Supporting Information for:

β-Amidoaldehydes *via* Oxazoline Hydroformylation

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General Considerations. Unless stated otherwise, all synthetic manipulations were carried out using standard Schlenk techniques under a nitrogen atmosphere, or in an MBraun Unilab glovebox under an atmosphere of purified nitrogen. Reactions were carried out in oven-dried glassware cooled under vacuum. Anhydrous toluene, hexanes, tetrahydrofuran, and diethyl ether were purchased from Fischer Scientific and sparged vigorously with nitrogen for 40 minutes prior to first use. The solvents were further purified by passing them under nitrogen pressure through two packed columns of neutral alumina (for diethyl ether and tetrahydrofuran; the tetrahydrofuran was also passed through a third column packed with activated 4Å molecular sieves) or through neutral alumina and copper(II) oxide (for toluene, hexanes and pentane). All non-dried solvents used were reagent grade or better.

IR spectra were recorded on a Mattson RS-10500 Research Series FTIR using NaCl salt plates. ^{1}H NMR spectra were recorded on a Varian 400 MHz instrument, with shifts reported relative to the residual solvent peak. ^{19}F NMR spectra were recorded on a Varian 400 MHz instrument, with shifts referenced to an external standard of neat $CFCl_3$ (0 ppm). ^{13}C NMR spectra were recorded on a 500 MHz instrument, with shifts referenced relative to the solvent peak. NMR solvents were purchased from Cambridge Isotope Laboratories; $CDCl_3$ was deacidified by passing through basic alumina prior to use, $(CD_3)_2CO$ was used as received.

The starting materials 2-phenyl-2-oxazoline (**1a**) (TCI America), benzonitrile (Aldrich), ethylene glycol (Mallinckrodt), potassium carbonate (Mallinckrodt), L-tryptophanol (Aldrich), Europium(III) tris[3-(trifluoromethylhydroxymethylene)-(+)-camphorate] (Aldrich), Carbon monoxide (Matheson, 99.99% min. purity) and hydrogen

(Airgas, 99.999% min. purity) were used as received. Dicobalt octacarbonyl (Strem Chemical) was stored at –30 °C in a glove box freezer. L-Isoleucinol,[1] 2-(4-fluorophenyl)-2-oxazoline (**1b**),[2] and 4-((*tert*-butyldimethylsilyloxy)methyl)-2-(4-*tert*-butylphenyl)-2-oxazoline (**1k**)[3] were prepared by known literature methods. The following previously synthesized oxazolines were prepared by reaction of the appropriate 2-amino alcohol with an aromatic nitrile in ethylene glycol solution at 125 °C[4] and compared with spectral data found in the literature: 2-(4-methoxyphenyl)-2-oxazoline (**1c**),[4] (*S*)-2-phenyl-4-methyl-2-oxazoline (**1d)**,[5] (*R*)-2-phenyl-4-ethyl-2-oxazoline (**1e**),[6] (*S*)-2-phenyl-4-isopropyl-2-oxazoline (**1f**),[7] (*S*)-2-phenyl-4-isobutyl-2-oxazoline (**1g**),[8] (*R*)-2,4-diphenyl-2-oxazoline (**1i**),[9] (*S*)-2-phenyl-4-benzyl-2-oxazoline (**1j**),[6] 2-phenyl-5-methyl-2-oxazoline.[10] Liquid oxazolines were purified by distillation and were stored in a nitrogen glove box over activated 4Å molecular sieves. The enantiomeric purities of all chiral oxazolines were assumed to be the same as the amino alcohols from which they were derived (> 99% ee). The enantiomeric purities of all chiral amido aldehydes was determined using the chiral shift reagent europium(III) tris[3-

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[1] Luo, S.-P.; Xu, D.-Q.; Yue, H.-D.; Wang, L.-P.; Yang, W.-L.; Xu, Z.-Y. *Tetrahedron: Asymm.* **2006**, *17*, 2028–2033.
[2] Lobert, M.; Koehn, U.; Hoogenboom, R.; Schubert, U. S. *Chem. Commun.* **2008**, 1458–1460
[3] Byrne, C, M.; Church, T. L.; Kramer, J. W.; Coates, G. W. *Angew. Chem., Int. Ed.* **2008**, *47*, 3979–3983.
[4] Karade, N. N.; Tiwari, G. B.; Gampawar, S. V. *Synlett* **2007**, 1921–1924.
[5] Ikeda, S.; Kondo, H.; Arii, T.; Odashima, K. *Chem. Commun.* **2002**, 2422–2423.
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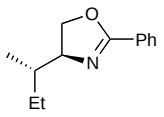
[7] Ohshima, T.; Iwasaki, T.; Mashima, K. *Chem. Commun.* **2006**, 2711–2713.
[8] Fukuhara, T.; Hasegawa, C.; Hara, S. *Synthesis* **2007**, 1528–1534.
[9] Gorunova, O. N.; Keuseman, K. J.; Goebel, B. M.; Kataeva, N. A.; Churakov, A. V.; Kuz'mina, L. G.; Dunina, V. V.; Smoliakova, I. P. *J. Organomet. Chem.* **2004**, 689, 2382–2394.
[10] Chamchaang, W.; Pinhas, A. R. *J. Org. Chem.* **1990**, *55*, 2943–2950.

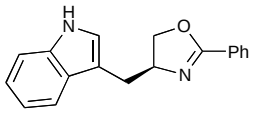
(trifluoromethylhydroxymethylene)-(+)-camphorate] relative to racemic and/or enantiomerically pure samples.

Oxazoline Synthesis



(4*S*)-4-((*S*)-*sec*-Butyl)-2-phenyl-2-oxazoline (1h). A Schlenk flask equipped with a Teflon-coated magnetic stir bar was charged with L-Isoleucinol (3.35 g, 28.6 mmol), potassium carbonate (0.366 g, 2.65 mmol) and ethylene glycol (5 mL). A nitrogen atmosphere was established and the reaction mixture was heated to 140 °C. Benzonitrile (2.70 mL, 26.5 mmol) was added and the flask was heated at 140 °C while vented through a mercury bubbler. After 20 h, the flask was cooled to room temperature and water (60 mL) was added. The reaction mixture was extracted with hexanes (3 x 20 mL). The organic extracts were combined and washed with brine, dried with $MgSO_4$, filtered and concentrated *in vacuo*. The resulting yellow oil was fractionally distilled under vacuum to afford the title compound as a colorless oil (3.74 g, 70%). ^{1}H NMR ($CDCl_3$): δ 7.95 (d, ^3J = 7.0 Hz, 2H, *o*-C<u>H</u>), 7.47 (t, ^3J = 7.2 Hz, 1H, *p*-C<u>H</u>), 7.40 (t, ^3J = 7.3 Hz, *m*-C<u>H</u>), 4.38 (pseudo t, J = 8.4 Hz, 1H, C<u>H</u>$_2$O), 4.21 (m, 1H, C<u>H</u>^{s}Bu), 4.13 (pseudo t, J = 7.60 Hz, 1H, C<u>H</u>$_2$O), 1.71 (m, 1H, C<u>H</u>Me), 1.61 (m, 1H, C<u>H</u>$_2$Me), 1.26 (m, 1H, C<u>H</u>$_2$Me), 0.96 (t, ^3J = 7.4 Hz, 3H, C<u>H</u>$_3$) 0.86 (d, ^3J = 6.7 Hz, 3H, C<u>H</u>$_3$). ^{13}C NMR ($CDCl_3$): δ 163.0, 131.3, 128.5, 128.4, 128.2, 71.4, 69.7, 39.4, 26.4, 14.5, 11.9. IR (NaCl plate, cm^{-1}): 2962, 2876, 1652, 1450, 1081, 1066, 1025. $[\alpha]_D^{23}$ –68.6 (c = 1.0 $CHCl_3$). HRMS (ESI) calculated for $C_{13}H_{18}NO^-$ (M – H$^+$): 204.1388; measured 204.1385.

(*S*)-4-((3-Indolyl)methyl)-2-phenyl-2-oxazoline (1l). A Schlenk flask equipped with a Teflon-coated magnetic stir bar was charged



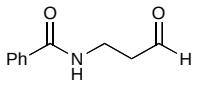
with L-tryptophanol (2.60 g, 13.7 mmol), potassium carbonate (0.174 g, 1.26 mmol) and ethylene glycol (2 mL). A nitrogen atmosphere was established and the reaction mixture was heated to 140 °C. Benzonitrile (1.30 mL, 12.7 mmol) was added and the flask was heated at 140 °C while vented through a mercury bubbler for 20 h. The flask was then cooled to room temperature and water (50 mL) was added and the reaction mixture was extracted with dichloromethane (2 x 50 mL). The organic extracts were combined and washed with brine, dried with $MgSO_4$, filtered and concentrated *in vacuo* to afford an oily solid. The crude product was purified by passing through a plug of silica gel (built with NEt_3/ethyl acetate/hexanes (2:49:49)) and eluted with hexanes/ethyl acetate (1:1). Upon concentration, the cream-colored foam was further purified by trituration with hexanes to yield an off-white solid (2.08 g, 60%, mp = 103–106 °C). IR (NaCl plate, cm^{-1}): 3411, 3181, 3058, 2921, 1643, 1450, 1359, 1089, 742, 695. $[\alpha]_D^{23}$ +24.3 (*c* = 1.0 $CHCl_3$). HRMS (EI) calculated for $C_{18}H_{16}N_2O$: 276.1263; measured 276.1251.

Oxazoline Hydroformylation

General Procedure for Oxazoline Hydroformylation. Unless otherwise noted, the following procedure was used: In a glove box, vials equipped with Teflon-coated magnetic stir bars were charged with the appropriate oxazoline starting material (1.0 mmol) and a toluene solution of $Co_2(CO)_8$ (0.040 mmol; 4.0 mL of a 0.010 M toluene stock solution) was added. The vials were then loaded into a custom-made 6-well high-

pressure reactor.[11] The reactor was sealed, taken out of the glove box and pressured with hydrogen (41 atm partial pressure) and carbon monoxide (41 atm partial pressure). The reactor was then sealed, heated to 80 °C and the reaction mixtures were stirred for the specified reaction time (6 or 20 h). The reactor was then cooled with dry ice for 10 min, vented carefully and warmed to room temperature in a water bath. The crude reaction mixtures concentrated *in vacuo* and immediately purified by column chromatography with silica gel that was pretreated with 1% NEt_3 in CH_2Cl_2 and using CH_2Cl_2 and then 50:50 EtOAc/C_6H_{14} as the eluent. Reported yields are for individual runs and may differ from those reported in Table 2, which are averages of at least two runs.

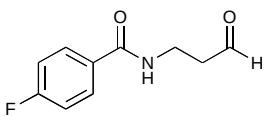
3-Benzamidopropanal (2a). General procedure was followed with a 6 h reaction time except that a catalyst loading of 2 mol % was employed.



Instability on silica gel precluded isolation of the title compound in satisfactory purity and yields were determined by ^{1}H NMR spectroscopy of the crude reaction mixture relative to an internal standard of mesitylene (81%, average of two runs). Chemical shifts were compared to those previously reported to verify identity.[12] ^{1}H NMR ($CDCl_3$): δ 9.81 (s, 1H, O=C<u>H</u>), 7.72 (d, ^3J = 7.2 Hz, 2H), 7.47 (t, ^3J = 7.4 Hz, 1H), 7.38 (t, ^3J = 7.2 Hz, 2H), 6.86 (br s, 1H, N<u>H</u>), 3.71 (pseudo q, ^3J = 5.8 Hz, 2H, NC<u>H</u>$_2$), 2.82 (t, ^3J = 5.7 Hz, 2H, C<u>H</u>$_2$C(O)H). ^{13}C NMR ($CDCl_3$): δ 202.0 (O=<u>C</u>H), 167.9 (O=<u>C</u>N), 134.2, 131.8, 128.8, 127.1, 43.9, 33.7. The branched isomer of the title compound (7%) was formed as judged by ^{1}H NMR analysis of the crude reaction mixture.

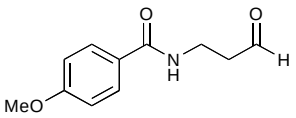
[11] Getzler, Y. D. Y. L.; Mahadevan, V.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **2002**, *124*, 1174–1175.
[12] Chan, S.; Braish, T. F. *Tetrahedron* **1994**, *50*, 9943–9950.

3-(4-Fluorobenzamido)propanal (2b). General procedure was followed with a 6 h reaction time except that a catalyst loading of



2 mol % was employed. Instability on silica gel precluded isolation of the title compound in satisfactory purity and reported yields were determined by ^{1}H NMR spectroscopy of the crude reaction mixture relative to an internal standard of mesitylene (83%, average of two runs). ^{1}H NMR ($CDCl_3$): δ 9.85 (s, 1H, OC<u>H</u>), 7.75 (dd, ^{3}J = 8.5 Hz, $^{4}J_{H–F}$ = 5.4, 2H), 7.08 (pseudo t, J = 8.5 Hz, 2H), 6.68 (br s, 1H, N<u>H</u>), 3.73 (pseudo q, ^{3}J = 5.7 Hz, 2H, NC<u>H</u>$_2$), 2.86 (t, ^{3}J = 5.6 Hz, 2H, C<u>H</u>$_2$C(O)H). ^{13}C NMR ($CDCl_3$): δ 201.9, 166.6, 164.8 (d, $^{1}J_{C–F}$ = 253 Hz), 130.5 (d, $^{4}J_{C–F}$ = 3.0 Hz), 129.4 (d, $^{3}J_{C–F}$ = 8.4 Hz), 115.7 (d, $^{2}J_{C–F}$ = 21.4 Hz), 43.8, 33.7. ^{19}F NMR = δ –111.1. The branched isomer of the title compound (7%) was formed as judged by ^{1}H NMR analysis of the crude reaction mixture.

3-(4-Methoxybenzamido)propanal (2c). General procedure was followed with a 6 h reaction time except that a catalyst



loading of 2 mol % was employed. Instability on silica gel precluded isolation of the title compound in satisfactory purity and reported yields were determined by ^{1}H NMR spectroscopy of the crude reaction mixture relative to an internal standard of mesitylene (63%, average of two runs). ^{1}H NMR ($CDCl_3$): δ 9.84 (s, 1H, O=C<u>H</u>), 7.70 (d, ^{3}J = 8.8 Hz, 2H), 6.89 (d, ^{3}J = 8.8 Hz, 2H), 6.63 (br s, 1H, N<u>H</u>), 3.83 (s, 3H, OC<u>H</u>$_3$), 3.71 (pseudo q, ^{3}J = 5.9 Hz, 2H, NC<u>H</u>$_2$), 2.84 (t, ^{3}J = 5.6 Hz, 2H, C<u>H</u>$_2$C(O)H). ^{13}C NMR ($CDCl_3$): δ 202.1 (O<u>C</u>H), 167.1 (O<u>C</u>N), 162.4, 128.9, 126.6, 113.9, 55.6, 44.0, 33.5. The branched

isomer of the title compound (4%) was formed as judged by ^{1}H NMR analysis of the crude reaction mixture.

(*S*)-3-Benzamidobutanal (2d). The general procedure was followed with a 6 h reaction time except that a catalyst loading of 2 mol % was employed to afford the title compound as a colorless solid (0.160 g, 84%; mp = 71–73 °C). The reaction was repeated at 70 °C and 90 °C with isolated yields of 71% and 86% respectively (average of two runs). ^{1}H NMR ($CDCl_3$): δ 9.76 (s, 1H, OC<u>H</u>), 7.72 (d, ^3J = 7.4 Hz, 2H, *o*-C<u>H</u>), 7.44 (t, ^3J = 7.4 Hz, 1H, *p*-C<u>H</u>), 7.36 (t, ^3J = 7.5 Hz, *m*-C<u>H</u>), 6.82 (br d, ^3J = 7.2 Hz, 1H, N<u>H</u>), 4.58 (pent, ^3J = 6.8 Hz, 1H, C<u>H</u>Me), 2.78–2.64 (m, 2H, C<u>H</u>$_2$C(O)H), 1.31 (d, ^3J = 6.8 Hz, 3H, C<u>H</u>$_3$). ^{1}H NMR (0.037 M $CDCl_3$, (+)-Eu(tfc)$_3$ (1 eq), OC<u>H</u>) = $\delta_{(S)}$ 10.45, $\delta_{(R)}$ 10.29. The product % ee for reactions run at 70, 80 and 90 °C are 94, 90 and 80% respectively. ^{13}C NMR ($CDCl_3$): δ 201.4 (O<u>C</u>H), 167.0 (O<u>C</u>N), 134.4, 131.6, 128.6, 127.1, 49.8, 41.7, 20.6 (<u>C</u>H$_3$). IR (NaCl plate, cm^{-1}): 3296, 2971, 1724, 1635, 1533, 696. $[\alpha]_D^{23}$ –30.0 (*c* = 1.0 $CHCl_3$). HRMS (EI) calculated for $C_{11}H_{13}NO_2$: 191.0946; measured 191.0937.

3-Benzamido-2-methylpropanal. The general procedure was followed with a 6 h reaction time except that the reaction was carried out at 90 °C to afford the title compound as a colorless oil (0.108 g, 57%). The use of enantiopure 2-phenyl-5-methyl-2-oxazoline under the same reaction conditions produced racemic 3-benzamido-2-methylpropanal. ^{1}H NMR ($CDCl_3$): δ 9.69 (s, 1H, OC<u>H</u>), 7.72 (d, ^3J = 7.2 Hz, 2H, *o*-C<u>H</u>), 7.46 (pseudo-t, 1H, *p*-C<u>H</u>), 7.38 (pseudo-t, *m*-C<u>H</u>), 6.87 (br, 1H, N<u>H</u>), 3.68 (m, 1H, NC<u>H</u>$_2$), 3.52 (m, 1H, NC<u>H</u>$_2$), 2.76 (m, 1H, C<u>H</u>CH$_3$), 1.18 (d, ^3J = 7.6 Hz,

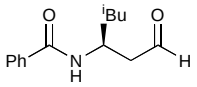
3H, C<u>H</u>$_3$). ^{13}C NMR ($CDCl_3$): δ 204.5 (O<u>C</u>H), 167.8 (O<u>C</u>N), 134.3, 131.7, 128.7, 127.1, 46.9, 40.0, 11.6 (<u>C</u>H$_3$). HRMS (ESI) calculated for $C_{11}H_{12}NO_2^-$ (M – H$^+$): 190.0868; measured 190.0860.

(*R*)-3-Benzamidopentanal (2e). General procedure was followed with a 6 h reaction time to afford the title compound as a colorless solid (0.170 g, 83%; mp = dec. 98 °C). ^{1}H NMR ($CDCl_3$): δ 9.77 (s, 1H, OC<u>H</u>), 7.73 (d, ^3J = 8.2 Hz, 2H, *o*-C<u>H</u>), 7.46 (t, ^3J = 8.0 Hz, 1H, *p*-C<u>H</u>), 7.38 (t, ^3J = 7.5 Hz, *m*-C<u>H</u>), 6.67 (br d, ^3J = 7.2 Hz, 1H, N<u>H</u>), 4.42 (m, 1H, C<u>H</u>Et), 2.80–2.64 (m, 2H, C<u>H</u>$_2$C(O)H), 1.73–1.64 (m, 2H, C<u>H</u>$_2$CH$_3$), 0.96 (t, ^3J = 7.41 Hz, 3H, C<u>H</u>$_3$). ^{1}H NMR (0.038 M $CDCl_3$, (+)-Eu(tfc)$_3$ (1 eq), OC<u>H</u>) = $\delta_{(R)}$ 10.28 (>99% ee). ^{13}C NMR ($CDCl_3$): δ 201.7 (O<u>C</u>H), 167.4 (O<u>C</u>N), 134.5, 131.7, 128.7, 127.1, 48.1, 47.3, 27.7, 10.9 (<u>C</u>H$_3$). IR (NaCl plate, cm^{-1}): 3295, 2962, 2931, 1719, 1637, 1533, 1310, 696. $[\alpha]_D^{23}$ +73.9 (*c* = 1.0 $CHCl_3$). HRMS (ESI) calculated for $C_{12}H_{14}NO_2^-$ (M – H$^+$): 204.1025; measured 204.1027.

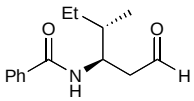
(*S*)-3-Benzamido-4-methylpentanal (2f). General procedure was followed with a 20 h reaction time to afford the title compound as a colorless solid (0.186 g, 85%; mp = dec. 95 °C). ^{1}H NMR ($CDCl_3$): δ 9.80 (s, 1H, O=C<u>H</u>), 7.73 (d, ^3J = 7.4 Hz, 2H, *o*-C<u>H</u>), 7.49 (t, ^3J = 7.2 Hz, 1H, *p*-C<u>H</u>), 7.41 (t, ^3J = 7.4 Hz, *m*-C<u>H</u>), 6.49 (br d, ^3J = 8.0 Hz, 1H, N<u>H</u>), 4.38 (pent, ^3J = 7.0 Hz, 1H, C<u>H</u>^{i}Pr), 2.77–2.65 (m, 2H, C<u>H</u>$_2$C(O)H), 1.99 (oct, ^3J = 6.8 Hz, 1H, C<u>H</u>(CH$_3$)$_2$), 0.99 (d, ^3J = 6.6 Hz, 3H, CH(C<u>H</u>$_3$)$_2$), 0.98 (d, ^3J = 6.6 Hz, 3H, CH(C<u>H</u>$_3$)$_2$). ^{1}H NMR (0.038 M $CDCl_3$, (+)-Eu(tfc)$_3$ (1 eq), OC<u>H</u>) = $\delta_{(R)}$ 10.60 (>99% ee). ^{13}C NMR ($CDCl_3$): δ 201.8 (O<u>C</u>H), 167.3

(O<u>C</u>N), 134.6, 131.8, 128.8, 127.1, 51.0, 46.2, 31.9 (<u>C</u>H(CH_3)$_2$), 19.6 (CH(<u>C</u>H_3)$_2$), 19.1 (CH(<u>C</u>H_3)$_2$). IR (NaCl plate, cm^{-1}): 3315, 2963, 1724, 1636, 1545, 696. $[\alpha]_D^{23}$ –63.7 (*c* = 1.0 $CHCl_3$). HRMS (EI) calculated for $C_{13}H_{17}NO_2$: 219.1259; measured 219.1255.

(*S*)-3-Benzamido-5-methylhexanal (2g). General procedure was followed with a 20 h reaction time to afford the title compound as a colorless solid (0.205 g, 88%; mp = dec. 46 °C) ^{1}H NMR ($CDCl_3$): δ 9.80 (s, 1H, OC<u>H</u>), 7.73 (d, ^3J = 7.2 Hz, 2H, *o*-C<u>H</u>), 7.48 (t, ^3J = 7.3 Hz, 1H, *p*-C<u>H</u>), 7.40 (t, ^3J = 7.4 Hz, *m*-C<u>H</u>), 6.54 (br d, ^3J = 7.9 Hz, 1H, N<u>H</u>), 4.60 (m, 1H, C<u>H</u>^{i}Bu), 2.82–2.66 (m, 2H, C<u>H</u>$_2$C(O)H), 1.74–1.63 (m, 2H, C<u>H</u>$_2$^{i}Pr), 1.40 (m, 1H, C<u>H</u>(CH_3)$_2$), 0.94 (t, ^3J = 6.2 Hz, 6H, CH(C<u>H</u>$_3$)$_2$. ^{1}H NMR (0.038 M $CDCl_3$, (+)-Eu(tfc)$_3$ 50 mol %, OC<u>H</u>) = $\delta_{(R)}$ 10.45 (>99% ee). ^{13}C NMR ($CDCl_3$): δ 201.7 (O<u>C</u>H), 167.1 (O<u>C</u>N), 134.5, 131.7, 128.7, 127.1, 49.0, 44.1, 43.8, 25.3, 23.1, 22.2. IR (NaCl plate, cm^{-1}): 3305, 2957, 1723, 1634, 1536, 695. $[\alpha]_D^{23}$ –55.6 (*c* = 1.0 $CHCl_3$). HRMS (EI) calculated for $C_{14}H_{19}NO_2$: 233.1416; measured 233.1411.



(3*R*,4*S*)-3-Benzamido-4-methylhexanal (2h). General procedure was followed with a 20 h reaction time to afford the title compound as a colorless solid (0.204 g, 87% mp = dec. 66 °C). ^{1}H NMR ($CDCl_3$): δ 9.77 (s, 1H, O=C<u>H</u>), 7.71 (d, ^3J = 8.5 Hz, 2H, *o*-C<u>H</u>), 7.46 (t, ^3J = 7.5 Hz, 1H, *p*-C<u>H</u>), 7.38 (t, ^3J = 7.8 Hz, *m*-C<u>H</u>), 6.62 (br d, ^3J = 8.0 Hz, 1H, N<u>H</u>), 4.44 (m, 1H, NC<u>H</u>), 2.72–2.63 (m, 2H, C<u>H</u>$_2$C(O)H), 1.76 (m, 1H, C<u>H</u>Me), 1.54 (m, 1H, CH_2CH_3), 1.17 (m, 1H, CH_2CH_3), 0.92 (m, 6H). ^{1}H NMR (0.037 M $CDCl_3$, (+)-Eu(tfc)$_3$ 50 mol %) OC<u>H</u> = $\delta_{(R)}$ 10.25 (>99%).



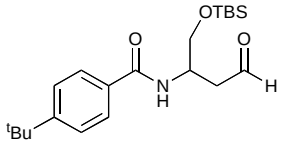
^{13}C NMR ($CDCl_3$): δ 201.9 (O<u>C</u>H), 167.3 (O<u>C</u>N), 134.5, 131.7, 128.7, 127.1, 49.8, 45.6, 38.3, 25.9, 15.6, 11.5. IR (NaCl plate, cm^{-1}): 3300, 2964, 2876, 1724, 1636, 1539, 1490, 696. $[\alpha]_D^{23}$ –59.2 (*c* = 1.0 $CHCl_3$). HRMS (EI) calculated for $C_{14}H_{19}NO_2$: 233.1416; measured 233.1424.

(*R*)-3-Benzamido-3-phenylpropanal (2i). General procedure was followed with a 20 h reaction time to afford the title compound as a colorless solid (0.169 g, 67% mp = 113–117 °C). ^{1}H NMR ($CDCl_3$): δ 9.81 (s, 1H, OC<u>H</u>), 7.77 (d, ^3J = 7.4 Hz, 2H), 7.50 (t, ^3J = 7.0 Hz, 1H), 7.41 (t, ^3J = 7.4 Hz, 2H), 7.38–7.28 (m, 6H), 7.00 (d, ^3J = 7.6 Hz, 2H, N<u>H</u>), 5.71 (dd, ^{3}J = 6.2 Hz, ^3J = 14.2 Hz, 1H, NC<u>H</u>), 3.21 (ddd, ^3J = 1.9 Hz, ^3J = 6.4 Hz, ^2J = 17.0 Hz, 1H), 3.06 (dd, ^3J = 5.8, ^2J = 17.0, 1H). ^{1}H NMR (0.056 M $CDCl_3$, (+)-Eu(tfc)$_3$ 25 mol %) OC<u>H</u> = $\delta_{(S)}$ 10.04 (44%, $\delta_{(R)}$ 9.98 (56%); ee 12%. ^{13}C NMR ($CDCl_3$): δ 200.8 (O<u>C</u>H), 167.0 (O<u>C</u>N), 140.5, 134.1, 131.9, 129.2, 128.8, 128.1, 127.2, 126.7, 49.3, 49.0. IR (NaCl plate, cm^{-1}): 3306, 1724, 1639, 1536, 699. $[\alpha]_D^{23}$ –0.2 (*c* = 1.0 $CHCl_3$). HRMS (ESI) calculated for $C_{16}H_{16}NO_2^+$ (M + H^+): 254.1181; measured 254.1171.

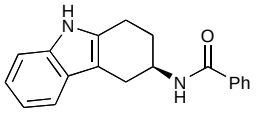
(*S*)-3-Benzamido-4-phenylbutanal (2j). General procedure was followed with a 6 h reaction time to afford the title compound as an off-white solid (0.217 g, 81%, mp = 109–114 °C). ^{1}H NMR ($CDCl_3$): δ 9.77 (s, 1H, OC<u>H</u>), 7.68 (d, ^3J = 7.2 Hz, 2H), 7.48 (t, ^3J = 7.4 Hz, 1H), 7.31 (t, ^3J = 7.0 Hz, 2H), 7.25 (m, 1H), 7.21 (d, ^3J = 7.0 Hz, 2H), 6.58 (br d, ^3J = 8.2 Hz, 1H, N<u>H</u>), 4.75 (m, 1H, NC<u>H</u>), 3.09 (dd, ^3J = 6.6 Hz, ^2J = 13.6 Hz, 1H), 2.97 (dd, ^3J = 7.8, ^2J = 13.5, 1H), 2.75 (m, 2H). ^{1}H

NMR (0.0.37 M $CDCl_3$, (+)-Eu(tfc)$_3$ (1 eq)) OC<u>H</u> = $\delta_{(S)}$ 10.27 (98%), $\delta_{(R)}$ 10.07 (2%); ee 96%. ^{13}C NMR ($CDCl_3$): δ 201.5 (O<u>C</u>H), 167.2 (O<u>C</u>N), 137.5, 134.4, 131.8, 129.4, 129.0, 128.8, 127.1, 127.0, 47.0, 46.8, 40.2. IR (NaCl plate, cm^{-1}): 3308, 1716, 1640, 1531, 1111, 696. $[\alpha]_D^{23}$ –40.6 (*c* = 1.0 $CHCl_3$). HRMS (EI) calculated for $C_{17}H_{17}NO_2$: 267.1259; measured 267.1263.

3-(4-*tert*-Butylbenzamido)-4-(*tert*-butyldimethylsiloxy)butanal (2k): General procedure was followed with a 6 h reaction time to afford the title compound as a colorless oil (0.319 g, 88%). ^{1}H NMR ($CDCl_3$): δ 9.83 (s, 1H, O=C<u>H</u>), 7.68 (d, ^3J = 7.8 Hz, 2H), 7.45 (d, ^3J = 7.8 Hz, 2H), 6.76 (br d, ^3J = 7.3 Hz, 1H, N<u>H</u>), 4.64 (m, 1H, NC<u>H</u>), 3.79 (m, 2H, C<u>H</u>$_2$OTBDMS), 2.83 (dd, ^3J = 3.9 Hz, ^2J = 16.6 Hz, 1H, C<u>H</u>$_2$C(O)H), 2.74 (dd, ^3J = 4.9 Hz, ^2J = 16.6 Hz, 1H, C<u>H</u>$_2$C(O)H), 1.32 (s, 9H, C(C<u>H</u>$_3$)$_3$), 0.91 (s, 9H, C(C<u>H</u>$_3$)$_3$), 0.06 (s, 6H, Si(C<u>H</u>$_3$)$_2$). ^{13}C NMR ($CDCl_3$): δ 201.3 (O<u>C</u>H), 166.9 (O<u>C</u>N), 155.4, 131.4, 126.9, 125.8, 64.5, 47.1, 45.4, 35.1, 31.3, 26.0, 18.4, –5.3. HRMS (ESI) calculated for $C_{21}H_{36}NO_3Si^-$ (M – H$^+$): 378.2464; measured 378.2475.



(*R*)-3-Benzamido-1,2,3,4,-tetrahydrocarbazole (3). General procedure was followed with a 6 h reaction time. A different work up procedure was used: the crude reaction mixture was filtered to give an off-white solid which was further purified by column chromatography using silica gel pretreated with a 1% solution of NEt_3 in CH_2Cl_2 and eluting with a 5% solution of EtOAc in CH_2Cl_2 to afford the title compound as a colorless microcrystalline solid (0.118 g, 42%, mp > 200



°C). The % ee of the crude **3** was not measured, but was assumed to be > 95% given the structural similarity of substrate **1l** to **1j**, and the enantiopurity of **3** in single crystals as determined by x-ray diffraction ($P2_12_12_1$ space group). The absolute configuration of **3** is assigned as *R* on the basis of the absolute configuration of the enantiomerically-pure starting material. ^{1}H NMR ($(CD_3)_2CO$): δ 9.86 (s, 1H, O=C<u>H</u>), 7.92 (d, ^3J = 7.6 Hz, 2H), 7.79 (br d, ^3J = 6.1 Hz, 1H, N<u>H</u>), 7.50 (t, ^3J = 7.0 Hz, 1H), 7.43 (t, ^3J = 8.0 Hz, 2H), 7.38 (d, ^3J = 7.6 Hz, 1H), 7.29 (d, ^3J = 8.0 Hz, 1H) 7.03 (t, ^3J = 7.2 Hz, 1H), 6.97 (t, ^3J = 7.4 Hz, 1H), 4.49 (m, 1H), 3.15 (dd, ^2J = 15.2 Hz, ^3J = 5.5 Hz, 1H), 2.92 (m, 2H), 2.74 (dd, ^3J = 8.8 Hz, ^2J = 15.0 Hz, 1H), 2.20 (m, 1H), 2.08 (m, 1H), ^{13}C NMR ($(CD_3)_2CO$): δ 167.0 (O<u>C</u>N), 137.7, 136.3, 134.4, 131.8, 129.1, 128.8, 128.2, 121.5, 119.4, 118.2, 111.5, 108.2, 47.4, 29.8, 28.3, 22.4. $[\alpha]_D^{23}$ –118 (*c* = 0.1 $CHCl_3$). HRMS (ESI) calculated for $C_{19}H_{19}N_2O^+$ ($M + H^+$): 291.1497; measured 291.1501.

X-Ray Crystallography

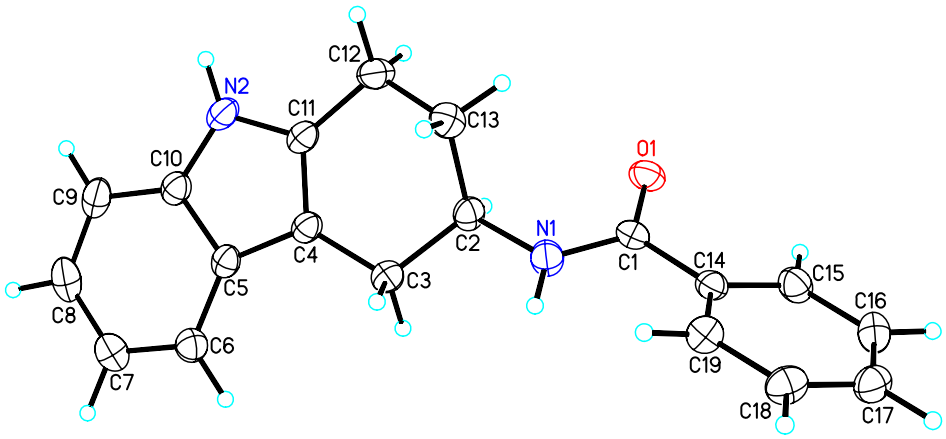


Table S1. Crystal data and structure refinement for **3.**

Identification code	dsl1	
Empirical formula	$C_{19}H_{18}N_2O$	
Formula weight	290.35	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 9.3075(4) Å	α= 90°
	b = 11.1765(7) Å	β= 90°
	c = 14.3598(11) Å	γ = 90°
Volume	1493.78(16) $Å^3$	
Z	4	
Density (calculated)	1.291 g/cm^3	
Absorption coefficient	0.081 mm^{-1}	
F(000)	616	
Crystal size	0.50 x 0.30 x 0.20 mm^3	
θ range for data collection	2.31 to 28.42°	
Index ranges	-12<=h<=11, -14<=k<=14, -7<=l<=19	
Reflections collected	8472	
Independent reflections	2145 [R(int) = 0.0409]	

Completeness to $\theta = 28.42°$	99.6 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9840 and 0.9608
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2145 / 0 / 271
Goodness-of-fit on F^2	0.996
Final R indices [$I>2\sigma(I)$]	$R1 = 0.0399$, $wR2 = 0.0850$
R indices (all data)	$R1 = 0.0564$, $wR2 = 0.0919$
Largest diff. peak and hole	0.148 and -0.186 e/Å^3

Table S2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for **3**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	1633(1)	2994(1)	9261(1)	34(1)
N(1)	-416(1)	3554(1)	9952(1)	36(1)
N(2)	1326(1)	5628(1)	13285(1)	34(1)
C(1)	314(2)	3106(2)	9235(1)	29(1)
C(2)	287(2)	3944(2)	10805(1)	31(1)
C(3)	-794(2)	3917(2)	11601(1)	33(1)
C(4)	-171(2)	4506(1)	12439(1)	28(1)
C(5)	-608(2)	4438(2)	13388(1)	29(1)
C(6)	-1714(2)	3850(2)	13861(1)	35(1)
C(7)	-1809(2)	3974(2)	14812(1)	42(1)
C(8)	-829(2)	4671(2)	15301(1)	46(1)
C(9)	254(2)	5274(2)	14855(1)	40(1)
C(10)	358(2)	5150(2)	13898(1)	32(1)
C(11)	1005(2)	5224(2)	12404(1)	29(1)
C(12)	1852(2)	5497(2)	11558(1)	37(1)
C(13)	963(2)	5177(2)	10700(1)	35(1)
C(14)	-516(2)	2746(2)	8396(1)	28(1)
C(15)	101(2)	1937(2)	7787(1)	36(1)
C(16)	-627(2)	1563(2)	7003(1)	40(1)
C(17)	-1978(2)	2007(2)	6815(1)	38(1)
C(18)	-2591(2)	2829(2)	7409(1)	38(1)
C(19)	-1871(2)	3195(2)	8199(1)	33(1)

Table S3. Bond lengths [Å] and angles [°] for **3.**

O(1)-C(1)	1.2348(18)		
N(1)-C(1)	1.331(2)	N(1)-C(2)-C(3)	109.17(13)
N(1)-C(2)	1.456(2)	N(1)-C(2)-C(13)	111.92(14)
N(2)-C(10)	1.368(2)	C(3)-C(2)-C(13)	111.47(15)
N(2)-C(11)	1.376(2)	C(4)-C(3)-C(2)	109.86(13)
C(1)-C(14)	1.486(2)	C(11)-C(4)-C(5)	107.28(14)
C(2)-C(3)	1.522(2)	C(11)-C(4)-C(3)	123.07(15)
C(2)-C(13)	1.523(2)	C(5)-C(4)-C(3)	129.64(15)
C(3)-C(4)	1.490(2)	C(6)-C(5)-C(10)	118.91(16)
C(4)-C(11)	1.358(2)	C(6)-C(5)-C(4)	134.52(15)
C(4)-C(5)	1.424(2)	C(10)-C(5)-C(4)	106.57(14)
C(5)-C(6)	1.398(2)	C(7)-C(6)-C(5)	118.91(17)
C(5)-C(10)	1.406(2)	C(6)-C(7)-C(8)	120.99(18)
C(6)-C(7)	1.375(2)	C(9)-C(8)-C(7)	121.55(17)
C(7)-C(8)	1.390(3)	C(8)-C(9)-C(10)	117.70(17)
C(8)-C(9)	1.371(3)	N(2)-C(10)-C(9)	130.15(16)
C(9)-C(10)	1.386(2)	N(2)-C(10)-C(5)	107.91(15)
C(11)-C(12)	1.479(2)	C(9)-C(10)-C(5)	121.93(16)
C(12)-C(13)	1.527(2)	C(4)-C(11)-N(2)	109.57(14)
C(14)-C(15)	1.382(2)	C(4)-C(11)-C(12)	125.53(15)
C(14)-C(19)	1.387(2)	N(2)-C(11)-C(12)	124.86(14)
C(15)-C(16)	1.379(3)	C(11)-C(12)-C(13)	109.04(13)
C(16)-C(17)	1.379(3)	C(2)-C(13)-C(12)	110.82(15)
C(17)-C(18)	1.377(3)	C(15)-C(14)-C(19)	119.03(16)
C(18)-C(19)	1.380(2)	C(15)-C(14)-C(1)	118.32(14)
		C(19)-C(14)-C(1)	122.65(15)
C(1)-N(1)-C(2)	122.27(13)	C(16)-C(15)-C(14)	120.74(16)
C(10)-N(2)-C(11)	108.65(14)	C(17)-C(16)-C(15)	119.90(18)
O(1)-C(1)-N(1)	121.49(15)	C(18)-C(17)-C(16)	119.81(17)
O(1)-C(1)-C(14)	120.91(14)	C(17)-C(18)-C(19)	120.38(17)
N(1)-C(1)-C(14)	117.60(13)	C(18)-C(19)-C(14)	120.12(17)

Symmetry transformations used to generate equivalent atoms:

Table S4. Anisotropic displacement parameters ($Å^2$ x 10^3) for **3.** The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	24(1)	42(1)	37(1)	3(1)	2(1)	-4(1)
N(1)	24(1)	52(1)	32(1)	-7(1)	-2(1)	2(1)
N(2)	31(1)	31(1)	39(1)	-9(1)	-5(1)	-2(1)
C(1)	27(1)	29(1)	30(1)	4(1)	4(1)	-3(1)
C(2)	27(1)	38(1)	27(1)	-3(1)	-5(1)	1(1)
C(3)	30(1)	38(1)	31(1)	-4(1)	-1(1)	-4(1)
C(4)	26(1)	28(1)	31(1)	-4(1)	-3(1)	1(1)
C(5)	27(1)	28(1)	30(1)	-5(1)	-3(1)	6(1)
C(6)	34(1)	36(1)	35(1)	-3(1)	1(1)	1(1)
C(7)	40(1)	48(1)	38(1)	0(1)	6(1)	3(1)
C(8)	47(1)	59(1)	31(1)	-6(1)	4(1)	14(1)
C(9)	38(1)	45(1)	37(1)	-15(1)	-6(1)	9(1)
C(10)	29(1)	31(1)	35(1)	-6(1)	-2(1)	4(1)
C(11)	27(1)	27(1)	34(1)	-5(1)	-5(1)	2(1)
C(12)	34(1)	35(1)	40(1)	1(1)	-2(1)	-8(1)
C(13)	35(1)	37(1)	33(1)	4(1)	-2(1)	0(1)
C(14)	27(1)	32(1)	26(1)	3(1)	1(1)	-4(1)
C(15)	30(1)	44(1)	33(1)	0(1)	3(1)	2(1)
C(16)	45(1)	46(1)	30(1)	-5(1)	3(1)	1(1)
C(17)	44(1)	39(1)	31(1)	5(1)	-8(1)	-8(1)
C(18)	35(1)	37(1)	41(1)	4(1)	-8(1)	0(1)
C(19)	33(1)	33(1)	35(1)	1(1)	-2(1)	3(1)

Table S5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3) for **3.**

	x	y	z	U(eq)
H(1N)	-1320(20)	3537(16)	9970(12)	41(5)
H(2N)	2040(20)	6123(19)	13424(13)	53(6)
H(2)	1049(16)	3347(15)	10961(11)	24(4)
H(3B)	-1709(18)	4347(16)	11396(11)	31(4)
H(3A)	-1019(17)	3031(17)	11727(11)	34(5)
H(6)	-2442(17)	3373(15)	13497(11)	25(4)
H(7)	-2630(20)	3548(16)	15152(11)	43(5)
H(8)	-950(18)	4703(18)	15980(13)	42(5)
H(9)	920(20)	5767(17)	15169(13)	47(6)
H(12B)	2245(17)	6302(17)	11522(12)	35(5)
H(12A)	2799(19)	5032(18)	11567(13)	45(5)
H(13B)	151(19)	5777(17)	10609(13)	42(5)
H(13A)	1563(17)	5204(15)	10156(11)	25(4)
H(15)	1050(20)	1640(20)	7897(14)	55(6)
H(16)	-210(20)	1030(20)	6555(14)	59(6)
H(17)	-2500(20)	1764(18)	6251(12)	44(5)
H(18)	-3560(20)	3145(18)	7258(13)	47(6)
H(19)	-2260(20)	3774(18)	8607(12)	43(5)