Dimethyl Amino[(phenylthio)methyl]malonate: A Useful C-3 Unit in a Mild, Direct Synthesis of Oxazole-4-carboxylates

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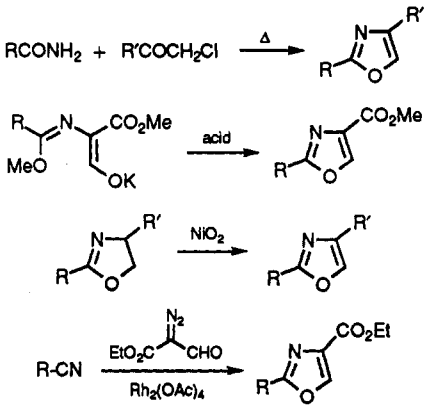
Received November 30, 1992 (Revised Manuscript Received June 29, 1993•)

N-Acyl derivatives of the title compound undergo oxidative cyclization upon treatment with *N*-chlorosuccinimide in DMF to form dimethyl 4,5-dihydro-5-(phenylthio)oxazole-4,4-dicarboxylates **4** which then are decarbomethoxylated with concomitant loss of thiophenoxide to form 2-substituted-4-carbomethoxy-5-unsubstituted oxazoles **1**. The mildness and generality of this method has been demonstrated by the synthesis of a variety of examples, including a fragment used for a synthesis of calyculin A.

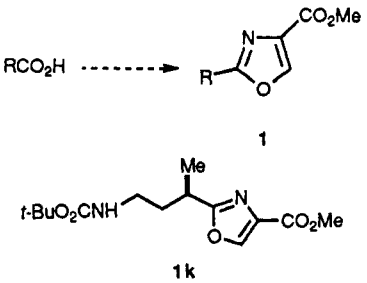
Introduction

The 2,4-disubstituted oxazole system is a component of increasing occurrence in complex natural products, such as the antibiotics virginiamycin M_1 and griseoviridin,[1] the protein phosphatase inhibitor calyculin A,[2] and the fungicidal ulapualide A,[3] which, in the latter, is prominently featured as a 2,4′:2′,4″-teroxazole system. An oxazole-containing synthetic thromboxane A_2 antagonist has also appeared in a recent report by a Bristol-Meyers Squibb group.[4]

Though structurally simple in comparison to the aforementioned polyfunctional and stereochemically complex natural products into which it is incorporated, the 5-unsubstituted oxazole ring bearing a functionalized 2-substituent can be troublesome to build, although there are essentially four known general methods,[5–8] represented by Equations 1–4.



Each of the methods outlined above suffers from one or more drawbacks, including low overall yields, limited tolerance for sensitive functionality, or potential hazards in a large-scale preparation. A new synthetic method for the conversion of carboxylic acids to homologous oxazoles (eq 5) was therefore sought in connection with a new synthesis of calyculin fragment **1k**.[9]



Results and Discussion

To accomplish this transformation, the possibility of using a cysteine derivative was investigated (Scheme I), but the attempted Pummerer rearrangement of **3** afforded primarily bis(nitrophenyl) disulfide and methyl α-(pro-

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• Abstract published in *Advance ACS Abstracts*, September 1, 1993.

(1) For synthetic studies and leading references, see: Meyers, A. I.; Lawson, J. P.; Walker, D. G.; , Linderman, R. J. *J. Org. Chem.* **1986**, *51*, 5111, and refs and reviews cited therein.

(2) (a) Matsunaga, S.; Fusetani, N. *Tetrahedron Lett.* **1991**, *32*, 5605. For synthetic studies and leading refs, see: (b) Evans, D. A.; Gage, J. R.; Leighton, J. L. *J. Am. Chem. Soc.* **1992**, *114*, 9434 [total synthesis of (+)-calyculin A]. (c) Evans, D. A.; Gage, J. R.; Leighton, J. L., Kim, A. S. *J. Org. Chem.* **1992**, *57*, 1961. (d) Evans, D. A.; Gage, J. R. *Ibid.* **1992**, *57*, 1958. (e) Smith, A. B., III; Salvatore, B. A.; Hull, K. G.; Duan, J. J.-W. *Tetrahedron Lett.* **1991**, *32*, 4859. (f) Barrett, A. G. M.; Edmunds, J. J.; Hendrix, J. A.; Malecha, J. W.; Parkinson, C. J. *J. Chem. Soc., Chem. Commun.* **1992**, 1240. (g) Vaccaro, H. A.; Levy, D. E.; Sawabe, A.; Jaetsch, T.; Masamune, S. *Tetrahedron Lett.* **1992**, *33*, 1937.

(3) For synthetic studies and leading refs, see: (a) Knight, D. W; Pattenden, G.; Rippon, D. E. *Synth. Lett.* **1991**, 36. (b) Pattenden, G. *J. Heterocycl. Chem.* **1992**, *29*, 607.

(4) Misra, R. N.; Brown, B. R.; Sher, P. M.; Patel, M. M.; Goldenberg, H. J.; Michel, I. M.; Harris, D. N. *Bioorg. Med. Chem. Lett.* **1991**, *9*, 461.

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(6) (a) Cornforth, J. W.; Cornforth, R. H. *J. Chem. Soc.* **1947**, 96. (b) Cornforth, J. W.; Cookson, E. *Ibid.* **1952**, 1085. A new synthetic method based on a *base-catalyzed* cyclization of a vinyl bromide was recently reported: (c) Das, J.; Reid, J. A.; Kronenthal, D. R.; Singh, J.; Pansegrau, P. D.; Mueller, R. H. *Tetrahedron Lett.* **1992**, *33*, 7835.

(7) (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. For an application to calyculin A oxazole fragments, see Yokokawa, F; Hamada, Y.; Shioiri, T. *Synth. Lett.* **1992**, 153. For other methods used to prepare the dihydrooxazoles, see Roush, D. M.; Patel, M. M. *Synth. Commun.* **1985**, *15*, 675 and refs cited therein. Hamada, Y.; Shibata, M..; Shioiri, T. *Tetrahedron Lett.* **1985**, *26*, 6501 ($SOCl_2$/AgOTf).

(8) (a) Connell, R.; Scaro, F.; Helquist, P.; Åkermark, B. *Tetrahedron Lett.* **1986**, *17*, 5559. (b) Connell, R. D.; Tebbe, M.; Helquist, P.; Åkermark, B. *Ibid.* **1991**, *32*, 17. (c) Yoo, S.-K. *Ibid.* **1992**, *33*, 2159. (d) Doyle, K. J.; Moody, C. J. *Ibid.* **1992**, *33*, 7769. A novel thermal rearrangement of alkyl *O*-vinylcarbohydroximates has also been recently reported to give oxazole-4-carboxylates: Yokoyama, M.; Irie, M.; Sujino, K; Kagemoto, T.; Togo, H; Funabashi, M. *J. Chem. Soc., Perkin Trans. 1* **1992**, 2127.

(9) The (*R*)-configuration of this target (ref 2c) was chosen before the absolute configuration of calyculin A was known (ref 2a) and is opposite to that in the natural product.

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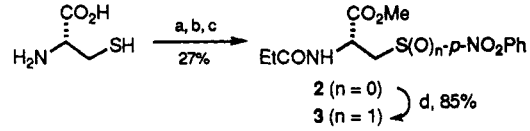
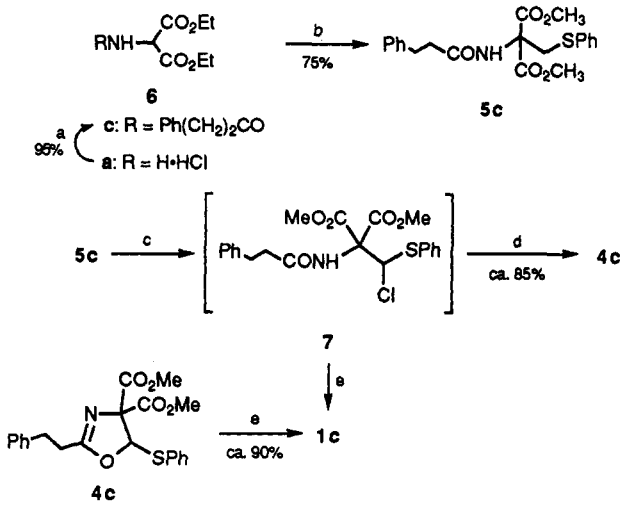
Scheme I[a]



[a] (a) *p*-FPhNO$_2$, aqueous NaHCO$_3$, EtOH, 78 °C; (b) SOCl$_2$, MeOH; (c) (EtCO)$_2$O, aqueous NaHCO$_3$, EtOAc; (d) *m*-CPBA, −20 °C.

Scheme II[a]



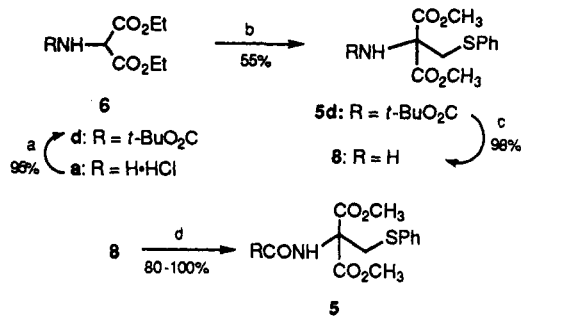
[a] (a) PhCH$_2$CH$_2$COCl, aqueous NaHCO$_3$, CH$_2$Cl$_2$; (b) NaOMe, MeOH; PhSCH$_2$Cl, DMF, cat. TBAB; (c) NCS, DMF; (d) EtN(i-Pr)$_2$; (e) K$_2$CO$_3$, MeOH, MeI.

pionylamino)acrylate, thus implicating a premature elimination reaction as the reason for the failure to produce an oxazole.

This strategy was abandoned in favor of one which replaced the C-2 methine in **2** with another carbomethoxy group, reasoning that the two events, cyclization and elimination, would be forced to occur in the desired sequence.

This plan was realized by the procedure outlined in Scheme II. In step b, enolization of diethyl (dihydrocinnamoylamino)malonate with sodium methoxide in methanol was accompanied by transesterification, and, after concentration and drying, the crude salts were alkylated with chloromethyl phenyl sulfide in DMF to give **5c** in 75% yield. The chlorination step c in DMF allowed both chlorination and cyclization to occur, and the cyclization was completed by allowing Hünig's base to react with the initially formed mixture of **7** and **4**. A few observations are worthy of mention. Anhydrous conditions are necessary to minimize sulfoxide formation, which is the exclusive process in a hydroxylic solvent such as methanol. Quite often, unreacted starting material **5**, the chlorinated intermediate **7**, and the oxazoline product **4** are very difficult to separate either by flash chromatography or by crystallization, resulting in yield losses during purification. In addition, although **1** is formed from **7** in the subsequent decarboxylative elimination step e, the yield is generally lower than that obtained from **4**, and so yields of purified **1** may sometimes not be optimum due to incomplete conversions in steps c or d. Still, small amounts of residual **5** could be removed by saponification to the readily-purified acid derivatives of **1**. Although oxazoline **4** could be thermally converted to **1**, treating it with potassium carbonate in methanol at room temperature (step e) in the presence of methyl iodide to trap thiophenol was the

Scheme III[a]

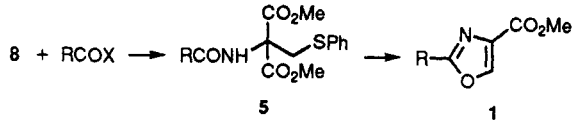


[a] (a) (*t*-BuO$_2$C)$_2$O, aqueous NaHCO$_3$, CH$_2$Cl$_2$; (b) NaOMe, MeOH; PhSCH$_2$Cl, DMF, cat. TBAB; (c) TFA; (d) RCOCl, pyr, or RCO$_2$H, 2,4,6-tri-ClPhCOCl, Et$_3$N, DMAP.

preferred procedure. This also served to supress a minor side reaction occasionally observed, namely ester demethylation of the product, presumably by thiophenoxide ion. It may be noted also that the byproduct, thioanisole, could in principle be recovered and used to regenerate the source of C-5, chloromethyl phenyl sulfide.

A refinement of this oxazole synthesis was necessary to make it more convergent and thus more attractive to applications involving valuable carboxylic acid precursors. To this end (Scheme III), it was found that multigram quantities of dimethyl amino[(phenylthio)methyl]malonate (**8**) could be prepared in three steps and 54% overall yield from diethyl aminomalonate, via *t*-BOC derivatives **6d**[10] and **5d**. The low nucleophilicity of **8**, a stable, weakly basic, low-melting solid, required that the acylation be performed with a quite active reagent for satisfactory results, and thus reaction with an acid chloride or a mixed anhydride formed from a carboxylic acid, triethylamine, and 2,4,6-trichlorobenzoyl chloride[11] turned out to be the methods of choice.

Table I summarizes examples of this new method, combining the results of Schemes II and III (eq 6).



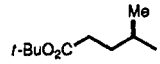
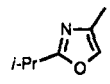
(6)

A teroxazole representative of the ulapualide fragment was prepared using this method from the corresponding bioxazole (entry 9 in Table I), but the yield was disappointing (20% overall) due to incomplete chlorination of the oxazole precursor. Of greater interest, however, was finding a reliable preparation of an oxazole fragment for the Evans synthesis of calyculin A.

During the application of this method to the preparation of enantiopure calyculin fragment **1k**, efforts were frustrated by the fact that the racemic model *t*-BOC amino acid prepared by the method of Grieco and co-workers[12] cyclized back to its precursor pyrrolidinone much faster than it could be coupled with **8**, in contrast to its desmethyl analog (compare entry 7 in Table I). The solution to this problem was to postpone the Curtius rearrangement until

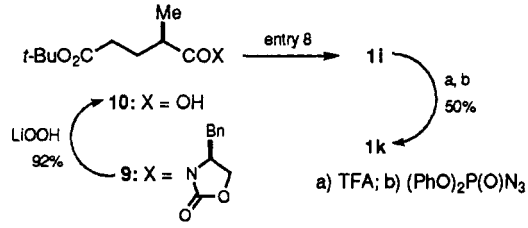
(10) Paik, Y. H.; Dowd, P. *J. Org. Chem.* **1986**, *51*, 2910.
(11) Inanaga, J.; Hirata, K.; Saeki, H; Katsuki, T.; Yamaguchi, M. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1989.
(12) Flynn, D. L.; Zelle, R. E.; Grieco, P. A. *J. Org. Chem.* **1983**, *48*, 2424.

Table I. Amides and Oxazoles by Eq 6

entry	R	X	5	yield (5), %	yield (1), %
1	Me	a	a	55[a]	43[b]
2	*i*-Pr	a	b	72[a]	46[b]
3	$PhCH_2CH_2$	a	c	75[a]	59
4	Ph	Cl	e	100	75
5	*trans*-PhCH=CH	Cl	f	82	59
6	$PhCH_2OCH_2$	Cl	g	100	60[b]
7	*t*-BOCNH$(CH_2)_3$	OH	h	86	40
8		OH	i	100	57[c]
9		OH	j	100	47

[a] 5a–c were prepared by phenylthiomethylation of amidomalonates. [b] Yield of saponified product. [c] Seventy percent yield based on NMR analysis of crude product.

Scheme IV



after the construction of the oxazole ring was accomplished (Scheme IV). Thus, the chiral auxiliary of enantiomerically pure **9**[2b] was cleaved by the LiOOH method[13] to provide in 92% yield chiral glutaric monoester **10** which was subjected to the new procedure to provide in 54% purified yield oxazole **1i** (78% for *ca.* 90% pure material). Debutylation and Curtius rearrangement[14] of **1i** gave a 50% yield of **1k** , indistinguishable in all respects from authentic material, including optical rotation, thus demonstrating that racemization of the potentially labile center had not occurred.

Experimental Section

Melting points were measured with a Büchi SMP-20 apparatus equipped with an Omega Model 450 AET thermocouple and are uncorrected. Infrared spectra were recorded with a Perkin-Elmer 1600 FT-IR instrument. ^1H NMR spectra were recorded using either a Bruker AM-250, AM-300, AM-400, or an AM-500 Fourier transform spectrometer at ambient temperature. Data are reported as follows: chemical shift (δ) in ppm downfield from tetramethylsilane (TMS) as an internal standard, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, sext = sextet, sep = septet, m = multiplet), integration, coupling constant(s) in hertz, and assignment (Ar = aryl, Ox = oxazole). ^{13}C NMR spectra were recorded using broad-band proton-decoupling on either a Bruker AM-300 (75 MHz) or AM-500 (125 MHz) and are reported in ppm downfield from TMS with the solvent resonance as internal standard (chloroform-*d* at 77.0 ppm). Optical rotations were recorded on a Jasco DIP-181 digital polarimeter with a sodium lamp (589 nm) and are recorded as $[\alpha]_D$ (concentration in g/100 mL, solvent). Combustion analyses were performed by Spang Microanalytical Laboratories (Eagle Harbor, MI). High-resolution mass spectra were obtained on JEOL AX-505 or SX-102 spectrometers in the Harvard University Mass Spectrometry Laboratory.

Thin-layer chromatographic analysis was conducted using EM Reagents 0.25-mm silica gel 60-F plates, and EM Reagents silica gel 60 (230–240 mesh) was used for flash column chromatography. Solvents used were reagent- or HPLC-grade, except for dimethylformamide, which was purchased from Aldrich as "anhydrous" (<0.015% H_2O). Hünig's base (*N,N*-diisopropylethylamine) and triethylamine were distilled from calcium hydride prior to use, and tetrahydrofuran was distilled from potassium–benzophenone. Starting materials such as chloromethyl phenyl sulfide and reagents such as *N*-chlorosuccinimide and 2,4,6-trichlorobenzoyl chloride were purchased from Aldrich Chemical Co. or Lancaster Synthesis and were used without further purification.

Dimethyl [*N*-(3-Phenylpropionyl)amino][(phenylthio)methyl]malonate (5c). To a suspension of 21.3 g (0.102 mol) of diethyl aminomalonate hydrochloride in 200 mL of CH_2Cl_2 was added 10 mL of water and 14.0 g (0.102 mol) of K_2CO_3 in portions. This was cooled to 0 °C, and 17.0 g (0.102 mol) of dihydrocinnamoyl chloride was added dropwise. The mixture was then allowed to warm to room temperature and separated, and the organic phase was washed with aqueous $NaHCO_3$, dried (Na_2SO_4), concentrated, and triturated with ether/hexanes to afford 28.2 g (92%) of diethyl [*N*-(3-phenylpropionyl)amino]malonate (**7c**) as a white solid. A portion of this (20.0 g, 63.0 mmol) was dissolved in 200 mL of MeOH containing 0.5 mL of 25% NaOMe/MeOH, allowed to stand for 2 h, evaporated, redissolved in a solution of 13 mL (total 63.0 mmol) of 25% NaOMe/MeOH in 200 mL of MeOH, concentrated, and dried *in vacuo* overnight. The residue was suspended in 40 mL of anhydrous DMF and stirred overnight at room temperature with 1 g of tetrabutylammonium bromide and 9.95 g (63.0 mmol) of chloromethyl phenyl sulfide. An additional 1 mL of 25% NaOMe/MeOH was added and the mixture was stirred for 1 h, poured onto 200 mL of aqueous $NaHCO_3$, and extracted with a 1:3 mixture of hexanes/Et_2O. The extracts were washed with H_2O, brine, dried (Na_2SO_4), concentrated to 1/3 volume, diluted with hexanes, and filtered to provide 18.6 g (75%) of **5c** as a white powder: mp 85–86 °C; IR (thin film) 3382, 3060, 3027, 2954, 1743, 1681, 1495, 1436, 1294, 1216 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.21 (t, 2, J = 7.5 Hz, CH_2CON), 2.75 (t, 2, J = 7.5 Hz, CH_2Ph), 3.63 (s, 6, 2 × CO_2CH_3), 3.93 (s, 2, CH_2SPh), 6.76 (br s, 1, N*H*), 7.1–7.5 (m, 10, Ar*H*). Anal. Calcd for $C_{21}H_{23}NO_5S$: C, 62.82; H, 5.78; N, 3.49. Found: C, 62.83; H, 5.90; N, 3.55.

Dimethyl [*N*-(Isobutyryl)amino][(phenylthio)methyl]malonate (5b). This was prepared by the procedure described above. Thus, crystalline diethyl [(isobutyryl)amino]malonate (**6b**) was prepared in 94% yield using isobutyric anhydride and was alkylated as above to provide **5b** in 72% yield: mp 62–63 °C; IR (thin film) 3383, 2967, 1746, 1677, 1497, 1294, 1215 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.02 (d, 6, J = 7 Hz, 2 × CH_3CH), 2.20 (sep, 1, J = 7 Hz, $CHCH_3$), 3.64 (s, 6, 2 × CO_2CH_3), 3.94 (s, 2, CH_2SPh), 6.85 (br s, 1, N*H*), 7.1–7.5 (m, 5, Ar*H*). Anal. Calcd for $C_{16}H_{21}NO_5S$: C, 56.62; H, 6.24; N, 4.13. Found: C, 56.69; H, 6.30; N, 4.18.

Dimethyl Acetamido[(phenylthio)methyl]malonate (5a). This was prepared as above from commercial diethyl acetamidomalonate in 55% yield: mp 89–90 °C; ^1H NMR (250 MHz, $CDCl_3$) δ 1.69 (s, 3, CH_3CO), 3.67(s, 6, 2 × CO_2CH_3), 3.92 (s, 2, CH_2SPh), 6.7 (br s, 1, N*H*), 7.1–7.5 (m, 5, Ar*H*). Anal. Calcd for $C_{14}H_{17}NO_5S$: C, 54.01; H, 5.50; N, 4.50. Found: C, 54.09; H, 5.59; N, 4.45.

Dimethyl [(*tert*-Butoxycarbonyl)amino][(phenylthio)methyl]malonate (5d). This was prepared using di-*tert*-butyl dicarbonate for the acylation step to provide **6d** as an oil which was alkylated as above (except that the transesterification required a reaction time of 16 h instead of 2 h) to provide **5d** in 55% yield (based on diethyl aminomalonate hydrochloride) after filter chromatography and trituration with Et_2O/hexanes: mp 89–90 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 1.35 (s, 9, 3 × $CH_3COCONH$), 3.63 (s, 6, 2 × CO_2CH_3), 3.9 (s, 2, CH_2S), 6.0 (br s, 1, N*H*), 7.1–7.5 (m, 5, Ar*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.0, 38.2, 53.1, 67.2, 80.3, 126.8, 128.8, 131.2, 135.1, 167.2 ppm. Exact mass calcd for $C_{17}H_{23}NNaO_6S$ (M + Na) 392.1144; found: 392.1163. Anal. Calcd for $C_{17}H_{23}NO_6S$: C, 55.27; H, 6.28; N, 3.79. Found: C, 55.29; H, 6.14; N, 3.87.

Dimethyl Amino[(phenylthio)methyl]malonate (8). To 73 g of trifluoroacetic acid containing 20 mL of CH_2Cl_2 was added 70.0 g of **5d** in portions (exotherm, gas evolution) and the mixture was allowed to stir at room temperature overnight. Concentration

(13) Evans, D. A.; Britton, T. C.; Ellman, J. A. *Tetrahedron Lett.* **1987**, *28*, 6141.

(14) Haefliger, W.; Klöppner, E. *Helv. Chim. Acta* **1982**, *65*, 1837. Ninomiya, K.; Siori, T.; Yamada, S. *Tetrahedron* **1974**, *30*, 1003.

and partitioning between water (650 mL) and Et_2O/hexane (1:2), basification of the aqueous phase with solid K_2CO_3, extraction with ether, drying ($MgSO_4$), concentration, and drying *in vacuo* provided 50.0 g (98%) of **8** as a solid: mp 23–24 °C; IR (film) 3382, 3316, 3005, 2952, 1736, 1580, 1438, 1215, 1032, 872 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.26 (br s, 2 NH), 3.59 (s, 8, 2 × CO_2CH_3 and CH_2S), 7.1–7.5 (m, 5, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 40.9, 52.9, 65.8, 127.1, 128.9, 131.3, 134.8, 170.4 ppm. Anal. Calcd for $C_{12}H_{15}NO_4S$: C, 53.52; H, 5.61; N, 5.20. Found: C, 53.66; H, 5.53; N, 5.24.

2(*R*)-Methylglutaric Acid 5-*tert*-Butyl Ester (10). To solution of **9** (44.0 g, 0.122 mol) in 350 mL of THF, precooled to 0 °C, was added a solution of 7.5 g of $LiOH·H_2O$ in 100 mL of ice–water and 42 mL of *ca.* 30% H_2O_2 over a 5-min period. After 30 min, a solution of 52 g of Na_2SO_3 in 800 mL of ice–water was added in portions with continued cooling. The resulting solution was thoroughly extracted with ether to recover the chiral auxiliary (19.3 g), and the aqueous layer was acidified with aqueous HCl and extracted with ether to provide 24 g (98%) of **10** as a pale yellow oil: $[\alpha]_D$ −16.6° (0.74, CH_2Cl_2); IR (film) 3200, 2978, 1710, 1461, 1420, 1370, 1254, 1157 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.37 (d, 3, J = 7 Hz, CH_3CH), 1.42 (s, 9, 3 × CH_3CO_2C), [1.90 (m, 1) and 2.10 m, 1), CH_2], 2.24 (t, 2, J = 7 Hz, CH_2CO), 3.08 (sext, 1, J = 7 Hz, CHMe), 3.91 (s, 3, CO_2CH_3), 8.17 (s, 1, Ox-5-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.0, 27.9, 29.8, 32.7, 33.1, 51.7, 80.1, 133.0, 143.5, 161.5, 168.4, 171.8 ppm; exact mass calcd for $C_{14}H_{21}NNaO_5$ (M + Na) 306.1317, found 306.1331.

General Procedures for the Acylation of 8. Procedure A: Acyl Halides. A solution of 10 mmol of **8** in 5–10 mL of pyridine optionally diluted with 20–30 mL of ether or dichloromethane was cooled to 0 °C, 10–11 mmol of a carboxylic acid chloride, optionally diluted with 2–10 mL of CH_2Cl_2, was added dropwise, and the mixture was allowed to warm and held at room temperature for up to 1 h. Dilution with ether, washing successively with 1 N HCl, aqueous $NaHCO_3$, and brine, drying ($MgSO_4$), concentration, chromatography (optional), and drying *in vacuo* afforded the acyl derivatives **5e-g** in high yield. The following compounds were prepared by this method.

Dimethyl Benzamido[(phenylthio)methyl]malonate (5e). From 2.93 g of **8** and 1.70 g of benzoyl chloride (neat pyridine, 10 mL) there was obtained 4.0 g (100%) of **5e** as a gum following flash column chromatography: IR (film) 3423, 2955, 1745, 1666, 1510, 1480, 1439, 1310, 1216 cm^{-1}; ^1H NMR (250 MHz) δ 3.69 (s, 6, 2 × CO_2CH_3), 4.05 (s, 2, CH_2S), 7.0–7.6 (m, 11, NH and ArH); exact mass calcd for $C_{19}H_{20}NO_5S$ (M + H) 374.1062, found 374.1083.

Dimethyl (*trans*-Cinnamoylamino)[(phenylthio)methyl]malonate (5f). From 3.30 g of **8** and 2.10 g of cinnamoyl chloride (CH_2Cl_2 and 1.2 mL of pyridine) there was obtained 4.3 g (88%) of **5f** as a glass following flash column chromatography: IR (film) 3408, 3059, 3026, 2954, 2847, 1746, 1668, 1629, 1578, 1501, 1437 cm^{-1}; ^1H NMR (300 MHz) δ 3.68 (s, 6, 2 × CO_2CH_3), 4.01 (s, 2, CH_2S), 6.16 (d, 1, J = 16 Hz, PhCH=CHCO), 6.9 (br s, 1, NH), 7.0–7.6 (m, 11, PhCH=CH and ArH). Anal. Calcd for $C_{21}H_{21}NO_5S$: C, 63.14; H, 5.30; N, 3.51. Found: C, 63.23; H, 5.25; N, 3.52.

Dimethyl (Benzyloxyacetamido)[(phenylthio)methyl]malonate (5g). From 2.70 g of **8** and 1.95 g of (benzyloxy)acetyl chloride (CH_2Cl_2 and 1.2 mL of pyridine), there was obtained 4.20 g (100%) of **5g** as a glass following flash column chromatography: IR (film) 3401, 3060, 3031, 2954, 2862, 1747, 1686, 1504, 1439, 1302, 1271 cm^{-1}; ^1H NMR (300 MHz) δ 3.64 (s, 2, OCH_2CO), 3.67 (s, 6, 2 × CO_2CH_3), 3.97 (s, 2, CH_2S), 4.48 (s, 2, $PhCH_2O$), 7.2–7.5 (m, 10, ArH), 8.95 (br s, 1, NH); exact mass calcd for $C_{21}H_{24}NO_6S$ (M + H) 418.1324, found 418.1331.

Procedure B: Mixed Anhydride Method. To an ice-cooled solution of a carboxylic acid (10 mmol) in 10–20 mL of anhydrous THF and 10 mmol of triethylamine was added 10 mmol of 2,4,6-trichlorobenzoyl chloride (hereafter referred to as TCBC), and the mixture was allowed to react at room temperature for 1–3 h, with monitoring by TLC (5% EtOAc/hexanes). At this point, the mixed anhydride intermediate could either be isolated by dilution with ether, filtration of $Et_3N·HCl$, and concentration and then coupled with 1.1 equiv of **8** in 20 mL of CH_2Cl_2 or, alternatively, it could more conveniently be coupled in the same flask. In either case, it was possible to use either 1 equiv of 4-(dimethylamino)pyridine (DMAP) or just a catalytic amount (50–100 mg), along with 1.1 equiv of triethylamine, to effect the coupling. In the former case, the reaction was generally complete within 1–3 h at room temperature, whereas the catalytic reactions were generally allowed to proceed overnight. Dilution with ether and workup as in procedure A afforded the following compounds:

Dimethyl [[4-[(*tert*-Butoxycarbonyl)amino]butyryl]amino][(phenylthio)methyl]malonate (5h). This was prepared from 1.98 g (9.78 mmol) of the protected 4-aminobutyric acid[15] by the *in situ* method, using 1.5 mL of triethylamine and 2.43 g of TCBC, followed by 2.80 g of **8**, 1.5 mL of Et_3N, and 0.1 g of DMAP to afford 3.80 g (86%) of the product after trituration with Et_2O/hexanes: mp 100–101 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 1.45 (s, 9, $CH_3COCONH$), 1.6 (quin, 2, J = 7 Hz, central CH_2), 1.93 (t, 2, J = 7 Hz, CH_2CO), 3.05 (q, 2, J = 6 Hz, CH_2NH), 3.66 (s, 6, 2 × CO_2CH_3), 3.92 (s, 2, CH_2S), 4.6 (br s, 1, $NHCO_2t$-Bu), 6.87 (br s, 1, $NHCOCH_2$) 7.2–7.5 (m, 5, ArH). Anal. Calcd for $C_{21}H_{30}N_2O_7S$: C, 55.49; H, 6.65; N, 6.16. Found: C, 55.63; H, 6.54; N, 6.15.

Dimethyl [[4-[(*tert*-Butoxycarbonyl)-2(*R*)-methylbutyryl]amino][(phenylthio)methyl]malonate (5i). This was prepared from 1.50 g (7.42 mmol) of **10** (*vide infra*) and 1.2 mL of Et_3N, 1.95 g (7.95 mmol) of TCBC, isolating the mixed anhydride, and adding 60 mL of dichloromethane, 2.20 g (8.23 mmol) of **8**, and 1.0 g of DMAP to afford 3.35 g (100%) of **5i** as a gum, a portion of which crystallized from Et_2O/hexane: mp 85–86 °C; $[\alpha]_D$ = −7.0° (1.0, CH_2Cl_2); IR (film) 3418, 2976, 1748, 1677, 1496, 1439, 1216, 1154 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.00 (d, 3, J = 7 Hz, CH_3CH), 1.45 (s, 9, 3 × $CH_3COCOCH_2$), 1.70 (m, 2, CH_2), 2.2 (m, 3, $CHCH_2CO$), 3.61 and 3.68 (two s, 6, 2 × CO_2CH_3), 3.94 (AB q, 2, CH_2S), 6.95 (br s, 1, $NHCOCH_2$), 7.2–7.5 (m, 5, ArH); exact mass calcd for $C_{22}H_{32}NO_7S$ (M + H) 454.1899, found 454.1913. A comparable yield was also obtained on a larger scale using the *in situ* catalytic DMAP procedure.

***N*-[1′,1′-Bis(methoxycarbonyl)-2′-(phenylthio)ethyl]-2-isopropyloxazole-4-carboxamide (5j).** This was prepared from 2.40 g (15.5 mmol) of **11b** (*vide infra*), 2.7 mL of Et_3N in 16 mL of THF, 4.00 g (16.2 mmol) of TCBC, isolating the mixed anhydride, and adding 30 mL of CH_2Cl_2, 4.30 g of **8**, 3.0 mL of Et_3N, and 75 mg of DMAP, to afford 6.33 g (100%) of **5j** as a gum after chromatography: IR (film) 3395, 3145, 3058, 2975, 1747, 1678, 1600, 1492, 1439, 1290, 1220 cm^{-1}; ^1H NMR (300 MHz) δ 1.36 (d, 6, J = 7 Hz, 2 × CH_3CH), 3.05 (sep, 1, J = 7 Hz, $CHCH_3$), 3.68 (s, 6, 2 × CO_2CH_3), 4.02 (s, 2, CH_2S), 7.03 (m, 1, ArH), 7.13 (m, 2 , ArH), 7.4 (m, 2, ArH), 7.90 (s, 1, OxH), 8.15 (br s, 1, NH); exact mass calcd for $C_{19}H_{22}N_2NaO_6S$ (M + Na) 429.1096, found 429.1076.

N-[1″,1″-Bis(methoxycarbonyl)-2″-(phenylthio)ethyl]-2′-isopropyl-[2,4′-bioxazole]-4-carboxamide (5l). This was prepared from 1.18 g (5.35 mmol) of **11j** (*vide infra*) by the *in situ* method, using 0.80 mL of triethylamine and 1.32 g (5.40 mmol) of TCBC, followed by 1.45 g (5.40 mmol) of **8**, 0.90 mL of Et_3N, and 0.1 g of DMAP to afford 2.55 g of **5l** as a colorless gum: IR (film) 3394, 3143, 2975, 1747, 1681, 1594, 1493 cm^{-1}; ^1H NMR (300 MHz) δ 1.43 (d, 6, J = 7 Hz, 2 × CH_3CH), 3.21 (sep, 1, J = 7 Hz, $CHCH_3$), 3.68 (s, 6, 2 × CO_2CH_3), 4.04 (s, 2, CH_2S), 7.06 (m, 1, ArH), 7.12 (m, 2 , ArH), 7.4 (m, 2, ArH), 8.05 (s, 1, OxH), 8.21 (br s, 1, NH); exact mass calcd for $C_{22}H_{23}N_3NaO_7S$ (M + Na) 496.1154, found 496.1151.

Oxazole Ring Synthesis. The general procedure is illustrated by the following preparation of **methyl 2-[3-(*tert*-butoxycarbonyl)-1(*R*)-methylpropyl]oxazole-4-carboxylate (1i):** To a cooled (0–10 °C) solution of 1.50 g (3.30 mmol) of **5i** in 6 mL of dry DMF was added 450 mg (3.40 mmol) of *N*-chlorosuccinimide. The mixture was allowed to warm slowly to room temperature and allowed to stir an additional 1–2 h, after which time there was added 600 μL (3.42 mmol) of *N,N*-diisopropylethylamine. After 16 h, the mixture was diluted with 50 mL of water and extracted with ether. The ether extracts were washed with water and brine, dried ($MgSO_4$), and concentrated to dryness *in vacuo*. The residue, which consisted mainly of the oxazoline **4i** as evidenced by the methine signal in the ^1H NMR spectrum at δ 6.4, was dissolved in 30 mL of MeOH and 0.66 g (4.2 mmol) of

(15) Moroder, L.; Hallet, A.; Wünsch, E.; Keller, O.; Wersin, G. *Z. Physiol. Chem.* **1976**, *357*, 1651.

anhydrous potassium carbonate was added. The suspension was heated at reflux for 1 h, after which time the mixture had become homogeneous and smelled strongly of thiophenol. Methyl iodide (0.5 mL) was added, the mixture was concentrated *in vacuo*, partitioned between ether and water, washed with brine, dried ($MgSO_4$), concentrated, and chromatographed to remove thioanisole, providing 530 mg (57%) of **1i** as an oil: $[\alpha]_D$ −19.7° (0.91, CH_2Cl_2); IR (film) 2978, 1729, 1584, 1466, 1438, 1380, 1154, 1110 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.37 (d, 3, J = 7 Hz, CH_3CH), 1.42 (s, 9, 3 × CH_3CO_2C), [1.90 (m, 1) and 2.10 m, 1), CH_2], 2.24 (t, 2, J = 7 Hz, CH_2CO), 3.08 (sext, 1, J = 7 Hz, CHMe), 3.91 (s, 3, CO_2CH_3), 8.17 (s, 1, Ox*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.0, 27.9, 29.8, 32.7, 33.1, 51.7, 80.1, 133.0, 143.5, 161.5, 168.4, 171.8 ppm; exact mass calcd for $C_{14}H_{21}NNaO_5$ (M + Na) 306.1317, found 306.1331.

Compounds **1a-c** and **1e-j** were prepared by the procedure outlined above and the carboxylic acids **11a,b,e,g**, and **j** were prepared by saponification with methanolic NaOH at room temperature overnight.

2-Methyl-4-oxazolecarboxylic Acid (11a). This was prepared from 3.47 g (11.1 mmol) of **5a** (15 mL of DMF, 1.50 g (11.3 mmol) of NCS, 16 h; 2.0 mL Hünig's base, 5 h). The crude intermediate (3.4 g of an orange oil) was stirred in 25 mL of MeOH, 1.1 g of chloroacetic acid, and 3.1 g of K_2CO_3 at room temperature overnight and worked up as above to provide crude **1a**, which was saponified to 0.42 g (30%) of the corresponding acid **11a**: mp 176–177 °C dec [lit.[6a] mp 183–184 °C dec]; ^1H NMR (250 MHz, $CDCl_3$) δ 2.57 (s, 3, CH_3), 8.23 (s, 1, Ox*H*).

2-Isopropyl-4-oxazolecarboxylic Acid (11b). This compound was prepared as described above, except that the intermediate oxazoline **4b** was purified prior to decarboxylative elimination. Thus, from 10.2 g (30.0 mmol) of **5b** (20 mL of DMF, 4.20 g of NCS, 20 min, rt; 6.8 mL of Hünig's base, 16 h) there was obtained 5.8 g (57%) of **4b** after flash chromatography (some losses in discarded mixed fractions). From 1.0 g of this there was obtained, after workup as for **1i**, a mixture of thioanisole and **1b** which was saponified to afforded 340 mg (75%, 43% overall) of **11b**: mp 105–106 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 1.38 (d, 6, J = 7 Hz, 2 × CH_3), 3.18 (sep, 1, J = 7 Hz, CH), 8.25 (s, 1, Ox*H*), 10.0 (br, 1, COO*H*). Anal. Calcd for $C_7H_9NO_3$: C, 54.19; H, 5.85; N, 9.03. Found: C, 54.22; H, 5.78; N, 8.92.

Methyl 2-(2-Phenylethyl)-4-oxazolecarboxylate (1c). This compound was prepared as described above, except that the intermediate oxazoline **4c** was purified prior to decarboxylative elimination. Thus, from 9.70 g (24.2 mmol) of **5c** (20 mL DMF, 3.30 g of NCS, 1 h, rt; 5.0 mL of Hünig's base, 16 h) there was obtained 8.0 g (82%) of **4c** after flash chromatography: IR (film) 3115, 1727, 1586, 1453, 1318, 1268, 1202, 1162 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 2.70 (t, 2, J = 7.5 Hz, CH_2Het), 3.00 (t, 2, J = 7.5 Hz, PhCH_2), 3.82 (s, 3, CO_2CH_3), 3.85 (s, 3, CO_2CH_3), 6.43 (s, 1, CHS), 7.1–7.5 (m, 10, Ar*H*). From 7.9 g of this there was obtained, after trituration with hexanes and chromatography of the mother liquors, 3.28 g (72%, 59% overall) of **1c**: mp 68–69 °C (lit.[1] mp 64–66 °C).

Methyl 2-Phenyl-4-oxazolecarboxylate (1e). Crude **4e** (4.0 g) was prepared as above from 3.80 g (10.2 mmol) of **5e**, 15 mL of DMF, and 1.33 g (10.0 mmol) of NCS. This was stirred for 1 h at room temperature with a solution of 2.30 g (10.6 mmol) of 25% NaOMe/MeOH in 50 mL of MeOH, worked up as above, and chromatographed to afford 1.52 g (75%) of **1e**: mp 87–88 °C (lit.[6b] mp 85.5–87 °C); ^1H NMR (300 MHz, $CDCl_3$) δ 3.91 (s, 3, CO_2CH_3), 7.5 (m, 3, Ar*H*), 8.1 (m, 2, Ar*H*), 8.30 (s, 1, Ox*H*).

Methyl 2-[2(*E*)-Phenylvinyl]-4-oxazolecarboxylate (1f). A. Dimethyl 4,5-Dihydro-5-(phenylthio)-2-[2(*E*)-phenylvinyl]oxazole-4,4-dicarboxylate (4f). This was prepared from 3.44 g (8.62 mmol) of **5f**, 13 mL of DMF, 1.20 g (9.00 mmol) of *N*-chlorosuccinimide (0 °C to rt, 16 h) and 1.5 mL of Hünig's base (10 h, rt), affording 2.18 g (64%) of **5f** after flash chromatography (some losses in mixed fractions) as a yellow gum: ^1H NMR (300 MHz, $CDCl_3$) δ 3.90 (s, 3, CO_2CH_3), 3.91 (s, 3, CO_2CH_3), 6.50 (s, 1, CHS), 6.52 (d, 1, J = 15 Hz, CH=CHHet), 7.1–7.5 (m, 11, Ar*H* and CH=CHPh); exact mass calcd for $C_{21}H_{20}NO_5S$ 398.1062, found 398.1070. B. This intermediate (2.00 g, 5.04 mmol) was converted with potassium carbonate in MeOH (1.0 g/ 30 mL, 2 h, rt) to 1.04 g (92%, 60% overall) of the title compound: mp 134–135 °C; ^1H-NMR (300 MHz, $CDCl_3$) δ 3.95 (s, 3, CO_2CH_3), 6.95 (d, 1, J = 15 Hz, CH=CHHet), 7.4–7.6 (m, 5, Ar*H*), 7.57 (d, 1, J = 16.5 Hz CH=CHPh), 8.22 (s, 1, Ox*H*). Anal. Calcd for $C_{13}H_{11}NO_3$: C, 68.11; H, 4.84; N, 6.11. Found: C, 68.16; H, 4.80; N, 6.17.

2-[(Benzyloxy)methyl]-4-oxazolecarboxylic Acid (11g). From 4.0 g (9.8 mmol) of **5g**, 15 mL DMF, 1.30 g (9.8 mmol) of NCS, and 2.2 mL of Hünig's base, there was obtained after chromatography 3.43 g (86%) of slightly impure **4g**. After treatment with K_2CO_3/MeOH (5 h, rt), chromatography, and saponification, there was obtained 1.10 g (60%, 52% overall) of **11g** as a white solid: mp 121–122 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 4.65 (s, 2), 4.69 (s, 2), 7.35 (m, 5, Ar*H*), 8.34 (s, 1, Ox*H*). Anal. Calcd for $C_{12}H_{11}NO_4$: C, 61.78; H, 4.76; N, 6.01. Found: C, 61.72; H, 4.78; N, 5.94.

Methyl 2-{3-[(*tert*-Butoxycarbonyl)amino]propyl}-4-oxazolecarboxylate (1h). From 3.32 g (7.30 mmol) of **5h**, 10 mL of DMF, 1.0 g (7.5 mmol) of *N*-chlorosuccinimide (2 h at rt), and 1.9 mL of EtN(*i*-Pr)$_2$ (16 h at rt), there was obtained after chromatography 1.90 g (58%) of slightly impure **4h**. After treatment with K_2CO_3/MeOH (5 h, rt), and workup as in the first example, substituting 0.5 mL of AcOH and 0.5 mL of 30% aqueous H_2O_2 for methyl iodide (to quench the odor without the risk of N-methylation), chromatography, and recrystallization (Et_2O/hexane), there was obtained 1.10 g (63%, 37% overall) of **11g** as white plates: mp 64–65 °C; IR (film) 3365, 2976, 1712, 1588, 1522, 1438 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.43 (s, 9, 3 × CH_3COCONH), 2.0 (quin, 2, J = 7 Hz, central CH_2), 2.87 (t, 2, J = 7 Hz, CH_2CO), 3.20 (br q, 2, J = 6 Hz), 3.91 (s, 3, CO_2CH_3), 4.67 (br s, 1, N*H*CO_2t-Bu), 8.16 (s, 1, Ox*H*). Anal. Calcd for $C_{13}H_{20}N_2O_5$: C, 54.92; H, 7.09; N, 9.85. Found: C, 54.98; H, 6.94; N, 9.92.

Methyl 2′-Isopropyl-[2,4′-bioxazole]-4-carboxylate (1j). The general procedure used for **1i** was followed, with the resulting intermediate being only partially cyclized. Prolonged reaction times afforded no noticeable increase in the conversion of **7j** to **4j**. Thus, from 6.23 g of **5j**, 20 mL of DMF, 2.05 g of *N*-chlorosuccinimide, and 3.5 mL of Hünig's base, there was obtained after chromatographic separation (4:1 hexane/EtOAc), 1.23 g (18%) of the less-polar product **7j** [^1H NMR (250 MHz, $CDCl_3$) δ 1.38 (d, 6, J = 7 Hz, 2 × CH_3CH), 3.12 (sep, 1, J = 7 Hz, CHCH$_3$), 3.87 (two s, 6, CO_2CH_3), 6.03 (s, 1, ClC*H*SPh), 7.3 (m, 3, Ar*H*), 7.63 (m, 2, Ar*H*), 8.12 (s, 1, Ox*H*), 8.19 (br s, 1, N*H*), is converted to **1j** in 30% yield by K_2CO_3/MeOH] and 3.2 g (52%) of **4j** (triturated with Et_2O/hexane): mp 119–120 °C; IR (film) 2974, 1742, 1678, 1580, 1440 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.37 (d, 6, J = 7 Hz, 2 × CH_3CH), 3.86 (s, 3, CO_2CH_3), 3.87 (s, 3, CO_2CH_3), 6.60 (s, 1, OC*H*SPh), 7.37 (m, 3, Ar*H*), 7.6 (m, 2, Ar*H*), 8.14 (s, 1, Ox*H*). A portion of this (3.02 g, 7.46 mmol) was decarboxylatively eliminated as above with 1.2 g of K_2CO_3 in 25 mL of MeOH (2 mL of MeI, 4 h at rt, extraction with EtOAc) to the oxazole, which was triturated with hexanes to provide 1.56 g (90%, 47% overall) of **1j** as a shiny white solid: mp 126–127 °C; IR (film) 3146, 3111, 2964, 1719, 1638, 1569, 1536, 1316, 996, 966 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.40 (d, 6, J = 7 Hz, 2 × CH_3), 3.18 (sep, 1, J = 7 Hz, CH), 3.95 (s, 3, CO_2CH_3), 8.2 (s, 2, 2 × Ox*H*); exact mass calcd for $C_{11}H_{13}N_2O_4$ (M + H) 237.0875, found 237.0857. This was converted to the corresponding acid **11j** in 96% yield by saponification in MeOH as above: mp 232–233 °C; ^1H NMR (300 MHz, DMSO-d_6) δ 1.32 (d, 6, J = 7 Hz, 2 × CH_3), 3.18 (sep, 1, J = 7 Hz, CH), 8.83 (s, 1, Ox*H*), 8.84 (s, 1, Ox*H*).

Methyl 2″-Isopropyl-[2,4:2,4″-teroxazole]-4-carboxylate (1l). This was prepared from 2.40 g (5.09 mmol) of **5l**, 13 mL of DMF, and 715 mg (5.35 mmol) of NCS (6 h, rt), followed by 1.1 mL of Hünig's base (16 h, rt). Extraction with Et_2O and treatment of the mixture (*ca.* 1:1:1 **5l**/**7l**/**4l** by ^1H NMR analysis) with K_2CO_3/MeOH as above afforded an extremely insoluble product which was extracted with a large volume of EtOAc containing CH_2Cl_2, concentrated, and triturated with ether to provide 0.35 g (23%) of **1l** as a highly electrostatic white powder: mp 224–226 °C; IR (film) 1745, 1654, 1577 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.41 (d, 6, J = 7 Hz, 2 × CH_3), 3.19 (sep, 1, J = 7 Hz, CH), 3.96 (s, 3, CO_2CH_3), 8.28 (s, 1, Ox*H*), 8.32 (s, 1, Ox*H*), 8.42 (s, 1, Ox*H*). Anal. Calcd for $C_{14}H_{13}N_3O_5$: C, 55.45; H, 4.32; N, 13.86. Found: C, 55.06; H, 4.70; N, 13.58.

Methyl 2-{3-[(*tert*-Butoxycarbonyl)amino]-1(*R*)-methylpropyl}oxazole-4-carboxylate (1k). A mixture of 0.98 g (3.4 mmol) of **2i** and 2 mL of trifluoroacetic acid was allowed to stand at room temperature for 16 h. Excess TFA was evaporated, and the residue was partitioned between Et_2O and aqueous $NaHCO_3$. The deprotected product was isolated by acidification of the aqueous layer, extraction with EtOAc, drying (Na_2SO_4), concentration, and drying *in vacuo*, affording 0.68 g (88%) of an oil: ^1H NMR (400 MHz, $CDCl_3$) δ 1.38 (d, 3, J = 7 Hz, CH_3CH), [1.90 (m, 1) and 2.10 (m, 1), CH_2], 2.37 (t, 2, J = 7 Hz, CH_2CO), 3.13 (sext, 1, J = 7 Hz, CHMe), 3.91 (s, 3, CO_2CH_3), 8.17 (s, 1, Ox*H*). A mixture of 200 mg (0.88 mmol) of this acid was heated in 3 mL of *tert*-butyl alcohol, 150 μL of triethylamine, and 250 mg (0.90 mmol) of diphenyl phosphorazidate [$(PhO)_2P(O)N_3$] for 14 h at reflux. The crude product was isolated by extraction from aqueous $NaHCO_3$ with EtOAc and was chromatographed (to remove 100 mg of a higher R_f, unidentified, byproduct, and baseline material) to afford 100 mg (47%) of **1k** as an oil: $[\alpha]_D$ −22.5° (1.0, CH_2Cl_2) [lit. $[\alpha]_D$ −21.5° (1.3, CH_2Cl_2)]; ^1H NMR spectrum same as that reported previously.[2b]

Acknowledgment. I am grateful for a paid leave of absence and financial support from DuPont Agricultural Products to pursue this research. I would also like to thank Prof. David A. Evans for kindly serving as my host for this leave and for helpful discussions. I also thank Dr. Andrew Tyler of the Harvard Mass Spectrometry Facility and Mssrs. Andrew Ratz and Scott Miller for obtaining mass spectra and acknowledge the NIH BRS Shared Instrumentation Grant Program 1 s10 RRO01748–01A1 and NSF (CHE88–14019) for providing NMR facilities. I also thank members of the Evans group for helpful advice and Sharon Reid for helping to prepare the manuscript.

Supplementary Material Available: ^1H NMR spectra for compounds **1i**, **5d,e,g,i,j,l**, and **10** (10 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.