Supplementary Material (ESI) for Green Chemistry

One-pot chemoenzymatic syntheses of enantiomerically-enriched *O*-acetyl cyanohydrins from aldehydes in ionic liquid

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Supporting Information

General Methods

All aldehydes were purified before using. Pseudomonas cepacia lipase (powder, light beige, ~50 units/mg) was purchased from Fluka Company. Candida antarctica lipase (acrylic resin, ≥10,000 U/g), Amano Lipase PS (from Pseudomonas cepacia), and Amano Lipase AK were purchased from Aldrich corporation. TMSCN (97%), Ac_2O (>99%), Vinyl acetate (>99%, redistilled before use) and all ionic liquids were purchased from Fluka company.

Analytical thin layer chromatography (TLC) was performed using Merck 60 F254 precoated silica gel plate (0.2 mm thickness). Subsequent to elution, plates were visualized using UV radiation (254 nm) on Spectroline Model ENF-24061/F 254 nm. Further visualization was possible by staining with acidic solution of ceric molybdate.

Flash chromatography was performed using Merck silica gel 60 with freshly distilled solvents. Columns were typically packed as slurry and equilibrated with the appropriate solvent system prior to use.

Infrared spectra were recorded on a Bio-Rad FTS 165 FTIR spectrometer. The oil samples were examined under neat conditions.

High Resolution Mass (HRMS) spectra were obtained using Finnigan MAT95XP GC/HRMS (Thermo Electron Corporation).

Proton nuclear magnetic resonance spectra (^{1}H NMR) were recorded on Bruker Avance DPX 300 and Bruker AMX 400 spectrophotometer ($CDCl_3$ as solvent). Chemical shifts for ^{1}H NMR spectra are reported as δ in units of parts per million (ppm) downfield from $SiMe_4$ (δ 0.0) and relative to the signal of chloroform-*d* (δ 7.2600, singlet). Multiplicities were given as: s (singlet); d (doublet); t (triplet); q (quartet); or m (multiplets). The number of protons (n) for a given resonance is indicated by nH. Coupling constants are reported as a *J* value in Hz. Carbon nuclear magnetic resonance spectra (^{13}C NMR) are reported as δ in units of parts per million (ppm) downfield from $SiMe_4$ (δ 0.0) and relative to the signal of chloroform-*d* (δ 77.03, triplet).

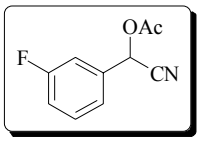
The enantioselectivities and configuration of *O*-acetyl cyanohydrins were determined using chiral HPLC analysis and by comparison with the reported data.[1-6] The enantioselectivities of cyanohydrins were determined after converting to the corresponding *O*-acetyl cyanohydrins using standard method [Ac_2O/Pyridine/DMAP (cat.)/CH_2Cl_2].

Experimental procedure

General procedure for the synthesis of cyanohydrin followed by lipase-catalyzed kinetic resolution: To a 10 mL oven-dried round-bottomed flask (RBF) was added [omim]PF_6 (1 mL), benzaldehyde (1 mmol) and TMSCN (1.5 mmol). After stirring at room temperature for 1 day, excess TMSCN was evaporated under *vacuo*. Then Pseudomonas Cepacia lipase (30 mg) was added to the RBF and the reaction system was dried azeotropically using freshly distilled THF (2 mL x 3) for three times. After that, vinyl acetate (5 mmol) was introduced into the RBF and the whole reaction system stirred at 40 ^{o}C for several days as shown in Table 2. After reaction, 2 mL aq. HCl (1 M) and 2 mL THF were added to the flask, stirred for half an hour, then it was extracted with diethyl ether (20 mL x 3), dried over anhydrous magnesium sulfate, filtered and evaporated the solvent under *vacuo* to afford the crude product. It was subjected to silica gel column chromatography using ethyl acetate and hexane as eluent to afford the desired product cyanohydrin and *O*-acetyl cyanohydrin.

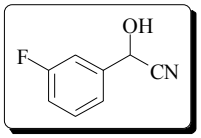
General procedure for one-pot synthesis of *O*-acetyl cyanohydrin followed by lipase-catalyzed resolution: To a 10 mL round-bottomed flask was added [omim]PF_6 (1 mL), aldehyde (1 mmol) and TMSCN (1.5 mmol). After stirring at room temperature for 1 day, Ac_2O (1.2 mmol) was added to the flask and continued to stir for 1 day. After that, TMSCN was removed under *vacuo*. Then *n*-BuOH (4 mmol), Candida antarctica lipase (50 mg) and Ac_2O (1 mmol) were introduced into the flask and it was stirred at 45 ^oC for 1 day. After reaction, 2 mL aq. HCl (1 M) and 2 mL THF were added to the flask, stirred for half an hour, then it was extracted with diethyl ether (20 mL x 3), dried over anhydrous magnesium sulfate, filtered and evaporated the solvent under *vacuo* to afford the crude product. It was subjected to silica gel column chromatography using ethyl acetate and hexane as eluent to afford the desired product cyanohydrin and *O*-acetyl cyanohydrin.

Spectroscopic data of products

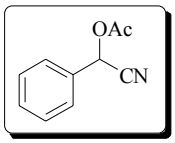


α-Acetoxy-2-(*m*-fluorophenyl)acetonitrile:[7] R_f = 0.21 (Ethyl acetate/Hexane = 1/4); FTIR (NaCl, neat): ν 1748 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.19 (s, 3H), 6.41 (s, 1H), 7.13-7.20 (m, 1H), 7.22-7.27 (m, 1H), 7.30-7.33 (m, 1H), 7.41-7.48 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.7 (C), 162.8 (d, J = 248.7 Hz, C), 133.9 (d, J = 7.6 Hz, C), 131.0 (d, J = 8.1 Hz, CH), 123.4 (d, J = 3.2 Hz, CH), 117.5 (d, J = 21.0 Hz, CH), 115.7 (C), 114.9 (d, J = 23.3 Hz, CH), 62.0 (d, J = 1.8 Hz, CH), 20.4 (CH_3) ppm; HRMS (EI, m/z): $[M]^+$, Calcd. for $C_{10}H_8FNO_2$: 193.0539, found: 193.0537.

HPLC analysis: The enantiomeric excess was determined by chiral HPLC employing Daicel Chiracel OD-H column (hexane : *i*-propanol 99.5:0.5, 0.5 mL/min): t_1 = 39.5 min, t_2 = 43.2 min.

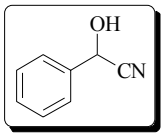


2-Hydroxy-2-(*m*-fluorophenyl)acetonitrile: FTIR (NaCl, neat): ν 3418, 2249 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.50 (d, J = 6.32 Hz, 1H), 5.54 (d, J = 6.20 Hz, 1H), 7.10-7.15 (m, 1H), 7.23-7.26 (m, 1H), 7.29-7.31 (m, 1H), 7.39-7.45 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.0 (d, J = 248.3 Hz, C), 137.4 (d, J = 7.3 Hz, C), 130.9 (d, J = 8.3 Hz, CH), 122.1 (d, J = 3.0 Hz, CH), 118.4 (C), 116.9 (d, J = 21.1 Hz, CH), 113.8 (d, J = 23.3 Hz, CH), 62.8 (d, J = 1.8 Hz, CH) ppm; HRMS (EI, m/z): $[M]^+$, Calcd. for C_8H_6FNO: 151.0433, found: 151.0423.



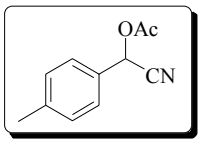
α-Acetoxy-2-phenylacetonitrile:[8,10,12,13] R_f = 0.50 (Ethyl acetate/Hexane = 1/4); FTIR (NaCl, neat): ν 2250, 1746 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.17 (s, 3H), 6.41 (s, 1H), 7.43-7.54 (m, 5H) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 20.2 (CH_3), 62.7 (CH), 116.0 (CN), 127.7 (CHx2), 129.1 (CHx2), 130.2 (CH), 131.7 (C), 168.8 (CO) ppm; HRMS (EI, m/z): $[M]^+$, Calcd. for $C_{10}H_9NO_2$: 175.0633, found: 175.0633.

HPLC analysis: The enantiomeric excess was determined by chiral HPLC analysis employing Daicel Chiracel OD-H (x2) column (hexane : *i*-propanol 95:5, 0.4 mL/min): t_1 = 39.4 min, t_2 = 42.4 min.



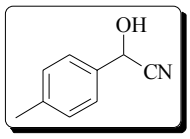
2-Hydroxy-2-phenylacetonitrile:[6,8,11,14] R_f = 0.6 (Ethyl acetate/Hexane = 1/2); FTIR (NaCl, neat): ν 3417, 2248 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 3.74 (br, s, 1H), 5.50 (s, 1H), 7.41-7.52 (m, 5H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 63.4 (CH), 118.8 (CN), 126.6 (CHx2),

129.1 (CHx2), 129.7 (CH), 135.2 (C) ppm; HRMS (EI, m/z): $[M]^+$, Calcd. for C_8H_7NO 133.0528, found 133.0554.

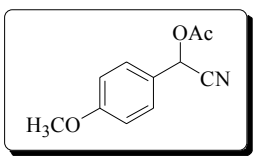


α-Acetoxy-2-(*p*-methylphenyl)acetonitrile:[8] R_f = 0.52 (Ethyl acetate/Hexane = 1/4); FTIR (NaCl, neat): ν 2250, 1747 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.12 (s, 3H), 2.36 (s, 3H), 6.35 (s, 1H), 7.23 (d, J = 8.43 Hz, 2H), 7.39 (d, J = 8.01 Hz, 2H) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 168.8 (C=O), 140.5 (C), 129.7 (CHx2), 128.8 (C), 127.7 (CHx2), 116.2 (CN), 62.6 (CH), 21.1 (CH_3), 20.3 (CH_3) ppm; HRMS (EI, m/z): $[M]^+$, Calcd. for $C_{11}H_{11}NO_2$: 189.0790, found: 189.0791.

HPLC analysis: The enantiomeric excess was determined by chiral HPLC analysis employing Daicel Chiracel OD-H column (hexane : *i*-propanol 97:3, 1 mL/min): t_1 = 8.0 min, t_2 = 9.9 min.



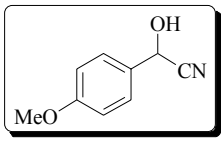
2-Hydroxy-2-(*p*-methylphenyl)acetonitrile:[8,14] R_f = 0.28 (Ethyl acetate/Hexane = 1/4); FTIR (NaCl, neat): ν 3434, 2247 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.33 (s, 3H), 4.30 (s, 1H), 5.38 (s, 1H), 7.18 (d, J = 8.01 Hz, 2H), 7.32 (d, J = 8.04 Hz, 2H) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 139.7 (C), 132.2 (C), 129.7 (CHx2), 126.6 (CHx2), 119.1 (CN), 63.0 (CH), 21.1 (CH_3) ppm; HRMS (EI, m/z): $[M]^+$, Calcd. for C_9H_9NO: 147.0684, found: 147.0684.



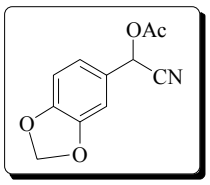
α-Acetoxy-2-(*p*-methoxyphenyl)acetonitrile:[8,10] R_f = 0.49 (Ethyl acetate/Hexane = 1/4); FTIR (NaCl, neat): ν 2250, 1741 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.12 (s, 3H), 3.81 (s,

3H), 6.34 (s, 1H), 6.94 (dd, J = 6.63, 2.4 Hz, 2H), 7.44 (dd, J = 6.63, 2.4 Hz, 2H) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 168.9 (C=O), 160.9 (C), 129.4 (CHx2), 123.7 (C), 116.2 (CN), 114.4 (CHx2), 62.4 (CH), 55.2 (CH_3), 20.2 (CH_3) ppm; HRMS (EI, m/z): $[M]^+$, Calcd. for $C_{11}H_{11}NO_3$: 205.0739, found: 205.0738.

HPLC analysis: The enantiomeric excess was determined by chiral HPLC analysis employing Daicel Chiracel OD-H column (hexane : *i*-propanol 99:1, 0.5 mL/min): t_1 = 38.1 min, t_2 = 44.1 min.

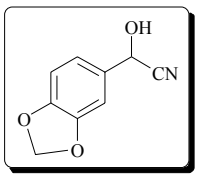


2-Hydroxy-2-(*p*-methoxyphenyl)acetonitrile:[6,8,11,14] R_f = 0.16 (Ethyl acetate/Hexane = 1/4); FTIR (NaCl, neat): ν 3418, 2240 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.80 (s, 3H), 4.04 (s, 1H), 5.42 (s, 1H), 6.91 (d, J = 8.82 Hz, 2H), 7.40 (d, J = 8.43 Hz, 2H) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 160.5 (C), 128.2 (CHx2), 127.5 (C), 119.1 (CN), 114.4 (CHx2), 63.0 (CH), 55.4 (CH_3) ppm; HRMS (EI, m/z): $[M]^+$, Calcd. for $C_9H_9NO_2$: 163.0633, found: 163.0633.

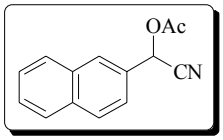


α-Acetoxy-2-(3,4-methylenedioxyphenyl)acetonitrile: R_f = 0.42 (Ethyl acetate/Hexane = 1/4); FTIR (NaCl, neat): ν 2252, 1751 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.14 (s, 3H), 6.00 (s, 2H), 6.30 (s, 1H), 6.83 (d, J = 8.01 Hz, 1H), 6.97-7.02 (m, 2H) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 168.8 (C=O), 149.2 (C), 148.2 (C), 125.2 (C), 122.2 (CH), 116.1 (CN), 108.4 (CH), 108.0 (CH), 101.7 (CH_2), 62.5 (CH), 20.3 (CH_3) ppm; HRMS (EI, m/z): $[M]^+$, Calcd. for $C_{11}H_9NO_4$: 219.0532, found: 219.0526.

HPLC analysis: The enantiomeric excess was determined by chiral HPLC analysis employing Daicel Chiracel OD-H column (hexane : *i*-propanol 99:1, 0.3 mL/min): t_1 = 79.7 min, t_2 = 89.4 min.

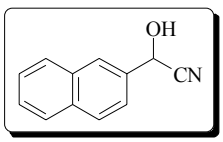


2-Hydroxy-2-(3, 4-methylenedioxyphenyl)acetonitrile:[6] R_f = 0.04 (Ethyl acetate/Hexane = 1/8); FTIR (NaCl, neat): ν 3418, 2245 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.72 (s, 1H), 5.40 (s, 1H), 5.99 (s, 2H), 6.80-6.82 (m, 1H), 6.96-6.98 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.8 (C), 148.3 (C), 129.1 (C), 120.7 (CH), 118.9 (CN), 108.5 (CH), 107.2 (CH), 101.6 (CH_2), 63.2 (CH) ppm; HRMS (EI, m/z): $[M]^+$, Calcd. for $C_9H_7NO_3$: 177.0426, found: 177.0426.



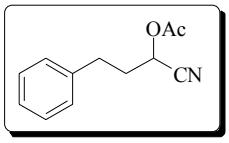
α-Acetoxy-2-(2-naphthyl)acetonitrile:[13] R_f = 0.22 (Ethyl acetate/Hexane = 1/8); FTIR (NaCl, neat): ν 1748 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.17 (s, 3H), 6.57 (s, 1H), 7.51-7.59 (m, 3H), 7.84-7.92 (m, 3H), 8.00 (s, 1H) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 168.9 (CO), 133.8 (C), 132.8 (C), 129.4 (CH), 128.9 (C), 128.3 (CH), 127.9 (CH), 127.8 (CH), 127.5 (CH), 127.0 (CH), 124.2 (CH), 116.1 (CN), 63.0 (CH), 20.4 (CH_3) ppm; HRMS (EI, m/z): $[M]^+$, Calcd. for $C_{14}H_{11}NO_2$: 225.0790, found: 225.0782.

HPLC analysis: The enantiomeric excess was determined by chiral HPLC analysis employing Daicel Chiracel OD column (hexane : *i*-propanol 99:1, 0.4 mL/min): t_1 = 76.3 min, t_2 = 86.7 min.



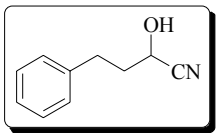
2-Hydroxy-2-(2-naphthyl)acetonitrile:[11] R_f = 0.07 (Ethyl acetate/Hexane = 1/8); FTIR (NaCl, neat): ν 3416 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.11 (d, J = 7.01 Hz, 1H), 5.72 (d,

J = 6.84 Hz, 1H), 7.54-7.62 (m, 3H), 7.87-7.95 (m, 3H), 8.03 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 133.7 (C), 133.0 (C), 132.6 (C), 129.4 (CH), 128.4 (CH), 127.8 (CH), 127.3 (CH), 127.0 (CH), 126.2 (CH), 123.7 (CH), 118.7 (CN), 63.9 (CH) ppm; HRMS (EI, m/z): $[M]^+$, Calcd. for $C_{12}H_9NO$: 183.0684, found: 183.0673.

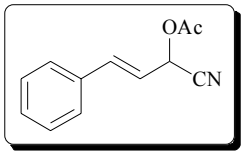


α-Acetoxy-4-phenylbutanenitrile:[9,13] R_f = 0.68 (Ethyl acetate/Hexane = 1/4); FTIR (NaCl, neat): *v* 2249, 1749 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.09 (s, 3H), 2.20 (m, 2H), 2.81 (t, *J* = 7.64 Hz, 2H), 5.24 (t, *J* = 6.83 Hz, 1H), 7.16-7.33 (m, 5H) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 168.9 (C=O), 139.0 (C), 128.6 (CHx2), 128.2 (CHx2), 126.5 (CH), 116.6 (CN), 60.4 (CH), 33.6 (CH_2), 30.6 (CH_2) 20.1 (CH_3) ppm; HRMS (EI, m/z): $[M]^+$, Calcd. for $C_{12}H_{13}NO_2$: 203.0946, found: 203.0951.

HPLC analysis: The enantiomeric excess was determined by chiral HPLC analysis employing Daicel Chiracel OD-H column (hexane : *i*-propanol 99:1, 0.5 mL/min): t_1 = 64.1 min, t_2 = 79.7 min.

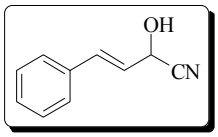


2-Hydroxy-4-phenylbutanenitrile:[6,11] R_f = 0.31 (Ethyl acetate/Hexane = 1/4); FTIR (NaCl, neat): *v* 3436, 2247 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.17 (m, 2H), 2.85 (m, 2H), 4.16 (s, 1H), 4.42 (t, *J* = 6.81 Hz, 1H), 7.22-7.37 (m, 5H) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 139.6 (C), 128.6 (CHx2), 128.3 (CHx2), 126.4 (CH), 120.0 (CN), 60.1 (CH), 36.4 (CH_2), 30.5 (CH_2) ppm; HRMS (EI, m/z): $[M]^+$, Calcd. for $C_{10}H_{11}NO$:161.0841, found: 161.0843.

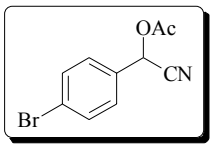


α-Acetoxy-4-phenyl-3-butenenitrile:[9,12,13] R_f = 0.43 (Ethyl acetate/Hexane = 1/8); FTIR (NaCl, neat): ν 2247, 1751 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.17 (s, 3H), 6.02 (dd, J = 6.72, 0.96 Hz, 1H), 6.19 (dd, J = 15.76, 6.72 Hz, 1H), 6.97 (d, J = 15.76 Hz, 1H), 7.33-7.44 (m, 5H) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 168.9 (CO), 137.8 (CH), 134.4 (C), 129.4 (CH), 128.8 (CHx2), 127.1 (CHx2), 118.3 (CH), 115.5 (CN), 61.5 (CH), 20.4 (CH_3) ppm; HRMS (EI, m/z): $[M]^+$, Calcd. for $C_{12}H_{11}NO_2$: 201.0790, found: 201.0778.

HPLC analysis: The enantiomeric excess was determined by chiral HPLC analysis employing Daicel Chiracel AS-H column (hexane : *i*-propanol 99:1, 0.3 mL/min): t_1 = 63.1 min, t_2 = 67.5 min.

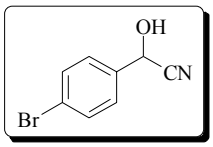


2-Hydroxy-4-phenyl-3-butenenitrile:[6,11] R_f = 0.19 (Ethyl acetate/Hexane = 1/4); FTIR (NaCl, neat): ν 3414, 2243 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.15 (d, J = 5.61 Hz, 1H), 6.25 (d, J = 6 Hz, 1H), 6.90 (d, J = 16.05 Hz, 1H), 7.31-7.42 (m, 5H) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 135.27 (CH), 134.75 (C), 129.08 (CH), 128.82 (CHx2), 127.07 (CHx2), 122.29 (CH), 118.25 (CN), 61.85 (CH) ppm; HRMS (EI, m/z): $[M]^+$, Calcd. for $C_{10}H_9NO$: 159.0684, found: 159.0688.

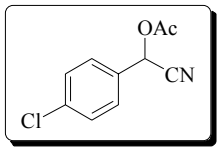


α-Acetoxy-2-(*p*-bromophenyl)acetonitrile:[10] R_f = 0.27 (Ethyl acetate/Hexane = 1/8); FTIR (NaCl, neat): ν 1748 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.16 (s, 3H), 6.37 (s, 1H), 7.38-7.41 (m, 2H), 7.57-7.59 (m, 2H) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 168.7 (CO), 132.4 (CHx2), 130.7 (C), 129.4 (CHx2), 124.7 (C), 115.7 (CN), 62.1 (CH), 20.3 (CH_3) ppm; HRMS (EI, m/z): $[M]^+$, Calcd. for $C_{10}H_8BrNO_2$: 252.9738, found: 252.9738.

HPLC analysis: The enantiomeric excess was determined by chiral HPLC analysis employing Daicel Chiracel OD-H column (hexane : *i*-propanol 95:5, 1 mL/min): t_1 = 10.6 min, t_2 = 13.3 min.

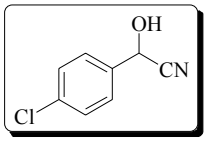


2-Hydroxy-2-(*p*-bromophenyl)acetonitrile:[14] FTIR (NaCl, neat): *v* 3420 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.20 (d, *J* = 6.68 Hz, 1H), 5.51 (d, *J* = 6.44 Hz, 1H), 7.41 (d, *J* = 8.44 Hz, 2H), 7.58 (d, *J* = 8.41 Hz, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 134.2 (C), 132.4 (CHx2), 128.3 (CHx2), 124.1 (C), 118.4 (CN), 63.0 (CH) ppm; HRMS (EI, m/z): $[M]^+$, Calcd. for C_8H_6BrNO: 210.9633, found: 210.9621.



α-Acetoxy-2-(*p*-chlorophenyl)acetonitrile:[8,10,13] R_f = 0.51 (Ethyl acetate/Hexane = 1/4); FTIR (NaCl, neat): *v* 2250, 1753 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.16 (s, 3H), 6.38 (s, 1H), 7.40-7.48 (m, 4H) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 168.7 (CO), 136.4 (C), 130.2 (C), 129.3 (CHx2), 129.1 (CHx2), 115.7 (CN), 62.0 (CH), 20.2 (CH_3) ppm; HRMS (EI, m/z): $[M]^+$, Calcd. for $C_{10}H_8ClNO_2$: 209.0244, found: 209.0241.

HPLC analysis: The enantiomeric excess was determined by chiral HPLC analysis employing Daicel Chiracel OD-H column (hexane : *i*-propanol 98:2, 1 mL/min): t_1 = 13.0 min, t_2 = 15.9 min.



2-Hydroxy-2-(*p*-chlorophenyl)acetonitrile:[6,8] R_f = 0.09 (Ethyl acetate/Hexane = 1/4); FTIR (NaCl, neat): *v* 3422, 2251 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 4.72 (s, 1H), 5.47 (s, 1H),

7.37 (d, J = 1.62 Hz, 4H) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 135.6 (C), 133.5 (C), 129.2 (CHx2), 127.9 (CHx2), 118.7 (CN), 62.5 (CH) ppm; HRMS (EI, m/z): $[M]^+$, Calcd. for C_8H_6ClNO: 167.0138, found: 167.0134.

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