Synthesis of Symmetrical 2,2',4,4'-Tetrasubstituted[4,4'-bioxazole]-5,5'(4*H*,4'*H*)-diones and their Reactions with some Nucleophiles

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Several symmetrical 2,2',4,4'-tetrasubstituted[4,4'-bioxazole]-5,5'(4*H*,4'*H*)-diones **1a-f** were obtained by dehydrodimerization of 5(4*H*)-oxazolones **2a-f**. The configurations of four were established; one by X-ray crystallography *rac*-**1c**, and three *rac*-**1a**, *meso*-**1a** and *rac*-**1b** by ^{1}H nmr spectroscopy of their derivatives. Upon being heated, the bioxazolones isomerized, presumably by breakage of the 4,4'-carbon-carbon bond to form free radicals followed by their recombination. The results of a crossover experiment were consistent with a radical nature for this isomerization reaction. Treatment of three of the bioxazolones *rac*-**1a**, *meso*-**1a** and *rac*-**1c** with methanol and amine nucleophiles led to ester and amide derivatives **7-11** of α,α'-dehydrodimeric amino acids.

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Introduction.

Symmetrical 2,2',4,4'-tetrasubstituted[4,4'-bioxazole]-5,5'(4*H*,4'*H*)-diones **1** can be obtained by dehydrodimerization of 5(4*H*)-oxazolones **2** [1], well known heterocyclic compounds formally derived by cyclization of α-amino acids by the elimination of water [2]. Since oxazolones **2** may undergo ring opening when treated with nucleophiles, it seemed likely that bioxazolones **1** might undergo a similar transformation to yield symmetrical α,α'-dehydrodimeric amino acids and their derivatives **3**. α,α'-Dehydrodimeric amino acids and derivatives **3** are of interest, since they may form when food is preserved by gamma ray irradiation. Indeed, irradiation of di- and tetra-peptides of alanine did yield dehydrodimers [3]. To see if bioxazolones **1** could serve as precursors for α,α'-dehydrodimeric amino acids and their derivatives **3**, several bioxazolones were synthesized and three were treated with nucleophiles. Nucleophilic attack, presumably at a carbonyl carbon of one of the bioxazole rings, was reported to cleave the 4,4'-carbon-carbon bond [4]. The present work shows that such cleavage is not universal; thus, some bioxazolones can serve as precursors to α,α'-dehydrodimeric amino acids and their derivatives.

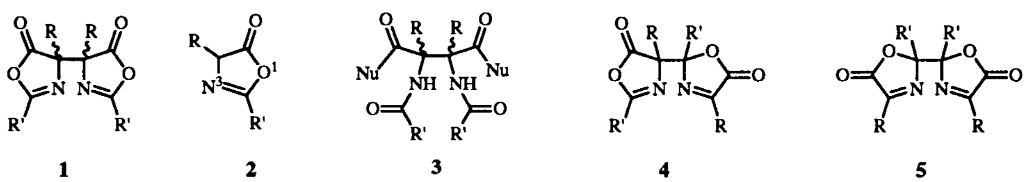
4,4'-Bioxazolones **1** were first described in 1949 by Wintersteiner and Stavely who prepared two examples by treating oxazolones **2** (R = $(CH_3)_2CHCH_2$ and $C_6H_5CH_2$, R' = C_6H_5) with mercuric acetate [1a]. Since then several other bioxazolones **1** have been prepared, but often they have been poorly characterized; in no instance has their stereochemistry been established, and very few of their reactions have been reported [1b-m]. Steglich found that basic hydrolysis of 2,2'-diphenyl-4,4'-diisopropyl[4,4'-bioxazole]-5,5'(4*H*,4'*H*)-dione (**1**, R = $(CH_3)_2CH$, R' = C_6H_5) resulted in cleavage of the 4,4'-carbon-carbon bond [4]. If this cleavage reaction were general, bioxazolones **1** would not be suitable precursors for the preparation of α,α'-dehydrodimeric amino acids or their derivatives; however, it is not general.

Results and Discussion.

Preparation of 2,2',4,4'-Tetrasubstituted[4,4'-bioxazole]-5,5'(4*H*,4'*H*)-diones (1).

Various oxidizing agents, besides mercuric acetate [1a], have been used to dehydrodimerize oxazolones **2** to bioxa-

Scheme 1



a R = CH_3, R' = 4-ClC_6H_4
b R = CH_3, R' = C_6H_5
c R = $C_6H_5CH_2$, R' = C_6H_5
d R = CH_3, R' = 3-BrC_6H_4
e R = $C_6H_5CH_2$, R' = CH_3
f R = $CH_3SCH_2CH_2$, R' = 4-ClC_6H_4
g R = C_6H_5CH, R' = CH_3

zolones **1**; *e.g.*, air [1b-d,g,k], singlet oxygen [1e,i], nickel(IV) oxide [1e,h,k] and manganese dioxide [1j]. In the present work, cupric acetate, manganese triacetate and benzoyl peroxide were found to be suitable as well. Formation of **1** from **2** was found to be consistent with a radical pathway as described below. Since a radical formed at position 4 in the oxazolone **2** is delocalized to position 2, coupling of two radicals can lead not only to *meso*- and *racemic*-bioxazolones **1**, but also to the 2,4'- and 2,2'-bioxazolones, **4** and **5**, respectively.

Six oxazolones **2a-f** were oxidized to dehydrodimers using cupric acetate and/or manganese triacetate. Chromatography and recrystallization led to the isolation of **1a-f**. Oxazolone **2a** was also oxidized using benzoyl peroxide.

Oxazolone **2a**, when treated with cupric acetate in tetrahydrofuran, gave the two 4,4'-bioxazolones *rac*-**1a** and *meso*-**1a** as well as a 2,4'-bioxazolone **4a**. Although reaction conditions were not maximized, isolated yields of *rac*-**1a** ranged from 12-15 percent, whereas *meso*-**1a** and **4a** were obtained pure in much lower yields, about one percent each. Benzoyl peroxide in benzene gave *rac*-**1a** in seven percent isolated yield. Manganese triacetate in tetrahydrofuran at room temperature gave the best result giving *rac*-**1a** in 27 percent yield. This yield dropped to six percent when the reaction was carried out at a higher temperature. In glacial acetic acid, the yield decreased slightly to 18 percent. Although the isolated yields of **1** are low, the precursors **2** are readily prepared in good yield from inexpensive compounds.

Oxazolone **2b** was treated with manganese triacetate in glacial acetic acid to give 4,4'-bioxazolones *rac*-**1b** (4 percent) and *meso*-**1b** as well as the 2,4'-bioxazolone **4b** (3 percent). These low yields reflect the greater difficulty encountered in isolating and purifying these compounds, whose physical properties are rather similar compared to the chloro analogs; *e.g.*, the melting points of the former span an eighteen degree range whereas the latter have melting points well-spaced over a 143 degree range. A small amount of *N*-acetylbenzamide was also isolated. Bioxazolone *rac*-**1c** was obtained in 16 percent yield using cupric acetate in tetrahydrofuran, and bioxazolones **1d** and **1f** in 10 and 17 percent yields, respectively, using cupric acetate in toluene.

Previously, all bioxazolones prepared by dehydrodimerization originated from 2-aryloxazolones [5], but dehydrodimerization was also successful when a 2-alkyloxazolone **2e** was oxidized. Bioxazolone **1e** was obtained in 8 percent yield from **2e** using cupric acetate in benzene.

Crystal Structure.

X-ray crystallography established the configuration of *rac*-**1c** and confirmed the basic structure of the 4,4'-bioxazolone ring system heretofore based on spectroscopy. The 4,4'-carbon-carbon bond length is 1.563 Å, which is longer than the average sp^3-sp^3 bond length of 1.53 Å (Figure 1). Each planar oxazolone ring is nearly coplanar with its phenyl group at positions 2 or 2'; *i.e.*, the torsion angle defined by N3', C2', C13'(*ipso* C) and C14'(*ortho* C) was -172° and that defined by N3, C2, C13, and C18 was -174°. The torsion angle about the 4,4'-bond measured between the benzyl methylene groups was about 39°. The crystal structures of related dehydrodimers, two bithiazolones [7] and two imidazolones [8] have been determined.

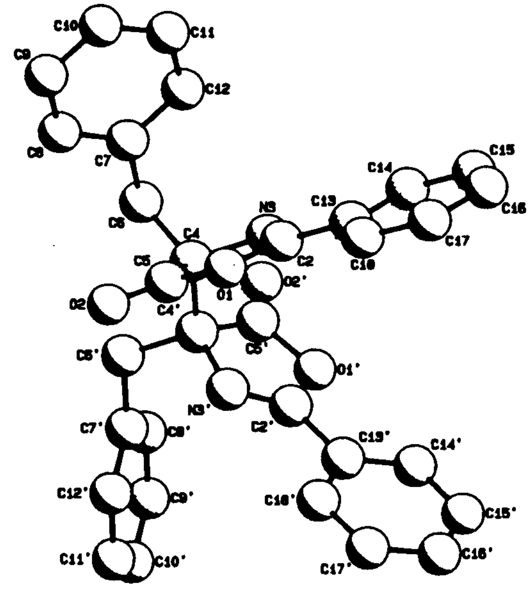


Figure 1. Ortep drawing of *rac*-**1c**. Tables 1, 2, 3 and 4

Cross Over Experiment.

When bioxazolone *rac*-**1a** was heated in benzene, *meso*-**1a** was formed. To see if this came about from recombination of two radicals formed by cleavage of the elongated, and thus weakened, 4,4'-bond, a mixture of *rac*-**1a** and **1d** was heated in toluene. The mass spectrum of the products gave molecular ion peaks not only for the parent bioxazolones *rac*-**1a** and **1d** (or their isomers), but also for the mixed "crossover" product(s) **6**. A control experiment showed that this mixed bromo-chloro isomer(s) was not formed in the inlet of the mass spectrometer. Apparently, radicals are formed which combine to give not only starting material and their isomers, but also the mixed chloro-bromo crossover products. The easy formation of radicals has been observed for somewhat similar molecules [1j].

Reactions of Bioxazolones with Nucleophiles.

Bioxazolone *rac*-**1a** was treated with a series of nucleophiles to give racemic ring-opened derivatives without cleavage of the 4,4'-carbon-carbon bond. Reaction with

Table 1

Fractional Coordinates and Isotropic Thermal Parameters for the Non-hydrogen Atoms of *rac*-**1c**, with their E.S.D.'s in Parentheses

Atom	x	y	z	B (Å)^2
O(1)	0.8506(1)	0.0326(2)	0.8434(1)	4.79(4)
O(1)'	0.6771(1)	0.4105(2)	0.7088(1)	4.22(4)
O(2)	0.7722(1)	-0.1139(2)	0.7394(1)	6.06(5)
O(2)'	0.5569(1)	0.3291(2)	0.7226(1)	5.30(4)
N(3)	0.7401(1)	0.1720(2)	0.8431(1)	4.03(4)
N(3)'	0.7360(1)	0.2094(2)	0.6866(1)	3.87(4)
C(2)	0.8241(2)	0.1426(3)	0.8762(1)	4.18(6)
C(2)'	0.7426(1)	0.3417(3)	0.6949(1)	3.60(5)
C(4)	0.6942(1)	0.0750(3)	0.7753(1)	3.86(5)
C(4)'	0.6572(1)	0.1645(3)	0.6966(1)	3.87(5)
C(5)	0.7722(2)	-0.0157(3)	0.7793(1)	4.41(6)
C(5)'	0.6204(2)	0.3035(3)	0.7112(1)	4.07(5)
C(6)	0.6234(2)	-0.0171(3)	0.7845(1)	4.72(6)
C(6)'	0.5866(2)	0.0875(3)	0.6220(1)	4.72(6)
C(7)	0.6639(2)	-0.1191(3)	0.8536(1)	4.64(6)
C(7)'	0.5582(2)	0.1694(3)	0.5453(1)	4.37(6)
C(8)	0.6669(2)	-0.2616(3)	0.8402(2)	6.00(8)
C(8)'	0.4861(2)	0.2609(3)	0.5185(2)	5.66(7)
C(9)	0.7027(2)	-0.3566(4)	0.9029(2)	7.6(1)
C(9)'	0.4591(2)	0.3347(4)	0.4478(2)	6.79(9)
C(10)	0.7367(2)	-0.3105(4)	0.9801(2)	8.10(9)
C(10)'	0.5034(2)	0.3183(4)	0.4023(2)	6.44(8)
C(11)	0.7349(2)	-0.1711(4)	0.9952(2)	6.87(8)
C(11)'	0.5740(2)	0.2275(4)	0.4273(2)	6.48(8)
C(12)	0.6981(2)	-0.0733(3)	0.9331(2)	5.56(7)
C(12)'	0.6031(2)	0.1530(3)	0.4990(1)	5.57(7)
C(13)	0.8948(2)	0.2140(3)	0.9454(1)	4.68(6)
C(13)'	0.8134(2)	0.4312(3)	0.6926(1)	3.84(5)
C(14)	0.8717(2)	0.3168(4)	0.9848(2)	6.01(8)
C(14)'	0.8210(2)	0.5726(3)	0.7122(1)	4.56(6)
C(15)	0.9380(3)	0.3872(4)	1.0494(2)	7.6(1)
C(15)'	0.8908(2)	0.6516(3)	0.7123(2)	5.46(7)
C(16)	0.0292(2)	0.3563(4)	0.0760(2)	7.8(1)
C(16)'	0.9542(2)	0.5886(3)	0.6935(2)	5.61(7)
C(17)	1.0521(2)	0.2525(4)	1.0367(2)	7.5(1)
C(17)'	0.9458(2)	0.4490(3)	0.6723(2)	5.82(7)
C(18)	0.9868(2)	0.1810(4)	0.9721(2)	5.84(8)
C(18)'	0.8755(20	0.3687(3)	0.6715(2)	5.22(6)

Table 2

Thermal Parameters for the Non-hydrogen Atoms of *rac*-**1c**, with their E.S.D.'s in Parentheses

Atom	β11	β22	β33	β12	β13	β23
O(1)	0.00449(6)	0.0136(2)	0.00521(6)	0.0028(2)	0.00493(9)	0.0012(2)
O(1)'	0.00462(6)	0.0106(2)	0.00472(5)	0.0018(2)	0.00509(8)	-0.0001(2)
O(2)	0.00739(9)	0.0131(2)	0.00695(7)	0.0025(3)	0.0078(1)	-0.0018(2)
O(2)'	0.00468(6)	0.0174(3)	0.00560(6)	0.0037(2)	0.00592(8)	0.0015(2)
N(3)	0.00398(8)	0.0127(2)	0.00356(6)	0.0006(3)	0.0033(1)	0.0010(2)
N(3)'	0.00456(7)	0.0107(2)	0.00385(6)	0.0000(2)	0.00466(9)	-0.0003(2)
C(2)	0.00453(9)	0.0123(3)	0.00393(7)	0.0007(3)	0.0042(1)	0.0031(3)
C(2)'	0.00413(9)	0.0105(3)	0.00319(6)	0.0014(3)	0.0035(1)	0.0002(2)
C(4)	0.00441(9)	0.0110(3)	0.00363(7)	0.0005(3)	0.0041(1)	0.0007(2)
C(4)'	0.00416(9)	0.0113(3)	0.00374(7)	-0.0011(3)	0.0041(1)	0.0001(3)
C(5)	0.0048(1)	0.0113(3)	0.00498(8)	0.0006(3)	0.0054(1)	0.0008(3)
C(5)'	0.00430(9)	0.0124(3)	0.00358(7)	0.0011(3)	0.0035(1)	0.0008(3)
C(6)	0.0045(1)	0.0145(3)	0.00454(8)	-0.0013(3)	0.0042(1)	0.0026(3)
C(6)'	0.0057(1)	0.0131(3)	0.00392(8)	-0.0022(3)	0.0040(1)	-0.0003(3)
C(7)	0.00372(9)	0.0150(3)	0.00467(8)	-0.0011(3)	0.0038(1)	0.0028(3)
C(7)'	0.0055(1)	0.0120(3)	0.00352(7)	-0.0039(3)	0.0039(1)	-0.0014(3)
C(8)	0.0058(1)	0.0155(4)	0.0058(1)	-0.0028(4)	0.0037(2)	0.0025(4)
C(8)'	0.0053(1)	0.0206(5)	0.00432(9)	0.0021(4)	0.0041(2)	0.0014(4)
C(9)	0.0068(2)	0.0164(4)	0.0089(2)	-0.0002(4)	0.0056(2)	0.0082(4)
C(9)'	0.0064(2)	0.0226(5)	0.0051(1)	0.0020(5)	0.003592)	0.0049(4)
C(10)	0.0060(2)	0.0274(5)	0.0073(1)	0.0013(5)	0.0044(2)	0.0157(4)
C(10)'	0.0075(2)	0.0197(4)	0.0042(1)	-0.0047(5)	0.0034(2)	0.0032(4)
C(11)	0.0061(1)	0.0267(5)	0.00531(9)	-0.0007(5)	0.0055(2)	0.0069(4)
C(11)'	0.0087(2)	0.0219(5)	0.00446(8)	-0.0039(5)	0.0075(2)	-0.0010(4)
C(12)	0.0054(1)	0.0207(5)	0.00435(8)	-0.0004(4)	0.0049(1)	0.0029(3)
C(12)'	0.007391)	0.0162(4)	0.00463(8)	0.0009(4)	0.0064(1)	-0.0008(3)
C(13)	0.0047(1)	0.0145(3)	0.00393(8)	-0.0012(3)	0.0034(1)	0.0032(3)
C(13)'	0.00413(9)	0.0115(3)	0.00357(7)	0.0002(3)	0.0038(1)	0.0003(3)
C(14)	0.0064(1)	0.0183(4)	0.0045(1)	-0.0013(5)	0.0035(2)	-0.0005(4)
C(14)'	0.0053(1)	0.0127(3)	0.00461(7)	-0.0025(3)	0.0056(1)	-0.0034(3)
C(15)	0.010692)	0.0188(5)	0.0051(1)	-0.0057)6)	0.0050(2)	-0.0020(4)
C(15)'	0.0066(1)	0.0139(3)	0.00569(9)	-0.0059(3)	0.0069(2)	-0.0054(3)
C(16)	0.0081(2)	0.0273(6)	0.0045(1)	-0.0100(5)	0.0026(2)	0.0051(4)
C(16)'	0.0055(1)	0.0177(4)	0.00565(9)	-0.0044(4)	0.0062(1)	-0.0013(4)
C(17)	0.0051(2)	0.0267(6)	0.0059(1)	-0.0048(5)	0.0019(2)	0.0079(4)
C(17)'	0.0060(1)	0.0161(4)	0.0073(1)	0.0019(4)	0.0091(1)	0.0016(4)
C(18)	0.0042(1)	0.0206(4)	0.0053(1)	-0.0010(4)	0.0034(2)	0.0038(4)
C(18)'	0.0064(1)	0.0117(3)	0.00626(9)	0.0005(3)	0.0078(1)	0.0004(3)

Table 3

Bond Distances (Å) of *rac*-**1c**, with their E.S.D.'s in Parentheses

Atom 1	Atom 2	Distance	Atom 1	Atom 2	Distance
O(1)	C(2)	1.381(3)	C(7)	C(12)	1.400(4)
O(1)'	C(2)'	1.394(3)	C(7)'	C(12)'	1.391(5)
O(1)	C(5)	1.383(2)	C(8)	C(9)	1.380(5)
O(1)'	C(5)'	1.398(3)	C(8)'	C(9)'	1.379(4)
O(2)	C(5)	1.194(3)	C(9)	C(10)	1.362(5)
O(2)'	C(5)'	1.194(4)	C(9)'	C(10)'	1.370(6)
N(3)	C(2)	1.271(3)	C(10)	C(11)	1.352(5)
N(3)'	C(2)'	1.260(3)	C(10)'	C(11)'	1.352(5)
N(3)	C(4)	1.466(3)	C(11)	C(12)	1.390(4)
N(3)'	C(4)'	1.471(3)	C(11)'	C(12)'	1.395(4)
C(2)	C(13)	1.456(3)	C(13)	C(14)	1.381(5)
C(2)'	C(13)'	1.467(4)	C(13)'	C(14)'	1.378(4)
C(4)	C(4)'	1.563(3)	C(13)	C(18)	1.408(4)
C(4)	C(5)	1.529(4)	C(13)'	C(18)'	1.398(4)
C(4)'	C(5)'	1.527(4)	C(14)	C(15)	1.378(4)
C(4)	C(6)	1.537(4)	C(14)'	C(15)'	1.379(4)
C(4)'	C(6)'	1.535(3)	C(15)	C(16)	1.395(4)
C(6)	C(7)	1.504(4)	C(15)'	C(16)'	1.392(5)
C(6)'	C(7)'	1.507(3)	C(16)	C(17)	1.364(4)
C(7)	C(8)	1.377(4)	C(16)'	C(17)'	1.367(4)
C(7)'	C(8)'	1.373(4)	C(17)	C(18)	1.377(4)
			C(17)'	C(18)'	1.389(4)

Scheme 2

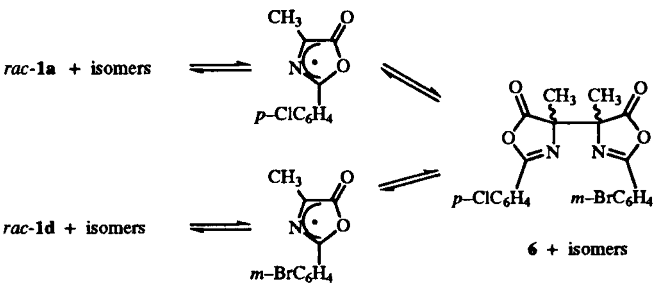


Table 4

Bond Angles of *rac*-**1c**, with their E.S.D.'s in Parentheses

Atom 1	Atom 2	Atom 3	Angle	Atom 1	Atom 2	Atom 3	Angle
C(2)	O(1)	C(5)	105.7(2)	C(6)'	C(7)'	C(8)'	120.8(3)
C(2)'	O(1)'	C(5)'	105.4(2)	C(6)	C(7)	C(12)	121.5(3)
C(2)	N(3)	C(4)	107.7(2)	C(6)'	C(7)'	C(12)'	121.2(2)
C(2)'	N(3)'	C(4)'	107.6(2)	C(8)	C(7)	C(12)	117.9(3)
O(1)	C(2)	N(3)	116.8(2)	C(8)'	C(7)'	C(12)'	118.1(2)
O(1)'	C(2)'	N(3)'	117.2(2)	C(7)	C(8)	C(9)	121.2(3)
O(1)	C(2)	C(13)	117.0(2)	C(7)'	C(8)'	C(9)'	121.0(3)
O(1)'	C(2)'	C(13)'	116.4(2)	C(8)	C(9)	C(10)	120.3(3)
N(3)	C(2)	C(13)	126.2(3)	C(8)'	C(9)'	C(10)'	120.8(3)
N(3)'	C(2)'	C(13)'	126.5(2)	C(9)	C(10)	C(11)	119.8(3)
N(3)	C(4)	C(4)'	107.6(2)	C(9)'	C(10)'	C(11)'	119.2(3)
N(3)'	C(4)'	C(4)	106.9(2)	C(10)	C(11)	C(12)	121.1(3)
N(3)	C(4)	C(5)	102.6(2)	C(10)'	C(11)'	C(12)'	121.0(3)
N(3)'	C(4)'	C(5)'	103.3(2)	C(7)	C(12)	C(11)	119.6(3)
N(3)	C(4)	C(6)	112.2(2)	C(7)'	C(12)'	C(11)'	120.0(3)
N(3)'	C(4)'	C(6)'	111.8(2)	C(2)	C(13)	C(14)	119.6(2)
C(4)	C(4)'	C(5)'	108.2(2)	C(2)'	C(13)'	C(14)'	121.9(3)
C(4)'	C(4)	C(5)	107.8(2)	C(2)	C(13)	C(18)	121.0(3)
C(4)	C(4)'	C(6)'	114.1(2)	C(2)'	C(13)'	C(18)'	118.2(2)
C(4)'	C(4)	C(6)	115.2(2)	C(14)	C(13)	C(18)	119.4(2)
C(5)	C(4)	C(6)	110.7(2)	C(14)'	C(13)'	C(18)'	119.8(3)
C(5)'	C(4)'	C(6)'	111.8(2)	C(13)	C(14)	C(15)	120.3(3)
O(1)	C(5)	O(2)	122.1(2)	C(13)'	C(14)'	C(15)'	120.1(3)
O(1)'	C(5)'	O(2)'	121.6(2)	C(14)	C(15)	C(16)	120.0(3)
O(1)'	C(5)'	O(2)'	121.6(2)	C(14)'	C(15)'	C(16)'	120.2(3)
O(1)	C(5)	C(4)	107.2(2)	C(15)	C(16)	C(17)	120.3(3)
O(1)'	C(5)'	C(4)'	106.6(2)	C(15)'	C(16)'	C(17)'	119.9(3)
O(2)	C(5)	C(4)	130.7(2)	C(16)	C(17)	C(18)	120.3(3)
O(2)'	C(5)'	C(4)'	131.9(2)	C(16)'	C(17)'	C(18)'	120.3(3)
C(4)	C(6)	C(7)	113.5(2)	C(13)	C(18)	C(17)	119.4(3)
C(4)'	C(6)'	C(7)'	113.5(2)	C(13)'	C(18)'	C(17)'	119.6(3)
C(6)	C(7)	C(8)	120.6(2)				

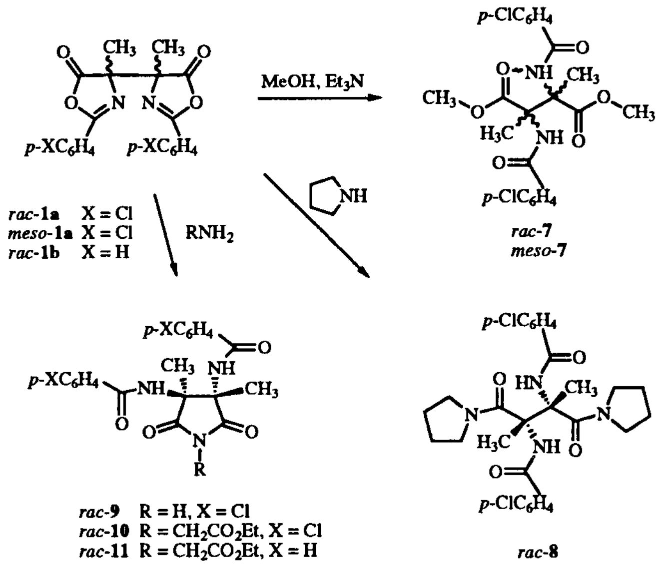
methanol gave methyl ester *rac*-**7** (91 percent yield); with pyrrolidine, amide *rac*-**8** (92 percent yield); with ammonia, imide *rac*-**9** (92 percent yield); and with the ethyl ester of glycine, imide *rac*-**10** (34 percent yield). Bioxazolone *rac*-**1b** reacted with the ethyl ester of glycine to give imide *rac*-**11** (90 percent yield). Treatment of *meso*-**1a** with methanol gave ester *meso*-**7**.

The α-protons of the glycine moiety of *rac*-**10** were shown to be diastereotopic, since they appeared as an AB quartet in the ^{1}H nmr spectrum. This established the stereochemistry of *rac*-**1a** as racemic. Therefore, the other 4,4'-dehydrodimer, *meso*-**1a**, must be the *meso* isomer. Prior to this observation, the assignment of configurations to *rac*-**1a** and *meso*-**1a** had not been made.

No reaction was observed when *rac*-**1a** was treated with diisopropylamine or with the methyl ester of L-proline. Perhaps lack of reaction is due to the steric bulk of the nucleophiles.

Bioxazolone *rac*-**1b** was treated with the ethyl ester of glycine to give *rac*-**11**. The ^{1}H nmr spectrum of the

Scheme 3



crude reaction mixture showed an AB pattern for the α-protons of the glycine moiety indicating that *rac*-**1b** was the racemate.

These reactions of *rac*-**1a**, *meso*-**1a** and *rac*-**1b** demonstrate that the 4,4'-bioxazolone system can undergo efficient nucleophilic ring opening in some cases.

EXPERIMENTAL SECTION

All reagents were used as received from Aldrich Chemical Co. or Lancaster Synthesis Inc. All solvents were reagent grade and were used without purification and redistillation, unless otherwise stated. Oxazolones used were the racemates. Thin layer chromatography was carried out with silica gel (Kieselgel 60F 254) tlc plates. Column chromatography was performed using silica gel (200-400 mesh, 60 Å). Melting points are uncorrected. Infrared spectra were measured with a Nicolet FT-IR model MX-1 or a Nicolet FT-IR Model 205 spectrometer. Nuclear magnetic resonance spectra (^{1}H and ^{13}C nmr) were recorded on a 360 MHz spectrometer in deuteriochloroform using tetramethylsilane as an internal standard, unless otherwise stated. Low resolution mass spectra were obtained on a Hewlett Packard 5890 spectrometer. Isotope peaks due to ^{37}Cl are not reported. Chemical ionization was carried out using methane. High resolution chemical ionization mass spectra were obtained at Boston University on a Finnegan MAT 90 spectrometer with an accuracy of 3 ppm or better. Elemental analyses were performed at the University of New Hampshire Instrumentation Center.

X-ray Crystal Structure of *rac*-**1c**.

Data were collected on an Enraf-Nonius CAD-4 diffractometer using a graphite monochromator. 3063 unique observed reflections with $|Fo| > 3\sigma(|Fo|)$ were measured. The space group is $P2_1/c$ with a = 16.632(4)Å, b = 9.4594(3)Å, c = 18.775(2)Å, β = 117.42(1)°. The structure was solved by direct methods (MULTAN 82; Main, Fisk, Hull, Lessinger, Germain, Declerq & Woolfson, 1982). Hydrogen atoms were located by difference Fourier synthesis. Anisotropic full-matrix least-squares refinement (on F) was done on non-hydrogen atoms; isotropic refinement on H atoms. In the last cycle, the H atoms were fixed at ideal positions. The function minimized was $\Sigma w(|Fo| - |Fc|)^2$, with $w = 4F^2/[\sigma(I)^2 + (pF^2)^2]$ and p = 0.04. Final R = 0.059 and wR = 0.068, max Δ/σ = 0.05. Maximum peak height in the final difference Fourier was 0.26 eÅ^{-3}, and S = 2.860 for 344 variables.

(4*R**,4'*R**)-2,2'-Bis(4-chlorophenyl)-4,4'-dimethyl[4,4'-bioxazole]-5,5'(4*H*,4'*H*)-dione (**1a**).

A mixture of 2-(4-chlorophenyl)-4-methyl-5(4*H*)-oxazolone (**2a**) [1d, 1h, 9] (4.00 g, 19.1 mmoles) and cupric acetate (9.50 g, 47.6 mmoles) in tetrahydrofuran (100 ml) was stirred at room temperature for 20 minutes. The reaction mixture was filtered, and then ethylenediaminetatraacetic acid was added to the filtrate to precipitate the remaining copper. The mixture was filtered, dried over magnesium sulfate, and concentrated. Purification of the residue by recrystallization (hexanes/ethyl acetate) gave *rac*-**1a** (0.500 g, 1.20 mmoles, 13%), mp 214-215°; ir (potassium bromide): 3093, 3051, 2995, 2945, 1820, 1659 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.80 (s, 6H) 7.34 (AA' of AA'XX', J = 7.8 Hz, 4H) 7.76 (XX' of AA'XX', J = 7.8 Hz, 4H); ^{13}C nmr (deuteriochloroform): δ 17.3, 71.7, 123.4, 129.2 (2 peaks), 139.6, 161.5, 176.2; ms: m/z (relative intensity) (CI) 457 ($M^+ + C_3H_5$, 3), 445 ($M^+ + C_2H_5$, 6), 417 (M^+ + H, 100).

Anal. Calcd. for $C_{20}H_{14}Cl_2N_2O_4$: C, 57.57; H, 3.38; N, 6.71. Found: C, 57.28; H, 3.35; N, 6.48. Two additional reactions were carried out at room temperature for 10 minutes each to give *rac*-**1a** in yields of 12 and 15 percent, respectively.

From a similar reaction carried out at reflux temperature it was possible to isolate (4*R**,4'*S**)-2,2'-bis(4-chlorophenyl)-4,4'-dimethyl[4,4'-bioxazole]-5,5'(4*H*,4'*H*)-dione (*meso*-**1a**) (0.026 g, 0.063 mmole, 1%), mp 72-73°; ir (potassium bromide): 3100, 2994, 2938, 1820, 1652 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.79 (s, 6H), 7.46 (AA' of AA'XX' J = 8.3 Hz, 4H), 7.92 (XX' of AA'XX' J = 8.3 Hz, 4H); ^{13}C nmr (deuteriochloroform): δ 18.5, 72.9, 123.7, 129.2, 129.6, 139.7, 161.2, 177.1; ms: [the mass spectrum and CHN analyses were done on mixtures of *meso*-**1a** and the 2,4' isomer **4a** reported directly below] m/z (relative intensity) (CI) 457 ($M^+ + C_3H_5$, 1), 445 ($M^+ + C_2H_5$, 2), 417 (M^+ + H, 36), 210 (1/2 (M^+ + H), 100).

Anal. Calcd. for $C_{20}H_{14}Cl_2N_2O_4$: C, 57.57; H, 3.38; N, 6.71. Found: C, 57.46; H, 3.52; N, 6.45. Also isolated was 2,2'-bis(4-chlorophenyl)-4,4'-dimethyl[2,4'-bioxazole]-5,5'(2*H*,4'*H*)-dione (**5a**) (0.030 g, 0.072 mmole, 1%), mp 144-148° dec [10]; ir (potassium bromide): 1833, 1820, 1787, 1653 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.61 (s, 3H), 2.29 (s, 3H), 7.42 (AA' of AA'XX' J = 8.5 Hz, 2H), 7.49 (AA' of AA'XX' J = 8.5 Hz, 2H), 7.60 (XX' of AA'XX' J = 8.5 Hz, 2H), 7.91 (XX' of AA'XX' J = 8.5 Hz, 2H); ^{13}C nmr (deuteriochloroform): δ 14.0, 19.9, 73.5, 105.6, 123.5, 128.2, 129.4 (2 peaks), 129.9, 131.8, 136.2, 139.9, 161.4, 162.9, 163.9, 174.9.

rac-**1a** *via* Benzoyl Peroxide.

Oxazolone **2a** (0.520 g, 2.49 mmoles) was added to a solution, previously dried over calcium chloride, of benzoyl peroxide (70%, 1.72 g, 5.00 mmoles) in benzene (50 ml). The mixture was heated to reflux for 5 hours and then cooled and diluted with benzene (25 ml). Decolorizing charcoal was added after which the mixture was filtered and concentrated to give an oil (0.450 g). Bioxazole *rac*-**1a** was isolated by circular chromatography (hexanes/ethyl acetate: 10/1, 4/1), (0.070 g, 0.168 mmoles, 7%).

rac-**1a** *via* Manganese Triacetate.

A mixture of oxazolone **2a** (1.60 g, 7.65 mmoles) and manganese triacetate dihydrate (4.00 g, 15.0 mmoles) in methylene chloride (80 ml) was stirred at room temperature for 1 hour. The insoluble manganese(III) salts were reduced to water soluble manganese(II) salts by the addition of an aqueous saturated solution of sodium bisulfite (30 ml), the layers were separated, and the aqueous layer was extracted with methylene chloride (3 x 30 ml). The combined organic layers were dried over magnesium sulfate, filtered and concentrated to give a solid which was further purified by recrystallization (hexanes/ethyl acetate: 1/1) to give *rac*-**1a** (0.440 g, 1.06 mmoles, 27%). When the reaction was carried out in tetrahydrofuran at reflux for 1 hour, the isolated yield was 6%; in glacial acetic acid at room temperature for 1.5 hours, the yield was 18%.

(4*R**,4'*R**)-4,4'-Dimethyl-2,2'-diphenyl[4,4'-bioxazole]-5,5'(4*H*,4'*H*)-dione (*rac*-**1b**), (4*R**,4*S**)-4,4'-Dimethyl-2,2'-diphenyl[4,4'-bioxazole]-5,5'(4*H*,4'*H*)-dione (*meso*-**1b**); 4,4'-Dimethyl-2,2'-diphenyl-[2,4'-bioxazole]-5,5'(2*H*,4'*H*)-dione (**4b**), and *N*-Acetylbenzamide.

4-Methyl-2-phenyl-5(4*H*)-oxazolone (**2b**) [1g, 11] (1.60 g, 9.13 mmoles) and manganese triacetate dihydrate (5.00 g, 18.3 mmoles) in glacial acetic acid (80 ml) were stirred at room temperature for 5 hours. The reaction mixture was worked up as for the synthesis of *rac*-**1a** *via* manganese triacetate described above. Separation by chromatography (hexanes/ethyl acetate: 4/1) followed by recrystallization gave the following four products: (*rac*-**1b**) (aqueous ethanol) (0.060 g, 0.172 mmole, 4%), mp 148-148.5°; ir (potassium bromide): 1820, 1659 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.82 (s, 6H), 7.34 (t, J = 7.89 Hz, 4H), 7.46 (tt, J = 1.24, 6.71 Hz, 2H), 7.82-7.85 (m, 4H); ^{13}C nmr (deuteriochloroform): δ 17.3, 71.7, 125.1, 128.0, 128.6, 133.0, 162.3, 176.7; ms: m/z (relative intensity) (CI) 389 (M^+ + C_3H_5, 0.002), 377 (M^+ + C_2H_5, 2.5), 349 (M^+ + H, 100).

Anal. Calcd. for $C_{20}H_{16}N_2O_4$: C, 68.94; H, 4.63; N, 8.05. Found: C, 68.63; H, 4.70; N, 7.93.

Compound *meso*-**1b** was obtained from chloroform/hexanes, mp 134-136°; ir (potassium bromide): 1826, 1813, 1645 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.80 (s, 6H), 7.47 (t, J = 7.7 Hz, 4H), 7.59 (t, J = 7.41 Hz, 2H), 7.99 (d, J = 7.43 Hz, 4H); ^{13}C nmr (deuteriochloroform): δ 18.6, 72.8, 125.3, 128.3, 128.8, 133.2, 161.9, 177.5; ms: m/z (relative intensity) (CI) 377 (M^+ +C_2H_3, 1), 349 (M^+ + H, 100).

Anal. Calcd. for $C_{20}H_{16}N_2O_4$: C, 68.94; H, 4.63; N, 8.05. Found: C, 68.71; H, 4.97; N, 7.97.

N-acetylbenzamide [12] was also obtained (0.025 g, 0.153 mmole, 2%); ir (potassium bromide): 3307, 3065, 1724, 1683 cm^{-1}; ^1H nmr (deuteriochloroform): δ 2.62 (s, 3H), 7.48 (t, J = 7.45 Hz, 2H), 7.59 (t, J = 7.07 Hz, 1H), 7.92 (d, J = 7.45 Hz, 2H); ^{13}C nmr (deuteriochloroform): δ 25.6, 127.7, 129.0, 132.6, 133.3, 165.8, 173.7; ms: m/z (relative intensity) (CI) 192 (M^+ + C_2H_5, 4), 164 (M^+ + H, 100), 150 (3), 122 (7), 105 (12). Compound **4b** was also obtained (0.030 g, 0.086 mmole, 3%), mp 152-154.5°; ir (potassium bromide): 3065, 2973, 2917, 1820, 1792, 1652 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.63 (s, 3H), 2.28 (s, 3H), 7.42-7.45 (m, 5H), 7.60-7.64 (m, 1H), 7.67-7.70 (m, 2H), 7.97-8.0 (m, 2H); ^{13}C nmr (deuteriochloroform): δ 13.9, 19.8, 73.4, 106.2, 125.2, 127.9, 128.2, 128.5, 128.9, 129.8, 133.3, 133.3, 162.1, 162.6, 164.2, 175.4; ms: m/z (relative intensity) (CI) 389 (M^+ + C_3H_5, 4), 377 (M^+ + C_2H_5, 5), 349 (M^+ + H, 100).

Anal. Calcd. for $C_{20}H_{16}N_2O_4$: C, 68.94; H, 4.63; N, 8.05. Found: C, 68.70; H, 4.76, N, 7.93.

(4*R**,4'*R**)-4,4'-Bis(phenylmethyl)-2,2'-diphenyl[4,4'-bioxazole]-5,5'(4*H*,4'*H*)-dione (*rac*-**1c**).

A mixture of 4-phenylmethyl-2-phenyl-5(4*H*)-oxazolone (**2c**) (0.300 g, 1.19 mmoles) and cupric acetate (0.480 g, 2.40 mmoles) in tetrahydrofuran (10 ml) was heated to reflux for 10 minutes. The reaction mixture was diluted with diethyl ether (100 ml) and then washed with water (20 ml). The aqueous wash was extracted with diethyl ether (50 ml) and the organic layers were combined and washed with brine (3 x 30 ml). The organic layer was dried over magnesium sulfate and then concentrated to give a residue (0.270 g) which was furthered purified by fractional recrystallization (ethanol) to give *rac*-**1c** (0.047 g, 0.094 mmole, 16%), mp 201-203° dec, lit [1a] mp 201-202.5°, lit [1e] mp 210°, lit [1m] mp 209-210°; ir (potassium bromide): 3072, 3030, 2938, 1827, 1659 cm^{-1}; ^1H nmr (deuteriochloroform): δ 3.58 (AA' of AA'XX', J = 13.1 Hz, 2H), 4.03 (XX' of AA'XX', J = 13.1 Hz, 2H) 7.10-7.26 (m, 14H), 7.26-7.38 (m, 2H), 7.61-7.64 (m, 4H); ^{13}C nmr (deuteriochloroform): δ 36.6, 76.6, 124.8, 127.4, 127.8, 128.2, 128.4, 130.5, 132.7, 133.2, 162.0, 176.0; ms: m/z (relative intensity) (CI) 529 (M^+ + C_2H_5, 9), 501 (M^+ + H, 100).

Anal. Calcd. for $C_{32}H_{24}N_2O_4$: C, 76.77; H, 4.84; N, 5.60. Found: C, 76.54; H, 4.66; N, 5.53.

rac-*N*-(3-Bromobenzoyl)alanine.

Standard Schotten-Baumann conditions were employed to couple 3-bromobenzoyl chloride (6.85 g, 31.2 mmoles) and *rac*-alanine (2.22 g, 25.0 mmoles) to give *rac*-*N*-(3-bromobenzoyl)alanine (3.50 g, 12.9 mmoles, 43%), mp 165-167°; ir (potassium bromide): 3269, 3058, 1715, 1637, 1539 cm^{-1}; ^1H nmr (acetone-d_6): δ 1.50 (d, J = 7.3 Hz, 3H), 4.66 (quint, J = 7.34 Hz, 1H), 7.34-7.44 (m, 1H), 7.69-7.71 (m, 1H), 7.89-7.91 (m, 1H), 8.06 (m, 2H); ^{13}C nmr (acetone-d_6): δ 17.1, 48.8, 122.3, 126.7, 130.7, 130.8, 134.6, 136.9, 165.5, 173.7; ms: m/z (relative intensity) (EI) 273 (M^+, 1.6), 271 (M^+, 1.4), 229 (28), 228 (43), 227 (27), 226 (40), 185 (96), 183 (100), 157 (36), 155 (37).

Anal. Calcd. for $C_{10}H_{10}BrNO_3$: C, 44.14; H, 3.72; N, 5.15. Found: C, 43.98; H, 3.72; N, 5.01.

2,2'-Bis(3-bromophenyl)-4,4'-dimethyl[4,4'-bioxazole]-5,5'(4*H*,4'*H*)-dione (**1d**).

N,N-Dicyclohexylcarbodiimide (1.52 g, 7.35 mmoles) in methylene chloride (75 ml) was added dropwise to a slurry of *rac*-*N*-(3-bromobenzoyl)alanine (2.00 g, 7.35 mmoles) in methylene chloride (75 ml) and the mixture was stirred at room temperature for 7 days. The mixture was filtered and concentrated to give the presumed 2-(3-bromophenyl)-4-methyl-5(4*H*)-oxazolone (**2d**) (1.72 g, 6.79 mmoles, 92%); ^1H nmr (deuteriochloroform): δ 1.59 (d, J = 7.60 Hz, 3H), 4.47 (q, J = 7.60 Hz, 1H), 7.38 (dd, J = 7.89, 7.89 Hz, 1H), 7.72 (d, J = 8.0 Hz, 1H), 7.92 (d, J = 7.83 Hz, 1H), 8.16 (s, 1H). A mixture of oxazolone **2d** (1.17 g, 4.61 mmoles) and cupric acetate (0.460 g, 2.31 mmoles) in toluene (40 ml) was heated at reflux for 1.5 hours, then concentrated and passed through silica (hexanes/ethyl acetate: 10/1). The copper-free eluate was concentrated to give an oil (1.30 g). Analysis (^1H nmr) indicated the presence of both the *racemic* and *meso* isomers. The crude mixture was recrystallized (hexanes/ethyl acetate) to give one isomer, **1d** (0.120 g, 0.237 mmole, 10%), mp 124.5-126°; ir (potassium bromide): 3072, 2988, 1827, 1652, 1567 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.81 (s, 6H), 7.26-7.28 (m, 2H), 7.61-7.63 (m, 2H), 7.77-7.79 (m, 2H), 8.00 (s, 2H); ^{13}C nmr (deuteriochloroform): δ 17.3, 71.7, 122.8, 126.6, 126.9, 130.3, 130.9, 136.1, 161.2, 175.9; ms: m/z (relative intensity) (CI) 509 (M^+ + H, 6), 507 (M^+ + H, 12), 505 (M^+ + H, 5), 256 (52), 254 (100), 228 (19), 226 (18), 185(20), 183 (20).

Anal. Calcd. for $C_{20}H_{14}Br_2N_2O_4$: C, 47.46; H, 2.79; N, 5.53. Found: C, 47.18; H, 2.93; N, 5.28.

4,4'-Bis(phenylmethyl)-2,2'-dimethyl[4,4'-bioxazole]-5,5'(4*H*,4'*H*)-dione (**1e**).

A mixture of 2-methyl-4-phenylmethyl-5(4*H*)-oxazolone (**2e**) [13] (0.500 g, 2.64 mmoles) and cupric acetate (0.800 g, 4.00 mmoles) in benzene (30 ml) was stirred at reflux for 25 hours, then cooled to room temperature and extracted with water (15 ml). The organic layer was dried over magnesium sulfate, filtered and concentrated. The mixture was separated by flash chromatography (hexanes/ethyl acetate: 4/1) to give **1e** (0.040 g, 0.106 mmole, 8%), mp 180-182°; ir (potassium bromide): 1825, 1801, 1694, 1496 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.85 (s, 6H), 3.41 (AA' of AA'BB' J = 13.1 Hz, 2H), 3.83 (BB' of AA'BB' J =13.1 Hz, 2H), 7.15-7.17 (m, 4H), 7.24-7.28 (m, 6H); ^{13}C nmr (deuteriochloroform): δ 14.3, 35.9, 75.5, 127.5, 128.2, 130.5, 133.1, 163.4, 176.1; ms: m/z (relative intensity) (CI) 417 (M^+ + C_3H_5, 1), 405 (M^+ + C_2H_5, 3), 377 (M^+ + H, 100), 349 (11), 307 (7).

Anal. Calcd. for $C_{22}H_{20}N_2O_4$: C, 70.20; H, 5.35; N, 7.44. Found: C, 69.91; H, 5.25; N, 7.30.

(*Z*)-4-Benzylidene-2-methyl-5(4*H*)-oxazolone (**2g**).

This compound was obtained as above (0.025 g, 0.133 mmole, 5%), mp 153-154° (lit [14] mp 152-153°); ^1H nmr (deuteriochloroform): δ 2.42 (s, 3H), 7.16 (s, 1H), 7.44-7.46 (m, 3H), 8.07-8.08 (m, 2H); ^{13}C nmr (acetone-d$_6$) δ 22.5, 38.1, 54.2, 127.4, 129.1, 130.1, 138.3, 170.0, 173.1; ms: m/z (relative intensity) (EI) 187 (M^+, 13), 159 (10), 117 (86), 89 (43), 43 (100).

rac-N-acetylphenylalanine.

This compound was obtained as above (0.010 g, 0.048 mmole, 2%), mp 152°; (lit [15] mp 152-153°); ms: m/z (relative intensity) (CI) 248 ($M^+ + C_3H_5$, 2), 236 ($M^+ + C_2H_5$, 5), 208 (M^+ + H, 100), 190 (12), 166 (24), 162 (24), 148 (8), 120 (7), 91 (1), 41 (78).

2,2'-Bis(4-chlorophenyl)-4,4'-bis[2-(methylthio)ethyl][4,4'-bioxazole]-5,5'(4*H*,4'*H*)-dione (**1f**).

A solution of *N,N*-dicyclohexylcarbodiimide (0.440 g, 2.21 mmoles) in methylene chloride (40 ml) was added dropwise to a slurry of *N*-(4-chlorobenzoyl)-*rac*-methionine (0.610 g, 2.12 mmoles) in methylene chloride (40 ml) and the mixture was stirred at room temperature for 20 hours. The reaction mixture was chilled, filtered, and then concentrated to give a solid which was presumed to be the corresponding oxazolone **2f** (0.750 g). A mixture of **2f** (0.750 g) and cupric acetate (0.210 g, 1.06 mmoles) in toluene was heated to reflux for 5 minutes, at which time tlc analysis of the reaction mixture indicated that the starting material had been consumed. The reaction mixture was concentrated and the copper salts were removed by passing the mixture through silica (hexanes/ethyl acetate: 4/1). The eluent was concentrated and the residue was recrystallized (hexanes/chloroform): to give **1f** (0.070 g, 0.130 mmole, 12%), mp 148.5-149.5°; ir (potassium bromide): 3086, 1813, and 1652 cm^{-1}; ^1H nmr (deuteriochloroform): δ 2.05 (s, 6H), 2.24-2.52 (m, 6H), 2.92-2.98 (m, 2H), 7.33 (AA' of AA'XX', J = 7.1 Hz, 4H) 7.76 (XX' of AA'XX', J = 7.1 Hz, 4H); ^{13}C nmr (deuteriochloroform): δ 14.9, 28.0, 29.2, 74.9, 123.2, 129.2, 129.3, 139.7, 162.6, 176.2; ms: m/z (CI) 537 (M^+ + H, 1).

Anal. Calcd. for $C_{24}H_{22}Cl_2N_2O_4S_2$: C, 53.63; H, 4.13; N, 5.21. Found: C, 53.60; H, 3.99; N, 5.08.

Crossover Experiment.

A solution of chlorobioxazolone *rac*-**1a** (0.016 g, 0.039 mmoles) and bromobioxazolone **1d** (0.020 g, 0.039 mmoles) in toluene was heated to reflux for 19 hours. The solution was then concentrated to give a solid; ms: m/z (relative intensity) (CI) 509 (M^+ + H, 1.51), 507 (M^+ + H, 0.88), 505 (M^+ + H, 1.00), 465 (M^+ + H, 0.46), 463 (M^+ + H, 1.21), 461 (M^+ + H, 1.00), 421 (M^+ + H, 0.09), 419 (M^+ + H, 0.70), 417 (M^+ + H, 1.00), 208 (100), 254 (19). As a control, **6** (0.016 g, 0.039 mmole) and **13** (0.020 g, 0.039 mmole) were dissolved in toluene at room temperature after which the solution was concentrated to give a solid. The ms gave peaks at m/z values of 417, 419 and 421 due to **1a** and at 505, 507 and 509 due to **1d**, but no peaks at 465, 463 or 461 due to a mixed bromochlorobioxazolone **6** or its isomers.

(2*R**,3*R**)-Dimethyl 2,3-Dimethyl-2,3-bis(4-chlorobenzamido)-butanedioate (*rac*-**7**).

A mixture of 4,4'-bioxazolone *rac*-**1a** (0.200 g 0.481 mmole) and triethylamine (catalytic) in methanol (10 ml) was stirred at room temperature for 3 hours. The mixture was then concentrated to give *rac*-**7a** (0.211 g 0.437 mmole, 91 %), mp 193.4-195.5°; ^1H nmr (deuteriochloroform): δ 1.63 (s, 6H), 3.92 (s, 6H), 7.41 (AA' of AA'XX', J = 8.6 Hz, 4H), 7.76 (XX' of AA'XX', J = 8.6 Hz, 4H), 8.50 (br s, 2H); ^{13}C nmr (deuteriochloroform): δ 18.0, 53.5, 62.7, 128.5, 129.0, 131.3, 138.5, 165.4, 172.1; ms: m/z (relative intensity) (CI) 481 (M^+ + 1, 100), 369 (8), 303 (8), 242 (8), (EI) 241 (1/2M^+ + 1, 16), 139 (100).

Anal. Calcd. for $C_{22}H_{22}Cl_2N_2O_6$: C, 54.90; H, 4.61; N, 5.82. Found: C, 54.47; H, 4.54; N, 5.63.

(2*R**,3*S**)-Dimethyl 2,3-Dimethyl-2,3-bis(4-chlorobenzamido)-butanedioate (*meso*-**7a**).

Similar treatment of 4,4'-bioxazolone *meso*-**1a** with triethylamine in methanol gave *meso*-**7a**, mp 147-149° (from ethanol); ir (potassium bromide): 3367, 3267, 1746, 1733, 1659 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.98 (s, 6H), 3.80 (s, 6H), 7.43 (AA' of AA'XX', J = 8.4 Hz, 4H), 7.79 (XX' of AA'XX', J = 8.4 Hz, 4H), 8.28 (br s, 2H); ^{13}C nmr (deuteriochloroform): δ 18.5, 53.4, 66.3, 128.7, 128.9, 132.1, 138.3, 166.8, 172.3; ms: m/z (relative intensity) (CI) 521 ($M^+ + C_3H_5$, 4), 509 ($M^+ + C_2H_5$, 10), 481 (M^+ +1, 100).

Anal. Calcd. for $C_{22}H_{22}Cl_2N_2O_6$: C, 54.90; H, 4.61; N, 5.82. Found: C, 54.71; H, 4.52; N, 5.53.

(2*R**,3*R**)-*N,N'*-Ditetramethylene-2,3-dimethyl-2,3-bis(4-chlorobenzamido)butanediamide (*rac*-**8**).

A mixture of 4,4'-bioxazolone *rac*-**1a** (0.030 g, 0.072 mmole) and pyrrolidine (0.5 ml, 6 mmoles) in tetrahydrofuran (20 ml) was stirred at room temperature for 5 minutes. The reaction mixture was concentrated, taken up in ether (15 ml), and washed with hydrochloric acid (1*M*, 15 ml). The organic layer was dried over magnesium sulfate, filtered, and concentrated to give *rac*-**8** (0.037 g, 0.066 mmole, 92%), mp 195° discoloration, 212-214°, total dec; ir (potassium bromide): 3311, 1673, 1595 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.70-1.88 (m, 8H), 2.05 (s, 6H), 3.33-3.47 (m, 6H), 3.65-3.70 (m, 2H), 7.45 (AA' of AA'XX', J = 8.7 Hz, 4H), 7.84 (XX' of AA'XX', J = 8.7 Hz, 4H) 8.98 (br s, 2H); ^{13}C nmr (deuteriochloroform): δ 19.3, 22.8, 27.6, 47.5, 49.5, 65.9 128.5, 129.1, 132.5, 138.2, 164.9, 172.5; ms: m/z (relative intensity) (EI) 558 (M^+, 0.004), 139 (100), 111 (30).

Anal. Calcd. for $C_{28}H_{32}Cl_2N_4O_4$: C, 60.20; H, 5.78; N, 10.03. Found: C, 60.07; H, 5.88; N, 9.73.

(3*R**,4*R**)-3,4-Dimethyl-3,4-bis(4-chlorobenzamido)-2,5-pyrrolidinedione (*rac*-**9**).

4,4'-Bioxazolone *rac*-**1a** (0.063 g, 0.151 mmole) was added to a solution of tetrahydrofuran (15 ml) saturated with ammonia gas. The reaction mixture was stirred at room temperature for 2 hours. Analysis (tlc) indicated complete consumption of starting material (hexanes/ethyl acetate: 4/1). Concentration of the reaction mixture gave *rac*-**9** (0.060 g, 0.139 mmole, 92%), mp > 210°; ir (potassium bromide): 3416, 1729, 1659 cm^{-1}; ^1H nmr (acetone-d$_6$): δ 1.68 (s, 6H), 7.50 (AA' of AA'XX', J = 8.5 Hz, 4H), 7.91-7.93 (XX' of AA'XX', J = 8.5 Hz, 6H), 10.52 (s, 1H); ^{13}C nmr (acetone-d$_6$): δ 20.5, 64.7, 128.9, 129.7, 133.1, 137.6, 166.1, 175.6; ms: m/z (relative intensity) (EI) 433 (M^+, 4), 208 (7), 139 (100), 111 (34); hrms: m/z (CI) Calcd. for $C_{20}H_{18}Cl_2N_3O_4$ (M^+ + 1): 434.0676. Found: 434.0687.

Anal. Calcd. for $C_{20}H_{17}Cl_2N_3O_4$: C, 55.32: H, 3.95; N, 9.68. Found: C, 55.18; H, 4.06; N, 9.32.

(3*R**,4*R**)-3,4-Dimethyl-3,4-bis(4-chlorobenzamido)-1-ethoxycarbonylmethyl-2,5-pyrrolidinedione (*rac*-**10**).

A mixture of 4,4'-bioxazolone *rac*-**1a** (0.150 g, 0.361 mmole), the hydrochloride salt of ethyl glycinate (0.500 g, 3.58 mmoles) and triethylamine (0.25 ml, 1.8 mmoles) in tetrahydrofuran (30 ml) was stirred at room temperature for 6 days. The mixture was concentrated and the components were separated by flash chromatography (hexanes/ethyl acetate: 4/1). Purification by recrystallization (hexanes/ethyl acetate) gave *rac*-**10** (0.065 g, 0.125 mmoles, 34%), mp 210-211°; ir (potassium bromide): 3402, 1799, 1750, 1722, 1666 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.31 (t, J = 7.1 Hz, 3H), 1.74 (s, 6H), 4.25 (m, 2H), 4.36 (A of AB, J = 17.2 Hz, 1H), 4.48 (B of AB, J = 17.2 Hz, 1H), 7.00 (br s, 2H), 7.46 (AA' of AA'XX', J = 8.6, 4H), 7.81 (XX' of AA'XX', J = 8.6, 4H); ^{13}C nmr (deuteriochloroform): δ 14.1, 21.9, 40.1, 62.3, 64.8, 128.6, 129.1, 131.5, 138.7, 166.5, 174.5; ms: m/z (relative intensity) (EI) 519 (M^+, 1), 209 (4), 139 (100), 111 (18); *Anal.* Calcd. for $C_{24}H_{23}Cl_2N_3O_6$: C, 55.48; H, 4.47; N, 8.09. Found: C, 55.54; H, 4.60; N, 8.03.

(3*R**,4*R**)-3,4-Dimethyl-3,4-bis(benzamido)-1-ethoxycarbonylmethyl-2,5-pyrrolidinedione (*rac*-**11b**).

A mixture of 4,4'-bioxazolone *rac*-**1b** (0.026 g, 0.063 mmole), the hydrochloride salt of ethyl glycinate (0.021 g, 0.151 mmole) and triethylamine (0.03 ml, 0.15 mmole) in anhydrous ether (10 ml) stirred at room temperature for 72 hours yielded *rac*-**11** (0.03 g, 0.066 mmole, 90%) as an oil; ir (potassium bromide): 3409, 1722, 1666 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.30-1.34 (m, 3H), 1.77 (s, 6H), 4.12-4.31 (m, 2H), 4.37 (A of AB, J = 17.1 Hz, 1H), 4.51 (B of AB, J = 17.1 Hz, 1H), 7.07 (br s, 2H), 7.47-7.57 (m, 6H), 7.88 (d, J = 7.73 Hz, 4H); ^{13}C nmr (deuteriochloroform): δ 14.1, 21.9, 40.1, 62.2, 64.8, 127.2, 128.8, 132.3, 133.3, 166.4, 167.5, 174.8; hrms: m/z (CI) Calcd. for $C_{24}H_{26}N_3O_6$ (M^+ + 1): 452.1823. Found: 452.1794.

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