

New Strategies for Organic Catalysis: The First Enantioselective  
Organocatalytic 1,3-Dipolar Cycloaddition

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Supporting Information

**General Information.** Commercial reagents were purified prior to use following the guidelines of Perrin and Armarego.<sup>1</sup> Organic solutions were concentrated under reduced pressure on a Buchi rotary evaporator. Chromatographic purification of products was accomplished using forced-flow chromatography on ICN 60 32-64 mesh silica gel 63 according to the method described by Still.<sup>2</sup> Thin-layer chromatography (TLC) was performed on EM Reagents 0.25 mm silica gel 60-F plates. Visualization of the developed chromatogram was performed by fluorescence quenching or KMnO<sub>4</sub> stain.

<sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were recorded on Bruker AM-400 (400 MHz and 100 MHz, respectively), Bruker DRX-500 (500 MHz and 125 MHz, respectively), Varian Mercury-300 (300 MHz and 75 MHz, respectively), or Varian I-500 (500 MHz and 125 MHz, respectively) instruments, as noted, and are internally referenced to residual protio solvent signals. Data for <sup>1</sup>H NMR are reported with chemical shift ( $\delta$  ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), integration, coupling constant (Hz), and assignment. Data for <sup>13</sup>C NMR are reported with chemical shift. IR spectra were recorded on an ASI React-IR 1000 spectrometer and are reported in terms of frequency of absorption (cm<sup>-1</sup>). Optical Rotations were recorded on a Jasco P-1010 polarimeter (WI lamp, 589 nm, 25°C). Mass spectra were obtained from the UC Irvine Mass Spectral Facility. Gas Chromatography was performed on Hewlett-Packard 5890A and 6890 Series gas chromatographs equipped with a split-mode capillary injection system and flame ionization detectors using a Bodman Chiraldex  $\Gamma$ -TA (30 m x 0.25 mm) column. HPLC analysis was performed on a Hewlett-Packard 1100 Series HPLC at

<sup>1</sup> Perrin, D. D.; Armarego, W.L.F. *Purification of Laboratory Chemicals*; 3rd ed., Pergamon Press, Oxford, 1988.

<sup>2</sup> Still, W.C.; Kahn, M.; Mitra, A. *J. Org. Chem.* 1978, 43, 2923.

254nm using the following Chiralcel columns: OD-H (25 cm) and OD guard (5 cm), AD (25 cm) and AD guard (5 cm).

**(5S)-5-Benzyl-2,2,3-trimethylimidazolidin-4-one trifluoromethanesulfonic acid salt**

(5). Prepared from the hydrochloride salt **1a**<sup>3</sup> by treatment with saturated aq. NaHCO<sub>3</sub> (100 mL) and extraction of the free amine with CHCl<sub>3</sub> (3 x 100 mL). The solution was dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated. The residue was taken up in Et<sub>2</sub>O and trifluoromethanesulfonic acid was added to precipitate **5**. The precipitate was recrystallized from 2-propanol to provide the title compound as colorless crystals. IR (CH<sub>2</sub>Cl<sub>2</sub>) 2363, 1730, 1290, 1182 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, *d*<sub>6</sub>-DMSO) δ 10.35 (br s, 1H, \*NH<sub>2</sub>), 9.27 (br s, 1H, \*NH<sub>2</sub>), 7.19–7.38 (m, 5H, C<sub>6</sub>H<sub>5</sub>), 4.67 (br d, *J* = 8.6 Hz, 1H, COCH), 3.30 (dd, *J* = 3.3, 15.4 Hz, 1H, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 2.93 (dd, *J* = 11.0, 15.4 Hz, 1H, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 2.79 (s, 3H, CH<sub>3</sub>NCO), 1.62 (s, 3H, CH<sub>3</sub>), 1.48 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 166.8, 136.6, 129.7, 129.3, 127.8, 77.5, 57.9, 34.4, 25.7, 24.6, 22.5; LRMS (CI) *m/z* 219 (MH)<sup>+</sup>; HRMS (CI) exact mass calcd for (C<sub>17</sub>H<sub>19</sub>N<sub>2</sub>O)<sup>+</sup> requires *m/z* 219.1497, found *m/z* 219.1497; [α]<sub>D</sub> = -58.8 (c = 1.0, CH<sub>3</sub>OH).

**(5S)-5-Benzyl-2,2,3-trimethylimidazolidin-4-one trifluoroacetic acid salt (6).**

Prepared from the hydrochloride salt **1a** by treatment with saturated aq. NaHCO<sub>3</sub> (100 mL) and extraction of the free amine with CHCl<sub>3</sub> (3 x 100 mL). The solution was dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated. The residue was taken up in Et<sub>2</sub>O and trifluoroacetic acid was added to precipitate the title compound as white crystals. IR (film) 3437, 2920, 2742, 2518, 2418, 1722, 1653, 1491, 1429, 1398, 1274, 1182, 1074, 834, 695 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, *d*<sub>6</sub>-DMSO) δ 9.97 (br s, 1H, \*NH<sub>2</sub>), 7.22–7.37 (m, 5H, C<sub>6</sub>H<sub>5</sub>), 4.53 (br d, *J* = 7.1 Hz, 1H, COCH), 3.27 (dd, *J* = 3.3, 14.8 Hz, 1H, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 3.00 (dd, *J* = 10.2, 14.8 Hz, 1H, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 2.76 (s, 3H, CH<sub>3</sub>NCO), 1.59 (s, 3H, CH<sub>3</sub>), 1.46 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 167.6, 136.9, 129.8, 129.1, 127.5, 77.2, 58.0, 34.7, 25.6, 24.7, 22.8; LRMS (EI) *m/z* 218 (M)<sup>+</sup>; HRMS (EI) exact mass calcd for (C<sub>17</sub>H<sub>19</sub>N<sub>2</sub>O)<sup>+</sup> requires *m/z* 219.1497, found *m/z* 219.1494; [α]<sub>D</sub> = -63.2 (c = 1.0, CHCl<sub>3</sub>).

<sup>3</sup> Ahrendt, K. A.; Borths, C. J.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2000**, *122*, 4243.

**(5S)-5-Benzyl-2,2,3-trimethylimidazolidin-4-one hydrobromide (7).** Prepared from the hydrochloride salt **1a** by treatment with saturated aq. NaHCO<sub>3</sub> (100 mL) and extraction of the free amine with CHCl<sub>3</sub> (3 x 100 mL). The solution was dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated. The residue was taken up in Et<sub>2</sub>O and hydrobromic acid was added to precipitate the title compound as white crystals. IR (film) 3414, 2912, 2711, 2557, 1707, 1607, 1390, 1274, 1197, 1159, 1058, 989, 703 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, *d*<sub>6</sub>-DMSO) δ 10.41 (brs, 1H, \*NH<sub>2</sub>), 9.69 (br s, 1H, \*NH<sub>2</sub>), 7.24–7.43 (m, 5H, C<sub>6</sub>H<sub>5</sub>), 4.69 (br d, *J* = 7.1 Hz, 1H, COCH), 3.28 (dd, *J* = 3.0, 15.1 Hz, 1H, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 3.15 (dd, *J* = 10.4, 14.8 Hz, 1H, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 2.77 (s, 3H, CH<sub>3</sub>NCO), 1.67 (s, 3H, CH<sub>3</sub>), 1.49 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 166.8, 136.7, 129.9, 129.2, 127.7, 77.6, 58.1, 33.9, 25.8, 24.5, 22.6; LRMS (EI) *m/z* 218 (M)<sup>+</sup>; HRMS (EI) exact mass calcd for (C<sub>17</sub>H<sub>18</sub>N<sub>2</sub>O)<sup>+</sup> requires *m/z* 218.1419, found *m/z* 218.1420; [α]<sub>D</sub> = -21.3 (c = 1.0, CHCl<sub>3</sub>).

**(5S)-5-Benzyl-2,2,3-trimethylimidazolidin-4-one perchloric acid salt (8).** Prepared from the hydrochloride salt **1a** by treatment with saturated aq. NaHCO<sub>3</sub> (100 mL) and extraction of the free amine with CHCl<sub>3</sub> (3 x 100 mL). The solution was dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated. The residue was taken up in Et<sub>2</sub>O and perchloric acid was added to precipitate the title compound as white crystals. IR (film) 3514, 3059, 2927, 2850, 1707, 1607, 1398, 1267, 1097, 927, 703 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, *d*<sub>6</sub>-DMSO) δ 10.37 (br s, 1H, \*NH<sub>2</sub>), 9.25 (br s, 1H, \*NH<sub>2</sub>), 7.26–7.43 (m, 5H, C<sub>6</sub>H<sub>5</sub>), 4.66 (br d, *J* = 8.8 Hz, 1H, COCH), 3.33 (dd, *J* = 3.3, 15.1 Hz, 1H, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 2.94 (dd, *J* = 10.7, 15.1 Hz, 1H, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 2.78 (s, 3H, CH<sub>3</sub>NCO), 1.62 (s, 3H, CH<sub>3</sub>), 1.48 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 166.8, 136.5, 129.7, 129.3, 127.8, 77.6, 58.0, 34.4, 25.7, 24.6, 22.5; LRMS (EI) *m/z* 218 (M)<sup>+</sup>; HRMS (CI) exact mass calcd for (C<sub>17</sub>H<sub>18</sub>NO<sub>2</sub>)<sup>+</sup> requires *m/z* 218.1419, found *m/z* 218.1428; [α]<sub>D</sub> = -61.1 (c = 1.0, CH<sub>3</sub>NO<sub>2</sub>).

**General Procedure A.** A flask containing nitron and imidizolidinone catalyst was charged with CH<sub>3</sub>NO<sub>2</sub>, then treated with the appropriate amount of H<sub>2</sub>O. After cooling the solution to the desired temperature, α,β unsaturated aldehyde was added dropwise to the flask. After the appropriate reaction time, the resulting solution was passed through a silica gel column with ethyl acetate. Removal of volatiles resulted in an oily residue, which was purified by silica gel chromatography to afford the title compounds.

**General Procedure B.** A flask containing nitron and imidizolidinone catalyst was charged with  $\text{CH}_3\text{NO}_2$ , then treated with the appropriate amount of  $\text{H}_2\text{O}$ . After cooling the solution to the desired temperature,  $\alpha,\beta$  unsaturated aldehyde was added dropwise to the flask. Additional aldehyde was added to the reaction mixture at 24 h intervals until the specified reaction time was reached. The resulting solution was passed through a silica gel column with ethyl acetate. Removal of volatiles resulted in an oily residue, which was purified by silica gel chromatography to afford the title compounds.

**General Procedure C: The Reduction of Isoxazolidine Products.** To a solution of the isoxazolidine aldehyde in absolute ethanol (1ml) were added 3 equivalents of  $\text{NaBH}_4$ . After 0.5 hours, the reaction mixture was quenched with  $\text{H}_2\text{O}$ , and extracted with 2 x 10mL of  $\text{CH}_2\text{Cl}_2$ . The organic layer was dried over  $\text{Na}_2\text{SO}_4$ , filtered, and concentrated. Purification of the resultant residue by silica gel chromatography provided the corresponding primary alcohol.

**(3R,4S,5R)-2-Benzyl-4-formyl-5-methyl-3-phenylisoxazolidine (Table 3, entry 1).** Prepared according to general procedure B from (*Z*)-*N*-benzylidenebenzylamine *N*-oxide (5.28 g, 25.0 mmol), (*5S*)-5-Benzyl-2,2,3-trimethylimidazolidin-4-one perchloric acid salt (**8**) (1.59 g, 5.00 mmol), crotonaldehyde (8.28 mL, 100.0 mmol followed by 5 x 6.21 mL, 75.0 mmol over 24 h intervals) and  $\text{H}_2\text{O}$  (1.35 mL, 75.0 mmol) in  $\text{CH}_3\text{NO}_2$  (250.0 ml) at  $-20^\circ\text{C}$  over the course of 144 h. The resulting solution was passed through a silica gel column with  $\text{CH}_2\text{Cl}_2$  to provide the title compound as an oil in 98% yield (6.85 g); 94:6 *endo:exo*. *Endo* isomer: IR ( $\text{CH}_2\text{Cl}_2$ ) 2853, 1722, 1494, 1455, 1374  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.81 (d,  $J = 2.4$  Hz, 1H, CHO), 7.24–7.58 (m, 10H,  $\text{C}_6\text{H}_5$  and  $\text{CH}_2\text{C}_6\text{H}_5$ ), 4.57 (dq,  $J = 6.1, 12.2$  Hz, 1H,  $\text{CHCH}_3$ ), 4.21 (d,  $J = 7.8$  Hz, 1H,  $\text{CHC}_6\text{H}_5$ ), 4.02 (d,  $J = 14.4$  Hz, 1H,  $\text{CH}_2\text{C}_6\text{H}_5$ ), 3.84 (d,  $J = 14.3$  Hz, 1H,  $\text{CH}_2\text{C}_6\text{H}_5$ ), 3.15 (m, 1H,  $\text{CHCHO}$ ), 1.52 (d,  $J = 6.2$  Hz, 3H,  $\text{CH}_3$ );  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  198.5, 138.4, 137.3, 129.0, 128.6, 128.3, 128.2, 127.5, 127.1, 73.4, 71.5, 71.1, 59.5, 21.2; LRMS (CI)  $m/z$  281 (M) $^+$ ; HRMS (CI) exact mass calcd for ( $\text{C}_{18}\text{H}_{19}\text{NO}_2$ ) requires  $m/z$  281.1418, found  $m/z$  281.1413 (M) $^+$ ;  $[\alpha]_D = +82.5^\circ$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ). Diastereomeric ratios were determined by  $^1\text{H}$  NMR analysis. A portion of the title compound was reduced to the corresponding primary alcohol (general procedure C) and purified by silica gel chromatography (3:7 EtOAc/hexane) for the determination of enantiomeric purity; *endo* 94% ee.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.22–7.47

(m, 10H, ArH), 4.22-4.24 (m, 1H, CHON), 4.00 (d,  $J = 14.6$  Hz, 1H,  $\text{CH}_2\text{C}_6\text{H}_5$ ), 3.81 (d,  $J = 14.6$  Hz, 1H,  $\text{CH}_2\text{C}_6\text{H}_5$ ), 3.74-3.75 (m, 2H,  $\text{CH}_2\text{OH}$ ), 3.65 (d,  $J = 8.3$  Hz, 1H,  $\text{CHC}_6\text{H}_5$ ), 2.36-2.42 (m, 1H,  $\text{CHCH}_2\text{OH}$ ), 1.46 (d,  $J = 6.4$  Hz, 3H,  $\text{CH}_3$ ). Enantiomeric ratios were determined by HPLC with a Chiralcel OD-H column and OD guard column (1:39 *i*PrOH/hexane, 1 mL/min flow rate); *endo* isomers  $t_r = 59.3$  min (major enantiomer) and 76.3 min (minor enantiomer).

**(3*R*,4*S*,5*R*)-2-Allyl-4-formyl-5-methyl-3-phenylisoxazolidine** (Table 3, entry 2).

Prepared according to general procedure B from (*Z*)-*N*-benzylideneallylamine *N*-oxide (63 mg, 0.30 mmol), (*5*S**)-5-Benzyl-2,2,3-trimethylimidazolidin-4-one perchloric acid salt (**8**) (19 mg, 0.08 mmol), crotonaldehyde (133  $\mu\text{L}$ , 1.6 mmol followed by 5 x 75  $\mu\text{L}$ , 1.2 mmol over 24 h intervals) and  $\text{H}_2\text{O}$  (22  $\mu\text{L}$ , 1.2 mmol) in  $\text{CH}_3\text{NO}_2$  (4.0 ml) at  $-20$  °C over the course of 132 h to provide the title compound as a colorless oil in 73% yield (68 mg); 93:7 *endo:exo*. *Endo* isomer: IR ( $\text{CH}_2\text{Cl}_2$ ) 2981, 2842, 1722, 1645, 1498, 1376  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  9.77 (d,  $J = 2.2$  Hz, 1H, CHO), 7.14-7.24 (m, 5H,  $\text{C}_6\text{H}_5$ ), 5.84-5.98 (m, 1H,  $\text{CH}_2=\text{CHCH}_2$ ), 5.06-5.28 (m, 2H,  $\text{CH}_2=\text{CH}$ ), 4.51 (dq,  $J = 6.0, 6.0$  Hz, 1H,  $\text{CHCH}_3$ ), 4.10 (d,  $J = 7.7$  Hz, 1H,  $\text{CHC}_6\text{H}_5$ ), 3.46 (dd,  $J = 5.5, 14.3$  Hz, 1H,  $\text{CH}_2=\text{CHCH}_2\text{N}$ ), 3.31 (dd,  $J = 6.6, 14.3$  Hz, 1H,  $\text{CH}_2=\text{CHCH}_2\text{N}$ ), 3.09 (ddd,  $J = 2.5, 5.8, 8.0$  Hz, 1H,  $\text{CHCHO}$ ), 1.50 (d,  $J = 6.0$  Hz, 3H,  $\text{CH}_3$ );  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  198.7, 138.6, 133.9, 129.1, 128.4, 127.8, 118.1, 73.7, 71.9, 71.3, 59.1, 21.3; LRMS (CI)  $m/z$  231 ( $\text{M}^+$ ); HRMS (CI) exact mass calcd for ( $\text{C}_{14}\text{H}_{17}\text{NO}_2$ ) requires  $m/z$  231.1259, found  $m/z$  231.1256 ( $\text{M}^+$ );  $[\alpha]_D = +63.8$  ° ( $c = 1.0$ ,  $\text{CHCl}_3$ ). Diastereomeric ratios were determined by  $^1\text{H}$  NMR analysis. A portion of the title compound was reduced to the corresponding primary alcohol (general procedure C) and purified by silica gel chromatography (3:7 EtOAc/hexane) for the determination of enantiomeric purity; *endo* 98% ee.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.13-7.41 (m, 5H,  $\text{C}_6\text{H}_5$ ), 5.83-5.97 (m, 1H,  $\text{CH}_2=\text{CHCH}_2$ ), 5.08-5.22 (m, 2H,  $\text{CH}_2=\text{CH}$ ), 4.21 (dq,  $J = 6.4, 6.4$  Hz, 1H,  $\text{CHCH}_3$ ), 3.64-3.83 (br s, 2H,  $\text{CH}_2\text{OH}$ ), 3.57 (d,  $J = 8.0$  Hz, 1H,  $\text{CHC}_6\text{H}_5$ ), 3.44 (dd,  $J = 5.2, 14.3$  Hz, 1H,  $\text{CH}_2=\text{CHCH}_2\text{N}$ ), 3.28 (dd,  $J = 6.6, 14.3$  Hz, 1H,  $\text{CH}_2=\text{CHCH}_2\text{N}$ ), 2.34 (m, 1H,  $\text{CHCH}_2\text{OH}$ ), 1.44 (d,  $J = 6.1$  Hz, 3H,  $\text{CH}_3$ ). Enantiomeric ratios were determined by HPLC with a Chiralcel AD column and AD guard column (3:97 EtOH/hexane, 1 mL/min flow rate); *endo* isomers  $t_r = 18.2$  min and 24.2 min.

**(3R,4S,5R)-2,5-Dimethyl-4-formyl-3-phenylisoxazolidine (Table 3, entry 3).** Prepared according to general procedure B from (*Z*)-*N*-benzylidenemethylamine *N*-oxide (54.1 mg, 0.40 mmol), (*S*)-5-Benzyl-2,2,3-trimethylimidazolidin-4-one perchloric acid salt (**8**) (26 mg, 0.08 mmol), crotonaldehyde (133  $\mu$ L, 1.6 mmol followed by 5 x 100  $\mu$ L, 1.2 mmol, over 24 h intervals) and H<sub>2</sub>O (22  $\mu$ L, 1.2 mmol) in CH<sub>3</sub>NO<sub>2</sub> (4.0 ml) at -20 °C over the course of 132 h to provide the title compound as a colorless oil in 66% yield (54 mg); 95:5 *endo:exo*. *Endo* >99% ee *Endo* isomer: IR (CH<sub>2</sub>Cl<sub>2</sub>) 2974, 2873, 1722, 1552 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  9.74 (d, *J* = 2.5 Hz, 1H, CHO), 7.26–7.39 (m, 5H, C<sub>6</sub>H<sub>5</sub>), 4.54 (dq, *J* = 6.0, 12.3 Hz, 1H, CHCH<sub>3</sub>), 3.83 (br s, 1H, CHC<sub>6</sub>H<sub>5</sub>), 3.09 (m, 1H, CHCHO), 2.60 (s, 3H, NCH<sub>3</sub>), 1.50 (d, *J* = 6.3 Hz, 3H, CHCH<sub>3</sub>); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  198.6, 137.8, 129.1, 128.5, 127.8, 73.5, 72.2, 66.3, 43.6, 21.9; LRMS (CI) *m/z* 205 (M)<sup>+</sup>; HRMS (CI) exact mass calcd for (C<sub>12</sub>H<sub>15</sub>NO<sub>2</sub>) requires *m/z* 205.1103, found *m/z* 205.1100 (M)<sup>+</sup>; [ $\alpha$ ]<sub>D</sub> = +77.2° (c = 1.0, CHCl<sub>3</sub>). Diastereomeric ratios were determined by <sup>1</sup>H NMR analysis. Enantiomeric ratios were determined by GLC with a Bodman  $\beta$ -PH column (100 °C, 23 psi); *endo* isomers t<sub>r</sub> = 38.0 min and 39.8 min.

**(3R,4S,5R)-2-Benzyl-4-formyl-5-methyl-3-(4-chlorophenyl) isoxazolidine (Table 3, entry 4).** Prepared according to general procedure B from (*Z*)-*N*-*para*-chlorobenzylidenebenzylamine *N*-oxide (74 mg, 0.30 mmol), (*S*)-5-Benzyl-2,2,3-trimethylimidazolidin-4-one perchloric acid salt (**8**) (19 mg, 0.06 mmol), crotonaldehyde (100  $\mu$ L, 1.2 mmol followed by 7 x 75  $\mu$ L, 0.90 mmol, over 24 h intervals) and H<sub>2</sub>O (16  $\mu$ L, 0.90 mmol) in CH<sub>3</sub>NO<sub>2</sub> (3.0 ml) at -20 °C over the course of 160 h. The resulting solution was passed through a silica gel column with CH<sub>2</sub>Cl<sub>2</sub> to provide the title compound as an oil in 78% yield (74 mg); 92:8 *endo:exo*. *Endo* isomer: IR (film) 3429, 3066, 2981, 2873, 2835, 2726, 1722, 1599, 1491, 1452, 1375, 1089, 1020, 819, 734, 703 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  9.79 (d, *J* = 2.2 Hz, 1H, CHO), 7.24–7.38 (m, 9H, C<sub>6</sub>H<sub>4</sub>Cl and CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 4.55 (m, 1H, CHCH<sub>3</sub>), 4.16 (d, *J* = 7.7 Hz, 1H, CHC<sub>6</sub>H<sub>4</sub>Cl), 3.97 (d, *J* = 14.0 Hz, 1H, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 3.84 (d, *J* = 14.3 Hz, 1H, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 3.06 (ddd, *J* = 7.4, 5.5, 2.2 Hz, 1H, CHCHO), 1.50 (d, *J* = 6.0 Hz, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  198.6, 137.5, 137.2, 134.1, 129.8, 129.6, 129.4, 129.1, 128.8, 128.6, 127.6, 21.3; LRMS (CI) *m/z* 315 (M)<sup>+</sup>; HRMS (CI) exact mass calcd for (C<sub>18</sub>H<sub>18</sub>NCIO<sub>2</sub>) requires *m/z* 315.1026, found *m/z* 315.1023 (M)<sup>+</sup>; [ $\alpha$ ]<sub>D</sub> = +69.8° (c = 1.0, CHCl<sub>3</sub>). Diastereomeric ratios were determined by <sup>1</sup>H NMR analysis. A portion of the title compound was reduced to the

corresponding primary alcohol (general procedure C) and purified by silica gel chromatography (3:7 EtOAc/hexane) for the determination of enantiomeric purity; *endo* 95% ee.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.24–7.39 (m, 9H, ArH), 4.23 (m, 1H, CHON), 3.97 (d,  $J = 14.2$  Hz, 1H,  $\text{CH}_2\text{C}_6\text{H}_5$ ), 3.84 (d,  $J = 14.2$  Hz, 1H,  $\text{CH}_2\text{C}_6\text{H}_5$ ), 3.73–3.81 (m, 2H,  $\text{CH}_2\text{OH}$ ), 3.67 (d,  $J = 7.8$  Hz, 1H,  $\text{CHC}_6\text{H}_4\text{Cl}$ ), 2.31–2.33 (m, 1H,  $\text{CHCH}_2\text{OH}$ ), 1.44 (d,  $J = 6.4$  Hz, 3H,  $\text{CH}_3$ ). Enantiomeric ratios were determined by HPLC with a Chiralcel AD column and AD guard column (3:125 EtOH/hexane, 1 mL/min flow rate); *endo* isomers  $t_r = 47.7$  min and 83.6 min.

**(3*R*,4*S*,5*R*)-2,5-Dimethyl-4-formyl-3-(4-chlorophenyl) isoxazolidine (Table 3, entry 5).** Prepared according to general procedure B from (*Z*)-*N*-*para*-chlorobenzylidenemethylamine *N*-oxide (68 mg, 0.40 mmol), (*5S*)-5-Benzyl-2,2,3-trimethylimidazolidin-4-one perchloric acid salt (**8**) (26 mg, 0.08 mmol), crotonaldehyde (133  $\mu\text{L}$ , 1.6 mmol followed by 8 x 100  $\mu\text{L}$ , 1.20 mmol, over 24 h intervals) and  $\text{H}_2\text{O}$  (22  $\mu\text{L}$ , 1.20 mmol) in  $\text{CH}_3\text{NO}_2$  (4.0 ml) at  $-20$  °C over the course of 160 h. The resulting solution was passed through a silica gel column with  $\text{CH}_2\text{Cl}_2$  to provide the title compound as an oil in 76% yield (73 mg); 93:7 *endo:exo*. *Endo* isomer: IR (film) 3429, 2974, 2927, 2850, 2781, 2734, 1908, 1722, 1599, 1490, 1460, 1375, 1344, 1298, 1205, 1089, 1020, 911.4, 818.7, 679.7  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.74 (d,  $J = 2.3$  Hz, 1H, CHO), 7.25–7.33 (m, 4H, ArH), 4.51 (dq,  $J_d = 5.9$ ,  $J_q = 6.1$  Hz, 1H,  $\text{CHCH}_3$ ), 3.82–4.01 (m, 1H,  $\text{CHC}_6\text{H}_4\text{Cl}$ ), 3.02 (ddd,  $J = 8.0, 5.5, 2.3$  Hz, 1H,  $\text{CHCHO}$ ), 2.59 (s, 3H,  $\text{NCH}_3$ ), 1.55 (d,  $J = 6.2$  Hz, 3H,  $\text{CHCH}_3$ );  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  198.3, 136.7, 134.3, 129.6, 129.5, 129.3, 129.1, 73.5, 73.1, 72.2; LRMS (FAB)  $m/z$  239 (M) $^+$ ; HRMS (FAB) exact mass calcd for ( $\text{C}_{12}\text{H}_{14}\text{ClNO}_2$ ) requires  $m/z$  239.0713, found  $m/z$  239.0707 (M) $^+$ ;  $[\alpha]_D^{25} = +64.1$  ° ( $c = 1.0$ ,  $\text{CHCl}_3$ ). Diastereomeric ratios were determined by  $^1\text{H}$  NMR analysis. A portion of the title compound was reduced to the corresponding primary alcohol (general procedure C) and purified by silica gel chromatography (2:3 EtOAc/hexane) for the determination of enantiomeric purity; *endo* 94% ee.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.24–7.38 (m, 4H, ArH), 4.20 (dq,  $J_d = 6.2$ ,  $J_q = 6.0$ , 1H, CHON), 3.66–3.75 (m, 2H,  $\text{CH}_2\text{OH}$ ), 3.35 (d,  $J = 8.52$  Hz, 1H,  $\text{CHC}_6\text{H}_4\text{Cl}$ ), 2.28–2.34 (m, 1H,  $\text{CHCH}_2\text{OH}$ ), 1.43 (d,  $J = 6.3$  Hz, 3H,  $\text{CH}_3$ ). Enantiomeric ratios were determined by HPLC with a Chiralcel OD-H column and OD guard column (3:97 iPrOH/hexane, 1 mL/min flow rate); *endo* isomers  $t_r = 29.0$  min and 45.3 min.

**(3R,4S,5R)-2-Benzyl-4-formyl-5-methyl-3-(4-methoxyphenyl) isoxazolidine (Table 3, entry 6).** Prepared according to general procedure B (*Z*)-*N*-*para*-methoxybenzylidenebenzylamine *N*-oxide (72 mg, 0.30 mmol), (*S*)-5-Benzyl-2,2,3-trimethylimidazolidin-4-one perchloric acid salt (**8**) (19 mg, 0.06 mmol), crotonaldehyde (100  $\mu$ L, 1.2 mmol followed by 5 x 75  $\mu$ L, 0.90 mmol, over 24 h intervals) and H<sub>2</sub>O (16  $\mu$ L, 0.90 mmol) in CH<sub>3</sub>NO<sub>2</sub> (3.0 ml) at -20 °C over the course of 136 h. The resulting solution was passed through a silica gel column with CH<sub>2</sub>Cl<sub>2</sub> to provide the title compound as an oil in 93% yield (86 mg); 98:2 *endo:exo*. *Endo* isomer: IR (film) 3429, 3035, 2974, 2935, 2835, 2726, 1722, 1614, 1514, 1452, 1375, 1298, 1251, 1174, 1035, 826, 734, 703 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  9.76 (d, *J* = 2.5 Hz, 1H, CHO), 7.23–7.38 (m, 7H, ArH), 6.87–6.91 (m, 2H, ArH), 4.52 (m, 1H, CHCH<sub>3</sub>), 4.06 (d, *J* = 8.2 Hz, 1H, CHC<sub>6</sub>H<sub>4</sub>OCH<sub>3</sub>), 3.99 (d, *J* = 14.3 Hz, 1H, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 3.80 (s, 3H, OCH<sub>3</sub>), 3.76 (d, *J* = 14.6 Hz, 1H, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 3.08 (ddd, *J* = 8.0, 5.5, 2.5 Hz, 1H, CHCHO), 1.50 (d, *J* = 6.3 Hz, 3H, CHCH<sub>3</sub>); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  199.1, 159.8, 137.7, 130.1, 129.1, 128.7, 128.5, 137.4, 114.6, 73.6, 71.8, 71.2, 59.5, 55.6, 21.5; LRMS (CI) *m/z* 311 (M)<sup>+</sup>; HRMS (CI) exact mass calcd for (C<sub>19</sub>H<sub>21</sub>NO<sub>3</sub>) requires *m/z* 311.1521, found *m/z* 311.1514 (M)<sup>+</sup>; [ $\alpha$ ]<sub>D</sub> = +71.8 ° (c = 1.0, CHCl<sub>3</sub>). Diastereomeric ratios were determined by <sup>1</sup>H NMR analysis. A portion of the title compound was reduced to the corresponding primary alcohol (general procedure C) and purified by silica gel chromatography (3:7 EtOAc/hexane) for the determination of enantiomeric purity; *endo* 91% ee. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.17–7.41 (m, 7H, ArH), 6.86–6.93 (m, 2H, ArH), 4.17 (dq, *J*<sub>d</sub> = 5.9, *J*<sub>q</sub> = 6.0, 1H, CHON), 3.96 (d, *J* = 14.6 Hz, 1H, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 3.80 (s, 3H, OCH<sub>3</sub>), 3.73 (d, *J* = 14.3 Hz, 1H, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 3.69–3.73 (m, 2H, CH<sub>2</sub>OH), 3.56 (d, *J* = 8.5 Hz, 1H, CHC<sub>6</sub>H<sub>4</sub>OCH<sub>3</sub>), 2.29–2.38 (m, 1H, CHCH<sub>2</sub>OH), 1.43 (d, *J* = 6.0 Hz, 3H, CH<sub>3</sub>). Enantiomeric ratios were determined by HPLC with a Chiralcel AD column and AD guard column (3:97 EtOH/hexane, 1 mL/min flow rate); *endo* isomers *t*<sub>r</sub> = 37.7 min and 69.5 min.

**(3R,4S,5R)-2,5-Dimethyl-4-formyl-3-(4-tolyl) isoxazolidine (Table 3, entry 7).** Prepared according to general procedure B from (*Z*)-*N*-*para*-methylbenzylidenemethylamine *N*-oxide (60 mg, 0.40 mmol), (*S*)-5-Benzyl-2,2,3-trimethylimidazolidin-4-one perchloric acid salt (**8**) (26 mg, 0.08 mmol), crotonaldehyde (133  $\mu$ L, 1.6 mmol followed by 7 x 100  $\mu$ L, 1.20 mmol, over 24 h intervals) and H<sub>2</sub>O (22  $\mu$ L, 1.20 mmol) in CH<sub>3</sub>NO<sub>2</sub> (4.0 ml) at -20 °C over the course



of 160 h. The resulting solution was passed through a silica gel column with  $\text{CH}_2\text{Cl}_2$  to provide the title compound as an oil in 82% yield (72 mg); 93:7 *endo:exo*. *Endo* isomer: IR (film) 3429, 2974, 2927, 2873, 2726, 1722, 1514, 1452, 1375, 1344, 1112, 1066, 911, 811, 687  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  9.74 (d,  $J = 2.5$  Hz, 1H, CHO), 7.12-7.26 (m, 4H, ArH), 4.53 (dq,  $J_d = 5.9$ ,  $J_q = 6.3$  Hz, 1H, CHCH<sub>3</sub>), 3.78 (bs, 1H, CHC<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 3.09 (ddd,  $J = 8.4$ , 5.4, 2.5 Hz, 1H, CHCHO), 2.59 (s, 3H, NCH<sub>3</sub>), 2.34 (s, 3H, C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 1.51 (d,  $J = 6.3$  Hz, 3H, CHCH<sub>3</sub>);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  198.7, 138.3, 134.5, 130.0, 129.6, 128.0, 127.5, 73.6, 72.2, 43.7, 21.6; LRMS (CI)  $m/z$  219 (M)<sup>+</sup>; HRMS (CI) exact mass calcd for (C<sub>13</sub>H<sub>17</sub>NO<sub>2</sub>) requires  $m/z$  219.1259, found  $m/z$  219.1262 (M)<sup>+</sup>;  $[\alpha]_D = +67.9^\circ$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ). Diastereomeric ratios were determined by  $^1\text{H}$  NMR analysis. A portion of the title compound was reduced to the corresponding primary alcohol (general procedure C) and purified by silica gel chromatography (3:7 EtOAc/hexane) for the determination of enantiomeric purity; *endo* 97% ee.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.13-7.26 (m, 4H, ArH), 4.20 (dq,  $J_d = 6.2$ ,  $J_q = 6.0$  Hz, 1H, CHON), 3.63-3.71 (m, 2H, CH<sub>2</sub>OH), 3.29 (d,  $J = 7.7$  Hz, 1H, CHC<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 2.55 (s, 3H, NCH<sub>3</sub>), 2.33 (s, 3H, C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 2.31-2.39 (m, 1H, CHCH<sub>2</sub>OH), 1.44 (d,  $J = 6.0$  Hz, 3H, CHCH<sub>3</sub>). Enantiomeric ratios were determined by HPLC with a Chiralcel AD column and AD guard column (3:97 *i*PrOH/hexane, 1 mL/min flow rate); *endo* isomers  $t_r = 40.2$  min and 47.6 min.

**(3R,4S,5R)-2-Benzyl-4-formyl-5-methyl-3-(2-naphthyl) isoxazolidine (Table 3, entry 8).** Prepared according to general procedure B from (*Z*)-*N*-2-naphthylidenebenzylamine *N*-oxide (78 mg, 0.30 mmol), (*5S*)-5-Benzyl-2,2,3-trimethylimidazolidin-4-one perchloric acid salt (**8**) (19 mg, 0.06 mmol), crotonaldehyde (100  $\mu\text{L}$ , 1.2 mmol followed by 5 x 75  $\mu\text{L}$ , 0.90 mmol, over 24 h intervals) and H<sub>2</sub>O (16  $\mu\text{L}$ , 0.90 mmol) in  $\text{CH}_3\text{NO}_2$  (3.0 ml) at  $-20^\circ\text{C}$  over the course of 138 h. The resulting solution was passed through a silica gel column with  $\text{CH}_2\text{Cl}_2$  to provide the title compound as an oil in 98% yield (97 mg); 95:5 *endo:exo*. *Endo* isomer: IR (film) 3429, 3059, 2981, 2927, 2866, 2726, 1954, 1722, 1607, 1498, 1452, 1375, 1313, 1120, 819, 742, 703  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.83 (d,  $J = 2.3$  Hz, 1H, CHO), 7.84-7.89 (m, 5H, ArH), 7.61 (dd,  $J = 1.6$  Hz, 1H, ArH), 7.49-7.52 (m, 2H, ArH), 7.24-7.38 (m, 2H, ArH), 4.61 (dq,  $J_d = 5.9$ ,  $J_q = 6.1$  Hz, 1H, CHCH<sub>3</sub>), 4.35 (d,  $J = 7.7$  Hz, 1H, CHNaph), 4.06 (d,  $J = 14.3$  Hz, 1H, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 3.89 (d,  $J = 14.3$  Hz, 1H, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 2.20 (ddd,  $J = 7.8$ , 5.5, 2.3 Hz, 1H, CHCHO), 1.55 (d,  $J = 6.2$  Hz, 3H, CHCH<sub>3</sub>);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  198.8, 137.5, 136.0, 133.5,

133.4, 129.1, 128.7, 128.4, 128.1, 127.9, 137.4, 127.1, 126.6, 126.5, 125.1, 73.8, 71.6, 71.5, 59.8, 21.3; LRMS (CI)  $m/z$  331 (M)<sup>+</sup>; HRMS (FAB) exact mass calcd for (C<sub>22</sub>H<sub>21</sub>NO<sub>2</sub>) requires  $m/z$  331.1572, found  $m/z$  331.1567 (M)<sup>+</sup>; [ $\alpha$ ]<sub>D</sub> = +53.1 ° (c = 1.0, CHCl<sub>3</sub>). Diastereomeric ratios were determined by <sup>1</sup>H NMR analysis. A portion of the title compound was reduced to the corresponding primary alcohol (general procedure C) and purified by silica gel chromatography (3:7 EtOAc/hexane) for the determination of enantiomeric purity; *endo* 93% ee. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.84–7.86 (m, 4H, ArH), 7.66–7.67 (m, 1H, ArH), 7.48–7.52 (m, 2H, ArH), 7.20–7.40 (m, 5H, ArH), 4.28 (dq,  $J_d$  = 6.1,  $J_q$  = 5.9, 1H, CHON), 4.04 (d,  $J$  = 14.2 Hz, 1H, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 3.75–3.87 (m, 4H, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>, CH<sub>2</sub>OH, CHNaph), 2.46–2.51 (m, 1H, CHCH<sub>2</sub>OH), 1.50 (d,  $J$  = 5.9 Hz, 3H, CH<sub>3</sub>). Enantiomeric ratios were determined by HPLC with a Chiralcel AD column and AD guard column (1:39 EtOH/hexane, 1 mL/min flow rate); *endo* isomers  $t_r$  = 57.7 min and 107.6 min.

**(3R,4S,5R)-2-Benzyl-4-formyl-5-methyl-3-cyclohexyl isoxazolidine** (Table 3, entry 9). Prepared according to general procedure A from (*Z*)-*N*-cyclohexylmethylidenebenzylamine *N*-oxide (65 mg, 0.30 mmol), (*5S*)-5-Benzyl-2,2,3-trimethylimidazolidin-4-one perchloric acid salt (**8**) (19 mg, 0.06 mmol), crotonaldehyde (200  $\mu$ L) and H<sub>2</sub>O (16  $\mu$ L, 0.90 mmol) in CH<sub>3</sub>CN (3.0 ml) at –40 °C over the course of 96 h. The resulting solution was passed through a silica gel column with CH<sub>2</sub>Cl<sub>2</sub> and purified by silica gel chromatography (2:23 EtOAc/Hexane) to provide the title compound as an oil in 69% yield (59 mg); 99:1 *endo:exo*. *Endo* isomer: IR (film) 2927, 2858, 2719, 1722, 1498, 1452, 1383, 1328, 1074, 1027, 973, 703 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  9.80 (d,  $J$  = 3.0 Hz, 1H, CHO), 7.23–7.40 (m, 5H, ArH), 4.57–4.64 (dq,  $J_d$  = 7.7,  $J_q$  = 6.1 Hz, 1H, CHON), 4.08 (d,  $J$  = 13.5 Hz, 1H, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 3.82 (d,  $J$  = 13.2 Hz, 1H, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 3.05 (dd,  $J$  = 7.7, 5.5 Hz, 1H, CH-chex), 2.86–2.91 (m, 1H, CHCHO), 1.35 (d,  $J$  = 6.1 Hz, 3H, CHCH<sub>3</sub>), 0.70–2.03 (m, 11H, chex-H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  73.6, 72.8, 67.2, 62.0, 42.6, 30.9, 29.8, 26.7, 26.3, 26.2, 18.1; LRMS (EI)  $m/z$  287 (M)<sup>+</sup>; HRMS (EI) exact mass calcd for (C<sub>18</sub>H<sub>25</sub>NO<sub>2</sub>) requires  $m/z$  287.1885, found  $m/z$  287.1881 (M)<sup>+</sup>; [ $\alpha$ ]<sub>D</sub> = +48.6 ° (c = 1.0, CHCl<sub>3</sub>). Diastereomeric ratios were determined by <sup>1</sup>H NMR analysis. A portion of the title compound was reduced to the corresponding primary alcohol (general procedure C) and purified by silica gel chromatography (3:7 EtOAc/hexane) for the determination of enantiomeric purity; *endo* 99% ee. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.32–7.41 (m, 5H, ArH), 4.32–4.34 (m, 1H, CHON), 4.14 (d,  $J$

= 12.7 Hz, 1H, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 3.88 (d, *J* = 13.2 Hz, 1H, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 3.73-3.84 (m, 2H, CH<sub>2</sub>OH), 2.58 (dd, *J* = 6.1, 5.4 Hz, 1H, CH-chex), 2.14-2.18 (m, 1H, CHCH<sub>2</sub>OH), 1.34 (d, *J* = 6.4 Hz, 3H, CHCH<sub>3</sub>), 0.82-1.74 (m, 11H, chex-H). Enantiomeric ratios were determined by HPLC with a Chiralcel OD-H column and OD guard column (3:97 iPrOH/hex, 1 mL/min flow rate); *endo* isomers *t*<sub>r</sub> = 22.9 min and 26.7 min.

**(3*R*,4*S*)-2-Benzyl-4-formyl-3-phenylisoxazolidine (Table 3, entry 11).** Prepared according to general procedure A from (*Z*)-*N*-benzylidenebenzylamine *N*-oxide (63 mg, 0.30 mmol), (5*S*)-5-benzyl-2,2,3-trimethylimidazolidin-4-one trifluoromethanesulfonic acid salt (**5**) (22 mg, 0.06 mmol), acrolein (71 μL, 1.2 mmol) and H<sub>2</sub>O (16 μL, 0.90 mmol) in CH<sub>3</sub>NO<sub>2</sub> (3.0 ml) at -18 °C over the course of 120 h to provide the title compound as a colorless oil in 80% yield (63 mg); 86:14 *endo:exo*. *Endo* isomer: IR (CH<sub>2</sub>Cl<sub>2</sub>) 2873, 1722, 1498, 1452, 1050 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.80 (d, *J* = 2.1 Hz, 1H, CHO), 7.27-7.51 (m, 10H, C<sub>6</sub>H<sub>5</sub> and CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 4.27-4.30 (m, 2H, CH<sub>2</sub>ON), 4.07 (d, *J* = 7.1 Hz, 1H, CHC<sub>6</sub>H<sub>5</sub>), 3.99 (d, *J* = 14.2 Hz, 1H, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 3.78 (d, *J* = 14.2 Hz, 1H, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 3.44 (m, 1H, CHCHO); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 198.4, 138.1, 137.1, 128.9, 128.6, 128.3, 128.2, 127.8, 127.3, 70.6, 65.8, 64.3, 59.6; LRMS (CI) *m/z* 267 (M)<sup>+</sup>; HRMS (CI) exact mass calcd for (C<sub>17</sub>H<sub>17</sub>NO<sub>2</sub>) requires *m/z* 267.1259, found *m/z* 267.1268; [α]<sub>D</sub> = +43.4 ° (*c* = 1.0, CHCl<sub>3</sub>). Diastereomeric ratios were determined by <sup>1</sup>H NMR analysis. A portion of the title compound was reduced to the corresponding primary alcohol (general procedure C) and purified by silica gel chromatography (3:7 EtOAc/hexane) for the determination of enantiomeric purity; *endo* 92% ee. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.19-7.51 (m, 10H, C<sub>6</sub>H<sub>5</sub> and CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 4.19 (dd, *J* = 8.2, 8.2 Hz, 1H, CH<sub>2</sub>ON), 3.94 (d, *J* = 14.3 Hz, 1H, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 3.88-3.92 (dd, *J* = 4.4, 8.2 Hz, 1H, CH<sub>2</sub>ON), 3.65-3.83 (m, 2H, CH<sub>2</sub>OH), 3.70 (d, *J* = 14.0 Hz, 1H, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 3.47 (d, *J* = 7.7 Hz, 1H, CHC<sub>6</sub>H<sub>5</sub>), 2.72-2.83 (m, 1H, CHCH<sub>2</sub>OH). Enantiomeric ratios were determined by HPLC with a Chiralcel AD column (1:24 EtOH/hexane, 1 mL/min flow rate); *endo* isomers *t*<sub>r</sub> = 15.8 min and 20.4 min.

**(3*R*,4*S*)-2-Benzyl-4-formyl-3-(4-methylphenyl)isoxazolidine (Table 3, entry 12).** Prepared according to general procedure B from (*Z*)-*N*-*para*-methylbenzylidenebenzylamine *N*-oxide (72 mg, 0.30 mmol), (5*S*)-5-benzyl-2,2,3-trimethylimidazolidin-4-one trifluoromethanesulfonic acid salt (**5**) (22 mg, 0.06 mmol), acrolein (71 μL, 1.2 mmol) followed

by 4 x 36  $\mu\text{L}$ , 0.60 mmol, over 24 h intervals),  $\text{H}_2\text{O}$  (16  $\mu\text{L}$ , 0.90 mmol), and in  $\text{CH}_3\text{NO}_2$  (3.0 ml) at  $-18^\circ\text{C}$  over the course of 112 h to provide the title compound as a colorless oil in 80% yield (66 mg) after silica gel chromatography (17:83 EtOAc/hexane); 85:15 *endo:exo*. *Endo* isomer: IR ( $\text{CH}_2\text{Cl}_2$ ) 2873, 1722, 1514, 1050  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  9.77 (d,  $J = 2.2$  Hz, 1H, CHO), 7.19–7.47 (m, 7H,  $\text{C}_6\text{H}_4\text{CH}_3$  and  $\text{CH}_2\text{C}_6\text{H}_5$ ), 4.24–4.28 (m, 2H,  $\text{CH}_2\text{ON}$ ), 3.97–4.02 (m, 2H, CHNO and  $\text{CH}_2\text{C}_6\text{H}_5$ ), 3.75 (d,  $J = 14.0$  Hz, 1H,  $\text{CH}_2\text{C}_6\text{H}_5$ ), 3.38–3.46 (m, 1H, CHCHO), 2.39 (s, 3H,  $\text{C}_6\text{H}_4\text{CH}_3$ );  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  199.1, 138.4, 137.5, 135.0, 129.9, 128.9, 128.5, 128.0, 127.5, 70.9, 66.2, 64.6, 59.9, 21.6; LRMS (CI)  $m/z$  281 ( $\text{M}^+$ ); HRMS (CI) exact mass calcd for ( $\text{C}_{18}\text{H}_{19}\text{NO}_2$ ) requires  $m/z$  281.1416, found  $m/z$  281.1415;  $[\alpha]_{\text{D}} = +39.8^\circ$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ). Diastereomeric ratio was determined by  $^1\text{H}$  NMR analysis. A portion of the title compound was reduced to the corresponding primary alcohol (general procedure C) and purified by silica gel chromatography (3:7 EtOAc/hexane) for the determination of enantiomeric purity; *endo* 90% ee.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.16–7.37 (m, 9H,  $\text{C}_6\text{H}_4\text{CH}_3$  and  $\text{CH}_2\text{C}_6\text{H}_5$ ), 4.18 (dd,  $J = 8.2, 8.2$  Hz, 1H,  $\text{CH}_2\text{ON}$ ), 3.94 (d,  $J = 14.8$  Hz, 1H,  $\text{CH}_2\text{C}_6\text{H}_5$ ), 3.87–3.91 (dd,  $J = 4.3, 8.1$  Hz, 1H,  $\text{CH}_2\text{ON}$ ), 3.67–3.82 (m, 2H,  $\text{CH}_2\text{OH}$ ), 3.65 (d,  $J = 14.3$  Hz, 1H,  $\text{CH}_2\text{C}_6\text{H}_5$ ), 3.44 (d,  $J = 7.7$  Hz, 1H,  $\text{CHC}_6\text{H}_4\text{CH}_3$ ), 2.70–2.81 (m, 1H,  $\text{CHCH}_2\text{OH}$ ), 2.35 (s, 3H,  $\text{C}_6\text{H}_4\text{CH}_3$ ). Enantiomeric ratios were determined by HPLC with Chiralcel AD column and AD guard column (1:9 EtOH/hexane, 1 mL/min flow rate); *endo* isomers  $t_r = 9.1$  min and 10.0 min.

**(3*R*,4*S*)-2-Benzyl-4-formyl-3-(4-chlorophenyl)isoxazolidine (Table 3, entry 13).**

Prepared according to general procedure B from (*Z*)-*N*-*para*-chlorobenzylidenebenzylamine *N*-oxide (74 mg, 0.30 mmol), (*5S*)-5-benzyl-2,2,3-trimethylimidazolidin-4-one trifluoromethanesulfonic acid salt (**5**) (22 mg, 0.06 mmol), acrolein (71  $\mu\text{L}$ , 1.2 mmol followed by 3 x 36  $\mu\text{L}$ , 0.60 mmol, over 24 h intervals) and  $\text{H}_2\text{O}$  (16  $\mu\text{L}$ , 0.90 mmol) in  $\text{CH}_3\text{NO}_2$  (3.0 ml) at  $-18^\circ\text{C}$  over the course of 96 h to provide the title compound as a colorless oil in 80% yield (70 mg) after silica gel chromatography (1:4 EtOAc/hexane); 80:20 *endo:exo*. *Endo* isomer: IR ( $\text{CH}_2\text{Cl}_2$ ) 2881, 1722, 1599, 1491  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.78 (d,  $J = 2.0$  Hz, 1H, CHO), 7.26–7.44 (m, 9H,  $\text{C}_6\text{H}_4\text{Cl}$  and  $\text{CH}_2\text{C}_6\text{H}_5$ ), 4.27–4.29 (m, 2H,  $\text{CH}_2\text{ON}$ ), 4.08 (d,  $J = 7.0$  Hz, 1H,  $\text{CHC}_6\text{H}_4\text{Cl}$ ), 3.96 (d,  $J = 14.0$  Hz, 1H,  $\text{CH}_2\text{C}_6\text{H}_5$ ), 3.80 (d,  $J = 14.2$  Hz, 1H,  $\text{CH}_2\text{C}_6\text{H}_5$ ), 3.34–3.40 (m, 1H, CHCHO);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  198.4, 136.8, 134.0, 136.7, 129.1, 128.7, 128.2, 127.4, 129.1, 69.6, 65.8, 64.3, 59.7; LRMS (CI)  $m/z$  ( $\text{M}$ ); HRMS (CI) exact mass

calcd for (C<sub>17</sub>H<sub>16</sub>ClNO<sub>2</sub>) requires  $m/z$  301.0870 (M)<sup>+</sup>, found  $m/z$  301.0862;  $[\alpha]_D = +36.5^\circ$  (c = 1.0, CHCl<sub>3</sub>). Diastereomeric ratios were determined by <sup>1</sup>H NMR analysis. A portion of the title compound was reduced to the corresponding primary alcohol (general procedure C) and purified by silica gel chromatography (2:3 EtOAc/hexane) for the determination of enantiomeric purity; *endo* 91% ee. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.04–7.42 (m, 9H, C<sub>6</sub>H<sub>4</sub>Cl and CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 4.17 (dd,  $J = 8.2, 8.2$  Hz, 1H, CH<sub>2</sub>ON), 3.91 (d,  $J = 14.0$  Hz, 1H, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 3.86–3.90 (dd,  $J = 4.7, 8.2$  Hz, 1H, CH<sub>2</sub>ON), 3.72–3.78 (m, 2H, CH<sub>2</sub>OH), 3.72 (d,  $J = 14.0$  Hz, 1H, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 3.49 (d,  $J = 7.7$  Hz, 1H, CHC<sub>6</sub>H<sub>4</sub>Cl), 2.68–2.76 (m, 1H, CHCH<sub>2</sub>OH). Enantiomeric ratios were determined by HPLC with a Chiralcel AD column and AD guard column (1:19 *i*PrOH/hexane, 1 mL/min flow rate); *endo* isomers  $t_r = 20.7$  min and 23.5 min.

**(3R,4S)-2-Benzyl-4-formyl-3-naphthylisoxazolidine (Table 3, entry 14).** Prepared according to general procedure A from (*Z*)-*N*-2-naphthylidenebenzylamine *N*-oxide (78 mg, 0.30 mmol), (*5S*)-5-benzyl-2,2,3-trimethylimidazolidin-4-one trifluoromethanesulfonic acid salt (**5**) (22 mg, 0.06 mmol), acrolein (71  $\mu$ L, 1.2 mmol), H<sub>2</sub>O (16  $\mu$ L, 0.90 mmol), and in CH<sub>3</sub>NO<sub>2</sub> (3.0 ml) at  $-18^\circ\text{C}$  over the course of 112 h to provide the title compound as a colorless oil in 82% yield (75 mg) after silica gel chromatography (1:3 EtOAc/hexane); 81:19 *endo:exo*. *Endo* isomer: IR (CH<sub>2</sub>Cl<sub>2</sub>) 3059, 2835, 1722, 1498, 1607 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  9.83 (d,  $J = 2.0$  Hz, 1H, CHO), 7.27–7.95 (m, 12H, C<sub>10</sub>H<sub>7</sub> and CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 4.32–4.36 (m, 2H, CH<sub>2</sub>ON), 4.28 (d,  $J = 7.0$  Hz, 1H, CHC<sub>10</sub>H<sub>7</sub>), 4.01 (d,  $J = 14.1$  Hz, 1H, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 3.85 (d,  $J = 14.2$  Hz, 1H, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 3.53 (m, 1H, CHCHO); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  198.7, 137.1, 135.4, 133.3, 133.2, 128.9, 128.7, 128.2, 127.9, 127.8, 127.7, 127.3, 127.2, 126.4, 126.3, 125.0, 110.4, 70.8, 65.9, 64.2, 59.7; LRMS (CI)  $m/z$  317 (M)<sup>+</sup>; HRMS (CI) exact mass calcd for (C<sub>21</sub>H<sub>19</sub>NO<sub>2</sub>) requires  $m/z$  317.1416, found  $m/z$  317.1416;  $[\alpha]_D = +20.3^\circ$  (c = 1.0, CHCl<sub>3</sub>). Diastereomeric ratio was determined by <sup>1</sup>H NMR analysis. A portion of the title compound was reduced to the corresponding primary alcohol (general procedure C) and purified by silica gel chromatography (3:7 EtOAc/hexane) for the determination of enantiomeric purity; *endo* 90% ee. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.21–7.89 (m, 12H, C<sub>10</sub>H<sub>7</sub> and CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 4.26 (dd,  $J = 8.2, 8.2$  Hz, 1H, CH<sub>2</sub>ON), 3.98 (d,  $J = 14.0$  Hz, 1H, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 3.93–3.98 (dd,  $J = 4.6, 8.2$  Hz, 1H, CH<sub>2</sub>ON), 3.75 (d,  $J = 14.0$ , 1H, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 3.72–3.83 (m, 2H, CH<sub>2</sub>OH), 3.67 (d,  $J = 7.7$  Hz, 1H, CHC<sub>10</sub>H<sub>7</sub>), 2.82–2.93 (m, 1H, CHCH<sub>2</sub>OH). Enantiomeric ratios were determined by HPLC with Chiralcel

AD column and AD guard column (1:9 EtOH/hexane, 1 mL/min flow rate); *endo* isomers  $t_r$  = 12.7 min and 17.5 min.

**(3*R*,4*S*)-2-Benzyl-4-formyl-3-(4-methoxyphenyl)isoxazolidine (Table 3, entry 15).**

Prepared according to general procedure B from (*Z*)-*N*-*para*-methoxybenzylidenebenzylamine *N*-oxide (72 mg, 0.30 mmol), (*5S*)-5-benzyl-2,2,3-trimethylimidazolidin-4-one trifluoromethanesulfonic acid salt (**5**) (22 mg, 0.06 mmol), acrolein (71  $\mu$ L, 1.2 mmol followed by 3 x 36  $\mu$ L, 0.60 mmol, over 24 h intervals), H<sub>2</sub>O (16  $\mu$ L, 0.90 mmol), and in CH<sub>3</sub>NO<sub>2</sub> (3.0 ml) at -18 °C over the course of 87 h to provide the title compound as a colorless oil in 83% yield (73 mg) after silica gel chromatography (3:7 EtOAc/hexane); 91:9 *endo:exo*. *Endo* isomer: IR (CH<sub>2</sub>Cl<sub>2</sub>) 2935, 1722, 1614, 1514, 1460, 1251 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  9.77 (d, *J* = 2.1 Hz, 1H, CHO), 7.26–7.42 (m, 7H, C<sub>6</sub>H<sub>4</sub>OCH<sub>3</sub> and CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 6.94 (d, *J* = 8.7 Hz, 2H, ortho C<sub>6</sub>H<sub>4</sub>OCH<sub>3</sub>), 4.22–4.28 (m, 2H, CH<sub>2</sub>ON), 3.96–4.00 (m, 2H, CHNO and CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 3.82 (s, 3H, OCH<sub>3</sub>), 3.73 (d, *J* = 14.2 Hz, 1H, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 3.40 (m, 1H, CHCHO); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  198.9, 159.6, 137.3, 129.6, 129.0, 128.6, 128.2, 127.2, 114.3, 70.3, 65.8, 64.1, 59.4, 55.2; LRMS (CI) *m/z* 297 (M)<sup>+</sup>; HRMS (CI) exact mass calcd for (C<sub>18</sub>H<sub>19</sub>NO<sub>3</sub>) requires *m/z* 297.1365, found *m/z* 297.1361. [ $\alpha$ ]<sub>D</sub> = +31.9 ° (c = 1.0, CHCl<sub>3</sub>). Diastereomeric ratio was determined by <sup>1</sup>H NMR analysis. A portion of the title compound was reduced to the corresponding primary alcohol (general procedure C) and purified by silica gel chromatography (2:3 EtOAc/hexane) for the determination of enantiomeric purity; *endo* 90% ee. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.19–7.40 (m, 7H, C<sub>6</sub>H<sub>4</sub>OCH<sub>3</sub> and CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 6.92 (d, *J* = 1.9 Hz, 2H, C<sub>6</sub>H<sub>4</sub>OCH<sub>3</sub>), 4.16 (dd, *J* = 8.2, 8.2 Hz, 1H, CH<sub>2</sub>ON), 3.90 (d, *J* = 14.3 Hz, 1H, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 3.87 (dd, *J* = 4.4, 8.2 Hz, 1H, CH<sub>2</sub>ON), 3.81 (s, 3H, C<sub>6</sub>H<sub>4</sub>OCH<sub>3</sub>), 3.66–3.79 (m, 2H, CH<sub>2</sub>OH), 3.65 (d, *J* = 14.3 Hz, 1H, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 3.42 (d, *J* = 7.6 Hz, 1H, CHC<sub>6</sub>H<sub>5</sub>OCH<sub>3</sub>), 2.69–2.80 (m, 1H, CHCH<sub>2</sub>OH). Enantiomeric ratios were determined by HPLC with Chiralcel AD column and AD guard column (2:23 *i*PrOH/hexane, 1 mL/min flow rate); *endo* isomers  $t_r$  = 15.4 min and 17.0 min.



provide (3*S*,4*R*,5*S*)-2-Benzyl-4-formyl-5-methyl-3-phenylisoxazolidine. A portion of this product was reduced to the corresponding primary alcohol (general procedure C) and purified by silica gel chromatography (3:7 EtOAc/hexane) for the determination of enantiomeric purity; *endo* 41% ee. Enantiomeric ratios were determined by HPLC with a Chiralcel OD-H column and OD guard column (1:39 *i*PrOH/hexane, 1 mL/min flow rate); *endo* isomers  $t_r = 59.3$  min (minor enantiomer) and 76.3 min (major enantiomer). The remainder of the product (59.4 mg, 0.21 mmol) was dissolved in *tert*-butanol (4.4 mL). To this solution was added 2-methyl-2-butene (1 mL, 90 mmol) and, dropwise, a solution of NaClO<sub>2</sub> (175 mg, 1.93 mmol) and NaH<sub>2</sub>PO<sub>4</sub> (203 mg, 1.47 mmol) in H<sub>2</sub>O (1.8 mL). The biphasic solution was stirred for 11 h. The reaction was concentrated, diluted with H<sub>2</sub>O (25 mL), and washed with hexanes (25 mL). The aqueous layer was acidified with 1*N* HCl to pH 2, and extracted with Et<sub>2</sub>O (2 x 30 mL). The combined organic layers were washed with cold H<sub>2</sub>O (15 mL), dried (Na<sub>2</sub>SO<sub>4</sub>), and concentrated. To this oil was added CH<sub>2</sub>Cl<sub>2</sub> (0.75 mL), 4-dimethylamino-pyridine (1.0 mg, 0.008 mmol), and 2-propanol (0.023 mL, 0.3 mmol). This solution was added to dicyclohexylcarbodiimide (19.3 mg, 0.09 mmol) and the reaction was stirred for 2 h at which time the mixture was filtered and concentrated. The resulting residue was taken up in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) and filtered again. The filtrate was then washed sequentially with 0.5*N* HCl (10 mL) and sat. aq. NaHCO<sub>3</sub> (10 mL), dried (Na<sub>2</sub>SO<sub>4</sub>), and concentrated. The resulting residue was purified by silica gel chromatography (1:9 EtOAc/hexane) to afford an oil that was identical in all respects to the compound (3*S*,4*R*,5*S*)-2-benzyl-4-formyl-5-methyl-3-phenylisoxazolidine isopropyl ester;<sup>4</sup>  $[\alpha]_D$  (literature) = -28.1 ° (c = 1.0, CHCl<sub>3</sub>);  $[\alpha]_D$  (found) = -7.4 ° (c = 1.0, CHCl<sub>3</sub>).

**(1*R*,2*R*,3*R*)-1-(Benzylamino)-2-(hydroxymethyl)-1-phenyl-butan-3-ol.** Following general procedure C, (3*R*,4*S*,5*R*)-2-benzyl-4-formyl-5-methyl-3-phenylisoxazolidine (Table 3, entry 1) (25.0 mg, 0.09 mmol), of known absolute configuration (*vide supra*), was reduced to the corresponding primary alcohol and purified by silica gel chromatography (3:7 EtOAc/hexane). The resulting oil was dissolved in EtOH (1.2 mL) and heated to reflux. Sodium metal (180 mg, 7.83 mmol) was added in 25 mg portions to the solution. Upon formation of a white solid (2.5 h), the reaction was cooled to room temperature and added to H<sub>2</sub>O (5 mL). The resulting mixture was diluted with EtOAc (10 mL), washed with NH<sub>4</sub>Cl (5 mL), and then extracted with EtOAc (3

<sup>4</sup> Gothelf, K. V., Thomsen, I., Jørgensen, K. A., *J. Am. Chem. Soc.*, 1996, 118, 59-64.



x 10 mL). The organic extracts were combined, dried ( $\text{Na}_2\text{SO}_4$ ), and concentrated. Purification of the resulting oil by silica gel chromatography (1:39  $\text{Et}_3\text{N}/\text{EtOAc}$ ) afforded (1*R*,2*R*,3*R*)-1-(benzylamino)-2-(hydroxymethyl)-1-phenyl-butan-3-ol as a white solid:  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.42–7.20 (m, 10H,  $\text{C}_6\text{H}_5$ ), 4.07 (dq,  $J = 2.2, 6.0$  Hz, 1H,  $\text{CHCH}_3$ ), 3.99 (d,  $J = 9.3$  Hz, 1H,  $\text{NCHC}_6\text{H}_5$ ), 3.60 (d,  $J = 12.6$  Hz, 1H,  $\text{CH}_2\text{C}_6\text{H}_5$ ), 3.54 (d,  $J = 12.6$  Hz, 1H,  $\text{CH}_2\text{C}_6\text{H}_5$ ), 3.52 (dd,  $J = 3.9, 11.3$  Hz, 1H,  $\text{CH}_2\text{OH}$ ), 3.19 (dd,  $J = 3.3, 11.3$  Hz, 1H,  $\text{CH}_2\text{OH}$ ), 1.74–1.66 (m, 1H,  $\text{CHCH}_2\text{OH}$ ), 1.25 (d,  $J = 6.3$  Hz, 3H,  $\text{CH}_3$ );  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  141.4, 139.0, 129.1, 128.8, 127.9, 127.6, 127.5, 69.6, 64.9, 61.6, 51.9, 51.7, 22.3;  $[\alpha]_D = +41.5^\circ$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ).

**Determination of the absolute configuration of (3*R*,4*S*,5*R*)-2-allyl-4-formyl-5-methyl-3-phenylisoxazolidine (Table 3, entry 2) by correlation with (1*R*,2*R*,3*R*)-1-(allylbenzylamino)-2-(hydroxymethyl)-1-phenyl-butan-3-ol.**

To a solution of (1*R*,2*R*,3*R*)-1-(Benzylamino)-2-(hydroxymethyl)-1-phenyl-butan-3-ol (23.0 mg, 0.08 mmol), of known absolute configuration (*vide supra*) and  $\text{K}_2\text{CO}_3$  (44.8 mg, 0.32 mmol) in 1 : 1  $\text{H}_2\text{O} : \text{CH}_3\text{CN}$  (0.5 mL : 0.5 mL), was added allyl bromide (0.05 mL, 0.32 mmol), and the resulting solution was stirred for 63 h. The reaction was extracted with  $\text{Et}_2\text{O}$  (3 x 10 mL). The organic extracts were combined, dried ( $\text{Na}_2\text{SO}_4$ ), and concentrated. The resulting oil was purified by silica gel chromatography (2:3  $\text{EtOAc}/\text{hexane}$ ) to afford (1*R*,2*R*,3*R*)-1-(allylbenzylamino)-2-(hydroxymethyl)-1-phenyl-butan-3-ol:  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.45–7.21 (m, 10H,  $\text{C}_6\text{H}_5$ ), 5.93–5.87 (m, 1H,  $\text{CH}_2=\text{CHCH}_2$ ), 5.25–5.21 (m, 2H,  $\text{CH}_2=\text{CH}$ ), 4.17–4.10 (m, 1H,  $\text{CHCH}_3$ ), 4.07 (d,  $J = 11.2$  Hz, 1H,  $\text{NCHC}_6\text{H}_5$ ), 4.02 (d,  $J = 13.7$  Hz, 1H,  $\text{CH}_2\text{C}_6\text{H}_5$ ), 3.55–3.49 (m, 2H,  $\text{CH}_2\text{OH}$ ,  $\text{CH}_2=\text{CHCH}_2\text{N}$ ), 3.31 (dd,  $J = 3.4, 11.3$  Hz, 1H,  $\text{CH}_2\text{OH}$ ), 2.95 (d,  $J = 13.7$  Hz, 1H,  $\text{CH}_2\text{C}_6\text{H}_5$ ), 2.55 (dd,  $J = 8.8, 13.2$  Hz, 1H,  $\text{CH}_2=\text{CHCH}_2\text{N}$ ), 2.26–2.22 (m, 1H,  $\text{CHCH}_2\text{OH}$ ), 1.33 (d,  $J = 6.3$  Hz, 3H,  $\text{CH}_3$ );  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  138.5, 135.7, 133.9, 130.1, 129.4, 128.9, 128.5, 128.0, 127.6, 119.1, 70.2, 65.0, 61.8, 54.4, 53.1, 46.1, 21.2;  $[\alpha]_D = +74.3^\circ$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ).

A solution of (3*R*,4*S*,5*R*)-2-allyl-4-formyl-5-methyl-3-phenylisoxazolidine (Table 3, entry 2) (51.0 mg, 0.22 mmol) was reduced to the corresponding primary alcohol (general procedure C) and purified by silica gel chromatography (3:7  $\text{EtOAc}/\text{hexane}$ ). The resulting oil (24.8 mg, 0.11 mmol) was dissolved in  $\text{EtOH}$  (3.5 mL) and heated to reflux. Sodium metal (150

mg, 6.52 mmol) was added in 25 mg portions to the solution. Upon formation of a white solid (3 h), the reaction was cooled to room temperature and added to H<sub>2</sub>O (5 mL). The resulting mixture was diluted with EtOAc (10 mL), washed with NH<sub>4</sub>Cl (5 mL), and then extracted with EtOAc (3 x 10 mL). The organic extracts were combined, dried (Na<sub>2</sub>SO<sub>4</sub>), and concentrated. Purification of the resulting oil by silica gel chromatography (4:21 Et<sub>3</sub>N/EtOAc) afforded a white solid. The solid (5.4 mg, 0.023 mmol) was dissolved in CH<sub>3</sub>CN (1.0 mL). To the stirring solution was added benzyl bromide (3.0 μL, 0.025 mmol) and K<sub>2</sub>CO<sub>3</sub> (5.7 mg, 0.041 mmol). The reaction was heated to reflux for 12 hours. The solution was then filtered and concentrated. The resulting residue was purified by silica gel chromatography (1:1 EtOAc/hexane) to afford an oil that was identical in all respects to the compound (1*R*,2*R*,3*R*)-1-(allylbenzylamino)-2-(hydroxymethyl)-1-phenyl-butan-3-ol (*vide supra*);  $[\alpha]_D^{25} = +72.1^\circ$  ( $c = 1.0$ , CHCl<sub>3</sub>).

**Determination of the absolute configuration of (3*R*,4*S*,5*R*)-2,5-dimethyl-4-formyl-3-phenylisoxazolidine (Table 3, entry 3) by correlation with (1*R*,2*R*,3*R*)-1-(benzylmethylamino)-2-(hydroxymethyl)-1-phenyl-butan-3-ol.**

To a solution of (1*R*,2*R*,3*R*)-1-(benzylamino)-2-(hydroxymethyl)-1-phenyl-butan-3-ol (26.8 mg, 0.09 mmol), of known absolute configuration (*vide supra*), and K<sub>2</sub>CO<sub>3</sub> (52.0 mg, 0.38 mmol) in CH<sub>3</sub>CN (1.5 mL) was added iodomethane (5.8 μL, 0.09 mmol) and the resulting mixture was stirred for 48h. The reaction was diluted with H<sub>2</sub>O (10 mL) and extracted with EtOAc (3 x 10 mL). The organic extracts were combined, dried (Na<sub>2</sub>SO<sub>4</sub>), and concentrated. The resulting oil was purified by silica gel chromatography (1:1 EtOAc/hexane) to afford (1*R*, 2*R*, 3*R*)-1-(benzylmethylamino)-2-(hydroxymethyl)-1-phenyl-butan-3-ol: <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.45–7.22 (m, 10H, C<sub>6</sub>H<sub>5</sub>), 4.24 (dq,  $J = 2.4, 6.4$  Hz, 1H, CHCH<sub>3</sub>), 4.14 (d,  $J = 11.2$  Hz, 1H, NCHC<sub>6</sub>H<sub>5</sub>), 3.61 (dd,  $J = 2.4, 11.8$  Hz, 1H, CH<sub>2</sub>OH), 3.48 (m, 2H, NCH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 3.37 (dd,  $J = 3.9, 11.7$  Hz, 1H, CH<sub>2</sub>OH), 2.20–2.13 (m, 1H, CHCH<sub>2</sub>OH), 2.12 (s, 3H, NCH<sub>3</sub>), 1.38 (d,  $J = 6.4$  Hz, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 138.1, 133.5, 130.1, 129.3, 128.9, 128.5, 128.1, 127.7, 70.3, 69.9, 61.7, 60.0, 45.9, 37.0, 21.9;  $[\alpha]_D^{25} = -10.3^\circ$  ( $c = 1.0$ , CHCl<sub>3</sub>).

A solution of (3*R*,4*S*,5*R*)-2,5-dimethyl-4-formyl-3-phenylisoxazolidine (Table 3, entry 3), (51.0 mg, 0.25 mmol) was reduced to the corresponding primary alcohol (general procedure C) and purified by silica gel chromatography (3:7 EtOAc/hexane). The resulting oil was dissolved in EtOH (5.0 mL) and heated to reflux. Sodium metal (180 mg, 7.83 mmol) was added in 25 mg

portions to the solution. Upon formation of a white solid (4 h), the reaction was cooled to room temperature and added to H<sub>2</sub>O (5 mL). The resulting mixture was diluted with EtOAc (10 mL), washed with NH<sub>4</sub>Cl (5 mL), and then extracted with EtOAc (3 x 10 mL). The organic extracts were combined, dried (Na<sub>2</sub>SO<sub>4</sub>), and concentrated. Purification of the resulting oil by silica gel chromatography (1:9 Et<sub>3</sub>N/EtOAc) afforded a white solid. The solid (9.1 mg, 0.047 mmol) was dissolved in CH<sub>3</sub>CN (1.0 mL). To the stirring solution was added benzyl bromide (5.8 μL, 0.048 mmol) and K<sub>2</sub>CO<sub>3</sub> (12.0 mg, 0.086 mmol). The reaction was heated to reflux for 14 h. The solution was then filtered and concentrated. The resulting residue was purified by silica gel chromatography (1.9:1 EtOAc/hexane) to afford a clear oil that was identical in all respects to the compound (1*R*,2*R*,3*R*)-1-(benzylmethylamino)-2-(hydroxymethyl)-1-phenyl-butan-3-ol (*vide supra*);  $[\alpha]_D = -8.4^\circ$  ( $c = 1.0$ , CHCl<sub>3</sub>).

**Determination of the absolute configuration of (3*R*,4*S*,5*R*)-2-benzyl-4-formyl-5-methyl-3-(4-chlorophenyl) isoxazolidine (Table 3, entry 4) by correlation with (1*R*,2*R*,3*R*)-1-(benzylamino)-2-(hydroxymethyl)-1-phenyl-butan-3-ol.**

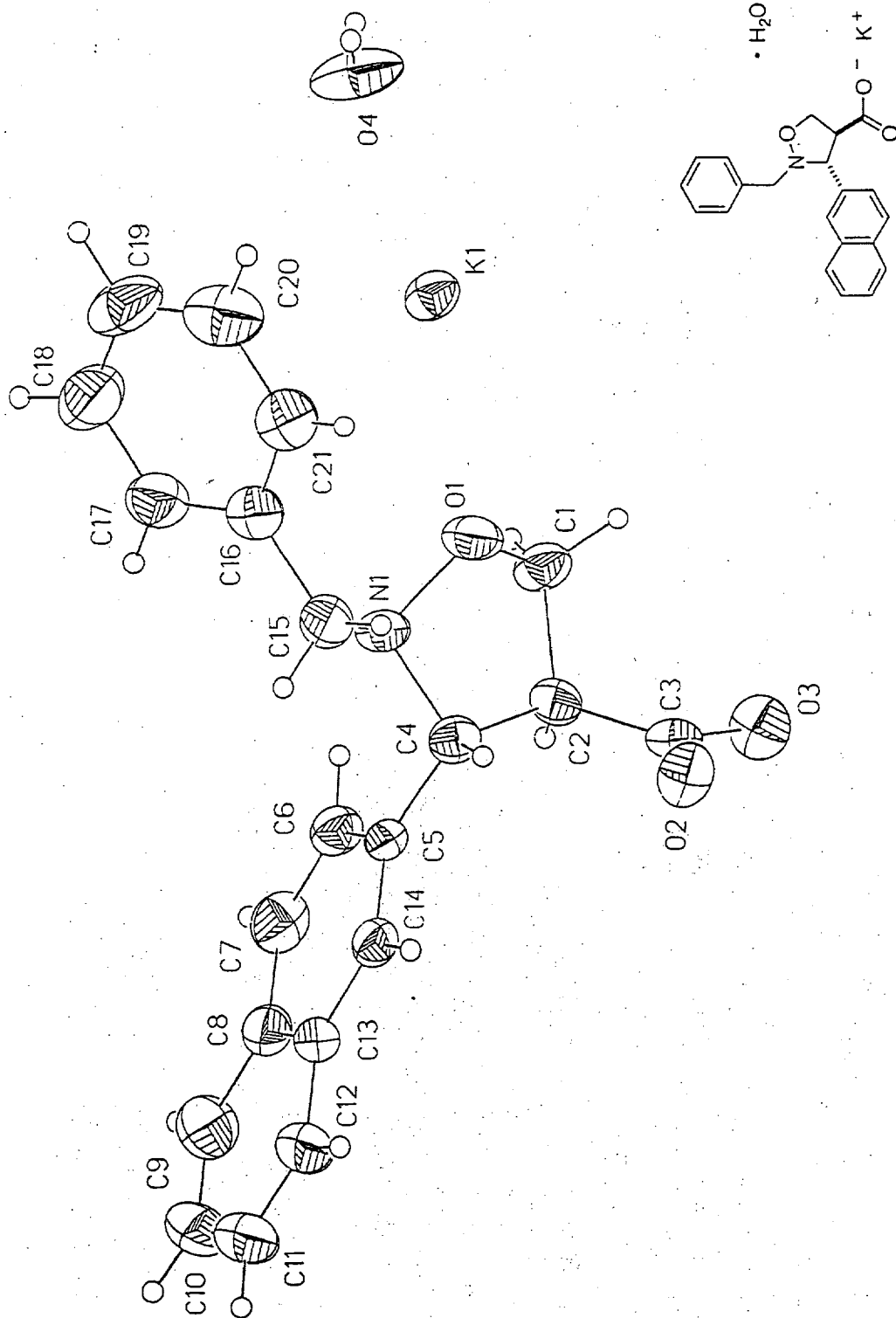
Following general procedure C, a solution of (3*R*,4*S*,5*R*)-2-benzyl-4-formyl-5-methyl-3-(4-chlorophenyl) isoxazolidine (Table 3, entry 4), (25.0 mg, 0.08 mmol) was reduced to the corresponding primary alcohol and purified by silica gel chromatography (3:7 EtOAc/hexane). The resulting oil was dissolved in EtOH (1.2 mL) and heated to reflux. Sodium metal (180 mg, 7.82 mmol) was added in 25 mg portions to the solution. Upon formation of a white solid (2 h), the reaction was cooled to room temperature and added to H<sub>2</sub>O (5 mL). The resulting mixture was diluted with EtOAc (10 mL), washed with NH<sub>4</sub>Cl (5 mL), and then extracted with EtOAc (3 x 10 mL). The organic extracts were combined, dried (Na<sub>2</sub>SO<sub>4</sub>), and concentrated. Purification of the resulting oil by silica gel chromatography (1:39 Et<sub>3</sub>N/EtOAc) afforded a white solid that was identical in all respects to the compound (1*R*,2*R*,3*R*)-1-(benzylamino)-2-(hydroxymethyl)-1-phenyl-butan-3-ol (*vide supra*);  $[\alpha]_D = +35.5^\circ$  ( $c = 1.0$ , CHCl<sub>3</sub>).

**Determination of the absolute configuration of (3*R*,4*S*)-2-benzyl-4-formyl-3-phenylisoxazolidine (Table 3, entry 11) by correlation with (S)-3-benzylamino-3-phenylpropan-1-ol.** To Wilkinson's catalyst (72.2 mg, 0.078 mmol) was added a solution of (3*R*,4*S*)-2-benzyl-4-formyl-3-phenylisoxazolidine (Table 3, entry 11) (20.4 mg, 0.078 mmol) in degassed

benzene (3.5 mL). The stirring solution was heated to reflux under a nitrogen atmosphere. After 20 h, the reaction was cooled to room temperature and H<sub>2</sub>O (10 mL) was added. The mixture was extracted with Et<sub>2</sub>O (3 x 15 mL), dried (Na<sub>2</sub>SO<sub>4</sub>), and concentrated to give a red oil which was purified by silica gel chromatography (1:9 EtOAc/hexane). The resulting residue was dissolved in EtOH (2 mL) and heated to reflux. Sodium metal (120 mg, 5.22 mmol) was added in 25 mg portions to the solution. Upon formation of a white solid (4 h), the reaction was cooled to room temperature and added to H<sub>2</sub>O (5 mL). The resulting mixture was diluted with EtOAc (10 mL), washed with NH<sub>4</sub>Cl (5 mL), and then extracted with EtOAc (3 x 10 mL). The organic extracts were combined, dried (Na<sub>2</sub>SO<sub>4</sub>), and concentrated. Purification of the resulting residue by silica gel chromatography (EtOAc) afforded an oil that was identical in all respects to the compound (*S*)-3-benzylamino-3-phenyl-propan-1-ol;<sup>5</sup>  $[\alpha]_D$  (literature) =  $-24.7^\circ$  (c = 0.93, MeOH);  $[\alpha]_D$  (found) =  $+20.8^\circ$  (c = 0.93, MeOH).

**Determination of the relative configuration of (3*R*,4*S*)-2-benzyl-4-formyl-3-naphthylisoxazolidine (Table 3, entry 14) by X-ray crystallography.** To a solution of 2-Benzyl-4-formyl-3-naphthylisoxazolidine (54 mg, 0.18 mmol) *tert*-butanol (3.9 mL) was added 2-methyl-2-butene (1 mL, 90 mmol), followed by dropwise of a solution of NaClO<sub>2</sub> (152 mg, 1.69 mmol) and NaH<sub>2</sub>PO<sub>4</sub> (178 mg, 1.29 mmol) in H<sub>2</sub>O (1.7 mL). The biphasic solution was stirred for 12h. The reaction was then concentrated, diluted with H<sub>2</sub>O (10 mL) and EtOAc (10 mL), and extracted with EtOAc (2 x 10 mL). The combined organic extracts were washed with cold H<sub>2</sub>O, dried (Na<sub>2</sub>SO<sub>4</sub>), and concentrated. Purification of the resulting residue by silica gel chromatography (2:3 EtOAc/hexane) afforded a yellow oil which was subsequently taken up in methanol (0.5 mL) and cooled to 0 °C. To the reaction mixture was added 53 μL of a 1.7*N* solution of KOH in methanol. After stirring for 3 hours, the solution was concentrated and the resulting yellow solid was recrystallized from ethanol/THF to afford crystals suitable for single crystal X-ray diffraction.

<sup>5</sup> Shimizu, M.; Maruyama, S.; Suzuki, Y.; Fujisawa, T. *Heterocycles* 1997, 45, 1883.



**Table 1. Crystal data and structure refinement for WSJ01.**

Empirical formula	$[\text{C}_{21}\text{H}_{18}\text{NO}_3]^+ \text{K}^+ \text{H}_2\text{O}$
Formula weight	389.48
Crystallization Solvent	Ethanol/THF
Crystal Habit	Blade
Crystal size	0.31 x 0.25 x 0.11 mm <sup>3</sup>
Crystal color	Colorless

**Data Collection**

Preliminary Photos	Rotation	
Type of diffractometer	CCD area detector	
Wavelength	0.71073 Å MoK $\alpha$	
Data Collection Temperature	98(2) K	
$\theta$ range for 7998 reflections used in lattice determination	2.50 to 25.50°	
Unit cell dimensions	a = 6.7539(13) Å b = 8.2935(16) Å c = 34.251(7) Å	$\beta = 91.678(3)^\circ$
Volume	1917.7(6) Å <sup>3</sup>	
Z	4	
Crystal system	Monoclinic	
Space group	P2 <sub>1</sub> /n	
Density (calculated)	1.349 Mg/m <sup>3</sup>	
F(000)	816	
Data collection program	Bruker SMART	
$\theta$ range for data collection	2.38 to 28.67°	
Completeness to $\theta = 28.67^\circ$	92.4 %	
Index ranges	$-8 \leq h \leq 9, -10 \leq k \leq 10, -45 \leq l \leq 44$	
Data collection scan type	$\omega$ scans at 7 $\phi$ settings	
Data reduction program	Bruker SAINT v6.1	
Reflections collected	33077	
Independent reflections	4566 [ $R_{\text{int}} = 0.1032$ ]	
Absorption coefficient	0.303 mm <sup>-1</sup>	
Absorption correction	None	
Max. and min. transmission (theory)	0.9671 and 0.9105	

Table 1 (cont.)

## Structure solution and Refinement

Structure solution program	SHELXS-97 (Sheldrick, 1990)
Primary solution method	Direct methods
Secondary solution method	Difference Fourier map
Hydrogen placement	Difference Fourier map
Structure refinement program	SHELXL-97 (Sheldrick, 1997)
Refinement method	Full matrix least-squares on $F^2$
Data / restraints / parameters	4566 / 0 / 324
Treatment of hydrogen atoms	Unrestrained
Goodness-of-fit on $F^2$	1.798
Final R indices [ $I > 2\sigma(I)$ , 3026 reflections]	$R1 = 0.0733$ , $wR2 = 0.0929$
R indices (all data)	$R1 = 0.1131$ , $wR2 = 0.0960$
Type of weighting scheme used	Sigma
Weighting scheme used	$w = 1/\sigma^2(Fo^2)$
Max shift/error	0.000
Average shift/error	0.000
Largest diff. peak and hole	0.605 and -0.385 e.Å <sup>-3</sup>

## Special Refinement Details

Refinement of  $F^2$  against ALL reflections. The weighted R-factor ( $wR$ ) and goodness of fit ( $S$ ) are based on  $F^2$ , conventional R-factors ( $R$ ) are based on  $F$ , with  $F$  set to zero for negative  $F^2$ . The threshold expression of  $F^2 > 2\sigma(F^2)$  is used only for calculating R-factors(gt) etc. and is not relevant to the choice of reflections for refinement. R-factors based on  $F^2$  are statistically about twice as large as those based on  $F$ , and R-factors based on ALL data will be even larger.

All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.

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Table 2. Atomic coordinates ( $\times 10^4$ ) and equivalent isotropic displacement parameters ( $\text{\AA}^2 \times 10^3$ ) for WSJ01.  $U(\text{eq})$  is defined as the trace of the orthogonalized  $U^{\text{ij}}$  tensor.

	x	y	z	$U_{\text{eq}}$
K(1)	9902(1)	7017(1)	9649(1)	39(1)
O(1)	6333(3)	5665(2)	9377(1)	46(1)
O(2)	1388(3)	4094(2)	9634(1)	45(1)
O(3)	3030(2)	1983(2)	9870(1)	46(1)
O(4)	13167(4)	8714(3)	9781(1)	72(1)
N(1)	5728(3)	5485(3)	8958(1)	36(1)
C(1)	6302(4)	4064(4)	9509(1)	42(1)
C(2)	4406(4)	3321(3)	9330(1)	34(1)
C(3)	2798(4)	3142(3)	9630(1)	33(1)
C(4)	3909(4)	4476(3)	8992(1)	34(1)
C(5)	3433(4)	3665(3)	8609(1)	30(1)
C(6)	4816(4)	2617(3)	8443(1)	39(1)
C(7)	4389(5)	1804(4)	8110(1)	48(1)
C(8)	2529(4)	1988(4)	7911(1)	43(1)
C(9)	2041(6)	1171(5)	7562(1)	63(1)
C(10)	240(6)	1381(5)	7379(1)	75(1)
C(11)	-1143(5)	2419(6)	7541(1)	70(1)
C(12)	-736(4)	3218(5)	7878(1)	52(1)
C(13)	1128(4)	3038(4)	8076(1)	37(1)
C(14)	1639(4)	3859(3)	8424(1)	33(1)
C(15)	5256(4)	7128(4)	8838(1)	43(1)
C(16)	7090(4)	8137(3)	8809(1)	40(1)
C(17)	8462(5)	7830(4)	8522(1)	52(1)
C(18)	10192(5)	8717(5)	8506(1)	64(1)
C(19)	10583(6)	9911(5)	8772(1)	65(1)
C(20)	9263(6)	10220(4)	9058(1)	64(1)
C(21)	7510(5)	9346(4)	9074(1)	49(1)



Table 4. Bond lengths [Å] and angles [°] for WSJ01.

K(1)-O(2)#1	2.625(2)	C(15)-H(15B)	0.96(3)
K(1)-O(4)	2.644(2)	C(16)-C(21)	1.377(4)
K(1)-O(3)#2	2.743(2)	C(16)-C(17)	1.392(4)
K(1)-O(2)#2	2.789(2)	C(17)-C(18)	1.383(5)
K(1)-O(1)	2.7932(18)	C(17)-H(17)	0.95(4)
K(1)-C(3)#2	3.117(3)	C(18)-C(19)	1.366(5)
K(1)-C(21)	3.167(3)	C(18)-H(18)	1.02(3)
K(1)-C(20)	3.359(4)	C(19)-C(20)	1.368(6)
K(1)-C(1)	3.475(3)	C(19)-H(19)	0.98(3)
K(1)-C(16)	3.525(3)	C(20)-C(21)	1.391(5)
K(1)-K(1)#3	4.1212(14)	C(20)-H(20)	0.90(4)
O(1)-C(1)	1.403(3)	C(21)-H(21)	0.83(2)
O(1)-N(1)	1.486(3)		
O(2)-C(3)	1.237(3)	O(2)#1-K(1)-O(4)	100.22(8)
O(2)-K(1)#4	2.625(2)	O(2)#1-K(1)-O(3)#2	125.05(6)
O(2)-K(1)#2	2.789(2)	O(4)-K(1)-O(3)#2	110.44(8)
O(3)-C(3)	1.271(3)	O(2)#1-K(1)-O(2)#2	80.89(7)
O(3)-K(1)#2	2.743(2)	O(4)-K(1)-O(2)#2	107.79(8)
O(4)-H(4AA)	0.92(4)	O(3)#2-K(1)-O(2)#2	47.15(6)
O(4)-H(44B)	0.73(3)	O(2)#1-K(1)-O(1)	87.11(6)
N(1)-C(15)	1.457(4)	O(4)-K(1)-O(1)	167.96(7)
N(1)-C(4)	1.493(3)	O(3)#2-K(1)-O(1)	71.99(6)
C(1)-C(2)	1.531(4)	O(2)#2-K(1)-O(1)	82.67(6)
C(1)-H(1A)	0.96(2)	O(2)#1-K(1)-C(3)#2	102.09(7)
C(1)-H(1B)	1.05(3)	O(4)-K(1)-C(3)#2	113.03(8)
C(2)-C(3)	1.523(4)	O(3)#2-K(1)-C(3)#2	23.98(6)
C(2)-C(4)	1.534(4)	O(2)#2-K(1)-C(3)#2	23.35(6)
C(2)-H(2A)	1.03(3)	O(1)-K(1)-C(3)#2	74.22(6)
C(3)-K(1)#2	3.117(3)	O(2)#1-K(1)-C(21)	137.69(9)
C(4)-C(5)	1.500(4)	O(4)-K(1)-C(21)	100.92(9)
C(4)-H(4A)	0.99(2)	O(3)#2-K(1)-C(21)	79.94(9)
C(5)-C(14)	1.360(3)	O(2)#2-K(1)-C(21)	125.63(9)
C(5)-C(6)	1.408(4)	O(1)-K(1)-C(21)	67.55(7)
C(6)-C(7)	1.348(4)	C(3)#2-K(1)-C(21)	102.65(10)
C(6)-H(6)	0.97(2)	O(2)#1-K(1)-C(20)	139.56(10)
C(7)-C(8)	1.420(4)	O(4)-K(1)-C(20)	76.92(9)
C(7)-H(7)	0.95(3)	O(3)#2-K(1)-C(20)	92.34(10)
C(8)-C(9)	1.405(4)	O(2)#2-K(1)-C(20)	138.95(10)
C(8)-C(13)	1.415(4)	O(1)-K(1)-C(20)	91.29(7)
C(9)-C(10)	1.364(5)	C(3)#2-K(1)-C(20)	116.30(11)
C(9)-H(9)	0.96(3)	C(21)-K(1)-C(20)	24.38(9)
C(10)-C(11)	1.397(5)	O(2)#1-K(1)-C(1)	67.22(7)
C(10)-H(10)	0.95(4)	O(4)-K(1)-C(1)	167.33(8)
C(11)-C(12)	1.352(5)	O(3)#2-K(1)-C(1)	77.39(8)
C(11)-H(11)	0.93(3)	O(2)#2-K(1)-C(1)	69.73(7)
C(12)-C(13)	1.420(4)	O(1)-K(1)-C(1)	22.71(6)
C(12)-H(12)	1.02(3)	C(3)#2-K(1)-C(1)	69.90(8)
C(13)-C(14)	1.409(4)	C(21)-K(1)-C(1)	90.11(8)
C(14)-H(14)	0.88(2)	C(20)-K(1)-C(1)	113.42(8)
C(15)-C(16)	1.501(4)	O(2)#1-K(1)-C(16)	115.12(7)
C(15)-H(15A)	0.90(3)	O(4)-K(1)-C(16)	115.23(8)

O(3)#2-K(1)-C(16)	91.73(7)	C(5)-C(4)-C(2)	114.6(2)
O(2)#2-K(1)-C(16)	129.18(7)	N(1)-C(4)-H(4A)	106.9(12)
O(1)-K(1)-C(16)	52.75(6)	C(5)-C(4)-H(4A)	112.2(12)
C(3)#2-K(1)-C(16)	110.15(7)	C(2)-C(4)-H(4A)	108.4(13)
C(21)-K(1)-C(16)	22.96(8)	C(14)-C(5)-C(6)	118.5(3)
C(20)-K(1)-C(16)	40.86(8)	C(14)-C(5)-C(4)	121.3(3)
C(1)-K(1)-C(16)	73.44(7)	C(6)-C(5)-C(4)	120.2(2)
O(2)#1-K(1)-K(1)#3	41.93(4)	C(7)-C(6)-C(5)	121.5(3)
O(4)-K(1)-K(1)#3	108.65(6)	C(7)-C(6)-H(6)	120.4(16)
O(3)#2-K(1)-K(1)#3	84.58(5)	C(5)-C(6)-H(6)	117.9(16)
O(2)#2-K(1)-K(1)#3	38.96(4)	C(6)-C(7)-C(8)	121.1(3)
O(1)-K(1)-K(1)#3	83.20(4)	C(6)-C(7)-H(7)	121.3(17)
C(3)#2-K(1)-K(1)#3	60.80(6)	C(8)-C(7)-H(7)	117.6(17)
C(21)-K(1)-K(1)#3	149.91(7)	C(7)-C(8)-C(9)	122.6(3)
C(20)-K(1)-K(1)#3	174.29(7)	C(7)-C(8)-C(13)	117.9(3)
C(1)-K(1)-K(1)#3	61.24(5)	C(9)-C(8)-C(13)	119.5(3)
C(16)-K(1)-K(1)#3	134.26(5)	C(10)-C(9)-C(8)	120.9(4)
C(1)-O(1)-N(1)	102.03(19)	C(10)-C(9)-H(9)	119.2(17)
C(1)-O(1)-K(1)	107.07(14)	C(8)-C(9)-H(9)	119.8(17)
N(1)-O(1)-K(1)	124.89(14)	C(9)-C(10)-C(11)	119.6(4)
C(3)-O(2)-K(1)#4	152.17(17)	C(9)-C(10)-H(10)	119(2)
C(3)-O(2)-K(1)#2	93.37(16)	C(11)-C(10)-H(10)	121(2)
K(1)#4-O(2)-K(1)#2	99.11(6)	C(12)-C(11)-C(10)	121.3(3)
C(3)-O(3)-K(1)#2	94.74(16)	C(12)-C(11)-H(11)	117(2)
K(1)-O(4)-H(4AA)	117(2)	C(10)-C(11)-H(11)	121.7(19)
K(1)-O(4)-H(44B)	135(3)	C(11)-C(12)-C(13)	120.7(4)
H(4AA)-O(4)-H(44B)	104(3)	C(11)-C(12)-H(12)	126.3(15)
C(15)-N(1)-O(1)	103.4(2)	C(13)-C(12)-H(12)	112.9(15)
C(15)-N(1)-C(4)	111.8(2)	C(14)-C(13)-C(8)	119.0(2)
O(1)-N(1)-C(4)	100.70(19)	C(14)-C(13)-C(12)	123.0(3)
O(1)-C(1)-C(2)	105.8(2)	C(8)-C(13)-C(12)	118.0(3)
O(1)-C(1)-K(1)	50.22(11)	C(5)-C(14)-C(13)	122.0(3)
C(2)-C(1)-K(1)	155.79(19)	C(5)-C(14)-H(14)	118.4(13)
O(1)-C(1)-H(1A)	111.1(15)	C(13)-C(14)-H(14)	119.4(13)
C(2)-C(1)-H(1A)	113.9(14)	N(1)-C(15)-C(16)	111.5(2)
K(1)-C(1)-H(1A)	77.7(14)	N(1)-C(15)-H(15A)	105(2)
O(1)-C(1)-H(1B)	105.2(17)	C(16)-C(15)-H(15A)	111.2(18)
C(2)-C(1)-H(1B)	116.2(16)	N(1)-C(15)-H(15B)	109.8(16)
K(1)-C(1)-H(1B)	78.6(17)	C(16)-C(15)-H(15B)	111.5(15)
H(1A)-C(1)-H(1B)	104(2)	H(15A)-C(15)-H(15B)	107(2)
C(1)-C(2)-C(3)	112.1(2)	C(21)-C(16)-C(17)	118.0(3)
C(1)-C(2)-C(4)	102.2(2)	C(21)-C(16)-C(15)	121.1(3)
C(3)-C(2)-C(4)	115.2(2)	C(17)-C(16)-C(15)	120.8(3)
C(1)-C(2)-H(2A)	109.9(13)	C(21)-C(16)-K(1)	63.76(15)
C(3)-C(2)-H(2A)	108.7(15)	C(17)-C(16)-K(1)	99.94(17)
C(4)-C(2)-H(2A)	108.5(14)	C(15)-C(16)-K(1)	103.01(17)
O(2)-C(3)-O(3)	123.8(3)	C(18)-C(17)-C(16)	120.8(4)
O(2)-C(3)-C(2)	120.6(2)	C(18)-C(17)-H(17)	120(2)
O(3)-C(3)-C(2)	115.6(2)	C(16)-C(17)-H(17)	119(2)
O(2)-C(3)-K(1)#2	63.28(14)	C(19)-C(18)-C(17)	120.3(4)
O(3)-C(3)-K(1)#2	61.28(14)	C(19)-C(18)-H(18)	124.6(18)
C(2)-C(3)-K(1)#2	169.60(15)	C(17)-C(18)-H(18)	115.0(18)
N(1)-C(4)-C(5)	109.9(2)	C(18)-C(19)-C(20)	119.8(4)
N(1)-C(4)-C(2)	104.23(19)	C(18)-C(19)-H(19)	120.3(19)

C(20)-C(19)-H(19)	119.9(19)	C(20)-C(21)-C(16)	120.9(4)
C(21)-C(20)-C(19)	120.2(4)	C(20)-C(21)-K(1)	85.54(18)
C(21)-C(20)-K(1)	70.07(18)	C(16)-C(21)-K(1)	93.29(18)
C(19)-C(20)-K(1)	102.0(2)	C(20)-C(21)-H(21)	119.8(18)
C(21)-C(20)-H(20)	119(2)	C(16)-C(21)-H(21)	119.3(18)
C(19)-C(20)-H(20)	121(2)	K(1)-C(21)-H(21)	91.0(17)
K(1)-C(20)-H(20)	98(2)		

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Symmetry transformations used to generate equivalent atoms:

#1  $x+1, y, z$

#2  $-x+1, -y+1, -z+2$

#3  $-x+2, -y+1, -z+2$

#4  $x-1, y, z$

Table 5. Anisotropic displacement parameters ( $\text{\AA}^2 \times 10^4$ ) for WSJ01. The anisotropic displacement factor exponent takes the form:  $-2\pi^2 [ h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12} ]$

	$U^{11}$	$U^{22}$	$U^{33}$	$U^{23}$	$U^{13}$	$U^{12}$
K(1)	298(3)	364(3)	490(4)	71(3)	-36(3)	-18(3)
O(1)	451(12)	431(13)	483(13)	54(10)	-191(10)	-98(10)
O(2)	347(10)	452(12)	548(13)	134(10)	66(9)	138(10)
O(3)	472(11)	368(11)	527(12)	73(11)	12(9)	88(10)
O(4)	414(14)	412(15)	1310(30)	64(15)	-340(16)	-46(12)
N(1)	313(12)	328(13)	429(15)	15(11)	-91(11)	-55(10)
C(1)	276(16)	442(19)	530(20)	80(16)	-59(15)	-18(14)
C(2)	315(15)	353(18)	344(16)	7(13)	-65(12)	32(12)
C(3)	290(14)	312(15)	382(16)	-44(14)	-77(12)	-45(13)
C(4)	271(14)	344(16)	397(18)	-27(14)	-8(13)	20(13)
C(5)	277(14)	313(15)	298(15)	30(12)	-12(12)	-73(12)
C(6)	296(15)	442(19)	434(18)	-20(14)	17(14)	-9(13)
C(7)	447(18)	454(19)	540(20)	-89(18)	122(16)	13(16)
C(8)	463(16)	481(18)	358(17)	-70(16)	66(14)	-147(16)
C(9)	650(20)	760(30)	490(20)	-200(20)	108(19)	-100(20)
C(10)	720(30)	1100(40)	420(20)	-260(20)	-20(20)	-320(20)
C(11)	480(20)	1130(40)	470(20)	-80(20)	-100(19)	-190(20)
C(12)	417(18)	700(20)	420(19)	-19(19)	-73(15)	-58(18)
C(13)	354(15)	438(17)	320(15)	3(15)	-10(12)	-94(15)
C(14)	273(15)	363(16)	347(17)	18(14)	30(13)	-12(13)
C(15)	350(16)	510(20)	421(19)	96(17)	-63(15)	23(16)
C(16)	415(16)	306(15)	457(18)	79(15)	-77(14)	41(14)
C(17)	500(20)	560(20)	510(20)	40(20)	-89(17)	-51(18)
C(18)	510(20)	680(30)	730(30)	180(20)	10(20)	-100(20)
C(19)	480(20)	530(20)	920(30)	320(20)	-170(20)	-170(20)
C(20)	740(30)	330(20)	820(30)	50(20)	-270(20)	-25(19)
C(21)	470(20)	430(20)	570(20)	77(18)	-46(19)	62(17)

Table 6. Hydrogen coordinates ( $\times 10^4$ ) and isotropic displacement parameters ( $\text{\AA}^2 \times 10^3$ ) for WSJ01.

	x	y	z	$U_{iso}$
H(1A)	7490(40)	3500(30)	9442(7)	31(7)
H(1B)	6380(40)	4140(40)	9815(10)	64(10)
H(2A)	4710(30)	2200(40)	9216(7)	48(8)
H(4A)	2830(30)	5210(30)	9073(6)	17(6)
H(6)	6130(40)	2550(30)	8565(7)	47(8)
H(7)	5300(40)	1070(40)	8005(8)	54(9)
H(9)	2960(40)	420(40)	7456(9)	53(10)
H(10)	-10(50)	870(50)	7134(12)	99(13)
H(11)	-2380(40)	2590(40)	7423(9)	58(9)
H(12)	-1630(40)	4020(30)	8009(8)	43(8)
H(14)	740(30)	4460(30)	8538(6)	10(6)
H(15A)	4620(40)	7040(40)	8604(8)	49(8)
H(15B)	4340(40)	7590(30)	9014(7)	36(8)
H(17)	8190(40)	7000(40)	8337(10)	79(12)
H(18)	11090(40)	8420(40)	8283(10)	65(10)
H(19)	11810(40)	10540(40)	8760(9)	65(10)
H(20)	9510(50)	11000(40)	9238(10)	73(12)
H(21)	6700(30)	9550(30)	9246(7)	20(8)
H(4AA)	13020(50)	9790(50)	9838(11)	95(15)
H(44B)	14180(50)	8520(40)	9846(10)	69(13)

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Table 7. Hydrogen bonds for WSJ01 [ $\text{\AA}$  and  $^\circ$ ].

D-H...A	d(D-H)	d(H...A)	d(D...A)	$\angle$ (DHA)
O(4)-H(4AA)...O(3)#5	0.92(4)	1.82(4)	2.730(3)	169(4)
O(4)-H(44B)...O(3)#3	0.73(3)	2.14(3)	2.861(3)	171(4)

Symmetry transformations used to generate equivalent atoms:

#1  $x+1, y, z$ #2  $-x+1, -y+1, -z+2$ #3  $-x+2, -y+1, -z+2$ #4  $x-1, y, z$ #5  $x+1, y+1, z$