Organoselenium Chemistry. Conversion of Ketones to Enones by Selenoxide Syn Elimination

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Abstract: The scope and limitation of the transformation of ketones to enones by selenenylation followed by selenoxide elimination have been examined. Several procedures for the preparation of α-phenylseleno ketones have been developed. The most useful are direct selenenylation of ketone enolates using PhSeBr and the reaction of enol acetates with electrophilic selenium species such as benzeneselenenyl trifluoroacetate. Several oxidants (ozone, hydrogen peroxide, sodium metaperiodate) and reaction conditions are described to allow optimization of the yield obtained in the transformation of α-phenylseleno ketones to enones. The reaction is quite general for acyclic carbonyl compounds and for tertiary selenides. Difficulties in achieving high yields may be anticipated when very strained double bonds are introduced, when the α-phenylseleno ketone is cyclic and has an α-hydrogen, or when the product is extremely reactive. Qualitative mechanistic studies have revealed two types of side reactions: (1) Pummerer-like transformations to give α,β-diketones and (2) reactions between the enolate or enol of α-phenylseleno ketones and selenenylation species formed during the disproportionation of benzeneselenenic acid. Reaction conditions which minimize these side reactions have been developed. The utility of benzeneseleninyl chloride as a seleninylating agent has been explored. One pot transformations of ketones to enones using this reagent can be achieved in satisfactory yield, but the procedure is prone to side reactions because of the sensitivity of the selenoxide function.

The many synthetic transformations originating from α,β-unsaturated carbonyl compounds have made their preparation a long standing important synthetic problem. The most straightforward method is the dehydrogenation of carbonyl compounds. There are a number of methods for performing this conversion,1,2 the most important of which is the α-bromination-dehydrobromination method.1 Oriental control is difficult to achieve in direct bromination of ketones, but Stotter and Hill12 have recently shown that bromination of cyclohexanone enolates can be carried out in high yield, and also that dehydrobromination can be performed without loss of regiospecificity. Isomerization of α-bromo ketones under conditions of the debrominations has been frequently reported,1,6 however, particularly for bromides of β-dicarbonyl compounds.13 The vigorous reaction conditions (frequently temperatures in excess of 120°) also severely limit this method because of the sensitivity of many enones.

Direct dehydrogenations can be performed by a number of reagents, including selenium dioxide,2a,b dichlorodiecyanquinone,2c periodic acid,2d oxygen in the presence of transition metal catalysts,2e and pyridine N-oxide-acetic anhydride. The first two methods have been studied in great detail, and some excellent procedures have been developed, but yields vary greatly, and effective control of regioselectivity is frequently a problem.

The discovery by Jones, Mundy, and Whitehouse3 that ketone enolates do not react with diphenyl diselenide, respectively. Diphenyl diselenide does not react with nitrogenous bases or dehydrogenation, occurs.14 This method may be useful in special cases.

Reinboldt and Perrier15 found that α-nitrobenzenselenenyl thiocyante (ArSeSCN) reacts with acetone to form α,β-unsaturated ketone. The reagent is not readily available, however, and the reaction has not been shown to be general. Although selenenyl bromides often brominate ketones, the chlorides behave as selenenylation agents.5e,16 Sharpless, Lauer, and Teranishi discovered that benzeneselenenyl chloride converts aldehydes and ketones to their α-phenylseleno derivatives, and this represents an important route to compounds which are not accessible by other methods.5c

We have developed three routes to α-phenylseleno ketones, as shown for 2 in Scheme I. A number of specific examples are summarized in Table I. The most widely useful method is the reaction of ketone (and ester) enolates with benzeneselenenyl bromide or chloride (PhSeBr, PhSeCl). These reagents are prepared by cleavage of diphenyl diselenide (PhSeSePh) with bromine and chlorine (or sulfuryl chloride), respectively. Diphenyl diselenide does not react with lithium enolates of ketones but does react with ester enolates5c,7 and more reactive carbonates.8,12

The failure of ketone enolates to react with diphenyl diselenide is apparently the result of an unfavorable equilibrium rather than of a kinetic barrier. Treatment of 2 with PhSeLi at −78° results in the rapid and almost quantitative
of organocuprates, or by metalation of ketones with potassium hydride, can also be converted to α-phenylseleno ketones regioisomeric with those prepared from the kinetic enolate.1d We have in this way prepared isomeric enones from 2-phenylcyclohexanone (runs 16-18) and 2-benzylcyclopentanone (runs 11-12).

The conversion of acetylenes to α-phenylseleno ketones (Scheme I) has not been examined extensively as to generality and regioselectivity.46

The Oxidation Reaction. With adequate methods for the preparation of keto selenides available, we can turn to the question of the oxidation reaction. The majority of the results described in Table I were obtained using the following oxidation methods, which are discussed in more detail below:

A. H₂O₂: one pot procedure.46
B. H₂O₂: two phase (H₂O₂-dichloromethane) usually buffered with pyridine.4b
C. O₃: Ozonization at -78° in dichloromethane followed by warm up.
D. O₃: Ozonization at -78° in dichloromethane followed by addition to refluxing carbon tetrachloride in the presence of diisopropylamine.
E. Selenoxide prepared directly by reaction of enolate with benzeneseleninyl chloride.

Since all keto selenoxides we have worked with have undergone the fragmentation reaction at or below room temperature, the oxidation must either be performed at low temperature, or the product enone must not itself be readily oxidized by the oxidizing agent chosen. We have explored sodium metaperiodate,22a ozone,22b hydrogen peroxide,22c and to a lesser extent m-chloroperbenzoic acid (m-CPBA) as oxidants. Because of its expense and the necessity of working in an aqueous methanolic medium, sodium metaperiodate is a reagent of last resort. Two selenides for which superior yields were obtained using this reagent are shown in runs 1 and 19 of Table I.

Even stabilized lithium and sodium enolates such as those formed from β-keto esters (runs 32-35), β-diketones (runs 36-40), β-keto sulfoxides (run 41), β-keto selenoxides,4b and phosphonooacetates20 react cleanly and rapidly with PhSeBr and PhSeCl.

Enol acetates can be cleanly converted to seleno ketones via the enolates (run 18) or by direct reaction with electrophilic selenium reagents. The reagent we have found most useful for this reaction is benzeneselenenyl trifluoroacetate4c,6 (PhSeO₂CCF₃) which is prepared by treatment of PhSeCl or PhSeBr with silver trifluoroacetate. The only enol acetate we have encountered which does not react with PhSeO₂CCF₃ is 1-acetoxy-2-phenylcyclohexene (run 18). By using enol acetates formed under acid catalyzed conditions,21 it is often possible to achieve the preparation of α-phenylseleno ketones regioisomeric with those prepared from the kinetic enolate.1d We have in this way prepared isomeric enones from 2-phenylcyclohexanone (runs 16-18) and 2-benzylcyclopentanone (runs 11-12).

The selenenylation of ketones via the enolate is limited primarily by the availability of the enolate. Yields are frequently almost quantitative. The major by-product we have detected is starting ketone, usually present to the extent of 2-10% in the product. Where this is objectionable, the more volatile starting material can be removed by distillation or sublimation; or the selenides, which are frequently crystalline, can be purified by crystallization. In a few systems, we have tentatively identified traces of bis-selenenylation materials. Since reaction of enolate with selenenyl halide is very rapid at -78°, enolate equilibration is not normally a problem (runs 11, 13, 16, and 25). Brattesani and Heathcock8 have recently reported that proton transfer during selenenylation of nitrile anions is unavoidable. Nitrile anions, perhaps because of their immunity to steric inhibition of resonance, frequently undergo disubstitution in competition with, or in preference to, monosubstitution.18

For most of the examples shown, we have prepared enolates by deprotonation of ketones using lithium diisopropylamide (LDA), but enolates prepared by cleavage of enol acetates with methyllithium (run 18), by conjugate addition of organocuprates, or by metalation of ketones with potassium hydride, can also be converted to α-phenylseleno ketones.

It is important to use a quantity of selenenylation agent equal to or slightly in excess of the total strong base present since organocupper reagents, lithium amides, alkoxides, etc. may react with PhSeBr. The choice between PhSeBr and PhSeCl is dictated mainly by the availability of the reagents; PhSeBr can conveniently be prepared in solution as needed, and we have used this method for most of the examples reported here. Care must be taken to avoid excess bromine and to ensure mixing of the solution during the reaction with PhSeSePh to prevent formation of PhSeBr₂, which is a brominating agent toward enolates.

The selenenylation of copper enolates prepared by conjugate addition of organocuprates to enones is complicated by the formation of small amounts of α-bromo and α-iodo ketones when pure PhSeBr is used.4b We have found that use of a mixture of PhSeBr and PhSeSePh solves this problem, although overall yields are not always high. A more satisfactory route may be to trap the enolate as the enol acetate. The purified enol acetate can then be converted to α-phenylseleno ketone in high yield.4c,6a (Stottlemyer and Hill14 reported difficulty in the bromination of copper enolates; they found that clean bromination could be achieved through the enol acetate.) Thus, formation of selenide 3 and easy transformation to 4 represent a net β-alkylation of the enone.

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Table I. Conversion of Carbonyl Compounds to \(\alpha,\beta\)-Unsaturated Carbonyl Compounds

<table>
<thead>
<tr>
<th>Starting material</th>
<th>Olefin</th>
<th>Run no.</th>
<th>Oxidation method</th>
<th>Yields (\text{%}^b)</th>
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<td>80</td>
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<td><img src="image16" alt="Structure" /></td>
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<td><img src="image18" alt="Structure" /></td>
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<td>B</td>
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<td>B</td>
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<tr>
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<td><img src="image40" alt="Structure" /></td>
<td>20</td>
<td>B</td>
<td>80 72</td>
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<td>D</td>
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<td>A</td>
<td>79</td>
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<td><img src="image56" alt="Structure" /></td>
<td>28</td>
<td>A</td>
<td>96</td>
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</table>
Ozonization of selenides\textsuperscript{2b} at \(-78^\circ\) stops cleanly at the selenoxide stage so that, in the absence of other readily oxidized functionalities or solvents (such as THF), one can simply add excess ozone. We have used ozonization when an aqueous work-up is undesirable because of substrate reactivity or water solubility (run 31), when the enone product is sensitive to excess hydrogen peroxide (as in runs 10, 36), when further transformations of the selenoxide are to be carried out,\textsuperscript{4b,d} or when oxidation and elimination are best carried out in separate steps (method D). The enone can sometimes be distilled directly out of the ozonization mixture provided that the volatility of the PhSeSePh [bp 202-203° (1 mm)] formed is not near that of the product. \textsuperscript{\textsuperscript{m}-Chloroperbenzoic acid cleanly oxidizes selenides to selenoxides, usually at temperatures (\(-30 \text{ to } 0^\circ\)) where elimination is slow. This oxidant can thus often be used in situations similar to those described above for ozone with the added advantage that selective oxidation of selenides or ketones to enones is done directly without the ozonization mixture provided that the volatility of the PhSeSePh [bp 202-203° (1 mm)] formed is not near that of the product.}

Hydrogen peroxide is the oxidant of choice under aqueous conditions. Hydrogen peroxide is the oxidant of choice under aqueous conditions.

### Table 1 (Continued)

<table>
<thead>
<tr>
<th>Starting material</th>
<th>Olefin</th>
<th>Run no.</th>
<th>Oxidation method\textsuperscript{a}</th>
<th>Yields\textsuperscript{b}</th>
<th>Selenide</th>
<th>Olefin</th>
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<td>CO(\text{CH}_2)</td>
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<td>A</td>
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<td>CO(\text{CH}_2)</td>
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<td>E</td>
<td>68</td>
<td>68</td>
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<tr>
<td>CO(\text{CH}_2)</td>
<td>CO(\text{CH}_2)</td>
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<td>C</td>
<td>70</td>
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<td>B\textsuperscript{f}</td>
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<td>36</td>
<td>C\textsuperscript{f}</td>
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<td>B\textsuperscript{f}</td>
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<td>B</td>
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<td>B</td>
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<td></td>
<td>41</td>
<td>B</td>
<td>78</td>
<td>71</td>
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</table>

\textsuperscript{a}See text for a description of the oxidation procedures. \textsuperscript{b}Olefin yields are overall unless yields of selenide are given. \textsuperscript{c}Selenides were prepared from the lithium enolate, except for runs 3 and 12. \textsuperscript{d}Diketone (6%) was also formed. \textsuperscript{e}See ref 4a for experimental details. \textsuperscript{f}Pyridine was added during selenoxide elimination. \textsuperscript{g}Diethylamine rather than diisopropylamine was used during selenoxide elimination (method D). \textsuperscript{h}Selenide prepared by reaction of sodium enolate (NaH) with PhSeBr or PhSeCl. \textsuperscript{i}No pyridine was added during H\textsubscript{2}O\textsubscript{2} oxidation.
that the carbonyl group significantly accelerates the elimina-
tion compared with simple alkyl selenoxides. We have
similarly observed that the ethylene ketals of keto selenox-
ides (see below) undergo significantly slower elimination
than the keto selenoxides themselves. The accelerating ef-
fect is even more pronounced for selenoxides derived from
β-dicarbonyl compounds. Here the elimination is rapid well
below 0° and for 6 appears to occur even at ~78°. Similar
trends are clearly present in sulfoxide eliminations.10

Cyclic systems where the carbon bearing selenium also
bears a hydrogen are subject to side reactions which lower
the yield to varying extent depending on reaction conditions
and subtle conformational and other factors in the sub-
strate. Apparently the cyclic transition state1,5a for the syn
elimination conflicts to a greater or lesser extent with con-
formational preferences of the cyclic ketone.

A four-membered cyclic system in which the selenide is
tertiary (run 9) gives cyclobutene in good yield. The reac-
tion is still feasible for the preparation of 3-phenylcyclo-
butenone (run 10), but compound 724 gives no detectable cy-
clobutenone on oxidation. It is not clear whether no product
is formed or whether that which is formed is destroyed sub-
sequent to elimination. 2-Benzylcyclopentanone can be con-
verted to 5-benzylcyclopent-2-enone in fair yield (run 11).
Note that an almost quantitative yield of the isomeric en-
ones is formed from the tertiary selenide (run 12). The
yields of cyclohexenones vary from fair to good depending
on substituents and reaction conditions. Cycloheptenone
and cyclooctenone are formed in very low yield when oxida-
tion of the respective selenides with hydrogen peroxide at
room temperature (method A or B), ozonization followed
by slow warm-up to 250 (method C), or oxidation with sodi-
um metaperiodate is employed. The conversion of 2-cy-
loheptenone to cyclohepta-2,6-diene, however, proceeds
without complication, possibly because the ring is flattened
by the two additional sp2 carbons in the ring. This could
make the cycloelimination occur more readily. A similar ef-
fect may be responsible for the somewhat higher yield ob-
tained for 2-p-tolylenecyclohexanone (run 19) when com-
pared with those of the other cyclohexanones.

We have attempted to improve yields for the cyclic en-
one by determining the nature of the side reactions which
are occurring. This information should then be of use in
modifying substituents or reaction conditions to eliminate
by-products. Most of these studies were carried out using
2-arylselenocyclooctanones (8), although cycloheptanone

and 2-methylcyclohexanone were also used. We have isolat-
ed and characterized two major types of by-productsb formed
in cyclic systems: α-arylseleno enones (10) and α-
diketones (11). When hydrogen peroxide is used, acyclic di-
carboxylic acids (12) are also formed, probably by further
oxidation of the diketone.25 The replacement of phenylese-
leno by benzylseleno in 8 does not improve the ratio of elimi-
nation to side reactions. However, the use of more strongly
electron-withdrawing groups (8b) increases the rate of syn
elimination27 and gives some improvement in yield of enone
with hydrogen peroxide as oxidant (Table II), although still
not to synthetically useful levels for cycloheptenone or cy-
clooctenone. Attempts to improve yields by changing pH
during sodium metaperiodate oxidation also failed.

A procedure which sacrifices some of the mildness of the
usual conditions but dramatically improves the reaction in
some cases, was the following: the selenide was ozonized at
~78° and then added while cold to refluxing carbon tetra-
chloride containing disopropylamine (method D, see runs
21 and 22, Table I; Table II). Unfortunately, this procedure
is not the whole answer. Yields are still less than quantita-
tive for the more troublesome systems, and no improvement
was obtained for 2-phenylcyclohexanone (runs 16 and 17).

Small amounts of α-phenylseleno enones are still formed
using method D, but less than 2% of α-diketone is present
(see Table II). This lends support to our postulateb that
Pummerer-like reactions are responsible for α-diketone for-
mations. The base prevents protonation of the selenoxide
(13, Scheme II).

Under highly acidic conditions, the Pummerer reaction is
the only pathway observed. No enone is formed (eq 7 gives
an example). This reaction also illustrates another problem
that arises under acidic conditions—the occurrence of redox
reactions. The hydrolysis of the presumed Pummerer inter-
mediate (e.g., 14) gives benzenseselenol, which reduces sele-
oxides to selenides. Small amounts of reduction were ob-
erved for method C (Table II). Under these conditions, the
PhSeO2H formed makes the reaction mixture slightly acid-
ic. Redox reactions are also illustrated in eq 8, again under
the conditions of method C. Such redox reactions are com-

<table>
<thead>
<tr>
<th>Oxidizing conditions</th>
<th>Yields (^a)</th>
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<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Aryl = phenyl (8a)</td>
<td></td>
</tr>
<tr>
<td>NaOAc-NaHCO₃</td>
<td>14</td>
</tr>
<tr>
<td>Method B</td>
<td>14</td>
</tr>
<tr>
<td>Method C</td>
<td>14</td>
</tr>
<tr>
<td>Method D, HN/-Pr₅</td>
<td>14</td>
</tr>
<tr>
<td>Method D, HNEt₂</td>
<td>14</td>
</tr>
<tr>
<td>Aryl = 3-CF₃CCl₃</td>
<td>14</td>
</tr>
<tr>
<td>Method B</td>
<td>14</td>
</tr>
<tr>
<td>Method C</td>
<td>14</td>
</tr>
<tr>
<td>Method D, HN/-Pr₅</td>
<td>14</td>
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</table>

\(^a\) Absolute yields.
The formation of 2-phenylseleno-2-cycloocten-1-one (10a) could conceivably occur by three mechanisms (eq 4, 5, and 6, in Scheme II). The first involves deprotonation of the Pummerer intermediate (14); the second involves addition of selenenic acid to enone, followed by dehydration (eq 5). This mechanism seemed unlikely (conditions were sufficiently mild that the hydroxyl compound 15 should have been isolated) and could be ruled out by generating PhSeOH (by elimination of 18) in the presence of cyclooctenone (9); no 10a was formed. The third plausible mechanism (eq 6) involves reaction of the stabilized enolate 16 (or the enol) with some selenenylating agent, most probably PhSeO-SePh produced during the disproportionation of PhSeOH (PhSO-SPh is formed during the disproportionation of PhSOH; it behaves as a sulfenylating reagent). The intermediate 17 would then undergo selenoxide elimination. Oxygen scrambling between the two arylseleno groups is unlikely, at least under basic conditions.

A straightforward test for the above mechanism is based on the fact that the arylseleno group in 10, formed according to eq 6, would not be the same one originally present in 13 whereas, in eq 4, the carbon-selenium bond is never broken. We thus carried out the elimination reaction on a mixture of two different arylseleno ketones. The acyclic selenoxide 18 undergoes high-yield elimination under most conditions. It was used as an in situ source of PhSeOH.

Some results of crossover experiments are summarized in Table III. Reversing the aryl groups gave similar results. The formation of the crossover product 10a from 13b is fully consistent with the mechanism of eq 6, even to the extent of a pronounced decrease in the relative yield of enone 9 when more PhSeX is present to react with enolate 16. Clearly, the formation of 10 according to eq 6 could be prevented by the presence of a nuclophilc which reacts more rapidly with PhSeO-SePh than does 16. In fact, if the selenoxide elimination is carried out in the presence of diethylamine (rather than diisopropylamine) using method D, the formation of 10 is completely suppressed (Table III). Only moderate increases in yields of enones are obtained, however (runs 22 and 23). The selenenamide (PhSeNEt2) is formed in high yield under these conditions. The reaction in the presence of HN-i-Pr2 also gives the selenenamide (PhSeN-i-Pr2), but formation of 10 is not prevented. Apparently disopropylamine is of lower or comparable reactivity toward PhSeO-SePh than 16, whereas diethylamine is much more reactive than 16.

Thus in the presence of an unhindered secondary or primary amine, the formation of by-product α-diketones and α-phenylseleno enones can be prevented, although at some cost in the mildness of the reaction conditions; i.e., with reactive enones, products resulting from Michael addition of the amine (and of selenenamide) may be formed. We have not been able to find a trapping agent for PhSeX which

Table III. Cross Over Experiments

<table>
<thead>
<tr>
<th>Ratio</th>
<th>Relative yields</th>
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<tbody>
<tr>
<td>13b:18</td>
<td>9</td>
</tr>
<tr>
<td>1:0sb</td>
<td>76</td>
</tr>
<tr>
<td>1:1sb</td>
<td>43</td>
</tr>
<tr>
<td>1:4sb</td>
<td>25</td>
</tr>
<tr>
<td>1:0tc</td>
<td>74</td>
</tr>
<tr>
<td>1:1tc</td>
<td>43</td>
</tr>
<tr>
<td>1:4tc</td>
<td>45</td>
</tr>
</tbody>
</table>

Note: Relative yields (NMR integration) of products 9 and 10 only are shown. Elimination by method D (HN-i-Pr2). Elimination by method C. The absolute yields are considerably lower (see Table II) than for method D.
does not have the potential of participating in Michael additions.

Our conclusion that the activating effect of the carbonyl function is required for the formation of by-products is supported by the observation that the ketals 19 and 20 are formed in good yield by selenoxide elimination, whereas the α-phenyleneseleno ketones themselves do not undergo clean elimination under comparable conditions. By similar reasoning, esters should be less prone toward these side reactions than ketones, because of the lower acidity of the α-hydrogen. In fact, an ε-lactone (run 31) can be successfully dehydrogenated (compare run 21).

In summary, given the successful preparation of an α-phenyleneseleno carbonyl compound, the following is suggested: if products are stable to hydrogen peroxide, use method A or preferably method B; if not, try method C (pyridine) or D (diisopropylamine). If seleno enone formation is a problem, try method D with diethylamine. If above methods fail, or if selective ozonization is difficult, try sodium metaperiodate in aqueous methanol, with or without sodium bicarbonate. Other potentially useful oxidizing agents which we have not explored in detail are tert-butyl hydroperoxide, peracetic acid, and MoO₃-Py-HMPA.

We have briefly explored the deselenylation of α-phenyleneseleno enones as an approach to improving the yields of enones. Selenium dioxide dehydrogenation of ketones often gives selenium containing by-products. Kocor and Tuszyl-Maczka found that these by-products could be removed and yields improved by treatment of the oxidation products with ammonium sulfide. The structure of these by-products has not been often determined, but Marx and Norman recently reported the isolation of 21 in 14% yield. If one assumes that by-products like 21 are usually formed during SeO₂ oxidations, then the ammonium sulfide purification results imply that analogs of 21 were deselenolated to enones by this reagent. Accordingly, we have treated the α-phenyleneseleno enone 23 with (NH₄)₂S as well as PhSeLi and find that both reagents do result in the conversion to enone (24). Apparently, Michael reaction subsequently leads to 25 since 24 disappears at a rate comparable to its rate of formation from 23. Oxidation of the reaction mixture gives back enone 24 by selenoxide elimination of 25. We postulate that this deselenization proceeds as shown (see eq 2).

The product 21 isolated by Marx and Norman is quite analogous to the by-products we have found in the selenoxide elimination and may actually be formed by a similar mechanism.

**Reaction of Benzeneseleninyl Chloride (26) with Enolates.** Difficulties in the oxidation in several systems led us to explore the utility of benzeneseleninyl chloride (26) as a seleninylation agent. This compound is prepared by ozonization of PhSeCl₂ and was conveniently isolated by crystallization. The reagent is very hygroscopic and, to avoid hydrolysis, contact with moist air must be avoided. This is a major disadvantage of this reagent; crystalline PhSeBr or PhSeCl can be handled in air with no special precautions.

Ketone and other enones undergo C-seleninylation with 26, and satisfactory yield of enone can be obtained in some cases (Method E, Table 1, runs 5 and 30). Yields are rather variable, however, and frequently lower than obtained by the two-step procedure. Major by-products which are formed are starting ketone and α-phenyleneseleno ketone. The use of amine-free solutions of sodium or potassium enolates (from the reaction of carbonyl compounds with NaH or KH) did not improve matters significantly. The use of benzeneseleninyl chloride is recommended only when the normal selenide oxidation procedure fails because of competing or preferential oxidation elsewhere in the molecule.

**Conclusion**

The methods described here, together with related published procedures employing the selenoxide elimination, provide techniques for the preparation of α,β-unsaturated carbonyl compounds and nitriles under uniquely mild conditions. A wide range of carbonyl compounds can be dehydrogenated, and good control of positional selectivity in unsymmetric ketones can often be achieved.

The power of the method is shown in the conversion of β-dicarbonyl compounds to sensitive β-dicarbonyl enones (runs 32 to 40), for which the dehydrobromination often fails completely. The procedure described here effects this conversion in excellent yield for most systems, with the further advantage that products are not detectably converted to the often more stable enol forms.

We have tried to explore in some detail the limitations of the methods described here. There are systems where the reaction fails to give high yields, and the results reported here should permit anticipation of systems where difficulties may be encountered and lead to quick selection of appropriate procedures to optimize yields.

The closely related sulfoxide elimination procedure developed by Trost and Salzmann does not suffer from the necessity of working with toxic compounds and appears to be somewhat less prone to side reactions. The advantages of the selenoxide route, however, include the almost ideal stoichiometry of the selenenylation reaction (which compensates for the somewhat higher expense of the reagent), the
mildness of the selenenylation reaction, and, of course, the extreme mildness of the olefin forming step (Jones, Mundy, and Whitehouse\(^3\) have reported that the selenoxide elimination proceeds at ca. 80–100° lower temperatures than the sulfoxide elimination). This point is illustrated in run 41, where an \(\alpha\)-phenylsulfino-\(\alpha\)-phenylselenenyl ketone undergoes selenoxide elimination to give a vinyl sulfoxide. A further advantage of the selenoxide route is the great relunctance of selenoxides to undergo further oxidation to selenones so that a wide range of oxidants is available, and these may be used in excess.

**Experimental Section**

Nuclear magnetic resonance spectra were obtained on a Varian A-60A, Joel MH-100, or Brucker WH270 spectrometer. Infrared spectra were obtained on a Beckman IR-8 or Perkin-Elmer IR-267 spectrophotometer and mass spectra on an AEI MS-902 spectrometer. Infrared spectra were measured in CCl\(_4\) solution.

Starting materials were commercially available or prepared according to the literature references cited. n-Butyllithium in hexane was purchased from Foote Mineral Co. or Alfa. Tetrahydrofuran (THF) was freshly distilled from lithium aluminum hydride; disopropylamine was distilled from potassium hydroxide and stored over 4A molecular sieves. All reactions involving ketone or ester enolates were run under an atmosphere of dry nitrogen.

Preparative thin layer chromatography (preparative TLC) was carried out using Merck PF-254 silica gel, with 10% ether–pentane as eluent unless indicated otherwise.

Elemental analyses were performed according to the procedure of Gould\(^2\) (Se) or by Spang Micronalytical Laboratories (C, H).

The normal work-up procedure involved addition of the reaction mixture to 30 ml of 50% ether–pentane and 30 ml of saturated NaHC\(_2\)O\(_4\) solution. The aqueous layer was separated and washed with ether, and the combined organic portions were washed with 10% H\(_2\)SO\(_4\) solution and dried by filtering through a cone of Na\(_2\)SO\(_4\). Solvent was removed on a rotary evaporator.

**CAUTION.** Selenium containing compounds are toxic and should be handled with due care. Most of the selenium containing compounds described here are sufficiently high boiling that volatility does not pose a severe toxicity or odor problem. PhSeCl and PhSeBr, however, are volatile enough to have pronounced odors.

**Oxidation Procedures.** Typical experimental procedures for the other oxidations are given below: method A (run 28 and ref 44), method B (runs 4, 6, 9, 34, and 35), method C (runs 10, 31, and 37), method D (run 15), method E (run 5), Na\(_2\)O\(_4\) (run 1), m-chloroperbenzoic acid (run 38).

The oxidation of divalent selenium compounds using hydrogen peroxide is highly exothermic and appears to be autocatalytic (i.e., PhSeO\(_2\)H is a catalyst, either because of its acidity or through the formation of PhSeOH). Under no conditions should oxidations of amounts greater than 5 mmol be carried out by adding the full amount of H\(_2\)O\(_2\) before oxidation has commenced (see runs 4 and 6 for larger scale oxidations).

**Lithium Dilsopropylamide.** Solutions of LDA in THF were usually prepared as needed (see run 1). For small scale experiments, preformed solution was convenient, prepared as follows: a dry septum-capped flask was flushed with nitrogen and cooled to \(-78^\circ\)C. THF (5 ml) and disopropylamine (7.9 ml) were added, followed by 40 ml of 1.40 M n-butyllithium in hexane. The 1 M LDA solution was warmed to 0° and stored at that temperature. It keeps indefinitely if air and moisture are carefully excluded.

**Diphenyl Diselenide.** This process is based on the organic synthesis preparation of benzeneselenenyl chloride.\(^{1a}\) We have used the air oxidation of benzeneselenenyl developed by Sharpless and Young,\(^2a\) or the alternative procedure below, which is essentially odorless since it avoids the necessity for acid work-up of the Grignard reaction, during which hydrogen selenide and benzeneselenenyl are liberated.

To a 2-L, three-neck flask purged with nitrogen (condenser, mechanical stirrer, 250-ml addition funnel) were added 24.0 g (1 mol) of Mg turnings, 50 ml of anhydrous ether, and 30 ml of a solution of 160 g (1.02 mol) of bromobenzene in 100 ml of ether. When the Grignard reaction had started, 400 ml of ether was added; the remainder of the bromobenzene solution was added over a period of 30 min. The solution was refluxed for an additional 30 min after completion of the addition. The addition funnel was replaced by a Y adapter, and 74 g (0.94 mol) of gray powdered selenium was added during 15 min in small portions through one arm of the Y tube, while nitrogen purge was continued through the other. The reaction was again refluxed for 30 min after completion of the selenium addition.

The flask was placed in an ice bath, and 23.5 ml (70 g, 0.435 mol) of bromine was added dropwise at a rate such that the solution did not reflux. A solution of 33.5 g (1 mol) of N\(_2\)Cl\(_2\) in 150 ml of ether was then slowly added, while vigorous stirring was continued. The ether layer was decanted from the precipitated magnesium salts and gravity filtered, the salts were washed with three 50-ml portions of ether, and the ether was evaporated on the steam bath. After most of the ether had evaporated, air was blown through the hot solution for 10 min, 500 ml of hexane was added, and the solution was again filtered if necessary and allowed to crystallize overnight at 5°. If the crystallized diphenyl diselenide was red (due to the presence of small amounts of amorphous selenium), it was redissolved by swirling and warming gently, filtered, and again allowed to crystallize. Filtration gave 82 g (56% yield) of yellow diphenyl diselenide, mp 60–62° (lit.\(^{3b}\) mp 63.5°). A second crop (14 g) can be obtained by concentration of the mother liquor to 200 ml for a total yield of 66%. Material prepared in this way contains a small amount of selenium (probably as diphenyl triselenide) but is adequate for most purposes.

Diphenyl diselenide can be recovered in high yield from high pressure applications such as those described below. A procedure for reduction of the PhSeO\(_2\)H and recovery of Ph\(_2\)Se\(_2\) is given in the Experimental Section following run 6.

**Benzeneselenenyl Chloride.** Chlorine gas was passed into a magnetically stirred solution of 25.0 g (80 mmol) of Ph\(_2\)Se\(_2\) in 190 ml of hexane until the weight had increased by 5.4 g. The white precipitate of PhSeCl \(_3\) which forms at the entrance point of the chlorine does not redissolve when the end point is passed—this can be used to determine the correct amount of chlorine (if excess chlorine was added, the PhSeCl\(_3\) can be removed by addition of a further small quantity of Ph\(_2\)Se\(_2\)). The solution was heated to dissolve any crystallized PhSeCl\(_3\) (if the solution is cloudy at this point, it should be filtered) and allowed to crystallize (0°), giving 27.3 g (89%) of PhSeCl\(_2\) as large orange crystals, mp 62–64° (lit.\(^{3c}\) mp 64–65°). If the starting Ph\(_2\)Se\(_2\) was pure, a second crop can be obtained, giving an almost quantitative yield.

**Benzeneselenenyl Bromide.** This procedure was usually prepared in situ and used directly. A typical procedure for 12 mmol of PhSeBr is as follows: 1.88 g (6 mmol) of Ph\(_2\)Se\(_2\) were dissolved in 5 ml of THF, and 0.324 ml (0.96 g, 6 mmol) of Br\(_2\) were added dropwise with stirring. The reaction is essentially instantaneous, and the solution can be used directly. Larger scale preparations require cooling (10°), because the reaction is slightly exothermic.

**Benzeneselenenyl Chloride.** A solution of 5.0 g (26 mmol) of PhSeCl\(_2\) in 25 ml of dichloromethane was ozonolized through a CaSO\(_4\) drying tube at \(-5^\circ\) until the color has faded to a light yellow. The solution was warmed to \(25^\circ\), and the drying tube was replaced by a septum in a dry bag. Care must be taken to avoid moisture since the chloride is extremely hygroscopic. After crystallization at \(-24^\circ\) overnight, the mother liquor was transferred by cannula to a flask equipped with a septum. The pale white crystals were washed with 5 ml of cold dichloromethane, which was added to the mother liquor. After crystallization in vacuum andair, the white crystals were obtained, mp 56–64° (lit.\(^{2b}\) mp 75°). A second crop (2.12 g) was obtained by adding 10 ml of cold hexane to the mother liquor and cooling overnight at \(-24^\circ\) for a combined yield of 92%.


3,3'-Bis(trifluoromethyl)diphenyl Diselenide. A 1-L, three-neck round-bottomed flask was fitted with a reflux condenser, a mechanical stirrer, and a dropping funnel, and a nitrogen inlet tube. The exit tube is attached to an NaOH bubbler. m-Trifluoromethylphennyl magnesium bromide was prepared using 28.1 g (0.125 mol) of m-bromobenzotrifluoride, 3.0 g (0.125 mol) of magnesium turnings, and 250 ml of dry ether. The dropping funnel was removed, and 9.5 g (0.12 mol) of powdered black selenium was added gradually over a 10-min period through the side arm. It is important to
avoid the introduction of oxygen during this operation. After stirring for an additional 20 min, 100 g of ice were slowly added to the flask followed by 20 ml of concentrated HCl. The reaction mixture was worked up (water wash), 100 ml of methanol was added to the yellow solution, and air was bubbled through overnight. Distillation of the residue gave 23.2 g (88%) of diselenide, an orange liquid, bp 121-123°C (0.25 mm).

Anal. Caled for C12H4F8Se3: Se, 53.55%. Found: Se, 54.42.


3-Trifluoromethylbenzeneselenenyl Chloride. To a solution of 4.48 g (10 mmol) of diselenide in 10 ml of dichloromethane at 25°C under nitrogen was added, dropwise, a solution of 1.35 g (10 mmol) of SOCl2 in 1 ml of dichloromethane with stirring over a 15-min period. Solvent was removed under vacuum, and distillation gave 4.62 g (89%) of chloride, a dark orange liquid, bp 54-55°C (0.25 mm).

Anal. Caled for C6H7ClF3Se: Se, 31.74%. Found: Se, 31.52.

Anal. Caled for C6H7ClF3Se: Se, 35.24. Found: Se, 35.10.

1-Phenyl-2-phenylseleno-1-propane (2). A. Run 1. The following serves as a typical procedure for the preparation of an a-phenylseleno ketone via the lithium enolate of propiophenone with acetic anhydride and purified by distillation and recrystallization from petroleum ether (bp 70-80°C). To a solution of 1.89 g (10 mmol) of 4-heptanone in 0.5 ml of THF, and a solution of 0.53 mmol of PhSeCl was added. When the PhSeCl had dissolved (72% yield, 76% based on recovered 4-heptanone) of trans-enone: bp 53-54°C (15 mm); lit. bp 72-73°C (15 mm); NMR δ 1.89 (d, J = 7.2 Hz, 1 H), 7.1-7.5 (m, 8 H), 7.78 (m, 2 H); IR 1672, 1599, 1582 cm⁻¹.

Anal. Caled for C16H160Se: c, 63.37; H, 5.32; Se, 26.04. Anal. Calcd for C16H160Se: c, 63.37; H, 5.32; Se, 26.04. Found: c, 63.45; H, 5.28; Se, 25.86.

B. Run 5. To a magnetically stirred solution of 1.22 ml of LDA in 5 ml of freshly distilled THF under nitrogen at −78°C was added a solution of 148 mg (1 mmol) of n-butyrylphenone in 0.5 ml of THF. After stirring the reaction mixture for 10 min, a solution of 374 mg (1.8 mmol, weighed in a dry bag) of benzene-seleninyl chloride (26) in 1 ml of THF was added, followed immediately by 0.01 mmol of PhAl3, cooled by an ice-salt bath, to keep the temperature between 30 and 35°C (CAUTION). The reaction mixture was stirred vigorously at 25°C for an additional 15 min after removing the bath and then was added to 25 ml of dry dichloromethane and 30 ml of 7% NaHCO3 solution. The aqueous layer was washed with 25 ml of dichloromethane, and the combined organic layers were washed with 30 ml of 10% HCl solution and 30 ml of saturated NaCl solution and dried (Na2SO4). After solvent removal, distillation gave 186 g (92%) of trans-enone: bp 53-54°C (15 mm); lit. bp 53-54°C (15 mm); NMR δ 1.58 (sextet, J = 7.2 Hz, 2 H), 1.87 (dd, J = 2, 15.8 Hz, 2 H), 2.13 (m, 2 H), 2.44 (t, J = 7.2 Hz, 2 H), 7.2-7.5 (m, 8 H), 7.78 (m, 2 H), 7.84 (s, 1 H).

trans-2-Hepten-4-one (Run 6). The selenide preparation in run 1 was followed using 0.105 mol of LDA in 50 ml of THF, a solution of 11.42 g (0.1 mol) of 4-heptanone in 10 ml of THF, and a solution of 0.11 mol of PhSeBr in 30 ml of THF. The reaction mixture was added to 100 ml of 10% HCl solution and 100 ml of 50% ether–pentane. The aqueous layer was worked up with 50 ml of ether–pentane, and the combined organic layers were washed with 50 ml of 7% NaHCO3 solution, 50 ml of saturated NaCl solution, and dried (Na2SO4). After solvent removal, remaining 4-heptanone (~5%) was removed under vacuum with a Dry Ice trap, leaving crude 3-phenyl-4-hepten-4-one: NMR δ 0.7-1.1 (m, 6 H), 1.3-2.0 (m, 4 H), 2.1-2.8 (m, 2 H), 3.51 (t, J = 7 Hz, 1 H), 7.0-7.5 (m, 4 H).

The oxidation procedure outlined in run 4 was followed by slowly (CAUTION!), adding 0.3 mol of H2O2 (34.1 g of 30% H2O2 in 30 ml of water) to a solution of the crude selenide in 150 ml of dichloromethane containing 17 ml (0.2 mol) of pyridine, cooled by an ice–salt bath, to keep the temperature between 30 and 35°C. The reaction was worked up by washing with a solution of 15.5 g (0.125 mol) of Na2CO3·H2O in 50 ml of water (save), twice with 100 ml of 10% HCl solution, and 50 ml of saturated NaCl solution and drying (Na2SO4). Distillation gave 4.07 g (72% yield, 76% based on recovered 4-heptanone) of trans-enone: bp 53-54°C (15 mm); lit. bp 53-54°C (15 mm); NMR δ 1.89 (d, J = 7.2 Hz, 3 H), 1.58 (sextet, J = 7.2 Hz, 2 H), 1.87 (dd, J = 2, 15.8 Hz, 2 H), 2.44 (t, J = 7.2 Hz, 2 H), 6.04 (dd, J = 2, 15.8 Hz,
1.76 (dd, J = 15.8, 6.8 Hz, 1 H).

**Recovery of Diphenyl Diselenide.** The aqueous sodium carbonate wash from the oxidation procedure outlined in run 7 was neutralized with concentrated HCl and kept acidic by further additions of acid, while 48.2 g (30.06 mmol) of sodium thiosulfate was added gradually over a 30-min period. After stirring the solution for 2 hr, an additional 7.9 g (0.05 mmol) of sodium thiosulfate was added, and the solution was stirred for 18 hr as Ph2Se2 precipitated. The crude Ph2Se2 was isolated by filtration (15.26 g, 89%) and was recrystallized from ethanol to give 12.0 g (70%, two crops), mp 59-60°C.

1-Cyclobutylphenyl Ketone (Run 9). Following the selenide preparation outlined in run 1, 400 mg (2.5 mmol) of cyclobutylphenyl ketone gave 679 mg (87%) of 1-phenylseleneno-1-cyclobutylphenyl ketone, after preparative TLC: NMR δ 1.7-2.3 (m, 4 H), 2.07 (s, 3 H), 2.5 cm⁻¹; ir 172.08878 cm⁻¹.

To a stirred solution of 315 mg (1 mmol) of selenide in 5 ml of dichloromethane containing 0.2 ml of 24% pyridine was added 8.8 mmol of H2O2 in 3 ml of water, and the reaction mixture was stirred at 25°C for 30 min. Normal work-up gave 131 mg (83%) of enone, after preparative TLC: NMR δ 2.14-2.63 (m, 4 H), 3.40 (m, 2 H); ir (neat) 1643, 1600, 1585 cm⁻¹;

A mixture containing predominantly one isomer: NMR δ 2.8-3.8 (m, 2 H); ir (neat) 1643, 1600, 1585 cm⁻¹;

1-Benzylcyclopentanone. This compound was prepared by the procedure of Forward and Whiting: 2-Benzylcyclopentanone.

Following the selenide preparation outlined in run 1, except that CrO3 formation and quench at -100°C, 146 mg (1 mmol) of 3-phenylcyclopentanone gave, after preparative TLC. 230 mg (65% pure, ca. 50% yield) of a mixture containing predominantly one isomer: NMR δ 2.8-3.8 (m, 4 H), 4.42 (d, J = 7.3 Hz, 1 H), 7.0-7.4 (br s, 5 H), 7.55 (m, 2 H).

A solution of 151 mg (0.5 mmol) of impure selenide prepared in run 1 except with CrO3 formation and quench at -10°C was warmed to 25°C and was worked up as usual. Preparative TLC (50% ether-pentane) gave 30 mg of enone (83% pure, ca. 53% yield).

2-Benzylcyclopentanone. The selenide was prepared by the method of House, Gall, and Olmstead, 2 a solution of 2.12 g of 2-phenylcyclohexane in 35 ml of benzene containing 5 ml of ethylene glycol and 58 mg p-TsOH.H2O was refluxed for 2.5 hr with water removal. Normal work-up (four water washes) followed by preparative TLC gave the ketal selenide: yield 0.389 g (81%): mixture of cis and trans isomers; NMR δ 1.06, 1.14 (d, J = 6.8 Hz, 3 H), 1.45-2.55 (m, 5 H), 5.91 (dd, J = 10, 2 Hz, 1 H), 6.88 (dt, J = 10, 4, -2 Hz, 1 H).

2-Benzylcyclopenten-1-one (Run 11). Following the selenide preparation outlined in run 1 and 147 mg (1 mmol) of 2-benzyl-2-phenylselenocyclopentanone, after preparative TLC: mp 52-54°C (recrystallized from ether-pentane); NMR δ 1.6-2.5 (m, 6 H), 2.99 and 3.25 (ABq, J = 13.8 Hz, 2 H), 6.9-7.6 (m, 10 H); ir 1727, 1601 (w), 1580 (w) cm⁻¹.

Anal. Caled for C16H16OSe: C, 58.75; H, 3.03.

2-Benzylcyclopenten-1-one (Run 12). Following the selenide preparation outlined in run 3, 432 mg (2 mmol) of 1-acetoxy-2-benzylcyclopentanone gave 603 mg (96%) of 1-acetoxy-2-benzylcyclopenten-1-one, after preparative TLC: mp 52-54°C (recrystallized from ether-pentane); NMR δ 1.6-2.5 (m, 6 H), 2.99 and 3.25 (ABq, J = 13.8 Hz, 2 H), 6.9-7.6 (m, 10 H); ir 1727, 1601 (w), 1580 (w) cm⁻¹.

Anal. Caled for C16H16OSe: C, 58.75; H, 3.03.

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yloxychlohexane was quenched with acetic anhydride, and the product was analyzed by GLC as above, showing a 99/1 ratio of 6-phenyl to 2-phenyl compounds: NMR δ 1.5-2.4 (m, 6 H), 1.73 (s, 3 H), 3.7 (m, 1 H), 5.50 (td, J = 3.7, 1.2 Hz, 1 H), 7.1 (m, 5 H).

2-Phenyl-2-cyclohexen-1-one (Run 18). A solution of 1.6 ml of 1.5 M methyllithium (2.5 mmol) in 2 ml of THF was cooled to -20° under nitrogen. To the stirred solution was added a solution of 0.216 g (1.0 mmol) of 1-acetoxy-2-phenylcyclohexene in THF. The mixture was warmed to 0°, stirred for 10 min, and cooled to -78°, and a solution of 2.75 ml of PhSeBr in 3 ml of THF was added rapidly. The contents of the flask was added to 0.5 N HCl and 50% ether–pentane. Normal work-up and preparative TLC purification (chloroform–hexane) gave 0.202 g (94% yield) of enone: mp 92-94° (lit.1e mp 94-95°); NMR δ 1.97 (q, J = 12.5, 1.7 Hz, 1 H), 5.54 (d, J = 12.5, 5.2 Hz, 1 H), 5.78 (dt, J = 12.2, 5.0 Hz, 1 H); ir (CHC13) 1718 cm−1.

Oxidation of 0.404 g (1.2 mmol) of the above selenide as in run 9 followed by preparative TLC (chloroform–hexane) gave 0.202 g (94% yield) of enone: mp 92-94° (lit.1f mp 94-95°); NMR δ 1.97 (q, J = 12.5, 1.7 Hz, 1 H), 5.54 (d, J = 12.5, 5.2 Hz, 1 H), 5.78 (dt, J = 12.2, 5.0 Hz, 1 H); ir (CHC13) 1718 cm−1.

6-(p-Tolylidine)-2-cyclohexen-1-one (Run 19). To a solution of 6 mmol of LDA (from 0.92 ml of NH4Pr2 and 2.94 ml of 2.05 M n-ButLi) in 10 ml of THF at -78° was added 1.2 ml of hexamethyldisilazane. A solution of (6-p-tolylidine)cyclohexanone (1.0 g, 5 mmol) in 3 ml of THF was added dropwise, followed after 10 min by a solution of 6 ml of PhSeBr (from 0.94 g Ph2Se2 and 0.162 ml of Br2) in 3 ml of THF. The reaction mixture was worked up as usual. Crystallization from methanol gave selenide with mp 116-117°: NMR δ 1.5-2.1 (m, 4 H), 2.1-2.9 (m, 4 H), 6.9-7.4 (m, 10 H); ir (CHC13) 1718 cm−1.

Ethylene Ketal of 2-Cyclohepten-1-one (Run 20). Following the oxidation procedure outlined in run 9 (stirred for 2 hr with H2O2), 157 mg (0.5 mmol) of the ethylene ketal of 2-phenylselenocycloheptanone gave 67 mg (87%) of reaction mixture outlined in run 20 after preparative TLC: NMR δ 1.5-1.9 (m, 6 H), 2.2 (m, 2 H), 3.86 (s, 4 H), 5.59 (d, J = 12 Hz, 1 H), 5.78 (dt, J = 12.2, 5.0 Hz, 1 H). Sp(2)-non-5-en-4-one (Run 24). Following the selenide preparation outlined in run 1, 138 mg (1 mmol) of sp(2)-sp(2)-non-4-one gave 249 mg (85% yield) of 5-phenylselenospi(2)-sp(2)-non-4-one after preparative TLC: mp 50-52° (recrystallized from ether–pentane): NMR δ 0.64 (m, 2 H), 1.24 (m, 2 H), 1.4-2.2 (m, 8 H), 4.23 (dd, J = 6.6, 4.2 Hz, 1 H), 7.1-7.5 (m, 7 H); ir (neat) 3095, 1600 (sh), 1645, 1450 cm−1; m/e (calcd for C16H16OSe: 278, 278) (found 278, 278).}


2-Phenylseleno-2-cyclohepten-1-one. A solution of 1.6 ml of methyl lithium (2.5 mmol) in 2 ml of THF was cooled to -78°, and a solution of 2.75 ml of PhSeBr in 2 ml of THF was added slowly to the stirred solution at 0° (ice water bath). Upon warming the reaction to 0° (ice water bath), water (3 ml) and acetic acid (0.6 ml, 10 mmol) were added, followed by the slow addition of 30% H2O2, keeping the temperature below 25°. Upon standing for 30 min at 25°, the reaction was worked up as usual. Distillation gave 0.675 g (96%) of methyl 1-cyclohexene-1,2-dicarboxylate: bp 75-76° (2 mm); lt.44 bp 47-50° (2 mm); NMR δ 1.45-1.85 (m, 4 H), 2.0-2.4 (m, 4 H), 3.67 (s, 3 H), 6.90 (m, 1 H).

Methyl 1-cyclohexene-1,2-dicarboxylate can be isolated by work-up prior to oxidation: mp 46-47° (crystallized from pentane); NMR δ 1.18 (t, J = 12.5, 4.4 Hz, 1 H), 4.08 (q, J = 7 Hz, 3 H), 7.55 (m, 2 H); ir (CHC13) 1716 (br), 1581 (w) cm−1.


A solution of 135 mg (0.5 mmol) of the above seldene in 2 ml of dichloromethane was ozonized at -78° and then warmed to room temperature with stirring (10 min). Solvent was removed, and the residue was immediately sublimed at 50° (Dry Ice cold finger, 0.2 mm) to give 60 mg of material [80% α,α,β,β-unsaturated lactone (ca. 66% yield), 6% PhSeBr, 14% unknown]: NMR δ 1.8-2.3 (m, 2 H), 2.3-2.7 (m, 2 H), 4.17 (m, 2 H), 5.91 (dt, J = 12.5, 1.7 Hz, 1 H), 6.25 (dt, J = 12.5, 4.4 Hz, 1 H); ir (neat) 1604 (sh) cm−1; m/e (calcd for C12H12O2Se: 182.102540) 182.10231.

2-Butyroxy-2-cyclohexen-1-one (Run 34). To a stirred suspension 0.63 g (15 mmol) of NaOH (37% dispersion in mineral oil; washed free of oil with 3 ml of 50% ether–pentane) in 30 ml of THF under nitrogen at 0° was added dropwise a solution of 1.86 g (10 mmol) of 2-carboxoxylactone in 2 ml of THF over a 15 min period. A solution of 2.11 g (11 mmol) of benzene-selenenyl chloride in 5 ml of THF was added rapidly, and the reaction mixture was slowly added with stirring to 50 ml of 50% ether–pentane, 25 ml of saturated NaHCO3 solution, and some ice. The aqueous layer was washed with 50% ether–pentane, and the organic layers were washed with 25 ml of saturated NaCl solution and dried (Na2SO4). 2-Butyroxy-2-phenylselenocyclohexanone: NMR δ 1.18 (t, J = 7 Hz, 3 H), 1.3-2.6 (m, 8 H), 4.08 (q, J = 7 Hz, 2 H), 7.24 (m, 3 H), 7.48 (m, 2 H); ir 1712 cm−1.

Into a 100-ml three-necked round-bottomed flask equipped with a dropping funnel, condenser, and thermometer was added the crude seldene in 30 ml of CH3Cl2. To the magnetically stirred so...
solution was gradually added 25 mmol of H2O2 (2.83 g of 30% H2O2 in 2.5 ml of water) over a 10-min period with occasional cooling in an ice bath to keep the temperature between 20 and 30°C (CAUTION: do not add more than 10% of the H2O2 solution until oxidation has begun). After stirring for an additional 10 min at 25°C, the reaction mixture was poured into 25 ml of CH2Cl2 and 10 ml of 10% Na2CO3 with stirring. The aqueous layer was washed with 25 ml of CH2Cl2. The combined organic layers were washed with 25 ml of saturated NaCl solution and dried (Na2SO4). The reaction mixture gave 1.63 g (89%) of a 92:8 mixture of keto:enol forms of the cyclohexenone (to minimize enolization), which was isolated by heating at 10°C (0.08 mm) to give 1.88 g of product. The crude reaction mixture was poured into 25 ml of CH2Cl2 and 10 ml of 10% Na2CO3 solution and 5 ml of NaHCO3 solution. The solution was added to 2.62 g (12 mmol) of diphenyl disulfide (m.p. 95-96°C). The reaction mixture was stirred at 25°C while cooling in Dry Ice cold finger (0.2 mm) to give 1.157 g of crude product. The粗制产品 was isolated by heating at 10°C (0.07 mm) to give 582 mg (84%) of pure product.

2-Benzothio-2-cyclopenten-one (Run 35). The commercially available 2:1 mixture of 2-benzothio- and 2-cyclopropenylketones (0.76 g, 5 mmol) was converted to selenide using the procedure for run 34. The reaction mixture gave 1.77 g of crude product (84% yield). The crude selenide was dissolved in 30 ml of pyridine and the mixture was added to 2.15 ml of 15% H2O2 solution (27% purity). After the oxidation, the organic layer was washed twice with 10 ml of H2O2, and each aqueous portion was back extracted with two 2-ml portions of CH2Cl2. The combined organic layers were dried (Na2SO4) and evaporated. The residue was added to 10 ml of ether to precipitate the benzeneseleninic acid, which was filtered and washed with ether. The crude product was isolated by heating at 10°C (0.07 mm) to give 1.17 g (46%) of sulfide: m.p. 40-42°C.

Additional Spectral Data. Spectral properties of selenides and α,β-unsaturated carbonyl compounds are not described in detail above. Additional spectral data are given below.

Run 20. 3-Phenylselenobicyclo[3.2.1]oct-2-ene-1-one (major isomer, m.p. 54°-96°) and 3-Phenylselenobicyclo[3.2.1]oct-2-ene-2-one (minor isomer, m.p. 54°-96°). NMR δ (CDCl3) 1.5-2.3 (m, 8 H), 2.35 (s, 3 H), 2.5-2.8 (m, 1 H), 7.28 (s, 5 H); ir 46c 1692, 1661, 1580 cm-1.

Run 21. 7-Phenylseleno-2-cyclohepten-1-one: NMR δ 1.4 (6 H), 3.99 (dd, J = 8.5, 1 H, 1 H), 5.95 (dt, J = 12.5, ~1.5 Hz, 1 H, 1 H), 6.26 (dt, J = 12.5, 4.8 Hz, 1 H), 7.0-7.7 (m, 5 H); ir 1550 cm-1. 2-Cycloheptadien-1-one: NMR δ 1.5-2.6 (m, 14 H) 1.6-2.1 (m, 1 H). 2.1-2.6 (m, 1 H), 3.7-4.0 (m, 2 H), 4.96 (m, 2 H). 5.67 (dd, J = 4.8, 1 H); ir 1705, 1675 cm-1. 255-295 (m, 1 H), 7.0-8.2 (m, 15 H); ir (CHCl3) 1655, 1598, 1580, 1228, 1075, 1040 cm-1.

Run 22. 7-Phenylseleno-2-cyclohepten-1-one: NMR δ 1.5-2.6 (m, 14 H), 1.6-2.1 (m, 1 H). 2.1-2.6 (m, 1 H), 3.7-4.0 (m, 2 H), 4.96 (m, 2 H). 5.67 (dd, J = 4.8, 1 H); ir 1705, 1675 cm-1. 255-295 (m, 1 H), 7.0-8.2 (m, 15 H); ir (CHCl3) 1655, 1598, 1580, 1228, 1075, 1040 cm-1.

Run 23. Ethyl 2-Phenylcarbathio-2-butanonate: NMR δ 1.0 (s, 3 H), 1.16 (t, J = 7 Hz, 3 H), 2.08 (m, 2 H), 4.18 (q, J = 7 Hz, 2 H), 7.25 (m, 10 H). (E)- and (Z)-Ethyl 2-Phenyl-2-butanonates (54:46 mixture): NMR δ 1.18, 1.22 (t, J = 7 Hz, 3 H), 2.02, 1.72 (d, J = 7.2 Hz, 3 H), 4.22, 4.14 (q, J = 7 Hz, 2 H, 2 H), 6.16, 7.06 (q, J = 7.2 Hz, 1 H), 7.0-7.4 (m, 5 H); ir 1717 cm-1.

Run 24. Ethyl Bicyclo[2.2.2]octa-2,5-diene-2-carboxylate: NMR δ 1.30 (t, J = 7.1 Hz, 3 H), 1.33 (m, 4 H), 1.39 (m, 4 H), 1.49 (q, J = 7 Hz, 2 H), 1.6-1.9 (m, 14 H), 2.20, 1.72 (d, J = 7 Hz, 3 H), 2.08 (m, 2 H), 4.18 (q, J = 7 Hz, 2 H), 7.25 (m, 10 H). (E)- and (Z)-Ethyl 2-Phenyl-2-butanonates (54:46 mixture): NMR δ 1.18, 1.22 (t, J = 7 Hz, 3 H), 2.02, 1.72 (d, J = 7.2 Hz, 3 H), 4.22, 4.14 (q, J = 7 Hz, 2 H, 2 H), 6.16, 7.06 (q, J = 7.2 Hz, 1 H), 7.0-7.4 (m, 5 H); ir 1717 cm-1.

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After solvent removal, sublimation at 50-60° (Dry Ice cold finger. buten-I-one in 1 ml of ether was added, followed by a solution of 6.62 (m, J = 7 Hz, 3 H), 1.6-2.0 (m, 4 H), 2.3-2.7 (m, 4 H), 4.13 (q, J = 7.2 Hz, 2 H), 7.1-7.6 (m, 5 H) ir; 1724 (sh), 1708, 1580 (w), 1224 cm⁻¹.

2-Buten-1-carboxylic acid (1). NMR δ 1.06 (d, J = 7 Hz, 3 H), 2.3-2.5 (m, 4 H), 6.4 (s, 1 H), 7.3-7.7 (m, 3 H), 7.77 (m, 2 H); ir 1705, 1672, 1591 cm⁻¹. This material was used in the mechanistic and yield experiments involving the oxidation procedures of run 9 (method C, no pyridine added) and run 15 (method D) were done on 1 mmol samples of 8a and 8b as listed. The isolation and characterization techniques described above were used. With 8b, 2-(m-trifluoromethylphenylseleno)-2-cycloheptanone (2) was obtained. NMR δ 1.4-2.0 (m, 6 H), 2.2-2.6 (m, 4 H), 6.40 (t, J = 5.7 Hz, 1 H), 7.2-7.9 (m, 4 H); ir 1688, 1659, 1590 (w) cm⁻¹; m/e (calcd for C₁₄H₁₈O₃Se, 280.0366) 280.0364.

The aqueous Na₂CO₃ layer was acidified, washed with 25 ml of ethyl acetate, and dried (Na₂SO₄) to give 118 mg of a 60:40 mixture of 1,8-octanediol acid (12) and PhSeOH by NMR analysis. Pure 12 was obtained by reducing the PhSeOH to Ph₂Se by Na/Hg, mp 140-142°.

For the other entries in Table II, the oxidation procedures of run 1 (NaO₂/NaHCO₃), run 10 (method C, no pyridine added), and run 15 (method D) were followed on mixtures of 8b and 1-phenyl-2-phenylseleno-1-butanone as indicated in Table III. The relative yields of products 9, 10a, and 10b were determined using the isolation and characterization techniques described in the Experimental Section for Table II.

Redox Studies. A. Selenium oxide (18) plus Selenide (2) (Equation 8). A solution of 76 mg (0.25 mmol) of 1-phenyl-2-phenylseleno-1-butanone in 1 ml of dichloromethane was ozonized at ~78°, and 72 mg (0.25 mmol) of 2 was added. The reaction mixture was warmed to 25° and worked up as usual. The relative yields of products as indicated in eq 8 were determined by NMR comparison with known compounds. The addition of 0.5 mmol of pyridine or diisopropylamine before warm-up gave only 1-phenyl-2-buten-1-one and recovered 2.

B. Selenium oxide (18) plus Selenol (8) (Equation 9). A solution of 152 mg (0.5 mmol) of 1-phenyl-2-phenylseleno-1-butanone in 4 ml of methanol was ozonized at ~40°, and 0.11 ml of concentrated H₂SO₄ was added to give 0.5 M methanolic H₂SO₄. The reaction mixture was warmed to ~5° with stirring for 4 hr and then left at 0° for an additional 64 hr. Normal work-up and preparative TLC gave 106 mg (68%) of recovered selenide and 28 mg (80% pure, ca. 22% yield) of 2,2-dimethoxy-1-phenyl-1-butanone. NMR δ 0.74 (t, J = 7.7 Hz, 3 H), 1.93 (q, J = 7.7 Hz, 2 H), 3.28 (s, 6 H), 7.4 (m, 3 H), 8.16 (m, 2 H); ir 1697, 1598, 1579 cm⁻¹. Quinolizidine derivative: mp 159-161°; m/e (calcd for C₁₄H₁₈O₃Se, 280.0366) 280.0364.
and (a) H. J. Reich, 39, 2133 (1974); 947 (1975).

We thank Professor B. M. Trost for a sample of spiro[4,3]-octan-1,6-dione.

(b) D. DeFilippo and F. Monicchioli, Tetrahedron, 28, 5733 (1969).


(26) K. B. Sharpless and M. W. Young have also observed that electron-withdrawing substituents increase the facility of selenoxide elimination.

(27) We have, however, observed that intramolecular additions of selenenic acids to give β-hydroxy-2-selenoles can occur, and also that selenenamides can add to Michael acceptors to give β-amino-2-selenoles (H. J. Reich, J. E. Trend, and J. M. Renga, unpublished results).


(29) Garbich has effectively used ketals as a protecting group in the preparation of enynes by dehydrobromination.


(35) It is advisable to add approximately 10% of peroxide solution at 25°C and then cool the reaction mixture with an ice bath when the reaction begins.


