A New Approach to the Synthesis of β-Hydroxy-α-amino Acids Using (Arylthio)nitrooxiranes

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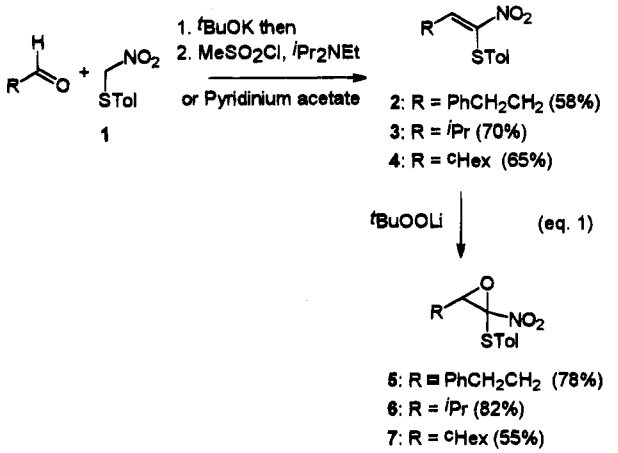
2-(Arylthio)-2-nitrooxiranes, prepared by the nucleophilic epoxidation of 1-(arylthio)-1-nitroalkenes using anhydrous metal alkyl peroxides in tetrahydrofuran, react with aqueous ammonia to give α-amino thioesters in good yield, without significant formation of the primary amide by subsequent reaction of the thioester with ammonia. *In situ* protection of the amino group is possible, leading to a range of protected derivatives. Diastereoselective epoxidation of 1-(arylthio)-1-nitroalkenes with an allylic, oxygen-substituted stereogenic center using metal alkyl peroxides is possible, and the sense of diastereoselectivity can be controlled simply by use of lithium or potassium as the counterion. Enhanced *syn* selectivity (15:1) in lithium *tert*-butyl peroxide mediated epoxidations can be achieved by using toluene as solvent. Use of potassium triphenylmethyl peroxide, rather than potassium *tert*-butyl peroxide, generally gives higher *anti* selectivity (12:1). Reactions of enantiomerically and diastereoisomerically pure 2-(arylthio)-2-nitrooxiranes with ammonia proceed stereospecifically with inversion of configuration, establishing a stereocontrolled route to β-hydroxy-α-amino acids. Use of other nitrogen nucleophiles, for example amino acid esters, is also possible, leading to a stereospecific approach to α-amino dicarboxylic acids. Applications of this methodology, which constitutes a stereocontrolled Strecker reaction, to the synthesis of γ-hydroxy threonine derivatives **19**–**22**, polyoxamic acid (**26**), and the C-5 epimer of the sugar fragment of polyoxin C (**27**) are described.

Over the past 50 years, many nonproteinogenic amino acids have been isolated from natural sources. β-Hydroxy-α-amino acids represent an important class of these compounds, and a number of excellent methods for their construction have been established,[1] the most general and direct of which have employed the reaction of chiral nucleophilic glycine equivalents with aldehydes.[2]

In a previous paper we have shown that 2-nitro-2-(phenylthio)oxiranes, prepared by nucleophilic epoxidation of 1-nitro-1-(phenylthio)alkenes, react with oxygen and halide nucleophiles under mild conditions to give α-substituted *S*-phenyl thioesters.[3] We now report a new method for generating α-amino acid derivatives *via* an extension of this ring opening methodology to include nitrogen nucleophiles, together with applications to the stereoselective synthesis of β-hydroxy-α-amino acids.[4]

Results and Discussion

The alkenes **2**, **3**, and **4** were prepared from the corresponding aldehydes by condensation with [(4-methylphenyl)thio]nitromethane (**1**, eq 1). [(4-Methylphenyl)thio]nitromethane (**1**)[5] was used in preference to (phenylthio)nitromethane since compounds derived from **1** carry a distinctive marker in the ^{1}H NMR. Treatment of the electron deficient alkenes **2**, **3**, and **4** with lithium *tert*-butyl peroxide (^{t}BuOOLi) in THF at −78 °C according to our previously reported method[3] resulted in rapid epoxidation to give the corresponding 2-(tolylthio)-2-nitrooxiranes **5**, **6**, and **7** in good yield.



Many examples of the reaction of oxiranes with amines as a method for regio- and stereoselective introduction of amino functionality into a molecule have been described, and several of these methods have been em-

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(1) For a general review, see: Williams, R. M. *Synthesis of Optically Active* α-Amino Acids; Pergamon Press: Oxford, 1989. Duthaler, R. O. *Tetrahedron* 1994, 50, 1539.

(2) For some representative examples, see: Schöllkopf, U.; Groth, U.; Gull, M.-R.; Nozulak, J. *Liebigs Ann. Chem.* **1983**, 1133. Evans, D. A.; Weber, A. E. *J. Am. Chem. Soc.* **1986**, *108*, 6757. Reno, D. S.; Lotz, B. T.; Miller, M. J. *Tetrahedron Lett.* **1990**, *31*, 827. Blaser, D.; Seebach, D. *Liebigs Ann. Chem.* **1991**, 1067.

(3) Ashwell, M.; Jackson, R. F. W.; Kirk, J. M. *Tetrahedron* **1990**, *21*, 7429.

(4) For preliminary accounts of some of the work reported in this paper, see: Jackson, R. F. W.; Kirk, J. M.; Palmer, N. J.; Waterson, D.; Wythes, M. J. *J. Chem. Soc., Chem. Commun.* **1993**, 889. Jackson, R. F. W.; Palmer, N. J.; Wythes, M. J. *J. Chem. Soc., Chem. Commun.* **1994**, 95.

(5) Prepared by coupling of nitromethane with 4-methylbenzenesulfenyl chloride according to Barrett's procedure for the preparation of (phenylthio)nitromethane: Barrett, A. G. M.; Dhanak, D.; Graboski, G. G.; Taylor, S. J. *Org. Synth.* **1989**, *68*, 8. See also: Seebach, D.; Lehr, F. *Helv. Chim. Acta* **1979**, *62*, 2239.

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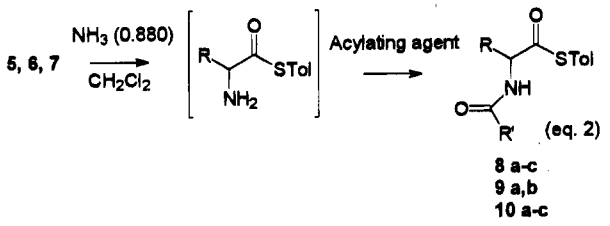
Table 1. Ring Opening of Oxiranes 5, 6, and 7 with Ammonia and *in Situ* Protection

oxirane	R	R′	product	yield (%)
5	$PhCH_2CH_2$	Me	**8a**	81
5	$PhCH_2CH_2$	^{t}BuO	**8b**	70
5	$PhCH_2CH_2$	$PhCH_2O$	**8c**	74
6	^{i}Pr	Me	**9a**	77
6	^{i}Pr	^{t}BuO	**9b**	69
7	c-Hex	Me	**10a**	63
7	c-Hex	^{t}BuO	**10b**	67
7	c-Hex	$PhCH_2O$	**10c**	61

ployed in the synthesis of β-hydroxy-α-amino acids.[6] One of the most direct of these methods involves ring opening of epoxy acids with ammonia or benzylamine. 2-(Arylthio)-2-nitrooxiranes **5**, **6**, and **7** are too hydrophobic to dissolve in the aqueous media usually employed in these reactions.[7] However, treatment of oxiranes **5**, **6**, and **7** in dichloromethane with aqueous ammonia (specific gravity 0.880, about 35%) at room temperature resulted in ring opening of the oxirane and loss of the nitro group to give the corresponding α-amino thioester. The rate of reaction of the isopropyl (**6**) and cyclohexyl (**7**) substituted oxiranes with ammonia is considerably slower than the phenylethyl derivative **5**, probably due to steric hindrance. The free amine can be isolated or, more conveniently, treated with an acylating agent *in situ* to provide the protected α-amino *S*-tolyl thioester (eq 2) (see Table 1). The mildness of the reaction conditions together with the variety of different protecting groups that can be introduced make this a useful method for preparing racemic N-protected α-amino thioesters. The biphasic conditions employed are essential for clean reaction; treatment of the oxiranes with NH_3 in MeOH or THF, under homogeneous reaction conditions, resulted in extensive decomposition.



An X-ray crystal structure analysis of the cyclohexyl-substituted oxirane **7** illustrates the distortion in the oxirane (Figure 1).[8] The degree of asymmetry in the C–O bonds of the oxirane ring[9] is the largest we have seen during our studies of hetero-substituted oxiranes, being slightly more pronounced than the (large) distortion observed in sulfoximinooxiranes.[10] The preferential nucleophilic attack at C(2) can be partly explained by fission of the longer, weaker O(1)–C(2) bond, with the short

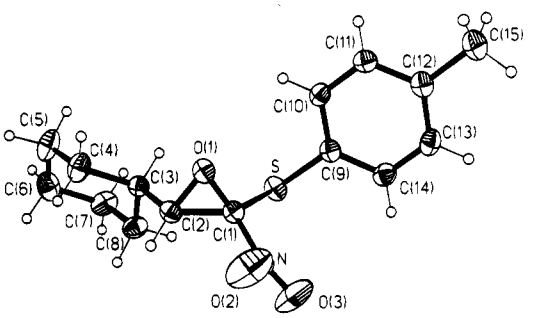


Figure 1. Structure of **7** with atom labeling and 40% ellipsoids. Selected bond lengths (Å): O(1)–C(1) 1.394 (2), O(1)–C(2) 1.466 (2), C(1)–C(2) 1.468 (3).

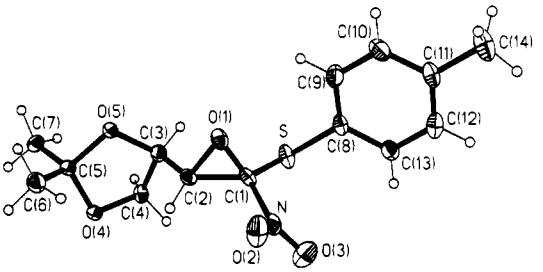
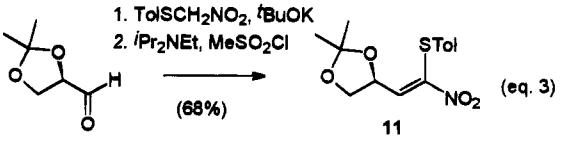


Figure 2. Structure of **12** with atom labeling and 40% ellipsoids. Selected bond lengths (Å): O(1)–C(1) 1.398 (7), O(1)–C(2) 1.463 (6), C(1)–C(2) 1.478 (6).

O(1)–C(1) bond ultimately becoming the double bond of the carbonyl group of the thioester. Although we have no quantitative data, there appears to be a reasonable correlation between the degree of asymmetry in the oxirane and the reactivity toward nucleophilic reagents.

We decided to examine the possibility of stereoselective nucleophilic epoxidation of the 1-nitro-1-(tolylthio)alkene **11** containing an allylic oxygen stereocenter as a potential stereocontrolled route to γ-hydroxythreonine. Related diastereoselective additions to 1-nitro-1-(phenylthio)-alkenes have been reported,[11] and attention has been drawn to the importance of the steric bulk (and shape) of the nucleophile.[12] The alkene **11** was prepared from D-isopropylideneglyceraldehyde by condensation with [(4-methylphenyl)thio]nitromethane (eq 3).



Epoxidation of **11** with ^{t}BuOOLi in THF at −78 °C gave a mixture of *syn* and *anti* oxiranes **12** and **13** (ratio 5:1), from which the major *syn* isomer **12** could be obtained pure (60%) by crystallization from pentane (eq 4). An X-ray crystal structure analysis of the oxirane **12** established its structure unambiguously (Figure 2).[8] Significant distortion in the oxirane ring was observed, analogous to that in the structure of oxirane **7**. This result suggests that the distortion is principally due to the arylthio and nitro substituents and is therefore a general characteristic of this functional group. Epoxidation of **11** with potassium *tert*-butyl peroxide (^{t}BuOOK) in THF at −78 °C resulted in a reversal in the diastereoselec-

(6) For example, see: Pons, D.; Savignac, M.; Durand, J. O.; Genêt, J.-P. *Tetrahedron Lett.* **1992**, *33*, 2497. Caldwell, C. G.; Bondy, S. S. *Synthesis*, **1990**, 34. Cardini, S.; Bernardi, A.; Colombo, L.; Gennari, C.; Scolastico, C.; Venturini, I. *Tetrahedron* **1988**, *44*, 5563.

(7) For a discussion of the role of solvent on the reaction of amines with oxiranes, see: Parker, R. E.; Rockett, B. W. *J. Chem. Soc.* **1965**, 2569.

(8) The authors have deposited atomic coordinates for compounds **7** and **12** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from The Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, U.K.

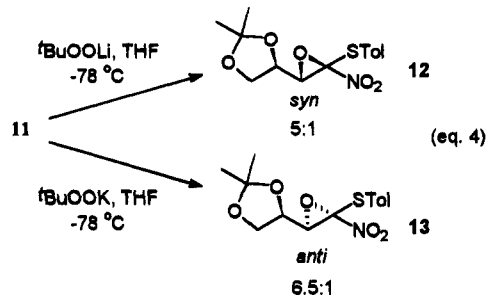
(9) A typical value for the C–O bond length in an oxirane is 1.44 Å; for a comprehensive discussion, see Allen, F. H. *Tetrahedron* **1982**, *38*, 2843.

(10) Bailey, P. L.; Clegg, W.; Jackson, R. F. W.; Meth-Cohn, O. *J. Chem. Soc., Perkin Trans. 1* **1993**, 343.

(11) Barrett A. G. M.; Lebold, S. A. *J. Org. Chem.* **1990**, *55*, 3853.

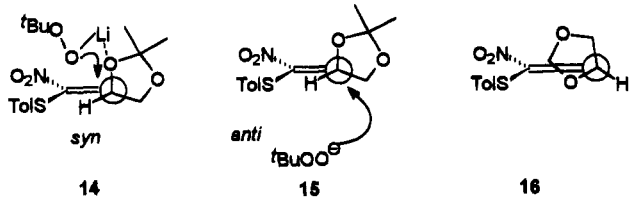
(12) Barrett, A. G. M.; Weipert, P. D.; Dhanak, D.; Husa, R. K; Lebold, S. A. *J. Am. Chem. Soc.* **1991**, *113*, 9820.

tivity, with the *anti* oxirane **13** now the major isomer (ratio of **12** to **13** 1:6.5) (eq 4). Column chromatography afforded **13** as a pure diastereoisomer (63%).



(eq. 4)

These results can be rationalized by assuming that the alkene adopts a reactive conformation in which the allylic hydrogen occupies the inside position, minimizing 1,3-allylic strain.[13] We ascribe the preferential *syn* epoxidation observed when ^{t}BuOOLi is used as the oxidizing agent to coordination between the lithium cation, the allylic oxygen, and the peroxide oxygen, which results in the peroxide oxygen being delivered to the most sterically hindered face (see conformation **14**). When ^{t}BuOOK is used, the possibility of coordination is much reduced, so steric and electronic effects[14] play a larger part. This results in delivery of the reagent to the least sterically hindered face, *anti* to the allylic oxygen (see conformation **15**). In principle, an alternative conformation in which the allylic C–O bond eclipses the carbon–sulfur bond (conformer **16**, methyl groups omitted for clarity) could also account for the observed stereoselectivity. In this case, *syn* epoxidation would be due to coordination of lithium to the δ-oxygen,[15] while attack from the less sterically hindered face would lead to the *anti* isomer. In a related system, Barrett has drawn attention to the possibility that allylic strain may not always be a critical factor in controlling the stereochemical outcome of nucleophilic additions to 1-(arylthio)-1-nitroalkenes.[16] Specifically, the point was made that the long carbon-sulfur bond, and the possibility for the *S*-aryl substituent to rotate out of the plane of the double bond, results in a significant reduction in allylic strain, so that conformations with a relatively bulky group in the inside position are not expected to be especially disfavored. Nevertheless in our case, we believe that the bulky isopropylidene group means that conformation **16** is unlikely to be important.



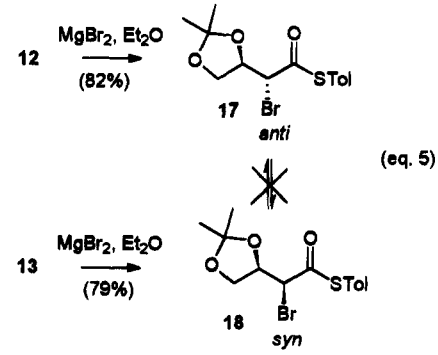
To investigate the balance between steric effects and coordination control further, the reactions were repeated using bulkier epoxidizing reagents.[17] Epoxidation with lithium triphenylmethyl peroxide (Ph_3COOLi) in THF at −78 °C resulted in a mixture of oxiranes **12** and **13**, in a 1:4 ratio. Using potassium triphenylmethyl peroxide (Ph_3COOK) as the oxidant, under the same reaction conditions, gave the oxiranes **12** and **13**, in a 1:12 ratio. In both cases the *anti* oxirane **13** is the major product. While the result for epoxidation with potassium triphenylmethyl peroxide was expected from the proposed model, it appears that for the very bulky lithium triphenylmethyl peroxide steric effects now outweigh those due to coordination.

Table 2. Epoxidation of Alkene 11 with a Range of Nucleophilic Epoxidizing Reagents

	products	
reagent	*syn* **12**	*anti* **13**
^{t}BuOOLi/THF	5	1
^{t}BuOOLi/Toluene	15	1
^{t}BuOOK/THF	1	6.5
Ph_3COOLi/THF	1	4
Ph_3COOK/THF	1	12

With a view to enhancing the effects of coordination control, and therefore the extent of *syn* selectivity, the epoxidation reaction with lithium *tert*-butyl peroxide was repeated using toluene, rather than THF, as solvent. To our satisfaction, the diastereoselectivity rose to 15:1 in favor of the *syn* oxirane **12**, suggesting that the effects of coordination had indeed been enhanced. These results are summarized in Table 2.

The purified oxiranes **12** and **13** were converted into the stereoisomeric *anti* and *syn* α-bromo *S*-tolyl thioesters **17** (85%) and **18** (83%), respectively, using magnesium bromide in ether (eq 5). No interconversion of the two diastereoisomers was observed under the reaction conditions. An X-ray crystal structure analysis of the α-bromo *S*-tolyl thioester **17** confirmed that it possessed the *anti* configuration[18] and therefore that the oxirane ring-opening reaction had proceeded with inversion of configuration.

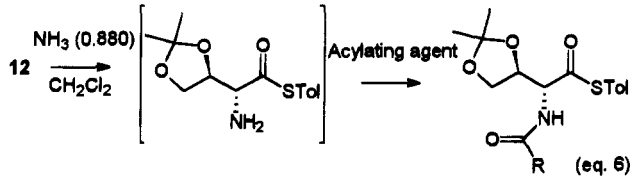


(eq. 5)

Reaction of oxirane **12** in dichloromethane with aqueous ammonia at room temperature yielded the α-amino thioester, which was treated, as before, with a number of different acylating agents *in situ* to provide the corresponding protected α-amino *S*-tolyl thioesters **19**–**22** in good yield (eq 6). Each of these products was diastereoisomerically pure. An X-ray crystal structure analysis of the γ-hydroxythreonine derivative **20** estab-

(13) Hoffmann, R. W. *Chem. Rev.* **1989**, *89*, 1841.
(14) Chérest, M.; Felkin, H.; Prudent, N. *Tetrahedron Lett.* **1968**, 2199. Chérest, M.; Felkin, H. *Tetrahedron Lett.* **1968**, 2205. Anh, N. T. *Top. Curr. Chem.* **1980**, *88*, 145.
(15) For related suggestions in the reaction of alkyllithium reagents with unsaturated esters derived from isopropylideneglyceraldehyde, see: Leonard, J.; Ryan, G.; Swain, P. A. *Synlett* **1990**, 613.
(16) Barrett, A. G. M.; Rys, D. J. *J. Chem. Soc., Perkin Trans. 1* **1995**, 1009.
(17) For an example of the use of triphenylmethyl hydroperoxide/benzyltrimethylammonium isopropoxide, see: Corey, E. J.; Kang, M.-c.; Desai, M. C.; Ghosh, A. K.; Houpis, I. N. *J. Am. Chem. Soc.* **1988**, *110*, 649.
(18) Clegg, W.; Dunbar, J. M.; Elsegood, M. R. J.; Jackson, R. F. W.; Palmer, N. J. *Acta Crystallogr.* **1995**, *C51*, in press.

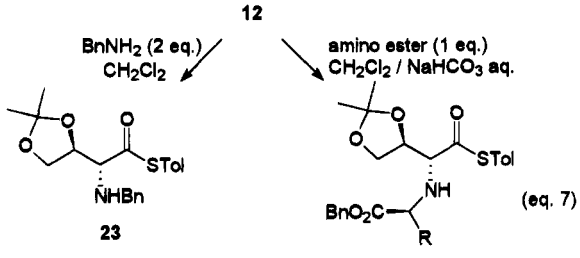
lished that the α-nitrogen and β-oxygen are *anti* to each other.[18] This in turn established that ring opening of oxirane **12** with ammonia proceeds stereospecifically with inversion of configuration.



19: R = *t*BuO (67%)
20: R = BnO (69%)
21: R = Ph (61%)
22: R = Me (65%)

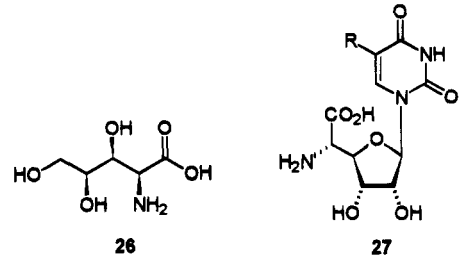
Analogous reactions using the *anti* oxirane **13** provided access to the diastereoisomeric compounds. Thus, these procedures provide rapid access to a variety of diastereoisomerically pure, fully protected γ-hydroxythreonine derivatives.[19]

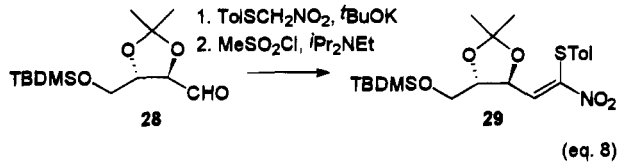
The ring opening reaction of 2-(tolylthio)-2-nitrooxiranes can be extended to include primary amines. Thus oxirane **12** was found to react with benzylamine in dichloromethane to give the benzyl protected derivative **23** directly (eq 7). Two equivalents of the amine are required, with 1 equiv acting as a base. Other primary amines such as leucine benzyl ester and phenylalanine benzyl ester also react satisfactorily. The need for 2 equiv of these more expensive reagents can be avoided by treating oxirane **12** with 1 equiv of the amine in a vigorously stirred biphasic system consisting of dichloromethane and aqueous sodium bicarbonate. Using this method, good yields of the α-amino thioester products **24** and **25** were obtained diastereoisomerically pure (eq 7). These products are amino dicarboxylic acid derivatives and closely resemble the structural unit found in ACE inhibitors like enalapril.[20]



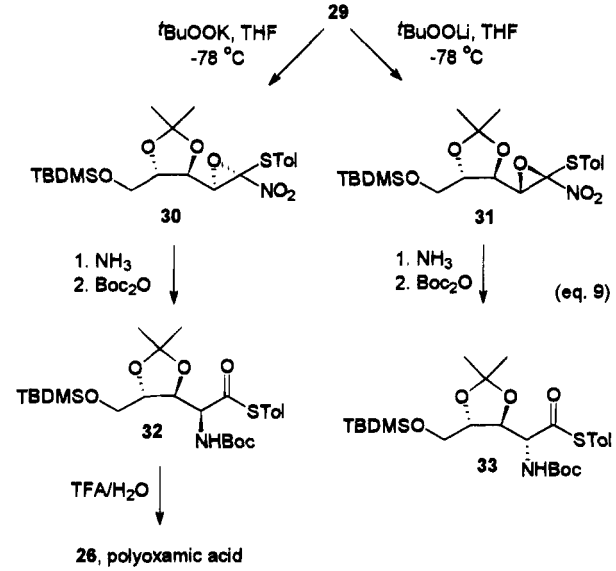
24: R = Bn (87%)
25: R = $CH_2{}^iPr$ (79%)

We wished to exploit further this diastereoselective epoxidation reaction. With this in mind we selected the polyoxins as suitable targets as both of the components, polyoxamic acid (**26**)[21-24] and polyoxin C (**27**),[11,25] should in principle be accessible using this methodology. The alkene **29** was prepared by condensation of [(4-methylphenyl)thio]nitromethane with the aldehyde **28**, itself prepared in two steps[23,26] from commercially available 2,3-isopropylidene-L-threitol (eq 8).





Nucleophilic epoxidation of the alkene **29** with *t*BuOOK gave a mixture of the two diastereoisomeric oxiranes **30** and **31**, (87%) (eq 9). Analytical HPLC indicated a stereoisomeric ratio of 25:1. The major isomer **30** was assigned *anti* stereochemistry on the basis of epoxidation of alkene **11** to give oxirane **13**, and also on the basis of subsequent transformations. Epoxidation of the alkene **29** with *t*BuOOLi in THF gave the oxiranes **30** and **31** (86%), with a ratio of 5:1 in favor of **31** (eq 9). This ratio increased to 15:1 in favor of the *syn* oxirane **31** when toluene was used as the solvent.



Reaction of the *anti* oxirane **30** with ammonia, followed by treatment with *tert*-butyl pyrocarbonate, gave the *syn* Boc-protected α-amino thioester **32** (65%), after chro-

(19) For recent approaches to the synthesis of γ-hydroxythreonine derivatives, see: Saito, S.; Bunya, N.; Inaba, M.; Moriwake, T.; Torii, S. *Tetrahedron Lett.* **1985**, *26*, 5309. Hirama, M.; Hioki, H.; Itô, S. *Tetrahedron Lett.* **1988**, *29*, 3125. Bols, M.; Lundt, I. *Acta Chem. Scand., Ser. B* **1988**, *42*, 67. Palomo, C.; Cabré, F.; Ontoria, J. M. *Tetrahedron Lett.* **1992**, *33*, 4819.

(20) Iwasaki, G.; Kimura, R.; Numao, N.; Kondo, K. *Chem. Lett.* **1988**, 1691 and references therein. For a recent alternative approach to the synthesis of amino dicarboxylic acids, see: D'Angeli, F.; Marchetti, P.; Salvadori, S.; Balboni, G. *J. Chem. Soc., Chem. Commun.* **1993**, 304.

(21) For the original isolation and structure determination, see: Isono, K.; Asahi, K.; Suzuki, S. *J. Am. Chem. Soc.* **1969**, *91*, 7490.

(22) For recent synthetic approaches and references to previous work see: Marshall, J. A.; Seletsky, B. M.; Coan, P. S. *J. Org. Chem.* **1994**, *59*, 5139. Matsuura, F.; Hamada, Y; Shiori, T. *Tetrahedron Lett.* **1994**, *25*, 733. Chida, N.; Koizumi, K.; Kitada, Y.; Yokoyama, C.; Ogawa, S. *J. Chem. Soc., Chem. Commun.* **1994**, 111. Dondoni, A.; Franco, S.; Merchán, F. L.; Merino, P.; Tejero, T. *Tetrahedron Lett.* **1993**, *43*, 5479. Paz, M. M.; Sardina, F. J. *J. Org. Chem.* **1993**, *58*, 6990.

(23) Savage, I.; Thomas, E. J. *J. Chem. Soc., Chem. Commun.* **1989**, 717.

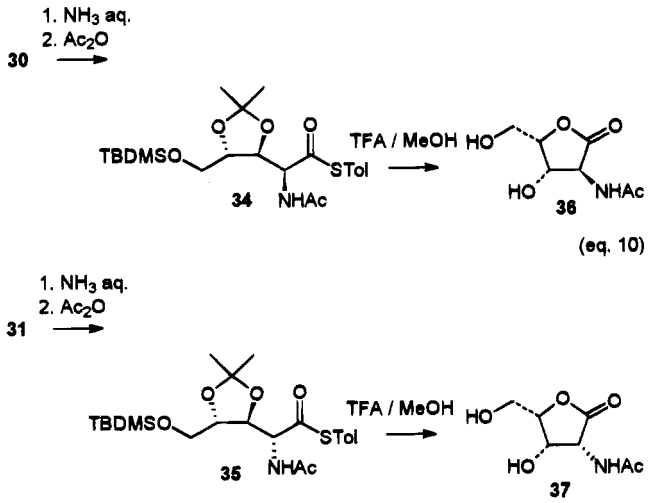
(24) Bani, B. K.; Manhas, M. S.; Bose, A. K. *J. Org. Chem.* **1993**, *58*, 307.

(25) For a recent synthetic approach, and references to earlier work, see: Dondoni, A.; Junquera, F.; Merchán, F. L.; Merino, P.; Tejero, T. *Tetrahedron Lett.* **1994**, *35*, 9439.

(26) Marshall, J. A.; Beaudoin, S. *J. Org. Chem.* **1994**, 59, 6614.

matographic separation of a trace of the *anti* thioester **33** (eq 9). Analogous treatment of the *syn* oxirane **31** gave the *anti* Boc-protected α-amino thioester **33** (55%). Each of these compounds appeared to be stereoisomerically pure by ^{1}H NMR analysis. Subsequent treatment of the α-amino thioester **32** with aqueous trifluoroacetic acid gave polyoxamic acid (**26**) (95%) (eq 9), whose spectroscopic properties were identical with those previously reported.[23]

For further confirmation of their structures, the oxiranes **30** and **31** were converted to the corresponding *N*-acetyl γ-lactones **36** and **37** (eq 10). Lactone **36** has frequently been prepared as a stable derivative of polyoxamic acid itself.[23,24,27,28] Hence reaction of the oxirane **30** with ammonia as before, followed by treatment with acetic anhydride, gave the corresponding *N*-acetylamino thioester **34**, which could not be separated from a trace amount of the other isomer. However, treatment of this mixture of thioesters with trifluoroacetic acid in methanol resulted in conversion to the γ-lactones, from which **36** was isolated by chromatography and recrystallization.



γ-Lactone **36** was found to be identical by comparison of ^{1}H and ^{13}C NMR with spectra of authentic material supplied by earlier workers.[23,24] In addition, the mp and specific rotation of our sample compared favorably with the literature values. Conversion of oxirane **31** to the γ-lactone **37** was carried out in the same way.

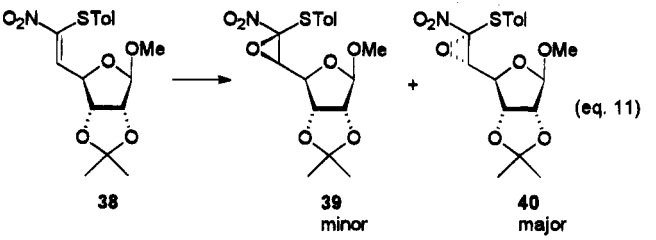
Studies toward Polyoxin C. Barrett has demonstrated the versatility of 1-(phenylthio)-1-nitroalkenes as synthetic intermediates in the synthesis of polyoxin C.[11] We envisaged that our methodology could provide an alternative synthesis of this compound. A similar approach to that already reported was adopted for the synthesis of the ribose-derived alkene **38**. Epoxidation of alkene **38** with a variety of nucleophilic epoxidizing reagents was examined, and the results obtained are summarized in Table 3. In every case the alkene was epoxidized to give a mixture of diastereoisomeric oxiranes **39** and **40** which could not be separated by flash chromatography (eq 11). Unfortunately, with the ribose-derived alkene **38**, it was not possible to reverse the diastereoselectivity by changing from lithium to potassium as counterion.

To establish the sense of epoxidation, it was necessary to convert one of the oxiranes into a derivative which

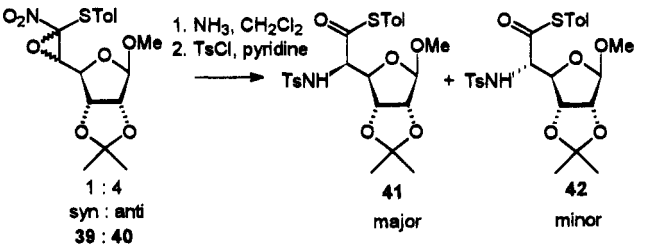
(27) Ikota, N. *Chem. Pharm. Bull.* **1989**, *37*, 3399.
(28) Saksena, A. K.; Lovey, R. G.; Girijvallabahan, V. M.; Ganguly, A. K.; McPhail, A. T. *J. Org. Chem.* **1986**, *51*, 5024.

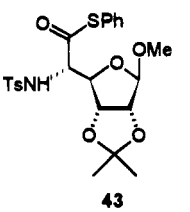
Table 3. Epoxidation of Alkene 38 with a Range of Nucleophilic Epoxidizing Reagents

reagent	products: *syn* **39**	products: *anti* **40**
^{t}BuOOLi/THF	1	6
^{t}BuOOK/THF	1	12
Ph_3COOK/THF	1	20
Ph_3COOLi/THF	1	5
^{t}BuOOLi/Toluene	1	4



could be compared with a known compound. The α-sulfonamido thioester **43** appeared to be an appropriate compound for comparison, since the two closely related derivatives **41** and **42** should be accessible from the appropriate oxirane precursor using the methodology we had developed. Thus, ring opening of the 4:1 mixture of oxiranes with ammonia produced an inseparable mixture of α-amino thioesters which were isolated (eq 12). Treatment of this mixture with *p*-toluenesulfonyl chloride gave the sulfonamides **41** and **42**, which were separated by flash chromatography. This two-step procedure was necessary in this instance as *in situ* protection was not efficient when *p*-toluenesulfonyl chloride was used. The spectral data and specific rotation of the minor diastereoisomer **42** closely matched those reported for the known compound **43**,[12] while those for the major diastereoisomer **41** were quite distinct.[29]





Since ring opening of these oxiranes occurs with inversion of configuration, the major component of the 4:1 mixture of oxiranes must have been the *anti* diastereoisomer **40**. By comparison of the ^{1}H NMR spectra we concluded that the *anti* oxirane was the major product in all the epoxidation reactions. Unfortunately ring opening with ammonia provides the unnatural diastereoisomer as the major product, so this methodology cannot be applied to a total synthesis of the polyoxins. It does

(29) See supporting information for a detailed comparison of the spectral data.

however provide an efficient route to compound **41**, epimeric with the natural series, provided the epoxidation of the alkene **38** is carried out with potassium triphenylmethyl peroxide.

In conclusion, we have developed a new and flexible approach to the synthesis of β-hydroxy-α-amino acids in which the key steps are diastereoselective nucleophilic epoxidation of 1-(arylthio)-1-nitroalkenes followed by amine ring opening to furnish the amino acid. The overall process constitutes a stereocontrolled Strecker reaction, providing fully protected amino acid derivatives which are suitable for subsequent transformations.

Experimental Section

General experimental procedures have already been described.[3] Specific rotations were measured at 20 °C, unless otherwise stated. NMR spectra were recorded in $CDCl_3$ as solvent, referenced to TMS, unless stated otherwise. Coupling constants are given in hertz. Mass spectral data refer to the isotope ^{79}Br. [(4-Methylphenyl)thio]nitromethane was prepared according to the procedure described for the preparation of (phenylthio)nitromethane.[5] Isopropylideneglyceraldehyde was prepared by the literature procedure.[30] Organic extracts were dried over $MgSO_4$, and the solvent was then removed using a rotary evaporator.

General Procedures for Preparation of 2-Nitro-2-(tolylthio)oxiranes. Method A: ^{t}BuOOH/BuLi/Toluene. ^{n}BuLi (0.81 mmol, in hexanes) was added to a solution of ^{t}BuOOH (1.02 mmol, ~3.8 M in toluene) in toluene (4 mL) at −78 °C. The alkene (0.678 mmol) in toluene (3 mL) was added dropwise at −78 °C, the reaction mixture was stirred for 1 h, and then the reaction was quenched with a saturated aqueous NH_4Cl solution (20 mL). The organic layer was separated and washed with 10% Na_2SO_3 solution (15 mL) and dried, and the solvent was removed under reduced pressure. The residue was purified by trituration with cold pentane or flash chromatography using petroleum ether−ethyl acetate as eluent to yield the oxirane.

Method B: ^{t}BuOOH/BuLi/THF. ^{n}BuLi (3.73 mmol) was added to a solution of ^{t}BuOOH (5.1 mmol, ~3.8 M in toluene) in THF (30 mL) at −78 °C. The alkene (3.39 mmol) in THF (7 mL) was added dropwise at −78 °C, the reaction mixture was stirred for 1 h, and then the reaction was quenched with a saturated aqueous NH_4Cl solution (20 mL). The reaction mixture was then worked up as described in procedure A.

Method C: Trityl Hydroperoxide/KH/THF. Triphenylmethyl hydroperoxide (0.28 g, 1.01 mmol) in THF (7 mL) was added to a suspension of KH (35 wt % dispersion in mineral oil) (0.11 g, 0.88 mmol) in THF (10 mL) at −78 °C. The alkene (0.68 mmol) in THF (3 mL) was added dropwise at −78 °C and the mixture stirred for 1 h. The yellow color due to the alkene was still present at the end of this time so the reaction was allowed to warm to −60 °C by which time the yellow color faded. The reaction was quenched with a saturated aqueous NH_4Cl solution (10 mL). The organic layer was separated and washed with a 10% Na_2SO_3 solution (10 mL) and then dried and the solvent removed under reduced pressure. The residue was washed with cold pentane, and the washings were collected and evaporated to give the oxirane.

Method D: ^{t}BuOOH/KH/THF. ^{t}BuOOH (2.25 mmol) was added to a suspension of KH (35 wt % dispersion in mineral oil) (0.188 g, 1.65 mmol) in THF (20 mL) at −78 °C. The alkene (1.5 mmol) in THF (5 mL) was added dropwise at −78 °C, the reaction mixture was stirred for 1 h, and the reaction was then quenched with a saturated aqueous NH_4Cl solution (10 mL). The reaction mixture was then worked up as described in procedure A.

Method E: Ph_3COOH/BuLi/THF. ^{n}BuLi (3.73 mmol) was added to a solution of trityl hydroperoxide (0.94 g, 5.01 mmol) in THF (30 mL) at −78 °C. The alkene (3.39 mmol) in THF (7 mL) was added dropwise at −78 °C, the reaction mixture was stirred for 1 h, and then the reaction was quenched with a saturated aqueous NH_4Cl solution (20 mL). The reaction mixture was then worked up as described in procedure A.

(*Z*)-(4*S*)-2,2-Dimethyl-4-[2′-[4″-methylphenyl)thio]-2′-nitroethenyl]-1,3-dioxolane (11). ^{t}BuOK (5.5 mL, 1 M solution in ^{t}BuOH, 0.1 equiv) was added to a solution of [(4-methylphenyl)thio]nitromethane (**1**, 10.13 g, 55.0 mmol) in a mixed solvent system of 1:1 ^{t}BuOH/THF (120 mL) at 0 °C. After 15 min, the D-isopropylideneglyceraldehyde (7.19 g, 55.0 mmol) in THF (20 mL) was added, and the reaction was allowed to warm to rt and stirred for a further 5 h. The reaction was quenched by pouring the solution into pH 7.0 phosphate buffer (80 mL), the organic layer was removed, and the aqueous layer was extracted with ether (3 × 20 mL). The organic layers were combined and dried, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography using 8:1 petroleum ether−ethyl acetate as eluent to yield a mixture of diastereoisomeric alcohols as a pale yellow oil (13.67 g, 79%). The alcohols were not characterized and used directly in the next step. Methanesulfonyl chloride (0.74 mL, 9.58 mmol) followed by ^{i}Pr$_2$NEt (1.67 mL, 9.58 mmol) was added to a solution of the alcohols (1.0 g, 3.19 mmol) in CH_2Cl_2 (20 mL) at −78 °C. The reaction was allowed to warm to rt over 2 h and then stirred at rt for a further 2 h. The reaction was quenched by pouring the solution into saturated aqueous $NaHCO_3$ (10 mL), and the organic layer was washed with $NaHCO_3$ (2 × 10 mL). The aqueous layers were combined and extracted with CH_2Cl_2 (10 mL). The organic layers were combined and dried, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography using 20:1 petroleum ether−ethyl acetate as eluent to yield the alkene (0.64 g, 68%) as a yellow oil: $[\alpha]_D$ +78.3° (*c* 1.0 in CH_2Cl_2); HRMS 295.0886, $C_{14}H_{17}NO_4S$ requires 295.0875; ν/cm^{-1} (Cap. film) 3411, 3044, 1537, 1493, 1383, 1373; δ_H (200 MHz) 1.43 (s, 3H), 1.49 (s, 3H), 2.32 (s, 3H), AB part of an ABX system (δ_A 4.22, δ_B 3.77, J_{AB} = 8.6, J_{AX} = 6.7, J_{BX} = 6.3), 5.20 (dt, 1H, *J* = 7.9, 6.5), 7.10−7.26 (AA′BB′ system, 4H), 7.53 (d, 1H, *J* = 7.9); δ_C (50 MHz) 149.0, 143.5, 138.8, 132.3, 130.4, 127.4, 111.1, 73.6, 68.6, 26.5, 25.6, 21.2; *m*/*z* (EI) 295 (M^+, 53), 123 (STol, 65), 91 (Tol, 51). Anal. Calcd for $C_{14}H_{17}NO_4S$: C, 56.93; H, 5.80; N, 4.74. Found: C, 56.43; H, 5.30; N, 4.70.

(2′*S*,3′*S*,4*R*)-2,2-Dimethyl-4-[3′-[(4″-methylphenyl)thio]-3′-nitrooxiran-2′-yl]-1,3-dioxolane (12) was prepared using the general procedure method A. Examination of the crude ^{1}H NMR spectrum showed that a mixture of oxiranes **12** and **13** had been obtained in a ratio of 15:1. The minor *anti* oxirane component was removed by trituration with cold pentane or flash chromatography using 40:1 petroleum ether−ethyl acetate 40:1 as eluent to yield oxirane **12** (71%) as a white solid (mp 41−42 °C): $[\alpha]_D$ +23.7° (*c* 0.118 in CH_2Cl_2); ν/cm^{-1} (KBr disk) 2996, 2969, 1568, 1385, 1375; δ_H (200 MHz) 1.40 (s, 3H), 1.50 (s, 3H), 2.36 (s, 3H), 3.72 (d, 1H, *J* = 7.5), AB part of an ABX system (δ_A 4.18, δ_B 3.88, J_{AB} = 8.9, J_{AX} = 6.8, J_{BX} = 5.7), 4.30 (m, 1H), 7.18−7.48 (AA′BB′ system, 4H); δ_C (50 MHz) 140.9, 134.7, 130.6, 122.0, 111.2, 94.6, 74.4, 66.0, 65.6, 26.6, 25.2, 21.3; *m*/*z* (EI) 296 ($M^+ - CH_3$, 25), 123 (STol, 90), 91 (Tol, 83). Anal. Calcd for $C_{14}H_{17}NO_5S$: C, 54.01; H, 5.50; N, 4.50. Found: C, 54.14; H, 5.57; N, 4.38.

(2′*R*,3′*R*,4*R*)-2,2-Dimethyl-4-[3′-[(4″-methylphenyl)thio)-3′-nitrooxiran-2′-yl]-1,3-dioxolane (13) was prepared as described in the general procedure using method C. Examination of the crude ^{1}H NMR spectrum showed that a 12:1 mixture of oxiranes **13** and **12** had been obtained. The residue was washed with cold petroleum ether, and the supernatant was evaporated to yield oxirane **13** (61%) as a pale yellow oil: $[\alpha]_D$ −37.9° (*c* 0.98 in CH_2Cl_2); HRMS ($M - CH_3$) 296.0625, $C_{13}H_{14}NO_5S$ requires 296.0592; ν/cm^{-1} (Cap. film) 2990, 1568, 1383, 1375, 1339; δ_H (500 MHz) 1.40 (s, 3H), 1.48 (s, 3H), 2.35 (s, 3H), 3.73 (d, 1H, *J* = 7.3), AB part of an ABX system (δ_A 4.22, δ_B 4.15, J_{AB} = 9.1, J_{AX} = 6.2, J_{BX} = 4.3), 4.34 (m, 1H), 7.17−7.48 (AA′BB′ system, 4H).

***S*-(4″-Methylphenyl) (2′*R*,4*R*)-2′-Bromo-2′-(2,2-dimethyl-1,3-dioxolan-4-yl)ethanethioate (17).** $MgBr_2$·Et_2O (0.114 g, 0.44 mmol) was added to a solution of oxirane **12** (0.115 g, 0.37 mmol) in diethyl ether (2 mL). The reaction mixture was

(30) Jackson, D. Y. *Synth. Commun.* **1988**, *18*, 337.

stirred at rt for 2 h, and then the reaction was quenched by pouring the solution into water (10 mL). The aqueous layer was extracted with ether (2 × 10 mL), the organic layers were combined and dried, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography using 30:1 petroleum ether–ethyl acetate as eluent to yield the *anti* α-bromo thioester **17** (0.105 g, 82%) as a white solid (mp 39–41 °C): $[\alpha]_D$ +39.6° (*c* 3.4 in CH_2Cl_2); HRMS 344.0113, $C_{14}H_{17}O_3BrS$ requires 344.0082; ν/cm^{-1} (KBr disk) 3020, 2988, 2936, 2885, 1701; δ_H (200 MHz) 1.35 (s, 3H), 1.51 (s, 3H), 2.38 (s, 3H), 4.08 (dd, 1H, J = 4.2, 9.2), 4.17 (dd, 1H, J = 5.8, 9.2), 4.39 (d, 1H, J = 8.6), 4.59 (m, 1H), 7.21–7.36 (m, 4H); δ_C (50 MHz) 192.7, 140.3, 134.4, 130.2, 122.98, 111.1, 76.1, 67.6, 51.6, 27.1, 25.3, 21.4; *m*/*z* (EI) 296 ($M^+ - CH_3$, 25), 123 (STol, 90), 91 (Tol, 83).

S-(4″-Methylphenyl) (2′S,4R)-2′-bromo-2′-(2,2-dimethyl-1,3-dioxolan-4-yl)ethanethioate (18) was prepared in exactly the same way as the α-bromo thioester **17** but starting with oxirane **13**. The residue was purified by flash chromatography using 30:1 petroleum ether–ethyl acetate as eluent to yield the *syn* α-bromo thioester **18** (79%) as a colorless oil: $[\alpha]_D$ −67.4° (*c* 2.4 in CH_2Cl_2); HRMS 344.0090, $C_{14}H_{17}O_3BrS$ requires 344.0082; ν/cm^{-1} (Cap. film) 2988, 2936, 1694; δ_H (200 MHz) 1.38 (s, 3H), 1.49 (s, 3H), 2.39 (s, 3H), 3.98 (dd, 1H, J = 4.9, 9.1), 4.14 (dd, 1H, J = 6.1, 9.1), 4.50 (m, 2H), 7.22–7.37 (m, 4H); δ_C (50 MHz) 193.3, 140.6, 134.6, 130.5, 128.1, 110.8, 76.8, 67.3, 53.7, 26.8, 25.3, 21.6; *m*/*z* (EI) 296 ($M^+ - CH_3$, 15), 223 (M^+ − STol, 48), 123 (STol, 90), 101 (M^+ − CHBrCOSTol, 100), 91 (Tol, 83).

General Procedure for Ammonia Ring Opening of Oxiranes and *in Situ* Amine Protection. Aqueous ammonia (3.25 mmol, 16 M, 0.88 specific gravity) was added to a solution of the oxirane (0.64 mmol) in CH_2Cl_2 (4 mL). The reaction mixture was stirred at rt for 2 h and then cooled to 0 °C, and the acylating agent (4.55 mmol) was added. The reaction mixture was allowed to warm to rt and stirred until TLC indicated no remaining amine (between 0.5 and 2 h depending on the acylating reagent). CH_2Cl_2 (10 mL) was added, the solution was dried, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography using petroleum ether–ethyl acetate as eluent to yield the N-protected α-amino thioester.

S-(4″-Methylphenyl) (2′R,4S)-2′-[(*tert*-butyloxycarbonyl)amino]-2′-(2,2-dimethyl-1,3-dioxolan-4-yl)ethanethioate (19) was prepared as described in the general procedure starting with oxirane **12** and using *tert*-butyl pyrocarbonate as the acylating agent. The crude product was purified using 8:1 petroleum ether–ethyl acetate as eluent to give the α-amino thioester **19** (67%) as a white solid (mp 87–90 °C): $[\alpha]_D$ +56.0° (*c* 3.25 in CH_2Cl_2); HRMS (MH) 382.1691, $C_{19}H_{28}NO_5S$ requires 382.1688; ν/cm^{-1} (KBr disk) 3393, 2978, 1705, 1690; δ_H (200 MHz) 1.34 (s, 3H), 1.49 (s, 12H), 2.37 (s, 3H), AB part of an ABX system (δ_A 4.08, δ_B 4.03, J_{AB} = 9.3, J_{AX} = 4.7, J_{BX} = 6.5), 4.45 (m, 1H), 4.62 (dd, 1H, J = 4.5, 8.6), 5.34 (d, 1H, J = 8.6), 7.19–7.30 (AA′BB′ system, 4H); δ_C (50 MHz) 198.1, 155.6, 139.9, 134.5, 130.1, 123.6, 110.3, 80.7, 75.6, 65.4, 62.1, 28.4, 26.3, 24.9, 21.4; *m*/*z* (EI) 382 (MH^+, 2), 366 ($M^+ - CH_3$, 9), 258 (M^+ − STol, 10), 230 (M^+ − COSTol, 18), 124 (HSTol, 62), 91 (Tol, 60).

S-(4″-Methylphenyl) (2′R,4S)-2′-[(benzyloxycarbonyl)amino]-2′-(2,2-dimethyl-1,3-dioxolan-4-yl)ethanethioate (20) was prepared as described in the general procedure staring with oxirane **12** and using benzyl chloroformate as the acylating agent. The crude product was purified using 3:1 petroleum ether–ethyl acetate as eluent to give the α-amino thioester **20** (69%) as a white solid (mp 86–88 °C): $[\alpha]_D$ +46.4° (*c* 1 in CH_2Cl_2); ν/cm^{-1} (KBr disk) 3341, 1723, 1682; δ_H (200 MHz) 1.32 (s, 3H), 1.43 (s, 3H), 2.36 (s, 3H), 4.05 (m, 2H), 4.44 (dt, 1H, J = 4.8, 10.9), 4.68 (m, 1H, J = 4.8, 8.7), 5.17 (s, 2H), 5.62 (d, 1H, J = 8.7), 7.19–7.39 (m, 9H); δ_C (50 MHz) 197.6, 156.1, 140.0, 136.1, 134.5, 130.2, 128.6, 128.4, 128.3, 123.3, 110.4, 75.6, 67.6, 65.4, 62.6, 26.4, 24.9, 21.5; *m*/*z* (EI) 400 ($M^+ - CH_3$, 21), 292 (M^+ − STol, 17), 123 (STol, 43), 91 (Tol, 100). Anal. Calcd for $C_{22}H_{25}NO_5S$: C, 63.59; H, 6.06; N, 3.37. Found: C, 63.74; H, 6.12; N, 3.14.

S-(4″-Methylphenyl) (2′R,4S)-2′-(benzoylamino)-2′-(2,2-dimethyl-1,3-dioxolan-4-yl)ethanethioate (21) was prepared as described in the general procedure starting with oxirane **12** and using benzoyl chloride as the acylating agent. The crude product was purified using 3:1 petroleum ether–ethyl acetate as eluent to give the α-amino thioester **21** (61%) as a white solid (mp 135–136 °C): $[\alpha]_D$ +30.7° (*c* 0.935 in CH_2Cl_2); ν/cm^{-1} (KBr disk) 3312, 1696, 1642; δ_H (200 MHz) 1.35 (s, 3H), 1.45 (s, 3H), 2.35 (s, 3H), AB part of an ABX system (δ_A 4.26, δ_B 4.10, J_{AB} = 9.3, J_{AX} = 4.4, J_{BX} = 6.6), 4.53 (m, 1H), 5.14 (dd, 1H, J = 4.5, 8.2), 7.02 (d, 1H, J = 8.2), 7.41–7.49 (AA′BB′ system, 4H), 7.51–7.63 (m, 3H), 7.84–7.89 (m, 2H); *m*/*z* (EI) 386 (MH^+, 20), 262 (M^+ − STol, 32), 123 (STol, 31), 105 (PhCO, 100), 91 (Tol, 23), 77 (Ph, 60). Anal. Calcd for $C_{21}H_{23}NO_4S$: C, 65.43; H, 6.01; N, 3.63. Found: C, 65.70; H, 5.89; N, 3.64.

S-(4″-Methylphenyl) (2′R,4S)-2′-(acetylamino)-2′-(2,2-dimethyl-1,3-dioxolan-4-yl)ethanethioate (22) was prepared as described in the general procedure starting with oxirane **12** and using acetic anhydride as the acylating agent. The crude product was purified by flash chromatography using 2:1 petroleum ether–ethyl acetate as eluent to yield the α-amino thioester **22** (65%) as a white solid (mp 121–122 °C): $[\alpha]_D$ +88.2° (*c* 1.05 in CH_2Cl_2); ν/cm^{-1} (KBr disk) 3322, 2984, 1694; δ_H (200 MHz) 1.35 (s, 3H), 1.48 (s, 3H), 2.11 (s, 3H), 2.38 (s, 3H), AB part of an ABX system (δ_A 4.17, δ_B 4.07, J_{AB} = 9.30, J_{AX} = 4.6, J_{BX} = 6.7), 4.42 (m, 1H), 4.93 (dd, 1H, J = 4.6, 8.5), 6.24 (d, 1H, J = 8.5), 7.20–7.30 (AA′BB′ system, 4H); *m*/*z* (EI) 324 (MH^+, 69), 308 ($M^+ - CH_3$, 9), 200 (M^+ − STol, 91), 172 (M^+ − COSTol, 30), 123 (STol, 48), 91 (Tol, 23). Anal. Calcd for $C_{16}H_{21}NO_4S$: C, 59.42; H, 6.54; N, 4.33. Found: C, 59.74; H, 6.73; N, 4.48.

S-(4″-Methylphenyl) (2′R,4S)-2′-(Benzylamino)-2′-(2,2-dimethyl-1,3-dioxolan-4-yl)ethanethioate (23). Benzylamine (0.31 mL, 2.82 mmol) was added to a solution of oxirane **12** (0.44 g, 1.41 mmol) in CH_2Cl_2 (10 mL) at rt. The reaction was stirred for 4 h, then washed with water, and dried and the solvent removed under reduced pressure. The residue was purified by flash chromatography using 10:1 petroleum ether–ethyl acetate as eluent to yield the α-amino thioester **23** (0.403 g, 77%) as a viscous colorless oil: $[\alpha]_D$ +54.8° (*c* 1.1 in CH_2Cl_2); HRMS 371.1585, $C_{21}H_{25}NO_6S$ requires 371.1538; ν/cm^{-1} (Cap. film) 3341, 2988, 1696; δ_H (200 MHz) 1.34 (s, 3H), 1.49 (s, 3H), 2.05 (br s, 1H), 2.39 (s, 3H), 3.59 (d, 1H, J = 6.3), AB system (δ_A 4.00, δ_B 3.82, J_{AB} = 13.0), 4.03–4.12 (m, 2H), 4.31 (m, 1H), 7.23–7.40 (m, 9H); δ_C (50 MHz) 201.6, 139.7, 139.4, 134.5, 130.1, 128.6, 128.4, 127.5, 124.5, 109.9, 76.5, 69.8, 66.3, 52.7, 26.7, 25.1, 21.5; *m*/*z* (EI) 372 (MH^+, 22), 356 ($M^+ - CH_3$, 50), 220 (M^+ − COSTol, 75), 123 (STol, 32), 91 (Tol, 100).

S-(4‴-Methylphenyl) (1″S,2′R,4S)-2′-[N-[1″-(benzyloxycarbonyl)-2″-phenylethyl]amino]-2′-(2,2-dimethyl-1,3-dioxolan-4-yl)ethanethioate (24). Phenylalanine benzyl ester *p*-toluenesulfonic acid salt (0.069 g, 0.161 mmol) was dissolved in CH_2Cl_2 (2 mL), and saturated aqueous $NaHCO_3$ solution (1 mL) was added. The oxirane **12** (0.05 g, 0.161 mmol) in CH_2Cl_2 (1 mL) was added, and the mixture reaction was stirred at rt for 48 h. Water (9 mL) was added, and the aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL). The organic layers were combined and dried, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography using 12:1 petroleum ether–ethyl acetate as eluent to yield **24** (0.071 g, 87%) as a colorless oil: $[\alpha]_D$ +44.4° (*c* 3.05 in CH_2Cl_2); HRMS (MH) 520.2150, $C_{30}H_{34}NO_5S$ requires 520.2157); ν/cm^{-1} (Cap. film) 3335, 3030, 2988, 1736, 1697; δ_H (200 MHz) 1.30 (s, 3H), 1.41 (s, 3H), 2.37 (s, 3H), 2.4 (br s, 1H), AB part of an ABX system (δ_A 3.00, δ_B 2.90, J_{AB} = 13.6, J_{AX} = 6.2, J_{BX} = 7.3), 3.40 (d, 1H, J 7.3), 3.73 (m, 2H), 3.90 (dd, 1H, J = 6.3, 8.9), 4.18 (m, 1H), 5.08 (s, 2H), 7.13–7.33 (m, 14H); δ_C (50 MHz) 199.8, 173.5, 139.7, 137.0, 135.4, 134.3, 130.0, 129.5, 128.5, 128.4, 126.8, 124.0, 109.9, 76.4, 76.2, 69.3, 66.9, 66.5, 62.3, 39.8, 26.8, 25.3, 25.1, 21.4; *m*/*z* (EI) 520 (MH^+, 28), 504 ($M^+ - CH_3$, 8), 384 ($M^+ - PHCH_2CO_2$, 8), 368 ($M^+ - COSTol$, 89), 124 (HSTol, 63), 91 (Tol, 100).

S-(4‴-Methylphenyl) (1″S,2′R,4S)-2′-[N-[1″-(benzyloxycarbonyl)-2″-methylbutyl]amino]-2′-(2,2-dimethyl-1,3-dioxolan-4-yl)ethanethioate (25) was prepared in exactly the

same way as compound **24** but using L-leucine benzyl ester *p*-toluenesulfonate salt. The residue was purified by flash chromatography using 16:1 petroleum ether–ethyl acetate as eluent to yield **25** (79%) as a colorless oil: $[\alpha]_D$ +26.6° (*c* 2.41 in CH_2Cl_2); ν/cm^{-1} (Cap. film) 3328, 2957, 1736, 1697; δ_H (200 MHz) 0.89 (d, 6H, *J* = 6.9), 1.33 (s, 3H), 1.45 (m, 2H), 1.49 (s, 3H), 1.69 (m, 1H), 2.16 (m, 1H), 2.36 (s, 3H), 3.47 (m, 2H), 4.03 (d, 2H, *J* = 5.6), 4.24 (q, 1H, *J* = 5.6), AB system (δ_A 5.14, δ_B 5.09, J_{AB} = 12.2), 7.17–7.40 (m, 9H); δ_C (50 MHz) 199.9, 174.8, 139.6, 135.7, 134.2, 130.0, 128.6, 128.4, 124.1, 110.0, 76.5, 69.5, 66.7, 59.6, 42.8, 26.9, 25.1, 24.7, 22.7, 22.4, 21.4; *m*/*z* (EI) 470 ($M^+ - CH_3$, 11), 350 ($M^+ - PhCH_2CO_2$, 23), 334 (M^+ – COSTol, 75), 123 (STol, 18), 91 (Tol, 100). Anal. Calcd for $C_{27}H_{35}NO_5S$: C, 66.77; H, 7.26; N, 2.88. Found: C, 66.62; H, 7.07; N, 3.03.

***Z*-(4*S*,5*S*)-2,2-Dimethyl-5-[(*tert*-butyldimethylsilyloxy)methyl]-4-[2′-[(4″-methylphenyl)thio]-2′-nitroethenyl]-1,3-dioxolane (29).** ^{t}BuOK (1.22 mL, 1 M solution in ^{t}BuOH) was added to a solution of [(4-methylphenyl)thio]nitromethane (**1**, 2.23 g, 12.16 mmol) in a mixed solvent system of 1:1 ^{t}BuOH/THF (120 mL) at 0 °C. After 15 min, the aldehyde **28** (3.33 g, 12.16 mmol) in THF (20 mL) was added, and then the reaction mixture was allowed to warm to rt and stirred for a further 2.5 h. The reaction was quenched by pouring the solution into a pH 7.0 phosphate buffer (50 mL), the organic layer was removed, and the aqueous layer was extracted with ether (3 × 20 mL). The organic layers were combined and dried, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography using 15:1 petroleum ether–ethyl acetate as eluent to yield a mixture of diastereoisomeric alcohols as a pale yellow oil (5.05 g, 91%). The alcohols were not characterized and used directly in the next step. Methanesulfonyl chloride (0.51 mL, 6.56 mmol) followed by ^{i}Pr$_2$NEt (1.14 mL, 6.56 mmol) was added to a solution of the alcohols (1.0 g, 2.19 mmol) in CH_2Cl_2 (20 mL) at −78 °C. The reaction mixture was allowed to warm to rt over 2 h; then the reaction was quenched by pouring the solution into saturated aqueous $NaHCO_3$ (10 mL). The organic layer was washed with $NaHCO_3$ (2 × 10 mL). The aqueous layers were combined and extracted with CH_2Cl_2 (10 mL). The organic layers were combined and dried, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography using 30:1 petroleum ether–ethyl acetate as eluent to yield alkene **29** (68%) as a yellow oil: $[\alpha]_D$ +66.7° (*c* 0.168 in CH_2Cl_2); HRMS (MH − CH_3) 424.1614, $C_{20}H_{30}NO_5SSi$ requires 424.1613; ν/cm^{-1} (Cap. film) 2930, 2859, 1541, 1327; δ_H (200 MHz) 0.07 (s, 3H), 0.08 (s, 3H), 0.89 (s, 9H), 1.48 (s, 6H), 2.32 (s, 3H), 3.80 (m, 2H), 4.00 (dt, 1H, *J* = 4.2, 7.7), 5.13 (dd, 1H, *J* = 7.7, 8.8), 7.10–7.28 (AA′BB′ system, 4H), 7.47 (d, 1H, *J* = 8.8); δ_C (50 MHz) 150.4, 141.6, 138.7, 130.6, 130.4, 127.6, 111.1, 81.2, 75.6, 62.2, 27.0, 26.9, 25.9, 21.2, 18.4, −5.3, −5.4; *m*/*z* (EI) 424 ($M^+ - CH_3$, 10), 382 ($M^+ - {}^t$Bu, 5), 324 ($M^+ - {}^t$BuMe$_2$Si, 78), 294 (^{t}BuMe$_2$SiOCH$_2$, 27), 123 (STol, 40), 91 (Tol, 63).

(2′*R*,3′*R*,4*R*,5*S*)-2,2-Dimethyl-5-[(*tert*-butyldimethylsilyloxy)methyl]-4-[3′-[(4″-methylphenyl)thio]-3′-nitrooxiran-2′-yl]-1,3-dioxolane (30) was prepared from alkene **29** using the general procedure method D. The crude product was purified by flash chromatography using 50:1 petroleum ether–ethyl acetate as eluent to yield the *anti* oxirane **30** (67%) as a colorless oil: $[\alpha]_D$ −51.0° (*c* 1.05 in CH_2Cl_2); ν/cm^{-1} (Cap. film) 2955, 2930, 2858, 1568, 1383, 1373, 1339; δ_H (200 MHz) 0.10 (s, 6H), 0.92 (s, 9H), 1.45 (s, 3H), 1.46 (s, 3H), 2.35 (s, 3H), 3.75 (d, 1H, *J* = 7.4), AB part of an ABX system (δ_A 3.86, δ_B 3.78, J_{AB} = 11.1, J_{AX} = 3.6, J_{BX} = 3.4), 4.22 (m, 2H), 7.16–7.48 (AA′BB′ system, 4H); *m*/*z* (EI) 440 ($M^+ - CH_3$, 80), 398 ($M^+ - {}^t$Bu, 5), 340 ($M^+ - {}^t$BuMe$_2$Si, 17), 310 ($M^+ - {}^t$BuMe$_2$SiOCH$_2$, 15), 91 (Tol, 80). Anal. Calcd for $C_{21}H_{33}NO_6SSi$: C, 55.36; H, 7.31; N, 3.08. Found: C, 55.16; H, 7.51; N, 3.03.

(2′*S*,3′*S*,4*R*,5*S*)-2,2-Dimethyl-5-[(*tert*-butyldimethylsilyloxy)methyl]-4-[3′-[(4″-methylphenyl)thio]-3′-nitrooxiran-2′-yl]-1,3-dioxolane (31) was prepared from alkene **29** using the general procedure method B. The crude product was purified by flash chromatography using 50:1 petroleum ether–ethyl acetate as eluent to give a 5:1 *syn*:*anti* mixture of oxiranes (86%) as a colorless oil: $[\alpha]_D$ +9.2° (*c* 1.09 in CH_2Cl_2); HRMS (M − CH_3) 440.1575, $C_{20}H_{30}NO_6SSi$ requires 440.1563; ν/cm^{-1} (Cap. film) 2955, 2930, 2859, 1568, 1383; δ_H (200 MHz) 0.12 (s, 3H), 0.13 (s, 3H), 0.92 (s, 9H), 1.46 (s, 3H), 1.47 (s, 3H), 2.35 (s, 3H), 3.72 (d, 1H, *J* = 7.8), 3.88 (d, 2H, *J* = 4.3), 4.15 (m, 1H), 4.28 (t, 1H, *J* = 7.7), 7.17–7.49 (AA′BB′ system, 4H); *m*/*z* (EI) 440 ($M^+ - CH_3$, 95), 340 ($M^+ - {}^t$BuMe$_2$Si, 40), 91 (Tol, 62). Anal. Calcd for $C_{21}H_{33}NO_6SSi$: C, 55.36; H, 7.31; N, 3.08. Found: C, 55.41; H, 7.80; N, 3.17.

(2′*S*,4*S*,5*S*)-2,2-Dimethyl-5-[(*tert*-butyldimethylsilyloxy)methyl]-4-[2′-(4″-methylphenyl)thio]-1′-[(*tert*-butyloxycarbonyl)amino]-2′-oxoethyl]-1,3-dioxolane (32) was prepared from oxirane **30** following the general procedure and using *tert*-butyl pyrocarbonate as the acylating agent. The crude product was purified by flash chromatography using 20:1 petroleum ether–ethyl acetate as eluent to yield the α-amino thioester **32** (65%) as a white solid, mp 92–93 °C: $[\alpha]_D$ −64.2° (*c* 1.0 in CH_2Cl_2); ν/cm^{-1} (KBr disk) 3403, 2928, 1719, 1686; δ_H (200 MHz) 0.08 (s, 6H), 0.90 (s, 9H), 1.37 (s, 3H), 1.46 (s, 3H), 1.51 (s, 9H), 2.37 (s, 3H), 3.70–3.89 (m, 3H), 4.56 (m, 2H), 5.52 (d, 1H, *J* = 9.6), 7.20–7.33 (AA′BB′ system, 4H); *m*/*z* (EI) 468 ($M^+ - {}^t$Bu, 5), 123 (STol, 55), 57 (^{t}Bu, 100).

(2′*R*,4*S*,5*S*)-2,2-Dimethyl-5-[(*tert*-butyldimethylsilyloxy)methyl]-4-[2′-(4″-methylphenyl)thio]-1′-[(*tert*-butyloxycarbonyl)amino]-2′-oxoethyl]-1,3-dioxolane (33) was prepared following the general procedure, starting with a 5:1 mixture of oxiranes **31** and **30** and using *tert*-butyl pyrocarbonate as the acylating agent. The crude product was purified by flash chromatography using 20:1 petroleum ether–ethyl acetate as eluent to yield the α-amino thioester **33** (55%) as a colorless oil. The minor diastereoisomeric impurity was removed during purification. **33**: ν/cm^{-1} (Cap. film) 3339, 2955, 2930, 1709; δ_H (200 MHz) 0.10 (s, 6H), 0.91 (s, 9H), 1.41 (s, 6H), 1.48 (s, 9H), 2.37 (s, 3H), AB part of an ABX system (δ_A 3.80, δ_B 3.65, J_{AB} = 10.3, J_{AX} = 3.2, J_{BX} = 5.6), 4.14–4.27 (m, 2H), 4.41 (m, 1H), 5.66 (d, 1H, *J* = 7.7), 7.18–7.31 (AA′BB′ system, 4H); *m*/*z* (EI) 454 ($M^+ - {}^t$Bu − CH_3, 32), 394 ($M^+ - {}^t$BuMe$_2$SiO, 17). Anal. Calcd for $C_{26}H_{43}NO_6SSi$: C, 59.39; H, 8.25; N, 2.67. Found: C, 59.62; H, 8.26; N, 2.58.

(3*S*,4*S*)-3,4,5-Trihydroxy-L-norvaline (Polyoxamic Acid) (26). Trifluoroacetic acid (2 mL) was added to the α-amino thioester **32** (0.200 g, 0.38 mmol) at 0 °C. Water (0.4 mL) was added at 0 °C, and the reaction mixture was stirred for 10 min and then warmed to rt and stirred for 1.5 h. The solvent was removed under reduced pressure and the residue was purified by ion exchange chromatography using Amberlite gel IR-120 (H^+) form with 0.6 M NH_4OH as eluent to give the free acid (0.060 g, 95%) as a white solid: δ_H (300 MHz, D_2O) 3.72 (m, 2H), 4.00 (m, 2H), 4.33 (m, 1H); δ_C (75 MHz, D_2O) 175.0, 75.4, 70.4, 64.7, 60.3; *m*/*z* (CI, NH_3) 166 (MH^+, 15).

(2′*S*,4*S*,5*S*)-2,2-Dimethyl-5-[(*tert*-butyldimethylsilyloxy)methyl]-4-[2′-(4″-methylphenyl)thio]-1′-acetamido-2′-oxoethyl]-1,3-dioxolane (34) was prepared from oxirane **30** following the general procedure and using acetic anhydride as the acylating agent. The crude product was purified by flash chromatography using 4:1 petroleum ether–ethyl acetate as eluent to yield the α-amino thioester **34** (84%) as a viscous, colorless oil: $[\alpha]_D$ −72.8° (*c* 1.0 in CH_2Cl_2); ν/cm^{-1} (Cap. film) 3287, 2988, 2955, 2930, 2859, 1701, 1665; δ_H (200 MHz) 0.08 (s, 3H), 0.09 (s, 3H), 0.91 (s, 9H), 1.39 (s, 3H), 1.45 (s, 3H), 2.16 (s, 3H), 2.38 (s, 3H), 3.72–3.84 (m, 3H), 4.58 (m, 1H), 4.98 (dd, 1H, *J* = 1.5, 9.4), 6.36 (d, 1H, *J* = 9.4), 7.20–7.32 (AA′BB′ system, 4H); *m*/*z* (EI) 452 ($M^+ - CH_3$, 100), 410 ($M^+ - {}^t$Bu, 31), 352 ($M^+ - {}^t$BuMe$_2$Si, 20), 344 (M^+ – STol, 65), 124 (HSTol, 47), 91 (Tol, 63). Anal. Calcd for $C_{23}H_{37}NO_5SSi$: C, 59.07; H, 7.98; N, 3.00. Found: C, 59.22; H, 8.21; N, 2.71.

(2′*R*,4*R*,5*S*)-2,2-Dimethyl-5-[(*tert*-butyldimethylsilyloxy)methyl]-4-[2′-(4″-methylphenyl)thio]-1′-(acetylamino)-2′-oxoethyl]-1,3-dioxolane (35) was prepared following the general procedure, starting with a 5:1 mixture of oxiranes **31** and **30** and using acetic anhydride as the acylating agent. The crude product was purified by flash chromatography using 4:1 petroleum ether–ethyl acetate as eluent to yield an inseparable 5:1 mixture of the α-amino thioesters **35** and **34** (67%) as a colorless viscous oil: $[\alpha]_D$ +36.0° (*c* 1.35 in MeOH); HRMS (M − CH_3) 452.1910. $C_{22}H_{34}NO_5SSi$ requires 452.1926); ν/cm^{-1} (Cap. film) 3293, 2955, 2930, 2859, 1701, 1664; δ_H (200 MHz)

0.09 (s, 6H), 0.91 (s, 9H), 1.40 (s, 3H), 1.45 (s, 3H), 2.16 (s, 3H), 2.38 (s, 3H), 3.65–3.84 (m, 3H), 4.61 (m, 1H), 4.98 (dd, 1H, J = 1.4, 9.4), 6.40 (d, 1H, J = 9.4), 7.15–7.40 (AA'BB' system, 4H); m/z (EI) 452 ($M^+ - CH_3$, 58), 410 ($M^+ - {}^t$Bu, 22), 352 ($M^+ - {}^t$BuMe$_2$Si, 18), 344 (M^+ − STol, 58), 124 (HSTol, 60).

[3S-(3α,4β,5β)]-3-(Acetylamino)-3,4-dihydro-4-hydroxy-5-(hydroxymethyl)-2(5*H*)-furanone (36). Trifluoroacetic acid (3 mL) was added dropwise to a solution of acetamide **34** (0.36 g, 0.77 mmol) in methanol (4.5 mL) at 0 °C. The reaction mixture was allowed to warm to rt and stirred for 24 h. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography using 20:1 methanol–ethyl acetate as eluent to give the γ-lactone **36** (0.093 g, 64%) as a crystalline solid (mp 141–142 °C): $[\alpha]_D$ −105.5° (*c* 3.25 in MeOH);[31] ν/cm^{-1} (KBr disk) 3320, 1787, 1655; δ_C (75 MHz, CD_3OD) 175.1, 173.6, 81.8, 72.7, 60.7, 56.3, 22.4; m/z (CI, NH_3) 207.1 (MNH_4^+, 100), 190.2 (MH^+, 18). Anal. Calcd for $C_7H_{11}NO_5$: C, 44.43; H, 5.86; N, 7.40. Found: C, 44.06; H, 6.01; N, 7.00.

[3*R*-(3β,4β,5β)]-3-(Acetylamino)-3,4-dihydro-4-hydroxy-5-(hydroxymethyl)-2(5*H*)-furanone (37). Trifluoroacetic acid (2 mL) was added dropwise to a 5:1 mixture of the acetamides **35** and **34** (0.196 g, 0.42 mmol) in methanol (3 mL) at 0 °C. The reaction mixture was allowed to warm to rt and stirred for 24 h. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography using 20:1 ethyl acetate–methanol as eluent to give the γ-lactone **37** (0.055 g, 69%) as a white solid which was recrystallized from ethanol (mp 160–162 °C) to remove the minor diastereoisomer: $[\alpha]_D$ −101° (*c* 1.0 in MeOH); ν/cm^{-1} (KBr disk) 3370, 3302, 1775, 1760, 1655; δ_C (75 MHz, CD_3OD) 176.3, 174.1, 84.0, 70.2, 61.4, 55.6, 22.5; m/z (CI, NH_3) 207.1 (MNH_4^+, 100).

Methyl 5,6-Dideoxy-2,3-*O*-isopropylidene-6-nitro-6-[(4'-methylphenyl)thio]-β-D-*ribo*-hex-5(*Z*)-enofuranoside (38). ^{t}BuOK (1.06 mL, 1 M solution in ^{t}BuOH) was added to a solution of [(4-methylphenyl)thio]nitromethane (**1**, 1.94 g, 10.62 mmol) in a mixed solvent system of 1:1 ^{t}BuOH/THF (90 mL) at 0 °C. After 15 min methyl 2,3-*O*-isopropylidene-β-D-*ribo*-pentodialdo-1,4-furanoside[11] (2.135 g, 10.62 mmol) in THF (20 mL) was added, and the reaction was allowed to warm to rt and stirred for a further 12 h. The reaction was quenched by pouring the solution into a pH 7.0 phosphate buffer (100 mL), the organic layer was removed, and the aqueous layer was extracted with ether (3 × 50 mL). The organic layers were combined and dried, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography using 12:1 petroleum ether–ethyl acetate as eluent to yield a mixture of diastereoisomeric alcohols (3.63 g, 89%) that were not characterized but used directly in the next step. Methanesulfonyl chloride (0.68 mL, 8.76 mmol) followed by ^{i}Pr$_2$NEt (1.53 mL, 8.76 mmol) was added to a solution of the alcohols (1.122 g, 2.92 mmol) in CH_2Cl_2 (40 mL) at −78 °C. The solution was allowed to warm to −30 °C and stirred for 30 min, resulting in a yellow solution. The reaction was quenched by pouring the solution into saturated aqueous $NaHCO_3$ (25 mL), and the organic layer was washed with $NaHCO_3$ (3 × 10 mL). The aqueous layers were combined and extracted with CH_2Cl_2 (10 mL). The organic layers were combined and dried, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography using 7:1 petroleum ether–diethyl ether as eluent to yield the alkene **38** (0.503 g, 47%) as a yellow crystalline solid (mp 75–76 °C): $[\alpha]_D$ −53° (*c* 1.1 in CH_2Cl_2); ν/cm^{-1} (KBr disk) 3074, 2918, 1534, 1381; δ_H (200 MHz) 1.34 (s, 3H), 1.53 (s, 3H), 2.32 (s, 3H), 3.40 (s, 3H), 4.70 (m, 2H), 5.09 (s, 1H), 5.35 (d, 1H, J = 8.6), 7.10–7.30 (AA'BB' system 4H), 7.45 (d, 1H, J = 8.6); δ_C (50 MHz) 149.5, 143.0, 139.0, 131.1, 130.4, 127.1, 113.1, 109.9, 85.3, 84.7, 84.2, 55.1, 26.4, 25.0, 21.2; m/z (EI) 367 (M^+, 60), 352 ($M^+ - CH_3$, 25), 123 (STol, 40), 91 (Tol, 50). Anal. Calcd for $C_{17}H_{21}O_6NS$: C, 55.57;H, 5.89; N, 3.81. Found: C, 55.74; H, 5.94; N, 3.76.

(6*R*)-Methyl 5,6-anhydro-2,3-*O*-isopropylidene-6-*C*-nitro-6-*C*-[(4'-methylphenyl)thio]-α-L-talofuranoside (39) was prepared following the general procedure method A. The residue was purified by flash chromatography using 12:1 petroleum ether–diethyl ether as eluent to yield an inseparable 4:1 *anti*:*syn* mixture of oxiranes (81%) as a colorless oil. The ^{1}H NMR for the minor isomer **39** is clearly distinguishable: δ_H (200 MHz) 1.35 (s, 3H), 1.51 (s, 3H), 2.36 (s, 3H), 3.43 (s, 3H), 3.74 (d, 1H, J = 8.7), 4.44 (d, 1H, J = 8.7), 4.67 (d, 1H, J = 6.6), 4.80 (d, 1H, J = 6.6), 5.10 (s, 1H), 7.17–7.52 (AA'BB' system, 4H).

(6*S*)-Methyl 5,6-anhydro-2,3-*O*-isopropylidene-6-*C*-nitro-6-*C*-[(4'-methylphenyl)thio]-β-D-allofuranoside (40) was prepared using the general procedure method C. The crude product was purified by flash chromatography using 12:1 petroleum ether–diethyl ether as eluent to yield an inseparable 20:1 *anti*:*syn* mixture of oxiranes (82%) as a colorless oil: $[\alpha]_D$ +34.2° (*c* 1.03 in CH_2Cl_2); HRMS 383.0998, $C_{17}H_{21}NO_7S$ requires 383.1038; ν/cm^{-1} (Cap. film) 2990, 2939, 1566, 1375, 1339; δ_H (200 MHz) 1.35 (s, 3H), 1.51 (s, 3H), 2.36 (s, 3H), 3.35 (s, 3H), 3.73 (d, 1H, J = 8.5), 4.40 (d, 1H, J = 8.5), 4.69 (d, 1H, J = 5.9), 4.97 (d, 1H, J = 5.9), 5.06 (s, 1H), 7.17–7.52 (AA'BB' system, 4H); δ_C (50 MHz) 140.7, 134.8, 130.5, 122.3, 113.0, 109.4, 96.4, 84.9, 83.9, 82.4, 63.9, 55.1, 26.3, 24.8, 21.3; m/z (EI) 383 (M^+, 22), 368 ($M^+ - CH_3$, 20), 123 (STol, 100), 91 (Tol, 80).

4'-Methylphenyl[Methyl 2,3-*O*-isopropylidene-5-(toluene-4-sulfonamido)-5-deoxy-α-L-talofuranoside]thiouronate (41). Aqueous ammonia (0.05 mL, 0.825 mmol, 16 M, specific gravity 0.88) was added to a solution of oxirane **40** (0.063 g, 0.164 mmol) in CH_2Cl_2 (2 mL). The reaction mixture was stirred at rt for 2 h, then CH_2Cl_2 (10 mL) was added and the reaction was dried, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography using 4:1 petroleum ether–ethyl acetate as eluent to yield the *syn* α-amino thioester (0.043 g, 74%) which was not characterized but used directly in the next step. *p*-Toluenesulfonyl chloride (0.139 g, 0.731 mmol, 6 equiv), ^{i}Pr$_2$NEt (0.049 mL, 0.284 mmol, 2.3 equiv), and DMAP (5 mg, 0.04 mmol, 0.3 equiv) were added to a solution of the *syn* α-amino thioester (0.043 g, 0.122 mmol) in CH_2Cl_2 (4 mL) at 0 °C. The reaction was stirred at 0 °C for 4 h, poured into water (10 mL), and extracted with CH_2Cl_2 (2 × 10 mL). The organic layers were combined and dried, and the solvent was removed under reduced pressure. The residues were purified by flash chromatography using 4:1 petroleum ether–ethyl acetate as eluent to give the *syn* sulfonamide **41** (0.045 g, 73%) as a white solid (mp 162–163 °C): $[\alpha]_D$ +73.0° (*c* 2.25 in CH_2Cl_2); ν/cm^{-1} (KBr disk) 3279, 2994, 2940, 1686; δ_H (200 MHz) 1.24 (s, 3H), 1.45 (s, 3H), 2.35 (s, 3H), 2.44 (s, 3H), 3.45 (s, 3H), 4.30 (dd, 1H, J = 10.1, J = 3.0), 4.55 (AB system δ_A 4.57, δ_B 4.53, J_{AB} = 6.1), 4.93 (d, 1H, J = 2.9), 4.95 (s, 1H), 6.79 (d, 1H, J = 10.0), 7.02–7.19 (AA'BB' system, 4H), 7.31–7.80 (AA'BB' system, 4H); δ_C (50 MHz) 196.0, 143.9, 140.1, 137.3, 134.4, 130.1, 129.8, 127.3, 123.0, 112.7, 111.1, 87.9, 85.6, 82.1, 63.7, 56.7, 26.3, 24.6, 21.6, 21.4; m/z (EI) 492 ($M^+ - CH_3$, 22), 384 (M^+ − TolSCO, 20), 155 ($TolSO_2$, 85), 123 (STol, 65), 91 (Tol, 100). Anal. Calcd for $C_{24}H_{29}NO_7S_2$: C, 56.78; H, 5.75; N, 2.76. Found: C, 56.85; H, 5.46; N, 2.55.

4'-Methylphenyl[methyl 2,3-*O*-isopropylidene-5-(toluene-4-sulfonamido)-5-deoxy-β-D-allofuranoside]thiouronate (42) was prepared in exactly the same way as compound **41** but starting with a 1:4 mixture of oxiranes **39** and **40**, respectively. A 4:1 mixture of sulfonamides **41** and **42** was obtained (64% combined yield), from which **42** could be obtained pure by flash chromatography using 6:1 petroleum ether–ethyl acetate as eluent: mp 189–192 °C; $[\alpha]_D$ −43.5° (*c* 1.25 in CH_2Cl_2); ν/cm^{-1} (KBr disk) 3279, 2932, 1684; δ_H (200 MHz) 1.31 (s, 3H), 1.45 (s, 3H), 2.35 (s, 3H), 2.45 (s, 3H), 3.49 (s, 3H), 4.18 (m, 2H), 4.62 (d, 1H, J = 5.9), 5.01 (s, 1H), 5.05 (d, 1H, J = 5.9), 5.46 (d, 1H, J = 8.2), 6.92–7.18 (AA'BB' system, 4H), 7.32–7.80 (AA'BB' system, 4H); m/z (EI) 492 ($M^+ - CH_3$, 70), 384 (M^+ − TolSCO, 35), 155 ($TolSO_2$, 80), 123

(31) Literature values are 141–142 °C and $[\alpha]_D$ −99.7° (*c* 2 in MeOH).[27] Previous reports had indicated a slightly higher mp: 150–152 °C[21] and 147–150 °C.[28]

(STol, 80), 91 (Tol, 100). Anal. Calcd for $C_{24}H_{29}NO_7S_2$: C, 56.78; H, 5.75; N, 2.76. Found: C, 56.98; H, 5.67; N, 2.73.

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Supporting Information Available: Experimental procedures for the preparation of (4-methylphenyl)nitromethane (**1**), the alkenes **2**, **3**, and **4**, the oxiranes **5**, **6**, and **7**, and the N-protected amino thioesters **8a–c**, **9a**, **9b**, and **10a–c**; ^{1}H NMR spectra for compounds **13**, **17–19**, **23–26**, **29**, **32**, **35–37**, and **40**; ^{13}C NMR spectra for compounds **17–19**, **23**, **25**, **26**, and **29** and COSY spectra for **26**, **36**, and **37**; comparison of ^{1}H NMR spectra for compounds **42** and **43** (35 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of this journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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