SUPPORTING INFORMATION

Enantioselective Synthesis of Vicinal Halohydrins *via* Dynamic Kinetic Resolution

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General experimental methods. Solvents were purified and dried by standard procedures. Flash chromatography was carried out on silica-gel (0.040-0.063 mm or 0.015-0.040 mm). Melting points were recorded in a metal block and are uncorrected. ^{1}H NMR spectra were recorded at 300 MHz, 400 MHz or 500 MHz; ^{13}C NMR spectra were recorded at 75 MHz, 100 MHz or 125 MHz with the solvent peak used as the internal reference; ^{19}F NMR{^{1}H} spectra were recorded at 377 MHz with CF_3CO_2H as external reference. The diastereomeric excesses (de) of the products were determined by ^{1}H NMR and ^{19}F NMR and the enantiomeric excesses (ee) by HPLC on chiral stationary phases with ^{i}PrOH/hexane mixtures as the eluent. Mixtures of enantiomers required as references were prepared by mixing products obtained independently with (*R*,*R*)-**I** and (*S*,*S*)-**I**. The catalysts were synthesized according to described procedures.[1]

Transfer Hydrogenation of α-Halo Ketones.

Method A. To a solution of catalyst (*R,R*)-**I** or (*S*,*S*)-**I** (0.01 mmol) in HCO_2H/Et_3N mixture was added the α-haloketone (2 mmol) and the mixture was stirred at room temperature until

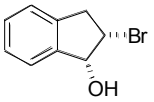
(1) (a) A. Fujii, S. Hashiguchi, N. Uematsu, T. Ikariya, R. Noyori, *J. Am. Chem. Soc.* **1996**, *118*, 2521-2522. (b) K. Haack, S. Hashiguchi, A. Fujii, T. Ikariya, R. Noyori, *Angew. Chem. Int. Ed. Engl*. **1997**, *36*, 285-288.

completion. The reaction mixture was then diluted with CH_2Cl_2 (20 mL) and washed with a satd. solution of $HNaCO_3$ (2 × 15 mL). The organic layer was dried and concentrated, and the residue was purified by flash chromatography

Method B. To a solution of the catalyst (*R,R*)-**I** or (*S*,*S*)-**I** (0.004-0.02 mmol), HCO_2Na (1.36 g, 20 mmol) and Bu_4NBr (2-30%) in a 1:1 H_2O/CH_2Cl_2 mixture (4-8 mL) was added the α-halo ketone (4 mmol) and the mixture was stirred at room temperature for 4-6 days. The reaction was then diluted with CH_2Cl_2 (10 mL), and the aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layer was dried and concentrated, and the residue was purified by flash chromatography.

Starting material, method used for the synthesis, catalyst, eluants, yields and spectral and analytical data for compounds **6-9**, **12**, **13**, and **18-21** are as follows:

(1*R*,2*S*)-2-Bromoindan-1-ol (6).



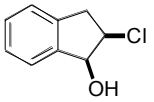
From 2-bromoindan-1-one **1**[2] (845 mg, 4 mmol) and following the method **B** with (*S,S*)-**I** as the catalyst; flash chromatography (1:8 EtOAc-hexane) gave 715 mg (84%) of **6** (>98% de, 99% ee) as a white solid: M.p. = 109-111 °C. $[\alpha]^{20}_D$ +59.4 (*c* 0.8, $CHCl_3$) [Lit.[3]: (1*S*,2*R*)-**6**: $[\alpha]^{25}_D$ –61.0 (*c* 0.62, $CHCl_3$)]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.45 (d, 1H, *J* = 9.6 Hz), 3.35 (dd, 1H, *J* = 16.8, 3.2 Hz), 3.33 (dd, 1H, *J* = 16.8, 5.2 Hz), 4.90 (m, 1H), 4.96 (dd, 1H, *J* = 9.6, 4.8 Hz), 7.23-7.45 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 40.5, 61.1, 76.6, 124.9, 125.3, 127.8, 129.0, 139.5, 141.9; mass spectrum (EI) *m/z* (rel intensity) 214 (M^+, 5), 212 (M^+, 5),

(2) H. M. Meshram, P. N. Reddy, K. Sadashiv, J. S. Yaday, *Tetrahedron Lett.* **2005**, *46*, 623-626.
(3) Bowers, N. I.; Boyd, D. R.; Sharma, N. D.; Goodrich, P. A.; Groocock, M. R.; Blacker, A. J.; Goode, P.; Dalton, H. *J. Chem. Soc., Perkins Trans 1*, **1999**, 1453-1461.

195 (17), 133 (100). HRMS calcd for C_9H_9OBr 213.9816 and 211.9837, found 213.9815 and 211.9832.

HPLC (Chiracel OB, 2-propanol/hexane 8:92, flow = 1 mL/min, T = 40 °C): t_R (1*S*,2*R*)-**6**, 7.17 min; (1*R*,2*S*)-**6,** 8.79 min.

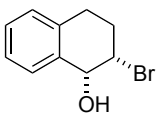
(1*S*,2*R*)-2-Chloroindan-1-ol (7).



From 2-chloroindan-1-one **2** (330 mg, 2 mmol) and following the method **A** with 2:1 HCO_2H/Et_3N mixture and (*R,R*)-**I** as the catalyst; flash chromatography (1:8 EtOAc-hexane) gave 282 mg (83%) of **7** (>98% de, 99% ee) as a white solid: M.p. = 110-112 °C. $[\alpha]^{20}_D$ −51.5 (*c* 0.9, $CHCl_3$) [Lit.[3] $[\alpha]^{25}_D$ −52.0 (*c* 0.6, $CHCl_3$)]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.52 (d, 1H, *J* = 9.5 Hz), 3.25 (dd, 1H, *J* = 17.0, 3.5 Hz), 3.33 (dd, 1H, *J* = 17.0, 5.5 Hz), 4.79 (td, 1H, *J* = 5.5, 3.5 Hz), 5.14 (dd, 1H, *J* = 9.5, 5.5 Hz), 7.23-7.45 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 39.7, 66.0, 76.4, 124.7, 125.1, 127.5, 128.8, 138.9, 141.5; mass spectrum (EI) *m/z* (rel intensity) 170 (M^+, 10), 168 (M^+, 40), 169 (35), 167 (100). HRMS calcd for C_9H_9OCl 168.0342, found 168.0344.

HPLC (Chiracel OB, 2-propanol/hexane 10:90, flow 1 mL/min, T = 30 °C): t_R (1*S*,2*R*)-**7**, 7.50 min; (1*R*,2*S*)-**6**, 9.88 min.

(1*R*,2*S*)-2-Bromo-1,2,3,4-tetrahydro-naphthalen-1-ol (8).

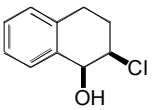


From 2-bromotetral-1-one **3** (900 mg, 4 mmol) and following the modified method **B** (using 384 mg, 30% mol of Bu_4NBr) with (*S,S*)-**I** as the catalyst; flash chromatography (1:10 EtOAc-hexane) gave 580 mg (64%) of **8** (>98% de, 96% ee) as a white solid: M. p. = 98-100 °C. $[\alpha]^{20}_D$ +7.25 (*c* 0.8, $CHCl_3$) ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.28 (m, 1H), 2.39 (d, 1H, *J* = 8.0 Hz), 2.50 (m, 1H), 2.85 (dt, 1H, *J* = 17.2, 6.8 Hz), 3.09 (dt, 1H, *J* = 17.2, 6.8 Hz), 4.69 (dt, 1H, *J* = 8.4, 3.2 Hz), 4.78 (d, 1H, *J* = 8.0 Hz), 7.09-7.47 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 27.8, 28.6, 58.8, 70.4, 126.8, 128.5, 128.8, 128.9, 134.9, 136.3; mass spectrum (EI) *m/z* (rel intensity) 228 (M^+, 4), 226 (M^+, 4) (100), 147 (100), 129 (77). HRMS calcd for $C_{10}H_{11}OBr$ 227.9973 and 225.9993, found 227.9966 and 225.9995.

HPLC (Chiracel OB, 2-propanol/hexane 1:99, flow 1 mL/min, T = 30 °C): t_R (1*R*,2*S*)-**8,** 23.74 min; (1*S*,2*R*)-**8** 29.46 min.

The opposite (1*S*,2*R*)-**8** enantiomer, obtained as above but using (*R*,*R*)-**I** as the catalyst, was crystallized from CH_2Cl_2-hexane and its absolute configuration was determined by single-crystal X-ray diffractometry.

(1*S*,2*R*)-2-Chloro-1,2,3,4-tetrahydro-naphthalen-1-ol (9).

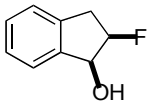


From 2-chlorotetral-1-one **4**[2] (360 mg, 2 mmol) and following the method **A** with 1.2:1 HCO_2H/Et_3N mixture and (*R,R*)-**I** as the catalyst; flash chromatography (1:14 EtOAc-hexane) gave 258 mg (71%) of **9** (>98% de, 99% ee) as a white solid: M. p. = 90-92 °C. $[\alpha]^{20}_D$ –8.2 (*c* 0.8, $CHCl_3$) ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.18 (dtd, 1H, *J* = 14.0, 7.0, 3.0 Hz), 2.37-2.44 (m, 2H), 2.82 (dt, 1H, *J* = 17.5, 7.0 Hz), 3.09 (dt, 1H, *J* = 17.0, 7.0 Hz), 4.53 (d, 1H, *J* = 9.0, 3.0 Hz), 4.83 (d, 1H, *J* = 3.0 Hz), 7.10-7.48 (m, 4H); ^{13}C NMR (125 MHz,

$CDCl_3$) δ 26.7, 27.6, 63.3, 70.1, 126.5, 128.2, 128.6, 128.9, 134.9, 135.8; mass spectrum (EI) *m/z* (rel intensity) 184 (M^+, 10), 182 (M^+, 36) (100), 167 (14), 165 (50), 129 (100). HRMS calcd for $C_{10}H_{11}OCl$ 182.0498, found 182.0496.

HPLC (Chiracel OB, 2-propanol/hexane 10:90, flow 1 mL/min, T = 30 °C): t_R (1*S*,2*R*)-**9**, 7.60 min; (1*R*,2*S*)-**9**, 10.09 min.

(1*S*,2*R*)-2-Fluoroindan-1-ol (12).

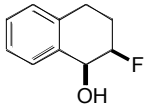


From 2-fluoroindan-1-one **10**[4] (300 mg, 2 mmol) and following the method **A** with 1.2:1 HCO_2H/Et_3N mixture and (*R,R*)-**I** as the catalyst; flash chromatography (1:8 EtOAc-hexane) gave 280 mg (92%) of **12** (>98% de, 92% ee) as a white solid: M.p. = 98-100 °C. $[\alpha]^{20}_D$ −67.4 (*c* 0.8, $CHCl_3$) ^1H NMR (500 MHz, $CDCl_3$) δ 2.42 (d, 1H, *J* = 9.5 Hz), 3.09 (ddd, 1H, $J_{H,F}$ = 34.5 Hz, *J* = 17.0, 4.5 Hz), 3.21 (dd, 1H, $J_{H,F}$ = 22.5 Hz, *J* = 17.0 Hz), 5.10 (ddd, 1H, $J_{H,F}$ = 18.5 Hz, *J* = 9.5, 4.5 Hz), 5.29 (dtd, 1H, $J_{H,F}$ = 54.0 Hz, *J* = 4.5, 1.5 Hz), 7.23-7.47 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 36.7 (d, $J_{C,F}$ = 22.0 Hz) , 76.4 ($J_{C,F}$ = 18.0 Hz), 94.4 ($J_{C,F}$ = 180.0 Hz), 124.6, 125.2, 127.5, 128.8, 138.4, 141.6; $^{19}F\{^1H\}$ NMR (377 MHz, $CDCl_3$) δ −125.1; mass spectrum (EI) *m/z* (rel intensity) 152 (M^+, 37), 151 (13), 135 (100), 91 (16). HRMS calcd for C_9H_9OF 152.0637, found 152.0632.

HPLC (Chiracel OB, 2-propanol/hexane 10:90, flow 1 mL/min, T = 30 °C): t_R (1*S*,2*R*)-**12** 8.42 min; (1*R*,2*S*)-**8,** 11.63 min.

(4) S. Stayber, M. Zupan, *Tetrahedron Lett.* **1996**, *37*, 3591-3594.

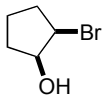
(1*S*,2*R*)-2-Fluoro-1,2,3,4-tetrahydro-naphthalen-1-ol (13).



From 2-fluorotetral-1-one **11**[4] (328 mg, 2 mmol) and following the modified method **A** with in 4 mL 1.2:1 HCO_2H/Et_3N mixture and (*R,R*)-**I** as the catalyst; flash chromatography (1:7 EtOAc-hexane) gave 325 mg (98%) of **13** (94% de, 97% ee) as a white solid: $[\alpha]^{20}_D$ −32.8 (*c* 1.16, $CHCl_3$) ^1H NMR (500 MHz, $CDCl_3$) δ 1.99 (m, 1H), 2.30-2.40 (m, 2H), 2.78 (dt, 1H, *J* = 17.0, 7.5 Hz), 3.03 (dtd, 1H, *J* = 17.0, 7.5, 2.0 Hz), 4.79 (d, 1H, $J_{H,F}$ = 17.5 Hz), 4.98 (ddt, 1H, $J_{H,F}$ = 50.0 Hz, *J* = 9.0, 3.0 Hz), 7.09-7.52 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.4 (d, $J_{C,F}$ = 19.9 Hz), 25.6 (d, $J_{C,F}$ = 8.9 Hz), 69.0 ($J_{C,F}$ = 19.0 Hz), 91.1 ($J_{C,F}$ = 172.5 Hz), 126.6, 128.2, 128.4, 129.2, 135.5, 135.7; $^{19}F\{^1H\}$ NMR (377 MHz, $CDCl_3$) δ −121.5; mass spectrum (EI) *m/z* (rel intensity) 166 (M^+, 14), 149 (100), 147 (45). HRMS calcd for $C_{10}H_{11}OF$ 166.0794, found 166.0801.

HPLC (Chiracel OB, 2-propanol/hexane 10:90, flow 1 mL/min, T = 30 °C): t_R *trans* isomers, 6.83 min, (1*S*,2*R*)-**13** 7.66 min; (1*R*,2*S*)-**13,** 15.95 min.

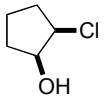
(1*S*,2*R*)-2-Bromocyclopentan1-ol (18).



From 2-bromocyclopentanone **14**[2] (492.0 mg, 3 mmol) and following the method **B** with (*S*,*S*)-**I** as the catalyst; flash chromatography (1:6 EtOAc-hexane) gave 400 mg (80%) of (1*S*,2*R*)-**18** (>98% de, 45% ee) as a colorless oil: $[\alpha]^{20}_D$ +3.9 (*c* 0.88, $CHCl_3$) (>98% de, 45% ee); ^1H NMR (300 MHz, $CDCl_3$): 1.50-2.25 (m, 7H), 3.99 (td, 1H, *J* = 3.9, 6.2 Hz), 4.28

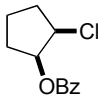
(td, 1H, *J* = 3.9, 6.2 Hz).; ^{13}C NMR (75 MHz, $CDCl_3$): 20.6, 30.5, 32.9, 60.1, 74.7; mass spectrum (CI) *m/z* (rel intensity) 166 (M^+, 9), 164 (M^+, 9), 149 (4), 147 (4), 85 (100). HRMS calcd for C_5H_9BrO 165.9814 and 163,9833, found 165.9816 and 163.9837.

(1*S*,2*R*)-2-clorocyclohexanol (19).



From 2-chlorocyclopentanone **15** (484 mg, 4mmol) and following the method **A** with 1.2:1 HCO_2H/Et_3N mixture and (*S*,*S*)-**I** as the catalyst; flash chromatography (1:6 EtOAc-hexane) gave 410 mg (80%) of (1*S*,2*R*)-**19** (>98% de, 60% ee) as a light brown oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.49-2.42 (m, 7H), 4.05-4.13 (m, 1H), 4.13-4.22 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.9, 30.2, 32.0, 65.7, 74.4. This compound was fully characterized as its benzoate.

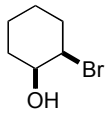
(1*S*,2*R*)-2-chlorocyclopentyl benzoate [(1*S*,2*R*)-22].



To a solution of **19** (120.5 mg, 1 mmol) in CH_2Cl_2 (1 mL) was added pyridine (0.2 mL, 2.40 mmol) and benzoyl chloride (0.14 mL, 1.20 mmol). The mixture was stirred at rt for 2 h, diluted with CH_2Cl_2 (10 mL) and washed with H_2O (2 x 10 mL). The organic layer was dried, concentrated, an purified by flash chromatography (1:8 EtOAc:Hexane) to yield (1*S*,2*R*)-**22** (190 mg, 80%) as a colorless oil. $[\alpha]^{20}_D$ + 9.2 (*c* 1.0, $CHCl_3$) (>98% de, 60% ee); ^{1}H-RMN (300 MHz, $CDCl_3$): 1.60-1.80 (m, 1H), 1.95-2.32 (m, 5H), 4.40-4.55 (m, 1H), 5.25-5.40 (m, 1H), 7.43 (t, 2H, *J* = 7.5 Hz), 7.55 (t, 1H, *J* = 7.5 Hz), 8.07 (d, 2H, *J* = 7.5 Hz); ^{13}C-RMN (75

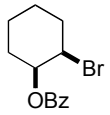
MHz, $CDCl_3$): 21.8, 22.4, 27.8, 32.7, 60.9, 73.3, 128.7, 130.0, 130.5, 133.3, 166.0; mass spectrum (EI) m/z (rel intensity) 227 (M^++1, 18), 225 (58), 123 (57), 105 (100). HRMS calcd for $C_{12}H_{14}ClO$ 225.0680, found 225.0682.

(1*S*,2*R*)-2-Bromo-ciclohexanol (20).



From 2-bromocyclohexanone **16**[2] (531 mg, 3 mmol) and following the method **B** with (*S*,*S*)-**I** as the catalyst; flash chromatography (1:6 EtOAc-hexane) gave 450 mg (84%) of (1*S*,2*R*)-**20** (70% de, 80% ee) as a light brown oil: $[\alpha]^{20}_D$ –7.0 (*c* 0.5, $CHCl_3$) (70% de, 80% ee); ^{1}H NMR (400 MHz, $CDCl_3$): 1.22-1.42 (m, 2H), 1.55-2.00 (m, 5H), 2.05-2.25 (m, 2H), 3.60-3.75 (m, 1H), 4.40-4.55 (m, 1H).; ^{13}C NMR (100 MHz, $CDCl_3$): 21.6, 23.1, 31.2, 32.5, 62.2, 70.5, mass spectrum (CI) m/z (rel intensity) 179 (M^+, 30), 177 (M^+, 30), 161 (12), 159 (12), 99 (51), 97 (100). HRMS calcd for $C_6H_{10}BrO$ 178,9887 and 176.9923, found 178.9894 and 176.9915.

(1*S*,2*R*)-2-bromocyclohexyl benzoate [(1*S*,2*R*)-23].

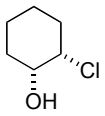


(1*S*,2*R*)-**20** (44.6 mg, 0.25 mmol) was benzoylated as described for **22** and the mixture was purified by flash chromatography (1:8 EtOAc:hexane) to yield (1*S*,2*R*)-**23** (60 mg, 85%) as a colorless oil: $[\alpha]^{20}_D$ –5.8 (*c* 0.4, $CHCl_3$) (92% de, 80% ee); ^{1}H NMR (400 MHz, $CDCl_3$): 1.40-1.60 (m, 2H), 1.68-1.90 (m, 3H),1.98-2.15 (m, 2H), 2.17-2.32 (m, 1H), 4.50-4.60 (m, 1H), 5.05-5.15 (m, 1H), 7.44 (t, 2H, *J* = 7.4 Hz), 7.56 (t, 1H, *J* = 7.4 Hz), 8.08 (d, 2H, *J* = 7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): 22.2, 22.5, 28.3, 33.1, 54.5, 73.0, 128.4, 129.8, 130.2,

133.1, 165.7; mass spectrum (CI) m/z (rel intensity) 286 (M^++1, 16), 285 (93), 284 (18), 283 (93), 203 (19), 123 (100). HRMS calcd for $C_{13}H_{16}BrO$ 285.0293, found 285.0313.

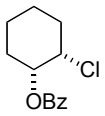
HPLC (Chiralcel OJ, 2-propanol/hexane 1:99, flow 0.5 mL/min, T = 30 °C): t_R (1*S*,2*R*)-**23**, 16.38 min; (1*R*,2*S*)-**23**, 19.86.

(1*R*,2*S*)-2-chloro-cyclohexanol [(1*R*,2*S*)-21].



From 2-chlorocyclohexanone **17** (535 mg, 4 mmol) and following the method **A** with 1.2:1 HCO_2H/Et_3N mixture and (*R*,*R*)-**I** as the catalyst; flash chromatography (1:6 EtOAc-hexane) gave 431 mg (79%) of (1*R*,2*S*)-**21** (78% de, 90% ee) as a light brown oil: $[\alpha]^{20}_D$ +4.5 (*c* 0.2, $CHCl_3$) (86% de, 90% ee); ^{1}H NMR (500 MHz, $CDCl_3$): 1.22-1.42 (m, 2H), 1.55-1.83 (m, 5H), 1.97-2.08 (m, 1H), 3.75-3.83 (m, 1H), 4.22-4.31 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): 21.7, 22.4, 30.8, 32.0, 66.2, 70.7. HRMS calcd for $C_6H_{11}ClO$ 134.0497, found 134.0498.

(1*R*,2*S*)-2-chlorocyclohexyl benzoate [(1*R*,2*S*)-24].



(1*R*,2*S*)-**21** (134.5 mg, 1 mmol) was benzoylated as described for **22** and the mixture was purified by flash chromatography (1:8 EtOAc:hexane) to yield (1*R*,2*S*)-**24** (190 mg, 79.7%) as a colorless oil: $[\alpha]^{20}_D$ + 6.0 (*c* 0.5, $CHCl_3$) (86% de, 90% ee); ^{1}H NMr (300 MHz, $CDCl_3$): 1.45-1.60 (m, 2H), 1.61-2.20 (m, 6H), 4.34-4.47 (m, 1H), 5.16-5.30 (m, 1H), 7.46 (t, 2H, *J* = 7.4 Hz), 7.55 (t, 1H, *J* = 7.4 Hz), 8.07 (d, 2H, *J* = 7.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): 21.8, 22.4, 27.8, 32.7, 60.9, 73.3, 128.7, 130.0, 130.5, 133.3, 166.0; mass spectrum (CI) m/z (rel

intensity) 239.(M^++1, 3), 203 (4), 225 (58), 123 (58), 105 (100). HRMS calcd for $C_{13}H_{16}ClO_2$ 239.0817, found 239.0838.

HPLC (Chiralcel OJ, 2-propanol/hexane 0.5:99.5, flow 0.5 mL/ min, T = 30 °C): t_R (1*S*,2*R*)-**24**, 18.45 min; (1*R*,2*S*)-**24**, 21.77 min.