Supporting Information

for

KetoABNO/NOₓ Co-Catalytic Aerobic Oxidation of Aldehydes to Carboxylic Acids and Access to α-Chiral Carboxylic Acids via Sequential Asymmetric Hydroformylation/Oxidation

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Materials and Methods:

Unless otherwise stated, all reactions were conducted in borosilicate vials with anhydrous organic solvents. All commercially available reagents were purchased from Aldrich and used as received, unless otherwise noted [note: Rh(acac)(CO)\textsubscript{2} (CAS 14874-82-9)]. All chiral aldehydes were synthesized as reported below and used without further purification. The \((R,R,R)\)- and \((S,S,S)\)-bis(diazaphospholane ligand was synthesized according to a literature protocol.\textsuperscript{1} All other commercially obtained reagents were used as received. Thin-layer chromatography (TLC) was conducted with Silicycle silica gel UV254 precoated plates (0.25 mm), and visualized using UV lamps or KMnO\textsubscript{4} staining. \textsuperscript{1}H NMR spectra and \textsuperscript{13}C NMR spectra were recorded on a Bruker 400 MHz Avance III or a Bruker 500 MHz Avance and are reported relative to residual solvent CDCl\textsubscript{3} (\textsuperscript{1}H, 7.26 ppm, \textsuperscript{13}C, 77.0ppm), (CD\textsubscript{3})\textsubscript{2}CO (\textsuperscript{1}H, 2.05 ppm, \textsuperscript{13}C, 206.26ppm), D\textsubscript{2}O (\textsuperscript{1}H, 4.79 ppm). High resolution mass spectral analysis was performed on at the mass spectrometry facility at the University of Wisconsin-Madison.

General Procedures:

General procedure for the hydroformylation of olefins:

All chiral aldehydes were used without further purification.

Inside a N\textsubscript{2}-purged glovebox, an oven-dried 15 mL Ace Glass pressure bottle equipped with a magnetic stir bar was charged with THF stock solutions of Rh(acac)(CO)\textsubscript{2} (0.001 mmol) and \((R,R,R)\)-bis(diazaphospholane ligand 1 (0.0012 mmol) using 1000\textmu L and 200\textmu L Eppendorf pipets. THF was added as necessary to afford a final volume of 1 mL once olefin is added. The pressure bottle was attached to a pressure reactor and removed from the glovebox, placed in a fume hood, subjected to 5 pressurization (140 psi)/depressurization (15 psi) cycles with syngas (1:1 H\textsubscript{2}:CO) to ensure replacement of the dinitrogen atmosphere with syngas, then filled to 150 psig syngas. The solution was allowed to stir at high speed to ensure gas mixing for 30-60 min in an oil bath at the reaction temperature. The reaction vessel was removed from the oil bath and allowed to cool for 5 minutes, then the pressure was reduced to <10 psig and the olefin (1.0 mmol) was injected with a gas-tight syringe with a 12'' needle. Solid olefins were injected as a solution in THF. The reaction was repressurized to the reaction pressure after additional pressurization/depressurization cycles and replaced in the oil bath to react overnight. Upon completion of the reaction, the pressure bottle was removed from the oil bath, allowed to cool to room temperature, and vented in a fume hood. NMR spectra are initially obtained of the crude reaction mixture by adding CDCl\textsubscript{3} or acetone-d\textsubscript{6} directly to the reaction mixture. For larger scale synthesis of the crude aldehyde (cf. product \textbf{2e}), a modified version of this general reaction procedure was employed, in
which a larger (210 mL) pressure bottle was used and additional syngas was added to the reactor whenever pressure dropped below 120 psig. All other steps in the protocol were unchanged.

**General procedure for the aerobic oxidation of chiral aldehydes to carboxylic acids:**

To a 4 mL borosilicate glass vial was added 9-azabicyclo[3,3,1]nonan-3-one-9-oxyl (keto-ABNO; 7.9 mg, 0.05 mmol), sodium nitrite (6.7 mg, 0.10 mmol) and a stir bar and capped with Teflon coated rubber septum cap. The vial was purged with oxygen and then solution of the aldehyde (1 mmol) in acetonitrile (1 mL), and water (180 µL) was added. Nitric acid (9.4 µL, 20 mol%) was then added to this reaction mixture and the reaction was capped and stirred at 23 °C for 8h. The reaction was diluted with dichloromethane (DCM) and transferred to a separatory funnel and acidified with 1 M HCl to a pH of about 2. The aqueous layer was washed with DCM (3 x 15 mL) and the organic layers were combined and washed with brine. The combined organic layers were dried with MgSO$_4$, concentrated under vacuum, and the crude mixture was purified by column chromatography to yield the pure acid.

**Characterization of Products:**

(S)-2-phenylpropanoic acid (2a):

This reaction was performed according to the general procedure for the aerobic oxidation of chiral aldehydes to carboxylic acids using the crude aldehyde obtained from the reaction of styrene under the general AHF reaction procedure. The crude product was purified by column chromatography on silica gel (Hexanes/EtOAc gradient 80/20 to 60/40) to give 89% of the product (134 mg, 0.89 mmol, 72% ee) as a colorless oil. The enantiomeric excess was determined by HPLC using a Chiracel OD-H, 250 x 4.6 mm, 0.40 mL/min, 97:3:0.1 hexane: iPrOH: trifluoroacetic acid, 210 nm, $t_R[R] = 19.0$ min, $t_R[S] = 21.4$ min, phenylpropionic acid $t_R = 22.7$ min. $^1$H NMR (500 MHz, CDCl$_3$): 11.57 (br s, 1H), 7.23 (m, 5H), 3.67 (q, $J = 7.1$, 1H), 1.45 (d, $J = 7.1$, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$): 181.04, 139.70, 128.65, 127.58, 127.37, 45.37, 18.05. HRMS (ESI) calculated for C$_9$H$_9$O$_2$ [M-H] requires m/z 149.0608, found 149.0613. Spectroscopic data are in accordance with those described in the literature.$^2$
(S)-2-(p-tolyl)propanoic acid (2b):

This reaction was performed according to the general procedure for the aerobic oxidation of chiral aldehydes to carboxylic acids using the crude aldehyde obtained from the reaction of 4-methylstyrene under the general AHF reaction procedure. The crude product was purified by column chromatography on silica gel (Hexanes/EtOAc gradient 80/20 to 50/50) to give 90% of the product (148 mg, 0.90 mmol, 81% ee) as a colorless solid. The enantiomeric excess was determined by HPLC using a Chiracel OD-H, 250 x 4.6 mm, 0.80 mL/min, 98:2:0.1 hexane: iPrOH: trifluoroacetic acid, 210 nm, t<sub>R</sub>[S] = 12.7 min, t<sub>R</sub>[R] = 11.5 min. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): 11.38 (br s, 1H), 7.20 (d, <i>J</i> = 8.1, 2H), 7.13 (d, <i>J</i> = 8.1, 2H), 3.68 (q, <i>J</i> = 7.1, 1H), 1.47 (d, <i>J</i> = 7.1, 3H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): 181.14, 137.04, 136.75, 129.33, 127.43, 44.94, 21.01, 18.05. HRMS (ESI) calculated for C<sub>10</sub>H<sub>11</sub>O<sub>2</sub> [M-H] requires m/z 163.0765, found 163.0769. Spectroscopic data are in accordance with those described in the literature. 3
(S)-2-(4-fluorophenyl)propanoic acid (2c):

This reaction was performed according to the general procedure for the aerobic oxidation of chiral aldehydes to carboxylic acids using the crude aldehyde obtained from the reaction of 4-fluorostyrene under the general AHF reaction procedure. The crude product was purified by column chromatography on silica gel (Hexanes/EtOAc gradient 80/20 to 50/50) to give 87% of the product (146 mg, 0.87 mmol, 83% ee) as a white solid. The enantiomeric excess was determined by HPLC using a Chiracel OJ-H, 250 x 4.6 mm, 0.40 mL/min, 98:2:0.1 hexane: iPrOH: trifluoroacetic acid, 220 nm, t\(_R\)[R] = 25.9 min, t\(_R\)[S] = 33.2 min. \(^1\)H NMR (500 MHz, CDCl\(_3\)): 10.50 (br s, 1H), 7.21 (m, 2H), 7.94 (t, J = 8.6, 2H), 3.65 (q, J = 7.1, 1H), 1.43 (d, J = 7.1, 3H). \(^13\)C NMR (125 MHz, CDCl\(_3\)): 180.58, 138.06, 133.30, 128.98, 128.80, 44.74, 18.01. HRMS (ESI) calculated for C\(_9\)H\(_8\)FO\(_2\) [M-H] requires m/z 167.0516, found 167.0512.

Spectroscopic data are in accordance with those described in the literature.\(^4\)

![HPLC trace of crude racemic 2-(4-fluorophenyl)propanoic acid (220 nm)](image1)

![HPLC trace of (S)-2-(4-fluorophenyl)propanoic acid (220 nm)](image2)

(S)-2-(4-chlorophenyl)propanoic acid (2d):

This reaction was performed according to the general procedure for the aerobic oxidation of chiral aldehydes to carboxylic acids using the crude aldehyde obtained from the reaction of 4-chlorostyrene under the general AHF reaction procedure. The crude product was purified by column chromatography on silica gel (Hexanes/EtOAc gradient 80/20 to 50/50) to give 89% of the product (164 mg, 0.89 mmol, 82% ee) as a white solid. The enantiomeric excess was determined by HPLC using a Chiracel OD-H, 250 x 4.6 mm, 0.70 mL/min, 98:2:0.1 hexane: iPrOH: trifluoroacetic acid, 210 nm, t\(_R\)[R] = 22.7 min, t\(_R\)[S] = 26.0 min. \(^1\)H NMR (400 MHz, CDCl\(_3\)): 11.35 (br s, 1H), 7.29 (d, J = 8.3, 2H), 7.24 (d, J = 8.3, 2H), 7.24 (t, J = 8.2, 2H), 3.70 (q, J = 7.2, 1H), 1.49 (d, J = 7.2, 3H). \(^13\)C NMR (125 MHz, CDCl\(_3\)): 180.58, 138.06, 133.30, 128.98, 128.80, 44.74, 18.01. mp: 63 – 66 °C. HRMS (ESI) calculated for C\(_9\)H\(_8\)ClO\(_2\) [M-H] requires m/z 183.0218, found 183.0219.

Spectroscopic data are in accordance with those described in the literature.\(^5\)
(R)-2-(benzoyloxy)propanoic acid (2e):

This reaction was performed according to the general procedure for the aerobic oxidation of chiral aldehydes to carboxylic acids using the crude aldehyde obtained from the reaction of vinyl benzoate under the general AHF reaction procedure. The crude product was purified by column chromatography on silica gel (Hexanes/EtOAc gradient 80/20 to 50/50) to give 89% of the product (186 mg, 0.96 mmol, 93% ee) as a white solid. For the one gram scale reaction, the crude aldehyde, (R)-1-oxopropan-2-yl benzoate, was weighed before oxidation. One gram (5.61 mmol) was oxidized to give 97% of the product (1.057 g, 5.44 mmol, 92% ee) as a white solid. The enantiomeric excess was determined by HPLC using a Chiracel OD-H, 250 x 4.6 mm, 0.80 mL/min, 95:5:0.1 hexane:iPrOH:trifluoroacetic acid, 220 nm, t<sub>S</sub>[S] = 9.8 min, t<sub>R</sub>[R] = 8.6 min. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 8.5 (br s, 1H), 8.07 (d, J = 7.2, 2H), 7.58 (t, J = 7.5, 1H), 7.45 (t, J = 7.5, 2H), 5.36 (q, J = 7.1, 1H), 1.67 (d, J = 7.1, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): 176.39, 165.92, 133.41, 129.86, 129.21, 128.43, 68.60, 16.92. HRMS (ESI) calculated for C<sub>10</sub>H<sub>10</sub>O<sub>4</sub> [M+H]<sup>+</sup> requires m/z 195.0652, found 195.0656.

Spectroscopic data are in accordance with those described in the literature.\textsuperscript{6}
(R)-2-acetoxypropanoic acid (2f):

This reaction was performed according to the general procedure for the aerobic oxidation of chiral aldehydes to carboxylic acids using the crude aldehyde obtained from the reaction of vinyl acetate under the general AHF reaction procedure. $^1$H NMR yield was obtained using dioxane as the internal standard (91%, see spectrum below for details). The crude product was purified by aqueous extraction using NaHCO$_3$. The NaHCO$_3$ aqueous layer was washed with Et$_2$O (2 x 15 mL) followed by acidification with HCl to pH 2 and extractions with DCM (3x 20mL) to give the pure product (92% ee) as a colorless oil. The enantiomeric excess was determined by chiral GC (Supelco’s Beta Dex 225, 80 °C ramp to 120 °C (5 °C/min) and hold at 120 °C for 5 min, then ramp to to 160 °C (5 °C/min) and hold at 160 °C for 5 min. Slight variance in retention time is due to manual injection.; $t_R$= 17.0 min, $t_R[S] = 19.5$ min. $^1$H NMR (400 MHz, CDCl$_3$): 9.60 (br s, 1H), 5.10 (q, $J = 7.1$, 1H), 1.53 (d, $J = 7.1$, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$): 176.56, 170.49, 68.13, 20.57, 16.75. HRMS (ESI) calculated for C$_5$H$_7$O$_4$[M+NH$_4$]$^+$ requires m/z 164.0918, found 164.0916.

Spectroscopic data are in accordance with those described in the literature.$^7$

(R)-2-(1,3-dioxoisindolin-2-yl)propanoic acid (2g):

This reaction was performed according to the general procedure for the aerobic oxidation of chiral aldehydes to carboxylic acids using the crude aldehyde obtained from the reaction of 2-vinylisoindoline-1,3-dione under the general AHF reaction procedure. The crude product was purified by column chromatography on silica gel (Hexanes/EtOAc gradient 80/20 to 50/50) to give 87% of the product (191 mg, 0.87 mmol, 84% ee) as a white solid. The enantiomeric excess was determined by HPLC using a Chiracel OD-H, 250 x 4.6 mm, 0.40 mL/min, 97:3:0.1 hexane: iPrOH: trifluoroacetic acid, 220 nm, $t_R[S] = 19.2$ min, $t_R[R] = 16.2$ min. $^1$H NMR (400 MHz, CDCl$_3$): 9.78 (br s, 1H), 7.90 (m, 2H), 7.78 (m, 2H), 5.05 (q, $J = 7.3$, 1H), 1.73 (d, $J = 7.3$, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$): 175.34, 167.38,
134.16, 131.77, 123.52, 47.32, 15.01. mp: 129 – 131 °C. HRMS (ESI) calculated for C_{11}H_{9}NO_{4} [M+Na]^+ requires m/z 242.0424, found 242.0420.

Spectroscopic data are in accordance with those described in the literature. 

HPLC trace of crude racemic 2-(1,3-dioxoisooindolin-2-yl)propanoic acid (210 nm)

HPLC trace of (R)-2-(1,3-dioxoisooindolin-2-yl)propanoic acid (210 nm)

(R)-2-(2-oxopyrrolidin-1-yl)propanoic acid (2h):

This reaction was performed according to the general procedure for the aerobic oxidation of chiral aldehydes to carboxylic acids using the crude aldehyde obtained from the reaction of 1-vinylpyrrolidin-2-one under the general AHF reaction procedure. $^1$H NMR yield was obtained using dioxane as the internal standard (94%, see spectrum below for details). The crude product was purified by aqueous extraction using NaHCO$_3$. The NaHCO$_3$ aqueous layer was washed with Et$_2$O (2 x 15 mL) followed by acidification with HCl to pH 2 and extractions with DCM (3 x 20mL) to give the pure product (83% ee) as a colorless oil. The enantiomeric excess was determined by chiral GC (GC, Supelco's Beta Dex 120, 90 °C ramp to 130 °C (5 °C/min), then ramp to 156 °C (1 °C/min) and hold at 156 °C for 22 min, then ramp to 165 °C (1 °C/min) and finally ramp to 170 °C (5 °C/min) and hold for 2 min.); $t_r[R]= 52.0$ min, $t_r[S] = 55.2$ min. $^1$H NMR (500 MHz, D$_2$O): 4.65 (q, $J = 7.4$, 1H), 4.65 (m, 2H), 2.46 (t, $J = 8.0$, 2H), 2.08 (qt, $J = 7.3$, 2H), 1.73 (d, $J = 7.3$, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$): 178.70, 175.21, 50.38, 44.88, 30.88, 17.39, 13.68. HRMS (ESI) calculated for C$_7$H$_{11}$NO$_3$ [M+H]^+ requires m/z 158.0812, found 158.0808.
(R)-2-acetamidopropanoic acid (2i):

This reaction was performed according to the general procedure for the aerobic oxidation of chiral aldehydes to carboxylic acids using the crude aldehyde obtained from the reaction of N-vinylacetamide under the general AHF reaction procedure. H NMR yield was obtained using dioxane as the internal standard (91%, see spectrum below for details). The crude product was purified by aqueous extraction using NaHCO₃. The NaHCO₃ aqueous layer was washed with Et₂O (2 x 15mL) followed by acidification with HCl to pH 2 and extractions with DCM (3 x 20mL) to give the pure product (84% ee) as a colorless oil. The enantiomeric excess was determined by chiral GC (GC, Supelco’s Beta Dex 120, 80 °C ramp to 185 °C (5 °C/min) and hold at 185 °C for 24 min.,) t_R[R]= 33.9 min, t_R[S] = 33.4 min. H NMR (500 MHz, D₂O): 4.31 (q, J = 7.2, 1H), 1.99 (s, 3H), 1.39 (d, J = 7.2, 3H). C NMR (125 MHz, CDCl₃): 176.66, 173.97, 48.56, 21.44, 15.97. HRMS (ESI) calculated for C₅H₉NO₃ [M+H]+ requires m/z 132.0655, found 132.0651.

Spectroscopic data are in accordance with those described in the literature.
Octanoic acid (3a)

This reaction was performed according to the general procedure using octanal (128 mg, 1.0 mmol). The crude product was purified by aqueous extraction using NaHCO₃. The NaHCO₃ aqueous layer was washed with Et₂O (2x 15 mL) followed by acidification with HCl to pH 2 and extractions with DCM (3x 20mL) to give 85% of the product (118 mg, 0.82 mmol) colorless oil. ¹H NMR (400 MHz, CDCl₃): 10.83 (br s, 1H), 2.35 (t, J = 7.5, 2H), 1.64 (qt, J = 7.3, 2H), 1.30 (m, 8H), 0.88 (t, J = 6.8, 3H). Octanoic acid is a known compound (CAS: 124-07-2). Spectroscopic data matches pure sample purchased from Sigma Aldrich.

Hydrocinnamic acid (3b):

This reaction was performed according to the general procedure using hydrocinnamylaldehyde (134 mg, 1.0 mmol). The crude product was purified by aqueous extraction using NaHCO₃. The NaHCO₃ aqueous layer was washed with Et₂O (2x 15 mL) followed by acidification with HCl to pH 2 and extractions with DCM (3x 20mL) to give 85% of the product (120 mg, 0.80 mmol) white solid. ¹H NMR (400 MHz, CDCl₃): 11.64 (br s, 1H), 7.29 (m, 2H), 7.21 (m, 3H), 2.95 (t, J = 7.7, 2H), 2.67 (t, J = 7.7, 2H). ¹³C NMR (100 MHz, CDCl₃): 179.53, 140.09, 128.52, 128.23, 126.34, 35.62, 30.51. Hydrocinnamic acid is a known compound (CAS: 501-52-0). Spectroscopic data matches pure sample purchased from Sigma Aldrich.

Cyclohexane carboxylic acid¹⁰ (3c):

This reaction was performed according to the general procedure using cyclohexanecarbaldehyde (112 mg, 1.0 mmol). The crude product was purified by aqueous extraction using NaHCO₃. The NaHCO₃ aqueous layer was washed with Et₂O (2x 15 mL) followed by acidification with HCl to pH 2 and extractions with DCM (3x 20mL) to give 85% of the product (116 mg, 0.91 mmol) colorless oil. ¹H NMR (400 MHz, CDCl₃): 11.78 (br s, 1H), 2.33 (tt, J = 3.5 Hz, J = 11.0 Hz, 1H), 1.94 (m, 2H), 1.76 (m, 2H), 1.65 (m, 1H), 1.46 (m, 2H), 1.27 (m, 2H). ¹³C NMR (100 MHz, CDCl₃): 182.51, 42.89, 28.76, 25.67, 25.32.

Picolinic acid hydrochloride (3d):

This reaction was performed according to the general procedure using 2-pyridine carbaldehyde (107 mg, 1.0 mmol). The crude product was cooled to 0 °C and then concentrated HCl (0.1 mL, 12 M) was added slowly and the mixture was stirred for 15 min. A white precipitate formed and was isolated via vacuum filtration and washed with cold water (1 x 2 mL) and Et₂O (2 x 5 mL) to give 91% of the product (145 mg, 0.91 mmol) as a white solid. ¹H NMR (500 MHz, (CD₃)₂SO): 8.77 (d, J = 4.7 Hz, 1H), 8.17 (m, 2H), 7.78 (m, 1H). ¹³C NMR (125 MHz, CDCl₃): 164.05, 147.01,
Picolinic acid hydrochloride is a known and commercially available compound (CAS 636-80-6).

**Nicotinic acid hydrochloride (3e):**

This reaction was performed according to the general procedure using 3-pyridine carbaldehyde (107 mg, 1.0 mmol). The crude product was cooled to 0 °C and then concentrated HCl (0.1 mL, 12 M) was added slowly and the mixture was stirred for 15 min. A white precipitate formed and was isolated via vacuum filtration and washed with cold water (1 x 2 mL) and Et₂O (2 x 5 mL) to give 89% of the product (142 mg, 0.89 mmol) as a white solid. ¹H NMR (500 MHz, D₂O): 9.29 (s, 1H), 9.07 (dd, J = 1.4 Hz, J = 6.7 Hz, 1H), 8.95 (d, J = 5.7 Hz, 1H), 8.18 (m, 1H). ¹³C NMR (125 MHz, D₂O): 164.94, 147.11, 144.03, 142.65, 130.99, 127.50. Nicotinic acid hydrochloride is a known and commercially available compound (CAS 636-79-3).

**Isonicotinic acid hydrochloride (3f):**

This reaction was performed according to the general procedure using 4-pyridine carbaldehyde (107 mg, 1.0 mmol). The crude product was cooled to 0 °C and then concentrated HCl (0.1 mL, 12 M) was added slowly and the mixture was stirred for 15 min. A white precipitate formed and was isolated via vacuum filtration and washed with cold water (1 x 2 mL) and Et₂O (2 x 5 mL) to give 91% of the product (145 mg, 0.91 mmol) as a white solid. ¹H NMR (500 MHz, D₂O): 8.89 (d, J = 5.6 Hz, 2H), 8.38 (d, J = 6.6 Hz, 2H). ¹³C NMR (125 MHz, D₂O): 167.31, 150.54, 142.16, 126.45. Isonicotinic acid hydrochloride is a known and commercially available compound (CAS 37832-54-5).

**2,3,4,5,6-pentafluorobenzoic acid¹¹ (3g):**

This reaction was performed according to the general procedure using 2,3,4,5,6-pentafluorobenzaldehyde (196 mg, 1.0 mmol). The crude product was purified by aqueous extraction using NaHCO₃. The NaHCO₃ aqueous layer was washed with Et₂O (2x 15 mL) followed by acidification with HCl to pH 2 and extractions with DCM (3x 20mL) to give 85% of the product (180 mg, 0.85 mmol) as a white solid. 2,3,4,5,6-pentafluorobenzoic acid is a commercially available compound (CAS: 602-94-8). Spectroscopic data matches pure sample purchased from Sigma Aldrich. ¹⁹F NMR is in exact accordance with spectra reported in the literature.

**3-(pyridin-2-yl)propanoic acid¹² (3h):**

This reaction was performed according to the general procedure using 3-(pyridin-2-yl)propanal (135 mg, 1.0 mmol). The crude product was purified by column chromatography on silica gel (DCM/MeOH 90/10) to
give 60% of the product (91 mg, 0.60 mmol) as a white solid. $^1$H NMR (500 MHz, DMSO-$d_6$): 8.47 (d, $J = 4.0$ Hz, 1H), 7.68 (dt, $J = 1.8$, 7.7 Hz, 1H), 7.20 (dd, $J = 4.9$ Hz, $J = 7.7$ Hz, 1H), 3.0 (t, $J = 7.4$ Hz, 2H), 2.7 (t, $J = 7.4$ Hz, 2H). $^{13}$C NMR (125 MHz, CDCl$_3$:CD$_3$CN 3:1): 174.47, 159.37, 146.99, 138.23, 123.61, 122.14, 34.05, 31.03.

**Adamantane-1-carboxylic acid**$^{13}$ (3i):

This reaction was performed according to the general procedure using adamantane-1-carbaldehyde (164 mg, 1.0 mmol). The crude product was purified by column chromatography on silica gel (DCM/MeOH 98/2) to give 55% of the product (98 mg, 0.54 mmol) as a white solid. $^1$H NMR (500 MHz, CDCl$_3$): 2.02 (br s, 3H), 1.90 (d, $J = 2.6$, 6H), 1.71 (m, 6H). $^{13}$C NMR (125 MHz, CDCl$_3$): 184.42, 40.46, 38.53, 36.38, 27.79.

**Aldehyde Starting Materials:**

The hydroformylation of N-vinyl acetamide was performed at 60 °C by the general procedure above. Characterization data agrees with literature report.$^{14}$

The hydroformylation of N-vinyl phthalimide was performed at 60 °C by the general procedure above. Characterization data agrees with literature report.$^{15}$

Hydroformylation of vinyl benzoate was performed at 60 °C according to the general procedure above, except olefin was added directly to the pressure bottle inside the glovebox and no pre-activation of the catalyst was performed. Characterization data agrees with literature report.$^{16}$ Enantiomeric excess was determined to be 92% by chiral GC analysis (Supelco β-DEX 225, 135 °C, isothermal); $t_{R}(R) = 14.3$ min, $t_{R}(S) = 15.2$ min.

The hydroformylation of vinyl acetate was performed at 60 °C by the general procedure above. Characterization data agree with literature report.$^{17}$

Hydroformylation of N-vinyl pyrrolidinone was performed at 60 °C according to the general procedure above. Characterization data agrees with literature report.$^{15}$

The hydroformylation of styrene, 4′-methylstyrene, 4′-fluorostyrene, 4′-methoxystyrene, and 4′-chlorostyrene were performed at 40 °C by the general procedure reported above. Characterization data agree with literature report.
All styrene substrates were synthesized according to literature.\textsuperscript{18}

The hydroformylation of styrene, 4'-methylstyrene, 4'-fluorostyrene, 4'-methoxystyrene, and 4'-chlorostyrene were performed at 40 °C by the general procedure reported above. Characterization data agree with the literature report.\textsuperscript{18} Enantiomeric excess was determined to be 73\% by chiral GC analysis (Supelco β-DEX 225, 100 °C for 2 min, then 3 °C/min to 140 °C, hold at 140 °C), $t_R(R) = 8.17$ and $t_R(S) = 8.33$ min.

Adamantane-1-carbaldehyde: The aldehyde was prepared using the Cu(MeCN)$_4$OTf/$\text{OMe}$bpy/ABNO/NMI alcohol oxidation procedure reported previously, and the $^1$H NMR and $^{13}$C NMR spectra match the reported spectra.\textsuperscript{19}
References

(S)-2a

CDCl₃, 500 MHz
(S)-2a

CDCl₃, 125 MHz
CDCl$_3$, 125 MHz
2c

CDCl₃, 125 MHz
CDCl₃, 400 MHz
$2d$

CDCl$_3$, 125 MHz
$^1$H NMR (400 MHz, D$_2$O) yield determination
(20µL (0.234 mmol) dioxane added)

2f
2f

CDCl₃, 400 MHz
2f
CDCl₃, 125 MHz
2g
CDCl₃, 400 MHz
$^{13}C$ NMR spectrum of compound 2g

CDCl$_3$, 125 MHz
$^{1}$H NMR (500 MHz, D$_2$O) yield determination
(20µL (0.234 mmol) dioxane added)
D2O, 500 MHz

2h
$^1$H NMR (500 MHz, D$_2$O) yield determination
(30µL (0.352 mmol) dioxane added)
D2O, 500 MHz

2i

linear aldehyde oxidation product

S34
D$_2$O, 125 MHz

$2i$
octanoic acid

3a

CD$_2$Cl$_2$, 400 MHz
3b

CD$_3$Cl, 100 MHz
3c

CD$_3$Cl, 400 MHz
CD$_3$Cl, 100 MHz

3c
DMSO-$d_6$, 500 MHz
DMSO-d$_6$, 125 MHz
$\text{D}_2\text{O, 125 MHz}$

$\text{3e}$
S45
$^{1}H$NMR of 3f in D$_2$O, 125 MHz
$3h$

CD$_3$Cl, 500 MHz
$^{3:1} \text{CDCl}_3: \text{CD}_3\text{CN}$

$3h$

CD$_3$Cl, 125 MHz
3i
CD$_3$Cl, 500 MHz
3i
CD$_3$Cl, 125 MHz