for many years.

My own attention was directed[24] towards these selenium compounds by two noteworthy observations that appeared in the then current literature:

The selenoxide 6 (as a mixture of *R* and *S* isomers) was observed to decompose in hexane to 5α-cholest-6-ene. The process was rapid at room temperature and the yield greater than 95%.[25] The (*S*)-selenoxide 7 actually collapsed quantitatively within 4 hr at 0°.



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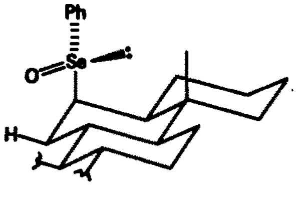

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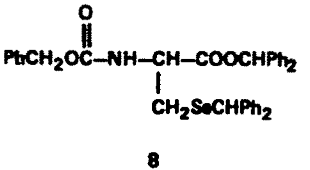
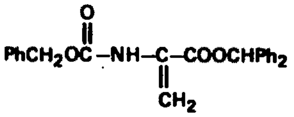
The second report[26] was an account of attempts to oxidise the selenide 8 to the corresponding selenoxide. None of the desired material was isolated. Instead, the selenide 6 was converted completely at room temperature to the (protected) dehydroalanine 9.



$$\mathrm{PhCH_2O}\overset{\overset{\mathrm{O}}{\|}}{\mathrm{C}}\mathrm{–NH–}\underset{\underset{\mathrm{CH_2SeCHPh_2}}{|}}{\mathrm{CH}}\mathrm{–COOCHPh_2}$$

8



$$\mathrm{PhCH_2O}\overset{\overset{\mathrm{O}}{\|}}{\mathrm{C}}\mathrm{–NH–}\underset{\underset{\mathrm{CH_2}}{\|}}{\mathrm{C}}\mathrm{–COOCHPh_2}$$

9

It was clear from the above observations[25,26] that selenoxides are synthetically equivalent to olefins and this conclusion definitely merited experimental study.

The preparation of selenoxides from selenides had fortunately been investigated before in some detail[23b,27] and adequate methods were therefore available for oxidising selenides to the selenoxide level. The use of selenoxide fragmentation (eqn 2, p. 1050) in synthesis would depend critically upon effective methods for introducing selenium as, for example, PhSe– into organic molecules. These,[4] and similar considerations made elsewhere,[5,6] led to a comprehensive examination of selenide chemistry and methods were found for the controlled introduction of selenium into organic structures. The techniques involve nucleophilic displacement (see p. 1064) by $PhSe^-$ or the capture of electrophilic selenium compounds (such as PhSeBr) by enolates (p. 1057) and olefins (p. 1081) or more sophisticated processes employing selenium-containing synthons (p. 1069).

These procedures, together with some auxiliary developments, have established selenoxide fragmentation as a reliable and efficient method for making unsaturated systems, especially α,β-unsaturated carbonyl compounds, terminal olefins and allylic alcohols. The literature on the subject is now extensive and I analyse it under the following general aspects:

(i) Types of selenoxide that undergo fragmentation readily.

(ii) Methods for making suitable selenides.

(iii) Methods for oxidising selenides to selenoxides and practical details for fragmentation of selenoxides.

(iv) Stereo- and regiochemistry of selenoxide fragmentation.

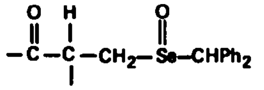
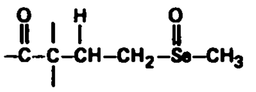
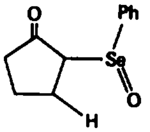
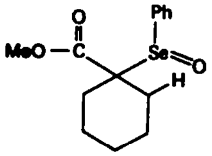
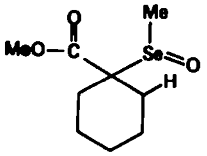
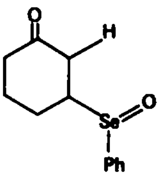
(B) *Types of selenoxide that fragment readily*

Examination of the types of selenoxide that can be isolated at room temperature reveals the structures most suitable for the fragmentation process (see Table 2).

In those cases where an α,β-unsaturated carbonyl system is being generated by fragmentation involving a hydrogen atom *alpha* to the carbonyl then the selenium atom need not necessarily be attached to an aromatic ring (compare entries 3 and 8). Entries 6 and 7 show the isomeric situation in which an α,β-unsaturated carbonyl system is formed but the hydrogen removed is *beta* to the carbonyl group. Here an aryl selenoxide (entry 6) is preferable but not essential.

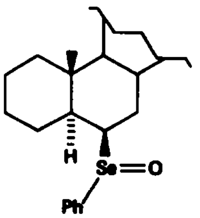
Where the resulting double bond is not conjugated and the hydrogen removed is unactivated, then the selenium atom should carry an aromatic ring (compare entries 1

Table 2.

Compound	Stability	Ref.
1  $\text{alkyl}-\overset{\overset{O}{\|}}{Se}-\text{alkyl}'$	isolable	23b; 28; 29
2  $\text{alkyl}-\overset{\overset{O}{\|}}{Se}-Ph$	fragments	5; 25
3  $-\overset{\overset{O}{\|}}{C}-\underset{\|}{\overset{\overset{H}{\|}}{C}}-CH_2-\overset{\overset{O}{\|}}{Se}-CHPh_2$	fragments	26
4  $-\overset{\overset{O}{\|}}{C}-\underset{\|}{\overset{\|}{C}}-\overset{\overset{H}{\|}}{C}H-CH_2-\overset{\overset{O}{\|}}{Se}-CH_3$	isolable	26
5 	fragments	4
6 	fragments (olefin yield: 90%)	30
7 	fragments (olefin yield: 40%)	30
8 	fragments	5

and 2). However, not all aryl-alkyl selenoxides collapse easily. Excluding the possibility that situations may arise where the conformation necessary for *syn* elimination is inaccessible[31] or where the resulting double bond would generate excessive ring strain, it appears that phenyl cycloalkyl selenoxides (e.g. **10**[25] and **11**[5]) fragment easily as do phenyl secondary-alkyl selenoxides[5] (e.g. **12**). However, phenyl primary alkyl selenoxides (e.g. **13**) collapse much less readily[5,32–36] especially when the β or γ carbons carry alkyl groups.[32,37] Three methods are available to cope with such problems.

Method 1. The aryl group can be made strongly electron-withdrawing.[5,34,38] As Table 3 shows substituents on the aromatic ring have an appreciable influence on the



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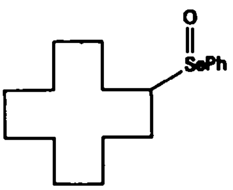

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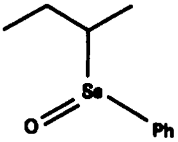
rate of selenoxide fragmentation and on the yield of olefin.[32] Unfortunately, the substituted selenides (and hence the selenoxides) are not always as easy to prepare in good yield as the unsubstituted parent compounds.[32]



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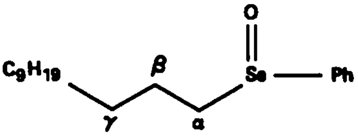

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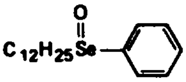
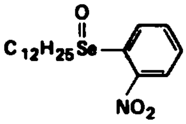
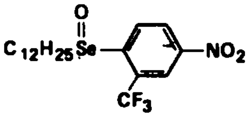
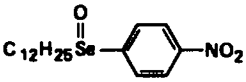
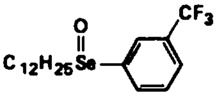
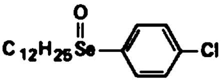
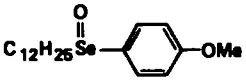
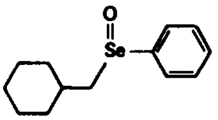
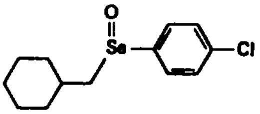
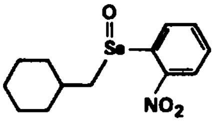
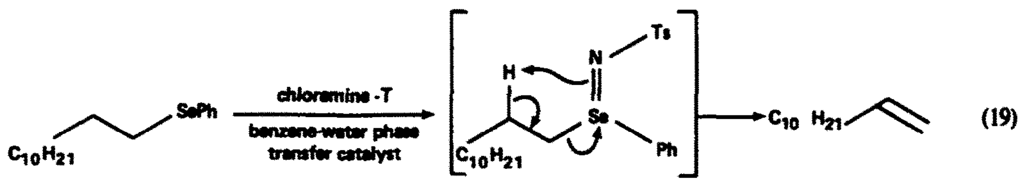
Method 2. A promising, but as yet unexplored, technique for increasing the facility of olefin formation is to use a selenonium imide 14 instead of the corresponding selenoxide.[35] In the single example published (eqn 19) the imide 14 was made *in situ* by the action of Chloramine-T on the selenide. Both the oxidation and elimination are complete in less than 20 min at room temperature to give 1-dodecene in 77% yield. The corresponding selenoxide fragmentation requires 20 hr at room temperature to generate the same yield of dodecene.[35]

Method 3. It is sometimes possible to improve the efficiency of selenoxide fragmentation by adding the

Table 3.[32]

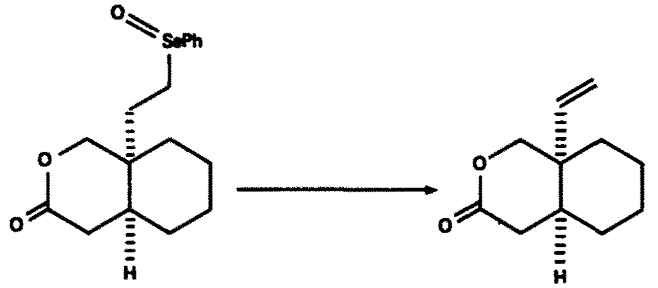
	Selenoxide	Fragmentation Conditions		Yield of Olefin
		Temp.	Time[a]	
1		25°C	20 h	77%
2		0	0.5	91%
3		25	0.5	88%
4		25	1.5	93%
5		25	2.0	70%
6		25	6.0	77%
7		25	7.0	60%
8		25 25	9.5 48.0	47% 46%
9		25	9.5	85%
10		25	9.5	92%

[a] Times were measured after completion of oxidation of the corresponding selenides. For the last three entries it is not clear from the literature whether the times shown include a brief [~30 min] period for oxidation of the selenides.



14

(19)



15 16

selenoxide to a refluxing solvent[36,39] (see p. 1106). For example, addition of selenoxide 15 to boiling carbon tetrachloride[36] (as opposed to heating a solution of 15) gave the olefin 16 in 61% yield (calculated from the selenide corresponding to 15).

4. SELENOXIDE FRAGMENTATION: PREPARATION OF SELENIDES AND SELENOXIDES

The methods used to make selenides suitable for the fragmentation reaction or for other processes (see later) are of 4 types:

(i) Replacement of an activated hydrogen (e.g. conversion of a ketone into an α-phenylselenoketone).

(ii) Use of a nucleophilic selenium anion (e.g. $PhSe^-$) to displace a leaving group, to open an epoxide, or for Michael addition to an α,β-unsaturated system.

(iii) Use of selenium-containing synthons.

(iv) Addition of reagents of the general class PhSe–X across a multiple bond.

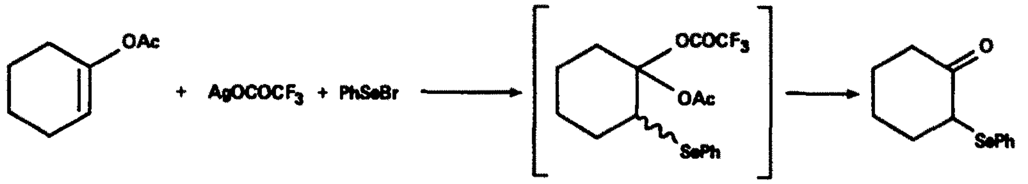
(A) CONVERSION OF COMPOUNDS WITH AN ACTIVATED HYDROGEN INTO SELENIDES

This important class of reactions deals mainly with the *alpha*-selenenylation of ketones, esters and lactones. Other compound types such as aldehydes and nitriles have not been studied so thoroughly.

The approach in all cases is to generate some species in which charge density is available at the *alpha* carbon so that reaction occurs with a selenenylating agent, PhSe–X. Enols, enolates, enol esters and enol silyl ethers are suitable and X can be Br, Cl, $OCOCF_3$ or PhSe.[c]

(a) Phenylselenenylation of ketones and aldehydes

(i) *Phenylselenenylation via enol derivatives.* In my own experiments[4] enol acetates[d] were converted into α-phenylselenoketones by treatment [0–25°] with PhSeBr in the presence of a slight excess of silver trifluoroacetate. Possibly, an intermediate of type 17 is formed. Very mild hydrolysis gives the α-phenylselenoketone (eqn 20).



17

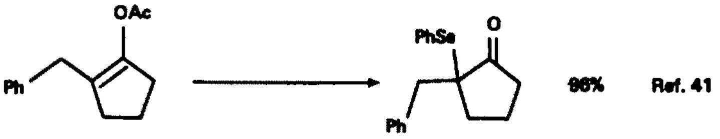
(20)

The phenylseleno-derivative of cyclohexanone was isolated in 70% yield; that from cyclopentanone in 62%. Conditions for the overall transformation were not optimised in this early work but the reactivity of enol acetates under extremely mild conditions[45] has been confirmed by independent experiments[41] and an alternative procedure has been developed.[46] In this, the enol acetate is added to a slight excess of $PhSe–OCOCF_3$, preformed in benzene from PhSeBr and CF_3COOAg. Reaction appears to be almost instantaneous at room

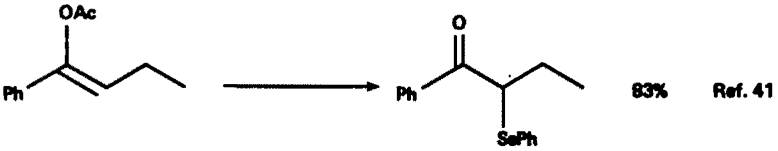
---

[c] Diphenyl diselenide (PhSe–SePh)[32,40,41] and phenyl selenenyl chloride (PhSe–Cl)[41,42] are commercially available but also easy to prepare. Phenylselenenyl bromide (PhSe–Br)[41,42,43] can be made *in situ* by adding bromine to diphenyl diselenide.[41] Tetrahydrofuran is a convenient solvent as it is frequently used for generation of enolates. An excess of bromine must be avoided because the $PhSeBr_3$ produced is a brominating agent.[41]

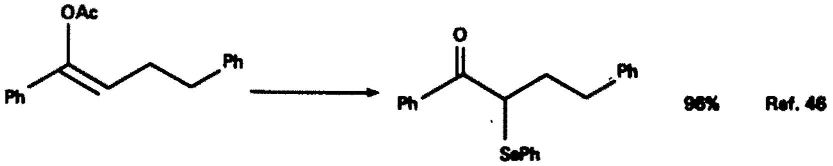
[d] The suitability of silyl enol ethers for reaction with selenenyl reagents (PhSe–X) has been recognised[e] but no details are yet available. Silyl enol ethers react with benzene sulphenyl chloride.[44]



98% Ref. 41 (21)



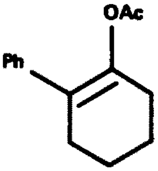
83% Ref. 41 (22)



98% Ref. 46 (23)

temperature and brief exposure to water serves for the hydrolysis stage. The product can be isolated in good yield (eqns 21–23).

The range of enol acetates that has been studied has not been reported[41] but several have evidently been examined[41] and only compound **18** failed to react.



18

Most methods for making α-phenylselenoketones involve basic conditions; therefore, the present method is a potentially valuable option. Moreover, for unsymmetrical ketones, it is generally possible to prepare the more highly substituted enol acetate isomer[47] and so α-phenylselenoketones regioisomeric with those derived from the kinetic enolate (see p. 1059) are accessible.[41] Besides direct reaction with $PhSeOCOCF_3$, an enol acetate can be converted into the corresponding enolate which is then selenenylated (see p. 1059). This variation is sometimes preferable[41] (as in the case of the enol acetate **18**).

(ii) *Phenylselenenylation via enols.* Both ketones and aldehydes react with benzeneselenenyl chloride (PhSeCl) and are converted into the corresponding α-phenylseleno-carbonyl compound[35,42] (e.g. eqn 24). The reaction, which is run in ethyl acetate solution and proceeds through the enol, is usually slow but can be accelerated by deliberate addition of HCl.[e] Prior to oxidation[f] it is essential to remove all HCl[g] but apart from this operation it is not usual to purify the selenide. Typical results[42] are collected in Table 4 in which the yield of enone gives some indication of the efficiency of the selenenylation process.

The following compounds (**19**–**22**) show the range of functional groups that appraently do not interfere with the use of PhSeCl.[35,h]

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[e] PhSeBr cannot be used instead of PhSeCl.

[f] Oxidation of selenides is discussed on p. 1087.

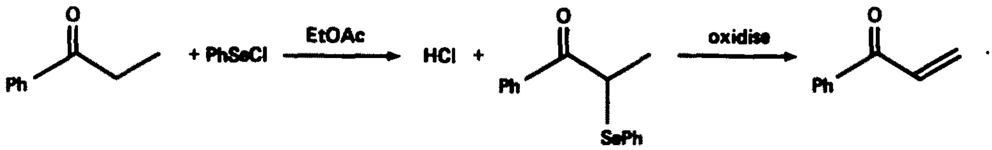
[g] As described on p. 1107 acid interferes with selenoxide fragmentation.

[h] In all these cases a complication is met in the oxidation stage. The initial products undergo Baeyer–Villiger rearrangement.

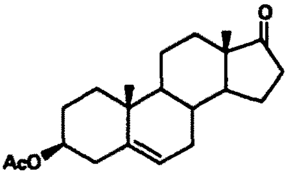
Table 4.

Carbonyl Compound	Time for reaction with PhSeCl	Yield of enone[a]
4-*tert*-butylcyclohexanone	0.25 h	74% (5%)
4-acetoxycyclohexanone	1.	53 (12)
cyclodecanone	5.	77 (5)
3-cholestanone	0.75	84[b] (4)
4-heptanone	5.	64 (13)
2-heptanone	2.	34[c] (29)
propiophenone	35.	84 (7)
hydrocinnamaldehyde	36.	67 (8)
dodecylaldehyde	20.	46 (13)

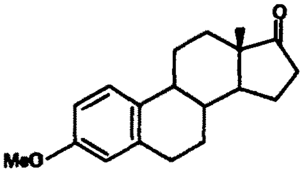
[a] Yields in parentheses refer to recovered starting carbonyl compound. [b] This is the yield of cholest-1-en-3-one. [c] Presumably 1- and 3-phenylselenoheptanones were formed.



(24)



19



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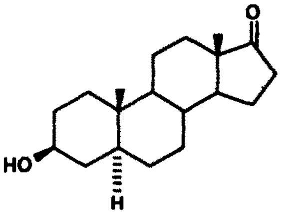
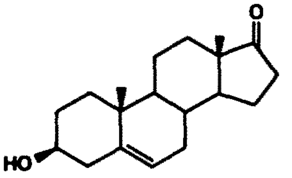


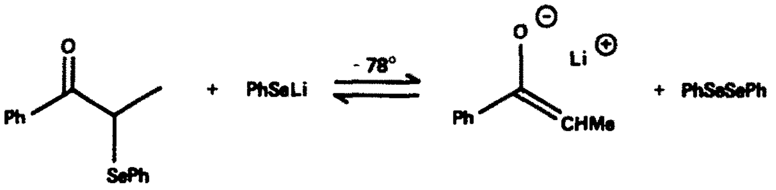
21



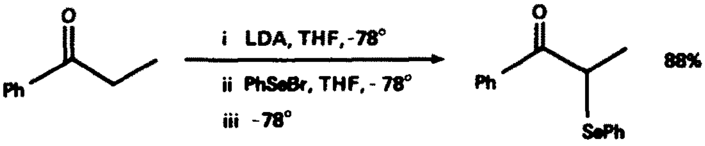
22

(iii) *Phenylselenenylation via enolates.* The majority of published α-selenenylation reactions of ketones (*not* aldehydes) have used the kinetic lithium enolate which is usually generated by adding the ketone in tetrahydrofuran to a slight excess of lithium diisopropylamide[i] in the same solvent at −78°. After keeping the mixture for about 10 min at this temperature a THF solution containing PhSeBr[j] [equivalent in molar amount to the LDA used[6,41] or slightly in excess[41] is then added rapidly to the resulting enolate. Reaction is almost instantaneous and, in the following typical example (eqn 26),[41] the cold mixture was subjected directly to aqueous work-up. In other cases[6] the mixture appears to have been warmed first to 0° before treatment with water.

This general procedure has been applied to the following ketones (Table 5).



(25)



(26)

A number of modifications to the general experimental technique are sometimes needed. Occasionally the enolate is best formed, and quenched, at very low temperature [−100° in the case of 3-phenylcyclobutanone[41] (entry 10 of Table 5)] and it can also be advantageous to generate the enolate in the presence of hexamethylphosphoric triamide,[6,41] as was done with entry 6 of Table 5.

The use of LDA is, of course, not the only way of making enolates of ketones and two examples of alternative procedures have been published[41,49] in selenium chemistry (see the following Sections 4 and 5).

(iv) *Phenylselenenylation of enolates derived from enol acetates.*[k] The enol acetate 18, which does not react with $PhSe\text{-}OCOCF_3$,[41] was converted[41,49] by standard methods [2.5 equiv. MeLi at −20-0°] into its enolate to which PhSeBr [2.75 equiv.] was then added rapidly at

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[i] This is not the only lithium amide that is suitable. Lithium *N*-isopropylcyclohexylamide[42] has also been used.

[j] PhSeCl can also be used[41] as can *meta*-trifluoromethylbenzeneselenenyl chloride.[41] PhSeSePh can be used with ester, lactone and nitrile enolates (see p. 1061) but is is not suitable with ketone enolates. For example, the equilibrium shown in eqn (25) lies well to the right.[41] The reaction of ketone enolates with PhSe–X (X = Cl or Br) is probably more rapid than proton transfer from the α-phenylseleno-ketone to residual enolate. For this reason, 2-methylcyclohexanone gave only the product of monosubstitution at the 6-position and no disubstituted product.[41] Equilibration between enolates is therefore not usually a problem.[41] For the acidity of α-phenylthioketones (See Ref. 48).

[k] See also p. 1057.

Table 5.

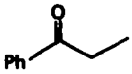
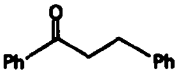
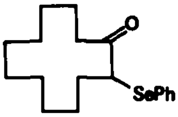
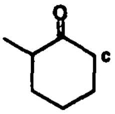
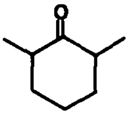
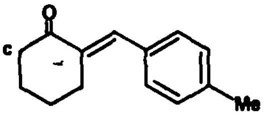
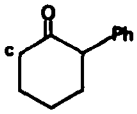
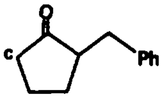
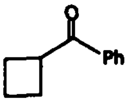
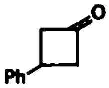
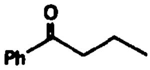
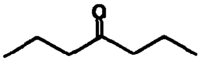
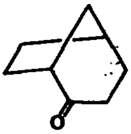
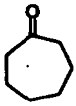
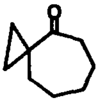
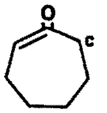
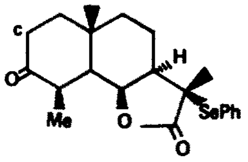
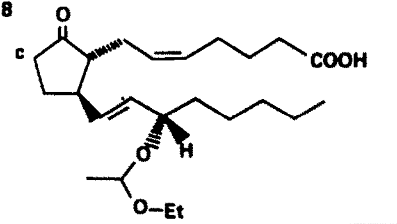
	Ketone	Yield of Selenide[a, b]	Ref.
1		88	6,41
2		(84)	6, 41
3		(72)	6, 41
4		89	41
5		76	6
6		68	41
7		(60)	41, 49
8		(66)	41, 49
9		87	41, 49
10		47 50	49 41
11		83	41
12		(80)	41
13		80	41
14		(55)	41
15		85	41

Table 5 (*Contd.*).

16		81	41
17		76[d]	50
18		(48)	51

[a] Yields in parentheses are a lower limit because they refer to an overall sequence that includes the reaction in question, the yield for the latter not being reported. In the present case yields in parentheses are based on starting *ketone* and refer to the *enone* obtained by selenoxide fragmentation. [b] The stereochemistry of PhSe- group relative to other substituents is not usually relevant. Sometimes mixtures of isomers are obtained (e.g. entry 10). [c] Position of selenenylation. [d] The PhSe- group enters from the *alpha* face.

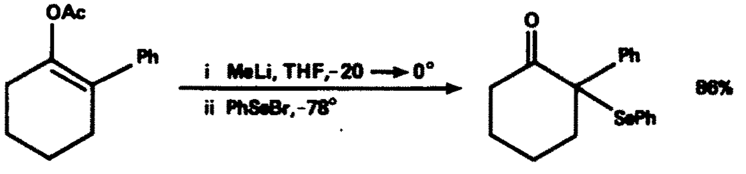
−78°. Aqueous work-up gave the product shown.[41,49]

(v) *Phenylselenenylation of copper enolates.* Copper enolates can be trapped by an excess of PhSeBr (eqn 28[49] and eqn 29[41,49]). It is advantageous to mix the PhSeBr with a small amount of PhSeSePh because the selenenylation of copper enolates is complicated by the production of α-bromo- and α-iodoketones when pure PhSeBr is used.[41,49] In the procedure summarised by the equations the PhSeSePh serves as a halogen trap but it may be better still to quench the copper enolate with acetic anhydride and to use the purified enol acetate as the starting material for selenenylation.[41]

(b) *Phenylselenenylation of esters*

The lithium enolates of esters used in the selenenylation reaction have usually been made by the action of LDA on the ester.[52,53] For example,[52] using THF solutions, each of the aliphatic esters 23 was added to LDA at −78° and, after a 10 min reaction period for deprotonation PhSeBr was added. The mixture was kept at −78° for up to 30 min before the products were isolated in the yields shown (eqn 30). In these experiments equimolar quantities of LDA, ester and PhSeBr were used.

The other published examples demonstrate the tech-



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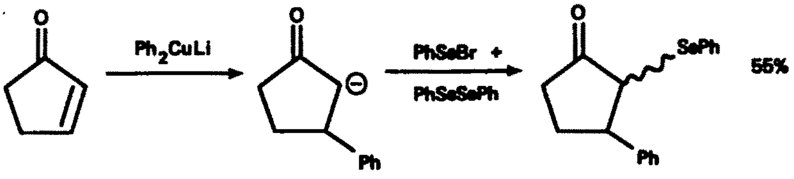
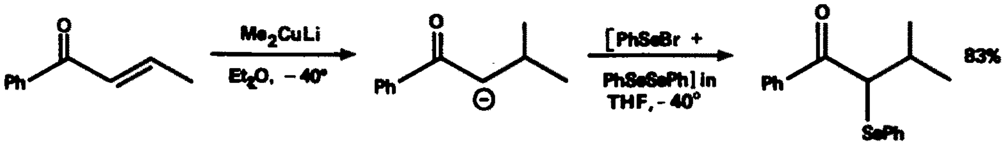
(27)

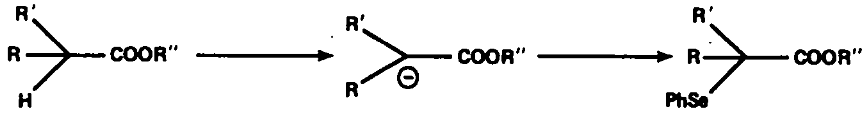


1:4 · 5::cis: trans

(28)



(29)


(30)

23

R = R′ = Me, R″ = Et 85%
R = R′ = H, R″ = Et 80%
R = Bu, R′ = H, R″ = Me 60%

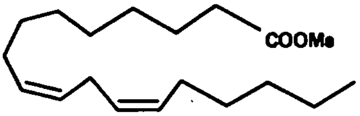
nical variations that have proved successful. For the esters, **24**–**26** lithium *N*-isopropylcyclohexylamide [1 equiv.] was the base and the enolates were quenched with a slight excess of PhSeBr [−78°, 1 hr, then warm to room temperature].[42] As shown, the yields are good.

The esters **27**–**29** have also been selenenylated (eqns 31–33) but in these cases a substantial excess (20%) of LDA was used for deprotonation. The amount of PhSeBr taken was equivalent to the LDA and reaction of the enolate was allowed to proceed in the range of −78° (at the start) to 0° before further processing.

In contrast to the situation with ketone enolates (see p. 1059) the enolates of esters react successfully with PhSeSePh and, in the case of the enolate derived from the olefinic ester **30**, it was actually essential to use the diselenide because PhSeBr adds across the double bonds.[42]

(c) *Phenylselenenylation of lactones*

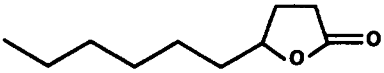
As with other carbonyl compounds the lactone enolates required are made by the action of LDA in THF and they are quenched with PhSeSePh, PhSeBr or PhSeCl.



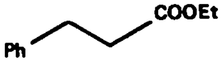
30

The selenenylation of ε-caprolactone is a typical example: the lactone was added to an excess of LDA in THF at −78°. After 15 min PhSeBr [equivalent to the amount of LDA] was introduced rapidly in THF solution and work-up gave the α-phenylselenolactone in 70% yield.[41]

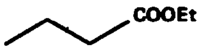
A similar process was applied to the lactone 31 except that the base was lithium N-isopropylcyclohexylamide and the mixture was not worked up immediately after addition of PhSeBr.[42]



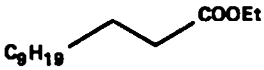
31



24
(80%)*

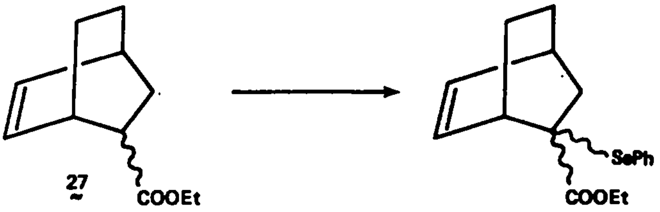


25
(83%)*



26
(79%)*

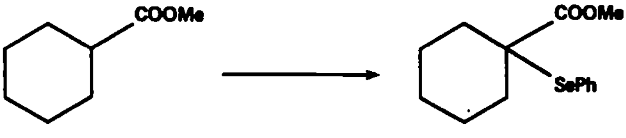
* See Ref. 54


(79%)* Ref. 6, 41 (31)

27


(79%)* Ref. 6, 41 (32)

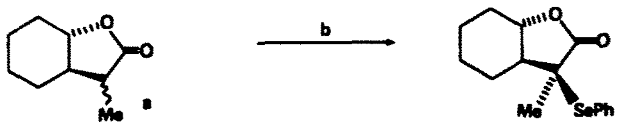
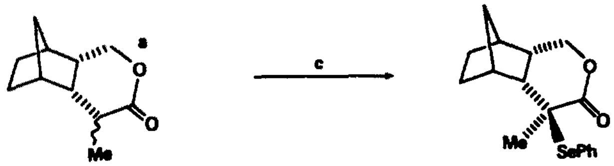
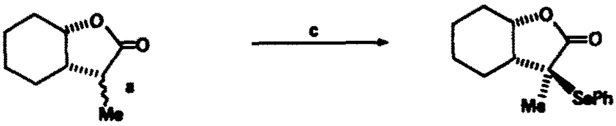
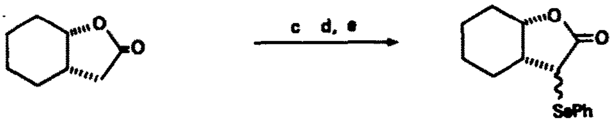
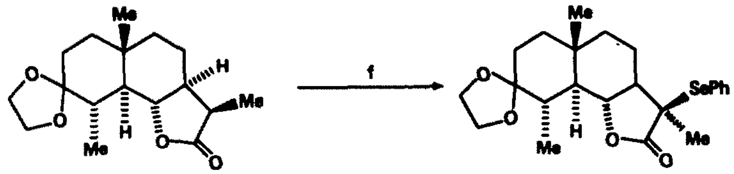
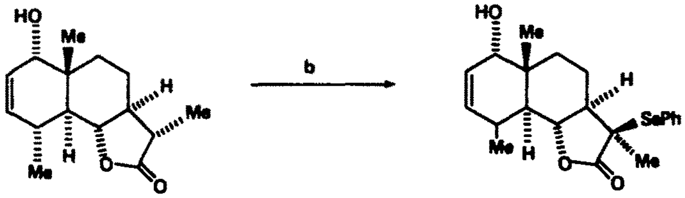
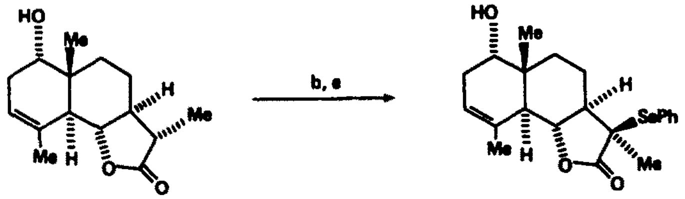
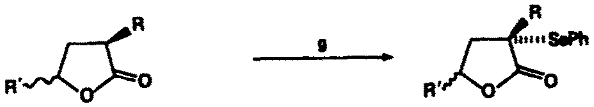
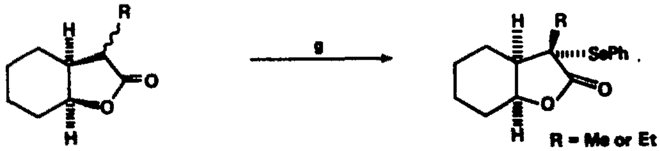
28


(96%)* Ref. 41 (33)

29

*See Ref. 54

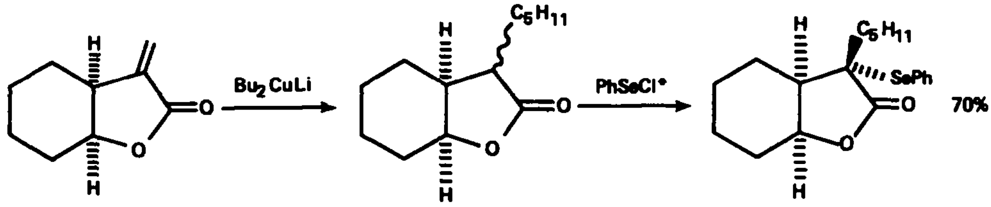
Table 6.

	Reaction	Yield	Ref.
1		85%	55
2		62	55
3		88	55
4		—	55
5		85	50
6		90	56
7		—	56
8	 R' = C_6H_{13}; R = Et, Bu, $PhCH_2$: 70 to 80% R' = C_4H_9; R = C_4H_9, $PhCH_2$: 72 to 83%		57
9		85 to 88	57

[a] Stereochemistry of alkyl group not specified. [b] Procedure of footnote *l* on p. 1064 used.[55] [c] Probably footnote *b* applied. [d] Stereochemistry of product not specified. [e] Yield of product not stated. [f] Selenenylation run at −20°. [g] A similar procedure to that specified in *b* was followed but with PhSeCl. It is not clear from the preliminary report[57] that PhSeCl was used throughout instead of PhSeSePh.

A number of lactones have been selenenylated in an extensive programme of natural product synthesis and a well-established procedure[l] is available. It has been used for the following transformations (Table 6).

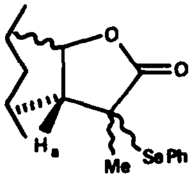
The selenenylation of lactone enolates generated by copper-mediated Michael addition is also known (eqn 34).[57]



(34)

*It is not clear whether PhSeCl or PhSeSePh was used.

Finally, it is important to comment on the stereochemistry of selenenylated lactones. For lactones of type 32 the relative stereochemistry of H_a and PhSe determines the nature of the product resulting from selenoxide fragmentation. If they are *trans* an α-methylene lactone will form; if *cis* the major product will be the endocyclic olefin (see p. 1105).[55,57]



32

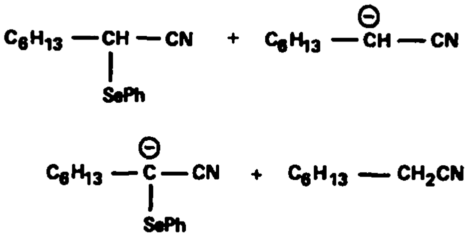
(d) *Selenylation of nitriles*

The selenenylation of octanonitrile has been studied in some detail.[58] The procedure developed differs from that described above for carbonyl compounds in that the anion 33 must be generated by using two equivalents of base. LDA or lithium N-isopropylcyclohexylamide in THF at −75° are suitable and the anion can be quenched successfully with PhSeSePh [1 equiv.] at room temperature (96% yield) or with PhSeBr (at −78°) (100% yield).[58,m] If only one equivalent of base is used, the initial selenenylated product equilibrates with α-lithiated nitrile (eqn 36) faster than selenenylation—even when the reagent is PhSeBr. Substantial amounts of octanonitrile are then recovered but bis-selenenylation does not occur.

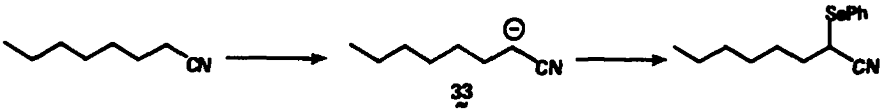
(e) *Selenenylation of α,β-unsaturated esters, β-ketosulphoxides, β-ketoesters, β-diketones and β-ketoselenoxides*

The heterocyclic systems 34 can be selenenylated in greater than 71% yield at the γ-position by deprotonation [1.1 equiv. LDA, −78° (at the start) to 0°] and reaction with PhSeBr [1.1 equiv., −78° (at the start) to 0°].[59]

The β-ketoesters 35 have been selenenylated efficiently at 0° by PhSeCl[41,49] or PhSeBr[49] after conversion to enolate with an excess of NaH. The same procedure was used to selenenylate the β-diketones 37 to 39 and the β-ketosulphoxide 40.



$$C_6H_{13}-\underset{SePh}{\underset{|}{CH}}-CN + C_6H_{13}-\overset{\ominus}{CH}-CN \longrightarrow C_6H_{13}-\underset{SePh}{\underset{|}{\overset{\ominus}{C}}}-CN + C_6H_{13}-CH_2CN \quad (36)$$



(35)

In a comparable process the ketoselenoxide 41, generated by low temperature ozonolysis, was deprotonated [$LiNR_2$, −78°] and quenched at −78° with PhSeCl to give 42 in at least 57% yield.[49]

The selenenylating properties of PhSe–NEt_2 have been examined briefly.[60,n] This reagent carries out the transformation shown (eqns 37–40) at room temperature without prior enolate formation:[60]

B. PREPARATION OF SELENIDES BY NUCLEOPHILIC DISPLACEMENT

Selenides can often be made by displacement of halide or sulphonate anions or by ring opening of an epoxide. Numerous examples of the displacement reaction using $ArSe^{-}$[o] are to be found in the older literature.[2c] In the context of modern organoselenium chemistry the methods described below are important.

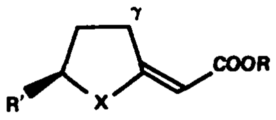
---

[l] Typically,[55] the γ-lactone [1 equiv.] in THF is added slowly to LDA [1.2 equiv.] in THF at −78°. 20 min after the end of the addition a THF solution of PhSeSePh [1.2 equiv.] containing hexamethylphosphoric triamide [1.2 equiv.] is added rapidly and the mixture is kept at −78° for 40 min, then warmed to −40° and kept at −40° for 1.5 hr. Work-up after quenching with 0.1 N HCl, gives the phenylselenolactone, usually in high yield.

[m] EtSeBr is also effective.

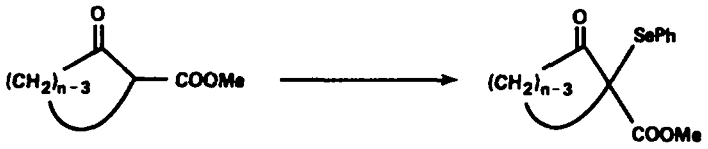
[n] Other members of this compound class have been studied in less detail.[60]

[o] The aryl selenide anions are generated by the action of $NaBH_4$ on ArSeCN or ArSe–SeAr. In the former case 1 mole $NaBH_4$ per mole ArSeCN is used.[32] but the latter requires 2 moles $NaBH_4$ per mole ArSeSeAr.[33,34,36,40] (Sometimes amounts slightly in excess of these quantities are employed.) Absolute ethanol is a suitable solvent[32,40] and DMF has been used for selenocyanate reduction.[38] Although electron-withdrawing substituents on the aryl ring may be necessary in order to facilitate selenoxide fragmentation (see p. 1055), the reactions of the substituted aryl selenide anions are sometimes inefficient[32] possibly because of reduced nucleophilicity.



X = N-alkyl, R = Me, R′ = H
X = O, R = Et, R′ = Me
X = S, R = Et, R′ = Me

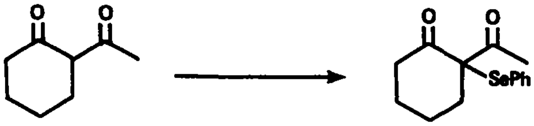
34



35 **36**

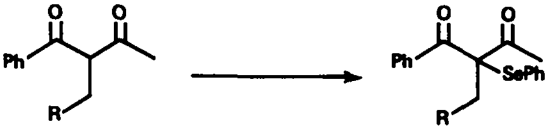
* See Ref. 54

n	Yield
8	96%
7	90%
6	(89%)*
5	(81%)*



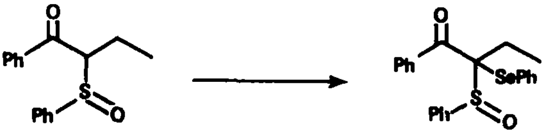
86% Ref. 49, 41

37



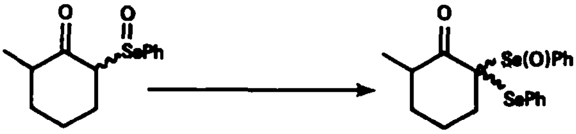
38 R = H
39 R = Pr^n

R = H 93% Ref. 49, 41
R = Pr^n 96% Ref. 49, 41

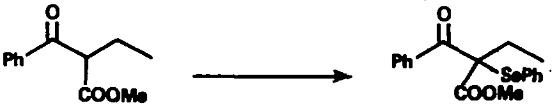


78% Ref. 41

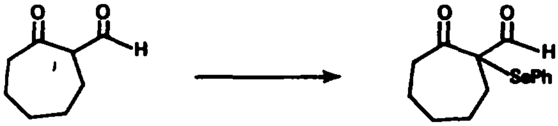
40



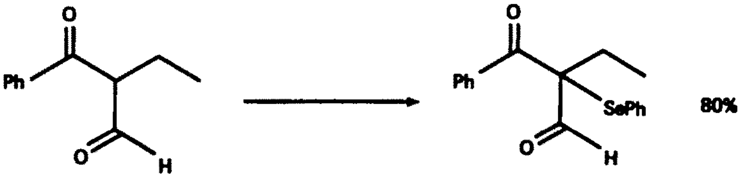
41 **42**



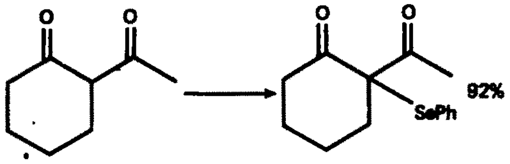
92% (37)



90% (38)



(39)



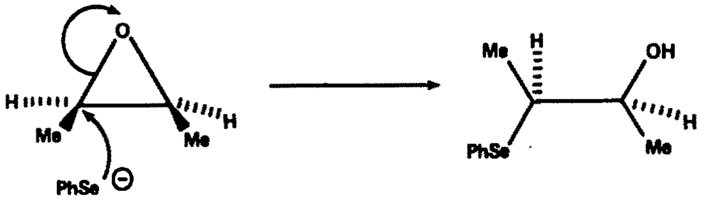
(40)

(a) *Opening of epoxides to β-hydroxyalkyl selenides*

Colourless ethanol solutions of PhSe$^-$Na$^+$ are easily generated as required by slow addition of NaBH$_4$ to PhSeSePh in dry ethanol.[40] Addition of an epoxide, followed by an appropriate reaction period at room temperature or at reflux, produces a β-hydroxyalkyl selenide (eqn 41) by normal S_N2 opening[35] of the ring. Other solvent systems can be used[40,61] according to the requirements of solubility and reaction temperature. The following transformations have been reported (Table 7).

The opening of epoxides by PhSeH and PrSeH in the presence of a catalytic amount of sodium selenolate has also been described.[64]

Although long reaction times may be needed for hindered epoxides, PhSe$^-$ is a powerful nucleophile and it usually gives β-hydroxyalkyl selenides in good yield. Evidently, preparation of the anion from the diselenide is an efficient process. Preliminary attempts to use the same method with 4,4'-dinitrodiphenyldiselenide gave β-hydroxyalkyl selenides in poor yield.[65]



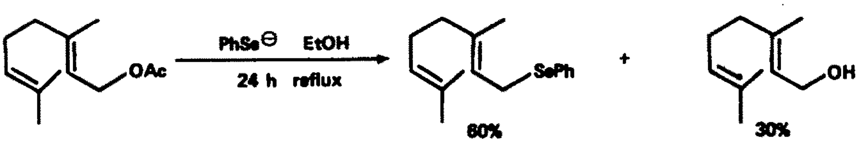
(41)

(b) *Displacement of halide anions*

The displacement of halide by selenide anions is a well-tried route to alkyl phenyl selenides[2c] and modern work of this type is collected in Table 8. It can be seen that the reaction is widely general but yields with substituted aryl selenide anions are not always as high as those with PhSe$^-$.[32] The displacement of allylic halides[35,68–70] is complicated. Both S_N2 and S_N2' reactions can occur and superimposed on this is the fact that allylic [1,3] shifts of PhSe take place under mild conditions (see p. 1108). By using a low reaction temperature for the displacement substantial control is sometimes possible.[35,68]

(c) *Displacement of sulphonate anions*

Aryl selenide anions generally effect smooth S_N2 displacement of methane- and toluenesulphonates at room temperature, a reaction period of several hours being necessary (Table 9). Displacement of acetate does not appear to be a useful procedure. In the single example[35] reported (eqn 42) displacement competes with acyl transfer.[p]



(42)

(d) *Direct conversion of alcohols into selenides*

Conversion of alcohols directly into selenides is expected to constitute a useful means of dehydration because the derived selenides are synthetically equivalent to olefins. The known conversion of alcohols into sulphides (eqn 43)[71] suggested a method of approach but the corresponding reaction does not occur with PhSeSePh.[37],[q] The use of selenocyanates, however, results in the desired transformation (eqn 44 and Table 10). The alcohols listed were converted at room temperature into 2-nitrophenylselenides in the yields indicated.[37],[r] It is clear that this method works very well for primary alcohols but its performance with secondary

$$\mathrm{ROH + PhSSPh + Ph_3P \longrightarrow RSPh + Ph_3P = O} \qquad (43)$$

$$\mathrm{RCH_2OH + ArSeCN \xrightarrow[\text{THF or Pyridine}]{Bu_3P} RCH_2SeAr} \qquad (44)$$

$$\mathrm{Ar = C_6H_5 \text{ or } 2\text{–}NO_2\text{–}C_6H_4\text{–}}$$

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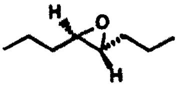
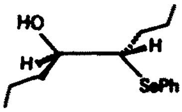
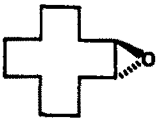
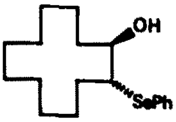
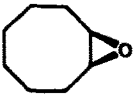
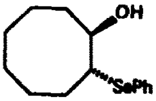
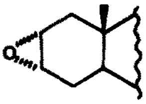
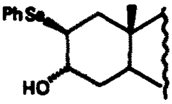
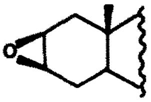
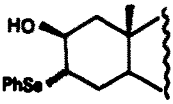
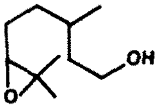
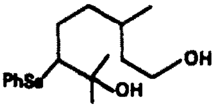
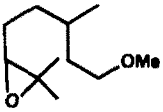
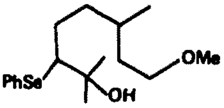
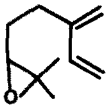
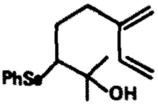
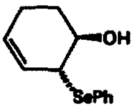
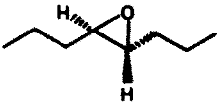
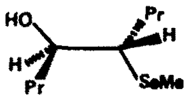
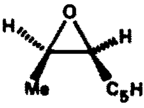
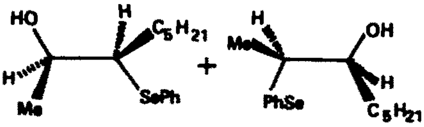
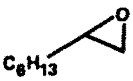
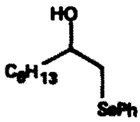
[p] The product of S_N2' displacement would not be detected under these conditions. See p. 1108.

[q] Diaryldiselenides react more sluggishly with phosphines than do the corresponding disulphides.[72]

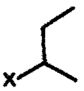
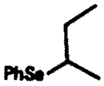
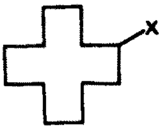
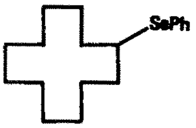
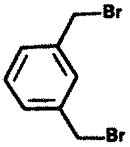
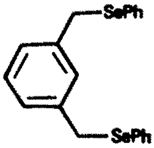
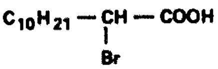
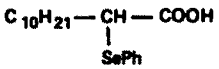
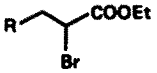
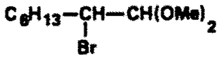
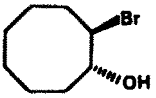
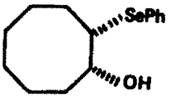
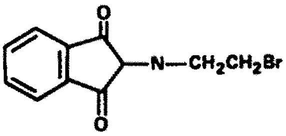
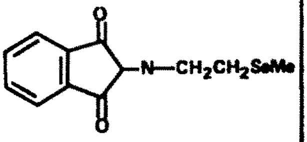
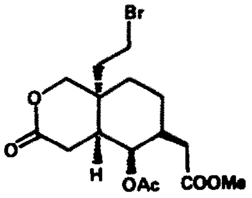
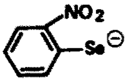
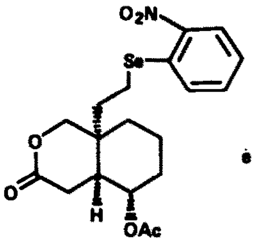
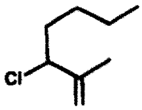
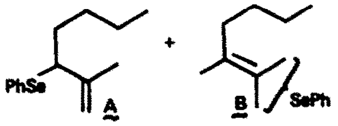
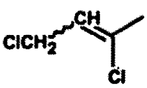
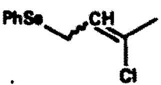
[r] Phenylselenides are also available by this method from PhSeCN.

Table 7.[a]

				Yield[b]	Ref.
1		EtOH 2 h room temp.		(98%)	40
2		BuOH 16 h reflux		(85)	35, 40
3		BuOH 16 h reflux		(75)	40
4	 (c)	1:1 EtOH:THF 14 h reflux		(40)	40
5	 (c)	1:1 EtOH:THF 8.5 h reflux		(51)	40
6		EtOH 0.5 h reflux		(95)	40
7		EtOH 2h reflux		(79)	40
8		EtOH 2h reflux		(50)	40
9		EtOH 0.5 h reflux		(50)	40
10		$MeSe^{\ominus}$		–	62
11		d		–	62
12		EtOH 2h reflux		86	13, 63

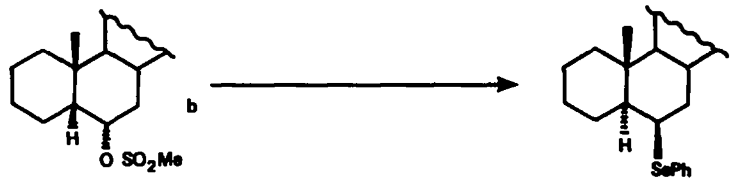
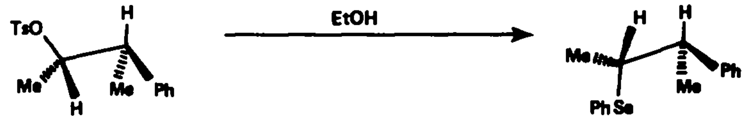
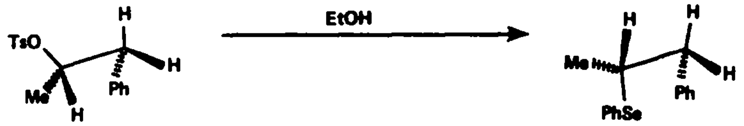
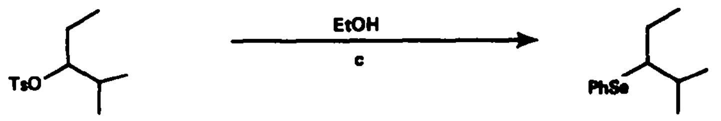
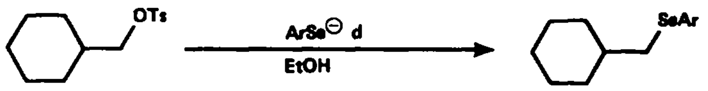
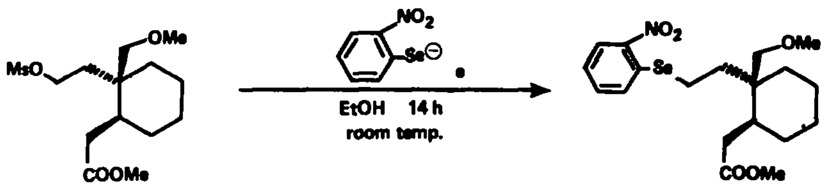
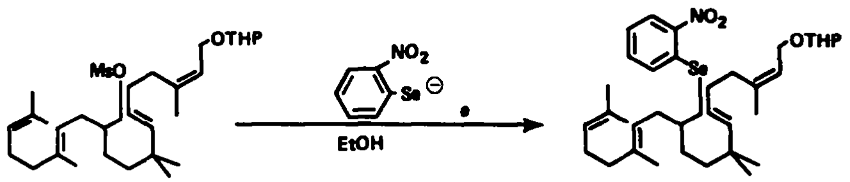
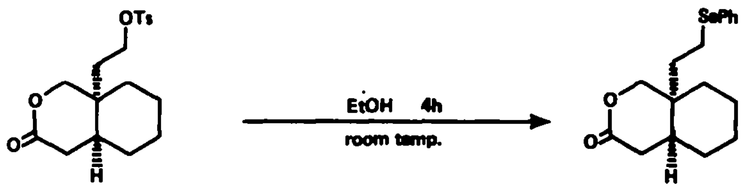
[a] Except where indicated $PhSe^-Na^+$ was used. [b] Ref. 54. [c] Cholestane skeleton. [d] Although not explicitly revealed in Ref. 62 both products would be formed.

Table 8.[a,54]

1.		$\xrightarrow{\text{b}}$		—	5
2		$\xrightarrow{\text{b}}$		—	5
3	$ArCH_2X$	$\xrightarrow{\text{c}}$	$ArCH_2SePh$	—	66
4	$PhCH_2Br$	$\xrightarrow[\text{reflux}]{\text{EtOH 2h}}$	$PhCH_2SePh$	(76)	31
5		$\xrightarrow[\text{reflux}]{\text{EtOH 2h}}$		(82)	31
6	$C_{12}H_{25}Br$	$\xrightarrow{ArSe^{\ominus}\text{EtOH several h}}$	$C_{12}H_{25}SeAr$ (d)	—	32
7	 $C_{10}H_{21}-\underset{\mid\atop Br}{CH}-COOH$	$\xrightarrow[\text{1 equiv. HO}^{\ominus}]{\text{EtOH room temp.}}$	 $C_{10}H_{21}-\underset{\mid\atop SePh}{CH}-COOH$	(91)	(35)
8	$Cl\,CH_2COOEt$	$\xrightarrow{\text{EtOH}}$	$PhSeCH_2COOEt$	—	42
9		$\xrightarrow[\text{R = Ph, Me, }C_9H_{19}]{\text{EtOH room temp.}}$	 R = Ph R = Me R = C_9H_{19}	(78) (89) (82)	42
10	 $C_6H_{13}-\underset{\mid\atop Br}{CH}-CH(OMe)_2$	$\xrightarrow[\text{ii hydrolysis}]{\text{i EtOH room temp.}}$	 $C_6H_{13}-\underset{\mid\atop SePh}{CH}-CHO$	—	13, 63
11		$\xrightarrow[\text{reflux}]{\text{EtOH 12 h}}$		—	13, 63
12		$\xrightarrow[\text{2 h reflux}]{MeSe^{\ominus}\text{ EtOH}}$		50	28
13		 $\xrightarrow[\text{room temp.}]{\text{DMF}}$	 e	87	38
14		$\xrightarrow[\text{f}]{\text{EtOH 0°}}$		76	35
15		$\xrightarrow{\quad}$		—	67

[a] $PhSe^-Na^+$ was used unless stated otherwise. Yields and conditions are given where reported. [b] Halide not specified. Some further examples—without details—are given in Ref. 39. [c] Various substituted benzyl halides were used. [d] Phenyl- and aryl-substituted selenide anions were used [(i) 2-NO_2, (ii) 2-CF_3-4NO_2, (iii) 4-NO_2, (iv) 3-CF_3, (v) 4-Cl, (vi) 4-MeO]. The substituted selenide anions were made by $NaBH_4$ reduction of the corresponding diselenides [(ii), (iv), (v), (vi)] or selenocyanates [(i), (iii)] in EtOH. [e] The 2-nitrophenylselenide anion was generated in DMF by $NaBH_4$ reduction. [f] The major product (76% yield) may have contained 6% of the (*Z*) and (*E*) isomers of the minor product.[68] If the reaction is run at reflux *B* is formed (100%).

Table 9.[a]

		Yield	Ref.
1		—	25
2		—	5
3		—	5
4		—	5
5		-	32
6		84%	33
7		75	34
8		98	36

[a] $PhSe^-Na^+$ used except where indicated otherwise. Yields and conditions given where reported. [b] Cholestane skeleton. [c] For some other examples—without details—see Ref. 39. [d] $ArSe^- = PhSe^-$, 4-Cl-C_6H_4Se, $2\text{-NO}_2\text{-C}_6H_4Se^-$. The latter was made from the selenocyanate; the other two from the diselenides. [e] Made from diselenide.

alcohols has not yet been established with the same thoroughness.

(e) *Michael addition to α,β-unsaturated systems*

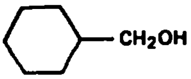
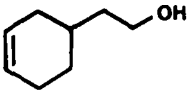
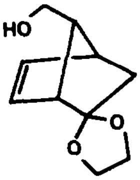
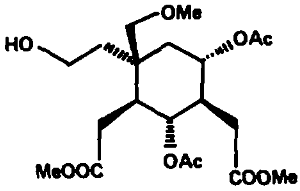
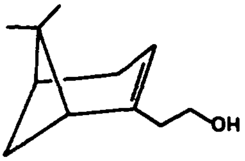
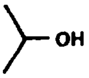
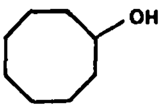
Reactions of $PhSe^-$ with unsaturated ketones and lactones are the only published examples in this category (eqns 45–47).

Where reported, the yield is poor, but with improvement, the process could become important for protection of carbon–carbon double bonds conjugated with a carbonyl group. The double bond is regenerated in excellent yield by selenoxide fragmentation.[5,73]

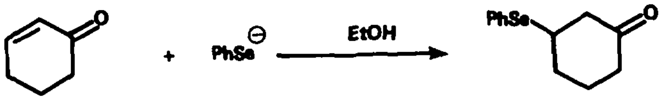
C. INTRODUCTION OF SELENIUM BY MEANS OF SELENIUM-CONTAINING SYNTHONS

The methods dealt with here involve generation of Se^{II}- or selenoxide-stabilized carbanions 43 and 44 which can react with H_2O, D_2O, alkyl halides, ketones, aldehydes

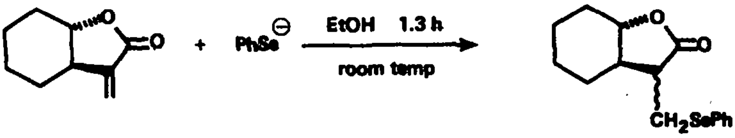
Table 10.[a]

Alcohol	Yield of Selenide	
	Solvent = Pyridine	Solvent = THF
1 $C_{12}H_{25}OH$	92	94
2 $C_7H_{15}OH$	85	—
3 $CH_3CH_2C\equiv CCH_2CH_2OH$	93	88
4 $PhCH_2OH$	97	93
5 	99	88
6 	98	95
7 	91	90
8 	—	91
9 	98	85
10 	93	—
11 	—	

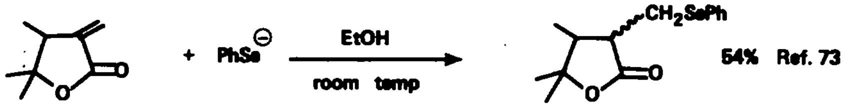
[a] Reaction times were probably about 30 min.



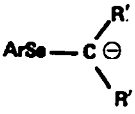
Ref. 5 (45)



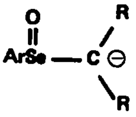
60% Ref. 73 (46)



(47)



43

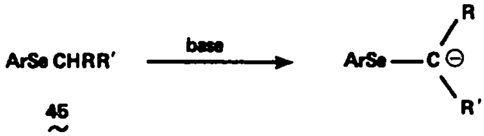


44

and other species. Both **43** and **44** *can* be made by deprotonation (eqns 48 and 49) and in the latter case there are few restrictions on the permissible structures of R and R′.[39,74] For deprotonation of **45**, however, there are severe restrictions (see p. 1077) in this respect[31,39,67,74,75] but a route to **43** is available by Se–C bond cleavage (eqn 50). In the case of compound **45** two competing reactions are possible when the selenide is treated with base: deprotonation, which depends *inter alia* on proton acidity,[a] or nucleophilic attack on selenium leading to cleavage. The fundamental studies[75] on the response of selenides to strong bases are summarised by eqns (51)–(56). It can be seen that lithium amides are suitable for deprotonation while BuLi has a strong tendency to bring about Se–C bond cleavage, and this latter process has been utilised frequently.

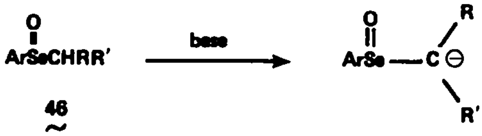
---

[a] $(PhSe)_2CH_2$ has a pK_a of ~35; $(PhS)_2CH_2$ has a pK_a of ~32–33.[75] $(PhSe)_3CH$ and $(PhS)_3CH$ are of comparable acidity (pK_a ~31).[75]



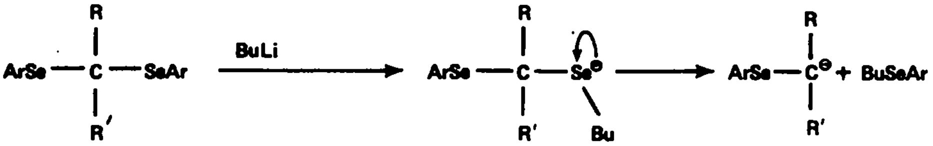
45

(48)



46

(49)



(50)

$$\mathrm{PhSeCH_3} \xrightarrow[>0^\circ\ \text{[No reaction below }0^\circ]]{\text{BuLi TMEDA THF}} \mathrm{PhSe\overset{\ominus}{C}H_2} \quad (38\%)^* \tag{51}$$

$$\mathrm{(PhSe)_2CH_2} \xrightarrow{\text{BuLi THF }-78^\circ} \mathrm{PhSe\overset{\ominus}{C}H_2} \quad (>95\%)^* \tag{52}$$

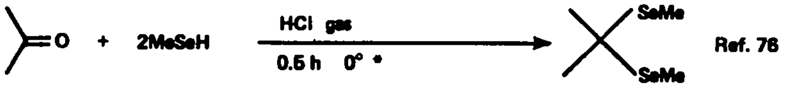
$$\mathrm{(PhSe)_3CH} \xrightarrow{\text{BuLi THF }-78^\circ} \mathrm{(PhSe)_3\overset{\ominus}{C}} + \mathrm{(PhSe)_2\overset{\ominus}{C}H} \tag{53}$$

$$\mathrm{(PhSe)_4C} \xrightarrow{\text{BuLi THF }-78^\circ} \mathrm{(PhSe)_3\overset{\ominus}{C}} \quad (\sim 100\%)^* \tag{54}$$

$$\mathrm{(PhSe)_2CH_2} \xrightarrow{\underline{i}\text{-}\mathrm{Bu_2NLi}\text{ THF }-78^\circ} \mathrm{(PhSe)_2\overset{\ominus}{C}H} \quad (91\%)^* \tag{55}$$

$$\mathrm{(PhSe)_3CH} \xrightarrow{i\text{-}\mathrm{Bu_2NLi}\text{ THF }-78^\circ} \mathrm{(PhSe)_3\overset{\ominus}{C}} \quad (\sim 100\%)^* \tag{56}$$

*Ref. 54



(57)

*The temperature throughout the reaction, which was allowed to proceed for 1 hr after passage of HCl, is not clear from the preliminary report.[76]

(a) *Preparation of bis-selenoketals*

Bis-selenenoketals are easily prepared from aldehydes and ketones by reaction with a selenol (usually PhSeH or MeSeH) in the presence of an acid (eqn 57).

A number of examples of this process have been published[76-78] and yields appear generally to be good (80–95%).[t]

(b) *Applications of Se–C bond cleavage: reactions with ketones and aldehydes*

The following general procedure,[78] or slight modifications of it, have been used in the large number of reported transformations based on Se–C bond cleavage of ketals: Addition of BuLi[u] [1 equiv.] to a cold [−78°] THF solution of the diselenoketal[v] generates the selenium-stabilized carbanion (eqn 50). After about 1.5 hr[w] a THF solution of ketone or aldehyde is introduced,[x] and the mixture is kept for 2 hr at −78° and then for several hr[y] at room temperature. Work-up affords a β-hydroxyalkyl selenide. The results obtained by this method are collected in Table 11.

It is clear that selenium stabilized carbanions react efficiently with hindered ketones (entry 23) and even with readily enolizable ketones such as $PhCOCH_2Ph$. It is

Table 11.[a]

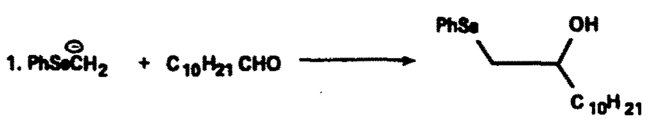
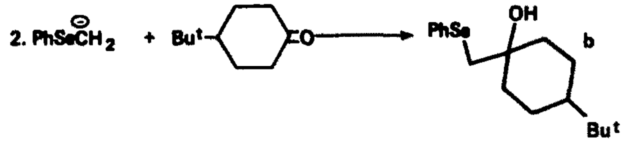
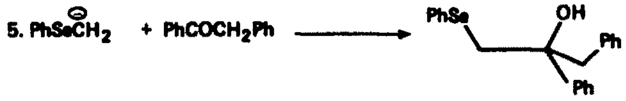
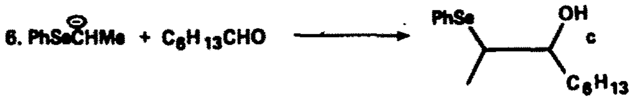
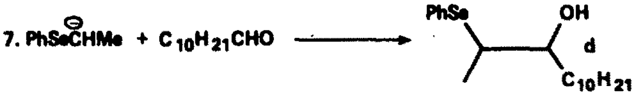
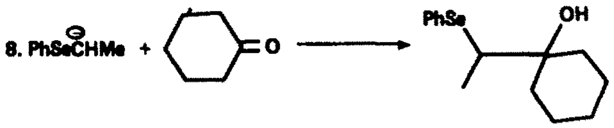
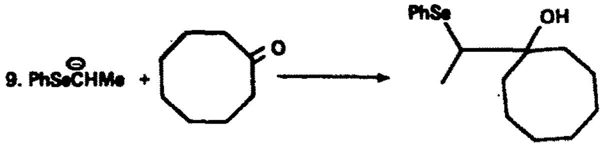
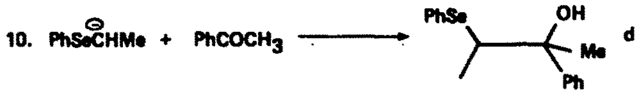
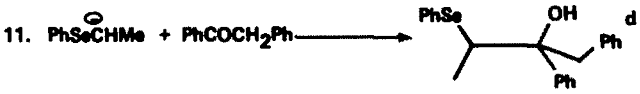
	Yield	Ref.
	71%	62
	45 68	80 62
	66	80
	71	80
	82	80
	49	78
	80	62
	72	77
	65	77
	57	80
	69	80

Table 11 (*Contd.*)

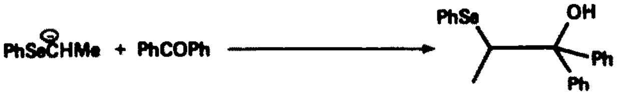
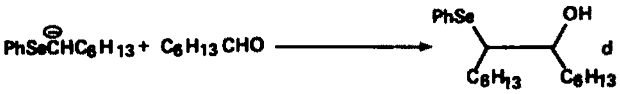
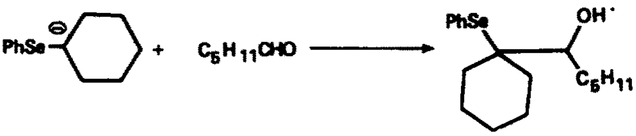
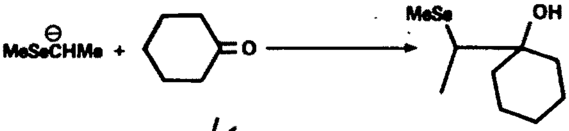
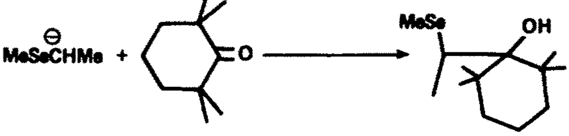
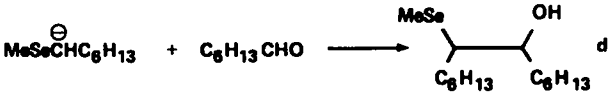
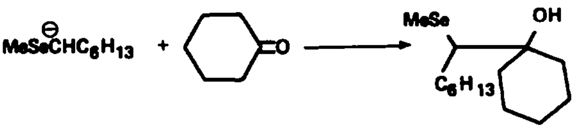
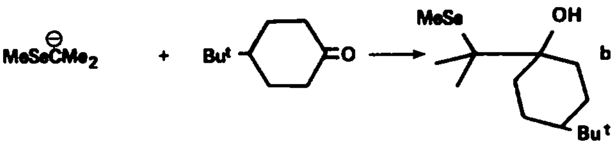
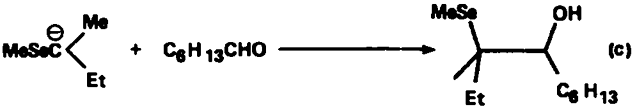
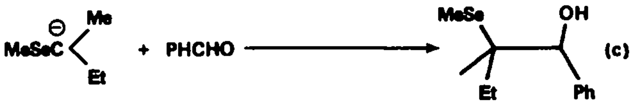
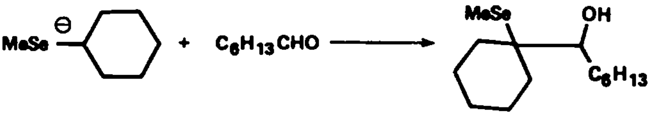
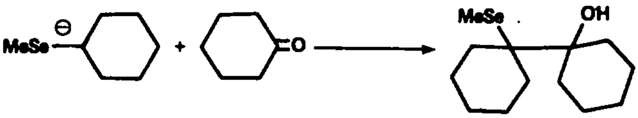
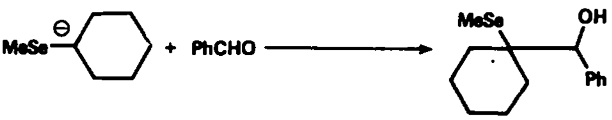
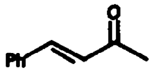
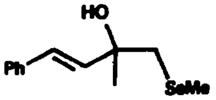
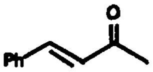
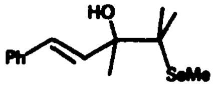
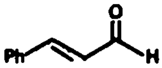
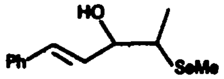
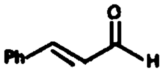
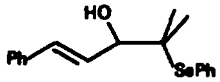
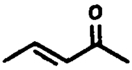
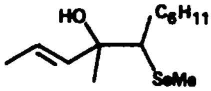
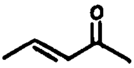
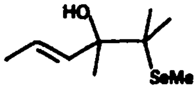
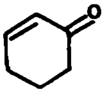
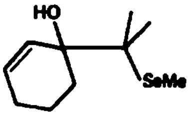
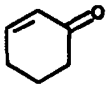
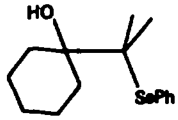
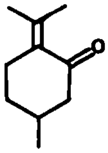
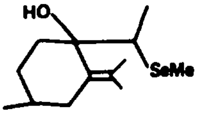
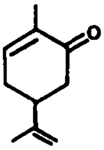
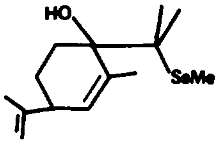
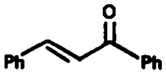
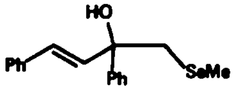
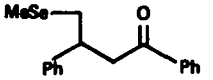
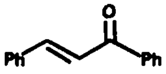
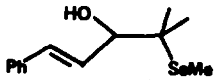
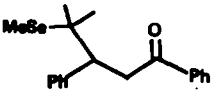
12. 	41	80
13. 	60 50	78 80
14. 	(97)[e]	80
15. 	75	62
16. 	70	78
17. 	78 85	78 77
18. 	67	78, 80
19. 	80	77
20. 	71	62
21. 	87	76
22. 	94	76
23. 	82	76
24. 	90	76
25. 	88	76

Table 11 (*Contd.*)

26.		–	81
27.		82	62
28.		60	76
29.		(60)ᵉ	76
30.		88	76
31.		(84)ᵉ 80	76 62
32.		82	76
33.		60	76
34.		81	76
35.		76	76
36.		41	76
37.		85	76

[a] The selenium stabilized anions were generated from selenoketals $(RSe)_2CRR'$. [b] Relative stereochemistry not established. [c] Presumably, a mixture of diastereoisomers is formed. [d] Explicit statement in literature that diastereoisomeric mixture was obtained. [e] Ref. 54.

Table 12.

1.	$\text{MeSe}\overset{\ominus}{\text{C}}\text{H}_2$	+		⟶			87%
2.	$\text{MeSe}\overset{\ominus}{\text{C}}\text{Me}_2$	+		⟶			80
3	$\text{MeSe}\overset{\ominus}{\text{C}}\text{HMe}$	+		⟶		(a)	90
4.	$\text{PhSe}\overset{\ominus}{\text{C}}\text{Me}_2$	+		⟶			78
5.	$\text{MeSe}\overset{\ominus}{\text{C}}\text{HC}_6\text{H}_{11}$	+		⟶		(a)	65
6.	$\text{MeSe}\overset{\ominus}{\text{C}}\text{Me}_{1\,2}$	+		⟶			45
7.	$\text{MeSe}\overset{\ominus}{\text{C}}\text{Me}_2$	+		⟶			55
8.	$\text{PhSe}\overset{\ominus}{\text{C}}\text{Me}_2$	+		⟶			63
9.	$\text{MeSe}\overset{\ominus}{\text{C}}\text{HMe}$	+		⟶		(a)	65
10.	$\text{MeSe}\overset{\ominus}{\text{C}}\text{Me}_2$	+		⟶		(a)	
11	MeSeCH_2	+		⟶			35
							35
12	MeSeCMe_2	+		⟶			21
							47

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[a] Presumably a mixture of isomers is obtained.

also apparent that the unsymmetrical carbanions (e.g. $RR'\overset{\ominus}{C}SeMe$) do not equilibrate (to give $RR'CHSe\overset{\ominus}{C}H_2$) under the experimental conditions.

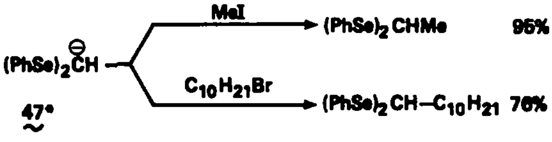
The response of α,β-unsaturated carbonyl compounds to phenylseleno- and methylseleno-carbanions has also been examined.[79] Reaction occurs smoothly [THF, −78°, 2 hr; then −25° for 1 hr] and takes place at the carbonyl carbon almost exclusively. Of the examples studied[79] (Table 12), chalcone is the only case where the regiospecificity is low.

(c) *Applications of Se–C bond cleavage: reactions with alkyl halides*

Selenium-stabilized carbanions react[82] with simple or activated alkyl halides (bromides and iodides) to form selenides as shown in eqn (58). The experimental technique[82] is very similar to that described on p. 1072 and the published[82] examples are collected in Table 13.

$$RCH(SeMe)_2 \xrightarrow{BuLi} R\overset{\ominus}{C}HSeMe \xrightarrow{R'-X} \underset{\substack{|\\ SeMe}}{R-CH}-R' \qquad (58)$$

This type of alkylation process has been used to make selenoketals:[77]



(d) *Applications of Se–C bond cleavage: acylation of selenium-stabilized carbanions*

Selenium-stabilized carbanions can be acylated by reaction with the common reagents shown in Table 14. Unlike the processes already described the yields are not uniformly high although some attempt at optimisation was evidently made. For best results the carbanion [in THF at −78°] should be added to a cold [−78°] solution of the acylating agent.[30]

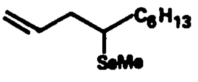
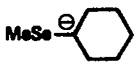
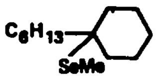
(e) *Applications of Se–C bond cleavage: reaction with non-carbon electrophiles*

The previous sections have dealt with the formation of carbon–carbon bonds, but selenium-stabilized carbanions can also be quenched with the electrophiles that are *formally* equivalent to PhS^+, R_3Si^+, H^+ and D^+ to give products (Table 15) that have synthetic utility in their own right (see later). The general procedure is similar to that already familiar from previous sections but few details are available.[82]

(f) *Selenium-stabilized carbanions by deprotonation*

As mentioned p. 1071, carbanions such as **48** can be generated by deprotonation of PhSeCHRR′ for certain constitutions of R and R′.

Table 13.[a]

1	$MeSe\overset{\ominus}{C}H_2$	+	$C_{10}H_{21}X$	$\longrightarrow$	$C_{10}H_{21}-CH_2-SeMe$	60%
2	$MeSe\overset{\ominus}{C}HC_6H_{13}$	+	$C_6H_{13}X$	$\longrightarrow$	$C_6H_{13}-\underset{\substack{\vert\\ SeMe}}{CH}-C_6H_{13}$	85
3	$PhSe\overset{\ominus}{C}HC_6H_{13}$	+	$C_6H_{13}X$	$\longrightarrow$	$C_6H_{13}-\underset{\substack{\vert\\ SePh}}{CH}-C_6H_{13}$	40
4	$MeSe\overset{\ominus}{C}HC_6H_{13}$	+	$C_7H_{15}X$	$\longrightarrow$	$C_7H_{15}-\underset{\substack{\vert\\ SeMe}}{CH}-C_6H_{13}$	75
5	$MeSe\overset{\ominus}{C}HC_6H_{13}$	+		$\longrightarrow$		56
6	$MeSe\overset{\ominus}{C}Me_2$	+	$C_6H_{13}X$	$\longrightarrow$	$C_6H_{13}-\underset{\substack{\vert\\ SeMe}}{CMe_2}$	85
7		+	$C_6H_{13}X$	$\longrightarrow$		84

[a] The nature of X (Br or I) is not explicitly given.

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[t] For further examples—without experimental details—see the preparation of selenium stabilized-carbanions.

[u] Bu^tLi can also be used.[77]

[v] The diselenoketal is sometimes used in slight excess[76] over BuLi.

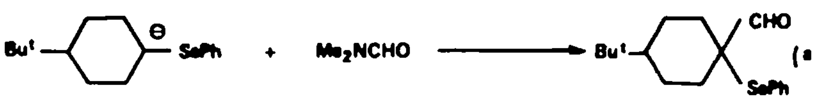
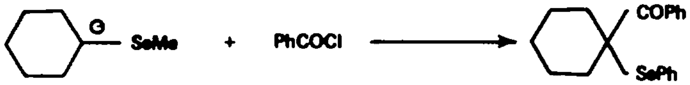
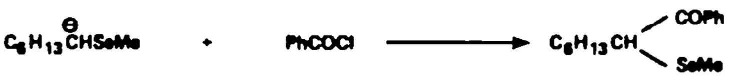
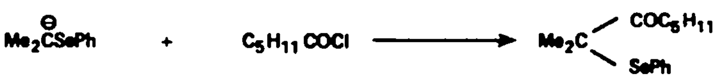
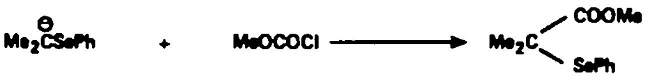
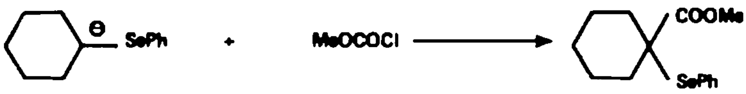
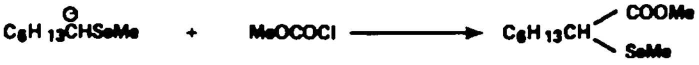
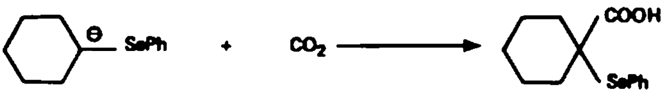
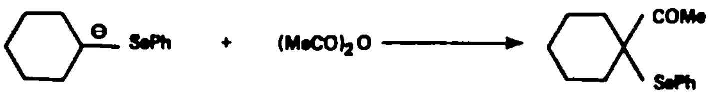
[w] There is substantial variation in the reaction times reported.[77,79]

[x] The selenium-stabilized carbanion is used in slight excess.[76,78]

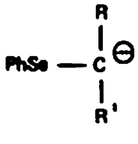
[y] Exact time depends on the individual case.[76,78]

[*] In view of the observations[75] described on p. 1071, carbanion **47** was, presumably, made by deprotonation [R_2NLi] of $(PhSe)_2CH_2$.

Table 14.

		Yield
1		46%
2		79
3		66
4		44
5		80
6		40
7		60
8		40
9		70
10		25

[a] Relative stereochemistry not established.



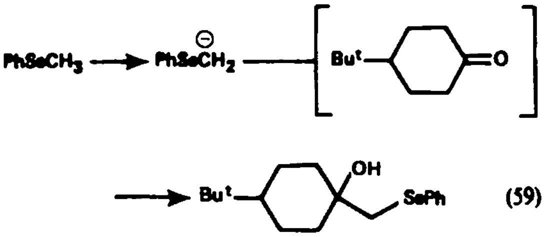
48

$PhSeCH_2SiMe_3$

49

In addition, a proper choice of base must be made. Alkyl lithium reagents generally produce Se–C bond cleavage[31,39,67,75] although in the case of **49** this type of cleavage amounts[39] only to 15% when the base used is *sec*-BuLi [25°, 1.5 hr, hexane solution, TMEDA]. LDA or, for sterically hindered cases, Et_2NLi usually avoids cleavage[67] and effects deprotonation. t-BuOK has been tried[31] unsuccessfully with benzyl selenides. Deprotonation of selenides has been achieved in five general situations, the known examples being as follows:

(i) *Deprotonation of phenyl alkyl selenides.* One case has been described (eqn 59):[74,85]



76%[a,b]

[a] No reaction conditions are given. Use of LDA can be presumed on the basis of the discussion on p. 1071.

[b] Relative stereochemistry not reported.

(ii) *Deprotonation of a selenoketal.* The selenoketal **50** has been deprotonated[74,75,77] [LDA or Bu_2^tNLi[75]] and the carbanion **47** quenched with benzophenone,[75] isobutyraldehyde[74] (eqn 60) or simple alkyl halides (see p. 1076).[75,77]

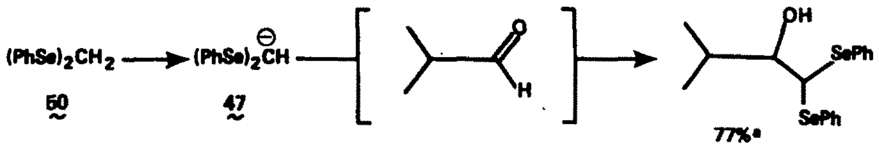
(iii) *Deprotonation of benzyl selenides.* The benzyl selenide **51** has been deprotonated[31,39] with LDA (eqn 61). t-BuOK does not produce the anion[31] and the substituted benzyl selenide **52**[**] could not[39] be depro-

---

[**] For deprotonation of a benzyl selenide carrying an additional activating group see p. 1081.

Table 15.

		Yield	Ref.
1	$Ph Se\overset{\ominus}{C}HMe + PhS{-}SPh \longrightarrow \underset{\displaystyle SPh}{PhSe{-}CHMe}$	80% 55	77 83
2	$PhSe\overset{\ominus}{C}Me_2 + PhS{-}SPh \longrightarrow \underset{\displaystyle SPh}{PhSe{-}CMe_2}$	70	77
3		50	83
4	$PhSe\overset{\ominus}{C}Me_2 + ClSiMe_3 \longrightarrow \underset{\displaystyle SiMe_3}{PhSe{-}CMe_2}$	75	83
5	$MeSe\overset{\ominus}{C}HMe + ClSiEt_3 \longrightarrow \underset{\displaystyle SiEt_3}{MeSe{-}CHMe}$	80	84
6	$MeSe\overset{\ominus}{C}HC_6H_{13} + ClSiEt_3 \longrightarrow \underset{\displaystyle SiEt_3}{MeSe{-}CHC_6H_{13}}$	91	84
7	$MeSe\overset{\ominus}{C}HC_6H_{13} + ClSiMe_3 \longrightarrow \underset{\displaystyle SiMe_3}{MeSe{-}CHC_6H_{13}}$	85	84
8	$PhSe\overset{\ominus}{C}HC_6H_{13} + ClSiMe_3 \longrightarrow \underset{\displaystyle SiMe_3}{PhSe{-}CHC_6H_{13}}$	51	84
9	$MeSe\overset{\ominus}{C}Me_2 + Cl\,SiEt_3 \longrightarrow \underset{\displaystyle SiEt_3}{MeSe{-}CMe_2}$	91	84
10	$MeSe\overset{\ominus}{C}HC_{13}H_{17} \overset{H_2O}{\longrightarrow} MeSeCH_2C_{13}H_{17}$	86	82
	$MeSe\overset{\ominus}{C}HC_{13}H_{17} \overset{D_2O}{\longrightarrow} MeSeCHDC_{13}H_{17}$	87	82
11	$MeSe\overset{\ominus}{C}(C_{10}H_{21})_2 \overset{H_2O}{\longrightarrow} MeSeCH(C_{10}H_{21})_2$	87	82
	$MeSe\overset{\ominus}{C}(C_{10}H_{21})_2 \overset{D_2O}{\longrightarrow} MeSeCD(C_{10}H_{21})_2$	87	82
12	$PhSe\overset{\ominus}{C}(C_{10}H_{21})_2 + H_2O \longrightarrow PhSeCH(C_{10}H_{21})_2$	92	82
13	$PhSe\overset{\ominus}{C}Me_2 + D_2O \longrightarrow PhSeCDMe_2$	> 98	77
14	$PhSe\overset{\ominus}{C}HMe + D_2O \longrightarrow PhSeCHDMe$	> 98	77
15	$PhSe\overset{\ominus}{C}HC_{10}H_{21} \overset{H_2O}{\longrightarrow} PhSeCH_2C_{10}H_{21}$	> 95	77
	$PhSe\overset{\ominus}{C}HC_{10}H_{21} \overset{D_2O}{\longrightarrow} PhSeCHDC_{10}H_{21}$	> 95	77



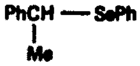
50 47 77%[a] (60)

[a]See footnote *a* to eqn (59).

$$\mathrm{PhCH_2SePh} \xrightarrow[\text{THF low temp.}]{\text{LDA}} \mathrm{Ph\overset{\ominus}{C}HSePh} \quad (61)$$

51 (76%)[a]

[a]See Ref. 54.



$\underset{\mathrm{Me}}{\mathrm{PhCH}}\mathrm{-SePh}$

52

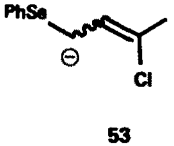
tonated under conditions successful with the parent compound 51.

(iv) *Deprotonation of allylic selenides.* Several examples in this category have been studied (Table 16).[67]

Some assessment of the ease of anion formation can be made from the Table. The acidifying effect of substituents such as Ph and Cl is evident and it is also clear that for allyl selenides the *alpha* position must not carry on alkyl substituent (entry 7). It is not surprising, therefore, that selenides of the type $\mathrm{PhSeCH_2R}$ cannot be deprotonated successfully if R is a simple alkyl group.[39]

All of the carbanions described in the above sections on deprotonation are powerful nucleophiles and, apart from the examples already given (see eqns 59 and 60 and associated discussion) they have been used for the reactions collected in Table 17.

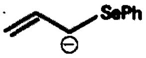
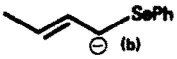
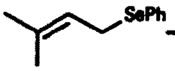
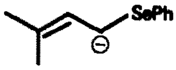
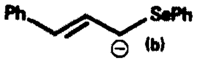
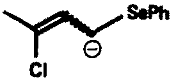
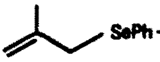
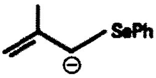
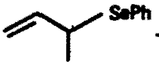
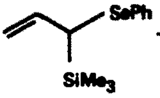
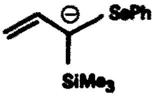
Some of the carbanions also react with secondary halides but reaction is slower and some increase in temperature and/or reaction time is needed. The anion 53[bb] decomposes appreciably within 0.5 hr at −78° and there-



53

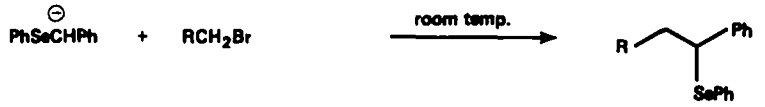
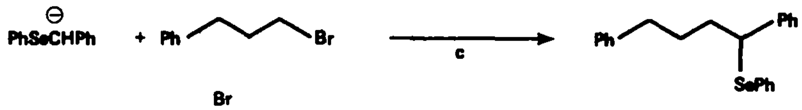
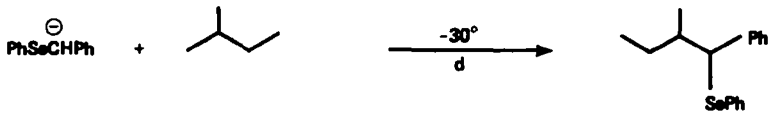
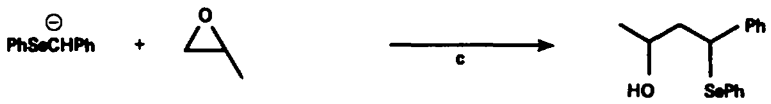
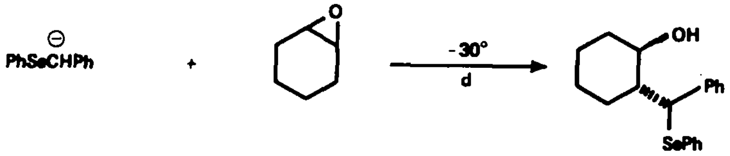
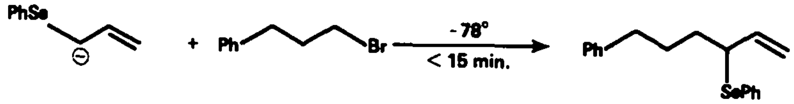
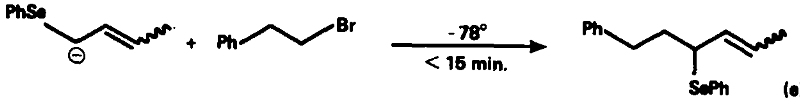
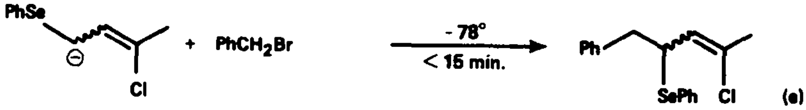
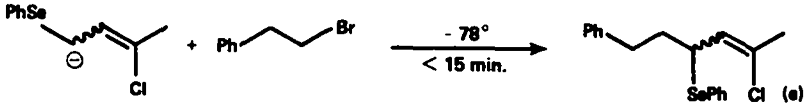
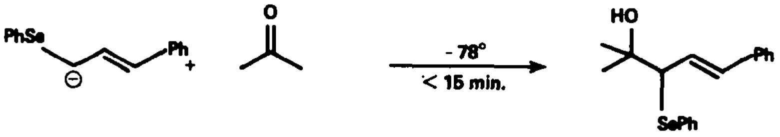
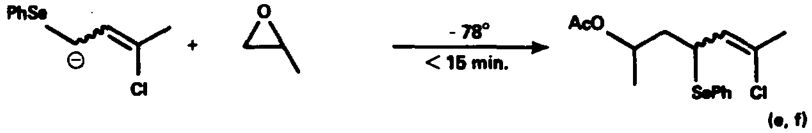
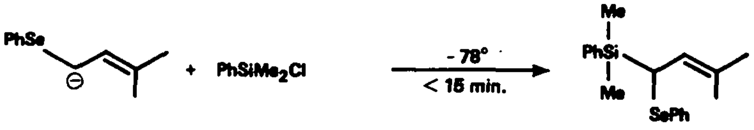
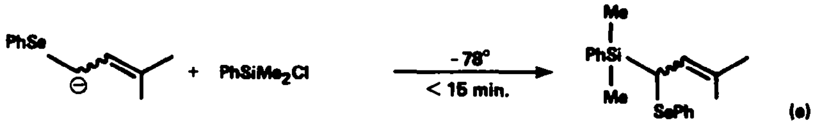
[bb]The products derived by alkylation of 53 have synthetic utility as precursors to α,β-unsaturated ketones (see p. 1108).

Table 16.[a]

1.		→		< 10 min.	− 78°
2		→		20 min.	−78°
3		→		20 min.	0°
4		→		< 5 min.	−78°
5		→		< 5 min. Rapid	−78° −100°
6		→	 c		
7		→	— d		
8		$\xrightarrow{\mathrm{Et_2NLi^e}}$			

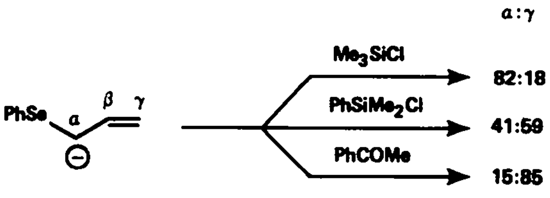
[a]LDA in THF unless otherwise stated. Times shown are those necessary for deprotonation. For the regiochemical integrity of the anions on quenching see p. 1081. [b]Presumed stereochemistry. [c]Conditions not stated. [d]Clean deprotonation not observed. [e]Less hindered bases such as lithium isobutylamide cause desilylation.

Table 17.[a]

			Yield	Ref.
1	 R = H, Me, CH_2Ph	room temp.	(78-81%)[b]	31
2		c	(81)	39
3		−30°, d	(78)	39
4		c	(66)	39
5		−30°, d	—	39
6		−78°, < 15 min.	(68)	67
7		−78°, < 15 min.	(80)	67
8		−78°, < 15 min.	(70)	67
9		−78°, < 15 min.	(85)	67
10		−78°, < 15 min.	(55)	67
11		−78°, < 15 min.	(80)	67
12		−78°, < 15 min.	(74)	67
13		−78°, < 15 min.	(63)	67

[a] All reactions run in THF. [b] Ref. 54. [c] It is not clear if the reaction was run at −78° or at −30°. [d] Reaction takes ~1.5 hr at −78° but is "rapid" at −30°. [e] Mixture of isomers. [f] Total product was acetylated.

fore its reactions with epoxides or with secondary bromides are not successful.[67] The results of Table 17 disguise the fact that reactions of the allyl-stabilized anions involve a competition between α and γ attack. Alkylation usually occurs predominantly α (Table 18) but the regioselectivity depends on the nature of the electrophile (eqn 62).[67]

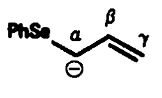
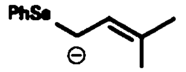
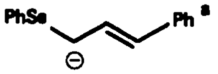
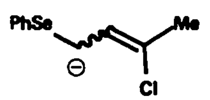


(62)

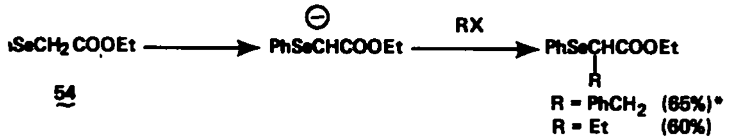
In those cases where γ-substitution occurs the products are usually 1:1 mixtures of *E* and *Z* isomers.[67] Attempts to suppress γ-alkylation were unsuccessful.[67,bb]

(v) *Deprotonation of other stabilized selenides.* The ester **54** is easily deprotonated [lithium N-isopropylcyclohexylamide, THF, −78°] and the anion reacts with alkyl halides at room temperature in the presence of dimethyl sulphoxide (eqn 63).[42]

Table 18.[67]

	~80%	α-alkylation
	> 90%	α-alkylation
	> 90%	α-alkylation
	~50%	α-alkylation
	mainly	α-alkylation

ᵃPresumed geometry.



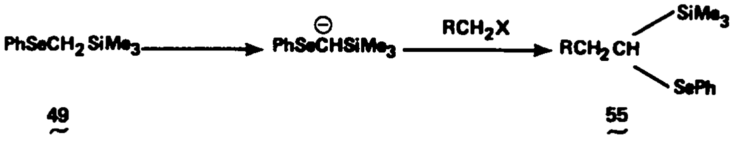
$$\text{SeCH}_2\text{COOEt} \longrightarrow \text{PhSe}\overset{\ominus}{\text{C}}\text{HCOOEt} \xrightarrow{\text{RX}} \text{PhSe}\underset{\text{R}}{\text{C}}\text{HCOOEt} \qquad (63)$$

54

R = PhCH₂ (65%)*
R = Et (60%)

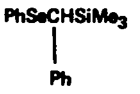
*Ref. 54.

The selenide **49** can also be deprotonated[39,87,cc] [LDA, THF, −78°, 45 min] and then alkylated [−78°–25°] by primary alkyl bromides and iodides in better than 88% overall yield (eqn 64).[87] The products **55** are convertible into aldehydes (RCH_2CHO) by oxidation.[87] The selenide **56** can be deprotonated with Et_2NLi [THF, 0°, 30 min].[39]

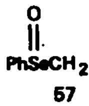


$$\text{PhSeCH}_2\text{SiMe}_3 \longrightarrow \text{PhSe}\overset{\ominus}{\text{C}}\text{HSiMe}_3 \xrightarrow{\text{RCH}_2\text{X}} \text{RCH}_2\text{CH}(\text{SiMe}_3)(\text{SePh}) \qquad (64)$$

49 **55**



56



57

(g) *Selenoxide-stabilized carbanions by deprotonation*

Unlike most phenyl alkyl selenides, the corresponding selenoxides (**57**, R = H or alkyl) can be deprotonated easily by LDA.[dd]

Methyl phenyl- and benzyl phenyl selenoxides cannot undergo selenoxide fragmentation but longer chain selenoxides must be handled below 0° to avoid olefin formation.[39] A procedure has been developed in which the phenyl alkyl selenide is oxidised *in situ* [*m*-chloroperbenzoic acid, THF, 0°[74] or −10°[39]; or ozone[39] in ether,[ee] −78°] and then deprotonated [LDA, THF, −78°].[39,74,ff] Reagents **58**–**62** were thereby generated from the corresponding selenides and found to react at −78° with aldehydes,[39,74] ketones[39,74] and reactive alkyl halides.[39] The products were then allowed to fragment[39] to olefin or reduced[74] by acidified iodide or bisulphite solution.[gg] These experiments are summarised by Table 19.

It is clear that yields are frequently good but it should be noted that the reaction with esters (entry 13) is limited to aromatic esters.

(h) *Introduction of selenium by addition across double bonds*

The double bonds of enols and their derivatives react with certain selenium reagents as already described (see

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[cc] Selenide **49** can be deprotonated successfully with sec-BuLi–TMEDA in hexane [25°, 1.5 hr].

[dd] Lithium dialkylamides do not readily cleave selenoxides.[39]

[ee] THF is unsuitable because it is attacked too rapidly by ozone.

[ff] Anion formation needs two equivalents of LDA if *m*-chloroperbenzoic acid is used.

[gg] For uses of the resulting selenides see p. 1110.

Table 19.[a]

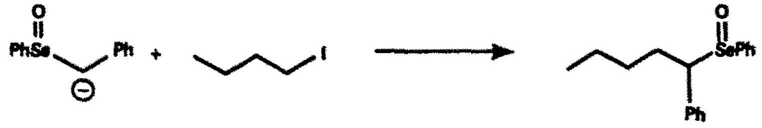
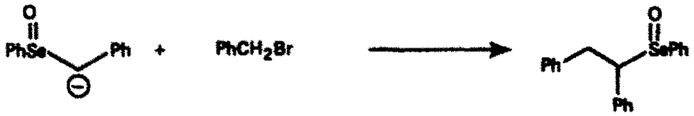
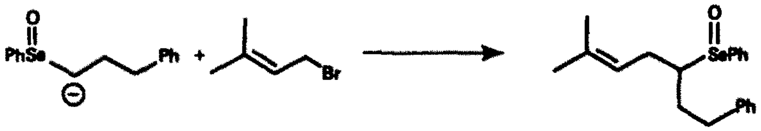
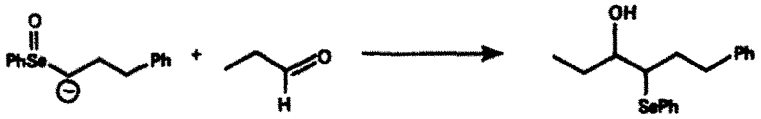
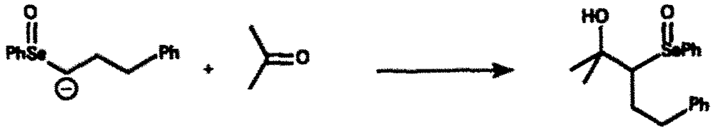
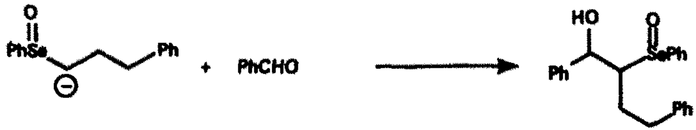
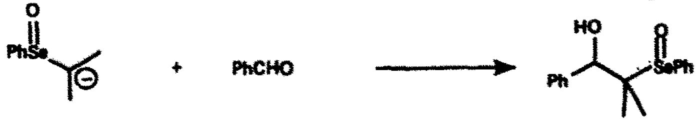
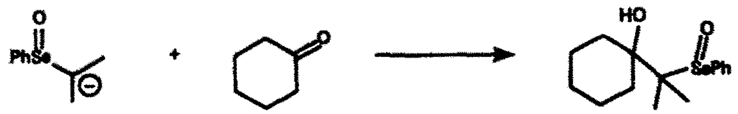
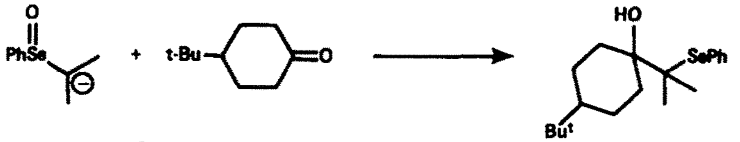
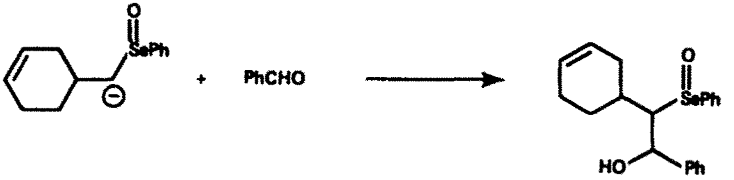
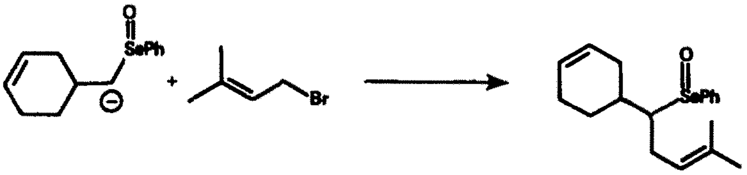
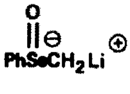
			Yield	Ref.
1		(b)	(76%)	39
2		(b)	(88)	39
3		(b)	(81)	39
4		(b)	(63)	39
5		(b, c)	(64)	39
6		(d, e, f)	87	74
7		(b)	(59)	39
8		(d, f)	88	74
9		(b)	(81) (76)[f]	39 39
10		(b, g)	(72)	39
11		(b)	(81)	39
12		(b)	(56)	39
13		(b)	(73) (81)[f]	39 39

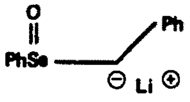
Table 19 (*Contd.*).

14		(d, f, h)	82	74
15		(b, f, g)	(50)	39
16		(b, f, g)	(46)	39

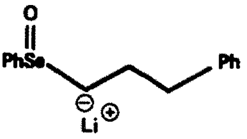
[a]Reactions conducted at −78° usually in 1:1 THF:Et_2O, Et_2O being the solvent used for ozonization of the selenides. Yields are given in the notation of Ref. 54. [b]This selenoxide was allowed to fragment (see later). [c]Reaction time specified as 15 min. [d]Reaction run in THF and initial product reduced. [e]Mixture of diastereoisomers. [f]*m*-Chloroperbenzoic acid used. [g]Presumably a mixture of diastereoisomers. [h]Relative stereochemistry not determined.



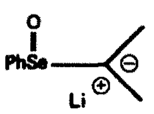
58 Ref. 39



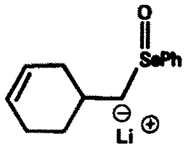
59 Ref. 39



60 Ref. 39, 74



61 Ref. 39, 74

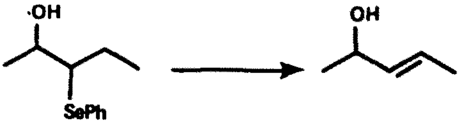


62* Ref. 39

*Ozone cannot be used to make the selenoxide but *m*-chloroperbenzoic acid [−10°] works well.

p. 1057). This section deals with reactions involving unactivated double bonds and reagents of the type PhSeX where X can be (formally) equivalent to Cl, Br, $OCOCF_3$, OAc, OMe or OH. A few early examples were carried out under quite vigorous conditions usually employing complex selenium compounds.[45]

My own experiments were based on the finding that hydroxyalkyl selenides[hh] are synthetically equivalent to allylic alcohols (eqn 65)[40] and it was, therefore, worthwhile to develop a method for converting simple olefins into β-hydroxyalkyl selenides under conditions that were just as mild as those used for the process summarized by eqn (65). This objective was achieved[63] by adding ethereal PhSeBr [1.2 equiv.] to a cold [−10°] ether solution of the olefin [1 equiv.] and an excess of CF_3COOAg. After a 2-hr period at +20° treatment with aqueous methanolic sodium bicarbonate [room temperature, 3 hr] effected hydrolysis of the trifluoroacetyl group incorporated by the process and *trans*-β-hydroxyalkyl selenides were formed (eqns 66–68).[63]

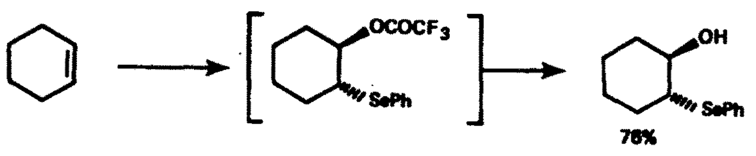


(65)

Mechanistically, the adduct 63 and/or the reagent 64 (generated *in situ*) are involved (eqns 69 and 70). Other work[46] has, in fact, shown that 64 is formed on mixing the reagents described by eqn 70 and that 64 adds rapidly to olefins in an inert solvent.

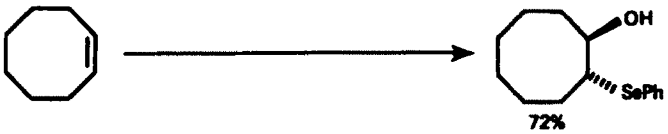
The trifluoroacetyl group was chosen on account of the solubility of the silver salt in organic solvents and also because the final product can be hydrolised under conditions that do not sacrifice the mildness of the addition process. The following β-hydroxyalkyl selenides (Table 20) were made[46] from preformed reagent and in these experiments ethanolic potassium hydroxide was used for the hydrolysis.

The addition is stereospecific (*trans*) but the regioselectivity is poor. Nevertheless, the reaction is a potentially useful supplememt to the opening of epoxides by $PhSe^-$. The conditions are extremely mild and, in

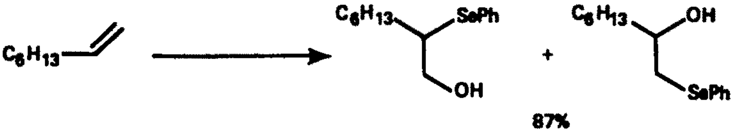


(66)

[hh]These had previously been obtained by treating an epoxide with $PhSe^-Na^+$.

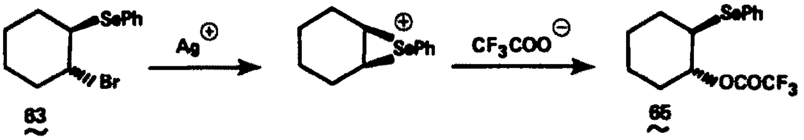


(67)



(68)

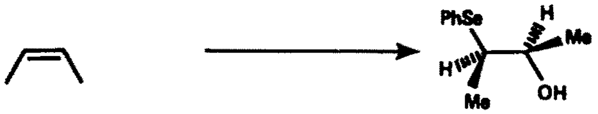
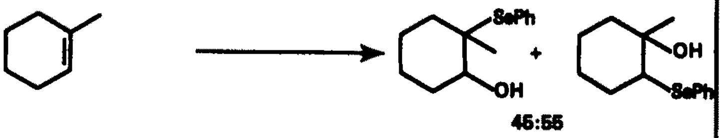
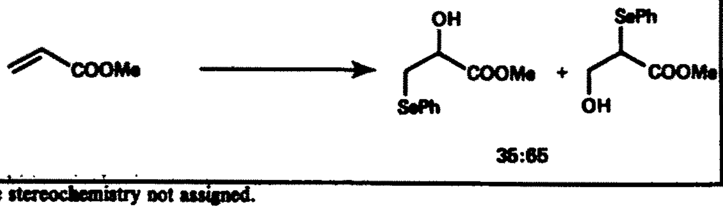
*Slight predominance of this isomer.



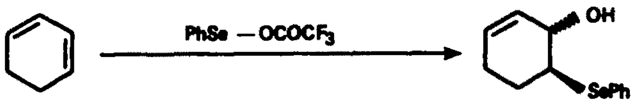
(69)

$$PhSeBr + AgOCOCF_3 \longrightarrow \underset{64}{PhSe{-}OCOCF_3} \longrightarrow 65 \qquad (70)$$

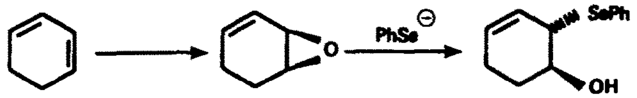
Table 20.

1		92%
2		94
3		90
4		Total yield: 93%*
5		69
6		96
7		Total yield: 71%

*Relative stereochemistry not assigned.



Ref. 46 (71)



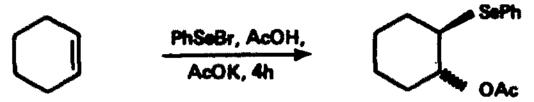
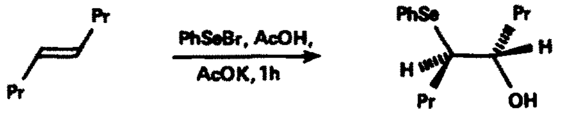
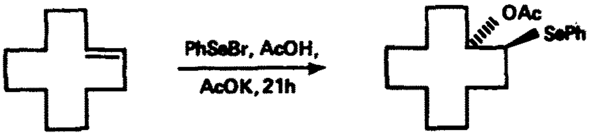
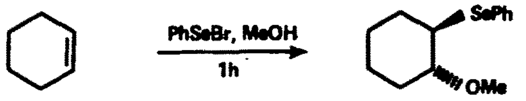
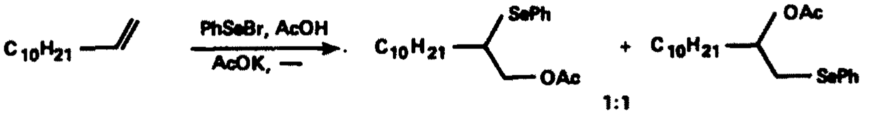
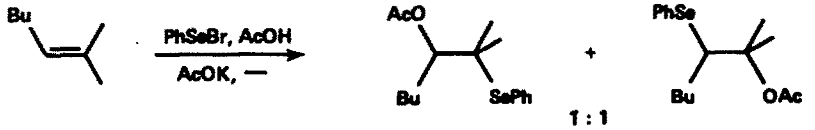
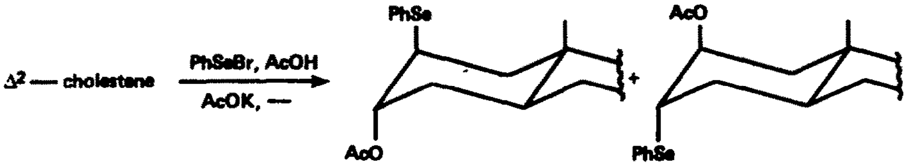
Ref. 40 (72)

some cases, the regiochemical result is opposite to that of the epoxide route (see eqns 71 and 72).

The general process is not limited to trifluoroacetates. Use of PhSeBr with silver *acetate* in acetic acid gives PhSe–OAc which also adds to olefins but the same result can be accomplished without expensive silver salts; the olefin is simply added to an acetic acid solution of PhSeBr followed by treatment with an excess of potassium acetate.[58] Acetolysis of an initially formed β-bromoalkyl selenide is occurring or else there is direct addition of PhSe–OAc across the double bond. If the reaction is run in methanol then a β-methoxyalkyl selenide is formed.[58] Again, the mechanism remains to be established.[u] Table 21 summarizes the results obtained[58] with the silver-free method.

Cholesterol failed to react with PhSeOAc,[58] while the allylic alcohol **66** gave [v] the selenenyl ester (which collapsed to ketone) (eqn 73).[69]

Table 21.

		Yield
1		(78%)[a]
2		(91)
3		(85)
4		(93)
5		—
6		—
7		—

[a]Notation of Ref. 54.

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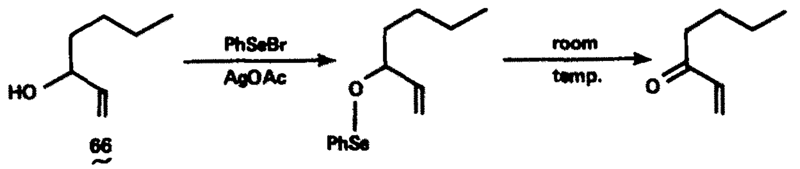
[u] The facility with which PhSeBr adds to double bonds, even in the presence of other nucleophiles, has been noted (p. 1062).

[v] The conditions used could have allowed reversible addition of PhSe–X across the double bond.



(73)

Finally, some unusual observations have been made, which merit attention.

(i) When cyclohexane is refluxed in acetic acid with one equivalent of PhSe(O)OH, then the *trans*-β-acetoxyalkyl selenide, previously made with PhSe–OAc, is obtained in 90% yield.[88]

(ii) An apparently simple way of making β-acetoxyalkyl selenides is[89] to reflux the olefin with dimethyl selenoxide for several hours in $CHCl_3$ containing AcOH. The results reported[89] are shown in Table 22.

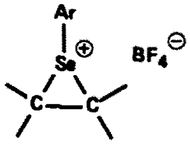
The regiospecificity observed with hex-1-ene is unusual[kk] and it should also be noted that selenoxide fragmentation of methyl (as opposed to phenyl) selenoxides has not been studied in much detail (see p. 1054).

(iii) The reagent PhSe–OAc can be generated by reaction of PhSe–NMe_2 with acetic anhydride.[60] The selenenamide itself does not react with cyclohexene but it does combine with some Michael acceptors, apparently as shown (eqn 74).[60]

For completeness a few miscellaneous studies concerning additions across double bonds should be cted:

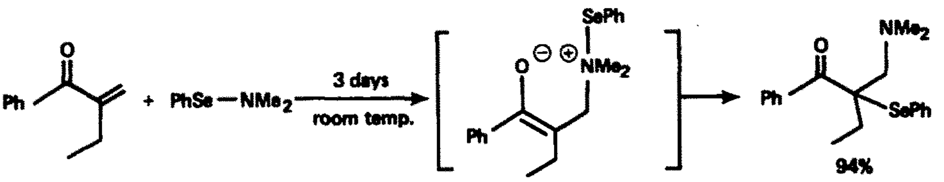
The regioselectivity of the reaction of PhSeCl with olefins has been examined briefly[90,91] and the mechanism of the addition is being investigated.[92–94]

Treatment of β-haloalkyl selenides with Ag^+ salts gives compounds of type 67. These in turn, afford β-substituted selenides on treatment with Cl^-, Br^- or AcO^- by attack at carbon.[95]



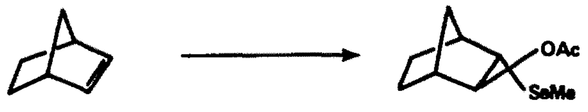
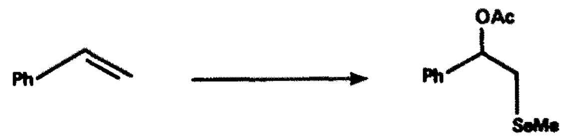
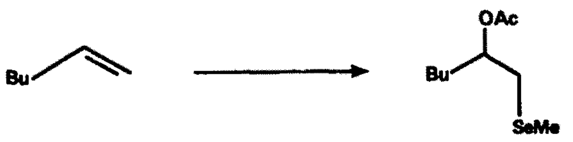
67

Finally, an intramolecular version has been found of the addition of ArSe–OH across a double bond.[96]



(74)

Table 22.

		Yield
1		83%
2		88
3		84
4		87

[kk] Possibly the thermodynamically more stable product is the one isolated and it accummulates via isomerisation of the kinetic product.[90]

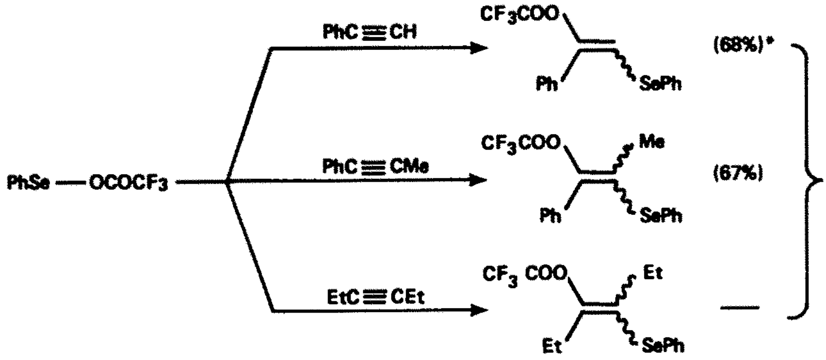
(i) *Introduction of selenium by addition across triple bonds*

Synthetic utility has not so far been demonstrated for the products that result from the reaction of ArSeX with acetylenes but some examples have been reported,[97–99] as well as a study[95] that is a mechanistic relevance.

PhSeCl reacts[97–99] with acetylenes to give halovinyl selenides largely[ll] of *trans* stereochemistry (e.g. eqn 75) and $PhSeOCOCF_3$ gives trifluoroacetoxyvinyl selenides (of unestablished stereochemistry) (eqn 76).[46]

The vinyl trifluoroacetates may possibly find use as precursors to the enolates of α-phenylselenoketones.

(75)



(76)

*Notation of Ref. 54.

but nitrophenyl alkyl selenides (see p. 1055) have not been tested. Over-oxidation did not occur.

In my experiments[4] with α-phenylselenoketones a three-fold excess of $NaIO_4$ in aqueous glyme was used, the composition of the mixture being such as to dissolve both reagent and substrate. Although the minimum reaction period was not determined it is clearly less than 12 hr at room temperature. V.p.c. analysis at the end of this time indicated very high yields of the enones produced by selenoxide fragmentation (eqns 77 and 78).[4]

The choice of periodate was made for the reason that the enones appeared to be inert to it and the use of the reagent in excess ensured that PhSe–OH, a product of the selenoxide fragmentation was not oxidised to PhSe(O)OH at the expense of residual selenoxide.[100]

The other cases where $NaIO_4$ has been used are listed in Table 23. Usually the selenoxide fragments *in situ* and only the unsaturated product is isolated.

(D) SELENOXIDE FRAGMENTATION: PROCEDURES FOR OXIDATION OF SELENIDES AND FOR FRAGMENTATION OF SELENOXIDES

In this Section a few introductory comments are made about each of the methods and the published examples are listed. The conclusions to be drawn from these data are then examined.

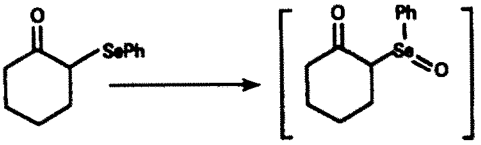
(a) *Oxidation-fragmentation*: *use of sodium periodate*

Early work[27] had established that phenyl alkyl selenides[mm] are convertible into selenoxides in good yield by treatment at 0° in aqueous methanol with $NaIO_4$. Di-(*p*-nitrophenyl)selenide was inert to the reagent[27,nn]

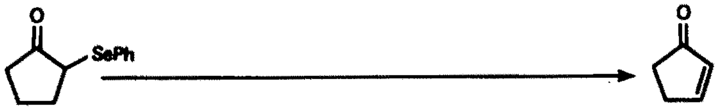
(b) *Oxidation-fragmentation*: *use of peracids*

A number of selenides have been oxidised with peracids below 0°[oo] and the resulting selenoxides have been allowed to collapse directly or have been deprotonated and used (at low temperatures) for further transformations (see p. 1081). The oxidation and fragmentation stages are summarised by Table 24.

The use of peracids as opposed to other reagents is frequently a matter of personal preference but in the case of the olefinic selenide of entries 6 and 7, peracid was more selective than ozone.



(77)



(78)

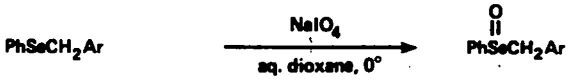
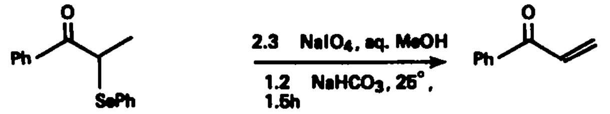
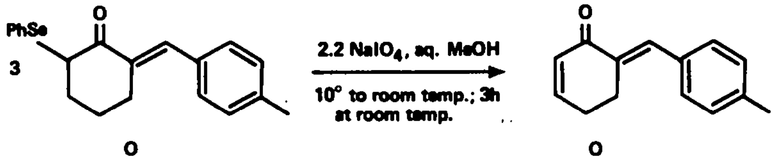
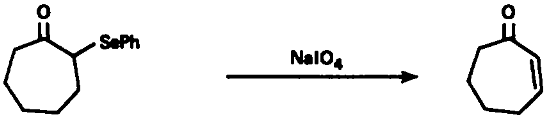
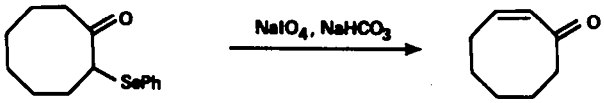
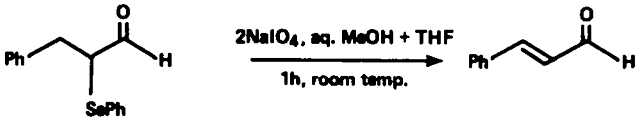
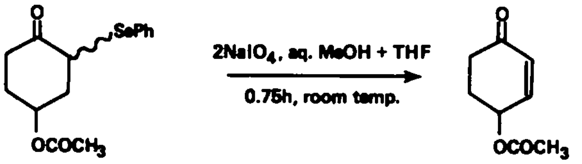
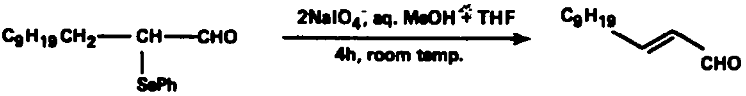
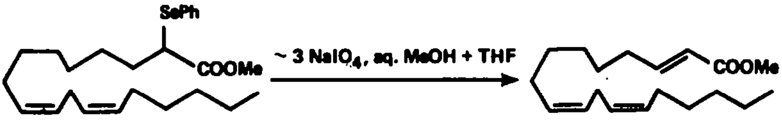
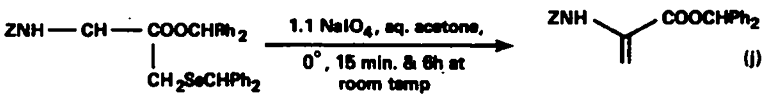
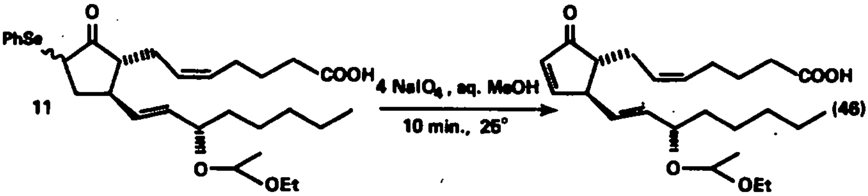
[ll] The compounds may have been pure *trans* isomers.

[mm] $PhSeCH_3$ and $PhSeCH_2Ph$. The selenoxides cannot undergo the fragmentation process.

[nn] $PhICl_2$ reacted with all the selenides studied and may merit renewed attention.

[oo] Modern practice calls for −78°.

Table 23.[a]

		Yield	Ref.
1	 (b)	~ 100%	66
2	 (e)	89 84^{c,d}	6, 41 42
3		68^d 74	6 6, 41
4	 (f)	< 10%	41, 49
5	 (g)	14	41, 49
6		67^d	42
7	 (h) (i)	47	42
8		46^d	42
9		80^d	42
10	 (j)		26
11		(46)	51

[a] Amounts of reagent, where reported, are here given relative to 1 millimole of starting material: 1 NaIO$_4$ denotes 1 equivalent of reagent; NaIO$_4$ indicates an unspecified amount. Yields are quoted using the notation of Ref. 54. [b] Ar = Ph or substituted phenyl: 4-Me-C$_6$H$_4$–, 3-Me-C$_6$H$_4$–, 4-NO$_2$-C$_6$H$_4$–, 3-NO$_2$-C$_6$H$_4$–, 4-Cl-C$_6$H$_4$–, 4-MeO-C$_6$H$_4$–. No selenoxide could be isolated for Ar = 2-Me-C$_6$H$_4$–. [c] Yield without buffer. [d] This yield refers to overall conversion (including selenenylation) of the carbonyl compound to enone. [e] See use of H$_2$O$_2$: Table 27, entry 36. See also Table 28, entry 1. [f] See use of O$_3$: Table 26, entry 15 and use of H$_2$O$_2$: Table 27, entry 53. [g] Of various procedures tried (Ref. 41) only use of O$_3$ under special conditions (Table 26, entry 17) gave modest yields of enone. [h] Stereochemistry not specified. [i] See use of H$_2$O$_2$: Table 27, entry 48. [j] The material consisted of roughly equal amounts of olefin and the starting selenide. See use of H$_2$O$_2$: Table 27, entry 69.

Table 24.[a]

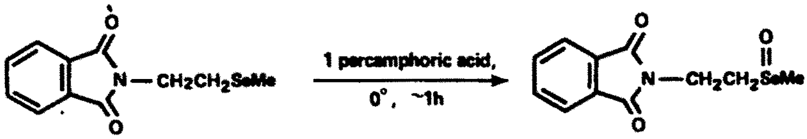
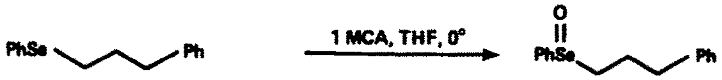
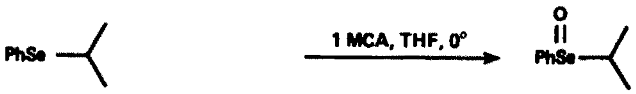
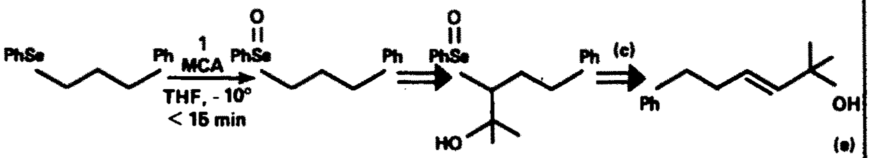
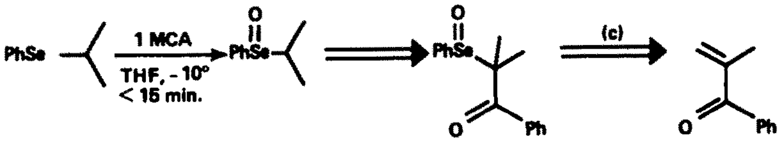
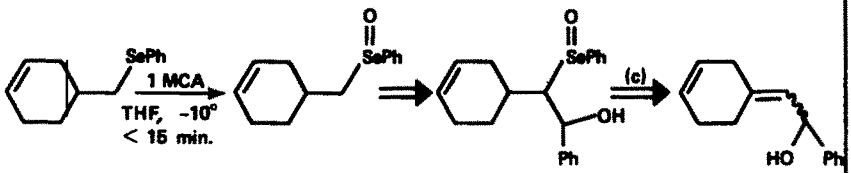
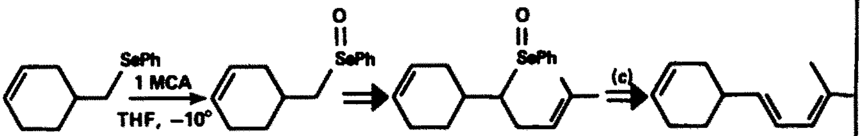
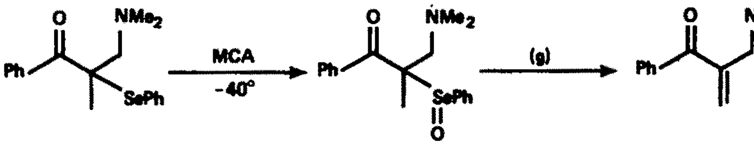
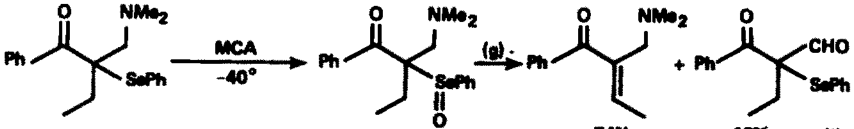
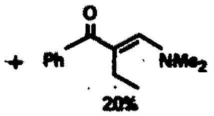
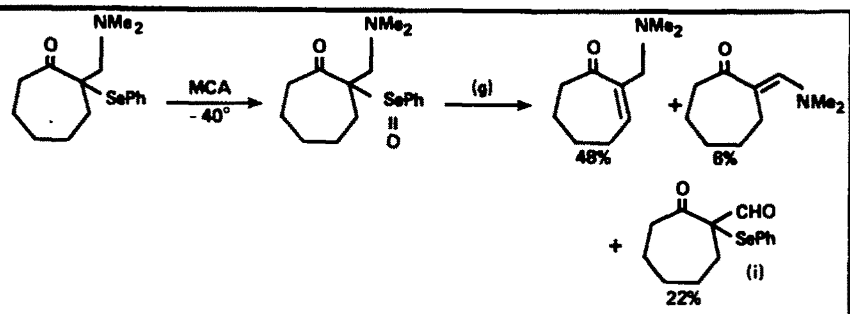
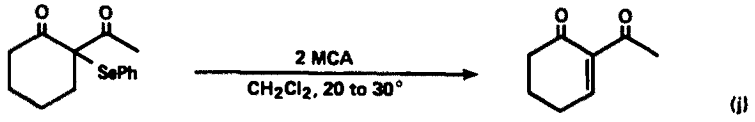
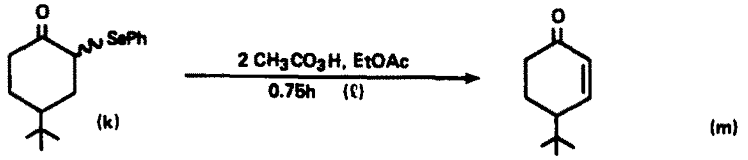
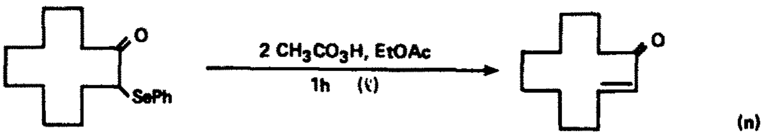
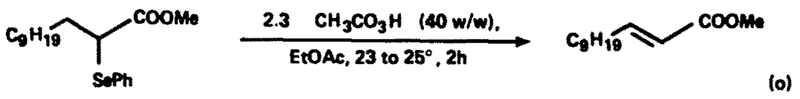
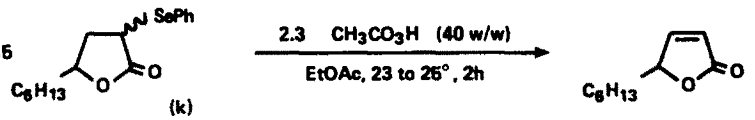
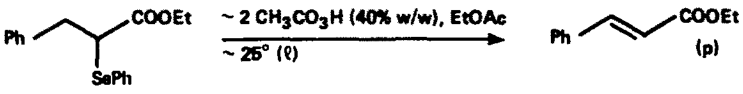
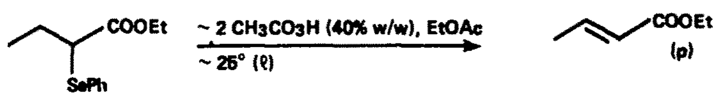
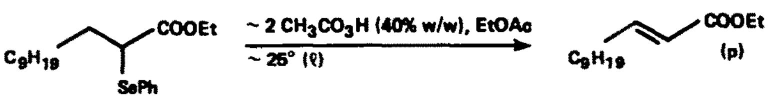
		Yield	Ref.
1	 (b)	89%	28
2		(87)	74
3		(82)	74
4	 (e)	76[d]	39
5	 (f)	81[d]	39
6		50[d]	39
7		46[d]	39
8	 (h)	84	60
9	 54% 10% (i)  20%		60

Table 24 (*Contd.*).

10			60
11		86	41
12		(45)	42
13		(75)	42
14		(83)	42
15		(56)	42
16		(65-80)[q]	42
17		(60-83)[q]	42
18		(79-82)[q]	42

[a] The notation explained in footnote *a* to Table 23 is used. MCA stands for *m*-chloroperbenzoic acid. [b] Optically inactive selenoxide was obtained. See use of H_2O_2: Table 27, entry 1. [c] The following procedure for decomposition of the selenoxide was probably used: sufficient AcOH is added to neutralise strong base in the mixture and to protonate half the amine present. The cold selenoxide solution is then added to refluxing CCl_4 or CH_2Cl_2 under these mildly basic conditions. The elimination is complete almost instantaneously. [d] Overall yield from selenide. [e] See use of O_3: Table 26, entry 31. [f] See use of O_3: Table 26, entry 35. [g] Reaction mixture was warmed to room temperature. [h] Only traces of product formed from the other direction of elimination. [i] This is a selenenylation product of the imine, which can itself be isolated in about 20% yield, as shown. [j] Crude material less than 2% enolized; distilled material is a 60:40 keto-enol mixture. See use of O_3: Table 26, entries 20 and 21. See use of H_2O_2: Table 27, entry 78. [k] Stereochemistry not reported. [l] These, probably, are the conditions used. [m] See use of H_2O_2: Table 27, entry 47. [n] (*Z*)-Isomer not detected. See use of H_2O_2: Table 27, entry 55. [o] (*Z*)-Isomer not detected. For α-phenylselenoesters peracids are just as effective as H_2O_2. This is not true of α-phenylselenoketones. [p] See use of H_2O_2: Table 27, entry 20. [q] Yield depends on selenenylation procedure. It is not clear whether both CH_3CO_3H and H_2O_2 were examined in the oxidation of this compound.

(c) *Oxidation-fragmentation: use of ozone*

In principle use of ozone has certain advantages. The reagent is easy to handle and an excess is removable without difficulty. Moreover a certain amount of background information has been available for some years.

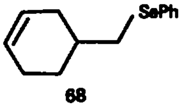
Selenides react[23b] quantitatively with O_3 in an inert solvent (CCl_4, $CHCl_3$, $MeNO_2$) at −10 to −50°.[99] The reaction is clean, and brief exposure to an excess of the reagent does not yield selenones. The following rate data are reported (Table 25). Sulphides appear to react some 50 times less rapidly than do olefins.[101]

Other ozonolyses,[102] carried out at −5–10°, showed that, at least for dialky selenides, further oxidation to selenone occurs at a rate comparable to formation of selenoxide.

Table 25.

Substrate	Relative Rate of Oxidation
PhSePh	1
PhSeBu	4.1
BuSeBu	34
$Me_2C{=}CHEt$	<1
BuSBu	<<1

Although selenide oxidation is fast (see Table 25) O_3 is not always the oxidant of choice if the substrate contains a carbon–carbon double bond. Phenyl allyl selenide can be oxidized cleanly[39] but in the case of the compound **68**, MCA is more selective than O_3.



68

The following ozonolyses are reported and Table 26 also gives, where available, the conditions under which the selenoxides were allowed to fragment. The protocol for selenoxide fragmentation can be critical.

(d) *Oxidation-fragmentation: use of hydrogen-peroxide*

Hydrogen peroxide is very frequently used for oxidising selenides. The reagent is cheap, it usually performs well, and it can often be added directly to the reaction vessel in which the selenide has been prepared. The following examples have been published (Table 27):

Table 26.[a]

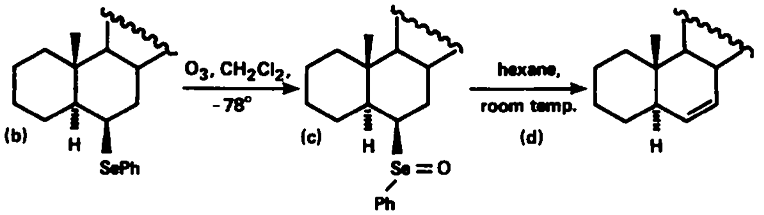
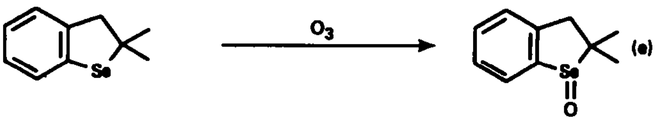
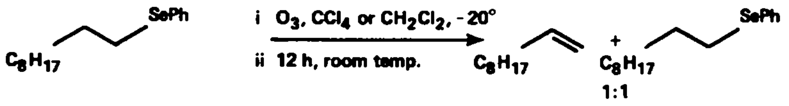
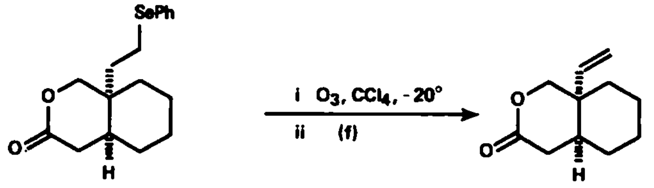
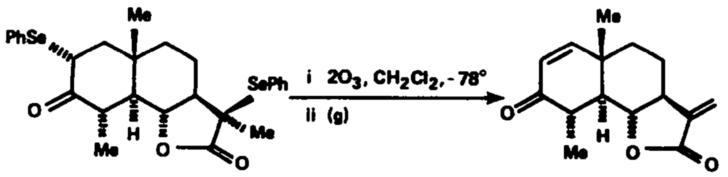
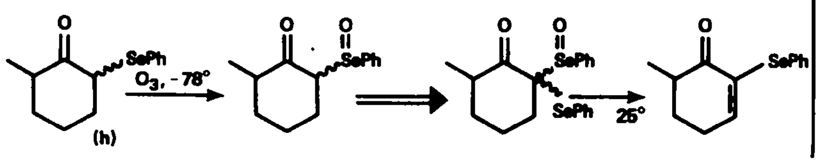
		Yield	Ref.
1		> 95%	25
2			96
3		~100	36
4		~60.5	36
5		60	50
6		57[i]	49

Table 26 (*Contd.*).

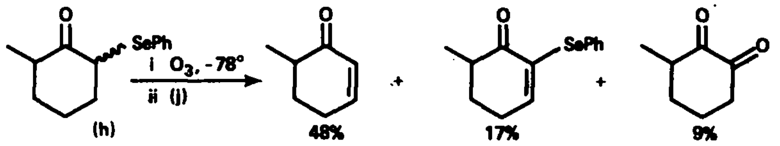
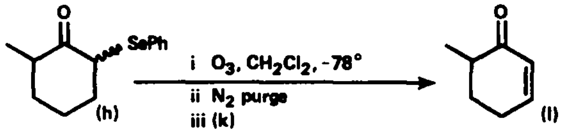
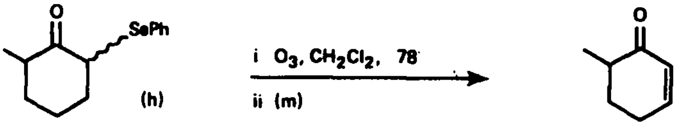
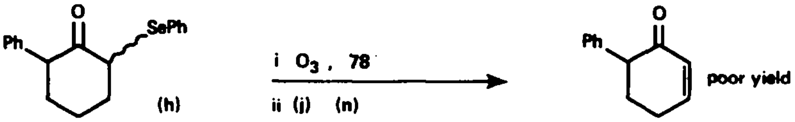
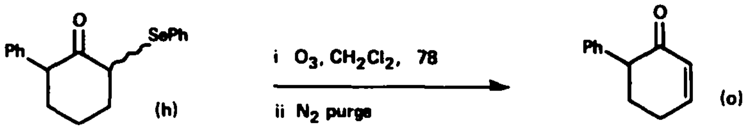
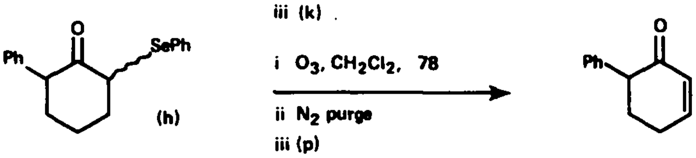
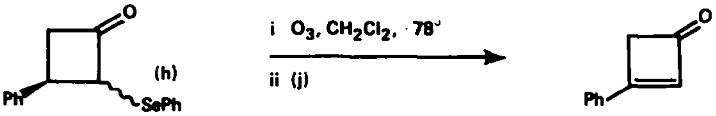
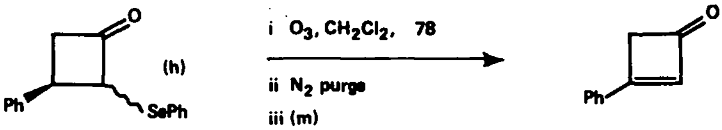
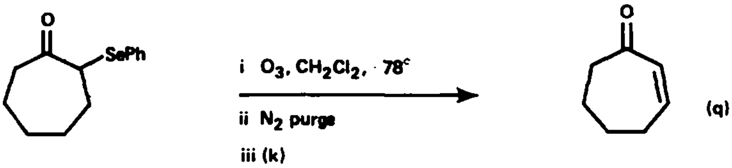
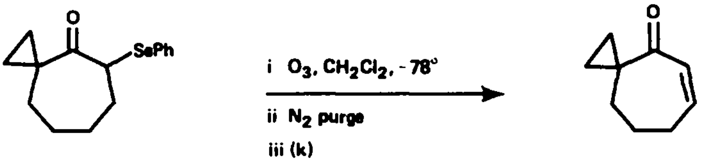
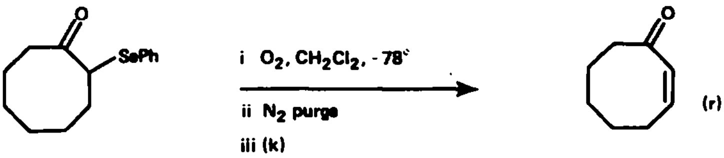
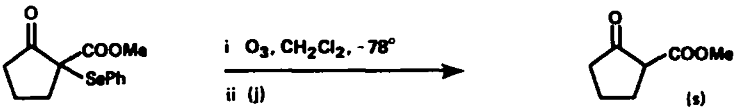
7			49
8		(73)	41
9		48	41
10			49
11		(62)	41
12		(58)	41
13		(58)	49
14		53	41
15		50 55^p	41
16		85	41
17		56	41
18		(28)	49

Table 26 (*Contd.*).

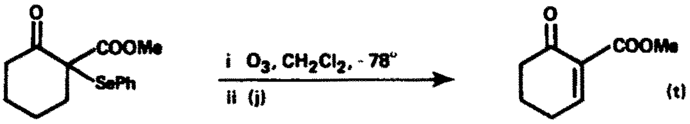
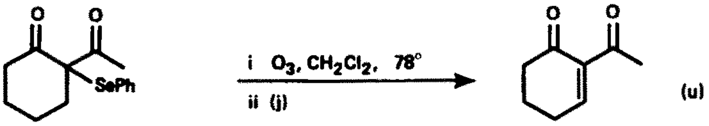
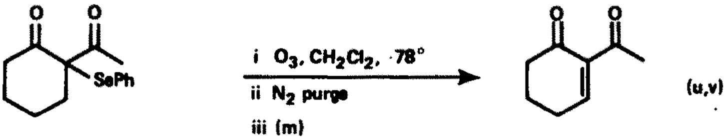
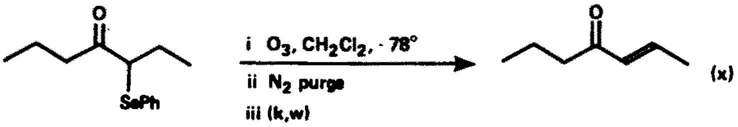
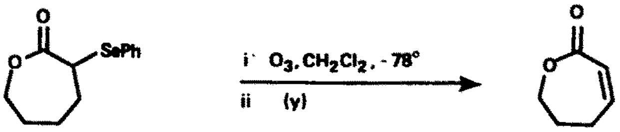
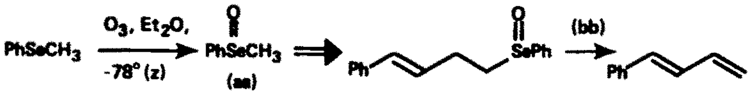
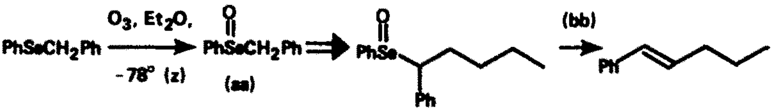
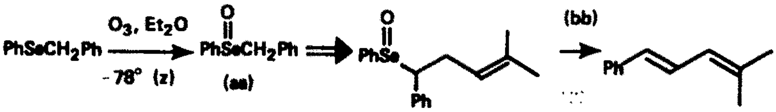
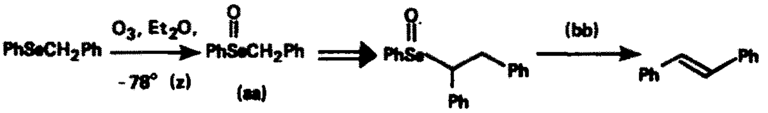
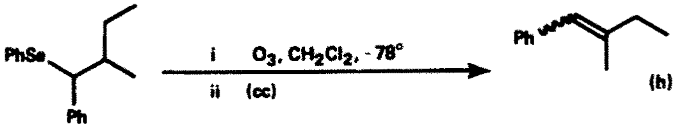
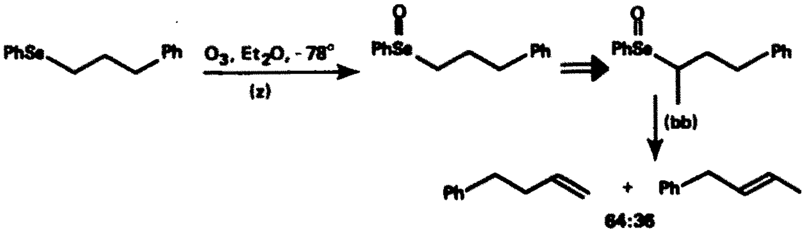
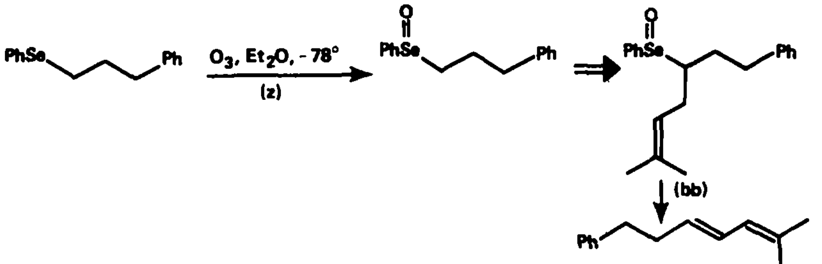
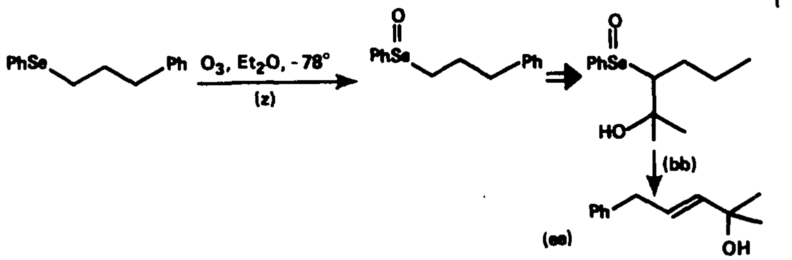
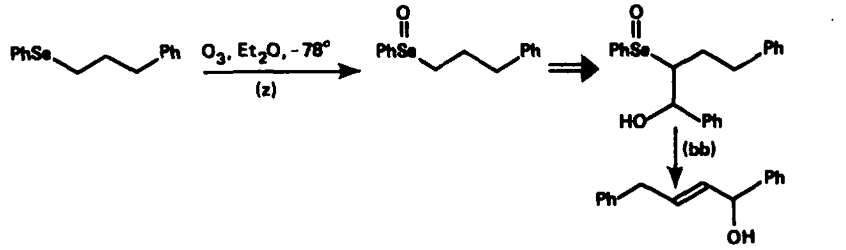
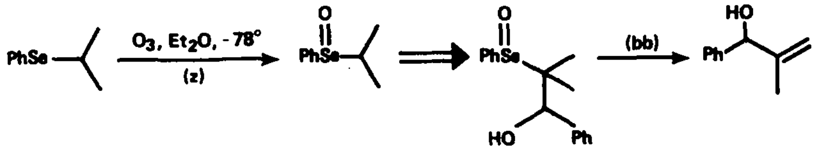
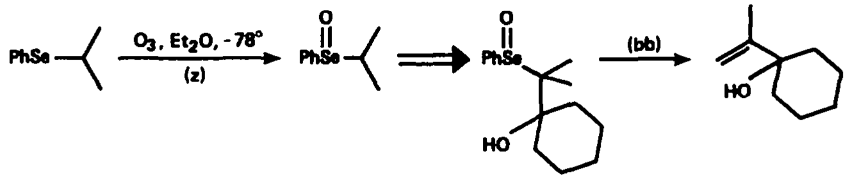
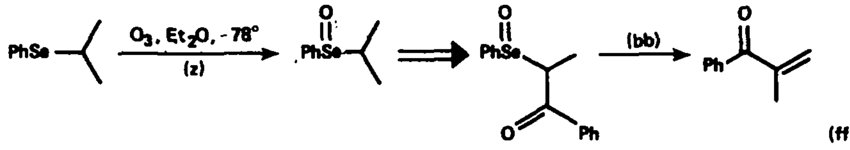
19		(81)	49
20		(90)	49
21		(84)	41
22		(80)	41
23		66	41
24		75^{i}	39
25		81^{i}	39
26		88^{i}	39
27		63^{i}	39
28		78^{dd}	39
29		59^{i}	39

Table 26 (*Contd.*).

30		64^i	39
31	 (ee)	81^i	39
32		72^i	39
33		81^i	39
34		55^i	39
35	 (ff)	73^i	39

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[a] The notation explained in footnote *a* to Table 23 is used. [b] Cholestane skeleton. [c] (*R*)- and (*S*)-isomers were produced in 2 : 1 ratio. [d] The (*S*)-selenoxide decomposes completely at 0° within 4 hr. The isomer is stable under these conditions. [e] Decomposes at room temperature. [f] The cold selenoxide solution was added over 10 min to refluxing CCl_4. If the selenoxide solution is merely heated from room temperature to reflux a mixture of olefin and selenoxide results. See entry 3 of this Table. [g] Warm reaction mixture to room temp. over 1 hr. [h] Stereochemistry not specified. [i] Overall yield from starting selenide. [j] Warm reaction mixture to room temp. [k] Cold Pr_2^iNH [1 mmole] was added and the solution [− 78°] was transferred isothermally to refluxing CCl_4 containing 0.5 mmole Pr_2^iNH. These quantities are stated explicitly for entries 8, 15, 16, 19. [l] See use of H_2O_2: Table 27, entry 45. [m] Pyridine [2.4 mmole] was added to reaction mixture [− 78°] which was then allowed to reach room temperature. The quantity of pyridine is given explicitly for entries 14 and 21. [n] The method used for oxidation is not absolutely clear from Ref. 49. [o] See use of H_2O_2: Table 27, entry 43. [p] Procedure of footnote *k* followed but Et_2NH was used instead of Pr_2^iNH. [q] See use of $NaIO_4$: Table 23, entry 4 and use of H_2O_2: Table 27, entry 53. [r] Of various procedures tried (Ref. 41) only the techniques of footnotes *k* and *p* gave modest yields of enone. For use of $NaIO_4$ see Table 23, entry 5. [s] See use of H_2O_2: Table 27, entry 72. [t] See use of H_2O_2: Table 27, entry 73. [u] See use of peracid: Table 24, entry 11 and use of H_2O_2: Table 27, entry 78. [v] Less than 1% enolized but material was not heated above 40°. [w] Details not reported. From the context the method shown was probably used. [x] See use of H_2O_2: Table 27, entry 34. [y] Warm to room temperature over 10 min. There is no indication whether or not O_3 was first removed at low temp. [z] Et_2O is used for ozonolysis as it is less rapidly attacked than THF. [aa] It is not absolutely clear from Ref. 39 whether the selenoxide was generated *in situ*. From the context the method shown would have been used for *in situ* generation. [bb] Sufficient AcOH is added to protonate all basic species present except half of the Pr_2^iNH (from LDA). The cold selenoxide solution is then added to refluxing CCl_4 or CH_2Cl_2. Fragmentation is almost instantaneous. These conditions were probably used. [cc] Selenoxide added to refluxing CCl_4. Possibly no base was present. [dd] Yield from $PhSeCh_2Ph$ (which was deprotonated with LDA). [ee] See use of peracid: Table 24, entry 4. [ff] See use of peracid: Table 24, entry 5.

Table 27[a]

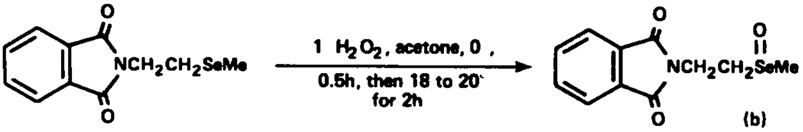
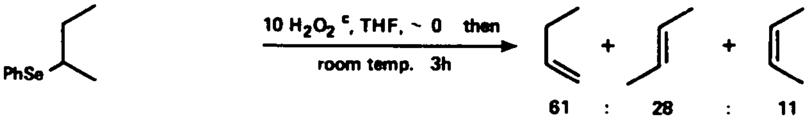
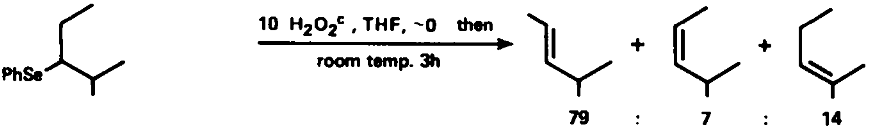
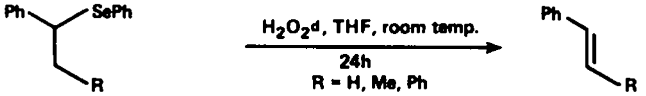
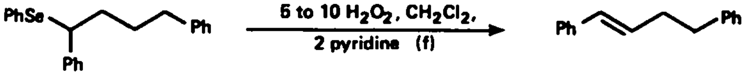
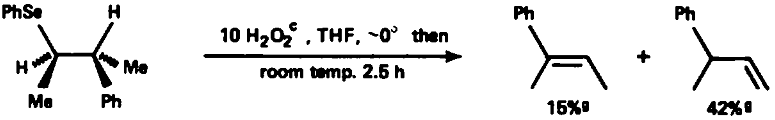
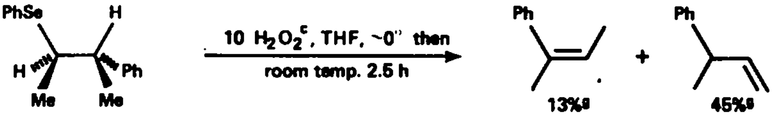
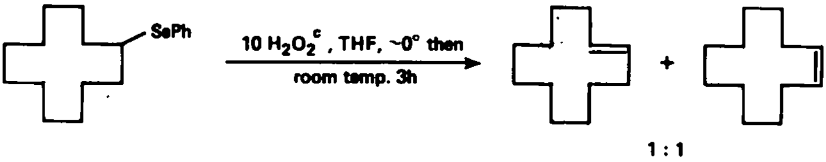
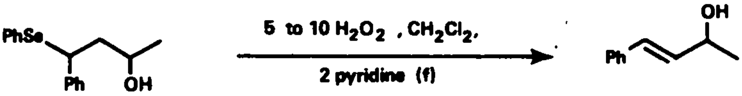
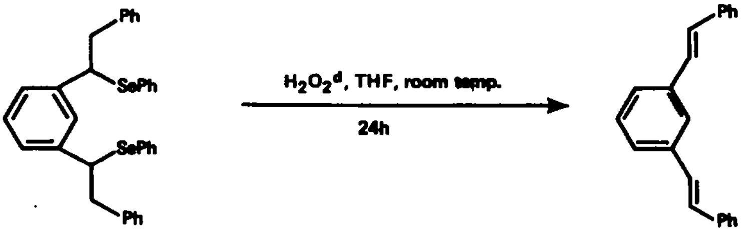
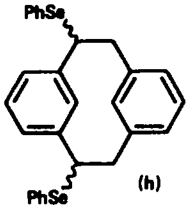
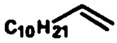
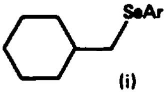
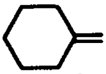
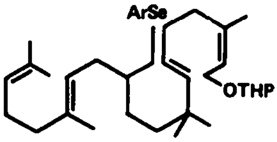
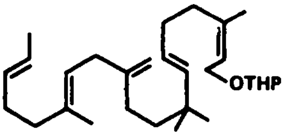
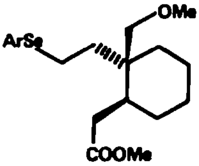
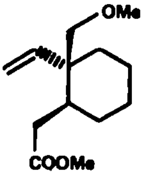
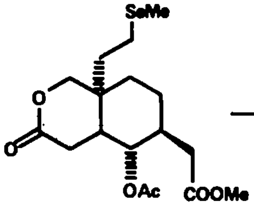
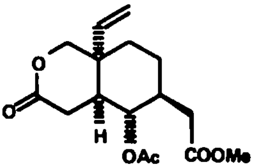
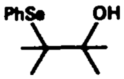
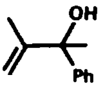
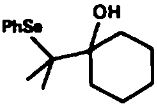
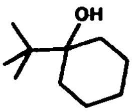
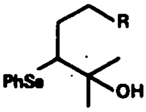
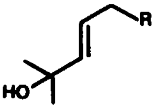
		Yield	Ref.
1		60	28
2		Total 71%	5
3		Total 100%	5
4		(76-81)[e]	31
5		(81)	39
6			5
7			5
8		Total 94	5
9		(66)	39
10		(62)	31

Table 27 (*Contd.*).

11	 (h)	$H_2O_2{}^d$, THF, room temp. 24h	no cyclophanediene	–	31
12	$C_{12}H_{25}SeAr$ (i)	10 $H_2O_2{}^d$, THF, ~0° then room temp. 20h for Ar=Ph	 Ar = Ph	77	32
			Ar = 2 $NO_2C_6H_4$ conditions: 0°, 0.5h	91	32
13	 (i)	10 $H_2O_2{}^d$, THF, ~0° then room temp. 9.5hr	 Ar = Ph	47	32
			Ar = 2 $NO_2C_6H_4$	92	32
14		2 $H_2O_2{}^j$, THF, 3.5h	 Ar = 2 $NO_2C_6H_4$	75	34
			Ar = Ph	< 4	34
15		4.8 $H_2O_2{}^{j,k}$, THF, 0° then room temp. 12 h, Ar = 2–NO_2–C_6H_4		92	33
16		$H_2O_2{}^j$, THF, Ar = 2–NO_2–C_6H_4		(81)	38
17		10 to 20 $H_2O_2{}^d$, THF; ~0° to room temp. (l)		80	78
18		10 to 20 $H_2O_2{}^d$, THF, ~0° to room temp. (l)		93	78
19		10 to 20 $H_2O_2{}^d$, THF, < 20°, then room temp. 5 to 12 h (e)		(50%) to (95%)^e	40

R ,

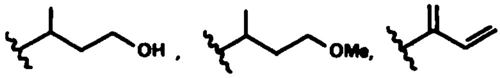


Table 27 (*Contd.*).

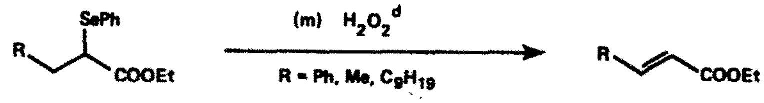
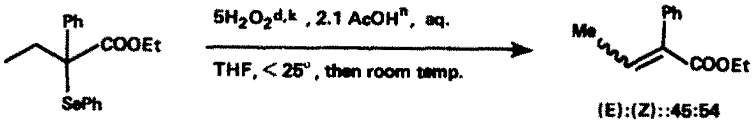
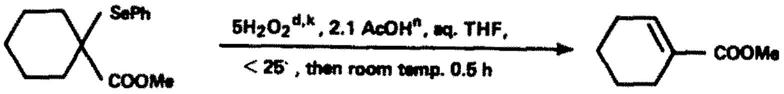
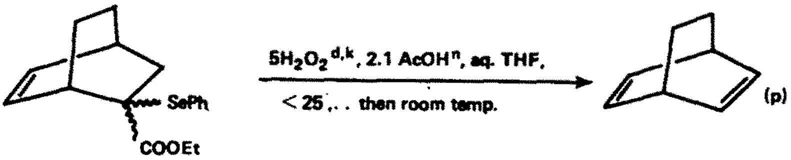
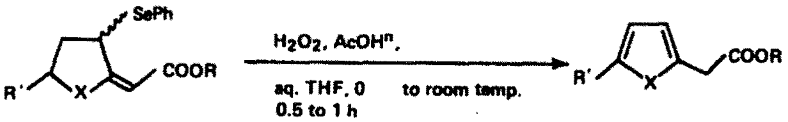
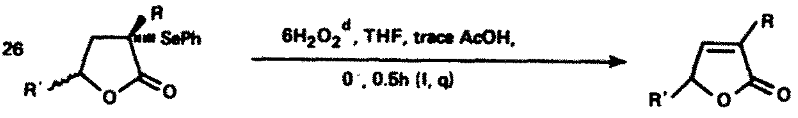
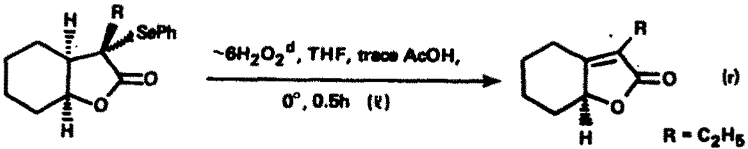
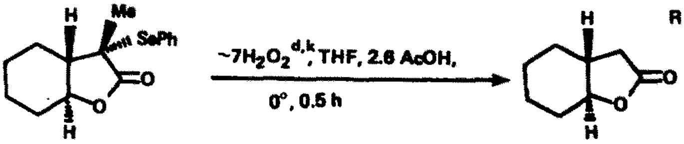
20		(~60 ~80%)	42
21		(79)	6, 41
22		(96) 90 o	41, 49 30
23		40	30
24		(79)	6, 41
25	 X = N–alkyl, R = Me, R' = H X = O , R = Et, R' = Me X = S , R = Et, R' = Me	(71%-95%) e	59
26			57
	R' R		
	C_4H_9 $PhCH_2$	85	
	C_6H_{13} $PhCH_2$	85	
	C_6H_{13} C_4H_9	98	
	C_4H_9 C_4H_9	99	
	C_6H_{13} C_2H_5	80	
27			
	$R = C_2H_5$	98	57
	$R = C_5H_{11}$	97	
28		98	56

Table 27 (*Contd.*).

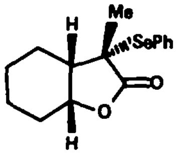
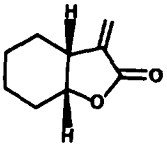
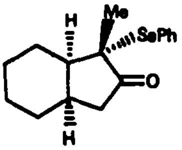
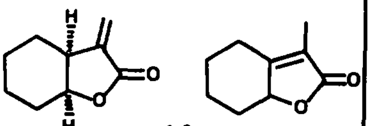
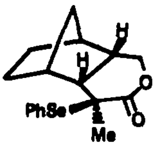
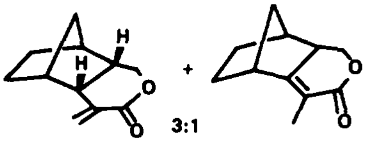
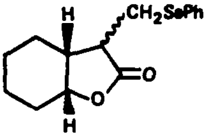
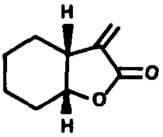
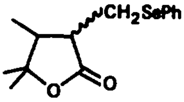
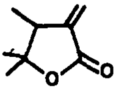
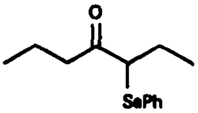
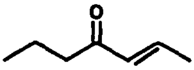
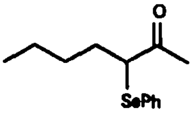
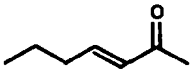
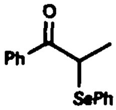
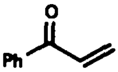
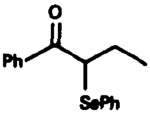
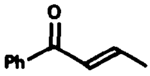
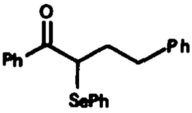
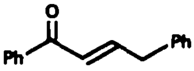
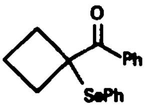
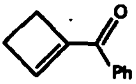
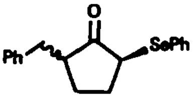
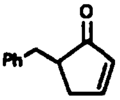
29		$\sim 7H_2O_2^{d,k}$, THF, 2.6 AcOH, 0°, 0.5h (ℓ)		very high	55
30		$\sim 7H_2O_2^{d,k}$, THF, 2.6 AcOH, 0°, 0.5 h (ℓ)	 .1:9	Total ~100%	55, 57
31		$\sim 7H_2O_2^{d,k}$, THF, 2.6 AcOH, 0°, 0.5 h (ℓ)	 3:1	Total 99%	56
32		$H_2O_2^{d}$, THF, trace AcOH, 0°, 0.5 h (ℓ)		97	73
33		$H_2O_2^{d}$, THF, trace AcOH 0°, 0.5 h (ℓ)		99	73
34		$3H_2O_2^{d,s}$ CH_2Cl_2, 2 pyridine, 30-35° $\sim 3H_2O_2^{d}$, THF, EtOAc,^{u} < 35°, 1 h (ℓ)		(72)$^{(t)}$ (64)	41 42
35		$\sim 3H_2O_2^{d}$, THF, EtOAc ^{u}, < 35°, 0.5 h	 (v)	(34)	42
36		5 to $10H_2O_2$, CH_2Cl_2, 2 pyridine (f)	 (w)	(56)	41
37		$2.7H_2O_2^{s}$, CH_2Cl_2, 2 pyridine, < 35°, then 25° 0.25 hr	 (x)	92	41
38		$5H_2O_2^{d}$, 2.1 AcOH^{n}, aq. THF, < 25°, 0.5h		(84)	6, 41
39		$8.8H_2O_2^{s}$, CH_2Cl_2, 2.4 pyridine, 25°, 0.5 h		83	41, 49
40		$8.8H_2O_2^{s}$, CH_2Cl_2, 2.4 pyridine, 25°, 0.5 h		(66)	41

Table 27 (*Contd.*).

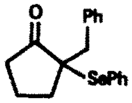
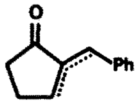
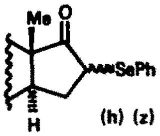
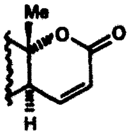
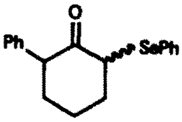
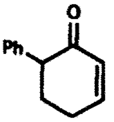
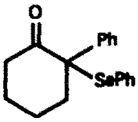
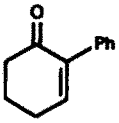
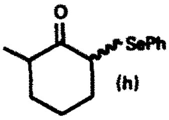
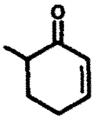
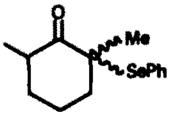
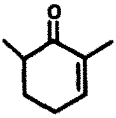
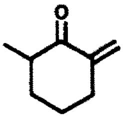
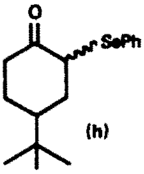
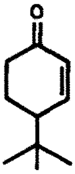
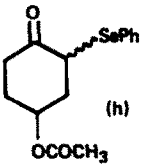
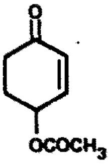
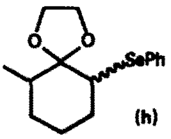
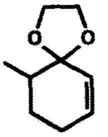
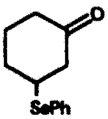
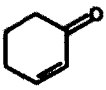
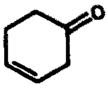
41		$\xrightarrow[25°,\ 0.5\ h]{8.8H_2O_2{}^{s},\ CH_2Cl_2,\ 2.4\ pyridine,}$	 (y)	95	41, 49
42		$\xrightarrow{H_2O_2}$		(39)	35
43		$\xrightarrow[25°,\ 5\ min.]{8.8H_2O_2{}^{s},\ CH_2Cl_2,\ 2.4\ pyridine,}$	 (aa)	(60)	41, 49
44		$\xrightarrow[25°,\ 0.5\ h]{8.8H_2O_2{}^{s},\ CH_2Cl_2,\ 2.4\ pyridine,}$		(94)	41, 49
45		$\xrightarrow[<25°,\ 0.5\ h]{5H_2O_2{}^{d},\ 2.1\ AcOH,\ aq.\ THF,}$	 (bb)	(36)	6, 41
46		$\xrightarrow{H_2O_2{}^{d},\ MeOH}$	 +  67 : 33	Total (76%)	6
		$\xrightarrow[<25°,\ 0.5h]{5H_2O_2{}^{d},\ 2.1\ AcOH\ {}^{n},\ aq.\ THF}$	80 : 20	Total (69%)	6
		$\xrightarrow{H_2O_2,\ CCl_4\quad (cc)}$	89 : 11	–	6
47		$\xrightarrow[<35°,\quad 0.75\ h]{\sim 3H_2O_2{}^{d},\ THF,\ EtOAc^{u},}$	 (dd)	(74)	42
48		$\xrightarrow[<35°,\ 0.75h]{\sim 3H_2O_2{}^{d},\ THF,\ EtOAc^{u},}$	 (ee)	(53)	42
49		$\xrightarrow[ii\ \ Heat\quad (f,\ l)]{i\ 5\ to\ 10H_2O_2,\ CH_2Cl_2,\ 2\ pyridine,}$	 (ff)	80	49
50		$\xrightarrow[then\ room\ temp.,\ 3\ h]{10H_2O_2{}^{c},\ THF,\ \sim 0°}$	 +  100 : 0	Total 96%	5

Table 27 (*Contd.*).

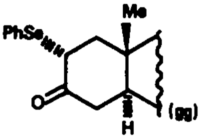
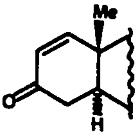
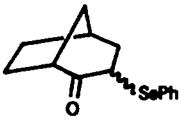
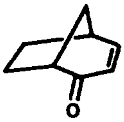
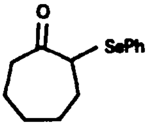
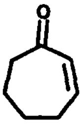
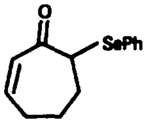
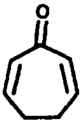
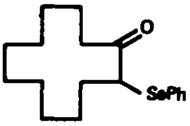
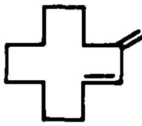
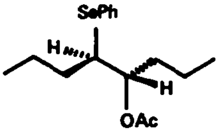
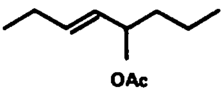
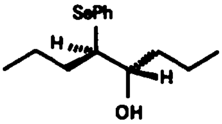
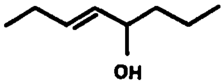
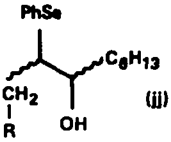
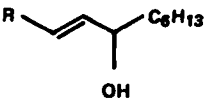
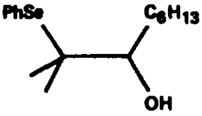
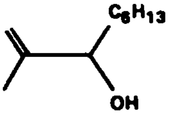
51		~3H_2O_2^{d}, THF, EtOAc^u, < 35°, 1 h		(45)	42
52		5 to 10H_2O_2 , CH_2Cl_2, 2 pyridine, 25°, ~10 min. (f)		72	41
53		5 to 10 H_2O_2^{s}, CH_2Cl_2, 2 pyridine ~ 10 min. (f)	 (hh)	(< 10%)	41
54		5 to 10 H_2O_2^{s}, CH_2Cl_2,2 pyridine, ~ 10 min. (f)		61	41
55		5 H_2O_2^{d} , 2.1 AcOH^n aq. THF, <25°, 25°, 0.5h	 (ii)	(72)	6, 41
		~3H_2O_2^{d}, THF, EtOAc^u, < 35°, 1h (l)		(77)	42
56		5 H_2O_2^{d}, THF, ~6°, room temp., 2.5 h		(85)	88
57		10 to 20 H_2O_2^{d} EtOH, THF, 0 to 25°, room temp. 10h (l)		(98)	40
58		10 to 20 H_2O_2^{d} THF, 25° (l)	 R = H	78	78
			R = Me	74	
59		10 to 20 H_2O_2^{d}, THF, 25° (l)		90	78

Table 27 (*Contd.*).

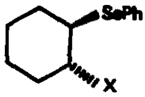
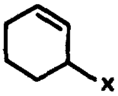
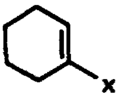
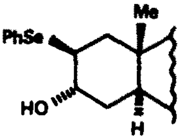
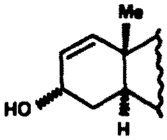
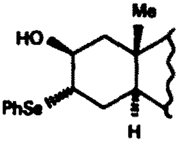
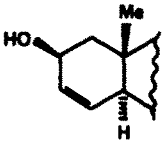
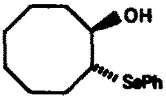
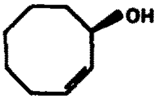
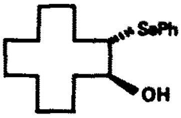
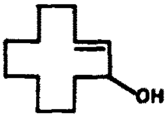
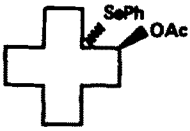
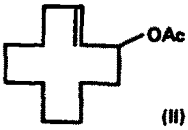
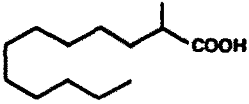
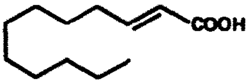
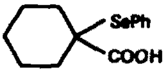
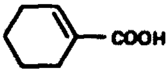
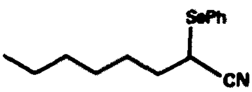
60		$5H_2O_2^d$, THF, 6° then:		+ 	—	88
		room temp., 44 h X = OAc	97	3	Total 73%	
		reflux 0.8 h X = OAc	—	—	78	
		room temp. 2 h X = OMe	98	3	93	
		— X = Cl	51	49	—	
		— X = OH	99.8	0.2	—	
61	 (gg)	10 to 20 $H_2O_2^d$, EtOH, THF, < 25°, reflux, 2.5 h (l)			(40)	40
62	 (gg)	10 to 20 $H_2O_2^d$, EtOH, THF, < 25°, reflux, 4 h (l)			(51)	40
63		10 to 20 $H_2O_2^d$, BuOH, THF, < 25°, room temp. 4 h (l)			(75)	40
64		10 to 20 $H_2O_2^d$, BuOH, THF, < 25°, reflux, 1 h (l)	 (kk)		(85)	40
65		5 $H_2O_2^d$, THF, ~6° then room temp., 1.5 h (l)	 (ll)		(85)	88
66		H_2O_2, THF, AcOH, 0° to room temp.			(91)	35
67		H_2O_2, THF, 0°, 2h (l)			60	30
68		$3H_2O_2^d$, THF, room temp., 2.3 h	 (E):(Z)::54:46		(~96%)	58

Table 27 (*Contd.*).

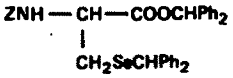
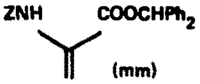
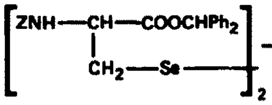
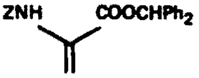
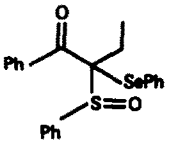
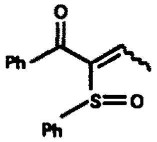
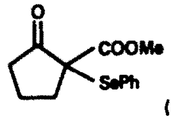
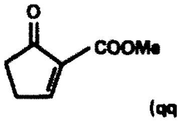
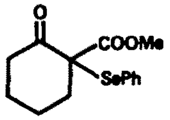
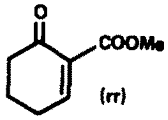
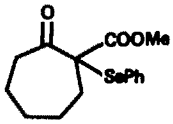
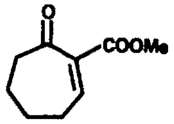
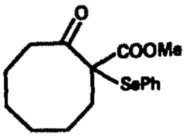
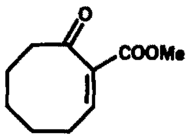
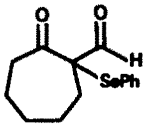
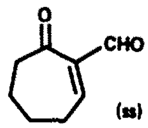
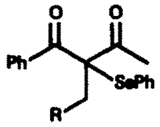
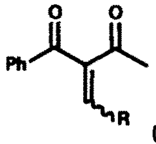
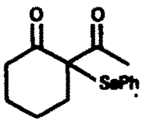
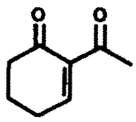
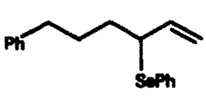
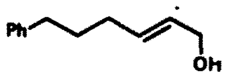
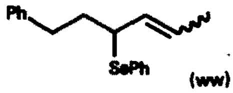
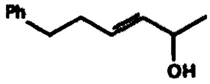
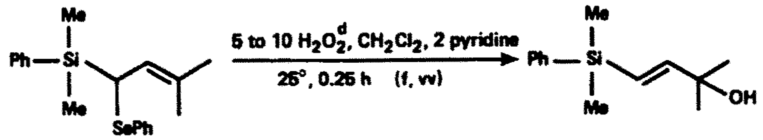
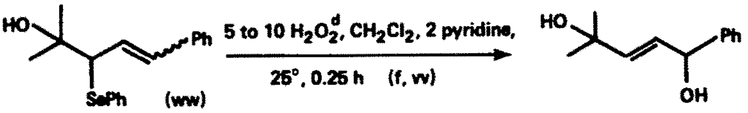
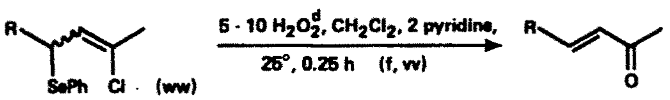
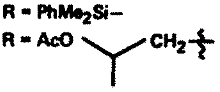
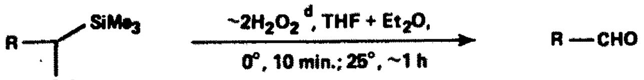
69		~15 H_2O_2[d], acetone, room temp. 0.25 h (k)	 (mm)	100	26
70		~37 H_2O_2[d], acetone 0°, 0.5 h; room temp. 1 h		~100%	26
71		3 H_2O_2[s], CH_2Cl_2, 2.4 pyridine, 25°, 0.3 h	 (nn)	71	41
72	 (oo)	1.9 H_2O_2[pp], CH_2Cl_2, ~25° ~0.3 h	 (qq)	(81)	41
73		2.5 H_2O_2[pp], CH_2Cl_2, 20 to 30°, 25°, 0.3 h	 (rr)	(89)	41
74		5 to 10 H_2O_2, CH_2Cl_2, 2 pyridine, ~10 min. (f)		93	41
75		5 to 10 H_2O_2[d], CH_2Cl_2, 2 pyridine, ~10 min. (f)		93	41, 49
76		2H_2O_2, 25°	 (ss)	74	60
77		5 to 10 H_2O_2[d], CH_2Cl_2, 2 pyridine, ~10 min. (f)	 R = H R = Pr (tt)	80 93	41, 49
78		2 H_2O_2[d], CH_2Cl_2, 20 to 30° ~0.3 h	 (uu)	(84)	41
79		5 to 10 H_2O_2[d], CH_2Cl_2, 2 pyridine, 25°, 0.25 h (f, vv)		(68)	67
80	 (ww)	5 to 10 H_2O_2[d], CH_2Cl_2, 2 pyridine, 25°, 0.25 h (f, vv)		(80)	67

Table 27 (*Contd.*).

81	 5 to 10 $H_2O_2^d$, CH_2Cl_2, 2 pyridine 25°, 0.25 h (f, vv)	(74)	67
82	 (ww) 5 to 10 $H_2O_2^d$, CH_2Cl_2, 2 pyridine, 25°, 0.25 h (f, vv)	(55)	67
83	 (ww) 5 - 10 $H_2O_2^d$, CH_2Cl_2, 2 pyridine, 25°, 0.25 h (f, vv)		67
	R = $PhCH_2$	(70)	
	R = $PhCH_2CH_2$	(85)	
	R = $PhMe_2Si$–	(63)	
	R = 	(80)	
84	 ~$2H_2O_2$ ^{d}, THF + Et_2O, 0°, 10 min.; 25°, ~1 h		87
	R = C_5H_{11}	80	
	R = C_6H_{13}	80	
	R = $C_{14}H_{29}$	90	
	R = $Ph(CH_2)_3$	75	

[a] Quantities are specified by the notation of footnote *a* to Table 23 (p. 1089). Where no initial temperature is stated it should be understood that H_2O_2 was added with cooling. [b] This selenoxide is stable. See use of peracid: Table 24, entry 1. [c] The H_2O_2 used was 70% (units not stated). [d] The H_2O_2 used was 30% (units not stated). [e] Depending on R (and, for entry 25 the nature of X and R'). [f] 5 to 10 equiv. of 15% aqueous H_2O_2 were stirred for ~ 10 min with a CH_2Cl_2 solution of the selenide containing 2 equiv. of pyridine. This *general* two-phase method was used for the present case but specific details have not been published. [g] These are absolute yields. [h] Stereochemistry not specified. [i] Ar can have various values (see Table 3, p. 1056). For reactions conducted at room temp. on a large scale, ice-bath cooling was probably used during the oxidation stage. This step is exothermic.[41] [j] The H_2O_2 used was 50% (units not stated). [k] The proportions shown assume the units to be w/w for the concentration of H_2O_2. [l] This *general* procedure was used: specific details are not reported. [m] It is not clear if H_2O_2 was tried in the oxidation of each of these esters. See use of peracid: Table 24, entries 16, 17, 18. [n] The reaction mixture contains 1 equiv. of Pr_2^iNH from LDA. [o] Using H_2O_2, THF, probably in neutral solution. Entries 22 and 23 should be compared. [p] See use of PhSe(O)Cl: Table 28, entry 2. [q] Specific details are given only for $R' = C_6H_{13}$, $R = PhCH_2$. [r] The compounds have the double bond largely (≥ 95%) in the endocyclic location shown. [s] 30% w/w H_2O_2 was diluted with about an equal volume of water. [t] In this case specific details are given. See footnote *f* above. See use of O_3: Table 26, entry 22. [u] The reaction mixture must be freed from HCl (generated during the selenenylation) prior to oxidation. [v] The low yield may be due, in part, to poor regioselectivity for the selenenylation. [w] See use of $NaIO_4$: Table 23, entry 2. [x] See use of PhSe(O)Cl: Table 28, entry 1. [y] The product is a 56:40 mixture of *endo* and *exo* isomers. The stereochemistry of the *exo* isomer is not given. [z] Various steroidal nuclei. Presumably the lactone arises by a Baeyer–Villiger reaction of the normal enone product. [aa] See use of O_3: Table 26, entry 11. [bb] See use of O_3: Table 26, entry 8. [cc] Presumably the selenide was sitrred in a two-phase H_2O_2–CCl_4 system. [dd] See use of peracid: Table 24, entry 12. [ee] See use of $NaIO_4$: Table 23, entry 7. [ff] Selenoxide fragmentation was completed by refluxing for 5 min in CCl_4 containing 2 equiv. of pyridine. [gg] Cholestane skeleton. [hh] See use of $NaIO_4$: Table 23, entry 4 and use of O_3: Table 26, entry 15. [ii] See use of peracid: Table 24, entry 13. (*Z*)-Isomer not detected. [jj] Mixture of diastereoisomers. [kk] (*Z*) and (*E*) isomers. [ll] (*Z*)-Isomer not detected. [mm] See use of $NaIO_4$: Table 23, entry 10. [nn] > 93% of one isomer. [oo] The starting material is actually a mixture of methyl and ethyl esters. [pp] Approximately 15% aq H_2O_2 was used. An excess must be avoided. The products are sensitive to *base-catalysed* epoxidation. [qq] See use of O_3: Table 26, entry 18. [rr] See use of O_3: Table 26, entry 19. The product is a 98:2 keto–enol mixture. [ss] Distillation gives material that is almost completely enolised. Before distillation the product is a 56:44 keto–enol mixture. [tt] A 95:5 mixture of geometrical isomers is formed. The compound is nonenolised.[49] [uu] The H_2O_2 used was ~ 15%. The product was an 85:15 keto–enol mixture. See use of O_3: Table 26, entries 20 and 21, and use of peracid: Table 24, entry 11. [vv] In *general* use of H_2O_2 in EtOH can give complex mixtures.[67] [ww] Mixture of geometrical isomers.

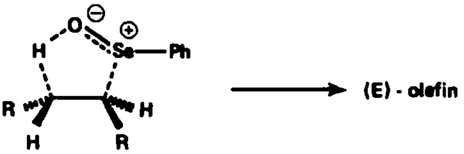
(e) *Direct introduction of phenylseleninyl group*

Direct introduction of the phenylseleninyl group has not been studied in detail. The reagent, PhSe(O)Cl, is reported to be exceedingly hygroscopic and the known examples of its use are summarised by Table 28.

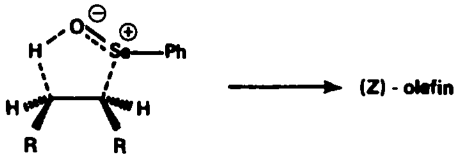
Finally, it has been observed[103] that the α-lithio-salts of esters react with diphenylseleninic anhydride to give α,β-unsaturated esters directly. However, no experimental details are yet available.

(f) *Selenoxide fragmentation: stereochemistry*

Fragmentation of selenoxides is a *syn* elimination process (e.g. Table 27, entries 6 and 7) and, in non-cyclic systems, the product is almost always the olefin of (*E*)-geometry, a fact that can be understood[104] as a consequence of the relative steric interactions in the transition states 69 and 70. The non-bonded interactions in the former are clearly less serious and so the (*E*)-isomer is the strongly favoured product but, for trisubstituted olefins, there is less discrimination (Table 24, entry 6; Table 27, entry 21 and, possibly, entry 41).



69



70

If the *syn* conformation is not accessible (or if the resultant strain from a double bond produced by fragmentation is high) then the process might be expected not to occur. Entry 11 of Table 27 may be such a case.

Among non-cyclic compounds only the fragmentation of α-phenylseleninylnitriles (Table 27, entry 68) (but not acids, esters, aldehydes or ketones) affords both geometrical isomers. However, it should be noted that the relatively insensitive technique of IR spectroscopy has often been used to establish the absence of the (*Z*)-product.

In most cyclic systems geometrical restraints ensure that a *cis*-olefin is produced. Oxidation of cyclododecyl phenyl selenide (Table 27, entry 8) gives[5] a 1:1 mixture of *cis* and *trans* cyclododecene, but fragmentation of 1-acetoxy-2-phenylseleninylcyclododecane[pp] (Table 27, entry 65) affords only the *trans* olefin as does fragmentation of 2-phenyl-seleninylcyclododecane (Table 27, entry 55). 1-Hydroxy-2-phenylseleninylcyclododecane[qq] (Table 27, entry 64) gives (*Z*) and (*E*) isomers. Evidently, double bond geometry is determined by conformational effects of the ring.

(g) *Selenoxide fragmentation: regiochemistry*

The regiochemistry of selenoxide fragmentation is characterised by several trends.

(i) In situations of type 71 elimination away from an electronegative substituent X is the rule (71→72) even when the double bond of the alternative product (73) would be conjugated with a phenyl group (Table 26, entries 32 and 33). In the case where X is chlorine both routes are equally easy (at least for a cyclohexyl skeleton) (Table 27, entry 60). When X is Me_2N then removal of the adjacent hydrogen (H_a in 71) is moderately disfavoured (Table 24, entries 8–10).

(ii) In the case of *sulphoxides* with partial structure 74 loss of H_a or H_b depends on the nature (H or C) of the other substituents present and, with non-cyclic compounds, the following sequence has been found[105] for the types of H that are removed preferentially: allylic ≃ propargylic > benzylic ≃ methyl > methylene ≫ methine. The evidence collected in Table 29 shows that the same sequence probably holds for selenoxide fragmentation and it is seen that production of a conjugated

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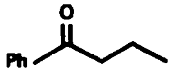
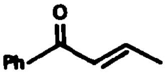
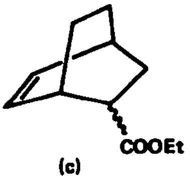
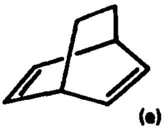
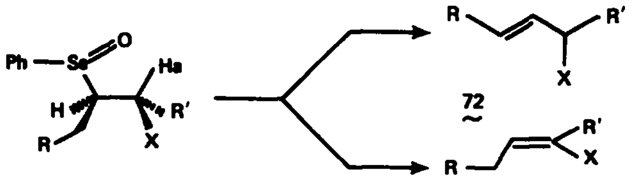
[pp] The parent selenide was made by *trans* addition to *trans* olefin.

[qq] The parent selenide was made by reaction of $PhSe^-$ with *trans*-cyclododecene epoxide.

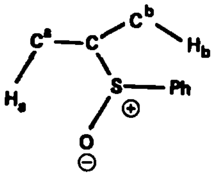
Table 28.[a]

				Yield	Ref.
1		i 1.2 LDA, THF, -78° ii 1.8 PhSe(O)Cl, -78° iii 1.2 AcOH, warm to room temp. over 0.25 h	 (b)	80%	41
2	 (c)	i 1.2 LDA, THF, -78° ii 1.8 PhSe(O)Cl, -78° iii 1.2 AcOH, warm to room temp. over 0.25 h (d)	 (e)	68%	41

[a] Quantities are specified by the notation of footnote *a* to Table 23 (p. 1088). [b] See use of H_2O_2: Table 27, entry 37. [c] Stereochemistry not specified. [d] Specific experimental details not given. Presumably the procedure used for entry 1 was followed. [e] See entry 24 of Table 27.



71 72 73 (79)



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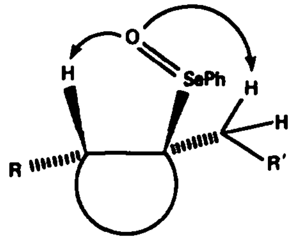


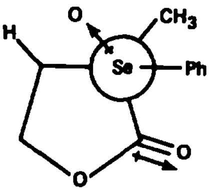
R = H or C
R' = H or C

75

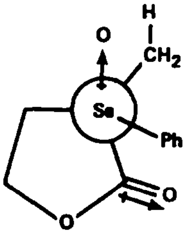
olefin is favoured over formation of an isolated double bond (Table 29, entry 1).

For cyclic compounds where a hydrogen on a ring carbon can be removed in competition with a hydrogen on an exocyclic carbon (see structure 75) then the general preference (evaluated largely with lactones) is as shown in Table 30.

Possibly, as explained[105] for sulphoxides, the trends shown in Table 30 arise because the conformation leading to *endo* olefinic product involve a smaller dipole-dipole interaction (76) than that (77) leading to the *exo* isomer.

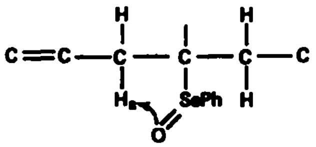
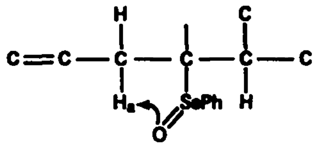
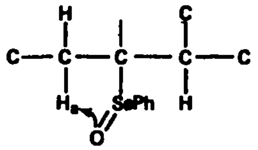
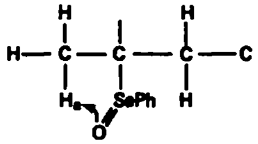
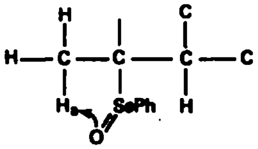


76



77

Table 29.[a]

		Table	Entry
1		26	30
2		24	7
3		27	3
4		26 27	29 2
5		27	6,7

[a] Hydrogen removed preferentially is denoted by H_a.

Table 30.[a]

				Table	Entry
CH_2 (ring)	(b)	$> CH_3$ (exocyclic)	(c)	27	46
CH_2 (ring)	(b)	$> CH_2$ (exocyclic)	(d)	27	26, 41[f]
CH (ring)	(e)	$> CH_3$ (exocyclic)	(c)	27	30[g]
CH (ring)	(e)	$> CH_2$ (exocyclic)	(d)	27	27

[a] In each case H attached to a ring C is removed preferentially.

[b] R = H in structure 75.

[c] R' = H in structure 75.

[d] R' = C in structure 75.

[e] R = C in structure 75.

[f] Here the exocyclic double bond is conjugated with a phenyl group.

[g] See Table 27, entry 31 for a possible exception.

(h) *Selenoxide fragmentation: oxidising agents and fragmentation procedures—general considerations*

For olefinic materials of the highest purity it is frequently essential that the starting selenides be themselves free of contaminants (such as unselenenylated carbonyl substrates). However, it often is convenient to carry out the oxidation on the crude selenide as it is isolated from the selenenylation reaction or even, as is frequent practice when using H_2O_2, to simply perform the oxidation on the selenide generated *in situ*.

Four types of oxidant are in common use: $NaIO_4$, peracids (usually MCA or CH_3CO_3H), O_3,[rr] and H_2O_2. Obviously, the choice is guided by the selectivity of the reagent and, where an excess is used, by the sensitivity to it of the fragmentation product. There is, however, a further complication. In those situations where fragmentation is sluggish an excess of oxidant is needed to quench the PhSe–OH [by immediate conversion to PhSe(O)OH]. If this is not done, residual selenoxide is usually consumed so that a mixture of olefin and selenide is obtained.[36, ss] Sometimes selenoxides of this type should be added to refluxing CCl_4 or CH_2Cl_2 and under these conditions fragmentation (unimolecular) is faster than transoxidation (bimolecular).[36]

It is usual to employ $NaIO_4$ in excess, and fragmentation then occurs in the oxidation mixture (which is an aqueous organic solvent) at, or below, room temperature. Occasionally, the system is buffered with $NaHCO_3$.

Peracids are commonly used in an organic solvent either in stoicheiometric amounts at −10 to −40°[tt] or in sufficient quantity to oxidise the PhSeOH formed. The latter process, conducted at room temperature, is confined to situations where the olefin does not react rapidly with peracid (e.g. Table 24, entries 11 to 18).

Ozone is invariably used at a low temperature (usually −78°) and CH_2Cl_2, CCl_4 or Et_2O have been the preferred solvents. THF is too sensitive to O_3 to be useful. The selenoxides are stable at the ozonolysis temperature and a variety of techniques—specifically cited in the Tables—have been developed for effecting the fragmentation.

The selenoxide—whether generated by low temperature ozonolysis or low temperature peracid treatment, or by direct use of PhSe(O)Cl—can be made to fragment by the following techniques or slight variations of them.

(i) Warm the cold selenoxide solution to room temperature. Sometimes a controlled rate of warming is specified.

(ii) Add pyridine to the cold selenoxide solution and let it attain room temperature.

(iii) Add the cold [−78°] selenoxide solution to refluxing CH_2Cl_2 or CCl_4. The decomposition is complete essentially instantaneously. An important variation is to have $Pr_2{}^iNH$ (from LDA or deliberately added) in the selenoxide solution initially.[uu] Sometimes $Pr_2{}^iNH$ is added to the refluxing solvent before the addition is begun. Occasionally, Et_2NH is used in place of $Pr_2{}^iNH$.

Hydrogen peroxide is employed very frequently[vv]—usually in excess over that needed to oxidise both the selenide and PhSeOH—in strengths from 15 to 70% w/w. The 30% reagent has found most use and, for one-phase oxidations, THF is the solvent almost always chosen. Where the selenide has been generated in EtOAc it is convenient just to dilute the solution with THF. Typically the temperature is kept near 0° during the beginning of the H_2O_2 addition and sometimes it is allowed to rise before all the oxidant has been added. The mixtures are then usually left at room temperature for a suitable period. AcOH is sometimes added to neutralise $Pr_2{}^iNH$ (from LDA) or even when $Pr_2{}^iNH$ is not initially present. Presumably this precaution protects compounds sensitive to basic H_2O_2. Mineral acid must *not* be present, however.[42, ww]

A two-phase method has been found to give superior results: an excess of H_2O_2 is stirred with a CH_2Cl_2 solution containing the selenide and usually also 2 equiv. of pyridine. Under these conditions the selenide is oxidised efficiently and it collapses in high yield, often within about 15 min (when the product is an enone).

(i) *Selenoxide fragmentation: efficiency of the process*

The mildness of selenoxide fragmentation is evident not only from the moderate conditions of pH and temperature used but also from the fact that it has been possible to isolate, without special difficulty, compounds that are sensitive to nucleophiles (α-methylene lactones), to polymerisation (e.g. Table 23, entry 2) or to enoliza-

---

[rr] Oxidation by photochemically-generated singlet oxygen has been examined briefly.[106]

[ss] See p. 1057 and Table 26, entry 3. Entry 10 of Table 23 may be another example of selenoxide reduction by PhSeOH.

[tt] The selenoxide can then be used for further transformations. Fragmentation is eventually allowed to occur (at a higher temperature) in the absence of oxidant.

[uu] Any other strong bases present can be neutralised with AcOH at low temp.

[vv] Careful temperature control is necessary[41] because the oxidation is highly exothermic and appears to be autocatalytic.

[ww] See also p. 1107.

tion.[xx] Olefins can also be obtained in which the double bond is not in its thermodynamically stable position (Table 27, entry 38).

The formation of terminal unconjugated olefins can be slow unless special techniques are used (see p. 1055) but other olefins are produced within a few hours and the formation of enones is generally a rapid process that frequently is over within minutes (see Table 27, entries 45 and 49). In β-dicarbonyl systems fragmentation can occur at temperatures approaching −78° as seems[41] to be the case for entry 72 of Table 27. Most selenoxide fragmentations, however, have been carried out between 0° and room temperature. Occasionally a long reaction time[88] (Table 27, entry 60) or a higher temperature[40] are employed. The use of refluxing CH_2Cl_2 (b.p. 40°) or CCl_4 (b.p. 77°) sacrifices the extreme thermal mildness generally characteristic of the fragmentation but under these conditions the process is complete almost instantaneously.

The general practice of selenoxide fragmentation calls for temperatures that are ~50 to ~120° lower than those required in the corresponding sulphoxide fragmentations. Direct comparison can be made in a number of cases.[55,104,107]

[redacted]

The yields of some cyclic enones are low. Possibly, the requirement for a cyclic transition state conflicts with the conformational preference of the cyclic ketone and so the incursion of other reaction pathways for the selenoxide is seen. For example, oxidation under a variety of conditions of 2-arylselenocyclooctanone gives the products shown (eqn 80) and the origin of the by-products can be understood[41] in terms of the properties of the intermediate selenoxide **78**. This compound has an acidic hydrogen and so a Pummerer-type reaction can occur (eqn 81) leading to the α-diketone and thence, if the oxidant is H_2O_2, to the diacid **82**. Loss of the acidic hydrogen in **78** can also generate the anion **83** which can quench species of type PhSe–X (produced from PhSe–OH). The mode of formation of the vinyl selenide **80** can, therefore, be summarised by eqn (82).

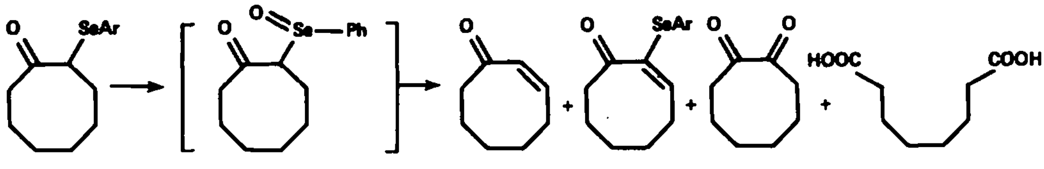
A suitable amine might trap PhSe–X and thereby suppress vinyl selenide formation. The Pummerer-type reaction (eqn 81) is favoured by low pH—hence the need to remove[42] mineral acid before oxidising selenides. The presence of a hindered base in the selenoxide mixture suppresses the Pummerer reaction. Thus, the rational for the different protocols for selenoxide fragmentation can be largely understood.

(j) *Selenoxide fragmentation*: *fate of the selenium*

[redacted]

and reduced back to PhSeSePh.[40,41] In the absence of an oxidant [and assuming that fragmentation is fast (see p. 1106)] the PhSeOH disproportionates to give PhSeSePh, PhSe(O)OH and water. In those experiments where it is convenient[39] to remove selenium compounds by extraction into base the diselenide can be oxidised to PhSe(O)OH with H_2O_2.

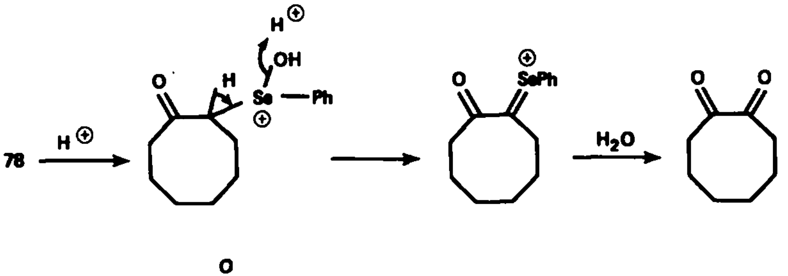
[xx] E.g. the product of Table 27, entry 77 was isolated in a non-enolized form.



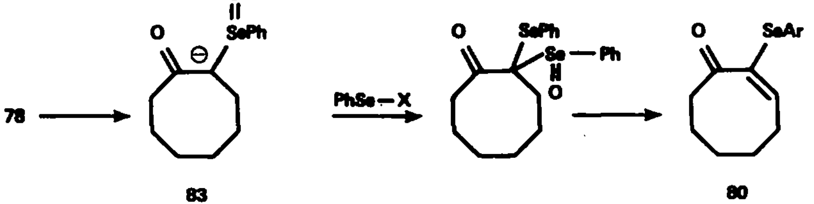
(80)

78 79 80 81 82*

*Produced if H_2O_2 is the oxidant.



(81)



(82)

83 80

5. REACTIONS OF ALLYLIC SELENIDES AND THEIR DERIVATIVES

Certain aspects of the chemistry of allylic selenides merit explicit comment.

(A) *The selenoallylic rearrangement*

Allylic selenides undergo a reversible 1,3 shift (eqn 83) whose mechanism and stereochemistry are not known.[108]

(83)

Treatment[35] of the allylic chloride **84** with PhSe⁻ at 0° gave the thermodynamically less stable selenide **85** which contained about 6% of the (*Z*) and (*E*) isomers of **86**. At 52° in $CHCl_3$, **85** rearranges to **86** with a half-life of ~1.3 hr.[68] In MeOH the rearrangement is slower ($t_{1/2}$ = 2.0 hr at 52°).[ν] Treatment of **84** with KSeCN gave[68] exclusively **87**. The 1,3 shift evidently, occurs very readily in the case of selenocyanates. Likewise, the allylic chloride **88** gave quantitatively the terminal selenocyanate **89**.

(B) [2,3]-*Sigmatropic rearrangement of allylic selenoxides*

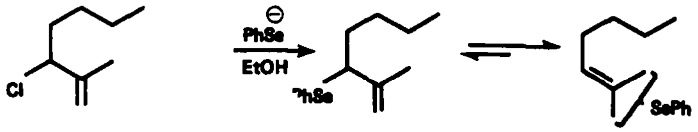
The equilibrium of eqn (84) lies largely on the right in contrast to the situation with sulphoxides,[86] and the selenenic esters **90** are readily hydrolised to the corresponding allylic alcohol.[5] As in the sulphur series[86,109] the olefin arising by the [2,3]-sigmatropic shift is of *trans* geometry.[67]

It is sometimes possible to use the 1,3 and [2,3] shifts to exert regiochemical control as shown by the following example (eqn 85).[35]

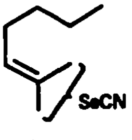
The [2,3]-sigmatropic rearrangement also accounts for the production of *trans*-diol in the following process (eqn 86).[40]

A number of [2,3]-sigmatropic reactions have been examined[67] as routes to allylic alcohols or to α,β-unsaturated ketones. These experiments have been listed (Table 27, entries 79–83) but additional comment should be made for the reactions summarised by eqns (87–89). Evidently, the [2,3]-sigmatropic rearrangement is faster[67] than selenoxide fragmentation and, in point of fact, the rearrangement shown by eqn (90) has a half-life at −40° of less than 60 min[67] while fragmentation of phenyl alkyl selenoxides (to olefins) does not occur rapidly below 0°. In the example of eqn (89) above the [2,3] shift is probably retarded by γ-substitution and fragmentation is facilitated by the resulting phenyl conjugation.

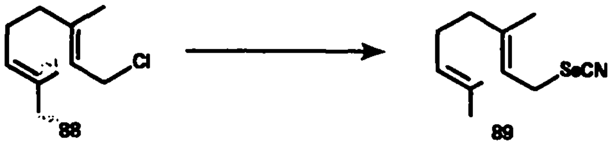
[ν] Geranyl linalyl selenide appears to be stable at 25°.[68] For other allylic selenides see Refs. 40 and 67.



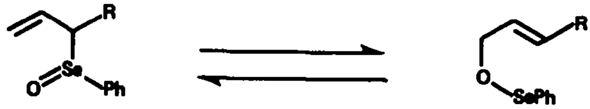
84 85 86



87

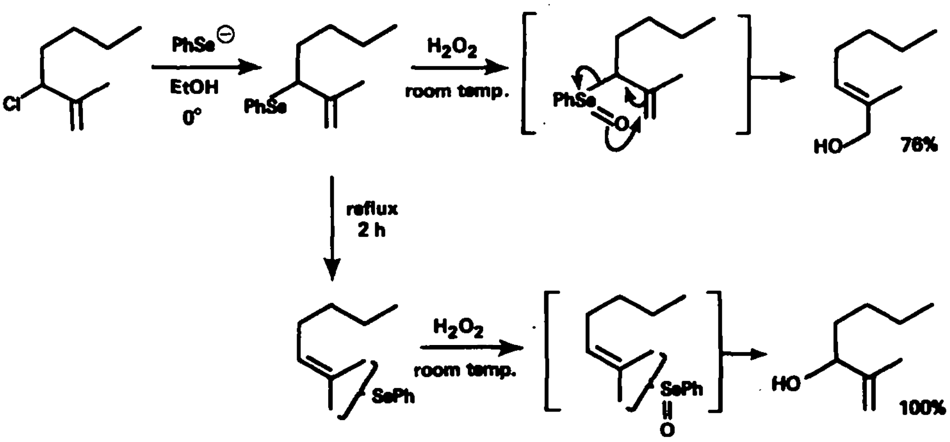


88 89

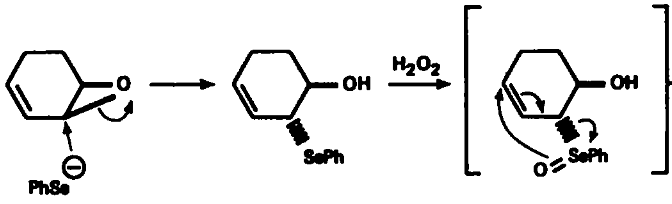


90

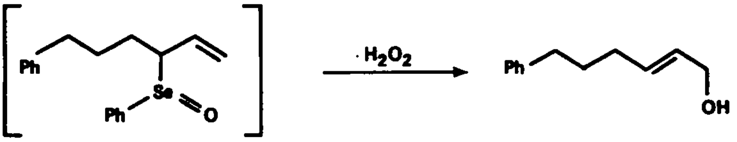
(84)



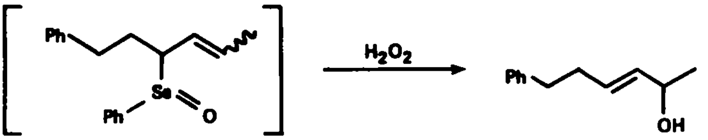
(85)



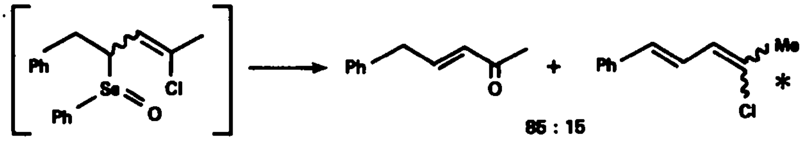
(86)



(87)

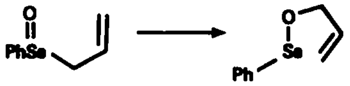


(88)



(89)

*Stereochemistry not specified



(90)

(C) [2,3]-*Sigmatropic rearrangement of selenium ylides*

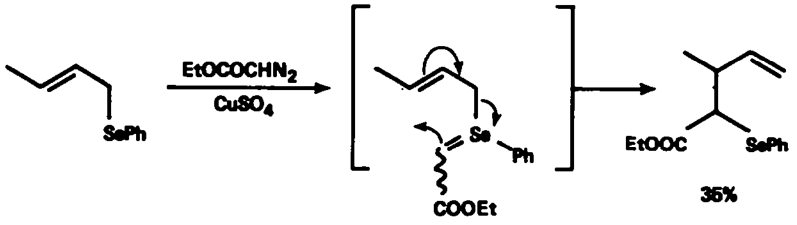
Little work has been reported on the reactions of selenium–carbon ylides in an allylic environment. The sequence[35] shown by eqn (91) should afford a general route to dienoic esters but the efficiency needs to be improved.

(D) *Reaction of allylic selenides with copper ate complexes*

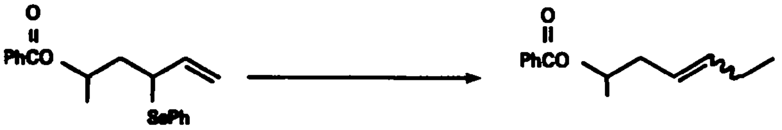
A few allylic selenides have been treated with lithium dimethyl cuprate [Et_2O, 0–20°] with the results[67] shown (eqns 92–94).

6. β-HYDROXYALKYL SELENIDES

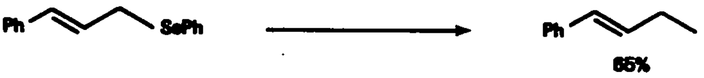
β-Hydroxyalkyl selenides promise to be useful in chemical synthesis and it is appropriate, therefore, to summarise in one place both their methods of preparation and their reactions.



(91)



(92)



(93)

(94)

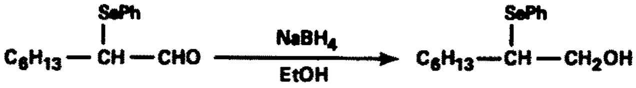
(A) *Preparation of β-hydroxyalkyl selenides*

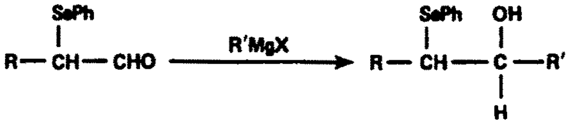
β-Hydroxyalkyl selenides are available from the following starting materials and all but the last route have already been dealt with as shown:

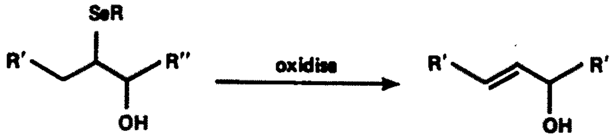
(i) Epoxides (see p. 1066).
(ii) Olefins (see p. 1081).
(iii) Selenium-stabilized anions (see p. 1072).
(iv) Selenoxide-stabilized anions (see p. 1081).
(v) α-Keto-selenides.

Selenides carrying an α-carbonyl group can be reduced[63] to β-hydroxyalkyl selenides (e.g. eqn 95). More extensive work[110] has shown that $LiAlH_4$ [2 equiv.] in Et_2O [−15°, 2 hr; then 25°, 1 hr] is the preferred reagent and that the process is fairly stereoselective.

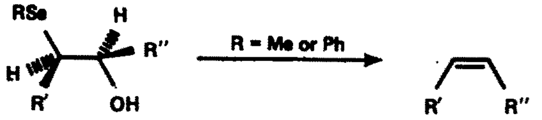
β-Hydroxyalkyl selenides can also be made[110] from α-selenoaldehydes by treatment with Grignard reagents (eqn 96). This process is highly stereoselective[zz] but it is not generally applicable to α-selenoketones. The results[110] with both processes are shown in Table 31.


$$C_6H_{13}-\overset{SePh}{CH}-CHO \xrightarrow[EtOH]{NaBH_4} C_6H_{13}-\overset{SePh}{CH}-CH_2OH$$
(95)

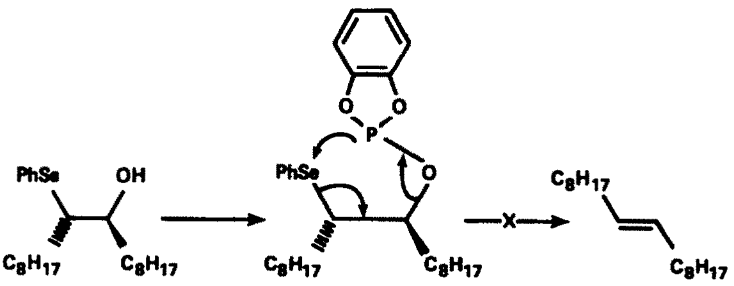

$$R-\overset{SePh}{CH}-CHO \xrightarrow{R'MgX} R-\overset{SePh}{CH}-\underset{H}{\overset{OH}{C}}-R'$$
(96)



(97)



(98)



(99)

(B) *Reactions of β-hydroxyalkyl selenides*

β-Hydroxyalkyl selenides are versatile intermediates and, as discussed below, they can be converted into allylic alcohols, olefins, epoxides or bromohydrins. β-Hydroxyalkyl selenoketals behave as precursors to vinyl selenides.

(a) *Conversion of β-hydroxyalkyl selenides into allylic alcohols.* This process (eqn 97) has already been dealt with in Table 27, entries 9, 17, 18, 19, 57–54[aaa] and in the discussion on the regiochemistry of selenoxide fragmentation (p. 1104). It is not limited to simple compounds but is also successful[79] for α,β,α′,β′-unsaturated alcohols (R″ = CH=CH– in eqn 97).

(b) *Conversion of β-hydroxyalkyl selenides into olefins.* Regio- and stereospecific (*trans*) elimination of the type represented by eqn (98) can be achieved in acidic or basic media and the following combination of reagents and conditions has been found successful: *p*-toluene sulphonic acid[bbb,a] in refluxing pentane,[62] excess of perchloric acid[b] in ether at room temperature,[62] excess of triethylamine in the presence of either trifluoroacetic anhydride,[c,62] or methanesulphonyl chloride,[d,74] or thionyl chloride[e,111]—all at room temperature. The work done on this important reaction is collected in Table 32.

The generally long reaction times but high yields are clear from the tabulated data. The reaction works well for *di*-, *tri*- and *tetra*-substituted olefins and it involves a *trans* elimination.[62,111,112]

An attempt[111] to effect *syn* elimination (eqn 99) followed, instead, the usual *trans* pathway. Reaction of β-hydroxyalkyl phenyl selenides, in which the phenyl ring carries an *ortho* or *para* nitro group, with Et_2P–Cl gives the same result.[63]

As entry 7 shows, the present method can be used to produce olefins that are *not* available by other routes. Vinyl selenides can also be made (entry 21).

[zz] Reaction conditions: R′MgX [1.16 equiv.] in Et_2O [−110°; 2 hr, then −78°, 1 hr]. See Table 31 for the stereochemical consequences of the $LiAlH_4$ and R′MgX reactions.

[aaa] See Table 24, entries 4 and 6 and Table 25, entries 31–34.

[bbb] The molar proportions of the reagents per mole of hydroxyalkyl selenide are: [a] 1 $TsOH–H_2O$; [b] 4.1 $HClO_4$; [c] 4 Et_3N + 2 $(CF_3CO)_2O$; [d] 5 Et_3N + 3 $MeSO_2Cl$; [e] 7 Et_3N + 2 $SOCl_2$.

Table 31.

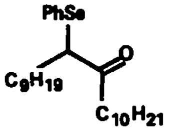
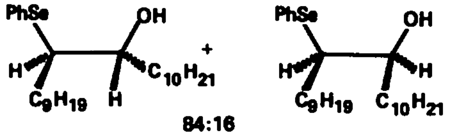
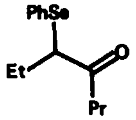
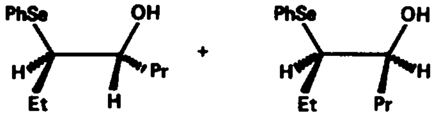
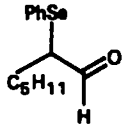
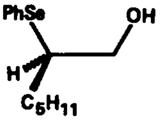
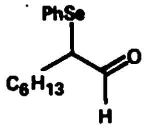
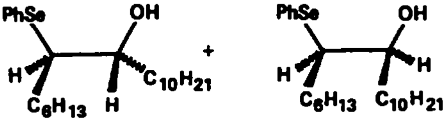
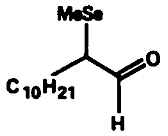
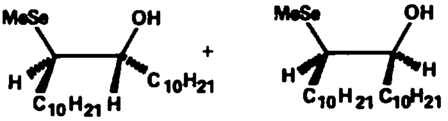
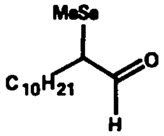
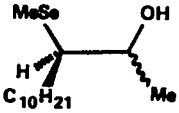
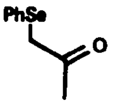
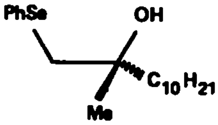
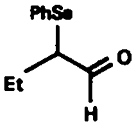
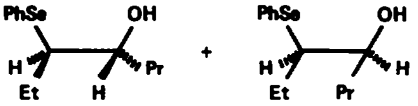
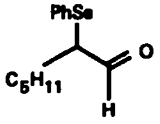
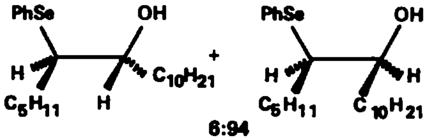
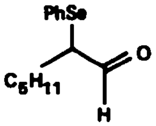
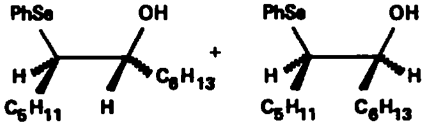
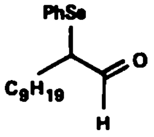
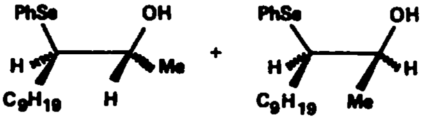
				Yield
1		LiAlH$_4$ →	 84:16	60%
2		LiAlH$_4$ →	 77:23	71
3		LiAlH$_4$ →		60
4		C$_{10}$H$_{21}$MgX →	 19:81	50
5		C$_{10}$H$_{21}$MgX →	 15:85	68
6		MeMgX →		75
7		C$_{10}$H$_{21}$MgX →		24
8		PrMgX →	 3:97	80
9		C$_{10}$H$_{21}$MgX →	 6:94	65
10		C$_6$H$_{13}$MgX →		75
11		MeMgX →	 3:97	67

Table 32.[a]

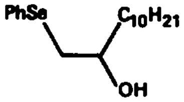
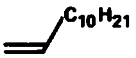
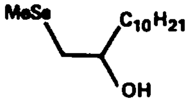
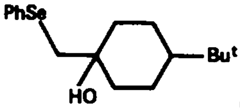
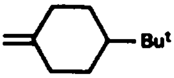
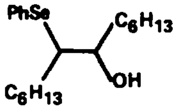
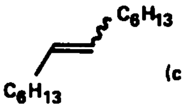
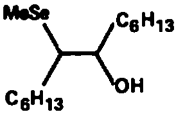
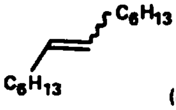
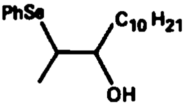
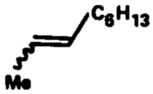
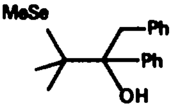
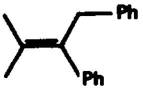
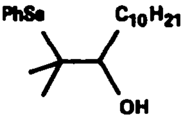
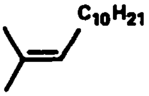
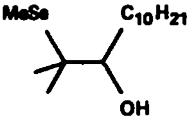
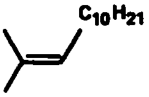
β-Hydroxyalkyl Selenide	Reagent[a]	Time	Olefin	Yield	Ref
1 	TsOH SOCl$_2$	40 22		71 70	62 111
2 	TsOH (CF$_3$CO)$_2$O	18 15		35 25	62 62
3  (b)	TsOH MsCl	18 —		65 98	62 74
4 	TsOH HClO$_4$ (CF$_3$CO)$_2$O	8 7 15	 (c)	70 94 65	62 62 62
5 	TsOH HClO$_4$ (CF$_3$CO)$_2$O SOCl$_2$	7 72 15 3	 (c)	62 85 75 88	62 62 62 111
6 	TsOH	10	 (c)	65	62
7 	TsOH (CF$_3$CO)$_2$O SOCl$_2$	8 1 2	 (d)	48 93 85	62, 111 111 111
8 	TsOH HClO$_4$ SOCl$_2$	26 13 2		30 31 90	111 111 111
9 	TsOH HClO$_4$ SOCl$_2$	9 9 2		59 22 80	111 111 111

Table 32 (*Contd.*).

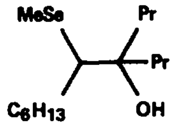
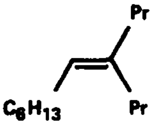
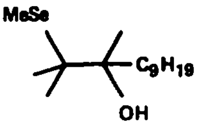
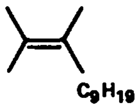
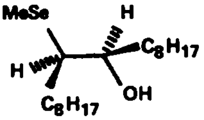
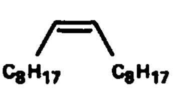
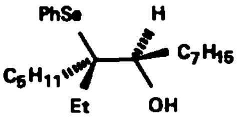
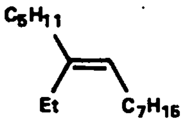
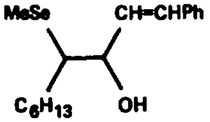
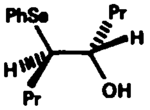
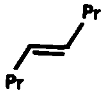
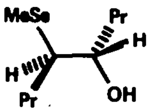
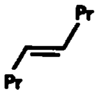
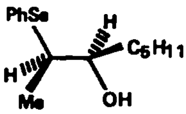
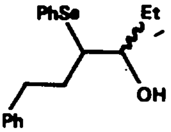
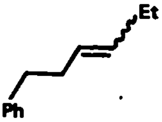
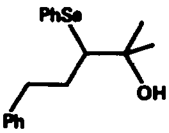
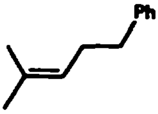
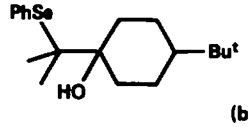
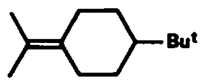
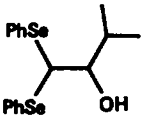
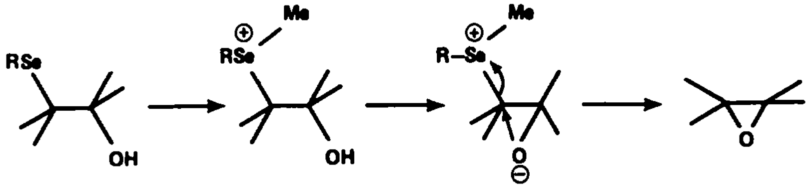
10		TsOH $SOCl_2$	17 2		61 80	111 111
11		$SOCl_2$	1		83	111
12		$SOCl_2$	–		94	111
13		$SOCl_2$	–		80	111
14	 (b)	$SOCl_2$	–	C_6H_{13}–CH=CH–Ph (b)	90	111
15		TsOH $HClO_4$ $(CF_3CO)_2O$	– – –		– – –	62 62 62
16		TsOH $HClO_4$ $(CF_3CO)_2O$	– – –		– – –	62 62 62
17		TsOH $(CF_3CO)_2O$	– –		– –	62 62
18		MsCl	–		70	74
19		MsCl	–		73	74

Table 32 (*Contd.*).

20	 (b)	MsCl	–		91	74
21		MsCl	–		81	74

[a] The proportions of reagents used are as indicated in footnote *bbb* on p. 1110. [b] Stereochemistry not specified. [c] Mixture of geometric isomers because hydroxyalkyl selenide is an isomer mixture. [d] This compound is not available by other olefin-forming processes.

(c) *Conversion of β-hydroxyalkyl selenides into epoxides.* Epoxides can be made efficiently from β-hydroxyalkyl selenides by the sequence shown (eqn 100). The reaction of phenyl selenides (R = Ph in eqn 100) with MeI[ccc] [Et_2O, room temperature, 2 hr] requires the presence of $AgBF_4$,[80] but methyl selenides (R = Me in eqn 100) are sufficiently reactive not to require assistance by silver ion[76] and they can be methylated easily [MeI or Me_2SO_4, 25°, 2–~4 hr].[76,79] The alkylation of β-hydroxyalkyl selenides is an efficient process and yields are generally well above 70%. The resulting species can be deprotonated with Bu^{t}OK in DMSO to afford the epoxides shown in Table 33.[ddd]



(100)

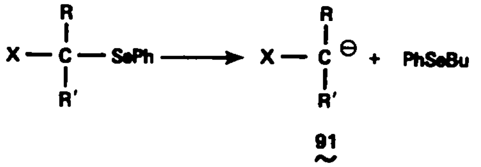
Some general features are contained in the above results. β-Hydroxyalkyl *phenyl* selenides may not be suitable for making *tetra*-substituted epoxides (entry 10)[79,80] but such hindered epoxides can be made in the methyl selenide series (entries 18, 19, 21, 26, 29, 30). A few hydroxyalkyl selenides give olefins in the methylation stage of this route (entry 24). The reaction works well for making α,β-unsaturated epoxides.

(d) *Conversion of β-hydroxyalkyl selenides into bromohydrins.* This topic is dealt with on p. 1120.

(e) *Conversion of β-hydroxyalkyl selenides into vinyl selenides.* The last entry of Table 32 shows that vinyl selenides are available from β-hydroxyalkyl selenoketals.

7. GENERATION OF CARBANIONS STABILIZED BY A HETEROATOM OTHER THAN SELENIUM

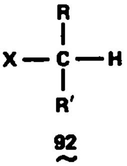
The Se–C bond cleavage reaction of eqn (101) consititutes a route to a variety of nucleophilic carbanions **91**.



$$X-\overset{R}{\underset{R'}{C}}-SePh \longrightarrow X-\overset{R}{\underset{R'}{C}}{}^{\ominus} + PhSeBu \qquad (101)$$

91

Some of these are not accessible in a synthetically useful yield by deprotonation of the corresponding hydrides **92**. Thus, although $PhSCH_3$ can be converted into $Ph\bar{S}CH_2$, species of the type PhSCHRR′ in which R or R′ (or both) are alkyl groups cannot be deprotonated effectively.[77,113] However, the Se–C bond cleavage reaction makes such



$$X-\overset{R}{\underset{R'}{C}}-H$$

92

carbanions readily available[77,113] (e.g. eqn 102) and a number of examples of the preparation and use of $Ph\bar{S}CHRR'$ have been published.[77,113]

Some complications to the general process of eqn (101) should be noted. Attempts to make the carbanion **93** from the ether–selenide **94** by reaction with BuLi failed[113] as did similar experiments[84] with the substrates **95** and **96**.

The silyl selenides **97**–**99** could be converted into carbanions [BuLi, THF, 0°, 1 h] which react with aldehydes and ketones to give β-hydroxyalkyl silanes. Unfortunately, the yields were less than 50%.[84]

8. FORMATION OF EPOXIDES FROM SELENONIUM YLIDES

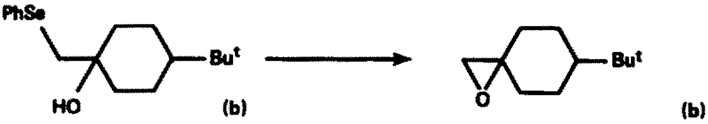
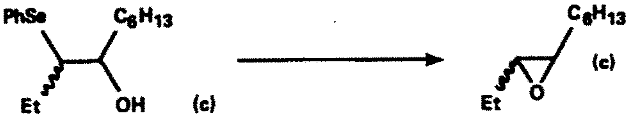
A few selenonium ylides have been generated[114] (*in situ*) and have been found to convert *non-enolizable* aldehydes and ketones into epoxides. The precursors of the ylides, compounds **100**–**103**, are made by the action of

---

[ccc] Sometimes Me_2SO_4 at 100° can be used[80] in the absence of a silver salt.

[ddd] In experiments with phenyl selenides (R = Ph in eqn 100) epoxide formation was run at 20° for 2 hr.[80] Similar conditions are used with methylselenides.[76,79]

Table 33.[a]

		Yield	Ref.
1		72%	80
2		73	80
3		67	80
4		46	80
5		63	80
6		46	80
7		57	80
8		70	80
9		70	80
10		80	80
11		90	76
12		97	76

Tab 33 contd.

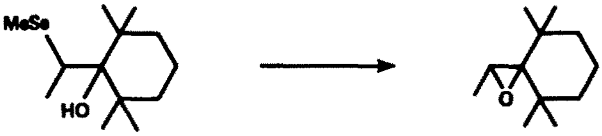
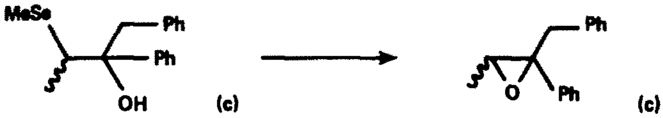
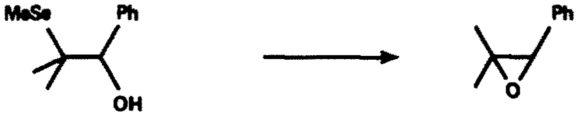
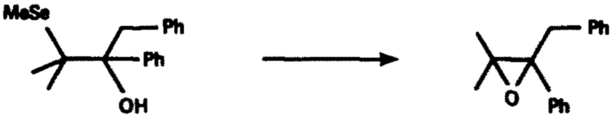
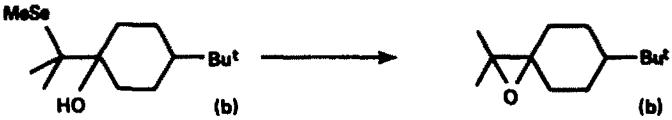
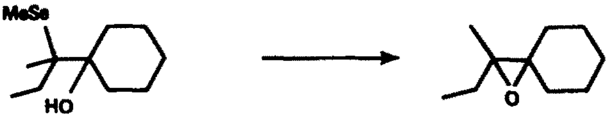
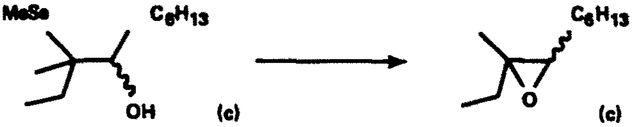
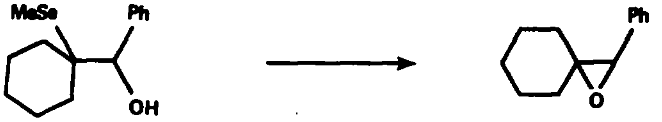
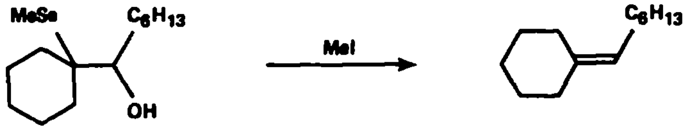
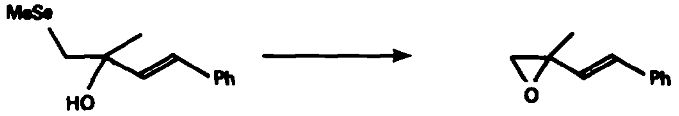
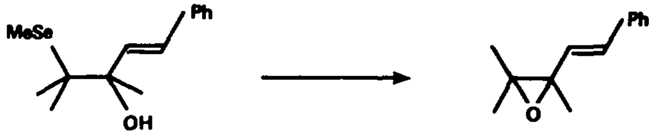
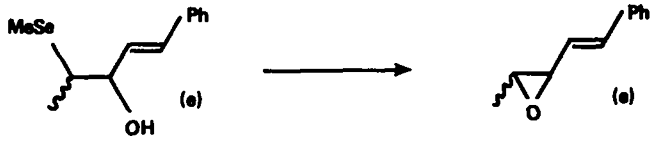
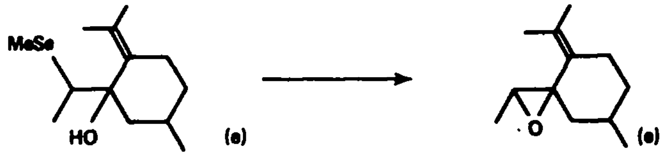
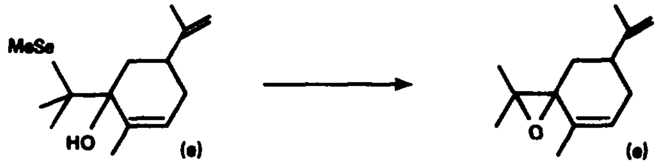
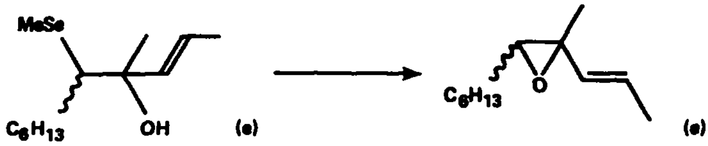
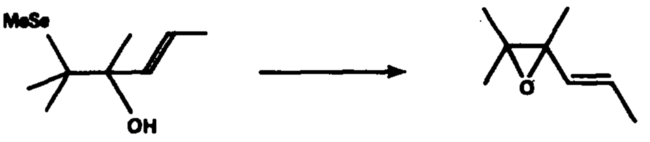
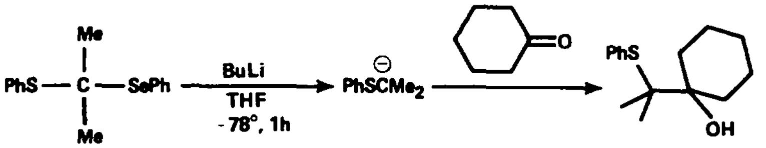
13		87	76
14		83	76
15	 (c) (c)	98	76
16		72	76
17		80	76
18		84^{d}	76
19	 (b) (b)	60^{d}	76
20	 (c) (c)	90	76
21		86	76
22	 (c) (c)	66	76

Table 33 (*Contd.*).

23		93	76
24		90	76
25		75	79
26		89	79
27		94	79
28		98	79
29		75	79
30		95	79
31		40	79
32		50	79

[a]Yield from selenonium salt except for the α,β-unsaturated epoxides where the yield is based[79] on β-hydroxyalkyl selenides. [b]Stereochemistry not given. [c]Mixture of stereoisomers. [d]Yield from ketone used to make the β-hydroxyalkyl selenide. [e]Probably an isomer mixture.



(102)

51% Ref. 113

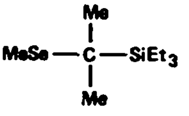
95% Ref. 77

$\overset{\ominus}{MeOCH_2}$

93

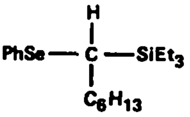
$MeOCH_2SePh$

94



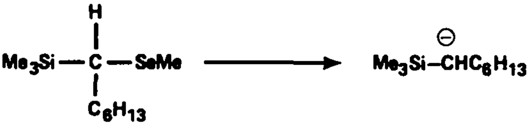
$MeSe-\overset{\overset{Me}{|}}{\underset{\underset{Me}{|}}{C}}-SiEt_3$

95



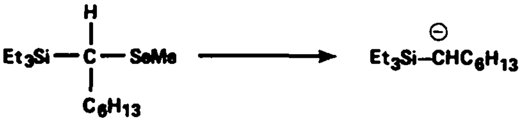
$PhSe-\overset{\overset{H}{|}}{\underset{\underset{C_6H_{13}}{|}}{C}}-SiEt_3$

96



$Me_3Si-\overset{\overset{H}{|}}{\underset{\underset{C_6H_{13}}{|}}{C}}-SeMe \longrightarrow Me_3Si-\overset{\ominus}{C}HC_6H_{13}$

97



$Et_3Si-\overset{\overset{H}{|}}{\underset{\underset{C_6H_{13}}{|}}{C}}-SeMe \longrightarrow Et_3Si-\overset{\ominus}{C}HC_6H_{13}$

98

$Et_3Si-\overset{\overset{H}{|}}{\underset{\underset{Me}{|}}{C}}-SeMe \longrightarrow Et_3Si-\overset{\ominus}{C}H-CH_3$

99

$Me_2\overset{\oplus}{Se}Me\ \ I^{\ominus}$ **100**

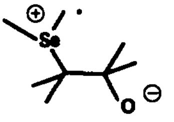
$Ph_2\overset{\oplus}{Se}Me\ \ BF_4^{\ominus}$ **101**

$Ph_2\overset{\oplus}{Se}CH_2Me\ \ BF_4^{\ominus}$ **102**

$Ph_2\overset{\oplus}{Se}CHMe_2\ \ BF_4^{\ominus}$ **103**

an alkyl halide on the selenide. In the case of diphenyl selenide a stoichiometric amount of a silver salt is needed on account of the poor nucleophilicity of selenium in this compound. Addition of Bu^{t}OK to a DMSO solution of one of these selenonium salts in the presence of a non-enolizable aldehyde or ketone leads to an epoxide. Table 34 summarizes the published work.[114]

The intermediate in each of these reactions is of the type **104** and such species can also be generated from β-hydroxyalkyl selenides (see p. 1114).



104

9. TRANSFER OF ALKYL AND ARYL GROUPS FROM SELENONIUM SALTS AND SELENIDES

(A) *Via selenonium salts*

Treatment of selenonium salts with BuLi in THF [−78°, 10 min] generates selenanes, such as **105**,[78] which react with aromatic and aliphatic aldehydes and ketones [−78°, 2 hr; then 20°, 1 hr] so as to transfer an alkyl group to the carbonyl component (e.g. eqn 103).

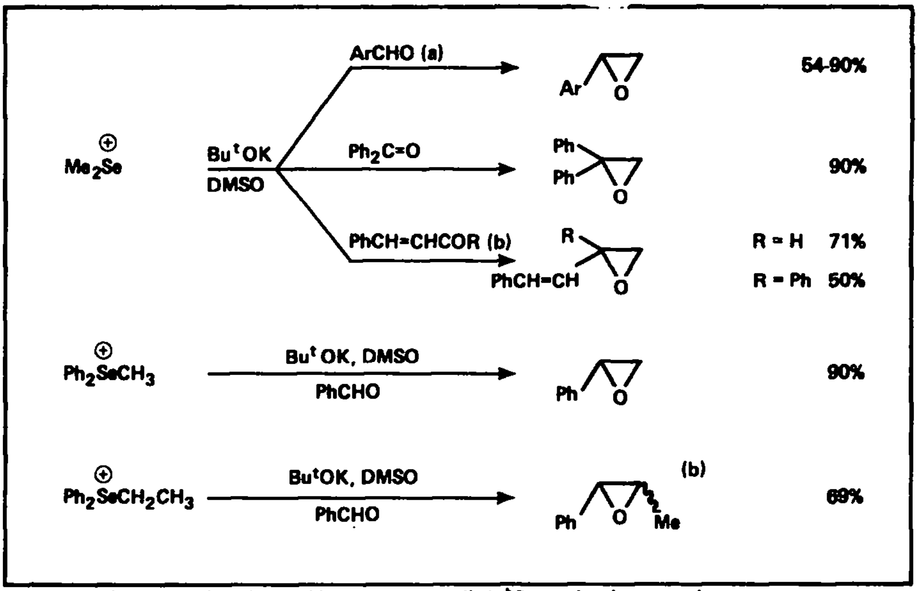
Monoaryl- or diarylselenonium salts, such as **101** behave in the same way but in these cases the phenyl group is transferred preferentially. Yields of alcohols from the few selenonium salts examined are generally modest.

In the example cited (eqn 103) butyl transfer is evidently a significant pathway; the proportion of butylation products is even greater with α,β-unsaturated substrates.[78] These react both by 1,2- and 1,4-addition.

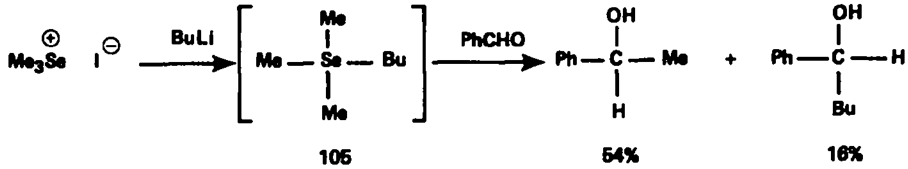
(B) *Via monoselenides*[78]

Treatment of the selenides **106**–**111** with BuLi [THF, 0°, 0.25 hr; then 20°, 0.5 hr] generates anionic species (e.g. **112**) which transfer alkyl groups to ketones and aldehydes [THF, room temperature, 2 hr]. Typical examples[78] are shown by eqns (104) and (105), and it can be seen that if the anion carries only alkyl groups then products arising from migration of each of these will result. Phenyl migrates in preference to alkyl, benzyl, or

Table 34.



[a] A few simply substituted benzaldehydes were studied. [b] Stereochemistry not given.



(103)

MeSeMe **106**

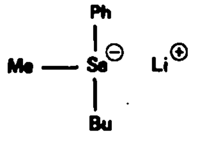
PhSeMe **107**

PhSePh **108**

$PhSeCH_2Ph$ **109**

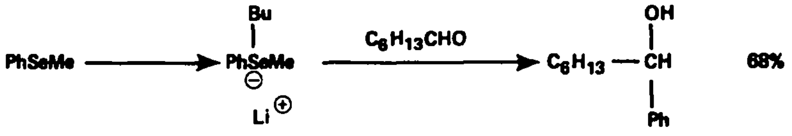
$PhCH_2SeMe$ **110**

$PhSeCH_2{-}CH{=}CH_2$ **111**

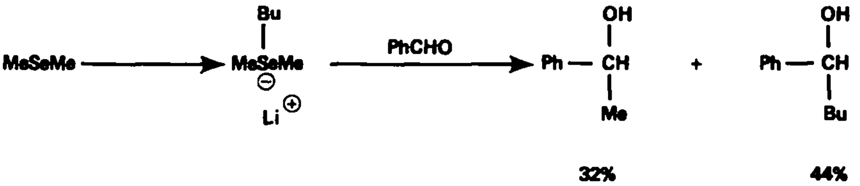


$$Me-\underset{Bu}{\overset{Ph}{Se^{\ominus}}}\ Li^{\oplus}$$

112



(104)



(105)

allyl and migratory aptitude of a benzyl group appears to be greater than that of a methyl.

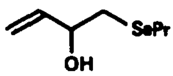
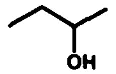
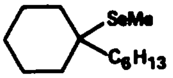
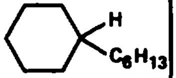
18. SIMPLE TRANSFORMATIONS OF SELENIDES AND SELENOXIDES: FORMATION OF HYDROCARBONS AND ALKYL HALIDES

The use of selenium-containing synthons for making carbon frameworks places some importance on the ability to transform the selenides into a wide range of compounds. This section deals with the conversion of selenides into hydrocarbons or halides, and of selenoxides into halides.

(A) *Hydrogenolysis of selenides*

Situations can conceivably arise in which selenium has served its purpose and has to be removed from an organic molecule by a process other than selenoxide fragmentation. Raney nickel in refluxing xylene[64a] or in refluxing ethanol [24 hr][82] can be used for this process

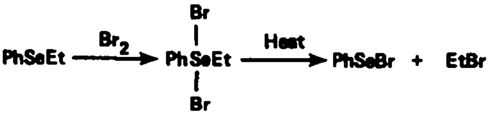
Table 35.

				Yield	Ref.
1		Raney Nickel xylene		—	64a
2	$C_{13}H_{27}CHDSeMe$	$Li/EtNH_2$	$C_{13}H_{27}CH_2D$	75%	82
3	$(C_{10}H_{21})_2CHSePh$	$Li/EtNH_2$	$(C_{10}H_{21})_2CH_2$	80	82
4		$Li/EtNH_2$		77	82
5	$(C_{10}H_{21})_2C(SeMe)_2$	Raney Nickel EtOH or $Li/EtNH_2$	$(C_{10}H_{21})_2CH_2$	Li 84 Ni 80	82 82

but an alternative exists in which the selenide is treated with an excess of lithium in $EtNH_2$ at −15° [1.25 hr].[82] Yields are usually better than 70%.[82] The following are typical results[64a,82] (Table 35).

(B) *Conversion of selenides into halides*

The preparation of halides from selenides has been known[115] for many years (e.g. eqn 106) but the method



$$PhSeEt \xrightarrow{Br_2} PhSe\overset{Br}{\underset{Br}{|}}Et \xrightarrow{Heat} PhSeBr + EtBr \quad (106)$$

has recently[81] been refined into three experimental procedures.

(i) The selenide is treated with 1 mole equiv. of Br_2 in aqueous EtOH at room temperature for up to 48 hr or for 1 hr at 80°.

(ii) The reaction can be conducted at room temperature in the same solvent mixture by using 2 mole equiv. of NBS.

(iii) This method calls for adding a CH_2Cl_2 solution of the selenide to a suspension, in the same solvent, of an excess of Et_3N [20 mmole per mole of selenide] and Br_2 [2 mole equiv.]. A reaction period of up to 3 hr at room temperature is sufficient.[81]

These procedures are applicable[81] to secondary and tertiary methyl or phenyl selenides (MeSeR; PhSeR) as shown by the following typical examples (Tables 36).

It appears that high yields of primary bromides are not obtained by any of these techniques but primary iodides can be made[81] by the modified scheme[***] summarized by eqn (107).

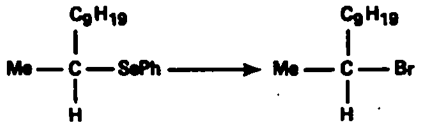
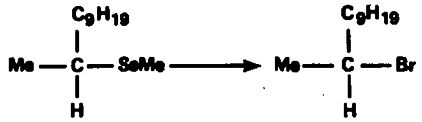
This method also has its limitations; it appears to be ineffective for preparing secondary or tertiary iodides.

Finally, the β-hydroxyalkyl selenides 113 have been converted[81] into bromohydrins as shown by methods (i) and (ii):

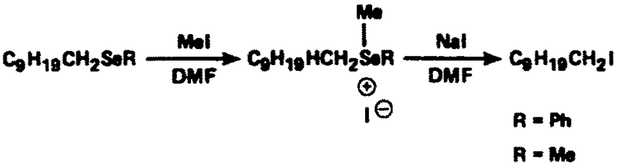
(C) *Conversion of selenoxides into halides*

A selenoxide, generated by ozonolysis in CH_2Cl_2 at −78° can be converted[116] efficiently into a secondary or

Table 36.

		Method	Yield	Ref.
1	 $Me-\overset{C_9H_{19}}{\underset{H}{C}}-SePh \longrightarrow Me-\overset{C_9H_{19}}{\underset{H}{C}}-Br$	Br_2 NBS Et_3N/Br_2	70% 60 84	81
2	 $Me-\overset{C_9H_{19}}{\underset{H}{C}}-SeMe \longrightarrow Me-\overset{C_9H_{19}}{\underset{H}{C}}-Br$	Br_2 NBS Et_3N/Br_2	50% 22 75	81
3		Et_3N/Br_2	68%	81

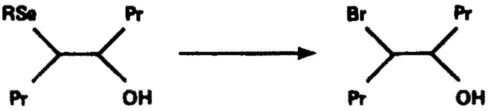
[***] Specific experimental details have not been reported.



$$\mathrm{C_9H_{19}CH_2SeR} \xrightarrow[\text{DMF}]{\text{MeI}} \mathrm{C_9H_{19}HCH_2\overset{Me}{\underset{\oplus}{Se}}R}\ \mathrm{I^{\ominus}} \xrightarrow[\text{DMF}]{\text{NaI}} \mathrm{C_9H_{19}CH_2I} \qquad (107)$$

R = Ph 80%

R = Me 65%

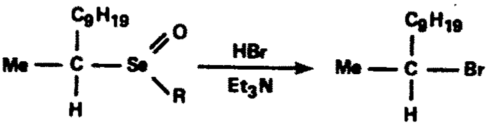


113*

R	Method	Time	Yield
Ph	Br_2	1 h	72%
Ph	NBS	24	70
Me	Br_2	1.5	40

*Stereochemistry not specified.

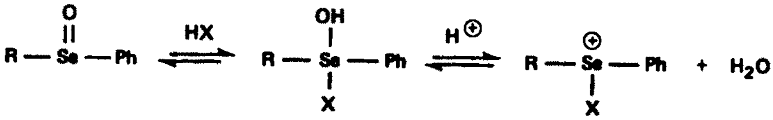
tertiary (but not primary) alkyl bromide by passing an excess of HBr into the cold solution and then adding Et_3N (2 mole per mole selenide).[fff] The mixture is allowed to attain, and is kept at, room temperature before isolation of the product (e.g. eqn 108). The reaction works better for the formation of alkyl bromides than of alkyl chlorides, and phenyl selenides give superior yields to methyl selenides. Mechanistically the following processes are probably involved (eqns 109 and 110).



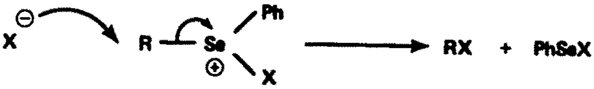
$$\mathrm{Me-\overset{C_9H_{19}}{\underset{H}{C}}-Se(=O)R} \xrightarrow[\mathrm{Et_3N}]{\mathrm{HBr}} \mathrm{Me-\overset{C_9H_{19}}{\underset{H}{C}}-Br} \qquad (108)$$

R = Me, 18 h, 77%

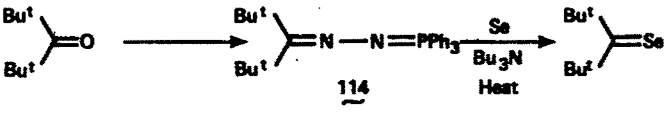
R = Ph, 2.5 h, 94%



$$\mathrm{R-\overset{O}{\overset{\|}{Se}}-Ph} \overset{\mathrm{HX}}{\rightleftharpoons} \mathrm{R-\overset{OH}{\underset{X}{Se}}-Ph} \overset{\mathrm{H^{\oplus}}}{\rightleftharpoons} \mathrm{R-\overset{\oplus}{\underset{X}{Se}}-Ph} + \mathrm{H_2O} \qquad (109)$$

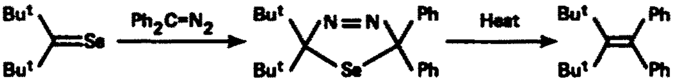


(110)



114

(111)



(112)

11. NEW USES FOR ELEMENTAL SELENIUM

(A) *Synthesis of selones* (*selenoketones*)

A few non-enolizable ketones such as di-*t*-butyl ketone and fenchone, have been converted into selones[117,118] by the sequence[ggg] shown (eqn 111) and the selones have served as precursors to hindered olefins (eqn 112).

(B) *Catalytic uses of selenium*[hhh]

A number of new uses, frequently of a catalytic nature, have been discovered recently for selenium. The reactions are for the synthesis of carbonyl compounds, X–CO–Y where X and Y are heteroatoms.

(a) *Formation of ureas.* If CO is passed through a THF solution of $BuNH_2$ at 20° containing a catalytic amount of suspended Se then the metal dissolves within a few minutes. If a controlled amount[iii] of O_2 is now admixed with the CO and passage of the gas stream is continued for several hours all of the amine is converted into $(BuNH)_2CO$.[120] At this stage selenium metal can be

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[fff] The reaction mixture must remain acidic but, except for benzyl selenoxides, Et_3N is required for a good yield.

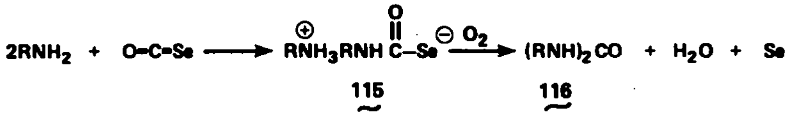
[ggg] Reaction of $Bu_2{}^tC{=}N^+{=}N^-$ and of $Bu_2{}^tC{=}PPh_3$, potential thermal products of 114,[119] with selenium would shed light on the mechanism.

[hhh] (i) A few of the processes discussed here are not catalytic in selenium but all the reactions in this Section are very closely related. (ii) Because of the simplicity of most of the compounds the tables give only *representative* examples.

[iii] If too much O_2 is added at this stage Se is deposited and urea formation stops.

precipitated by passing in pure O_2 and isolation of the urea in almost quantitative yield is then straightforward. The following are typical results (Table 37).[120,121]

These reactions probably involve COSe, formed from Se and CO in the presence of a base. Reaction with the amine produces a salt, **115**, which sometimes can be isolated[120,122] and oxidation then affords the urea (**115**→**116**)[123] (eqn 113). The pathway from **115** to **116** is not yet clear. It may involve formation of a diselenide[122] or attack of amine on the salt and, in fact, it is possible to obtain an unsymmetrical urea by treating the intermediate salt **115** with a second amine[120,123a] followed by oxidation. (Production of the urea is not then catalytic in Se.) In the case of anilines a modification is needed[124] in that a stoicheiometric amount of Et_3N must be added to the reaction mixture. Although absolute yields are now generally less than 50%, on the basis of the aniline consumed, yields are quantitative.



$$2RNH_2 + O{=}C{=}Se \longrightarrow \underset{115}{\overset{\oplus}{RNH_3}RNH\overset{O}{\overset{\|}{C}}{-}Se^{\ominus}} \xrightarrow{O_2} \underset{116}{(RNH)_2CO} + H_2O + Se \qquad (113)$$

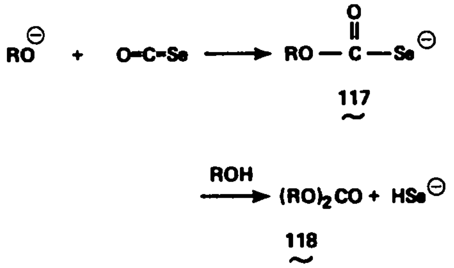
(b) *Conversion of alcohols into carbonates.* A procedure similar to that just described in Section (a) serves to convert alcohols into symmetrical carbonates. For example,[125,126] CO was passed into THF containing EtOH, EtONa and Se in the molar ratio of 5:5:1 and, after 2 hr at room temperature, O_2 was used to precipitate dissolved Se. $(EtO)_2CO$ was obtained in 92% yield (based on reacted Se). Methyl-, propyl- and butylcarbonates were likewise obtained in near quantitative yields. The yield of benzyl carbonate was 76% but with secondary and tertiary alcohols yields are less than 20%. Phenols do not react. The process can be conducted in a fashion[126] that is catalytic in Se. The details follow those just described except that after initial passage of CO a stream of CO containing a *controlled* amount of O_2 is passed in for several hours. Dissolved Se is finally precipitated as before.

THF is the preferred solvent except that DMF is better for converting diols into cyclic carbonates.[126]

The mechanism involves[126] formation of the salt **117** probably by rapid[126] reaction of COSe formed *in situ* (eqns 114 and 115). When the reaction is not done in the catalytic manner, i.e. when no O_2 is used, the salt probably suffers rapid alcoholysis (**117**→**118**). In the catalytic process (i.e. O_2 being used) the NaSeH could be oxidised to Se, the metal being recycled.[126] Alternatively,[123b] the salt may be oxidised to ROCO–Se–Se–COOR which could give *inter alia* $(RO)_2C{=}O$ and Se (to be recycled).

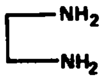
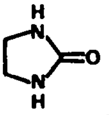
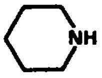
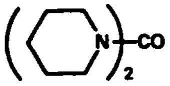
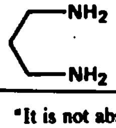
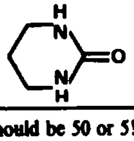
(c) *Formation of heterocycles.* A number of carbonylations of the following type (eqn 116) have also been performed and the mechanism can be understood on the basis of the intervention of COSe (eqn 117).

$$Se + CO \xrightarrow{RO^{\ominus}} O{=}C{=}Se \qquad (114)$$

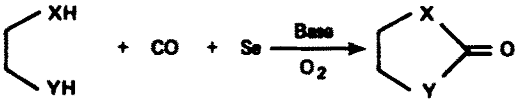


$$RO^{\ominus} + O{=}C{=}Se \longrightarrow \underset{117}{RO-\overset{O}{\overset{\|}{C}}-Se^{\ominus}} \xrightarrow{ROH} \underset{118}{(RO)_2CO} + HSe^{\ominus} \qquad (115)$$

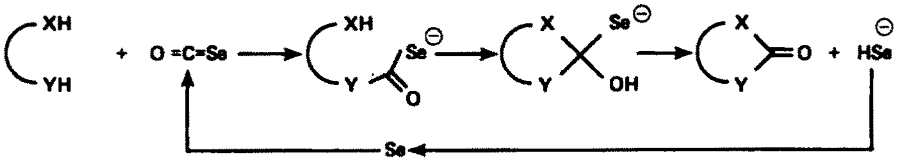
Table 37.

	Amine	Conditions			Urea	Yield
		CO	Temp.	Se		
1	$BuNH_2$	1 atm	20°	5 mole %	$(BuNH)_2CO$	100%
2	$C_6H_{13}NH_2$	1	20	5	$(C_6H_{13}NH)_2CO$	95 to 99
3	$C_8H_{17}NH_2$	1	20	5	$(C_8H_{17}NH)_2CO$	
4	$C_6H_{11}NH_2$	1	20	5	$(C_6H_{11}NH)_2CO$	
5	$PhCH_2NH_2$	1	20	5	$(PhCH_2NH)_2CO$	74
6		1	20	5		14
		50	60	50[a]		98
7		1	20	5		26
8		50	40	50[a]		96

[a] It is not absolutely clear whether this should be 50 or 5!



(116)

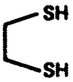
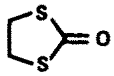
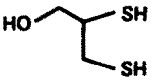
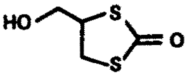
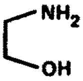
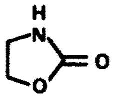
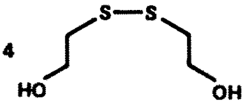
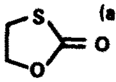
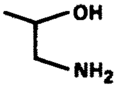
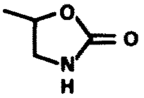
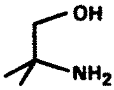
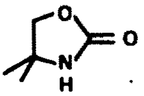
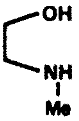
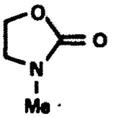
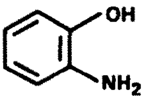
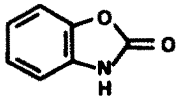
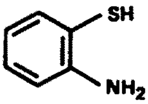
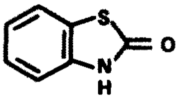


(117)

Typically,[127] the reaction is run in THF for several hours at a fixed temperature in the range 25 to 60°. The starting material is treated with a catalytic amount of Se and a mixture of CO and O_2 under a pressure of 3 atmospheres. If the starting material contains no amino-group then Et_3N is needed as a co-catalyst. Results of the following type can be obtained by this, or by a similar[128] procedure (Table 38).

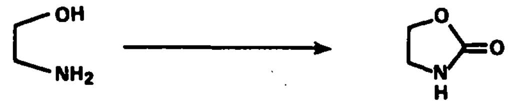
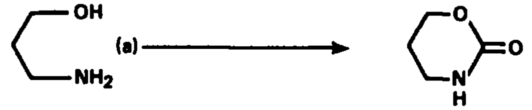
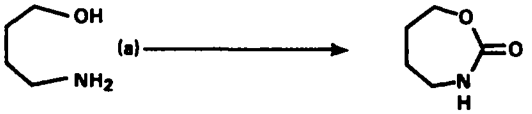
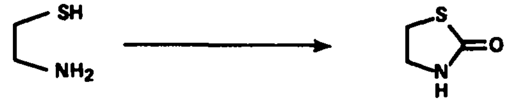
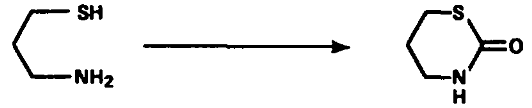
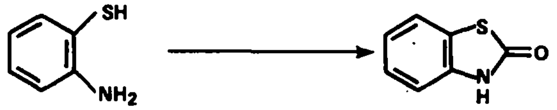
Heterocycles can also be made by a stoicheiometric synthesis (Table 39) in which an amino-alcohol or amino-thiol is treated with CO in the presence of an equimolar amount of Se and an excess of Et_3N.[128] The reaction

Table 38.

				Yield	Ref.
1		10h, 25°		90%	127
2		10h, 25°		85	127
3		2h, 60°		95	127, 128
4		20 h, 60°	 (a)	60	127
5		6 h room temp.		99	128
6		6 h room temp.		90	128
7		6 h room temp.		90	128, 123[a]
8		6 h room temp.		84	128
9		6 h room temp.		64	128

[a] The thiol, $HOCH_2CH_2SH$, is produced but it is converted into the heterocycle.

Table 39.[128]

		Yield
1		94%
2		85
3		68
4		77
5		76
6		64

[a] At high concentration of the amino alcohol, ureas are formed.[128] Ureas are the major product when the catalytic procedure is used.[128]

proceeds at room temperature in DMF and when it is over oxygen is used to precipitate the Se.

(d) *Formation of formanilides.* Treatment of various substituted anilines with a small amount of $Et_3N \cdot H_2Se$ in the presence of CO under pressure gives the corresponding anilide (eqn 118). This reaction[129] is run at 100° for 45 hr.

$$ArNH_2 + CO + Et_3N \cdot H_2Se \longrightarrow ArNHCHO \qquad (118)$$

(e) *Conversion of formates into carbonates.* Simple alkyl formates, ROCHO (R = Me, Et, Pr^i, Bu) are converted into carbonates. ROCOOR' (R' selected from Me, Et, Pr^i, Bu) by treatment in THF with an equivalent of an alkoxide (R'ONa) and Se. In this noncatalytic process the yield of carbonate (based on Se consumed) is generally greater than 80%.[130]

If a catalytic reaction is to be performed—as opposed to a stoicheiometric process—then O_2 is added at a controlled rate after the initial charge of Se has dissolved.[130]

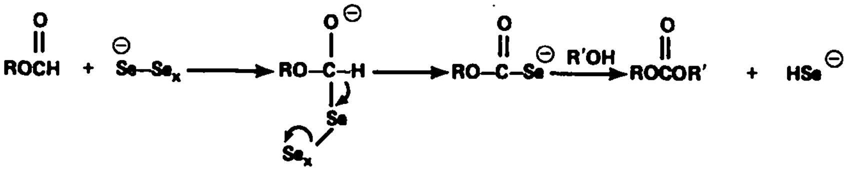
Equation (119) summarises a possible[131] mechanism.

(f) *Conversion of formamides into carbamates.* In a process analogous to that of Section (e), formamides are converted into carbamates[131] (eqn 120), but yields are less than 36% (based on Se consumed):

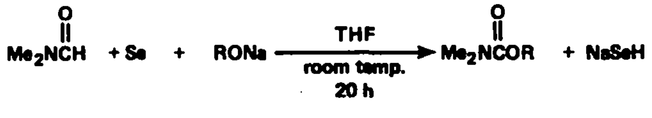
(g) *Formation of carbamates and thiolcarbamates.* Treatment of amines with CO under pressure in the presence of Se (a catalytic amount) and a disulphide produces[132] thiolcarbamates, usually in high yield (eqn 121).

A variety of simple aromatic and aliphatic amines have been used together with both alkyl and aryl *sym* disulphides (Table 40). In the case of anilines, Et_3N is needed as a co-catalyst.

A number of simple primary amines have been converted[133] into carbamates by treatment with CO in the presence of an equimolar amount of Se and an excess of both Et_3N and an alcohol (eqn 122). This is not a true

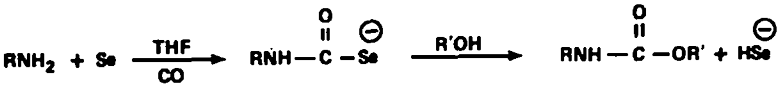


$$ROCHO + {}^{\ominus}Se\text{—}Se_x \longrightarrow RO\text{—}CH(O^{\ominus})\text{—}Se\text{—}Se_x \longrightarrow RO\text{—}C(=O)\text{—}Se^{\ominus} \xrightarrow{R'OH} ROCOR'(=O) + HSe^{\ominus} \qquad (119)$$



$$Me_2NCHO + Se + RONa \xrightarrow[\text{room temp.}\ 20\ h]{THF} Me_2NCOOR + NaSeH \qquad (120)$$

$$\mathrm{RNH_2} + \mathrm{Se} \xrightarrow[\mathrm{CO}]{\mathrm{MeCN}} \mathrm{RNH}-\overset{\overset{\displaystyle \mathrm{O}}{\|}}{\mathrm{C}}-\mathrm{Se}^{\ominus} \xrightarrow{\mathrm{R'SSR'}} \mathrm{RNH}-\overset{\overset{\displaystyle \mathrm{O}}{\|}}{\mathrm{C}}-\mathrm{SR'} \qquad (121)$$



$$\mathrm{RNH_2} + \mathrm{Se} \xrightarrow[\mathrm{CO}]{\mathrm{THF}} \mathrm{RNH}-\overset{\overset{\displaystyle \mathrm{O}}{\|}}{\mathrm{C}}-\mathrm{Se}^{\ominus} \xrightarrow{\mathrm{R'OH}} \mathrm{RNH}-\overset{\overset{\displaystyle \mathrm{O}}{\|}}{\mathrm{C}}-\mathrm{OR'} + \mathrm{HSe}^{\ominus} \qquad (122)$$

Table 40.

Thiolcarbonate	Yield	Reaction Temp.	Half-Time
1 $Pr^iNHCOSPh$	85%	20°	very fast
2 $Bu^t NHCOSPh$	84	20	very fast
3 $C_6H_{11}NHCOSPh$	87	20	very fast
4 BuNHCOSMe	73	-5^a	3h
5 $Pr^iNHCOSMe$	77	-5^a	3
6 $p-Me-C_6H_4-NHCOSPr^i$	92	60	0.5
7 $o-Me-C_6H_4-NHCOSPr^i$	92	60	3.5
8 $PhNHCOSBu^i$	87	60	1
9 $PhNHCOSBu^s$	83	60	2.5
10 $PhNHCOSBu^t$	0	60	—
11 PhNHCOSPh	50	60	1.2
12 $p-Cl-C_6H_4-NHCOSBu^i$	90	60	1.5
13 $p-NO_2-C_6H_4-NHCOSBu^i$	0	60	—

[a] Run at 20°, the reaction affords ureas.

catalytic process. Evidently, the intermediate salt undergoes alcoholysis, and at the end of the reaction O_2 is used to precipitate Se. Yields are in the range of 16–90%.

12. THE MECHANISM OF SELENIUM DIOXIDE OXIDATION

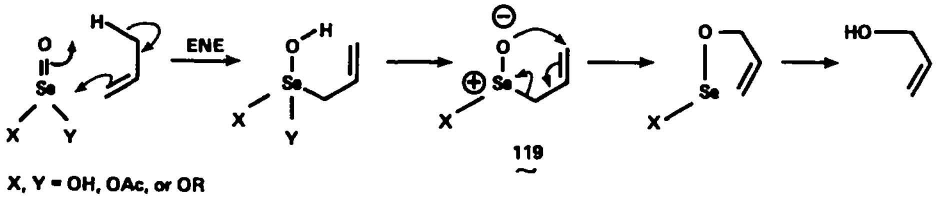
Selenium dioxide has long been employed for certain types of oxidation[1a] but its use has been without mechanistic understanding. The mode of action of this reagent has now been clarified to a substantial degree.

(A) *Allylic oxidation*

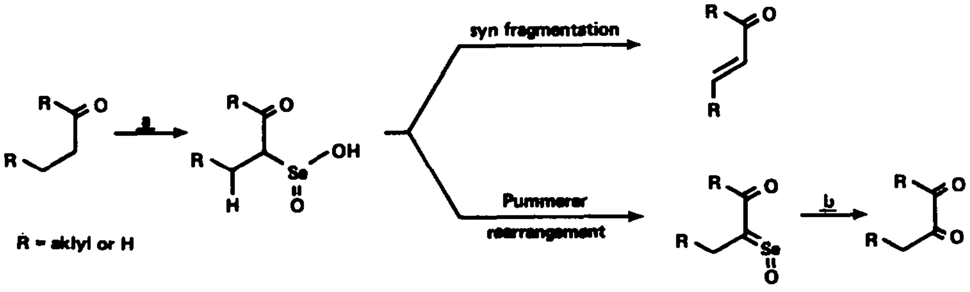
Many of the results of allylic oxidation by SeO_2 can be understood in terms of an ene reaction followed by a [2,3]-sigmatropic rearrangement and hydrolysis of a Se(II) ester (eqn 123). Strong evidence in support of the intermediate **119** and of the [2,3] shift has been acquired.[69,134,135]

(B) *Oxidation of ketones and aldehydes*

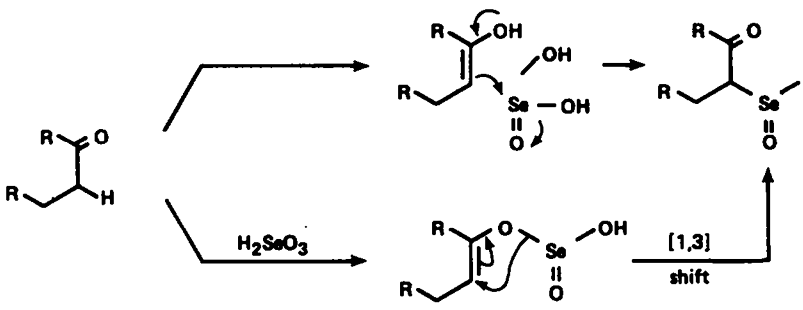
Evidence is now available[136] to support the following pathway (eqn 124) but some minor details remain to be clarified. Steps *a* and *b* could each occur by two routes (eqns 125 and 126) and no decision between them can yet be made.



(123)



(124)



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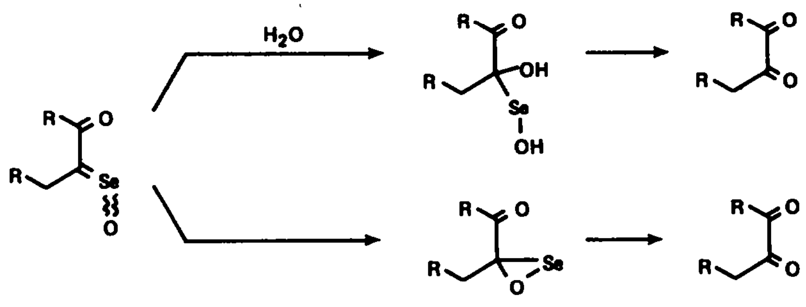


(126)

13. AZA ANALOGUES OF SELENIUM DIOXIDE

Several reagents[137] represented by structure **120**, have been found to react with olefins (and acetylenes) to effect allylic (or propargylic) amination (e.g. eqn 127).


$R{-}N{=}Se{=}N{-}R$

R= Bu^t –; $ArSO_2$ –

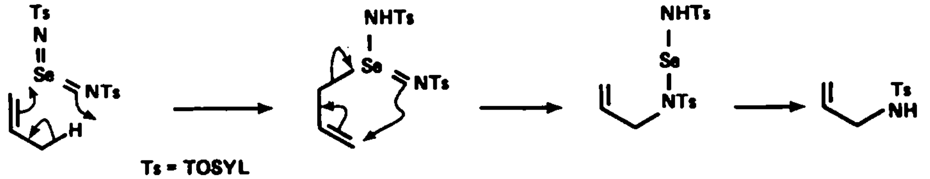
120

Reagent **120** (R = 4-Me–$C_6H_4SO_2$, for example) is easily made by letting selenium metal react with anhydrous Chloramine-T at room temperature over 24 hr. It reacts with an excess[jjj] of the olefinic substrate and the process is the first case of direct allylic amination of olefins. [The corresponding sulphur compound[138] may be superior in this regard.] The reagent also reacts with 1,3-dienes, the products usually[kkk] being *vicinal cis* disulphonamides,[139] e.g. eqn (128). For this type of process the reagent is generated (from Se and Chloramine-T) in the presence of 4-$MeC_6H_4SO_2NH_2$, whose role in the subsequent amination is shown below.

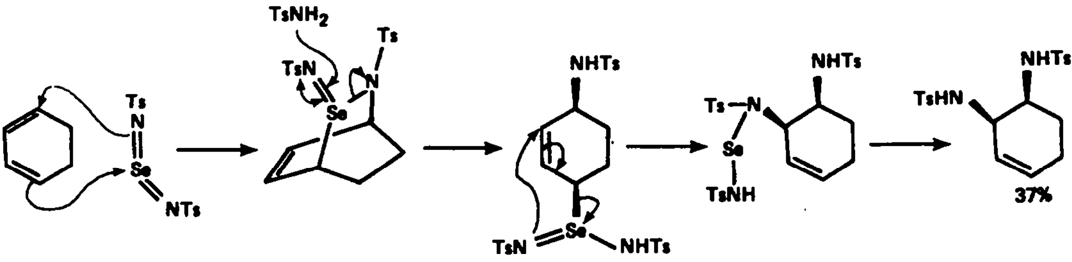
14. FORMATION OF 1,2,3-SELENADIAZOLES AND THEIR FRAGMENTATION INTO ACETYLENES

A new application of SeO_2 has been found in its use to convert[140–149] semicarbazones into 1,2,3-selenadiazoles, a heterocyclic system which affords[141–149] acetylenes on heating, as shown by eqn (129).[141]

The general procedure involves oxidising the semicarbazone with SeO_2, usually in warm glacial AcOH[141–145] or in dioxane[141,146–149] and mixing the resulting selenadiazole with sand[141–145] or glass powder.[146–149] Pyrolysis at an appropriate temperature within the range 160–220° (sometimes[145,147–149] under reduced pressure) then affords the acetylene. Table 41 shows *typical* examples. Yields of selenadiazoles are variable and for aldehydes are generally poor. In compounds with the



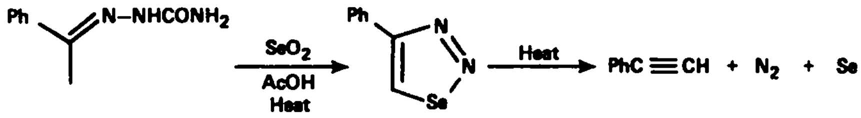
(127)



(128)

[jjj] An excess is needed to avoid polyamination. More than one of the sulphonamide units of the reagent is formally available. Molar ratios of reagent to olefin of 0,63 and 0.83 generally result in better yields.

[kkk] Occasionally, allylic amination is the main process.[139]



(129)

part structure, $-CH_2COCH_2-$, ring closure discriminates in favour of the carbon bearing the more acidic hydrogens.

The pyrolysis stage works extremely well with many simple compounds; in those cases where it is not efficient 1,4-diselenines and/or selenophenes are usually produced,[144,146,147,149,150] sometimes in substantial amounts.[149] In certain cases the selenophenes arise by reaction between the initial pyrolysis products—Se and the acetylene[150,151]—but in other cases the precursor is the corresponding 1,4-diselenine.[149]

15. OXIDATION OF AMINES

Conversion of amines by means of selenoxide fragmentation into imines and thence, by hydrolysis, into carbonyl compounds (eqn 130) is a process that occurs[aa]

[aa] The corresponding reaction in the oxygen series does not appear to take place: the ethyl ester of benzeneseleninic acid is a distillable, low-melting solid.[23b] Benzylamine, with two equivalents of $[PhSe(O)]_2O$ or of PhSe(O)Cl affords benzonitrile.

Table 41.

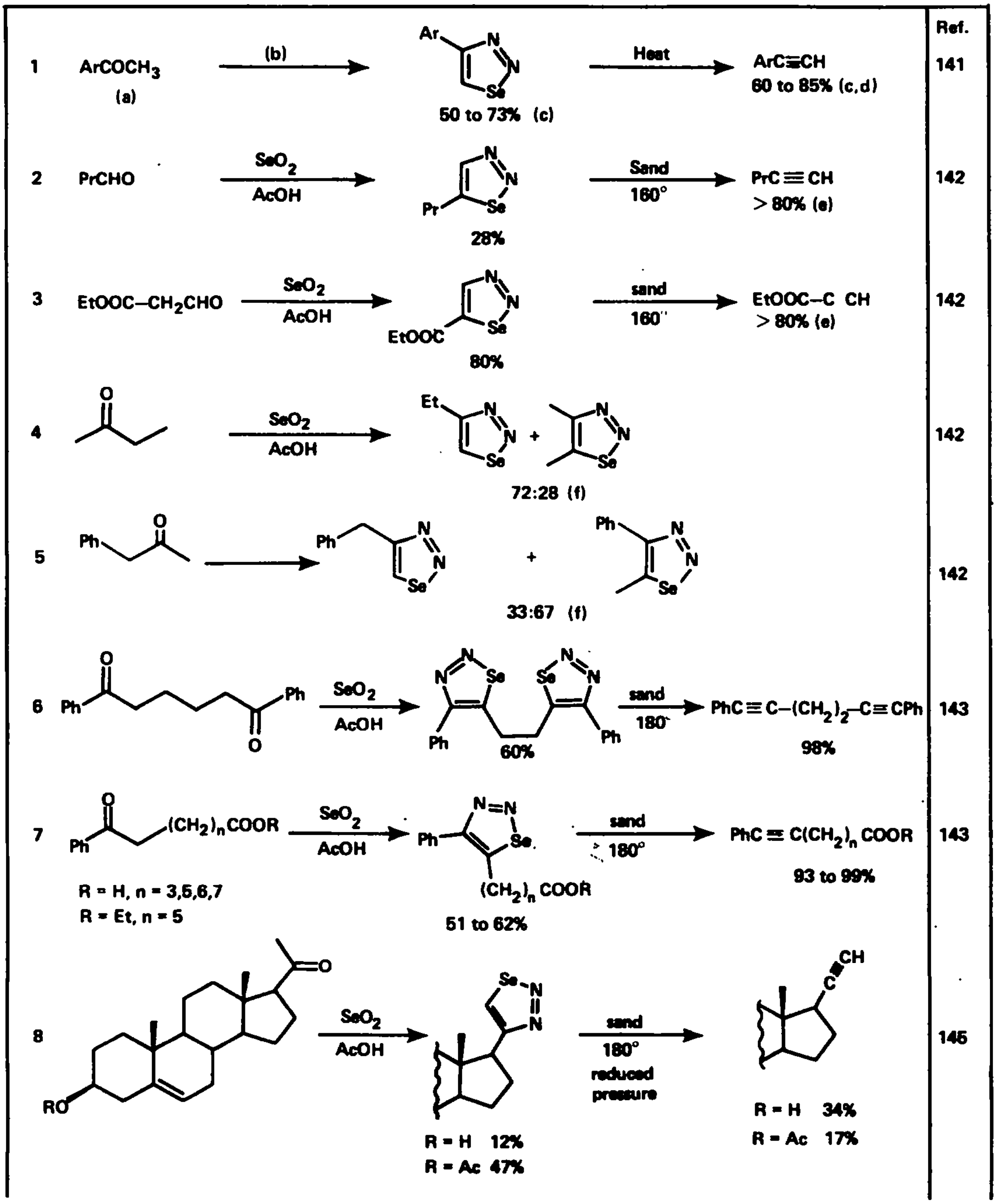
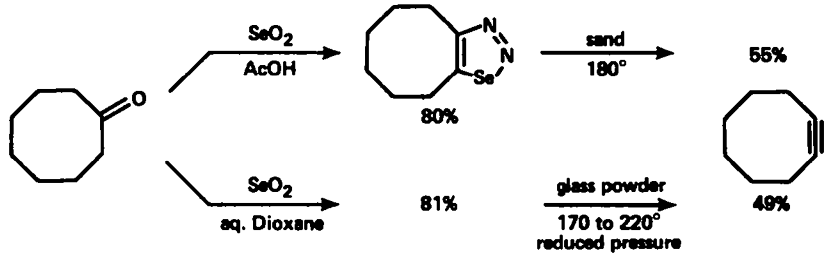
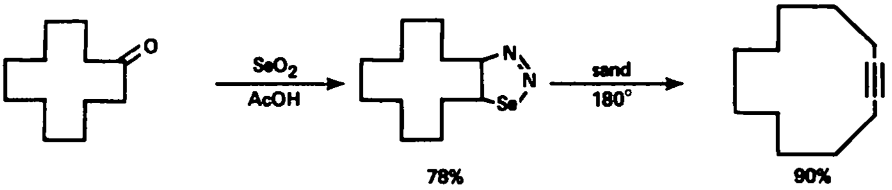
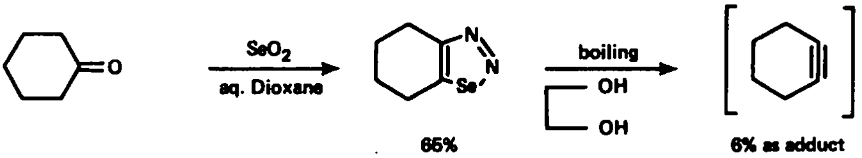
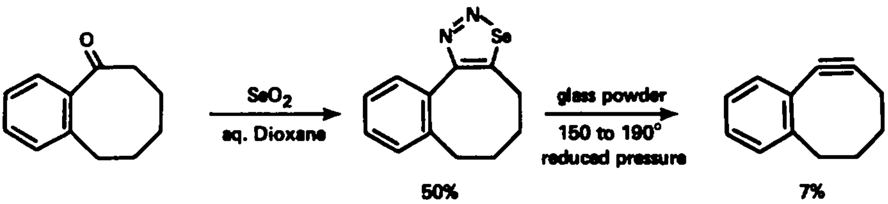
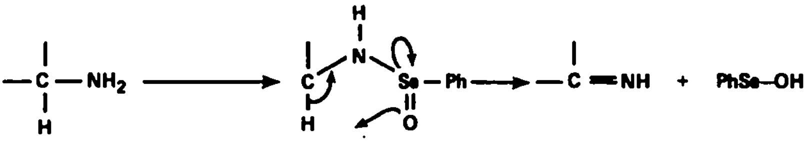


Table 41 (*Contd.*).

9		144 146,147
10		144
11		147
12		149

[a] A variety of simple acetophenones was used. [b] Oxidation of semicarbazone generally done in warm AcOH. [c] Yield depends on particular case. [d] If Ar = 4-F–C_6H_4– yield is 11%. [e] Precise yield not given. [f] These are relative yields.



121

(130)

in high yield.[152,153] The method appears to be limited, however, to production of non-enolizable ketones (e.g. adamantanone, fluorenone). The intermediate 121 is generated by treating the amine with $[PhSe(O)]_2O$ in CH_2Cl_2 at room temperature and it collapses spontaneously.[mmm] It is not clear whether hydrolysis of the imine occurs during work-up or *in situ*. (Water is formed by disproportionation of PhSe–OH.) In a modified procedure,[152] which does not seem to offer special advantages, the primary amine is treated with a CH_2Cl_2 solution of PhSe(O)Cl [1 equiv.].

The overall conversion of amine to ketone is a slow process,[154] but the rate-determining step has not been identified.

16. ORTHO-HYDROXYLATION OF PHENOLS

The principle of using a valence contraction of selenium (123→124) to effect *ortho*-hydroxylation of a phenol has been demonstrated[103] by examples that have relevance to tetracycline chemistry (eqn 131).[155] The phenol 122 (R = OMe or NH_2) was converted into its monosodium salt and treated with $[PhSe(O)]_2O$. Compounds 125 (R = OMe or NH_2) were isolated in yields of 75 and 68% respectively.

17. 1,2 SHIFTS IN SELENOXIDES

A number of processes, formally involving a 1,2 shift of an alkyl carbon from selenium to oxygen in selenoxides are known[35,66] and synthetic possibilities have been demonstrated by the case (eqn (132); Ar = simple substituted benzene nucleus) in which an aryl benzyl selenoxide is converted into an aldehyde.[66] This transformation

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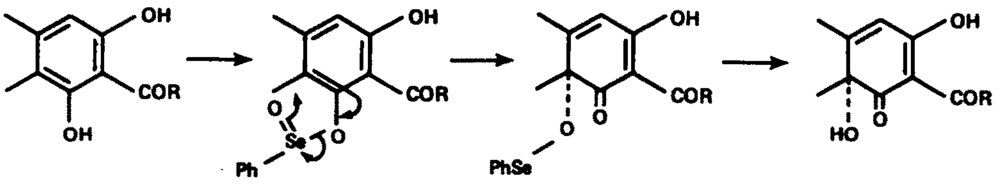
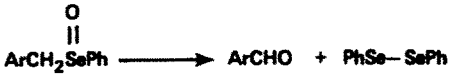
[mmm] The fragmentation of 121 may be simply a 1,2-elimination.



122 123 124 125 (131)



$$ArCH_2\overset{\overset{O}{\|}}{Se}Ph \longrightarrow ArCHO + PhSe{-}SePh \qquad (132)$$

is brought about by brief (2–3 min) heating to 110–130°. The mechanism is being investigated.[66]

18. FLUORINATION WITH SELENIUM TETRAFLUORIDE AND ITS PYRIDINE SALT

Selenium tetrafluoride which, if pure, can be used in ordinary glass apparatus, converts ketones[156,157] and aldehydes[157] into *gem* difluorides (eqns 133 and 134). In the simple examples examined the reagent was sometimes used in excess and yields are between 65 and 100%. Reaction times ranged from 0.25 hr at −20° for cyclohexanecarboxaldehyde to 15 hr at 20° for adamantanone.

$$R_2C{=}O \longrightarrow R_2CF_2 \ (R = \text{alkyl or aryl}) \qquad (133)$$

$$RCHO \longrightarrow RCHF_2 \ (R = \text{alkyl or aryl}) \qquad (134)$$

SeF_4 also converts carboxylic acids and their anhydrides into acyl fluorides. The reaction occurs at room temperature and has given simple products in yields that are generally better than 85%. Alcohols are likewise converted into alkyl fluorides. Usually the yield is greater than 50% and the range of compounds for which the reaction is successful includes primary, secondary, tertiary, allylic and benzylic alcohols.

Hydrogen fluoride is produced in the reactions involving acids and alcohols and it is preferable to mix pyridine [1 equiv.] with SeF_4 before adding the substrate.

19. PREPARATION OF VINYL SELENIDES

The chemistry of vinyl selenides[158] has not yet been examined in detail. As described on p. 1114 they can be made from β-hydroxyalkyl selenoketals. The following modern information is also available:

(a) The borate salt 126 reacts[159] with PhSeCl in a stereospecific fashion (eqn 135). The migrating alkyl group and the entering electrophile are *trans* and protonolysis affords the (*E*)-vinyl selenide. In the sulphur series (use of PhSCl) a mixture of (*Z*) and (*E*) isomers is obtained.

(b) Vinyl selenides are available[160] by Wittig reactions (eqns 136 and 137) and, in the case of the phosphonate reagents (eqn 137) there is high stereoselectivity in favour of the (*E*) product.

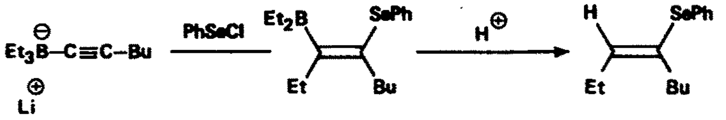
(c) Vinyl selenides can be hydrolised ($HgCl_2$, aq MeCN; 24 hr, 50°) to carbonyl compounds.[160b]

20. SELENOXIDES AS OXIDISING AGENTS

Selenoxides have mild oxidising properties. A few acyl hydrazides have been converted efficiently into *sym* diacyl hydrazines by diphenyl selenoxide. The general procedure[161] involves mildly acidic conditions (AcOH as cosolvent) at 60–70° for 1–2 hr.

Catechols can, similarly, be converted into *o*-quinones.[162]

A number of simple aliphatic and benzylic sulphides have been oxidised[163] to the corresponding sulphoxides

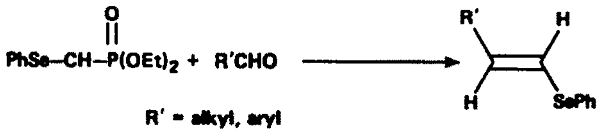


126 (135)

$$Ph_3P{=}C(R)(SePh) + R'CHO \longrightarrow R'CH{=}C(R)(SePh) \qquad (136)$$

R = H, Me R' = alkyl; aryl 63-99%

*Corresponding Wittig reactions with ketones sometimes follow an anomolous pathway.[160a]



(137)

R' = alkyl, aryl

by dibenzyl selenoxide in AcOH at room temp. (2 hr). An acid medium is essential for these oxidations. Diphenyl selenoxide is less reactive than the dibenzyl analogue.

REFERENCES

[1] [a]E. N. Trachtenberg, *Oxidation* (Edited by R. L. Augustine). Vol. 1, p. 119. Marcel Dekker, New York (1961); [b]E.g. R. E. A. Dear and F. L. M. Pattison, *J. Am. Chem. Soc.* **85**, 622 (1963).

[2] [a]Houben-Weyl, *Methoden der Organischen Chemie*, Vol. 9, p. 917. Georg Thieme Verlag, Stuttgart (1955); [b]*Selenium* (Edited by R. A. Zingaro and W. C. Cooper). Van Nostrand Reinhold, New York (1974); [c]*Organic Selenium Compounds: Their Chemistry and Biology*, (Edited by D. L. Klayman and W. H. H. Günther). Wiley-Interscience, New York (1973); [d]J. Gosselck, *Angew. Chem. Internat. Edn.* **2**, 660 (1963).

[3] D. L. J. Clive and C. V. Denyer, *Chem. Comm.* 253 (1973).

[4] D. L. J. Clive, *Chem. Comm.* 695 (1973).

[5] K. B. Sharpless, M. W. Young and R. F. Lauer, *Tetrahedron Letters* 1979 (1973).

[6] H. J. Reich, I. L. Reich and J. M. Renga, *J. Am. Chem. Soc.* **95**, 5813 (1973).

[7] M. Narita and C. U. Pittman, Jr., *Synthesis* 489 (1976).

[8] T. H. Chan and J. R. Finkenbine, *J. Am. Chem. Soc.* **94**, 2880 (1972).

[9] [a]C. C. J. Culvenor, W. Davies and N. S. Heath, *J. Chem. Soc.* 278 (1949); [b]C. C. J. Culvenor, W. Davies and K. H. Pausacker, *J. Chem. Soc.* 1050 (1946).

[10] [a]W. J. R. Tyerman, W. B. O'Callaghan, P. Kebarle, O. P. Strausz and H. E. Gunning, *J. Am. Chem. Soc.* **88**, 4277 (1966); [b]A. B. Callear and W. J. R. Tyerman, *Trans. Faraday Soc.* **62**, 371 (1966).

[11] [a]J. W. Cornforth, R. H. Cornforth and K. K. Mathew, *J. Chem. Soc.* 112 (1959); [b]S. F. Brady, M. A. Ilton and W. S. Johnson, *J. Am. Chem. Soc.* **90**, 2882 (1968).

[12] A. Michaelis and H. v. Soden, *Annalen* **229**, 295 (1885).

[13] D. L. J. Clive, unpublished observations.

[14] E. M. Lown, H. S. Sandhu, H. E. Gunning and O. P. Strausz, *J. Am. Chem. Soc.* **90**, 7164 (1968).

[15] T. H. Chan and J. R. Finkenbine, *Tetrahedron Letters* 2091 (1974).

[16] F. Mathey and G. Muller, Comptes Rend. **281**, 881 (1975).

[17] R. F. Hudson and C. Brown, *Accounts Chem. Res.* **5**, 204 (1972).

[18] V. Calò, L. Lopez, A. Mincuzzi and G. Pesce, *Synthesis* 200 (1976).

[19] D. Hadzi, C. Klofutar and S. Oblak, *J. Chem. Soc.* (A), 905 (1968).

[20] T. van Es, *Carbohydrate Res.* **5**, 282 (1967).

[21] J. M. Behan, R. A. W. Johnstone and M. J. Wright, *J. Chem. Soc. Perkin I*, 1216 (1975).

[22] D. Van Ende and A. Krief, *Tetrahedron Letters* 2709 (1975).

[23] [a]Ref. 2*a*, p. 1028; [b]G. Ayrey, D. Barnard and D. T. Woodbridge, *J. Chem. Soc.* 2089 (1962); [c]D. G. Foster and S. F. Brown, *J. Am. Chem. Soc.* **50**, 1182 (1928).

[24] See Ref. 35.

[25] D. N. Jones, D. Mundy and R. D. Whitehouse, *Chem. Comm.* 86 (1970).

[26] R. Walter and J. Roy, *J. Org. Chem.* **36**, 2561 (1971).

[27] M. Cinquini, S. Colonna and R. Giovini, *Chem. and Ind.* 1737 (1969).

[28] K. Balenović, M. Malnar, Z. Cibilić and N. Kovačević, *Bull. Sci. Conseil Acad. R.S.F., Yougoslavie, Section A*, **18**, 130 (1973).

[29] J. Rabelo and T. van Es, *Carbohydrate Res.* **32**, 1975 (1974).

[30] J. N. Denis, W. Dumont and A. Krief, *Tetrahedron Letters* 453 (1976).

[31] R. H. Mitchell, *Chem. Comm.* 990 (1974).

[32] K. B. Sharpless and M. W. Young, *J. Org. Chem.* **40**, 947 (1975).

[33] P. A. Grieco, K. Hiroi, J. J. Reap and J. A. Noguez, *J. Org. Chem.* **40**, 1450 (1975).

[34] P. A. Grieco, Y. Masaki and D. Boxler, *J. Am. Chem. Soc.* **97**, 1597 (1975).

[35] K. B. Sharpless, K. M. Gordon, R. F. Lauer, D. W. Patrick, S. P. Singer and M. W. Young, *Chemica Scripta* **8A**, 9 (1975).

[36] R. D. Clark and C. H. Heathcock, *J. Org. Chem.* **41**, 1396 (1976).

[37] P. A. Grieco, S. Gilman and M. Nishizawa, *J. Org. Chem.* **41**, 1485 (1976).

[38] P. A. Grieco, J. A. Noguez and Y. Masaki, *Tetrahedron Letters* 4213 (1975).

[39] H. J. Reich and S. K. Shah, *J. Am. Chem. Soc.* **97**, 3250 (1975).

[40] K. B. Sharpless and R. F. Lauer, *J. Am. Chem. Soc.* **95**, 2697 (1973).

[41] H. J. Reich, J. M. Renga and I. L. Reich, *J. Am. Chem. Soc.* **97**, 5434 (1975).

[42] K. B. Sharpless, R. F. Lauer and A. Y. Teranishi, *J. Am. Chem. Soc.*, **95**, 6137 (1973).

[43] [a]O. Behaghel and H. Seibert, *Ber.* **65**, 812 (1932); [b]G. Bergson and S. Wold, *Ark. Kemi.* **19**, 215 (1963).

[44] S. Murai, Y. Kuroki, K. Hasegawa and S. Tsutsumi, *Chem. Comm.* 946 (1972).

[45] For use of vigorous conditions see G. Hölzle and W. Jenny, *Helv. Chim. Acta* **73**, 593 (1958).

[46] H. J. Reich, *J. Org. Chem.* **39**, 428 (1974).

[47] H. O. House, M. Gall and H. D. Olmstead, *J. Org. Chem.* **36**, 2361 (1971).

[48] R. M. Coates, H. D. Pigott and J. Ollinger, *Tetrahedron Letters* 3955 (1974).

[49] H. J. Reich, J. M. Renga and I. L. Reich, *J. Org. Chem.* **39**, 2133 (1974).

[50] P. A. Grieco and M. Nishizawa, *Chem. Comm.* 582 (1976).

[51] G. Stork and S. Raucher, *J. Am. Chem. Soc.* **98**, 1583 (1976).

[52] T. J. Brocksom, N. Petragnani and R. Rodrigues, *J. Org. Chem.* **39**, 2114 (1974).

[53] [a]M. W. Rathke and A. Lindert, *J. Am. Chem. Soc.* **93**, 2318 (1971); [b]M. W. Rathke and A. Lindert, *Tetrahedron Letters* 3995 (1971).

[54] Notation similar to that of Table 5, footnote *a* is used here so that yields quoted are lower limits.

[55] P. A. Grieco and M. Miyashita, *J. Org. Chem.* **39**, 120 (1974).

[56] K. Yamakawa, T. Tominaga and K. Nishitani, *Tetrahedron Letters* 4137 (1975).

[57] P. A. Grieco, C. S. Pogonowski and S. Burke, *J. Org. Chem.* **40**, 542 (1975).

[58] D. N. Brattesani and C. H. Heathcock, *Tetrahedron Letters* 2279 (1974).

[59] C. A. Wilson II and T. A. Bryson, *J. Org. Chem.* **40**, 800 (1975).

[60] H. J. Reich and J. M. Renga, *J. Org. Chem.* **40**, 3313 (1975).

[61] See Ref. 38.

[62] J. Rémion, W. Dumont and A. Krief, *Tetrahedron Letters* 1385 (1976).

[63] D. L. J. Clive, *Chem. Comm.* 100 (1974).

[64] [a]L. A. Khazemova and V. M. Al'bitskaya, *J. Org. Chem.* (*U.S.S.R.*) **5**, 1873 (1969); [b]L. A. Khazemova and V. M. Al'bitakaya, *J. Org. Chem.* (*U.S.S.R.*) **6**, 941 (1970).

[65] D. L. J. Clive, W. Kiel and S. Menchen, unpublished observations.

[66] I. D. Entwistle, R. A. W. Johnstone and J. H. Varley, *Chem. Comm.* 61 (1976).

[67] H. J. Reich, *J. Org. Chem.* **40**, 2570 (1975).

[68] K. B. Sharpless and R. F. Lauer, *J. Org. Chem.* **37**, 3973 (1972).

[69] K. B. Sharpless and R. F. Lauer, *J. Am. Chem. Soc.* **94**, 7154 (1972).

[70] E. G. Kataev, G. A. Chmutova and É. G. Yarkova, *J. Org. Chem.* (*U.S.S.R.*) **3**, 2139 (1967).

[71] I. Nakagawa and T. Hata, *Tetrahedron Letters* 1409 (1975).

[72] [a]J. Michalski and J. Wieczorkowski, *J. Chem. Soc.* 885 (1960); [b]I. A. Nurethdinov, E. V. Bayandina and G. M. Vinokurova, *J. Gen. Chem.* (*U.S.S.R.*) **44**, 2548 (1974); [c]R. J. Cross and D. Millington, *Chem. Comm.* 455 (1975); [d]See R. H. Mitchell, *Can. J. Chem.* 238 (1976); [e]C.-Y. Shiue and S.-H. Chu, *J. Org. Chem.* **41**, 1847 (1976).

[73] P. A. Grieco and M. Miyashita, *Tetrahedron Letters* 1869 (1974).

[74] H. J. Reich and F. Chow, *Chem. Comm.* 790 (1975).

[75] D. Seebach and N. Peleties, *Chem. Ber.* **105**, 511 (1972).

[76]D. Van Ende, W. Dumont and A. Krief, *Angew. Chem. Internat. Edn.* **14**, 700 (1975).

[77]D. Seebach and A. K. Beck, *Angew Chem. Internat. Edn.* **13**, 806 (1974).

[78]W. Dumont, P. Bayet and A. Krief, *Ibid.* **13**, 804 (1974).

[79]D. Van Ende and A. Krief, *Tetrahedron Letters* 457 (1976).

[80]W. Dumont and A. Krief, *Angew. Chem. Internat. Edn.* **14**, 350 (1975).

[81]M. Sevrin, W. Dumont, L. Hevesi and A. Krief, *Tetrahedron Letters* 2647 (1976).

[82]M. Sevrin, D. Van Ende and A. Krief, *Ibid.* 2643 (1976).

[83]A. Anciaux, A. Eman, W. Dumont, D. Van Ende and A. Krief, *Ibid.* 1613 (1975).

[84]W. Dumont and A. Krief, *Angew. Chem. Internat. Edn.* **15**, 161 (1976).

[85]See Ref. 75.

[86]D. A. Evans and G. C. Andrews, *Accounts Chem. Res.* **7**, 147 (1974).

[87]K. Sachdev and H. S. Sachdev, *Tetrahedron Letters* 4223 (1976).

[88]K. B. Sharpless and R. F. Lauer, *J. Org. Chem.* **39**, 429 (1974).

[89]N. Miyoshi, S. Furui, S. Murai and N. Sonoda, *Chem. Comm.* 293 (1975).

[90]E. G. Kataev, T. G. Mannafov, E. A. Berdnikov and O. A. Komarovskaya, *J. Org. Chem.* (*U.S.S.R.*) **9**, 1998 (1973).

[91]See M. Ōki, W. Nakanishi and M. Fukunaga, *Chemistry Letters* 1277 (1975).

[92]H. J. Reich and J. E. Trend, *Can. J. Chem.* **53**, 1922 (1975).

[93]D. G. Garratt, G. H. Schmid and I. G. Csizmadia, *J. Mol. Structure* **22**, 117 (1974).

[94]G. H. Schmid and D. G. Garratt, *Chemica Scripta* **8A**, 111 (1975).

[95]G. H. Schmid and D. G. Garratt, *Tetrahedron Letters* 3991 (1975).

[96]H. J. Reich and J. E. Trend, *J. Org. Chem.* **41**, 2503 (1976).

[97]E. G. Kataev and T. G. Mannafov, *J. Org. Chem.* (*U.S.S.R.*) **6**, 1971 (1970).

[98]E. G. Kataev, T. G. Mannafov and O. O. Saidov, *J. Org. Chem.* (*U.S.S.R.*) **7**, 2318 (1971).

[99]E. G. Kataev, T. G. Mannafov and Yu. Yu. Samitov, *J. Org. Chem.* (*U.S.S.R.*) **11**, 2366 (1975).

[100]See Ref. 36.

[101][a]D. Barnard, *J. Chem. Soc.* 4547 (1957); [b]Footnote 15 in Ref. 23*b*.

[102]R. Paetzold and G. Bochmann, *Z. Anorg. Chem.* **360**, 293 (1968).

[103]D. H. R. Barton, P. D. Magnus and M. N. Rosenfeld, *Chem. Comm.* 301 (1975).

[104]B. M. Trost, T. N. Salzmann and K. Hiroi, *J. Am. Chem. Soc.* **98**, 4887 (1976).

[105]B. M. Trost and K. K. Leung, *Tetrahedron Letters* 4197 (1975).

[106]L. Hevesi and A. Krief, *Angew. Chem. Internat. Edn.* **15**, 381 (1976).

[107]P. A. Grieco and J. J. Reap, *Tetrahedron Letters* 1097 (1974).

[108]See P. Brownbridge and S. Warren, *J. Chem. Soc.* (C), 2125 (1976).

[109]See J. E. Baldwin and J. E. Patrick, *J. Am. Chem. Soc.* **93**, 3556 (1971).

[110]A. M. Léonard-Coppens and A. Krief, *Tetrahedron Letters* 3227 (1976).

[111]J. Rémion and A. Krief, *Tetrahedron Letters* 3743 (1976).

[112]See Refs. 93 and 95.

[113]For similar work in the sulphur series see A. Anciaux, A. Eman, W. Dumont and A. Krief, *Tetrahedron Letters* 1617 (1975).

[114]W. Dumont, P. Bayet and A. Krief. *Angew. Chem. Internat. Edn.* **13**, 274 (1974).

[115]G. Hölzle and W. Jenny, *Helv. Chim. Acta* **41**, 712 (1958) and Refs. therein.

[116]L. Hevesi, M. Sevrin and A. Krief, *Tetrahedron Letters* 2651 (1976).

[117]T. G. Back, D. H. R. Barton, M. R. Britten-Kelly and F. S. Guziec, Jr., *Chem. Comm.* 539 (1975).

[118]T. G. Back, D. H. R. Barton, M. R. Britten-Kelly and F. S. Guziec, Jr., *J. Chem. Soc.* (C), 2079 (1976).

[119]H. Staudinger and G. Lüscher, *Helv. Chim. Acta* **5**, 75 (1922).

[120]N. Sonoda, T. Yasuhara, K. Kondo, T. Ikeda and S. Tsutsumi, *J. Am. Chem. Soc.* **93**, 6344 (1971).

[121]See K. Kondo, N. Sonoda and H. Sakurai, *Chemistry Letters* 1429 (1974).

[122]K. Kondo, N. Sonoda, K. Yoshida, M. Koishi and S. Tsutsumi, *Chemistry Letters* 401 (1972).

[123][a]See Ref. 121; [b]See Ref. 122.

[124]K. Kondo, N. Sonoda and S. Tsutsumi, *Chem. Comm.* 307 (1972).

[125]K. Kondo, N. Sonoda and S. Tsutsumi, *Tetrahedron Letters* 4885 (1971).

[126]K. Kondo, N. Sonoda and H. Sakurai, *Bull. Chem. Soc. Japan* **48**, 108 (1975).

[127]P. Koch and E. Perrotti, *Tetrahedron Letters* 2899 (1974).

[128]N. Sonoda, G. Yamamoto, K. Natsukawa, K. Kondo and S. Murai, *Tetrahedron Letters* 1969 (1975).

[129]K. Kondo, N. Sonoda and H. Sakurai, *Chem. Comm.* 853 (1973).

[130]K. Kondo, N. Sonoda and H. Sakurai, *Tetrahedron Letters* 803 (1974).

[131]K. Kondo, N. Sonoda and H. Sakurai, *Chem. Comm.* 160 (1974).

[132]P. Koch, *Tetrahedron Letters* 2087 (1975).

[133]K. Kondo, N. Sonoda and S. Tsutsumi, *Chemistry Letters* 373 (1972).

[134]D. Arigoni, A. Vasella, K. B. Sharpless and H. P. Jensen, *J. Am. Chem. Soc.* **95**, 7917 (1973).

[135]H. P. Jensen and K. B. Sharpless, *J. Org. Chem.* **40**, 264 (1975).

[136]K. B. Sharpless and K. M. Fordon, *J. Am. Chem. Soc.* **98**, 300 (1976).

[137]K. B. Sharpless, T. Hori, L. K. Truesdale and C. O. Dietrich, *J. Am. Chem. Soc.* **98**, 269 (1976).

[138]K. B. Sharpless and T. Hori, *J. Org. Chem.* **41**, 176 (1976).

[139]K. B. Sharpless and S. P. Singer, *J. Org. Chem.* **41**, 2504 (1976).

[140]I. Lalezari, A. Shafiee and M. Yalpani, *Tetrahedron Letters* 5105 (1969).

[141]I. Lalezari, A. Shafiee and M. Yalpani, *Angew Chem. Internat. Edn.* **9**, 464 (1970).

[142]I. Lalezari, A. Shafiee and M. Yalpani, *J. Org. Chem.* **36**, 2836 (1971).

[143]I. Lalezari, A. Shafiee and H. Golgolab, *J. Heterocyclic Chem.* **10**, 655 (1973).

[144]I. Lalezari, A. Shafiee and M. Yalpani, *J. Heterocyclic Chem.* **9**, 1411 (1972).

[145]H. Golgolab and I. Lalezari, *J. Heterocyclic Chem.* **12**, 801 (1975).

[146]H. Meier and I. Menzel, *Chem. Comm.* 1059 (1971).

[147]H. Meier and E. Voigt, *Tetrahedron* **28**, 187 (1972).

[148]H. Meier and H. Gugel, *Synthesis* 338 (1976).

[149]H. Meier, M. Layer, W. Combrink and S. Schniepp, *Chem. Ber.* **109**, 1650 (1976).

[150]I. Lalezari, A. Shafiee, F. Rabet and M. Yalpani, *J. Heterocyclic Chem.* **10**, 953 (1973).

[151]I. Lalezari, A. Shafiee and A. Rashidbaigi, *J. Heterocyclic Chem.* **13**, 57 (1976).

[152]M. R. Czarny, *Chem. Comm.* 81 (1976).

[153]M. R. Czarny, *Synthetic Commun.* **6**, 285 (1976).

[154]D. L. J. Clive and S. Menchen, unpublished observations.

[155]D. L. J. Clive, *Quart. Rev.* **22**, 435 (1968).

[156]Br. Pat. 1,136,075, *Chem. Abstr.* **70**, 88124 (1969).

[157]G. A. Olah, M. Nojima and I. Kerekes, *J. Am. Chem. Soc.* **96**, 925 (1974).

[158]I. N. Azerbaev, A. V. Asmanova, L. A. Tsoi and M. K. Dzhamaletdinova, *Chem. Abs.* **74**, 12766v. (1971); I. N. Azerbaev, A. B. Asmanova, L. A. Tsoi and V. S. Basalitskya, *Ibid.* **73**, 76788r (1970); I. N. Azerbaev, A. B. Asmanova, L. A. Tsoi, G. P. Von and R. A. Mashurova, *Ibid.* **79**, 115254j (1972); I. N. Azerbaev, A. B. Asmanova, L. A. Tsoi and G. P. Von, *Ibid.* 115279w (1972); I. N. Azerbaev, A. B. Asmanova and L. A. Tsoi, *Ibid.* **79**, 78298d (1972); I. N. Azerbaev, L. A. Tsoi and A. K. Pataaev, *J. Org. Chem. U.S.S.R.* **12**, 748 (1976); E. G.

Kataev, T. G. Mannafov, A. B. Remizov and O. A. Komarovskya, *Ibid.* **11**, 2363 (1974); J. Gosselck and E. Wolters, *Z. Naturforsch.* **17b**, 131 (1962).

[159] J. Hooz and R. Mortimer, *Tetrahedron Letters* 805 (1976).

[160a] N. Petragnani and R. Rodrigues, *Chemica Scripta* **8A**, 110 (1975); [b] N. Petragnani, R. Rodrigues and J. V. Comasseto, *J. Organometallic Chem.* **114**, 281 (1976).

[161] K. Balenović, R. Lazic, V. Polak and P. Stern, *Bull. Sci., Conseil Acad. RSF., Yougoslavie, Section A* **17**, 147 (1972).

[162] K. Balenović, N. Bregant and I. Perina, *Synthesis* 172 (1973).

[163] D. Barnard and D. T. Woodbridge, *Chem. Indust.* 1603 (1959).