Practical Modifications and Applications of the Sharpless Asymmetric Aminohydroxylation in the One-Pot Preparation of Chiral Oxazolidin-2-ones

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Supporting Information

Experimental Section

Melting points were determined by using the Thomas-Hoover capillary melting point apparatus and were uncorrected. IR spectra were obtained as thin films on disposable, poly(tetrafluoroethylene) cards on Nicolet Magna-IR spectrometer 550. ^{1}H and ^{13}C spectra were recorded on a Bruker AVANCE-400 NMR spectrometer (operating at 400 and 100 MHz, respectively), and the chemical shifts were reported as ppm (δ unit) downfield from TMS. Coupling constants (*J*) are reported in Hz. Elemental analyses were performed by Quantitative Technologies Inc., Whitehouse, NJ. Chiral assays were performed by SFC using the following conditions: Chiralcel OD-H column, 25 cm, 300 bar, 1.5 mL/min, 35 C, 3% - 7% MeOH at 0.1%/min, at 210 nm.

General Procedure for Synthesis of Oxazolidinones. A 250 mL round-bottom flask was charged with distilled water (72 mL) and sodium hydroxide (40 mmol) and stirred to dissolve. A 2 mL portion of this solution was used to put potassium osmate (VI) oxide hydrate (0.3 mmol) into solution in a separate vial. n-PrOH (36 mL), urethane (40 mmol), and 1,3-dichloro-5,5-dimethylhydantoin (20 mmol) were added to the remaining NaOH solution. In a separate flask, the olefin (13 mmol) was taken up in n-PrOH (10mL) and the ligand, DHQ_2(PHAL) or $DHQD_2$(PHAL) (0.3 mmol) was added. This solution was added to the NaOH solution. n-PrOH (26 mL) was used to rinse the flask and was also added. The potassium osmate solution was then transferred to the reaction. The solution was stirred for 3 hours. Sodium hydroxide (40 mmol) was added and the solution was stirred for 1 hour. The reaction was quenched with sodium sulfite (24 mmol). Once diluted with water (60 mL), the organics were extracted with 1:1 MTBE: hexanes (1 x 240 mL). The yellow aqueous layer was removed and re-extracted with 1:1 MTBE: hexanes (1 x 120 mL). The organics were combined and washed with distilled water (5 x 60 mL). The organic layer was dried with $MgSO_4$, filtered, concentrated to an oil, diluted with toluene (50 mL), and concentrated again. The oil was then purified via chromatography (silica, 50:50 hexane: ethyl acetate) to separate the regioisomers. Each regioisomer was recrystallized in CH_2Cl_2/hexanes. The resulting suspension was filtered *in vacuo*, and the collected solid as dried *in vacuo* at 40 °C to afford the desired product as crystalline solid.

4(S)-Methyl-5(S)-phenyl-oxazolidin-2-one: mp 96-99 °C; IR (CH_2Cl_2) 3243, 2966, 2921, 1745, 1716 cm^{-1}; ^{1}H NMR (CD_3CN) δ 7.43 (m, 5H), 5.95 (s, 1H), 5.04 (d, *J* = 7.0, 1H), 3.78 (m, 1H), 1.30 (d, *J* = 6.0, 3H); ^{13}C NMR (CD_3CN) δ 158.1, 138.5, 128.9, 128.8, 126.2, 84.6, 56.1, 19.0.

5(S)-Methyl-4(S)-phenyl-oxazolidin-2-one: mp 119-22 °C; IR (CH_2Cl_2) 3242, 2969, 2904, 1751 cm^{-1}; ^{1}H NMR (CD_3CN) δ 7.41 (m, 5H), 6.16 (s, 1H), 4.49 (dd, *J* = 7.0, 1.0, 1H), 4.36

(m, 1H), 1.44 (d, *J* = 6.0, 3H); ^{13}C NMR (CD_3CN) δ 158.5, 139.9, 128.9, 128.4, 126.4, 81.1, 63.2, 18.5. Anal. Calcd for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.26; N, 7.90. Found: C, 67.65; H, 6.36; N, 7.75.

5(S)-Methyl-4(S)-(4-methoxy)phenyl-oxazolidin-2-one: mp 106-9 °C; IR (CH_2Cl_2) 3215, 2966, 2904, 2837, 1760, 1710 cm^{-1}; ^{1}H NMR (CD_3CN) δ 7.31 (d, *J* = 8.7 Hz, 2H), 6.96 (d, *J* = 8.7 Hz, 2H), 6.10 (s, 1H), 4.43 (d, *J* = 7.3 Hz, 1H), 4.33 (m, 1H), 3.80 (s, 3H), 1.41 (d, *J* = 6.1 Hz, 3H); ^{13}C NMR (CD_3CN) δ 159.8, 158.5, 131.6, 127.7, 117.3, 114.2, 81.2, 62.8, 55.0, 18.4. Anal. Calcd for $C_{11}H_{13}NO_3$: C, 63.76; H, 6.32; N, 6.76. Found: C, 63.73; H, 6.46; N, 6.70.

4(S)-Methyl-5(S)-(4-methoxy)phenyl-oxazolidin-2-one: mp 149-51 °C; IR (CH_2Cl_2) 3253, 3140, 2910, 2843, 1757, 1734 cm^{-1}; ^{1}H NMR (CD_3CN) δ 7.34 (d, *J* = 8.7 Hz, 2H), 6.96 (d, *J* = 8.8 Hz, 2H), 5.87 (s, 1H), 4.95 (d, *J* = 7.5 Hz, 1H), 3.79 (s, 3H), 3.77 (m, 1H), 1.25 (d, *J* = 6.1 Hz, 3H); ^{13}C NMR (CD_3CN) δ 160.2, 158.1, 130.2, 128.0, 117.3, 114.1, 84.6, 56.0, 55.0, 18.7.

4(S), 5(S)-Diphenyl-oxazolidin-2-one: mp 129-32 °C; IR (CH_2Cl_2) 3247, 3056, 3033, 1752 cm^{-1}; ^{1}H NMR (CD_3CN) δ 7.38 (m, 10H), 6.33 (s, 1H), 5.27 (d, *J* = 7.6 Hz, 1H), 4.82 (d, *J* = 7.5 Hz, 1H); ^{13}C NMR (CD_3CN) δ 158.1, 139.0, 137.7, 129.1, 129.0, 129.9, 128.7, 126.6, 126.5, 117.3, 85.6, 64.2. Anal. Calcd for $C_{15}H_{13}NO_2$: C, 75.30; H, 5.48; N, 5.85. Found: C, 74.90; H, 5.64; N, 5.80.

Ethyl-3(S)-carboethoxyamino-2(S)-hydroxy-3-(4-nitrophenyl)-propionate: IR (CH_2Cl_2) 3329, 2977, 2933, 2904, 1719, 1693, 1519 cm^{-1}; ^{1}H NMR (CD_3CN) δ 8.35 (m, 2H), 7.75 (m, 2H), 6.36 (m, 1H), 5.40 (m, 1H), 4.62 (m, 1H), 4.39 (m, 2H), 4.18 (m, 2H), 2.32 (s, 1H), 1.78 (m, 6H).