Supporting Information

Practical Synthesis of Optically Active Styrene Oxides via Reductive Transformation of 2-Chloroacetophenones with Chiral Rhodium Catalysts

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General methods. The NMR spectra were recorded in CDCl₃ with TMS (δ 0.00) as internal standard on BRUKER Advance 400 MHz. Infrared (IR) spectra were obtained by placing neat samples directly on the DiComp probe of an ASI Applied Systems React IR 1000 in situ IR instrument. Enantiomer excess of samples were determined by HPLC. Optical rotations were recorded on JASCO DIP-370. The mass spectra were performed by JEOL HICHTECH Co., Inc. Elemental analyses were performed by Tokyo Kasei Kogyo Co., Inc.

Preparation of 2-chloro-1-phenylethanol derivatives (3a-3m). A mixture of 2-chloroacetophenone **2a** (1 mmol) and catalyst **1a** (0.001 mmol) in a 5:2 mixture of formic acid to triethylamine (0.2 mL) and ethylacetate (1.0 mL) was stirred at 25 °C for 1 h. The reaction mixture was then passed through a SiO₂ column chromatography (eluent: 20% C₂H₅OAc in Hexane) to give 2-chlorophenylethanol **3a** in 93% yield. No impurities were detectable by NMR and HPLC. The ee value was determined by HPLC analysis. Absolute configuration was determined by the sign of rotation of the isolated product. Table 1 and Table 2 list experimental results on asymmetric transfer hydrogenation of **2a-2l**.

Large-scale preparation. 2-Chloro-*m*-chloroacetophenone **2c** (4.73 g, 25.0 mmol) was added to a solution of ethylacetate (31.3 mL) with catalyst **1a** (3.4 mg, 0.001 mmol), formic acid (1.03 mL, 26.3 mmol), and triethylamine (3.76 mL, 26.3 mmol). The reaction mixture was stirred at 25 °C for 2 h and washed with 2 M HCl aq. and brine. Organic layer was passed through a short SiO₂ and MgSO₄ column and concentrated to give **3c** (4.63 g, 97%). The 2-propanol solution (12.5 mL) of **3c** (4.60 g, 24.0 mmol) was treated with 4M NaOH aq. at 0 °C for 1 h. The mixture was extracted with hexane and water. Organic layer was dried over MgSO₄ and concentrated to give *m*-chlorostyrene oxide **4b** (3.54g, 96%).

Spectral data. Optically active 2-chloro-1-phenylethanol, **3a**¹, **3b**², **3c**³, **3d**², **3g**², **3h**², **3j**², **3k**⁴ and **3m**⁵ were identified by the spectral data described in the literature. Absolute configuration was determined by the sign of rotation of the isolated product.

2-Chloro-1-(*o*-methoxyphenyl)ethanol (3e). $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 3.60–3.90 (m, 2H), 3.85 (s, 3H), 5.05–5.15 (m, 1H), 6.85–7.45 (m, 4H), $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ 156.62, 129.60, 127.60, 121.50, 120.97, 110.83, 70.64, 55.72, 49.90; IR (neat, cm^{-1}), 3321, 1692, 1603, 1534, 1235, 1158; $[\alpha]^{20}_{\text{D}} +51.2$ (c 2.0, CHCl_3); MS(FAB), m/z 186 $[\text{M}]^+$, Anal. Calcd for $\text{C}_9\text{H}_{11}\text{ClO}_2$: C, 57.92; H, 5.94. Found; C, 57.79; H, 5.94.

2-Chloro-1-(*m*-methoxyphenyl)ethanol (3f). $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 3.58–3.73 (m, 2H), 3.99 (s, 3H) 4.82 (dd, 1H, $J = 8.6$ Hz, 3.6 Hz), 6.82–7.46 (m, 4H), $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ 160.22, 142.10, 130.10, 118.77, 114.32, 112.03, 74.38, 55.67, 51.13; IR (neat, cm^{-1}), 3329, 1603, 1586, 1258, 1150, 1040; $[\alpha]^{20}_{\text{D}} +41.5$ (c 2.0, CHCl_3); MS(FAB), m/z 186 $[\text{M}]^+$, Anal. Calcd for $\text{C}_9\text{H}_{11}\text{ClO}_2$: C, 57.92; H, 5.94. Found; C, 57.91; H, 5.97.

2-Chloro-1-(*m*-trifluoromethylphenyl)ethanol (3i). $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 3.42–3.91 (m, 2H), 4.94 (dd, 1H, $J = 8.4$ Hz, 3.4 Hz), 7.46–7.66 (m, 4H), $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ 141.33, 131.58, 131.26, 130.94, 129.86, 129.85, 129.52, 129.72, 129.67, 125.60, 125.56, 123.39, 123.35, 123.31, 123.27, 123.02, 73.78, 50.84 (observed complexity due to C–F splitting); IR (neat, cm^{-1}), 3334, 1328, 1164, 1119, 1071; $[\alpha]^{20}_{\text{D}} +42.8$ (c 1.0, CHCl_3); MS(FAB), m/z 224 $[\text{M}]^+$, Anal. Calcd for $\text{C}_9\text{H}_8\text{ClF}_3\text{O}$: C, 48.13; H, 3.59. Found; C, 47.97; H, 3.48.

Preparation of styrene oxides 4a–4c. The ethylacetate solution of **3a** (0.93 mmol) was treated with 2 M NaOH aqueous solution. (10.0 mL) at 0 °C for 1 h. After usual work up procedure, (*R*)-styrene oxide **4a** with 96.8% ee was obtained in 83% yield. The ee value was determined by HPLC analysis using a Chiralpak AS column (250 x 4.6 mm).

One-pot preparation of 4a. A mixture of 2-chloroacetophenone **2a** (5 mmol) and catalyst **1a** (0.005 mmol) in a 5:2 formic acid to triethylamine (1.0 mL) and 2-propanol (6.0 mL) was stirred at 25 °C for 2 h. The mixture was cooled to 0 °C. 2M NaOH aq. (10.0 mL) was added to the mixture and stirred at 0 °C for 1 h. The 2-propanol layer was extracted,

concentrated and diluted with hexane (10 mL). The hexane solution was washed with 1M HCl aq. (10 mL x 2) and passed through a short SiO₂ column chromatography (eluent: hexane) to give styrene oxide **4a** in 83% yield. The ee value was determined by HPLC analysis.

Spectral data. These compounds **4a**⁶, **4b**⁶ and **4c**⁶ were identified by the spectral data described in the literature.

References

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Table 1. Asymmetric Transfer Hydrogenation of 2-Chloroacetophenone, **2a**, Catalyzed by

Chiral Catalysts with a Mixture of HCOOH/N(C ₂ H ₅) ₃ or 2-propanol ^a							
catalyst	S/C	HCOOH/ N(C ₂ H ₅) ₃	solvent	time, h	yield, % ^b	ee, % ^b	config ^c
1a	1,000	5:2	CH ₃ CO ₂ C ₂ H ₅	1	99	97	<i>S</i>
1a	5,000	5:2	CH ₃ CO ₂ C ₂ H ₅	2	99	96	<i>S</i>
1a	1,000	5:2	CH ₃ CN	1	99	93	<i>S</i>
1a	1,000	5:2	THF	1	99	95	<i>S</i>
1a	1,000	5:2	acetone	1	99	96	<i>S</i>
1a	1,000	5:2	DMF	1	99	96	<i>S</i>
1a	1,000	5:2	CH ₂ Cl ₂	1	99	94	<i>S</i>
1a	1,000	5:2	toluene	1	99	92	<i>S</i>
1a	1,000	5:2	—	1	99	89	<i>S</i>
1a	100	2-propanol	2-propanol	14	94	98	<i>S</i>
1a	1,000	2-propanol	2-propanol	16	trace	—	
1b	1,000	1:1	CH ₃ CO ₂ C ₂ H ₅	24	36	91	<i>S</i>
1c	1,000	5:2	CH ₃ CO ₂ C ₂ H ₅	4	99	71	<i>S</i>

^aThe reaction of **2a** in a 1.0 M solution containing the (*R,R*)-Rh catalyst (**1a**) was conducted with a mixture of HCOOH and N(C₂H₅)₃ at 25 °C. ^bUnless otherwise noted, yields and ee values were determined by HPLC analysis using a Daicel Chiralcel OB or OB-H column. Configuration was determined from the sign of rotation of the isolated product. 2-Formyloxyacetophenone was formed as a main byproduct.

Table 2. Asymmetric Transfer Hydrogenation of the ring-substituted 2-chloroacetophenones (**2b-2l**) Catalyzed by Chiral Rh complex **1a** with a Mixture of HCOOH/N(C₂H₅)₃^a

product alcohol	R	yield, % ^b	ee, % ^b
3b	<i>o</i> -Cl	81	88
3c	<i>m</i> -Cl	93	95
3d	<i>p</i> -Cl	90	92
3e	<i>o</i> -CH ₃ O	90	95
3f	<i>m</i> -CH ₃ O	90	95
3g	<i>p</i> -CH ₃ O	94	94
3h	<i>m</i> -OH	93	95
3i	<i>m</i> -CF ₃	80	96
3j	<i>p</i> -MsNH	80	97
3k	<i>m</i> -CH ₃	92	96
3l	3',4'-OCH ₂ O	93	98

^aThe reaction of **2a** in a 1.0 M solution containing the (*R,R*)-Rh catalyst (**1a**) was conducted with a mixture of HCOOH and N(C₂H₅)₃ at 25 °C. ^bIsolated yields. ^cThe ee values were determined by HPLC analysis using a Daicel Chiralcel OB or OB-H column. Configuration was determined from the sign of rotation of the isolated product. 2-Formyloxyacetophenone was formed as a main byproduct.