Oxidation of Oxazolines and Thiazolines to Oxazoles and Thiazoles. Application of the Kharasch−Sosnovsky Reaction

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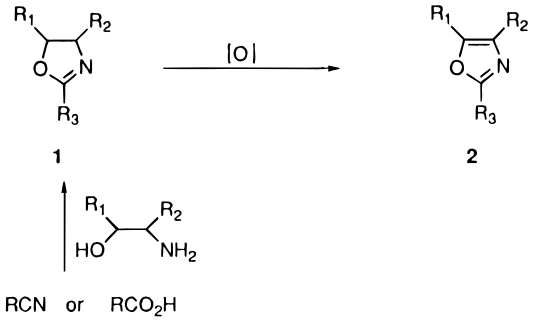
Using a modification of the Kharasch−Sosnovsky reaction, the oxidation of oxazolines and thiazolines bearing a variety of 2-alkyl substituents (chiral and achiral) were smoothly oxidized to their corresponding oxazoles and thiazoles, respectively. The key feature involved in the successful implementation of this important oxidation was the use of a mixture of Cu(I) and Cu(II) salts to enhance the oxidation of the intermediate captodative radical, **24**. The main limitation of this method was shown when the oxidation failed with oxazolines/thiazolines lacking the carboalkoxy group at C-4.

The isolation of a wide range of compounds containing the oxazole and/or thiazole moiety from secondary metabolites have spurred considerable interest in synthetic efforts to reach them.[1] This interest arises from the fact that these compounds, for example, Ulapualide A and Diazonamides A and B (Figure 1), have been found to possess significant biological activity as cytotoxic, antifungal, antibacterial, antitumor, and antiviral agents.[2]

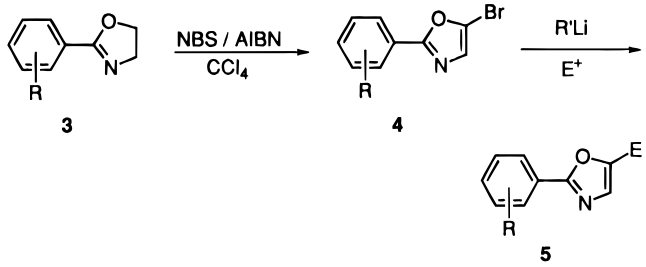
The efforts to reach the oxazole and/or thiazole units have centered mainly on ring synthesis from acyclic precursors;[3] however, several methods have been reported[4] wherein direct oxidation of oxazolines **1** have led to oxazoles **2**. The latter approach to 1,3-oxazoles is particularly attractive since both functionalized and chiral oxazolines are readily prepared from the appropriate nitriles or carboxylic acids and amino alcohols.[5]



Most of the above methods however, have one or more drawbacks such as low yields, limited stability to reaction conditions, loss of optical purity, and hazardous reaction conditions.[5]

During the course of a synthetic program to reach oxazole- and thiazole-containing natural products,[6] an effort was initiated to search for alternative and efficient methods to oxidize 2-oxazolines and/or thiazolines containing a variety of substituents. Perhaps the most general method to date was the oxidations of oxazoles and thiazoles using nickel peroxide.[4a] However, the yields of oxidized products were oftentimes erratic and rarely exceeded 40−50%.

Two additional oxidation methods have been recently reported. The first involves a variation of a previously described route to 1,3-oxazoles wherein treating 2-aryl-2-oxazoline **3** with *N*-bromosuccinimide/azobis(isobutyronitrile) gave the 5-bromo-1,3-oxazole **4** in ca 50%



yield.[4b] Halogen−metal exchange and electrophilic quench of the latter provided the oxazoles **5** in 70−80% yield. The additional step required to remove the bromo substituent detracts from the efficiency of the method; therefore, another method was sought to completely avoid the bromo intermediate **4**. Furthermore, this study narrowly dealt only with a single ring derivative (**5**), whereas oxazoles containing a 4-carboxy substituent (**14**) derived from serine were the main focus of the present study.

The desired oxazolines (Table 1, entries a−e) were made by condensing the imidate hydrochlorides **6** (prepared in quantitative yield from the nitriles and alcohol in presence of anhydrous hydrogen chloride) with DL-serine methyl ester.[7] The reactions proceeded smoothly

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(1) (a) Evans, D. A.; Gage, J. R.; Leighton, J. L. *J. Am. Chem. Soc.* **1992**, *114*, 9434. (b) Wipf, P.; Miller, C. P. *Tetrahedron Lett.* **1992**, *33*, 907. (c) Gangloff, A. R.; Akermark, B.; Helquist, P. *J. Org. Chem.* **1992**, *57*, 4797. (d) Doyle, K. J.; Moody, C. J. *Tetrahedron Lett.* **1992**, *33*, 7769. (e) Vaccaro, H. A.; Levy, D. E.; Sowabe, A.; Jaetsch, T.; Masamune, S. *Tetrahedron Lett.* **1992**, *33*, 1937. (f) Short, K. M.; Ziegler, C. B., Jr. *Tetrahedron Lett.* **1993**, *34*, 71.

(2) (a) Michael, J. P.; Pattenden, G. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1. (b) Fusetani, N.; Matsunaga, S. *Chem. Rev.* **1993**, *93*, 1793. (c) Davidson, B. S. *Chem. Rev.* **1993**, *93*, 1771. (d) Kobayashi, J.; Ishibashi, M. *Chem. Rev.* **1993**, *93*, 1753. (e) Lewis, J. R. *Nat. Prod. Rep.*, **1993**, *10*, 29. (f) Lewis, J. R. *Nat. Prod. Rep.* **1992**, *9*, 81. (g) Evans, D. A.; Gage, J. R.; Leighton, J. L. *J. Am. Chem. Soc.* **1992**, *114*, 9434. (h) Salvatore, B. A.; Smith A. B. *Tetrahedron Lett.* **1994**, *35*, 1329. (i) Wipf, P. *Chem. Rev.* **1995**, *95*, 2115 and references cited therein.

(3) (a) Turchi, I. J. *Oxazoles*; Weissberger, A., Taylor, E. C., Eds.; J. Wiley: New York, 1986. (b) Shapiro, R. *J. Org. Chem.* **1993**, *58*, 5759. (c) Wipf, P.; Miller, C. P. *J. Org. Chem.* **1993**, *58*, 3604. (d) Meyers, A. I.; Lawson, J. P.; Walker, D. G.; Linderman, R. J. *J. Org. Chem.* **1986**, *51*, 5111. (e) Das, J.; Reid, J. A.; Kronenthal, D. R.; Singh, J. P.; Pansegrau, P. D.; Mueller, R. H. *Tetrahedron Lett.* **1992**, *33*, 7835.

(4) (a) Evans, D. L.; Minster, D. K.; Jordis, U.; Hecht, S. M.; Mazzu, A. L., Jr.; Meyers, A. I. *J. Org. Chem.* **1979**, *44*, 497. (b) Kashima, C.; Arao, H. *Synthesis* **1989**, 873. (c) Barrish, J. C.; Singh, J.; Spergel, S. H.; Han, W-C.; Kissick, T. P.; Kronenthal, D. R.; Mueller, R. H. *J. Org. Chem.* **1993**, *58*, 4494.

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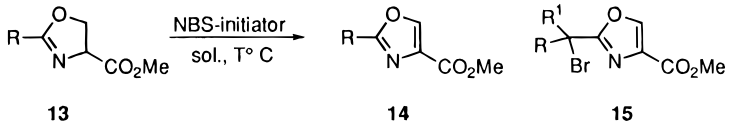
Table 1. Oxazoline−Oxazole Transformation



Entry	R in **13**	Oxazole (%) **14**	Oxazole (%) **15**	Solvent	T°C	Equiv NBS (initiator)	Rxn time (h)
a)	Ph	83	<1	benzene	80	1.2 (Bz_2O_2)	2
b)	Me	62	<1	CH_2Cl_2	-15 to -10	1.5 (hν)	7
c)	n-C_5H_{11}	65	<1	CH_2Cl_2	-40 to -25	5.0 (hν)	12
d)	i-Pr	<1	76	CH_2Cl_2	0	2.6 (hν)	10
e)	Cyclohexyl	<1	66	CH_2Cl_2	0	2.6 (hν)	12

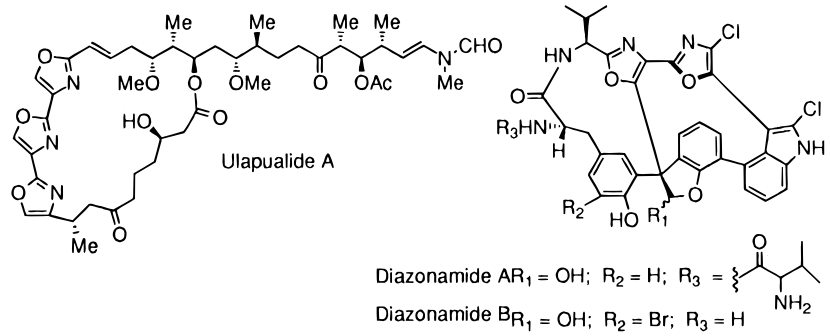
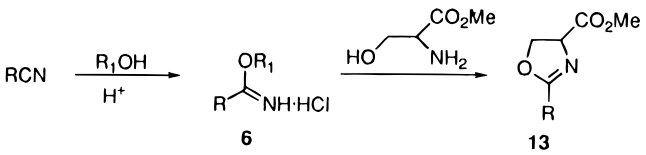


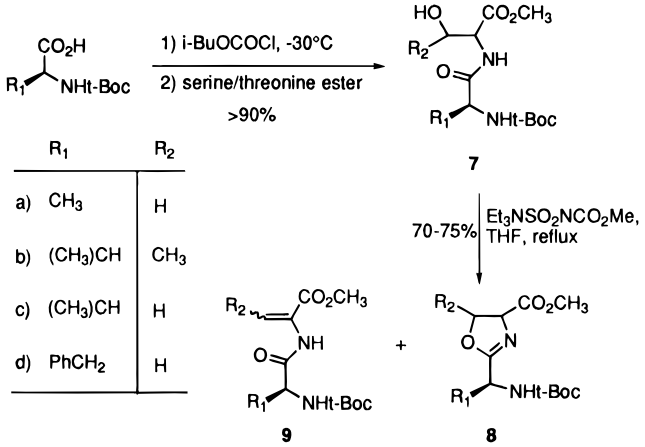
Figure 1.



with the precipitation of ammonium chloride as a byproduct to give the oxazolines **13** in very good yield. The oxazolines[8] **8** containing a stereocenter at the 2α position were prepared by treating the dipeptides **7**, obtained from the requisite amino acid (serine or threonine) with Burgess reagent[9] as shown in Scheme 1. A small amount (6−8%) of the opened chain dehydration product **9** was also obtained. The enantiomerically pure thiazolines **12** were prepared[10] by formation of the carboxamides **10** of the *N*-protected amino acids followed by the direct alkylation of the carboxamides using triethyloxonium hexafluorophosphate to obtain the corresponding imino ethers **11**. The crude, moisture-sensitive, imino ethers were directly condensed with the ethyl cysteinate to give the desired thiazolines **12** (Scheme 2).

Oxidations were conducted using NBS with either benzoyl peroxide or light as the radical initiator and

Scheme 1

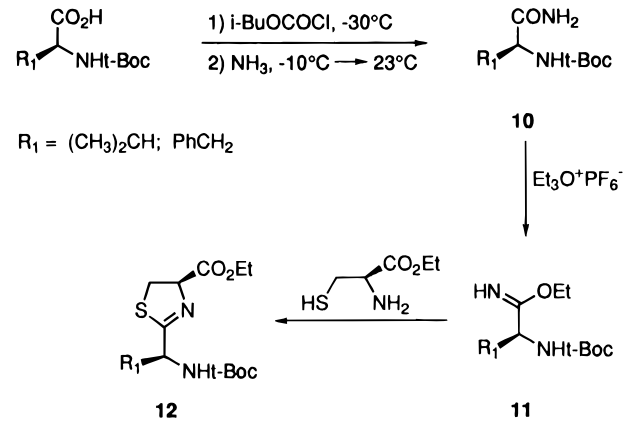


	R_1	R_2
a)	CH_3	H
b)	$(CH_3)CH$	CH_3
c)	$(CH_3)CH$	H
d)	$PhCH_2$	H

varying temperatures and stoichiometry. The results are presented in Table 1. Thermal conditions were well suited for the oxidation of 2-aryl-substituted oxazolines with NBS/benzoyl peroxide in refluxing benzene. Furthermore, the nature of the substituent on the 4-position of the oxazoline was found to be important. For example, the presence of a carbomethoxy group completely eliminated the formation of the 5-bromo product. On the other hand, the presence of an alkyl or aryl group at the 4-position of the oxazoline seemed to favor the formation of the 5-bromo product as reported earlier.[4b] In order to render the oxidation more general in nature, we focused on the oxidation of 2-alkyl-4-carbomethoxy oxazolines and/or thiazolines, since these systems would serve as important precursors to a large number of oxazole- and/or thiazole-containing natural products. When conditions

(5) For a recent review on oxazolines, see: Gant, T.; Meyers, A. I. *Tetrahedron* **1994**, *8*, 2297.
(6) (a) Meyers, A. I.; Tavares, F. *Tetrahedron Lett.* **1994**, *35*, 2481. (b) Tavares, F.; Meyers, A. I. *Tetrahedron Lett.* **1994**, *35*, 6803. (c) Aguilar, E.; Meyers, A. I. *Tetrahedron Lett.* **1994**, *35*, 2473. (d) Aguilar, E.; Meyers, A. I. *Tetrahedron Lett.* **1994**, *35*, 2477.
(7) Cornforth, J. W.; Cornforth, R. H. *J. Chem. Soc.* **1947**, 96.
(8) Wipf, P.; Miller, C. P. *Tetrahedron Lett.* **1992**, *33*, 907.
(9) (a) Burgess,E. M.; Penton, Jr., H. R.; Taylor, E. A. *J. Org. Chem.* **1973**, *38*, 26. (b) Burgess, E. M.; Penton, H. R., Jr.; Taylor, E. A.; Williams W. M. *Organic Syntheses*; Wiley: New York, 1988; Coll. Vol. VI, 1988; p 788.
(10) North, M.; Pattenden, G. *Tetrahedron* **1990**, *24*, 8267.

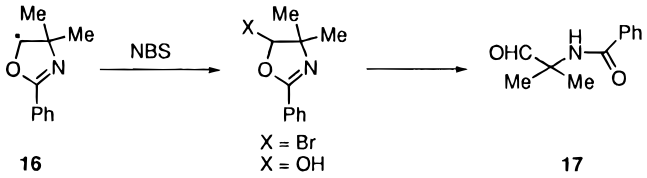
Scheme 2



similar to the oxidation of 2-aryl-substituted oxazolines were employed for the 2-alkyl-4-carbomethoxy derivatives, a mixture of brominated products were obtained. This necessitated the use of lower temperatures and photolytic conditions. As seen from Table 1, oxidation of the methyl-substituted oxazoline gave the desired oxazole in >60% yield (Table 1, entry b). Reaction of 2-(*n*-pentyl)-4-carbomethoxyoxazoline with NBS at −15 °C gave the desired oxazole along with some starting material and side chain-brominated product. Lowering the temperature and using excess NBS (5 equiv) ultimately resulted in a satisfactory yield of the desired oxazole (Table 1, entry c).

However, application of these oxidation conditions to isopropyl and cyclohexyl substituted oxazolines, wherein both contained a tertiary hydrogen atom, were not met with success. In both cases considerable bromination products were formed. In order to increase the selectivity of the reaction, dichloromethane was replaced by aromatic solvents. The latter are well known to form an intermediate π complex with halogen atoms.[11] This, too, failed to avoid the bromination products, **15** (Table 1, entries d, e). The extension of the NBS method to the oxidation of thiazolines, however, failed to give the desired thiazoles under various conditions (*hν*, peroxide).

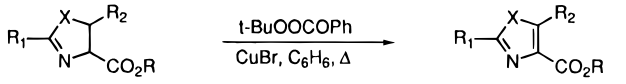
In the interest of determining the site of radical formation, 4,4-dimethyl-2-phenyloxazoline was treated with 2.2 equiv of NBS in the presence of benzoyl peroxide. Proposed formation of the radical intermediate **16** at the 5-position would be followed by trapping of the bromine atom, and the resulting product could then lead to the open chained aldehyde **17** on aqueous workup. However,



the absence of any of the above intermediates or aldehyde **17** precluded this reaction pathway. An alternative mechanism for the oxidation of 2-substituted-4-carbomethoxy oxazolines might be expected to involve the initially formed radical **18**, a relatively stable captodative

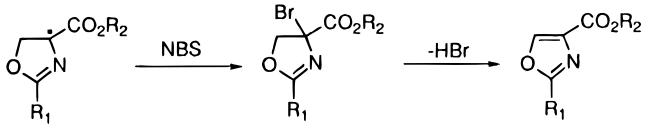
(11) Russell, G. A. *J. Am. Chem. Soc.* **1958**, *80*, 4987.
(12) Rawlinson, D. J.; Sosnovsky, G. *Synthesis* **1972**, 1. *Ibid* **1973**, 567.

Table 2. Radical Oxidation of Oxazolines/Thiazoline

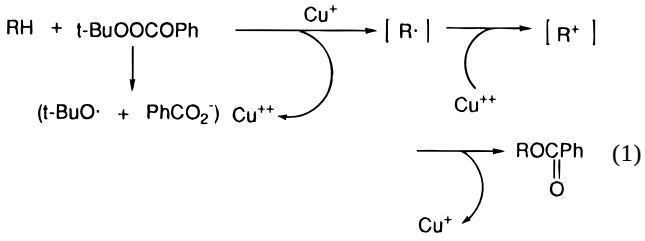


Entry	R	R_1	R_2	X	Rxn time	Yield, %
a)	Me	i-Pr	H	O	12 h	60
b)	Me	Et	Me	O	12 h	63
c)	Et	n-Pr	H	S	4.5 h	83
d)	Me	Cyclohexyl	H	O	12 h	55
e)	Me	$(CH_3)_2CH$(H)NHt-Boc	H	O	12 h	45
f)	Me	CH_3(H)NHt-Boc	H	O	12 h	25
g)	Me	$PhCH_2$(H)NHt-Boc	H	O	12 h	31

radical.[13] Trapping of the bromine atom followed by elimination of hydrogen bromide would afford the desired oxazole **19**.



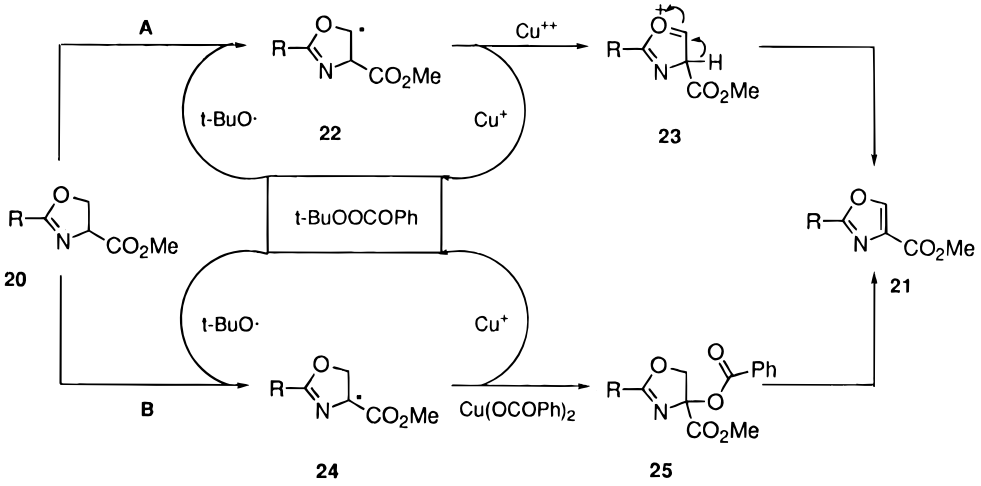
In view of the limited applicability of the reaction wherein side chain radical bromination in the tertiary alkyl groups was unavoidable, an effort was made to search for alternative methods. With the knowledge that radical formation most likely occurs at the 4-position of the oxazoline, methods were evaluated that could selectively generate the appropriate radical species. One such method was the so-called Kharasch−Sosnovsky[12] reaction, which involves a copper ion-catalyzed decomposition of a peroxyester resulting in the formation of an alkoxy radical. Subsequent reaction with a C−H substrate then generates an alkyl radical which is oxidized to a cation and captured by the carboxylate anion (eq 1).



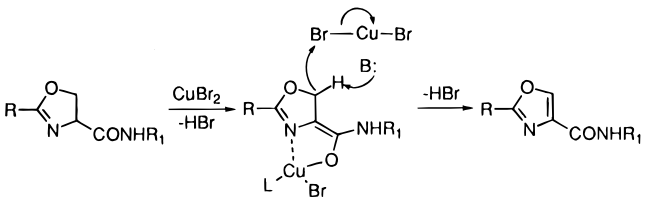
This process was initially found to be moderately successful when applied to the oxidation of oxazolines and thiazolines.[6a] The early experimental conditions required that we utilize 1.1 equiv of Cu(I)Br and 1.5 equiv of *tert*-butyl perbenzoate in benzene at reflux. The yields of the oxidation are given in Table 2. Oxazolines containing either the isopropyl or cyclohexyl substituents (Table 2, entries a, d) gave only the oxazole **21** devoid of any side chain substitution as previously observed with NBS (Table 1, entries d, e). Additionally, thiazoline ester **20c**

(13) Viehe, H. G.; Janousek, Z.; Merenyi, R.; Stella, L. *Acc. Chem. Res.* **1985**, *18*, 148.

Scheme 3

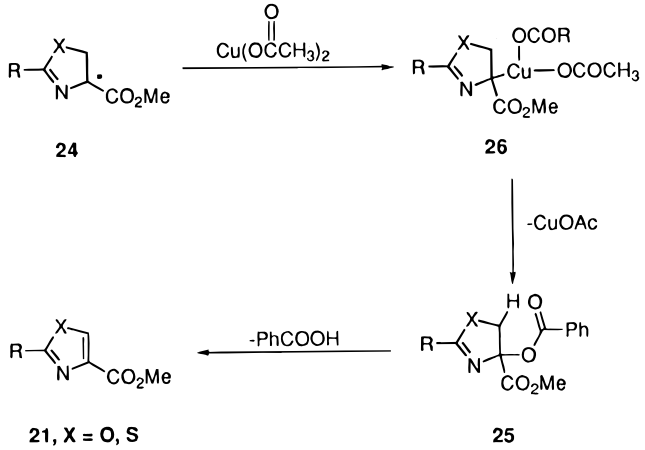


Scheme 4



was smoothly oxidized to the corresponding thiazole **21c** (Table 2, entry c) in good yield. The presence of a 5-methyl substituent in the oxazoline **20** (R_2 = Me, X = O, Table 2, entry b) was found not to interfere with the oxidation to the oxazole. This copper-mediated process did not limit the nature of the side chain to aryl or *n*-alkyl, but also allowed secondary and tertiary hydrogens to remain intact at the α-position. When applied to oxazolines **20** (Table 2, entries e, f, g) containing stereocenters at the 2-(α) position, the corresponding oxazoles **21** were obtained, albeit in low yields ranging from 30−45% compared to the simple alkyl or aryl substituted oxazoles. Based on these results, the following mechanisms (A and B, Scheme 3) were proposed. The intermediate α-oxa radical **22** in mechanism A has precedent in the Kharasch−Sosnovsky reactions[12] involving tetrahydrofurans and thiophenes, which were oxidized by Cu(II) *via* oxonium ions to their dihydro derivatives. In the case of **22** this would readily lead to **23**, and rapid proton loss would provide the observed oxazole **21**. On the other hand (mechanism B), formation of the more favorable captodative radical[13] **24** followed by ligand transfer[14] with Cu(II) benzoate would produce the intermediate **25**. The latter would undergo a syn elimination with the loss of benzoic acid to give the oxazole **21**. It is also be reasonable to expect that the captodative radical **24** may be formed from **22**, *via* H-atom transfer. Interestingly, while this study was in progress a Cu(II)Br-mediated oxidation of 2-oxazolines was reported by a Bristol-Myers Squibb group[4c] wherein a mechanism involving an ionic pathway was proposed (Scheme 4).

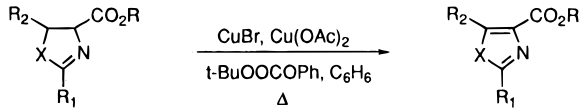
From Scheme 3 above, it was felt that mechanism A or B would be favored by the presence of excess Cu(II) species in the reaction mixture. This might serve to increase the solubility of the oxazoline in the benzene solution and may also provide the higher copper(II) ion concentration which could enhance the rate of oxidation and/or ligand transfer between the presumed radical **24** (X = O) and the Cu(II) salts. It was assumed that this would lead to the Cu(III) species[14] **26** *via* oxidative addition which subsequently reductively eliminates to the acyloxy oxazoline **25**. Syn elimination, on heating, would then provide the oxazole **21** (or thiazole, X = S). Some evidence for this pathway was acquired when the oxidation was performed using the stoichiometric ratios: CuBr (1.1), $Cu(OAc)_2$ (1.1), and *tert*-butyl perbenzoate (1.5) in refluxing benzene for the time specified in Table 3. In this manner, yields of the oxazoles and thiazoles increased to 55−81% (*vs* 25−45%, Table 2, entries e, f, g) and 76−84%, respectively. The oxazole fragment **21** (Table 3, entry k), a precursor[2g,h] to Calyculin A was also



prepared in good yield without any loss of optical purity. The reaction times were also significantly decreased to 4−8 h (*vs* 12 h, Table 2). Chiral HPLC analysis of the valine derived oxazole and thiazole (Table 3, entries a, c) indicated that there was no racemization occuring during the oxidations (see supporting information). Additional support for mechanism B above (Scheme 3) was obtained when the adduct ester **25** was isolated in 8% yield from a run that was performed at 60 °C in benzene rather than at reflux. Presumably, the benzoate ester eliminates somewhat slower than the acetate, thus allowing for its isolation. The structure of the benzoate **25**, derived from valine derivative **20e**, was supported by ^{1}H NMR, ^{13}C, DEPT 135, and 90 spectra. Subsequent heating of the solution containing the benzoate **25** gave the expected oxazole **21e**. Extension of this oxidation

(14) Jenkins, C. L.; Kochi, J. K. *J. Am. Chem. Soc.* **1972**, *94*, 843 and 856.

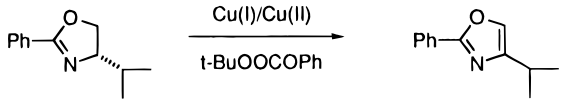
Table 3. Radical Oxidations to Oxazoles/Thiazoles



20 **21**

Entry	R	R_1	R_2	X	Rxn time	Yield, %
e)	Me	$(CH_3)_2CH$, NHt-Boc	H	O	8.5 h	65
f)	Me	CH_3, NHt-Boc	H	O	8.5 h	51
g)	Me	$PhCH_2$, NHt-Boc	H	O	8.0 h	54
h)	Me	$(CH_3)_2CH$, NHt-Boc	Me	O	8.5 h	56
i)	Et	$(CH_3)_2CH$, NHt-Boc	Me	S	4.5 h	84
j)	Et	$PhCH_2$, NHt-Boc	H	S	4.5 h	76
k)	Et	CH_3, N_3	H	O	8.5 h	56
l)	Me	TBSO, O	H	O	7.5 h	81

protocol to 4-alkyl substituted oxazoline **27**, however, gave very poor yields (10%) of the oxazoles **28** even after prolonged reflux (24 h) with the unreacted oxazoline **27** being returned as the major component of the reaction



27 **28**

(eq 2). In retrospect this is not surprising, since the incipient radical (**22** or **24**) to be formed at the 5-position may not be expected to be as stable, even if it did form initially, as that having an electron-withdrawing group at this position.

In summary, a useful Cu(I)/Cu(II)/peroxide oxidation has been developed in this laboratory for the synthesis of 4-carboxyoxazoles and thiazoles. The method tolerates a wide range of functional groups without loss of optical purity. The limitations previously observed in the bromination of oxazolines was nicely avoided using the copper-mediated process. The latter process has already been utilized in the total synthesis of several important classes of compounds such as, the streptogramin antibiotic, madumycin II,[16] Bistatramides[6d] C and D, and the potent HIV-1 inhibitor thiangazole.[15] This should open the way toward the synthesis of other biologically active oxazole/thiazole-containing natural products.

Experimental Section

General Procedure for the Preparation of Oxazolines. 4-Carbomethoxy-2-methyl-2-oxazoline, 13b.[4] A suspension of 20.25 g (164 mmol) of methyl acetimidate hydrochloride[17] in 250 mL of CH_2Cl_2 at 0 °C was treated with 21.46 g (180.4 mmol) of racemic serine methyl ester and the reaction mixture allowed to warm to room temperature. After 24 h at room temperature, 50 mL water was added, and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 30 mL), and the combined organic phases were dried (Na_2SO_4) and concentrated under vacuum. The residue was then purified by flash chromatography on SiO_2 using hexane/ethyl acetate (65:35) to give 23.45 g (96% yield) of **13b** as a colorless oil. IR (thin film, cm^{-1}) 2957, 1744, 1670, 1439; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.00 (s, 3H), 3.76 (s, 3H), 4.34−4.49 (m, 2H), 4.66−4.73 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.8, 52.6, 68.2, 69.4, 167.7, 171.7.

(*S*)-(+)-4-Carbomethoxy-2-ethyl-5-methyl-2-oxazoline, 20b. Prepared as described in the general procedure using 1.5 g (12.20 mmol) of ethyl imidate, 1.596 g (13.42 mmol) of L-threonine methyl ester and 20 mL CH_2Cl_2. Flash chromatography on SiO_2 using hexane/ethyl acetate (70:30) gave 1.85 g (89% yield) of **20b** as a colorless oil. $[\alpha]^{23}_D$ 170.5 (*c* 3.12, $CHCl_3$); IR (thin film, cm^{-1}) 2982, 1743, 1658, 1439, 1020; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.08 (t, J = 7.62 Hz, 3H), 1.30 (d, J = 6.34 Hz, 3H), 2.21 (q, J = 7.49 Hz, 2H), 3.66 (s, 3H), 4.09−4.13 (dd, J = 0.69, 7.31 Hz, 1H), 4.61−4.69 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.95, 20.7, 21.5,52.2, 74.4, 78.2, 170.8, 171.5. Anal. Calcd for $C_8H_{13}NO_3$: C, 56.13; H, 7.65. Found C, 56.07; H, 7.69.

4-Carbomethoxy-2-isopropyl-2-oxazoline, 20a. Prepared as described in the general procedure using isopropyl imidate[18] (3.7 g, 27 mmol), racemic serine methyl ester (3.53 g,29.7 mmol), and 45 mL of CH_2Cl_2. Flash chromatography on SiO_2 using hexane/ethyl acetate (70:30) gave 3.96 g (86% yield) of **20a** as a colorless oil. IR (thin film, cm^{-1}) 2975, 1743, 1657, 1472; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.13 (d, J = 6.99 Hz, 6H), 2.51−2.61 (m, 1H), 3.71 (s, 3H), 4.28−4.43 (m, 2H), 4.61−4.68 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 19.5, 28.1, 52.5, 67.9, 69.1, 171.7, 174.7.

4-Carbomethoxy-2-pentyl-2-oxazoline, 13c. Prepared as described in the general procedure using 1.82 g (12.2 mmol) of *n*-pentyl imidate,[18] racemic serine methyl ester (1.60 g, 13.42 mmol), and 20 mL of CH_2Cl_2. Flash chromatography on SiO_2 using hexane/ethyl acetate (70:30) gave 1.99 g (91% yield) of **13c** as a colorless oil. IR (thin film, cm^{-1}) 2956, 1744, 1661, 1467, 1178, 1039; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.81 (t, J = 6.81Hz, 3H), 1.19−1.25 (m, 4H), 1.53−1.60 (m, 2H), 2.22 (t, J = 7.89 Hz, 2H), 3.68 (s, 3H), 4.26−4.40 (m, 2H), 4.60−4.66 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.7, 22.1, 25.4, 27.7, 31.1, 52.4, 67.8, 69.0, 170.8, 171.6.

4-Carbomethoxy-2-cyclohexyl-2-oxazoline, 20d. Prepared as described in the general procedure using 2.17 g (12.2 mmol) of cyclohexyl imidate,[18] racemic serine methyl ester (1.596 g, 13.42 mmol), and 20 mL of CH_2Cl_2. Flash chromatography on SiO_2 using hexane/ethyl acetate (70:30) gave 2.37 g (92% yield) of **20d** as a colorless oil. IR (thin film, cm^{-1}) 2932, 1743, 1654, 1037; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.16−1.87 (m, 10 H), 2.17−2.29 (m, 1H), 3.70 (s, 3H), 4.27−4.44 (m, 2H), 4.53−4.69 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.4, 25.6, 29.5, 29.6, 37.3, 52.4, 67.8, 68.9, 171.8, 173.7. Anal. Calcd for $C_{11}H_{17}NO_3$: C, 62.54; H, 8.11; Found: C, 62.52; H, 8.10.

(*S*)-(+)-4-Carbomethoxy-2-propyl-2-thiazoline, 20c. Prepared as described in the general procedure using 1.68 g (12.2 mmol) of *n*-propyl imidate, 1.99 g (13.42 mmol) of L-cystine ethyl ester and 20 mL of CH_2Cl_2. Flash chromatography on SiO_2 using hexane/ethyl acetate (65:35) gave **20c** as a colorless oil. $[\alpha]^{23}_D$ 108.8 (*c* 10.9, $CHCl_3$); IR (thin film, cm^{-1}) 2963, 1740, 1622, 1463, 1095; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.92 (t, J = 7.32 Hz, 3H), 1.26 (t, J = 7.11 Hz, 3H), 1.59−1.70 (m, 2H), 2.46−2.52 (m, 2H), 3.41−3.55 (m, 2H), 4.19 (q, J = 7.11 Hz, 2H), 4.97−5.04 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.5, 14.1, 21.0, 36.2, 61.6, 77.9, 170.9, 174.7.

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(17) (a) Dox, A. W. *Organic Syntheses*, Wiley: New York, 1990; Coll. Vol. VII, p 5. (b) See ref 3d above.

(18) Iminium Salts in Organic Chemistry, Bohme, H., Viehe, H. G., Ed.; John Wiley and Sons: Canada, 1976; Vol. 9, Part 1.

4-Carbomethoxy-2-phenyl-2-oxazoline, 13a.[19] Prepared as described in the general procedure using 2.74 g (16 mmol) of benzimidate hydrochloride, 2.74 g (17.6 mmol) of racemic serine methyl ester and 27 mL of CH_2Cl_2. Flash chromatography on SiO_2 using hexane/ethyl acetate (80:20) gave **13a** as a colorless oil. IR (thin film, cm^{-1}) 3062, 2953, 1210, 1178, 1069; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.71 (s, 3H), 4.44−4.51 (dd, J = 8.75, 10.53 Hz, 1H), 4.59 (app t, J = 8.59 Hz, 1H), 4.82−4.88 (dd, J = 8.02, 10.4 Hz, 1H), 7.28−7.41 (m, 3H), 7.88 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 52.4, 68.3, 69.3, 126.7, 128.1, 128.3, 131.6, 165.9, 171.3.

General Procedure for the Preparation of BOC Protected Amino Acids. To a stirred solution of 1 equiv of the amino acid in THF/H_2O (1:1) (0.30 M) at rt was added 2.2 equiv of sodium hydroxide. To this was added 1.1 equiv of Boc_2O, and the reaction mixture esd stirred at rt for 18 h. The organic layer was concentrated under vacuum, and the aqueous layer was extracted with CH_2Cl_2. The aqueous layer was then acidified with 1 N HCl to pH 4 and the precipitated acid extracted with CH_2Cl_2. Concentration under vacuum gave the desired product in quantitave yield as a white solid, used without further purification for the next step.

(*S*)-(+)-*N*-(*tert*-Butyloxycarbonyl)valine.[10] Prepared as described in the general procedure using 0.710 g (6.06 mmol) of (*S*)-(+)-valine, 1.46 g (6.67 mmol) of $(Boc)_2O$, and 0.533 g (13.3 mmol) of sodium hydroxide. $[\alpha]^{23}_D$ 11.7 (*c* 2.35, $CHCl_3$); IR (thin film, cm^{-1}) 3328, 3103, 2974, 1717, 1661, 1510, 1406, 1164; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.89 (d, J = 6.84 Hz, 3H), 0.94 (d, J = 6.84 Hz, 3H), 1.41 (s, 9H), 2.14−2.20 (m, 1H), 5.04 (m, 1H), 6.28 (d, J = 7.44), 11.53 (br, s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 17.4, 18.9, 28.3, 31.0, 58.3, 80.0, 155.8, 177.2.

(*S*)-(+)-*N*-(*tert*-Butyloxycarbonyl)phenylalanine.[10] Prepared as described in the general procedure using 1.0 g (6.06 mmol) of (*S*)-phenylalanine, 1.46 g (6.67 mmol) of $(Boc)_2O$, and 0.533 g (13.3 mmol) of sodium hydroxide; $[\alpha]^{23}_D$ 7.29 (*c* 7.0); IR (thin film, cm^{-1}) 3314, 2978, 1718, 1498, 1404, 1165; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.30 (s, 9H), 3.20 (m, 2H), 5.20 (m, 1H), 6.61 (d, J = 7.5 Hz, 1H), 7.18−7.31 (m, 5H), 11.35 (br, s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 28.3, 38.2, 54.6, 80.6, 127.4, 128.9, 129.7, 136.2, 155.7, 176.4.

(*S*)-(−)-*N*-(*tert*-Butyloxycarbonyl)alanine.[10] Prepared as described in the general procedure using 1.50 g (16.9 mmol) of (*S*)-alanine, 4.06 g (18.6 mmol) of $(Boc)_2O$, and 1.48 g (77.1 mmol) of sodium hydroxide; $[\alpha]^{23}_D$ −2.0 (*c* 1.8 $CHCl_3$); IR (thin film, cm^{-1}) 2970, 1700, 1655, 1417, 1161; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.38 (br, s, 9H), 1.79−2.25 (m, 4H), 3.30−3.54 (m, 2H), 4.16−4.31 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 23.6,28.3, 30.7, 46.3, 58.9,80.3, 153.9, 178.6.

General Procedure for the Preparation of Amides from the Boc Protected Amino Acids. To a stirred solution of the Boc protected amino acid (1 equiv) in CH_2Cl_2 (0.22 M) at −30 °C was added *N*-methylmorpholine (1.1 equiv) followed by isobutyl chloroformate (1.1 equiv). The reaction mixture was allowed to warm to −20 °C over 30 min, and gaseous ammonia was then bubbled through for 15 min. After warming to rt over 1 hour, the reaction mixture was diluted with water, and the layers were separated. The aqueous layer was extracted with CH_2Cl_2, and the combined organic extracts were dried (Na_2SO_4) and concentrated under vacuum to give the desired amides which were used without further purification for the next step.

(*S*)-(+)-*N*-(*tert*)-butyloxycarbonylvalinamide.[10] Prepared as described in the general procedure using 0.727 g (3.35 mmol) of (*S*)-(+)-*N*-(*tert*-butyloxycarbonyl)valine, 0.405 mL (3.69 mmol) of *N*-methylmorpholine, and 0.482 mL (3.69 mmol) of isobutyl chloroformate. $[\alpha]^{23}_D$ 0.30 (*c* 2.67, EtOH); IR (thin film, cm^{-1}) 3383, 3342, 3200, 1682, 1662, 1520, 1170; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.90 (d, J = 6.81 Hz, 3H), 0.94 (d, J = 6.78 Hz, 3H), 1.39 (s, 9H), 2.02−2.11 (m, 1H), 5.21 (m, 1H), 6.02 (br, s, 1H), 6.39 (br, s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 19.2, 28.3, 30.7, 59.4, 79.8, 155.9, 174.4.

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(*S*)-(+)-*N*-(*tert*-Butyloxycarbonyl)phenylalanamide.[10] Prepared as described in the general procedure using 1.30 g (4.91 mmol) of (*S*)-(+)-*N*-(*tert*-butyloxycarbonyl)phenylalanine, 0.594 mL (5.40 mmol) of *N*-methylmorpholine, and 0.706 mL (5.40 mmol) of isobutyl chloroformate; $[\alpha]^{23}_D$ 13.57 (*c* 3.42, EtOH); IR (thin film, cm^{-1}) 3383, 3342, 3190, 1682, 1657, 1520, 1165; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.36 (s, 9H), 3.03 (m, 2H), 5.23 (d, J = 6.54 Hz, 1H), 5.93 (br, s, 1H), 6.12 (br, s, 1H), 7.18−7.29 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 27.8, 38.5, 71.2, 80.1, 126.8, 128.6, 129.3, 136.6, 155.5, 174.0.

General Procedure for the Preparation of Imino Ethers 11 from the Acid Amides. A suspension of *N*-*tert*-butyloxycarbonyl amino acid (1 equiv) in dry CH_2Cl_2 (0.4 M) was cooled to 0 °C, to this was added triethyloxonium hexafluorophosphate (1.1 equiv), and the resulting solution was stirred at rt for 18 h. The reaction mixture was then washed with saturated $NaHCO_3$, dried (Na_2SO_4), and concentrated under vacuum to give a colorless oil that was carried on directly to the next step without further purification.

2(*S*)-[*N*-(*tert*-Butyloxycarbonyl)amino]-3-methylbutanimino Ethyl Ether.[10] Prepared as described in the general procedure using 2.0 g (9.26 mmol) of (*S*)-(+)-*N*-(*tert*-butoxycarbonyl) valinamide and 2.55 g (10.19 mmol) of triethyloxonium hexafluorophosphate and obtained in 96% yield (2.17 g). Used without further purification directly for the next step. ^1H NMR ($CDCl_3$, 300 MHz) δ 1.43 (t, J = 7.20 Hz, 3H), 0.93 (d, J = 7.01 Hz, 3H), 0.98 (d, J = 6.93 Hz, 3H), 1.42 (s, 9H), 2.08−2.21 (m, 1H), 3.98−4.49 (m, 3H), 4.8 (m, 1H), 5.81 (br, s, 1H), 6.10 (br, s, 1H).

2(*S*)-[*N*-(*tert*-Butyloxycarbonyl)amino]-3-phenylpropanimino Ethyl Ether.[10] Prepared as described in the general procedure using 1.0 g (3.79 mmol) of (*S*)-(+)-*N*-(*tert*-butoxycarbonyl)phenylalaninamide, and 1.04 g (4.17 mmol) of triethyloxonium hexafluorophosphate and obtained in 98% yield (1.08 g). Used without further purification directly for the next step. ^1H NMR ($CDCl_3$, 300 MHz) δ 1.40 (t, J = 7.21 Hz, 3H), 1.41 (s, 9H), 3.10 (m, 2H), 3.98−4.41 (m, 3H), 5.31 (br, s, 1H), 6.10 (br, s, 1H), 7.16−7.26 (m, 5H).

General Procedure for the Preparation of Dipeptides 7 from the Boc Protected Amino Acids. Dipeptide of (*S*)-*N*-*tert*-Butyloxycarbonyl Valine-Serine. To a solution of the (*S*)-(+)-*N*-(*tert*-butyloxycarbonyl)valine (4.0 g,18.4 mmol) in 80 mL of THF (0.23 M) at −30 °C was added 3.5 mL (38.6 mmol) of Et_3N, followed by 2.64 mL (20.2 mmol) of isobutyl chloroformate. After 30 min, 3.14 g (20.2 mmol) of racemic serine methyl ester hydrochloride was added as a solid. The reaction mixture was allowed to warm gradually to rt over 6 h and stirred further for an additional 12 h. The organic layer was concentrated under vacuum followed by dilution with water (30 mL) and ethyl acetate (50 mL). The layers were separated, and the organic layer was washed with saturated $NaHCO_3$ (30 mL). The aqueous layer was extracted with ethyl acetate (2 × 30 mL), and the combined organic extracts were dried (Na_2SO_4) and concentrated under vacuum to give 5.38 g (92% yield) of the desired product. Used without further purification for the next step. IR (thin film, cm^{-1}) 3314, 2965, 1654, 1522; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.87 (d, J = 6.72 Hz, 3H), 0.96 (d, J = 6.87 Hz, 3H), 1.41 (s, 9H), 2.14−2.23 (m, 1H), 3.75 (s, 3H), 3.85−3.93 (m, 3H), 4.62−4.66 (m, 1H), 5.09−5.19 (m, 1H), 6.96 (br, s, 1H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 17.9, 19.2, 28.2, 30.9, 52.6, 54.6, 59.9, 62.5, 80.2, 156.3, 170.9, 172.1.

Dipeptide of (*S*)-*N*-*tert*-Butyloxycarbonyl Phenylalanine-Serine. Prepared as described in the general procedure using 2.44 g (9.22 mmol) of (*S*)-(+)-*N*-(*tert*-butyloxycarbonyl)-phenylalanine, 2.13 mL (19.4 mmol) of *N*-methylmorpholine, 1.33 mL (10.1 mmol) of isobutyl chloroformate, and racemic serine methyl ester hydrochloride and obtained in 96% yield (3.24 g) as a colorless oil. Used without further purification for the next step. IR (thin film, cm^{-1}) 3311, 2979, 1740, 1659; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.36 (s, 3H), 2.96−3.14 (m, 2H), 3.26 (br, s, 1H), 3.72 (s, 3H), 3.88 (m, 2H), 4.33−4.39 (m, 1H), 4.56−4.61 (m, 1H), 5.18 (d, J = 7.65 Hz, 1H), 7.19 (d, J = 1.71 Hz, 1H), 7.21−7.30 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 28.2, 38.1, 52.7, 54.9, 55.9, 62.7, 80.5, 126.9, 128.6, 129.3, 136.4, 155.7, 170.5, 171.7.

Dipeptide of (*S*)-*N*-*tert*-Butyloxycarbonyl Valine-Threonine. Prepared as described in the general procedure using 2.0 g (9.22 mmol) of (*S*)-(+)-*N*-(*tert*-butyloxycarbonyl)valine, 2.13 mL (19.4 mmol) *N*-methylmorpholine, 1.33 mL (10.1 mmol) of isobutyl chloroformate, and 1.71 g (10.1 mmol) of L-threonine methyl ester and obtained in 93% yield (2.84 g) as a colorless oil. Used without further purification for the next step. IR (thin film, cm^{-1}) 3328, 2964, 1747, 1663; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.90 (d, J = 7.01 Hz, 3H), 1.19 (d, J = 6.21 Hz, 3H), 3.73 (s, 3H), 2.10 (m, 1H), 3.83−4.10 (m, 1H), 4.34−4.58 (m, 1H), 4.61 (m, 1H), 5.15−5.18 (m, 1H), 6.85 (br, s, 1H).

Dipeptide of (*S*)-*N*-*tert*-Butyloxycarbonyl Alanine-Serine. Prepared as described in the general procedure using 2.50 g (13.23 mmol) of (*S*)-(+)-*N*-(*tert*-butyloxycarbonyl)alanine, 2.51 mL (27.8 mmol) of Et_3N, 1.89 mL (14.6 mmol) of isobutyl chloroformate, and 2.26 g (14.6 mmol) of racemic serine methyl ester hydrochloride and obtained in 96% yield (3.68 g) as a colorless oil. Used without further purification for the next step. IR (thin film, cm^{-1}) 3343, 2983, 1739, 1661; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.23 (d, J = 7.01 Hz, 3H), 1.31 (s, 9H), 3.68 (s, 3H), 3.71−3.92 (m, 2H), 4.10−4.23 (m, 2H), 4.56 (m, 1H), 5.60 (d, J = 7.23 Hz, 1H), 7.34 (d, J = 7.56 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 18.1, 27.9, 49.8, 52.2, 54.3, 62.2, 79.8, 155.4, 170.6, 173.2.

General Procedure for the Preparation of Oxazolines 8 or 20 (e−l) from the Dipeptides *via* Burgess reagent. 2-[(*S*)-1-[*N*-(*tert*-Butoxycarbonyl)amino]-2-methylpropyl]-4-carbomethoxyoxazoline, 20e. To a solution of the dipeptide derived from (*S*)-*N*-*tert*-butyloxycarbonyl valine-serine (4.35 g, 13.7 mmol) in 90 mL of THF (0.15 M) was added 3.58 g (15.1 mmol) of Burgess reagent,[9] and the contents were heated to reflux for 1.5 h. The solvent was concentrated under vacuum and the residue flash chromatographed on SiO_2 using hexane/ethyl acetate (70:30) to give **20e** in 68% yield (4.08 g) as a colorless oil. IR (thin film, cm^{-1}) 3310, 2966, 1720, 1658; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.93 (d, J = 6.90 Hz, 3H), 0.97 (d, J = 6.84 Hz, 3H), 1.38 (s, 9H), 2.13 (m, 1H), 3.69 (s, 3H), 4.23−4.30 (dd, J = 3.10, 8.20 Hz, 1H), 4.75−4.78 (dd, J = 1.43, 10.22 Hz, 1H), 4.88−4.94 (m, 2H), 5.23 (d, J = 9.10 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 16.3, 16.7, 31.4, 52.1, 53.8, 71.0, 78.8, 79.2, 155.9, 170.7, 170.9.

2-[(*S*)-1-[*N*-(*tert*-Butoxycarbonyl)amino]-2-methylpropyl]-5-methyl-4-carbomethoxyoxazoline, 20h. Prepared as described in the general procedure using 2.50 g (7.53 mmol) dipeptide of (*S*)-*N*-*tert*-butyloxycarbonyl valine-threonine and 1.97 g (8.28 mmol) of Burgess reagent.[9] Flash chromatography on SiO_2 using hexane/ethyl acetate (70:30) gave 1.49 g (63% yield) of **20h** as a colorless oil. IR (thin film, cm^{-1}) 3300, 2964,-1715, 1658; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.91 (d, J = 6.90 Hz, 3H), 0.96 (d, J = 6.84 Hz, 3H), 1.24 (d, J = 6.45 Hz, 3H), 1.39 (s, 9H), 2.11 (m, 1H), 3.70 (s, 3H), 4.26−4.30 (dd, J = 3.12, 8.16 Hz, 1H), 4.73−4.76 (dd, J = 1.41, 10.14 Hz, 1H), 4.89−4.93 (m, 1H), 5.20 (d, J = 9.09 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 16.1,16.9, 28.3, 31.4, 51.9, 53.6, 70.7, 78.3, 79.5, 155.6, 170.0, 170.1.

2-[(*S*)-1-[*N*-(*tert*-Butoxycarbonyl)amino]-2-phenylethyl]-4-carbomethoxyoxazoline, 20g. Prepared as described in the general procedure using 3.0 g (8.20 mmol) of dipeptide of (*S*)-*N*-*tert*-butyloxycarbonyl phenylalanine-serine and 2.14 g (9.02 mmol) of Burgess reagent.[9] Flash chromatography on SiO_2 using hexane/ethyl acetate (75:25) gave 2.03 g (71% yield) of **20g** as a colorless oil. IR (thin film, cm^{-1}) 3335, 2977, 1745, 1709; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.37 (s, 9H), 2.97−3.14 (m, 2H), 3.71 (s, 3H), 4.37−4.41 (m, 1H), 4.51−4.71 (m, 2H), 5.14 (d, J = 7.68 Hz, 1H), 7.07−7.26 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 28.2, 38.8, 49.6, 52.6, 67.7, 69.9, 79.7, 126.7, 128.2, 129.3, 129.4, 129.5, 135.7, 154.8, 169.3, 170.8.

Oxazoline Azide, 20k.[1h] ^1H NMR ($CDCl_3$, 300 MHz) δ 1.20 (d, J = 7.0 Hz, 3H), 1.63−1.76 (m, 1H), 1.88−2.00 (m, 1H), 2.63−2.71 (m, 1H), 3.34 (t, J = 6.93 Hz, 2H), 3.76 (s, 3H),4.34−4.49 (ddd, J = 7.47, 8.67, 16.23 Hz, 2H), 4.68−4.74 (m, 1H).

2-[(S)-1-[*N*-(*tert*-Butoxycarbonyl)amino]-2-methyl]-4-carbomethoxyoxazoline, 20f. Prepared as described in the general procedure using 3.5 g (12.1 mmol) of dipeptide of (*S*)-*N*-*tert*-butyloxycarbonyl alanine-serine and 3.15 g (13.3 mmol) of Burgess reagent. Flash chromatography on SiO_2 using hexane/ethyl acetate (65:35) gave 2.10 g (64% yield) of **20f** as a colorless oil. IR (thin film, cm^{-1}) 3320, 2958, 1705, 1608; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.34 (d, J = 7.77 Hz, 3H), 1.38 (s, 9H), 3.73 (s, 3H), 4.38−4.55 (m, 2H), 4.68−4.74 (dd, J = 7.83, 10.59 Hz, 1H), 5.16 (br,s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 19.4, 28.1, 44.6,52.9, 67.6, 70.1, 80.2, 154.8, 171.0, 171.2.

General Procedure for the Preparation of Thiazolines from the Imino Ethers. To a solution of the imino ether (1.0 equiv) in anhydrous ethanol (0.32 M) was added L-cystine ethyl ester (1.1 equiv) and the resulting solution stirred at rt for 18 h. The solvent was evaporated and the residue flash chromatographed on SiO_2 using hexane/ethyl acetate to give the desired product.

2-[(S)-1-[*N*-(*tert*-Butyloxycarbonyl)amino]-2-methylpropyl]-4-carbethoxy-(*S*)-2-thiazoline, 20i. Prepared as described in the general procedure using 2.17 g (8.89 mmol) 2(*S*)-[*N*-(*tert*-butyloxycarbonyl)amino]-3-methylbutanimino ethyl ether and 1.32 g (8.89 mmol) of L-cystine ethyl ester. Flash chromatography on SiO_2 using hexane/ethyl acetate (85:15) gave 0.750 g (42% yield) of **20i** as a colorless oil. $[\alpha]^{23}_D$ −64.3 (*c* 1.1, $CHCl_3$); IR (thin film, cm^{-1}) 3350, 1705, 1618; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.81 (d, J = 6.78 Hz, 3H), 0.91 (d, J = 6.81 Hz, 3H), 1.20 (t, J = 7.11 Hz, 3H), 1.35 (s, 9H), 2.03−2.18 (m, 1H), 3.41−3.51 (m, 2H), 4.15 (q, J = 7.11 Hz, 2H), 4.40 (m, 1H), 5.05 (t, J = 8.10 Hz, 1H), 5.20 (d, J = 9.06 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.9, 16.4, 19.2, 28.1, 32.3, 35.6, 57.7, 61.5, 77.5, 79.4, 155.3, 170.4, 175.5.

2-[(S)-1-[*N*-(*tert*-Butyloxycarbonyl)amino]-2-phenylethyl]-4-carbethoxy-(*S*)-2-thiazoline, 20j. Prepared as described in the general procedure using 1.08 g (3.70 mmol) of 2(*S*)-[*N*-(*tert*-butyloxycarbonyl)amino]-3-methylbutanimino ethyl ether and 0.55 g (3.70 mmol) of L-cystine ethyl ester. Flash chromatography on SiO_2 using hexane/ethyl acetate (85:15) gave 0.630 g (45% yield) of **20j** as a colorless oil. $[\alpha]^{23}_D$ −49.1 (*c* 1.3, $CHCl_3$); IR (thin film, cm^{-1}) 3310, 2960, 1700, 1606; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.28 (t, J = 7.08 Hz, 3H), 1.37 (s, 9H), 3.00−3.23 (m, 2H), 3.44−3.60 (m, 2H), 4.23 (q, J = 7.05 Hz, 2H), 4.78−5.18 (m, 3H), 7.15−7.29 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.1, 28.2, 35.4, 39.9, 53.9, 61.8, 78.0, 79.8, 126.8, 128.3, 129.6, 136.1, 154.4, 170.3, 175.9.

Oxazoline, 20l.[16] To a solution of the amide (1.22 g, 2.94 mmol) in 30 mL of THF was added 0.804 g (3.23 mmol) of Burgess reagent, and the contents were refluxed for 1.5 h. The solvent was removed under vacuum to give the crude product. Column chromatography on SiO_2 using hexane/ethyl acetate (7:3) gave 0.806 g (69% yield) of the desired oxazoline **20l**, in 65−70% overall yield from the acid. IR (thin film, cm^{-1}) 1730, 1632; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.02 (d, J = 4.5 Hz, 6H), 0.84 (s, 9H), 1.30 (s, 3H), 1.35 (s, 3H), 1.65−1.91 (m, 2H), 2.52−2.55 (d, J =7.3 Hz, 1H), 3.48 (t, J = 7.65, 1H), 3.80 (s, 3H), 4.00−4.05 (dd, J = 5.94, 7.95 Hz, 1H), 4.18−4.23 (m, 2H), 4.31−4.37 (dd, J = 8.79, 10.74 Hz, 1H), 4.46 (dd, J = 8.01, 8.79 Hz, 1H), 4.69 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −4.9, −4.7, 17.9, 25.7, 25.8, 26.9, 35.8, 40.9, 52.6, 67.4, 68.1, 69.1, 69.8, 72.4, 108.6, 168.3, 171.5. Anal. Calcd for $C_{19}H_{35}NO_6Si$: C, 56.83; H, 8.78. Found C, 56.58; H, 8.71.

Synthesis of Oxazoles Using NBS and Peroxide. 4-Carbomethoxy-2-phenyl-2-oxazole, 14a.[19] To 4-carbomethoxy-2-phenyl-2-oxazoline (0.30 g, 1.46 mmol) and benzoyl peroxide (20 mg, 0.082 mmol) was added 10 mL of dry benzene (0.15 M) and the reaction mixture brought to gentle reflux for 15 min. To this was added NBS (0.311g, 1.75 mmol) and further refluxed for 1.5 h. The flask was cooled, and the contents were poured over crushed ice. The organic layer was separated and the aqueous layer extracted with CH_2Cl_2 (2 × 20 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated under vacuum to afford the crude oxazole, which was purified by radial chromatography using hexane/ethyl acetate (95:10) as eluent to afford 0.247 g (83% yield) of **14a** as a colorless oil. IR (thin film, cm^{-1}) 1725, 1612, 1572; ^1H NMR ($CDCI_3$, 300 MHz) δ 3.92 (s, 3H), 7.40−7.48 (m, 3H), 8.04 (m, 2H), 8.25 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 52.2, 126.3, 126.8, 128.8, 131.1, 134.3, 143.8, 161.7, 162.4; MS *m*/*z* 203 (M^+).

2-(2-Bromoisopropyl)-4-carbomethoxy-2-oxazole, 15d. To neat 4-carbomethoxy-2-isopropyl-2-oxazoline (0.200 g, 1.17 mmol) taken in a Pyrex test tube were added AIBN (10 mg 0.061 mmol) and NBS (0.540 g, 3.04 mmol). The reaction mixture was then evacuated and filled with argon. To this was added 10 mL of dry CH_2Cl_2 (0.12 M) under argon. The reaction mixture was photolyzed at 0 °C for 10 h using a 450 W lamp as the UV source. The crude reaction mixture was diluted with water (20 mL) and the organic layer separated. The aqueous layer was further extracted with CH_2Cl_2 (2 × 20 mL). The combined organic extract was dried (Na_2SO_4) and concentrated under vacuum and the crude product purified by radial chromatography using hexane/ethyl acetate (95:5) as eluent to afford 0.220 g (76% yield) of **15d** as a colorless oil. IR (thin film, cm^{-1}) 1730; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.18 (s, 6H), 3.88 (s, 3H), 8.20 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 32.1, 51.2, 52.2, 133.4, 144.2, 161.3, 166.6.

2-(1-Bromocyclohexyl)-4-carbomethoxy-2-oxazole, 15e. Procedure was followed as in the oxidation of 4-carbomethoxy-2-isopropyl-2-oxazoline using 0.247 g (1.17 mmol) of 4-carbomethoxy-2-cyclohexyl-2-oxazoline, 0.01 g (0.061 mmol) of AIBN, 0.54 g (3.04 mmol) of NBS, and 9.8 mL of CH_2Cl_2 (0.12 M). Radial chromatography on SiO_2 using hexane/ethyl acetate (95:5) gave 0.223 g (66% yield) of **15e** as a yellow oil. IR (thin film, cm^{-1}) 1749; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.34−1.84 (m, 6H), 2.34−2.55 (m, 4H), 3.88 (s, 1H), 8.21 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 23.3, 24.7, 39.0, 52.2, 59.3, 133.5, 144.0, 161.4, 166.0.

4-Carbomethoxy-2-pentyl-2-oxazole, 14c. To neat 4-carbomethoxy-2-pentyl-2-oxazoline (0.05 mmol, 0.1 g) in a Pyrex test tube was added NBS (0.445 g, 0.25 mmol). The reaction mixture was then evacuated and purged with argon. To this was added 10 mL of dry CH_2Cl_2 (0.05 M) under argon. The reaction mixture was photolyzed at −40 °C and gradually warmed to −25 °C over a 12 h period using a 450 W lamp as the UV source. The organic layer was then quickly decanted into a mixture of crushed ice and CH_2Cl_2 (30 mL), the reaction test tube was rinsed with ether (2 × 3 mL), the organic layers were combined, dried (Na_2SO_4), and concentrated under vacuum, and the crude product was subjected to flash chromatography on SiO_2 using hexane/ethyl acetate (85:15) to afford 0.064 g (65% yield) of the oxazole **14c** as a colorless oil. IR (thin film, cm^{-1}) 1744; ^1H NMR ($CDCl_3$, 300 MHz,) δ 0.92 (t, J = 7.21 Hz, 3H), 1.36 (m, 4H), 1.8 (m, 2H), 2.79 (t, J = 7.32 Hz, 2H), 3.88 (s, 3H), 8.11 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.1, 22.4, 26.8, 28.3, 31.4, 52.3, 133.2, 143.9, 162.2, 166.4. Anal. Calcd for $C_{10}H_{15}NO_3$: C, 60.89; H, 7.67. Found: C, 60.72; H, 7.61.

4-Carbomethoxy-2-methyl-2-oxazole, 14b.[17b] Procedure was followed as in the oxidation of 4-carbomethoxy-2-pentyl-2-oxazoline using 0.300 g (2.09 mmol) of 4-carbomethoxy-2-methyl-2-oxazoline, 0.552 g (3.14 mmol) of NBS, and 20 mL of CH_2Cl_2. The reaction mixture was photolyzed at −10 °C for 7 h. Flash chromatography on SiO_2 using hexane/ethyl acetate (60:40) gave 0.183 g (62% yield) of **14b** as a colorless oil. IR (thin film, cm^{-1}) 1749; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.48 (s, 3H), 3.87 (s, 3H), 8.11 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.1, 52.4, 133.5,144.1, 162.0, 162.7.

General Procedure for the Preparation of Oxazoles Using the Modified Sosnovsky Reaction; Cu(I), *tert*-Butyl Perbenzoate. To the oxazoline was added 1.1 equiv of CuBr. The reaction mixture was evacuated and purged with argon and to this was added dry benzene (0.23 M) under argon. The mixture was heated to 60 °C, and the peroxy ester was added dropwise (1.5 equiv) over 15 min. The mixture was then heated to reflux for 12 h. To the crude reaction mixture was added 10% ammonium hydroxide to remove the copper salts. The organic layer was washed with water, dried (Na_2SO_4), and concentrated under vacuum. The crude product was subjected to flash chromatography on SiO_2 using hexane/ethyl acetate to afford the oxazoles in 55−65% yields.

4-Carbomethoxy-2-isopropyl-2-oxazole, 21a.[3b] Prepared as described in the general procedure using 0.300 g (1.75 mmol) 4-carbomethoxy-2-isopropyl-2-oxazoline, 0.277 g (1.93 mmol) of Cu(I)Br, *tert*-butyl perbenzoate, and 7.63 mL of benzene (0.23 M). Flash chromatography on SiO_2 using hexane/ethyl acetate (80:20) gave 0.178 g (60% yield) of **21a** as a colorless oil. IR (thin film, cm^{-1}) 1748; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.23 (s, 3H), 1.26 (s, 3H), 2.98−3.07 (m, 1H), 3.78 (s, 3H), 8.06 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 19.9, 28.3, 51.8, 132.7, 143.4, 161.6, 169.7.

4-Carbomethoxy-2-cyclohexyl-2-oxazole, 21d. Prepared as described in the general procedure using 0.394 g (2.0 mmol) of 2-cyclohexyl-4-carbomethoxy-2-oxazoline, 0.315 g (2.20 mmol) of Cu(I)Br, 0.582 g (3.0 mmol) of *tert*-butyl perbenzoate, and 8.12 mL of benzene (0.23 M). Flash chromatography on SiO_2 using hexane/ethyl acetate (85:15) gave 0.215 g (55% yield) of **21d** as a colorless oil. IR (thin film, cm^{-1}) 1702; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.12−2.25 (m, 10 H), 2.71−2.82 (m, 1H), 3.82 (s, 3H), 8.08 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.2, 25.4, 25.6, 30.2, 37.4, 51.9, 132.7, 143.3, 161.8, 169.1.

4-Carbomethoxy-2-ethyl-5-methyl-2-oxazole, 21b. Prepared as described in the general procedure using 0.359 g (2.0 mmol) of 4-carbomethoxy-2-ethyl-5-methyl-2-oxazoline, 0.315 g (2.20 mmol) of Cu(I)Br, 0.582 g (3.0 mmol) of *tert*-butyl perbenzoate, and 7.77 mL of benzene (0.23 M). Flash chromatography on SiO_2 using hexane/ethyl acetate (80:20) gave 0.224 g (63% yield) of **21b** as a colorless oil. IR (thin film, cm^{-1}) 1714; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.28 (t, J = 7.62 Hz, 3H), 2.54 (s, 3H), 2.72 (q, J = 7.56 Hz, 2H), 3.84 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 11.1, 11.8, 21.4, 51.8, 126.9, 128.3, 130.0, 163.8.

4-Carboethoxy-2-propyl-2-thiazole, 21c. Prepared as described in the general procedure using 0.300 g (1.49 mmol) of 2-propyl-4-carboethoxy-2- thiazoline, 0.236 g (1.64 mmol) of Cu(I)Br, 0.434 g (2.24 mmol) of *tert*-butyl perbenzoate, and 6.49 mL of benzene (0.23 M). The reaction mixture was refluxed for 4.5 h. Flash chromatography on SiO_2, hexane/ethyl acetate (85:15), gave 0.247 g (83%) of **21c** as a colorless oil. IR (thin film, cm^{-1}) 1711, 1589; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.81 (t, J = 6.93 Hz, 3H), 1.22 (t, J = 3.70 Hz, 3H), 1.80 (m, 2H), 2.95 (t, J = 6.31 Hz, 2H), 4.3 (q, J = 6.70 Hz, 2H), 8.03 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.5, 14.3, 23.4, 35.3, 61.2, 126.7, 146.6, 161.4, 172.1.

General Procedure for the Cu(I)−Cu(II) Oxidation of Oxazolines and Thiazolines. 2-[(S)-1-[*N*-(*tert*-Butoxycarbonyl)amino]-2-methylpropyl]-4-carbomethoxyoxazole, 21e. To the oxazoline **20e** (0.300 g, 0.001 mol) in a 50 mL round bottomed flask were added CuBr (0.158 g, 1.10 mmol) and $Cu(OAc)_2$ (0.199 g, 1.10 mmol). The flask was evacuated and then filled with argon. The evacuation/argon addition was repeated twice. Benzene (6.5 mL) (0.16 M) was syringed into the flask and stirring initiated. The reaction was warmed to 60 °C, and *tert*-butyl perbenzoate (0.291 g, 1.50 mmol) was added gradually over 15 min. The reaction mixture was then heated to reflux for 7.5 h (4.5 h in case of thiazolines). After cooling to rt, ethyl acetate (10 mL) was added, and the mixture was washed with buffered 10% NH_4OH solution to remove all the copper salts. The aqueous layer was extracted with ethyl acetate (3 × 10 mL), the combined organic extracts were dried over Na_2SO_4, and the crude product, obtained after concentration under vacuum, was subjected to flash column chromatography on SiO_2. [hexane/ethyl acetate (80:20)]. This produced 0.194 g (65% yield) of **21e** as a white solid. mp 120−123 °C; $[\alpha]^{23}_D$ −53.9 (*c* 0.73 CH_2Cl_2); IR (thin film, cm^{-1}) 3334, 2970, 1749, 1715, 1584, 1522; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.86 (d, J = 6.69 Hz, 3H), 0.89 (d, J = 5.22 Hz, 3H), 1.39 (s, 9H), 2.00−2.21 (m, 1H), 3.88 (s, 3H), 4.76 (dd, J = 6.06, 9.15 Hz, 1H), 5.25 (d, J = 9.12 Hz, 1H), 8.15 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 17.7, 18.6, 28.2, 32.6, 52.1, 54.2, 79.9, 133.1, 143.7, 155.3, 161.5, 165.1. Anal. Calcd for $C_{14}H_{22}N_2O_5$: C, 56.36; H, 7.43; N, 9.39. Found C, 56.31; H, 7.43; N, 9.31.

2-[(*S*)-1-[*N*-(*tert*-Butoxycarbonyl)amino]-2-methylpropyl]-5-methyl-4-carbomethoxyoxazole, 21h. Oxidation was carried out as described in the general procedure using 0.330 g (1.05 mmol) of 2-[(*S*)-1-[*N*-(*tert*-butoxycarbonyl)amino]-2-methylpropyl]-5-methyl-4-carbomethoxyoxazoline, **20h**, 0.166 g (1.16 mmol) of Cu(I)Br, 0.210 g (1.16 mmol) of $Cu(OAc)_2$, and 0.307 g (1.58 mmol) of *tert*-butyl perbenzoate. Flash chromatography on SiO_2 using hexane/ethyl acetate (80:20) gave 0.184 g (56% yield) of **21h** as a colorless oil. $[\alpha]^{23}_D$ 20.9 (*c* 11.7, $CHCl_3$); IR (thin film, cm^{-1}) 3325, 2970, 1715, 1621,

1584; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.88 (d, J = 6.75 Hz, 3 H), 0.90 (d, J = 6.78 Hz, 3H), 2.10−2.17 (m, 1H), 2.58 (s, 3H), 3.78 (s, 3H), 4.69 (dd, J = 5.88, 9.18 Hz, 1H), 5.23 (d, J = 9.30 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 12.3, 18.3, 19.1, 28.6, 33.2, 52.3, 54.4, 80.2, 129.9, 155.7, 156.6, 162.0, 162.5.

2-[(*S*)-1-[*N*-(*tert*-Butoxycarbonyl)amino]-2-phenylethyl]-4-carbomethoxyoxazole, 21g. Oxidation was carried out as described in the general procedure using 0.40 g (1.15 mmol) of 2-[(*S*)-1-[*N*-(*tert*-butoxycarbonyl)amino]-2-phenylethyl]-4-carbomethoxyoxazoline, **20g**, 0.182 g (1.27 mmol) of Cu(I)Br, 0.230 g (1.27 mmol) of $Cu(OAc)_2$, and 0.335 g (1.73 mmol) of *tert*-butyl perbenzoate. Flash chromatography on SiO_2 using hexane/ethyl acetate (80:20) gave 0.227 g (57% yield) of **21g** as a colorless oil. $[\alpha]^{23}_D$ −16.0 (*c* 2.8, $CHCl_3$); IR (thin film, cm^{-1}) 3353, 2977, 1714, 1167; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.37 (s, 9H), 3.18−3.25 (dd, J = 6.72, 14.85 Hz, 2H), 3.88 (s, 3H), 5.18 (m, 2H), 6.99−7.02 (m, 2H), 7.18−7.22 (m, 3H), 8.10 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 28.2, 40.3, 50.1, 52.2, 80.2, 127.0, 128.5, 129.2, 133.2, 135.5, 143.8, 154.9, 161.4, 164.7. Anal. Calcd for $C_{18}H_{22}N_2O_5$: C, 62.42; H, 6.40. Found C, 62.18; H, 6.46.

Oxazole Azide, 21k. Oxidation was carried out as described in the general procedure using 0.020 g (0.089 mmol) of oxazoline azide, **20k**, 0.014 g (0.097 mmol) of Cu(I)Br, 0.018 g (0.097 mmol) of $Cu(OAc)_2$, and 0.026 g (0.013 mmol) of *tert*-butyl perbenzoate. Flash chromatography on SiO_2 using hexane/ethyl acetate (70:30) gave 0.011 g (56% yield) of **21k** as a colorless oil.[1h] $[\alpha]^{25}_D$ −32.7 (*c* 0.74, $CHCl_3$); lit. $[\alpha]^{25}_D$ −35.8 (*c* 0.74, $CHCl_3$); IR (thin film, cm^{-1}) 3330, 2952, 2099, 1653, 1583; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.34 (d, J = 7.05 Hz, 3H), 1.80−1.91 (m, 1H), 2.05−2.17 (m, 1H), 3.10−3.27 (m, 1H), 3.33 (t, J = 6.78 Hz, 2H), 3.89 (s, 3H), 8.15 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 18.4, 31.2, 33.7, 49.0, 52.2, 133.1, 143.8, 161.7, 168.1.

2-[(*S*)-1-[*N*-(*tert*-Butyloxycarbonyl)amino]-2-methylpropyl]-4-carbethoxythiazole, 21i. Oxidation was carried out as described in the general procedure using 1.00 g (3.03 mmol) of 2-[(*S*)-1-[*N*-(*tert*-butyloxycarbonyl)amino]-2-methylpropyl]-4-carbethoxy-(*S*)-2-thiazoline, **20i**, 0.478 g (3.33 mmol) of Cu(I)Br, 0.603 g (3.33 mmol) of $Cu(OAc)_2$, and 0.884 g (4.55 mmol) of *tert*-butyl perbenzoate. Flash chromatography on SiO_2 using hexane/ethyl acetate (80:20) gave 0.835 g (84% yield) of **21i** as a white solid.[6c] Mp 116−117 °C; $[\alpha]^{23}_D$ −39.1 (*c* 2.6, $CHCl_3$); IR (thin film, cm^{-1}) 3345, 2975, 1715, 1500, 1167; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.85 (d, J = 6.84 Hz, 3H), 0.93 (d, J = 6.78 Hz, 3H), 1.36 (t, J = 7.11 Hz, 3H), 1.40 (s, 9H), 2.37−2.46 (m, 1H), 4.36 (q, J = 7.14 Hz, 2H), 4.86 (dd, J = 5.52, 8.40 Hz, 1H), 5.26 (d, J = 8.46 Hz, 1H), 8.03 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.3,17.1, 19.3, 28.2, 33.2, 57.9, 61.3, 79.9, 126.7,147.3, 155.3, 161.2, 173.2. Anal. Calcd for $C_{15}H_{24}N_2O_4S$: C, 54.86; H, 7.37; N, 8.53. Found C, 54.58; H, 7.51; N, 8.49.

2-[(*S*)-1-[*N*-(*tert*-Butyloxycarbonyl)amino]-2-phenylethyl]-4-carbethoxythiazole, 21j. Oxidation was carried out as described in the general procedure using 0.30 g (0.794 mmol) of 2-[(*S*)-1-[(*tert*-butyloxycarbonyl)amino]-2-phenylethyl]-4-carbethoxy-(*S*)-2-thiazoline, **20j**, 0.126 g (0.873 mmol) of Cu(I)Br, 0.158 g (0.873 mmol) of $Cu(OAc)_2$, and 0.200 g (1.032 mmol) of *tert*-butyl perbenzoate. Flash chromatography on SiO_2 using hexane/ethyl acetate (85:15) gave 0.227 g (76% yield) of **21j** a colorless oil. $[\alpha]^{23}_D$ 5.1 (*c* 1.8, $CHCl_3$); IR (thin film, cm^{-1}) 3324, 2978, 1712, 1584; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.34 (s, 9H), 1.39 (t, J = 7.14 Hz, 3H), 3.25−3.35 (m, 2H), 4.38 (q, J = 7.14 Hz, 2H), 5.23−5.28 (m, 2H), 7.06−7.24 (m, 5H), 8.00 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.7, 28.5, 41.8, 54.2, 61.7, 80.6, 127.3, 127.5, 128.9, 129.7, 136.5, 147.6, 155.2, 161.7, 173.4.

2-[(*S*)-1-[*N*-(*tert*-Butoxycarbonyl)amino]ethyl]-4-carbomethoxyoxazole, 21f. Oxidation was carried out as described in the general procedure using 0.20 g (0.735 mmol) of 2-[1-[(*tert*-butoxycarbonyl)amino]ethyl]-4-carbomethoxyoxazoline, 0.116 g (0.809 mmol) of Cu(I)Br, 0.147 g (0.809 mmol) of $Cu(OAc)_2$, and 0.214 g (1.103 mmol) of *tert*-butyl perbenzoate. Flash chromatography on SiO_2, hexane/ethyl acetate (70:30), gave 0.101 g (51% yield) of **21f** as a colorless oil. $[\alpha]^{23}_D$ −29.0 (*c* 0.5, $CHCl_3$); IR (thin film, cm^{-1}) 3340, 2982, 1720, 1153; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.41 (s, 9H), 1.52 (d, J = 6.90 Hz, 3H), 3.89 (s, 3H), 5.19 (d, J = 6.1 Hz, 1H), 5.21 (br s, 1H), 8.02 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.2, 28.3, 52.2, 128.2, 129.0, 143.9, 161.5. HRMS-FAB $(M + H)^+$, $C_{12}H_{19}N_2O_5$, Calcd 271.1293; Found 271.1289.

Oxazole, 21l.[16] To the oxazoline **20l** (0.320 g, 0.80 mmol) in a 25 mL round bottomed flask were added CuBr (0.126 g, 0.88 mmol) and $Cu(OAc)_2$ (0.160 g, 0.88 mmol). The flask was evacuated and then filled with argon. The evacuation/argon addition was repeated two times. Benzene (5 mL) (0.16 M) was syringed into the flask and stirring initiated. The reaction was warmed to 60 °C, and *tert*-butyl perbenzoate (0.233 g, 1.20 mmol) was added gradually over 15 min. The reaction mixture was then heated to reflux for 7.5 h. After cooling to rt, ethyl acetate (10 mL) was added. The mixture was then washed with buffered 10% NH_4OH solution to remove all the copper salts. The aqueous layer was extracted with ethyl acetate (3 × 10 mL). The combined organic extracts were dried over Na_2SO_4, and the crude product obtained after rotary evaporation was subjected to flash column chromatography over SiO_2 using hexane/ethyl acetate (7:3) to afford the desired oxazole **21l**, in 81% yield (0.258 g). IR (thin film, cm^{-1}) 2953, 1750, 1583, 1369, 1322, 1252, 1109; ^{1}H NMR ($CDCl_3$, 300 MHz) δ −0.15 (s, 3H), −0.01 (s, 3H), 0.78 (s, 9H), 1.31 (s, 3H), 1.34 (s, 3H), 1.63−1.89 (m, 2H), 3.01 (d, J = 6.3 Hz, 2H), 3.47 (t, J = 7.53 Hz, 1H), 3.88 (s, 3H), 4.01−4.06 (dd, J = 5.91, 7.98 Hz, 1H), 4.18−4.44 (m, 2H), 8.12 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −4.9, −4.2, 17.8, 25.6, 25.7, 26.9, 35.7, 41.0, 52.1, 68.1, 69.7, 72.2, 108.8, 133.3, 143.7, 161.7, 163.6.

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Supporting Information Available: Proton and carbon spectra, HPLC chiral analyses for all compounds (62 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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