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Phenylseleno-[1] and Phenylsulfenolactonizations.[2] Two Highly Efficient and Synthetically Useful Cyclization Procedures

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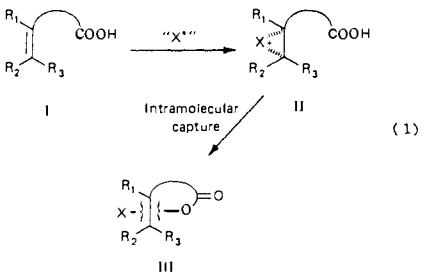
Abstract: Phenylselenolactonization and phenylsulfenolactonization, two new lactonization reactions, are described in detail. A series of unsaturated carboxylic acids was cyclized to phenylseleno- and phenylsulfenolactones by PhSeCl and PhSCl, respectively. These regio- and stereoselective ring closures are accompanied by the introduction into the organic structure of the synthetically useful PhSe and PhS groups and are, therefore, powerful synthetic methods. The phenylselenolactones so obtained are converted oxidatively with hydrogen peroxide and a variety of other oxidizing agents to unsaturated lactones and reductively to saturated lactones with Raney Ni or tri-*n*-butyltin hydride. The reversal of these cyclization reactions is effected with sodium in liquid ammonia. The mildness of the reactions described and their applicability to complex cases are demonstrated by the use of polyfunctional and sensitive substrates including prostanoid systems.

I. Introduction

Lactonization methodology plays an important role in modern organic synthetic chemistry not only because lactones occur in nature in great abundance and variety, but also because they constitute a particularly useful class of synthons. A major body of lactonizations involve the cyclization of open-chain hydroxy acids of which the most recent and elegant are the macrolide-forming reactions.[4] Another large category of lactonizations include those of unsaturated carboxylic acids (I) initiated by suitable electrophilic reagents. This latter class of ring closures, represented by eq 1 and proceeding by intramolecular capture of the reactive intermediate II, is a useful reaction in that not only does it form lactones (III) but also at the same time it offers selective functionalization of unsaturated substrates. In the past the initiation of these cyclizations of olefinic carboxylic acids has been carried out by acid,[5] lead tetraacetate,[6] mercuric reagents,[7] and halogens.[8] The most common and useful of these lactonizations, the halolactonization reaction, is a powerful process in organic synthesis for



(1)

regio- and stereoselective functionalization of olefinic bonds even in acyclic systems.[9a] Its application to the stereocontrolled construction of complex natural products has been amply demonstrated.[9b,c] However, the usual requirement for aqueous basic media and the rather drastic conditions required to convert the halolactones to useful synthetic intermediates impose severe limitations to the scope of this method. The use of the other aforementioned lactonization procedures is even less widespread owing to the drastic conditions of the reactions

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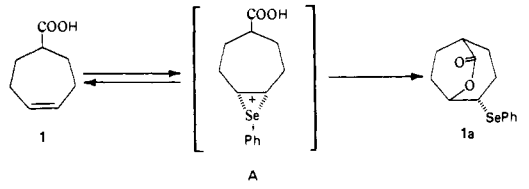
Scheme I. The Phenylselenolactonization Reaction



that are usually incompatible with a rather large number of important functionalities and protecting groups. In addition, the inability to elaborate the produced lactones to useful intermediates under acceptable conditions makes these conventional procedures even more limited.

The necessity for a milder lactonization procedure for unsaturated carboxylic acids coupled with the recent successful applications of organoselenium and sulfur reagents[10] in organic synthesis initiated by Sharpless[11] and Reich[12] prompted us to investigate these reagents in connection with the above problem. At the outset of our work, it was known that electrophilic selenium[13] and sulfur[14] reagents would add to double bonds in a trans fashion but in a nonregioselective manner. Our hope was to develop synthetically useful intramolecular reactions involving trapping of the initially formed episelenonium or episulfonium ion by internal nucleophiles strategically placed in positions of the molecule favoring ring closure. This type of reaction, although of great potential value in the synthesis of heterocycles, has escaped systematic investigation.[15]

In this paper we describe a new general method for internal lactonization of unsaturated carboxylic acids employing phenylselenenyl chloride (PhSeCl) or its sulfur counterpart, phenylsulfenyl chloride (PhSCl), which appears to be highly effective and can be carried out in organic media under very mild conditions and low temperatures. This discovery represents one of the most facile and mild lactonization procedures and introduces at the same time into the organic molecule the phenylselenenyl (PhSe) or the phenylsulfenyl (PhS) moieties, two highly desirable groups on account of their synthetically fertile chemistries.[10] This is the first of several important synthetic applications we have discovered of this facile type of organoselenium-induced ring closure.

II. Results and Discussion

The Phenylselenolactonization Reaction. The phenylselenolactonization of unsaturated carboxylic acids is exemplified in Scheme I by the reaction of 4-cycloheptene-1-carboxylic acid (**1**)[16] with PhSeCl in methylene chloride at −78 °C, to afford the phenylselenolactone **1a** in quantitative yield. This rapid reaction proceeds in the absence or presence of base such as triethylamine, pyridine, or solid potassium carbonate. The use of base, however, to remove the liberated hydrogen chloride is advisable in sensitive cases to avoid destruction of the products. A preformation of the carboxylate salt with the organic base is essential for optimum yields. The initial step of this facile ring closure is presumably the reversible electrophilic addition of the phenylselenononium ion[17] to the double bond of **1** to give intermediate A. The reactive positive center is then intercepted intramolecularly by the carboxylic group leading to the observed product, phenylselenolactone **1a**, with expulsion of hydrogen chloride. Based on the assumed S_N2-type mechanism of the intramolecular capture of the selenonium ion and by analogy to the halolactonization reaction, the stereochemistry of the phenylselenolactones was assumed to be trans. This assumption was confirmed by an X-ray diffraction analysis[18] carried out on the phenylselenolactone **8a** (vide infra) which showed, besides its six-membered-ring nature, the trans relationship of the phenylseleno group to the lactone functionality.

To show the generality of this method a series of unsaturated carboxylic acids was utilized for the cyclization reaction. As indicated in Table I good to excellent yields of phenylselenolactones were obtained. In general, the ring closure occurs at the carbon able to sustain the most stable carbonium ion, although subsequent rearrangement is possible to the thermodynamically most stable product. It appears that five-membered lactones are preferred over four- and six-membered and six- and seven- are preferred over seven- and eight-membered, respectively.

Table I. Phenylseleno- and Phenylsulfenolactonizations and Useful Transformation of the Products

Entry	Unsaturated acid	Reversal yield (percent)	Cyclization product	M.p (°C)	Yield (percent)	Oxidation product	Yield (percent)	Reduction product	Yield (percent)
1		82 80	 1a, X = SePh 1b, X = SPh	71-71.5 82-82.5	100 82	 1c	90	 1d	85,[a] 88[b]
2		77 79	 2a, X = SePh 2b, X = SPh	81-92 94-95	90 70	 2c	81 80	 2d	80[a]
3		78	 3a, X = SePh 3b, X = SPh	102.5-103.5 112.5-113	95 95			 3d	83,[a] 89[b] 85[a]
4			 4a, X = SePh 4b, X = SPh		83 86	 4c	92	 4d	76[a]
5			 5a		90				
6			 6a	113.5-114.5	98	 6c	82	4d	73[a]
7			 7a, X = SePh 7b, X = SPh	78.5-79	91 86	 7c	87	4d	84,[a] 85[b]
8			 8a	66-67	93	 8c	85	 8d[16]	86[b]
9			 9a		95	 9c	92	 8d	97[b]
10			 10a		35				
11			 11a	46-47.7	80				
12			 12a		75				
13			 13a		74				
14			14a		70				
15			15a		68			15d	80

[a] Reduction method A (Ra-Ni/H_2). [b] Reduction method B (*n*-Bu_3SnH).

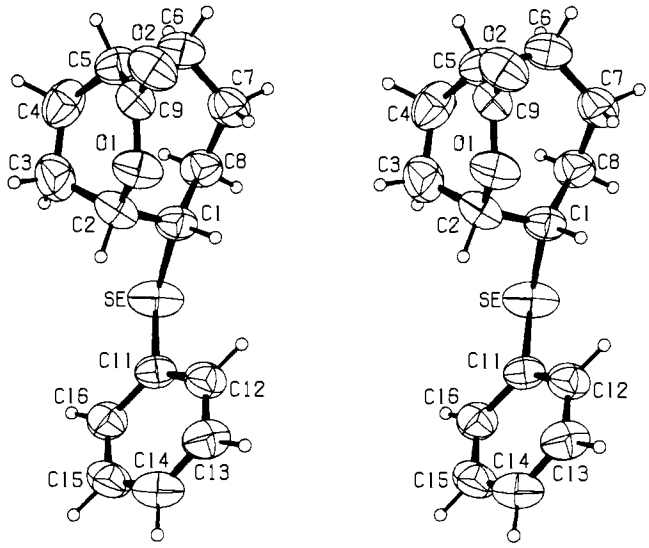
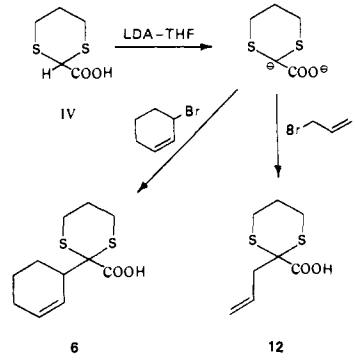


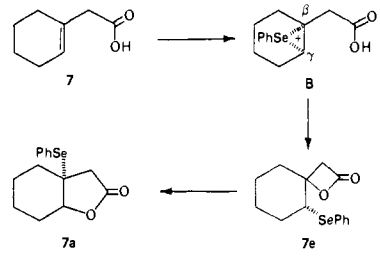
Figure 1. A stereoscopic structure of phenylselenolactone **8a**.

Most of the unsaturated acids employed were either obtained from commercial sources or prepared according to published procedures. The dithiane acids **6** and **12** were pre-



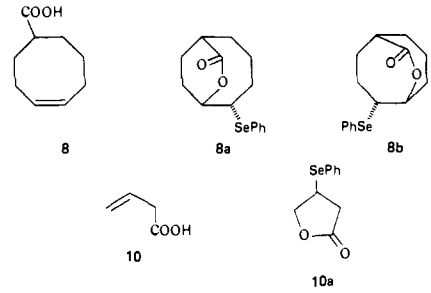
pared from the dianion (2.2 equiv of LDA, 0 → 25 °C, THF, 2 h) of the acid IV[19,20] and the corresponding bromide in 85 and 90% yields, respectively. The attachment of this useful two-carbon appendage by this method seems to be quite general and proceeds in high yield.[20] Alternatively the bromides were first coupled with dithiane and the products carboxylated (LDA-CO_2).

The high tendency to initially capture a tertiary carbonium ion (carbon β, intermediate B) and for the kinetic product to rearrange to a thermodynamically more stable lactone (**7e** → **7a**) was clearly seen in the phenylselenolactonization of the

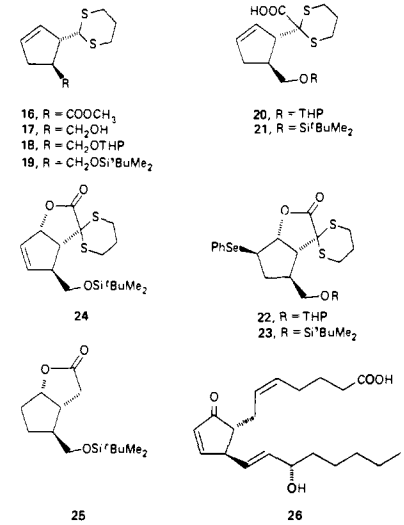


acid **7**. In this case the exclusive final product after chromatographic isolation on a silica column was the γ-lactone **7a** (IR ν_{max} 1765 cm^{-1}). However, careful IR analysis of the initially formed product revealed the β-lactone **7e** (IR ν_{max} 1820 cm^{-1}) as the sole substance. This material apparently rearranges rapidly to the thermodynamically more stable γ-lactone by silica gel or even by itself at ambient temperatures.

4-Cyclooctene-1-carboxylic acid (**8**)[16] on phenylselenolactonization at −78 °C produced a mixture of six- and seven-membered-ring lactones **8a** and **8b** observed by TLC and ^{1}H NMR (220 MHz, $CDCl_3$: **8a**, τ 5.27; **8b**, τ 5.50; **8a**:**8b** ca. 3:1) spectroscopy. On passage through a silica gel column, however, only one product, lactone **8a**, was obtained in 85% yield. An X-ray diffraction analysis of lactone **8a** established its bicyclo[4.2.2] nature. The stereoscopic structure of **8a** is shown in Figure 1.[18] The beneficial action of silica gel in converting rather cleanly the initially formed mixtures in these reactions to the thermodynamically stable product was also observed in the case of 3-buten-1-oic acid (**10**). Thus, initial TLC analysis revealed what was presumed to be simple addition of PhSeCl across the double bond, whereas chromatography on silica gel yielded lactone **10a**. Similar phenomena were observed with a number of other unsaturated acids.

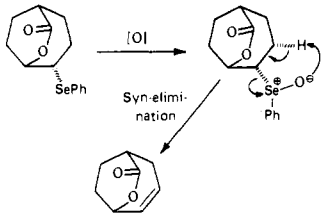


The application of this new selenium-based methodology for lactone formation in polyfunctional and sensitive cases and the illustration of its usefulness in natural product synthesis were shown by the following sequences that could eventually lead to prostaglandins. The readily available cyclopentene derivative **16**[17] was reduced to the alcohol **17** ($LiAlH_4$-ether, 97%) and protected as the tetrahydropyranyl (**18**, 100%) or

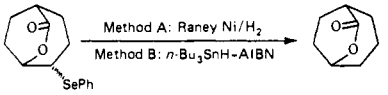


the *tert*-butyldimethylsilyl (**19**, 98%) ethers. Carboxylation (1. *n*-BuLi 2. CO_2) of **18** and **19** resulted in the high-yield formation of **20** (85%) and **21** (85%), respectively. Both of these highly functionalized acids underwent smooth phenylselenolactonization to afford their respective lactones **22** (90%) and **23** (92%). The survival of these important protecting groups, (tetrahydropyranyl, silyl, and dithiane) clearly demonstrates the wide scope and applicability of this method over the conventional halolactonization procedures. Oxidative (H_2O_2) removal of the phenylseleno group from **23** (vide infra) was achieved selectively with controlled amounts of H_2O_2 to afford the unsaturated lactone **24** in 86% yield. Raney Ni reduction of **23** (vide infra) resulted in the removal of both the phenylseleno and the dithiane groups giving rise to the saturated lactone **25**, a potential intermediate in the synthesis of prostaglandin A_2 (**26**).

Scheme II. Preparation of Unsaturated Lactones by Oxidative Elimination of the PhSe Group from Phenylselenolactones



Scheme III. Preparation of Saturated Lactones by Reductive Removal of the PhSe Group from Phenylselenolactones



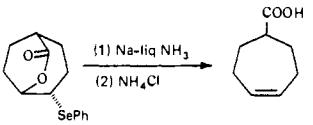
An excellent application of the described technology in a complex instance is the conversion of 6β-4-isoprostacyclin **15**[21] (Table I) to the novel phenylselenolactone **15a** (85%, diastereomeric mixture at C-4) and subsequently to the prostanoid **15b** (85% C-4 diastereoisomers) by reduction with tri-*n*-butyltin hydride in the presence of a radical initiator in toluene at 110 °C (vide infra).

Oxidative Removal of the Phenylseleno Group. The chemical fertility of the phenylseleno group was one of the important considerations for developing the phenylselenocyclization reactions. One of this group's most versatile and useful transformations is the formation of olefins by oxidation. The phenylselenolactones obtained from the cyclization reactions were converted to unsaturated lactones in good to excellent yields, (Scheme II, Table I). The majority of the oxidations were carried out using hydrogen peroxide in tetrahydrofuran (THF) or methylene chloride at 0–25 °C. To a lesser extent, ozone, chloramine T, or *m*-chloroperbenzoic acid were used. The selenoxides so obtained were allowed to decompose at ambient temperatures in the absence or presence of added base such as triethylamine or diisopropylamine. The use of base is recommended by Reich[22] to minimize undersirable side reactions in certain cases. The phenylseleno group in the presence of the dithiane moiety (examples **6a** and **23**) was selectively oxidized employing dilute hydrogen peroxide in THF at 0 °C.

In all cases examined, *the syn elimination of the resulting selenoxide occurred selectively away from the oxygen.* The strong directing effect of the oxygen on the syn elimination of the selenoxides could be due to the polar nature of this functionality which tends to align itself antiparallel to the oxygen lone electron pairs in order to minimize repulsion (Scheme II). This arrangement, first proposed by Trost[23] for sulfoxide syn eliminations, positions the selenoxide grouping favorably to eliminate away from the oxygen as observed. This selectivity is also observed in the case of cyclic ethers.[21,24]

Reductive Removal of the Phenylseleno Group. The ability of the phenylseleno group to be removed reductively from the phenylselenolactones is an important and attractive feature of this cyclization reaction for synthetic purposes since this operation leads to saturated lactones. Hydrogenolysis of the C–Se bond occurs rapidly with Raney Ni catalyst at ambient temperatures in THF, DME, or ether (method A, Scheme III).[25] Although this method for reducing off the PhSe group is generally efficient, it suffers from nonselectivity since it does not allow the survival of several other functionalities such as dithiane, unsaturation, and allylic oxygen. Furthermore, basic impurities remaining from the preparation of Raney Ni (which involves NaOH)[26] will damage the lactone and result in diminished yields if not carefully excluded. A milder and more selective method for removing the PhSe group consists of treatment with tri-*n*-butyltin hydride in toluene solution at 110 °C in the presence of traces of the radical initiator azobisisobutyronitrile (AIBN) (method B, Scheme III).[27] The reaction is presumed to proceed by a radical mechanism. Thus a tin radical attacks the selenium to give tri-*n*-butyltin phenylselenide and an alkyl radical which combines with a hydrogen radical to produce the observed saturated product.

Scheme IV. Reversal of the Phenylselenolactonization Reaction

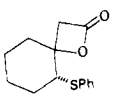


The mildness of this methodology and its applicability in complex and useful cases were demonstrated by the synthesis of the novel prostacyclin γ-lactone **15** (90%) from the phenylselenolactone **15a** and the use of 2 equiv of tri-*n*-butyltin hydride and 1% (by mole) of AIBN. Under similar conditions and in high yields 6α- and 6β-5,6-dihydroprostacyclins have also been prepared from the corresponding selenides.[27a,b] Furthermore, as pointed out by Clive,[27c] this tin hydride based procedure for the removal of the PhSe group could prove to be very valuable in deoxygenating organic molecules since both hydroxy and carbonyl compounds are easily converted to selenides.

Reversal of the Phenylselenolactonization Reaction. The scope and value of a synthetic operation are usually increased by the possibility of reversing it. Indeed, in certain instances, the reverse reaction becomes just as important and useful as the forward reaction itself. Although the reverse reaction concept is used extensively in retrosynthetic analysis, it is not always a feasible process. To enhance the power and utility of our selenium-induced ring closures we sought and found conditions for their reversal. Specifically the phenylselenolactonization reaction can be reversed by sodium in liquid ammonia to the unsaturated acids (Scheme IV).[28a] This reaction, exemplified in Scheme IV, proceeds rapidly at low (−78 to 33 °C) temperatures in very good yields. Several examples are shown in Table I. The mechanism of this ring-opening process presumably involves electron attack on the selenium resulting in radicals and radical anions followed by β-elimination of the carboxylate leading to the final products.

The Phenylsulfenolactonization Reaction. It was observed that phenylsulfenyl chloride (PhSCl) reacted with certain unsaturated carboxylic acids in a similar fashion to PhSeCl furnishing phenylsulfenolactones.[15a,28b] However, it was found that preformation of the carboxylate with triethylamine was necessary for this reaction to proceed in reasonable yields, whereas the phenylselenolactonization proceeds in the absence just as well as in the presence of base. In the sulfur case the simple adduct of PhSCl to the double bond[14] was observed in the absence of base. These adducts were usually obtained as mixtures of regio- and stereoisomers and were rather labile both thermally and solvolytically.

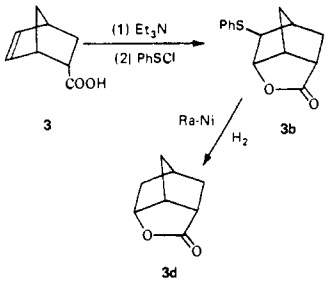
Under the proper conditions (1. Et_3N, CH_2Cl_2, 25 °C. 2. PhSCl, −78 °C), good yields of γ- and δ-phenylsulfenolactones (**1b–4b**) were obtained as shown in Table I and illustrated in Scheme V for the case of *endo*-norborn-5-enecarboxylic acid (**3**). We assume the mechanism of this cyclization reaction and the stereochemistry of the products to be similar to those of the phenylselenolactonization reaction discussed above. As in that case the β-lactone **4f** was observed by IR (ν_{max} 1820 cm^{-1}) as



4f

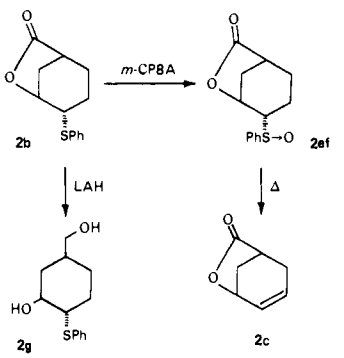
the kinetic product rearranging completely and spontaneously at room temperature or on silica gel to the thermodynamically

Scheme V. The Phenylsulfenolactonization Reaction



more stable γ-lactone **4b** (IR ν_{max} 1765 cm^{-1}). Owing to its numerous drawbacks as compared to the phenylselenolactonization, the phenylsulfenolactonization reaction was not pursued exhaustively. Among its disadvantages are the relative instability of PhSCl as compared to PhSeCl, the requirement of base, the generally less clean nature of the reaction, and relatively lower yields. In addition, the removal of the PhS group either reductively or oxidatively is generally more cumbersome than the manipulation of the PhSe group.

It was, however, demonstrated that phenylsulfenolactones could be quite useful intermediates. For instance, reductive removal of the phenylsulfeno group with Raney Ni[26] from **3b** furnished **3d** in 85% yield. Further, manipulations were demonstrated using the phenylsulfenolactone **2b**. Thus, reduction with $LiAlH_4$ in ether at 0 °C produced the diol **2g** (98%), mp 108.5–109 °C (ether), whereas oxidation with *m*-chloroperbenzoic acid (1.2 equiv) in CH_2Cl_2 at −78 → 25 °C furnished the sulfoxide **2ef**, mp 128–130 °C (mixture of diastereoisomers **2e**:**2f** (ca. 55:45) by ^1H NMR spectroscopy, 220 MHz, $CDCl_3$, τ 5.15, 5.22, CHO). Heating of **2ef** at reflux in toluene for 36 h yielded the unsaturated lactone **2c** in 80% yield. Termination of the pyrolysis after 10 h led to the isolation of pure **2e**, mp 154–155 °C (ether) (35%) as well as **2c** (50%).



The reversal of the phenylsulfenolactonization was realized under similar conditions to those described for its selenium counterpart, namely, excess sodium in liquid ammonia (Table I, examples **1** and **2**), leading to good yields of the starting unsaturated acids.

III. Conclusion

We have demonstrated that organoselenium and organosulfur reagents can be used effectively to induce lactonizations of unsaturated carboxylic acids in a regio- and stereocontrolled manner. Phenylselenolactonization is an extremely rapid and highly efficient cyclization process of unsaturated acids initiated by PhSeCl. Phenylsulfenolactonization, the corresponding reaction initiated by PhSCl, was also found to be a practical reaction. In general, the selenium-based methodology is superior to the sulfur-based method, being more convenient and efficient and leading to the usually crystalline phenylselenolactones, a class of easily manipulated intermediates.

The mildness of these cyclizations and their generality allowed the preparation of a series of phenylseleno- and phenylsulfenolactones which were utilized in a number of transformations leading to a variety of useful synthons. Thus, experimental conditions are reported for their conversion to (1) unsaturated lactones by oxidative removal of the PhSe and PhS groups, (2) saturated lactones by reductive removal of the PhSe and PhS groups, and (3) unsaturated acids (reversal) by Na–liquid NH_3. Most importantly our results demonstrate high efficiency coupled with compatibility of reaction conditions with a large array of functionalities including the tetrahydropyranyl, silyl, and dithiane protecting groups and the important hydroxyl and olefinic moieties.

The usefulness of the phenylselenolactonization technology was demonstrated by the preparation of advanced intermediates for prostaglandin synthesis and the construction of complex molecules in the prostacyclin series. It is envisioned that further and useful applications in complex sequences, particularly in advanced and sensitive cases, will be found.

Experimental Section

General. Melting points were recorded on a Thomas-Hoover Unimelt apparatus and are uncorrected. ^1H 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., or 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, or 2 mm × 20 cm^{-1} × 20 cm^{-1} 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.

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. The abbreviation Me_3Si is used for the trimethylsilyl group.

All yields refer to chromatographically and spectroscopically (^1H NMR) homogeneous materials.

Phenylselenolactonization. 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), pyridine (method C), or anhydrous potassium carbonate (method D). In methods B and C the acid was first stirred with the base (1.10 mmol) at 25 °C before cooling to −78 °C and adding the PhSeCl. In method D powdered anhydrous potassium carbonate (2 mmol) was added just prior to the addition of PhSeCl. The phenylselenolactones were isolated after allowing the reaction mixture to reach room temperature, concentrating, and chromatographing on silica gel (columns or plates). The procedure is exemplified by the preparation of (1α,4α,5α)-4-(phenylseleno)-6-oxabicyclo[3.2.2]nonan-7-one described below.

(1α,4α,5α)-4-(Phenylseleno)-6-oxabicyclo[3.2.2]nonan-7-one (1a). Method A. To a magnetically stirred solution of 4-cycloheptene-1-carboxylic acid **1**,[16] 140 mg, 1.0 mmol) in dry methylene chloride (5 mL) under argon at −78 °C was added solid PhSeCl (212 mg, 1.1 mmol) and the mixture stirred at that temperature. The completion of the reaction was signaled by the complete dissolution of the red-orange PhSeCl and was confirmed by TLC. The pale yellow solution was then allowed to reach room temperature, concentrated, and

chromatographed on a silica gel-methylene chloride column. The product was obtained after the elution of trace amounts of diphenyl diselenide. Removal of the solvent from the appropriate fractions furnished 293 mg (100%) of the phenylselenolactone as a pale yellow oil crystallizing on standing. Recrystallization from hexane-ether (3:1) gave analytically pure (1α,4α,5α)-4-(phenylseleno)-6-oxabicyclo[3.2.2]nonan-7-one (**1a**) as colorless crystals.

Methods B and C. In these methods the acid **1** (140 mg, 1.0 mmol) was stirred at 25 °C in dry methylene chloride (5 mL) at 25 °C with (method B) triethylamine (1.11 mg, 1.1 mmol) or (method C) pyridine (86 mg, 1.1 mmol) for 30 min prior to cooling to −78 °C and continuing as in method A. In both cases the yield of **1a** was quantitative.

Method D. This method was exactly the same as method A except that powdered anhydrous potassium carbonate (276 mg, 2 mmol) was added to the reaction mixture prior to the addition of PhSeCl. The yield of product (**1a**) was 100%.

Properties and Spectral Data of Phenylselenolactones. 1a (100%): colorless, crystalline solid, mp 71-71.5 °C (hexane-ether); R_f 0.19 (silica, CH_2Cl_2); IR (KBr) ν_{max} 2940, 2850, 1735 (δ-lactone), 1575, 1470, 1440, 1430,1375,1345, 1310, 1245, 1220, 1192, 1170, 1138, 1116, 1070, 1055, 1020, 987, 950, 932, 865, 823, 770, 745, 692, 665 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) τ 2.35 (m, 2 H, aromatic), 2.55 (m, 3 H, aromatic), 5.33 (m, 1 H, CHO), 6.37 (m, 1 H, CHSe), 7.14 (m, 1 H, CHCO), 7.66-8.24 (m, 8 H, CH_2); mass spectrum *m/e* (rel intensity) 296 ($^{80}Se - M^+$, 26), 158 ($PhSeH^+$, 13), 139 ($M^+ - PhSe$, 13.5), 111 (17), 110 (15.5), 95 (base peak). Anal. ($C_{14}H_{16}O_2Se$) C, H, Se.

2a (method B, 90%): colorless, crystalline solid, mp 91-92 °C (ether-petroleum ether); R_f 0.34 (silica, CH_2Cl_2); IR (KBr) ν_{max} 2940, 2840, 1765 (γ-lactone), 1575, 1478, 1435, 1348, 1320, 1270, 1195, 1155, 1130, 1070, 1012, 1000, 958, 906, 837, 752, 733, 708, 688, 665 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) τ 2.50 (m, 2 H, aromatic), 2.74 (m, 3 H, aromatic), 5.22 (m, 1 H, CHO), 6.36 (t, J = 5 Hz, 1 H, CHSe), 7.35 (m, 1 H, CHCO), 7.60-8.20 (m, 6 H, CH_2); mass spectrum *m/e* (rel intensity) 282 ($^{80}Se - M^+$, 26), 158 ($PhSeH^+$, 9), 125 ($M^+ - PhSe$, 18), 97 (17), 81 (base peak). Anal. ($C_{13}H_{14}O_2Se$) C, H, Se.

3a (method B, 95%): colorless, crystalline solid, mp 102.5-103.5 °C (ether-petroleum ether); R_f 0.33 (silica, CH_2Cl_2); IR (KBr) ν_{max} 2940, 1765 (γ-lactone), 1560, 1475, 1430, 1335, 1300, 1275, 1240, 1178, 1155, 1100, 1060, 1000, 970, 938, 895, 888, 876, 842, 735, 722, 688, 680, 665 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) τ 2.33 (m, 2 H, aromatic), 2.53 (m, 3 H, aromatic) 5.15 (d, J = 6 Hz, 1 H, CHO), 6.61 (d, J = 2.5 Hz, 1 H), 6.69 (m, 1 H), 7.40 (m, 2 H), 7.82 (m, 2 H), 8.18 (d, J = 14 Hz, 1 H), 8.30 (d, J = 11 Hz, 1 H); mass spectrum *m/e* (rel intensity) 294 ($^{80}Se - M^+$, 13), 158 ($PhSeH^+$, 15), 137 ($M^+ - PhSe$, 29), 116 (11), 93 (92), 91 (57), 79 (base peak). Anal. ($C_{14}H_{14}O_2Se$) C, H, Se.

6a (method B, 98%): colorless crystals, mp 113.5-114.5 °C (ether-petroleum ether); R_f 0.50 (silica, CH_2Cl_2); IR (liquid film) ν_{max} 2940, 1765 (γ-lactone), 1572, 1475, 1430, 1215, 1202, 1172, 1120, 1024, 980, 940, 740, 690 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) τ 2.40 (m, 2 H, aromatic), 2.68 (m, 3 H, aromatic), 5.16 (dd, J = 4, 4 Hz, 1 H, CHO), 6.13 (t, J = 15 Hz, 1 H, CH_2S), 6.21 (m, 1 H, CHSe), 6.73 (t, J = 13 Hz, 1 H, CH_2S), 7.20-8.60 (m, 11 H, CH_2, CH_2S, CH); mass spectrum *m/e* (rel intensity) 400 ($^{80}Se - M^+$, 6.5), 262 ($M - PhSeH^+$, 5.5), 199 (base peak). Anal. ($C_{17}H_{20}S_2SeO_2$) C, H, S, Se.

7a (method B, 91%): colorless crystals, mp 78.5-79 °C (ether-petroleum ether); R_f 0.31 (silica, CH_2Cl_2); IR (KBr) ν_{max} 2935, 2850, 1765 (γ-lactone), 1435, 1350, 1320, 1245, 1205, 1100, 1065, 1020, 992, 946, 925, 890, 853, 800, 745, 712, 692 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) τ 2.45 (m, 2 H, aromatic), 2.65 (m, 3 H, aromatic), 5.67 (bs, 1 H, CHO), 7.32 (d, J = 17 Hz, 1 H, CH_2CO), 7.54 (d, J = 17 Hz, 1 H, CH_2CO), 7.90-8.60 (m, 8 H, CH_2); mass spectrum *m/e* (rel intensity) 296 ($^{80}Se - M^+$, 8), 158 ($PhSeH^+$, 13), 139 ($M^+ - PhSe$, base peak), 121 (38). Anal. ($C_{14}H_{16}O_2Se$) C, H, Se.

8a (method B, 94%): colorless crystals, mp 67-69 °C (ether); R_f 0.61 (silica, 5% methanol in ether); IR (CCl_4) ν_{max} 3003, 2907, 2817, 1751 (δ-lactone), 1595, 1484, 1445, 1395, 1258, 1242, 1193, 1117, 1066, 1034, 943, 880, 690 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) τ 2.60 (m, 2 H, aromatic), 2.83 (m, 3 H, aromatic), 5.27 (m, 1 H, CHO), 6.30 (m, 1 H, CHSe), 7.03 (m, 1 H, CHCO), 7.81 (m, 4 H, CH_2), 8.11 (m, 4 H, CH_2), 8.33 (m, 1 H, CH_2), 8.47 (m, 1 H, CH_2); mass spectrum *m/e* (rel intensity) 310 ($^{80}Se - M^+$, 33), 158 ($PhSeH^+$, 19), 157 (23), 153 ($M^+ - PhSe$, 22), 135 (18), 125 (17), 109 (38), 107 (56), 97 (23), 91 (22), 81 (69), 79 (60), 77 (44), 67 (83), 55 (base peak). Anal. ($C_{15}H_{18}O_2Se$) C, H, Se.

9a (method A, 95%): pale yellow oil, R_f 0.37 (silica, CH_2Cl_2); IR (liquid film) ν_{max} 3057, 2985, 1770 (γ-lactone), 1563, 1471, 1429, 1312, 1295, 1163, 1002, 971, 951, 876, 738, 690, 667 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) τ 2.45 (m, 2 H, aromatic), 2.70 (m, 3 H, aromatic), 5.15 (d, J = 7 Hz, 1 H, CHO), 6.15 (m, 1 H, CHSe), 7.00 (m, 1 H), 7.28 (dd, J = 17, 10 Hz), 7.80 (m, 3 H), 8.23 (m, 1 H), 8.50 (m, 1 H); mass spectrum *m/e* (rel intensity) 282 ($^{80}Se - M^+$, 73), 158 ($PhSeH^+$, base peak), 125 ($M^+ - PhSe$, 25), 107 (38). Anal. ($C_{13}H_{14}O_2Se$) C, H, Se.

10a (method A, isolated after passage through a silica-CH_2Cl_2 column, 36%): pale yellow oil, R_f 0.26 (CH_2Cl_2); IR (CCl_4) ν_{max} 3067, 2985, 2890, 1786 (γ-lactone), 1582, 1477, 1439, 1418, 1366, 1299, 1258, 1176, 1087, 1071, 1020, 943, 901, 842, 732, 694, 674 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) τ 2.43 (m, 2 H, aromatic), 2.60 (m, 3 H, aromatic), 5.41 (dd, J = 7, 12 Hz, 1 H, CHO), 5.75 (dd, J = 7, 12 Hz, 1 H, CHO), 6.03 (m, 1 H, CHSe), 7.08 (dd, J = 7, 18 Hz, 1 H, CHCO), 7.46 (dd, J = 7, 18 Hz, 1 H, CHCO); mass spectrum *m/e* (rel intensity) 242 ($^{80}Se - M^+$, 74), 183 (9), 85 (96), 78 (100). Anal. ($C_{10}H_{10}O_2Se$) C, H.

22 (method B, 90%): pale yellow oil, R_f 0.41 (silica, CH_2Cl_2); IR (liquid film) ν_{max} 2920, 2840, 1765 (γ-lactone), 1577, 1476, 1440, 1260, 1160, 1125, 1065, 1015, 982, 735, 687, 665 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) τ 2.43 (m, 2 H, aromatic), 2.67 (m, 3 H, aromatic), 4.97 (m, 1 H, OCHO), 5.35 (m, 1 H, CHO), 5.95-6.76 (m, 7 H, CH_2O, CH_2S, CHSe), 7.12-8.52 (m, 15 H, CH_2, CH_2S, CH); mass spectrum *m/e* (rel intensity) 286 (16), 263 (21), 184 (31), 157 (14), 149 (base peak), 133 (12), 129 (19), 104 (19), 91 (12), 85 (16), 77 (40). Anal. ($C_{22}H_{28}O_4S_2Se$) C, H.

23 (method B, 92%): colorless crystals, mp 96.5-97 °C (ether-petroleum ether); R_f 0.65 (silica, CH_2Cl_2); IR (liquid film) ν_{max} 2940, 2920, 2850, 1765 (γ-lactone), 1570, 1475, 1438, 1250, 1170, 1140, 1110, 1025, 995, 945, 838, 778, 740, 690, 665 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) τ 2.54 (m, 2 H, aromatic), 2.77 (m, 3 H, aromatic), 5.07 (dd, J = 10, 3 Hz, 1 H, CHO), 6.09 (t, J = 17 Hz, 1 H, CH_2S), 6.29 (m, 1 H, CHSe), 6.29 (dd, J = 10, 3 Hz, 1 H, CH_2O), 6.41 (dd, J = 10, 6 Hz, 1 H, CH_2O), 6.75 (t, J = 17 Hz, 1 H, CH_2S), 7.22-8.28 (m, 7 H, CH_2, CH_2S, CH), 9.10 (s, 9 H, $SiC(CH_3)_3$), 9.92 and 9.93 (singlets, 3 H each, $Si(CH_3)_2$); mass spectrum *m/e* (rel intensity) 473 ($^{80}Se - M^+ - t$-Bu, 46), 471 (23), 316 ($M^+ - PhSe - t$-Bu), 288 (11), 271 (13), 241 (9), 210 (10), 197 (28), 186 (23), 185 (10), 183 (20), 167 (11), 158 (19), 137 (12), 123 (15), 121 (11), 119 (17), 109 (11), 106 (12.5), 105 (11), 91 (29), 89 (16), 79 (20), 78 (42), 77 (32), 75 (82.5), 73 (base peak). Anal. ($C_{23}H_{34}O_3S_2SeSi$) C, H, S, Se.

Oxidative Removal of the Phenylseleno Group. General Procedure. All reactions indicated in Table I were carried out on 1-mmol scale in THF using hydrogen peroxide as oxidant (method A). The successful use of other oxidants [ozone (method B), *m*-chloroperbenzoic acid (method C), and chloramine T (method D)] was demonstrated in the preparation of 6-oxabicyclo[3.2.2]non-3-en-7-one (**1c**). These procedures are exemplified below in the preparation of **1c**.

6-Oxabicyclo[3.2.2]non-3-en-7-one (1c). Method A (H_2O_2). A stirred solution of (1α,4α,5α)-4-(phenylseleno)-6-oxabicyclo[3.2.2]-nonan-7-one (**1b**, 295 mg, 1 mmol) in freshly distilled tetrahydrofuran (5 mL) was treated dropwise at 0 °C with a 3% tetrahydrofuran solution of H_2O_2 (made from 30% commercial H_2O_2) (275 μL, 1.5 mmol). The reaction mixture was allowed to reach room temperature and stirred for 15 h before dilution with ether (20 mL) and washing with water (2 × 5 mL) and saturated sodium chloride solution (5 mL). After drying ($MgSO_4$) and removal of the solvents the product was isolated by column chromatography (silica, CH_2Cl_2). 6-Oxabicyclo[3.2.2]non-3-en-7-one (**1c**) was obtained as an oil which slowly crystallized on standing (112 mg, 80%). An analytical sample was obtained by recrystallization from pentane.

Method B (O_3). Ozone was passed through a cold (−78 °C) solution of the selenide **1b** (295 mg, 1 mmol) in CH_2Cl_2 (25 mL) until a blue color persisted. The excess ozone was expelled with a stream of oxygen and the solution treated with diisopropylamine (101 mg, 1 mmol) and allowed to reach room temperature. After stirring at 25 °C for 15 h the product was isolated as in method A described above. Obtained was 6-oxabicyclo[3.2.2]non-3-en-7-one (**1c**, 135 mg, 95%).

Method C (*m*-CPBA). A magnetically stirred methylene chloride solution (10 mL) of the selenide **1b** (295 mg, 1 mmol) under argon was cooled to −20 °C and treated with *m*-chloroperbenzoic acid (237 mg,

80%, 1.1 mmol, in 5 mL of methylene chloride). The reaction mixture was stirred at −20 °C for 20 min and then allowed to reach room temperature, stirred for 10 min, and treated with diisopropylamine (202 mg, 2 mmol). After stirring at 25 °C for 15 h the solvent was removed and the product isolated by column chromatography as in method A. Obtained was 6-oxabicyclo[3.2.2]non-3-en-7-one (**1c**, 121 mg, 88%).

Method D (Chloramine T). A solution of the selenide **1b** (295 mg, 1 mmol) in freshly distilled THF (25 mL) was treated under argon with anhydrous chloramine T (341 mg, 1.5 mmol) and refluxed for 2 h. After cooling to room temperature the mixture was concentrated to one-fifth of its volume, diluted with ether (25 mL), and treated as in method A to furnish 6-oxabicyclo[3.2.2]non-3-en-7-one (**1c**, 105 mg, 75%).

Properties of Unsaturated Lactones. 1c: colorless crystals, mp 42-43 °C (pentane); R_f 0.19 (silica, CH_2Cl_2); IR (liquid film) ν_{max} 3033, 2924, 2874, 1724 (δ-lactone), 1433, 1377, 1362, 1305, 1225, 1139, 1053, 1033, 1012, 974, 960, 935, 922, 866, 855, 746, 719, 497 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) τ 3.90 (m, 1 H, olefin), 4.15 (m, 1 H, olefin), 5.19 (m, 1 H, CHO), 7.04 (m, 1 H, CHCO), 7.23-8.50 (m, 6 H, CH_2); mass spectrum *m/e* (rel intensity) 138 (M^+, 6), 110 (43), 94 (20), 91 (14), 82 (26), 81 (37), 79 (base peak). Anal. ($C_8H_{10}O_2$) C, H.

2c (method A, 81%): identical with previously reported compound;[29] ^1H NMR (220 MHz, $CDCl_3$) τ 3.75 (m, 1 H, olefin), 4.13 (m, 1 H, olefin), 5.22 (t, *J* = 6 Hz, 1 H, CHO), 7.08 (m, 1 H, CHCO), 7.50 (d, *J* = 12 Hz, 1 H), 7.50 (m, 2 H), 7.90 (d, *J* = 12 Hz, 1 H).

4c (method A, 92%): identical with previously reported compound;[30] ^1H NMR (220 MHz, $CDCl_3$) τ 3.80 (m, 1 H, olefin), 4.09 (m, 1 H, olefin), 5.16 (m, 1 H, CHO), 7.15-8.63 (m, 7 H).

6c (method A, 82%): colorless, crystalline solid, mp 117-118 °C; R_f 0.50 (silica, ether-petroleum ether, 1:1); IR ($CHCl_3$) ν_{max} 3030, 2950, 2857, 1770 (γ-lactone), 1463, 1445, 1439, 1425, 1404, 1377, 1355, 1333, 1314, 1290, 1238, 1183, 1176, 1157, 1089, 1050, 1013, 976, 957, 935, 912, 890, 877, 858, 819, 707, 660 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) τ 3.70 (m, 1 H, olefin), 4.00 (m, 1 H, olefin), 4.94 (m, 1 H, CHO), 5.94 (dt, *J* = 14, 3 Hz, 1 H, CHS), 6.63 (dt, *J* = 14, 3 Hz, 1 H, CHS), 7.20-8.70 (m, 9 H); mass spectrum *m/e* (rel intensity) 242 ($^{32}S - M^+$, 25), 198 ($M - CO_2$, 81), 145 (11), 124 (56), 123 (54), 119 (24), 106 (22), 91 (base peak). Anal. ($C_{11}H_{14}O_2S_2$) C, H.

8c (method A, 85%): colorless oil, R_f 0.17 (silica, CH_2Cl_2); IR (liquid film) ν_{max} 3021, 2941, 2865, 1745, 1468, 1393, 1319, 1253, 1238, 1198, 1159, 1091, 1057, 1010, 936, 895, 797, 752, 719, 699 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) τ 4.12 (m, 1 H, olefin), 4.62 (m, 1 H, olefin), 5.00 (m, 1 H, CHO), 6.95 (m, 1 H, CHCO), 7.60-8.35 (m, 8 H, CH_2); mass spectrum *m/e* (rel intensity) 152 (M^+, 5), 107 ($M - CO_2H$, 20), 96 (21), 95 (22), 93 (25), 80 (base peak). Anal ($C_9H_{12}O_2$) C, H.

7c (method A, 87%): identical with previously reported compound;[31] ^1H NMR (220 MHz, $CDCl_3$) τ 4.21 (s, 1 H, olefin), 5.73 (dd, *J* = 11, 6 Hz, 1 H, CHO), 7.08 (d, *J* = 14 Hz, 1 H), 7.43 (m, 1 H), 7.66 (dt, *J* = 14, 6 Hz, 1 H), 8.00 (m, 2 H), 8.60 (m, 3 H).

9c (method A, 92%): identical with previously reported compound;[32] ^1H NMR (60 MHz, $CDCl_3$) τ 3.90 (m, 1 H, olefin), 4.12 (m, 1 H, olefin), 4.48 (m, 1 H, CHO), 6.70-7.93 (m, 5 H).

24 (method A, 86%): pale yellow oil, R_f 0.52 (silica, CH_2Cl_2); IR (liquid film) ν_{max} 2924, 2882, 2817, 2849, 1770 (γ-lactone), 1471, 1408, 1385, 1361, 1332, 1314, 1282, 1258, 1161, 1105, 1106, 1020, 976, 954, 897, 903, 823, 816, 763, 671 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) τ 3.89 (d, *J* = 5.5 Hz, 1 H, olefin), 4.10 (m, 1 H, olefin), 4.62 (d, *J* = 6 Hz, 1 H, CHO), 5.93-6.68 (m, 5 H, CHO, CHS, CH), 7.38 (m, 3 H), 7.82 (d, *J* = 14 Hz, 1 H), 8.10 (t, *J* = 14 Hz, 1 H), 9.12 (s, 9 H, Si-*t*-Bu), 9.94 and 9.96 (singlets, 3 H each, $SiCH_3$); mass spectrum *m/e* (rel intensity) 315 ($M^+ - t$-Bu, 59), 285 (16), 271 (14), 211 (10), 197 (20), 195 (32), 183 (62), 181 (16), 179 (11), 169 (13), 163 (11), 149 (13), 139 (22), 135 (17), 123 (16), 121 (25), 106 (10), 84 (base peak). Anal. ($C_{17}H_{28}O_3S_2Si$) C, H.

Reductive Removal of the Phenylseleno Group. General Procedure. All reactions indicated in Table I were carried out on 1-mmol scale except for **15a** → **15d**, which was performed on 0.1 mmol. Raney Ni (method A) prepared according to Fieser and Fieser[26] or tri-*n*-butyltin hydride (method B) were used to effect the reduction. These two methods are exemplified below for the preparation of 6-oxabicyclo[3.2.2]nonan-7-one (**1d**).

6-Oxabicyclo[3.2.2]nonan-7-one (1d). Method A (Raney Ni). To a freshly prepared suspension of neutral Raney Ni (from 3 g of 50% Raney Ni alloy)[26] in THF (20 mL) at 25 °C was added under argon the phenylselenolactone **1a** (295 mg, 1 mmol) in THF solution (5 mL). The mixture was stirred at room temperature for 1 h (or refluxed for 15 min), at which time TLC (silica, CH_2Cl_2) indicated completion of the reaction. The Raney Ni was removed by filtration and washed thoroughly with THF. Removal of the solvent followed by column chromatography (silica, CH_2Cl_2) furnished 6-oxabicyclo[3.2.2]-nonan-7-one (**1d**, 119 mg, 85%) as an oil crystallizing on standing.

Method B (*n*-Bu_3SnH). A solution of the phenylselenolactone **1b** (295 mg, 1 mmol) in freshly distilled toluene (5 mL) was mixed with tri-*n*-butyltin hydride (582 mg, 390 μL, 2 mmol) and 0.02 M toluene solution of azobisisobutyronitrile (AIBN, 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. Removal of the solvent and column chromatography of the residue (silica, CH_2Cl_2) afforded pure 6-oxabicyclo[3.2.2]nonan-7-one (**1d**, 123 mg, 88%) as an oil crystallizing on standing.

Properties of Saturated Lactones. 1d (method A, 85%; Method B, 88%): colorless crystals, mp 149.0-150.5 °C (pentane); R_f 0.29 (silica, CH_2Cl_2); IR (CCl_4) ν_{max} 2941, 2857, 1745 (δ-lactone), 1458, 1451, 1445, 1431, 1381, 1348, 1321, 1305, 1267, 1250, 1218, 1202, 1189, 1149, 1106, 1055, 1029, 1005, 954, 939, 904, 851, 835 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) τ 5.28 (m, 1 H, CHO), 7.16 (m, 1 H, CHCO), 7.73-8.64 (m, 10 H, CH_2); mass spectrum *m/e* (rel intensity) 140 (M^+, 5), 97 (13), 96 (13), 84 (75), 83 (19), 81 (68), 69 (12), 68 (70), 67 (75), 66 (11), 56 (21), 55 (base peak), 54 (79), 53 (19). Anal. ($C_8H_{12}O_2$) C, H.

2d (method A, 80%): identical with the previously reported compound;[33] ^1H NMR ($CDCl_3$) τ 5.17 (t, *J* = 7 Hz, 1 H, CHO), 7.35 (m, 1 H, CHCO), 7.58 (m, 1 H, CH_2), 7.90-8.50 (m, 7 H, CH_2).

3d (method A, 83%; method B, 89%): colorless crystals, mp 154-155 °C (lit. mp 154.2-155.2,[34a] 157-158 °C[34b,c]), identical with the previously reported compound;[34] ^1H NMR (220 MHz, $CDCl_3$) τ 5.21 (dd, *J* = 10, 5 Hz, 1 H, CHO), 6.80 (m, 1 H, CHCO), 7.47 (dd, *J* = 11, 5 Hz, 1 H), 7.44 (bs, 1 H), 8.03 (m, 1 H), 8.20-8.55 (m, 5 H).

4d (from **4a**, method A, 76%; from **6a**, method A, 73%; from **7a**, method A, 84%; from **7a**, method B, 85%): identical with the previously reported compound;[35] ^1H NMR (220 MHz, $CDCl_3$) τ 5.45 (dd, *J* = 7, 5 Hz, 1 H, CHO), 7.36 (dd, *J* = 10, 6 Hz, 1 H), 7.59 (m, 1 H), 7.71 (dd, *J* = 16, 3 Hz, 1 H), 7.90 (dd, *J* = 15, 4 Hz), 8.1-8.8 (m, 7 H, CH_2)

Phenylsulfenolactonization. General Procedure. All phenylsulfenolactonizations were carried out on 1-mmol scale. The unsaturated carboxylic acid (1 mmol) was stirred with freshly distilled (CaH_2) triethylamine (111 mg, 154 μL, 1.1 mmol) in dry methylene chloride (5 mL) at 25 °C under argon for 30 min. The solution was cooled to −78 °C and treated dropwise while stirring with a solution of PhSCl in methylene chloride (2% w/v, 10 mL, 200 mg, 1.4 mmol) over a period of 10 min. The mixture was then allowed to reach room temperature, concentrated to 1-2 mL, and chromatographed on a silica gel-CH_2Cl_2 column to afford the following phenylsulfenolactones.

1b (82%): colorless crystals, mp 82-82.5 °C (ether-petroleum ether); R_f 0.26 (silica, CH_2Cl_2); IR (CCl_4) ν_{max} 3077, 2959, 2882, 1750 (δ-lactone), 1587, 1490, 1451, 1443, 1383, 1353, 1314, 1225, 1149, 1062, 1036, 951, 935, 873, 727, 692 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) τ 2.67 (m, 5 H, aromatic), 5.49 (d, *J* = 5 Hz, 1 H, CHO), 6.46 (dd, *J* = 13, 5 Hz, 1 H, CHS), 7.16 (m, 1 H, CHCO), 8.0 (m, 8 H, CH_2); mass spectrum *m/e* (rel intensity) 248 ($^{32}S - M^+$, 72), 136 (base peak), 135 (55), 110 (38), 109 (18), 95 (21). Anal. ($C_{14}H_{16}O_2S$) C, H, S.

2b (70%): colorless crystals, mp 94-95 °C (ether-petroleum ether); R_f 0.32 (silica, CH_2Cl_2); IR (CCl_4) ν_{max} 3096, 3021, 2703, 2882, 1776, (γ-lactone), 1585, 1486, 1464, 1453, 1361, 1332, 1277, 1215, 1193, 1172, 1142, 1081, 1053, 1029, 1017, 1010, 976, 909, 893, 858, 844, 718, 702, 691 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) τ 2.60 (m, 2 H, aromatic), 2.69 (m, 3 H, aromatic), 5.24 (m, 1 H, CHO), 6.32 (m, 1 H, CHS), 7.33 (m, 1 H), 7.54 (d, *J* = 11 Hz, 1 H), 7.75 (m, 2 H), 8.05 (m, 3 H); mass spectrum *m/e* (rel intensity) 234 ($^{32}S - M^+$, base peak), 136 (95), 124 ($M^+ - PhSH$, 28), 110 (51), 91 (26), 79 (47). Anal. ($C_{13}H_{14}SO_2$) C, H, S.

3b (95%): colorless crystals, mp 112.5-113 °C (hexane); R_f 0.29 (silica, CH_2Cl_2); IR ($CHCl_3$) ν_{max} 3077, 2985, 2882, 1770 (γ-lactone), 1587, 1493, 1449, 1443, 1348, 1312, 1285, 1250, 1188, 1174, 1152, 1133, 1105, 1066, 1014, 1000, 973, 936, 905, 891, 800, 690 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) τ 2.71 (m, 5 H, aromatic), 5.44 (d, *J* = 5 Hz, 1 H, CHO), 6.72 (d, *J* = 3 Hz, 1 H, CHS), 6.77 (m, 1

H, CHCO), 7.42 (dd, J = 11, 5 Hz, 1 H), 7.52 (s, 1 H), 7.80 (d, J = 12 Hz, 1 H), 7.89 (ddd, J = 14, 11, 4 Hz, 1 H), 8.20 (d, J = 14 Hz, 1 H), 8.37 (d, J = 12 Hz, 1 H); mass spectrum m/e (rel intensity) 246 ($^{32}S - M^+$, base peak), 149 (56), 136 ($M^+ - PhSH$, 24), 123 (22), 116 (21), 109 (55). Anal. ($C_{14}H_{14}SO_2$) C, H, S.

4b (71%): pale yellow oil, R_f 0.25 (silica, CH_2Cl_2); IR (CCl_4) ν_{max} 3012, 2941, 2857, 1776 (γ-lactone), 1575, 1471, 1435, 1333, 1282, 1224, 1170, 1136, 1087, 1010, 974, 943, 892, 852, 741, 687 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) τ 2.65 (m, 5 H, aromatic), 5.62 (m, 1 H, CHO), 6.85 (m, 1 H, CHS), 7.28 (m, 1 H, CH), 7.42 (dd, J = 17, 7 Hz, 1 H, CHCO), 7.75 (dd, J = 17, 3 Hz, 1 H, CHCO), 7.85-8.85 (m, 6 H, CH_2); mass spectrum m/e (rel intensity) 248 ($^{32}S - M^+$, 60), 138 ($M^+ - PhSH$, 43), 121 (18), 110 (base peak), 93 (22). Anal. ($C_{14}H_{16}O_2S$) C, H.

7b (86%): colorless crystals, mp 84–85 °C (ether-petroleum ether); R_f 0.36 (silica, CH_2Cl_2); IR (KBr) ν_{max} 2941, 2857, 1770 (γ-lactone), 1471, 1439, 1418, 1351, 1316, 1269, 1239, 1205, 1160, 1147, 1124, 1105, 1085, 1066, 1017, 992, 962, 948, 929, 891, 855, 806, 754, 718, 707, 692 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) τ 2.58 (m, 5 H, aromatic), 5.72 (m, 1 H, CHO), 7.40 (d, 1 H, J = 16 Hz, CHCO), 7.57 (d, 1 H, J = 16 Hz, CHCO), 8.10-8.60 (m, 6 H); mass spectrum m/e (rel intensity) 248 ($^{32}S - M^+$, 18), 139 (base peak, $M^+ - PhS$), 121 (34), 110 (47), 93 (19). Anal. ($C_{14}H_{16}O_2S$) C, H.

Oxidation of the Phenylsulfenolactone 2b to the Sulfoxides 2ef. The phenylsulfenolactone **2b** (234 mg, 1 mmol) was dissolved in dry methylene chloride (20 mL) and cooled to −78 °C under argon. A solution of m-chloroperbenzoic acid (203 mg, 85%, 1 mmol) in dry methylene chloride (10 mL) was added dropwise with magnetic stirring and the reaction mixture was stirred at −78 °C for 15 min before being poured into a separating funnel containing ether (50 mL) and 10% $NaHCO_3$ solution (50 mL). The organic layer was separated and washed with water (25 mL) and saturated sodium chloride solution (25 mL). The dried ($MgSO_4$) solvents were removed and the crystalline residue was recrystallized from ether-petroleum ether (1:1) affording the sulfoxide **2ef** (235 mg, 94%, mixture of diastereoisomers) as colorless crystals: mp 125–130 °C; R_f 0.15 (silica, ether); IR (Nujol) 2907, 2841, 1770 (γ-lactone), 1351, 1332, 1299, 1266, 1200, 1178, 1135, 1082, 1052, 1033, 1022, 1014, 968, 906, 893, 855, 840, 812, 756, 750, 712, 699, 687 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) τ 2.38 (m, 5 H, aromatic), 5.15 (t, J = 5 Hz, 0.55 H, CHO), 5.22 (t, J = 5 Hz, 0.45 H, CHO), 6.86 (m, 0.55 H, CHSO), 6.97 (m, 0.45 H, CHSO), 7.20-8.23 (m, 7 H); mass spectrum m/e (rel intensity) 250 ($^{32}S - M^+$, 3.1), 234 (6.8), 125 ($M^+ - PhS$, 37), 110 (15), 109 (12), 97 (20), 81 (base peak). Anal. ($C_{13}H_{14}O_3S$) C, H.

Pyrolysis of Sulfoxide 2ef. The sulfoxide **2ef** (250 mg, 1 mmol, mixture of diastereoisomers) was dissolved in freshly distilled toluene (10 mL) and heated under argon at 110 °C for 36 h. Removal of the solvent followed by column chromatography (silica, CH_2Cl_2) furnished the lactone **2c** (99.2 mg, 80%) as an oil identical in all respects with the reported compound.[29] When the pyrolysis was carried out for 10 h instead of 36 h, column chromatography led to the isolation of **2c** (62 mg, 50%) as well as the recovery of pure sulfoxide **2e** (75 mg, 30%) as colorless crystals: mp 154–155 °C (ether); R_f 0.15 (silica, ether); IR (Nujol) 2907, 2841, 1770 (γ-lactone), 1351, 1332, 1282, 1269, 1200, 1178, 1135, 1082, 1052, 1033, 1022, 1014, 968, 906, 893, 855, 840, 812, 757, 750, 712, 699, 687 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) τ 2.32 (m, 2 H, aromatic), 2.42 (3 H, aromatic), 5.15 (t, J = 5 Hz, 1 H, CHO), 6.86 (m, 1 H, CHSO), 7.26 (m, 1 H), 7.27 (d, J = 13 Hz, 1 H), 7.62 (m, 1 H), 8.04 (m, 4 H); mass spectrum m/e (rel intensity) 250 ($^{32}S - M^+$, 3), 234 (7), 125 ($M^+ - PhS$, 37), 110 (15), 109 (12), 97 (20), 81 (base peak). Anal. ($C_{13}H_{14}O_3S$) C, H.

$LiAlH_4$ Reduction of Phenylsulfenolactone 2b. The phenylsulfenolactone **2b** (234 mg, 1 mmol) in dry ether (5 mL) was added dropwise to a stirred suspension of $LiAlH_4$ (37.8 mg, 1 mmol) in dry ether (10 mL) at 0 °C under argon. Stirring was continued at 25 °C for 2 h and the reaction mixture was quenched cautiously with wet ether and finally a few drops of water while vigorously stirred until it became milky white. The mixture was then dried ($MgSO_4$), the solution filtered, and the solid washed thoroughly with ether. Removal of the solvent gave the diol **2a** as a white, crystalline solid (233 mg, 98%) recrystallized from ether: mp 108.5–109 °C; R_f 0.18 (silica, ether); IR ($CHCl_3$) 3650, 3597, 3030, 2959, 2882, 1582, 1475, 1449, 1433, 1379, 1282, 1081, 1063, 1042, 952, 966, 929, 690 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) τ 2.52 (m, 2 H, aromatic), 2.68 (m, 3 H, aromatic), 6.50 (m, 2 H, CH_2O), 6.6 (m, 1 H, CHO), 7.23 (m, 1 H, CHS), 7.83 (m, 2 H, CH_2), 8.2 (m, 1 H, $CHCH_2OH$), 8.4 (s, 2 H, OH), 8.63 (m, 2 H, CH_2), 8.90 (m, 2 H, CH_2); mass spectrum m/e (rel intensity) 238 ($^{32}S - M^+$, 16), 220 ($M^+ - H_2O$, 13), 132 (14), 111 (23), 110 ($M^+ - PhS - H_2O$, base peak). Anal. ($C_{13}H_{18}O_2S$) C, H.

Preparation of Alcohol 17. The dithiane methyl ester **16** (464 mg, 2 mmol) was dissolved in dry ether (10 mL) and added dropwise to a cold (0 °C), stirred suspension of $LiAlH_4$ (76 mg, 2 mmol) in dry ether (10 mL). The cooling bath was removed and the reaction mixture was stirred at ambient temperature for 2 h and then quenched cautiously with wet ether and finally a few drops of water. The reaction mixture was stirred vigorously at 25 °C until it became milky white, dried ($MgSO_4$), and filtered and the solid was thoroughly washed with ether. Removal of the solvent afforded the alcohol **17** as an oil (419 mg; 97%), homogeneous by TLC: R_f 0.55 (silica, ether); IR (liquid film) ν_{max} 3378 (OH), 3135, 2924, 2899, 2857, 1621, 1418, 1269, 1221, 1160, 1099, 1060, 1015, 917, 899, 862, 727, 707, 667 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) τ 4.23 (m, 2 H, olefin), 5.81 (d, J = 5 Hz, 1 H, SCHS), 6.40 (d, J = 5 Hz, 2 H, CH_2O), 6.9-8.3 (m, 11 H); mass spectrum m/e (rel intensity) 216 (M^+, 2), 121 (15), 120 (10), 119 (dithiane cation, base peak), 106 (6), 91 (10), 79 (13), 77 (11), 74 (10), 67 (6), 59 (15). Anal. ($C_{10}H_{16}OS_2$), C, H.

Preparation of the Tetrahydropyranyl Ether 18. The alcohol **17** (216 mg, 1 mmol) in dry methylene chloride (5 mL) was cooled to 0 °C and successively treated with dihydropyran (101 mg, 109 μL, 1.2 mmol) and p-toluenesulfonic acid (3.8 mg, hydrate, dissolved in 100 μL of THF) under argon. The cooling bath was removed and the reaction mixture was stirred for 4 h, diluted with ether (25 mL), and washed with 5% sodium bicarbonate solution (5 mL), water (5 mL), and brine (5 mL). The dried ($MgSO_4$) solvents were removed and the residue was purified by column chromatography (silica, 20% ether in petroleum ether, R_f 0.28) to afford pure tetrahydropyranyl ether **18** as an oil (312 mg, 100%): IR (liquid film) ν_{max} 3145, 2924, 1656, 1618, 1462, 1445, 1433, 1414, 1376, 1355, 1344, 1316, 1267, 1239, 1222, 1163, 1136, 1122, 1109, 1063, 1059, 1020, 967, 918, 895, 861, 806, 727, 703, 668 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) τ 4.20 (m, 1 H, olefin), 4.30 (m, 1 H, olefin), 5.36 (m, 1 H, OCHO), 5.68 (m, 1 H, SCHS), 6.13 (m, 2 H), 6.32 (m, 2 H), 6.48 (m, 2 H), 6.60 (m, 2 H), 7.0-8.6 (m, 12 H); mass spectrum m/e (rel intensity) 300 (M^+, 1.2), 215 (9), 119 (base peak). Anal. ($C_{15}H_{24}O_2S_2$) C, H.

Preparation of the Silyl Ether 19. The alcohol **17** (216 mg, 1 mmol) was dissolved in dry DMF (2 mL), cooled to −10 °C, and treated successively while stirring and under argon with imidazole (82 mg, 1.2 mmol) and *tert*-butyldimethylsilyl chloride (181 mg, 1.2 mmol). The reaction mixture was allowed to reach room temperature and stirred for 15 h. The mixture was then poured into water (10 mL) and extracted with ether (2 × 25 mL), and the combined ether extract was washed with water (3 × 5 mL) and brine (5 mL). The dried ($MgSO_4$) solvent was removed and the oily residued chromatographed by column (silica, 20% ether-petroleum ether, R_f 0.64) furnishing pure silyl ether **19** as an oil (323 mg; 98%): IR (liquid film) ν_{max} 3040, 2950, 2924, 2890, 2849, 1466, 1460, 1427, 1418, 1381, 1355, 1269, 1245, 1172, 1112, 1096, 1078, 1000, 936, 907, 833, 812, 773, 733, 710, 666 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) τ 4.28 (m, 2 H, olefin), 5.82 (d, J = 5.5 Hz, 1 H, SCHS), 6.45 (d, J = 6 Hz, 2 H, CH_2O), 6.97-7.30 (m, 5 H), 7.30-8.13 (m, 5 H), 9.11 (s, 9 H, Si-*t*-Bu), 9.97 (s, 6 H, $SiCH_3$); mass spectrum m/e (rel intensity) 330 (M^+, 0.2), 273 ($M^+ - t$-Bu, 4), 181 (14), 167 (6), 147 (15), 119 (base peak), 101 (9). Anal. ($C_{16}H_{30}OS_2Si$) C, H.

Preparation of the Dithiane Carboxylic Acid 20. To a stirred solution of the dithiane **18** (300 mg, 1 mmol) in dry THF (10 mL) under argon at −20 °C, n-butyllithium (700 μL, 1.60 M in hexane, 1.1 mmol) was added dropwise. Stirring was continued at −20 °C for 2 h and then the solution was withdrawn with a syringe and added at once to a saturated solution of CO_2 (dry ice) in THF (25 mL) at −78 °C. The cooling bath was removed and the solution allowed to reach room temperature with stirring and then poured into water (25 mL) and acidified to pH 4 with 1 N oxalic acid. The product was extracted with ether (4 × 25 mL), and the combined ether solution was washed with water (10 mL) and brine (10 mL) and dried ($MgSO_4$). The residue obtained after evaporation was chromatographed on a silica gel column using ether as eluant to afford the carboxylic acid **20** (292 mg, 85%): R_f 0.11 (silica, CH_2Cl_2); IR (liquid film) ν_{max} 2899, 1709, 1429, 1348, 1269, 1198, 1135, 1117, 1058, 1031, 976, 901, 866, 813, 735, 676 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) τ 0.35 (bs, 1 H, COOH), 4.07 (m, 1 H, olefin), 4.34 (m, 1 H, olefin), 5.30 (m, 1 H, OCHO), 6.0-8.50 (m, 20 H); mass spectrum m/e (rel intensity) 183

($M^+ - C_5H_7O_2S_2$, 18), 169 (10), 163 (14), 139 (18), 119 (14), 106 (7), 101 (13), 85 (83), 59 (base peak). Anal. ($C_{16}H_{24}O_4S_2$) C, H.

Preparation of the Dithiane Carboxylic Acid 21. The dithiane carboxylic acid **21** was prepared and purified from the dithiane silyl ether **19** (330 mg, 1 mmol) exactly in the same way as described above for the carboxylic acid **20**. Obtained was 318 mg (85%), oil: R_f 0.11 (silica, CH_2Cl_2); IR ($CHCl_3$) ν_{max} 2941, 2925, 1701, 1481, 1368, 1258, 1105, 1009, 942, 912, 840, 690 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) τ −1.50 (bs, 1 H, COOH), 4.1 (m, 1 H, olefin), 4.35 (m, 1 H, olefin), 6.3-8.80 (m, 12 H), 9.1 (s, 9 H, Si-*t*-Bu), 9.93 (s, 6 H, CH_3SiCH_3); mass spectrum *m/e* (rel intensity) 317 ($M^+ - t$-Bu, 4), 289 (16), 197 (31), 181 (14), 163 (53), 123 (11), 119 (52), 106 (69), 91 (24), 89 (42), 79 (30), 75 (base peak). Anal. ($C_{17}H_{30}O_3SiS_2$) C, H.

Cyclohexenyl Dithiane Carboxylic Acid 6. The dithiane carboxylic acid **111** (304 mg, 2 mmol) was dissolved in dry THF (10 mL) and added dropwise from a syringe to a cold (0 °C) stirred LDA solution (2.2 mmol, prepared from 1.38 mL of 1.6 M hexane solution of *n*-BuLi and 308 μL of diisopropylamine in 2.7 mL of THF) under argon. Stirring was continued at 25 °C for 3 h to complete the dianion formation and then a solution of cyclohexenyl bromide (322 mg, 2 mmol) in dry THF (2 mL) was added dropwise at 0 °C. The reaction mixture was stirred at 25 °C for 24 h and then poured into water (20 mL), acidified to pH 3 with 1 N hydrochloric acid, and extracted with ether (3 × 50 mL). The combined ether extract was washed with water (20 mL) and brine (20 mL). Removal of the dried ($MgSO_4$) solvents afforded crude **6**, which was purified by column chromatography (silica, ether): 415 mg (85%); colorless crystals, mp 112.5-113.5 °C (ether-petroleum ether); R_f 0.42 (silica, ether); IR (CCl_4) ν_{max} 3257-2331 (COOH), 3003, 2915, 1689 (C=O), 713 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) τ 4.17 (m, 2 H, olefin), 6.73 (m, 2 H, CHS), 7.06 (bs, 1 H), 7.31 (m, 2 H), 7.70-8.60 (m, 8 H); mass spectrum *m/e* (rel intensity) 244 (M^+, 1.3), 199 ($M - CO_2H$, 5), 163 (M − cyclohexenyl, base peak), 119 (20), 117 (16), 91 (16). Anal. ($C_{11}H_{16}O_2S_2$) C, H.

Allyl Dithiane Carboxylic Acid 12. The allyl dithiane carboxylic acid **12** was prepared from **111** in exactly the same way as described above for **6**. Obtained was 148 mg (90%) of colorless crystals: mp 71.0-72.5 °C (CCl_4); R_f 0.50 (silica, ether); IR (CCl_4) ν_{max} 3279-2364, 2907, 1692 (C=O), 1429, 1408, 1277, 1234, 991, 964, 924 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) τ −1.17 (s, 1 H, COOH), 3.70-5.10 (m, 3 H, olefin), 6.30-6.95 (m, 2 H, CHS), 6.95-7.42 (m, 4 H, CHS and allylic H), 7.42-8.20 (m, 2 H, CH_2CH_2S); ^1H NMR of methyl ester (360 MHz, $CDCl_3$) τ 4.21 (m, 1 H, $CH_2=CH$), 4.72 (d, J = 17 Hz, 1 H, $H_2C=CH$-), 4.78 (d, J = 10 Hz, 1 H, $H_2C=CH$-), 6.28 (s, 3 H, $-OCH_3$), 6.58 (dd, J = 12, 12 Hz, CHS), 7.32 (d, J = 7 Hz, 2 H, CHS), 7.46 (d, J = 12 Hz, 2 H, $CH_2=CHCH_2$-), 7.79 (m, 1 H, CH_2CH_2S), 8.22 (m, 1 H, CH_2CH_2S); mass spectrum *m/e* (rel intensity) 204 (M^+, 13), 163 (M − allyl, base peak), 159 ($M - CO_2H$, 42), 119 (10), 117 (7), 85 (53). Anal. ($C_8H_{12}O_2S_2$) C, H.

Reversal of the Phenylseleno- and Phenylsulfenolactonization Reactions. General Procedure. The reversal of the phenylseleno- and phenylsulfenolactonizations to the unsaturated hydroxy acids indicated in Table I was carried out on 1-mmol scale with sodium in liquid ammonia as illustrated below for the case of (1α,4α,5α)-4-(phenylseleno)-6-oxabicyclo[3.2.2]nonan-7-one (**1a**) (**1a** → **1**). To a stirred solution of sodium (230 mg, 10 mmol) in dry liquid ammonia (25 mL) cooled to −78 °C was added dropwise a solution of the phenylselenolactone **1a** (295 mg, 1 mmol) in dry ether (2 mL). The reaction mixture was stirred for 5 min at −78 °C and quenched with excess solid ammonium chloride and the cooling bath was removed. After the ammonia was allowed to evaporate by stirring at ambient temperature 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). Drying ($MgSO_4$) of the combined ether extracts and evaporation gave crude 4-cycloheptene-1-carboxylic acid (**1**), which was purified by preparative layer chromatography, 115 mg (82% yield), mp 66-67 °C (lit.[16] mp 65-67 °C), characterized by spectral comparison to an authentic sample; **1b** → **1** (80%, identical with an authentic sample); **2a** → **2** (77%, identical with an authentic sample); **2b** → **2** (79%, identical with an authentic sample); **3a** → **3** (78%, identical with an authentic sample); **9a** → **9** (80%, identical with an authentic sample; **11a** → **11** (75%, identical with an authentic sample).

X-ray Analysis of Phenylselenolactone 8a. Crystals of **8a**, obtained from ether-petroleum ether, were monoclinic, space group $P2_1/c$, with a = 8.434 (1), Å, b = 10.566 (1) Å, c = 15.137 (2) Å, β = 96.01 (1)°, and d_{calcd} = 1.461 g cm^{-3} for Z = 4 ($C_{15}H_{18}O_2Se$, mol wt 309.27).

The intensity data were measured on a Hilger-Watts diffractometer (Ni-filtered Cu Kα radiation, θ-2θ scans, pulse height discrimination). The size of the crystal used for data collection was approximately 0.10 × 0.20 × 0.25 mm; the data were corrected for absorption (μ = 39.8 cm^{-1}). Of the 1892 independent reflections for $\theta < 57°$, 1643 were considered to be observed [$I > 2.5\sigma(I)$]. The structure was solved by the heavy-atom method and was refined by full-matrix least squares. In the final refinement, anisotropic thermal parameters were used for the heavier atoms and isotropic temperature factors were used for the hydrogen atoms. The hydrogen atoms were included in the structure factor calculations but their parameters were not refined. The final discrepancy indices are R = 0.039 and wR = 0.046 for the 1643 observed reflections. The final difference map has no peaks greater than ±0.2 e A^{-3}.

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Supplementary Material Available: A listing of properties and full spectral data of compounds **4a, 5a, 11a-15a, 8d, 9d, 15d,** and **25** and Tables II-V listing the final atomic parameters, final anisotropic thermal parameters, bond lengths, and bond angles in **8a** (7 pages) Ordering information is given on any current masthead page.

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Conformation and Cope Rearrangement of *sym*-Oxepin Oxides

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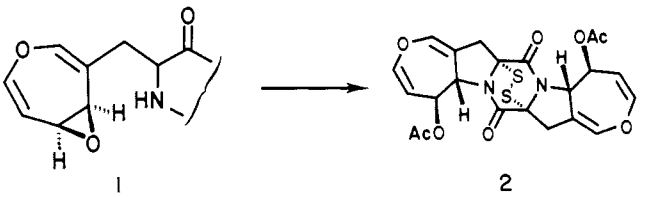
Abstract: The synthesis of a homologous series of transoid, bridged *sym*-oxepin oxides (**10a–c**) is described. The lower homologues, **10a,b**, do not undergo facile Cope rearrangement to the *sym*-oxepin oxides **15a,b**. The generation of transoid **10c** led rapidly to the production of the Cope rearrangement product **15c**. The differing reactivity in the series **10a–c** is attributed to the inability of **10a,b** to interconvert with their cisoid isomers, **14a,b**. The production of **15c** is thought to occur via ring inversion of transoid **10c** to cisoid **14c**, followed by rapid Cope rearrangement (**14c** → **15c**). Under forcing conditions **10a,b** undergo epoxide opening and a subsequent rearrangement.

In an elegant scheme Neuss and co-workers in 1968 postulated[1] the intermediacy of an oxepin oxide (**1**, Scheme I) during the fungal biogenesis of the aranotins (e.g., acetylaranotin, **2**). Thus, it was suggested, the stereochemistry of the dihydrooxepin moiety of the aranotins is established by intramolecular displacement at carbon with Walden inversion in enzyme-bound epoxide **1**.

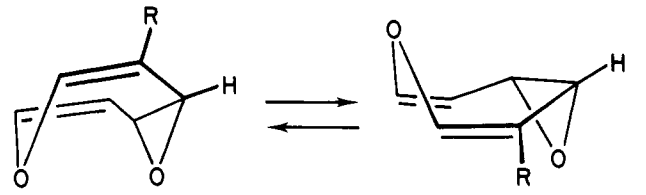
The first syntheses of an oxepin oxide were communicated by Klein and Grimme,[2a] and by us[2b] in 1974–1975. Subsequently, we detailed[3] our conversion of benzene oxide oxepin to *sym*-oxepin oxide (**3**, R = H, Scheme II), and studied the conformation and Cope rearrangement of **3** (R = H) by ^{1}H NMR spectroscopy.[4] Other studies revealed the Cope rearrangement of a methylated derivative[5] and helped define the scope[6] of our synthetic approach to oxepin oxides. Further, we reported the synthesis of the bridgehead diene **10a**[7] (Scheme IV) and characterized a derivative of **10a** by X-ray crystal analysis.[8]

The possible intermediacy of an enzyme-bound oxepin oxide in biogenesis (Scheme I) raises an intriguing question of stereochemistry. A priori one must consider two stereochemical outcomes for the Cope rearrangement of a chiral oxepin oxide (**4**, Scheme III). In principle, **4** could interconvert, via Cope rearrangement, with its diastereomer **5** (**5** ≠ **4**) or with its rotamer **6** (**6** = **4**). The interconversion **4** ⇌ **5** would proceed via a transition state resembling cisoid conformation **3a** (Scheme II); the degenerate rearrangement **4** ⇌ **6** would proceed via a transoid transition state[9] (cf. **3b**, Scheme II). Thus, the stereochemical integrity of an intermediate, chiral oxepin oxide would depend on the rate and the geometrical requirements of the Cope rearrangement. Herein we report that *oxepin oxides locked in transoid conformations do not undergo facile Cope rearrangements*, in sharp contrast to conformationally mobile oxepin oxides.

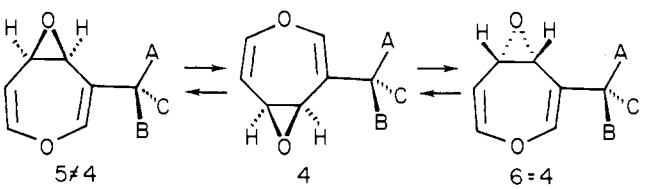
Scheme I



Scheme II



Scheme III



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