Preparation of Chiral Oxazolidin-2-ones and Vicinal Amino Alcohols

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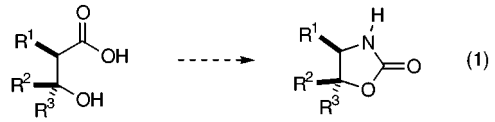
Chiral 4-substituted-, 4,5-disubstituted-, and 4-substituted-5,5-dimethyl-oxazolidin-2-ones are useful chiral auxiliaries for asymmetric synthesis.[1,2] They are typically prepared from chiral 1,2-amino alcohols, which in turn are prepared from the corresponding chiral α-amino acid.[3] In recent years a number of unnatural amino acid derived oxazolidinone chiral auxiliaries have been defined,[4−14] however the routes employed for their preparation either proceed via an asymmetric amino acid synthesis or are of relatively limited generality. In conjunction with another project, we needed access to a variety of chiral oxazolidinones in high enantiomeric purity, and in many cases, the obvious amino acid precursor was either not commercially available or relatively expensive. Rather than synthesizing the requisite amino acid, we optimized a simple, general alternative route that works well for a variety of unnatural aryl and alkyl substituents. As outlined in Scheme 1, the route employs the condensation of a chiral *N*-acyloxazolidinone titanium enolate with formaldehyde[15] followed by hydrolysis to the *β*-hydroxy acid and subsequent Curtius rearrangement with intramolecular capture of the intermediate isocyanate.

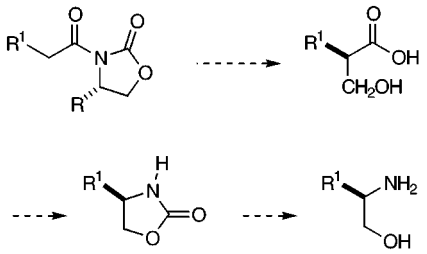
In a few cases, the chiral *N*-acyloxazolidinone enolates are condensed with acetone or a simple aldehyde and the corresponding 4-substituted-(5,5-dimethyl)oxazolidinone or 4,5-disubstituted-oxazolidinone are prepared (eq 1).



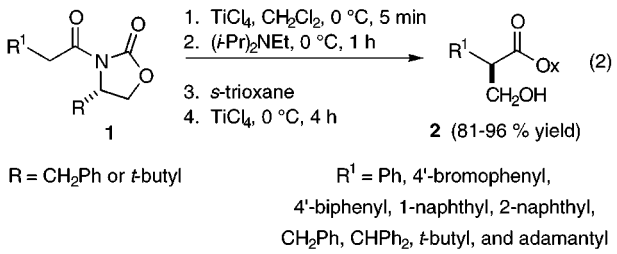
(1)

The preparation of oxazolidinones from *β*-hydroxy acids using the Curtius rearrangement followed by an intramolecular trapping has of course been carried out by other groups in the course of syntheses.[16−20] However, to our knowledge, the strategy has not previously been generalized for the preparation of chiral 4-substituted oxazolidin-2-ones in high enantiomeric purity. The route also permits the preparation of the corresponding *β*-amino alcohols by barium hydroxide hydrolysis of the oxazolidinone. Our results are summarized in Table 1.

Scheme 1



The requisite *β*-hydroxy acid intermediates are prepared according to Evans protocol.[15] An *N*-acyloxazolidinone is converted to its titanium enolate by treatment with $TiCl_4$ and $(i\text{-Pr})_2NEt$ and condensed with formaldehyde in the form of *s*-trioxane. The condensation proceeds in good yield (81−96%) and with near complete stereochemical control as judged by analysis of the crude ^1H NMR spectrum, for a variety of *N*-acyloxazolidinones.



In most cases, hydrolysis of the *β*-hydroxy-*N*-acyloxazolidinone proceeds smoothly upon treatment with $LiOH/H_2O_2$ (77−98% yield).[21] However, two relatively hindered substrates, suffer LiO_2H-promoted hydrolysis cleavage of the oxazolidinone ring. Fortunately, in these cases, the intermediate hydroxy amide **4** is efficiently hydrolyzed with aqueous KOH (75−79% overall yield) (Scheme 2).

N-Acyloxazolidinone enolates derived from **1** (R = CH_2Ph) can also be condensed with acetone to afford,

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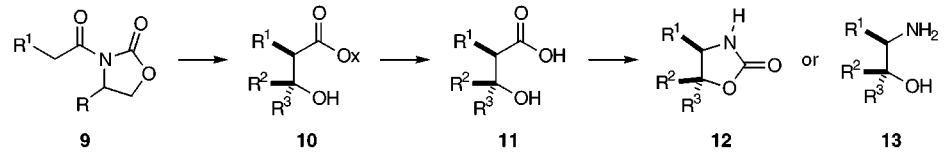
Table 1. Summary Data for the Preparation of Chiral Oxazoldin-2-ones and Vicinal Amino Alcohols

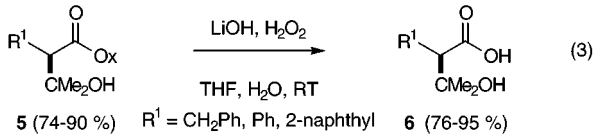


9 10 11 12 13

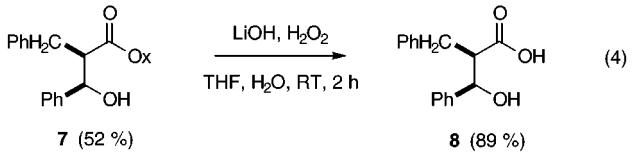
					% yield				
entry	R for **9** (abs config)	R^1	R^2	R^3	**10**	**11**	**12**	**13**	er[i]
1	$PhCH_2$ (*R*)	$PhCH_2$	Me	Me	90[a]	76[d]	88[f]		95:5
2	$(CH_3)_3C$ (*S*)	$PhCH_2$	Ph	H	52[a]	89[d]	82[g]		>98:2
3	$PhCH_2$ (*S*)	Ph_2CH	H	H	94[b]	77[d]	79[f]	71[j]	>98:2
4	$PhCH_2$ (*S*)	$(CH_3)_3C$	H	H	83[b]	79[e]	76[h]		>98:2
5	$PhCH_2$ (*S*)	1-adamantyl	H	H	81[b]	79[e]	79[f]		>98:2
6	$PhCH_2$ (*S*)	Ph	H	H	96[b]	91[d]	86[f]		96:4
7	$(CH_3)_3C$ (*S*)	Ph	Me	Me	74[c]	94[d]	81[f]		>98:2
8	$PhCH_2$ (*S*)	4′-BrC_6H_4	H	H	96[b]	95[d]	72[f]		92:8
9	$PhCH_2$ (*S*)	4′-biphenyl	H	H	87[b]	95[d]	74[f]	80[j]	95:5
10	$PhCH_2$ (*S*)	1-naphthyl	H	H	96[b]	98[d]	83[f]	71[j]	97:3
11	$PhCH_2$ (*S*)	2-naphthyl	H	H	92[b]	89[d]	87[f]	84[j]	95:5
12	$PhCH_2$ (*S*)	2-naphthyl	Me	Me	86[c]	79[d]	74[f]		>98:2

[a] DIPEA/Bu_2BOTf, −78 °C, CH_2Cl_2 then acetone or benzaldehyde. [b] DIPEA/$TiCl_4$, 0 °C, CH_2Cl_2 then *s*-trioxane/$TiCl_4$. [c] DIPEA/$TiCl_4$, 0 °C, CH_2Cl_2 then acetone/$TiCl_4$. [d] LiO_2H, THF/H_2O. [e] LiO_2H, THF/H_2O then KOH, Δ. [f] $(PhO)_2P(O)N_3$/TEA/toluene, 80 °C, 12 h. [g] $(PhO)_2P(O)N_3$/TEA/toluene, reflux, 8 h. [h] $(PhO)_2P(O)N_3$/TEA/xylenes, Δ, 12 h. [i] The enantiomer ratio (er) is determined as the diastereomer ratio of the corresponding camphorsulfonyl derivative. [j] $(PhO)_2P(O)N_3$/TEA/toluene, 80 °C, 12 h, then $Ba(OH)_2$·$8(H_2O)$, THF/H_2O, Δ.

after hydrolysis, the corresponding dimethyl derivatives. Such oxazolidinones have been recently shown to be useful chiral auxiliaries.[22] Two condensation procedures prove effective: reaction of the titanium enolate described above and reaction via the corresponding boron enolate (Bu_2BOTf/(*i*-Pr)$_2$NEt). The latter conditions are also useful for the stereoselective condensation with higher aldehydes; for example, condensation of **1** (R = *t*-Bu, R^1 = CH_2Ph) with benzaldehyde to afford **7**.[23] The hydrolyses of **5** and **7** proceed smoothly. We find it quite surprising that despite their rather hindered looking structures, the dimethyl derivatives **5** hydrolyze readily and without the initial oxazolidinone cleavage observed with the hydroxymethyl derivatives **2** bearing sterically demanding R^1 groups.



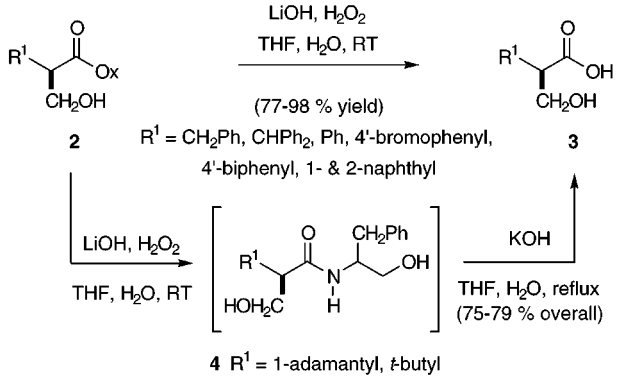
5 (74-90 %) **6** (76-95 %) (3)



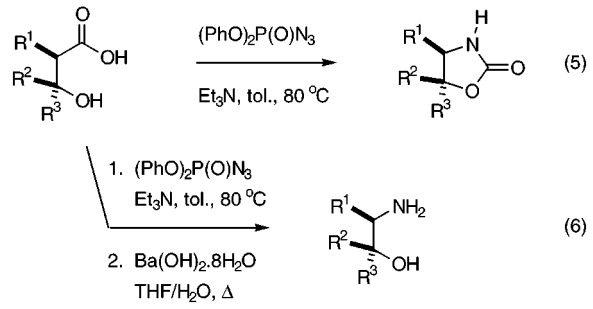
7 (52 %) **8** (89 %) (4)

Having the requisite β-hydroxy acids in hand, they were subjected to the Curtius rearrangement via the acyl azide by treatment with $(PhO)_2P(O)N_3$ followed by heating in toluene or xylene.[24] The one-pot formation of acyl azide, Curtius rearrangement, and intramolecular trapping proceeds smoothly to afford 4-substituted-oxazolidin-2-ones, 4,5-disubstituted-oxazolidin-2-ones, and 4-substituted-(5,5-dimethyl)oxazolidin-2-ones in good yields

Scheme 2



(72−88%, Table 1). The Curtius rearrangement is of course known to proceed with retention of configuration at the migrating chiral center, and the products obtained herein are consistent with that expectation. In each case, we find that the enantiomeric purity of the oxazolidinone can be conveniently assayed by derivatizing with camphor sulfonyl chloride and assessing the resulting diastereomer ratio from the ^{1}H NMR spectrum.



Chiral 1,2-amino alcohols are also useful intermediates and auxiliaries for asymmetric synthesis.[3] Chiral β-hydroxy acids can also be converted to the corresponding amino alcohols using the same approach. Curtius rearrangement in toluene followed by removal of the

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solvent and hydrolysis of the crude oxazolidinone ($Ba(OH)_2$, THF/H_2O, reflux)[17,19] affords the amino alcohol (71−84%, Table 1).

In summary, we have generalized a method for the enantioselective syntheses of 4-substituted-oxazolidin-2-ones, 4,5-disubstituted-oxazolidin-2-ones, and 4-substituted-(5,5-dimethyl)oxazolidin-2-ones. The corresponding vicinal amino alcohols can be obtained by hydrolysis of the crude oxazolidinone. The approach involves stereoselective condensation of *N*-acyloxazolidinone enolates with formaldehyde, and in a few cases a higher aldehyde or acetone, removal of the chiral auxiliary to give an intermediate *β*-hydroxy acid, followed by the Curtius rearrangement, and has been carried out on scales up to 50 mmol. In addition, we find that the enantiomeric purity of these oxazolidinones can be easily determined by analyzing the camphor sulfonyl derivatives.

Experimental Section

General. All solvents were distilled immediately before use under nitrogen. THF and toluene were distilled from Na/benzophenone. CH_2Cl_2 and xylenes were distilled from CaH_2. Flash column chromatography used 230−400 mesh silica gel. Melting points were determined using a capillary melting point apparatus and are not corrected. Optical rotations were recorded at ambient temperature. ^1H NMR and ^{13}C spectra were recorded in $CDCl_3$ unless noted otherwise. Combustion analyses were performed by M−H−W Analytical Labs, and High-Resolution Mass Spectral determinations were performed by the Midwest Center for Mass Spectrometry.

General Procedures to Prepare *β*-Hydroxyoxazolidinones. (A) Via the Boron Aldol Reaction.[23] To a stirred, cooled (0 °C) solution of *N*-acyloxazolidinone (1 equiv) in CH_2Cl_2 (ca. 0.2 M) was added Bu_2BOTf (1.0 M solution in CH_2Cl_2, 1.1 equiv). After 5 min, $(i\text{-Pr})_2NEt$ (1.15 equiv) was added dropwise. After an additional 30 min at 0 °C, the reaction mixture was cooled to −78 °C and the appropriate aldehyde or ketone (1.1 equiv) added dropwise. The resulting mixture was stirred for additional 45 min at −78 °C, then warmed to rt. After ca. 45 min at rt, the reaction was recooled to 0 °C and quenched by the addition of pH 7 phosphate buffer (ca. 10 mL on a 3 mmol scale reaction) and 30% aqueous H_2O_2 (ca. 1 mL). After being stirred for 1 h at 0 °C, the mixture was partitioned between CH_2Cl_2: water, and the organic layer was dried (Na_2SO_4) and concentrated. Flash chromatography on silica afforded the *β*-hydroxyoxazolidinone.

(B) Via the $TiCl_4$-Catalyzed Aldol Reaction.[15] To a stirred, cooled (0 °C) solution of *N*-acyloxazolidinone (1.0 equiv) in CH_2Cl_2 (ca. 0.2 M) was added $TiCl_4$ (1.05 equiv) dropwise. The resulting yellow solution was stirred for ca. 5 min (0 °C) after which $(i\text{-Pr})_2NEt$ (1.1 equiv) was added dropwise. The resulting dark red-to-purple mixture was stirred for 1 h at 0 °C, then *s*-trioxane (1.15 equiv as a ca. 10% solution in CH_2Cl_2) and additional $TiCl_4$ (1.05 equiv) were added. The resulting mixture was stirred for an additional 4 h at 0 °C and then quenched by the addition of saturated aqueous NH_4Cl (approximately an equal volume) and extracted with additional CH_2Cl_2. The organic layer was washed with water, dried (anhydrous Na_2SO_4), and concentrated. Flash chromatography on silica and/or recrystallization afforded the *β*-hydroxyoxazolidinone.

(4*R*)-4-Benzyl -3-((2*R*)-2-benzyl-3-hydroxy-3-methyl-1-oxobutyl)-oxazolidin-2-one. (4*R*)-4-Benzyl-3-(3-phenyl-1-oxopropyl)-2-oxazolidinone (1.03 g, 3.33 mmol) was condensed with acetone (0.27 mL, 3.7 mmol) via procedure A using Bu_2BOTf (3.66 mL, 1.0 M in CH_2Cl_2, 3.7 mmol) and $(i\text{-Pr})_2NEt$ (0.65 mL, 3.7 mmol) to afford the *β*-hydroxyoxazolidinone (1.10 g, 90%) after flash chromatography (4:1 hexane:EtOAc): TLC analysis (3:2 hexane:EtOAc) $R_f = 0.36$; mp 140−143 °C; $[\alpha]_D = -141°$ (*c* 1.14, $CHCl_3$); ^1H NMR (300 MHz) *δ* 7.40−7.20 (10 H, m), 4.38 (1 H, dd, *J* = 5.2, 6.0 Hz), 4.20−4.15 (1 H, m), 3.87 (1 H, d, *J* = 8.9 Hz), 3.52 (1 H, br s), 3.41 (1 H, dd, *J* = 7.7, 8.5 Hz), 3.20 (1 H, dd, *J* = 3.6, 10.1 Hz), 3.10−3.00 (2 H, m), 2.64 (1 H, dd, *J* = 9.7, 3.6 Hz), 1.40 (3 H, s), 1.39 (3 H, s); ^{13}C NMR (75 MHz) *δ* 173.3, 153.1, 138.7, 135.1, 129.3, 128.9, 128.8, 128.4, 128.3, 127.3, 126.4, 71.7, 65.7, 55.6, 52.9, 37.8, 34.8, 29.9, 25.9; HRMS analysis (CI, $C_{22}H_{25}NO_4 + H^+ = 368.1861$) found *m/z* 368.1865.

(4*S*)-4-*tert*-Butyl -3-((2*R*)-2-benzyl-3-hydroxy-3-phenyl-1-oxopropyl)-oxazolidin-2-one. (4*S*)-4-*tert*-Butyl-3-(3-phenyl-1-oxopropyl)-2-oxazolidinone (2.00 g, 7.26 mmol) was condensed with benzaldehyde (0.81 mL, 8.0 mmol) via procedure A using Bu_2BOTf (8.0 mL, 1.0 M in CH_2Cl_2, 8.0 mmol) and $(i\text{-Pr})_2NEt$ (1.42 mL, 8.13 mmol) to afford recovered starting oxazolidinone (800 mg, 40%) and the *β*-hydroxyoxazolidinone (1.40 g, 52%) after flash chromatography (2:1 hexane:EtOAc): TLC analysis (2:1 hexane:EtOAc) $R_f = 0.28$; mp 184−186 °C; $[\alpha]_D = +55.5°$ (*c* 1.26, $CHCl_3$); ^1H NMR (500 MHz) *δ* 7.50−7.10 (10 H, m), 5.05−4.97 (1 H, m), 4.91 (1H, d, *J* = 6.8 Hz), 3.95 (1 H, d, *J* = 7.2 Hz), 3.91 (1 H, d, *J* = 9.3 Hz), 3.44 (1 H, dd, *J* = 8.5, 8.5 Hz), 3.27 (1 H, dd, *J* = 4.0, 9.7 Hz), 3.09 (1 H, dd, *J* = 2.0, 11.3 Hz), 0.46 (9 H, s); ^{13}C NMR (125 MHz) *δ* 173.8, 153.9, 141.2, 138.5, 129.1, 128.2, 128.1, 128.0, 127.8, 126.5, 126.4, 126.2, 75.7, 64.7, 61.3, 50.5, 35.0, 34.7, 25.2; HRMS analysis (FAB, $C_{23}H_{27}NO_4 + H^+ = 382.2018$) found *m/z* 382.2027.

(4*S*)-4-Benzyl-3-((2*R*)-2-(diphenylmethyl)-3-hydroxy-1-oxopropyl)-2-oxazolidinone. (4*S*)-4-Benzyl-3-(3,3-diphenyl-1-oxopropyl)-2-oxazolidinone (1.00 g, 2.59 mmol) was condensed with *s*-trioxane (270 mg, 3.00 mmol) via procedure B using $TiCl_4$ (two 0.30 mL, 2.7 mmol portions) and $(i\text{-Pr})_2NEt$ (0.50 mL, 2.8 mmol) to afford the *β*-hydroxyoxazolidinone (1.01 g, 94%) after flash chromatography (3:1 hexane:EtOAc): TLC analysis (3:2 hexane:EtOAc) $R_f = 0.50$; mp 76−80 °C; $[\alpha]_D = +114°$ (*c* 1.08, $CHCl_3$); ^1H NMR (300 MHz) *δ* 7.50−7.20 (15 H, m), 5.25−5.17 (1 H, m), 4.41 (1 H, d, *J* = 11.7 Hz), 4.25−4.15 (1 H, m), 3.95 (1 H, dd, *J* = 2.0, 6.8) 3.85−3.75 (2 H, m), 3.60 (1 H, dd, *J* = 8.1, 8.5 Hz), 3.20 (1 H, dd, *J* = 3.6, 10.1), 2.73 (1 H, dd, *J* = 4.0, 9.7 Hz), 2.41 (1 H, br s); ^{13}C NMR (75 MHz) *δ* 175.0, 143.4, 142.0, 140.8, 135.1, 129.3, 128.8, 128.7, 128.4, 128.0, 127.8, 127.1, 126.9, 126.6, 65.8, 62.9, 55.4, 51.3, 48.6, 37.7; HRMS analysis (CI, $C_{26}H_{25}NO_4 + H^+ = 416.1862$) found *m/z* 416.1863.

(4*S*)-4-Benzyl-3-((2*R*)-2-(*tert*-butyl)-3-hydroxy-1-oxopropyl)-2-oxazolidinone. (4*S*)-4-benzyl-3-(3,3-dimethyl-1-oxobutyl)-2-oxazolidinone (14.90 g, 54.11 mmol) was condensed with *s*-trioxane (5.65 g, 62.8 mmol) via procedure B using $TiCl_4$ (two 6.23 mL, 56.8 mmol portions) and $(i\text{-Pr})_2NEt$ (10.37 mL, 59.5 mmol) to afford the *β*-hydroxyoxazolidinone (12.72 g, 77%) after recrystallization (ca. 9:1 hexane:CH_2Cl_2): TLC analysis (6:1 hexane:EtOAc) $R_f = 0.12$; mp 137−139 °C; $[\alpha]_D = +62°$ (*c* 1.03, $CHCl_3$); ^1H NMR (300 MHz) *δ* 7.35−7.21 (5 H, m), 4.77−4.66 (1 H, m), 4.22 (1 H, dd, *J* = 10.0, 4.3 Hz), 4.18−4.10 (2 H, m), 4.06 (1 H, dd, *J* = 10.3, 10.0 Hz), 3.94 (1 H, dd, *J* = 4.3, 10.0 Hz), 3.39 (1 H, dd, *J* = 3.1, 13.4 Hz), 2.81 (1 H, dd, *J* = 9.3, 13.4 Hz), 2.23 (1 H, s), 1.02 (9 H, s); ^{13}C NMR (75 MHz) *δ* 175.3, 153.8, 135.3, 129.5, 128.7, 127.1, 65.6, 62.3, 55.6, 53.1, 37.5, 33.0, 27.9; combustion analysis ($C_{17}H_{23}NO_4$: C, 66.86; H, 7.59) found C, 66.68; H, 7.79.

(4*S*)-4-Benzyl-3-((2*R*)-2-(1-adamantyl)-3-hydroxy-1-oxopropyl)-2-oxazolidinone. (4*S*)-4-Benzyl-3-(2-(1-adamantyl)-1-oxopropyl)-2-oxazolidinone (1.14 g, 3.21 mmol) was condensed with *s*-trioxane (335.8 mg, 3.73 mmol) via procedure B using $TiCl_4$ (two 0.37 mL, 3.4 mmol portions) and $(i\text{-Pr})_2NEt$ (0.62 mL, 3.5 mmol) to afford the *β*-hydroxyoxazolidinone (1.00 g, 81%) after flash chromatography (3:1 hexane:EtOAc): TLC analysis (3:2 hexane:EtOAc) $R_f = 0.50$; mp 160−162 °C; $[\alpha]_D = +71°$ (*c* 1.16, $CHCl_3$); ^1H NMR (300 MHz) *δ* 7.40−7.20 (5 H, m), 4.80−4.70 (1 H, m), 4.20−4.07 (4 H, m), 3.96 (1 H, dd, *J* = 2.4, 6.1 Hz), 3.28 (1 H, dd, *J* = 3.2, 10.1), 2.80 (1 H, dd, *J* = 4.4, 9.3 Hz), 1.90−1.50 (15 H, m); ^{13}C NMR (75 MHz) *δ* 174.9, 153.8, 135.3, 129.5, 128.8, 127.1, 65.6, 61.2, 55.6, 54.4, 40.0, 37.6, 36.7, 35.5, 28.4; HRMS analysis (CI, $C_{23}H_{29}NO_4 + H^+ = 384.2175$) found *m/z* 384.2168.

(4*S*)-4-(*tert*-Butyl)-3-((2*R*)-3-hydroxy-2-phenyl-1-oxopropyl)-2-oxazolidinone. (4*S*)-4-(*tert*-Butyl)-3-(2-phenyl-1-oxoethyl)-2-oxazolidinone (650.0 mg, 2.49 mmol) was condensed with *s*-trioxane (270 mg, 3.0 mmol) via procedure B using $TiCl_4$ (two 0.29 mL, 2.6 mmol portions) and $(i\text{-Pr})_2NEt$ (0.48 mL, 2.7 mmol) to afford the *β*-hydroxyoxazolidinone (570.0 mg, 78%) after flash chromatography (5:1 hexane:EtOAc): TLC analysis (5:2 hexane:EtOAc) $R_f = 0.44$; mp 123−125 °C; $[\alpha]_D = +113°$ (*c* 1.30, $CHCl_3$); ^1H NMR (300 MHz) *δ* 7.45−7.21 (5 H, m), 5.27 (1

H, dd, J = 9.3, 5.0 Hz), 4.42 (1 H, d, J = 7.6 Hz), 4.24−4.12 (2 H, m), 4.04 (1 H, dd, J = 9.1, 7.6 Hz), 3.83 (1 H, dd, J = 11.0, 5.3 Hz), 2.39 (1 H, br s), 0.97 (9 H, s); ^{13}C NMR (75 MHz) δ 172.9, 153.9, 134.7, 128.7, 128.6, 127.7, 65.5, 64.9, 61.4, 51.8, 35.7, 25.6; combustion analysis ($C_{16}H_{21}NO_4$: C, 65.96; H, 7.27) found C, 65.81; H, 7.41.

(4*S*)-4-Benzyl-3-((2*R*)-3-hydroxy-3-methyl-2-phenyl-1-oxobutyl)-2-oxazolidinone. (4*S*)-4-Benzyl-3-(2-phenyl-1-oxoethyl)-2-oxazolidinone (1.00 g, 3.39 mmol) was condensed with acetone (0.29 mL, 3.90 mmol) via procedure B using $TiCl_4$ (two 0.39 mL, 3.6 mmol portions) and (i-Pr)$_2$NEt (0.65 mL, 3.7 mmol) to afford the β-hydroxyoxazolidinone (1.15 g, 96%) after flash chromatography (0.5% MeOH in CH_2Cl_2): TLC analysis (3:2 hexane:EtOAc) R_f = 0.37; mp 133−135 °C; $[\alpha]_D$ = +118° (*c* 0.99, $CHCl_3$); ^{1}H NMR (300 MHz) δ 7.51−7.48 (2 H, m), 7.38−7.20 (8 H, m), 5.13 (1 H, s), 4.68−4.57 (1 H, m), 4.08 (1 H, dd, J = 9.3, 2.2 Hz), 3.99 (1 H, dd, J = 7.9, 8.8 Hz), 3.91 (1 H, s), 3.39 (1 H, dd, J = 13.4, 3.3 Hz), 2.80 (1 H, dd, J = 13.4, 9.8 Hz), 1.45 (3 H, s), 1.06 (3 H, s); ^{13}C NMR (75 MHz) δ 174.7, 152.7, 135.0, 134.4, 130.4, 129.3, 129.0, 128.2, 127.7, 127.4, 72.6, 65.7, 56.4, 55.6, 38.0, 30.0, 26.9; combustion analysis ($C_{21}H_{23}NO_4$: C, 71.37; H, 6.56) found C, 71.25; H, 6.66.

(4*S*)-4-Benzyl-3-((2*R*)-2-(4′-bromophenyl)-3-hydroxy-1-oxopropyl)-2-oxazolidinone. (4*S*)-4-Benzyl-3-(2-(4′-bromophenyl)-1-oxoethyl)-2-oxazolidinone (1.06 g, 2.68 mmol) was condensed with *s*-trioxane (280 mg, 3.11 mmol) via procedure B using $TiCl_4$ (two 0.31 mL, 2.8 mmol portions) and (i-Pr)$_2$NEt (0.51 mL, 2.95 mmol) to afford the β-hydroxyoxazolidinone (960 mg, 84%) after flash chromatography (4:1 hexane:EtOAc): TLC analysis (4:1 hexane:EtOAc) R_f = 0.44; mp 78−82 °C; $[\alpha]_D$ = +146° (*c* 2.4, $CHCl_3$); ^{1}H NMR (300 MHz) δ 7.50−7.25 (9 H, m), 5.20 (1 H, dd, J = 4.8, 4.0 Hz), 4.70−4.60 (1 H, m), 4.20 (1 H, dd, J = 8.9, 2.0), 4.08−4.00 (2 H, m), 3.84 (1 H, dd, J = 4.8, 6.0 Hz), 3.31 (1 H, dd, J = 3.2, 10.1), 2.85 (1 H, dd, J = 9.3, 4.4 Hz), 2.42 (1 H, br s); ^{13}C NMR (75 MHz) δ 172.5, 152.6, 134.9, 133.8, 131.8, 130.5, 129.4, 128.9, 127.4, 121.9, 65.9, 64.8, 55.5, 51.3, 37.7; HRMS analysis (CI, $C_{19}H_{18}NO_4Br + H^+$ = 404.0497), found m/z 404.0496.

(4*S*)-4-Benzyl-3-((2*R*)-2-(4′-biphenyl)-3-hydroxy-1-oxopropyl)-2-oxazolidinone. (4*S*)-4-Benzyl-3-(2-(4′-biphenyl)-1-oxoethyl)-2-oxazolidinone (1.10 g, 2.97 mmol) was condensed with *s*-trioxane (310 mg, 3.44 mmol) via procedure B using $TiCl_4$ (two 0.34 mL, 3.1 mmol portions) and (i-Pr)$_2$NEt (0.57 mL, 3.3 mmol) to afford the β-hydroxyoxazolidinone (1.03 g, 87%) after flash chromatography (4:1 hexane:EtOAc): TLC analysis (3:2 hexane:EtOAc) R_f = 0.45; mp 152−154 °C; $[\alpha]_D$ = +148° (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz) δ 7.60−7.25 (14 H, m), 5.32 (1 H, dd, J = 4.8, 4.0 Hz), 4.70−4.63 (1 H, m), 4.18−4.08 (1 H, m), 4.12 (1 H, dd, J = 2.4, 6.8 Hz), 4.07 (1 H, dd, J = 8.0, 8.9 Hz), 3.98−3.90 (1 H, m), 3.36 (1 H, dd, J = 3.6, 10.1 Hz), 2.89 (1 H, dd, J = 9.3, 4.4 Hz), 2.42 (1 H, br s); ^{13}C NMR (75 MHz) δ 172.9, 152.7, 140.7, 140.4, 135.0, 133.76, 129.4, 129.2, 128.9, 128.7, 127.4, 127.3, 126.9, 65.9, 65.0.0, 55.5, 51.6, 37.8; HRMS analysis (CI, $C_{25}H_{23}NO_4 + H^+$ = 402.1705) found m/z 402.1704.

(4*S*)-4-Benzyl-3-((2*R*)-3-hydroxy-2-(1′-naphthyl)-1-oxopropyl)-2-oxazolidinone. (4*S*)-4-Benzyl-3-(2-(1′-naphthyl)-1-oxopropyl)-2-oxazolidinone (2.50 g, 7.24 mmol) was condensed with *s*-trioxane (756 mg, 8.39 mmol) via procedure B using $TiCl_4$ (two 0.83 mL, 7.6 mmol portions) and (i-Pr)$_2$NEt (1.39 mL, 7.96 mmol) to afford the β-hydroxyoxazolidinone (2.60 g, 96%) after flash chromatography (5:1 hexane:EtOAc): TLC analysis (3:2 hexane:EtOAc) R_f = 0.36; mp 54−56 °C; $[\alpha]_D$ = +228° (*c* 1.08, $CHCl_3$); ^{1}H NMR (300 MHz) δ 8.28 (1 H, d, J = 8.4 Hz), 7.81 (1 H, d, J = 8.1 Hz), 7.75 (1 H, dd, J = 6.4, 2.6 Hz), 7.60−7.42 (2 H, m), 7.40−7.19 (7 H, m), 6.02 (1 H, dd, J = 9.1, 4.3 Hz), 4.75−4.64 (1 H, m), 4.25 (1 H, dd, J = 11.2, 9.3 Hz), 4.04 (1 H, dd, J = 9.1, 2.4 Hz), 4.00−3.87 (2 H, m), 3.35 (1 H, dd, J = 13.4, 3.1 Hz), 2.88 (1 H, dd, J = 13.4, 9.3 Hz), 2.80−2.40 (1 H, br s); ^{13}C NMR (75 MHz) δ 173.6, 152.6, 135.1, 134.0, 131.5, 131.3, 129.4, 128.9, 128.7, 128.4, 127.3, 126.7, 125.9, 125.0, 124.5, 123.3, 65.9, 64.4, 55.6, 48.3, 37.7; HRMS analysis (CI, $C_{23}H_{21}NO_4 + H^+$ = 376.1548) found m/z 376.1541.

(4*S*)-4-Benzyl-3-((2*R*)-3-hydroxy-2-(2′-naphthyl)-1-oxopropyl)-2-oxazolidinone. (4*S*)-3-(2-(2′-Naphthyl)-1-oxoethyl)-4-benzyl-2-oxazolidinone (2.42 g, 7.02 mmol) was condensed with *s*-trioxane (733 mg, 8.14 mmol) via procedure B using $TiCl_4$ (two 0.81 mL, 7.4 mmol portions) and (i-Pr)$_2$NEt (1.22 mL, 7.7 mmol) to afford the β-hydroxyoxazolidinone (2.42 g, 92%) after flash chromatography (4:1 hexane:EtOAc): TLC analysis (3:2 hexane:EtOAc) R_f = 0.42; mp 142−143 °C; $[\alpha]_D$ = +176° (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz) δ 7.90−7.25 (12 H, m), 5.44 (1 H, dd, J = 5.2, 4.0 Hz), 4.70−4.60 (1 H, m), 4.38 (1 H, dd, J = 10.5, 9.7 Hz), 4.07 (1 H, d, J = 8.9 Hz), 3.99−3.90 (2 H, m), 3.36 (1 H, dd, J = 7.9, 8.8 Hz), 3.38 (1 H, d, J = 13.3 Hz), 2.88 (1 H, dd, J = 9.3, 4.0 Hz), 2.55 (1 H, br s); ^{13}C NMR (75 MHz) δ 172.9, 152.6, 135.1, 133.2, 132.7, 132.3, 129.4, 128.9, 128.4, 127.8, 127.7, 127.5, 127.3, 126.7, 126.2, 126.1, 65.8, 65.0, 55.5, 52.0, 37.7; combustion analysis ($C_{23}H_{21}NO_4$: C, 73.58; H, 5.64) found C, 73.44; H, 5.80.

(4*S*)-Benzyl-3-((2*R*)-3-hydroxy-3-methyl-2-(2′-naphthyl)-1-oxobutyl)-2-oxazolidinone. (4*S*)-4-Benzyl-3-(2′-naphthyl)-1-oxoethyl)-2-oxazolidinone (1.00 g, 2.89 mmol) was condensed with acetone (0.25 mL, 3.3 mmol) via procedure B using $TiCl_4$ (two 0.33 mL, 3.0 mmol portions) and (i-Pr)$_2$NEt (0.55 mL, 3.2 mmol) to afford the β-hydroxyoxazolidinone (1.00 g, 86%) after flash chromatography (4:1 hexane:EtOAc): TLC analysis (3:2 hexane:EtOAc) R_f = 0.52; mp 174−176 °C; $[\alpha]_D$ = +148° (*c* 1.1, $CHCl_3$); ^{1}H NMR (300 MHz) δ 8.00 (1 H, s), 7.90−7.25 (11 H, m), 5.35 (1 H, s), 4.70−4.60 (1 H, m), 4.10−4.00 (2 H, m), 3.94 (1 H, dd, J = 7.9, 8.8 Hz), 3.45 (1 H, dd, J = 3.3, 10.0 Hz), 2.84 (1 H, dd, J = 9.8, 3.6 Hz), 1.55 (3 H, s), 1.18 (3 H, s); ^{13}C NMR (75 MHz) δ 174.6, 152.6, 135.0, 133.0, 132.7, 132.0, 129.4, 129.3, 128.9, 128.3, 128.0, 127.6, 127.4, 127.3, 126.0, 125.9, 72.8, 65.6, 56.5, 55.6, 37.9, 30.0, 27.0; HRMS analysis (CI, $C_{25}H_{25}NO_4$ + H^+ = 404.1862) found m/z 404.1860.

General Procedures for the Hydrolyses of β-Hydroxyoxazolidinones to β-Hydroxy Acids. (A) Procedure A. To a cooled (0 °C) solution of the β-hydroxyoxazolidinone (1 equiv) in THF:water (4:1, ca. 0.05 M) was added 30% aqueous H_2O_2 (ca. 10 equiv) dropwise followed by the portionwise addition of LiOH(H_2O) (ca. 2 equiv). The resulting mixture was warmed to rt, stirred for 3 h, and then recooled (0 °C) and quenched by the addition of excess 1.0 M aqueous Na_2SO_3. The resulting mixture was partitioned between CH_2Cl_2:water. The aqueous phase was acidified to pH 2 with 1 N aqueous HCl and extracted three times with EtOAc. These latter organic extracts were combined, dried (anhydrous Na_2SO_4), and concentrated. The crude β-hydroxy acid product was used without further purification.

(B) Procedure B. To a cooled (0 °C) solution of the β-hydroxyoxazolidinone (1 equiv) in THF:water (3:1, ca. 0.2 M) was added 30% aqueous H_2O_2 (ca. 10 equiv) dropwise followed by the portionwise addition of LiOH(H_2O) (ca. 2 equiv). The resulting mixture was warmed to rt and stirred for 3 h. KOH (ca. 2 equiv) was then added and the resulting mixture was heated at reflux for 1.5 h. Afterward, the reaction mixture was recooled (0 °C) and quenched by the addition of excess 1.0 M aqueous Na_2SO_3. The resulting mixture was partitioned between CH_2Cl_2:water. The aqueous phase was acidified to pH 2 with 1 N aqueous HCl and extracted three times with EtOAc. These latter organic extracts were combined, dried (anhydrous Na_2SO_4), and concentrated. The crude β-hydroxy acid product was used without further purification.

(2*R*)-2-Benzyl-3-hydroxy-3-methylbutanoic Acid. (4*R*)-4-Benzyl-3-((2*R*)-2-benzyl-3-hydroxy-3-methyl-1-oxobutyl)-2-oxazolidinone (530 mg, 1.45 mmol) was hydrolyzed via procedure A using 30% aqueous H_2O_2 (1.18 mL, 11.6 mmol) and LiOH-(H_2O) (120 mg, 2.9 mmol) to afford crude β-hydroxy acid (240 mg, 80%), which was used without further purification: TLC analysis (1:1 hexane:EtOAc) R_f = 0.10; mp 96−98 °C; $[\alpha]_D$ = −29° (*c* 1.05, acetone); ^{1}H NMR (300 MHz, acetone-d_6) δ 7.34−7.14 (5 H, m), 3.06−2.91 (2 H, m), 2.73 (1 H, dd, J = 5.7, 9.3 Hz), 1.35 (6 H, s); ^{13}C NMR (75 MHz, acetone-d_6) δ 179.4, 139.0, 128.7, 128.4, 126.4, 71.5, 58.0, 33.7, 28.7, 26.7; combustion analysis ($C_{12}H_{16}O_3$: C, 69.21; H, 7.74) found C, 69.27; H, 7.59.

(2*S*,3*S*)-2-Benzyl-3-hydroxy-3-phenylpropanoic Acid.[28] (4*S*)-4-*tert*-Butyl--3-((2*R*)-2-benzyl-3-hydroxy-3-phenyl-1-oxopro-

(25) CAS Registry Number (racemate) 51439-23-7; see: Gladiali, S.; Chelucci, G.; Marchetti, M.; Azzena, U. *Chim. Ind. (Milan)* **1985**, *67*, 387−91.

(26) CAS Registry Number (racemate) 529-64-6; see: Cox, R. J. O. H., David *J. Chem. Soc., Perkin Trans. 1* **1991**, 2537−40.

(27) CAS Registry Number (racemate) 6343-61-9; see: Meier, I. K.; Schwartz, J. *J. Org. Chem.* **1990**, *55*, 5619−24.

pyl)oxazolidin-2-one (500 mg, 1.31 mmol) was hydrolyzed via procedure A using 30% aqueous H_2O_2 (0.80 mL, 7.86 mmol) and LiOH(H_2O) (109.9 mg, 2.62 mmol) to afford the crude β-hydroxy acid (300 mg, 89%), which was used without further purification: $[\alpha]_D = -46.5°$ (*c* 1.63, acetone).

(2*R*)-2-(Diphenylmethyl)-3-hydroxypropanoic Acid. (4*S*)-4-Benzyl-3-((2*R*)-2-(diphenylmethyl)-3-hydroxy-1-oxopropyl)-2-oxazolidinone (470 mg, 1.12 mmol) was hydrolyzed via procedure A using 30% aqueous H_2O_2 (0.92 mL, 9.0 mmol) and LiOH(H_2O) (94.4 mg, 2.2 mmol) to afford the β-hydroxy acid (220 mg, 77%), which was used without further purification: TLC analysis (1:4 hexane:EtOAc) $R_f = 0.20$; mp 161−163 °C; $[\alpha]_D = -59°$ (*c* 0.74, acetone); ^{1}H NMR (300 MHz, acetone-d_6) δ 7.40−7.10 (10 H, m), 4.21 (1 H, d, J = 11.7 Hz), 3.70−3.50 (3 H, m); ^{13}C NMR (75 MHz, acetone-d_6) δ 174.8, 143.9, 129.1, 128.8, 128.5, 127.0, 126.8, 63.3, 52.9, 51.5; HRMS analysis (CI, $C_{16}H_{16}O_3 + H^+ = 257.1177$) found *m*/*z* 257.1183.

(2*R*)-2-(*tert*-Butyl)-3-hydroxypropanoic Acid.[25] (4*S*)-4-Benzyl-3-((2*R*)-2-(*tert*-butyl)-3-hydroxy-1-oxopropyl)-2-oxazolidinone (14.10 g, 46.2 mmol) was hydrolyzed via procedure B using 30% aqueous H_2O_2 (28.3 mL, 277 mmol), LiOH(H_2O) (3.87 g, 92.3 mmol), and KOH (5.18 g, 92.3 mmol) to afford the β-hydroxy acid. Recrystallization from EtOAc gave the title compound (5.47 g, 81%): $[\alpha]_D = +4.5°$ (*c* 1.38, acetone).

(2*R*)-2-(1′-Adamantyl)-3-hydroxypropanoic Acid. (4*S*)-4-Benzyl-3-((2*R*)-2-(1′-adamantyl)-3-hydroxy-1-oxopropyl)-2-oxazolidinone (320 mg, 0.84 mmol) was hydrolyzed via procedure B using 30% aqueous H_2O_2 (0.52 mL, 5.1 mmol), LiOH(H_2O) (70.9 mg, 1.7 mmol), and KOH (94.8 mg, 1.7 mmol) to afford crude β-hydroxy acid (150 g,79%), which was used without further purification: TLC analysis (1:4 hexane:EtOAc) $R_f = 0.24$; mp 180−181 °C; $[\alpha]_D = -6°$ (*c* 1.0, acetone); ^{1}H NMR (300 MHz, acetone-d_6) δ 4.30 (1 H, br s), 3.62−3.50 (2 H, m), 2.02 (1 H, dd, J = 4.84, 4.83 Hz), 1.90−1.80 (3 H, m), 1.70−1.50 (10 H, m), 1.45−1.35 (2 H, m); ^{13}C NMR (75 MHz, acetone-d_6) δ 174.9, 59.8, 58.7, 42.0, 40.1, 36.6, 36.5, 33.4, 28.1; HRMS analysis (CI, $C_{13}H_{20}O_3 + H^+ = 225.1491$) found *m*/*z* 225.1488.

(2*R*)-3-Hydroxy-2-phenylpropanoic Acid.[26] (4*S*)-4-*tert*-Butyl-3-((2*R*)-3-hydroxy-2-phenyl-1-oxopropyl)-2-oxazolidinone (184 mg, 0.63 mmol) was hydrolyzed via procedure A using 30% aqueous H_2O_2 (0.51 mL, 5.0 mmol) and LiOH(H_2O) (52.9 mg, 1.3 mmol) to afford the crude β-hydroxy acid (95.7 mg, 91%), which was used without further purification: $[\alpha]_D = +70°$ (*c* 1.11, acetone).

(2*R*)-3-Hydroxy-3-methyl-2-phenylbutanoic Acid.[27] (4*S*)-4-Benzyl-3-((2*R*)-3-hydroxy-3-methyl-2-phenyl-1-oxobutyl)-2-oxazolidinone (462 mg, 1.31 mmol) was hydrolyzed via procedure A using 30% aqueous H_2O_2 (1.07 mL, 10.45 mmol) and LiOH(H_2O) (109 mg, 2.25 mmol) to afford the crude β-hydroxy acid (242 mg, 95%), which was used without further purification: $[\alpha]_D = +93°$ (*c* 1.01, acetone).

(2*R*)-2-(4′-Bromophenyl)-3-hydroxypropanoic Acid.[29] (4*S*)-4-Benzyl-3-((2*R*)−(4′-bromophenyl)-3-hydroxy-1-oxopropyl)-2-oxazolidinone (456 mg, 1.13 mmol) was hydrolyzed via procedure A using 30% aqueous H_2O_2 (0.92 mL, 9.0 mmol) and LiOH(H_2O) (94.6 mg, 2.2 mmol) to afford the crude β-hydroxy acid (266 mg, 96%), which was used without further purification: $[\alpha]_D = +53°$ (*c* 1.42, acetone).

(2*R*)-2-(4′-Biphenyl)-3-hydroxypropanoic Acid.[30] (4*S*)-4-Benzyl-3-((2*R*)-2-(4′-biphenyl)-3-hydroxy-1-oxopropyl)-2-oxazolidinone (53.0 mg, 1.33 mmol) was hydrolyzed via procedure A using 30% aqueous H_2O_2 (1.08 mL, 10.6 mmol) and LiOH(H_2O) (111 mg, 2.7 mmol) to afford the crude β-hydroxy acid (307 mg, 95%), which was used without further purification: $[\alpha]_D = +63°$ (*c* 1.09, acetone).

(2*R*)-3-Hydroxy-2-(1′-naphthyl)propanoic Acid.[31] (4*S*)-4-Benzyl-3-((2*R*)-3-hydroxy-2-(1′-naphthyl)-1-oxopropyl)-2-oxazolidinone (1.00 g, 2.66 mmol) was hydrolyzed via procedure A using 30% aqueous H_2O_2 (2.17 mL, 21.3 mmol) and LiOH(H_2O) (223 mg, 5.3 mmol) to afford the crude β-hydroxy acid (563 mg, 98%), which was used without further purification: $[\alpha]_D = +136°$ (*c* 1.06, acetone).

(2*R*)-3-Hydroxy-2-(2′-naphthyl)propanoic Acid. (4*S*)-4-Benzyl-3-((2*R*)-3-hydroxy-2-(2′-naphthyl)-1-oxopropyl)-2-oxazolidinone (544 mg, 1.45 mmol) was hydrolyzed via procedure A using 30% aqueous H_2O_2 (1.18 mL, 11.6 mmol) and LiOH(H_2O) (121 mg, 2.9 mmol) to afford the crude β-hydroxy acid (279 mg, 90%), which was used without further purification: TLC analysis (1:4 hexane:EtOAc) $R_f = 0.14$; mp 132−138 °C; $[\alpha]_D = 90°$ (*c* 1.02, acetone); ^{1}H NMR (300 MHz, acetone-d_6) δ 7.85−7.80 (4 H, m), 7.52−7.40 (3 H, m) 4.21 (1 H, dd, J = 8.5, 2.0 Hz), 4.00 (1 H, dd, J = 5.6, 2.8 Hz), 3.90 (1 H, dd, J = 6.0, 4.4 Hz); ^{13}C NMR (75 MHz, acetone-d_6) δ 173.6, 134.9, 133.8, 133.5, 128.3, 128.0, 127.8, 127.4, 126.7, 126.4, 126.1, 64.3, 54.6; HRMS analysis (EI, $C_{13}H_{12}O_3 = 216.0786$) found *m*/*z* 216.0788.

(2*R*)-3-Hydroxy-3-methyl-2-(2′-naphthyl)butanoic Acid. (4*S*)-4-Benzyl-3-((2*R*)-3-hydroxy-3-methyl-2-(2′-naphthyl)-1-oxobutyl)-2-oxazolidinone (503 mg, 1.25 mmol) was hydrolyzed via procedure A using 30% aqueous H_2O_2 (0.76 mL, 7.48 mmol) and LiOH(H_2O) (105 mg, 2.49 mmol) to afford the expected crude product (242 mg, 77%) fairly cleanly: TLC analysis (1:4 hexane:EtOAc) $R_f = 0.20$; mp 85−88 °C; $[\alpha]_D = +53°$ (*c* 1.03, acetone); ^{1}H NMR (300 MHz, acetone-d_6) δ 7.95 (1 H, d, J = 1.2 Hz), 7.90−7.80 (3 H, m), 7.65 (1 H, dd, J = 1.6, 6.8 Hz), 7.50−7.40 (2 H, m), 3.95 (1 H, s), 1.39 (3 H, s), 1.18 (3 H, s); ^{13}C NMR (75 MHz, acetone-d_6) δ 174.6, 134.2, 133.4, 132.9, 128.9, 128.1, 128.0, 127.6, 127.5, 126.2, 126.0, 71.8, 60.7, 28.8, 26.8; HRMS analysis (CI, $C_{15}H_{16}O_3 + H^+ = 245.1178$), found *m*/*z* 245.1176.

The Curtius Rearrangements of β-Hydroxy Acids. (A) Preparation of Oxazolidinones. To a mixture of β-hydroxy acid (1.0 equiv) and Et_3N (1.1 equiv) in toluene heated to 80 °C or xylenes (ca. 0.1 M) was added $(PhO)_2P(O)N_3$ (1.05 equiv). The resulting mixture was heated at 80−130 °C (ca. 6−12 h) and then cooled to rt and partitioned between CH_2Cl_2:water. The organic layer was dried (Na_2SO_4) and concentrated. Chromatography on silica afforded the oxazolidin-2-one.

(B) Preparation of 1,2-Amino Alcohols. To a mixture of β-hydroxy acid (1.0 equiv) and Et_3N (1.1 equiv) in toluene heated to 80 °C or xylenes (ca. 0.1 M) was added $(PhO)_2P(O)N_3$ (1.05 equiv). The resulting mixture was heated at 80−130 °C (ca. 6−12 h) and then cooled to rt and concentrated in vacuo. The residue was taken up in dioxane:water (2:1, ca. 0.1 M), $Ba(OH)_2 \cdot 8H_2O$ (ca. 5 molar equiv) added, and the resulting mixture heated at reflux (ca. 12 h). The resulting pasty mixture was cooled to rt and filtered, and the filtrate was concentrated in vacuo. The residue was partitioned between CH_2Cl_2:water, and the organic extract dried (Na_2SO_4) and concentrated. Flash chromatography on silica afforded the amino alcohol.

(4*R*)-4-Benzyl-5,5-dimethyloxazolidin-2-one.[22] (2*R*)-2-Benzyl-3-hydroxy-3-methylbutanoic acid (150 mg, 0.72 mmol) was reacted in toluene at 80 °C for 8 h via procedure A using Et_3N (0.11 mL, 0.84 mmol) and $(PhO)_2P(O)N_3$ (0.16 mL, 0.76 mmol) to afford the known oxazolidin-2-one (130 g, 88%) after flash chromatography (1:1 hexane:EtOAc).

(4*S*,5*R*)-4-Benzyl-5-phenyloxazolidin-2-one. (2*S*,3*S*)-2-Benzyl-3-hydroxy-3-phenylpropanoic acid (126 mg, 0.49 mmol) was reacted in refluxing toluene for 8 h via procedure A using Et_3N (75.3 mL, 0.54 mmol) and $(PhO)_2P(O)N_3$ (0.11 mL, 0.52 mmol) to afford the title compound (102 mg, 82%) after flash chromatography (2:1 hexane:EtOAc): TLC analysis (2:1 hexane:EtOAc) $R_f = 0.10$; mp 93−95 °C; $[a]_D = -197.8°$ (*c* 0.9, $CHCl_3$); ^{1}H NMR (500 MHz) δ 7.50−7.00 (10 H, m), 5.80 (1 H, d, J = 7.2 Hz), 5.25 (1 H, s), 4.23−4.20 (1 H, m), 2.30−2.20 (2 H, m); ^{13}C NMR (125 MHz) δ 158.4, 136.6, 134.7, 128.8, 128.7, 128.6, 128.5, 127.0, 126.0, 80.5, 57.9, 38.0; HRMS analysis (FAB, $C_{16}H_{15}NO_2 + H^+ = 254.1181$) found *m*/*z* 254.1175.

(4*R*)-4-(Diphenylmethyl)oxazolidin-2-one.[32] (2*R*)-2-(Diphenylmethyl)-3-hydroxypropanoic acid (44.0 mg, 0.17 mmol) was reacted in toluene at 80 °C for 8 h via procedure A using Et_3N (26.4 μL, 0.18 mmol) and $(PhO)_2P(O)N_3$ (39.2 μL, 0.18

(28) CAS Registry Number (racemate) 158664-77-8; see: Galatsis, P.; Manwell, J. J.; Blackwell, J. M. *Can. J. Chem.* **1994**, *72*, 1656−9.

(29) CAS Registry Number (racemate) 23007-97-8; see: Caldwell, H. C.; Finkelstein, J. A.; Arbakov, D.; Pelikan, C.; Groves, W. G. *J. Med. Chem.* **1969**, *12*, 477−80.

(30) CAS Registry Number (racemate) 99802-44-5; see: Guarnieri, A.; Burnelli, S.; Varoli, L.; Ghendini, N.; Scapini, G.; Ferri, S.; Cavicchini, E. *Pharmazie* **1985**, *40*, 529−31.

(31) CAS Registry Number (racemate) 1105903-99-9; see: Testa, E.; Fontanella, L.; Cristiani, G.; Mariani, L. *Ann.* **1961**, *639*, 166−80.

(32) R enantiomer (CAS Registry Number 173604-33-6); see: Sibi, M.; Despande, D. K.; Ji, J. *Tetrahedron Lett.* **1995**, *36*, 8965−8.

mmol) to afford the oxazolidin-2-one (33.7 mg, 79%) after flash chromatography (2:1 hexane:EtOAc).

(2*R*)-2-Amino-3,3-diphenyl-1-propanol.[33] (2*R*)-2-(Diphenylmethyl)-3-hydroxypropanoic acid (25.2 mg, 0.0983 mmol) was reacted via procedure B in toluene at 80 °C for 8 h then in dioxane:water for an additional 8 h using Et_3N (15.1 μL, 0.11 mmol), $(PhO)_2P(O)N_3$ (22.0 μL, 0.10 mmol), and $Ba(OH)_2{\cdot}8H_2O$ (155 mg, 0.49 mmol) to afford the amino alcohol (15.8 mg, 71%) after flash chromatography (EtOAc): $[\alpha]_D = -38°$ (*c* 0.48, MeOH).

(4*R*)-4-(*tert*-Butyl)oxazolidin-2-one.[34] (*R*)-2-*tert*-Butyl-3-hydroxypropanoic acid (5.47 g, 37.41 mmol) was reacted via procedure A using Et_3N (5.74 mL, 4.16 g, 41.2 mmol) and $(PhO)_2P(O)N_3$ (8.55 mL, 10.9 g, 39.7 mmol) in refluxing xylenes (240 mL, 12 h) to afford the known oxazolidinone (3.55 g, 74%) after flash chromatography (1:1 hexane:EtOAc).

(4*R*)-4-(1′-Adamantyl)oxazolidin-2-one. (*R*)-2-(1′-Adamantyl)-3-hydroxypropanoic acid (130 mg, 0.58 mmol) was reacted via procedure A using Et_3N (89 μL, 64.5 mg, 0.64 mmol) and $(PhO)_2P(O)N_3$ (0.16 mL, 0.17 g, 0.61 mmol) in hot toluene (5 mL, 80 °C, 12 h) to afford the titled oxazolidinone (100 mg, 79%) after flash chromatography (1:1 hexane:EtOAc): TLC analysis (1:4 hexane:EtOAc) $R_f = 0.43$; mp 172−174 °C; $[\alpha]_D = 8.1°$ (*c* 0.78, $CHCl_3$); ^{1}H NMR (300 MHz) δ 4.25 (2 H, d, $J = 7.2$ Hz), 3.37 (1 H, t, $J = 7.2$ Hz), 2.03−1.90 (3 H, m), 1.70−1.50 (6 H, m), 1.50−1.38 (6 H, m); ^{13}C NMR (75 MHz) δ 160.8, 65.0, 61.6, 42.3, 37.1, 36.6, 34.8, 27.6; HRMS analysis (CI, $C_{13}H_{19}NO_2 + H^+$ = 222.1494) found *m*/*z* 222.1591.

(4*R*)-4-Phenyloxazolidin-2-one.[35] (2*R*)-3-Hydroxy-2-phenylpropanoic acid (120 mg, 0.72 mmol) was reacted in toluene at 80 °C for 8 h via procedure A using Et_3N (0.11 mL, 0.79 mmol) and $(PhO)_2P(O)N_3$ (0.16 mL, 0.76 mmol) to afford the titled oxazolidinone (102 mg, 86%) after flash chromatography (1:1 hexane:EtOAc).

(4*R*)-5,5-Dimethyl-4-phenyloxazolidin-2-one.[22] (2*R*)-3-Hydroxy-3-methyl-2-phenylbutanoic acid (220 mg, 1.13 mmol) was reacted in toluene at 80 °C for 8 h via procedure A using Et_3N (0.17 mL, 1.2 mmol) and $(PhO)_2P(O)N_3$ (0.26 mL, 1.2 mmol) to afford the title compound (173 mg, 81%) after flash chromatography (1:1 hexane:EtOAc).

(4*R*)-4-(4′-Bromophenyl)oxazolidin-2-one.[36] (2*R*)-2-(4′-Bromophenyl)-3-hydroxypropanoic acid (66.6 mg, 0.27 mmol) was reacted in toluene at 80 °C for 8 h via procedure A using Et_3N (41.6 mL, 0.3 mmol) and $(PhO)_2P(O)N_3$ (62.1 mL, 0.29 mmol) to afford the title compound (47.8 mg, 73%) after flash chromatography (1:1 hexane:EtOAc): $[\alpha]_D = -13°$ (*c* 2.0, $CHCl_3$).

(4*R*)-4-(4′-Biphenyl)oxazolidin-2-one.[37] (2*R*)-2-(4′-Biphenyl)-3-hydroxypropanoic acid (55.5 mg, 0.23 mmol) was reacted in toluene at 80 °C for 8 h via procedure A using Et_3N (35.1 μL, 0.25 mmol) and $(PhO)_2P(O)N_3$ (52.3 μL, 0.24 mmol) to afford the title compound (46.0 mg, 84%) after flash chromatography (1:1 hexane:EtOAc): $[\alpha]_D = +124°$ (*c* 1.13, $CHCl_3$).

(2*R*)-2-Amino-3,3-(4′-biphenyl)-1-propanol.[38] (2*R*)-2-(4′-biphenyl)-3-hydroxypropanoic acid (62.0 mg, 0.098 mmol) was reacted via procedure B in toluene at 80 °C for 8 h then in dioxane:water for an additional 8 h using Et_3N (39.2 μL, 0.28 mmol), $(PhO)_2P(O)N_3$ (58.0 μL, 0.27 mmol), and $Ba(OH)_2{\cdot}8H_2O$ (404 mg, 1.3 mmol) to afford the title compound (43.8 mg, 80%) after flash chromatography (EtOAc).

(4*R*)-4-(1′-Naphthyl)oxazolidin-2-one.[39] (2*R*)-3-Hydroxy-2-(1′-naphthyl)propanoic acid (255 mg, 2.28 mmol) was reacted in toluene at 80 °C for 8 h via procedure A using Et_3N (0.18 mL, 1.29 mmol) and $(PhO)_2P(O)N_3$ (0.27 mL, 1.25 mmol) to afford the title compound (208 mg, 83%) after flash chromatography (1:1 hexane:EtOAc).

(2*R*)-2-Amino-2-(1′-naphthyl)ethanol [CAS Registry Number (Racemate) 157142-34-2]. (2*R*)-3-Hydroxy-2-(1′-naphthyl)-propanoic acid (217 mg, 1.00 mmol) was reacted via procedure B in toluene at 80 °C for 8 h then in dioxane:water for an additional 8 h using Et_3N (0.15 mL, 1.10 mmol), $(PhO)_2P(O)N_3$ (0.23 mL, 1.05 mmol), and $Ba(OH)_2{\cdot}8H_2O$ (1.58 g, 5.00 mmol) to afford the title compound (162 mg, 86%) after flash chromatography (EtOAc): $[\alpha]_D = -85°$ (*c* 0.5, MeOH); ^{1}H NMR (360 MHz) δ 8.00−7.40 (7 H, m), 4.90−4.80 (1 H, m), 3.90−380 (1 H, m), 3.70−3.60(1 H, m), 2.90−2.60 (2 H, br s).

(4*R*)-4-(2′-Naphthyl)oxazolidin-2-one. (*R*)-3-Hydroxy-2-(2′-naphthyl)propanoic acid (120 mg, 0.56 mmol) was reacted in toluene at 80 °C for 8 h via procedure A using Et_3N (85.1 μL, 0.61 mmol) and $(PhO)_2P(O)N_3$ (130 μL, 0.59 mmol) to afford the title compound (130 mg, 87%) after flash chromatography (1:1 hexane:EtOAc): TLC analysis (1:4 hexane:EtOAc) $R_f = 0.45$; mp 145−147 °C; $[\alpha]_D = -14°$ (*c* 1.14, $CHCl_3$); ^{1}H NMR (300 MHz) δ 7.91 (1 H, d, $J = 8.5$ Hz), 7.87−7.83 (2 H, m), 7.79 (1 H, s), 7.58−7.53 (2 H, m), 7.47 (1 H, dd, $J = 1.6$, 6.8 Hz), 5.52 (1 H, s), 5.12 (1 H, dd, $J = 8.0$, 7.7 Hz), 4.81 (1 H, dd, $J = 8.9$, 8.4 Hz), 4.28 (1 H, dd, $J = 6.4$, 2.0 Hz); ^{13}C NMR (75 MHz) δ 159.9, 136.7, 133.3, 129.6, 129.3, 127.9, 127.7, 126.7, 126.5, 125.3, 123.2; HRMS analysis (EI, $C_{13}H_{11}NO_2$ = 214.0868) found *m*/*z* 214.0865.

(2*R*)-2-Amino-2-(2′-naphthyl)ethanol [CAS Registry Number (Racemate) 153875-87-7]. (2*R*)-3-Hydroxy-2-(2′-naphthyl)-propanoic acid (61.2 mg, 0.28 mmol) was reacted via procedure B in toluene at 80 °C for 8 h and then in dioxane:water for an additional 8 h using Et_3N (43.4 μL, 0.31 mmol), $(PhO)_2P(O)N_3$ (64.0 μL, 0.3 mmol), and $Ba(OH)_2{\cdot}8H_2O$ (446 mg, 1.4 mmol) to afford the title compound (44.3 mg, 84%) after flash chromatography (EtOAc): $[\alpha]_D = -10°$ (*c* 0.32, MeOH); ^{1}H NMR (360 MHz) δ 7.80−7.40 (7 H, m), 4.20−4.10 (1 H, m), 3.80−3.70 (1 H, m), 6.65−3.55 (1 H, m), 2.70−2.40 (2 H, br s).

((4*R*)-5,5-Dimethyl-4-(2′-naphthyl)oxazolidin-2-one. (*R*)-3-Hydroxy-3-methyl-2-(2′-naphthyl)butanoic acid (150 mg, 0.61 mmol) was reacted in toluene at 80 °C for 8 h via procedure A using Et_3N (94.0 μL, 0.68 mmol) and $(PhO)_2P(O)N_3$ (140 μL, 0.65 mmol) to afford the title compound (110 mg, 74%) after flash chromatography (1:1 hexane:EtOAc): TLC analysis (1:4 hexane:EtOAc) $R_f = 0.50$; mp 177−180 °C; $[\alpha]_D = -36°$ (*c* 1.06, $CHCl_3$); ^{1}H NMR (300 MHz) δ 7.90−7.80 (3 H, m), 7.74 (1 H, s), 7.55−7.50 (2 H, m), 7.34 (1 H, dd, $J = 0.9$, 3.9 Hz), 6.40 (1 H, s), 4.80 (1 H, s), 1.62 (3 H, s), 0.92 (3 H, s); ^{13}C NMR (75 MHz) δ 159.1, 134.3, 133.2, 133.0, 128.6, 127.9, 127.6, 126.5, 126.4, 125.5, 124.1, 84.6, 66.0, 28.2, 23.7; HRMS analysis (EI, $C_{15}H_{15}NO_2$ = 242.1181) found *m*/*z* 242.1181.

Illustrative Procedure for the Preparation of Sulfonamide Derivatives of Chiral Oxazolidin-2-ones. (4*R*)-4-Benzyl-3-((1′*S*,4′*R*)-camphorsulfonyl)-5,5-dimethyloxazolidin-2-one. To a cooled (−78 °C) solution of (4*R*)-4-benzyl-5,5-dimethyloxazolidin-2-one (86.1 mg, 0.42 mmol) in THF (2 mL) was added *n*-BuLi (0.17 mL of a 2.50 M solution in hexanes, 0.42 mmol). The resulting mixture was stirred for 30 min at −78 °C, after which (1*S*)−(+)-10-camphorsulfonyl chloride (95.6 mg, 0.38 mmol) was added as a solution in THF (ca. 1 mL). The resulting mixture was warmed to rt, stirred for an additional 2 h, and then quenched by the addition of saturated aqueous NH_4Cl (1 mL). The resulting mixture was partitioned between CH_2Cl_2 (5 mL):water (5 mL), and the organic phase was separated, dried, and concentrated. Flash chromatography on silica (4:1 hexane:EtOAc) afforded the sulfonamide derivative (150 mg, 93%): TLC analysis (3:2 hexane:EtOAc) $R_f = 0.45$; mp 95−97 °C; $[\alpha]_D = +9.5°$ (*c* 0.86, $CHCl_3$); ^{1}H NMR (500 MHz) δ 7.30−7.20 (5 H, m, phenyl), 4.47 (1 H, dd, $J = 4.4$, 4.8 Hz), 3.65 (1 H, d, $J = 14.5$ Hz), 3.38 (1 H, d, $J = 14.9$), 3.34 (1 H, dd, $J = 4.8$, 9.3 Hz), 3.00 (1 H, dd, $J = 9.3$, 4.8 Hz), 2.40−2.30 (2 H, m), 2.10−1.90 (3 H, m), 1.65−1.60 (1 H, m), 1.40 (3 H, s), 1.38 (3 H, s), 1.17 (3 H, s), 0.85 (3 H, s); ^{13}C NMR (125 MHz) δ 213.6, 152.1, 136.0, 129.0, 128.6, 126.8, 83.9, 65.5, 58.5, 52.0, 47.8, 42.5, 42.2, 36.1, 28.0, 26.7, 25.1, 22.0, 19.7, 19.5; HRMS analysis (EI, $C_{22}H_{29}NO_5S$ = 419.1766) found *m*/*z* 419.1769. The 4*S* diastereomeric oxazolidinone shows a resolved peak at 4.00 for the C−H protons. The diastereomeric ratio as determined by relative integration of the peaks at 3.65 and 4.00 is 95:5.

(33) CAS Registry number (racemate) 92646-33-8; see: Kanemasa, S.; Onimura, K. *Tetrahedron* **1992**, *48*, 8631−44.

(34) CAS Registry Number 142618-93-7; see: Drauz, K.; Jahn, W.; Schwarm, M. *Chem.*- -Eur. J. **1995**, *1*, 538−40.

(35) Evans, D. A.; Sjorgen, E. B. *Tetrahedron Lett.* **1985**, *26*, 3783−6.

(36) CAS Registry Number (racemate) 85288-37-5; see: Meth-Cohn, O.; Patel, D.; Rhouati, S. *Tetrahedron Lett.* **1982**, *23*, 5085−8.

(37) 69776-91-6; see: Huth, A. N., Franz *Liebigs Ann. Chem.* **1979**, 56−62.

(38) CAS Registry Number 110480-85-8, see: Pirkle, W. H. S.; Thomas J. *J. Chromatogr.* **1987**, *396*, 83−92.

(39) Ishizuka, T.; Kimura, K.; Ishibuchi, S.; Kunieda, T. *Chem. Lett.* **1992**, 991−4.

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Supporting Information Available: Details of the experimental procedures and characterization data for the sulfonamide derivatives (24 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.

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