Stereoselective Synthesis of Highly Substituted γ-Lactones and Butenolides by Intramolecular Michael Addition of Enantiomerically Enriched γ-[(Phenylthio)acyl]oxy α,β-Unsaturated Esters

Carmen M. Rodríguez, Tomás Martín, Miguel A. Ramírez, and Victor S. Martín*

Centro de Productos Naturales Orgánicos "Antonio González", Instituto Universitario de Bio-Orgánica, Carretera la Esperanza, 2, 38206 La Laguna, Tenerife, Spain

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The synthesis of polysubstituted γ-lactones by the base-induced cyclization of enantiomerically enriched γ-[(phenylthio)acyl]oxy α,β-unsaturated esters obtained from 2,3-epoxy alcohols is described. The procedure is highly stereoselective and compatible with a wide range of functionalities (ester, tetrahydropyranyl ether, silyl ether, etc.). Varying degrees of substitution, including quaternary centers, in the final γ-lactone were synthesized with excellent stereoselectivity. Useful functional interconversions were successfully demonstrated, in particular those resulting in butenolides. By the use of AM1 it was concluded that the intramolecular Michael reaction can be described as a kinetically controlled reaction in which the relative stability of the transition states for all possible final configurations led to geometries in agreement with the experimental results.

Introduction

The synthesis of butenolides and saturated γ-lactones as optically active fragments is currently receiving considerable attention in light of their utility as synthons for the synthesis of biologically active natural products.[1,2] The γ-lactone chemistry also plays a very important role in the synthesis of nucleosides and related bioactive compounds.[3] Although the cyclocarbonylation of unsaturated alcohols catalyzed by transition metals is a well-known procedure for the synthesis of γ-lactones,[4] relatively few methods using carbon–carbon formation from an acyclic ester are reported in the literature.[5] The use of the carbon–carbon strategy is even more limited when the cyclization step is performed by an intramolecular Michael addition of a suitable linear precursor.[6] Considering our recently obtained results in the enantioselective synthesis of γ-[(phenylthio)acyl]oxy α,β-unsaturated esters[7] we were very interested in exploring a new methodology for the synthesis of substituted γ-lactones by the intramolecular cyclization of a suitable linear precursor. In this paper we report on our studies of highly alkylated systems by base-promoted cyclization of γ-[(phenylthio)acyl]oxy α,β-unsaturated esters (Scheme 1).

Results and Discussion

Enantioselective Synthesis of γ-[(Phenylthio)-acyl]oxy α,β-Unsaturated Esters. Our strategy for the enantioselective synthesis of γ-lactones is based on the possibility of opening 2,3-epoxy alcohols with carboxylic acids assisted by titanium tetraisopropoxide.[8] Since 2,3-epoxy alcohols are easily synthesized by the Sharpless asymmetric epoxidation for a broad range of allylic alcohols in either enantiomer,[9] our methodology (Scheme 2) would be general for obtaining defined absolute stereochemistry and functionality in the final γ-lactone unity.

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(6) (a) Koft, E. R.; Kotnis, A. S.; Broadbent, T. A. *Tetrahedron Lett.* **1987**, *28*, 2799. (b) Li, T. T.; Wu, Y. L. *Tetrahedron Lett.* **1988**, *29*, 4039. (c) Laabassi, M.; Grée, R. *Synlett* **1990**, 265.

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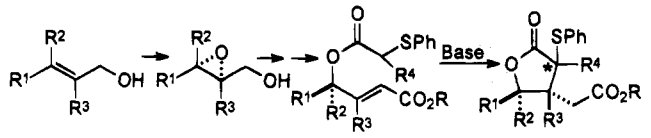
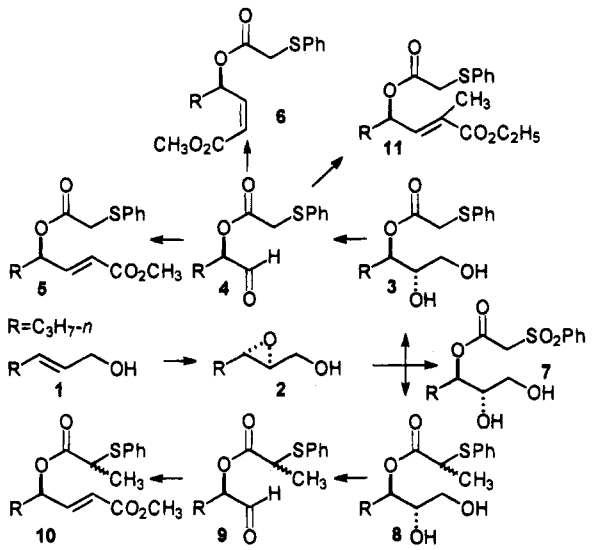
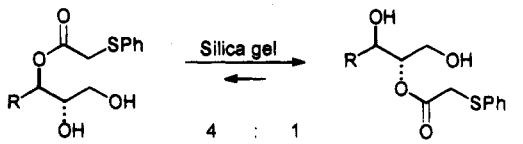
Scheme 1



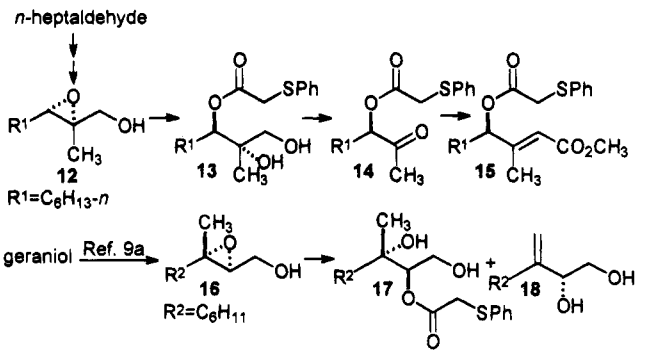
Scheme 2



Scheme 3



Scheme 4



The diol **3** was obtained by the above-mentioned opening reaction using (phenylthio)acetic acid as the nucleophilic reagent. This reagent was selected for several related reasons: the phenylthio group acidifies the adjacent proton and facilitates the Michael addition, and the same group in the ester–lactone product could then be removed reductively or used to obtain the olefin and to facilitate C-alkylations. The opening reaction could be performed using the isolated epoxy alcohol, although to achieve the highest conversion and yield we also ran the asymmetric epoxidation in the catalytic manner[9c] performing the "in situ" opening of the formed 2,3-epoxy alcohol without any intermediate isolation step. The choice of the method depends on the degree of optical purity to be reached in the final products since it is well-known that asymmetric epoxidation in the catalytic version yields 2–5% lower enantiomeric excess than in the stoichiometric version.[9c] In cases where a crystalline product appears during the synthetic sequence the catalytic version is the recommended one, since simple recrystallization then yields in most cases enantiomerically pure products. Although the opening reaction is highly regioselective (C3 vs C2, ≈100:1) the oxidative cleavage should be performed without the purification of the obtained diol since transesterification was observed in presence of silica gel, increasing the amount of undesired product bearing the ester functionality in the C2 carbon (Scheme 3).

The diol ester **3** was submitted to degradative oxidation with sodium periodate, and the resulting aldehyde **4**, without purification, was treated with the sodium salt of (trimethylphosphono)acetate, in benzene, affording the α,β-unsaturated ester **5** with a ratio *E*-**5**/*Z*-**6** (>20:1). In order to check the influence of the double-bond geometry in the cyclization stereochemistry the aldehyde **4** was also treated with $Ph_3P{=}CHCO_2CH_3$, under protic conditions (MeOH), giving a separable mixture of **6**/**5** (2:1). On the other hand, considering the ability of the benzenesulfonyl group to activate α-anions toward Michael addition[10] the benzenesulfonyl derivative **7** was prepared in a similar manner. In this case, however, the opening reaction led to poorer regioselectivity (C3 vs C2, 10:1) and lower yields (≈70%). By following similar methodology the 1:1 diastereoisomeric mixture of the diol **8** (C3 vs C2, ≈50:1) was obtained when racemic 2-(phenylthio)propionic acid was used as the opening reagent. When **8** was submitted to the series of reactions similar to those described for **3**, the diastereoisomeric mixture **10** was obtained in excellent yield.

In order to extend our methodology to the broadest range of substituted compounds we prepared the α-methyl α,β-unsaturated ester **11** by a Wittig reaction over the aldehyde **4** using, in benzene, the stabilized phosphorane $Ph_3C{=}C(CH_3)CO_2C_2H_5$ (*E*/*Z*, 12:1). On the other hand, when the opening reaction was performed on the epoxy alcohol **12** (obtained from *n*-heptaldehyde by Wittig's reaction with $Ph_3P{=}C(CH_3)CO_2C_2H_5$, reduction with DIBAL, and asymmetric epoxidation) the diol ester **13** was obtained with the usual regioselectivity (C3 vs C2 ≈100:1). Oxidative cleavage with $Pb(OAc)_4$ gave the methyl ketone **14**, which, when submitted to the sodium salt of (trimethylphosphono)acetate, in benzene, afforded the β-methyl α,β-unsaturated ester **15** (*E*/*Z*, 10:1). In an effort to fulfill the entire substitution pattern possible we attempted to open the epoxide **16**.[9a] In this case, however, a mixture of the C2-ester–1,3-diol **17** and the elimination product[11] **18** was obtained (Scheme 4).

Because the general methodology could not be used in the synthesis of the tertiary carbinol (phenylthio)acetate, an alternative route was developed (Scheme 5). Thus the geraniol epoxide **16**[9a] was submitted to catalyic hydrogenation and the resulting saturated product **19** was transformed into the quaternary vinyl alcohol **21** by reductive opening of the corresponding iodide obtained

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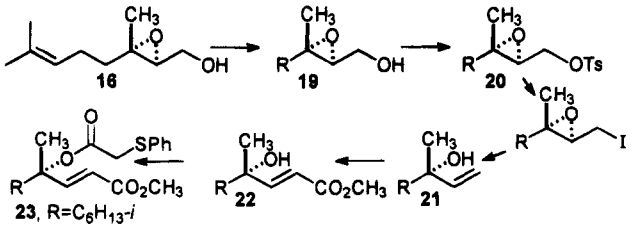
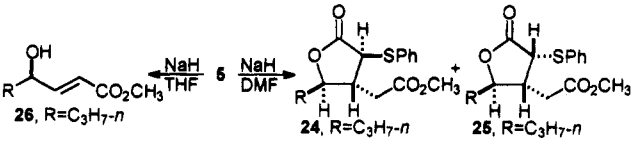
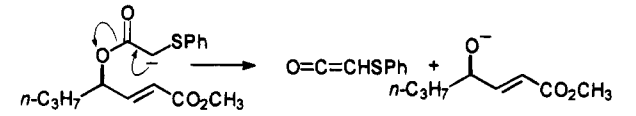
Scheme 5



Scheme 6



Scheme 7



from the epoxy tosylate **20**.[12] The ozonolysis of **21** and homologation of the resulting aldehyde with the sodium salt of (trimethylphosphono)acetate, in benzene, yielded the γ-hydroxy α,β-unsaturated ester **22** which was esterified with (phenylthio)acetic acid yielding the desired unsaturated ester **23**.[13]

Synthesis of γ-Lactones by Intramolecular Michael Addition. With the linear precursors in our hands we began the cyclization studies. We found that when the *E*-isomer **5** was treated with an equivalent amount of sodium hydride, in DMF, at −50 °C, the γ-lactone **24** was obtained as the sole stereoisomer (Scheme 6).

The reaction rate and stereochemistry depend on the reaction conditions (Table 1). Thus, when the temperature was increased, in DMF, to 0 °C the reaction time was shorter but the amount of **25** increased reaching at room temperature a **24/25** ratio of 2:1. The stereochemical results were similar in a HMPA−THF mixture, when NaH was used as the deprotonating base. However, when lithium bis(trimethylsilyl)amide or potassium *tert*-butoxide was used, even at −50 °C, **25** was detected in at least a ratio of 9:1 or 4:1, respectively.

Surprisingly the free α,β-unsaturated alcohol **26** was the only product obtained, when the reaction was performed in THF (Scheme 7). This result is interpreted by basic elimination to the corresponding ketene. In less polar solvents such as benzene, even at room temperature, no reaction was obtained.

In order to check the influence of the double-bond geometry of the unsaturated ester, we studied the cyclization of the *Z*-isomer **6**. When the reaction was run using DMF, at −50 °C, the same γ-lactone **24** was the only obtained product. In this case, however, the hydrolysis of the ester was not observed when the reaction was performed in THF, although at 0 °C (the deprotection conditions of the *E*-isomer) a poor conversion was reached (Table 2).

The great asymmetric induction imposed by the oxygenated stereogenic center suggests to us the possibility

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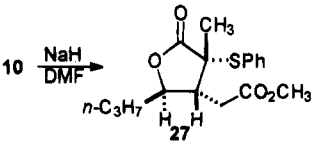
Scheme 8



Scheme 9

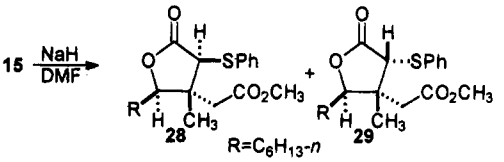


Table 1. Influence of the Reaction Conditions on the Cyclization of the *E*-Isomer 5

base/solvent	temp (°C)	time	yield (%)	24	25	26
NaH/DMF or	−50	4 h	95	100		
NaH/THF-	0	0.5 h	94	85	15	
HMPA, 3:1	rt	5 min	92	66	33	
KOBu-*t*/DMF	−60 → −30	0.5 h	94	80	20	
LiN (TMS)$_2$/DMF	−60 → −30	2 h	93	90	10	
NaH/THF	−78 → −30	>12 h				
	0	4 h	80			100
	rt	1 h	80			100
NaH/CH_2Cl_2	−78 → −30	>12 h				
	0	>12 h				
	rt	12 h	60			100
NaH/C_6H_6	rt	>12 h				

Table 2. Influence of the Reaction Conditions on the Cyclization of the *Z*-Isomer 6

base/solvent	temp (°C)	time	yield (%)	24	25
NaH/DMF or	−50	2 h	95	100	
NaH/THF-	0	15 min	91	85	15
HMPA, 3:1	rt	5 min	93	66	33
NaH/THF	−78 → −30	>12 h			
	0	12 h	40	90	10
	rt	4 h	80	80	20
NaH/CH_2Cl_2	−78 → rt	>12 h			
NaH/C_6H_6	0 → rt	>12 h			

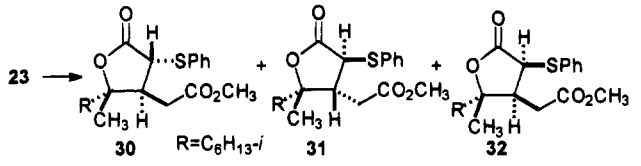
of controling the stereochemistry in a quaternary center located in α to the carbonyl position, if a suitable linear precursor is used. In this sense the diastereoisomeric mixture **10** was treated with NaH, in DMF at −50 °C, giving rise to the only stereoisomer **27** (Scheme 8). In this case, however, the phenylthio group is oriented *cis* relative to the (methoxycarbonyl)methylene group.

In a similar manner and in an attempt to control the stereochemistry in all the carbons in the γ-lactone moiety in highly substituted systems, the β-methyl α,β-unsaturated ester **15** was submitted to our standard basic conditions yielding the stereoisomers **28** and **29** in a ratio of 8:1 (Scheme 9).

It should be pointed out that the diastereomeric mixture is obtained only in the vicinal carbon to the carbonyl lactone, complete stereocontrol being obtained in the quaternary center.

Control in the stereoselectivity in a quaternary carbon located in the γ-carbon of the lactone was equally achieved by the cyclization of the suitable unsaturated precursor. Thus, when **23** was submitted to our standard basic conditions (NaH, DMF) (Scheme 10), **30** was obtained with a ratio relative to **31** and **32** of 20:3:1. When the reaction was performed at a lower temperature using a lithium base, **32** was not detected and the ratio **30:31** was slightly higher (7:1).

Scheme 10



Scheme 11

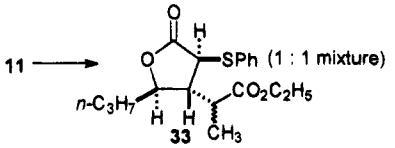
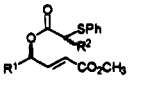
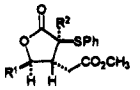
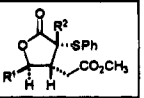


Table 3. Stereoselective Intramolecular Michael Addition with Different Functionalities

Entry	Substrate	Product	
			
1.	R^1=$(CH_2)_2$OTBDPS R^2=H, **34**	**35**, 95%	-
2.	R^1=$(CH_2)_2$OTBDPS R^2=CH_3, **36**	-	**37**, 95%
3.	R^1=*E*-CH_2CH=$CHCH_2$OTHP R^2=H, **38**	**39**, 95%	-
4.	R^1=*E*-CH_2CH=$CHCH_2$OAc R^2=H, **40**	**41**, 95%	-

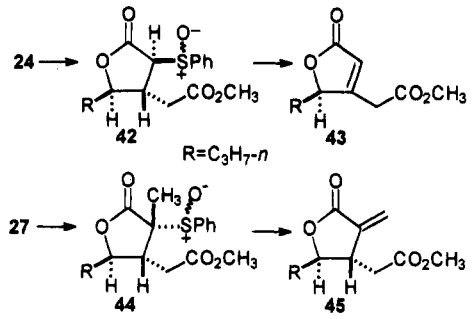
The obtained results prompted us to investigate the stereoselection in those cases in which an additionally created stereocenter is located in the carboxyalkyl branch. However, when the ester **11** was submitted to cyclization a disappointing 1:1 mixture of the γ-lactones **33** was obtained (Scheme 11).

As expected, our methodology was general in terms of functionalities existent in the molecule. Thus, with substrates in which acidic or basic sensitive groups were present the procedure works smoothly affording the corresponding γ-lactones with the expected stereochemistries and yields. Thus, *tert*-butyldiphenylsilyl, tetrahydropyranyl, or acetyl groups are totally compatible with the reaction conditions. In similar terms the presence of nonelectrophilic double bonds is perfectly possible (Table 3).

In order to explore the versatility of the obtained substances a series was performed with the γ-lactones. Thus, the oxidation of **24** and **27** with a stoichiometric amount of *m*-chloroperbenzoic acid proceeded without any problem, (Scheme 12) yielding the diastereomeric mixtures of sulfoxides[14] **42** and **44** which, submitted to thermal elimination,[14] yielded the butenolide **43** and the methylene lactone **45**, respectively, with excellent yields.

In a similar manner, oxidation of **24** and **27** to the sulfones using our recently reported procedure using

Scheme 12



Scheme 13

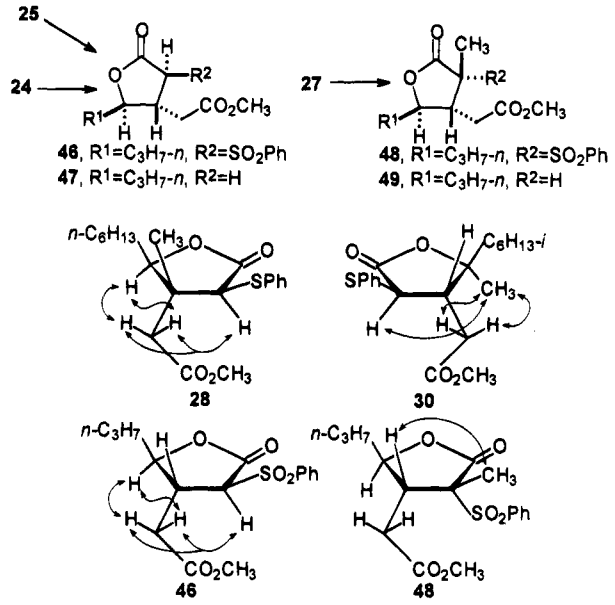


Figure 1.

ruthenium tetroxide[15] and reductive desulfonation[16] yielded the γ-lactones **47** and **49** (Scheme 13). Noteworthy is the fact that when the less abundant diastereoisomer **25** was oxidized to the sulfone, the α-carbonyl carbon was completely epimerized. This inversion of the configuration suggests that the *all-trans*-substituted ring is the thermodynamically more stable compound. It should also be pointed out that such a reaction occurred when other oxidants were used (MCPBA[17] and Oxone[18]).

The stereochemistry in all the cyclic products and the corresponding sulfones were determined by ROESY[19] and/or NOEDIFF[20] experiments assuming the stereochemistry of the epoxy alcohol[9] (Figure 1).

Discussion of the Stereochemical Results. In order to clarify the stereochemical course of the reaction we considered the use of semiempirical calculations as a tool to obtain models for such reactions. Although the

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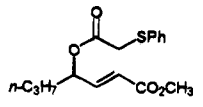
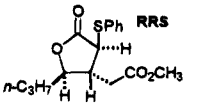
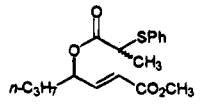
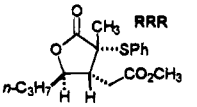
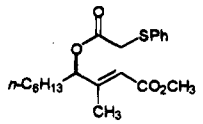
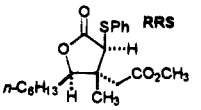
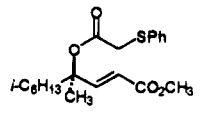
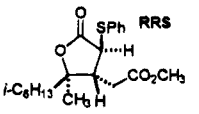
Table 4. Heat of Formations in kcal/mol of All Diastereoisomers Obtained by the Cyclization of 5, 10, 15, and 23 Using MOPAC/AM1

Substrate	Conf.[a]	ΔH (s)[b]	ΔH (f)[c]	ΔH (Na^+)[d]	Isolated product.
 **5**	2R,3R,4S	**-160.02**	-182.15	**-239.36**	 **24**
	2R,3S,4S	-155.28	-182.95	-235.86	
	2R,3R,4R	-157.40	**-184.52**	-237.68	
	2R,3S,4R	-157.82	-180.78	-235.62	
 **10**	2R,3R,4S	-156.51	-181.49	**-237.01**	 **27**
	2R,3S,4S	-154.79	-181.84	-233.32	
	2R,3R,4R	**-158.70**	**-185.95**	-236.23	
	2R,3S,4R	-154.89	-180.70	-236.07	
 **15**	2R,3R,4S	**-178.40**	-200.78	-256.35	 **28**
	2R,3S,4S	-177.47	**-204.23**	-256.16	
	2R,3R,4R	-174.20	-203.15	**-256.66**	
	2R,3S,4R	-177.35	-199.97	-254.20	
 Enantiomer of **23**	2R,3R,4S	**-177.17**	-193.67	-253.68	 Enantiomer of **30**
	2R,3S,4S	-174.93	**-201.90**	-254.69	
	2R,3R,4R	-175.16	-201.77	-253.89	
	2R,3S,4R	-175.73	-199.82	**-256.44**	

a) Possible configuration of the final γ-lactone; b) ΔH (Kcal/mol) protonated compound; c) Δ (Kcal/mol) free anion; d) ΔH (Kcal/mol) using a Na^+ "sparkles".

Michael-addition reaction has extraordinary importance in synthetic chemistry, relatively few mechanistic studies have been reported,[21] and they are mainly devoted to the intermolecular version of the reaction.[21d,e,22]

In order to clarify the high diastereoselection found in the cyclization reaction and thinking of a possible thermodynamic control, we studied using AM1, the energies of each of the four possible diastereoisomers which can be obtained when such a reaction is performed on **5**, **10**, **15**, and **23** (Table 4). In Table 4 are shown the heat of formation of both the free enolates and the sodium salts, although in this last case because sodium parametrization is not available, a "sparkles" entity was used, considering its definition as a simplified atom of nuclear charge of +1, ionic radius of 0.7 Å and zero heat of formation, no orbitals and no ionization potential.[23] Although the less energetic structures correspond to the isolated diastereoisomers when protonated species are compared, it should be considered, however, that because the reaction is performed in basic conditions the final products should be the ester enolates instead of the protonated species. When similar calculations were performed over such anions the energies obtained were not in agreement with the experimental results.

Considering such calculated results, a thermodynamically controlled reaction looks to be highly unlikely.[24] Thus, a kinetic control was speculated for the intramolecular cyclization. The forming carbon—carbon bond (C3···C4 in the γ-lactone ring) was chosen as the reaction coordinate. The reaction path was calculated for the "breaking" of the C3—C4 bond, starting for all the free enolate esters, by systematically increasing the bond length value in successive increments and optimizing all the remaining geometrical parameters. The geometry corresponding to the maximum potential along all the paths was then fully optimized by gradient minimization routines and characterized as true transition states by calculating force constants. The main features of the found transition states for all possible final configurations are summarized in Table 5.

As can be observed in Table 5 for each γ-[(phenylthio)-acyl]oxy α,β-unsaturated ester, the less energetic transition states found are those which correctly lead to the isolated γ-lactone. In Figure 2 are indicated the geometries of such transition states.

A picture with the three species, starting enolate, transition state and final product for the γ-[(phenylthio)-acyl]oxy α,β-unsaturated ester **5**, is shown in Figure 3. The lower energy structure **50** derives from the *Si* face attack of the *E*-enolate ion **54** to the *Re*-π-face at the β-carbon of the conjugate ester.[25] The geometry of the enolate carbon changes from planar (dihedral angle S—C^-—C=O ≈ 6°) necessary to stabilize the carbanion with the vicinal carbonyl group, to nearly orthogonal

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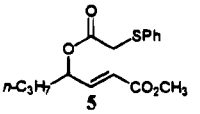
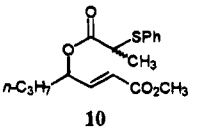
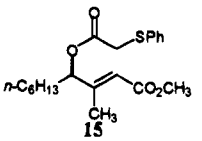
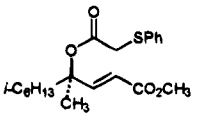
(22) Bernardi, A.; Capelli, A. M.; Gennari, C.; Scolastico, C. *Tetrahedron: Asymmetry* **1990**, *1*, 21.

(23) Stewart, J. J. P. *MOPAC Manual* **1990**.

(24) In our preliminary note (ref 7) we speculated that such thermodynamic control is mainly based on the fact that both *E*- and *Z*-unsaturated esters (**5** and **6**) gave the same ratio of γ-lactones. However, we now have strong evidence that under the cyclization reaction conditions (NaH, DMF) it is not possible to revert the final lactones to the starting unsaturated esters.

Table 5. Main Features of the Found Transition States for all Possible Final Configurations, Using MOPAC/AM1

Substrate	Conf.[a]	δ [b] (Å)	O=C–S (deg)	C–C=C (deg)	ν[c] (cm^{-1})	ΔH (Kcal/mol)
 5	**2(R),3(R),4S**	2.17	93.98	107.94	174.59	**-165.93**
	2(R),3(S),4S	2.10	95.54	113.55	284.99	-163.75
	2(R),3(R),4R	2.11	-99.85	113.29	248.52	-164.43
	2(R),3(S),4R	2.15	-96.73	107.60	175.19	-164.09
 10	2(R),3(R),4S	2.08	95.78	109.75	316.58	-168.57
	2(R),3(S),4S	2.12	92.76	111.70	271.86	-164.84
	2(R),3(R),4R	2.06	-102.49	112.27	307.51	**-168.66**
	2(R),3(S),4R	2.06	-100.90	109.92	330.10	-167.83
 15	**2(R),3(R),4S**	2.06	45.61	108.89	364.06	**-187.70**
	2(R),3(S),4S	2.10	96.81	109.31	311.58	-186.05
	2(R),3(R),4R	2.10	-93.70	111.97	287.48	-184.80
	2(R),3(S),4R	2.10	-89.93	104.48	296.38	-186.53
 Enantiomer of **23**	**2(R),3(R),4S**	2.17	92.91	106.15	164.26	**-182.75**
	2(R),3(S),4S	2.12	95.35	113.15	246.49	-182.23
	2(R),3(R),4R	2.12	-95.45	113.49	125.73	-182.28
	2(R),3(S),4R	2.18	-93.48	106.26	234.82	-182.68

a) Configuration based on the possible final γ-lactone (in bold type the one corresponding to the isolated product); b) C3-C4 distance; c) Imaginary frequencies obtained in the harmonic vibrational frequency analysis.

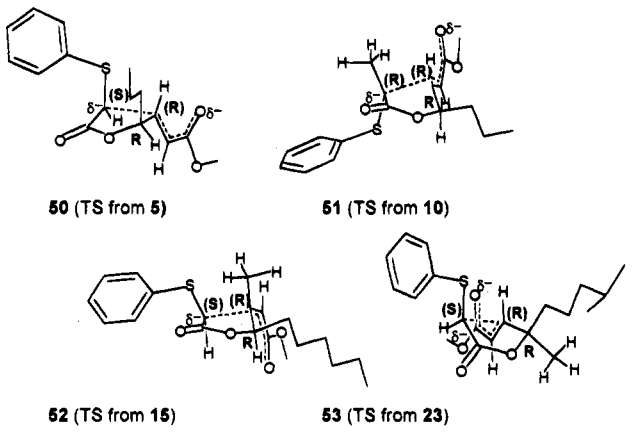


Figure 2. Transition-state geometries.

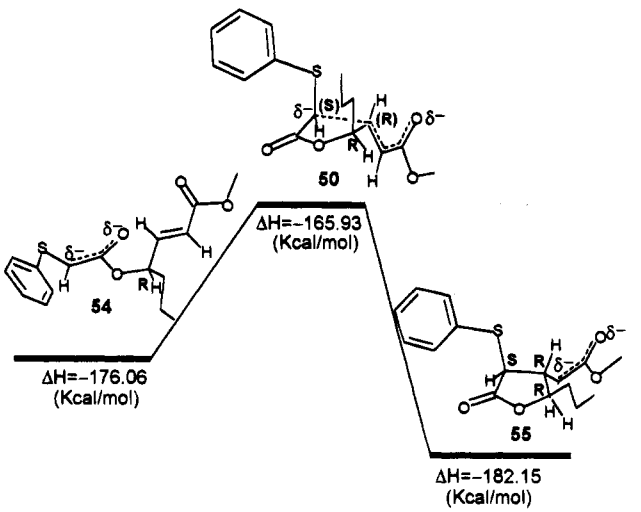


Figure 3. Schematic representation of the minimum-energy path for the intramolecular Michael cyclization of the enolates **54** (generated from **5**).

relative to the plane containing such a group (angle S–C⁻–C=O ≈ 94°). This structural feature is similar in all the TSs for the cyclization of **15** and **23**. However, in the cyclization of the methyl-α-carbonyl-substituted **10** the lower energy TS **51** corresponds to the one derived from the *Re*-face attack of the planar *E*-enolate to the *Re*-π-face of the electrophilic double bond with nearly interchange between the methyl and the phenylthio group (dihedral angle S–C⁻–C=O ≈ −102°).[25]

(25) Although we do not have experimental evidence about the stereochemistry of the enolate generated (any attempt at trapping the formed enolate was fruitless because of all conditions the cyclization was the observed reaction) our calculations suggests that the *E*-enolate is 0.8–3 kcal/mol more stable than the *Z*-isomer.

Conclusions

The intramolecular Michael cyclization of γ-[(phenylthio)acyl]oxy α,β-unsaturated esters obtained from enantiomerically enriched 2,3-epoxy alcohols has proved to be an excellent way to obtain α-(phenylthio) γ-lactones of high stereochemical purity. The method is extended to the synthesis of highly substituted systems. Thus those substrates presenting quaternary centers in all possible stereocenters in the ring were obtained with absolute stereochemical control. The methodology is general in terms of functionalities present in the final compound

since a wide range of protecting groups have been used in the study. The versatility of the methodology was extended by interconversion into other functionalities.

In order to rationalize the stereochemical course of such a procedure extensive semiempirical calculations were performed. Thus it can be concluded that the intramolecular Michael addition is very well described as a kinetically controlled reaction. The relative stability of the transition states for all possible final configurations led to geometries in agreement with the experimental results.

Experimental Section

Materials and Methods. ^1H and ^{13}C NMR spectra were recorded on a Bruker AMX 400 and/or Bruker AC 200 spectrometer in $CDCl_3$ or C_6D_6 as solvent, and chemical shifts are reported relative to Me_4Si. Low- and high-resolution mass spectra were taken using a Hewlett-Packard Model 257 and VG Micromass ZAB-2F spectrometers, respectively. Elemental analyses were performed on a Carlo-Erba Model 1106. Optical rotations were determined for solutions in chloroform or diethyl ether with a Perkin-Elmer Model 241 polarimeter. Infrared spectra were recorded on a Perkin-Elmer Model 257 and Perkin-Elmer Model 1605 FTIR spectrophotometer. GC analyses were performed on a Hewlett-Packard HP-5890 instrument with a capillary column, OV-1, 25 m. Melting points were determined on a Büchi model 535 melting point apparatus and are uncorrected. HPLC chromatography was performed using a LKB pump Model 2248 with a LKD 2MD Rapid Spectral detector using a μ-Porasil Silica 10-μm WATERS column. Column chromatography was performed on silica gel, 0.015–0.04 and 0.04–0.063 mm, and TLC and PLC were performed on silica gel, all Merck products. Visualization of spots was effected with UV light and/or phosphomolybdic acid in ethanol stain. All solvents were purified by standard techniques. Reactions requiring anhydrous conditions were performed under argon. Anhydrous magnesium sulfate was used for drying solutions.

Computational methods. Semiempirical calculations were carried out using standard MNDO,[26] AM1,[27] and PM3[28] Hamiltonians implemented in MOPAC 6.0.[29] Geometries for products were previously optimized using force field calculations (PCMODEL 3.3[30]) and further optimized with respect to all geometrical parameters using Broyden–Flecher–Goldfarb–Shanno or Eigenvector-Following routine[31] algorithms. All structures were refined using the keyword PRECISE with a gradient norm of energy, $[\Sigma(\delta E/\delta r)^2]^{0.5}$, lower than 0.01 kcal/Å. Transition states, for the intramolecular Michael addition, were calculated using the best-suited reaction coordinate, viz. C4–C3 bond lengths, which were further optimized with either NLLSQ[32] or TS[31] algorithms. Inspection of the number of negative eigenvalues occurring in their corresponding force constant matrices accordingly led to classification of the stationary structures.[33] In the context of the present work, only Δ (ΔH) is really meaningful, since ΔH corresponds to "gas-phase" conditions.

Preparation of (2*S*,3*S*)-2,3-Epoxy-1-hexanol (2). Crushed, activated 3-Å molecular sieves (20% w) were added to stirred CH_2Cl_2 (600 mL) under argon. The flask was cooled to −20 °C and Ti(OPr-*i*)$_4$ (35.66 mL, 0.12 mol), (*R*,*R*)-(+)-diethyl tartrate (23.94 mL, 0.14 mol), and (*E*)-2-hexen-1-ol (11.78 mL, 0.1 mol) in CH_2Cl_2 (65 mL) were added sequentially with stirring. The mixture was stirred for 15 min, and *tert*-butyl hydroperoxide (39.93 mL, 4.5 M in isooctane, 0.18 mol)[9b] was added slowly. After the addition, the reaction was maintained with stirring for 4 h. Tartaric acid aqueous solution (15% w/v, 600 mL) was added, and the stirring was continued until clear phases were reached (30 min). The phases were separated, and the aqueous phase was extracted with CH_2Cl_2 (2 × 200 mL). The combined organic phases were concentrated, diluted with ether (300 mL), and treated with a precooled (0 °C) solution of 15% NaOH (w/v) aqueous (300 mL). The two-phase mixture was stirred vigorously for 15 min at 0 °C. The organic phase was separated, and the aqueous phase extracted with ether (2 × 100 mL). The combined organic phases were washed with saturated brine (100 mL), dried, evaporated, and chromatographed on a silica gel column, to yield **2** (9.28 g, 80% yield, >95% ee by ^1H NMR analysis of the Mosher's ester[34]): $[\alpha]^{25}_D$ −46.5° (*c* 0.93, $CHCl_3$) [lit.[35] $[\alpha]^{25}_D$ −46.6° (*c* 1.0, $CHCl_3$)]; ^1H NMR ($CDCl_3$) δ 0.95 (t, J = 7.09 Hz, 3 H), 1.46 (m, 4 H), 2.33 (m, 1 H), 2.90 (m, 2 H), 3.72 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 13.76 (q), 19.16 (t), 33.53 (t), 55.83 (d), 58.41 (d), 61.83 (t); IR ($CHCl_3$) (cm^{-1}) 3524, 2972, 2963, 2873, 1460, 1370, 1264, 1103; MS *m/z* (relative intensity) 115 $(M - 1)^+$ (27), 99 (14), 81 (25), 73 (81), 57 (100); HRMS calcd. for $C_6H_{11}O_2$ $(M - 1)^+$ 115.0759, found 115.0741.

General Procedure To Obtain 3-[(Phenylthio)acyl]oxy 1,2-Diols. Preparation of (1*R*)-1-[1(*S*)-1,2-Dihydroxyethyl]butyl (Phenylthio)acetate (3). To a stirred solution of 2,3-epoxy-1-hexanol **2** (5 g, 0.043 mol) in dry CH_2Cl_2 (430 mL, 0.1 M) was added (phenylthio)acetic acid (10.88 g, 0.065 mol) at 0 °C under argon. The mixture was stirred for 15 min, and Ti(OPr-*i*)$_4$ (15.4 mL, 0.0517 mol) was added. After the addition, the mixture was allowed to warm to room temperature and the solution was stirred for 2 h. A tartaric acid aqueous solution (15% w/v, 400 mL) was added, and the two were stirred until clear phases were reached (30 min). The phases were separated, and the aqueous phase was extracted with CH_2Cl_2 (2 × 100 mL). The combined organic phases were washed with a saturated aqueous solution of $NaHCO_3$ (200 mL) and brine (200 mL), dried, concentrated, and purified by column chromatography, to yield **3** (11.51 g, 94% yield): $[\alpha]^{25}_D$ +11.1° (*c* 1.32, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.85 (t, J = 7.21 Hz, 3 H), 1.28 (m, 2 H), 1.57 (m, 2 H), 3.12 (br s, 1 H), 3.45 (br s, 1 H), 3.56 (m, 3 H), 3.66 (s, 2 H), 4.88 (m, 1 H), 7.25 (m, 2 H), 7.39 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 13.78 (q), 18.41 (t), 32.32 (t), 36.68 (t), 62.56 (t), 72.83 (d), 75.66 (d), 127.08 (d), 129.09 (d), 129.91 (d), 134.80 (s), 170.08 (s); IR ($CHCl_3$) (cm^{-1}) 3555, 2962, 2934, 2874, 1727, 1463, 1281, 1129, 1069; MS *m/z* (relative intensity) 284 $(M)^+$ (25), 253 (2), 168 (61), 123 (100); HRMS calcd for $C_{14}H_{20}O_4S$ $(M)^+$ 284.1082, found 284.1078.

General Procedure To Transform 3-[(Phenylthio)acyl]-oxy 1,2-Diols into γ-[(Phenylthio)acyl]oxy α,β-Unsaturated Esters. Preparation of Methyl (4*R*)-4-[(Phenylthio)-acetoxy]hept-2(*E*)-enoate (5). To a stirred solution of **3** (10 g, 0.035 mol) in MeOH/H_2O (20:1, 70 mL) was added $NaIO_4$ (18.83 g, 0.088 mol) and a catalytic amount of tetrabutylammonium periodate at rt. After 1 h, the mixture was filtered through a pad of Celite and washed with ether (3 × 30 mL). The resulting solution was concentrated, yielding an oil of the crude aldehyde **4**, which was used without purification.

To a suspension of sodium hydride (1.9 g, 0.063 mol, 80% in mineral oil) in benzene (500 mL), at 0 °C was added slowly (trimethylphosphono)acetate (11.34 mL, 0.070 mol) in benzene (50 mL). After complete addition the mixture was stirred for 5 min and the crude aldehyde dissolved in benzene (150 mL) was added dropwise. The reaction mixture was stirred for 30 min, after which time TLC showed complete conversion to the unsaturated ester. The reaction was quenched with acetic acid (4 mL), extracted with ether (500 mL), and washed with saturated aqueous solution of $NaHCO_3$ (200 mL) and brine (200 mL), dried over $MgSO_4$, filtered, and concentrated. Flash chromatography provided pure samples of esters **5** (7.92 g, 73%

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(28) Stewart, J. J. P. *J. Comput. Chem.* **1989**, *10*, 221.
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(34) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543. The ee >95% signifies that no absorption caused by the presence of the other enantiomer could be observed.
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yield) and **6** (0.33 g, 3% yield). Compound **5**: $[\alpha]^{25}_D$ +19.9° (*c* 1.24, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.84 (t, *J* = 7.19 Hz, 3 H), 1.24 (m, 2 H), 1.57 (m, 2 H), 3.64 (s, 2 H), 3.69 (s, 3 H), 5.37 (m, 1 H), 5.90 (dd, *J* = 15.7, 1.5 Hz, 1 H), 6.77 (dd, *J* = 15.7, 5.35 Hz, 1 H), 7.24 (m, 3 H), 7.38 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 13.35 (q), 17.70 (t), 35.39 (t), 36.29 (t), 51.23 (q), 72.96 (d), 121.08 (d), 126.75 (d), 128.73 (d), 129.77 (d), 134.44 (s), 144.71 (d), 165.87 (s), 166.40 (s); IR ($CHCl_3$) (cm^{-1}) 2962, 2875, 1725, 1719, 1659, 1438, 1316, 1279, 1129; MS *m/z* (relative intensity) 308 $(M)^+$ (18), 168 (6), 141 (54), 123 (100); HRMS calcd for $C_{16}H_{20}O_4S$ $(M)^+$ 308.1082, found 308.1093. Compound **6**: $[\alpha]^{25}_D$ +3.3° (*c* 2.6, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.88 (t, *J* = 7.24 Hz, 3 H), 1.34 (m, 2 H), 1.60 (m, 2 H), 3.65 (s, 2 H), 3.67 (s, 3 H), 5.77 (dd, *J* = 11.59, 0.86 Hz, 1 H), 5.95 (dd, *J* = 11.59, 7.74 Hz, 1 H), 6.22 (m, 1 H), 7.24 (m, 3 H), 7.36 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 13.39 (q), 17.72 (t), 35.50 (t), 36.21 (t), 51.16 (q), 72.24 (d), 119.84 (d), 126.75 (d), 128.48 (d), 129.54 (d), 134.79 (s), 146.84 (d), 165.25 (s), 168.61 (s); IR ($CHCl_3$) (cm^{-1}) 2942, 2933, 2873, 1730, 1719, 1659, 1457, 1282, 1130, 901.

Preparation of Methyl (4*R*)-4-[(Phenylthio)acetoxy]-hept-2(*Z*)-enoate (6). To a stirred solution of **3** (1 g, 3.52 mmol) in MeOH/H_2O (20:1, 7 mL) was added $NaIO_4$ (1.88 g, 8.8 mmol) and a catalytic amount of tetrabutylammonium periodate at rt. After 1 h, the mixture was filtered through a pad of Celite and washed with ether (3 × 5 mL). The resulting solution was concentrated, yielding an oil of the crude aldehyde **4**, which was used without purification.

To a stirred solution of the crude aldehyde in dry MeOH (35 mL) was added methyl (triphenylphosphoranylidene)-acetate (2.35 g, 7.04 mmol) at rt, under argon. The mixture was stirred for 24 h at the same temperature after which time the mixture was extracted in ether (30 mL) and washed with water (30 mL), dried over $MgSO_4$, and concentrated, yielding after flash chromatography **5** (304 mg, 28% yield) and **6** (618 mg, 57% yield).

Preparation of (1*R*)-1-[(1*S*)-1,2-Dihydroxyethyl]butyl (Benzenesulfonyl)acetate (7). The general procedure to obtain 3-[(phenylthio)acyl]oxy 1,2-diols was applied to **2** on a 1 g (8.62 mmol) scale using (benzenesulfonyl)acetic acid (2.59 g, 12.93 mmol) for 6 h, yielding **7** (2.02 g, 74% yield): $[\alpha]^{25}_D$ +18.3° (*c* 2.42, $CHCl_3$); ^1H NMR ($CDCl_3$) δ: 0.92 (t, *J* = 7.34 Hz, 3 H), 1.52 (m, 4 H), 2.35 (br s, 1 H), 2.91 (br s, 1 H), 3.74 (m, 3 H), 4.17 (s, 2 H), 4.34 (m, 1 H), 7.62 (m, 3 H), 7.95 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 14.39 (q), 19.38 (t), 35.12 (t), 61.60 (t), 67.74 (t), 72.47 (d), 79.94 (d), 128.75 (d), 129.88 (d), 132.0 (s), 134.99 (d), 162.79 (s); IR ($CHCl_3$) (cm^{-1}) 3534, 3018, 2958, 1744, 1327, 1282, 1160, 1084; MS *m/z* (relative intensity) 285 $(M - OCH_3)^+$ (2) 255 (4), 201 (49), 182 (87), 141 (100), 77 (98); HRMS calcd for $C_{13}H_{17}O_5S$ $(M - OCH_3)^+$ 285.0797, found 285.0816.

Preparation of (1*R*)-1-[(1*S*)-1,2-Dihydroxyethyl]butyl (2*R*)- and (2*S*)-2-(Phenylthio)propionate (8). The general procedure to obtain 3-[(phenylthio)acyl]oxy 1,2-diols was applied to **2** on a 5 g (43.1 mmol) scale using 2-(phenylthio)-propionic acid (11.78 g, 64.65 mmol) for 2 h, yielding **8** (11.30 g, 88% yield): ^1H NMR ($CDCl_3$) δ 0.88 (t, *J* = 7.09 Hz, 3 H), 1.22 (m, 2 H), 1.46 (d, *J* = 7.16 Hz, 3 H), 1.48 (m, 2 H), 3.17 (br s, 2 H), 3.46 (m, 3 H), 3.89 (q, *J* = 7.16 Hz, 1 H), 4.81 (m, 1 H), 7.28 (m, 3 H), 7.38 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 13.81 (q), 17.46 (q), 18.39 (t), 32.43 (t), 45.17 (d), 62.58 (t), 72.88 (d), 75.20 (d) 127.84 (d), 127.91 (s), 128.98 (d), 132.49 (d), 173.04 (s); IR ($CHCl_3$) (cm^{-1}) 3548, 2934, 2874, 1732, 1377, 1358, 1070; MS *m/z* (relative intensity) 298 $(M)^+$ (14), 182 (25), 137 (100), 109 (27); HRMS calcd for $C_{15}H_{22}O_4S$ $(M)^+$ 298.1239, found 298.1227.

Preparation of Methyl (4*R*)-4-[[(2*R*)- and (2*S*)-2-(Phenylthio)propionyl]oxy]hept-2(2*E*)-enoate (10). The general procedure to transform 3-[(phenylthio)acyl]oxy 1,2-diols into γ-[(phenylthio)acyl]oxy α,β-unsaturated esters was applied to **8** on a 10 g (33.56 mmol) scale, yielding **10** (8.21 g, 76% yield): ^1H NMR ($CDCl_3$) δ 0.74 (t, *J* = 7.25 Hz, 3 H), 1.14 (m, 2 H), 1.32 (d, *J* = 7.0 Hz, 3 H), 1.45 (m, 2 H), 3.33 (q, *J* = 7.0 Hz, 1 H), 3.58 (s, 3 H), 5.22 (m, 1 H), 5.74 (dd, *J* = 15.82, 1.58 Hz, 1 H), 6.62 (dd, *J* = 15.82, 5.39 Hz, 1 H), 7.14 (m, 3 H), 7.30 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 13.65 (q), 17.36 (q), 18.01 (t), 37.79 (t), 45.26 (d), 51.49 (q), 72.95 (d), 121.43 (d), 127.75 (d), 127.95 (s), 128.91 (d), 132.72 (d), 145.18 (d), 166.24 (s), 171.64 (s); IR ($CHCl_3$) (cm^{-1}) 2960, 2933, 2874, 1722, 1663, 1454, 1313, 1163, 1068; MS *m/z* (relative intensity) 322 $(M)^+$ (6), 182 (2), 137 (100); HRMS calcd for $C_{17}H_{22}O_4S$ $(M)^+$ 322.1239, found 322.1243.

Preparation of Ethyl (4*R*)-2-Methyl-4-(phenylthioacetoxy)hept-2(*E*)-enoate (11). To a stirred solution of **3** (1 g, 3.52 mmol) in MeOH/H_2O (20:1, 7 mL) was added $NaIO_4$ (1.88 g, 8.8 mmol) and a catalytic amount of tetrabutylammonium periodate at rt. After 1 h, the mixture was filtered through a pad of Celite and washed with ether (3 × 5 mL). The resulting solution was concentrated, yielding an oil of the crude aldehyde **4**, which was used without purification.

To a stirred solution of crude aldehyde in dry benzene (35.2 mL, 0.1 M) was added carbethoxyethylidene–triphenylphosphorane (2.55 g, 7.04 mmol) at 0 °C under argon. The mixture was stirred for 12 h at the same temperature, after which time the mixture was extracted in ether (30 mL) and washed with water (30 mL), dried over $MgSO_4$, and concentrated, yielding after flash chromatography **11** (816.3 mg, 72% yield): $[\alpha]^{25}_D$ +2.4° (*c* 2.42, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.86 (t, *J* = 7.2 Hz, 3 H), 1.3 (t, *J* = 7.16 Hz, 3 H), 1.55 (m, 4 H), 1.89 (d, *J* = 1.45 Hz, 3 H), 3.63 (s, 2 H), 4.20 (q, *J* = 7.16 Hz, 2 H), 5.52 (ddd, *J* = 9.08, 5.96, 5.96 Hz, 1 H), 6.48 (dd, *J* = 9.08, 1.45 Hz, 1 H), 7.24 (m, 3 H), 7.38 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 13.02 (q), 13.76 (q), 14.21 (q), 18.07 (t), 35.86 (t), 36.79 (t), 60.67 (t), 71.99 (d), 127.02 (d), 128.0 (s), 129.0 (d), 130.1 (d), 137.87 (d), 155.1 (s), 172.3 (s), 174.6 (s); IR ($CHCl_3$) (cm^{-1}) 2962, 2935, 2874, 1715, 1657, 1466, 1368, 1271, 1152, 1085; MS *m/z* (relative intensity) 336 $(M)^+$ (1), 169 (19), 123 (100), 77 (21); HRMS calcd for $C_{18}H_{24}O_4S$ $(M)^+$ 336.1395, found 336.1409.

Preparation of (1*R*)-1-[(1*S*)-1,2-Dihydroxy-1-methylethyl]heptyl (Phenylthio)acetate (13). The general procedure to obtain 3-[(phenylthio)acyl]oxy 1,2-diols was supplied to **12** on a 2 g (0.012 mol) scale, yielding **13** (3.08 g, 78% yield): $[\alpha]^{25}_D$ +17.6° (*c* 1.41, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.88 (t, *J* = 6.53 Hz, 3 H), 0.97 (s, 3 H), 1.29 (m, 8 H), 1.55 (m, 1 H), 1.77 (m, 1 H), 2.65 (br s, 1 H), 2.77 (br s, 1 H), 3.17 (m, 1 H), 3.29 (m, 1 H), 3.69 (s, 2 H), 4.79 (dd, *J* = 10.56, 2.05 Hz, 1 H), 7.34 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 14.01 (q), 17.94 (q), 22.52 (t), 26.24 (t), 28.12 (t), 28.97 (t), 31.62 (t), 36.43 (t), 66.56 (t) 73.14 (s), 77.20 (d), 127.13 (d), 129.15 (d), 129.64 (d), 134.55 (s), 171.09 (s); IR ($CHCl_3$) (cm^{-1}) 3679.1, 3542.1, 3021.4, 2957.5, 2930.1, 2857.0, 1711.4, 1483.1, 1460.2, 1437.4, 1405.4, 1286.7, 1131.4, 1044.6; MS *m/z* (relative intensity) 342 $(M + 2)^+$ (1), 341 $(M + 1)^+$ (3), 340 $(M)^+$ (14), 266 (10), 207 (27), 168 (43), 123 (100), 110 (92); HRMS calcd for $C_{18}H_{28}O_4S$ $(M)^+$ 340.1708, found 340.1679.

Preparation of (1*R*)-1-Acetylheptyl (Phenylthio)acetate (14). To a stirred solution of **13** (3 g, 8.82 mmol) in benzene (88.2 mL, 0.1 M) was added $Pb(OAc)_4$ (4.69 g, 0.0106 mol) at 0 °C under argon. The reaction mixture was allowed to warm at rt, and the solution was stirred for 1 h. It was then diluted in AcOEt (100 mL) and filtered through a pad of Celite. The resulting solution was treated and solid sodium bicarbonate and filtered. The solvent was evaporated in vacuo and the resulting residue was passed through a column of silica gel to give the ketone **14** (2.55 g, 94% yield): $[\alpha]^{25}_D$ +10.1° (*c* 2.38, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.88 (t, *J* = 6.39 Hz, 3 H), 1.25 (m, 8 H), 1.71 (m, 2 H), 2.09 (s, 3 H), 3.74 (s, 2 H), 4.98 (dd, *J* = 7.33, 5.32 Hz, 1 H), 7.27 (m, 3 H), 7.42 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 13.98 (q), 22.47 (t), 24.90 (t), 26.00 (q), 28.84 (t), 30.23 (t), 31.44 (t), 36.18 (t), 79.63 (d), 126.99 (d), 129.05 (d) 129.76 (d), 134.72 (s), 169.31 (s), 179.92 (s); IR ($CHCl_3$) (cm^{-1}) 3021.4, 2957.5, 2930.1, 2857.0, 1732.2, 1725.1, 1483.1, 1464.8, 1437.4, 1359.8, 1263.8, 1213.6, 1126.8, 1026.3; MS *m/z* (relative intensity) 310 $(M + 2)^+$ (3), 309 $(M + 1)^+$ (8), 308 $(M)^+$ (41), 157 (11), 151 (18), 150 (21), 123 (85), 116 (34), 97 (100); HRMS calcd for $C_{17}H_{24}O_3S$ $(M)^+$ 308.1446, found 308.1444.

Preparation of Methyl (4*R*)-3-Methyl-4-[(phenylthio)-acetoxy]-dec-2(*E*)-enoate (15). Crushed, activated 4-Å molecular sieves (20% w) were added to a suspension of sodium hydride (438.3 mg, 14.6 mmol, 80% in mineral oil) in dry benzene (100 mL), at 0 °C. (Trimethylphosphono)acetate (2.63 mL, 16.2 mmol) in benzene (40 mL) was slowly added to this mixture. After complete addition the mixture was stirred for

5 min, and the ketone **14** (2.5 g, 8.12 mmol) in benzene (30 mL) was added dropwise. The reaction mixture was stirred for 20 h, after which time TLC showed complete conversion to the unsaturated ester. The reaction was quenched with acetic acid (1 mL), extracted with ether (150 mL) and washed with saturated aqueous solution of $NaHCO_3$ (150 mL) and brine (150 mL), dried over $MgSO_4$, filtered, and concentrated. Flash chromatography provided test **15** (2.07 g, 70% yield): $[\alpha]^{25}_D$ +8.6° (*c* 2.34, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.88 (t, J = 6.7 Hz, 3 H), 1.25 (m, 8 H), 1.62 (m, 2 H), 2.14 (s, 3 H), 3.66 (s, 2 H), 3.69 (s, 3 H), 5.12 (t, J = 6.42 Hz, 1 H), 5.81 (s, 1 H), 7.26 (m, 3 H), 7.39 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 13.98 (q), 14.94 (q), 22.49 (t), 24.96 (t), 28.85 (t), 31.53 (t), 32.57 (t), 36.57 (t), 51.0 (q), 78.75 (d), 116.08 (d), 126.95 (d), 129.01 (d), 129.83 (d), 134.32 (s), 155.83 (s), 166.75 (s), 168.69 (s); IR ($CHCl_3$) (cm^{-1}) 3030.0, 2956.2, 2924.5, 2861.3, 1727.7, 1717.2, 1656.6, 1481.3, 1440.0, 1336.9, 1264.7, 1223.4, 1156.4; MS *m/z* (relative intensity) 366 $(M + 2)^+$ (1), 365 $(M + 1)^+$ (3), 364 $(M)^+$ (9), 197 (60), 137 (30), 125 (61), 123 (100), 97 (59), 69 (48); HRMS calcd for $C_{20}H_{29}O_4S$ $(M + 1)^+$ 365.1787, found 365.1779.

Preparation of (2*S*,3*S*)-2,3-Epoxy-3,7-dimethyl-1-octanol (19). To a stirred solution of **16**[9a] (3 g, 17.62 mmol) in dry ethyl acetate (120 mL) was added PtO_2 (200 mg, 0.88 mmol) at rt under 2 atm of H_2. The reaction mixture was stirred for 4 h, after which time TLC showed the end of the reaction. The solution was filtered through Whatman paper no. 2 and washed with ethyl acetate (2 × 30 mL). The combined organic phases were concentrated, and the crude obtained was purified by flash chromatography to yield the epoxide **19** (2.88 g, 95% yield): $[\alpha]^{25}_D$ −7.4° (*c* 2.78, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.86 (d, J = 6.4 Hz, 6 H), 1.14 (m, 2 H), 1.27 (s, 3 H), 1.39 (m, 3 H), 1.54 (m, 2 H), 2.30 (br s, 1 H), 2.95 (dd, J = 6.8, 4.0 Hz, 1 H), 3.66 (dd, J = 12.0, 6.8 Hz, 1 H), 3.82 (dd, J = 12.0, 4.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 16.69 (q), 22.49 (q), 22.49 (q), 27.86 (d), 38.66 (t), 38.77 (t), 61.41 (t), 61.41 (s), 63.00 (d); IR ($CHCl_3$) (cm^{-1}) 3606.2, 3456.0, 3005.3, 2951.6, 2865.8, 1467.0, 1386.6, 1231.0, 1209.5, 1080.7, 1021.7, 866.1; MS *m/z* (relative intensity) 157 $(M - CH_3)^+$ (1), 141 (1), 129 $(M - Pr\text{-}i)^+$ (8), 115 (23), 111 (13), 95 (13), 71 (100), 69 (93), 59 (64), 55 (93); HRMS calcd for $C_{10}H_{19}O_2$ $(M - 1)^+$ 171.1385, found 171.13698.

Preparation of (2*S*,3*S*)-2,3-Epoxy-3,7-dimethyloctyl *o*-Toluenesulfonate (20). To a stirred solution of **19** (2.5 g, 14.51 mmol) in dry pyridine (72.6 mL, 0.2 M), was added TsCl (3.32 g, 17.42 mmol) at 0 °C. The reaction mixture was stirred for 6 h, after which time TLC showed the end, and then was diluted with H_2O (100 mL) and the aqueous layer was extracted with Et_2O (3 × 50 mL). The ethereal extracts were washed with H_2O (100 mL), saturated $CuSO_4$ solution (100 mL), and saturated NaCl solution (100 mL), dried, and concentrated. Chromatography of the crude product on silica gel gave the tosylate **20** (4.26 g, 90% yield): $[\alpha]^{25}_D$ +16.1° (*c* 0.69, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.84 (d, J = 6.8 Hz, 6 H), 1.12 (m, 2 H), 1.18 (s, 3 H), 1.29 (m, 3 H), 1.45 (m, 2 H), 2.44 (s, 3 H), 2.94 (dd, J = 5.6, 5.6 Hz, 1 H), 4.08 (dd, J = 11.2, 5.6 Hz, 1 H), 4.15 (dd, J = 11.2, 5.6 Hz, 1 H), 7.34 (d, J = 8.2 Hz, 2 H), 7.79 (d, J = 8.2 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 17.06 (q), 22.06 (t), 22.91 (q), 23.03 (t), 28.27 (d), 38.54 (t), 39.12 (t), 59.09 (d), 61.56 (s), 69.01 (t), 128.38 (d), 130.33 (d), 133.25 (s), 145.47 (s); IR ($CHCl_3$) (cm^{-1}) 3036.2, 3017.8, 2953.4, 2870.7, 1599.0, 1465.8, 1369.3, 1190.1, 1171.7, 1098.2, 974.1, 813.3; MS *m/z* (relative intensity) 283 $(M - Pr\text{-}i)^+$ (1), 241 (1), 200 (34), 172 (4), 156 (10), 155 (100), 141 (12), 111 (39), 110 (10), 91 (90); HRMS calcd for $C_{14}H_{19}O_4S$ $(M - Pr\text{-}i)^+$ 283.1004, found 283.1007.

Preparation of (3*S*)-3,7-Dimethyloct-1-en-3-ol (21). To a stirred solution of **20** (4 g, 12.27 mmol) in dry acetone (41 mL, 0.3 M) was added sodium iodide (7.36 g, 49.08 mmol) at rt, under argon. The reaction was stirred for 4 h until TLC showed it to be completed. The reaction mixture was then diluted in Et_2O (100 mL) and filtered through a pad of Celite. The organic phase was concentrated, yielding the iodide, which was used without purification.

Activated zinc powder was prepared by washing commercially available zinc powder with 1 M HCl for 2 min, H_2O, EtOH, and Et_2O successively and drying under reduced pressure (3 mm Hg). A mixture of the iodide and activated zinc powder (4.81 g, 73.62 mmol) in dry Et_2O (75 mL) and AcOH (7.5 mL) at rt was stirred for 1 h and then was filtered through a pad of Celite, and the organic phase was washed with saturated aqueous solution of $NaHCO_3$ (3 × 75 mL) and NaCl (100 mL). The ethereal solution was concentrated, and the crude product was purified by chromatography on silica gel to afford **21** (1.72 g, 90% yield): $[\alpha]^{25}_D$ +9.6° (*c* 2.02, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.86 (d, J = 6.48 Hz, 6 H), 1.17 (m, 3 H), 1.27 (s, 3 H), 1.30 (m, 2 H), 1.49 (m, 3 H), 5.03 (dd, J = 10.72, 1.40 Hz, 1 H), 5.19 (dd, J = 17.45, 1.40 Hz, 1 H), 5.91 (dd, J = 17.45, 10.72 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 21.63 (t), 22.56 (q), 27.83 (d), 27.88 (q), 39.31 (t), 42.57 (t), 73.27 (s), 111.42 (t), 145.26 (d); IR ($CHCl_3$) (cm^{-1}) 3595.5, 2994.5, 2951.6, 2865.8, 1461.7, 1365.1, 1214.9, 1177.3, 925.1; MS *m/z* (relative intensity) 156 $(M)^+$ (6), 155 $(M - 1)^+$ (70), 111 (28), 91 (100), 71 (26), 69 (76), 57 (56); HRMS calcd for $C_{10}H_{19}O$ $(M - 1)^+$ 155.1436, found 155.1435.

Preparation of Methyl (4*S*)-4-Hydroxy-4,8-dimethylnon-2(*E*)-enoate (22). A solution of the alcohol **21** (1.5 g, 9.62 mmol) in CH_2Cl_2/MeOH, 4:1 (0.05 M) was stirred at −78 °C under O_3 atm, until the solution turned blue. The excess O_3 was removed by a flow of argon until the blue color disappeared from the solution. Then Me_2S (1.41 mL, 19.23 mmol) was added and the reaction mixture was stirred 1 h at −78 °C. After this period it was allowed to warm to room temperature and stirred for a further 12 h. The reaction was extracted with CH_2Cl_2 (2 × 25 mL) and the combined organic layers were washed with NaCl saturated aqueous solution (100 mL), dried over $MgSO_4$, and concentrated, yielding the aldehyde, which was used without purification.

To a suspension of sodium hydride (721 mg, 24.04 mmol, 80% in mineral oil) in dry benzene (75 mL) at 0 °C was slowly added (trimethylphosphono)acetate (4.2 mL, 25.96 mmol) in benzene (50 mL). After complete addition the mixture was stirred for 5 min and the crude aldehyde dissolved in benzene (50 mL) was added dropwise. The reaction mixture was stirred for 1 h, after which time TLC showed complete conversion into the unsaturated ester. The reaction was quenched with acetic acid (1.5 mL) and extracted with ether (200 mL). The combined organic phases were washed with $NaHCO_3$ saturated aqueous solution (150 mL) and brine (150 mL), dried over $MgSO_4$, filtered, and concentrated. Flash chromatography provided a pure sample of ester **22** (1.44 g, 70% yield): $[\alpha]^{25}_D$ +8.7° (*c* 2.54, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.84 (d, J = 6.6 Hz, 6 H), 1.17 (m, 3 H), 1.26 (m, 2 H), 1.31 (s, 3 H), 1.52 (m, 2 H), 1.76 (br s, 1 H), 3.73 (s, 3 H), 6.02 (d, J = 15.66 Hz, 1 H), 6.95 (d, J = 15.66 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 21.94 (t), 22.97 (q), 28.14 (q), 28.22 (d), 39.60 (t), 42.72 (t), 51.97 (q), 73.50 (s), 118.59 (d), 153.01 (d), 167.66 (s); IR ($CHCl_3$) (cm^{-1}) 3598.0, 3489.4, 3015.3, 2956.1, 2867.2, 1712.6, 1657.9, 1460.4, 1435.7, 1366.6, 1312.3, 1282.6, 1198.7, 1174.0, 1149.3, 981.4, 956.7, 922.2, 818.5; MS *m/z* (relative intensity) 215 $(M + 1)^+$ (1), 183 $(M - OCH_3)^+$ (2), 171 $(M - Pr\text{-}i)^+$ (40), 129 (100), 111 (22), 98 (40), 97 (81), 69 (99), 55 (80); HRMS calcd for $C_{12}H_{23}O_3$ $(M + 1)^+$ 215.1647, found 215.1650.

Preparation of Methyl (4*S*)-4,8-Dimethyl-4-[(phenylthio)acetoxy]non-2(*E*)-enoate (23). To a stirred solution of (phenylthio)acetic acid (1.89 g, 11.21 mmol) in dry CH_2Cl_2 (56 mL, 0.1 M) under argon were added sequentially with stirring DMAP (479 mg, 3.93 mmol) and the ester **22** (1.2 g, 5.61 mmol) at 0 °C. The mixture was stirred for 15 min, and DCC (2.08 g, 10.09 mmol) was slowly added; it was then allowed to warm to room temperature and additionally stirred for 3 h. The reaction mixture was diluted in CH_2Cl_2 (100 mL), filtered through a pad of Celite and washed with 5% (w/v) HCl aqueous solution (2 × 100 mL), saturated aqueous solution of $NaHCO_3$ (100 mL) and saturated brine (100 mL). The organic phase was dried over $MgSO_4$, concentrated, and purified by chromatography on silica gel, to afford **23** (1.69 g, 83% yield): $[\alpha]^{25}_D$ +2.7° (*c* 2.63, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.83 (d, J = 6.60 Hz, 6 H), 1.09 (m, 2 H), 1.18 (m, 2 H), 1.46 (m, 1 H), 1.51 (s, 3 H), 1.66 (m, 1 H), 1.84 (m, 1 H), 3.61 (s, 2 H), 3.74 (s, 3 H), 5.84 (d, J = 15.92 Hz, 1 H), 6.88 (d, J = 15.92 Hz, 1 H), 7.23 (m, 1 H), 7.28 (m, 2 H), 7.41 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 21.54 (t), 22.94 (q), 23.96 (q), 28.14 (d), 37.75 (t), 39.26 (t), 39.94 (t), 52.06

(q), 83.63 (s), 119.60 (d), 127.39 (d), 129.45 (d), 130.38 (d), 135.33 (s), 151.04 (d), 167.06 (s), 168.54 (s); IR ($CHCl_3$) (cm^{-1}) 3062.8, 3018.2, 2955.8, 2929.0, 2866.5, 1723.7, 1720.2, 1660.0, 1480.1, 1467.2, 1437.3, 1377.3, 1313.1, 1278.8, 1176.0, 1128.9, 1068.9, 979.0; MS *m/z* (relative intensity) 366 $(M + 2)^+$ (1), 365 $(M + 1)^+$ (2), 364 $(M)^+$ (10), 274 (14), 168 (23), 137 (41), 123 (100), 109 (19), 95 (21), 81 (21), 77 (20), 69 (16), 55 (11); HRMS calcd for $C_{20}H_{28}O_4S$ $(M)^+$ 364.1708, found 364.1715.

General Cyclization Procedure of γ-[(Phenylthio)acyl]-oxy α,β-Unsaturated Esters. Preparation of Methyl (2*R*,3*R*,4*S*)-[5-Oxo-4-(phenylthio)-2-propyltetrahydrofuran-3-yl]acetate (24). To a suspension of sodium hydride (10.7 mg, 0.357 mmol, 80% in mineral oil) in dry DMF (1.6 mL) under argon at −50 °C was added dropwise the unsaturated ester **5** (100 mg, 0.325 mmol) in dry DMF (1.6 mL). The reaction mixture was stirred for 4 h, after which time TLC showed complete conversion into the lactone. The reaction was quenched with acetic acid (30 μL) and extracted with ether (2 × 10 mL). The combined organic phases were washed with saturated aqueous solution of $NaHCO_3$ (10 mL) and brine (10 mL), dried, and concentrated. Purification by column chromatography gave the lactone **24** (95 mg, 95% yield): $[\alpha]^{25}_D$ +7.1° (*c* 1.39, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.86 (t, *J* = 7.05 Hz, 3 H), 1.35 (m, 4 H), 2.40 (m, 1 H), 2.56 (d, *J* = 5.82 Hz, 2 H), 3.68 (s, 3 H), 3.75 (d, *J* = 10.28 Hz, 1 H), 4.22 (m, 1 H), 7.32 (m, 3 H), 7.55 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 13.64 (q), 18.39 (t), 34.67 (t), 36.01 (t), 43.11 (d), 51.28 (d), 51.79 (q), 82.24 (d), 128.74 (d), 129.16 (d), 131.53 (s), 134.10 (d), 171.05 (s), 173.5 (s); IR ($CHCl_3$) (cm^{-1}) 2960, 2934, 2875, 1770, 1735, 1438, 1172, 974; MS *m/z* (relative intensity) 308 $(M)^+$ (86), 277 (3), 249 (7), 168 (32), 109 (96); HRMS calcd for $C_{16}H_{20}O_4S$ $(M)^+$ 308.1082, found 308.1083.

Cyclization of 5 Using NaH/DMF at 0 °C. The cyclization was performed in accordance with the general cyclization procedure described above at 0 °C in 0.5 h, yielding **24** (78 mg, 78% yield) and **25** (16 mg, 16% yield): $[\alpha]^{25}_D$ +79.2° (*c* 1.4, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.95 (t, *J* = 7.08 Hz, 3 H), 1.42 (m, 1 H), 1.6 (m, 3 H), 2.5 (dd, *J* = 14.56, 2.76 Hz, 1 H), 2.87 (m, 2 H), 3.69 (s, 3 H), 4.08 (d, *J* = 10.12 Hz, 1 H), 4.12 (m, 1 H), 7.32 (m, 3 H), 7.55 (m, 2 H); ^1H NMR (C_6D_6) δ 0.75 (t, *J* = 7.18 Hz, 3 H), 1.11 (m, 3 H), 1.34 (m, 1 H), 2.0 (dd, *J* = 17.12, 5.4 Hz, 1 H), 2.46 (ddd, *J* = 9.32, 9.32, 5.4 Hz, 1 H), 2.46 (dd, *J* = 17.12, 9.32 Hz, 1 H), 3.32 (s, 3 H), 3.76 (m, 1 H), 4.03 (d, *J* = 7.68 Hz, 1 H), 6.99 (m, 3 H), 7.65 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 14.14 (q), 19.23 (t), 32.42 (t), 35.83 (t), 42.55 (d), 50.85 (d), 52.46 (q), 83.01 (d), 128.97 (d) 129.72 (d), 132.57 (s), 133.54 (d), 171.93 (s), 174.39 (s).

Preparation of Methyl (4*R*)-4-Hydroxyhept-2(*E*)-enoate (26). To a suspension of sodium hydride (10.71 mg, 0.357 mmol, 80% in mineral oil) in dry THF (1.6 mL) under argon was slowly added **5** (100 mg, 0.325 mmol) in dry THF (1.6 mL) at 0 °C. The reaction mixture was stirred for 4 h until no starting material was detected by TLC. It was then quenched with acetic acid (30 μL) and extracted in ether (2 mL), and the combined organic extracts were washed with saturated aqueous solution of $NaHCO_3$ (2 mL) and brine (2 mL), dried, and concentrated to yield, after chromatographic separation the alcohol **26** (41 mg, 80% yield): $[\alpha]^{25}_D$ +33.6° (*c* 3.55, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.94 (t, *J* = 7.08 Hz, 3 H), 1.22 (m, 2 H), 1.55 (m, 2 H), 2.20 (br s, 1 H), 3.74 (s, 3 H), 4.30 (m, 1 H), 6.0 (dd, *J* = 15.64, 1.58 Hz, 1 H), 6.96 (dd, *J* = 15.64, 4.9 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 13.78 (q), 18.37 (t), 38.73 (t), 51.45 (q), 70.70 (d), 119.57 (d), 150.72 (d), 167.0 (s); IR ($CHCl_3$) (cm^{-1}) 3555, 2972, 2963, 2874, 1725, 1665, 1454, 1370, 1103; MS *m/z* (relative intensity) 159 $(M + 1)^+$ (1), 141 (2), 129 (24), 115 (41); HRMS calcd for $C_8H_{15}O_3$ $(M + 1)^+$ 159.0943, found 159.0945.

Preparation of Methyl (2*R*,3*R*,4*R*)-[4-Methyl-5-oxo-4-(phenylthio)-2-propyltetrahydrofuran-3-yl]acetate (27). The general cyclization procedure was used over **10** on a 100 mg (0.310 mmol) scale, yielding **27** (95 mg, 95% yield): $[\alpha]^{25}_D$ +64.1° (*c* 0.82, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.93 (t, *J* = 6.91 Hz, 3 H), 1.40 (s, 3 H), 1.5 (m, 4 H), 2.54 (dd, *J* = 16.01, 6.35 Hz, 1 H), 2.68 (ddd, *J* = 9.96, 6.22, 6.22 Hz, 1 H), 2.91 (dd, *J* = 16.01, 5.86 Hz, 1 H), 3.74 (s, 3 H), 4.20 (m, 1 H), 7.36 (m, 3 H), 7.52 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 13.71 (q), 18.85 (t), 22.08 (q), 31.25 (t), 35.12 (t), 49.33 (d), 51.98 (q), 55.00 (s), 81.03 (d), 128.27 (s), 128.89 (d), 129.99 (d), 137.40 (d), 171.63 (s), 174.74 (s); IR ($CHCl_3$) (cm^{-1}) 2944, 2932, 2874, 1763, 1736, 1378, 1208, 1096, 992; MS *m/z* (relative intensity) 322 $(M)^+$ (100), 291 (12), 263 (6), 213 (31); HRMS calcd for $C_{17}H_{22}O_4S$ $(M)^+$ 322.1239, found 322.1229.

Preparation of Methyl (2*R*,3*R*,4*S*)-[2-Hexyl-3-methyl-5-oxo-4-(phenylthio)tetrahydrofuran-3-yl]acetate (28). The general cyclization procedure was used over **15** on a 500 mg (1.37 mmol) scale, yielding **28** (2*R*,3*R*,4*S*) (420 mg, 84% yield) and **29** (2*R*,3*R*,4*R*) (55 mg, 11% yield). Compound **28**: $[\alpha]^{25}_D$ −31.3° (*c* 0.91, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.88 (t, *J* = 6.66 Hz, 3 H), 1.26 (s, 3 H), 1.31 (m, 8 H), 1.57 (m, 2 H), 2.42 (d, *J* = 15.16 Hz, 1 H), 2.57 (d, *J* = 15.16 Hz, 1 H), 3.59 (s, 3 H), 4.32 (s, 1 H), 4.35 (dd, *J* = 9.64, 2.52 Hz, 1 H), 7.29 (m, 3 H), 7.60 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 14.42 (q), 16.98 (q), 22.92 (t), 26.86 (t), 29.37 (t), 29.41 (t), 31.97 (t), 39.33 (t), 46.23 (s), 52.11 (q), 58.26 (d), 84.52 (d), 128.30 (d), 129.53 (d), 132.82 (d), 134.50 (s), 171.11 (s), 174.63 (s); IR ($CHCl_3$) (cm^{-1}) 3018.4, 2959.3, 2925.6, 2858.1, 1771.1, 1733.1, 1454.7, 1437.9, 1349.3, 1231.2, 1205.9, 1172.2, 1108.9, 1016.1, 965.5; MS *m/z* (relative intensity) 366 $(M + 2)^+$ (7), 365 $(M + 1)^+$ (18), 364 $(M)^+$ (80), 291 (71), 207 (58), 149 (100), 109 (61), 95 (55), 57 (76); HRMS calcd for $C_{20}H_{28}O_4S$ $(M)^+$ 364.1708, found 364.1687. Compound **29**: $[\alpha]^{25}_D$ +111.7° (*c* 1.19, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.89 (t, *J* = 6.72 Hz, 3 H), 1.21 (s, 3 H), 1.29 (m, 8 H), 1.55 (m, 2 H), 2.46 (d, *J* = 16.58 Hz, 1 H), 2.80 (d, *J* = 16.58 Hz, 1 H), 3.71 (s, 3 H), 3.75 (s, 1 H), 4.24 (dd, *J* = 10.02, 2.14 Hz, 1 H), 7.33 (m, 3 H), 7.59 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 14.42 (q), 19.65 (q), 22.92 (t), 26.96 (t), 29.37 (t), 29.41 (t), 31.97 (t), 38.92 (t), 46.23 (s), 52.11 (q), 57.90 (d), 85.97 (d), 129.05 (d), 129.65 (d), 134.03 (d), 134.50 (s), 171.11 (s), 174.63 (s); IR ($CHCl_3$) (cm^{-1}) 3021.1, 2953.3, 2933.5, 2855.7, 1766.4, 1737.2, 1440.5, 1362.7, 1221.6, 1211.3, 1168.1, 1012.5, 963.8.

Preparation of Methyl (2*S*,3*S*,4*R*)-[2-Methyl-2-(4-methylpentyl)-5-oxo-4-(phenylthio)tetrahydrofuran-3-yl]-acetate (30). The general cyclization procedure was used over **23** on a 200 mg (0.55 mmol) scale, yielding **30** (2*S*,3*S*,4*R*) (150 mg, 75% yield), **31** (2*S*,3*R*,4*S*) (22.5 mg, 11% yield), and **32** (2*S*,3*S*,4*S*) (7.5 mg, 4% yield). Compound **30**: $[\alpha]^{25}_D$ +13.1° (*c* 2.34, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.80 (d, *J* = 6.60 Hz, 6 H), 1.04 (m, 4 H), 1.25 (s, 3 H), 1.38 (m, 2 H), 1.56 (m, 1 H), 2.45 (dd, *J* = 14.20, 7.80 Hz, 1 H), 2.66 (ddd, *J* = 11.60, 7.80, 5.80 Hz, 1 H), 2.72 (dd, *J* = 14.20, 5.80 Hz, 1 H), 3.53 (d, *J* = 11.60 Hz, 1 H), 3.72 (s, 3 H), 7.34 (m, 3 H), 7.60 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 20.88 (t), 22.12 (q), 22.89 (q), 28.20 (d), 34.13 (t), 39.23 (t), 40.33 (t), 43.77 (d), 52.44 (q), 52.50 (d), 86.69 (s), 129.63 (d), 130.97 (s), 135.55 (d), 172.03 (s), 173.30 (s); IR ($CHCl_3$) (cm^{-1}) 3020.6, 2957.7, 28.67.8, 1764.6, 1737.6, 1440.3, 1386.4, 1305.5, 1265.1, 1229.1, 1220.1, 1134.8, 955.1; MS *m/z* (relative intensity) 366 $(M + 2)^+$ (5), 365 $(M + 1)^+$ (14), 364 $(M)^+$ (62), 275 (22), 237 (15), 197 (39), 168 (40), 149 (72), 123 (71), 109 (94), 85 (62), 69 (100), 55 (56); HRMS calcd for $C_{20}H_{28}O_4S$ $(M)^+$ 364.1708, found 364.1706. Compound **31**: $[\alpha]^{25}_D$ −52.1° (*c* 1.57, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.86 (d, *J* = 6.60 Hz, 6 H), 1.15 (m, 2 H), 1.29 (s, 3 H), 1.44 (m, 5 H), 2.50 (dd, *J* = 14.48, 8.60 Hz, 1 H), 2.59 (ddd, *J* = 12.08, 8.60, 5.44 Hz, 1 H), 2.75 (dd, *J* = 14.48, 5.44 Hz, 1 H), 3.56 (d, *J* = 12.08 Hz, 1 H), 3.73 (s, 3 H), 7.34 (m, 3 H), 7.59 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 21.39 (t), 22.85 (q), 22.94 (q), 25.49 (q), 28.28 (d), 33.65 (t), 36.32 (t), 39.58 (t), 48.27 (d), 52.45 (d), 52.63 (q), 86.64 (s), 129.31 (d), 129.61 (d), 131.69 (s), 134.76 (d), 172.02 (s), 173.56 (s); IR ($CHCl_3$) (cm^{-1}) 3024.0, 2953.7, 2874.6, 1764.8, 1738.4, 1465.9, 1439.6, 1386.8, 1312.1, 1263.8, 1228.6, 1197.9, 1131.9, 995.7, 956.2. Compound **32**: $[\alpha]^{25}_D$ −98.4° (*c* 1.36, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.87 (d, *J* = 6.60 Hz, 6 H), 1.21 (m, 3 H), 1.35 (s, 3 H), 1.42 (m, 1 H), 1.55 (m, 2 H), 1.68 (m, 1 H), 2.47 (dd, *J* = 16.96, 4.12 Hz, 1 H), 2.94 (dd, *J* = 16.96, 10.76 Hz, 1 H), 3.08 (ddd, *J* = 10.76, 8.80, 4.12 Hz, 1 H), 3.65 (s, 3 H), 4.10 (d, *J* = 8.80 Hz, 1 H), 7.32 (m, 3 H), 7.57 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 21.72 (t), 22.64 (q), 22.96 (q), 28.26 (d), 31.57 (t), 39.36 (t), 41.07 (t), 44.08 (d), 51.37 (d), 52.42 (q), 87.73 (s), 128.62 (d), 129.62 (d), 132.85 (d), 134.59 (s), 172.08 (s), 175.13 (s); IR ($CHCl_3$) (cm^{-1}) 3021.9, 2957.5, 2856.2, 1756.3, 1737.9, 1466.5, 1438.9, 1383.7, 1305.4, 1264.0, 1218.0, 1199.6, 1176.6, 1139.8, 860.3.

Cyclization of 23 Using $LiN(SiMe_3)_2$. To a suspension

of unsaturated ester **23** (200 mg, 0.55 mmol) in dry THF/HMPA (1:1) (5.5 mL) at −78 °C was slowly added lithium bis(trimethylsilyl)amide (604 μL, 0.604 mmol) 1 M in THF. The reaction mixture was stirred for 4 h, after which time TLC showed complete conversion into the lactone. The reaction was quenched with acetic acid (40 μL) and extracted with ether (2 mL). The organic phases were washed with saturated aqueous solution of $NaHCO_3$ (2 mL) and brine (2 mL), dried, concentrated, and purified by flash chromatography to give the lactones **30** (2*S*,3*S*,4*R*) (158 mg, 79% yield) and **31** (2*S*,3*R*,4*S*) (22 mg, 11% yield).

Preparation of Methyl (2*S*)- and (2*R*)-2-[(2*R*,3*R*,4*S*)-5-Oxo-4-(phenylthio)-2-propyltetrahydrofura-3-yl]propionate (33). The general cyclization procedure was used over **11** on a 500 mg (1.49 mmol) scale, yielding **33** (460 mg, 92% yield), as a 1:1 diastereoisomer mixture: ^{1}H NMR ($CDCl_3$) δ 0.77 (t, *J* = 6.8 Hz, 6 H), 1.11 (d, *J* = 7.2 Hz, 6 H), 1.13 (t, *J* = 7.2 Hz, 6 H), 1.35 (m, 8 H), 2.25 (m, 2 H), 2.64 (m, 2 H), 3.66 (d, *J* = 7.6 Hz, 1 H), 3.72 (d, *J* = 7.6 Hz, 1 H), 4.02 (q, *J* = 7.2 Hz, 4 H), 4.09 (m, 2 H), 7.24 (m, 6 H), 7.49 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 14.03 (q), 14.33 (q), 14.45 (q), 18.75 (t), 37.74 (t), 41.26 (d), 48.45 (d), 49.50 (d), 61.35 (t), 81.63 (d), 129.60 (d), 132.0 (s), 134.54 (d), 134.81 (d), 174.0 (s), 174.6 (s); IR ($CHCl_3$) (cm^{-1}) 2963, 2937, 2876, 1774, 1719, 1474, 1371, 1268, 1182, 1100, 1025; MS *m/z* (relative intensity) 336 $(M)^+$ (1), 169 (19), 123 (100), 77 (21).

Preparation of Methyl (2*R*,3*R*,4*S*)-[5-Oxo-4-(phenylthio)-2-[2-[(*tert*-butyldiphenylsilyl)oxy]ethyl]tetrahydrofuran-3-yl]acetate (35). The general cyclization procedure was used over **34** for 4 h, yielding **35** (95 mg, 95% yield): $[\alpha]^{25}_D$ +5.5° (*c* 2.01, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.04 (s, 9 H), 1.81 (m, 2 H), 2.43 (m, 1 H), 2.63 (d, *J* = 5.98 Hz, 2 H), 3.69 (s, 3 H), 3.75 (t, *J* = 6.10 Hz, 2 H), 3.82 (d, *J* = 10.2 Hz, 1 H), 4.47 (ddd, *J* = 8.7, 8.7, 3.13 Hz, 1 H), 7.31 (m, 3 H), 7.39 (m, 8 H), 7.60 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 19.17 (s), 26.87 (q), 34.44 (t), 37.21 (t), 43.38 (d), 51.21 (d), 51.90 (q), 59.72 (t), 79.22 (d), 127.75 (d), 128.84 (d), 129.23 (d), 129.77 (d), 133.41 (s), 134.15 (d), 134.82 (s), 135.50 (d), 171.03 (s), 173.55 (s); IR ($CHCl_3$) (cm^{-1}) 2954, 2931, 2858, 1771, 1736, 1361, 1215, 1112; MS *m/z* (relative intensity) 491 $(M - Bu\text{-}t)^+$ (10), 255 (100), 199 (81), 77 (35); HRMS calcd for $C_{27}H_{27}O_5SSi$ $(M - Bu\text{-}t)^+$ 491.1348, found 491.1344.

Preparation of Methyl (2*R*,3*R*,4*R*)-[4-Methyl-5-oxo-4-(phenylthio)-2-[2-[(*tert*-butyldiphenylsilyl)oxy]ethyl]tetrahydrofuran-3-yl]acetate (37). The general cyclization procedure was used over **36** for 4 h, yielding **37** (475 mg, 95% yield): $[\alpha]^{25}_D$ +46.1° (*c* 3.56, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.08 (s, 9 H), 1.44 (s, 3 H), 1.74 (m, 2 H), 2.54 (dd, *J* = 16.14, 5.94 Hz, 1 H), 2.73 (ddd, *J* = 6.31, 5.94, 5.94 Hz, 1 H), 2.95 (dd, *J* = 16.14, 6.31 Hz, 1 H), 3.76 (s, 3 H), 3.85 (t, *J* = 6.10 Hz, 2 H), 4.50 (ddd, *J* = 9.69, 9.69, 2.56 Hz, 1 H), 7.39 (m, 9 H), 7.60 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 19.21 (s), 22.34 (q), 26.93 (q), 31.18 (t), 36.38 (t), 49.52 (d), 52.01 (q), 55.12 (s), 60.10 (t), 78.05 (d), 127.33 (d), 128.97 (d), 129.72 (d), 130.05 (d), 133.57 (s), 135.51 (d), 137.40 (d), 171.63 (s), 174.64 (s); IR ($CHCl_3$) (cm^{-1}) 2954, 2931, 2858, 1766, 1737, 1379, 1292, 1112; MS *m/z* (relative intensity) 505 $(M - Bu\text{-}t)^+$ (78), 255 (100), 183 (24), 109 (17); HRMS calcd for $C_{28}H_{29}O_5SSi$ $(M - Bu\text{-}t)^+$ 505.1505, found 505.1508.

Preparation of Methyl (2*R*,3*R*,4*S*)-[5-Oxo-4-(phenylthio)-2-[4-(tetrahydropyran-2-yloxy)but-2(*E*)-enyl]tetrahydro-furan-3-yl]acetate (39). The general cyclization procedure was used over **38** for 4 h, yielding after flash chromatography **39** (95 mg, 95% yield): ^{1}H NMR ($CDCl_3$) δ 1.59 (m, 6 H), 2.39 (m, 3 H), 2.61 (d, *J* = 5.95 Hz, 2 H), 3.50 (m, 1 H), 3.70 (s, 3 H), 3.77 (d, *J* = 10.44 Hz, 1 H), 3.85 (m, 2 H), 4.16 (dd, *J* = 11.88, 4.45 Hz, 1 H), 4.59 (t, *J* = 3.33 Hz, 1 H), 5.60 (m, 1 H), 5.72 (m, 2 H), 7.34 (m, 3 H), 7.54 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 19.34 (t), 25.28 (t), 30.45 (t), 34.32 (t), 36.33 (t), 42.17 (d), 51.02 (q), 51.83 (d), 62.10 (t), 65.37 (t), 81.21 (d), 97.89 (d), 126.16 (d), 128.82 (d), 129.11 (d), 131.10 (d), 132.85 (s), 134.17 (d), 170.91 (s), 173.31 (s); IR ($CHCl_3$) (cm^{-1}) 2948, 2884, 1772, 1734, 1640, 1352, 1158, 1130, 1024; MS *m/z* (relative intensity) 336 $(M - C_5H_8O)^+$ (55), 318 (12), 287 (6), 205 (19), 149 (33), 85 (100); HRMS calcd for $C_{17}H_{20}O_5S$ $(M - C_5H_8O)^+$ 336.1031, found 336.1039.

Preparation of Methyl (2*R*,3*R*,4*S*)-[2-(4-Acetoxybut-2-(*E*)-enyl)-5-oxo-4-(phenylthio)tetrahydrofuran-3-yl]acetate (41). The general cyclization procedure was used over **40** for 4 h, yielding after chromatography **41** (95 mg, 95% yield): $[\alpha]^{25}_D$ + 5.4° (*c* 1.72, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 2.04 (s, 3 H), 2.38 (m, 3 H), 2.60 (d, *J* = 5.68 Hz, 2 H), 3.69 (s, 3 H), 3.72 (d, *J* = 10.26 Hz, 1 H), 4.23 (m, 1 H), 4.41 (d, *J* = 4.55 Hz, 2 H), 5.59 (m, 2 H), 7.33 (m, 3 H), 7.54 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 20.82 (q), 34.40 (t), 36.16 (t), 41.98 (d), 51.12 (q), 51.95 (d), 64.32 (t), 81.08 (d), 128.06 (d), 128.64 (d), 129.02 (d), 129.21 (d), 130.99 (s), 134.43 (d), 170.5 (s), 170.97 (s), 173.24 (s); IR ($CHCl_3$) (cm^{-1}) 2959, 1734, 1646, 1362, 1221, 1084; MS *m/z* (relative intensity) 378 $(M)^+$ (51), 347 (3), 318 (57), 149 (100), 109 (73); HRMS calcd for $C_{19}H_{22}O_6S$ $(M)^+$ 378.1137, found 378.1130.

Preparation of Methyl (2*R*,3*R*,4*S*)-[4-(Benzenesulfinyl)-5-oxo-2-propyltetrahydrofuran-3-yl]acetate (42). To a stirred solution of lactone **24** (100 mg, 0.325 mmol) in dry CH_2Cl_2 (3.25 mL) was added *m*-chloroperbenzoic acid (88 mg, 0.357 mmol) at 0 °C. The reaction was stirred for 1 h and was then quenched with potassium fluoride (37.7 mg, 0.65 mmol) and vigorously stirred for 0.5 h. The mixture was filtered through a pad of Celite and washed with ether (3 × 3 mL). The resulting solution was concentrated, and the crude was purified by flash chromatography to yield **42** (100.99 mg, 96% yield) as an isomeric mixture: ^{1}H NMR ($CDCl_3$) δ 0.69 (t, *J* = 6.98 Hz, 3 H), 0.86 (t, *J* = 7.18 Hz, 3 H), 1.12 (m, 2 H), 1.40 (m, 4 H), 1.62 (m, 2 H), 1.91 (dd, *J* = 17.02, 3.85 Hz, 2 H), 2.62 (d, *J* = 2.3 Hz, 2 H), 2.81 (m, 2 H), 3.49 (s, 3 H), 3.64 (s, 3 H), 3.89 (d, *J* = 7.98 Hz, 1 H), 4.05 (m, 1 H), 4.21 (m, 1 H), 4.31 (m, 1 H), 7.5 (m, 6 H), 7.59 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 13.58 (q), 18.53 (t), 35.18 (t), 36.53 (t), 38.25 (d), 52.06 (q), 67.68 (d), 82.40 (d), 129.12 (d), 129.64 (d), 134.59 (d), 136.86 (s), 166.73 (s), 170.95 (s); IR ($CHCl_3$) (cm^{-1}) 2961, 2936, 1765, 1736, 1444, 1362, 1086, 1052; MS *m/z* (relative intensity) 293 $(M - OCH_3)^+$ (6), 199 (100), 125 (89).

Preparation of Methyl (2*R*)-(5-Oxo-2-propyl-2,5-dihydrofuran-3-yl)acetate (43). A solution of the mixture of sulfoxides **42** (100 mg, 0.309 mmol) in dry toluene (3.09 mL, 0.1 M) was submitted to reflux (6−8 h). After that time, TLC showed that the starting material had disappeared. The solvent was then evaporated, and the obtained residue was purified by column chromatography yielding **43** (36.67 mg, 60% yield): $[\alpha]^{25}_D$ + 2.2° (*c* 2.78, $CHCl_3$), ^{1}H NMR ($CDCl_3$) δ 0.95 (t, *J* = 7.11 Hz, 3 H), 1.47 (m, 2 H), 1.84 (m, 2 H), 3.30 (dd, *J* = 17.25, 1.49 Hz, 1 H), 3.51 (d, *J* = 17.25 Hz, 1 H), 3.74 (s, 3 H), 5.07 (m, 1 H), 6.03 (d, *J* = 1.49 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 13.55 (q), 17.83 (t), 33.40 (t), 33.91 (t), 52.43 (q), 83.43 (d), 119.08 (d), 129.08 (s), 163.51 (s), 168.27 (s); IR ($CHCl_3$) (cm^{-1}) 3018, 2962, 1747, 1644, 1438, 1163; MS *m/z* (relative intensity) 199 $(M + 1)^+$ (65), 167 (11), 155 (26), 139 (20), 127 (100); HRMS calcd for $C_{10}H_{14}O_4$ $(M)^+$ 198.0892, found 198.0891.

Preparation of Methyl (2*R*,3*R*,4*R*)-[4-(Benzenesulfinyl)-4-methyl-5-oxo-2-propyltetrahydrofuran-3-yl]acetate (44). The procedure (used above to obtain **42**) was utilized to oxidize **27** on a (100 mg (0.311 mmol) scale for 1 h, yielding after purification **44** (100.77 mg, 96% yield) as an isomeric mixture: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, *J* = 7.16 Hz, 3 H), 0.89 (t, *J* = 7.16 Hz, 3 H), 1.21 (s, 3 H), 1.38 (m, 4 H), 1.42 (m, 4 H), 1.51 (s, 3 H), 2.33 (dd, *J* = 15.79, 8.72 Hz, 1 H), 2.86 (dd, *J* = 15.79, 4.25 Hz, 1 H), 2.89 (m, 2 H), 3.31 (m, 1 H), 3.48 (m, 1 H), 3.73 (s, 3 H), 3.77 (s, 3 H), 4.10 (m, 1 H), 4.50 (m, 1 H), 7.63 (m, 6 H), 7.98 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 13.62 (q), 14.37 (q), 18.32 (t), 33.17 (t), 35.52 (t), 40.70 (d), 52.12 (q), 69.85 (s), 82.27 (d), 128.83 (d), 131.37 (d), 134.60 (d), 134.70 (s), 166.73 (s), 170.96 (s); IR ($CHCl_3$) (cm^{-1}) 2934, 2876, 1774, 1738, 1310, 1218, 1085; MS *m/z* (relative intensity) 323 $(M - CH_3)^+$ (7), 213 (89), 181 (61); HRMS calcd for $C_{16}H_{19}O_5S$ $(M - CH_3)^+$ 323.0953, found 323.0956.

Preparation of Methyl (2*R*,3*R*)-(4-Methylene-5-oxo-2-propyltetrahydrofuran-3-yl)acetate (45). The pyrolysis (used above to obtain **43**) of the sulfoxides **44** on a 100 mg (0.296 mmol) scale for 8 h yielded after flash chromatography **45** (37.63 mg, 60% yield): $[\alpha]^{25}_D$ +13.7° (*c* 2.39, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.93 (t, *J* = 6.99 Hz, 3 H), 1.44 (m, 2 H), 1.65 (m, 2 H), 2.58 (d, *J* = 6.92 Hz, 2 H), 3.10 (m, 1 H), 3.70 (s, 3

H), 4.22 (m, 1 H), 5.63 (d, J = 2.49 Hz, 1 H), 6.27 (d, J = 2.49 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 13.65 (q), 18.24 (t), 37.71 (t), 38.23 (t), 40.83 (d), 51.84 (q), 82.57 (d), 122.79 (t), 138.29 (s), 169.38 (s), 171.17 (s); IR ($CHCl_3$) (cm^{-1}) 2934, 2874, 1746, 1738, 1640, 1124, 972; MS m/z (relative intensity) 212 $(M)^+$ (2), 180 (28), 169 (65), 141 (68); HRMS calcd for $C_{11}H_{16}O_4$ $(M)^+$ 212.1048, found 212.1033.

General RuO_4 Oxidation of Sulfides to Sulfones. Preparation of Methyl (2*R*,3*R*,4*S*)-[4-(Benzenesulfonyl)-5-oxo-2-propyltetrahydrofuran-3-yl]acetate (46). To a stirred solution of lactone **24** (100 mg, 0.325 mmol) in a biphasic solvent system (0.33 mL of CH_3CN–0.33 mL of CCl_4–0.5 mL of H_2O/mmol of compound) was added periodic acid as the stoichiometric oxidant (155.4 mg, 0.682 mmol) and $RuCl_3xH_2O$ (1.35 mg, 0.0065 mmol) at rt. The reaction mixture was vigorously stirred for 2 h, and then ether (3 mL) was added and the stirring was continued for 10 min. After that time $MgSO_4$ was added and the mixture was filtered through Whatman paper no. 2 and washed with ether (3 × 3 mL). The combined organic phases were concentrated, and the residue obtained was purified by flash chromatography to yield **46** (100.45 mg, 91% yield) as a white solid: mp 80–82 °C; $[\alpha]^{25}_D$ +8.2° (*c* 1.75, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.91 (t, J = 7.16 Hz, 3 H), 1.43 (m, 2 H), 1.65 (m, 2 H), 2.72 (dd, J = 16.86, 4.75 Hz, 1 H), 2.86 (dd, J = 16.86, 5.77 Hz, 1 H), 3.07 (m, 1 H), 3.70 (s, 3 H), 4.24 (m, 1 H), 4.39 (d, J = 8.26 Hz, 1 H), 7.65 (m, 3 H), 7.98 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 13.53 (q), 16.46 (t), 35.16 (t), 36.46 (t), 38.22 (d), 51.99 (q), 67.65 (d), 82.41 (d), 129.08 (d), 129.55 (d), 134.55 (d), 136.77 (s), 166.72 (s), 170.93 (s); IR ($CHCl_3$) (cm^{-1}) 2944, 2935, 2875, 1774, 1733, 1323, 1220, 1150; MS m/z (relative intensity) 341 $(M + 1)^+$ (49), 309 (20), 199 (43), 77 (100); HRMS calcd for $C_{16}H_{21}O_6S$ $(M + 1)^+$ 341.1059, found 341.1041. Anal. Calcd for $C_{16}H_{20}O_6S$: C, 56.45; H, 5.93. Found: C, 56.29; H, 5.92.

Preparation of Methyl (2*R*,3*R*)-(5-Oxo-2-propyltetrahydrofuran-3-yl)acetate (47). To a stirred solution of sulfone **46** (100 mg, 0.294 mmol) in a biphasic solvent system THF/H_2O, 20:1 (1.61 mL/84 μL) was added excess of amalgamated aluminum (aluminum paper was shaken in a 2% $HgCl_2$ aqueous solution, washed with ethanol and ether, and cut into thin strips). The heterogenous mixed was vigorously stirred for 4 h, until TLC showed complete conversion. The mixture was diluted in ether (6 mL), filtered through a pad of Celite, and washed with ether (3 × 3 mL). The resulting solution was concentrated and the obtained crude was purified by flash chromatography to yield **47** (45.88 mg, 78% yield): $[\alpha]^{25}_D$ +21.5° (*c* 0.92, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.79 (t, J = 7.0 Hz, 3 H), 1.45 (m, 4 H), 2.16 (dd, J = 17.06, 7.0 Hz, 1 H), 2.37 (m, 3 H), 2.64 (dd, J = 17.06, 7.81 Hz, 1 H), 3.53 (s, 3 H), 4.03 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 13.57 (q), 18.61 (t), 34.55 (t), 36.31 (t), 36.79 (t), 37.02 (d), 51.57 (q), 84.39 (d), 171.36 (s), 175.39 (s); IR ($CHCl_3$) (cm^{-1}) 2961, 2935, 2876, 1768, 1730, 1438, 1180; MS m/z (relative intensity) 169 $(M - OCH_3)^+$ (12), 157 (68), 140 (8), 127 (48); HRMS calcd for $C_9H_{13}O_3$ $(M - OCH_3)^+$ 169.0865, found 169.0865.

Preparation of Methyl (2*R*,3*R*,4*R*)-[4-(Benzenesulfonyl)-4-methyl-5-oxo-2-propyltetrahydrofuran-3-yl]acetate (48). The procedure (used above to obtain **46**) was utilized to oxidize **27** on a 100 mg (0.311 mmol) scale for 2 h, yielding **48** (100.04 mg, 91% yield): $[\alpha]^{25}_D$ +66.7° (*c* 0.54, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.96 (t, J = 6.7 Hz, 3 H), 1.54 (s, 3 H), 1.55 (m, 4 H), 2.76 (dd, J = 17.04, 5.84 Hz, 1 H), 2.89 (ddd, J = 7.9, 5.94, 5.94 Hz, 1 H), 3.5 (dd, J = 17.04, 7.9 Hz, 1 H), 3.77 (s, 3 H), 4.72 (m, 1 H), 7.56 (m, 3 H), 7.78 (m, 2 H); ^{1}H NMR (C_6D_6) δ 0.73 (t, J = 6.92 Hz, 3 H), 1.18 (m, 4 H), 1.52 (s, 3 H), 2.43 (dd, J = 17.5, 5.42 Hz, 1 H), 2.73 (ddd, J = 9.15, 5.2, 5.2 Hz, 1 H), 3.44 (s, 3 H), 3.62 (dd, J = 17.5, 9.15 Hz, 1 H), 4.67 (ddd, J = 9.6, 9.6, 2.3 Hz, 1 H), 6.89 (m, 3 H), 7.74 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 13.71 (q), 18.92 (t), 20.57 (q), 31.31 (t), 35.79 (t), 48.48 (d), 52.01 (q), 70.59 (q), 82.71 (d), 128.57 (d), 130.60 (d), 134.86 (d), 135.45 (s), 171.14 (s), 171.63 (s); IR ($CHCl_3$) (cm^{-1}) 2959, 2876, 1769, 1736, 1383, 1310, 1148; MS m/z (relative intensity) 354 $(M)^+$ (2), 323 (23), 213 (100), 181 (67); HRMS calcd for $C_{17}H_{22}O_6S$ $(M)^+$ 354.1137, found 354.1139.

Preparation of Methyl (2*R*,3*R*,4*R*)-(4-Methyl-5-oxo-2-propyltetrahydrofuran-3-yl)acetate (49). The procedure (used above to obtain **47**) was utilized to reduce **48** on a 100 mg (0.282 mmol) scale with amalgamated aluminum for 4 h at rt, yielding **49** (47.15 mg, 78% yield): $[\alpha]^{25}_D$ +21.2° (*c* 2.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.93 (t, J = 6.98 Hz, 3 H), 1.25 (d, J = 5.83 Hz, 3 H), 1.59 (m, 4 H), 2.20 (m, 1 H), 2.35 (m, 1 H), 2.65 (d, J = 7.66 Hz, 2 H), 3.70 (s, 3 H), 4.08 (ddd, J = 8.23, 8.23, 3.12 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 13.72 (q), 14.14 (q), 18.92 (t), 35.65 (t), 36.14 (t), 41.24 (d), 45.56 (d), 51.80 (q), 82.49 (d), 171.39 (s), 177.95 (s); IR ($CHCl_3$) (cm^{-1}) 2962, 1767, 1737, 1439, 1181, 908; MS m/z (relative intensity) 214 $(M)^+$ (4), 186 (16), 183 (25), 171 (89), 141 (90); HRMS calcd for $C_{11}H_{18}O_4$ $(M)^+$ 214.1205, found 214.1195.

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Supplementary Material Available: Full geometries and energies of the transition states of Table 5 and copies of ^{13}C NMR spectra for the new compounds (49 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.