Phenylselenoetherification. A Highly Efficient Cyclization Process for the Synthesis of O- and S-Heterocycles[1]

K. C. Nicolaou,*[2a] R. L. Magolda, W. J. Sipio, W. E. Barnette, Z. Lysenko, and M. M. Joullie*

Contribution from the Department of Chemistry, University of Pennsylvania, Philadelphia, Pennsylvania 19104. *Received March 29, 1979*

Abstract: Phenylselenoetherification, a new cyclization procedure based on organoselenium chemistry, is described in detail. Unsaturated hydroxy and thio compounds were subjected to this new cyclization process to afford a series of phenyl selenoethers and phenyl selenothioethers which were transformed to a variety of heterocyclic systems by reductive or oxidative removal of the selenium group. Applications to the synthesis of muscarine analogues are described.

I. Introduction

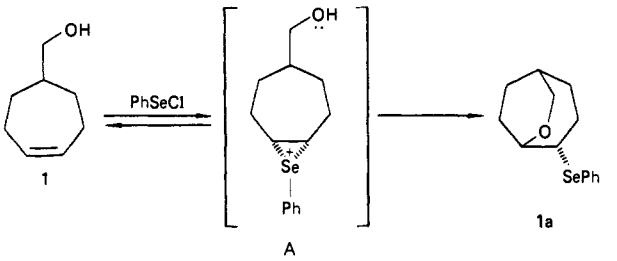
O- and S-heterocycles are quite common in nature and in the laboratory as useful synthetic intermediates. Of particular importance are the tetrahydrofuran and tetrahydropyran systems, which occur in many naturally occurring substances[2b] of biological interest. Several methods have been used for the synthesis of these systems including the manipulation of furan derivatives and the utilization of unsaturated hydroxy compounds in cyclization reactions induced by oxygen,[3] halogen,[4] mercury,[5] lead,[6] and thallium[7] reagents. These methods, however, suffer from lack of generality, from the drastic nature of some of the reagents and conditions, and also from severe limitations of elaborating the products to useful synthetic intermediates or targets. The haloetherification reaction is clearly the most general and useful ring-closure reaction leading to cyclic halo ethers which can be elaborated reductively to saturated cyclic systems or oxidatively by base-induced elimination to unsaturated compounds. An important and useful feature of this latter reaction is its tendency to proceed selectively toward the oxygen (when allowed) by an E_2 trans type mechanism leading to enol ethers of defined geometry.

We now wish to introduce a new selenium-based and versatile method for the construction of O- and S-heterocycles by cyclization of unsaturated hydroxy and thio compounds, respectively.[1,8] This mild procedure is accompanied by the introduction into the organic framework of the phenylseleno group, a modern and synthetically unique group leading to phenyl selenoethers. In contrast to the halogen-based methodology, this new method provides entry into the allylic cyclic ether class by syn elimination of the corresponding phenylselenoxides. *In this regard this technology is unique and complementary to the halogen-based method and is, therefore, an extremely powerful and useful reaction for the construction of O-containing complex heterocyclics.* In the case of S-heterocycles the selenium-based methodology provides stereoselective routes to *Z* or *E* cyclic vinyl sulfoxides and sulfones.

II. Results and Discussion

1. The Phenylselenoetherification Reaction. The cyclization of unsaturated hydroxy compounds with phenylselenenyl chloride (PhSeCl),[9] termed phenylselenoetherification, is illustrated in Scheme I for the case of 4-cycloheptene-1-methanol (**1**). This reaction proceeds rapidly in methylene chloride at −78 °C, presumably via the intermediacy of the initially formed selenium species A which is captured intramolecularly by the hydroxy group leading to the formation of the phenyl selenoether **1a** in high yield (95%). Assuming an S_N2 mode of ring closure and by analogy to the phenylselenolactonization

Scheme I. The Phenylselenoetherification Reaction



reaction[10] the stereochemistry of the phenylseleno group is assigned trans to the oxygen. Table I indicates the successful application of this new ring-closure reaction to a wide variety of substrates. A series of phenyl selenoethers was formed in good to excellent yields. It was observed in certain cases that it was advantageous to carry out the reaction in the presence of base (e.g., triethylamine or anhydrous potassium carbonate) to neutralize the liberated hydrogen chloride. This highly regioselective process leads preferentially to the formation of five-membered rings rather than four- or six-membered. A six-membered ring is formed in preference to a seven-membered ring (example **16**) and is also found when no five-membered ring option is available (example **1**). It is presumed that the initial addition of the oxygen function proceeds at least predominantly in a Markownikoff fashion and that subsequent rearrangement to the thermodynamically most stable isomer (often a tetrahydrofuran system) occurs leading to the observed products in a clean manner.

As shown in Table I, primary, secondary, and tertiary alcohols enter this reaction as well as phenols.[8b] The compatibility of the cyclization reaction with a variety of functionalities, including silyl ether (example **9**), dithiane (examples **8–10** and **13**), and carbonyl, is worth noting and it clearly enhances the utility of the method in complex situations. The phenyl selenoethers obtained are subject to a variety of transformations, the most useful ones being their conversion to allylic ethers and their reduction discussed in detail below.

2. Synthesis of Allylic Ethers. Perhaps the most important and useful feature of the phenylselenoetherification reaction is its unique and complementary nature to the haloetherification in the synthesis of unsaturated cyclic ethers. Scheme II exemplifies the preparation of allylic cyclic ethers by the oxidative removal of selenium from the phenyl selenoethers. Oxidation of the phenyl selenoether **2a** (C* epimeric mixture) with hydrogen peroxide (1.5 equiv) in tetrahydrofuran at 0 → 25 °C leads after 15 h at 25 °C to the allylic ether **2b** (85%, C* epimeric mixture). In comparing the selenium-based methodology to the halogen-based technique two points should be

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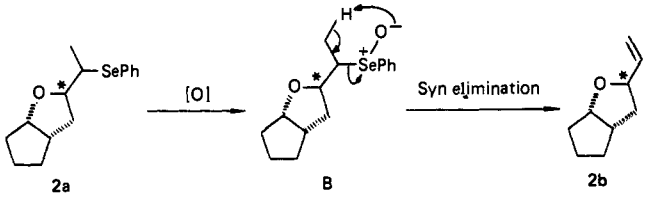
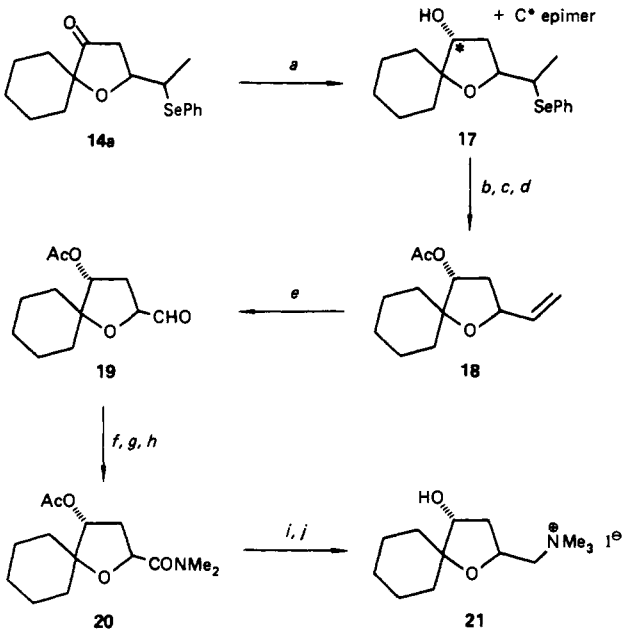
Scheme II. Synthesis of Allylic Ethers



Scheme III. Synthesis of Muscarine Analogue 21



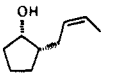
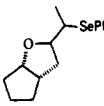
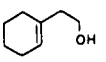
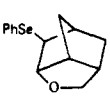
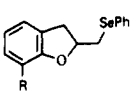
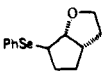
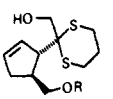
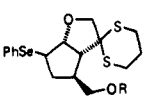
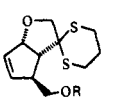
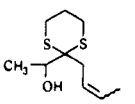
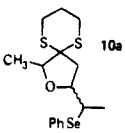
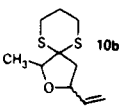
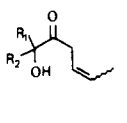
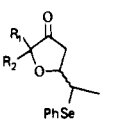
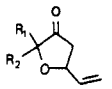
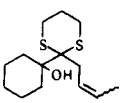
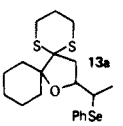
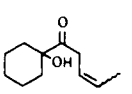
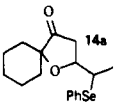
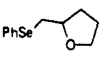
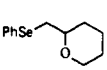
Reagents: a, $NaBH_4$, MeOH; b, Ac_2O, DMAP, C_5H_5N, CH_2Cl_2; c, O_3, CH_2Cl_2; d, Et_3N, Δ; e, O_3, CH_3OH; f, $H_2Cr_2O_7$, Me_2CO; g $(COCl)_2$; h, Me_2NH; i, $LiAlH_4$, ether; j, MeI.

emphasized. First, the introduction of the unsaturation proceeds under much milder conditions in the case of selenium; second, *the syn elimination of the selenoxide proceeds selectively away from the oxygen*[11,12] as opposed to the *toward-oxygen base-induced elimination of hydrogen halide* from the halo ethers. Thus, the present methodology constitutes an excellent and selective procedure for the preparation of allylic ethers. The most satisfactory explanation for this interesting and useful course of the syn elimination has been suggested by Trost[13] in the case of the parallel sulfur-based methodology and assumes an antiparallel orientation of the selenoxide or sulfoxide and the oxygen lone electron pairs.

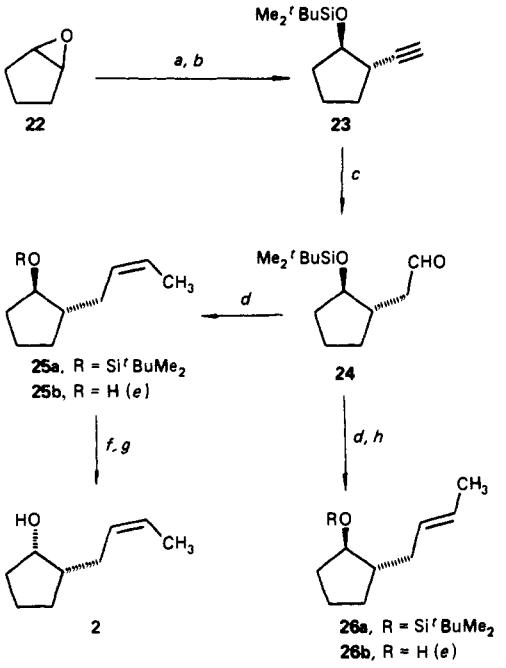
Table I indicates all the examples of allylic ethers synthesized in very good to excellent yields by this method. Noteworthy is the survival of the dithiane moiety under the conditions of the oxidation procedure.

The potential value of this new seleniun-based methodology in the synthesis of natural products was demonstrated by the construction of the muscarine[14] analogue **21** from the phenyl selenoether **14a** (Scheme III). The choice of this spiro system was made because of the large number of natural products containing this particular furanoid structure. Treatment of the keto selenide **14a** with sodium borohydride in methanol at 25 °C furnished **17** in 80% yield together with its C* epimer (20%) separated chromatographically. The major isomer **17** (more polar, doublet in the ^1H NMR spectrum, τ 7.60, J = 8 Hz, for OH as expected for the trans isomer[14c]) was protected as the acetate using acetic anhydride in CH_2Cl_2 at 25 °C in the presence of pyridine and dimethylaminopyridine as catalyst and oxidized (1, O_3, CH_2Cl_2, −78 °C; 2, Et_3N) to the allylic ether **18** (78% overall from **17**). The rather unstable aldehyde **19** was obtained by ozonolysis of **18** (MeOH, −78 °C) followed by Me_2S workup and oxidized directly to the acid by Jones reagent. Conversion to the dimethylamide **20** via the acid chloride (1, $(COCl)_2$; 2, Me_2NH) was achieved in 46% overall

Table I. Phenyl Selenoethers and Allylic Ethers

Entry	Unsaturated substrate	Phenylselenoether	Yield (percent)	Allylic ether	Yield (percent)
1		 **1a**	95	 **1b**	87
2		 **2a**	83	 **2b**	84
3		 **3a**	87		
4		 **4a**	93		
5	 R = H	 **5a**	85		
6	R = CH_3	**6a**	82		
7		 **7a**	92	 **7b**	82
8	 R = H	 **8a**	90	 **8b**	75
9	R = Si^tBuMe_2	**9a**	86		
10		 **10a**	83	 **10b**	83
11	 R_1 = H, R_2 = CH_3	 **11a**	80	 **11b**	82
12	R_1 = R_2 = CH_3	**12a**	80		
13		 **13a**	83		
14		 **14a**	80		
15		 **15a**	86		
16		 **16a**	90		

Scheme IV, Preparation of Cyclopentanols 2, 25a,b, and 26a,b



a, Li-acetylide: EDA; b, $^tBuMe_2SiCl$–imid; c, 9-BBN–H_2O_2–NaOH; d, $Ph_3P{=}CHMe$; e, AcOH–THF–H_2O (3:2:2); f, Et_3N–MesCl; g, KO_2, 18-C-6; h, PhSSPh–$h\nu$.

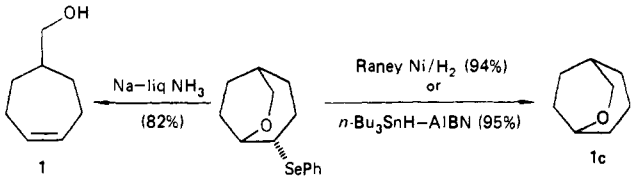
yield from **18**. The synthesis was finally completed by reducing the amide **20** to the amine and treating with MeI to afford the muscarine analogue **21** (50% overall from **20**) as colorless needles, mp 149–150 °C (toluene–acetone).

3. Synthesis of Unsaturated Substrates. The hydroxy compounds **1**, **3**, **4**, **7**, and **9** were obtained from the corresponding carboxylic acids via reduction ($LiAlH_4$–ether) of the methyl esters (CH_2N_2). Alcohol **8** was obtained by acid-catalyzed removal of the silyl ether from **9**. The cyclopentanol **2** was synthesized from cyclopentene oxide as indicated in Scheme IV. Thus, lithium acetylide–ethylenediamine complex reacted with cyclopentene oxide (**22**) in dimethyl sulfoxide to afford acetylene **23** after protection of the alcohol with *tert*-butyldimethylchlorosilane and imidazole (88% overall yield). The aldehyde **24** produced from **23** by hydroboration–oxidation with 9-BBN was condensed with methylmethylenetriphenylphosphorane to afford the cis olefin **25a**, deprotection of which led to the trans alcohol **25b** (66% overall yield). The cis hydroxy compound **2** was finally obtained by inversion of **25b** via its mesylate with potassium superoxide in the presence of 18-crown-6.[15]

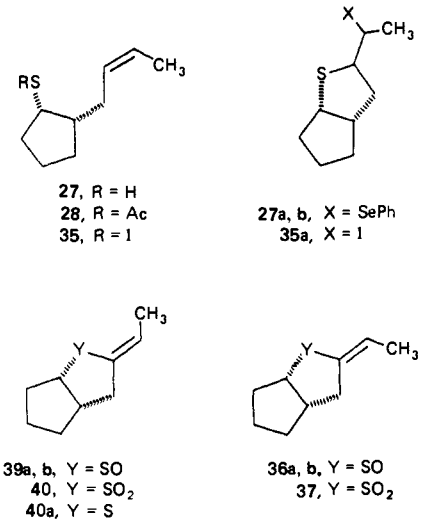
For the preparation of the dithiane hydroxy compounds (e.g., **10** and **13**), dithiane was sequentially lithiated and reacted with crotyl bromide[16] (>95% trans) and the appropriate carbonyl compound.[16] Unmasking[16] of the ketone function gave rise to the keto hydroxy substrates **11**, **12**, and **14** which were directly cyclized without isolation with PhSeCl.

4. Reduction of Phenyl Selenoethers. The phenyl selenoethers are useful intermediates for the synthesis of saturated ethers owing to the readiness of the phenylseleno group to be cleaved reductively from the molecule. Scheme V indicates the action of various reducing agents on these intermediates. Thus, hydrogenolysis of the carbon–selenium bond by Raney Ni[17] occurs at 25 °C in tetrahydrofuran (**1a** → **1c**) in high yield (94%). An alternative procedure for the reductive removal of the phenylseleno group involves treatment with tri-*n*-butyltin hydride in toluene at 110 °C in the presence of small amounts of azobisisobutyronitrile (AIBN) as a radical initiator.[19-21] The latter method is particularly useful in cases

Scheme V, Removal of the PhSe Group from Phenylseleno Ethers



Scheme VI. Synthesis of S-Heterocycles



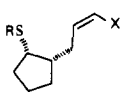
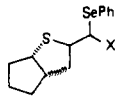
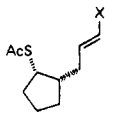
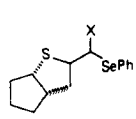
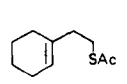
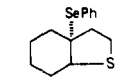
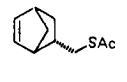
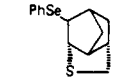
where selectivity is desired over unsaturation, sulfur, or other reducible functionalities.

While tri-*n*-butyltin hydride and Raney Ni–H_2 remove the phenylseleno group leaving the cyclic ether functionality intact, it was observed that excess sodium in liquid ammonia (−78 → −33 °C) results in efficient reversal of the phenylselenoetherification reaction yielding the starting hydroxy olefin (**1a** → **1**, 82%).[22] The ability to carry out this reverse reaction enhances the potential uses of this methodology and suggests the phenyl selenoether moiety as a possible internal protecting group of the hydroxy olefin system.

5. Synthesis of S-Heterocycles. As an extension to the selenium-induced cyclizations of hydroxy unsaturated substrates and because of the increasing importance of S-heterocycles in the β-lactam and prostacyclin fields we investigated the possibility of capturing the phenylselenonium intermediates with internally positioned sulfur nucleophiles. In many cases we found this to be a successful strategy and we report here a new and stereoselective construction of cyclic α,β-unsaturated sulfoxides and sulfones based on this principle.[1b]

Scheme VI and Table II demonstrate these reactions and their generality. The starting thiols were obtained from their acetates by cleavage in absolute methanol and anhydrous K_2CO_3 at 25 °C. The thioacetates in turn were formed from the corresponding mesylates by displacement with excess potassium thioacetate in Me_2SO at 45 °C. The *E* olefins were obtained by photolysis of the *tert*-butyl dimethylsilyl ether derivatives in the presence of PhSSPh followed by purification on silver nitrate impregnated silica columns (to remove the remaining *Z* isomers).

Table II. Organoselenium-Induced Cyclizations of Unsaturated Thioacetates and Thiols

Substrate	Product	Yield (%)[a]
27, R = H, X = CH_3 28, R = Ac, X = CH_3 29, R = H, X = $(CH_2)_3COOCH_3$ 30, R = Ac, X = $(CH_2)_3COOCH_3$	 	27a 80 27a 85 29a 77 29a 81
31, X = CH_3 32, X = $(CH_2)_3COOCH_3$	 	31a 88 32a 80
33	 	33a 77
34	 	34a 81

Yield of pure product isolated by preparative tlc or column chromatography (silica gel). Reactions were run on 0.1–1 mmole scale in methylene chloride at −78° C unless otherwise specified. [b] Reaction run in methanol at −78° C.

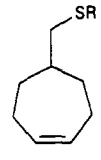
Thus, thiol **27** (obtained from **25b**, Scheme IV, as described) reacted rapidly with PhSeCl (−78 → 25 °C, CH_2Cl_2) to afford the cyclic thioether **27a** in 85% yield. This cyclization proceeded at least as well when the thioacetate **28** was utilized with the same product being formed. This observation is synthetically important since it allows the ring closure to take place from a stable, protected form of the often rather labile unsaturated thiols such as **27**. Treatment of the phenylseleno thioether **27a** with excess hydrogen peroxide (8 equiv, THF, 25 °C) for 24 h (method A) produced a mixture of *E* sulfone **37** and its unconjugated isomer **38a** (stereochemistry unassigned) in 92% yield [**37**:**38a** ca. 2:1 by ^1H NMR spectroscopy, τ 3.53 (q, J = 9 Hz, 0.66 H) for conjugated olefin and τ 4.20 (m, 0.34 H) for unconjugated olefin]. Stoichiometric amounts of hydrogen peroxide produced a complex mixture of products containing sulfoxides **36a,b**, their unconjugated isomers, and sulfones **37** and **38a**. However, treatment of the selenide **27a** with 1 equiv of *m*-chloroperbenzoic acid (CH_2Cl_2, −78 °C) followed by another 1 equiv at −20 °C and warming to 25 °C (method B) led selectively to the formation of two isomeric *E* sulfoxides **36a** and **36b** (sulfoxide isomerism). Further amounts of *m*-chloroperbenzoic acid (3 equiv total, −78 → 25 °C, method C) led directly to the *E* sulfone **37** (95%). Alternatively, a combination of *m*-chloroperbenzoic acid (2 equiv, −78 → 25 °C) and hydrogen peroxide (4 equiv, 25 °C, 24 h) (method D) can be used for the production of the *E* sulfone **37** in high yield (95%). The observed oxidation of sulfoxide to sulfone is apparently effected by benzeneperoxyselenenic acid (PhSe(=O)OOH)[23a] produced in situ under the reaction conditions. Reich has recently reported similar observations.[23b] It, therefore, appears that benzeneperoxyselenenic acid (H_2O_2 + catalytic PhSeSePh) is an excellent reagent for selectively oxidizing sulfides to sulfoxides and sulfones under very mild conditions and in the presence of olefinic bonds.

The geometry of the double bond in **36a,b** and **37** was based on mechanistic considerations, namely, an assumed trans addition during the cyclization reaction and a syn elimination of the phenyl selenoxide. A clear view of the mechanism of these reactions is not, however, evident at present and must await further investigations. As expected from the above assumptions, the trans thioacetate **31** on cyclization with PhSeCl followed by oxidation led stereoselectively to the *Z* sulfoxides **39a,b** (mixture of sulfoxide diastereoisomers) via selenide **27b** (stereochemistry unassigned) in similarly high yield.

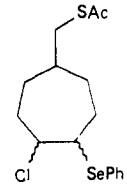
The same *Z* isomer **39b** was also obtained by a sequence beginning with the *Z* thioacetate **28** and (a) cleaving the acetate, (b) cyclizing with iodine (1.1 equiv, CH_2Cl_2, K_2CO_3, −78 °C) (reaction presumably proceeding via the sulfenyl iodide **35** undergoing intramolecular addition to the double bond affording the iodide **35a**), (c) eliminating (note the E_2 trans type elimination) with 1,5-diazabicyclo[5.4.0]undec-5-ene (benzene, 0 °C), and (d) oxidizing with *m*-chloroperbenzoic acid (30% overall yield from **28**). The latter sequence provides only one sulfoxide (**39b**) presumably due to steric reasons. The β,γ-unsaturated sulfone **38b** (stereochemistry unassigned) was produced as a mixture with its conjugated isomer **40** (**38b**:**40** ca. 1:3 by ^1H NMR spectroscopy, τ 4.17 (m, 0.25 H, CH=C), 3.53 (q, J = 9 Hz, 0.75 H, CH=C)) in 87% total yield. Decoupling experiments on the iodide **35a** [irradiating at τ 5.95 (CHI) collapses doublet at τ 8.30 (CH_3) to a singlet] established the five-membered-ring nature of this series of compounds rather than the six-membered.

Thus by changing the ring-closure initiator, using the proper double-bond isomer, and choosing the correct oxidizing conditions, the described methodology offers versatile and selective routes to either the *Z* or the *E* isomers of cyclic α,β-unsaturated sulfoxides and sulfones. In view of the available methodology for converting the sulfoxides to sulfides, the reported reactions also represent stereoselective syntheses of α,β-unsaturated sulfides, a rather important class of compounds.

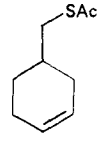
In cases where the geometry of the substrate is not favorable for a ring closure and/or when the expected cyclic product would be severely strained the reaction takes alternative pathways. Thus, the thiol **41** on treatment with PhSeCl under the cyclization conditions afforded cleanly the thioselenide **42**,



41, R = H
42, R = SePh
43, R = Ac



44



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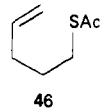


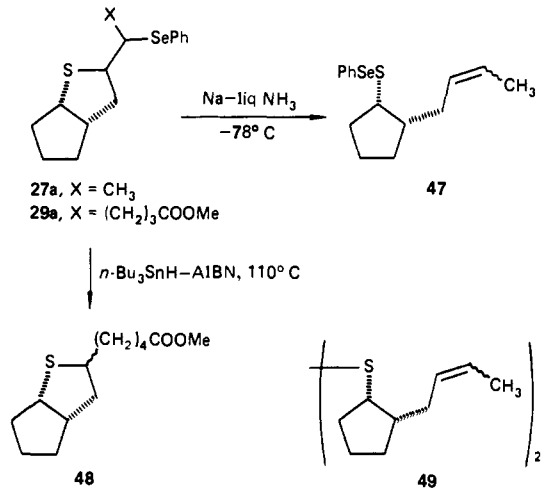
46

whereas the thioacetate **43** led to the chloroselenide **44** (mixture of isomers). Similarly the thioacetates **45** and **46** failed to yield cyclic thioethers on treatment with PhSeCl, simple addition of the reagent across the double bond being the predominant observation.

Reduction of the thioselenide **27a** with excess sodium in liquid NH_3 afforded after workup (air oxidation) diphenyl diselenide (50%), the thioselenide **47** (30%), and the disulfide **49** (55%). Tri-*n*-butyltin hydride reduction of **29a** in toluene at 110 °C in the presence of a radical initiator (AIBN) produced the sulfide **48** isolated in 76% yield as a mixture of diastereoisomers (ca. 1:1 by ^1H NMR, τ 6.18 and 6.28 for CHS). The same mixture of **48** but in a different ratio (ca. 3:2 by ^1H NMR) was observed by direct cyclization of the thiol **29** under acid (*p*-toluenesulfonic acid) conditions in anhydrous benzene.

III. Conclusion

The effective use of PhSeCl to synthesize phenyl selenoethers from unsaturated hydroxy compounds has been dem-



onstrated. This new class of compounds, which are usually formed in excellent yields, can be transformed to saturated O-heterocycles or to unsaturated allylic O-heterocycles by reductive or oxidative manipulation of the phenylseleno group. Although the cyclization mode of this selenium-based methodology parallels that of the halogen-based methodology, it provides a unique approach to the synthesis of cyclic allylic ethers owing to the high selectivity of selenoxide eliminations away from oxygen, Furthermore, the methodology described involves extremely mild conditions and as a consequence a plethora of sensitive functionalities survive the reactions. Examples are the dithiane, silyl ether, ketone, hydroxy, and aryl functions.

Extension of this selenium-based methodology to the formation of S-heterocycles has also been achieved. The cyclization products are converted by oxidation selectively to either *Z* or *E* cyclic α,β-unsaturated sulfoxides or sulfones, depending on the geometry of the starting olefin. This route provides the opposite geometry to that obtained by the parallel halogen-based method and thus again provides a complementary approach to these systems.

The potential of the present technology in the construction of complex systems was demonstrated by the synthesis of a spiro analogue of muscarine, a compound with potential biological value. The application of this methodology to the synthesis of even more complex, O- and S-containing biologically active stable analogues of prostacyclin has been achieved[1b,12] and will be fully described in due course.

Experimental Section

General, Melting points were recorded on a Thomas-Hoover Unimelt apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Varian 220-MHz NMR spectrometer in $CDCl_3$ unless otherwise stated and are reported in τ from Me_4Si. IR spectra were obtained with a Perkin-Elmer Model 237 spectrophotometer and the IR figures reported are ν_{max} in cm^{-1}. Mass spectra were provided by the Mass Spectral Service of Merck Sharp and Dohme, Rahway, N.J., and the Chemistry Department, University of Pennsylvania, and are within acceptable limits unless otherwise stated. Microanalyses were performed by Galbraith Laboratories.

Thin layer chromatography (TLC) was carried out on 0.25-mm E. Merck precoated silica gel plates (60F-254) using UV light and/or 7% polyphosphomolybdic acid in ethanol–heat as developing agent. Preparative layer (PLC) was performed on 0.25, 0.5, 1, and 2 mm × 20 cm × 20 cm E. Merck precoated silica gel plates (60F-254). For column chromatography E. Merck silica gel (60, particle size 0.063–0.200 mm) was used.

Silver nitrate impregnated silica was prepared as follows. Column silica gel 60 (EM, 100 g) was added to a solution of silver nitrate (10 g) in distilled water (200 mL). From the slurry, the water was then evaporated on the rotary evaporator (60–70 °C) while the silica was protected from light (aluminum foil). The now free-flowing $AgNO_3$–silica was dried further at 80 °C for 24 h with protection from light. The preparation of the column proceeded in the usual manner, preferably with protection from light (aluminum foil wrapping column).

Silver nitrate impregnated TLC plates were prepared from commercial silica plates (0.25 mm, E. Merck, 60F-254) by dipping into a $AgNO_3$ (10% w/v) solution in anhydrous acetonitrile for 10 s and then allowing to dry at ambient temperature and in the dark for at least 1 h. Visualization of these plates was carried out with polyphosphomolybdic acid in absolute ethanol (7% w/v).

All reactions were carried out under an argon atmosphere using dry, freshly distilled solvents under anhydrous conditions unless otherwise stated. Ethereal and hydrocarbon solvents were dried and distilled under argon from sodium–benzophenone ketyl. Methylene chloride was distilled under argon from calcium hydride. Reaction temperatures were measured externally. NMR multiplicities are reported using the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; b, broad; *J*, coupling constant (Hz). Only the strongest and/or structurally most important peaks are reported for the IR and mass spectra. Selenium-containing compounds exhibited the characteristic isotopic family in their mass spectra [^{74}Se(1), ^{76}Se(10), ^{77}Se(9), ^{78}Se(27), ^{80}Se(57), ^{82}Se(11)] but only the peaks due to the most abundant isotope (^{80}Se) are reported. Yields refer to chromatographically and spectroscopically pure compounds.

Phenylselenoetherification, General Procedure. All reactions indicated in Table I were carried out on 1-mmol scale in dry methylene chloride (5 mL) at −78 → 25 °C using commercial (Aldrich) PhSeCl (1.10 mmol) without base (method A) or with triethylamine (method B). The phenyl selenoethers were isolated after the reaction mixture was allowed to reach room temperature, concentrated, and chromatographed on silica gel (columns or plates). The procedure is exemplified by the preparation of (1α,4α,5α)-4-(phenylseleno)-6-oxabicyclo[3.2.2]nonane (**1a**) described below.

(1α,4α,5α)-4-(Phenylseleno)6-oxabicyclo[3.2.2]nonane (1a), Method A. To a magnetically stirred solution of 4-cycloheptene-1-methanol (**1**, 126 mg, 1.0 mmol) in dry methylene chloride (5 mL) was added solid PhSeCl (212 mg, 1.1 mmol) and the mixture was stirred at that temperature until the red-orange PhSeCl solid dissolved and TLC indicated completion of the reaction. The pale yellow solution was allowed to reach room temperature, concentrated, and chromatographed on a silica gel–methylene chloride column. The product (**1a**) was obtained after the elution of small amounts of diphenyl diselenide. Obtained was (1α,4α,5α)-4-(phenylseleno)-6-oxabicyclo[3.2.2]-nonane (**1a**, 269 mg, 95%).

Method B. Method B involved exactly the same procedure as in method A except that triethylamine (111 mg, 1.1 mmol) was also used in the reaction. The yield of **1a** was the same as above.

Method C. Method C is identical with method A except that methylene chloride–petroleum ether (30–60 °C) (1:1) was used as solvent for the reaction. The yield of **1a** was the same as in methods A and B.

Properties and Spectral Data of Phenyl Selenoethers. 1a (methods A, B, C, 95%): pale yellow oil; R_f 0.33 (silica, CH_2Cl_2); IR (liquid film) ν_{max} 3022, 2899, 2827, 1573, 1479, 1437, 1312, 1250, 1220, 1205, 1125, 1099, 1085, 1062, 1033, 1024, 1010, 997, 985, 966, 922, 885, 853, 789, 737, 690, 667 cm^{-1}; ^{1}H NMR (220 MHz, $CDCl_3$) τ 2.52 (m, 2 H, aromatic), 2.80 (m, 3 H, aromatic), 6.04 (m, 1 H, OCH), 6.16 and 6.35 (d, J = 4.0 Hz, 1 H each, $-OCH_2$), 6.47 (m, 1 H, -SeCH), 7.70–8.50 (m, 9 H, CH_2 and CH); mass spectrum *m/e* (rel intensity) 282 (M^+, 82), 156 (73), 125 (M^+ − PhSe, base peak), 91 (79). Anal. ($C_{14}H_{18}OSe$) C, H,

2a (method A, 83%, mixture of diastereoisomers, ca. 1:1): pale yellow oil; R_f 0.42 (silica, CH_2Cl_2); IR (liquid film) ν_{max} 3040, 2933, 2849, 1575, 1477, 1449, 1435, 1374, 1316, 1238, 1042, 1024, 738, 693 cm^{-1}; ^{1}H NMR (220 MHz, $CDCl_3$) τ 2.35 (m, 2 H, aromatic), 2.65 (m, 3 H, aromatic), 5.35 and 5.58 (multiplets, 0.5 H each, OCH–), 5.95 and 6.24 (multiplets, 0.5 H each, SeCH), 6.60 (m, 1 H, –OCH–), 7.30 (m, 1 H), 7.70–8.50 (m, 8 H), 8.55 and 8.60 (doublets, J = 7.0 Hz, 1.5 H each, CH_3); mass spectrum *m/e* (rel intensity) 296 (M^+, 7), 139 (M^+ − PhSe, 16), 111 (46), 93 (10), 81 (15), 67 (base peak). Anal. ($C_{15}H_{20}OSe$) C, H.

4a (method A, 93%): pale yellow oil; R_f 0.38 (silica, CH_2Cl_2); IR (liquid film) ν_{max} 3096, 3003, 2907, 1595, 1493, 1449, 1366, 1312, 1290, 1272, 1258, 1211, 1193, 1147, 1076, 1062, 1035, 1025, 1000, 988, 970, 962, 948, 912, 883, 867, 844, 791, 769, 735, 692, 671 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$) τ 2.53 (m, 2 H, aromatic), 2.77 (m, 3 H, aromatic), 5.69 (d, 1 H, J = 5.0 Hz, OCH), 6.22 (dd, 1 H, J = 4.0,

8.0 Hz, $-OCH_2-$), 6.32 (d, 1 H, J = 8.0 Hz, OCH_2-), 6.92 (d, 1 H, J = 3.0 Hz, SeCH), 7.35 (m, 1 H), 7.64 (m, 1 H), 7.80 (m, 1 H), 7.97 (m, 2 H), 8.42 (m, 1 H), 8.81 (m, 1 H); mass spectrum m/e (rel intensity) 280 (M^+, 39), 157 (12), 123 (M^+ − PhSe, 93), 105 (33), 95 (48), 93 (base peak), 91 (46), 77 (61). Anal. ($C_{14}H_{16}OSe$) C, H.

5a (method A, 85%): colorless crystals, mp 61–62 °C (petroleum ether); R_f 0.29 (silica, 5% ether in petroleum ether); IR ($CHCl_3$) ν_{max} 3115, 3049, 2967, 2899, 1618, 1613, 1592, 1471, 1449, 1408, 1339, 1242, 1176, 1104, 1079, 1029, 1022, 1007, 962, 877, 709, 692 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) τ 2.48 (m, 2 H, aromatic), 2.77 (m, 3 H, aromatic), 2.90 (d, J = 8.0 Hz, 1 H, aromatic), 2.93 (t, J = 7.0 Hz, 1 H, aromatic), 3.20 (t, J = 8.0 Hz, 1 H, aromatic), 3.28 (d, J = 8.0 Hz, 1 H, aromatic), 5.1 (m, 1 H, OCH), 6.68 (dd, J = 12.0, 6.0 Hz, 1 H, benzylic), 6.70 (dd, J = 11.0, 5.0 Hz, 1 H, benzylic), 6.95 (dd, J = 12.0, 8.0 Hz, 1 H, $SeCH_2$), 7.01 (dd, J = 15.0, 7.0 Hz, 1 H, $SeCH_2$); mass spectrum m/e (rel intensity) 290 (M^+, 36), 133 (M^+ − PhSe, base peak), 119 (23), 105 (61), 91 (45), 77 (54); high-resolution mass spectrum m/e 290.0202 (calcd for $C_{15}H_{14}OSe$, 290.0209).

7a (method A, 92%): pale yellow oil; R_f 0.42 (silica, CH_2Cl_2); IR (liquid film) ν_{max} 3030, 2929, 2841, 1570, 1471, 1433, 1290, 1212, 1064, 1038, 1022, 998, 948, 917, 898, 738, 692 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) τ 2.67 (m, 2 H, aromatic), 2.85 (m, 3 H, aromatic), 5.69 (d, J = 7.0 Hz, 1 H, OCH), 6.34 (m, 3 H, OCH_2- and SeCH), 7.2 (m, 1 H), 7.95 (m, 3 H), 8.20–8.67 (m, 3 H); mass spectrum m/e (rel intensity) 268 (M^+, 37), 157 (17), 111 (M^+ − PhSe, 38), 110 (41), 93 (94), 77 (46), 55 (base peak). Anal. ($C_{13}H_{16}OSe$) C, H.

8a (method A, 90%): pale yellow oil; R_f 0.41 (silica, ether); IR (liquid film) ν_{max} 3390 (OH), 3012, 2899, 2817, 1563, 1468, 1425, 1408, 1370, 1339, 1289, 1266, 1227, 1143, 1099, 1053, 1018, 996, 962, 929, 903, 867, 845, 808, 735, 687, 667 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) τ 2.47 (m, 2 H, aromatic), 2.74 (m, 3 H, aromatic), 5.24 (dd, J = 3.0, 2.0 Hz, 1 H, OCH), 5.78 and 6.05 (doublets, J = 4.0 Hz, 1 H each, $-OCH_2-$), 6.20 (dd, J = 4.5, 2.0 Hz, 1 H, -SeCH-), 6.37 (m, 2 H, CH_2OH), 7.50 (s, 1 H, OH), 7.12 (m, 4 H), 7.54 (m, 2 H), 8.00 (m, 2 H), 8.30 (m, 1 H); mass spectrum m/e (rel intensity) 402 (M^+, 1), 245 (M^+ − PhSe, 2), 110 (1), 106 (1), 86 (25), 84 (base peak), 77 (2). Anal. ($C_{17}H_{22}O_2S_2Se$) C, H.

9a (method A, 86%): colorless crystals, mp 76–77 °C (pentane); R_f 0.36 (silica, CH_2Cl_2): IR (liquid film) ν_{max} 3030, 2924, 2841, 1567, 1471, 1433, 1416, 1379, 1353, 1295, 1274, 1250, 1215, 1147, 1087, 1020, 999, 937, 906, 840, 810, 725, 735, 690, 667 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) τ 2.45 (m, 2 H, aromatic), 2.74 (m, 3 H, aromatic), 5.26 (dd, J = 3.0, 2.0 Hz, 1 H, OCH), 5.79 and 6.06 (doublets, J = 4.0 Hz, 1 H each, OCH_2), 6.22 (dd, J = 4.5, 2.0 Hz, 1 H, SeCH), 6.43 (m, 2 H, $SiOCH_2$), 7.16 (m, 4 H), 7.27 (t, J = 3.0 Hz, 1 H), 7.64 (m, 2 H), 8.00 (m, 2 H), 8.30 (m, 1 H), 9.10 [s, 9 H, $-SiC(CH_3)_3$], 9.93 [s, 6 H, $-Si(CH_3)_2$]; mass spectrum m/e (rel intensity) 516 (M^+, 2), 459 (M^+ − ^{t}Bu, 36), 353 (11), 209 (23), 195 (46), 181 (17), 165 (17), 149 (20), 133 (10), 119 (26), 106 (10), 91 (37), 73 (base peak). Anal. ($C_{23}H_{36}O_2SiSeS_2$) C, H.

Preparation of Alcohols 1, 3, 4, 7, and 9 from the Corresponding Acids, General Procedure. The unsaturated hydroxy compounds **1**, **3**, **4**, **7**, and **9** (Table I) were prepared from the corresponding carboxylic acids via the methyl esters by reduction with $LiAlH_4$ as illustrated below in the case of cycloheptene-1-methanol (**1**). Cycloheptene-1-carboxylic acid (1.40 g, 10 mmol) was treated at 0 °C in ether with excess diazomethane to give after removal of the solvent its methyl ester quantitatively (1.54 g). The methyl ester was dissolved in dry ether (20 mL), cooled to 0 °C, and treated with lithium aluminum hydride (0.76 g, 20 mmol). After stirring at ambient temperature for 1 h the reaction was quenched with (i) wet ether (10 mL) and (ii) traces of water until milky white. The dry ($MgSO_4$) ether solution was filtered and the solid washed thoroughly with ether. Evaporation of the solvent followed by column chromatography (silica, CH_2Cl_2) furnished pure alcohol **1** (1.20 g, 95%) as a colorless oil: R_f 0.58 (silica, ether); IR (liquid film).

3[25] (96%): colorless oil; R_f 0.58 (silica, ether); IR (liquid film) ν_{max} 3340 cm^{-1} (OH).

4[26] (90%): colorless oil; R_f 0.39 (silica, ether); IR (liquid film) ν_{max} 3300 cm^{-1} (OH).

7[27] (98%): colorless oil; R_f 0.50 (silica, ether); IR (liquid film) ν_{max} 3400 cm^{-1} (OH).

8 (90%, from **9** by desilylation in AcOH–THF–H_2O, 3:1:1, 45 °C, 16 h); colorless crystals, mp 121–122 °C (pentane); R_f 0.20 (silica, ether); IR (Nujol) ν_{max} 3226 (OH), 2941, 2857, 1460, 1418, 1408, 1370, 1351, 1274, 1239, 1220, 1155, 1096, 1060, 1034, 948, 924, 909, 753 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) τ 4.15 (m, 2 H, olefinic), 6.05 (m, 2 H, OCH_2), 6.39 (dd, J = 10, 5 Hz, 1 H, OCH_2), 6.55 (t, J = 10 Hz, 1 H, OCH_2), 6.9–8.30 (m, 12 H); mass spectrum m/e (rel intensity) 246 (M^+, 2), 228 (M^+ − H_2O, 2), 149 (base peak), 106 (8), 91 (12). Anal. ($C_{11}H_{18}S_2O_2$) C, H.

9 (95%, from the corresponding acid[10]): colorless oil; R_f 0.53 (silica, hexane–ether, 1:1); IR (liquid firm) ν_{max} 3390 (OH), 2899, 2841, 1462, 1437, 1416, 1374, 1355, 1323, 1271, 1250, 1198, 1093, 1003, 935, 906, 833, 811, 773, 719 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) τ 4.20 (m, 2 H, olefinic), 6.06 (d, J = 7.0 Hz, 2 H, OCH_2), 6.42 (m, 2 H, OH, $SiOCH_2$), 6.60 (t, J = 9.0 Hz, 1 H, $SiOCH_2$), 6.90–8.30 (m, 10 H), 9.10 (s, 9 H, $SiC(CH_3)_3$), 9.90 (s, 6 H, $Si(CH_3)_2$); mass spectrum m/e (rel intensity) 369 (M^+, 1), 329 (M^+ − CH_2OH, 3), 303 (M − t-Bu, 3), 263 (30), 197 (13), 189 (14), 149 (base peak), 106 (10), 91 (15). Anal. ($C_{17}H_{32}O_2S_2Si$) C, H.

14a (method C, 80%): pale yellow oil; R_f 0.30 (silica, CH_2Cl_2); IR (liquid film) ν_{max} 2880, 1750, 1540, 1470, 1440, 1430, 1390, 1365, 1250, 1230, 1190, 1145, 1070, 1050, 1020, 995, 885, 740, 690 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) τ 2.30–2.50 (m, 2 H, aromatic), 2.70–2.85 (m, 3 H, aromatic), 5.70–5.90 (m, 1 H, OCH), 6.45–6.65 (m, 1 H, SeCH), 7.30–7.65 (m, 2 H, $COCH_2$), 8.30–8.50 (m, 13 H); high-resolution mass spectrum m/e 338.0879 (calcd for $C_{17}H_{22}O_2Se$, 338.0876).

16a (method A, 90%): pale yellow oil; R_f 0.39 (silica, CH_2Cl_2); IR (liquid film) ν_{max} 3077, 2959, 2874, 1572, 1473, 1451, 1361, 1342, 1297, 1266, 1250, 1217, 1183, 1085, 1047, 1020, 995, 966, 909, 891, 858, 844, 810, 733, 690, 667 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) τ 2.52 (m, 2 H, aromatic), 2.82 (m, 3 H, aromatic), 6.00 (m, 1 H, OCH), 6.62 (m, 2 H, OCH_2), 7.01 (dd, J = 2.0, 1.0 Hz, 1 H, $SeCH_2$), 7.10 (dd, J = 2.0, 2.0 Hz, 2 H, $SeCH_2$), 8.00–8.80 (m, 6 H); mass spectrum m/e (rel intensity) 256 (M^+, 16), 172 (11), 157 (7.5), 99 (10), 85 (base peak), 77 (15). Anal. ($C_{12}H_{16}OSe$) C, H.

Preparation of Crotyldithiane. To a magnetically stirred solution of dithiane (1.2 g, 10 mmol) in dry THF (50 mL) under argon at −20 °C, n-butyllithium (7.0 mL, 1.60 M in hexane, 11 mmol) was added dropwise. Stirring was continued at −20 °C for 2 h and the dithiane anion cooled to −78 °C and quenched with crotyl bromide (>95% trans, 1.62 g, 12 mmol). The reaction mixture was stirred at −20 °C for 3 h and then poured onto water (150 mL) and extracted with petroleum ether (3 × 75 mL). The organic solution was washed with (i) water (2 × 20 mL) and (ii) brine (20 mL), dried ($MgSO_4$), and concentrated to afford crude crotyldithiane, which was purified by column chromatography (silica, petroleum ether). Obtained was 1.6 g (92%): ^1H NMR (60 MHz, $CDCl_3$) τ 4.52 (m, 2 H, olefinic), 6.00 (t, J = 7.0 Hz, 1 H, SCHS), 7.20 (m, 4 H, SCH_2), 7.48–8.50 (m, 7 H); IR (liquid film) ν_{max} 2870, 1415, 1365, 1270, 1235, 1175, 1065, 964, 908, 863, 768, 748, 708 cm^{-1}; mass spectrum m/e (rel intensity) 174 (M^+, 8), 119 (M^+ − C_4H_7, base peak), 106 (6), 85 (22). Anal. ($C_8H_{14}S_2$) C, H.

Reactions of Crotyldithiane. Crotyldithiane (1.74 g, 10 mmol) was dissolved in dry THF (50 mL), cooled to −20 °C under argon, and treated dropwise with n-butyllithium (7.0 mL, 1.60 M in hexane) while stirring. Stirring was continued at −20 °C for 2 h and the anion so obtained was cooled to −78 °C and quenched with acetaldehyde, acetone, or cyclohexanone (11 mmol) or syringed into a saturated THF solution of CO_2 (−78 °C, 50 mL, dry ice) to afford the corresponding hydroxydithiane compound or the dithianecarboxylic acid after allowing to reach room temperature, workup, and column chromatography (silica, CH_2Cl_2) or by vacuum distillation. The workup was the same as described above for the preparation of crotyldithiane except that methylene chloride was used as extraction solvent. In the case of the dithianecarboxylic acid, the aqueous phase was acidified to pH 4 with 1 N oxalic acid prior to extraction.

10 (82%): pale yellow oil; bp 120–125 °C (0.06 mm); R_f 0.25 (silica, CH_2Cl_2); IR (liquid film) ν_{max} 3420 (OH), 2880, 1420, 1380, 1355, 1275, 1240, 1170, 1125, 1100, 1057, 968, 910, 865 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) τ 4.40 (m, 2 H, olefinic), 5.79 (q, J = 6.5 Hz, 1 H, C*H*OH), 6.70–7.60 (m, 7 H), 8.00 (m, 2 H, allylic CH_2), 8.30 (m, 3 H, allylic CH_3), 8.64 (d, J = 6.5 Hz, 3 H, CH_3); mass spectrum m/e (rel intensity) 218 (M^+, 2), 173 (M^+ − C_2H_5O, base peak), 163 (33), 119 (13), 106 (16). Anal. ($C_{10}H_{18}OS_2$) C, H.

13 (84%): pale yellow oil; R_f 0.33 (silica, CH_2Cl_2); IR (liquid film) ν_{max} 3450 (OH), 2880, 1440, 1365, 1340, 1305, 1270, 1250, 1170, 1150, 1125, 1080, 1050, 1038, 965, 926, 908, 850 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) τ 4.33 (m, 2 H, olefinic), 7.18 (m, 4 H), 7.80–8.70 (m,

18 H); mass spectrum *m/e* (rel intensity) 173 (M − $C_6H_{12}O$, 10), 119 (14), 106 (4), 99 (15), 84 (base peak). Anal. ($C_{14}H_{24}OS_2$) C, H.

Preparation of Hydroxy Ketones 11, 12, and 14, General Procedure. A solution of the dithiane (1.0 mmol) in acetonitrile (2 mL) was added at once to a magnetically stirred solution of NCS (4.0 mmol) and silver nitrate (4.5 mmol) in aqueous 80% acetonitrile (20 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 15 min, then at 25 °C for 5 min, and then treated successfully with (i) saturated aqueous sodium sulfite (1 mL), (ii) 5% sodium carbonate (1 mL), and (iii) brine (1 mL). Hexane–methylene chloride (1:1, 20 mL) mixture was added and after stirring the solution was filtered through Celite. After the solid residue was washed with hexane–methylene chloride (1:1) the solvents were dried ($MgSO_4$) and evaporated to leave the crude hydroxy ketones **11** (66%), **12** (68%), and **14** (76%), which were cyclized with PhSeCl directly without purification owing to their relative instability.

Preparation of Allylic Ethers, General Procedure. All reactions indicated in Table I were carried out on 1-mmol scale in THF using hydrogen peroxide as oxidizing agent (method A). The successful use of ozone as on oxidizing agent was demonstrated in the preparation of the allylic ether **18** (vide infra). The preparation of the allylic ether **1b** described below illustrates the hydrogen peroxide procedure for the preparation of allylic ethers from phenyl selenoethers.

6-Oxabicyclo[3,2,2]non-3-ene (1b). A stirred solution of (1α,4α,5α)-4-(phenylseleno)-6-oxabicyclo[3.2.2]nonane (**1a**, 283 mg, 1 mmol) in freshly distilled THF (5 mL) was treated dropwise at 0 °C with a 3% THF solution of hydrogen peroxide (made from commercial 30% hydrogen peroxide and THF) (1.5 mL, 1.5 mmol). The reaction mixture was allowed to reach room temperature and stirred for 18 h before dilution with ether (20 mL) and washing with water (2 × 5 mL) and saturated sodium chloride solution (5 mL). After removal of the dried ($MgSO_4$) solvents the residue was chromatographed (column, silica, CH_2Cl_2) to afford 6-oxabicyclo[3.2.2]non-3-ene (**1b**, 108 mg, 87%) as a colorless oil crystallizing on standing.

Properties and Spectral Data of Allylic Ethers, 1b (method A, 87%): colorless, crystalline solid, mp 60–61 °C (sublimed); R_f 0.10 (silica, CH_2Cl_2); IR ($CHCl_3$) ν_{max} 3028, 2954, 2890, 1654, 1471, 1449, 1375, 1352, 1275, 1248, 1132, 1070, 1010, 965, 925, 899, 845, 820 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) τ 4.04 and 4.21 (multiplets, 1 H each, olefinic), 5.85 (m, 1 H, OCH), 5.98 and 6.14 (m, 1 H each, OCH_2), 7.30–8.50 (multiplets, 11 H, CH_2 and CH); mass spectrum *m/e* (rel intensity) 124 (M^+, 3), 110 (4), 95 (20), 85 (43), 71 (65), 57 (base peak); high-resolution mass spectrum *m/e* 124.0880 (calcd for $C_8H_{12}O$, 124.0888).

2b (method A, 84%, mixture of diastereoisomers, ca. 1:1): colorless oil; R_f 0.36 (silica, CH_2Cl_2); IR (liquid film) ν_{max} 3115, 2985, 2899, 1668, 1479, 1462, 1439, 1339, 1244, 1220, 1149, 1066, 1047, 995, 926, 885, 816, 755 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) τ 3.80–5.10 (m, 3 H, olefinic), 5.55 (m, 2 H, OCH), 7.50–9.00 (m, 9 H); mass spectrum *m/e* (rel intensity) 138 (M^+, 3), 109 (12), 96 (10), 85 (15), 79 (20), 67 (base peak); high-resolution mass spectrum *m/e* 138.1042 (calcd for $C_9H_{14}O$, 138.1044).

7b (method A, 82%): pale yellow oil; R_f 0.24 (silica, CH_2Cl_2); IR (liquid film) ν_{max} 3077, 2941, 2874, 1460, 1374, 1242, 1183, 1070, 1040, 996, 933, 905, 738, 717 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) τ 4.20 (m, 2 H, olefinic), 4.92 (m, 1 H, OCH), 6.30 (m, 2 H, OCH_2), 7.05–8.34 (m, 5 H); mass spectrum *m/e* (rel intensity) 110 (M^+, base peak), 109 (30), 95 (22), 82 (18), 79 (88), 69 (20); high-resolution mass spectrum *m/e* 110.0730 (calcd for $C_7H_{10}O$, 110.0732).

9b (method A, 75%): pale yellow oil; R_f 0.45 (silica, CH_2Cl_2); IR (liquid film) ν_{max} 3021, 2907, 2841, 1466, 1418, 1379, 1355, 1274, 1250, 1099, 1067, 1026, 1003, 976, 948, 926, 909, 833, 810, 775, 735 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) τ 4.10 and 4.30 (multiplets, 1 H each, olefinic), 4.68 (m, 1 H, OCH), 5.90 and 6.43 (doublets, J = 4.0 Hz, 1 H each, OCH_2), 6.47 (d, J = 3.0 Hz, 2 H, $SiOCH_2$), 6.72 (m, 1 H), 7.15 (m, 5 H), 7.98 (m, 2 H, CH_2 and CH), 9.12 (s, 9 H, $SiC(CH_3)_3$), 9.95 (s, 6 H, $Si(CH_3)_2$); mass spectrum *m/e* (rel intensity) 358 (M^+, 1), 301 (M^+ − ^{t}Bu, 24), 226 (36), 195 (32), 183 (33), 165 (35), 148 (42), 119 (22), 106 (12), 75 (base peak). Anal. ($C_{17}H_{30}O_2S_2Si$) C, H.

Reduction of the Phenyl Selenoether 1a, Preparation of 6-Oxabicyclo[3,2,2]nonane (1c), Method A (Raney Ni). To a freshly prepared suspension of neutral Raney Ni (from 3 g of 50% Raney Ni alloy) in THF (20 mL) at ambient temperature was added under argon the phenyl selenoether **1a** (283 mg, 1.0 mmol) in THF solution (5 mL). The reaction mixture was stirred at 25 °C for 1 h, at which time TLC indicated completion of the reduction. The solution was filtered and the Raney Ni washed thoroughly with THF. Removal of the solvent followed by column chromatography (silica, CH_2Cl_2) afforded pure 6-oxabicyclo[3.2.2]nonane (**1c**, 118.5 mg, 94%) as a colorless, crystalline solid: mp 119–120 °C (sublimed); R_f 0.19 (silica, CH_2Cl_2); IR ($CHCl_3$) ν_{max} 3030, 2959, 2890, 1471, 1449, 1379, 1348, 1279, 1258, 1134, 1073, 1016, 964, 926, 897, 851, 826 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) τ 5.96 (m, 1 H, OCH), 6.05 and 6.25 (b doublets, J = 4.5 Hz, 1 H each, OCH_2), 7.80–8.50 (m, 11 H, CH_2 and CH); mass spectrum *m/e* (rel intensity) 126 (M^+, 74), 111 (10), 97 (71), 83 (30), 67 (base peak). Anal. ($C_8H_{14}O$), C, H.

Method B (*n*-Bu_3SnH). To a solution of the phenyl selenoether **1a** (283 mg, 1.0 mmol) in freshly distilled toluene (2.5 mL) were added freshly prepared tri-*n*-butyltin hydride (582 mg, 390 μL, 2 mmol) and azobisisobutyronitrile (AIBN, 0.02 M toluene solution, 1 mL, 0.02 mmol). The mixture was degassed with a stream of argon for 15 min, sealed with a plastic cap, and heated to 110 °C for 1 h (TLC indicated completion of the reaction). Column chromatography (silica, CH_2Cl_2) afforded pure 6-oxabicyclo[3.2.2]nonane (**1c**, 120 mg, 95%) as colorless crystals.

Reversal of the Phenylselenoetherification Reaction, Reduction of Phenyl Selenoether 1a with Na–Liquid NH_3. To a stirred solution of sodium (230 mg, 10 mmol) in dry liquid ammonia (25 mL) cooled to −78 °C was added (syringe) a solution of the phenyl selenoether **1a** (283 mg, 1 mmol) in ether (2 mL). The reaction mixture was stirred at −78 °C for 5 min and then quenched with excess solid ammonium chloride (1 g) and the cooling bath was removed. After evaporation of the ammonia the residue was partitioned between water (25 mL) and ether (50 mL). The ether layer was separated and the aqueous phase extracted with ether (2 × 25 mL). The combined ether extracts were dried ($MgSO_4$) and evaporated to give 4-cycloheptene-1-methanol (**1**), which was purified by preparative layer chromatography, 98 mg (78%), spectroscopically and chromatographically identical with an authentic sample.

Preparation of Silyl Ether 23. To a stirred solution of cyclopentene oxide (4.2 g, 50 mmol) in dry Me_2SO (50 mL) was added lithium acetylide–EDA complex (6.9 g, 75 mmol). The mixture was stirred for 72 h and then diluted with petroleum ether (75 mL) and washed with 5% sodium bicarbonate solution (20 mL), water (20 mL), and brine (20 mL). The dried ($MgSO_4$) solvents were removed on the rotary evaporator to yield 4.84 (88%) of crude alcohol which was silylated without purification by dissolving in dry DMF (10 mL) and stirring with imidazole (5.98 g, 88 mmol) and *tert*-butyldimethylchlorosilane (13.26 g, 88 mmol) at 25 °C for 15 h. The product was isolated by pouring onto water (25 mL) and extracting with ether (3 × 30 mL), removing the dried ($MgSO_4$) solvents, and chromatography (column, silica, petroleum ether, R_f 0.17). Obtained was 9.85 g (100%): IR (liquid film) ν_{max} 2985, 2899, 2132 (alkyne), 1481, 1471, 1393, 1368, 1259, 1176, 1124, 1093, 1064, 1047, 1031, 1010, 941, 897, 870, 840, 778 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) τ 5.86 (m, 1 H, OCH), 7.55 (bs, 1 H, C≡CH), 7.90–8.70 (m, 7 H), 9.18 (s, 9 H, $SiC(CH_3)_3$), 9.96 (s, 6 H, $Si(CH_3)_2$). Anal. ($C_{13}H_{24}OSi$) C, H.

Preparation of Aldehyde 24. To a stirred solution of **23** (9.85 g, 44 mmol) in anhydrous THF at −10 °C was added 9-BBN (105 mL, 0.5 M in THF, 52.76 mmol) under argon. The reaction mixture was allowed to warm up and stirred at ambient temperature for 1.5 h. The mixture was then cooled to −10 °C and 15% aqueous H_2O_2 (35.87 mL, 158.28 mmol) and NaOH (52.76 mL, 1 M, 52.76 mmol) were added simultaneously over a period of 15 min. The mixture was diluted with ether (200 mL) and washed with water (2 × 50 mL) and brine (2 × 50 mL). The dried solvent ($MgSO_4$) was removed and the crude aldehyde was purified by column chromatography (silica, CH_2Cl_2) to yield 9.05 g (85%) of **24** as an oil: R_f 0.42; IR (liquid film) ν_{max} 2924, 2841, 2703, 1725 (CHO), 1460, 1399, 1379, 1355, 1253, 1111, 1053, 1005, 938, 870, 837, 772 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) τ 0.06 (m, 1 H, CHO), 6.23 (m, 1 H, OCH), 7.37–9.00 (m, 9 H), 9.15 (s, 9 H, $SiC(CH_3)_3$), 9.96 (s, 6 H, $Si(CH_3)_2$); mass spectrum *m/e* (rel intensity) 185 (M^+ − *t*-Bu, 3), 183 (48), 157 (10), 109 (15), 81 (29), 75 (base peak); high-resolution mass spectrum *m/e* 185.0856 (calcd for $C_9H_{17}O_2Si$ (M^+ − *t*-Bu), 185.0997).

Preparation of Trans Alcohol 25b. To a stirred solution of ethyltriphenylphosphonium bromide (12.74 g, 34 mmol) in dry Me_2SO (20 mL) under argon was slowly added at 25 °C a solution of dimsyl sodium (24.3 mL, 1 M, 34.30 mmol) and the red-orange solution stirred for 15 min. The aldehyde **24** (7.52 g, 31 mmol) in dry Me_2SO

(5 mL) was then added to 25 °C and the mixture was stirred at that temperature for 2 h. The reaction mixture was then diluted with water (50 mL) and extracted with petroleum ether (2 × 100 mL); the extracts were washed with (i) water (25 mL) and (ii) brine (25 mL), dried ($MgSO_4$), and concentrated to afford crude olefin **25b** (6.80 g, 82%), which was deprotected without purification as follows. The oily silyl ether **25b** (6.8 g) was stirred under argon at 50 °C in AcOH–THF–H_2O (3:2:2) (20 mL) for 24 h and then poured onto water (50 mL) and extracted with ether (2 × 50 mL). The combined ether solution was washed with 5% sodium bicarbonate (2 × 10 mL), water (10 mL), and brine (10 mL), dried ($MgSO_4$), and evaporated to yield the crude product which was purified by column chromatography (silica, hexanes–ether, 1:1, R_f 0.32), leading to pure **25b** (3.4 g, 95%): IR (liquid film) ν_{max} 3280 (OH), 2985, 2925, 2857, 1440, 1400, 1333, 1244, 1070, 1020, 963, 905, 873, 831, 769, 733 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) τ 4.55 (m, 2 H, olefinic), 6.18 (m, 1 H, OCH), 7.52–8.90 (m, 13 H); mass spectrum *m/e* (rel intensity) 140 (M^+, 8), 122 (40), 107 (32), 94 (21), 81 (45), 79 (base peak). Anal. ($C_9H_{16}O$) C, H.

Preparation of Cis Alcohol 2. The trans alcohol **25b** (170 mg, 1.21 mmol) in dry CH_2Cl_2 (1 mL) was cooled to −20 °C under argon and while stirring treated with triethylamine (255 μL, 1.82 mmol) and then mesyl chloride (140 μL, 1.82 mmol). After stirring at −20 °C for 2 h, the reaction mixture was allowed to reach room temperature, diluted with CH_2Cl_2 (25 mL), and washed with (i) water (2 × 5 mL) and (ii) brine (5 mL). Removal of the dried ($MgSO_4$) solvent afforded the crude mesylate (258 mg, 98%), which was dissolved in dry Me_2SO (1 mL) and added dropwise to a stirred mixture of potassium superoxide (338 mg, 4.76 mmol) and 18-crown-6 (314 mg, 1.18 mmol) in dry Me_2SO (1 mL) under argon and 20 °C. The reaction mixture was stirred at ambient temperature for 12 h, diluted with water (10 mL), and extracted with ether (2 × 25 mL). The combined ether solution was washed with (i) water (10 mL) and (ii) saturated KCl solution (3 × 10 mL) and dried ($MgSO_4$). Removal of the solvent followed by column chromatography (silica, hexanes–ether, 1:1) afforded pure cis alcohol **2** (130 mg, 78%): R_f 0.48; IR (liquid film) ν_{max} 3390 (OH), 3067, 2985, 2915, 1439, 1397, 1370, 1316, 1149, 1117, 1029, 984, 926 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) τ 4.55 (m, 2 H, olefinic), 5.83 (m, 1 H, OCH), 7.70–8.80 (m, 13 H); mass spectrum *m/e* (rel intensity) 140 (M^+, 5), 122 (40), 107 (30), 94 (21), 81 (45), 79 (base peak); high-resolution mass spectrum *m/e* 140.1197 (calcd for $C_9H_{16}O$, 140.1201).

Reduction of Ketone 14a. The ketone **14a** (338 mg, 1 mmol) in absolute methanol (5 mL) at 25 °C was treated with sodium borohydride (45 mg, 1.2 mmol). After 30 min of stirring the mixture was poured onto water (10 mL) and extracted with methylene chloride (2 × 20 mL). The organic layer was washed with (i) water (5 mL) and (ii) brine (5 mL) and the solvent dried ($MgSO_4$) and evaporated. Column chromatography (silica, CH_2Cl_2) afforded the hydroxy compound **17** as the major product as well as its C* epimer as a minor product. **17** (80%) was a colorless oil: R_f 0.15 (silica, CH_2Cl_2); IR (liquid film) ν_{max} 3400 cm^{-1} (OH); ^1H NMR (220 MHz, $CDCl_3$) τ 2.30–2.50 (m, 2 H, aromatic), 2.70–2.85 (m, 3 H, aromatic), 5.85–5.95 (m, 1 H, OCH), 6.00–6.10 (m, 1 H, OCH), 6.40–6.55 (m, 1 H, SeCH), 7.06 (d, J = 8 Hz, 1 H), 7.40–7.60 (m. 1 H), 8.15–8.75 (m, 14 H). *epi*-**17** (20%): colorless oil; R_f 0.33 (silica, CH_2Cl_2); IR (liquid film) ν_{max} 3400 cm^{-1} (OH); ^1H NMR (220 MHz, $CDCl_3$) τ 2.30–2.50 (m, 2 H, aromatic), 2.70–2.85 (m, 3 H, aromatic), 5.75–5.90 (m, 1 H, OCH), 5.95–6.05 (m, 1 H, OCH), 6.70–6.85 (m, 1 H, SeCH), 7.75 (bs, 1 H, OH), 7.95–8.05 (m, 1 H), 8.15 -8.75 (m, 14 H). Anal. ($C_{17}H_{24}SeO_2$) C, H.

Preparation of the Allylic Ether 18. The alcohol **17** (340 mg, 1 mmol) in dry methylene chloride (5 mL) was cooled to 0 °C and treated with pyridine (0.5 mL), acetic anhydride (250 μL), and 4-(dimethylamino)pyridine (5 mg, 0.04 mmol). The reaction mixture was allowed to reach room temperature and stirred for 12 h. The solution was then diluted with methylene chloride (20 mL) and washed with (i) saturated $CuSO_4$ solution (2 × 5 ml), (ii) 0.1 N HCl solution (5 mL), (iii) water (5 mL), and (iv) brine (5 mL). Drying ($MgSO_4$) and removal of the solvent furnished the acetate selenide (382 mg, 100%), which was oxidized with ozone without further purification as follows. A methylene chloride solution (25 mL) of the selenide obtained above (382 mg, 1 mmol) was cooled to −78 °C and a slow stream of ozone (Welsbach ozonator, Type T-20) was passed through until the blue color of ozone persisted. The excess ozone was removed by passing oxygen through the solution and triethylamine (140 μL, 1 mmol) was added. The reaction mixture was then stirred at 25 °C for 15 h, the solvent removed, and the residue chromatographed (column, silica, CH_2Cl_2) to afford the allylic ether **18** (175 mg, 78%) as a colorless oil: IR (liquid film) ν_{max} 1745 (acetate), 1625 cm^{-1} (olefin); ^1H NMR (220 MHz, $CDCl_3$) τ 4.0–5.0 (m, 3 H, olefinic), 4.90–5.00 (m, 1 H, C*H*OAc) 5.55–5.68 (m, 1 H, CHO), 7.22–7.50 (m, 1 H), 7.95 (s, 3 H, CH_3CO), 8.20–8.80 (m, 11 H). Anal. ($C_{13}H_{20}O_3$) C, H.

Preparation of Aldehyde 19. The olefin **18** (224 mg, 1 mmol) was dissolved in absolute methanol (10 mL) and cooled to −78 °C. Ozone was passed through the solution until a blue coloration persisted and then the excess ozone was expelled with a stream of oxygen. Dimethyl sulfide (147 μL, 2 mmol) was added at −78 °C and the reaction mixture was then stirred at −10 °C for 1 h, 0 °C for 1 h, and finally 25 °C for 2 h. The solvent was removed under vacuum and the aldehyde extracted with ether. The crude product obtained after removal of the ether [IR (liquid film) ν_{max} 2700 and 1725 (aldehyde), 1745 cm^{-1} (acetate)] was rather unstable and, therefore, was oxidized directly to the acid without purification.

Preparation of Amide 20. The crude aldehyde obtained above (from 1 mmol of **18**) was dissolved in acetone (5 mL) and cooled to −10 °C. Jones reagent was added dropwise until a yellow coloration persisted, the solution diluted with ether (50 mL), and the mixture treated with a few drops of 10% sodium bisulfite solution before the cooling bath was removed, dried ($MgSO_4$), and filtered. The solid residue was thoroughly washed with ether and the solvents were removed to afford the crude acid, which was dissolved in dry benzene (1 mL) and oxalyl chloride (0.5 mL). After the mixture was stirred at 25 °C for 6 h the solvents were removed under vacuum and under anhydrous conditions the acid chloride was dissolved in dry ether (5 mL) and excess dimethylamine gas was passed through the solution at 0 °C. The reaction mixture was stirred at 25 °C for 1 h, the solvents were removed, and the amide **20** was purified by column chromatography (silica, ether): 78 mg (46% overall from **18**); IR (liquid film) ν_{max} 1745 (acetate), 1640 cm^{-1} (amide); ^1H NMR (220 MHz, $CDCl_3$) τ 5.00–5.10 (m, 1 H, C*H*OAc), 5.40–5.52 (m, 1 H, OCHCO), 6.85 (s, 3 H, NCH_3), 7.05 (s, 3 H, NCH_3), 7.40–7.55 (m, 1 H), 7.95 (s, 3 H, CH_3CO), 8.20–8.70 (m, 11 H).

Preparation of Muscarine Analogue 21. Lithium aluminum hydride (108 mg, 3 mmol) was added to a solution of the amide **20** (160 mg, 1 mmol) in dry THF (5 mL) and the mixture refluxed under argon for 1 h. The reaction mixture was cooled to 0 °C and quenched with wet ether and finally a few drops of water until milky white. Drying ($MgSO_4$) and filtration of the solution followed by a thorough wash of the solid residue with THF gave after removal of the solvent the crude amine. Dissolution in THF–petroleum ether (1:1, 5 mL), cooling to 0 °C, and addition of methyl iodide (710 mg, 5 mmol) gave the muscarine analogue **21** as a crystalline solid which was purified by recrystallization from toluene–acetone (1:1) (50%): white needles, mp 149–150 °C; IR (KBr) ν_{max} 3350, 1040, 975, 915 cm^{-1}; ^1H NMR (220 MHz, Me_2SO-d_6/acetone-d_6) τ 5.00 (d, 1 H, OH), 5.50 (m, 1 H, OCH), 6.05–6.15 (m, 1 H, C*H*OH), 6.40–6.60 (m, 2 H, NCH_2), 6.85 (s, 9 H, $N(CH_3)_3$), 7.55–7.62 (m, 1 H, CH_2), 8.15–8.85 (m, 11 H, CH_2). Anal. ($C_{13}H_{20}NO_2I\cdot1.5H_2O$) C, H, N.

Preparation of Thioacetates from the Corresponding Mesylates. The mesylate (obtained from the corresponding alcohol by treatment with 1.5 equiv of mesyl chloride and 1.5 equiv of triethylamine in CH_2Cl_2 at −20 °C) (1.0 mmol) was dissolved in anhydrous dimethyl sulfoxide (Me_2SO, 5 mL) and treated under argon with recrystallized (EtOH) potassium thioacetate (571 mg, 5 mmol). The reaction mixture was stirred at 45 °C for 10–15 h, when TLC indicated complete reaction. After cooling to room temperature the mixture was diluted with petroleum ether (50 mL) and water (50 mL). After shaking, the organic phase was separated and washed with (i) water (2 × 50 mL) and (ii) brine (25 mL). The dried ($MgSO_4$) solvents were removed and the crude product was purified by flash column or preparative layer chromatography (silica, ether–petroleum ether mixtures) to afford the thioacetates (72–80%).

Properties of Thioacetates 28 (78%): pale yellow oil; R_f 0.42 (silica, 5% ether in petroleum ether); IR (liquid film) ν_{max} 2985, 2941, 2841, 1684 (thioacetate), 1645, 1437, 1346, 1133, 1107, 951 cm^{-1}; ^1H NMR (220 MHz, $CDCl_2$) τ 4.61 (m, 2 H, olefin), 6.09 (m, 1 H, CHS), 7.68 (s, 3 H, CH_3CO), 7.82–8.05 (m, 3 H), 8.18–8.45 (m, 8 H), 8.61–8.81 (m, 1 H); mass spectrum *m/e* (rel intensity) 198 (M^+, 2), 183 ($M^+ - CH_3$, 3), 157 (11), 156 (22), 155 (M^+ − Ac, base peak), 127 (36), 121 (31), 93 (83), 81 (66), 79 (68), 55 (90). Anal.

($C_{11}H_{18}OS$) C, H.

31 (80%): pale yellow oil; R_f 0.42 (silica, 5% ether in petroleum ether); IR (liquid film) ν_{max} 3008, 2955, 2865, 1687 (thioacetate), 1650, 1445, 1435, 1335, 1130, 1110, 960, 630 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) τ 4.64 (m, 2 H, olefin), 6.09 (m, 1 H, CHS), 7.66 (s, 3 H, CH_3CO), 7.91 (m, 3 H), 8.05-8.43 (m, 8 H), 8.73 (m, 1 H); mass spectrum *m/e* (rel intensity) 198 (M^+, 4), 183 ($M^+ - CH_3$, 6), 169 (2), 157 (20), 156 (38), 155 (base peak), 127 (62), 121 (53), 93 (92). Anal. ($C_{11}H_{18}OS$) C, H.

Preparation of Thioselenides. To a stirring solution of thioacetate (**27-34**) (1.0 mmol) in absolute methanol (10 mL) at −78 °C was added PhSeCl (1.1 mmol) under argon. Stirring was continued for 1-2 h until TLC indicated complete reaction. Methylene chloride (20 mL) was added and the solution was washed with brine (10 mL), 5% $NaHCO_3$ solution, and finally again with brine (10 mL). The organic phase was then dried ($MgSO_4$) and evaporated to afford the crude product which was purified by either flash column or preparative layer chromatography (silica, ether-petroleum ether mixtures).

Properties of Thioselenide 27a (85% from 28, 80% from 27): pale yellow oil; R_f 0.43 (silica, 5% ether in petroleum ether); IR (liquid film) ν_{max} 3030, 2915, 2849, 1684, 1460, 1471, 1445, 1433, 1370, 1312, 1292, 1225, 1171, 1073, 1063, 1018, 993, 736, 690, 668 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) τ 2.41 (m, 2 H, aromatic), 2.75 (m, 3 H, aromatic), 6.25-6.50 (m, 2 H, CHS), 6.64 (m, 1 H, CHSe), 7.23 (m, 1 H), 7.77 (m, 1 H), 8.07-8.60 (m, 10 H); ^{13}C NMR (25 MHz, CD_2Cl_2) δ 135.33, 135.09, 129.17, 127.77, 58.28, 51.39, 49.25, 44.26, 42.18, 35.90, 31.82, 25.11, 21.64; mass spectrum *m/e* (rel intensity) 312 (M^+, 6), 155 (M^+ − SePh, base peak); high-resolution mass spectrum *m/e* 312.0443 (calcd for $C_{15}H_{20}S^{80}Se$; 312.0451). Anal. ($C_{15}H_{20}SSe$) C, H, S.

Preparation of α,β-Unsaturated Sulfoxides 36a, 36b, 39a, and 39b. The thioselenide **27a** or **31a** (93.6 mg, 0.3 mmol) in CH_2Cl_2 (3 mL) was cooled to −78 °C and treated under argon and with stirring with a solution of *m*-CPBA in CH_2Cl_2 (2.4 mL, 0.125 M, 0.3 mmol). After 15 min at −78 °C TLC indicated complete conversion to the sulfoxide and at that time another portion of *m*-CPBA (2.4 mL, 0,125 M, 0.3 mmol) was introduced dropwise. The cooling bath was removed and the mixture was allowed to stir at ambient temperature for 12 h. The reaction mixture was then diluted with CH_2Cl_2 (25 mL) and washed with saturated $NaHCO_3$ (2 × 20 mL). The organic layer was then washed with 10% $NaHSO_3$ (20 mL) and brine (20 mL). The dried ($MgSO_4$) solvent was removed and the residue subjected to preparative layer chromatography to afford the conjugated sulfoxides **36a** (23.5 mg, 46%) and **36b** (21 mg, 41%) or **39a** (235 mg, 46%) and **39b** (20 mg, 40%).

α,β-Unsaturated Sulfoxide 36a: colorless oil; R_f 0.37 (silica, 5% methanol in ether); IR (CCl_4) ν_{max} 3030, 2955, 2865, 1660, 1465, 1445, 1376, 1035 (S=O) cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) τ 3.62 (m, 1 H, olefin), 6.63 (m, 1 H, CHSO), 6.85 (m, 2 H), 7.52 (d, J = 12 Hz, 1 H), 7.88 (m, 1 H), 8.12 (m, 1 H), 8.18 (d, J = 6 Hz, 3 H, CH_3), 8.40 (m, 1 H), 8.53 (m, 2 H), 8.80 (m, 1 H); mass spectrum *m/e* (rel intensity) 171 ($(M + 1)^+$, 4), 170 (M^+, 30), 154 (50), 153 (46), 125 (36), 104 (30), 93 (41) 67 (base peak); high-resolution mass spectrum *m/e* 170.0764 (calcd for $C_9H_{14}OS$, 170.0765).

36b: colorless oil; R_f 0.47 (silica, 5% methanol in ether); IR (CCl_4) ν_{max} 3010, 2950, 2860, 1665, 1430, 1375, 1350, 1118, 1038 (S=O), 740 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) τ 3.77 (q, J = 6 Hz, 1 H, olefin), 6.52 (m, 1 H, CHSO), 7.18 (m, 1 H), 7.30 (m, 1 H), 7.42 (m, 1 H), 7.77 (m, 1 H), 8.17 (m, 6 H), 8.30 (m, 1 H), 8.53 (m, 1 H); mass spectrum *m/e* (rel intensity) 171 ($(M + 1)^+$, 7), 170 (M^+, 46), 154 (91), 153 (75), 125 (73), 93 (80), 79 (base peak); high-resolution mass spectrum *m/e* 170.0762 (calcd for $C_9H_{14}OS$, 170.0765).

39a: colorless oil; R_f 0.31 (silica, 5% methanol in ether); IR (CCl_4) ν_{max} 2975, 2950, 2860, 2800, 1665, 1488, 1443, 1413, 1380, 1350, 1295, 1275, 1150, 1120, 1075, 1032 (S=O), 968, 933, 913, 842, 740 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) τ 3.90 (m, 1 H, olefin), 6.57 (m, 2 H), 6.90 (m, 1 H), 7.62 (m, 1 H), 7.83 (m, 1 H), 7.93 (dd, J = 9, 1.5 Hz, 3 H, CH_3), 8.10 (m, 1 H), 8.38 (m, 1 H), 8.55 (m, 2 H), 8.80 (m, 1 H); mass spectrum *m/e* (rel intensity) 171 ($(M + 1)^+$, 4), 170 (M^+, 26), 154 (28), 107 (10), 93 (28), 67 (base peak); high-resolution mass spectrum *m/e* 170.0781 (calcd for $C_9H_{14}OS$, 170.0765).

39b: colorless oil; R_f 0.44 (5% methanol in ether); IR (CCl_4) ν_{max} 3010, 2980, 2931, 2864, 2800, 1660, 1490, 1460, 1443, 1380, 1350, 1295, 1185, 1170, 1150, 1118, 1075, 1033, 908, 843, 832 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) τ 3.98 (q, J = 6 Hz, 1 H, olefin), 6.53 (m, 1 H), 7.25 (m, 3 H), 7.67 (m, 1 H), 7.93 (d, J = 6 Hz, 3 H, CH_3), 8.20 (m, 4 H), 8.45 (m, 1 H); mass spectrum *m/e* (rel intensity) 171 ($(M + 1)^+$, 3), 170 (M^+, 21), 154 (24), 93 (26), 67 (base peak); high-resolution mass spectrum *m/e* 170.0709 (calcd for $C_9H_{14}OS$, 170.0765).

Preparation of α,β-Unsaturated Sulfones 37 and 40. The thioselenides **27a** or **31a** (93.6 mg, 0.3 mmol) were oxidized to the α,β-unsaturated sulfones **37** or **40** exactly in the same way as in the preparation of the corresponding sulfoxides except that 3 equiv of *m*-CPBA was used. Isolation and purification as above led to sulfone **37** (50 mg, 90%) and **40** (49.6 mg, 89%).

37: colorless oil; R_f 0.20 (silica, ether-petroleum ether, 1:1); IR (CCl_4) ν_{max} 2985, 2930, 2860, 1665, 1440, 1380, 1348, 1300 (SO_2), 1115 (SO_2), 1073, 1040, 1020, 930, 840 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) τ 3.53 (q, J = 9 Hz, 1 H, olefin), 6.62 (m, 1 H, $CHSO_2$), 7.13 (m, 2 H), 7.65 (d, J = 15 Hz, 1 H), 7.85 (m, 1 H), 7.98 (m, 1 H), 8.08 (m, 1 H), 8.17 (d, J = 6 Hz, 3 H, CH_3), 8.23 (m, 1 H), 8.38 (m, 1 H), 8.58 (m, 1 H); mass spectrum *m/e* (rel intensity) 186 (M^+, 6), 169 (1), 138 (7), 121 (68), 120 (33), 107 (15), 105 (18), 94 (13), 93 (74), 91 (24), 79 (78), 68 (74), 67 (base peak); high-resolution mass spectrum *m/e* 186.0717 (calcd for $C_9H_{14}O_2S$, 186.0714).

40: colorless oil; R_f 0.20 (silica, ether-petroleum ether, 1:1), IR (CCl_4) ν_{max} 2978, 2932, 2891, 1442, 1380, 1350, 1300 (SO_2), 1118 (SO_2), 1075, 1043, 933, 843, 725 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) τ 3.98 (q, J = 6 Hz, 1 H, olefin), 6.55 (m, 1 H, $CHSO_2$), 7.13 (m, 1 H), 7.67 (m, 2 H), 7.90 (d, J = 6 Hz, 3 H, CH_3) 7.97 (m, 1 H), 8.17 (m, 2 H), 8.35 (m, 1 H), 8.52 (m, 1 H), 8.75 (m, 1 H); mass spectrum *m/e* (rel intensity) 186 (M^+, 5), 169 (1), 138 (6), 122 (7), 121 (53), 120 (24), 107 (10), 105 (13), 93 (61), 86 (23), 79 (47), 68 (40), 67 (base peak); high-resolution mass spectrum *m/e* 186.0720 (calcd for $C_9H_{14}O_2S$, 186.0714).

Preparation of β,γ-Unsaturated Sulfones 38a and 38b. The thioselenide **27a** or **27b** (93.6 mg, 0.3 mmol) in CH_2Cl_2 (3 mL) was cooled to 0 °C and treated with 1 M hydrogen peroxide solution (1.5 mL, 1.5 mmol, made from 30% hydrogen peroxide and THF). After 5 min the cooling bath was removed and stirring was continued at ambient temperature for 12 h, when TLC indicated complete reaction. The workup and purification of products proceeded in the same manner as for the preparation of sulfoxides **36a,b** and **39a,b.** Obtained, from **27a**, was a mixture of **38a** and **37** (51 mg, 92%): R_f 0.18 (silica, ether-petroleum ether, 1:1); ratio **38a**:**37** ca. 1:2 by ^1H NMR (360 MHz, $CDCl_3$). The ^1H NMR spectrum of this mixture revealed the following signals for **38a**: τ 4.20 (m, 1 H, olefin), 4.60 (m, 2 H, olefin), 6.30 (m, 1 H, $CHSO_2$), 6.50 (m, 1 H, $CHSO_2$), 7.13 (m, 2 H), 7.68 (m, 1 H), 7.88 (m, 1 H), 7.97 (m, 1 H), 8.08 (m, 1 H), 8.23 (m, 1 H), 8.39 (m, 1 H), 8.58 (m, 1 H). Obtained from **27b** was a mixture of **38b** and **40** (49 mg, 87%): R_f 0.18 (ether-petroleum ether, 1:1); ratio **38b**:**40** ca. 1:3 by ^1H NMR (360 MHz, $CDCl_3$). The ^1H NMR of this mixture revealed the following signals for **38b**: τ 4.17 (m, 1 H, olefin), 4.55 (m, 2 H, olefin), 6.33 (m, 1 H, $CHSO_2$), 6.41 (m, 1 H, $CHSO_2$), 7.13 (m, 2 H), 7.67 (m, 2 H), 7.97 (m, 1 H), 8.17 (m, 2 H), 8.30 (m, 1 H), 8.49 (m, 1 H).

Preparation of Sulfoxide 36b from Thioacetate 27a via Iodide 35a. Because of its relative instability thiol **27** was generated immediately prior to its cyclization with iodine. The thioacetate **27a** (115 mg, 0.58 mmol) was dissolved in absolute methanol (5 mL) and the mixture deoxygenated by bubbling dry argon through it for 15 min. Sodium methoxide (157 mg, 2.9 mmol) was added in one portion and the resulting solution stirred at room temperature under argon for 30 min. Water (30 mL) was then added and the mixture adjusted to pH 4 with 1 N oxalic acid. Extraction with ether (3 × 40 mL), washing of the combined ether layer with water (30 mL), and removal of the dried ($MgSO_4$) solvents afforded the crude thiol **27** (90 mg, 100%): R_f 0.55 (silica, hexane); IR (liquid film) ν_{max} 3000, 2950, 2855, 2200 (SH), 1440, 1400, 1365, 1315, 1255, 1090, 1010, 960, 800 cm^{-1}; ^1H NMR (360 MHz, benzene-d_6) τ 4.52 (m, 1 H, olefin), 4.60 (m, 1 H, olefin), 6.88 (m, 1 H, CHS), 7.73 (m, 1 H), 7.88 (m, 1 H), 8.08-8.83 (m, 8 H), 8.42 (d, J = 6 Hz, 3 H, CH_3); mass spectrum *m/e* (rel intensity) 156 (M^+, 24), 127 (base peak), 93 (52), 67 (34); high-resolution mass spectrum *m/e* 156.0942 (calcd for $C_9H_{16}S$, 156.0973).

Thiol **27** was dissolved in dry CH_2Cl_2 (75 mL), cooled to −78 °C under argon, and treated sequentially with powdered K_2CO_3 (325 mg, 2.32 mmol) and iodine (178 mg, 0.696 mmol). The reaction mixture was stirred at −78 °C for 3 h (all iodine crystals dissolved) and the orange-red mixture was washed with 10% sodium thiosulfate solution (40 mL) and water (40 mL) and dried over $MgSO_4$. Filtration and removal of the solvents gave the rather labile iodide **35a**, which was

immediately reacted with DBU. A rapidly purified sample (PLC, silica, 1% ether in hexane, R_f 0.26) exhibited the following properties: IR (liquid film) ν_{max} 2950, 2860, 1440, 1370, 1310, 1250, 1220, 1190, 1050, 1020, 905 cm^{-1}; ^1H NMR (360 MHz, benzene-d_6) τ 5.97 (m, 1 H, CHI), 6.55 (m, 1 H, CHS), 6.78 (m, 1 H, SC*H*CH1), 7.48 (m, 1 H), 7.68 (m, 1 H), 8.12–9.00 (m, 6 H), 8.33 (d, J = 6 Hz, 3 H, CH_3). Irradiation at τ 5.97 (CHI) collapsed the doublet at τ 8.33 (CH_3) to a singlet.

The crude iodide **35a** (125 mg) was dissolved in dry benzene (2.2 mL) and treated with diazabicyclo[5.4.0]undec-5-ene (DBU, 441 mg, 433 μL, 2.9 mmol) under argon and at room temperature. After stirring at room temperature for 15 h the reaction mixture was diluted with ether (30 mL), washed with water (2 × 10 mL), and dried ($MgSO_4$). The residue obtained after removal of the solvents was subjected to PLC (silica, 1% ether in hexane) yielding the thioenol ether **40a** (51 mg, 60% overall from **27a**); R_f 0.42 (silica, 1% ether in petroleum ether); IR (CCl_4) ν_{max} 3010, 2950, 2860, 1700, 1630, 1440, 900 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) τ 4.68 (q, J = 6 Hz, 1 H, olefin), 6.04 (m, 1 H, CHS), 7.25 (m, 1 H), 7.33 (m, 1 H), 7.50 (m, 1 H), 7.92–8.69 (m, 6 H), 8.36 (d, J = 6 Hz, CH_3); mass spectrum *m/e* (rel intensity) 156 (M^+, 45), 139 (12), 126 (16), 125 (83), 97 (43), 88 (23), 84 (base peak); high-resolution mass spectrum *m/e* 154.0825 (calcd for $C_9H_{14}S$, 154.0816).

The thioenol ether **40a** (16 mg, 0.1 mmol) was dissolved in anhydrous CH_2Cl_2 (2 mL) and cooled to −20 °C under argon. *m*-CPBA (21 mg, 85% purity, 0.1 mmol) dissolved in CH_2Cl_2 (1 mL) was added dropwise with stirring. After stirring at −20 °C for 5 min the reaction mixture was diluted with ether (50 mL), saturated sodium bicarbonate (5 mL), and water (5 mL) and dried ($MgSO_4$). Removal of the solvents after filtration followed by PLC (silica, 5% methanol in CH_2Cl_2) furnished a colorless oil corresponding to sulfoxide isomer **39a** (8.5 mg, 50%) with identical properties as described above.

Preparation of Trans Olefins 26a and 26b from the Corresponding Cis Olefins. The cis olefin **25a** (300 mg, 1.13 mmol) was dissolved in anhydrous benzene (68 mL) together with diphenyl disulfide (123 mg, 0.56 mmol) and the solution was degassed by bubbling through it a stream of argon for 15 min. Irradiation with a Hanovia UV lamp (150 W) (while maintaining the solution at ambient temperature by circulating water) for 6–12 h (until silver nitrate impregnated silica TLC revealed a constant equilibrium of cis/trans isomers) produced an enriched solution of the trans olefin **26a.** Column chromatography on silver nitrate impregnated silica (petroleum ether) afforded pure trans olefin **26a** (232 mg, 77%), R_f 0.27 ($AgNO_3$–silica, petroleum ether), and pure cis olefin **25a** (41 mg, 13.5%), R_f 0.20 ($AgNO_3$–silica, petroleum ether). **26a:** colorless oil; IR (liquid film) ν_{max} 2985, 2924, 2907, 2809, 1570, 1462, 1435, 1370, 1355, 1250, 1105, 1045, 100, 961, 871, 833, 772 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) τ 4.60 (m, 2 H, olefin), 6.28 (m, 1 H, CHO), 7.85 (m, 2 H), 8.22 (m, 3 H), 8.35 (m, 1 H), 8.05 (m, 2 H), 8.63 (d, J = 6 Hz, 3 H, CH_3) 8.88 (m, 1 H), 9.12 (s, 9 H, $C(CH_3)_3$), 9.95 (s, 3 H, CH_3Si), 9.98 (s, 3 H, CH_3Si); mass spectrum *m/e* (rel intensity) 254 (M^+, 1), 197 (32), 75 (base peak). Anal. ($C_{15}H_{30}OSi$) C, H. The *tert*-butyldimethylsilyl group was removed from **26a** to afford **26b** as described above for the preparation of **25b**, **26b** (95%): colorless oil; R_f 0.48 (silica, 50% ether in petroleum ether); IR (CCl_4) ν_{max} 3618 (OH), 3480 (OH), 3020, 2978, 2960, 2932, 2868, 1485, 1442, 1412, 1382, 1350, 1295, 1150, 1119, 1075, 1043, 1022, 968, 934, 914, 842, 832, 735 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) τ 4.52 (m, 2 H, olefin), 6.15 (m, 1 H, CHO), 7.90 (m, 1 H), 8.02 (m, 2 H), 8.10 (m, 2 H), 8.27 (m, 1 H), 8.30 (d, J = 9 Hz, 3 H, CH_3), 8.42 (m, 2 H), 8.77 (m, 2 H); mass spectrum *m/e* (rel intensity) 140 (M^+, 4), 122 ($M^+ - H_2O$, 10), 105 (56), 97 (71), 84 (base peak). Anal. ($C_8H_{16}O$) C, H.

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Supplementary Material Available: A listing of properties and full spectral data of compounds **3a**, **6a**, **10a**, **11a–13a**, **15a**, **10b**, **11b**, **30**, **32–34**, **29a**, **32a–34a**, **41–43**, and **45–49**, and the preparations and properties of the precursors of the *E* and *Z* thioacetates **30** and **32**, i.e., the trans hydroxy and *tert*-butyldimethylsilyl ether derivatives (numbers **50–53**) (10 pages). Ordering information is given on any current masthead page.

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