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PREPARATION AND REACTIVITY OF α-PHENYLSELENENYL ETHERS

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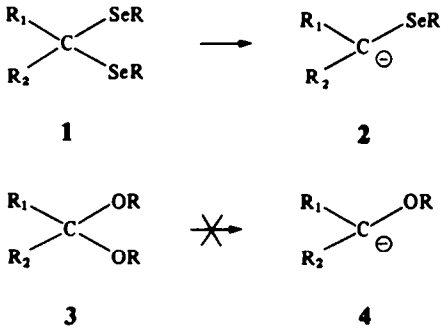
Abstract—α-Phenylselenenyl cyclic ethers may be prepared by the reactions of either lactols or lactol acetates with benzeneselenol, or from lactones by the "one-pot" process of reduction and Lewis acid catalyzed selenation. The tetrahydropyranyl phenyl selenides also exhibit a significant anomeric effect and its size has been estimated. The selenenyl ethers are converted to enol ethers through an oxidative elimination process, and an exploration of their reactivity toward amide bases and lithium alkyls has been made.

α-Selenenyl ethers constitute a special case of the class of compounds known as selenoacetals. Selenoacetals of type **1**, prepared from carbonyl compounds and benzeneselenol in the presence of acid, have been used for the preparation of selenium stabilized carbanions, anion **2** being generated by alkyl lithium induced carbon–selenium bond cleavage. These selenium stabilized anions have proven to be useful synthetic intermediates for the preparation of a variety of structural types.[1,2]

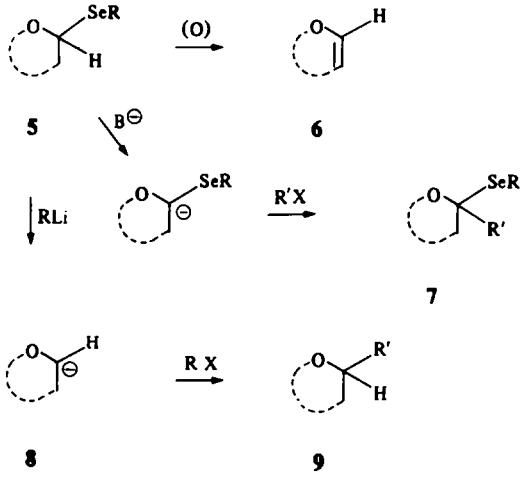


1 **2**

3 **4**

The generation of similar heteroatom stabilized anions from oxygen acetals (**3** to **4**) is not readily accomplished.[3] Oxygen substituted anions also lack the degree of stabilization provided by selenium (or sulfur).[1,4,5] Such anions have great potential utility, however, for the synthesis of a variety of naturally occurring ethers, including polyether antibiotics and carbohydrates, and several examples of their preparation have been reported. Cohen and Lin[6] for example have prepared tetrahydropyranyl and furanyl α-anions by reductive cleavage of phenylthio ethers, and in one case, utilized this methodology for the preparation of *trans*-roseoxide. Acyclic oxygen stabilized anions derived from alkoxystannane precursors have been reported from several laboratories.[7,8]

The cyclic α-selenenyl ethers, **5**, should also provide an entry into the chemistry of α-alkoxy anions as well as into that of several other types of useful intermediates and reactants. For example, oxidative elimination[9] of **5** should provide an alternative means for the formation of enol ethers, **6**. In principle it should also be possible to deprotonate compounds of type **5** and alkylate the resulting acyl anion equivalents[10] to form new selenenyl ethers of type **7**. Finally, protonation or alkylation of anion **8** derived from **5** would result in the net conversion of a hemiacetal into an ether, **9**.



5 **6** **7** **8** **9**

Preparation. As the first step in the exploration of the chemistry of α-seleno ethers we have examined methods for the preparation of cyclic members of the class. In principle the α-seleno ethers should be obtainable by displacement of the anomeric oxygen substituent of cyclic hemiacetals by nucleophilic selenium. Thus, a simple hemiacetal should react with benzeneselenol in the presence of acid[1] to produce the desired seleno ether. In practice, tetrahydropyranol, **10** (Table 1), on exposure to benzeneselenol in the presence of catalytic toluenesulfonic acid afforded 2-phenylselenenyltetrahydropyran, **11**, in 92% isolated yield. The reaction is carried out at room temperature overnight in benzene solution, and the product is readily purified by radial chromatography on silica gel.

Two variations on this method have also proven useful for the preparation of cyclic α-phenylselenenyl ethers. In one the cyclic hemiacetal acetate is employed as the substrate. The reaction is performed under conditions similar to those employed for the preparation of **11** from **10**. In the particular case of acetate **12**, for example, **11** is produced in an isolated yield of 97%. In cases where the hemiacetal itself may be unstable with respect to its open chain hydroxy

Table 1. Preparation of α-phenylselenenyl cyclic ethers

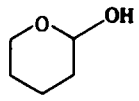
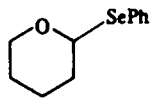
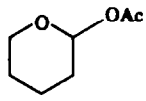
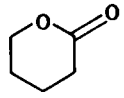
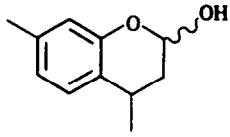
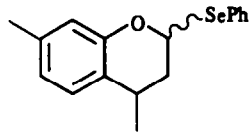
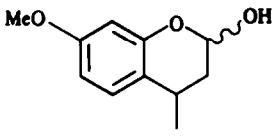
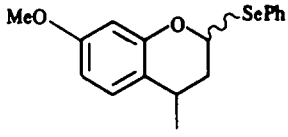
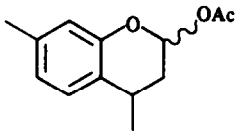
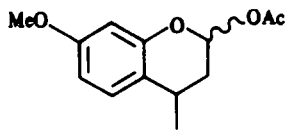
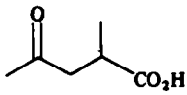
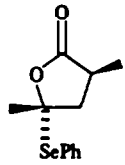
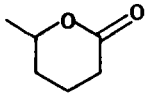
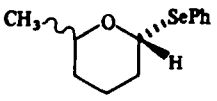
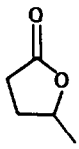
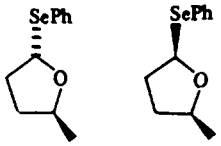
Entry	Substrate	Product(s)	Method	Yield
1	 **10**	 **11**	a	92%
2	 **12**	**11**	a	97%
3		**11**	c	88%
4	 **13**	 **15**	b	62%
5	 **14**	 **16**	b	55%
6	 **19**	**15**	a	90%
7	 **20**	**16**	a	62%
8		 **29**	a	90%

Table 1—*continued*

Entry	Substrate	Product(s)	Method	Yield
9	 **22**	 **21a** *trans* **21b** *cis*	c	100%
10	 **23**	 **24** **25**	c	100%

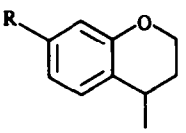
Reaction conditions: a, benzeneselenol, TsOH, C_6H_6, room temperature; b, benzeneselenol, TsOH, C_6H_6, reflux; c, (1) DIBAL, toluene, −78°, (2) BF_3–Et_2O, benzeneselenol, −78°.

aldehyde tautomer this second method should prove particularly useful.

In many cases cyclic hemiacetals are prepared from the corresponding lactones. To avoid the problems involved with the isolation and purification of the hemiacetals and their derivatives we sought a method for the preparation of the selenenyl ethers directly from lactones. In their work on the generation of α-lithio ethers Cohen and Lin[6] prepared α-phenylthio cyclic ethers by the one-pot reduction and phenylthioacetalization of lactones. In a similar fashion the diisobutylaluminum hydride (DIBAL) reduction of representative lactones followed by reaction with benzeneselenol in the presence of a Lewis acid affords the corresponding α-phenylseleno cyclic ethers. For example, treatment of δ-valerolactone with one equivalent of DIBAL in toluene at −78° followed by the addition of boron trifluoride etherate and benzeneselenol produces **11** in 88% yield.

These three routes for the preparation of α-phenylselenenyl ether **11** have been applied to a variety of other 5- and 6-membered cyclic systems. In Table 1 are listed representative examples of the substrates, the particular method employed and the structures and yields of products.

In the cases of lactols and lactol acetates as substrates (Entries 4–7) the selenation reaction can be carried out in the simplest possible fashion: exposure to benzeneselenol and catalytic toluenesulfonic acid at room temperature in benzene solution. Interestingly the bicyclic aromatic lactol substrates **13** and **14** when reacted in refluxing benzene yield selenides **15** and **16**, but they are also reduced in part to the corresponding chromans, **17** and **18**. The latter may be formed from either the cation produced by protonation of the lactol substrate or from reduction of the selenide product itself. In either case the hydride source is presumably benzeneselenol. In contrast to the behavior of the lactols, acetates **19** and **20** react with benzeneselenol at room temperature to form selenides **15** and **16** unadulterated with the derived chromans.

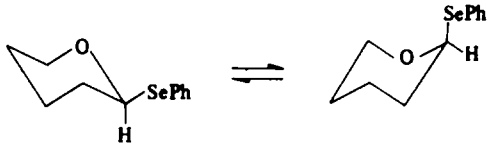


17 R = CH_3
18 R = OMe

When lactones (Entries 8–10) are used as precursors for α-phenylselenenyl ethers the two-step process may be carried out as a "one-pot" procedure[6] at low temperature. In these examples the selenation reaction appears to be considerably faster than it is with lactol or lactol acetate substrates. The aluminate species produced in the initial DIBAL reduction of lactones may function as a better leaving group in the presence of BF_3 than do protonated hydroxy or acetoxy groups.

The results shown in Table 1 also yield an indication of the magnitude of the anomeric effect for cyclic α-phenylselenenyl ethers, an effect that appears to be larger than that for the equivalent sulfur systems. For α-phenylselenenyl tetrahydropyran, **11**, one conformation predominates. The NMR spectrum of **11** exhibits a broad triplet at δ 5.70 ppm (J = 4.0 Hz) attributable to the proton attached to the anomeric center. Both the multiplicity and the coupling constants of this pattern clearly show that this proton must be largely equatorial in nature and that the seleno group must be predominantly axial. The amount of equatorial selenide conformer can be estimated by considering the spectral characteristics of the isomers of **21**. These diastereomers produced in a *cis*:*trans* ratio of 17:83 are obtained upon reduction and selenation of lactone **22**. (The equivalent conversion carried out employing thiophenol affords a similar mixture of diastereomers;

9:91, *cis*:*trans*.[9]) The stereochemistry of the major isomer **21a** is clearly *trans* and the phenylselenenyl group occupies an axial position. This conclusion again follows from examination of the NMR spectrum of the seleno ether. Thus compound **21a** exhibits a broadened multiplet for the equatorial anomeric proton at δ 5.88 ppm. The isomeric selenide **21b** exhibits the anomeric proton at δ 4.98 as a doublet of doublets. On the *assumption* that these values for **21a** and **21b** represent the chemical shifts for a *single* chair conformation in each case we calculate[11] an upper limit of $K = 2.5$ for the equilibrium **i** to **ii**. This 70:30 ratio in favor of the axial conformer **ii** is equivalent to an energy difference of approximately 0.55 kcal mol^{-1}, an anomeric effect sufficiently large to dominate what must be assumed to be a stereochemical preference for the equatorial selenide conformer.[12] It is to be expected as well that the anomeric effect for the phenylselenenyl group should exceed that for the equivalent sulfur substituent. The greater length of the C—Se bond[13] renders the phenylselenenyl group effectively smaller than the phenylthio species. As a consequence the orbital–orbital interaction[14] from which the anomeric effect results should have a stronger bearing on the conformations of the selenium compounds than it does for the α-phenylthio substituted cyclic ethers.



i **ii**

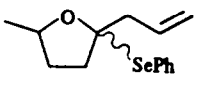
This anomeric effect appears to be diminished, however, when other conformational restraints are present in the phenylselenenyl ethers. Thus, for the chromanol substrates **13**, **14**, **19** and **20** (Entries 4–7) the presence of sp^2 centers in the pyranyl ring affects the stereochemistry of the selenation process. In the case of acetate **20** for example, two products, *trans*-**16** and *cis*-**16** are formed in a ratio of 1.5:1. For the related methyl compound **19** the *trans*-**15**:*cis*-**15** ratio is 3:1. The same reduction in stereoselectivity observed in the formation of these unsaturated phenylselenenyl ethers is also observed in 5-membered rings. Lactone **23** affords a 3:1 *trans*:*cis* mixture of **24** and **25** in quantitative yield.

Reactivity. Formation of a carbon–carbon double bond by the oxidation and elimination of a phenylselenenyl group[9] is a frequently employed technique. Application of this sequence to the α-phenylselenenyl ethers described above should yield enol ethers as the elimination products. In Table 2 are shown some representative examples of the preparation of cyclic vinyl ethers.

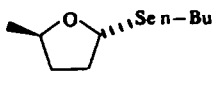
We have examined several methods for oxidation–elimination of α-phenylselenenyl ethers. Unlike the olefins usually obtained from simple alkyl selenides the vinyl ether products obtained here are highly susceptible to addition and secondary oxidation reactions. For example, the bicyclic ether **16** when treated with *m*-chloroperbenzoic acid (MCPBA) affords chromene **26** in 52% yield. With other oxidants, for example, hydrogen peroxide or ozone, no recognizable products are obtained. The simple selenenyltetrahydropyran **11** is also smoothly oxidized but the product, dihydropyran, reacts rapidly with *m*-chlorobenzoic acid to form **27** even in the presence of a carbonate buffer. Similarly, the tetrahydrofurans **24** and **25** are converted quantitatively to enol ether **28** in the presence of either hydrogen peroxide or ozone but the product, **29**, is rapidly hydrated on exposure to moisture.

A particularly useful case, however, is shown in Entry 4 of Table 2. Application of the oxidative elimination sequence to lactone selenide **29** (Table 1, Entry 8) cleanly affords the Δ^3-butenolide **30** in 80% isolated yield. The two-stage process is carried out under mild conditions which do not effect isomerization of the product. The oxidation step is carried out with ozone in methylene chloride, and elimination of the selenoxide results upon addition of the reaction mixture to refluxing methylene chloride containing pyridine. Exposure of the product to stronger basic conditions, for example, carrying out the elimination step in the presence of triethylamine, results in a mixture of both the Δ^2- and Δ^3-butenolides. Other methods for preparing Δ^3-butenolides, methods which involve the use of acidic or basic reaction conditions, usually result in extensive double bond isomerization.[15,16]

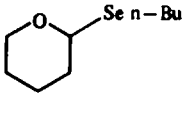
The α-phenylselenenyl ethers have potential for use as precursors of either acyl anion equivalents or α-alkoxyanions. They may also serve as synthetic equivalents of the latter. Thus, deprotonation of seleno ether **24** utilizing lithium hexamethyldisilazide followed by reaction with allyl bromide in the presence of HMPA affords a 3.1:1 mixture of *E*- and *Z*-**31**. Attempts to deprotonate other α-phenylselenenyl cyclic ethers with amide bases failed, however.[17] With alkyl lithium bases a second process competes with deprotonation and cleavage of a carbon–selenium bond occurs in preference to anion formation. With **24**, for example, exposure to n-butyl lithium and prenyl bromide results in the formation of dialkyl selenide **32** and prenyl benzene. Similarly selenide **11** on treatment with butyl lithium alone yields **33** and phenyl lithium. The "ate" complex **34** presumably formed as an intermediate in this reaction apparently decomposes with the loss of the most stable anion, i.e. phenyl lithium. The same type of result occurs with methyl lithium and **11**. These findings suggest the possibility for generation of α-alkoxy anions by utilizing a substituent on selenium less prone to depart as an anion



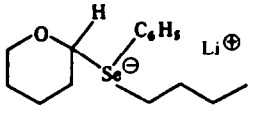
31



32

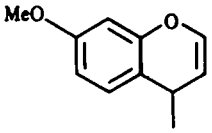
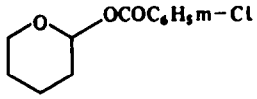
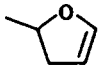
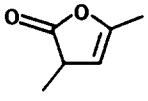


33



34

Table 2. Oxidative elimination of α-phenylselenenyl ethers

Entry	Substrate	Product
1	**16**	 **26**
2	**11**	 **27**
3	**24**	 **28**
4	**29**	 **30**

than either a phenyl or the alkoxy alkyl group.[7] An investigation of this process is currently underway.

EXPERIMENTAL

^{1}H-NMR spectra were recorded with either a Nicolet NMC 360 or a Varian EM-390 spectrometer. Spectra were obtained in $CDCl_3$ soln and chemical shifts are reported in ppm from internal TMS. ^{13}C-NMR spectra were measured with an IBM WP 200 spectrometer. IR spectra were recorded with a Perkin–Elmer 1430 spectrometer. Nominal mass spectra were measured with either a Finnigan 4000 or a Varian M-66 mass spectrometer, and precise mass measurements were made with the latter instrument. Solvents were purified and dried according to standard methods and m.ps are uncorrected. Microanalyses were performed by Atlantic Microlabs, Atlanta, Georgia.

3,4-Dihydro-4,7-dimethyl-2H-1-benzopyran-2-ol, **13**[18]

The title compound was prepared in 75% yield as previously reported.[18] It was obtained in a 2.6:1 ratio of *trans* to *cis* isomers. ^{1}H-NMR (360 MHz, $CDCl_3$): δ (axial OH) 7.11 (d, 1H, J = 7.6 Hz), 6.75 (d, 1H, J = 7.6 Hz), 6.65 (bs, 1H), 5.60 (dd, 1H, J = 2.6, 4.0 Hz), 3.4–3.2 (bs, 1H, —OH), 3.11 (m, 1H), 2.29 (s, 3H), 2.06 (ddd, 1H, J = 4.0, 5.6, 13.4 Hz), 1.72 (ddd, 1H, J = 2.6, 10.3, 13.4 Hz), 1.34 (d, 3H, J = 6.9 Hz); (equatorial OH) 7.09 (d, 1H, J = 7.9 Hz), 6.75 (buried d, 1H, J = 7.9 Hz), 6.66 (bs, 1H), 5.47 (dd, 1H, J = 2.5, 8.2 Hz), 3.4–3.2 (bs, 1H, —OH), 3.00 (m, 1H), 2.29 (s, 3H), 2.23 (ddd, 1H, J = 2.5, 5.8, 13.4 Hz), 1.66 (ddd, 1H, J = 8.2, 10.1, 13.4 Hz), 1.37 (d, 3H, J = 6.9 Hz).

3,4-Dihydro-7-methoxy-4-methyl-2H-1-benzopyran-2-ol, **14**

The lactol was prepared from 7-methoxy-4-methyl-2H-1-benzopyran-2-one[19] as described for **13**. It was obtained as a colorless oil in 75% yield after silica gel chromatography (1:1 EtOAc–pet ether). From integration of the 360 MHz NMR spectrum, the ratio of *trans* to *cis* isomers was determined to be 2.6:1. ^{1}H-NMR (360 MHz, $CDCl_3$): δ (axial OH) 7.13 (d, 1H, J = 8.6 Hz), 6.52 (dd, 1H, J = 2.6, 8.6 Hz), 6.39 (d, 1H, J = 2.6 Hz), 5.60 (dd, 1H, J = 2.6, 4.0 Hz), 3.76 (s, 3H), 3.2–3.1 (bs, 1H, —OH), 3.10 (m, 1H), 2.05 (ddd, 1H, J = 4.0, 5.6, 13.4 Hz), 1.71 (ddd, 1H, J = 2.6, 10.3, 13.4 Hz), 1.33 (d, 3H, J = 6.9 Hz); (equatorial OH) 7.08 (d, 1H, J = 8.7 Hz), 6.51 (dd, 1H, J = 2.7, 8.7 Hz), 6.41 (d, 1H, J = 2.7 Hz), 5.45 (dd, 1H, J = 2.5, 8.3 Hz), 3.76 (s, 3H), 3.2–3.1 (bs, 1H, —OH), 2.98 (m, 1H), 2.23 (ddd, 1H, J = 2.5, 5.8, 13.2 Hz), 1.65 (ddd, 1H, J = 8.3, 10.2, 13.2 Hz), 1.36 (d, 3H, J = 6.9 Hz); IR (neat): 3100–3700, 3020, 2975, 2950, 2890, 1620, 1590, 1510, 1470, 1450, 1430, 1380, 1360, 1315, 1280, 1260, 1200, 1170, 1140, 1100, 1040, 995, 885, 850, 800 cm^{-1}; ^{13}C-NMR (50 MHz, $CDCl_3$): (axial OH) 159.24, 152.27, 127.79, 119.67, 107.69, 102.05, 91.72, 55.30, 35.97, 23.83, 20.60; (equatorial OH) 159.33, 153.37, 127.61, 119.36, 107.74, 101.95, 94.42, 55.30, 37.96, 27.69, 20.86; *m/e* 194. Precise mass determination, calc for $C_{11}H_{14}O_3$, 194.09435; found, 194.09178.

3,4-Dihydro-7-methoxy-4-methyl-2H-1-benzopyranyl-2-acetate, **20**

Lactol **14** (1.18 g, 5.75 mmol) was dissolved in 30 ml $CHCl_3$. 4-Dimethylaminopyridine (0.70 g, 5.75 mmol) was added, followed by an excess (0.86 ml, 1.6 equiv) of Ac_2O. The reaction was stirred for 20 min at room temp (NMR indicated the disappearance of the anomeric proton signal at δ 5.5). Quenching (2 ml MeOH) followed by solvent removal *in vacuo* gave a clear yellow oil. Workup was effected by dissolving the crude oily residue in ether, at which point the DMAP began to precipitate. The soln was then filtered through cotton, washed with 40 + 20 ml 2 N HCl and 2 × 25 ml 5% $NaHCO_3$, dried over $MgSO_4$, and concentrated to give 1.20 g (88%) of **20** as a clear oil: 1:1 *trans*:*cis*. ^{1}H-NMR (360 MHz, $CDCl_3$): 7.14 (dd, 0.5 H, J = 8.6, 1 Hz), 7.07 (dd, 0.5 H, J = 8.5, 0.6 Hz), 6.55 (2 dd, 1H, J = 4.0, 8.5 Hz), 6.48 (t, 0.5 H, J = 2.7 Hz, axial OAc), 6.44 (bs and q, 1.5 H), 3.75 (s, 3H), 3.06 (m, 0.5 H, axial OAc), 2.98 (m, 0.5 H, eq OAc), 2.24 (ddd, 0.5 H, J = 6.3, 3.1, 14 Hz, eq OAc), 2.11 (s, 1.5 H), 2.07 (s, 1.5 H), 2.09 (ddd, 0.5 H, axial OAc), 1.86 (m, 0.5 H, eq OAc), 1.75 (ddd, 0.5 H, J = 2.6, 12, 14 Hz, axial OAc), 1.39 (d, 1.5 H, J = 7.1 Hz, eq OAc), 1.35 (d, 1.5 H, J = 6.8 Hz, axial OAc); IR (neat): 3020, 2975, 2945, 2890, 2845, 1750, 1620, 1585, 1505, 1465, 1445, 1425, 1375, 1325, 1290, 1275, 1245, 1205, 1165, 1135, 1085, 1035, 1025, 1000, 935, 885, 835, 805 cm^{-1}; ^{13}C-NMR (50 MHz, $CDCl_3$): 169.63, 169.44, 159.27, 159.24, 152.11, 151.74, 128.19, 127.21, 119.10, 118.97, 108.53, 108.37, 101.91, 101.86, 91.61, 90.37, 55.22, 34.06, 33.72, 26.32, 23.11, 21.79, 21.01, 19.51; *m/e* 236. (Found: C, 66.16%; H, 6.87%; $C_{13}H_{16}O_4$ requires: C, 66.09%; H, 6.83%.)

3,4-Dihydro-4,7-dimethyl-2H-1-benzopyranyl-2-acetate, **19**

Lactol **13** (418 mg, 2.35 mmol), DMAP (288 mg, 2.35 mmol), and Ac_2O (0.50 ml, 5.3 mmol) were combined in 20 ml $CHCl_3$ as described for **20**. Radial chromatography of the residue (CH_2Cl_2 load solvent, ether eluent) afforded 505 mg (98%) of **19** as a clear oil: 1:1 *trans*:*cis* mixture. ^{1}H-NMR (360 MHz, $CDCl_3$): 7.14 (d, 0.5 H, J = 7.9 Hz), 7.06 (d, 0.5 H, J = 7.9 Hz), 6.79 (2 dd, 1H, J = 4.7, 7.9 Hz), 6.71 (bs, 1H), 6.49 (t, 0.5 H, J = 2.7 Hz, axial OAc), 6.45 (dd, 0.5 H, J = 3.1, 5.6 Hz, eq OAc), 3.09 (m, 0.5 H, axial OAc), 3.00 (m, 0.5 H, eq OAc), 2.28 (s, 3H), 2.25 (ddd, 0.5 H, J = 6.5, 3.1, 14 Hz, eq OAc), 2.10 (ddd, 0.5 H, J = 5.6, 2.9, 14 Hz, axial OAc), 2.10 (s, 1.5 H), 2.06 (s, 1.5 H), 1.88 (m, 0.5 H, eq OAc), 1.76 (ddd, 0.5 H, J = 2.6, 12, 14 Hz, axial OAc), 1.41 (d, 1.5 H, J = 7.1 Hz, eq OAc), 1.36 (d, 1.5 H, J = 6.9 Hz, axial OAc); IR (neat): 3035, 2970, 2940, 2885, 1758, 1630, 1580, 1510, 1460, 1425, 1380, 1330, 1300, 1235, 1200, 1165, 1140, 1090, 1055, 1010, 945, 930, 895, 870, 810 cm^{-1}; ^{13}C-NMR (50 MHz, $CDCl_3$): 169.64, 169.47, 151.21, 150.83, 137.59, 137.54, 127.46, 126.44, 123.95, 123.92, 122.51, 122.44, 117.50, 117.37, 91.67, 90.42, 34.11, 33.77, 26.62, 23.43, 21.78, 21.06, 20.85, 19.46; *m/e* 220.

2-Phenylselenenyltetrahydropyran, **11**

(a) *From 2-hydroxytetrahydropyran.* The pyranol **10** (159 mg, 1.55 mmol), prepared by the method of Woods,[20] was dissolved in 10 ml benzene along with a few crystals of *p*-toluenesulfonic acid. After the soln had stirred under an argon atmosphere, benzeneselenol (270 mg, 1.1 equiv) was added via 1 cm^3 syringe, and the resulting mixture was stirred at 25° overnight. Reduced-pressure solvent evaporation followed by radial chromatography (pet ether) gave, in addition to diphenyl diselenide (first band), 344 mg (92%) of selenoacetal, **11**, as a light yellow free-flowing oil. ^{1}H-NMR (360 MHz, $CDCl_3$): 7.59 (m, 2H), 7.26 (m, 3H), 5.70 (t, 1H, J = 4.0 Hz), 4.17 (m, 1H), 3.67 (m, 1H), 2.12 (m, 1H), 2.00 (m, 1H), 1.78 (m, 1H), 1.75–1.60 (m, 3H); IR (neat): 3065, 2945, 2865, 1580, 1480, 1470, 1440, 1335, 1285, 1260, 1230, 1185, 1170, 1105, 1075, 1035, 1010, 885, 870, 815, 740, 690, 670 cm^{-1}; ^{13}C-NMR (50 MHz, $CDCl_3$): 133.55, 128.87, 128.29, 127.04, 84.66, 64.31, 32.77, 25.69, 21.46. Precise mass determination, calc for $C_{11}H_{14}OSe$, 242.02098; found, 242.02569.

(b) *From 2-acetoxytetrahydropyran.* The acetate **12**[21] (328 mg, 2.28 mmol) was converted into **11** by the procedure described for **10**. Yield (after chromatography): 97%.

2-Phenylselenenyl-3,4-dihydro-7-methoxy-4-methyl-2H-1-benzopyran, **16**

From acetate **20**. Compound **20** (104 mg, 0.44 mmol) was dissolved in 20 ml anhyd benzene in a 50 ml three-necked round-bottomed flask. After the addition of a few crystals of *p*-toluenesulfonic acid and a subsequent argon purge, benzeneselenol (218 mg, 1.4 mmol) was added in one portion, via syringe, to the stirred soln. After 3 hr, the solvent was evaporated to give a yellow residue. Radial chromatography (pet ether) afforded, along with diphenyl diselenide (first band), 91 mg (62%) of a 1.5:1 *trans*:*cis* mixture of selenoacetals **16** as a light yellow oil. ^{1}H-NMR (360 MHz, $CDCl_3$): (axial PhSe) 7.67–7.62 (m, 2H), 7.34–7.27 (m, 3H), 7.14 (d, 1H, J = 8.6 Hz), 6.57 (dd, 1H, J = 2.6, 8.6 Hz), 6.40 (d, 1H, J = 2.6 Hz), 6.06 (t, 1H, J = 3.6 Hz), 3.77 (s, 3H), 3.11 (m, 1H), 2.38 (ddd, 1H, J = 3.6, 5.8, 13.8 Hz), 2.13 (ddd, 1H, J = 3.6, 10.6, 13.8 Hz), 1.34 (d, 3H, J = 6.7 Hz); (equatorial PhSe) 7.71–7.66 (m, 2H), 7.34–7.27 (m, 3H), 7.08 (d, 1H, J = 8.5 Hz), 6.52 (dd, 1H, J = 2.6, 8.5 Hz), 6.45 (d, 1H, J = 2.6 Hz), 5.80 (dd, 1H, J = 3.0, 9.8 Hz), 3.76 (s, 3H), 2.98 (m, 1H), 2.48 (ddd, 1H, J = 3.0, 5.8, 13.6 Hz), 1.90 (m, 1H), 1.33 (d, 3H, J = 6.8 Hz); IR (neat): 3085, 3020, 2990, 2960, 2895, 2860, 1625, 1585, 1510, 1485, 1475, 1450, 1380, 1330–1280, 1260, 1215, 1205, 1170, 1135, 1050, 1000, 940, 890, 845, 810, 750, 700 cm^{-1}; ^{13}C-NMR (50 MHz, $CDCl_3$): (anomeric C) axial, 80.48; equatorial, 79.28; *m/e* 334 (^{80}Se), 332 (^{78}Se), 177 (M − PhSe), 162 (M − PhSe − CH_3). Precise mass determination, calc for $C_{17}H_{18}{}^{78}SeO_2$, 332.04798; found, 332.05398.

From lactol **14**. Compound **14** (215 mg) was dissolved in 30 ml anhyd benzene in a three-necked round-bottomed flask equipped with a condenser. After addition of a few crystals of *p*-TsOH and a subsequent argon purge, the soln was heated to reflux. Benzeneselenol (3 equiv) was added in one portion, via syringe, to the boiling soln. After 24 hr, solvent evaporation gave a yellow residue. The NMR spectrum of the crude product indicated not only the selenide **16** (in a 1.7:1 *trans*:*cis* ratio) but also the corresponding chroman **18**. Preparative TLC (pet ether, multiple elutions) afforded a 55% yield of selenoacetal–chroman mixture. (In some runs, chromene **26** could be detected as well. While the *trans*:*cis* isomer ratio did not vary with the reflux time or the amount of added PhSeH, the relative amount of chroman **18** did.) Compound **18** displayed ^{1}H-NMR (360 MHz, $CDCl_3$): 7.05 (d, 1H, J = 8.7 Hz), 6.48 (dd, 1H, J = 2.6, 8.7 Hz), 6.36 (d, 1H, J = 2.6 Hz), 4.21 (ddd, 1H, J = 3.5, 7, 11 Hz), 4.15 (ddd, 1H, J = 3.5, 7, 11 Hz), 3.76 (s, 3H), 2.90 (m, 1H), 2.06 (2 ddd, 1H, J = 3.5, 5.5, 7, 14 Hz), 1.70 (2 ddd, 1H, J = 3.5, 6.3, 7, 14 Hz), 1.30 (d, 3H, J = 7.0 Hz).

2-Phenylselenenyl-3,4-dihydro-4,7-dimethyl-2H-1-benzopyran, **15**

From acetate **19**. Compound **19** (160 mg, 0.73 mmol) was reacted in the manner described for **20** to afford selenoacetal **15**, a light yellow free-flowing oil (90%), as a 1.5:1 *trans*:*cis* isomer mixture. ^{1}H-NMR (360 MHz, $CDCl_3$): (axial PhSe) 7.67–7.62 (m, 2H), 7.34–7.27 (m, 3H), 7.14 (d, 1H, J = 7.8 Hz), 6.80 (d, 1H, J = 7.8 Hz), 6.67 (bs, 1H), 6.07 (t, 1H, J = 3.6 Hz), 3.13 (m, 1H), 2.38 (ddd, 1H, J = 3.6, 5.8, 13.8 Hz), 2.29 (s, 3H), 2.14 (ddd, 1H, J = 3.6, 10.7, 13.8 Hz), 1.36 (d, 3H, J = 6.8 Hz); (equatorial PhSe) 7.71–7.66 (m, 2H), 7.34–7.27 (m, 3H), 7.07 (d, 1H, J = 7.8 Hz), 6.75 (d, 1H, J = 7.8 Hz), 6.72 (bs, 1H), 5.81 (dd, 1H, J = 3.2, 9.6 Hz), 2.99 (m, 1H), 2.50 (ddd, 1H, J = 3.1, 5.9, 13.6 Hz), 2.28 (s, 3H), 1.90 (m, 1H), 1.35 (d, 3H, J = 6.9 Hz); IR (neat): 3050, 2970, 2950, 2900, 1620, 1575, 1510, 1455, 1420, 1380, 1360, 1330–1290, 1250, 1220, 1170, 1145, 1105, 1050, 930, 890, 870, 810, 755, 705 cm^{-1}; ^{13}C-NMR (50 MHz, $CDCl_3$): (anomeric C) axial, 80.28; equatorial, 79.19. Precise mass determination, calc for $C_{17}H_{18}{}^{78}SeO$, 316.05304; found, 316.05057.

From lactol **13**. Hemiacetal **13** (57 mg, 0.32 mmol) was combined with benzeneselenol (1.25 equiv) for 3 hr in the manner described for **14**. Chroman-free selenoacetal **15** was

obtained in 62% yield. The *trans*:*cis* product ratio was 1.7:1.

Chroman **17**, present in some runs, was identified by its ^{1}H-NMR spectrum (360 MHz, $CDCl_3$): 7.04 (d, J = 8.5 Hz), 6.72 (d, J = 8.5 Hz), 6.62 (bs), 4.19 (ddd, J = 3.7, 11 Hz), 4.13 (ddd, J = 3.7, 11 Hz), 2.91 (m), 2.27 (s), 2.05 (m), 1.69 (m), 1.30 (d, J = 7.0 Hz).

*7-Methoxy-4-methyl-*4H-1-*benzopyran*, **26**

Selenoacetal **16** (60 mg) was taken up in $CHCl_3$ (15 ml) and cooled to 0°. When 1.0 equiv of *m*-CPBA was added, the yellow hue of the soln rapidly intensified as diphenyl diselenide was formed. After 10 min at 0°, the solvent was evaporated *in vacuo* to give a yellow residue. The NMR spectrum indicated the complete disappearance of the anomeric carbon signals at δ 6.0 and 5.8 ppm and the appearance of the enol ether olefinic signal at δ 4.9. On preparative TLC (pet ether, multiple elutions), 16 mg (52%) of the chromene **26** were obtained as a clear oil. ^{1}H-NMR (360 MHz, $CDCl_3$): 7.01 (d, 1H, J = 8.5 Hz), 6.59 (dd, 1H, J = 2.6, 8.5 Hz), 6.45 (dd, 1H, J = 1.5, 6.3 Hz), 6.41 (d, 1H, J = 2.6 Hz), 4.89 (dd, 1H, J = 6.3, 3.9 Hz), 3.76 (s, 3H), 3.45 (m, 1H), 1.31 (d, 3H, J = 6.9 Hz); IR (neat): 3100, 3000, 2960, 2925, 2840, 1665, 1620, 1580, 1510, 1470, 1450, 1425, 1340, 1315, 1295, 1280, 1245, 1200, 1165, 1140, 1125, 1050, 935, 845, 815, 765 cm^{-1}; *m/e* 176.

cis-3,5-*Dimethyl*-5-*phenylselenenyltetrahydrofuran*-2-*one*, **29**

To a soln containing 1.3 g (10 mmol) of 2-methyllevulinic acid in dry, oxygen-free benzene (25 ml) was added a crystal of *p*-toluenesulfonic acid and 1.9 g (1.2 equiv) of benzeneselenol. The mixture was stirred at room temp for 36 h, washed with $NaHCO_3$ aq and dried over $MgSO_4$. After the solvent was removed *in vacuo*, the crude product was purified using preparative TLC (SiO_2) (5% ether:hexane), yielding 1.5 g (90%) of pure **29**. ^{1}H-NMR (90 MHz, $CDCl_3$): δ 7.7 (m, 2H), 7.25 (m, 3H), 2.8–2.3 (m, 3H), 1.8 (s, 3H), 1.2 (d, 3H, J = 7 Hz); IR: 1790 cm^{-1}; *m/e* 270.

2,4-*Dimethyl*-Δ^3-γ-*butyrolactone*, **30**

A soln containing 0.85 g (5 mmol) of **29** in 20 ml CH_2Cl_2 was ozonized until a blue color had developed. Excess O_3 was removed by bubbling N_2 through the soln for 15 min. This soln was then poured into a refluxing soln of pyridine (1.2 ml, 3 equiv) in 25 ml of CH_2Cl_2. Reflux was continued for 2 hr. The reaction was cooled to room temp, washed with water several times, and dried over $MgSO_4$. Solvent was stripped on a rotary evaporator to give a crude product. Purification using preparative TLC (SiO_2) (10% ether:hexane) yielded 0.45 g (80%) of **31**. ^{1}H-NMR (90 MHz, $CDCl_3$): δ 5.15 (m, 1H), 3.2 (m, 1H), 1.95 (d, 3H, J = 1.5 Hz), 1.3 (d, 3H, J = 7 Hz).

5-*Methyl*-2-*phenylselenenyltetrahydrofuran*, **24** and **25**

To a soln of 0.50 g (5 mmol) γ-valerolactone in 10 ml dry toluene at −78° was added 5.5 ml (1.1 equiv) diisobutylaluminum hydride (1.0 M in hexane). After 1 hr, a soln of 1.9 ml (3 equiv) boron trifluoride etherate and 0.95 g (1.2 equiv) benzeneselenol was added to this soln; reaction proceeded for 10 min at −78° before a water quench. The crude product was dissolved in diethyl ether, washed twice each with 10% HCl, sat $NaHCO_3$ aq, and water, and then dried with $MgSO_4$. Solvent evaporation and chromatography yielded **24** and **25** (1.2 g, 100%): ^{1}H-NMR (90 MHz, $CDCl_3$): δ 7.65 (m, 2H), 7.28 (m, 3H), 6.02 (dd, 1H, J = 3.5, 3.8 Hz), 4.36 (m, 1H), 2.50 (m, 1H), 2.10 (m, 2H), 1.45 (m, 1H), 1.32 (d, 3H, J = 6.1 Hz); IR ($CHCl_3$): 1580, 1480, 1070, 690 cm^{-1}; *m/e* 242.

2-*Phenylselenenyltetrahydropyran*, **11**, *from δ-valerolactone*

To a soln of 2.48 g (25 mmol) δ-valerolactone in 100 ml dry toluene at −78° was added 27 ml (1.1 equiv) diisobutylaluminum hydride (1.0 M in hexane). After 1.5 hr, a soln of 10 ml (3 equiv) boron trifluoride etherate and 4.75 g (1.2 equiv) benzeneselenol was added to this soln; reaction proceeded for 10 min at −78° before a water quench. The crude product was dissolved in diethyl ether, washed twice with 10% HCl, saturated $NaHCO_3$ aq, and water, and dried with $MgSO_4$. Solvent evaporation and chromatography yielded **11** (5.3 g, 88%).

6-*Methyl*-2-*phenylselenenyltetrahydropyran*, **21**

To a soln of 15 ml dry toluene and 0.15 g (1.3 mmol) δ-caprolactone at −78° was added 1.4 ml (1.1 equiv) diisobutylaluminum hydride (1.0 M in hexane). After this soln had stirred for 1 hr, a mixture of 0.55 g (3 equiv) boron trifluoride etherate and 0.25 g (1.2 equiv) benzeneselenol was added at −78° and allowed to react for 7 min before a sat NH_4Cl quench. The crude product was dissolved in diethyl ether and was washed twice each with sat $NaHCO_3$ aq, 10% HCl, and water. Drying with $MgSO_4$ followed by solvent evaporation and chromatography afforded **21** (0.33 g, 100%). ^{1}H-NMR (90 MHz, $CDCl_3$): δ 7.51 (m, 2H), 7.18 (m, 3H), 5.88 (t, 1H, J = 2.5 Hz), 4.17 (dd, 1H, J = 2.3, 11.1 Hz), 1.98 (m, 2H), 1.80–1.20 (m, 4H), 1.52 (d, 3H, J = 6.3 Hz); IR ($CHCl_3$): 1480, 1190, 1110, 1035, 900, 730, 650 cm^{-1}; *m/e* 256.

2-n-*Butylselenenyltetrahydropyran*, **33**

To a soln of 0.35 g (1.4 mmol) **11** in 20 ml dry THF at −78° was added 1.1 ml (1.1 equiv) n-BuLi (1.6 M in hexane). After 30 min, 0.8 ml (3 equiv) HMPA and then 2 ml water were added, and the THF was evaporated. The residue obtained was diluted with water and extracted with diethyl ether; the ether extracts were washed twice with water. $MgSO_4$ drying and solvent evaporation yielded **34** (0.32 g, 100%). ^{1}H-NMR (90 MHz, $CDCl_3$): δ 5.39 (t, 1H, J = 4.2 Hz), 4.05 (m, 1H), 3.57 (m, 1H), 2.65 (m, 2H, $SeCH_2$), 2.05–1.40 (m, 10H), 0.90 (t, 3H, J = 7.4 Hz); IR ($CHCl_3$): 1470, 1035, 555 cm^{-1}; *m/e* 222.

2-n-*Butylselenenyl-5-methyltetrahydrofuran*, **32**

To a soln of 0.35 g (1.4 mmol) **24** and **25** in 20 ml dry THF at −78° was added 1.1 ml (1.1 equiv) n-BuLi (1.6 M in hexane). After 30 min, 0.80 ml (3 equiv) HMPA and 0.20 ml (2 equiv) prenyl bromide were added in succession, and the reaction was allowed to warm to room temp. After 20 hr of stirring, this soln was quenched with sat NH_4Cl, the THF was evaporated, and the resultant residue was extracted with diethyl ether. The extracts were washed twice with water and dried with $MgSO_4$. Solvent evaporation and chromatography yielded **33** (0.18 g, 57%). ^{1}H-NMR (90 MHz, $CDCl_3$): δ 5.72 (dd, 1H, J = 3.9, 7.2 Hz), 4.22 (m, 1H), 2.70 (m, 2H, $SeCH_2$), 2.40–1.3 (m, 6H), 1.25 (d, 3H, J = 6.0 Hz), 0.88 (t, 3H, J = 7.4 Hz); IR ($CHCl_3$): 1460, 1205, 1075, 575 cm^{-1}; *m/e* 222. A minor product in this reaction is phenyl prenyl selenide (0.11 g, 35%). ^{1}H-NMR (90 MHz, $CDCl_3$): δ 7.50 (m, 2H), 7.20 (m, 3H), 5.35 (t, 1H, J = 7.5 Hz), 3.52 (d, 2H, J = 8.6 Hz), 1.60 (s, 3H), 1.45 (s, 3H); IR ($CHCl_3$): 1250, 900, 750, 650 cm^{-1}; *m/e* 222.

2-*Allyl*-2-*phenylselenenyl*-5-*methyltetrahydrofuran*, **31**

To a dry THF soln of 0.26 g (1.2 equiv) 1,1,1,3,3,3-hexamethyldisilazane and 1.2 ml (1.3 equiv) n-BuLi (1.6 M in hexane) at −78° was added 0.35 g (1.4 mmol) of **24**. After stirring at −78° for 30 min, this soln was warmed to −20° and was allowed to stir for 2.5 hr before 0.80 ml (3 equiv) HMPA and 0.20 ml (2 equiv) allyl bromide were added successively. This soln was allowed to warm to room temp with stirring for 20 hr and was quenched with sat NH_4Cl soln. The THF was evaporated and the crude product was diluted with diethyl ether, washed twice with sat NH_4Cl, washed once with water, and dried with $MgSO_4$. Solvent evaporation and chromatography afforded **32** (0.20 g, 50%). ^{1}H-NMR (90 MHz, $CDCl_3$): δ 7.40 (m, 2H), 7.13 (m, 3H), 5.69 (m, 1H), 4.70 (d, 2H, J = 9.1 Hz), 3.64 (m, 1H), 2.38 (t, 1H, J = 8.2 Hz), 2.30–1.40 (m, 3H), 0.80 (d, 3H, J = 6.1 Hz); IR ($CHCl_3$): 1480, 890, 715, 655 cm^{-1}; *m/e* 282.

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