Enantioselective Preparation of β-Alkyl-γ-butyrolactones from Functionalized Ketene Dithioacetals

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Received September 14, 1992 (Revised Manuscript Received February 8, 1993)

An efficient and general enantioselective synthesis of β-alkyl-γ-butyrolactones has been developed. The key step of this procedure is an oxazolidinone-directed alkylation of a lithiated ketene dithioacetal that proceeds with excellent regiochemical control and high diastereofacial selectivity. Reductive removal of the chiral auxiliary followed by acid-induced cyclization of the resultant hydroxy ketene dithioacetal gives the enantiomerically pure β-alkyl-γ-butyrolactone.

Introduction

Stereochemically defined γ-butyrolactones have played a key role in the synthesis of many types of natural products, serving as building blocks for alkaloids,[1] macrocyclic antibiotics,[2] lignan lactones,[3] pheromones,[4] antileukemics,[5] and flavor components.[6,7] Accordingly, there are a large number of methods for the enantioselective preparation of substituted γ-butyrolactones: from simple natural products such as amino acids, tartaric acid, ascorbic acids, carbohydrates, or ribonolactones;[8–10] from chiral sulfoxides, epoxides, or substituted acetylenic acids;[11] and by various enzymatic or synthetic reductions, oxidations, and hydrolyses.[12]

Additionally, the pharmacology of substituted γ-butyrolactones[13] is notable because they are potent antagonists or agonists—depending upon the substitution pattern—of the γ-aminobutyric acid (GABA) receptor, the major inhibitory neurotransmitter receptor in the mammalian central nervous system. The antagonist activity of β-substituted γ-butyrolactones 1 has led, in part, to the proposal

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that the pharmacophore of the convulsant drug picrotoxinin (2, Figure 1)[14] is the relatively simple bridged β-isopropenyl-γ-butyrolactone substructure 3 that is imbedded in the tetracyclic natural product.[15]

There are relatively few procedures for obtaining enantioselectively pure β-alkyl-γ-butyrolactones, and the neurological activity at the GABA receptor of the individual enantiomers of such derivatives has not been examined.[16] The synthetic methods that have been

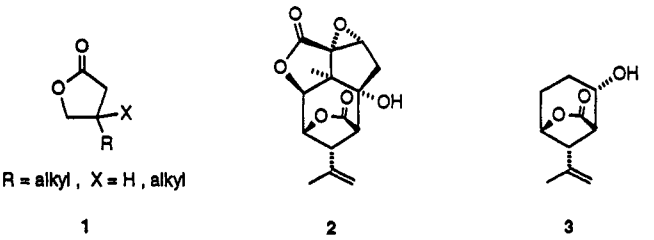
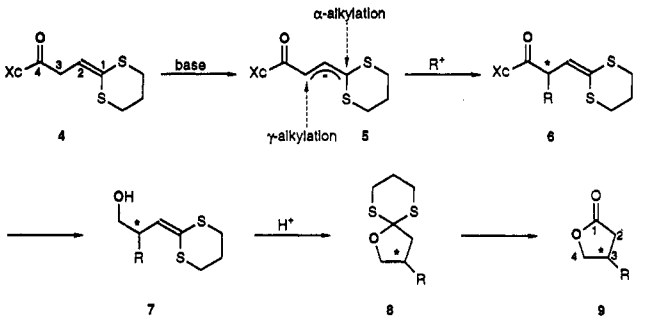


Figure 1. GABA receptor antagonist, 1; picrotoxinin, 2; proposed pharmacophore, 3.

Scheme I. Synthetic Outline for β-Substituted γ-Butyrolactones



reported, each of which relies on nucleophilic addition to stable electrophilic species, include addition to sulfoxide derivatives developed by Posner[17] and by Hua,[18] and Michael addition to oxazepinediones reported by Mukaiyama.[19] For some time we have been interested in the stereoselective synthesis of substituted γ-butyrolactones as intermediates for natural products synthesis,[2a,20] and as part of that effort we have developed a new and general enantioselective route to β-alkyl-substituted γ-butyrolactones that is complementary to the existing methods.

The basis of this new procedure (Scheme I) is the alkylation of an acyclic ketene dithioacetal anion (5, which is also a γ-extended enolate) containing all of the elements of the incipient lactone ring in latent form. The choice of a specific directing group was dictated by the tremendous success of the oxazolidinone chemistry developed by the Evans group, for which the stereochemical sense of

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(13) In this paper, in accord with the historical name for a five-membered lactone (γ-butyrolactone), the positions of substituents on the carbon centers of the lactone ring are designated as α-, β-, and γ- starting with the carbon adjacent to the carbonyl functionality. Note that the designators α- and β- do not imply stereochemistry. Relative stereochemical designations of *trans* and *cis* are used to relate substituents on the ring. Absolute stereochemical designators (*R*)- and (*S*)- are also used for specific stereogenic centers on the ring.

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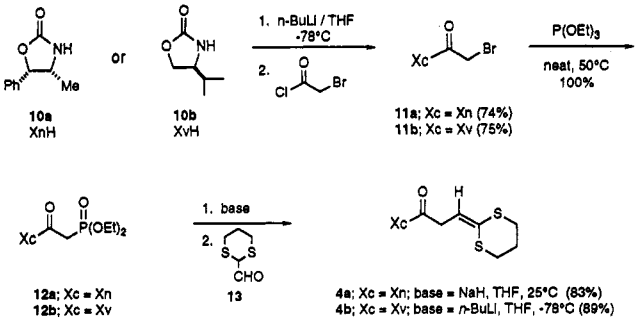
Scheme II. Synthesis of *N*-Acyloxazolidinone Ketene Dithioacetal

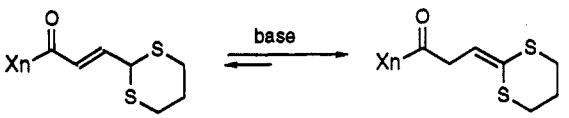


induction can be confidently predicted.[21] Conversely, the regioselectivity expected for this alkylation was not immediately obvious, since γ-extended enolates undergo α-alkylation but ketene dithioacetal-derived allylic anions can give either α- or γ-alkylation products, as discussed in more detail below.[22] If γ-alkylation of **5** were to occur (relative to the dithianyl group), reductive removal of the chiral auxiliary in **6** to give the hydroxy ketene dithioacetal **7** and acid-induced cyclization via the sulfur-stabilized cation[23] would give the 1,3-dithiane-protected lactone **8**, and subsequent hydrolysis of the dithioacetal would then produce the enantiomerically pure β-alkyl-γ-butyrolactone **9**.

Results and Discussion

The acyclic substrate **4** required for the alkylation was obtained by olefination of an acylated chiral auxiliary and a ketene dithioacetal equivalent (Scheme II). Thus, the oxazolidinones (**10a**, XnH or **10b**, XvH), derived from the optically pure amino alcohols, (1*S*,2*R*)-norephedrine and (*S*)-valinol, were deprotonated (n-BuLi/−78 °C) and then N-acylated by treatment with bromoacetyl chloride to give the α-bromo carboximide **11** in 75% yield.[24] (Each of the acylated oxazolidinones was successfully converted into the alkylation precursor; therefore subsequent text and schemes indicate this by the use of a generic abbreviaton (Xc) for both oxazolidinone derivatives.) The requisite Horner–Emmons precursor **12** was made via an Arbuzov reaction of the α-bromo carboximide **11** with neat triethyl phosphite at 50 °C to give the phosphonate ester **12** in quantitative yield, which was deprotonated with NaH at room temperature or alternatively, with n-butyllithium at −78 °C. Horner–Emmons coupling of the resultant phosphonate anion[25] with 2-formyl-1,3-dithiane (**13**, conveniently prepared and stored as the solid aldol dimer, which is cracked by vacuum distillation to give the liquid monomer[22c]) yielded exclusively the deconjugated carboximide ketene dithioacetal **4**, which was somewhat sensitive to acid but could be readily purified by silica gel chromatography in 85–90% yield.

The deconjugated isomer **4** is presumably formed under these reaction conditions via base-catalyzed isomerization of the initially formed Horner–Emmons product **14**. Consistent with this assumption, mixtures of the two isomers **4** and **14** are produced under the less basic conditions of a corresponding Wittig coupling reaction (a phosphorane corresponding to **12** was the substrate for the Wittig olefination). Furthermore, **14**, which can be separated from the Wittig product mixture, equilibrates completely to **4** when treated with base.



14 **4a**

As an interesting aside, when the usual basic workup of the acylation reaction is avoided (as was done to prevent possible base-induced hydrolysis of the resultant labile α-bromo N-acylated oxazolidinone) none of the desired acylated oxazolidinone product **11a** is isolated. Instead, an isomeric, enantiomerically pure oxazolidinone with a very different ^{1}H NMR spectrum is produced in high yield. Most significantly, the methyl doublet is shifted downfield dramatically (1.59 ppm in the isomer vs 0.94 ppm in **11a**). These observations are consistent with an acid-catalyzed epimerization of the phenyl substituent during this nonbasic workup, as shown in Scheme III. This epimerization is easily avoided, however, by employing low temperature, mildly basic workup conditions (−78 °C, aqueous $NaHCO_3$) under which the α-bromo N-acylated carboximide is stable.

With the enantiomerically pure carboximide ketene dithioacetal thus prepared, the alkylation of the lithiated ketene dithioacetal **5** could be investigated. Deprotonation of the carboximide ketene dithioacetal, **4a** or **4b**, with LDA generated an allylic enolate/allylic ketene dithioacetal anion, potentially capable of alkylating at either the α- or γ-carbon (position relative to the dithioacetal, Scheme I). As mentioned above, the regioselectivity of this process could not be predicted solely based on the reactivity pattern of extended enolates (which alkylate at the enolate α-position) or the alkylation of ketene dithioacetal allylic anions, since **5** contains both of these functionalities. Substituted ketene dithioacetal allylic anions have been reported to alkylate with either α- or γ-regioselectivity depending on the structure of the substrate, the counterion, the electrophile, and the ionic composition of the solution.[26-29] For example, the lithium anion of γ-phenyl ketene dithioacetal **15** gives exclusively α-alkylation prod-

(21) For a review, see (a) Evans, D. A. *Aldrichim. Acta* **1982**, *15*, 23. (b) Evans, D. A. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1984; Vol. 3, Chapter 1.

(22) For a review, see (a) Kolb, M. *Synthesis* **1990**, 171. Also, (b) Seebach, D.; Gröbel, B.-Th.; Braun, M.; Geiss, K.-H.; Beck, A. K. *Angew. Chem. Int. Ed. Engl.* **1972**, *11*, 443. (c) Meyers, A. I.; Strickland, R. C. *J. Org. Chem.* **1972**, *37*, 2579.

(23) Corey, E. J.; Beames, D. J. *J. Am. Chem. Soc.* **1973**, *95*, 5829.

(24) (a) Evans, D. A.; Mathre, D. J.; Scott, W. L. *J. Org. Chem.* **1985**, *50*, 1830. (b) Evans, D. A.; Bartroli, J.; Shih, T. L. *J. Am. Chem. Soc.* **1981**, *103*, 2129. The following conventions are used to designate the oxazolidinone auxiliaries: Xn represents the norephedrine-derived auxiliary, Xv represents the valinol-derived auxiliary, and Xc is a generic designation for both auxiliaries.

(25) A related phosphonate has been reported previously: Broka, C. A.; Ehrler, J. *Tetrahedron Lett.* **1991**, 5907.

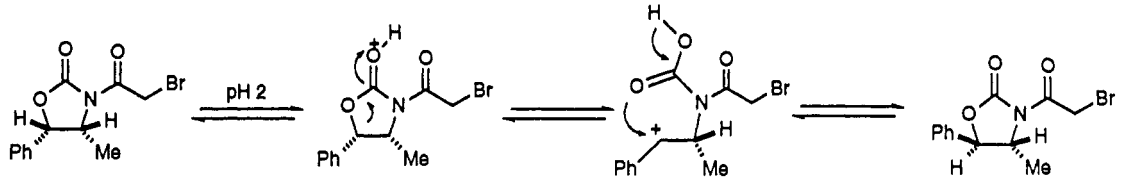
(26) See ref 22 and (a) Hünig, S.; Reichelt, H. *Chem. Ber.* **1986**, *119*, 1772. (b) Biellmann, J. F.; Ducep, J.-B. *Org. React.* **1982**, *27*, 1. (c) Murphy, W. S.; Wattanasin, S. *J. Chem. Soc., Perkin Trans. I* **1980**, 2678. (d) Ahlbrecht, H. *Chimia* **1977**, *31*, 391.

(27) (a) Fallis, A. G.; Bo, L. *Tetrahedron Lett.* **1986**, 5193. (b) Ziegler, F. E.; Tam, C. C. *J. Org. Chem.* **1979**, *44*, 3428.

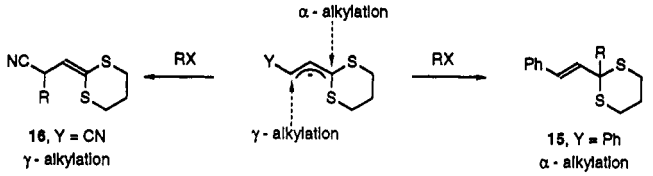
(28) (a) Dziadulewicz, E.; Hodgson, D.; Gallagher, T. *J. Chem. Soc. Perkin Trans. I* **1988**, 3367. (b) Dziadulewicz, E.; Gallagher, T. *Tetrahedron Lett.* **1985** *26*, 4547.

(29) Fang, J.-M.; Chen, M.-Y. *Tetrahedron Lett.* **1988**, 5939.

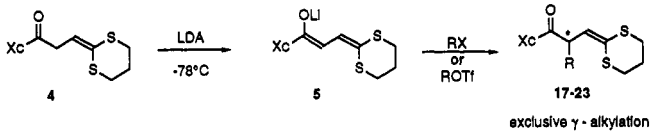
Scheme III. Acid-Catalyzed Epimerization of Norephedrine Oxazolidinone



Scheme IV. Alkylation Patterns for Other Ketene Dithioacetals



Scheme V. Regioselective and Stereoselective Alkylation



ucts;[30] however, the γ-cyano ketene dithioacetal **16** akylates exclusively at the γ-center (Scheme IV).[22c] As a reasonable extrapolation from this γ-cyano ketene dithioacetal alkylation, we anticipated that the lithiated carboximide ketene dithioacetal **5** would likely alkylate at the γ-site, a prediction that was borne out by experiment.

In practice, alkylation of the acyclic allylic ketene dithioacetal anion **5** did occur exclusively at the γ-position, and with a high diastereofacial bias, under standard lithium enolate alkylation conditions (LDA, THF, −78 °C; Scheme V). A variety of electrophiles reacted with the allylic enolate in this regio- and stereoselective manner (Table I). The proportion of the major diastereomeric product was readily determined by inspection of the ^{1}H NMR spectrum of the crude reaction mixture; subsequently, the major product was conveniently chromatographed or recrystallized to >99% diastereomeric excess. For the alkylations, typical reactive electrophiles (primary, allylic, benzylic, Table I, entries i–v) work quite well to give diastereomeric ratios (7:1 to 40:1) of products in accord with literature precedent[21,31] and purified diastereomers in 60–80% yield. The alkylated carboximide ketene dithioacetals **17–23**, like the alkylation precursors, were somewhat prone to hydrolysis and were sensitive to acidic environments. Thus, the alkylated products were stored as cold, dilute solutions in benzene and concentrated in the presence of potassium carbonate to prevent the hydrolysis of the ketene dithioacetal.[32]

Less reactive electrophiles were expected to present a problem in view of the documented failure of even β-branched primary halides to react satisfactorily with oxazolidinone carboximide-derived enolates.[33] We therefore tested trifluoromethanesulfonic esters (triflates; Table I) as electrophilic alkylation reagents[34] and found that the lithiated ketene dithioacetal **5** is efficiently alkylated with n-propyl triflate (entry vi), and even secondary electrophiles such as isopropyl triflate (entries vii and viii) and cyclohexyl triflate (entry ix) react satisfactorily. The alkyl triflates are easily generated from the corresponding alcohols by treatment with trifluoromethanesulfonic anhydride and pyridine, and after a simple decantation and partial concentration of the carbon tetrachloride solution are utilized in the alkylation reaction to give moderate yields (37–76%) of the alkyl ketene dithioacetal products **21–23**. Employing triflates as electrophiles in enolate alkylation reactions has received limited attention, but for the alkylation of these relatively unreactive ketene dithioacetal anions the triflate electrophiles were very successful and especially advantageous for alkylation with secondary electrophiles.[35] In fact, in the alkylations reported here, since even primary iodides react somewhat sluggishly, the corresponding triflates are preferred.

These alkylations provide the cyclization precursors of the target β-alkyl-γ-butyrolactones. The enantiomerically pure α-alkylated *N*-acyloxazolidinone ketene dithioacetal acyclic intermediates **17–23** were transformed in two steps to the β-alkyl-γ-butyrolactones (Scheme VI, Table I). First, reductive removal of the oxazolidinone chiral auxiliary by lithium aluminum hydride at 0 °C gave the primary hydroxy ketene dithioacetals **24–28** in 85–95% yield.[31] Subsequently, treatment of this intermediate with aqueous acid readily effected cyclization[22a,39d] and concomitant hydrolysis of the thioacetal, to give the enantiomerically pure β-alkyl-γ-butyrolactone in ~90% yield. Alternatively, the bicyclic dithioacetal orthoester (**29**, **30**) was isolated (95%) by treatment of the hydroxy ketene dithioacetal with anhydrous trifluoroacetic acid, which affected cationic cyclization without hydrolysis of the thioacetal. The dithioacetal-protected lactone was hydrolyzed in 91% yield by treatment with mercuric chloride to give the γ-butyrolactone.[23] The enantiomeric purity of each product was assessed by comparison of optical rotations with published values and by ^{1}H NMR chemical shift analysis in the presence of a chiral shift reagent.[36]

(30) (a) Seebach, D.; Kolb, M. *Justus Liebigs Ann. Chem.* **1977**, 811. (b) Corey, E. J.; Kozikowski, A. P. *Tetrahedron Lett.* **1975**, 925. (c) Seebach, D.; Kolb, M.; Gröbel, B.-Th. *Angew. Chem. Int. Ed. Engl.* **1973**, *12*, 69.

(31) Evans, D. A.; Ennis, M. D.; Mathre, D. J. *J. Am. Chem. Soc.* **1982**, *104*, 1737.

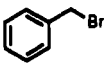
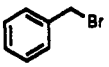
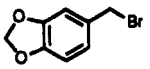
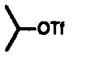
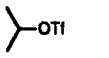
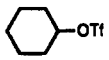
(32) For a discussion of the qualitative and mechanistic details of ketene dithioacetal hydrolysis, see: (a) Okuyama, T. and Fueno, T. *J. Org. Chem.* **1987**, *52*, 1405. (b) Okuyama, T. *Acc. Chem. Res.* **1986**, *19*, 370. (c) Kresge, A.; Straub, T. S. *J. Am. Chem. Soc.* **1983**, *105*, 3957. (d) Okuyama, T.; Kawao, S.; Fueno, T. *J. Org. Chem.* **1981**, *46*, 4372. (e) Okuyama, T.; Fueno, T. *J. Am. Chem. Soc.* **1980**, *102*, 6590. (f) Kankaanpera, A.; Aaltonen, R. *Acta. Chem. Scand.* **1972**, *26*, 1698. (g) Gold, V.; Waterman, D. C. A. *J. Chem. Soc. Sec. B* **1968**, *839*, 849.

(33) Evans, D. A.; Dow, R. L.; Shih, T. L.; Takacs, J. M.; Zahler, R. *J. Am. Chem. Soc.* **1990**, *112*, 5290, and refs therein.

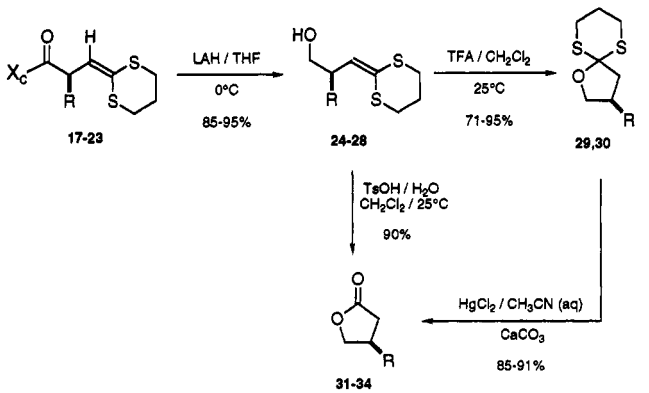
(34) (a) Stang, P. J.; Hanack, M.; Subramanian, C. R. *Synthesis* **1982**, 85. (b) Beard, C. D.; Baum, K.; Grakuakas, V. *J. Org. Chem.* **1973**, *38*, 3673.

(35) For examples of triflates as alkylation reagents, see: (a) Petit, Y.; Sanner, C.; Larchevêque, M. *Tetrahedron Lett.* **1990**, 2149. (b) Phillion, D. P.; Andrew, S. S. *Tetrahedron Lett.* **1986**, 1477. (c) Ikegami, S.; Hayama, T.; Katsuki, T.; Yamaguchi, M. *Tetrahedron Lett.* **1986**, 3403. (d) Masamune, S.; Ma, P.; Okumoto, H.; Ellingboe, J. W.; Ito, Y. *J. Org. Chem.* **1984**, *49*, 2837.

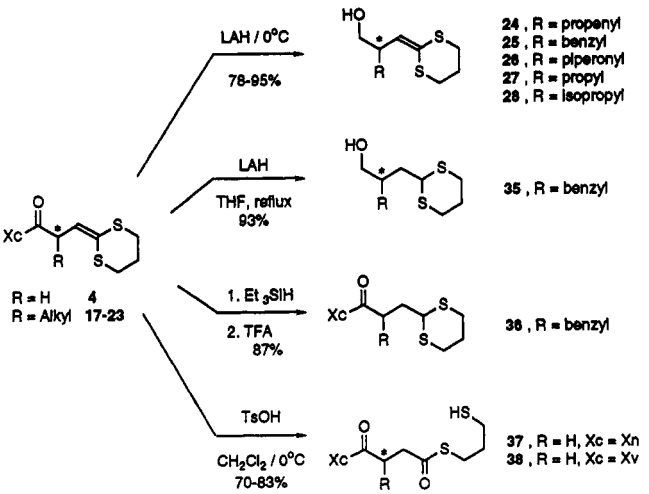
Table I. Stereoselective Alkylation of Lithiated Ketene Dithioacetal and β-Alkyl-γ-butyrolactones

entry		E^+	alkylation product R	alkylation product ratio of diastereomers (yield of major product)	β-alkyl-γ-butyrolactone configuration	β-alkyl-γ-butyrolactone % ee
i	$X_c = X_n$	CH_3I	methyl	7:1 (**17a**, 78)	–	–
ii	$X_c = X_n$		allyl	22:1 (**18a**, 57)	–	–
iii	$X_c = X_n$		benzyl	24:1 (**19a**, 67)	*R*	**31a**, >99
iv	$X_c = X_v$		benzyl	25:1 (**19b**, 60)	*S*	**31b**, >99
v	$X_c = X_n$		piperonyl	40:1 (**20a**, 60)	*R*	**32a**, 94
vi	$X_c = X_n$		n-propyl	16:1 (**21a**, 64)	*R*	**33a**, >99
vii	$X_c = X_n$		isopropyl	24:1 (**22a**, 58)	*S*	**34a**, >99
viii	$X_c = X_v$		isopropyl	24:1 (**22b**, 76)	*R*	**34b**, >99
ix	$X_c = X_n$		cyclohexyl	46:1 (**23a**, 37)	–	–

Scheme VI. Cyclization of Acyclic Substrate



Scheme VII. Ketene Dithioacetal Transformations



The butyrolactones are from 94 to >99% enantiomerically pure by these criteria.

Some of the intermediates in this route are also useful precursors of other derivatives. For example, the carboximide ketene dithioacetals (**4**, **17–23**) can be converted into 1,4-dicarbonyl derivatives (Scheme VII). For example, the ketene dithioacetals undergo hydrolysis with aqueous acid to give the carboximide thioesters **37** and **38**, differentially protected 1,4-diesters; in fact, as mentioned earlier, this hydrolysis is often difficult to avoid. Additionally, the carboximide and/or the ketene dithioacetal functionality could be selectively reduced depending on the choice of reagents. As described above, treatment of **17–23** with a solution of LAH in THF at 0 °C gave, by reduction of the oxazolidinone auxiliary, the hydroxy ketene dithioacetal γ-butyrolactone precursor. On the other hand, exposure of **19** to LAH in refluxing THF gave the fully reduced hydroxy dithiane **35**,[37] a differentially protected 1,4-bisaldehyde equivalent. The ketene dithioacetal could also be selectively reduced by treatment first with triethylsilane, followed by protonation with trifluoroacetic acid to give the carboximide dithioacetal **36**,[38] a four-carbon carboxylate/protected aldehyde component.

As an approach to disubstituted γ-butyrolactones, the carboximide ketene dithioacetal anion **5** could also be condensed with aldehyde electrophiles. The boron enolate was generated from **4**, and this anion showed very high γ-regioselectivity in the condensation with aldehydes (Scheme VIII). This regioselectivity is in accord with results from Fang's group which have reported that unsymmetrical ketene dithioacetal anions react with aldehydes and ketones to give γ-adducts.[39]

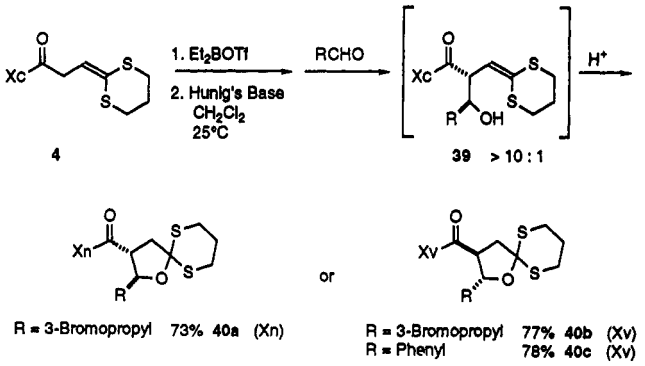
(36) (a) See ref 19; (b) Jones, J. B.; Jakovac, I. J. *J. Org. Chem.* **1979**, *44*, 2165.

(37) (a) Wong, M. Y. H.; Gray, G. R. *J. Am. Chem. Soc.* **1978**, *100*, 3548. (b) Wong, M. Y. H.; Gray, G. R. *Tetrahedron Lett.* **1977**, 1617.

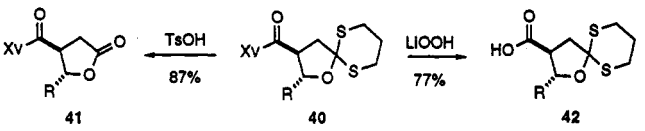
(38) (a) Carey, F. A.; Neergaard, J. R. *J. Org. Chem.* **1971**, *36*, 2731. (b) Carey, F. A.; Court, A. S. *J. Org. Chem.* **1972**, *37*, 1926. (c) Ceruti, M.; Degani, I.; Fochi, R. *Synthesis* **1987**, 79.

(39) (a) Fang, J.-M.; Chen, M.-Y.; Yang, W.-J. *Tetrahedron Lett.* **1988**, 5937. (b) Fang, J.-M.; Hong, B.-C.; Liao, L. F. *J. Org. Chem.* **1987**, *52*, 855. (c) Fang, J.-M.; Hong, B.-C. *J. Org. Chem.* **1987**, *52*, 3162. (d) Kozikowski, A. P.; Chen, Y.-Y. *J. Org. Chem.* **1980**, *45*, 2236.

Scheme VIII. Stereoselective Aldol Condensations of Ketene Dithioacetal Anion



Scheme IX. Bisfunctionalized Butyrolactones



Boron enolates are the standard substrates for enantioselective aldol condensations, and these can be prepared by reaction of dialkylboryl triflate and excess Hunig's base with the enolizable carbonyl substrate.[40] The necessary boryl triflate reagents are usually generated by reaction of a trialkylborane with trifluoromethane sulfonic anhydride.[19a,24b] The carboximide ketene dithioacetals, substrates for the aldol condensations, were rather sensitive to these typical conditions and tended to decompose on extended exposure to the boryl triflate reagent. Thus, a modified procedure for the generation of boron enolates, detailed by Oppolzer's group, was employed. The diethylboryl triflate was prepared in situ,[40a] and this allowed aldol adduct formation to be maintained at 70–80%. The initial aldol product **39** was not routinely isolated, but rather under slightly acidic workup conditions (pH 4 phosphate buffer) underwent a facile, electrophilic cyclization to give the β,γ-bisfunctionalized dithioacetal protected γ-butyrolactone **40**. ^{1}H NMR showed a >10:1 diastereomeric ratio of the trans-substituted lactones, the erythro products expected from the Evans' oxazolidinone-mediated aldol condensation.

The bis-substituted γ-butyrolactone obtained by this aldol sequence was selectively transformed to give a variety of lactones (Scheme IX). For example, the oxazolidinone auxiliary was hydrolyzed with lithium hydroperoxide[41] to give the dithioacetal-protected lactone acid **42**, or the dithioacetal was readily hydrolyzed with aqueous acid to give the acylated lactone **41**.

The procedures detailed here result in an efficient and general enantioselective synthesis of β-alkyl-γ-butyrolactones. The alkylation sequence proceeds with excellent regiochemical control and generally high diastereofacial selectivity. Subsequent cyclization of the ketene dithioacetal functionality efficiently generates protected or unprotected forms of various γ-butyrolactone ring systems. The γ-butyrolactones thus synthesized will serve as picrotoxinin analogues and will be assayed for convulsant activity at the GABA receptor.[42]

Several other useful transformations of some of the γ-butyrolactone intermediates are also possible. For instance, selective aldol condensation of the boron enolate of the ketene dithioacetal gave disubstituted γ-butyrolactones that could be converted into functionalized γ-butyrolactone acids. Finally, regioselective reduction and hydrolysis of the alkylated carboximide ketene dithioacetal produced four acyclic, differentially 1,4-bisfunctionalized chiral synthetic building blocks: a hydroxy ketene dithioacetal, a hydroxy thioacetal, a carboximide thioester, and a carboximide thioacetal, that could be valuable as intermediate substructures for complex organic syntheses.

Experimental Section

General Experimental. Proton and carbon nuclear magnetic resonance spectra (^{1}H NMR and ^{13}C NMR) were obtained on a Bruker WM 250, a General Electric GE 300, a GN 500, or an Omega 500 spectrometer using the solvent indicated. Proton chemical shifts are reported in parts per million (ppm) relative to chloroform ($CDCl_3$, 7.27 ppm) or other indicated solvent. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant (Hz), and integration. Carbon chemical shifts are reported in parts per million relative to chloroform (77.0 ppm) or other indicated solvent. Infrared spectra (IR) were recorded on a Perkin-Elmer 283 spectrophotometer or a Nicolet 5-DXB FT/IR spectrophotometer. IR peaks are reported in cm^{-1} with the following relative intensities: s (strong, 67–100%), m (medium, 34–66%), w (weak, 7–33%). Low-resolution mass spectra (LRMS), electron impact (EI) and chemical ionization (CI), were recorded on a Finnigan 4000 spectrometer. High-resolution mass spectra (HRMS) and fast atom bombardment mass spectra (FAB) were recorded on a Vacuum Generators 7070E-HF double sector spectrometer. Gas chromatography was performed on a Hewlett-Packard 5830A capillary gas chromatograph equipped with a cross-linked 5% phenyl methyl silicon capillary column (12 m) and an FID detector, using Helium carrier gas (flow rate 25 mL/min). Melting points were taken on a Laboratory Devices melting point apparatus and are reported uncorrected. Combustion analyses were performed by Galbraith Laboratories, Inc. (Knoxville, TN) or Desert Analytics (Tucson, AZ). Optical rotations were measured with a Perkin-Elmer 241 MC polarimeter or a Jazso DIP-360 polarimeter at the indicated wavelengths and were recorded after multiple chromatographies or recrystallizations of the particular compound. Flash chromatography[43] was performed using Alfa silica gel (58 μm) or ICN 200–400 mesh silica gel. Radial chromatography was performed on a Harrison Model 7923 Chromatotron with plates of 1, 2, or 4 mm thickness made with Merck silica 60 PF_{254} containing gypsum. Analytical thin-layer chromatography (TLC) was performed using 0.25-mm Merck precoated silica gel plates (60 F-254). Visualization was accomplished with UV light, iodine, and phosphomolybdic acid or anisaldehyde/sulfuric acid solution. Boiling points for bulb-to-bulb distillations refer to air bath temperatures and are uncorrected. Reaction solvents were routinely distilled prior to use. Anhydrous tetrahydrofuran (THF) and diethyl ether (Et_2O) were distilled from sodium and benzophenone; dichloromethane (CH_2Cl_2), triethylamine (Et_3N), ethyl acetate (EtOAc), and diisopropylamine were distilled from calcium hydride. Toluene was distilled from sodium, and anhydrous methanol (MeOH) was obtained by distillation from

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powdered 3-Å molecular sieves. Alkyllithiums were titrated by the method of Gilman and Haubein[44] or Ronald, Winkle, and Lansinger.[45] (*S*)-Valinol was prepared by the method of Smith and Gawley.[46] The oxazolidinone chiral auxiliaries, (4*R*,5*S*)-4-methyl-5-phenyl-2-oxazolidinone and (4*S*)-4-(1-methylethyl)-2-oxazolidinone, were prepared as described by Evans et al.[24] Starting materials were azeotropically dried prior to reaction as required and all reactions were conducted in flame-dried glassware under an anhydrous argon atmosphere with standard precautions taken to exclude moisture.

(4*R*,5*S*)-3-(1-Oxo-2-bromoethyl)-4-methyl-5-phenyl-2-oxazolidinone (11a). A three-necked, 2-L, round-bottomed flask equipped with a thermocouple probe, an addition funnel, septa, and stirring bar was charged with a solution of (4*R*,5*S*)-4-methyl-5-phenyl-2-oxazolidinone (30.0 g, 169 mmol) in THF (600 mL) and was cooled with a dry ice/acetone bath. Butyllithium (75.0 mL of a 2.59 M solution in hexanes, 186 mmol) was added dropwise so that the internal temperature was maintained below −60 °C. The resultant dark orange solution was treated dropwise with a solution of bromoacetyl chloride (26.6 g, 169 mmol, 13.9 mL) in THF (300 mL), while maintaining the internal temperature below −65 °C. The resultant pale orange solution was stirred for 1 h at −78 °C and then quenched at −78 °C with saturated aqueous NH_4Cl (30 mL) and saturated aqueous $NaHCO_3$ (60 mL) and allowed to warm to ambient temperature. The organic layer was separated and the aqueous layer was extracted with Et_2O (3 × 90 mL). The combined organic extracts were washed with H_2O and brine, dried ($MgSO_4$), and concentrated. Purification by flash chromatography (2:1 = hexanes/Et_2O) gave 37.0 g (73%) of **11a** as a colorless oil: $[\alpha]^{29}_D$ +17.2°, $[\alpha]^{29}_{577}$ +18.6°, $[\alpha]^{29}_{546}$ +20.9°, $[\alpha]^{29}_{435}$ +39.5°, $[\alpha]^{29}_{405}$ +51.5 (c = 1.46, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.43 (m, 3 H, aromatic H), 7.31 (m, 2 H, aromatic H), 5.75 (d, J = 7.3 Hz, 1 H, C*H*Ph), 4.80 (apparent quintet, J = 6.9 Hz, 1 H, NC*H*Me), 4.55 (ABq, J_{AB} = 12.7 Hz, $\Delta\nu_{AB}$ = 19.2 Hz, 2 H, CH_2Br), 0.94 (d, J = 6.9 Hz, 3 H, CH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.7, 152.5, 132.7, 129.0, 128.8, 125.6, 79.5, 55.2, 28.3, 14.2; IR (neat) 3070 w, 3020 w, 2980 w, 1780 s, 1700 m, 1355 s, 1220 m, 1200 m, 1180 m, 1120 m, 770 m cm^{-1}; MS (EI, 70 eV) m/e (rel inten) 299 (M^+, ^{81}Br, 3), 297 (M^+, ^{79}Br, 2), 200 (3), 107 (100), 91 (16), 77 (29), 70 (93); MS (CI, isobutane) m/e (rel inten) 300 (MH^+, ^{81}Br, 100), 298 (MH^+, ^{79}Br, 94), 256 (22), 254 (36), 220 (58), 178 (36), 107 (88); HRMS (EI, 70 eV) calcd for $C_{12}H_{12}{}^{81}BrNO_3$: 298.9979. Found: 298.9968. Anal. Calcd for $C_{12}H_{12}BrNO_3$: C, 49.49; H, 4.03; N, 4.70. Found: C, 49.51; H, 4.18; N, 4.80.

(4*R*,5*R*)-3-(1-Oxo-2-bromoethyl)-4-methyl-5-phenyl-2-oxazolidinone (11c). The trans-substituted oxazolidinone was prepared in a manner similar to that described for **11a**, except that excess bromoacetyl chloride was added. The reaction was quenched at −78 °C with only saturated NH_4Cl (no $NaHCO_3$ solution was added, thus rendering the aqueous layer to pH = 2–3). Following the complete workup, purification by flash chromatography (2:1 = hexanes/Et_2O) gave **11c** (79%) as a colorless oil: $[\alpha]^{26}_D$ +28.6°, $[\alpha]^{26}_{577}$ +32.9°, $[\alpha]^{26}_{535}$ +53.1° (c = 0.94, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.42 (m, 3 H, aromatic H), 7.33 (m, 2 H, aromatic H), 5.13 (d, J = 3.0 Hz, 1 H, C*H*Ph), 4.55 (collapsed ABq, 2 H, CH_2Br), 4.45 (apparent quintet, J = 3.0 Hz, 1 H, NC*H*Me), 1.59 (d, J = 6.0 Hz, 3 *H*, CH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.9, 152.7, 132.6, 129.5, 129.2, 125.3, 79.8, 67.9, 43.8, 14.4; IR (neat) 1783 s, 1710 s, 1495 w, 1455 w, 1415 w, 1370 s, 1337 s, 1210 m, 1200 s, 1170 m, 1160 m, 1125 w, 1047 m, 1000 w, 977 w, 760 m, 695 w cm^{-1}; MS (EI, 70 eV) m/e (rel inten) 299 (M^+, ^{81}Br, 4), 297 (M^+, ^{79}Br, 3), 200 (8), 174 (9), 146 (9), 132 (10), 117 (18), 107 (100), 91 (34), 77 (46), 70 (98); MS (CI, isobutane) m/e (rel inten) 300 (MH^+, ^{81}Br, 94), 298 (MH^+, ^{79}Br, 100), 254 (49), 220 (50), 178 (34), 107 (8), 85 (11); HRMS (CI, isobutane) calcd for $C_{12}H_{13}BrNO_3$: 298.0078. Found: 298.0090.

(4*S*)-3-(1-Oxo-2-bromoethyl)-4-(1-methylethyl)-2-oxazolidinone (11b). A three-necked, 250-mL, round-bottomed flask equipped with a thermocouple probe, an addition funnel, and a mechanical stirrer device was charged with a solution of (4*S*)-4-(1-methylethyl)-2-oxazolidinone (5.37 g, 41.6 mmol) in THF (107 mL) and was cooled to −78 °C. The internal temperature was maintained below −60 °C as butyllithium (19.2 mL of a 2.39 M solution in hexanes, 45.8 mmol) was added dropwise with vigorous stirring. The resultant white mixture was treated dropwise with a solution of bromoacetyl chloride (7.20 g, 45.8 mmol, 3.80 mL) in THF (54 mL), while maintaining the internal temperature below −65 °C. A clear yellow solution resulted, which was stirred at −78 °C for 40 min. The reaction was quenched at −78 °C with saturated aqueous NH_4Cl (11 mL) and saturated aqueous $NaHCO_3$ (12 mL) and allowed to warm to ambient temperature. The organic layer was separated and the aqueous layer was extracted with Et_2O (3 × 25 mL). The combined organic extracts were washed with H_2O and brine, dried ($MgSO_4$), and concentrated. Purification by flash chromatography (2:1 = hexanes/Et_2O) gave 7.76 g (75%) of **11b** as a colorless oil, which solidified on standing. Recrystallization from Et_2O/hexanes gave a white, crystalline solid: mp 50.5–51.0 °C; $[\alpha]^{29}_D$ +85.4°, $[\alpha]^{29}_{577}$ +90.3°, $[\alpha]^{29}_{546}$ +104.3°, $[\alpha]^{29}_{435}$ +181.1°, $[\alpha]^{29}_{405}$ +222.4° (c = 2.30, EtOH); ^1H NMR (500 MHz, $CDCl_3$) δ 4.61 (d, J = 12.2 Hz, 1 H, $COCH_aH_bBr$), 4.46 (m, 1 H, NC*H*), 4.44 (d, J = 12.2 Hz, 1 H, $COCH_aH_bBr$), 4.35 (apparent t, J = 9.1 Hz, 1 H, OCH_cH_d), 4.28 (dd, J = 9.1, 3.1 Hz, 1 H, OCH_cH_d), 2.42 (m, 1 H, $CH(Me)_2$), 0.95 (d, J = 7.0 Hz, 3 H, CH_3), 0.92 (d, J = 7.0 Hz, 3 H, CH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.0, 153.4, 63.8, 58.6, 28.1, 28.0, 17.8, 14.6; IR (neat) 2964 m, 2871 w, 1780 s, 1702 s, 1484 w, 1389 s, 1367 s, 1326 s, 1204 s, 1020 s, 971 m cm^{-1}; MS (EI, 70 eV) m/e (rel inten) 251 (M^+, ^{81}Br, 0.7), 249 (M^+, ^{79}Br, 0.7), 208 (6), 206 (6), 128 (8), 126 (7), 123 (11), 121 (12), 86 (100), 68 (21), 55 (12); MS (CI, isobutane) m/e (rel inten) 252 (MH^+, ^{81}Br, 100), 250 (MH^+, ^{79}Br, 96), 206 (21), 172 (23), 130 (23). Anal. Calcd. for $C_8H_{12}NO_3Br$: C, 38.40; H, 4.84; N, 5.60. Found: C, 38.69; H, 4.89; N, 5.45.

Diethyl 2-[(4*R*,5*S*)-4-Methyl-2-oxo-5-phenyl-3-oxazolidinyl]-2-oxoethanephosphonate (12a). A 100-mL round-bottomed flask equipped with an air-cooled reflux condenser and a stir bar was charged with (4*R*,5*S*)-3-(1-oxo-2-bromoethyl)-4-methyl-5-phenyl-2-oxazolidinone (19.1 g, 64.2 mmol) and purified, neat triethyl phosphite (11.7 g, 70.6 mmol, 12.1 mL). The solution was stirred at 50 °C for 8 h under a rapid flow of argon and then cooled to ambient temperature and concentrated under reduced pressure (~1 mmHg). The resultant oil was dried by azeotropic distillation with toluene to give 22.8 g (100%) of the phosphonate ester (**12a**) as a pale yellow oil: ^1H NMR (300 MHz, $CDCl_3$) δ 7.42 (m, 3 H, aromatic H), 7.29 (m, 2 H, aromatic H), 5.67 (d, J = 7.3 Hz, 1 H, C*H*Ph), 4.78 (apparent quintet, J = 6.7 Hz, 1 H, NC*H*Me), 4.18 (m, 4 H, 2 × CH_2CH_3), 3.88 (dd, J = 22, 14.1 Hz, 1 H, CH_aH_bP), 3.69 (dd, J = 22, 14.1 Hz, 1 H, CH_aH_bP), 1.33 (t, J = 7.1 Hz, 6 H, 2 × CH_2CH_3), 0.90 (d, J = 6.7 Hz, 3 H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.7, 164.6, 152.9, 132.9, 128.6, 125.5, 78.8, 62.7 (m), 55.0, 35.3, 33.5, 16.3, 16.2, 14.3; IR (neat) 3469 (broad) m, 2985 m, 2934 w, 1782 s, 1699 s, 1400 m, 1355 s, 1256 s, 1173 s, 1028 s, 972 s cm^{-1}; MS (EI 70 eV) m/e (rel inten) 355 (M^+, 2), 222 (11), 196 (4), 179 (72), 151 (41), 133 (38), 123 (63), 116 (31), 107 (100), 91 (43), 81 (49), 70 (57), 65 (32); MS (CI, isobutane) m/e (rel inten) 356 (MH^+, 32), 178 (100), 139 (34); HRMS (EI, 70 eV) calcd for $C_{16}H_{22}NO_6P$: 355.1184. Found: 355.1161.

Diethyl 2-[(4*S*)-4-(1-Methylethyl)-2-oxo-3-oxazolidinyl]-2-oxoethanephosphonate (12b). As described for **12a**, (4*S*)-3-(1-oxo-2-bromoethyl)-4-(1-methylethyl)-2-oxazolidinone (1.0 g, 4.0 mmol) was heated at 50 °C with triethyl phosphite (730 mg, 4.4 mmol, 0.75 mL) for 30 min. The crude product was purified by radial chromatography (gradient eluent system 2:1 to 1:1 = hexanes/ethyl acetate) to give 1.2 g (94%) of the phosphonate ester (**12b**) as a pale yellow oil: ^1H NMR (500 MHz, $CDCl_3$) δ 4.47 (m, 1 H, NC*H*), 4.28 (app t, J = 8.7 Hz, 1 H, OCH_aH_b), 4.23–4.15 (m, 5 H, OCH_aH_b and 2 × CH_2CH_3), 3.85 (dd, J = 22.3, 14.0 Hz, 1 H, CH_cH_dP), 3.72 (dd, J = 22.3, 14 Hz, 1 H, CH_cH_dP), 2.39 (m, 1 H, $CH(Me)_2$), 1.33 (t, J = 7.0 Hz, 6 H, 2 × CH_2CH_3), 0.92 (d, J = 6.9 Hz, 3 H, CH_3), 0.90 (d, J = 6.9 Hz, 3 H, CH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.9, 153.9, 63.3, 62.7 (m), 58.8, 34.8, 33.7, 28.4, 17.9, 16.3, 16.2, 14.6; IR (neat) 3474 w, 2968 s, 1779 s, 1698 s, 1486 m, 1391 s, 1367 s, 1322 s, 1260 s, 1208 s, 1166 s, 1051 s, 1023 s, 974 s, 835 m, 776 m cm^{-1}; MS (EI, 70 eV) m/e (rel inten) 308 ($(M + 1)^+$, 2), 307 (M^+, 1), 179 (100), 151 (47), 123

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(71), 109 (49), 81 (52), 69 (26), 55 (22); MS (CI, isobutane) *m/e* (rel inten) 308 (MH^+, 100), 179 (5), 130 (27). HRMS (CI, isobutane) calcd for $C_{12}H_{23}NO_6P$: 308.1263. Found: 308.1278.

2-Formyl-1,3-dithiane (13) and Aldol Dimer. This synthesis of the dimer is adapted from the preparation of 2-formyl-1,3-dithiane described by Meyers and Strickland.[22c] A solution of 1,3-dithiane (50.0 g, 416 mmol) in THF (870 mL) was cooled in a −40 °C bath and treated dropwise with butyllithium (144 mL of a 3.18 M solution in hexanes, 458 mmol) with stirring. The resulting yellow solution was stirred at −30 °C for 1 h and then was transferred via cannula to a flask containing a precooled (−30 °C) solution of dimethylformamide (128 mL, 1.64 mol). The mixture was allowed to warm to 0 °C and was stirred for 8 h and then was poured into ice water (800 mL). The mixture was extracted with pentane (3 × 500 mL) and the aqueous layer was adjusted to pH 2 with aqueous 3 N HCl. The acidic aqueous mixture was stirred vigorously at ambient temperature for 3 h, then extracted with Et_2O (5 × 300 mL). The combined organic solutions were washed with H_2O (700 mL) and brine (700 mL), dried ($MgSO_4$), and concentrated in vacuo. The aldol dimer 53.5 g (87%) was isolated as a white solid: mp 106–109 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 9.39 (s, 1 H, CHO), 4.35 (dd, J = 6.7, 4.4 Hz, 1 H, C*H*OH), 4.17 (d, J = 6.7 Hz, 1 H, S_2CH), 3.19 (d, J = 4.4 Hz, 1 H, O*H*), 3.11–2.67 (m, 8 H, dithiane H), 2.07–1.91 (m, 4 H, dithiane H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 185.7, 76.5, 62.7, 44.8, 26.7, 26.6, 26.2, 26.1, 24.4, 24.0; IR (neat) 3443 m, 2901 m, 2826 w, 1695 s, 1424 s, 1275 m, 1068 s cm^{-1}; MS (EI, 70 eV) *m/e* (rel inten) 148 (M^+ monomer, 16), 119 (100), 91 (12), 85 (13), 75 (19), 59 (13); MS (CI, isobutane) *m/e* (rel inten) 149 (MH^+ monomer, 100), 133 (3). The solid dimer can be stored at room temperature and, as needed, heated under vacuum (120 °C, 1.0 mm Hg) and distilled (95–97% recovery) to give the monomer, 2-formyl-1,3-dithiane as a colorless liquid whose ^1H NMR and IR spectra agree with the published data:[22c] ^1H NMR (500 MHz, $CDCl_3$) δ 9.5 (d, J = 0.9 Hz, 1 H, C*H*O), 4.1 (apparent s, 1 H, S_2CHCHO), 3.0 (ddd, J = 14.2, 12.2, 2.6 Hz, 2 H, 2 × SCH_aH_b), 2.6 (ddd, J = 14.2, 4.1, 3.3 Hz, 2 H, 2 × SCH_aH_b), 2.1 (m, 1 H, CH_cH_d), 2.0 (m, 1 H, CH_cH_d); ^{13}C NMR (126 MHz, $CDCl_3$) δ 188.2, 47.6, 25.4, 24.9; IR (neat) 2903 s, 2826 m, 2704 w, 1715 s, 1424 s, 1277 m, 1244 m, 1182 w, 1014 m, 907 m cm^{-1}; MS (EI, 70 eV) *m/e* (rel inten) 148 (M^+, 11), 119 (100), 108 (11), 91 (14), 85 (12), 74 (33), 59 (20); MS (CI, isobutane) *m/e* (rel inten) 149 (MH^+, 100), 133 (1), 119 (20), 87 (9); HRMS (CI, isobutane) calcd for $C_5H_8OS_2$: 148.0016. Found: 147.9995.

(4*R*,5*S*)-3-[1-Oxo-3-(1,3-dithian-2-ylidene)propyl]-4-methyl-5-phenyl-2-oxazolidinone (4a). A 3-necked 250-mL round-bottomed flask equipped with an addition funnel, septa, and stirring bar was charged with a 60% dispersion of NaH in mineral oil (1.50 g, 37.5 mmol). The NaH was rinsed free of mineral oil with dry hexanes (3 × 10 mL). The flask was successively evacuated and filled with dried Ar (3×). THF (17 mL) was added, and the NaH suspension was cooled with an ice/water bath as a solution of diethyl 2-[(4*R*,5*S*)-4-methyl-2-oxo-5-phenyl-3-oxazolidinyl)-2-oxoethanephosphonate (**12a**), 12.2 g, 34.4 mmol) in THF (17 mL) was added dropwise. The yellow solution was allowed to warm to ambient temperature and was stirred for 30 min. A solution of 2-formyl-1,3-dithiane (5.10 g, 34.4 mmol) in THF (34 mL) was added dropwise and the reaction solution was stirred for 30 min at ambient temperature. The reaction was diluted with H_2O (70 mL). The organic layer was separated and the aqueous layer was extracted with Et_2O (3 × 70 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated. Purification by flash chromatography (2:1 = hexanes/Et_2O) gave the olefination adduct **4a** 9.92 g (83%) as a pale yellow oil. Crystallization from Et_2O/hexanes gave a white solid: mp 80.0–81.5 °C; $[\alpha]^{27}_D$ +19.9°, $[\alpha]^{27}_{577}$ +15.9°, $[\alpha]^{27}_{546}$ +18.3°, $[\alpha]^{27}_{435}$ +33.2°, $[\alpha]^{27}_{405}$ +42.1° (*c* = 1.02, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.38 (m, 3 H, aromatic H), 7.31 (m, 2 H, aromatic H), 6.15 (apparent t, J_{AX} = J_{BX} = 6.9 Hz, 1 H, $CH_AH_BCH_X$=C), 5.68 (d, J = 7.3 Hz, 1 H, OC*H*Ph), 4.76 (apparent quintet, J = 6.9 Hz, 1 H, NC*H*Me), 3.96 (dd, J_{AB} = 18.9 Hz, J_{AX} = 6.9 Hz, 1 H, $CH_AH_BCH_X$=C), 3.88 (dd, J_{AB} = 18.9 Hz, J_{BX} = 6.9 Hz, 1 H, $CH_AH_BCH_X$=C), 2.88 (m, 4 H, dithiane H), 2.16 (m, 2 H, dithiane H), 0.88 (d, J = 6.9 Hz, 3 H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.8, 152.9, 133.2, 131.2, 128.7, 125.6, 122.9, 105.0, 79.0, 54.8, 36.1, 29.9, 29.3, 24.7, 14.5; IR (neat) 2910 w, 1780 s, 1700 m, 1365 s, 1197 m cm^{-1}; MS (EI, 70 eV) *m/e* (rel inten) 349 (M^+, 11), 172 (69), 145 (58), 116 (44), 98 (16), 91 (21), 87 (22), 77 (24), 71 (100); MS (CI, isobutane) *m/e* (rel inten) 350 (MH^+, 100), 178 (14), 145 (4), 107 (2). Anal. Calcd for $C_{17}H_{19}NO_3S_2$: C, 58.45; H, 5.44; N, 4.01. Found: C, 58.29; H, 5.38; N, 4.01.

(4*S*)-3-[1-Oxo-3-(1,3-dithian-2-ylidene)propyl]-4-(1-methylethyl)-2-oxazolidinone (4b). A 25-mL round-bottomed flask was charged with a solution of diethyl 2-[(4*S*)-4-(1-methylethyl)-2-oxo-3-oxazolidinyl)]-2-oxoethanephosphonate (307 mg, 1.00 mmol) in THF (1.5 mL) and cooled in a −78 °C dry ice/acetone bath. Butyllithium (0.42 mL of a 2.59 M solution in hexanes, 1.10 mmol) was added dropwise with a syringe and the resulting clear, pale yellow solution was stirred at −78 °C for 1 h. A −78 °C solution of 2-formyl-1,3-dithiane (148 mg, 1.00 mmol) in THF (1 mL) was added dropwise via cannula and the reaction solution was warmed to 0 °C and stirred for 30 min. The solution was concentrated; the residue was dissolved in Et_2O (5 mL) and washed once with H_2O and brine, dried ($MgSO_4$), and concentrated. Purification by radial chromatography (2:1 = hexanes/Et_2O) gave 267 mg (89%) of the olefination adduct **4b** as a colorless oil: $[\alpha]^{29}_D$ +77.6°, $[\alpha]^{29}_{577}$ +80.5°, $[\alpha]^{29}_{546}$ +92.2°, $[\alpha]^{29}_{435}$ +162°, $[\alpha]^{29}_{405}$ +198° (*c* = 2.16, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 6.14 (app t, J_{AX} = J_{BX} = 7.0 Hz, 1 H, $CH_AH_BCH_X$=C), 4.43 (app dt, J = 3.3, 8.7 Hz, 1 H, NC*H*), 4.29 (app t, J = 8.7 Hz, 1 H, OCH_aH_b), 4.22 (dd, J = 3.3, 8.7 Hz, 1 H, OCH_aH_b), 3.93 (dd, J_{AB} = 18.8 Hz, J_{AX} = 7.0 Hz, 1 H, $CH_AH_BCH_X$=C), 3.88 (dd, J_{AB} = 18.8 Hz, J_{BX} = 7.0 Hz, 1 H, $CH_AH_BCH_X$=C), 2.89 (m, 4 H, dithiane H), 2.38 (m, 1 H, C*H*Me$_2$), 2.18 (m, 2 H, dithiane H), 0.92 (d, J = 7.0 Hz, 3 H, CH_3), 0.88 (d, J = 7.0 Hz, 3 H, CH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.1, 153.9, 131.3, 122.9, 63.4, 58.5, 36.1, 29.9, 29.4, 28.3, 24.7, 17.9, 14.6; IR (neat) 2961 m, 1777 s, 1698 s, 1387 s, 1371 s, 1300 m, 1206 s cm^{-1}; MS (EI, 70 eV) *m/e* (rel inten) 301 (M^+, 3), 172 (89), 145 (41), 116 (28), 98 (12), 87 (14), 71 (100), 55 (6); MS (CI, isobutane) *m/e* (rel inten) 302 (MH^+, 100), 130 (18); HRMS (EI, 70 eV) calcd for $C_{13}H_{19}NO_3S_2$: 301.0806. Found: 301.0785. Anal. Calcd for $C_{13}H_{19}NO_3S_2$: C, 51.83; H, 6.31; N. 4.65. Found: C, 50.91; H, 6.32; N, 5.03.

General Procedure for the Preparation of Alkyl Triflates.[34] A solution of trifluoromethanesulfonic anhydride (8.4 mmol, 1.4 mL) in carbon tetrachloride (3 mL) was added under argon to a 25-mL round-bottomed flask which contained a 0 °C solution of the alcohol (7.0 mmol) and pyridine (8.4 mmol, 660 mg, 700 μL) in carbon tetrachloride (7 mL). An orange precipitate formed and the mixture was stirred at 0 °C for 1 h. The clear supernatant was transferred via cannula to a dry round-bottomed flask; the solution was concentrated with a stream of argon, the residue taken up in dry THF, and this solution was used directly for the alkylation reactions. The presence of alkyl triflate was detected with ^1H NMR by the downfield shift of proton(s) adjacent to the triflate oxygen. **Propyl trifluoromethane sulfonate: ^1H NMR (300 MHz, CCl_4/$CDCl_3$) δ 4.52 (m, 2 H, CH_2OTf), 1.88 (m, 2 H), 1.06 (m, 3 H). 2-Propyl trifluoromethanesulfonate:** ^1H NMR (500 MHz, CCl_4/$CDCl_3$) δ 5.16 (septet, J = 6.3 Hz, 1 H, C*H*OTf), 1.50 (d, J = 6.3 Hz, 6 H, $CH(CH_3)_2$. **Cyclohexyl trifluoromethanesulfonate:** ^1H NMR (300 MHz, CCl_4/$CDCl_3$) δ 5.66 (s, 1 H, C*H*OTf), 2.00 (m, 3 H), 1.64 (m, 2 H), 1.63 (m, 2 H), 1.62 (m, 3 H).

General Procedure for the Alkylation of Carboximide Ketene Dithioacetals. A 2-necked round-bottomed flask equipped with septa, a temperature thermocouple, and a stirring bar was charged with the acylated oxazolidinone (**4a** or **4b**, 21.2 mmol) and THF (20 mL) and the solution was cooled with a −78 °C dry ice/acetone bath. A −78 °C solution of freshly prepared lithium diisopropyl amide (23.3 mmol) in THF (22 mL) was added dropwise via cannula. The orange solution was warmed to 0 °C over 2.5 h. At −30 °C, a 1 M solution (THF) of the electrophile (organic halide or alkyl triflate, 1.5–3.0 equiv, 31.8–63.6 mmol) was added dropwise to the enolate solution via cannula. The yellow solution was warmed to 0 °C over 1 h and stirred for 1–2.5 h. The reaction was quenched at 0 °C with pH 7 phosphate buffer solution. The organic layer was separated and the aqueous layer was extracted with Et_2O (3 × 90 mL). The combined organic extracts were washed with H_2O and brine, dried ($MgSO_4$), and concentrated. Purification by flash or radial chromatography (5:1 = hexanes/Et_2O) gave the alkylated carboximide ketene dithioacetal (**17–23**) as a colorless oil. Some oils crystallized and

were further purified by recrystallization from dichloromethane/Et_2O/hexanes (1:1:1).

(4*R*,5*S*)-3-[1-Oxo-3-(1,3-dithian-2-ylidene)-2-methylpropyl]-4-methyl-5-phenyl-2-oxazolidinone (17a). Alkylation of the lithium enolate of **4a** with methyl iodide gave **17a**. Purification with radial chromatography gave a colorless oil (78%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (m, 3 H, aromatic H), 7.33 (m, 2 H, aromatic H), 6.12 (d, J = 9.0 Hz, 1 H, *H*C=C), 5.68 (d, J = 7.0 Hz, 1 H, C*H*Ph), 4.92 (dq, J = 9.0, 6.9 Hz, 1 H, COC*H*C=), 4.75 (apparent quintet, J = 7.0 Hz, 1 H, NC*H*Me), 2.90 (m, 4 H, dithiane H), 2.17 (m, 2 H, dithiane H), 1.32 (d, J = 6.9 Hz, 3 H, COCHCH_3), 0.89 (d, J = 7.0 Hz, 3 H, NCHCH_3); IR (neat) 2975 w, 2930 m, 1782 s, 1698 s, 1455 m, 1356 s, 1230 s, 1197 s, 1121 m, 960 m cm^{-1}; MS (EI, 70 eV) m/e (rel inten) 363 (M^+, 4), 186 (76), 159 (100), 130 (38), 85 (98); MS (CI, isobutane) m/e (relative intensity) 364 (MH^+, 100), 178 (9), 107 (4); HRMS (EI, 70 eV) calcd for $C_{18}H_{21}NO_3S_2$: 363.0963. Found: 363.0970.

(4*R*,5*S*)-3-[1-Oxo-3-(1,3-dithian-2-ylidene)-2-(2-propenyl)-propyl]-4-methyl-5-phenyl-2-oxazolidinone (18a). Alkylation of the lithium enolate of **4a** with allyl bromide gave **18a**. Purification with radial chromatography gave a colorless oil (57%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40 (m, 3 H, aromatic H), 7.32 (m, 2 H, aromatic H), 6.06 (d, J = 9.2 Hz, 1 H, *H*C=C), 5.83 (m, 1 H, allyl olefinic H), 5.66 (d, J = 7.0 Hz, 1 H, C*H*Ph), 5.08 (m, 3 H, COC*H*C= and allyl olefinic H), 4.76 (apparent quintet, J = 7.0 Hz, 1 H, NC*H*Me), 2.90 (m, 4 H, dithiane H), 2.55 (m, 1 H, CH_aH$_b$CH=CH$_2$), 2.40 (m, 1 H, CH$_a$$H_b$CH=CH$_2$), 2.16 (m, 2 H, dithiane H), 0.87 (d, J = 7.0 Hz, 3 H, NCHCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.0, 152.5, 149.6, 134.2, 133.3, 130.9, 128.9, 128.7, 125.6, 117.7, 78.8, 55.1, 43.3, 37.6, 30.0, 29.5, 24.7, 14.6; IR (neat) 2912 w, 1781 s, 1697 s, 1456 m, 1364 s, 1344 s, 1220 m, 1195 s, 1121 m, 1032 m, 989 m, 914 m, 766 m, 730 w, 701 m cm^{-1}; MS (EI, 70 eV) m/e (rel inten) 389 (M^+, 2), 348 (9), 304 (6), 212 (83), 185 (58), 172 (16), 143 (25), 137 (32), 119 (100), 91 (41), 77 (52), 67 (39); MS (CI, isobutane) m/e (rel inten) 390 (MH^+, 100), 178 (42), 107 (18). HRMS (EI, 70 eV) calcd for $C_{20}H_{23}NO_3S_2$: 389.1119. Found: 389.1122.

(4*R*,5*S*)-3-[1-Oxo-3-(1,3-dithian-2-ylidene)-2-benzylpropyl]-4-methyl-5-phenyl-2-oxazolidinone (19a). Alkylation of the lithium enolate of **4a** with benzyl bromide gave **19a**. Purification with flash chromatography and further by recrystallization gave a white solid (67%): mp 120–121 °C; $[\alpha]^{27}_D$ −25.0°, $[\alpha]^{27}_{577}$ −28.4°, $[\alpha]^{27}_{546}$ −30.9°, $[\alpha]^{27}_{435}$ −64.0°, $[\alpha]^{27}_{405}$ −84.2° (c = 0.85, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (m, 3 H, aromatic H), 7.29 (m, 7 H, aromatic H), 6.10 (d, J = 9.4 Hz, 1 H, *H*C=C), 5.63 (d, J = 7.0 Hz, 1 H, C*H*Ph), 5.37 (m, 1 H, COCHC=), 4.72 (apparent quintet, J = 7.0 Hz, 1 H, NC*H*Me), 3.17 (dd, J = 13.1, 6.8 Hz, 1 H, CH_aH$_b$Ph), 2.82 (m 4 H, dithiane H), 2.59 (collapsed ddd (7 lines), J = 13.1, 6.8, 2.4 Hz, 1 H, CH$_a$$H_b$Ph), 2.08 (m, 2 H, dithiane H), 0.73 (d, J = 7.0 Hz, 3 H, NCHCH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.0, 152.3, 137.7, 133.2, 130.3, 131.5, 129.7, 129.1, 128.7, 128.6, 128.1, 126.4, 125.6, 78.7, 54.9, 45.5, 39.2, 30.0, 29.5, 24.7, 14.3; IR (neat) 2923 m, 1781 s, 1695 s, 1496 m, 1455 m, 1367 s, 1342 s, 1226 s, 1197 s, 1122 m, 766 m, 732 m, 700 s cm^{-1}; MS (EI, 70 eV) m/e (rel inten) 439 (M^+, 2), 348 (29), 304 (8), 262 (15), 235 (12), 187 (19), 172 (20), 143 (31), 128 (51), 115 (51), 107 (35), 91 (100), 73 (56), 65 (35); MS (CI, isobutane) m/e (rel inten) 440 (MH^+, 100), 384 (3), 178 (27), 133 (13), 107 (13). Anal. Calcd for $C_{24}H_{25}NO_3S_2$: C, 65.60; H, 5.69; N, 3.19. Found: C, 65.61; H, 5.73; N, 3.19.

(4*R*,5*S*)-3-[1-Oxo-3-(1,3-dithian-2-ylidene)-2-[3,4-(methylenedioxy)benzyl]propyl)-4-methyl-5-phenyl-2-oxazolidinone (20a).[47] Alkylation of the lithium enolate of **4a** with piperonyl bromide gave **20a**. Purification with flash chromatography gave a colorless oil (60%): ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.34 (m, 5 H, aromatic H), 6.80 (s, 1 H, piperonyl H), 6.71 (s, 1 H, piperonyl H), 6.70 (s, 1 H, piperonyl H), 6.05 (d, J = 9.3 Hz, 1 H, *H*C=C), 5.90 (dd, J = 5.1, 1.5 Hz, 2 H, OCH_2O) 5.63 (d, J = 7.0 Hz, 1 H, C*H*Ph), 5.28 (m, 1 H, COC*H*C=), 4.72 (app quintet, J = 7.0 Hz, 1 H, NC*H*Me), 3.50 (dd, J = 13.2, 6.7 Hz, 1 H, CH_aH$_b$-Ar), 2.84 (m, 4 H, dithiane H), 2.70 (dd, J = 13.2, 6.7 Hz, 1 H, CH$_a$$H_b$Ar), 2.10 (m, 2 H, dithiane H), 0.78 (d, J = 7.0 Hz, 3 H, NCHCH_3); ^{13}C NMR (63 MHz, $CDCl_3$) δ 173.2, 152.5, 147.5, 146.3, 133.5, 132.0, 131.8, 128.9, 128.8, 128.7, 125.9, 122.9, 110.3, 108.1, 100.9, 79.0, 55.2, 45.9, 39.1, 30.2, 29.6, 24.9, 14.6; IR (neat) 2820 m, 1790 s, 1700 s, 1610 m, 1370 s, 1250 m, 1200 s, 1124 m, 1027 m, 701 m cm^{-1}; MS (EI, 70 eV) m/e (rel inten) 483 (M^+, 8), 348 (87), 304 (27), 172 (32), 135 (100); HRMS (EI, 70 eV) calcd for $C_{25}H_{25}NO_5S_2$: 483.1173. Found: 483.1145.

(4*R*,5*S*)-3-[1-Oxo-3-(1,3-dithian-2-ylidene)-2-propylpropyl]-4-methyl-5-phenyl-2-oxazolidinone (21a). Alkylation of the lithium enolate of **4a** with propyl trifluoromethanesulfonate gave **21a**. Purification with radial chromatography gave a colorless oil (64%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (m, 3 H, aromatic H), 7.31 (m, 2 H, aromatic H), 6.05 (d, J = 9.4 Hz, 1 H, HC=C), 5.66 (d, J = 7.0 Hz, 1 H, C*H*Ph), 4.97 (m, 1 H, COC*H*C=), 4.75 (apparent quintet, J = 7.0 Hz, 1 H, NC*H*Me), 2.88 (m, 4 H, dithiane H), 2.16 (m, 2 H, dithiane H), 1.78 (m, 1 H, propyl H), 1.54 (m, 1 H, propyl H), 1.39 (m, 2 H, propyl H), 0.93 (t, J = 7.3 Hz, 3 H, propyl CH_3), 0.88 (d, J = 7.0 Hz, 3 H, NCHCH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.8, 152.4, 133.3, 130.3, 130.0, 128.7, 128.6, 125.6, 78.8, 55.0, 43.6, 35.5, 30.0, 29.5, 24.8, 20.1, 14.5, 14.0; IR (neat) 2958 m, 2932 m, 2871 m, 1782 s, 1695 s, 1456 m, 1361 s, 1348 s, 1280 m, 1224 s, 1195 s, 1120 m, 1031 m, 766 m, 701 m cm^{-1}; MS (EI, 70 eV) m/e (rel inten) 391 (M^+, 6), 214 (100), 187 (57), 171 (10), 158 (21), 143 (25), 71 (44); MS (CI, isobutane) m/e (rel inten) 392 (MH^+, 100), 178 (86), 133 (34), 107 (27), 83 (21), 71 (17); HRMS (EI, 70 eV) calcd for $C_{20}H_{25}NO_3S_2$: 391.1276. Found: 391.1287.

(4*R*,5*S*)-3-[1-Oxo-3-(1,3-dithian-2-ylidene)-2-(2-propyl)-propyl]-4-methyl-5-phenyl-2-oxazolidinone (22a). Alkylation of the lithium enolate of **4a** with 2-propyl trifluoromethanesulfonate gave **22a**. Purification with radial chromatography and further by recrystallization gave a white, crystalline solid (58%): mp 176–177 °C; $[\alpha]^{29}_D$ −20.0°, $[\alpha]^{29}_{577}$ −16.5°, $[\alpha]^{29}_{546}$ −22.4°, $[\alpha]^{29}_{435}$ −54.9°, $[\alpha]^{29}_{405}$ −73.1° (c = 1.00, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (m, 3 H, aromatic H), 7.31 (m, 2 H, aromatic H), 6.05 (d, J = 9.9 Hz, 1 H, HC=C), 5.66 (d, J = 7.0 Hz, 1 H, C*H*Ph), 4.92 (dd, J = 9.9, 7.4 Hz, 1 H, COC*H*C=), 4.77 (app quintet, J = 7.0 Hz, 1 H, NC*H*Me), 2.89 (m, 4 H, dithiane H), 2.16 (m, 3 H, dithiane H and C*H*(Me)$_2$), 1.01 (d, J = 6.6 Hz, 3 H, CH(CH_3)$_2$), 0.96 (d, J = 7.0 Hz, NCHCH_3), 0.90 (d, J = 6.6 Hz, 3 H, CH(CH_3)$_2$); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.4, 152.5, 133.3, 131.2, 128.7, 128.6, 125.6, 78.7, 55.0, 49.4, 32.6, 30.0, 29.4, 24.7, 20.4, 19.0, 14.5; IR (neat) 2958 s, 2932 s, 2871 m, 1784 s, 1697 s, 1457 m, 1363 s, 1348 s, 1281 m, 1224 s, 1195 s, 1125 m, 1031 m, 767 m, 700 m cm^{-1}; MS (EI, 70 eV) m/e (rel inten) 391 (M^+, 5), 348 (3), 304 (3), 214 (100), 187 (72), 158 (16), 143 (20), 107 (22); MS (CI, isobutane) m/e (rel inten) 392 (MH^+, 100), 178 (6); HRMS (CI, isobutane) calcd for $C_{20}H_{28}NO_3S_2$: 392.1354. Found: 392.1342. Anal. Calcd for $C_{20}H_{25}NO_3S_2$: C, 61.36; H, 6.44; N, 3.58. Found: C, 61.40; H, 6.46; N, 3.30.

(4*R*,5*S*)-3-[1-Oxo-3-(1,3-dithian-2-ylidene)-2-(2-cyclohexyl)propyl]-4-methyl-5-phenyl-2-oxazolidinone (23a). Alkylation of the lithium enolate of **4a** with cyclohexyl trifluoromethanesulfonate gave **23a**. Purification with radial chromatography gave a colorless oil (37%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (m, 3 H, aromatic H), 7.30 (m, 2 H, aromatic H), 6.05 (d, J = 9.7 Hz, 1 H, *H*C=C), 5.66 (d, J = 7.0 Hz, 1 H, C*H*Ph), 4.92 (dd, J = 9.7, 7.4 Hz, 1 H, COC*H*C=), 4.77 (app quintet, J = 7.0 Hz, 1 H, NC*H*Me), 2.85 (m, 4 H, dithiane H), 2.16 (m, 2 H, dithiane H), 1.81–1.43 (m, 6 H, cyclohexyl H), 1.20 (m, 5 H, cyclohexyl H), 0.90 (d, J = 7.0 Hz, 3 H, NCHCH_3); IR (neat) 2926 s, 2851 s, 1783 s, 1693 s, 1450 m, 1364 s, 1339 s, 1225 s, 1195 s, 1119 s, 1032 m, 766 m, 734 m, 701 m cm^{-1}; MS (EI, 70 eV) m/e (rel inten) 431 (M^+, 24), 348 (6), 254 (90), 227 (34), 198 (12), 172 (53), 145 (76), 118 (36), 107 (35), 97 (36), 91 (71), 87 (35), 78 (10), 71 (94), 55 (100); MS (CI, isobutane) m/e (rel inten) 432 (MH^+, 100), 227 (8), 178 (95), 133 (44), 107 (54); HRMS (EI, 70 eV) calcd for $C_{23}H_{29}NO_3S_2$: 431.1589. Found: 431.1554.

(4*S*)-3-[1-Oxo-3-(1,3-dithian-2-ylidene)-2-benzylpropyl]-4-(1-methylethyl)-2-oxazolidinone (19b). Alkylation of the lithium enolate of **4b** with benzyl bromide gave **19b**. Purification with radial chromatography gave a colorless oil (60%): $[\alpha]^{28}_D$ +47.8°, $[\alpha]^{28}_{577}$ +50.3°, $[\alpha]^{28}_{546}$ +58.6°, $[\alpha]^{28}_{435}$ +110°, $[\alpha]^{28}_{405}$ +141° (c = 1.38, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (m, 5 H, aromatic H), 6.04 (d, J = 9.3 Hz, 1 H, *H*C=C), 5.40 (dt, J = 9.3, 7.6 Hz, 1 H, COC*H*C=), 4.38 (ddd, J = 8.9, 3.8, 2.8 Hz, 1 H, NC*H*), 4.22 (apparent t, J = 8.9 Hz, 1 H, OCH_aH$_b$), 4.14 (dd,

(47) Procedures for the preparation of all piperonyl derivatives: Nguyen, H. D. Ph.D. Thesis, University of California, Irvine, 1989.

J = 8.9, 2.8 Hz, 1 H, OCH_aH_b), 3.17 (dd, J = 13.1, 7.2 Hz, 1 H, CH_cH_dPh), 2.78 (m, 4 H, dithiane H), 2.59 (collapsed ddd (seven lines), J = 13.1, 7.2, 5.7 Hz, 1 H, CH_cH_dPh), 2.18 (m, 1 H, $CH(Me)_2$), 2.07 (m, 2 H, dithiane H), 0.84 (d, J = 6.9 Hz, 3 H, CH_3), 0.60 (d, J = 6.9 Hz, 3 H, CH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.1, 153.5, 137.8, 131.4, 129.6, 129.1, 128.1, 126.4, 63.0, 58.5, 45.4, 39.5, 30.0, 29.4, 28.4, 24.6, 17.9, 14.3; IR (neat) 2962 m, 2920 m, 2874 w, 1778 s, 1694 s, 1486 m, 1454 m, 1421 m, 1373 s, 1300 s, 1258 m, 1202 s, 1098 m, 1057 m, 1023 m, 912 m, 749 m, 699 s cm^{-1}; MS (EI, 70 eV) m/e (rel inten) 391 (M^+, 1), 300 (100), 262 (21), 235 (15), 187 (7), 143 (15), 119 (10), 91 (7), 73 (7); HRMS (EI, 70 eV) calcd for $C_{20}H_{25}NO_3S_2$: 391.1276. Found: 391.1275.

(4*S*)-3-[1-Oxo-3-(1,3-dithian-2-ylidene)-2-(2-propyl)propyl]-4-(1-methylethyl)-2-oxazolidinone (22b). Alkylation of the lithium enolate of **4b** with 2-propyl trifluoromethanesulfonate gave **22b**. Purification with radial chromatography and further by recrystallization gave colorless, translucent crystals (76%): mp 84–85 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 6.07 (d, J = 9.9 Hz, 1 H, HC=C), 4.95 (dd, J = 9.9, 6.7 Hz, 1 H, COCH=), 4.46 (app dt, J = 8.8, 3.0 Hz, 1 H, NCH), 4.28 (app t, J = 8.8 Hz, 1 H, OCH_aH_b), 4.22 (dd, J = 8.8, 3.0 Hz, 1 H, OCH_aH_b), 2.90 (m, 4 H, dithiane H), 2.38 (m, 1 H, $CH(Me)_2$), 2.18 (m, 3 H, dithiane H and $CH(Me)_2$), 1.03 (d, J = 7.0 Hz, 3 H, CH_3), 0.96 (d, J = 7.0 Hz, 3 H, CH_3), 0.95 (d, J = 7.0 Hz, 3 H, CH_3), 0.91 (d, J = 7.0 Hz, 3 H, CH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.5, 153.5, 131.2, 128.4, 63.0, 58.6, 49.3, 32.7, 30.1, 29.5, 28.5, 24.8, 20.6, 18.7, 18.0, 14.6; IR (neat) 2962 s, 2931 m, 2873 m, 1779 s, 1693 s, 1464 m, 1372 s, 1300 m, 1203 s, 1093 m, 1058 m, 1021 m cm^{-1}; MS (EI, 70 eV) m/e (rel inten) 343 (M^+, 7), 300 (16), 214 (99), 187 (100), 172 (21), 158 (26), 143 (51), 107 (54), 97 (46), 87 (24), 79 (57), 69 (77), 55 (41); MS (CI, isobutane) m/e (rel inten) 344 (MH^+, 100), 130 (14); HRMS (EI, 70 eV) calcd for $C_{16}H_{25}NO_3S_2$: 343.1276. Found: 343.1272.

General Procedure for the Reductive Removal of the Oxazolidinone Chiral Auxiliary. A solution of lithium aluminum hydride (1 M, 1.2 mmol) in THF was added to a solution of the carboximide ketene dithioacetal (**17–23**, 1.0 mmol) in THF (7 mL) at 0 °C and was stirred for 30 min. At 0 °C, the suspension was treated with solid $Na_2SO_4 \cdot 10H_2O$ (170 mg) and allowed to warm to ambient temperature over 30 min. The white mixture was filtered through a pad of Celite, the solid was washed with THF (5 × 2 mL), and the combined filtrates were concentrated. Flash or radial chromatography (5:1 = hexanes/Et_2O) of the residue gave the hydroxy ketene dithioacetal (**24–28**) as a colorless oil.

(2*R*)-2-(2-Propenyl)-3-(1,3-dithian-2-ylidene)propanol (24a). Reduction of **18** with lithium aluminum hydride in THF gave **24a**. Purification with radial chromatography gave a colorless oil (90%): ^1H NMR (500 MHz, $CDCl_3$) δ 5.78 (m, 2 H, HC=CS_2 and allyic H), 5.07 (m, 1 H, allylic H), 5.03 (m, 1 H, allylic H), 3.60 (dd, 1 H, J = 10.5, 4.6 Hz, CH_aH_bOH), 3.49 (dd, 1 H, J = 10.5, 7.3 Hz, CH_aH_bOH), 2.97 (m, 1 H, CHC=C), 1.89 (m, 4 H, dithiane H), 2.17 (m, 4 H, dithiane H and CH_2C=C); ^{13}C NMR (126 MHz, $CDCl_3$) δ 135.8, 133.6, 129.3, 116.5, 65.5, 42.1, 35.7, 30.2, 29.6, 25.0; IR (neat) 3385 (broad) s, 2914 s, 1641 m, 1583 w, 1422 m, 1277 m, 1027 s, 912 s cm^{-1}; MS (EI, 70 eV) m/e (rel inten) 216 (M^+, 12), 185 (28), 175 (100), 119 (20), 107 (36), 101 (62), 73 (50), 67 (41), 53 (12); MS (CI, isobutane) m/e (rel inten) 217 (MH^+, 100), 199 (12); HRMS (EI, 70 eV) calcd for $C_{10}H_{16}OS_2$: 216.0642. Found: 216.0656.

(2*R*)-2-Benzyl-3-(1,3-dithian-2-ylidene)propanol (25a). Reduction of **19a** with lithium aluminum hydride in THF gave **25a**. Purification with radial chromatography gave a colorless oil (88%): $[\alpha]^{28}_D$ −26.7°, $[\alpha]^{28}_{577}$ −56.5°, $[\alpha]^{28}_{546}$ −61.8°, $[\alpha]^{28}_{435}$ −107.4°, $[\alpha]^{28}_{405}$ −130.6° (c = 0.46, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.20 (m, 5 H, aromatic H), 5.83 (d, J = 9.6 Hz, 1 H, HC=C), 3.59 (dd, 1 H, J = 10.4, 5.3 Hz, CH_aH_bOH), 3.49 (dd, 1 H, J = 10.4, 6.5 Hz, CH_aH_bOH), 3.19 (m, 1 H, CHC=C), 2.81 (m, 4 H, dithiane H), 2.65 (m, 2 H, CH_2Ph), 2.09 (m, 2 H, dithiane H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 139.4, 134.1, 129.4, 129.2, 128.2, 126.0, 65.1, 44.0, 37.5, 30.3, 29.6, 25.0; IR (neat) 3387 (broad) s, 2913 s, 1602 w, 1582 w, 1494 m, 1453 m, 1421 m, 1276 m, 1062 m, 1031 s, 911 m, 745 s, 700 s cm^{-1}; MS (EI, 70 eV) m/e (rel inten) 266 (M^+, 4), 235 (5), 175 (100), 128 (20), 115 (13), 107 (27), 101 (39), 91 (56), 73 (38); MS (CI, isobutane) m/e (rel inten) 267 (MH^+, 100), 249 (14), 193 (13), 175 (16), 161 (26), 107 (22); HRMS (EI, 70 eV) calcd for $C_{14}H_{18}OS_2$: 266.0799. Found: 266.0790.

(2*R*)-2-[3,4-(Methylenedioxy)benzyl]-3-(1,3-dithian-2-ylidene)propanol (26a).[47] Reduction of **20a** with lithium aluminum hydride in THF gave **26a**. Purification with flash chromatography gave a colorless oil (88%): ^1H NMR (250 MHz, $CDCl_3$) δ 6.70 (m, 3 H, aromatic H), 5.93 (s, 2 H, OCH_2O), 5.80 (d, J = 8.8 Hz, 1 H, HC=C), 3.50 (m, 2 H, CH_2OH), 3.15 (m, 1 H, CHC=C), 2.70 (m, 6 H, dithiane H and CH_2Ar), 2.15 (m, 2 H, dithiane H); IR (neat) 3600 (broad) m, 2920 s, 2880 m, 1490 m, 1250 m, 700 s cm^{-1}; MS (EI, 70 eV) m/e (rel inten) 310 (M^+, 34), 236 (44), 175 (78), 135 (100); HRMS (EI, 70 eV) calcd for $C_{15}H_{18}O_3S_2$: 310.0697. Found: 310.0710.

(2*R*)-2-Propyl-3-(1,3-dithian-2-ylidene)propanol (27a). Reduction of **21a** with lithium aluminum hydride in THF gave **27a**. Purification with radial chromatography gave a colorless oil (95%): $[\alpha]^{27}_D$ −22.5°, $[\alpha]^{27}_{577}$ −35.7°, $[\alpha]^{27}_{546}$ −32.7°, $[\alpha]^{27}_{435}$ −56.6°, $[\alpha]^{29}_{405}$ −61.5° (c = 0.36, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 5.73 (d, J = 9.8 Hz, 1 H, HC=C), 3.57 (dd, 1 H, J = 10.5, 5.4 Hz, CH_aH_bOH), 3.44 (dd, 1 H, J = 10.5, 7.6 Hz, CH_aH_bOH), 2.87 (m, 5 H, dithiane H and CHC=C), 2.15 (m, 2 H, dithiane H), 1.48–1.25 (m, 4 H, CH_2CH_2), 0.90 (t, J = 6.9 Hz, 3 H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.1, 128.9, 66.2, 42.4, 33.4, 30.3, 29.7, 25.0, 20.3, 14.2; IR (neat) 3372 (broad) s, 2953 s, 2927 s, 2868 s, 1464 m, 1421 m, 1378 w, 1276 m, 1239 w, 1054 m, 1036 m, 1010 m, 912 m cm^{-1}; MS (EI, 70 eV) m/e (rel inten) 218 (M^+, 20), 187 (89), 175 (7), 145 (72), 113 (13), 107 (19), 97 (21), 85 (17), 79 (18), 71 (100), 55 (39); MS (CI, isobutane) m/e (rel inten) 219 (MH^+, 100), 201 (10); HRMS (EI, 70 eV) calcd for $C_{10}H_{18}OS_2$: 218.0799. Found: 218.0794.

(2*R*)-2-(2-Propyl)-3-(1,3-dithian-2-ylidene)propanol (28a). Reduction of **22a** with lithium aluminum hydride in THF gave **28a**. Purification with radial chromatography gave a colorless oil (85%): $[\alpha]^{29}_D$ −16.4°, $[\alpha]^{29}_{577}$ −20.3°, $[\alpha]^{29}_{546}$ −19.8°, $[\alpha]^{29}_{435}$ −30.1°, $[\alpha]^{29}_{405}$ −26.5° (c = 0.45, $CHCl_3$); HRMS (CI, isobutane) calcd for $C_{10}H_{19}OS_2$: 219.0877. Found: 219.0863. Spectral data for **28a** is identical to that for **28b**.

(2*S*)-2-Benzyl-3-(1,3-dithian-2-ylidene)propanol (25b). Reduction of **19b** with lithium aluminum hydride in THF gave **25b**. Purification with radial chromatography gave a colorless oil (78%): $[\alpha]^{27}_D$ +43.4°, $[\alpha]^{27}_{577}$ +42.4°, $[\alpha]^{27}_{546}$ +50.2°, $[\alpha]^{27}_{435}$ +94.0°, $[\alpha]^{27}_{405}$ +120 (c = 1.00, $CHCl_3$); HRMS (EI, 70 eV) calcd for $C_{14}H_{18}OS_2$: 266.0799. Found: 266.0798. Spectral data for **25b** is identical to that for **25a**.

(2*S*)-2-(2-Propyl)-3-(1,3-dithian-2-ylidene)propanol (28b). Reduction of **22b** with lithium aluminum hydride in THF gave **28b**. Purification with radial chromatography gave a colorless oil (58%): $[\alpha]^{29}_D$ +16.6°, $[\alpha]^{29}_{577}$ +11.2°, $[\alpha]^{29}_{546}$ +10.4°, $[\alpha]^{29}_{435}$ +19.9°, $[\alpha]^{29}_{405}$ +29.5° (c = 0.64, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 5.81 (d, J = 10.2 Hz, 1 H, HC=C), 3.68 (dd, J = 10.4, 5.0 Hz, 1 H, CH_aH_bOH), 3.47 (dd, J = 10.4, 8.2 Hz, 1 H, CH_aH_b-OH), 2.89 (m, 4 H, dithiane H), 2.71 (m, 1 H, CHC=C), 2.17 (m, 2 H, dithiane H), 1.73 (m, 1 H, $CH(Me)_2$), 0.92 (d, J = 6.8 Hz, 3 H, CH_3), 0.88 (d, J = 6.8 Hz, 3 H, CH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 133.3, 129.6, 64.3, 48.6, 30.4, 29.7, 29.1, 25.0, 20.7, 19.3; IR (neat) 3385 (broad) m, 2955 s, 2912 s, 2872 m, 1463 m, 1422 m, 1385 w, 1366 w, 1275 m, 1241 w, 1056 m, 1036 m, 1010 w, 913 m cm^{-1}; MS (EI, 70 eV) m/e (rel inten) 218 (M^+, 16), 187 (91), 175 (55), 113 (27), 107 (82), 101 (67), 97 (24), 81 (52), 73 (100), 69 (38), 53 (23); MS (CI, isobutane) m/e (rel inten) 219 (MH^+, 100), 201 (9); HRMS (EI, 70 eV) calcd for $C_{10}H_{18}OS_2$: 218.0799. Found: 218.0810.

General Procedure for the Cyclization of the Acyclic Hydroxy Ketene Dithioacetals: Dithiane-Protected Lactones. 2,2-[3-[3,4-(Methylenedioxy)benzyl]-1-oxa-1,4-butanediyl]-1,3-dithiane (30).[47] A 10-mL, round-bottomed flask was charged with a solution of 2-piperonyl hydroxy ketene dithioacetal (**26a**, 79 mg, 0.3 mmol) in dichloromethane (2.0 mL), and trifluoroacetic acid (20 μL, 0.3 mmol) was added via a microsyringe. The resulting yellow solution was stirred for 30 min at ambient temperature and concentrated to give a yellow oil. Purification by radial or flash chromatography (petroleum ether: ether = 1:1) gave 73 mg of **30** (90%) as a colorless oil: ^1H NMR (250 MHz, $CDCl_3$) δ 6.70 (m, 3 H, aromatic H), 5.95 (s, 2 H, OCH_2O), 4.05 (m, 1 H, CH_aH_bO), 3.75 (m, 1 H, CH_aH_bO), 3.40 (m, 2 H, dithiane H), 2.70 (m, 5 H, 2 × dithiane H, S_2CCH_2,

and C*H*CH$_2$Ar), 2.40–1.80 (m, 4 H, 2 × dithiane H and C*H*$_2$Ar); IR (neat) 2915 s, 2855 m, 1497 m, 1455 s, 1447 m, 1420 m, 1273 m, 1240 w cm^{-1}; MS (EI, 70 eV) *m/e* (rel inten) 310 (M$^+$, 38), 236 (60), 175 (27), 135 (100); HRMS (EI, 70 eV) calcd for $C_{15}H_{18}O_3S_2$: 310.0697. Found: 310.0699.

2,2-(3-Benzyl-1-oxa-1,4-butanediyl)-1,3-dithiane (29). As described above, 2-(hydroxy-1-benzylethyl)ketene dithioacetal (**25a**) was treated with trifluoroacetic acid in dichloromethane to give **29**. Purification by radial chromatography gave a colorless oil (71%): $[\alpha]^{29}_D$ +6.6°, $[\alpha]^{29}_{577}$ +0.8°, $[\alpha]^{29}_{546}$ +2.3°, $[\alpha]^{29}_{435}$ +6.6°, $[\alpha]^{29}_{405}$ +12.7° (*c* = 0.73, CHCl$_3$); ^{1}H NMR (250 MHz, CDCl$_3$) δ 7.24 (m, 5 H, aromatic H), 4.04 (dd, *J* = 9.8, 6.8 Hz, 1 H, C*H*$_a$H$_b$O), 3.76 (dd, *J* = 9.8, 4.7 Hz, 1 H, CH$_a$*H*$_b$O), 3.41 (td, *J* = 13.2, 2.4 Hz, 1 H, dithiane H), 3.34 (td, *J* = 13.2, 2.3 Hz, 1 H, dithiane H), 2.76 (m, 5 H, 2 × dithiane H, S$_2$CC*H*$_2$, and C*H*CH$_2$Ph), 2.33 (dd, *J* = 13.7, 7.8 Hz, 1 H, C*H*$_c$H$_d$Ph), 2.16 (m, 1 H, CH$_c$*H*$_d$Ph), 1.93 (m, 2 H, dithiane H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 139.7, 128.4, 128.3, 126.0, 90.7, 72.7, 47.4, 40.0, 39.2, 28.3, 27.9, 24.4; IR (neat) 3024 m, 2915 s, 2855 m, 1496 m, 1453 s, 1441 m, 1423 m, 1275 m, 1243 w cm^{-1}; MS (EI, 70 eV) *m/e* (rel inten) 266 (M$^+$, 2), 192 (7), 175 (31), 131 (19), 116 (48), 101 (18), 91 (100), 65 (28); MS (CI, isobutane) *m/e* (rel inten) 267 (MH$^+$, 100), 193 (15), 177 (35), 107 (10); HRMS (EI, 70 eV) calcd for $C_{14}H_{18}OS_2$: 266.0799. Found: 266.0792.

General Procedure for the Hydrolysis of Dithiane-Protected Lactones. (*R*)-β-[3,4-(Methylenedioxy)benzyl]-γ-butyrolactone (32a).[47] A solution of **30** (73 mg, 240 μmol) in 80% aqueous acetonitrile (5.0 mL) in a 25-mL round-bottomed flask was treated with mercuric chloride (130 mg, 470 μmol) and calcium carbonate (94 mg, 940 μmol) at ambient temperature. The resulting cloudy solution was stirred for 1 h and then filtered through a pad of Celite; the pad was rinsed with acetonitrile (3 × 2 mL). The combined filtrates were concentrated, the residue was taken up in chloroform (2 mL), and this solution was treated with Na$_2$S·9H$_2$O (0.5 mmol, 120 mg) and then allowed to stir at ambient temperature for 1 h, during which time a black precipitate formed. The mixture was dried (Na$_2$SO$_4$), filtered, and concentrated. Flash chromatography (ether:petroleum ether = 1.5:1) of the residue gave 62 mg of **32a** (60%) as an oil: $[\alpha]^{28}_D$ +4.4° (*c* = 1.08, CHCl$_3$) [lit.[48] of (*S*) enantiomer $[\alpha]_D$ −4.8° (*c* = 1.14, CHCl$_3$)]; ^{1}H NMR (250 MHz, CDCl$_3$) δ 6.7 (m, 3 H, aromatic H), 5.93 (s, 2 H, OC*H*$_2$O), 4.35 (dd, *J* = 9.0, 7.2 Hz, 1 H, C*H*$_a$H$_b$O), 4.05 (dd, *J* = 9.0, 6.8 Hz, 1 H, CH$_a$*H*$_b$O), 2.80 (m, 1 H, C*H*CH$_2$Ar), 2.70 (m, 2 H, C*H*$_2$C=O), 2.56 (dd, *J* = 17.3, 7.0 Hz, 1 H, C*H*$_c$H$_d$Ar), 2.24 (dd, *J* = 17.3, 7.2 Hz, 1 H, CH$_c$*H*$_d$Ar); ^{13}C NMR (63 MHz, CDCl$_3$) δ 176.8, 148.2, 146.6, 132.1, 121.8, 109.0, 108.6, 101.2, 72.6, 38.8, 37.4, 34.3; IR (neat) 2900 m, 1780 s cm^{-1}; MS (EI, 70 eV) *m/e* (rel inten) 220 (M$^+$, 24), 135 (100); HRMS (EI, 70 eV) calcd for $C_{12}H_{12}O_4$: 220.0735. Found: 220.0728.

(*R*)-β-Benzyl-γ-butyrolactone (31a). In a fashion similar to that described above, 2,2-(3-benzyl-1-oxa-1,4-butanediyl)-1,3-dithiane (**29**) was hydrolyzed with mercuric chloride/calcium carbonate in aqueous acetonitrile to give **31a** (91%). Bulb-to-bulb distillation gave a colorless oil: bp 100–120 °C (1.5 mmHg); $[\alpha]^{29}_D$ +6.6°, $[\alpha]^{29}_{577}$ +3.3°, $[\alpha]^{29}_{546}$ +6.8°, $[\alpha]^{29}_{435}$ +8.9°, $[\alpha]^{29}_{405}$ +12.6° (*c* = 0.92, EtOH); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.36 (m, 2 H, aromatic H), 7.29 (m, 1 H, aromatic H), 7.19 (m, 2 H, aromatic H), 4.37 (dd, *J* = 9.0, 7.0 Hz, 1 H, C*H*$_a$H$_b$O), 4.07 (dd, *J* = 9.0, 6.2 Hz, 1 H, CH$_a$*H*$_b$O), 2.90 (m, 1 H, C*H*CH$_2$Ph), 2.82 (m, 2 H, C*H*$_2$C=O), 2.64 (dd, *J* = 17.4, 8.0 Hz, 1 H, C*H*$_c$H$_d$Ph), 2.33 (dd, *J* = 17.4, 7.0 Hz, 1 H, CH$_c$*H*$_d$Ph); ^{13}C NMR (75 MHz, CDCl$_3$) δ 176.8, 138.2, 128.8, 128.6, 126.8, 72.6, 38.9, 37.2, 34.2; IR (neat) 3026 w, 2921 m, 2851 w, 1774 s, 1496 m, 1454 m, 1418 m, 1378 w, 1170 s, 1016 s, 745 m, 701 s cm^{-1}; MS (EI, 70 eV) *m/e* (rel inten) 176 (M$^+$, 27), 117 (10), 91 (100), 65 (14); MS (CI, isobutane) *m/e* (rel inten) 177 (MH$^+$, 100); HRMS (EI, 70 eV) calcd for $C_{11}H_{12}O_2$: 176.0837. Found: 176.0839.

General Procedure for the Cyclization and Concomitant Hydrolysis of Acyclic Hydroxy Ketene Dithioacetals To Give γ-Butyrolactones. A 10-mL, round-bottomed flask was charged with the hydroxy ketene dithioacetal (0.2 mmol) and dichloromethane (1 mL). At ambient temperature, the solution was treated with toluenesulfonic acid (10 mg) and stirred for 1 h. The solution was diluted with water (1 mL) and the layers were separated. The aqueous layer was extracted with Et$_2$O (3 × 1 mL). The combined organic extracts were washed with H$_2$O and brine, dried (MgSO$_4$), and concentrated. Purification by radial chromatography (5:1 = hexanes/Et$_2$O) gave the volatile lactone as a colorless oil. The lactone could be further purified by bulb-to-bulb distillation (60–120 °C, 1.5 mmHg).

(*R*)-β-Benzyl-γ-Butyrolactone (31a). Cyclization of (2*R*)-2-Benzyl-3-(1,3-dithian-2-ylidene)propanol (**25a**) with toluenesulfonic acid in dichloromethane gave **31a**. Bulb-to-bulb distillation gave a colorless oil (85%): $[\alpha]^{29}_D$ +5.6°, $[\alpha]^{29}_{577}$ +1.5°, $[\alpha]^{29}_{546}$ +6.0°, $[\alpha]^{29}_{435}$ +8.5°, $[\alpha]^{29}_{405}$ +12.7° (*c* = 1.00, EtOH); HRMS (EI, 70 eV) calcd for $C_{11}H_{12}O_2$: 176.0837. Found: 176.0835. Spectral data for the lactone obtained from this procedure is identical to that described for **31a** obtained from hydrolysis of the dithiane-protected lactone.

(*R*)-β-Propyl-γ-butyrolactone (33a). Cyclization of (2*R*)-2-Propyl-3-(1,3-dithian-2-ylidene)propanol (**27a**) with toluenesulfonic acid in dichloromethane gave **33a**. Bulb-to-bulb distillation gave a colorless oil (90%): $[\alpha]^{29}_D$ +7.4° (*c* = 0.31, CHCl$_3$) [lit.[19a] $[\alpha]^{26}_D$ +6.7° (*c* = 3.9, EtOH)]; ^{1}H NMR (300 MHz, CDCl$_3$) δ 4.42 (dd, *J* = 8.7, 8.0 Hz, 1 H, C*H*$_a$H$_b$O), 3.94 (dd, *J* = 8.7, 7.6 Hz, 1 H, CH$_a$*H*$_b$O), 2.61 (m, 2 H, C*H*$_2$C=O), 2.18 (m, 1 H, C*H*-propyl), 1.54 (m, 2 H, propyl H), 1.39 (m, 2 H, propyl H), 0.93 (t, *J* = 7.3 Hz, 3 H, C*H*$_3$); IR (neat) 2923 s, 1780 s, 1467 m, 1420 m, 1379 m, 1171 s, 1016 s cm^{-1}; MS (EI, 70 eV) *m/e* (rel inten) 129 (MH$^+$, 6), 128 (M$^+$, 2), 97 (7), 70 (39), 69 (34), 56 (100), 55 (99); MS (CI, isobutane) *m/e* (rel inten) 129 (MH$^+$, 100); HRMS (CI, isobutane) calcd for $C_7H_{13}O_2$: 129.0915. Found: 129.0917.

(*S*)-β-(2-Propyl)-γ-butyrolactone (34a). Cyclization of (2*R*)-2-(2-propyl)-3-(1,3-dithian-2-ylidene)propanol (**28a**) with toluenesulfonic acid in dichloromethane gave **34a**. Bulb-to-bulb distillation gave a colorless oil (48%): $[\alpha]^{29}_D$ −21.6°, $[\alpha]^{29}_{577}$ −19.3°, $[\alpha]^{29}_{546}$ −26.3°, $[\alpha]^{29}_{435}$ −45.9°, $[\alpha]^{29}_{405}$ −53.8° (*c* = 0.69, CHCl$_3$) [lit.[19a,49] $[\alpha]^{24}_D$ −13° (neat)]; HRMS (CI, isobutane) calcd for $C_7H_{13}O_2$: 129.0915. Found: 129.0910. Spectral data for this lactone is identical to **34b**.

(*S*)-β-Benzyl-γ-Butyrolactone (31b). Cyclization of (2*S*)-2-Benzyl-3-(1,3-dithian-2-ylidene)propanol (**25b**) with toluenesulfonic acid in dichloromethane gave **31b** (76% after chromatography). Bulb-to-bulb distillation gave a colorless oil: $[\alpha]^{29}_D$ −6.9°, $[\alpha]^{29}_{577}$ −7.7°, $[\alpha]^{29}_{546}$ −8.5°, $[\alpha]^{29}_{435}$ −12.4°, $[\alpha]^{29}_{405}$ −11.2° (*c* = 1.00, CHCl$_3$); HRMS (EI, 70 eV) calcd for $C_{11}H_{12}O_2$: 176.0837. Found: 176.0843. Spectral data for the lactone obtained from this procedure is identical to that described for **31a** obtained from hydrolysis of the dithiolane-protected lactone.

(*R*)-β-(2-Propyl)-γ-butyrolactone (34b). Cyclization of (2*S*)-2-(2-Propyl)-3-(1,3-dithian-2-ylidene)propanol (**28b**) with toluenesulfonic acid in dichloromethane gave **34b**. Bulb-to-bulb distillation gave a colorless oil (95%): $[\alpha]^{29}_D$ +15.0°, $[\alpha]^{29}_{577}$ +7.6°, $[\alpha]^{29}_{546}$ +13.3°, $[\alpha]^{29}_{435}$ +25.3°, $[\alpha]^{29}_{405}$ +36.5° (*c* = 0.92, CHCl$_3$) [lit.[19a,49] of (*S*) enantiomer $[\alpha]^{24}_D$ −13° (neat)]; ^{1}H NMR (500 MHz, CDCl$_3$) δ 4.42 (dd, *J* = 9.0, 7.7 Hz, 1 H, C*H*$_a$H$_b$O), 3.97 (app t, *J* = 8.7 Hz, 1 H, CH$_a$*H*$_b$O), 2.58 (dd, *J* = 16.9, 8.0 Hz, 1 H, C*H*$_c$H$_d$C=O), 2.30 (m, 1 H, C*H*CH(Me)$_2$), 2.23 (dd, *J* = 16.9, 9.6 Hz, 1 H, CH$_c$*H*$_d$C=O), 1.64 (m, 1 H, C*H*(Me)$_2$), 0.96 (d, *J* = 6.7 Hz, 3 H, C*H*$_3$), 0.92 (d, *J* = 6.7 Hz, 3 H, C*H*$_3$); ^{13}C NMR (126 MHz, CDCl$_3$) δ 177.3, 72.2, 42.7, 32.9, 31.7, 20.6, 19.9; IR (neat) 2964 m, 2923 w, 2872 w, 1774 s, 1467 w, 1384 w, 1292 w, 1174 m, 1010 m cm^{-1}; MS (EI, 70 eV) *m/e* (rel inten) 129 (MH$^+$, 2), 128 (M$^+$, 2), 113 (1), 69 (68), 58 (37), 55 (100); MS (CI, isobutane) *m/e* (rel inten) 129 (MH$^+$, 100); HRMS (EI, 70 eV) calcd for $C_7H_{12}O_2$: 128.0837. Found: 128.0841.

(2*S*)-(2-Benzyl-3-hydroxypropyl)-1,3-dithiane (35). The benzyl carboximide ketene dithioacetal **19b** (89.7 mg, 0.23 mmol) in THF (1.7 mL) was treated with a solution of LAH (1.1 M, 0.12 mL) in THF and heated at reflux for 1 h. The mixture was cooled to ambient temperature, solid Na$_2$SO$_4$·10H$_2$O (50.7 mg) and MgSO$_4$ were added, and the mixture was stirred at ambient temperature for 3 h. The white mixture was filtered through a pad of Celite, the solid was washed with THF (5 × 1 mL), and the combined filtrates were concentrated. Radial chromatog-

(48) (a) Reference 17b; (b) Tomioka, K.; Mizuguchi, H.; Koga, K. *Chem. Pharm. Bull. Jpn.* **1982**, *30*, 4304. (c) Kuhn, M.; von Wartburg, A. *Helv. Chim. Acta* **1967**, *50*, 1546.

(49) Kendall, M.; Wells, R. J. *Aust. J. Chem.* **1974**, *27*, 2293.

raphy (5:1 = hexanes/Et_2O) of the residue gave the hydroxy dithiane 57.7 mg (93%) **35** as a colorless oil: $[\alpha]^{28}_D$ +15.9°, $[\alpha]^{28}_{577}$ +14.4°, $[\alpha]^{28}_{546}$ +16.1°, $[\alpha]^{28}_{435}$ +29.6°, $[\alpha]^{28}_{405}$ +37.1° (c = 1.40, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.28 (m, 2 H, aromatic H), 7.21 (m, 3 H, aromatic H), 4.10 (t, J = 7.4 Hz, 1 H, CHS_2), 3.59 (dd, J = 10.9, 4.7 Hz, 1 H, CH_aH_bOH), 3.52 (dd, J = 10.9, 5.0 Hz, 1 H, CH_aH_bOH), 2.82 (m, 4 H, dithiane H), 2.66 (m, 2 H, CH_2-Ph), 2.20 (m, 1 H, $CH_cH_dCHS_2$), 2.10 (m, 1 H, $CH_cH_dCHS_2$), 1.86 (m, 2 H, dithiane H), 1.78 (m, 1 H, CH); ^{13}C NMR (126 MHz, $CDCl_3$) δ 139.8, 129.1, 128.3, 126.1, 64.3, 45.4, 39.3, 37.5, 36.8, 30.3, 30.2, 25.9; IR (neat) 3616–3160 (broad) m, 3058 w, 3018 w, 2929 s, 2899 s, 1602 w, 1494 m, 1453 m, 1422 m, 1276 m, 1243 m, 1182 w, 1030 s, 951 w, 907 m, 741 s, 701 s cm^{-1}; MS (EI, 70 eV) m/e (rel inten) 268 (M^+, 20), 161 (100), 143 (50), 134 (20), 91 (26); MS (CI, isobutane) m/e (rel inten) 269 (MH^+, 1), 268 (1), 251 (1), 161 (100); HRMS (EI, 70 eV) calcd for $C_{14}H_{20}OS_2$: 268.0955. Found: 268.1051.

2-[(2*S*)-2-Benzyl-3-oxo-3-[(4′*S*)-4′-(1-methylethyl)-2′-oxo-3-oxazolidinyl]propyl]-1,3-dithiane (36). The benzyl carboximide ketene dithioacetal **19b** (60.7 mg, 0.16 mmol) in CH_2Cl_2 (2 mL) was cooled to −78 °C, treated with triethylsilane (100 μL) and then with trifluoroacetic acid (100 μL), and allowed to warm to ambient temperature over 2 h. The solution was washed with saturated aqueous $NaHCO_3$ (2 mL), water (2 mL), and brine (2 mL), then dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified with flash chromatography (7:1 = hexanes/ether) to give the carboximide dithiane (54.7 mg, 87%) **36** as a colorless oil: $[\alpha]^{27}_D$ +40.1°, $[\alpha]^{27}_{577}$ +34.3°, $[\alpha]^{27}_{546}$ +38.7°, $[\alpha]^{27}_{435}$ +60.4°, $[\alpha]^{27}_{405}$ +69.4° (c = 1.01, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.22 (m, 5 H, aromatic H), 4.43 (m, 2 H, $CHC{=}O$ and NC*H*), 4.23 (t, J = 8.8 Hz, 1 H, OCH_aH_b), 4.14 (dd, J = 8.8, 2.7 Hz, 1 H, OCH_aH_b), 3.91 (t, J = 7.4 Hz, 1 H, HCS_2), 3.08 (dd, J = 13.1, 6.6 Hz, H, CH_cH_dPh), 2.74 (m, 4 H, dithiane H), 2.67 (dd, J = 13.1, 8.4 Hz, 1 H, CH_cH_dPh), 2.37 (dt, J = 13.9, 8.6 Hz, $CH_eH_fCHS_2$), 2.17 (m, 1 H, $CHMe_2$), 2.00 (m, 1 H, CH_eH_f-CHS_2), 1.85 (m, 2 H, dithiane H), 0.84 (d, J = 7.1 Hz, 3 H, CH_3), 0.62 (d, J = 7.1 Hz, 3 H, CH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.0, 153.7, 138.0, 129.3, 129.2, 128.4, 126.6, 63.1, 58.5, 44.9, 42.5, 39.6, 36.0, 29.3, 28.4, 25.6, 17.9, 14.4; IR (neat) 2961 m, 2926 m, 1777 s, 1696 s, 1490 w, 1458 w, 1421 w, 1387 s, 1300 m, 1277 w, 1237 m, 1205 m, 1141 w, 1102 w, 1054 w, 1019 w, 989 w, 948 w, 908 w, 774 w, 748 w, 701 m cm^{-1}; MS (EI, 70 eV) m/e (rel inten) 393 (M^+, 7), 261 (51), 193 (7), 150 (35), 145 (24), 130 (100), 119 (94), 104 (28), 91 (73), 85 (29), 69 (24), 59 (9), 55 (15); HRMS (CI, isobutane) calcd for $C_{20}H_{28}NO_3S_2$: 394.1510. Found: 394.1517.

5,8-Dioxo-4-thia-8-[(4*R*,5*S*)-4-methyl-2-oxo-5-phenyl-2-oxazolidinyl]octanethiol (37). A 10-mL, round-bottomed flask was charged with the carboximide ketene dithioacetal **4a** (69.8 mg, 0.20 mmol) and dichloromethane (1 mL). At ambient temperature, the solution was treated with toluenesulfonic acid (10.0 mg) and stirred for 1 h. The solution was diluted with water (1 mL) and the layers were separated. The aqueous layer was extracted with Et_2O (3 × 1 mL). The combined organic extracts were washed with H_2O and brine, dried ($MgSO_4$), and concentrated. Purification by radial chromatography (5:1 = hexanes/Et_2O) gave the thioester **37** (51.4 mg, 70%) as a yellow oil: ^1H NMR (500 MHz, $CDCl_3$) δ 7.39 (m, 5 H, aromatic H), 5.70 (d, J = 7.3 Hz, 1 H, OC*H*Ph), 4.76 (app quintet, J = 7.0 Hz, 1 H, NC*H*Me), 3.33 (m, 3 H), 3.00 (m, 2 H), 2.65 (m, 3 H), 2.45 (t, J = 7.4 Hz, 1 H, S*H*), 1.90 (m, 2 H), 1.88 (d, J = 7.0 Hz, 3 H, CH_3); IR (neat) 2918 w, 1781 s, 1696 s, 1458 w, 1380 m, 1347 s, 1260 m, 1218 m, 1199 m, 1121 m, 1031 w, 992 m, 767 m, 732 w, 700 m cm^{-1}; MS (EI, 70 eV) 349 ($M^+ - H_2O$, 2), 260 (2), 172 (89), 145 (37), 116 (26), 71 (100); MS (CI, isobutane) 368 (MH^+, 4), 350 (23), 178 (100), 107 (55); HRMS (CI, isobutane) calcd for $C_{17}H_{22}NO_4S_2$: 368.0990. Found: 368.0981.

5,8-Dioxo-4-thia-8-[(4*S*)-4-(1-methylethyl)-2-oxazolidinyl]octanethiol (38). A 10-mL, round-bottomed flask was charged with the carboximide ketene dithioacetal **4b** (60.2 mg, 0.20 mmol) and dichloromethane (1 mL). At ambient temperature, the solution was treated with toluenesulfonic acid (10.0 mg) and stirred for 1 h. The solution was diluted with water (1 mL) and the layers were separated. The aqueous layer was extracted with Et_2O (3 × 1 mL). The combined organic extracts were washed with H_2O and brine, dried ($MgSO_4$), and concentrated. Purification by radial chromatography (5:1 = hexanes/Et_2O) gave the thioester **38** (52.9 mg, 83%) as a yellow oil: ^1H NMR (500 MHz, $CDCl_3$) δ 4.42 (m, 1 H, NC*H*), 4.29 (dd, J = 16.2, 8.6 Hz, 1 H, OCH_aH_b), 4.21 (m, 1 H, OCH_aH_b), 3.31 (m, 3 H), 2.99 (m, 1 H), 2.93 (m, 1 H), 2.68 (m, 1 H), 2.61 (t, J = 7.2 Hz, 1 H, S*H*), 2.38 (m, 2 H), 2.04 (m, 1 H), 1.87 (m, 2 H), 0.91 (apparent t, J = 6.7 Hz, 3 H, CH_3), 0.88 (apparent dd, J = 6.9, 2.1 Hz, 3 H, CH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.6, 171.3, 154.0, 63.5, 58.4, 37.7, 33.6, 30.9, 28.3, 27.5, 27.2, 17.9, 14.6; IR (neat) 9262 m, 2927 w, 2875 w, 1780 s, 1696 s, 1484 w, 1466 w, 1388 s, 1301 m, 1260 m, 1208 s, 1142 w, 1104 m, 1056 m, 1019 m, 997 m, 973 m, 773 w, 756 w, 728 w, 692 w cm^{-1}; MS (EI, 70 eV) m/e (rel inten) 301 ($M^+ - H_2O$, 6), 212 (41), 172 (95), 145 (48), 126 (22), 116 (29), 100 (100), 86 (23), 71 (92), 55 (80); MS (CI, isobutane) m/e (rel inten) 320 (MH^+, 4), 302 (9), 212 (39), 130 (100), 107 (11); HRMS (CI, isobutane) calcd for $C_{13}H_{22}NO_4S_2$: 320.0990. Found: 320.0989.

4-Bromobutanal. Ethyl 4-bromobutanoate (5.45 g, 28.0 mmol) was dissolved in CH_2Cl_2 (50 mL) and cooled to −78 °C. Neat DIBAL (5.70 mL, 32.0 mmol) was added dropwise via syringe while the temperature of the reaction solution was maintained below −65 °C. After 30 min, the reaction mixture was poured into an ice-cold solution of 10% aqueous HCl and the mixture was stirred for 1 h. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic solution was washed with water, dried ($MgSO_4$), and concentrated under reduced pressure. Bulb-to-bulb distillation of the residue gave the bromo aldehyde (4.02 g, 96%) as a colorless liquid: bp 44–50 °C (1.5 mmHg). Analytical data agrees with that reported in the literature:[50] ^1H NMR (300 MHz, $CDCl_3$) δ 9.80 (s, 1 H, C*H*O), 3.45 (t, J = 6.4 Hz, 2 H, CH_2Br), 2.67 (t, J = 6.6 Hz, 2 H, CH_2CHO), 2.17 (apparent quintet, J = 6.6 Hz, 2 H, CH_2); IR (neat) 2963 m, 2831 m, 2724 w, 1725 s, 1439 m, 1390 m, 1364 m, 1277 w, 1246 m, 1123 m, 1041 m cm^{-1}; GCMS (EI, 70 eV; 50 m DB5 column: temperature 1 = 35 °C, time 1 = 3 min, rate = 25 °C/min, temperature 2 = 250 °C, time 2 = 5 min, retention time = 9.61 min) m/e (rel inten) 152 (M^+, ^{81}Br, 2), 150 (M^+, ^{79}Br, 2), 124(3), 122 (4), 95 (15), 93 (16), 81 (14), 79 (13), 71 (100), 43 (22), 42 (31), 41 (71), 39 (59).

2,2-[(2*S*,3*R*)-3-[[(4*R*,5*S*)-4-Methyl-2-oxo-5-phenyl-3-oxazolidinyl]carbonyl]-2-(3-bromopropyl)-1-oxa-1,4-butanediyl]-1,3-dithiane (40a). Diethylboryl triflate was generated in situ by the addition of trifluoromethanesulfonic acid (0.18 mL, 2.00 mmol) to a 1 M solution of commercial triethylborane (2.00 mL, 2.00 mmol in hexanes) at ambient temperature. The mixture was stirred under a rapid flow of argon at 40 °C for 30 min and a pale orange solution resulted. At −5 °C, a solution of the carboximide ketene dithioacetal **4a** (350 mg, 1.00 mmol) in CH_2Cl_2 (4 mL) was added to the boron triflate solution, and subsequently, a solution of Hunig's base (271 mg, 2.10 mmol) in CH_2Cl_2 (2.1 mL) was added. The dark orange solution was stirred at −5 °C for 30 min and then cooled to −78 °C and maintained at this temperature as a solution of bromobutanal (755 mg, 5.00 mmol) in CH_2Cl_2 (5 mL) was added dropwise. The resulting pale orange solution was stirred at −78 °C for 1 h and quenched with phosphate buffer (pH 7, 20 mL). The layers were separated, the aqueous layer was extracted three times with ether (20 mL), and the organic solution was washed with aqueous saturated NH_4Cl, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by radial chromatography (5:1 to 2:1 = hexanes/ethyl acetate) to give the cyclized aldol adduct **40a** (367 mg, 73%) as a colorless oil: $[\alpha]^{28}_D$ −50.4°, $[\alpha]^{28}_{577}$ −54.8°, $[\alpha]^{28}_{546}$ −62.1°, $[\alpha]^{28}_{435}$ −103.5°, $[\alpha]^{28}_{405}$ −122.6° (c = 3.13, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.42 (m, 3 H, aromatic H), 7.30 (m, 2 H, aromatic H), 5.69 (d, J = 7.3 Hz, 1 H, OC*H*Ph), 4.78 (apparent quintet, J = 6.7 Hz, 1 H, NC*H*Me), 4.62 (m, 1 H, OC*H* lactone), 4.05 (apparent q, J = 8.4 Hz, 1 H, O=CC*H*), 3.48 (m, 2 H, CH_2-Br), 3.42 (td, J = 12.2, 2.6 Hz, 1 H, SC*H*), 3.34 (td, J = 14.4, 2.6 Hz, 1 H, SC*H*), 2.86 (dd, J = 13.7, 9.8 Hz, 1 H, $CH_aH_bCS_2$), 2.78 (broadened dt, J = 13.6 Hz, 1 H, SC*H*), 2.71 (broadened dt, J = 14.2 Hz, 1 H, SC*H*), 2.31 (dd, J = 13.7, 8.2 Hz, 1 H, $CH_aH_bCS_2$), 2.13 (m, 2 H, dithiane and bromoalkyl chain), 1.99 (m, 2 H, dithiane and bromoalkyl chain), 1.86 (m, 2 H, bromoalkyl chain); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.2, 152.5, 132.9, 128.9, 128.7, 125.6, 90.1, 81.0, 79.1, 55.0, 47.9, 46.1, 33.5, 32.3, 29.6, 28.6, 28.5,

(50) Stork, G.; Kobayashi, Y.; Suzuki, T.; Zhao, K.; *J. Am. Chem. Soc.* **1990**, *112*, 1661.

24.5, 14.4; IR (neat) 2934 w, 1782 s, 1697 s, 1456 w, 1345 s, 1276 w, 1219 m, 1197 m, 1150 w, 1122 m, 1067 m, 1040 w, 977 m, 765 w, 735 w, 701 m cm^{-1}; MS (EI, 70 eV) *m/e* (rel inten) 501 (M^+, ^{81}Br, 2), 499 (M^+, ^{79}Br, 2), 349 (11), 286 (81), 244 (24), 215 (12), 172 (81), 160 (47), 145 (22), 134 (49), 118 (100), 107 (75), 91 (39), 87 (34), 81 (76), 71 (64), 61 (18), 55 (63); MS (CI, isobutane) *m/e* (rel inten) 502 (MH^+, ^{81}Br, 100), 500 (MH^+, ^{79}Br, 87), 420 (18), 350 (23), 133 (32), 107 (49); HRMS (EI, 70 eV) calcd for $C_{12}H_{26}NO_4S_2Br$: 499.0470. Found: 499.0470.

2,2-[(2*R*,3*S*)-3-[[(4*S*)-4-(Methylethyl)-2-oxo-3-oxazolidinyl]carbonyl]-2-(3-bromopropyl)-1-oxa-1,4-butanediyl]-1,3-dithiane (40b). As described for **40a**, the boron enolate of the carboximide ketene dithioacetal **4b** (100 mg starting material, 0.33 mmol in 1.25 mL of CH_2Cl_2) was condensed with bromobutanal (257 mg, 1.70 mmol in 2 mL of CH_2Cl_2) to give the cyclic aldol adduct **40b** (115 mg, 77%) as a colorless oil: ^1H NMR (500 MHz, $CDCl_3$) δ 4.64 (collapsed ddd (6 lines), *J* = 7.8, 5.2 Hz, 1 H, OC*H*), 4.46 (overlapping dt, *J* = 8.6, 3.4 Hz, 1 H, NC*H*), 4.30 (apparent t, *J* = 9.1 Hz, 1 H, OCH_aH_b), 4.25 (dd, *J* = 9.1, 3.4 Hz, 1 H, OCH_aH_b), 3.98 (overlapping dt, *J* = 10.2, 8.2 Hz, 1 H, O=CC*H*), 3.46 (m, 2 H, CH_2Br), 3.40 (overlapping ddd, *J* = 13.8, 12.4, 2.8 Hz, 1 H, SC*H*), 3.32 (overlapping ddd, *J* = 14.1, 12.6, 2.6 Hz, 1 H, SC*H*), 2.87 (dd, *J* = 13.7, 10.2 Hz, 1 H, CH_cH$_d$-CS_2), 2.77 (m, 1 H, SC*H*), 2.10 (m, 1 H, SC*H*), 2.35 (m, 1 H, *H*CMe$_2$), 2.26 (dd, *J* = 13.7, 7.9 Hz, 1 H, CH$_c$*H*$_d$$CS_2$), 2.12 (m, 2 H, dithiane and bromoalkyl chain), 1.97 (m, 2H, dithiane and bromoalkyl chain), 1.82 (m, 2H, bromoalkyl chain); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.4, 153.4, 90.0, 80.5, 63.5, 58.4, 48.0, 46.3, 33.4, 32.4, 29.6, 28.6, 28.5, 28.3, 24.5, 17.9, 14.7; IR (neat) 2962 m, 1777 s, 1694 s, 1386 s, 1372 s, 1300 s, 1204 s, 1095 m, 1056 m, 1019 m, 974 w, 912 w, 736 w, 714 w cm^{-1}; MS (EI, 70 eV) *m/e* (rel inten) 453 (M^+, ^{81}Br, 37), 451 (M^+, ^{79}Br, 33), 319 (54), 317 (52), 238 (100), 188 (40), 130 (99), 106 (59), 81 (53); HRMS (CI, isobutane) calcd for $C_{17}H_{27}NO_4S_2Br$: 452.0564. Found: 452.0561.

2,2-[(2*S*,3*S*)-3-[[(4*S*)-4-(Methylethyl)-2-oxo-3-oxazolidinyl]carbonyl]-2-phenyl-1-oxa-1,4-butanediyl]-1,3-dithiane (40c). As described for **40a**, the boron enolate of the carboximide ketene dithioacetal **4b** (100 mg starting material, 0.33 mmol in 1.25 mL of CH_2Cl_2) was condensed with benzaldehyde (1.70 mmol in 2 mL of CH_2Cl_2) to give the cyclic aldol adduct **40c** (105 mg, 78%) as a colorless oil: ^1H NMR (500 MHz, $CDCl_3$) δ 7.48 (m, 2 H, phenyl H), 7.35 (m, 3 H, phenyl H), 5.67 (d, *J* = 9.3 Hz, 1 H, OC*H*Ph), 4.39 (m, 1 H, NC*H*), 4.24 (m, 1 H, O=C-C*H*), 4.17 (m, 2 H, OCH_2), 3.48 (broadened dt, *J* = 11 Hz, Δν = 36.8 Hz, 2 H, SCH_2), 3.10 (dd, *J* = 13.5, 9.8 Hz, 1 H, C$H_aH_b$$CS_2$), 2.81 (collapsed dt, *J* = 13.9 Hz, 1 H, SCH), 2.73 (collapsed dt, *J* = 13.9 Hz, 1 H, SC*H*), 2.37 (m, 2 H, CH$_a$*H*$_b$$CS_2$ and C*H*Me$_2$), 2.14 (m, 1 H, dithiane H), 2.03 (m, 1 H, dithiane H); IR (neat) 2926 m, 2922 m, 1778 s, 1698 s, 1386 s, 1301 m, 1276 m, 1252 m, 1205 s, 1075 m, 1032 m, 977 m, 907 m, 731 m, 709 m cm^{-1}; MS (EI, 70 eV) *m/e* (rel inten) 407 (M^+, 21), 301 (18), 273 (27), 259 (42), 172 (100), 144 (80), 131 (67), 106 (77); MS (CI, isobutane) *m/e* (rel inten) 408 (MH^+, 10), 131 (54), 130 (100), 107 (52). HRMS (CI, isobutane) calcd for $C_{20}H_{26}NO_4S_2$: 407.1225. Found: 407.1215.

(β*S*,γ*R*)-γ-(3-Bromopropyl)-β-[[(4*S*)-4-(methylethyl)-2-oxo-3-oxazolidinyl]carbonyl]-γ-butyrolactone (41b). The cyclic aldol adduct **40b** (50.0 mg, 0.10 mmol) in dichloromethane (1 mL) was treated with toluenesulfonic acid (10 mg) and stirred for 1 h. The solution was diluted with water (1 mL) and the layers were separated. The aqueous layer was extracted with Et_2O (3 × 1 mL). The combined organic extracts were washed with H_2O and brine, dried ($MgSO_4$), and concentrated. Purification by radial chromatography (5:1 = hexanes/Et_2O) gave the acylated lactone (31.5 mg, 87%): ^1H NMR (500 MHz, $CDCl_3$) δ 4.81 (collapsed ddd (seven lines), *J* = 9.2, 5.8, 3.4 Hz, 1 H, OC*H*), 4.47 (m, 1 H, NC*H*), 4.35 (apparent t, *J* = 9.0 Hz, 1 H, OCH_aH_b), 4.27 (dd, *J* = 9.0, 2.9 Hz, 1 H, OCH_aH_b), 4.18 (dt, *J* = 8.2, 6.8 Hz, 1 H, O=CC*H*), 3.44 (m, 2 H, CH_2Br), 3.06 (dd, *J* = 17.6, 9.4 Hz, 1 H, CH_cH$_d$C=O), 2.69 (dd, *J* = 17.6, 7.4 Hz, 1 H, CH$_c$*H*$_d$C=O), 2.36 (m, 1 H, C*H*Me$_2$), 2.10 (m, 1 H, bromoalkyl chain), 1.95 (m, 2 H, bromoalkyl chain), 1.81 (m, 1 H, bromoalkyl chain), 0.93 (d, *J* = 7.0 Hz, 3 H, CH_3), 0.87 (d, *J* = 7.0 Hz, 3 H, CH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.8, 170.5, 153.6, 80.3, 63.8, 58.6, 45.0, 33.5, 32.8, 32.5, 28.6, 28.1, 17.8, 14.6; IR (neat) 2964 m, 2876 w, 1778 s, 1698 s, 1388 s, 1302 m, 1274 m, 1206 s, 1108 m, 1062 m, 1028 m, 978 w, 773 w, 710 w cm^{-1}; MS (EI, 70 eV) *m/e* (rel inten) 240 (6), 235 (4), 233 (4), 184 (62), 149 (20), 130 (100), 111 (27), 97 (15), 86 (66), 70 (55); MS (CI, isobutane) *m/e* (rel inten) 364 (MH^+, ^{81}Br, 19), 362 (MH^+, ^{79}Br, 20), 282 (7), 155 (12), 130 (100); HRMS (CI, isobutane) calcd for $C_{14}H_{21}NO_5Br$: 362.0603. Found: 362.0587.

2,2-[(2*R*,3*S*)-3-Carboxy-2-(3-bromopropyl)-1-oxa-1,4-butanediyl]-1,3-dithiane (42b). The cyclic aldol adduct **40b** (50.0 mg, 0.10 mmol) was treated with a solution of LiOOH (1.5 mL of a stock solution prepared from 30% H_2O_2 (1.1 mL, 10 mmol) in THF (10 mL) and H_2O (5 mL) and LiOH (120 mg, 5.0 mmol)) and stirred at ambient temperature overnight. The mixture was washed with aqueous HCl buffer (pH 4, 5 mL) and extracted three times with ether (5 mL). The organic solution was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by radial chromatography (1:1 = hexanes/ether, then 1:1:0.1 = hexanes/ether/MeOH) to give the dithiane lactone acid **42b** (26.3 mg, 77%) as a colorless film: ^1H NMR (500 MHz, $CDCl_3$) δ 4.34 (td, *J* = 8.6, 3.4 Hz, 1 H, OC*H*), 3.49 (m, 2 H, CH_2Br), 3.41 (overlapping ddd, *J* = 13.7, 2.6 Hz, 2 H, SC*H*), 3.32 (overlapping ddd, *J* = 12.7, 2.6 Hz, 1 H, SC*H*), 3.00 (dd, *J* = 9.7, 8.5 Hz, 1 H, O=CC*H*), 2.78 (broadened dt, *J* = 13.9, 3.1 Hz, 1 H, SC*H*), 2.72 (broadened dt, *J* = 13.9, 3.1 Hz, 1 H, SC*H*), 2.59 (dd, *J* = 13.9, 3.1 Hz, 1 H, C$H_aH_b$$CS_2$), 2.52 (dd, *J* = 13.9, 9.8 Hz, 1 H, CH$_a$*H*$_b$$CS_2$), 2.15 (m, 2 H, dithiane and bromoalkyl chain), 2.01 (m, 3 H, dithiane and bromoalkyl chain), 1.89 (m, 1 H, bromoalkyl chain); ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.2, 90.2, 81.2, 48.3, 44.6, 33.3, 32.9, 29.5, 28.4, 24.5; IR (neat) 3631–2533 (broad) m, 2913 s, 2851 m, 1708 s, 1424 m, 1276 m, 1251 m, 1215 w, 1026 m, 976 m, 907 m, 873 w, 809 w cm^{-1}; MS (CI, isobutane) *m/e* (rel inten) 343 (MH^+, ^{81}Br, 100), 341 (MH^+, ^{79}Br, 92), 313 (34), 261 (59), 243 (37), 207 (20), 190 (35), 163 (30), 106 (72). HRMS (CI, isobutane) calcd for $C_{11}H_{18}O_3S_2Br$: 340.9881. Found: 340.9883.

Acknowledgment. This research was supported by grants from the National Institutes of Health (NS 27600 and NS 01227). We are grateful to Laura J. Dardashti and Dr. Hua D. Nguyen for technical assistance.

Supplementary Material Available: ^1H NMR spectra for all compounds with HRMS (29 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.