Stereoselective Synthesis of Cyclic Ethers Using Vinylogous Sulfonates as Radical Acceptors: Effect of *E*/*Z* Geometry and Temperature on Diastereoselectivity

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Treatment of the *E*-vinylogous sulfonates **1a**−**g** with tris(trimethylsilyl)silane and triethylborane, in the presence of air, furnished the cyclic ethers **2/3a**−**g** with good to excellent diastereoselectivity favoring the *cis*-isomer **2**. This study demonstrated the level of stereocontrol in a 6-exo radical cyclization and may be attributed to the type of radical intermediate. Hence, the modest selectivity obtained for the cyclization of **1e** may be a function of the acyl radical geometry (sp^2) and high inversion barrier (29 kcal/mol) as compared to the alkyl (1 kcal/mol) and vinyl (2.9 kcal/mol) radicals. This is consistent with the acyl radical cyclization having an earlier transition state than the corresponding alkyl and vinyl radicals. The modest diastereoselectivity can be improved dramatically using the *Z*-vinylogous sulfonate (≥34:1; R = Ph) to promote kinetic trapping of the *s-trans* rotamer **I** and **III**, respectively (Figure 1). The 5-exo alkyl radical cyclization reaction under nonreductive Keck-allylation conditions was also examined, in which **8** was formed in 91% overall yield. This transformation provides a convenient method for in situ homologation and should be applicable to target directed synthesis.

Introduction

Cyclic ether containing natural products represent both architecturally challenging and biologically important molecules that have stimulated the development of an array of methods for their stereocontrolled syntheses.[1,2] Methods that utilize radicals as reactive intermediates have gained considerable prominence in recent times, primarily due to the excellent stereocontrol that can be obtained. Furthermore, the design and implementation of tandem-reaction sequences that allow the construction of multiple carbon−carbon bonds provides additional versatility to this methodology.[3] In a program directed towards the synthesis of cyclic ether containing natural products,[4] we had examined the merit of vinylogous carbonates[5,6] in a series of intramolecular cyclizations. We decided to extend our studies to vinylogous sulfonates (VINS)[7,8] since we anticipated that the sulfone would allow alternative modes of functionalization for the cyclic ether intermediate.[9]

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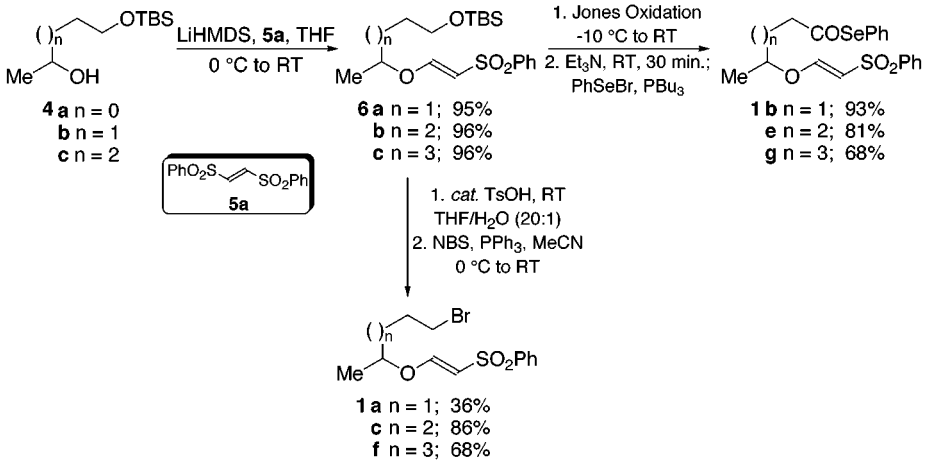
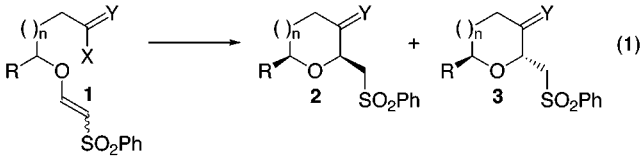
Scheme 1



Herein, we describe a full account of the intramolecular addition of acyl, alkyl, and vinyl radicals to vinylogous sulfonates (eq 1). In the course of this study, we provide



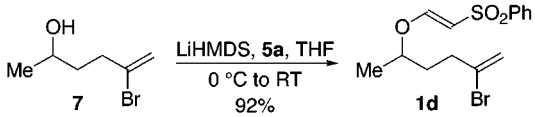
(1)

evidence to support the hypothesis that acyl radicals proceed through earlier transition states than the corresponding alkyl and vinyl radicals to explain the erroneous stereochemical result in the 6-exo acyl radical cyclization. Our expectation that the *Z*-vinylogous sulfonate would dramatically improve the level of diastereocontrol, through the kinetic trapping of the *s-trans* **III** rotamer (Figure 1), provides a convenient method for improving poor stereocontrol in this type of radical cyclization.[7,10]

Results and Discussion

Scheme 1 summarizes the synthetic routes utilized for the preparation of the alkyl bromides and acyl selenides required for the cyclization study. Treatment of the secondary alcohols **4a**−**c** with lithium hexamethyldisilyl azide, followed by *E*-bis(phenylsulfonyl)-1,2-ethylene **5a**, furnished the corresponding *E*-vinylogous sulfonates **6a**−**c** in excellent yield.[11] Oxidation of the primary *tert*-butyldimethylsilyl ethers **6a**−**c** with Jones reagent furnished the corresponding carboxylic acids,[12] which were then converted to the acyl selenides **1b**, **1e**, and **1g** using the Crich protocol in 68−93% overall yield.[13] The alkyl bromides were also available from the vinylogous sulfonates **6a**−**c** via acid-catalyzed removal of the *tert*-butyldimethylsilyl ether, followed by the treatment of the primary alcohol with *N*-bromosuccinimide and triphenylphosphine to afford the alkyl bromides **1a**,[14] **1c**, and **1f** in 36−86% overall yield from **6**.[15]

The vinyl bromide **1d** was prepared in a single step from the known secondary alcohol **7** in 92% yield (eq 2),[16]



(2)

completing the synthesis of the substrates required for the cyclization study. Table 1 provides a summary of the results from this study.

Tetrahydrofuran Construction. Treatment of the vinylogous sulfonates **1a**,**b** with tris(trimethylsilyl)-silane[17] and triethylborane at room temperature, in the presence of air, furnished the 2,5-disubstituted tetrahydrofurans **2/3a**,**b** in 87−99% yield, with excellent diastereoselectivity**,** favoring the *cis*-isomer (Table 1; entries 1 and 2). The stereochemical outcome for the cyclization reactions is consistent the *Beckwith Transition State Model*, which has been used extensively to predict the outcome of 5-hexenyl type radical cyclizations.[18] The cyclization was also extended to the Keck-type allylation,[19] which facilitates the tandem formation of two new carbon−carbon bonds. Treatment of the alkyl halide **1a** with allyltributyltin and triethylborane at room temperature, in the presence of air, furnished the cyclic ether **8** in 91% yield, epimeric (1.4:1) at the phenylsulfonyl group (eq 3).[10] This transformation provides a useful method for homologation, and should allow the introduction of various side chains in a single operation, thus avoiding

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(14) The vinylogous sulfonate **1a** could also be prepared via the following reaction sequence. Treatment of the diol **i** with *N*-bromosuccinimide at 0 °C afforded the primary bromide, which was then converted to the *E*-vinylogous sulfonate **1a** in an improved 53% overall yield.

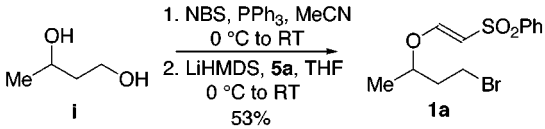

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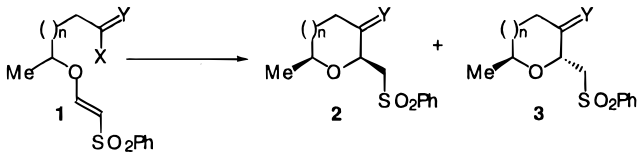
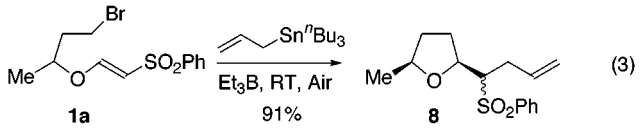
Table 1. Intramolecular Radical Cyclizations of the Vinylogous Sulfonates (VINS) 1a−g



entry	vinylogous sulfonate (VINS) **1**[a]				temp	conc,[b] M	cyclic ethers: ratio of **2**:**3**[c]	cyclic ethers: yield (%)[d]
1	**1a**	$n = 0$	X = Br	Y = H_2	rt	0.02	≥19:1	99
2	**1b**	$n = 0$	X = SePh	Y = O	rt	0.02	17:1	87
3	**1c**	$n = 1$	X = Br	Y = H_2	rt	0.01	≥19:1	90
4	**1c**	$n = 1$	X = Br	Y = H_2	Δ	0.01	≥19:1	89
5	**1d**	$n = 1$	X = Br	Y = CH_2	rt	0.01	≥19:1	90
6	**1d**	$n = 1$	X = Br	Y = CH_2	Δ	0.01	≥19:1	95
7	**1e**	$n = 1$	X = SePh	Y = O	rt	0.01	6:1	90
8	**1e**	$n = 1$	X = SePh	Y = O	Δ	0.01	3:1	95
9	**1f**	$n = 2$	X = Br	Y = H_2	rt	0.005	≥19:1	34
10	**1g**	$n = 2$	X = SePh	Y = O	rt	0.005	17:1	63

[a] All the cyclizations were carried out on a 0.3 mmol reaction scale. [b] $(TMS)_3SiH$, Et_3B, PhH. [c] Ratios of diastereoisomers were determined by 400 MHz ^1H NMR integration. [d] Isolated yields.

the alternative multistep sequences and carbanion mediated functionalization which leads to ring-opening through β-elimination.[8]



Tetrahydropyran Construction. The synthesis of tetrahydropyrans was initiated by treating the vinylogous sulfonates **1c**,**d** under analogous conditions, both at reflux and room temperature, to furnish the 2,6-disubstituted tetrahydropyrans **2/3c**,**d** in 89−95% yield, with excellent diastereoselectivity favoring the *cis*-isomer (Table 1; entries 3−6). However, the poor diastereocontrol in the 6-*exo*-trigonal acyl radical cyclization of **1e** (entry 7 and 8) was attributed to kinetic trapping of the *s-cis* rotamer **II**, as outlined in Figure 1, analogous to the vinylogous carbonates.[5b] Despite the fact that the mixture could be equilibrated to the thermodynamically more stable diastereoisomer **2e**, using a catalytic amount of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in refluxing benzene, the additional step and low recovery deemed it unsuitable for synthetic purposes.

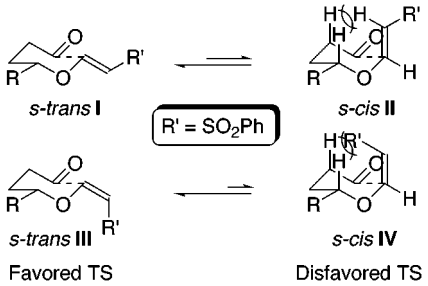
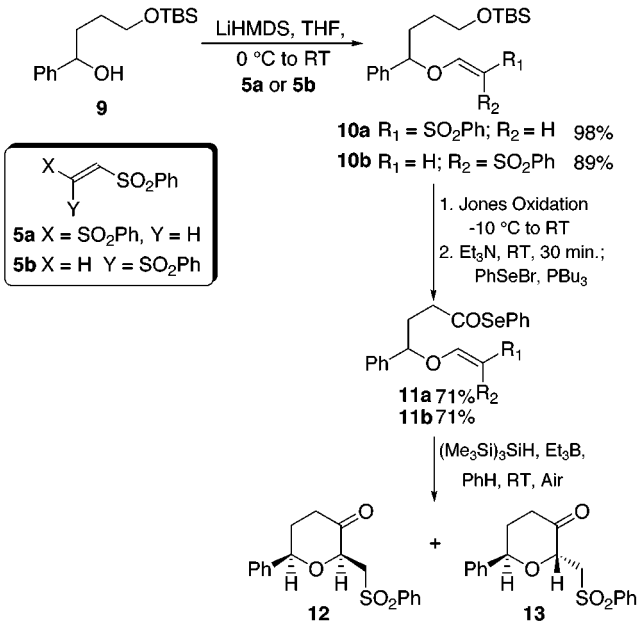


Figure 1.

The ability to prepare *E*- and *Z*-vinylogous sulfonates provided an opportunity to test the hypothesis, that the rotamer population could be altered using the acceptor geometry and thus improve the diastereoselectivity in the 6-exo acyl radical cyclization.[20] This study would determine whether the *s-trans* **III** rotamer could be promoted over the corresponding *s-cis* **IV** rotamer.[10] To this end, the secondary alcohol **9** was converted to the *E*- and *Z*-vinylogous sulfonates **10a** and **10b** using lithium hexamethyldisilyl azide (Scheme 2), followed by the addition of the *E*- or *Z*-bis(phenylsulfonyl)-1,2-ethylene **5a** or **5b,** respectively.[11] The primary *tert*-butyldimethylsilyl ethers **10a** and **10b** were then oxidized with Jones reagent to the corresponding carboxylic acids[12] and converted to the acyl selenides **11a** and **11b** using the Crich protocol in 71% overall yield in each case.[13]

Scheme 2



Treatment of the acyl selenides **11a** and **11b**, under the standard cyclization conditions furnished the cyclic ethers **12/13** in good yield, with 7:1 and ≥35:1 *cis*-diastereoselectivity (Table 2, entries 1−2), thus confirming the relevance of the vinylogous sulfonate geometry

(20) Hanessian, S.; Dhanoa, D. S.; Beaulieu, P. L. *Can. J. Chem.* **1987**, *65*, 1859.

Table 2. Intramolecular Radical Cyclizations of the *E*- and *Z*-Vinylogous Sulfonates 11a/b

					cyclic ethers	
entry	VINS	**11**[a]	method[b]	temp	ratio of **12**:**13**[c]	yield (%)[d]
1	**a**	*E*	A	rt	7:1	85
2	**b**	*Z*	A	rt	35:1	84
3	**a**	*E*	A	Δ	5:1	80
4	**b**	*Z*	A	Δ	34:1	82
5	**a**	*E*	B	Δ	5:1	83
6	**b**	*Z*	B	Δ	34:1	83

[a] All the cyclizations were carried out on a 0.3 mmol reaction scale. [b] Method A: $(TMS)_3SiH$, Et_3B, PhH. Method B: $(TMS)_3SiH$, AIBN, PhH. [c] Ratios of diastereoisomers were determined on crude reaction mixtures by HPLC. [d] Isolated yields.

to rotamer population. To further highlight the difference in the diastereochemical outcome for the two isomers, the cyclizations were repeated at elevated reaction temperature. As expected, the *Z*-isomer **11b** retains the very high diastereoselectivity (34:1), while the *E*-isomer **11a** furnished the 2,6-disubstituted tetrahydropyran-3-ones **12/13** as a slightly lower 5:1 mixture of diastereoisomers (entries 3 and 4). Finally, we decided to examine the propensity for triethylborane to act as a Lewis acid through chelation of the acyl or ring oxygen forcing the vinylogous sulfonate to become *s-cis* **II** (Figure 1), by repeating the cyclization with a noncoordinating initiator (AIBN). Treatment of the acyl selenides **11a** and **11b**, under the analogous reaction conditions, albeit with catalytic AIBN as the initiator, furnished the cyclic ethers **12/13** with analogous selectivity (entries 5 and 6). Hence, it appears the Lewis acidity of triethylborane plays a minimal role in diastereochemical outcome of these reactions.

Additional insight into the low diastereocontrol was also gleaned from high level ab initio calculations (MP2/6-311G**) on the acyl radical ($CH_3CO\cdot$).[21] These calculations indicate that the acyl radical is an sp^2-hybridized species with a barrier to inversion of 29 kcal/mol. Conversely, the corresponding alkyl and vinyl radicals have significantly lower barriers to inversion, 1 and 2.9 kcal/mol, respectively.[3] It is therefore plausible that acyl radicals commit to bond formation significantly earlier than the corresponding alkyl and vinyl radicals. This trend is also apparent in the 5- and 7-exo radical cyclizations summarized in Table 1 (entries 1/2 and 9/10).

Tetrahydrooxepine Construction. The synthesis of 2,7-disubstituted tetrahydrooxepines **2/3f**,**g** was also investigated. Treatment of the acyl selenides **1f**,**g** with tris(trimethylsilyl)silane[17] and triethylborane, in the presence of air, at room temperature afforded the 2,7-disubstituted tetrahydrooxepines **2/3f**,**g** in 34−63% yield, and with excellent diastereoselectivity (Table 1, entries 9−10). Interestingly, in the acyl radical cyclization the predominant byproduct was the aldehyde, formed from the direct reduction of the acyl radical intermediate. This provides another illustration of the effectiveness of the low-temperature reaction conditions for suppression of decarbonylation in demanding cyclization reactions of this nature.[5b] The vinylogous sulfonates, however, appear to be less efficient radical acceptors compared to the vinylogous carbonate from the relative efficiency of the cyclization reactions.

(21) Guerra, M. *J. Chem. Soc., Perkin Trans. 2* **1996**, 779.

In conclusion, we have demonstrated the intramolecular addition of acyl, alkyl, and vinyl radicals to vinylogous sulfonates for the efficient and stereoselective synthesis of *cis*-disubstituted cyclic ethers. The stereochemical outcome of the cyclization was confirmed with the aid of NOE experiments and attributed to kinetic trapping of the favored transition state **I** ($n = 0$, 1, and 2) which has the alkyl substituent pseudoequatorial with the vinylogous sulfonate *s-trans*, to alleviate $A^{1,3}$-allylic strain in the transition state. The excellent regiochemical control in the cyclization is a function of the intramolecular addition of a nucleophilic radical to the LUMO of the vinylogous sulfonate.[22] The ability to utilize the *Z*-vinylogous sulfonate to improve the diastereoselectivity, by favoring **III** over **IV**, in the 6-*exo*-trigonal acyl radical cyclization is particularly attractive for target-directed synthesis (Figure 1).[7a]

Experimental Section

General. The chemical shifts of the ^1H NMR and ^{13}C NMR spectra were all recorded relative to chloroform or benzene. Multiplicities were determined with the aid of an APT sequence, separating methylene and quaternary carbons = e (even), from methyl and methine = o (odd). Melting points are uncorrected. HPLC analysis was performed using a HP 1100 series HPLC system with a Zorbax RX-Sil column (4.6 mm ID × 25 cm) eluting with 20% ethyl acetate in hexane. All compounds were purified as specified, and gave spectroscopic data consistent with being ≥95% the assigned structure. Analytical TLC was carried out on precoated 0.2 mm thick Merck 60 F_{254} silica plates. Flash chromatography was carried out using Merck Silica Gel 60 (230−400 mesh).

All reagents and starting materials were obtained from commercial suppliers (Acros, Aldrich, Fluka, and Lancaster) and were used without purification except where indicated. Dichloromethane was dried over and freshly distilled from calcium hydride. All reactions were carried out under an inert atmosphere of nitrogen using oven-dried or flame-dried glassware unless specified to the contrary.

General Cyclization Procedure. The acyl selenide, alkyl bromide, or vinyl bromide (0.3 mmol, azeotroped with anhydrous benzene) were dissolved in anhydrous benzene (see note 1) and cooled with stirring to 5 °C protected from moisture by a drying tube packed with Drierite. Triethylborane (0.6 mL, 0.6 mmol, 2.0 equiv of a 1 M solution in hexane) was added via syringe, followed by the addition of tris(trimethylsilyl)-silane (190.8 μL, 0.6 mmol, 2.0 equiv). The mixture then was allowed warmed to room temperature and stirred under the atmosphere of dry air (TLC control). The solvent was then removed in vacuo to afford a crude oil. Purification by flash chromatography on silica gel (eluting with 10−20% ethyl acetate/hexane) furnished the *cyclic ethers* **2/3** as colorless oils.

Note 1: The concentrations of the various ring sizes were 0.2, 0.1, and 0.05 M for five-, six-, and seven-membered rings, respectively.

(2*S,5*S**)-[(5-Methyloxolan-2-yl)methyl]sulfonylbenzene (2a).** IR ($CHCl_3$) 3024 (m), 2974 (m), 2930 (m), 2875 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.92−7.89 (m, 2H), 7.64−7.60 (m, 1), 7.55−7.51 (m, 2H), 4.22 (pentet, $J = 6.5$ Hz, 1H), 3.92−3.84 (m, 1H), 3.42 (dd, A of ABX, $J_{AB} = 14.1$, $J_{AX} = 5.8$ Hz, 1H), 3.20 (dd, B of ABX, $J_{AB} = 14.1$, $J_{BX} = 6.6$ Hz, 1H), 2.14−2.05 (m, 1H), 1.99−1.91 (m, 1H), 1.77−1.69 (m, 1H), 1.45−1.36 (m, 1H), 1.07 (d, $J = 6.1$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.94 (e), 133.62 (o), 129.07 (o), 128.13 (o),

(22) The LUMO of a vinyl sulfone and a vinyl ether are known to have larger coefficients at the β- and α-carbons, respectively, thus reinforcing each other in α-alkoxy vinyl sulfone. See: (a) Sims, J.; Houk, K. N. *J. Am. Chem. Soc.* **1973**, *95*, 5798. (b) Fleming, I. *Frontier Orbitals and Organic Chemical Reactions*; John Wiley and Sons: New York, 1977; p 186.

75.83 (o), 72.86 (o), 61.80 (e), 32.37 (e), 31.49 (e), 21.10 (o); HRMS (FAB, M+Na$^+$) calcd for $C_{12}H_{16}O_3NaS$ 263.0718, found 263.0726.

(2*S,5*S**)-5-Methyl-2-[(phenylsulfonyl)methyl]-2,4,5-trihydrofuran-3-one (2b).** mp 143−144 °C; IR ($CDCl_3$) 3018 (s), 2981 (w), 2932 (w), 1764 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94−7.92 (m, 2H), 7.66−7.52 (m, 3H), 4.28−4.20 (m, 1H), 4.18 (dd, J = 7.9, 2.6 Hz, 1H), 3.57 (dd, A of ABX, J_{AB} = 14.8, J_{AX} = 2.7 Hz, 1H), 3.34 (dd, B of ABX, J_{AB} = 14.8, J_{BX} = 8.0 Hz, 1H), 2.58 (dd, A of ABX, J_{AB} = 18.0, J_{AX} = 7.7 Hz, 1H), 2.14 (dd, B of ABX, J_{AB} = 18.0, J_{BX} = 10.3 Hz, 1H), 1.36 (d, J = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.70 (e), 139.86 (e), 133.83 (o), 129.11 (o), 128.17 (o), 76.26 (o), 72.86 (o), 57.37 (e), 43.22 (e), 20.65 (o); HRMS (EI, M$^+$) calcd for $C_{12}H_{14}O_4S$ 254.0613, found 254.0602.

(2*S,6*S**)-[(6-Methylperhydro-2H-pyran-2-yl)methyl]-sulfonylbenzene (2c).** mp 62−63 °C; IR ($CHCl_3$) 3071 (w), 3025 (m), 2976 (m), 2939 (m), 2848 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92−7.89 (m, 2H), 7.63−7.58 (m, 1H), 7.53−7.49 (m, 2H), 3.87 (dddd, J = 11.5, 8.2, 3.2, 2.2 Hz, 1H), 3.36 (dd, A of ABX, J_{AB} = 14.6, J_{AX} = 8.2 Hz, 1H), 3.29−3.24 (tq, J = 6.2, 2.0 Hz, 1H), 3.12 (dd, B of ABX, J_{AB} = 14.6, J_{BX} = 3.3 Hz, 1H), 1.81−1.75 (m, 1H), 1.64−1.58 (m, 1H), 1.55−1.43 (m, 2H), 1.26−1.16 (m, 1H), 1.09−0.98 (m, 1H), 0.82 (d, J = 6.2 Hz, 3H); ^{13}C NMR (100, MHz, $CDCl_3$) δ 140.51 (e), 133.34 (o), 128.79 (o), 128.26 (o), 73.96 (o), 72.45 (o), 62.24 (e), 32.38 (e), 30.83 (e), 23.25 (e), 21.44 (o); HRMS (CI, M + NH_4^+) calcd for $C_{13}H_{22}NO_3S$ 272.1320, found 272.1334.

(2*S,6*S**)-[(6-Methyl-3-methylene-4,5,6-trihydro-2*H*-pyran-2-yl)methyl]sulfonylbenzene (2d).** mp 73−74 °C; IR ($CHCl_3$) 3071 (w), 3026 (m), 2976 (m), 2918 (m), 2848 (m), 1655 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92−7.89 (m, 2H), 7.61−7.56 (m, 1H), 7.52−7.48 (m, 2H), 4.78 (d, J = 1.8 Hz, 1H), 4.62 (s, 1H), 4.32 (dd, J = 8.1, 3.6 Hz, 1H), 3.54−3.42 (m, 3H), 2.34 (ddd, A of ABXY, J_{AB} = 13.8, J_{AX} = 4.7, J_{AY} = 2.5 Hz, 1H), 2.26−2.18 (m, 1H), 1.63 (dp, J = 13.1, 2.4 Hz, 1H), 1.27−1.17 (m, 1H), 0.77 (d, J = 6.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.12 (e), 140.70 (e), 133.28 (o), 128.71 (o), 128.31 (o), 107.46 (e), 73.87 (o), 73.47 (o), 58.62 (e), 35.05 (e), 33.17 (e), 20.82 (o); HRMS (EI, M + H$^+$) calcd for $C_{14}H_{19}O_3S$ 267.1055, found 267.1058.

(2*S,6*S**)-6-Methyl-2-[(phenylsulfonyl)methyl]-4,5,6-trihydro-2*H*-pyran-3-one (2e).** mp 89−91 °C; IR ($CHCl_3$) 3022 (s), 2980 (w), 2934 (w), 2858 (w), 1729 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.91−7.89 (m, 2H), 7.64−7.60 (m, 1H), 7.54−7.51 (m, 2H), 4.43 (dd, J = 8.7, 2.3 Hz, 1H), 3.83 (ddq, J = 12.4, 6.2, 2.5 Hz, 1H), 3.81 (dd, J = 15.1, 2.3 Hz, 1H), 3.30 (dd, J = 15.1, 8.7 Hz, 1H), 2.54 (ddd, A of ABXY, J_{AB} = 16.0, J_{AX} = 6.0, J_{AY} = 3.1 Hz, 1H), 2.46 (ddd, B of ABXY, J_{AB} = 16.0, J_{BX} = 12.2, J_{BY} = 6.7 Hz, 1H), 2.03 (ddt, J = 13.7, 6.5, 2.9 Hz, 1H), 1.82−1.72 (m, 1H), 1.00 (d, J = 6.1 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 204.20 (e), 140.29 (e), 133.55 (o), 128.93 (o), 128.14 (o), 77.67 (o), 73.12 (o), 56.11 (e), 37.47 (e), 33.69 (e), 20.53 (o); HRMS (EI, M + H$^+$) calcd for $C_{13}H_{17}O_4S$ 269.0848, found 269.0854.

(2*S,7*S**)-[(7-Methyloxepan-2-yl)methyl]sulfonylbenzene (2f).** mp 45−47 °C; IR ($CHCl_3$) 3019 (s), 2933 (s), 2858 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93−7.89 (m, 2H), 7.63−7.59 (m, 1H), 7.55−7.51 (m, 2H), 4.12−4.06 (m, 1H), 3.57−3.49 (m, 1H), 3.48 (dd, A of ABX, J_{AB} = 14.7, J_{AX} = 8.9 Hz, 1H), 3.10 (dd, B of ABX, J_{AB} = 14.7, J_{BX} = 2.8 Hz, 1H), 1.78−1.35 (m, 8H), 0.74 (d, J = 6.3 Hz, 3H); ^{13}C NMR (100, MHz, $CDCl_3$) δ 140.67 (e), 133.31 (o), 129.03 (o), 127.75 (o), 75.90 (o), 73.33 (o), 62.61 (e), 37.52 (e), 36.08 (e), 26.11 (e), 23.35 (e), 22.03 (o); HRMS (EI, M$^+$) calcd for $C_{14}H_{20}O_3S$ 268.1133, found 268.1131.

(2*S,7*S**)-7-Methyl-2-[(phenylsulfonyl)methyl]oxepan-3-one (2 g).** mp 112−113 °C; IR ($CHCl_3$) 3033 (w), 2974 (w), 2934 (m), 2869 (w), 1714 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93−7.90 (m, 2H), 7.65−7.61 (m, 1H), 7.57−7.52 (m, 2H), 4.42 (dd, J = 9.4, 2.2 Hz, 1H), 3.61 (dd, A of ABX, J_{AB} = 14.7, J_{AX} = 2.2 Hz, 1H), 3.59−3.51 (m, 1H), 3.38 (dd, B of ABX, J_{AB} = 14.8, J_{BX} = 9.4 Hz, 1H), 2.75 (ddd, A of ABXY, J_{AB} = 14.8, J_{AX} = 12.3, J_{AY} = 2.5 Hz, 1H), 2.52−2.47 (ddt, J = 14.8 Hz, 6.5, 1.4 Hz, 1H), 1.95−1.1.82 (m, 2H), 1.65−1.47 (m, 2H), 1.01 (d, J = 6.2 Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 212.17 (e), 140.30 (e), 133.64 (o), 129.18 (o), 127.85 (o), 82.11 (o), 80.61 (o), 58.26 (e), 42.04 (e), 38.46 (e), 22.20 (e), 22.16 (o); HRMS (EI, M$^+$) calcd for $C_{14}H_{19}O_4S$ 283.1004, found 283.1017.

(2*S,6*R**)-6-Phenyl-2-[(phenylsulfonyl)methyl]-4,5,6-trihydro-2*H*-pyran-3-one (12).** IR ($CHCl_3$) 3067 (m), 3028 (s), 2933 (m), 2857 (w), 1732 (vs), 1686 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82−7.80 (m, 2H), 7.45 (t, J = 7.5 Hz, 1H), 7.31 (t, J = 7.8 Hz, 2H), 7.26−7.04 (m, 3H), 7.04−7.01 (m, 2H), 4.78 (dd, J = 11.1, 2.4 Hz, 1H), 4.67 (dd, J = 8.7, 2.4 Hz, 1H), 3.88 (dd, A of ABX, J_{AB} = 15.2, J_{AX} = 2.5 Hz, 1H), 3.47 (dd, A of ABX, J_{AB} = 15.2, J_{AX} = 8.7 Hz, 1H), 2.70−2.66 (m, 2H), 2.35−2.29 (m, 1H), 2.17−2.06 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.60 (e), 140.19 (e), 139.72 (e), 133.36 (o), 128.88 (o), 128.26 (o), 128.01 (o), 127.84 (o), 125.59 (o), 78.57 (o), 78.53 (o), 56.24 (e), 37.94 (e), 34.13 (e); HRMS (FAB, M + Na$^+$) calcd for $C_{18}H_{18}O_4NaS$ 353.0824, found 353.0826.

(1*R*/*S*)-1-(2*S,5*S**)-[(5-Methyloxolan-2-yl)but-3-enyl]sulfonylbenzene (8).** The alkyl bromide **1a** (95.7 mg, 0.30 mmol, azeotroped with anhydrous benzene) was dissolved in anhydrous benzene (3.0 mL) and cooled with stirring to 5 °C protected from moisture by a drying tube packed with Drierite. Triethylborane (360 μL, 0.36 mmol, 1.2 equiv of a 1 M solution in hexane) was added via syringe, followed by the addition of allyltributyltin (287.7 μL, 0.90 mmol, 3.0 equiv). The reaction mixture was then warmed to room temperature and stirred under the atmosphere of dry air for ca. 2 h (TLC control; 3:7 ethyl acetate/hexane). The solvent was then removed in vacuo to afford a crude oil. Purification by flash chromatography on silica gel (eluting with 5−10% ethyl acetate/hexane) furnished the *cyclic ether* **8** (75.8 mg, 91%) as a colorless oil: IR ($CHCl_3$) 3070 (m), 3029 (m); 2972 (s), 2930 (s), 2875 (s), 1641 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87−7.84 (m, 2H), 7.61−7.46 (m, 3H), 5.84−5.69 (m, 1H), 5.02−4.92 (m, 2H), 4.32−4.27 (m, 0.6H), 4.19−4.14 (m, 0.4H), 3.90−3.76 (m, 1H), 3.32 (q, J = 5.7 Hz, 0.4H), 3.16 (dt, J = 5.7, 4.8 Hz, 0.6H), 2.69−2.43 (m, 2H), 2.05−1.76 (m, 3H), 1.39−1.28 (m, 1H), 1.08 (d, J = 6.1, 1.8H), 0.97 (d, J = 6.0, 1.2H); ^{13}C NMR (100 MHz, C_6D_6) δ 141.69 (e), 140.22 (e), 135.95 (o), 135.90 (o), 133.49 (o), 133.26 (o), 129.84 (o), 129.50 (o), 129.47 (o), 129.07 (o), 129.03 (o), 128.99 (o), 117.36 (e), 117.30 (e), 77.07 (o), 76.57 (o), 75.64 (o), 75.50 (o), 69.28 (o), 68.18 (o), 33.21 (e), 32.99 (e), 30.97 (e), 30.87 (e), 29.97 (e), 28.33 (e), 21.21 (o), 20.97 (o); HRMS (CI, M$^+$) calcd for $C_{15}H_{24}NO_3S$ 298.1477, found 298.1466.

Procedure for Preparing the *E*- and *Z*-Vinylogous Sulfonates 10a and 10b. The secondary alcohol **9** (221.7 mg, 0.79 mmol) dissolved in anhydrous THF (7.0 mL) and cooled with stirring to 0 °C. Lithium hexamethyldisilyl azide (1.00 mL, 1.00 mmol, 1.0 M solution in THF) was added dropwise and the reaction stirred for ca. 30 min and then warmed to room temperature where it was stirred for an additional 30 min. The reaction mixture was then cooled to 0 °C, and *E*-bis-(phenylsulfonyl)-1,2-ethylene **5a** (313.9 mg, 1.02 mmol, 1.3 equiv) added portionwise keeping the internal temperature ≤5 °C. The reaction mixture was then allowed to warm to room temperature where it was stirred for ca. 3 h (TLC control; 3:7 ethyl acetate/hexane). The reaction mixture was then partitioned between saturated aqueous $NaHCO_3$ solution and diethyl ether, the organic layers were combined, washed with saturated aqueous NaCl solution, dried (Na_2SO_4), and filtered, and the solvent removed in vacuo to afford a crude yellow oil. Purification by flash chromatography on silica gel (eluting with 10−20% ethyl acetate/hexane) furnished the *E*-vinylogous sulfonate **10a** (345.8 mg, 98%) as a yellow oil. The *Z*-vinylogous sulfonate **10b** was prepared in an analogous manner using the *Z*-bis(phenylsulfonyl)-1,2-ethylene **5b** in 89% yield.

(1*E*)-2-[1-Phenyl-4-(*tert*-butyldimethylsilyloxy)butoxy]-vinylsulfonylbenzene (10a). mp 48−49 °C; IR ($CHCl_3$) 3071 (w), 3028 (m), 3019 (m), 2956 (m), 2930 (m), 2884 (m), 2857 (m) 1627 (s), 1608 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73−7.70 (m, 2H), 7.54−7.49 (m, 2H), 7.46−7.41 (m, 2H), 7.35−7.27 (m, 3H), 7.21−7.19 (m, 2H), 5.66 (d, J = 12.0 Hz, 1H), 4.90−4.87 (m, 1H), 3.58 (dt, J = 6.2, 1.4 Hz, 2H), 2.04−1.94 (m, 1H), 1.90−1.82 (m, 1H), 1.62−1.42 (m, 2H), 0.84 (s, 9H), −0.01 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.18 (o), 142.51 (e), 139.31 (e), 132.57 (o), 128.98 (o), 128.84 (o), 128.50 (o),

126.68 (o), 126.16 (o), 108.00 (o), 85.84 (o), 62.44 (e), 33.91 (e), 28.38 (e), 25.91 (o), 18.28 (e), −5.36 (o); HRMS (FAB, M + Na^+) calcd for $C_{24}H_{34}O_4NaSiS$ 469.1845, found 469.1827.

(1*Z*)-2-[1-Phenyl-4-(*tert*-butyldimethylsilyloxy)butoxy]-vinylsulfonylbenzene (10b). mp 51−52 °C; IR ($CHCl_3$) 3081 (m), 3067 (m), 3027 (m), 2955 (s), 2930 (s), 2858 (s), 1626 (vs) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.03−8.00 (m, 2H), 7.62−7.57 (m, 1H), 7.53−7.48 (m, 2H), 7.27−7.23 (m, 3H), 6.99−6.95 (m, 2H), 6.42 (d, J = 6.5 Hz, 1H), 5.53 (d, J = 6.4 Hz, 1H), 4.78 (dd, J = 7.8, 5.7 Hz, 1H), 3.61−3.51 (m, 2H), 1.96−1.75 (m, 2H), 1.55−1.34 (m, 2H), 0.86 (s, 9H), 0.01 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.89 (o), 142.74 (e), 139.72 (e), 132.75 (o), 128.69 (o), 128.56 (o), 128.43 (o), 127.83 (o), 126.13 (o), 108.22 (o), 87.77 (o), 62.44 (e), 34.02 (e), 28.29 (e), 25.92 (o), 18.28 (e), −5.36 (o); HRMS (FAB, M + Na^+) calcd for $C_{24}H_{34}O_4NaSiS$ 469.1845, found 469.1832.

General Jones Oxidation Procedure. The *tert*-butyldimethylsilyl ether **10a** (188.7 mg, 0.42 mmol) was dissolved in acetone (4.2 mL) and cooled with stirring to −10 °C. Jones reagent (0.84 mL, 1.68 mmol, 2 M aqueous solution) was added dropwise, and the reaction mixture was allowed to warm to ambient temperature and stirred for ca. 16 h (TLC control; 7:3 ethyl acetate/hexane). Propan-2-ol (1.0 mL) was added dropwise to destroy excess Jones reagent, the reaction mixture was filtered through Celite and concentrated in vacuo to afford the crude acid. The crude acid was partitioned between saturated aqueous $NaHCO_3$ solution and diethyl ether. The aqueous layer was then cooled to 0 °C, carefully acidified with an aqueous 1 N HCl solution, and extracted with ethyl acetate. The organic layers were combined, washed with a saturated NaCl solution, dried (Na_2SO_4), and filtered, and the solvent was removed in vacuo to afford the carboxylic acid (127.9 mg, 87%) as a yellow oil. The *Z*-isomer **10b** was treated in an analogous manner to afford the carboxylic acid in 84% yield, as a pale yellow oil.

4-[(1*E*)-2-(Phenylsulfonyl)vinyloxy]-4-phenylbutanoic acid. IR ($CHCl_3$) 3600−2300 (bs), 3018 (s), 2927 (s), 2854 (m), 1772 (s), 1723 (s), 1688 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.73−7.70 (m, 2H), 7.54−7.41 (m, 4H), 7.36−7.28 (m, 3H), 7.22−7.20 (m, 2H), 5.70 (d, J = 12.2 Hz, 1H), 4.97 (dd, J = 7.7, 5.4 Hz, 1H), 2.49−2.34 (m, 2H), 2.28−2.07 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.84 (e), 159.68 (o), 142.25 (e), 138.31 (e), 132.69 (o), 129.02 (o), 128.84 (o), 126.71 (o), 126.07 (o), 108.67 (o), 84.13 (o), 32.06 (e), 29.47 (e); HRMS (FAB, M + Na^+) calcd for $C_{18}H_{18}O_5NaS$ 369.0773, found 369.0784.

4-[(1*Z*)-2-(Phenylsulfonyl)vinyloxy]-4-phenylbutanoic acid. IR ($CHCl_3$) 3500−2300 (bs), 3026 (s), 2927 (m), 1713 (s), 1629 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.02−8.00 (m, 2H), 7.64−7.60 (m, 1H), 7.55−7.51 (m, 2H), 7.28−7.25 (m, 3H), 6.98−6.96 (m, 2H), 6.41 (d, J = 6.5 Hz, 1H), 5.57 (d, J = 6.5 Hz, 1H), 4.87 (dd, J = 8.4, 4.7 Hz, 1H), 2.45−2.30 (m, 2H), 2.19−1.99 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.44 (e), 154.49 (o), 142.62 (e), 138.80 (e), 132.97 (o), 128.88 (o), 128.79 (o), 128.73 (o), 127.73 (o), 126.01 (o), 108.85 (o), 86.12 (o), 32.26 (e), 29.46 (e); HRMS (FAB, M + Na^+) calcd for $C_{18}H_{18}O_5NaS$ 369.0773, found 369.0764.

General Procedure for Acyl Selenide Formation. The carboxylic acid from **10a** (121.8 mg, 0.35 mmol) was dissolved in anhydrous dichloromethane (0.35 mL) and cooled with stirring to 0 °C. Triethylamine (58.8 μL, 0.42 mmol, 1.2 equiv) was added in anhydrous dichloromethane (0.7 mL) and the mixture allowed to warm to room temperature where it was allowed to stir for ca. 20 min. The reaction mixture was then concentrated in vacuo and further dried under high vacuum for ca. 1 h. Phenylselenyl bromide (173.4 mg, 0.72 mmol, 2.0 equiv) was dissolved in anhydrous tetrahydrofuran (2.8 mL), and the purple mixture was cooled with stirring to 0 °C. Tributylphosphine (181.1 μL, 0.7 mmol, 2 equiv) was then added slowly via syringe affording a canary yellow-colored solution. The mixture was allowed to warm to room temperature and stirred for 20 min, the triethylammonium salt was added in anhydrous tetrahydrofuran (2.0 mL), and the reaction mixture stirred at room temperature for ca. 19 h (TLC control; 5% AcOH in ethyl acetate). The reaction mixture was then partitioned between saturated $NaHCO_3$ and diethyl ether, and the organic layers were combined, dried (Na_2SO_4), filtered, and concentrated in vacuo to afford a crude oil. Purification by flash chromatography on silica gel (eluting with 5 and then 30% ethyl acetate/hexane) furnished the acyl selenide **11a** (140 mg, 82%) as a pale yellow oil. The *Z*-isomer **11b** was prepared in an analogous fashion in 84% yield as a pale yellow oil.

4-[(1*E*)-2-(Phenylsulfonyl)vinyloxy]-4-phenyl-1-phenylselenobutan-1-one (11a). IR ($CHCl_3$) 3070 (w), 3029 (m), 3012 (m), 2935 (w), 1716 (s), 1628 (s), 1609 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.74−7.71 (m, 2H), 7.54−7.50 (m, 1H), 7.47−7.28 (m, 11H), 7.20−7.17 (m, 2H), 5.69 (d, J = 12.1 Hz, 1H), 4.95 (dd, J = 7.9, 5.4 Hz, 1H), 2.84−2.68 (m, 2H), 2.29−2.03 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.47 (e), 159.49 (o), 142.11 (e), 138.10 (e), 135.65 (o), 132.62 (o), 129.33 (o), 128.90 (o), 128.94 (o), 126.75 (o), 126.61 (o), 125.92 (o), 125.86 (e), 108.59 (o), 83.66 (o), 42.76 (e), 32.35 (e); HRMS (EI, M^+) calcd for $C_{24}H_{23}O_4S^{78}Se$ 485.0490, found 485.0504.

4-[(1*Z*)-2-(Phenylsulfonyl)vinyloxy]-4-phenyl-1-phenylselenobutan-1-one (11b). IR ($CHCl_3$) 3070 (m), 3027 (m); 3016 (m); 1715 (s); 1628 (s) 1609 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.04−8.01 (m, 2H), δ 7.66−7.61 (m, 1H), 7.58−7.53 (m, 2H), 7.50−7.45 (m, 2H), 7.41−7.34 (m, 3H), 7.30−7.25 (m, 3H), 7.23−6.96 (m, 2H), 6.39 (d, J = 6.4 Hz, 1H), 5.58 (d, J = 6.4 Hz, 1H), 4.85 (dd, J = 8.0, 5.2 Hz, 1H), 2.78−2.63 (m, 2H), 2.17−2.03 (m, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 199.75 (e), 154.38 (o), 142.70 (e), 138.69 (e), 135.76 (o), 133.00 (o), 129.45 (o), 129.10 (o), 128.93 (o), 128.82 (o), 127.77 (o), 127.72 (o), 126.03 (e), 126.00 (o), 108.99 (o), 85.68 (o), 42.73 (e), 32.57 (e); HRMS (EI, M^+) calcd for $C_{24}H_{23}O_4S^{78}Se$ 485.0490, found 485.0504.

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Supporting Information Available: Experimental procedures and spectra data for the preparation of compounds **1a**−**g**, in addition to the ^1H NMR spectra for compounds **1a**−**g**, **2a**−**g**, **8**, **10a/b**, **11a/b**, and **12**. This material is available free of charge via the Internet at http://pubs.acs.org.

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