KINETIC RESOLUTION OF 2-OXAZOLIDINONES VIA CATALYTIC, ENANTIOSELECTIVE N-ACYLATION

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SUPPORTING INFORMATION: Experimental procedures (16 pages), ¹H NMR and ¹³C NMR spectra (46 pages).

EXPERIMENTAL PART.

1. GENERAL.

All reagents were obtained commercially and used as received unless otherwise specified. Catalysts **1**^{9a}, **2**^{9b}, and **3**^{9d} were prepared as previously described. Oxazolidinone substrates were prepared following existing general protocols as detailed in the next section.

Solvents and reagents used for KR experiments were purified as follows. Chloroform (OmniSolv® grade, stabilized with nonpolar hydrocarbons, EM Science) and N,N-diisopropylethylamine (Sigma-Aldrich) used for KR experiments were distilled from K₂CO₃ and CaH₂, respectively. *tert*-Amyl alcohol (2-methyl-2-butanol, Sigma-Aldrich) was distilled under atmospheric pressure before use. Isobutyric anhydride was taken from a recently opened bottle or distilled under reduced pressure if significant amounts of the isobutyric acid (>5%) were found by ¹H NMR analysis. Solvents used for chromatography were ACS or HPLC grade, as appropriate. Reactions were monitored by thin layer chromatography (TLC) and by ¹H NMR. EM Science 60F silica gel plates were used for TLC analyses. Flash column chromatography was performed over ICN Ecochrom silica gel (32-63 μm). HPLC analyses were performed on a Shimadzu LC system using Chiralcel AS-H and Chiralpak AD-H analytical chiral stationary phase columns (4.6x250 mm, Chiral Technologies, Inc.). ¹H NMR and ¹³C NMR spectra were recorded on a Mercury 300 MHz Varian spectrometer. The chemical shifts are reported as δ values (ppm) relative to TMS using residual CHCl₃ peak (7.26 ppm) as the reference. High-Resolution mass spectral analyses were performed at Washington University MS Center on a Kratos MS-50TA spectrometer using Electron Impact ionization (EI) and Fast Atom Bombardment (FAB) methods. Melting points were measured on a Mel-Temp II capillary melting point apparatus. Infrared spectra were recorded on a Perkin-Elmer Spectrum Bx FTIR spectrophotometer using potassium bromide plates. Optical rotations were measured at room temperature and 589 nm wavelength using a Perkin-Elmer 241 polarimeter.

2. PREPARATION AND CHARACTERIZATION OF THE SUBSTRATES

2.1. Synthesis of oxazolidinone substrates.

Oxazolidinones **4a**,¹⁶ **4b**,^{6a} **4d**,¹⁷ **4f**,^{6a} **5a**,¹⁸ **6a**,¹⁶ **6b**,¹⁹ **6c**,¹² and **6d**,^{12,13} have been previously described in racemic form. Oxazolidinones **4a**,²⁰ **4b**,^{6a,21} **4c**,^{21,22} **4d**,²³ **4f**,²⁰ **5a**,²⁴ **5c**,²¹ **6a**,²⁰ **6b**,²⁵ and **6d**,^{12,13} have been described as individual enantiomers.

Substrates **4a-f** and **5a-e** were obtained via the general sequence illustrated in Scheme 1S. (±)-N-Boc-□-phenylglycine methyl ester **7a** were prepared using a combination of previously described procedures^{26,27} starting with (±)-phenylglycine (Sigma-Aldrich). (±)-N-Boc-□-1-

naphthylglycine methyl ester **7b**²⁸ and (±)-N-Boc-□-naphthylglycine methyl ester **7c** were prepared as shown in Scheme 2S via a sequence of known protocols starting with 1- and 2-naphthaldehydes, respectively. (±)-N-carbomethoxy-□-2-furylglycine methyl ester **7d** and (±)-N-carbomethoxy-□-2-thienylglycine methyl ester **7e** were prepared by amidoalkylation³¹ of furan and thiophene, respectively (Scheme 3S). Intermediate **8f** was prepared from the commercially available (±)-valinol (Sigma-Aldrich) by treatment with Boc₂O. Oxazolidinone **6a** was prepared via a modification of the synthetic route described by Hamersak et al.¹² as illustrated in Scheme 4S. **6b** and **6c** were prepared analogously from *trans*- and *cis*-stilbene oxides, respectively. Racemic N-acyl-oxazolidinones were prepared by DMAP-catalyzed acylation with the respective anhydrides as described by Ager et al.^{7b}

Scheme 1S

Conditions: (A) NaBH₄, LiCl, THF [Ref.²⁹] (**8b**: 92%, **8c**: 86%); (B) MeMgBr, THF [Ref.²⁴] (**9b**: 93%, **9c**: 71%, **9d**: 84%, **9e**: 85%); (C) *t*-BuONa, THF [Ref.²⁴] (**4b**: 89%, **4c**: 76%, **4d**: 70% for 2 steps, **4e**: 81% for 2 steps, **4f**: 80%, **5b**: 72%, **5c**: 73%, **5d**: 90%, **5e**: 81%).

Scheme 2S

Conditions: (A) NaCN, NH₃ NH₄Cl; PhCHO, PhMe [Ref.³⁰]; (B) 2M HCl (**14b**: 61% from **10b**, **14c**: 66% from **10c**); (C) 6N HCl, 130 °C; (D) SOCl₂, MeOH [Ref.²⁶]; (E) Boc₂O, NEt₃, MeOH [Ref.²⁷] (**7b**: 75% from **14b**, **7c**: 74% from **14c**)

Scheme 3S.

Conditions: CH₂Cl₂, room temp [Ref.³¹] (**7d**: 80% **7e**: 74%)

Scheme 4S.

Conditions: (A) NaN₃, NH₄Cl, MeOH, reflux [Ref.³²] (93%) (B) ClCO₂Ph, Py (C) PPh₃, H₂O, THF, reflux [Ref.¹²] (80% for 2 steps)

2.2. Characterization of synthetic intermediates.

(±)-N-carbomethoxy-2-furylglycine methyl ester 7d: ¹H NMR (300 MHz, CDCl₃): δ 7.34 (d; J = 1.1 Hz; 1H), 6.32 (d; J = 1.1 Hz; 2H), 5.73 (s; 1H), 5.50 (d; J = 8.0 Hz; 1H), 3.75 (s; 3H), 3.68 (s; 3H); ¹³C NMR (75 MHz, CDCl₃): δ 169.3, 156.0, 148.7, 142.8, 110.6, 108.4, 52.9, 52.5, 51.9; **IR** (KBr, cm⁻¹) 3322.7 (br), 1751.8, 1720.5; **MS**: HR-FAB calculated for C₉H₁₁NO₅Li (M+Li⁺) m/z: 220.0797, measured m/z: 220.0796;

(±)-N-carbomethoxy-2-thienylglycine methyl ester 7e: ¹H NMR (300 MHz, CDCl₃): δ 7.29-7.24 (m; 1H), 7.07-7.04 (m; 1H), 6.97-6.93 (m; 1H), 5.78 (s; 1H), 5.64 (d; J = 7.4 Hz; 1H), 3.77 (s; 3H), 3.69 (s; 3H); ¹³C NMR (75 MHz, CDCl₃): δ 170.4, 155.8, 138.9, 127.0, 126.0, 125.8, 53.5, 52.9, 52.5; **IR** (KBr, cm⁻¹) 3322.2 (br), 1747.7, 1722.1; **MS**: HR-FAB calculated for C₉H₁₁NO₄SLi (M+Li⁺) m/z: 236.0569, measured m/z: 236.0573;

2-Methyl-1-(1-naphthyl)-1-(tert-butoxycarbamido)-propan-2-ol 9b: ¹H NMR (300 MHz, CDCl₃): δ 8.24 (d; J = 8.0 Hz; 1H), 7.87-7.78 (m; 2H), 7.56-7.44 (m; 4H), 5.75 (d; J = 8.2 Hz; 1H), 5.57 (d; J = 8.2 Hz; 1H), 1.88 (s; 1H), 1.45 (s; 3H), 1.40 (s; 9H), 1.00 (s; 3H); ¹³C NMR (75 MHz, CDCl₃): δ 155.8, 136.9, 133.6, 132.2, 128.8, 127.9, 126.2, 125.5, 125.1, 124.5, 123.7, 79.4, 73.5, 56.2, 28.3, 27.9, 27.7; **IR** (KBr, cm⁻¹) 3433.5 (br), 1693.5; **MS**: HR-FAB calculated for C₁₉H₂₅NO₃Li (M+Li⁺) m/z: 322.1994, measured m/z: 322.2004;

2-Methyl-1-(2-furyl)-1-(methoxycarbamido)-propan-2-ol 9d: ¹H NMR (300 MHz, CDCl₃): δ 7.34 (d; J = 1.9 Hz; 1H), 6.31 (dd; J₁ = 3.3 Hz, J₂ = 1.9 Hz; 1H), 6.24 (d; J = 3.3 Hz; 1H), 5.67 (s, br; 1H), 4.66 (d; J = 9.1 Hz; 1H), 3.65 (s; 3H), 1.27 (s; 3H), 1.11 (s; 3H); ¹³C NMR (125 MHz, DMSO): δ 156.2, 154.0, 140.9, 109.9, 106.6, 71.0, 57.9, 51.1, 26.6, 26.3; **IR** (KBr, cm⁻¹)

3406.3 (br), 3342 (br), 1709.2; **MS**: HR-FAB calculated for C₁₀H₁₅NO₄Li (M+Li⁺) m/z: 220.1161, measured m/z: 220.1158;

2-Methyl-1-(2-thienyl)-1-(methoxycarbamido)-propan-2-ol 9e: ¹H NMR (300 MHz, CDCl₃): δ 7.21-7.19 (m; 1H), 7.01-6.99 (m; 1H), 6.95-6.92 (m; 1H), 5.65 (d; J = 9.3 Hz; 1H), 4.86 (d; J = 9.3 Hz; 1H), 3.62 (s; 3H), 2.05 (s; 1H), 1.33 (s; 3H), 1.11 (s; 3H); ¹³C NMR (125 MHz, DMSO): δ 156.0, 143.2, 125.5, 124.4, 124.3, 71.0, 59.6, 52.1, 27.1, 26.0; **IR** (KBr, cm⁻¹) 3415.3 (br), 1704.1; **MS**: HR-FAB calculated for C₁₀H₁₅NO₃SLi (M+Li⁺) m/z: 236.0933, measured m/z: 236.0932.

2.3. Determination of absolute configurations.

The absolute configurations of the unreacted oxazolidinones *R*-($\square$)-**4a**,²⁰ *R*-($\square$)-**4b**,^{6a} *R*-($\square$)-**4c**,^{21,22} *S*-(+)-**4d**,²³ *R*-($\square$)-**5a**,²⁴ *R*-($\square$)-**5c**,²¹ *4R,5S*-(+)-**6a**,^{20,25a} *4R,5R*-(+)-**6b**,^{25a} and *4R,5R*-($\square$)-**6c**³³ recovered from KR experiments (described in Section 3) were assigned by comparison of the sign of optical rotation with the literature data. The configuration of *4R,5R*-($\square$)-**6c** was also confirmed by its conversion into the natural enantiomer of cytotoxazone *4R,5R*-($\square$)-**6d**.^{12,13} The configuration of oxazolidinone *R*-($\square$)-**5b** was assigned based on the sign of rotation of the amino alcohol *R*-($\square$)-**22b**³⁴ obtained by its alkaline hydrolysis.³⁵ In all these cases, the absolute configuration predicted by analogy with the KR of benzylic alcohols^{9a,b,d} was confirmed. The previously unreported oxazolidinones **4e**, **5d**, and **5e** were converted into Mosher amides and analyzed as described below.³⁶ The absolute configurations of the N-acylated products of KR were deduced from those of the unreacted substrates.

Mosher amides **23d**, **23e**, **24b**, **24d**, and **24e** were prepared from enantiomerically enriched samples of recovered oxazolidinones by hydrolysis to the corresponding 2-amino alcohols³⁵ followed by acylation with (S)-MTPA-Cl (Scheme 5S) and analyzed by ¹⁹F NMR.³⁶

Scheme 5S.

In the ¹⁹F NMR spectrum of the diastereomeric mixture of **23e**, the peak corresponding to the major diastereomers were observed upfield from those of the minor diastereomer, which is consistent with the expected absolute configuration.

For amides **24b** and **24e**, the analogous NMR patterns were observed, which is consistent with assigning a higher priority to an aromatic substituent (1-naphthyl, thienyl) than to the 2-hydroxyisopropyl group, by analogy with the relative ranking (phenyl>*tert*-butyl) in *tert*-butyl

phenyl carbinol.³⁶ The absolute configuration of **5b** has been verified independently by the sign of rotation of **22b** (*vide supra*). For Mosher amide **24d**, however, the ¹⁹F chemical shift of the major diastereomer was found to be downfield of the minor one. Since KR of all other substrates, including the furan derivative **4d**, has been established to proceed with the same absolute sense of enantioselection, reversal of this general trend in the single case of substrate **5d** is highly unlikely. Therefore, the absolute configuration of **5d** has been assigned by analogy with all other substrates. The reversal of the NMR pattern is deemed to result from the smaller size of 2-furyl compared with 1-naphthyl and 2-thienyl.

2.4. Characterization data and HPLC properties of oxazolidinone substrates and their N-acylated derivatives.

Note: The absolute configurations of oxazolidinones and their N-acyl derivatives shown below correspond to the predominant enantiomers obtained by KR using the (R)-enantiomers of catalysts **1**, **2** and **3**.

HPLC (Chiralcel AS-H, MeCN, 0.8 mL/min): (R)-enantiomer: 7 min; (S)-enantiomer: 12 min. **Note:** the enantiomer shown was recovered from KR with acetic, propionic and isobutyric anhydrides. The opposite enantiomer was recovered in the case of benzoic anhydride.

Previously described.³⁷

HPLC (Chiralcel AD-H, 7.5%IPA/hexane, 0.9 mL/min): (R)-enantiomer: 16 min; (S)-enantiomer: 12 min.

Previously described.^{7b}

HPLC (Chiralcel AD-H, 7.5%IPA/hexane, 0.9 mL/min): (R)-enantiomer: 12 min; (S)-enantiomer: 10 min.

¹H NMR (300 MHz, CDCl₃): δ 7.40-7.26 (m; 5H), 5.43 (dd; J₁ = 8.8 Hz, J₂ = 3.8 Hz; 1H), 4.68 (t; J = 8.8 Hz; 1H), 4.25 (dd; J₁ = 8.8 Hz, J₂ = 3.8 Hz; 1H), 3.79 (septet; J = 6.6 Hz; 1H), 1.14 (d; J = 6.6 Hz; 3H), 1.13 (d; J = 6.6 Hz; 3H); **¹³C NMR** (75 MHz, CDCl₃): δ 177.0, 153.3, 139.2, 129.2, 128.6, 125.7, 69.7, 57.7, 32.7, 19.1, 18.2; **IR** (KBr, cm⁻¹) 1780.9, 1705.1; **MS**: HR-EI calculated for C₁₃H₁₅NO₃ (M⁺) m/z: 233.1052, measured m/z: 233.1054; **mp** 78-79 °C;

HPLC (Chiralcel AD-H, 2%IPA/hexane, 1.0 mL/min): (R)-enantiomer: 18 min; (S)-enantiomer: 14 min.

Previously described.³⁸

HPLC (Chiralcel AD-H, 7.5%IPA/hexane, 1.0 mL/min): (R)-enantiomer: 25 min; (S)-enantiomer: 9 min.

HPLC (Chiralcel AS-H, MeCN, 0.65 mL/min): (R)-enantiomer: 9 min; (S)-enantiomer: 11 min.

¹H NMR (300 MHz, CDCl₃): δ 7.94-7.80 (m; 3H), 7.61-7.43 (m; 3H), 7.28 (d; J = 7.1 Hz; 1H), 6.26 (dd; J₁ = 8.7 Hz, J₂ = 3.6 Hz; 1H), 4.87 (t; J = 8.7 Hz; 1H), 4.23 (dd; J₁ = 8.7 Hz, J₂ = 3.6 Hz; 1H), 3.93 (septet; J = 6.9 Hz; 1H), 1.28 (d; J = 6.9 Hz; 3H), 1.20 (d; J = 6.9 Hz; 1H); **¹³C NMR** (75 MHz, CDCl₃): δ 177.2, 153.9, 134.5, 130.0, 129.7, 129.3, 127.2, 126.4, 125.7, 122.0, 121.3, 69.7, 54.6, 33.1, 19.7, 18.7; **IR** (KBr, cm⁻¹) 1780.9, 1705.8; **MS**: HR-EI calculated for C₁₇H₁₇NO₃ (M⁺) m/z: 283.1208, measured m/z: 283.1205; **mp** 101-102 °C;

HPLC (Chiralcel AD-H, 10% IPA/hexane, 1.0 mL/min): (R)-enantiomer: 20 min; (S)-enantiomer: 17 min.

HPLC: acylated with (*i*-PrCO)₂O^{7b} and analyzed as described below (cf. **4c-C**).

¹H NMR (300 MHz, CDCl₃): δ 7.90-7.76 (m; 4H), 7.54-7.47 (m; 2H), 7.38 (dd; J₁ = 8.5 Hz, J₂ = 1.9 Hz; 1H), 5.60 (dd; J₁ = 9.0 Hz, J₂ = 4.1 Hz; 1H), 4.75 (t; J = 9.0 Hz; 1H), 4.33 (dd; J₁ = 9.0 Hz, J₂ = 4.1 Hz; 1H), 3.83 (septet; J = 6.8 Hz; 1H), 1.15 (d; J = 6.8 Hz; 3H), 1.14 (d; J = 6.8 Hz; 3H); **¹³C NMR** (75 MHz, CDCl₃): δ 177.0, 153.4, 136.4, 133.21, 133.16, 129.4, 128.0, 127.7, 126.65, 126.52, 125.4, 122.8, 69.6, 57.9, 32.7, 19.1, 18.2; **IR** (KBr, cm⁻¹) 1779.6, 1701.5; **MS**: HR-EI calculated for C₁₇H₁₇NO₃ (M⁺) m/z: 283.1208, measured m/z: 283.1210; **mp** 104-105 °C;

HPLC (Chiralcel AD-H, 7% IPA/hexane, 1.0 mL/min): (R)-enantiomer: 16 min; (S)-enantiomer: 11 min.

HPLC (Chiralcel AS-H, MeCN, 0.65 mL/min): (R)-enantiomer: 10 min; (S)-enantiomer: 7 min.

¹H NMR (300 MHz, CDCl₃): δ 7.38 (t; *J* = 1.5 Hz; 1H), 6.35 (d; *J* = 1.5 Hz; 2H), 5.56 (dd; *J*₁ = 8.7 Hz, *J*₂ = 3.6 Hz; 1H), 4.57 (t; *J* = 8.7 Hz; 1H), 4.47 (dd; *J*₁ = 8.7 Hz, *J*₂ = 3.6 Hz; 1H), 3.75 (septet; *J* = 6.9 Hz; 1H), 1.16 (d; *J* = 6.9 Hz; 3H), 1.14 (d; *J* = 6.9 Hz; 3H); **¹³C NMR** (75 MHz, CDCl₃): δ 177.0, 150.0, 142.82, 142.79, 110.6, 108.7, 66.5, 51.5, 32.7; **IR** (KBr, cm⁻¹) 1780.7, 1706.8; **MS**: HR-EI calculated for C₁₁H₁₃NO₄ (M⁺) *m/z*: 223.0845, measured *m/z*: 223.0853; colorless oil; **HPLC** (Chiralcel AD-H, 2% IPA/hexane, 1.0 mL/min): (R)-enantiomer: 14 min; (S)-enantiomer: 17 min.

¹H NMR (300 MHz, CDCl₃): δ 7.28 (d; *J* = 5.0 Hz; 1H), 7.03 (d; *J* = 3.6 Hz; 1H), 6.96 (dd; *J*₁ = 5.0 Hz, *J*₂ = 3.6 Hz; 1H), 6.85 (s; 1H), 5.21 (apparent triplet; *J* = 7.5 Hz; 1H), 4.67 (apparent triplet; *J* = 8.7 Hz; 1H), 4.23 (dd; *J*₁ = 8.7 Hz, *J*₂ = 6.7 Hz; 1H); **¹³C NMR** (75 MHz, CDCl₃): δ 159.4, 143.0, 127.1, 125.8, 125.3, 72.4, 52.2; **IR** (KBr, cm⁻¹) 3246 (br), 1748.6; **MS**: HR-EI calculated for C₇H₇NO₂S (M⁺) *m/z*: 169.0198, measured *m/z*: 169.0204; **mp** 101-101.5 °C; **HPLC** (Chiralcel AS-H, MeCN, 0.8 mL/min): (R)-enantiomer: 9 min; (S)-enantiomer: 7 min.

¹H NMR (300 MHz, CDCl₃): δ 7.26 (dd; *J*₁ = 4.2 Hz, *J*₂ = 1.4 Hz; 1H), 7.07 (dd; *J*₁ = 4.2 Hz, *J*₂ = 1.4 Hz; 1H), 6.96 (t; *J* = 4.2 Hz; 1H), 5.76 (dd; *J*₁ = 8.6 Hz, *J*₂ = 3.3 Hz; 1H), 4.65 (t; *J* = 8.6 Hz; 1H), 4.38 (dd; *J*₁ = 8.6 Hz, *J*₂ = 3.3 Hz; 1H), 3.73 (septet; *J* = 6.8 Hz; 1H), 1.14 (d; *J* = 6.8 Hz; 3H), 1.136 (d; *J* = 6.8 Hz; 3H); **¹³C NMR** (75 MHz, CDCl₃): δ 176.8, 152.5, 141.6, 127.0, 125.7, 125.5, 69.6, 53.4, 32.7, 19.1, 18.2; **IR** (KBr, cm⁻¹) 1780.8, 1705.9; **MS**: HR-EI calculated for C₁₁H₁₃NO₃S (M⁺) *m/z*: 239.0616, measured *m/z*: 239.0621; colorless oil; **HPLC** (Chiralcel AD-H, 4% IPA/hexane, 1.0 mL/min): (R)-enantiomer: 12 min; (S)-enantiomer: 15 min.

HPLC (Chiralcel AS-H, MeCN, 0.8 mL/min): (R)-enantiomer: 9 min; (S)-enantiomer: 11 min.

¹H NMR (300 MHz, CDCl₃): δ 7.36-7.32 (m; 3H), 7.15-7.11 (m; 2H), 5.07 (s; 1H), 3.84 (septet; J = 6.9 Hz; 1H), 1.59 (s; 3H), 1.15 (d; J = 6.9 Hz; 6H), 0.98 (s; 3H); **¹³C NMR** (75 MHz, CDCl₃): δ 177.2, 152.8, 136.4, 128.8, 128.5, 126.2, 82.1, 67.0, 32.8, 29.0, 23.7, 19.0, 18.4; **IR** (KBr, cm⁻¹) 1768.4, 1697.2; **MS**: HR-EI calculated for C₁₅H₁₉NO₃ (M⁺) m/z: 261.1365, measured m/z: 261.1371; **mp** 115-117 °C;

HPLC (Chiralcel AD-H, 2% IPA/hexane, 1.0 mL/min): (R)-enantiomer: 14 min; (S)-enantiomer: 8 min.

¹H NMR (300 MHz, CDCl₃): δ 7.92-7.83 (m; 4H), 7.64 (d; J = 6.6 Hz; 1H), 7.57-7.50 (m; 3H), 6.40 (s; 1H), 5.53 (s; 1H), 1.79 (s; 3H), 0.87 (s; 3H); **¹³C NMR** (75 MHz, CDCl₃): δ 160.9, 134.1, 133.5, 131.4, 129.5, 129.2, 126.9, 126.1, 125.7, 124.3, 122.4, 84.9, 61.4, 29.0, 23.8; **IR** (KBr, cm⁻¹) 3220 (br), 1743.9; **MS**: HR-EI calculated for C₁₅H₁₅NO₂ (M⁺) m/z: 241.1103, measured m/z: 241.1103; **mp** 209.5-210.5 °C;

HPLC (Chiralcel AD-H, 8% IPA/hexane, 1.0 mL/min): (R)-enantiomer: 12 min; (S)-enantiomer: 18 min.

¹H NMR (300 MHz, CDCl₃): δ 7.91-7.88 (m; 2H), 7.83 (d; J = 8.2 Hz; 1H), 7.60-7.43 (m; 3H), 7.23 (t; J = 6.6 Hz; 1H), 6.06 (s; 1H), 3.92 (septet; J = 6.7 Hz; 1H), 1.77 (s; 3H), 1.22 (d; J = 6.7 Hz; 3H), 1.19 (d; J = 6.7 Hz; 3H), 0.91 (s; 3H); **¹³C NMR** (75 MHz, CDCl₃): δ 177.4, 153.2, 134.2, 132.7, 131.5, 129.6, 129.3, 127.1, 126.2, 125.5, 122.2, 122.1, 82.6, 62.4, 33.1, 29.2, 23.2, 19.3, 18.8; **IR** (KBr, cm⁻¹) 1773.7, 1705.6; **MS**: HR-EI calculated for C₁₉H₂₁NO₃ (M⁺) m/z: 311.1521, measured m/z: 311.1514; **mp** 138-139.5 °C;

HPLC (Chiralcel AD-H, 2% IPA/hexane, 1.0 mL/min): (R)-enantiomer: 13 min; (S)-enantiomer: 10 min.

HPLC (Chiralcel AS-H, MeCN, 0.8 mL/min): (R)-enantiomer: 10 min; (S)-enantiomer: 12 min.

¹H NMR (300 MHz, CDCl₃): δ 7.87-7.79 (m; 3H), 7.63 (s; 1H), 7.54-7.46 (m; 2H), 7.26-7.22 (m; 1H), 5.24 (s; 1H), 3.88 (septet; J = 6.6 Hz; 1H), 1.65 (s; 3H), 1.17 (d; J = 6.6 Hz; 6H), 1.02 (s; 3H); **¹³C NMR** (75 MHz, CDCl₃): δ 177.3, 152.9, 133.9, 133.2, 133.1, 128.8, 127.9, 127.7, 126.6, 126.4, 82.2, 67.2, 32.8, 29.1, 23.7, 19.0, 18.4; **IR** (KBr, cm⁻¹) 1772.3, 1705.0; **MS**: HR-EI calculated for C₁₉H₂₁NO₃ (M⁺) m/z: 311.1521, measured m/z: 311.1521; **mp** 134-135.5 °C;

HPLC (Chiralcel AD-H, 8% IPA/hexane, 1.0 mL/min): (R)-enantiomer:

13 min; (S)-enantiomer: 7 min.

¹H NMR (300 MHz, CDCl₃): δ 7.41 (m; 1H), 6.38-6.34 (m; 2H), 5.40 (s; 1H), 4.61 (s; 1H), 1.60 (s; 3H), 1.11 (s; 3H); **¹³C NMR** (75 MHz, CDCl₃): δ 159.0, 150.8, 142.7, 110.4, 107.9, 84.2, 60.0, 27.7, 22.8; **IR** (KBr, cm⁻¹) 3270.3 (br), 1748.2; **MS**: HR-EI calculated for C₉H₁₁NO₃ (M⁺) m/z: 181.0739, measured m/z: 181.0739; **mp** 97-97.5 °C; **HPLC** (Chiralcel AS-H, MeCN, 0.8 mL/min): (R)-enantiomer: 7 min; (S)-enantiomer: 11 min.

¹H NMR (300 MHz, CDCl₃): δ 7.37 (d; J = 1.8 Hz; 1H), 6.35 (dd; J₁ = 3.3 Hz, J₂ = 1.8 Hz; 1H), 6.26 (d; J = 3.3 Hz; 1H), 5.14 (s; 1H), 3.81 (septet; J = 6.9 Hz; 1H), 1.55 (s; 3H), 1.16 (d; J = 6.9 Hz; 3H), 1.14 (s; 3H); **¹³C NMR** (75 MHz, CDCl₃): δ 177.2, 152.2, 149.2, 142.6, 110.5, 108.4, 81.9, 61.0, 32.8, 28.0, 22.5, 19.0, 18.4; **IR** (KBr, cm⁻¹) 1781.6, 1700.3; **MS**: HR-EI calculated for C₁₃H₁₇NO₄ (M⁺) m/z: 251.1158, measured m/z: 251.1161; **mp** 93-94 °C; **HPLC** (Chiralcel AD-H, 4% IPA/hexane, 1.0 mL/min): (R)-enantiomer: 9 min; (S)-enantiomer: 6 min.

¹H NMR (300 MHz, CDCl₃): δ 7.25-7.23 (m; 1H), 6.99-6.97 (m; 2H), 6.91 (s; 1H), 4.86 (s; 1H), 1.54 (s; 3H), 1.04 (s; 3H); **¹³C NMR** (75 MHz, CDCl₃): δ 158.7, 140.2, 127.0, 125.2, 125.1, 84.4, 62.0, 27.4, 22.9; **IR** (KBr, cm⁻¹) 3242.3 (br), 1744.7; **MS**: HR-EI calculated for C₉H₁₁NO₂S (M⁺) m/z: 197.0511, measured m/z: 197.0523; **mp** 120.5-121.5 °C; **HPLC** (Chiralcel AD-H, 5% IPA/hexane, 0.9 mL/min): (R)-enantiomer: 13 min; (S)-enantiomer: 6 min.

¹H NMR (300 MHz, CDCl₃): δ 7.26-7.23 (m; 1H), 7.00-6.97 (m; 1H), 6.94-6.92 (m; 1H), 5.37 (s; 1H), 3.79 (septet; J = 6.6 Hz; 1H), 1.56 (s; 3H), 1.19-1.13 (m; 9H); **¹³C NMR** (75 MHz, CDCl₃): δ 177.1, 152.1, 139.5, 127.1, 125.7, 125.0, 82.2, 62.9, 32.9, 28.3, 22.9, 19.0, 18.3; **IR** (KBr, cm⁻¹) 1772.5, 1700.2; **MS**: HR-EI calculated for C₁₃H₁₇NO₃S (M⁺) m/z: 267.0929, measured m/z: 267.0928; **mp** 93.5-94.5 °C; **HPLC** (Chiralcel AD-H, 4% IPA/hexane, 0.9 mL/min): (R)-enantiomer: 7 min; (S)-enantiomer: 16 min.

HPLC (Chiralcel AS-H, MeCN, 0.8 mL/min): (4*R*,5*S*)-enantiomer: 7 min; (4*S*,5*R*)-enantiomer: 13 min.

4S, 5R-6a-C

¹H NMR (300 MHz, CDCl₃): δ 7.12-7.07 (m; 6H), 6.99-6.96 (m; 2H), 6.89-6.85 (m; 2H), 5.90 (d; J = 7.7 Hz; 1H), 5.69 (d; J = 7.7 Hz; 1H), 3.89 (septet; J = 6.9 Hz; 1H), 1.223 (d; J = 6.9 Hz; 3H), 1.216 (d; J = 6.9 Hz; 3H); **¹³C NMR** (75 MHz, CDCl₃): δ 176.7, 153.3, 134.6, 132.9, 128.3, 128.2, 128.0, 127.9, 126.4, 126.0, 80.0, 62.8, 32.8, 18.9, 18.6; **IR** (KBr, cm⁻¹) 1782.0, 1702.0; **MS**: HR-EI calculated for C₁₉H₁₉NO₃ (M⁺) m/z: 309.1365, measured m/z: 309.1360; **mp** 125-125.5 °C; **HPLC** (Chiralcel AD-H, 4% IPA/hexane, 1.0 mL/min): (R)-enantiomer: 21 min; (S)-enantiomer: 17 min.

4R, 5R-(+)-6b

HPLC (Chiralcel AS-H, MeCN, 0.8 mL/min): (4R,5R)-enantiomer: 8 min; (4S,5S)-enantiomer: 12 min.

4S, 5S-6b-C

¹H NMR (300 MHz, CDCl₃): δ 7.47-7.29 (m; 10H), 5.34 (d; J = 4.7 Hz; 1H), 5.27 (d; J = 4.7 Hz; 1H), 3.86 (septet; J = 6.6 Hz; 1H), 1.18 (d; J = 6.6 Hz; 3H), 1.15 (d; J = 6.6 Hz; 3H); **¹³C NMR** (75 MHz, CDCl₃): δ 177.1, 153.0, 138.7, 137.4, 129.3, 129.1, 128.7, 125.8, 125.2, 99.9, 82.5, 65.7, 33.0, 19.2, 18.1; **IR** (KBr, cm⁻¹) 1781.5, 1708.2; **MS**: HR-EI calculated for C₁₉H₁₉NO₃ (M⁺) m/z: 309.1365, measured m/z: 309.1366; **mp** 99-100 °C; **HPLC**: hydrolyzed to the oxazolidinone³⁹ and analyzed as above (cf. 6b)

4R, 5R-(-)-6c

HPLC (Chiralcel AS-H, MeCN, 0.8 mL/min): (4R,5R)-enantiomer: 5 min; (4S,5S)-enantiomer: 7 min.

4S, 5S-6c-C

¹H NMR (300 MHz, CDCl₃): δ 7.13 (d; J = 8.6 Hz; 2H), 6.84 (d; J = 8.6 Hz; 2H), 5.61 (d; J = 8.9 Hz; 1H), 5.23 (d; J = 8.9 Hz; 1H), 3.77 (s; 3H), 3.74 (septet; J = 6.6 Hz; 1H), 3.35 (s; 3H), 1.13 (d; J = 6.6 Hz; 6H); **¹³C NMR** (75 MHz, CDCl₃): δ 176.4, 165.7, 160.0, 151.9, 127.8, 126.4, 114.0, 75.4, 59.4, 55.2, 52.3, 32.9, 19.0, 18.2; **IR** (KBr, cm⁻¹) 3248.7, 1766.9, 1748.5, 1723.8; **MS**: HR-EI calculated for C₁₆H₁₉NO₆ (M⁺) m/z: 321.1212, measured m/z: 321.1217; **mp** 122-123 °C; **HPLC** (Chiralcel AD-H, 8% IPA/hexane, 0.95 mL/min): (4R,5R)-enantiomer: 24 min; (4S,5S)-enantiomer: 33 min.

3. KINETIC RESOLUTION EXPERIMENTS.

3.1. General remarks: Detection of several oxazolidinones during flash chromatography was problematic due to their weak UV absorption and difficulty visualizing them on TLC with common staining reagents (anisaldehyde, permanganate or phosphomolybdic acid stains). Therefore, chromatographic fractions were typically concentrated by directed airflow prior to TLC analysis in order to facilitate the detection. Some oxazolidinone substrates and their N-acylated derivatives crystallized after elution from the column or upon the concentration of the chromatographic fractions. In those cases, care was taken to dissolve the compounds completely in order to avoid possible errors in enantiomeric excess (ee) determination during the subsequent HPLC analysis. HPLC analyses were performed on a Shimadzu LC system using UV detection at 254 nm in all cases, except for 2-furyl derivatives **4d**, **4d-C**, **5d** and **5d-C** detected at 204 nm. Most oxazolidinones were separated on Chiralcel AS-H analytical column using acetonitrile as eluent. Most N-acyl oxazolidinones were separated on Chiralpak AD-H column using isocratic isopropanol-hexane eluent mixtures. Selectivity factors were calculated according to Kagan's equation:¹ $s = \ln((1-C_{HPLC})(1-ee_{SM}))/\ln((1-C_{HPLC})(1+ee_{SM}))$, wherein C_{HPLC} was calculated as $C_{HPLC} = ee_{SM}/(ee_P + ee_{SM})$, wherein ee_P is the enantiomeric excess of the N-acylated product and ee_{SM} is the enantiomeric excess of the unreacted oxazolidinone. **Note:** The higher the absolute value of the selectivity factor, the greater is the relative error associated with it. Therefore, high selectivity factors given below should only be viewed as approximate.

3.2. The proof-of-principle experiment

The stock solution of the catalyst was prepared by dissolving of (*R*)-CF₃-PIP **1** (13.2 mg, 0.050 mmol) and *i*-Pr₂NEt (242 mg, 1.87 mmol) in CHCl₃ in a 5.00 mL volumetric test tube and bringing the volume to the mark. Two one-dram vials were each charged with (±)-4-phenyl-oxazolidin-2-one **4a** (41 mg, 0.25 mmol) and 0.50 mL of the stock solution of the catalyst. The substrate was dissolved by gentle heating with a heatgun. The vial was cooled in an ice bath for 15 min. Then propionic anhydride (24 μ L, 0.187 mmol) was added, the vial was swirled and left in the ice bath for 24 h. The reaction mixture was quenched by adding 0.5 mL of methanol and leaving it at room temperature for 1 h. The mixture was diluted with CH₂Cl₂, washed with 1 M aqueous HCl, then saturated aqueous NaHCO₃ and brine and dried over Na₂SO₄. The resulting solution was concentrated and subjected to flash chromatography (20% $\rightarrow$ 30% EtOAc/hexanes). The unreacted substrate and the N-acylated derivative thus separated were analyzed by chiral stationary phase HPLC as described above. The data of the duplicate experiment are given in Table 1S.

Table 1S.

Expt	ee _{PR} %	ee _{SM} %	C _{HPLC} %	s	C _{AVG} %	s _{AVG}
1	64.9	46.5	42	7.3	39	7.8
2	69.6	39.8	36	8.2		

3.3. Variation of the anhydride

The stock solution of the catalyst was prepared by dissolving (*R*)-Cl-PIQ **2** (11.2 mg, 0.040 mmol) of and *i*-Pr₂NEt (0.13 mL, 0.75 mmol) of in CDCl₃ in a 5.00 mL volumetric flask and

bringing the volume to the mark. Ten one-dram vials, each charged with ($\pm$)-4-phenyl-oxazolidin-2-one **4a** (16 mg, 0.10 mmol), 0.50 mL of the stock catalyst solution, were divided into five pairs and cooled in an ice bath. 0.075 mmol of acetic, propionic, isobutyric, benzoic anhydrides and *tert*-butyl dicarbonate were added, respectively, to each of the 1st, the 2nd, the 3rd, the 4th, and the 5th pairs of vials. The reactions were monitored by periodically withdrawing aliquots and checking them by ¹H NMR. Since no reaction could be detected in the reaction mixtures with Boc₂O, they were allowed to warm to room temperature. The reactions were stopped by quenching with methanol after 24 h or after reaching 45-50% conversion. The workup and HPLC analysis followed the standard procedure. The results are summarized in Table 2S.

Table 2S

Entry	anhydride	t(h)	#	ee _{PR} %	ee _{SM} %	C _{HPLC} %	s	C _{AVG} %	s _{AVG}
1	Ac ₂ O	2.5	1	16.8	9.2	35	1.5	34	1.5
			2	16.7	8.0	32	1.5		
2	(EtCO) ₂ O	3.5	1	69.2	60.9	47	10	45	10
			2	70.6	55.1	44	10		
3	(i-PrCO) ₂ O	24	1	81.8	59.6	42	18	42	17
			2	79.7	59.2	43	16		
4	Bz ₂ O	24	1	67.0	12.9	16	5.7	16	5.5
			2	64.7	12.3	16	5.3		
5	Boc ₂ O ^a	24	1	nd	nd	nd	nd	<3	N/A
			2	nd	nd	nd	nd		

^a) room temperature, % conversion estimated from ¹H NMR spectrum

3.4. Variation of the solvent

Stock catalyst solutions in five different solvents each containing 0.0080 M of **2** and 0.15 M of *i*-Pr₂NEt were prepared. Five pairs of vials were each charged with ($\pm$)-4-phenyl-oxazolidin-2-one **4a** (16 mg, 0.10 mmol) and 0.50 mL of the respective stock catalyst solution. Gentle heating was employed to dissolve the substrate. The substrate was found to be poorly soluble in the toluene-based stock solution. Even after dilution with an equal volume of toluene, it did not dissolve completely. All the vials were cooled in an ice bath. Isobutyric anhydride (12 μ L, 0.075 mmol) was added to each vial. The reactions were monitored by TLC and were stopped by quenching with methanol after 24 h or after reaching *ca.* 50% conversion by TLC. The workup and HPLC analysis followed the standard procedure.

Table 3S

Entry	solvent	t(h)	#	ee _{PR} %	ee _{SM} %	C _{HPLC} %	s	C _{AVG} %	s _{AVG}
1	<i>tert</i> -amyl alcohol	19	1	83.9	67.4	42	18	44	24
			2	84.7	66.7	43	16		
2	THF	24	1	82.9	16.7	17	13	17	12
			2	82.2	17.2	17	12		

3	MeCN	24	1	48.3	17.2	26	3.4	25	3.4
			2	49.3	15.9	24	3.4		
4	EtOAc	24	1	75.0	10.2	12	7.8	12	7.9
			2	75.7	10.2	12	8.0		
5 ^a	PhMe	24	1	77.7	5.8	6.9	8.5	7.3	8.6
			2	78.5	6.5	7.7	8.8		

^a) 0.1 M substrate, not completely dissolved

3.5. Kinetic resolution with Cl-PIQ in tert-amyl alcohol

The procedure described in Section 3.3 was followed using various oxazolidinone substrates. In several cases listed in Table 4S below, the substrates were not completely soluble in the reaction mixture, as noted.

Table 4S

Entry	Substrate	t(h)	#	ee _{PR} %	ee _{SM} %	C _{HPLC} %	s	C _{AVG} %	s _{AVG}
1	4b	17	1	88.4	75.2	46	37	46	38
			2	88.9	75.1	46	39		
2 ^a	4c	19	1	90.9	72.2	44	46	44	44
			2	90.4	71.3	44	42		
3	4d	17	1	81.2	82.2	50	24	50	25
			2	82.1	81.6	50	26		
4	4e	15	1	77.0	70.7	48	16	47	16
			2	76.7	67.2	47	15		
5 ^b	5a	21.5	1	92.5	70.5	43	54	43	55
			2	92.8	70.7	43	57		
6 ^a	5b	10	1	96.3	65.9	40	105	40	105
			2	96.3	64.7	40	105		
7 ^{a,c}	5c	10	1	92.4	87.8	49	74	49	70
			2	91.8	87.7	49	67		
8 ^a	5c	16	1	94.3	69.7	42	72	42	75
			2	95.2	64.9	41	79		
9	5d	28	1	82.7	82.2	50	27	50	28
			2	83.7	82.1	50	29		
10	5e	19	1	78.4	75.1	49	18	49	18
			2	78.3	75.3	49	18		
11 ^a	6a	24	1	86.2	64.6	43	26	43	26
			2	86.3	64.2	43	26		
12	6b	15	1	79.6	72.8	48	19	48	19
			2	78.8	73.9	48	18		

^a) substrate not completely dissolved;

^b) substrate resolved under the standard conditions using double catalyst loading (8 mol %);

^c) reaction mixture diluted to half the standard concentration.

3.6. Preparative scale KR of (±)-5,5-dimethyl-4-(2-naphthyl)-oxazolidinone **5c** using Cl-PIQ

The racemic **5c** (0.814 g, 3.39 mmol) was added to 34 mL of a stock catalyst solution [Cl-PIQ (38 mg, 0.135 mmol) and *i*-Pr₂NEt (0.44 mL, 2.5 mmol) in *tert*-amyl alcohol). The substrate did not dissolve completely even when heated. The heterogeneous mixture was stirred magnetically in an ice bath for 15 minutes. Isobutyric anhydride (0.42 mL, 2.5 mmol) was added, and the stirring was continued for 10 h. The substrate gradually went into solution. The reaction was quenched by addition of methanol (10 mL) and stirring for an additional hour. The mixture was concentrated on a rotary evaporator, and the residue separated using flash chromatography (15/85→30/70 EtOAc/hexanes). The N-acylated product (0.416 g, 40% yield, 92.1% ee) was eluted first, followed by the unreacted substrate (0.391 g, 48% recovery, 75.6% ee). The eluent was changed to 20% isopropanol/2% Et₃N/78% hexanes in order to elute the catalyst (30 mg, pure by ¹H NMR, 79% recovery). Using the above ee values, the conversion was calculated to be 45%, and the selectivity factor, 56.

3.7. Kinetic resolution with BTM

The stock solution of the catalyst was prepared by dissolving (R)-BTM **3** (20 mg, 0.080 mmol) and *i*-Pr₂NEt (0.26 mL, 1.50 mmol) in CHCl₃ in a 10.0 mL volumetric flask and bringing the volume to the mark. Two one-dram vials were each charged with 0.10 mmol of a racemic oxazolidinone substrate and 0.50 mL of the stock solution of the catalyst. Sodium sulfate (100 mg) was added after the substrate was dissolved. The mixture was magnetically stirred at rt and treated with isobutyric anhydride (12.4 μ L, 0.075 mmol). of was added, the reaction was stirred under room temperature. The reaction was monitored by ¹H NMR and was quenched by adding 0.5 mL of methanol when no further progress was observed (less than 1% change of the conversion in 2 h). The resulting solution was concentrated and subjected to flash chromatography (EtOAc/hexanes 35/65). The unreacted substrate and the N-acylated derivative thus separated were analyzed by chiral stationary phase HPLC as described above. The results of the duplicate experiments are given in Table 5S.

Table 5S

Entry	Substrate	t(h)	#	ee _{pro} %	ee _{sm} %	C _{HPLC} %	s	C _{AVG} %	s _{AVG}
1 ^a	4a	8.5	1	98.3	53.9	35	196	36	199
			2	98.3	54.3	36	202		
2 ^b	4a	5	1	96.6	89.2	48	173	48	168
			2	96.3	90.0	48	163		
3 ^a	4b	21	1	99.1	68.9	41	448	42	452
			2	99.0	74.2	43	455		
4 ^a	4c	14	1	97.6	88.2	47	239	47	255
			2	97.9	87.0	47	272		
5 ^a	4d	8.5	1	95.7	69.9	42	96	42	96
			2	95.6	71.0	43	96		
6 ^a	4e	6	1	98.0	96.2	50	397	49	426
			2	98.3	95.7	49	455		

7 ^a	5a	8.5	1	98.4	17.5	15.1	144	15	134
			2	98.1	16.5	14.4	124		
8 ^b	5a	12	1	99.0	46.9	32	305	33	343
			2	99.1	49.9	33	381		
9 ^b	5b	7	1	98.9	97.10	44	456	45	517
			2	99.1	81.7	45	577		
10 ^b	5c	8.5	1	98.0	57.5	37	176	37	201
			2	98.5	55.6	36	226		
11 ^b	5d	7	1	95.8	69.1	42	97	43	88
			2	94.6	71.8	43	78		
12 ^b	5e	6.5	1	97.7	98.4	50	408	50	389
			2	97.2	98.9	50	369		
13 ^a	6a	6	1	98.5	71.9	42	290	43	303
			2	98.5	77.4	44	316		
14 ^a	6b	6	1	92.1	70.8	43	51	44	50
			2	91.4	73.7	45	49		
15 ^c	6c	5.75	1	92.8	96.8	51	111	51	113
			2	93.6	95.5	51	116		

^a) 0.2 M (±)-substrate, 4 mol % BTM, 0.75 equiv (*i*-PrCO)₂O

^b) 0.2 M (±)-substrate, 8 mol % BTM, 1.50 equiv (*i*-PrCO)₂O

^c) 0.1 M (±)-substrate, 4 mol % BTM, 0.75 equiv (*i*-PrCO)₂O

3.8. Preparative scale KR of (±)-4-(2-thienyl)-oxazolidinone 4e using BTM

The racemic substrate (1.00 g, 5.9 mmol) was dissolved in 30 mL of freshly distilled chloroform (0.2 M substrate concentration). Sodium sulfate (1.5 g), *i*-Pr₂NEt (0.77 mL, 4.4 mmol), (R)-BTM (60 mg, 0.24 mmol), and a stir bar were added. Isobutyric anhydride (0.73 mL, 4.4 mmol) was added to the mixture stirred magnetically at room temperature. The stirring was continued for 5 hours, whereupon the reaction was quenched by addition of methanol (3 mL) and stirring for an additional hour. The mixture was concentrated on a rotary evaporator, and the residue separated using flash chromatography (35/65 EtOAc/hexanes). Fractions were eluted in the following order: the pure N-acylated product (0.727 g, 51% yield, 96.7% ee), the catalyst contaminated with the product (48 mg total weight, estimated 40 mg of BTM by ¹H NMR, 66% recovery), and the unreacted substrate (0.482 g, 48% recovery, 99.4% ee). Using the above ee values, the conversion was calculated to be 51%, and the selectivity factor, 346.

3.9. Preparative scale KR of (±)-*cis*-5-carbomethoxy-4-(*p*-methoxyphenyl)-2-oxazolidinone 6c using BTM and its conversion to (□)-Cytosaxone 6d.

The above procedure was followed, except that a lower concentration of the racemic substrate (0.1 M) was used to ensure its complete dissolution [(±)-**6c** (0.735 g, 3.0 mmol) in 30 mL of CHCl₃, Na₂SO₄ (1.5 g), *i*-Pr₂NEt (0.39 mL, 2.2 mmol), BTM (30 mg, 0.12 mmol), (*i*-PrCO)₂O (0.37 mL, 0.22 mmol), 5h at rt]. Chromatography was performed using EtOAc/hexanes 20:80→35/65. Fractions were eluted in the following order: the pure N-acylated product (0.463 g, 48% yield, 91.3% ee), the catalyst contaminated with the product (25 mg total weight, estimated 14 mg of BTM by ¹H NMR, 62% recovery), and the unreacted substrate (0.330 g, 44% recovery, 97.3% ee). C_{HPLC}=52%, S=94.

A portion of the recovered starting material (100 mg) was recrystallized from Et₂O/hexane with 88% recovery. The recrystallized product having 99.0% ee was reduced with NaBH₄ and CaCl₂ according to a literature protocol¹² to give (R)-cytoxazone **6d** (mp 122-123 °C [lit.^{12,40} 122-123 °C], [α]_D +76.0 (c 1.0, MeOH) (lit.⁴⁰ [α]_D +75.7 (c 1.0, MeOH)

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