Preparation of *exo*- and *endo*-7-(3-Methoxyphenyl)-5,7-dimethyl-6,8-dioxabicyclo[3.3.1]octane (4b and 5b). The reaction was repeated with 3-bromoanisole (31.6 mmol, 4.00 mL), *n*-BuLi (32.5 mmol, 13 mL of 2.5 M), and ketone 1 (31.6 mmol, 4.42 g). It was unclear by ^{1}H NMR analysis of the mixture whether cyclization was complete, so the crude product was stirred for 18 h in 30 mL of benzene and 0.1 g of *p*-toluenesulfonic acid. The reaction was quenched with Na_2CO_3, extracted into CH_2Cl_2 (3 × 30 mL), dried ($MgSO_4$), concentrated, and filtered through Florisil. Only 2.835 g (11.4 mmol) was recovered (36%). Analysis of the mixture by GCMS indicated two isomers, ratio 56/44, having capillary GC retention times of 9.41 and 10.84 min, respectively. The earlier eluting isomer was tenatively identified as the *endo* isomer **5b** because the 2- and 4-methoxy-substituted ketals eluted in this order. Furthermore, the 2- and 4-methoxy-substituted endo ketals contain a *m/e* 233 peak in the mass spectrum, which is lacking in the mass spectrum of the exo ketal. Neither isomer ever crystallized, and no further separations were performed. NMR assignments are made on the basis of peak integrations for analogous protons or carbons. **4b*/5b#**: ^{1}H NMR (363 MHz) δ 1.2–2.2 (m, 6 H), 1.52# (s, 3 H), 1.53* (s, 3 H), 1.54* (s, 3 H), 1.59# (s, 3 H), 3.81* (s, 3 H), 3.80# (s, 3 H), 4.39* (br s, 1 H), 4.46# (br s, 1 H), 6.76 (td, 1 H, *J* = 8.2, 2.3 Hz), 6.92 (br t, 1 H, *J* = 9.6 Hz), 7.03 (dt, 1 H, *J* = 10.3, 1.8 Hz), 7.23 (td, 1 H, *J* = 8.4, 4.0 Hz); ^{13}C NMR δ 159.13, 150.35, 145.37, 129.28, 128.82 (2 C), 117.90, 116.87, 113.73, 111.51, 111.37, 110.75, 108.15#, 107.91*, 85.32#, 84.56*, 82.26*, 81.88#, 54.98*,#, 34.61*, 34.15#, 31.82#, 25.83#, 24.86*,#, 24.23*, 23.21*, 17.06*, 16.25#. **4b**: EIMS, *m/e* (rel intensity) 248 (25), 205 (7), 187 (30), 161 (32), 135 (20), 98 (80), 43 (100); exact mass calcd for $C_{15}H_{20}O_3$ 248.1412, found 248.1412. **5b**: EIMS, *m/e* (rel intensity) 248 (15), 233 (5), 205 (4), 187 (20), 161 (21), 135 (25), 98 (100), 43 (86); exact mass calcd for $C_{15}H_{20}O_3$ 248.1412, found 248.1407.

Preparation of *exo*- and *endo*-7-(4-Methoxyphenyl)-5,7-dimethyl-6,8-dioxabicyclo[3.2.1]octane (4c and 5c). As previously described, 4-bromoanisole (35.7 mmol, 4.47 mL) was reacted with *n*-BuLi (40.0 mmol, 16.0 mL of 2.5 M) and ketone 1 (35.7 mmol, 5.00 g). The reaction was quenched with 25 mL of 5% HCl, allowed to stir 12 h, and worked up as described in the synthesis of **4a** and **5a**. GCMS analysis showed two components only, ratio 54/46, eluting at 9.83 and 11.11 min. No further purifications were performed. Recovered material totalled 8.689 g (98.0%). After ca. 10 days at room temperature, flaky opaque crystals came out of solution. Capillary GC retention time and the mass spectrum of these crystals corresponded to that of the later eluting ketal. Crystals suitable for X-ray analysis were separated from the supernate and recrystallized from hexane as platelets. By X-ray analysis the platelets were determined to be the exo isomer **4c**. **4c**: mp 101 °C; ^{1}H NMR (250 MHz) δ 1.50 (s, 3 H), 1.58 (s, 3 H), 1.60–2.18 (m, 6 H), 3.78 (s, 3 H), 4.41 (br s, 1 H), 6.85 (d, 2 H, *J* = 8.4 Hz), 7.32 (d, 2 H, *J* = 8.4 Hz); ^{13}C NMR δ 157.99, 140.73, 125.57, (2 C), 113.13 (2 C), 107.82, 84.31, 82.23, 55.01, 34.18, 24.91, 24.26, 23.32, 17.06; EIMS, *m/e* (rel intensity) 248 (25), 205 (20), 187 (30), 161 (55), 135 (68), 98 (100), 43 (43); exact mass calcd for $C_{15}H_{20}O_3$ 248.1412, found 248.1408. **5c**: ^{1}H NMR (250 MHz) δ 1.48 (s, 3 H), 1.53 (s, 3 H), 1.1–1.8 (m, 6 H), 3.80 (s, 3 H), 4.36 (br s, 1 H), 6.85 (d, 2 H, *J* = 8.1 Hz), 7.29 (d, 2 H, *J* = 8.1 Hz); ^{13}C NMR δ 157.99, 135.69, 126.37 (2 C), 113.13 (2 C), 107.94, 85.06, 81.93, 55.01, 34.58, 31.90, 25.81, 24.91, 16.08; IR 1511, 1244, 1038, 845; EIMS, *m/e* (rel intensity) 248 (9), 233 (4), 205 (10), 161 (25), 135 (40), 98 (77), 43 (100); exact mass calcd for $C_{15}H_{20}O_3$ 248.1412, found 248.1406.

Crystal Structure Analyses: General Remarks. For both crystal structure analyses, intensity data were collected at 23 °C on a Nicolet R3mE four-circle diffractometer equipped with a graphite monochromator (Mo K_α radiation, λ = 0.71069 Å) using the ω-scan method with fixed scan speeds out to a $2\theta_{max}$ of 65.0°. Three standard reflections were collected periodically through the data collections, in both cases, to check for crystal alignment and deterioration. The structures were solved by direct methods.[17] All refinements were done by block-cascade least squares, minimizing $\Sigma w(|F_o| - |F_c|)^2$ with 101 parameters refined in each full-matrix block.[17] Hydrogen atoms were located from difference maps at an intermediate stage of refinement (unit weighing), refining until the hydrogen atom parameters converged (isotropic thermal parameters for the hydrogen atoms and anisotropic thermal parameters for the carbon and oxygen atoms), and held constant during the weighted refinement, which used the weighting scheme $w = k[\sigma^2F_o + 0.0015F_o^2]^{-1}$. The numbering scheme used in the two structures is shown in the thermal ellipsoid plots (Figures 1 and 2). Atomic parameters, bond distances, and unit cell data for both structures are available in the supplementary data.[18]

Ketal 4a. The crystal used for data collection had dimensions of 0.70 × 0.70 × 0.41 mm^3 and was mounted on a glass fiber with epoxy cement. The total data collection included 5084 intensity measurements of which 4759 were considered unique and 2039 were observed at the $6\sigma_F$ level (approximately equivalent to $3\sigma_I$). Lorentz and polarization corrections were applied to the data in the usual manner; no corrections were made for absorption or extinction (μ = 0.80 cm^{-1}). R = 0.048 for the observed data, R_w = 0.055, GOOF = 1.18, and R = 0.151 for the unique data set. The maximum residual electron density $\Delta\rho$ = 0.16 e Å^{-3} and the minimal value was −0.26 e Å^{-3}.

Ketal 4c. The crystal chosen for data collection was approximately 0.87 × 0.56 × 0.24 mm^3 and was mounted in the same manner as **4a**. The total data collection included 5679 intensity measurements of which 4848 were considered unique and 1570 were considered observed at the $6\sigma_F$ level. Lorentz and polarization corrections were applied to the data in the normal manner; no corrections were made for absorption or extinction (μ = 0.78 cm^{-1}). R = 0.046 for the observed data, R_W = 0.051, GOOF = 1.098, and R = 0.104 for the unique data set. The maximum residual electron density $\Delta\rho$ = 0.16 e Å^{-3} and the minimal value was −0.25 e Å^{-3}.

Acknowledgment. We thank Dr. L. Joseph Sears, Montana State University, for performing HRMS measurements and Montana State University for a grant covering computer time.

Supplementary Material Available: Full tables of crystallographic data, unit cell parameters, bond distances and angles, atomic coordinates, isotropic and anisotropic thermal parameters, and hydrogen atom coordinates and ^{1}H and ^{13}C NMR spectra of title compounds (22 pages). Ordering information is given on any current masthead page.

(17) Sheldrick, G. M. *SHELXTYL Users Manual*, Revision 5; Nicolet XRD Corporation, Madison, WI, 1987.

(18) See paragraph at end of paper about supplementary material.

A Rapid and Efficient Synthesis of Chiral 2-Hydro 2-Oxazolines

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During the course of our studies on asymmetric synthetic methods we required a fast, general, and efficient route to a variety of chiral 2-H oxazolines, **3**. In searching the literature, we found a number of methods[1-7] of varying

(1) For a recent review of oxazolines, see: Maryanoff, B. *The Chemistry of Heterocyclic Compounds—Oxazoles*; Turchi, I. J., Ed.; Interscience: New York, 1986; Vol. 45, 963.
(2) Meyers, A. I.; Brinkmeyer, R. S.; Collington, E. W. *Organic Syntheses*; Wiley: New York, 1988; Collect. Vol. VI, p 64.
(3) Schollkopf, U.; Gerhart, F.; Hoppe, I.; Harms, R.; Hantke, K.; Scheunemann, K.-H.; Eilers, E.; Blume, E. *Justus Liebigs Ann. Chem.* **1976**, 183.
(4) Ito, Y.; Sawamura, M.; Shirakawa, E.; Hayashizaki, K.; Hayashi, T. *Tetrahedron Lett.* **1988**, *29*, 235.
(5) Bates, G. S.; Varelas, M. A. *Can. J. Chem.* **1980**, *58*, 2562.
(6) Ito, Y.; et al. *Synth. Commun.* **1974**, *4*, 97. Bartel, K.; Fehlhammer, W. P. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 599.
(7) Gassman, P.; Guggenheim, T. L. *J. Am. Chem. Soc.* **1982**, *104*, 5849.

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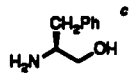
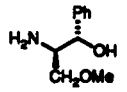
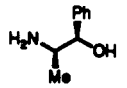
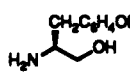
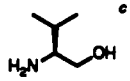
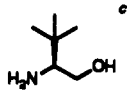
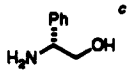
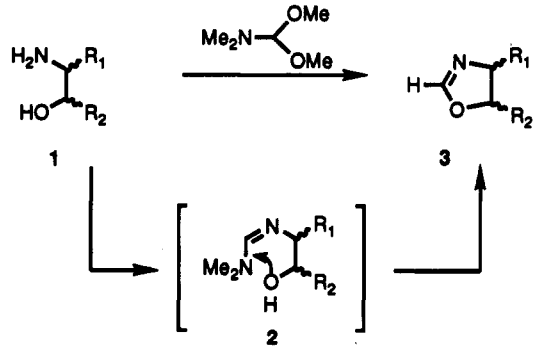
Table I. 2-H Oxazolines 3 from Amino Alcohols

amino	alcohol 1	method[a]	oxazoline 3 R_1	oxazoline 3 R_2	% yield[b]
a,		A	—CH_2Ph	H	90
b,		A	—CH_2OMe	····Ph	90
c,		A	—Me	—Ph	81
d,		A	—$CH_2C_6H_4OBn$	H	77
e,		B	—t-Pr	H	67
f,		B	—t-Bu	H	65
g,		B	····Ph	H	75

[a] See the Experimental Section. [b] Purified, isolated yields. [c] Prepared from the corresponding optically active amino acids according to the reduction described in ref 8 ($LiAlH_4$).

utility but none which allowed access to these compounds in an inexpensive and rapid manner. Furthermore, in order to reach oxazolines of a chiral nature, none of the existing methods utilized readily available chiral amino alcohols. The latter are now very accessible commercially or by simple reduction of many α-amino acids.[8]

In this report we describe a remarkably simple, high-yielding route to 2-H oxazolines 3 from a variety of β-amino alcohols 1. All of the latter were optically active materials which, when treated with dimethylformamide dimethyl acetal (DMF-DMA), most likely proceed through the formamidine 2, ejecting dimethylamine and producing the oxazolines.[9] The seven examples examined in this study



are presented in Table I. The procedure for the synthesis of the oxazolines differed slightly for high or low molecular weight amino alcohols but were equally simple to perform. For high molecular weight amino alcohols (Table I, 1a–d) a benzene solution containing a catalytic amount of *p*-toluenesulfonic acid or Amberlite resin was heated to reflux (method A), and the distillate was allowed to percolate through molecular sieves before reentering the solution (Soxhlet or a side-armed dropping funnel). For low boiling or lower molecular weight amino alcohol (Table I, 1e–f) the reactants were warmed neat and dissolved in a solvent and heated to reflux as above (method B).

Experimental Section

General. A continuous liquid/solid extraction device was constructed from a pressure-equalizing addition funnel and condenser; a small portion of glass wool was placed above the stopcock, and the addition funnel body filled with molecular sieves. The distillate was allowed to reflux through the side arm and condense over the sieves.

Excluding norephedrine, amino alcohols were prepared according to a general literature procedure.[8] Specific rotations were determined with a Rudolph Research Autopol III. NMR spectra were recorded on a Bruker AC-300 with TMS or $CHCl_3$ (^1H = 7.24, ^{13}C = 77.00 ppm) as internal standards.

4(*S*)-Benzyl-2-oxazoline (3a) (Method A). (*S*)-Phenylalinol, 1a (3.00 g, 19.8 mmol), dimethylformamide dimethyl acetal (DMF-DMA) (2.77 mL, 1.05 equiv), and Amberlite IR-120 resin (150 mg) in benzene (50 mL) were refluxed for 16 h in a flask equipped with a liquid/solid extraction apparatus containing 15 g of 4A molecular sieves. The reaction mixture was filtered of resin, washed with 10% $KHCO_3$ (30 mL) and brine (30 mL), and dried (Na_2SO_4). The solution was concentrated and subjected to Kugelrohr distillation (55 °C (5 mTorr)) to yield 2.37 g (90%) of the oxazoline 3a as a clear oil: $[\alpha]^{24}_D$ −77.9° (*c* 1.47, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 2.69 (dd, J = 8.2, 13.8 Hz, 1 H), 3.08 (dd, J = 5.8, 13.8 Hz, 1 H), 3.93 (dd, J = 7.3, 8.5 Hz, 1 H), 4.17 (dd, J = ~9.0, ~9.0 Hz, 1 H), 4.38 (m, 1 H), 6.82 (d, J = 1.9 Hz, 1 H), 7.21–7.35 (m, 5 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 41.59 (II), 66.47 (III), 70.49 (II), 126.51 (III), 128.51 (III), 129.13 (III), 137.67 (IV), 154.75 (III); IR (neat) ν 3062, 3029, 1629, 1091 cm^{-1}; HRMS calcd for $C_{10}H_{11}NO$ 161.0841, found 161.0843. Anal. Calcd for $C_{10}H_{11}NO$: C, 74.51; H, 6.88; N, 8.69. Found: C, 74.46; H, 6.89; N, 8.76.

4(*S*)-(Methoxymethyl)-5(*S*)-phenyl-2-oxazoline (3b) (Method A). The methoxyaminol 1b (2.50 g, 13.8 mmol), DMF-DMA (1.83 mL, 1.0 equiv), and Amberlite IR-120 resin (125 mg) in benzene (50 mL) were refluxed for 28 h in a flask equipped with a liquid/solid extraction apparatus containing 15 g of 4A

(8) Dickman, D. A., Meyers, A. I.; Smith, G. A.; Gawley, R. E. *Organic Syntheses*; Wiley: New York, 1990; Collect. Vol. VII, p 530.

(9) For other uses in the synthesis of heterocycles using DMF-acetal, see: Stanovnik, B.; Tisler, M. *Synthesis* **1974**, 121. Bredereck, H.; Simchen, G.; Kantelherner, K. *Chem. Ber.* **1971**, *104*, 932.

molecular sieves. The reaction mixture was filtered of resin, washed with 10% $KHCO_3$ (30 mL) and brine (30 mL), and dried (Na_2SO_4). The solution was concentrated and subjected to Kugelrohr distillation (75 °C 5 (mTorr)) to yield 2.37 g (90%) of the oxazoline **3b** as a clear oil: $[\alpha]^{24}_D$ +195° (*c* 1.63, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 3.42 (s, 3 H), 3.54 (dd, *J* = 6.1, 9.7 Hz, 1 H), 3.64 (dd, *J* = 4.2, 9.7 Hz, 1 H), 4.13 (dddd, *J* = 2.0, 4.2, 6.1, 7.1 Hz, 1 H), 5.29 (d, *J* = 7.1 Hz, 1 H), 7.02 (d, *J* = 2.0 Hz, 1 H), 7.26–7.40 (m, 5 H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 59.19 (I), 73.40 (III), 73.81 (II), 82.22 (III), 125.43 (III), 128.16 (III), 128.67 (III), 140.21 (IV), 154.85 (III); IR (neat) ν 3064, 1631, 1102 cm^{-1}. Anal. Calcd for $C_{11}H_{13}NO$: C, 69.09; H, 6.85; N, 7.32. Found: C, 68.94; H, 6.78; N, 7.33.

4(*S*)-Methyl-5(*R*)-phenyl-2-oxazoline (3c)[5] (Method A). (1*R*,2*S*)-Norephedrine, **1c** (10.0 g, 66.1 mmol), DMF-DMA (9.67 mL, 1.1 equiv), and TsOH (20 mg) in benzene (50 mL) were refluxed for 60 h in a flask equipped with a liquid/solid extraction apparatus containing 45 g of 4A molecular sieves. The reaction mixture was washed with 10% $KHCO_3$ (60 mL) and brine (60 mL) and dried (Na_2SO_4). The solution was concentrated and passed through a short column of silica gel with 30% ethyl acetate/hexane to remove residual formamidine. The residue was subjected to Kugelrohr distillation (80 °C (50 mTorr)) to yield 8.63 g (81%) of the oxazoline **3c** as a clear oil: $[\alpha]^{24}_D$ −228° (*c* 2.30, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 0.79 (s, 3 H), 4.43 (ddq, *J* = 2.0, 7.0, 10.0 Hz, 1 H), 5.56 (d, *J* = 10.0 Hz, 1 H), 7.02 (d, *J* = 2.0 Hz, 1 H), 7.19–7.39 (m, 5 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 17.69 (I), 64.06 (III), 82.74 (III), 126.08 (III), 127.88 (III), 128.25 (III), 136.39 (IV), 153.80 (III); IR ($CDCl_3$) ν 3064, 3033, 1632, 1098 cm^{-1}. Anal. Calcd for $C_{10}H_{11}NO$: C, 74.51; H, 6.88; N, 8.69. Found: C, 74.22; H, 6.90; N, 8.65.

2-Oxazoline 3d (Method A). (*S*)-Benzyltyrosinol, **1d** (2.50 g, 10.4 mmol), DMF-DMA (1.51 mL, 1.1 equiv), and TsOH (20 mg) in benzene (50 mL) were refluxed for 60 h in a flask equipped with a liquid/solid extraction apparatus containing 20 g of 4A molecular sieves. The reaction mixture was washed with 10% $KHCO_3$ (30 mL) and brine (30 mL) and dried (Na_2SO_4). The residue was subjected to Kugelrohr distillation (140–145 °C (5 mTorr)) to yield 2.04 g (74%) of the oxazoline **3d** as a clear oil that crystallized on standing. An analytical sample was recrystallized from ether: mp 61–62 °C; $[\alpha]^{24}_D$ −44.0° (*c* 1.56, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 2.62 (dd, *J* = 8.0, 13.9 Hz, 1 H), 3.01 (dd, *J* = 5.8, 13.9 Hz, 1 H), 3.91 (dd, *J* = 7.6, 8.5 Hz, 1 H), 4.14 (ddd, *J* = 0.5, 8.5, 9.5 Hz, 1 H), 4.33 (ddddd, *J* = 1.9, 5.8, 7.6, 8.0, 9.5 Hz, 1 H), 5.03 (s, 2 H), 6.80 (d, *J* = 1.9 Hz, 1 H), 6.90–7.42 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 40.76 (II), 66.71 (I), 70.04 (II), 70.53 (II), 114.95 (I), 127.48 (IV), 127.95 (I), 128.95 (I), 130.07 (I), 130.21 (I), 137.09 (IV), 154.74 (I), 157.57 (IV); IR ($CDCl_3$) ν 3035, 1630, 1511, 1114 cm^{-1}. Anal. Calcd for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.54; H, 6.34; N, 5.27.

4(*S*)-Isopropyl-2-oxazoline (3e) (Method B). With a water bath to moderate the exotherm, (*S*)-valinol, **1e** (9.50 g, 92.0 mmol), and DMF-DMA (14.7 mL, 1.2 equiv) were combined, neat. After the mixture was stirred for 4 h, the volatiles were removed by rotory evaporation and the mixture was twice azeotropically concentrated with the addition of a 30-mL portion of hexane (rotary evaporator). TsOH (40 mg) was added to the resultant formamidine, and the mixture was diluted with hexanes (50 mL), fitted with a liquid/solid extraction apparatus containing 30 g of 4A molecular sieves and refluxed for 48 h. The solution was washed with 10% $KHCO_3$ (30 mL) and brine (30 mL) and dried (Na_2SO_4). The hexanes were removed by distillation through a 10-cm helices column at atmospheric pressure. The mixture was then distilled at reduced pressure (69–70 °C (67 Torr)) to yield 6.96 g (67%) of the oxazoline **3e** as a clear liquid: $[\alpha]^{24}_D$ −117° (*c* 1.18, $CHCl_3$), −127° (*c* 3.09, EtOH); ^1H NMR ($CDCl_3$, 300 MHz) δ 0.86, 0.94 (d, *J* = 6.7 Hz, 3 H), 1.70 (d heptet, *J* = 6.7, 6.7 Hz, 1 H), 3.84–3.91 (m, 2 H), 4.17 (m, 1 H), 6.78 (d, *J* = 1.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 18.13 (I), 18.52 (I), 32.32 (III), 68.75 (II), 71.22 (III), 154.05 (III); IR (neat) ν 1632, 1386, 1368, 1094 cm^{-1}. Anal. Calcd for $C_6H_{11}NO$: C, 63.69; H, 9.80; N, 12.38. Found: C, 63.42; H, 9.89; N, 12.73.

4(*S*)-*tert*-Butyl-2-oxazoline (3f) (Method B). With a water bath to moderate the exotherm, (*S*)-*tert*-leucinol, **1f** (10.2 g, 86.8 mmol), and DMF-DMA (13.8 mL, 1.2 equiv) were combined, neat. After the mixture was stirred for 4 h, the volatiles were removed by rotory evaporation and the mixture was twice evaporated with the addition of a 30-mL portion of hexane (rotary evaporator). TsOH (40 mg) was added to the resultant formamidine, and the mixture was diluted with hexanes (50 mL), fitted with a liquid/solid extraction apparatus containing 30 g of 4A molecular sieves, and refluxed 48 h. The solution was washed with 10% $KHCO_3$ (30 mL) and brine (30 mL) and dried (Na_2SO_4). The hexanes were removed by distillation through a 10-cm helices column at atmospheric pressure. The mixture was then distilled at reduced pressure (74–75 °C (56 Torr)) to yield 7.19 g (65%) of the oxazoline **3f** as a clear liquid: $[\alpha]^{24}_D$ −104° (*c* 1.52, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 0.91 (s, 9 H), 3.86 (ddd, *J* = 2.0, 8.4, 10.4 Hz, 1 H), 4.00 (dd, *J* = 8.4, 8.4 Hz, 1 H), 4.14 (dd, *J* = 8.4, 10.4 Hz, 1 H), 6.82 (d, *J* = 2.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 25.74 (I), 33.25 (IV), 67.32 (II), 74.92 (I), 154.10 (I); IR (neat) ν 1635, 1395, 1366, 1102 cm^{-1}. Anal. Calcd for $C_7H_{13}NO$: C, 66.11; H, 10.30; N, 11.01. Found: C, 65.95; H, 10.23; N, 11.02.

4(*R*)-Phenyl-2-oxazoline (3g) (Method B). With a water bath to moderate the exotherm, (*R*)-phenylglycinol, **1g** (1.76 g, 12.9 mmol), and DMF-DMA (2.22 mL, 1.3 equiv) were combined, neat, and 5 mL of $CHCl_3$ was added to dissolve the solid. After the mixture was stirred for 16 h, the volatiles were removed by rotory evaporation and the mixture was twice azeotropically evaporated with the addition of a 20-mL portion of hexane. TsOH (20 mg) was added to the resultant formamidine, and the mixiture was diluted with hexanes (50 mL), fitted with a liquid/solid extraction apparatus containing 10 g of 4A molecular sieves, and refluxed 48 h. The solution was washed with 10% $KHCO_3$ (15 mL) and brine (15 mL) and dried (Na_2SO_4). The hexanes were removed by rotary evaporation, and the mixture was then subjected to Kugelrohr distillation (40–45 °C (50 mTorr)) to yield 1.43 g (75%) of the oxazoline **3g** as a clear liquid: $[\alpha]^{24}_D$ +133° (*c* 1.60, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 4.03 (dd, *J* = ~8.4, ~8.4 Hz, 1 H), 4.55 (ddd, *J* = 0.4, 8.7, 10.4 Hz, 1 H), 5.18 (ddd, *J* = 2.1, 8.3, 10.4 Hz, 1 H), 7.02 (d, *J* = 2.1 Hz, 1 H), 7.22–7.37 (m, 5 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 68.56 (III), 73.22 (II), 126.39 (III), 127.47 (III), 128.58 (III), 141.60 (IV), 155.28 (III); IR ($CDCl_3$) ν 3063, 3030, 1627, 1099 cm^{-1}. Anal. Calcd for C_9H_9NO: C, 73.45; H, 6.16; N, 9.52. Found: C, 73.29; H, 6.15; N, 9.57.

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An Enantioselective Synthesis of SK&F 93505, a Key Intermediate for Preparing Cardiotonic Agents

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A variety of 6-phenyl-5-substituted-4,5-dihydro-3-(2*H*)-pyridazinones (Figure 1) have demonstrated significant inhibitory activity against cardiac PDE III, making them attractive candidates for the treatment of congestive heart failure.[1] SK&F 95654 (Figure 2) has been found to be a potent inhibitor in this class. Approaches to racemic 6-phenyl-5-methyl-4,5-dihydro-3(2*H*)-pyridazinones based on the hydrazine condensation of 3-benzoylcrotonic acid derivatives **2** have been described in the literature.[1-3] The 3-benzoylcrotonic acid derivatives were prepared in about

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