The Enantioselective α-Benzylation of Aldehydes via Photoredox Organocatalysis

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Supporting Information

I. General Information. Commercial reagents were purified prior to use following the guidelines of Perrin and Armarego.[1] Dimethylsulfoxide (DMSO) and 2,6-lutidine were distilled from CaH_2 prior to use. Octanal and propanal were passed through a short plug of basic alumina and then distilled. All other solvents were purified according to the method of Grubbs.[2] Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator. Chromatographic purification of products was accomplished using force-flow chromatography according to the method of Still[3] on ICN 60 32-64 mesh silica gel 63. Davisil Grade 643 silica gel or Iatrobeads 6RS-8060 silica gel were used where specified. Thin-layer chromatography (TLC) was performed on Silicycle 250 mm silica gel F-254 plates. Visualization of the developed plates was performed by fluorescence quenching or by $KMnO_4$, anisaldehyde, ceric ammonium molybdate, or ninhydrin stain.

^1H and ^{13}C NMR spectra were recorded on a Varian Inova 400 (400 MHz or 100 MHz) or a Bruker Avance 500 (500 MHz or 125 MHz) and are internally referenced to residual protio solvent signals (note: $CDCl_3$ referenced at δ 7.27 ppm for ^1H and δ 77.0 ppm for ^{13}C). Data for ^1H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, bs = broad

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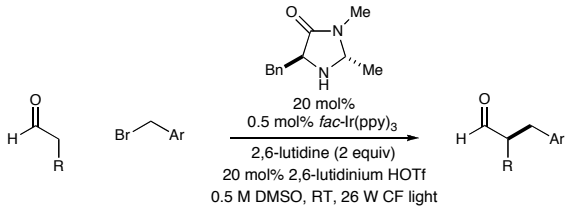
(1) Perrin, D. D.; Armarego, W. L. F. *Purification of Laboratory Chemicals*; 3rd ed., Pergamon Press, Oxford, 1988.
(2) Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics,* **1996**, *15*, 1518.
(3) Still, W. C.; Kahn, M.; Mitra, A. J. *J. Org. Chem.* **1978**, *43*, 2923.

singlet, d = doublet, t = triplet, q = quartet, hept = heptet, m = multiplet), integration, coupling constant (Hz), and assignment. Data for ^{13}C NMR are reported in terms of chemical shift. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in terms of frequency of absorption (cm^{-1}). High Resolution Mass spectra were obtained from the Princeton Mass Spectrometry Laboratory. Supercritical fluid chromatography (SFC) was performed on a Berger Minigram equipped with a diode array UV detector (λ = 214–280 nm) using a chiral column (25 cm) and guard column (5 cm) as noted for each compound. High Performance Liquid chromatography (HPLC) was performed on a Hewlett-Packard 1100 Series chromatographs using a chiral column (25 cm) and guard column (5 cm) as noted for each compound. Optical rotations were measured on a Jasco P-1010 polarimeter with $[\alpha]_D$ values reported in degrees; concentration (c) is in g/100 mL.

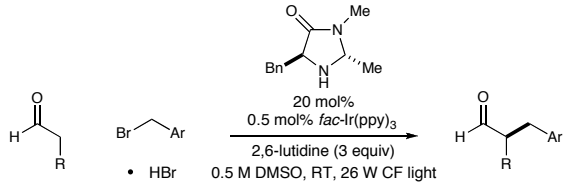
II. Method A. General Procedure for Enantioselective α-Benzylation using Non-basic Substrates:



To an oven-dried 8 mL vial equipped with a magnetic stir bar and rubber septum was added (2*R*,5*S*)-5-benzyl-2,3-dimethylimidazolidin-4-one (0.10 mmol, 0.20 equiv), tris-(2-phenylpyridinato-C^2,*N*)iridium(III) (*fac*-Ir(ppy)$_3$) (0.0025 mmol, 0.0050 equiv), 2,6-lutidinium triflate (0.10 mmol, 0.20 equiv), and the benzyl bromide (0.50 mmol, 1.0 equiv). The vial was then degassed by alternative evacuation and back filling with Ar or N_2 (1 min x4). Previously degassed DMSO (1.0 mL, 0.5 M), aldehyde (1.0 mmol, 2.0 equiv), and 2,6-lutidine (1.0 mmol, 2.0 equiv) were then added to the vial via syringe addition. The reaction vial was sealed with parafilm and positioned approximately 1 cm in front of two 13W compact fluorescent light bulbs for 6 h. Upon completion, the reaction mixture was poured into 8 mL of saturated aqueous NH_4Cl or $NaHCO_3$ and extracted with Et_2O (2 x 10 mL). The combined organic layers were dried over Na_2SO_4 or $MgSO_4$ and the solvent was removed *in vacuo*. The resulting crude oil was purified by flash chromatography with the solvent mixture as noted to provide the pure products.

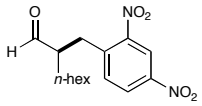
Racemic samples were obtained by running the reaction with equal amounts of each enantiomer of the catalyst. The corresponding alcohols were obtained for chiral SFC or HPLC analysis by the following procedure. The aldehyde starting material (1 equiv) was dissolved in a 5:1 mixture of CH_2Cl_2/MeOH (0.1 M) and $NaCNBH_3$ (10 equiv) was added to the stirring solution at room temperature. Upon consumption of the aldehyde (1-2 hours) the reaction mixture was poured into saturated aqueous NH_4Cl and extracted with CH_2Cl_2 (2 x 5 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo*. The product alcohol sample was submitted to chiral SFC or HPLC analysis without any further purification.

Method B. General Procedure for Enantioselective α-Benzylation using Basic Substrates:

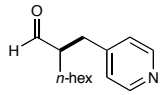


To an oven-dried 8 mL vial equipped with a magnetic stir bar and rubber septum was added (2*R*,5*S*)-5-benzyl-2,3-dimethylimidazolidin-4-one (0.10 mmol, 0.20 equiv), tris-(2-phenylpyridinato-C^2,*N*)iridium(III), (*fac*-Ir(ppy)$_3$) (0.0025 mmol, 0.0050 equiv), and the methylaryl bromide as the hydrobromic acid salt (0.50 mmol, 1.0 equiv). The vial was then degassed by alternative evacuation and back filling with Ar or N_2 (1 min x 4). Previously degassed DMSO (1.0 mL, 0.5 M), aldehyde (1.0 mmol, 2.0 equiv), and 2,6-lutidine (1.5 mmol, 3.0 equiv) were then added to the vial via syringe addition. The reaction vial was sealed wit parafilm and positioned approximately 1 cm in front of two 13W compact fluorescent light bulbs for 3 h. Upon completion, the reaction mixture was poured into 8 mL of saturated aqueous $NaHCO_3$ and extracted with Et_2O (2 x 10 mL). The combined organic layers were dried over Na_2SO_4 or $MgSO_4$ and the solvent was removed *in vacuo*. The resulting crude oil was either immediately purified by flash chromatography with the solvent mixture as noted to provide the pure aldehyde products or subjected to the following reduction conditions: The crude oil was dissolved in a 5:1 mixture of CH_2Cl_2/MeOH (0.1 M), $NaBH_4$ (10 equiv) was added, and the reaction mixture was stirred at room temperature for one hour. Water (10 mL) was added and the mixture was extracted with CH_2Cl_2 (2 x 10 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. The crude alcohol product was then purified by flash

chromatography with the solvent mixture as noted to provide the pure alcohol product. Racemic samples were obtained by running the reaction with equal amounts of each enantiomer of the catalyst.

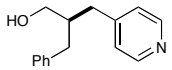


(*R*)-2-(2,4-Dinitrobenzyl)octanal (Table 1, entry 4). General α-benzylation method A was followed using (2*R*,5*S*)-5-benzyl-2,3-dimethylimidazolidin-4-one (20.4 mg, 0.10 mmol), *fac*-$Ir(ppy)_3$ (1.6 mg, 0.0025 mmol), 2,6-lutidinium triflate (25.7 mg, 0.10 mmol), 1-(bromomethyl)-2,4-dinitrobenzene (0.131 g, 0.50 mmol), octanal (0.128 g, 1.0 mmol), and 2,6-lutidine (0.107 g, 0.116 mL, 1.0 mmol) in DMSO (1.0 mL, 0.5 M). The crude oil was purified by flash chromatography (20% EtOAc/hexanes) to provide the pure title compound as a light yellow oil (145 mg, 94% yield, 90% ee). IR (thin film): 3100, 2930, 2858, 2731, 1724, 1605, 1532, 1346, 1457, 1346, 1276, 1197, 1150, 1065 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.63 (d, *J* = 1.5 Hz, 1H, C**H**O), 8.77 (d, *J* = 2.3 Hz, 1H, Ar**H**), 8.35 (dd, *J* = 8.5 Hz, 2.4, 1H, Ar**H**), 7.67 (d, *J* = 8.4 Hz, 1H, Ar**H**), 3.35 (dd, *J* = 13.7, 9.0 Hz, 1H, ArC$\mathbf{H}_2$), 3.10 (dd, *J* = 13.7, 4.7 Hz, 1H, ArC$\mathbf{H}_2$), 2.79 (m, 1H, CHOC**H**), 1.79 (m, 1H, C$\mathbf{H}_2(CH_2)_4CH_3$), 1.60 (m, 1H, C$\mathbf{H}_2(CH_2)_4CH_3$), 1.35 (m, 8H, $CH_2(C\mathbf{H}_2)_4CH_3$), 0.86 (m, 3H, $CH_2(CH_2)_4C\mathbf{H}_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.7, 149.4, 146.8, 142.1, 134.9, 127.0, 120.7, 52.7, 32.0, 31.7, 29.7, 29.5, 26.8, 22.7, 14.2; HRMS (ESI-) exact mass calculated for [M-H]- ($C_{15}H_{19}N_2O_5$) requires m/z 307.1300, found m/z 307.1300; $[\alpha]_D^{23}$ = +72.1 (c = 1.30, $CHCl_3$). HPLC analysis (AS, 5% ^{i}PrOH/hexanes, 1.0 mL/min, 254 nm) indicates 92% ee: t_R(major) = 19.75 minutes, t_R(minor) = 21.51 minutes.

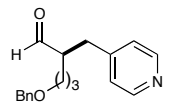


(*R*)-2-(Pyridin-4-ylmethyl)octanal (Table 2, entry 1). General α-benzylation method B was followed using (2*R*,5*S*)-5-benzyl-2,3-dimethylimidazolidin-4-one (20.4 mg, 0.10 mmol), *fac*-$Ir(ppy)_3$ (1.6 mg, 0.0025 mmol), 4-(bromomethyl)pyridinium bromide (0.127 g, 0.50 mmol), octanal (0.128 g, 1.0 mmol), and 2,6-lutidine (0.161 g, 0.174 mL, 1.5 mmol) in DMSO (1.0 mL, 0.5 M). The crude oil was purified by flash chromatography (Davisil, 40% EtOAc/hexanes) to provide the pure title compound (95 mg, 87% yield, 90% ee) as a light yellow oil. IR (thin film)

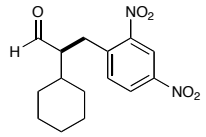
3024, 2926, 2856, 2711, 1724, 1601, 1457, 1415 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 9.67 (d, *J* = 1.2 Hz, 1H, C**H**O), 8.51 (d, *J* = 5.3 Hz, 2H, Ar**H**), 7.10 (d, *J* = 5.7 Hz, 2H, Ar**H**), 3.05 – 2.93 (m, 1H, ArC$\mathbf{H_2}$), 2.73 – 2.59 (m, 2H, ArC$\mathbf{H_2}$, $ArCH_2C\mathbf{H}$), 1.74 – 1.59 (m, 1H, CHOCHC$\mathbf{H_2}$), 1.56 – 1.44 (m, 1H, CHOCHC$\mathbf{H_2}$), 1.42 – 1.18 (m, 8H, $CH_2(C\mathbf{H_2})_4CH_3$), 0.87 (t, *J* = 6.8 Hz, 3H, $CH_2C\mathbf{H_3}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 203.4, 149.7, 148.4, 124.3, 52.4, 33.9, 31.5, 29.2, 28.6, 26.7, 22.5, 14.0; HRMS (ESI-TOF) calculated for $C_{14}H_{22}NO$ $[M+H]^+$ m/z 220.1696, found 220.1699. $[\alpha]_D^{23}$ = +43.6 (c = 0.90, $CHCl_3$). HPLC analysis of the corresponding alcohol (OD, 7% ^{i}PrOH/hexanes, 1.0 mL/min, 254 nm) indicates 90% ee: t_R(major) = 12.03 minutes, t_R(minor) = 10.83 minutes.



(*R*)-2-Benzyl-3-(pyridin-4-yl)propan-1-ol (Table 2, entry 2). General α-benzylation method B was followed using (2*R*,5*S*)-5-benzyl-2,3-dimethylimidazolidin-4-one (20.4 mg, 0.10 mmol), *fac*-$Ir(ppy)_3$ (1.6 mg, 0.0025 mmol), 4-(bromomethyl)pyridinium bromide (0.127 g, 0.50 mmol), hydrocinnamaldehyde (0.134 g, 0.132 mL, 1.0 mmol), and 2,6-lutidine (0.161 g, 0.174 mL, 1.5 mmol) in DMSO (1.0 mL, 0.5 M). The crude oil was subjected to the reduction conditions described and purified by flash chromatography (40% EtOAc/hexanes + 0.5% Et_3N) to provide the pure title compound (104 mg, 91% yield, 90% ee) as a light yellow oil. IR (thin film) 3296, 2921, 1603, 1418, 1030, 701 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 8.34 (d, 1H, *J* = 5.5 Hz, C**H**NC**H**), 7.20 (t, 2H, *J* = 7.4 Hz, Ar**H**), 7.12 (t, 1H, *J* = 7.2 Hz, Ar**H**), 7.08 (d, 2H, *J* = 7.5 Hz, Ar**H**), 7.02 (d, 2H, *J* = 5.3 Hz, C**H**CHNCHC**H**), 3.39 (d, 2H, *J* = 4.9 Hz, C$\mathbf{H_2}$OH), 2.9 (bs, 1H, $CH_2O\mathbf{H}$), 2.65 (dt, 2H, *J* = 15.9, 7.9 Hz, ArC$\mathbf{H_2}$), 2.53 (ddd, 2H, *J* = 13.5, 6.3, 4.3 Hz, ArC$\mathbf{H_2}$), 2.06 (m, 1H, $ArCH_2C\mathbf{H}$); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 150.4, 149.5, 140.2, 129.3, 128.6, 126.3, 124.9, 63.3, 44.0, 37.5, 36.7; HRMS (ESI-TOF) calculated for $C_{15}H_{18}NO$ $[M+H]^+$ m/z 228.1383, found 228.1383. $[\alpha]_D^{23}$ = –3.42 (c = 1.0, $CHCl_3$). HPLC analysis (AS, 6% EtOH/hexanes, 1.0 mL/min, 254 nm) indicates 90% ee: t_R(major) = 16.98 minutes, t_R(minor) = 18.67 minutes.

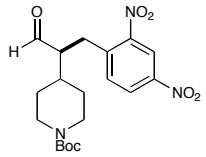


(*R*)-5-(Benzyloxy)-2-(pyridin-4-ylmethyl)pentanal (Table 2, entry 3). General α-benzylation method B was followed using (2*R*,5*S*)-5-benzyl-2,3-dimethylimidazolidin-4-one (20.4 mg, 0.10 mmol), *fac*-Ir(ppy)$_3$ (1.6 mg, 0.0025 mmol), 4-(bromomethyl)pyridinium bromide (0.127 g, 0.50 mmol), 5-(benzyloxy)pentanal (0.192 g, 1.0 mmol), and 2,6-lutidine (0.161 g, 0.174 mL, 1.5 mmol) in DMSO (1.0 mL, 0.5 M). The crude oil was purified by flash chromatography (Davisil, 50% EtOAc/hexanes) to provide the pure title compound (112 mg, 77% yield, 87% ee) as a light yellow oil. IR (thin film) 2931, 2858, 1721, 1607, 1496, 1454, 1417, 1362, 1206, 1102 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.67 (d, *J* = 1.6 Hz, 1H, C**H**O), 8.50 (d, *J* = 5.9 Hz, 2H, Pyr**H**), 7.39 – 7.29 (m, 5H, Ph**H**), 7.11 (d, *J* = 5.9 Hz, 2H, Pyr**H**), 4.48 (s, 2H, PhC**H$_2$**), 3.47 (t, *J* = 5.9 Hz, 2H, BnOC**H$_2$**), 3.01 (dd, *J* = 16.2, 9.7 Hz, 1H, PyrC**H$_2$**), 2.75 – 2.65 (m, 2H, PyrC**H$_2$**, PyrCH$_2$C**H**), 1.86 – 1.54 (m, 4H, CHOCH(C**H$_2$**)$_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 203.2, 149.5, 148.5, 138.2, 128.4, 127.7, 127.7, 124.4, 73.0, 69.6, 52.1, 33.9, 26.9, 25.4; HRMS (ESI-TOF) calculated for $C_{18}H_{22}NO_2$ $[M+H]^+$ m/z 284.1645, found 284.1648. $[\alpha]_D^{23}$ = +13.4 (c = 1.04, $CHCl_3$). HPLC analysis of the corresponding alcohol (OD, 3% EtOH/hexanes, 1.0 mL/min, 254 nm) indicates 87% ee: t_R(major) = 91.60 minutes, t_R(minor) = 85.47 minutes.

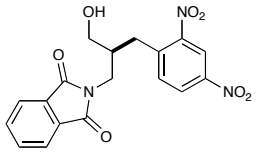


(*S*)-2-Cyclohexyl-3-(2,4-dinitrophenyl)propanal (Table 2, entry 4). General α-benzylation method A was followed using (2*R*,5*S*)-5-benzyl-2,3-dimethylimidazolidin-4-one (20.4 mg, 0.10 mmol), *fac*-Ir(ppy)$_3$ (1.6 mg, 0.0025 mmol), 2,6-lutidinium triflate (25.7 mg, 0.10 mmol), 1-(bromomethyl)-2,4-dinitrobenzene (0.131 g, 0.50 mmol), 2-cyclohexylethanal (0.126 g, 0.137 mL, 1.0 mmol), and 2,6-lutidine (0.107 g, 0.116 mL, 1.0 mmol) in DMSO (1.0 mL, 0.5 M). The crude oil was purified by flash chromatography (10% EtOAc/hexanes) to provide the pure title compound (113 mg, 73% yield, 90% ee) as a light yellow oil. IR (thin film) 2925, 2853, 1721, 1604, 1530, 1345 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.65 (s, 1H, C**H**O), 8.76 (d, 1H, *J* = 2.2 Hz, Ar**H**), 8.33 (dd, 1H, *J* = 8.5, 2.2 Hz, Ar**H**), 7.71 (d, 1H, *J* = 8.5 Hz, Ar**H**), 3.31 (dd, 1H, *J* = 13.4, 10.5 Hz, ArC**H$_2$**CH), 3.17 (dd, 1H, *J* = 13.5, 3.0 Hz, ArC**H$_2$**CH), 2.73 (m, 1H, ArCH$_2$C**H**CH), 2.02–1.55 (m, 6H, **Cy**), 1.43–1.06 (m, 5H, **Cy**); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 203.3, 149.3, 146.6, 142.7, 135.3, 126.9, 120.6, 58.5, 39.2, 30.7, 30.0, 29.2, 26.2; HRMS (ESI-

TOF) calculated for $C_{15}H_{18}N_2NaO_5$ $[M+Na]^+$ m/z 329.1108, found 329.1107. $[\alpha]_D^{24}$ = +81.07 (c = 1.0, $CHCl_3$). SFC analysis of the corresponding alcohol (IA, 5–50% MeOH gradient, 1.0 mL/min, 220 nm) indicates 90% ee: t_R(major) = 7.90 minutes, t_R(minor) = 7.16 minutes.

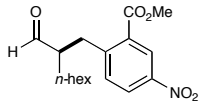


(*S*)-*tert*-Butyl 4-(1-(2,4-dinitrophenyl)-3-oxopropan-2-yl)piperidine-1-carboxylate (Table 2, entry 5). General α-benzylation method A was followed using (2*R*,5*S*)-5-benzyl-2,3-dimethylimidazolidin-4-one (20.4 mg, 0.10 mmol), *fac*-Ir(ppy)$_3$ (1.6 mg, 0.0025 mmol), 2,6-lutidinium triflate (25.7 mg, 0.10 mmol), 1-(bromomethyl)-2,4-dinitrobenzene (0.131 g, 0.50 mmol), *tert*-butyl 4-(2-oxoethyl)piperidine-1-carboxylate (0.227 g, 1.0 mmol), and 2,6-lutidine (0.107 g, 0.116 mL, 1.0 mmol) in DMSO (1.0 mL, 0.5 M). The crude oil was purified by flash chromatography (35% EtOAc/hexanes) to provide the pure title compound (152 mg, 75% yield, 90% ee) as a light yellow oil. IR (thin film) 2937, 2862, 1724, 1685, 1533, 1346, 1167 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.65 (s, 1H, C**H**O), 8.77 (d, 1H, *J* = 2.2 Hz, Ar**H**), 8.33 (dd, 1H, *J* = 8.5, 2.2 Hz, Ar**H**), 7.71 (d, 1H, *J* = 8.5 Hz, Ar**H**), 4.12 (bs, 2H, NBocC**H$_2$**), 3.29 (dd, 1H, *J* = 13.1, 10.8 Hz, ArC**H$_2$**CH), 3.18 (dd, 1H, *J* = 13.4, 2.4 Hz, ArC**H$_2$**CH), 2.81 (m, 1H, ArCH$_2$C**H**), 2.70 (bs, 2H, NBocC**H$_2$**), 2.05 (m, 1H, CH$_2$C**H**CH$_2$), 1.74 (d, 1H, *J* = 12.6 Hz, C**H$_2$**CHCH$_2$), 1.66 (d, 1H, *J* = 12.9 Hz, C**H$_2$**CHCH$_2$), 1.57–1.34 (m, 11H, C**H$_2$**CHCH$_2$, and C(C**H$_3$**)$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 202.2, 154.5, 148.9, 146.5, 142.0, 135.1, 126.9, 120.4, 79.6, 57.2, 37.3, 29.6, 29.4, 29.0, 28.3; HRMS (ESI-TOF) calculated for $C_{19}H_{25}N_3NaO_7$ $[M+Na]^+$ m/z 430.1585, found 430.1585. $[\alpha]_D^{24}$ = +70.21 (c = 1.0, $CHCl_3$). SFC analysis of the corresponding alcohol (IA, 5–50% MeOH gradient, 1.0 mL/min, 220 nm) indicates 90% ee: t_R(major) = 6.35 minutes, t_R(minor) = 5.55 minutes.



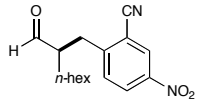
(*S*)-2-(2-(2,4-Dinitrobenzyl)-3-hydroxypropyl)isoindoline-1,3-dione (Table 2, entry 6). General α-benzylation method A was followed using (2*R*,5*S*)-5-benzyl-2,3-

dimethylimidazolidin-4-one (10.2 mg, 0.05 mmol), *fac*-Ir(ppy)$_3$ (0.8 mg, 0.00125 mmol), 2,6-lutidinium triflate (12.9 mg, 0.05 mmol), 1-(bromomethyl)-2,4-dinitrobenzene (0.065 g, 0.25 mmol), 3-(1,3-dioxoisoindolin-2-yl)propanal (0.102 g, 0.5 mmol), and 2,6-lutidine (0.54 g, 0.68 mL, 1.0 mmol) in DMSO (0.5 mL, 0.5 M). This procedure varies from the general procedure in that it is on half the scale. After 2 h, 5 mL of 4:1 CH_2Cl_2/MeOH was added and the reaction cooled to −78°C. 15 equiv of $NaCNBH_3$ was added to reduce the aldehyde to the alcohol. The reaction mixture was partitioned between saturated NH_4Cl and CH_2Cl_2 and extracted twice with CH_2Cl_2, dried with $MgSO_4$ and concentrated. The crude oil was purified by flash chromatography (Iatrobeads, 50% Et_2O/petroleum ether) to provide the pure title compound (69 mg, 72% yield, 90% ee) as a light yellow solid. IR (thin film) 3467, 1771, 1706, 1606, 1533, 1399, 1348 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.84 (s, 1H, Ar**H**), 8.41 (d, *J* = 8.4 Hz, 1H, Ar**H**), 7.91 – 7.86 (m, 2H, Ar**H**), 7.82 – 7.74 (m, 3H, Ar**H**), 3.84 (d, *J* = 6.7 Hz, 2H, C**H$_2$**OH), 3.58 – 3.50 (m, 1H NC**H$_2$**), 3.45 – 3.36 (m, 1H, NC**H$_2$**), 3.19 (dd, *J* = 6.2, 13.5 Hz, 1H, ArC**H$_2$**), 3.13 (dd, *J* = 8.4, 13.6 Hz, 1H, ArC**H$_2$**), 2.87 (m, 1H, CH_2C**H**OH), 2.30 (s, 1H, O**H**); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 169.0, 149.3, 146.6, 142.0, 134.4, 134.3, 131.6, 126.9, 123.6, 120.6, 60.6, 41.1, 38.3, 32.4; HRMS (ESI-TOF) calculated for $C_{18}H_{25}N_3O_7$ $[M+H]^+$ m/z 386.0983, found 386.0983. $[\alpha]_D^{23}$ = +16.8 (c = 1.02, $CHCl_3$). HPLC analysis (OD, 25% EtOH/hexanes, 1.0 mL/min, 230 nm) indicates 90% ee: t_R(major) = 31.15 minutes, t_R(minor) = 26.72 minutes.

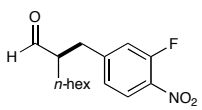


(*R*)-Methyl 2-(2-formyloctyl)-5-nitrobenzoate (Table 3, entry 1). General α-benzylation method A was followed using (2*R*,5*S*)-5-benzyl-2,3-dimethylimidazolidin-4-one (20.4 mg, 0.10 mmol), *fac*-Ir(ppy)$_3$ (1.6 mg, 0.0025 mmol), 2,6-lutidinium triflate (25.7 mg, 0.10 mmol), methyl 2-(bromomethyl)-5-nitrobenzoate (0.137 g, 0.50 mmol), octanal (0.128 g, 0.156 mL, 1.0 mmol), and 2,6-lutidine (0.107 g, 0.116 mL, 1.0 mmol) in DMSO (1.0 mL, 0.5 M). The crude oil was purified by flash chromatography (15% EtOAc/hexanes) to provide the pure title compound (122 mg, 76% yield, 93% ee) as a light yellow oil. IR (thin film) 2928, 2857, 1726, 1524, 1360, 1256, 1129, 1072 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.64 (d, 1H, *J* = 2.1 Hz, C**H**O), 8.78 (d, 1H, *J* = 2.0 Hz, Ar**H**), 8.25 (dd, 1H, *J* = 8.4, 2.2 Hz, Ar**H**), 7.47 (d, 1H, *J* = 8.5 Hz, Ar**H**), 3.95 (s, 3H, CO_2C**H$_3$**), 3.44 (dd, 1H, *J* = 13.1, 8.4 Hz, ArC**H$_2$**CH), 3.15 (dd, 1H, *J* = 13.2, 5.4 Hz, ArC**H$_2$**CH),

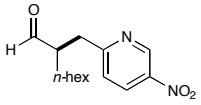
2.71 (m, 1H, $ArCH_2C\mathbf{H}$), 1.73 (m, 1H, $CHOCHC\mathbf{H_2}CH_2$), 1.56 (m, 1H, $CHOCHC\mathbf{H_2}CH_2$), 1.43–1.17 (m, 8H, $CH_2(C\mathbf{H_2})_4CH_3$), 0.85 (t, 3H, J = 7.0 Hz, $CH_2C\mathbf{H_3}$); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 203.9, 165.8, 149.4, 146.5, 133.5, 130.6, 126.5, 126.4, 53.5, 52.9, 33.6, 31.7, 29.6, 29.5, 26.9, 22.7, 14.2; HRMS (ESI-TOF) calculated for $C_{17}H_{23}NNaO_5$ $[M+Na]^+$ m/z 344.1468, found 344.1468. $[\alpha]_D^{22}$ = +6.01 (c = 0.75, $CHCl_3$). SFC analysis of the corresponding alcohol (IA, 5–50% MeOH gradient, 1.0 mL/min, 220 nm) indicates 93% ee: t_R(major) = 4.11 minutes, t_R(minor) = 3.74 minutes.



(*R*)-2-(2-Formyloctyl)-5-nitrobenzonitrile (Table 3, entry 2). General α-benzylation method A was followed using (2*R*,5*S*)-5-benzyl-2,3-dimethylimidazolidin-4-one (20.4 mg, 0.10 mmol), *fac*-$Ir(ppy)_3$ (1.6 mg, 0.0025 mmol), 2,6-lutidinium triflate (25.7 mg, 0.10 mmol), 2-(bromomethyl)-5-nitrobenzonitrile (0.121 g, 0.50 mmol), octanal (0.128 g, 0.156 mL, 1.0 mmol), and 2,6-lutidine (0.107 g, 0.116 mL, 1.0 mmol) in DMSO (1.0 mL, 0.5 M). The crude oil was purified by flash chromatography (15% EtOAc/hexanes) to provide the pure title compound (120 mg, 83% yield, 90% ee) as a light yellow oil. IR (thin film) 2932, 2855, 1722, 1529, 1353, 1168 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.67 (d, 1H, J = 1.4 Hz, C**H**O), 8.50 (d, 1H, J = 2.4 Hz, Ar**H**), 8.36 (dd, 1H, J = 8.6, 2.4 Hz, Ar**H**), 7.61 (d, 1H, J = 8.6 Hz, Ar**H**), 3.32 (dd, 1H, J = 14.1, 8.9 Hz, $ArC\mathbf{H_2}CH$), 3.03 (dd, 1H, J = 14.1, 5.2 Hz, $ArC\mathbf{H_2}CH$), 2.90–2.80 (m, 1H, $ArCH_2C\mathbf{H}$), 1.80 (m, 1H, $CHOCHC\mathbf{H_2}CH_2$), 1.60 (m, 1H, $CHOCHC\mathbf{H_2}CH_2$), 1.51–1.24 (m, 8H, $CH_2(C\mathbf{H_2})_4CH_3$), 0.89 (t, 3H, J = 6.8 Hz, $CH_2C\mathbf{H_3}$); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 202.2, 150.8, 146.3, 132.0, 127.9, 127.3, 115.9, 114.1, 52.6, 33.0, 31.5, 29.3, 29.2, 26.7, 22.5, 14.0; HRMS (ESI-TOF) calculated for $C_{16}H_{20}N_2NaO_3$ $[M+Na]^+$ m/z 311.1366, found 311.1365. $[\alpha]_D^{22}$ = +12.44 (c = 0.75, $CHCl_3$). SFC analysis of the corresponding alcohol (IC, 5–25% MeOH gradient, 1.0 mL/min, 220 nm) indicates 90% ee: t_R(major) = 5.95 minutes, t_R(minor) = 7.04 minutes.

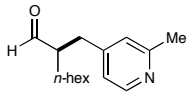


(*R*)-2-(3-Fluoro-4-nitrobenzyl)octanal (Table 3, entry 3). General α-benzylation method A was followed using (2*R*,5*S*)-5-benzyl-2,3-dimethylimidazolidin-4-one (30.6 mg, 0.15 mmol, 0.30 equiv), *fac*-Ir(ppy)$_3$ (1.6 mg, 0.0025 mmol), 2,6-lutidinium triflate (25.7 mg, 0.10 mmol), 4-(bromomethyl)-2-fluoro-1-nitrobenzene (0.117 g, 0.50 mmol), octanal (0.128 g, 0.156 mL, 1.0 mmol), and 2,6-lutidine (0.107 g, 0.116 mL, 1.0 mmol) in DMSO (1.0 mL, 0.5 M). This procedure differs from the general procedure in that 30 mol% of the organocatalyst is used. The crude oil was purified by flash chromatography (10% EtOAc/hexanes) to provide the pure title compound (103 mg, 74% yield, 90% ee) as a light yellow oil. IR (thin film) 2929, 2857, 1724, 1601, 1524, 1342, 841 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.67 (d, 1H, *J* = 1.8 Hz, C**H**O), 8.01 (t, 1H, *J* = 8.0 Hz, Ar**H**), 7.12 (m, 2H, (Ar**H**)$_2$), 3.09 (dd, 1H, *J* = 14.1, 7.8 Hz, ArC**H$_2$**CH), 2.76 (dd, 1H, *J* = 14.1, 6.2 Hz, Ar C**H$_2$**CH), 2.67 (m, 1H, ArCH$_2$C**H**), 1.70 (m, 1H, CHOCHC**H$_2$**CH$_2$), 1.52 (m, 1H, CHOCHC**H$_2$**CH$_2$), 1.42–1.19 (m, 8H, CH$_2$(C**H$_2$**)$_4$CH$_3$), 0.88 (t, 3H, *J* = 6.9 Hz, CH$_2$C**H$_3$**); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 202.9, 156.6, 154.4, 149.1 (d, *J* = 8.1 Hz), 126.3 (d, *J* = 2.5 Hz), 125.1 (d, *J* = 3.8 Hz), 118.7 (d, *J* = 20.7 Hz), 52.8, 34.1, 31.5, 29.2, 28.7, 26.7, 22.5, 14.0; HRMS (ESI-TOF) calculated for $C_{15}H_{21}FNO_3$ $[M+H]^+$ m/z 282.1500, found 282.1499. $[\alpha]_D^{22}$ = +39.62 (c = 1.0, $CHCl_3$). HPLC analysis of the corresponding alcohol (OD, 0.5% EtOH/hexanes, 1.0 mL/min, 254 nm) indicates 90% ee: t_R(major) = 86.76 minutes, t_R(minor) = 80.93 minutes.



(*R*)-2-((5-Nitropyridin-2-yl)methyl)octanal (Table 3, entry 4). General α-benzylation method A was followed using (2*R*,5*S*)-5-benzyl-2,3-dimethylimidazolidin-4-one (20.3 mg, 0.10 mmol, 0.32 equiv), tris-(2,2'-bipyridyl)ruthenium (II) chloride hexahydrate (1.9 mg, 0.0025 mmol), 2,6-lutidinium triflate (25.7 mg, 0.10 mmol), 2-(bromomethyl)-5-nitropyridine (109 mg, 0.50 mmol), octanal (0.128 g, 0.156 mL, 1.0 mmol), and 2,6-lutidine (0.107 g, 0.116 mL, 1.0 mmol) in DMSO (1.0 mL, 0.5 M). The vial was placed in a 17 °C cryocooler in between two 26 W lamps

and irradiated for 8 h.[4] The crude oil was purified by flash chromatography (Davisil, 80% EtOAc/petroleum ether) to provide the pure title compound (98 mg, 74% yield, 90% ee). IR (thin film) 2927, 2857, 1724, 1599, 1578, 1520, 1469, 1343, 861, 724 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.75 (d, 1H, *J* = 1.2 Hz, C**H**O), 9.31 (d, 1H, *J* = 2.6 Hz, Ar**H**), 8.37 (dd, 1H, *J* = 2.6, 8.4 Hz, Ar**H**), 7.39 (d, 1H, *J* = 8.4 Hz, Ar**H**), 3.30 (dd, 1H, *J* = 7.8, 14.3 Hz, C$\mathbf{H_2}$Ar), 3.09-3.02 (m, 1H, C$\mathbf{H_2}$Ar), 3.00 (dd, 1H, *J* = 5.2, 14.3 Hz, C**H**CHO), 1.78-1.72 (m, 1H, C$\mathbf{H_2}(CH_2)_4CH_3$), 1.55-1.47 (m, 1H, C$\mathbf{H_2}(CH_2)_4CH_3$), 1.42-1.27 (m, 8H, $CH_2(C\mathbf{H_2})_4CH_3$), 0.87 (t, 3H, *J* = 6.8 Hz, C$\mathbf{H_3}$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.6, 166.3, 144.7, 142.6, 131.3, 123.8, 50.9, 36.8, 31.5, 29.3, 28.8, 26.8, 22.5, 14.0; HRMS (ESI-TOF) calculated for $C_{14}H_{21}N_2O_3$ $[M+H]^+$ m/z 265.1552, found 265.1550. $[\alpha]_D^{23}$ = +41.2 (c = 0.76, $CHCl_3$); HPLC analysis (AS, 3.5% ^{i}PrOH/hexanes, 1.0 mL/min, 254 nm) indicates 90% ee: t_R (minor) = 18.4 minutes, t_R (major) = 23.3 minutes.



(*R*)-2-((2-Methylpyridin-4-yl)methyl)octanal (Table 3, entry 5). General α-benzylation method B was followed using (2*R*,5*S*)-5-benzyl-2,3-dimethylimidazolidin-4-one (16.3 mg, 0.08 mmol), *fac*-$Ir(ppy)_3$ (1.3 mg, 0.002 mmol), 4-(bromomethyl)-2-methylpyridinium bromide (0.107 g, 0.40 mmol), octanal (0.103 g, 0.8 mmol), and 2,6-lutidine (0.129 g, 0.140 mL, 1.2 mmol) in DMSO (0.8 mL, 0.5 M). The crude oil was purified by flash chromatography (Davisil, 15% EtOAc/hexanes) to provide the pure title compound (87 mg, 75% yield, 91% ee) as a light yellow oil. IR (thin film) 2955, 2930, 2857, 1726, 1606, 1561, 1457 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 9.67 (d, J = 1.7, 1H, C**H**O), 8.39 (d, J = 5.1, 1H, Ar**H**), 6.97 (s, 1H, Ar**H**), 6.91 (d, J = 5.1, 1H, Ar**H**), 2.96 (dd, J = 9.7, 16.2, 1H, ArC$\mathbf{H_2}$), 2.70 – 2.58 (m, J = 6.2, 2H, ArC$\mathbf{H_2}$, CHOC**H**), 2.53 (s, 3H, ArC$\mathbf{H_3}$), 1.76 – 1.60 (m, 1H, CHOCHC$\mathbf{H_2}$), 1.54 – 1.42 (m, 1H, CHOCHC$\mathbf{H_2}$), 1.42 – 1.16 (m, 8H, $CH_2(C\mathbf{H_2})_4CH_3$), 0.88 (t, J = 6.8, 3H, $(CH_2)_4C\mathbf{H_3}$); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 203.7, 158.4, 149.1, 148.6, 124.0, 123.9, 121.4, 52.5, 33.9, 31.5, 29.2, 28.6, 26.8, 24.3, 22.5, 14.0; HRMS (ESI-TOF) calculated for $C_{15}H_{24}NO$ $[M+H]^+$ m/z 234.1852, found 234.1852. $[\alpha]_D^{23}$ = +16.0 (c = 1.02, $CHCl_3$). HPLC analysis of the corresponding alcohol

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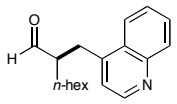
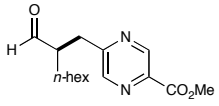
([4]) The apparatus used to irradiate the vial at a sub-ambient temperature was identical to that described in Nagib, D. A.; Scott, M. E.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2009**, *131*, 10875. The reaction can be conducted without cooling but the yield decreases by ca. 10%.

(OD, 6% ^{i}PrOH/hexanes, 1.0 mL/min, 254 nm) indicates 91% ee: t_R(major) = 11.76 minutes, t_R(minor) = 10.30 minutes.

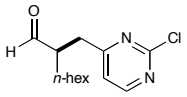


(*R*)-2-(Quinolin-4-ylmethyl)octanal (Table 3, entry 6). General α-benzylation method B was followed using (2*R*,5*S*)-5-benzyl-2,3-dimethylimidazolidin-4-one (20.4 mg, 0.10 mmol), *fac*-Ir(ppy)$_3$ (1.6 mg, 0.0025 mmol), 4-(bromomethyl)quinolinium bromide (0.152 g, 0.50 mmol), octanal (0.128 g, 1.0 mmol), and 2,6-lutidine (0.161 g, 0.174 mL, 1.5 mmol) in DMSO (1.0 mL, 0.5 M). The crude oil was purified by flash chromatography (Davisil, 15% EtOAc/hexanes) to provide the pure title compound (121 mg, 90% yield, 82% ee) as a light yellow oil. IR (thin film) 2927, 2857, 1724, 1592, 1569, 1509, 1464 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.72 (d, J = 2.2, 1H, C**H**O), 8.82 (d, J = 4.4, 1H, Ar**H**), 8.14 (d, J = 8.5, 1H, Ar**H**), 8.00 (d, J = 8.4, 1H , Ar**H**), 7.73 (dd, J = 4.1, 11.2, 1H, Ar**H**), 7.60 (t, J = 7.6, 1H, Ar**H**), 7.25 (d, J = 4.4, 1H, Ar**H**), 3.50 (dd, J = 7.4, 14.4, 1H, ArC**H$_2$**), 3.10 (dd, J = 6.8, 14.4, 1H, ArC**H$_2$**), 2.90 – 2.77 (m, 1H, ArCH$_2$C**H**), 1.81 – 1.68 (m, 1H, CHOCHC**H$_2$**), 1.66 – 1.55 (m, 1H, CHOCHC**H$_2$**), 1.48 – 1.12 (m, 8H, CH$_2$(C**H$_2$**)$_4$CH$_3$), 0.87 (t, J = 6.9, 3H, C**H$_3$**); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 203.5, 150.0, 148.4, 145.1, 130.5, 129.3, 127.3, 126.7, 123.1, 121.9, 51.8, 31.5, 30.9, 29.3, 29.25, 26.8, 22.5, 14.0; HRMS (ESI-TOF) calculated for $C_{18}H_{24}NO$ $[M+H]^+$ m/z 270.1852, found 270.1854. $[\alpha]_D^{23}$ = +34.8 (c = 1.2, $CHCl_3$). HPLC analysis of the corresponding alcohol (OD, 5% ^{i}PrOH/hexanes, 1.0 mL/min, 254 nm) indicates 82% ee: t_R(major) = 18.79 minutes, t_R(minor) = 21.82 minutes.



(*R*)-Methyl 5-(2-formyloctyl)pyrazine-2-carboxylate (Table 3, entry 7). Alternative conditions were employed: an oven-dried 40 mL vial equipped with a Teflon septum and magnetic stir bar was charged with 2,6-lutidinium triflate (7.8 mg, 0.030 mmol), methyl 5-

(bromomethyl)pyrazine-2-carboxylate[5] (34.7 mg, 0.150 mmol), bis[2-(2,4-difluorophenyl)-5-trifluoromethylpyridine)] (4,4'-di-*tert*-butyl-2,2'-dipyridyl) iridium(III) hexafluorophosphate ($Ir(dF(CF_3)ppy)_2(dtbbpy)PF_6$)(1.7 mg, 0.0016 μmol, 0.01 equiv.) and (2*R*, 5*S*)-5-benzyl-2,3-dimethylimidazolidin-4-one (6.1 mg, 0.030 mmol). The vial was purged with a stream of argon and dry acetonitrile (0.050 mL) followed by octanal (0.047 mL, 0.30 mmol), and dry 2,6-lutidine (0.032 mL, 0.90 mmol, 1.8 equiv.) were added. The mixture was degassed through freeze-pump-thaw at −78°C (×3) and then the vial was sealed with parafilm. The vial was then placed as close as possible to three 13 W lamps and irradiated for 6 h. Volatiles were removed *in vacuo*. Analysis of the residue by ^{1}H NMR spectroscopy using 1,3-benzodioxole as an internal standard indicated a 72% NMR yield of the title compound. The crude oil was purified by flash chromatography (60% EtOAc/petroleum ether) to yield an analytical sample of the title compound. IR (thin film) 2926, 2856 1747, 1723, 1436, 1281, 1157, 1031, 732 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.75 (d, 1H, *J* = 1.2 Hz, C**H**O), 9.17 (d, 1H, *J* = 1.4 Hz, Ar**H**), 8.60 (d, 1H, *J* = 1.4 Hz, Ar**H**), 4.01 (s, 3H, OC$\mathbf{H_3}$), 3.29 (dd, 1H, *J* = 8.0, 14.7 Hz, C$\mathbf{H_2}$Ar), 3.08-3.01 (m, 1H, C**H**CHO), 2.97 (dd, 1H, *J* = 5.4, 14.7 Hz, C$\mathbf{H_2}$Ar), 1.77-1.70 (m, 1H, C$\mathbf{H_2}(CH_2)_4CH_3$), 1.56-1.48 (m, 1H, C$\mathbf{H_2}(CH_2)_4CH_3$), 1.41-1.25 (m, 8H, $CH_2(C\mathbf{H_2})_4CH_3$), 0.86 (t, *J* = 6.0 Hz, 3H, C$\mathbf{H_3}$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.1, 164.5, 158.9, 145.3, 144.5, 140.7, 53.0, 50.5, 33.9, 31.5, 29.2, 28.7, 26.7, 22.5, 14.0; ; HRMS (ESI-TOF) calculated for $C_{15}H_{23}N_2O_3$ $[M+H]^+$ m/z 279.1703, found 279.1706; $[\alpha]_D^{23}$ = +26.0 (c = 0.51, $CHCl_3$); HPLC analysis (AS, 3.5% ^{i}PrOH/hexanes, 1.0 mL/min, 254 nm) indicates 87% ee: t_R (major) = 28.4 minutes, t_R (minor) = 32.2 minutes.



(*R*)-2-((2-Chloropyrimidin-4-yl)methyl)octanal (Table 3, entry 8). General α-benzylation method A was followed using (2*R*,5*S*)-5-benzyl-2,3-dimethylimidazolidin-4-one (20.3 mg, 0.10 mmol), *fac*-Ir(ppy)$_3$ (1.6 mg, 0.0025 mmol), 2,6-lutidinium triflate (25.7 mg, 0.10 mmol), 4-(bromomethyl)-2-chloropyrimidine (104 mg, 0.50 mmol), octanal (0.128 g, 0.156 mL, 1.0 mmol), and 2,6-lutidine (0.107 g, 0.116 mL, 1.0 mmol) in DMSO (1.0 mL, 0.5 M). After 7 h,

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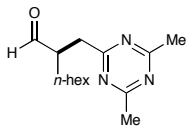
([5]) Mjalli, A. M. M.; Andrews, R. C.; Arimilli, M. N.; Rao, M.; Guzel, M.; Bondlela, M. Patent WO2005014534, **2005**; *Chem. Abstr.* 142:240711.

the reaction was subject to basic work up conditions and the crude oil was purified by flash chromatography (Davisil, 30% EtOAc/petroleum ether) to provide the pure title compound (99 mg, 78% yield, 87% ee) as a light yellow oil. IR (thin film) 2927, 2858, 1724, 1566, 1539, 1433, 1339, 1184, 722 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 9.72 (s, 1H, C**H**O), 8.47 (d, 1H, *J* = 5.2 Hz, Ar**H**), 7.16 (d, 1H, *J* = 5.2 Hz, Ar**H**), 3.17-3.05 (m, 2H, C$\mathbf{H_2}$Ar, C**H**CHO), 2.80 (dd, 1H, *J* = 4.4, 14.0 Hz, C$\mathbf{H_2}$Ar), 1.76-1.70 (m, 1H, C$\mathbf{H_2}(CH_2)_4CH_3$), 1.58-1.49 (m, 1H, C$\mathbf{H_2}(CH_2)_4CH_3$), 1.42-1.26 (m, 8H, $CH_2(C\mathbf{H_2})_4CH_3$), 0.86 (t, *J* = 6.8 Hz, 3H, C$\mathbf{H_3}$); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 203.1, 171.9, 161.2, 159.1, 119.7, 50.2, 35.8, 31.5, 29.2, 28.8, 26.6, 22.5, 14.0; HRMS (ESI-TOF) calculated for $C_{13}H_{20}ClN_2O$ $[M+H]^+$ m/z 255.1264 (^{35}Cl), 257.1235 (^{37}Cl), found 255.1282 (^{35}Cl), 257.1239 (^{37}Cl); $[\alpha]_D^{23}$ = +5.27 (c = 0.86, $CHCl_3$); HPLC analysis (AS, 3.5% ^{i}PrOH/hexanes, 1.0 mL/min, 254 nm) indicates 87% ee: t_R (minor) = 13.0 minutes, t_R (major) = 15.4 minutes.



(*R*)-2-((4,6-Dimethyl-1,3,5-triazin-2-yl)methyl)octanal (Table 3, entry 9). General α-benzylation method A was followed using (2*R*,5*S*)-5-benzyl-2,3-dimethylimidazolidin-4-one (20.3 mg, 0.10 mmol), bis[2-(2,4-difluorophenyl)-5-trifluoromethylpyridine)] (4,4'-di-*tert*-butyl-2,2'-dipyridyl) iridium(III) hexafluorophosphate ($Ir(dF(CF_3)ppy)_2(dtbbpy)PF_6$) (2.8 mg, 0.0025 mmol), 2,6-lutidinium triflate (25.7 mg, 0.10 mmol), 2-(bromomethyl)-4,6-dimethyl-1,3,5-triazine[6] (101 mg, 0.50 mmol), octanal (0.128 g, 0.156 mL, 1.0 mmol), and 2,6-lutidine (0.107 g, 0.116 mL, 0.90 mmol) in DMSO (1.0 mL, 0.5 M). After 3 h, the reaction was subject to basic work up conditions and the crude oil was purified by flash chromatography (Davisil, 80% EtOAc/petroleum ether) to provide the pure title compound (85 mg, 68% yield, 87% ee) as a light yellow oil. The enantiomeric excess was determined on the alcohol, which was prepared by treating a solution of the aldehyde (30.4 mg, 0.121 mmol) in 10% MeOH/THF (2 mL) with $NaBH_4$ (13.0 mg, 0.342 mmol) at 0 °C. After complete consumption of the aldehyde (10 min., as judged by TLC) the reaction was quenched with sat. NH_4Cl solution (5 mL) and product was

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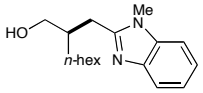
([6]) Schaefer, F. C.; Ross, J. H. Patent US3062818, **1962**; *Chem. Abstr.* 58:27384.

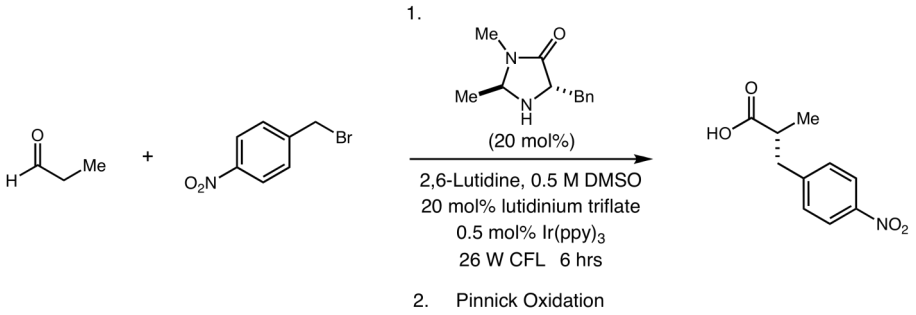
extracted into Et_2O (3 x 5 mL). The organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by flash chromatography using 3% MeOH/CH_2Cl_2 to afford the alcohol as a colourless oil (17.9 mg, 58% yield). IR (thin film) 2927, 2857, 1536, 1433, 1396 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.78 (s, 1H, , C**H**O), 3.21 (dd, 1H, *J* = 8.4, 15.7 Hz, C**H**$_2$Ar), 3.08-3.01 (m, 1H, C**H**CHO), 2.93 (dd, 1H, *J* = 5.0, 15.7 Hz, C**H**$_2$Ar), 2.56 (s, 6H, 2 x ArC**H**$_3$), 1.79-1.69 (m, 1H, C**H**$_2$$(CH_2)_4CH_3$), 1.53-1.46 (m, 1H, C**H**$_2$$(CH_2)_4CH_3$), 1.39-1.25 (m, 8H, CH-$_2$$(CH_2)_4CH_3$), 0.86 (t, 3H, *J* = 6.6 Hz, C**H**$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.7, 176.7, 176.0, 49.1, 37.6, 31.5, 29.2, 28.8, 26.7, 25.5, 22.5, 14.0; HRMS (ESI-TOF) calculated for $C_{14}H_{24}N_3O$ $[M+H]^+$ m/z 250.1919, found 250.1920. $[\alpha]_D^{23}$ = +25.8 (c = 1.18, $CHCl_3$); HPLC analysis of the corresponding alcohol (AS, 2% ^{i}PrOH/hexanes, 1.0 mL/min, 254 nm) indicates 91% ee: t_R (minor) = 13.7 minutes, t_R (major) = 15.5 minutes.



(*R*)-2-((1-Methyl-1*H*-benzo[*d*]imidazol-2-yl)methyl)octan-1-ol (Table 3, entry 10). General α-benzylation method B was followed using (2*R*,5*S*)-5-benzyl-2,3-dimethylimidazolidin-4-one (20.4 mg, 0.10 mmol), *fac*-Ir(ppy)$_3$ (1.6 mg, 0.0025 mmol), 2-(bromomethyl)-1-methyl-1*H*-benzo[*d*]imidazolium bromide (0.153 g, 0.50 mmol), octanal (0.128 g, 1.0 mmol), and 2,6-lutidine (0.161 g, 0.174 mL, 1.5 mmol) in DMSO (1.0 mL, 0.5 M). The crude oil was purified by flash chromatography (Davisil, 20% EtOAc/hexanes) and reduced to the alcohol using $NaBH_4$ (4 equiv) in CH_2Cl_2/MeOH (4:1) to provide the pure title compound (112 mg, 81% yield, 88% ee) as a light yellow solid. IR (thin film) 3215, 3054, 2925, 2855, 1615, 1508, 1466, 1443, 1400 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.69 (dd, *J* = 2.3, 6.3 Hz, 1H, Ar**H**), 7.32 (dd, *J* = 2.4, 6.4 Hz, 1H, Ar**H**), 7.29 – 7.22 (m, 2H, Ar**H**), 3.76 (s, 3H, NC**H**$_3$), 3.71 (dd, *J* = 3.4, 11.3 Hz, 1H, C**H**$_2$OH), 3.60 (dd, *J* = 6.5, 11.3 Hz, 1H, C**H**$_2$OH), 3.02 (dd, *J* = 4.5, 15.5 Hz, 1H, ArC**H**$_2$), 2.95 (dd, *J* = 8.6, 15.5 Hz, 1H, ArC**H**$_2$), 2.26 – 2.09 (m, 1H,C**H**CH_2OH), 1.52 – 1.44 (m, 1H,CHC**H**$_2$$CH_2$), 1.39 (m, 3H, CHC**H**$_2$C**H**$_2$), 1.29 (m, 6H, (C**H**$_2$)$_3$$CH_3$), 0.88 (t, *J* = 6.8 Hz, 3H, $(CH_2)_4$**CH**$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 154.5, 141.7, 135.5, 122.2, 122.1, 119.0, 109.1, 77.3, 77.0, 76.8, 65.7, 39.5, 32.1, 31.8, 30.7, 29.9, 29.5, 27.2, 22.6, 14.1; HRMS (ESI-TOF) calculated for $C_{17}H_{27}N_2O$ $[M+H]^+$ m/z 275.2118, found 275.2119. $[\alpha]_D^{23}$ = –15.9 (c = 1.18,

$CHCl_3$). HPLC analysis (OD, 8% ^{i}PrOH/hexanes, 1.0 mL/min, 254 nm) indicates 88% ee: t_R(major) = 14.42 minutes, t_R(minor) = 12.12 minutes.

III. Absolute stereochemical proof:



(*R*)-2-(4-Nitrobenzyl)propanoic acid. General α-benzylation method A was followed using (2*R*,5*S*)-5-benzyl-2,3-dimethylimidazolidin-4-one (81.6 mg, 0.40 mmol), *fac*-Ir(ppy)$_3$ (6.4 mg, 0.010 mmol), 2,6-lutidinium triflate (102.8 mg, 0.40 mmol), 1-(bromomethyl)-4-nitrobenzene (0.121 g, 2.0 mmol), propanal (0.232 g, 0.290 mL, 4.0 mmol), and 2,6-lutidine (0.428 g, 0.464 mL, 4.0 mmol) in DMSO (4.0 mL, 0.5 M). This procedure varies from the general procedure in that it is on four times the scale. The crude aldehyde isolated from the general benzylation workup was then subjected to a Pinnick Oxidation using the following procedure.

The crude aldehyde was dissolved in a 1:1:1 mixture of THF/*t*-BuOH/2-methyl-2-butene (9 mL), NaH_2PO_4 (0.56 g, 4.0 mmol) was added, and the mixture was stirred at room temperature. $NaClO_2$ (80% technical grade, 0.30 g, 2.6 mmol) dissolved in water (1 mL) was then added to the reaction mixture, which was left to stir at room temperature for 3 hours. Upon completion, aqueous HCl (1.0 M, 20 mL) was added and the solution was extracted with EtOAc (3x 20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. The crude acid was purified by flash chromatography (25% EtOAc in hexanes) to provide the pure title compound (105 mg, 26% yield over 2 steps, 88% ee) as a white solid. Spectroscopic data matched that reported in the literature.[7] SFC analysis (IA, 5–10% MeOH gradient, 1.0 mL/min, 220 nm) indicates 88% ee: t_R(major) = 6.89 minutes, t_R(minor) = 6.33 minutes. $[\alpha]_D^{24}$ = –32.53 (c = 1.14, $CHCl_3$). The experimental optical rotation indicates that the compound is

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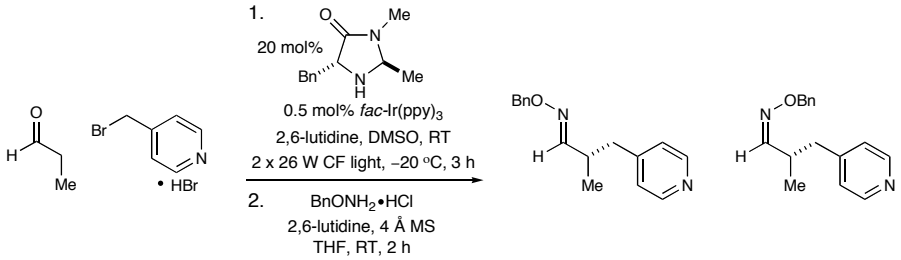
([7]) Kotake, T.; Hayashi, Y.; Rajesh, S.; Mukai, Y.; Takiguchi, Y.; Kimura, T.; Kiso, Y. *Tetrahedron* **2005**, *61*, 3819.

indeed (*R*)-2-(4-nitrobenzyl)propanoic acid when compared to the known data in the literature ($[\alpha]_D^{25}$ = –36.9 (c = 1.14, $CHCl_3$) for the same compound of 97% ee).[7] All other compounds in this publication were assigned the appropriate stereochemistry by analogy.

IV. Synthesis of Angiogenesis Inhibitor 12

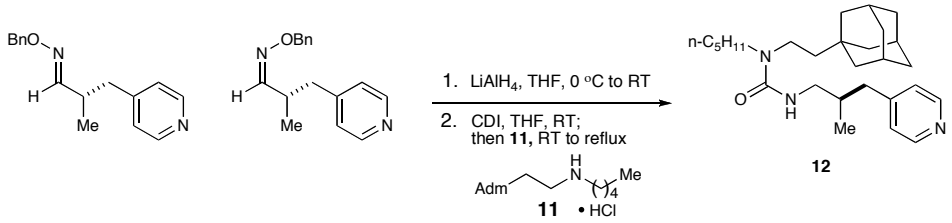


E- and *Z*-2-Methyl-3-(pyridin-4-yl)propanal *O*-benzyloxime

An oven-dried 8 mL vial equipped with a Teflon septum and magnetic stir bar was charged with 4-(bromomethyl)pyridine hydrobromide (127 mg, 0.503 mmol, 1.0 equiv.), tris-(2-phenylpyridinato-C^2,*N*)iridium(III) (1.7 mg, 2.6 μmol, 0.005 equiv.) and (2*S*, 5*R*)-5-benzyl-2,3-dimethylimidazolidin-4-one (20.3 mg, 0.100 mmol, 0.2 equiv.). The vial was purged with a stream of argon and propanal (73 μL, 1.01 mmol, 2.0 equiv.) followed by dry DMF (1.0 mL) and dry 2,6-lutidine (175 μL, 1.50 mmol, 3.0 equiv.) were added. Each of the liquids was degassed by sparging immediately before being added. The vial was sealed with parafilm and placed in a –20 °C cryocooler between two 26 W lamps and irradiated for 3 h. The mixture was then removed from the cryocooler and connected to an argon line. THF (2.5 mL), 2,6-lutidine (58 μL, 0.500 mmol, 1.0 equiv.), *O*-benzylhydroxylamine hydrochloride (194 mg, 1.22 mmol, 2.4 equiv.) and 4Å molecular sieves (200 mg) were added. The mixture was stirred until TLC indicated complete consumption of the aldehyde (2 h). The mixture was then filtered through a pad of celite and the solids washed with CH_2Cl_2 (25 mL). The filtrate was concentrated *in vacuo* and the residue was partitioned between Et_2O (17 mL) and sat. $NaHCO_3$ solution (17 mL). The layers were separated and additional product was extracted into Et_2O (2 × 17 mL). The combined organic phase was dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by flash chromatography (Davisil, 70% EtOAc/hexanes) to afford the title compound as a yellow oil (105 mg, 82% yield, 3.3:1 mixture of *E*/*Z* isomers). IR (thin film) 2929, 1601, 1454,

1415, 1025, 734 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.47 [d, 4H, *J* = 5.6 Hz, Pyr**H** (*E*- and *Z*-isomers)], 7.36 – 7.26 [m, 11H, C**H**N (*E*-isomer) and Ph**H** (*E*- and *Z*-isomers)], 7.07 – 7.05 [m, 4H, Pyr**H** (*E*- and *Z*-isomers)], 6.52 [d, 1H, *J* = 7.6 Hz, C**H**N (*Z*-isomer)], 5.08 – 5.02 [m, 1H, PhC**H$_2$** (*Z*-isomer)], 5.02 [s, 2H, PhC**H$_2$** (*E*-isomer)], 3.49 – 3.38 [m, 1H, PyrCH$_2$C**H** (*Z*-isomer)], 2.83 [dd, 1H, *J* = 13.2, 7.0 Hz, PyrC**H$_2$** (*E*-isomer)], 2.76 – 2.68 [m, 3H, PyrCH$_2$C**H** (*E*-isomer) and PyrC**H$_2$** (*Z*-isomer)], 2.62 [dd, 2H, *J* = 13.2, 7.0 Hz, PyrC**H$_2$** (*E*- and *Z*-isomers)], 1.09 [d, 3H, *J* = 6.4 Hz, C**H$_3$** (*E*-isomer)], 1.05 [d, 3H, *J* = 6.8 Hz, C**H$_3$** (*E*-isomer)]; ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.0, 153.8, 149.6, 148.4, 148.3, 137.7, 137.5, 128.4, 128.2, 127.88, 127.85, 127.82, 124.5, 124.4, 75.8, 75.6, 39.9, 39.6, 35.4, 31.1, 17.9, 17.2; HRMS (ESI-TOF) calculated for $C_{16}H_{19}N_2O$ $[M+H]^+$ m/z 255.1497, found 255.1504; HPLC analysis (OD, 2.5% ^{i}PrOH/hexanes, 1.0 mL/min, 254 nm) indicates 93% ee: t_R (minor, *E* and *Z*-isomers) = 36.3 minutes, t_R (major, *E*-isomer) = 42.2 minutes, t_R (major, *Z*-isomer) = 46.3 minutes.

(*S*)-1-[2-(1-(Adamantyl)ethyl]-3-[2-methyl-3-(4-pyridyl)propyl]-1-pentylurea

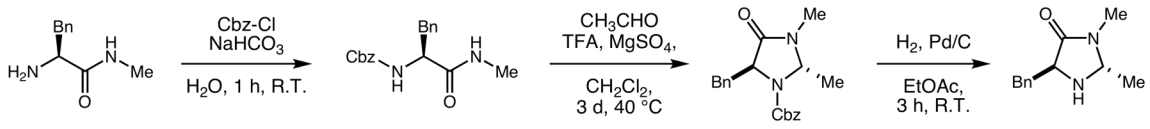


To a stirred solution of *E*- and *Z*-2-methyl-3-(pyridin-4-yl)propanal *O*-benzyloxime (59.2 mg, 0.233 mmol) in anhydrous THF (4.5 mL) at 0 °C was added a freshly prepared solution of lithium aluminium hydride (0.75 mL, 1.0 M in THF, 0.75 mmol). The mixture was stirred at 0°C for 20 min and then at r.t. for 40 min, quenched with methanol (5 mL) and concentrated *in vacuo*. H_2O (5 mL) was added and product was extracted into CH_2Cl_2 (3 × 5 mL). The combined organic phase was dried (Na_2SO_4) and concentrated *in vacuo*. The crude amine was taken up in THF (2 mL) and treated with 1,1'-carbonyldiimidazole (56.0 mg, 0.345 mmol). The mixture was stirred at r.t. for 20 min. and then 2-(1-adamantyl)-*N*-pentylethylamine hydrochloride[8] (84.9 mg, 0.297 mmol) was added. The mixture was refluxed for 1 hr. After it

([8]) Matsuoka, H.; Nishimura, K.; Seike, H.; Aono, H.; Murai, M. US Patent Application 20080161270, **2008**; *Chem. Abstr*. 139:22108.

had cooled to r.t. it was diluted with EtOAc (5 mL) and washed with sat. $NaHCO_3$ solution (5 mL) and brine (5 mL). The organic phase was dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by flash chromatography (57.5% EtOAc/hexanes + 0.5% NEt_3) to furnish the title compound as a white solid (42.4 mg, 42% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.47 (d, 2H, *J* = 4.5 Hz, Pyr**H**), 7.09 (d, 2H, *J* = 4.5 Hz, Pyr**H**), 4.33 – 4.31 (m, 1H, N**H**), 3.27 – 3.22 (m, 1H, C$\mathbf{H_2}$NH), 3.15 – 3.06 (m, 5H, C$\mathbf{H_2}$NH, BuC$\mathbf{H_2}$ and admCH_2C$\mathbf{H_2}$), 2.71 (dd, 1H, *J* = 13.5, 5.5 Hz, PyrC$\mathbf{H_2}$), 2.34 (dd, 1H, *J* = 13.5, 9.0 Hz, PyrC$\mathbf{H_2}$), 2.03 – 1.97 (m, 1H, PyrCH_2C**H**), 1.94 (s, 3H, CCH_2C**H**CH_2C), 1.70 (d, 3H, *J* = 12.0 Hz, CHC$\mathbf{H_2}$C), 1.61 (d, 3H, *J* = 12.0 Hz, CHC$\mathbf{H_2}$C), 1.53 – 1.47 (m, 8H, CHC$\mathbf{H_2}$CH and NCH_2C$\mathbf{H_2}$), 1.34 – 1.23 (m, 6H, CH_3(C$\mathbf{H_2}$)$_3$CH_2N), 0.89 (t, 3H, *J* = 7.3 Hz, C$\mathbf{H_3}$(CH_2)N), 0.86 (d, 3H, *J* = 6.5 Hz, C$\mathbf{H_3}$CH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.3, 149.8, 149.6, 124.5, 47.1, 46.6, 42.2, 41.9, 40.4, 37.0, 35.3, 31.6, 29.1, 28.45, 28.40, 22.5, 17.4, 14.0; HRMS (ESI-TOF) calculated for $C_{27}H_{44}N_3O$ $[M+H]^+$ m/z 426.3484, found 426.3485; $[\alpha]_D^{23}$ = - 4.23 (c = 0.76, $CHCl_3$), lit.[8] $[\alpha]_D$ = - 4.6; SFC analysis (IC, 5-25% MeOH gradient, 254 nm) indicates 93% ee: t_R (major) = 10.9 minutes, t_R (minor) = 12.1 minutes.

V. Synthesis of (2*R*,5*S*)-5-benzyl-2,3-dimethylimidazolidin-4-one organocatalyst.[9]



To a flask containing L-phenylalanine-*N*-methylamide[10] (13.9 g, 78 mmol, 1.0 equiv) was added $NaHCO_3$ (26 g, 312 mmol, 4.0 equiv), CbzCl (16 g, 13.5 mL, 93.5 mmol, 1.2 equiv), and H_2O (200 mL). The product immediately began to precipitate and the mixture was allowed to stand with stirring for one hour. The crude solid was then collected on a fritted glass funnel by suction filtration. The solid was rinsed with aqueous HCl (1.0 M, 1 L) to remove excess $NaHCO_3$ and dried under reduced pressure (~0.1 torr) overnight. To a 1 L flask containing this solid was added $MgSO_4$ (50 g, 2 wt equiv), acetaldehyde (10.3 g, 13.1 mL, 234 mmol, 3 equiv),

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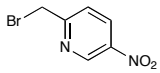
([9]) The synthesis of catalyst **10** has been described previously, see: Nagib, D. A.; Scott, M. E.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2009**, *131*, 10875, Supporting Information.
([10]) Li, J.; Luo, S.; Cheng, J.-P.; *J. Org. Chem.* **2009**, *74*, 1747.

TFA (44.5 g, 30 mL, 390 mmol, 5 equiv), and CH_2Cl_2 (300 mL, 0.25 M). The flask was then equipped with a reflux condenser and heated to 40 °C for three days. The solution was concentrated *in vacuo* giving a mixture of the *cis* and *trans* imidazolidinone products as a dark brown oil. The pure trans product was isolated by flash chromatography (25% EtOAc in hexanes) as a light yellow oil (2.77 g, 11% yield). To the Cbz protected catalyst (2.77 g, 8.2 mmol) dissolved in EtOAc (50 mL, 0.16 M) was added 10% dry Pd/C (0.25 g, 9 wt%) and the reaction mixture was stirred under an atmosphere of H_2 for 3 hours. The solution was then passed through a pad of celite eluting with EtOAc (250 mL). The organic solvent was removed *in vacuo* yielding the pure title compound (1.6 g, 96% yield, >99% ee) as a light yellow oil that solidified spontaneously upon standing. IR (thin film) 3308, 2922, 1682, 1399, 1083, 751, 700 cm^{-1}; ^1H NMR (500 HHz, $CDCl_3$) δ: 7.25–7.11 (m, 5H, Ar**H**), 4.00 (q, 1H, *J* = 5.7 Hz, NMeC**H**NH), 3.77 (dd, 1H, *J* = 7.1, 4.2 Hz, COC**H**NH), 2.98 (dd, 1H, *J* = 13.8, 4.1 Hz, ArC$\mathbf{H_2}$), 2.84 (dd, 1H, *J* = 13.8, 7.3 Hz, ArC$\mathbf{H_2}$), 2.65 (s, 3H, NC$\mathbf{H_3}$), 1.90 (bs, 1H, N**H**), 1.17 (d, 3H, *J* = 5.8 Hz, CHC$\mathbf{H_3}$); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 174.1, 137.5, 129.5, 128.3, 126.6, 70.8, 59.9, 37.7, 26.5, 20.2; HRMS (ESI-TOF) calculated for $C_{12}H_{17}N_2O$ $[M+H]^+$ m/z 205.1335, found 205.1336. $[\alpha]_D^{23} = -99.21$ (c = 1.0, $CHCl_3$). SFC analysis (IA, 5% MeOH, 1.0 mL/min, 220 nm) indicates >99% ee: t_R(major) = 4.86 minutes, t_R(minor) = 5.70 minutes.

VI. Synthesis of Starting Material Bromides.



2-(Bromomethyl)-5-nitropyridine. To a solution of 2-methyl-5-nitropyridine[11] (1.01 g, 7.29 mmol) in acetic acid (6 mL) was added bromine (185 μL, 3.61 mmol) and the mixture was refluxed for 30 min. After the solution had cooled to ambient temperature, it was diluted with H_2O (60 mL) and product was extracted into Et_2O (3 × 60 mL). The combined organic phase was washed with sat. $NaHCO_3$ solution (3 × 90 mL), dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by flash chromatography (10% EtOAc/petroleum ether) to provide the title compound as an orange solid (325 mg, 21% yield) followed by unreacted 2-methyl-5-nitropyridine (0.521 g). IR (thin film) 1599, 1577, 1519, 1471, 1343, 1294, 1017, 865, 852, 809,

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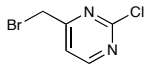
([11]) Bobrovskii, S. I.; Babaev, E. V.; Bundel, Y. G. *Chem. Heterocyc. Compd.* **1990**, *26*, 631.

721, 609 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.38 (d, 1H, *J* = 2.5 Hz, Ar**H**), 8.49 (dd, 1H, *J* = 2.5, 8.7 Hz, Ar**H**), 7.67 (d, 1H, *J* = 8.7 Hz, Ar**H**), 4.62 (s, 2H, C$\mathbf{H}_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.9, 145.0, 143.3, 132.2, 123.7, 31.8; HRMS (ESI-TOF) calculated for $C_6H_6BrN_2O_2$ $[M+H]^+$ m/z 216.9613 (^{79}Br), 218.9592 (^{81}Br), found 216.9607 (^{79}Br), 218.9586 (^{81}Br).



4-(Bromomethyl)-4-chloropyrimidine. *N*-Bromosuccinimide (7.14 g, 40.1 mmol) and benzoyl peroxide (1.76 g, 7.27 mmol) were added to a solution of 2-chloro-4-methylpyrimidine[12] (4.44 g, 34.5 mmol) in carbon tetrachloride (110 mL) and the mixture was refluxed for 24 h. The mixture was filtered and the solids washed with carbon tetrachloride. The filtrate was concentrated *in vacuo* and the residue was purified by flash chromatography (10% Et_2O/petroleum ether) to provide the title compound as a colourless oil (0.945 g, 13% yield). IR (thin film) 1565, 1541, 1427, 1337, 1204, 1182, 913, 718, 680 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 8.65 (d, 1H, *J* = 5.0 Hz, Ar**H**), 7.45 (d, 1H, *J* = 5.0 Hz, Ar**H**), 4.42 (s, 2H, C$\mathbf{H}_2$Br); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 168.2, 161.2, 160.4, 118.8, 30.4; HRMS (ESI-TOF) calculated for $C_5H_5BrClN_2$ $[M+H]^+$ m/z 206.9325 (^{35}Cl, ^{79}Br), 208.9295 (^{35}Cl, ^{81}Br), 208.9304 (^{37}Cl, ^{79}Br), 210.9265 (^{37}Cl, ^{81}Br), found 206.9319, 208.9298, 210.9269.

VII. Emission Quenching Experiments.

Emission intensities were recorded using a Perkin Elmer LS50 Luminescence specrometer. All *fac*-Ir(ppy)$_3$ solutions were excited at 385 nm and the emission intensity at 520 nm was observed. In a typical experiment, a 0.0656 M solution of *fac*-Ir(ppy)$_3$ in DMSO was added to the appropriate amount of quencher in a screw-top 1.0 cm quartz cuvette. After degassing with a stream of argon for 15 minutes, the emission spectrum of the sample was collected.

Figure S1: *fac*-Ir(ppy)$_3$ Emission Quenching by Imidazolidinone.

([12]) Adjabeng, G.; Bifulco, N.; Davis-Ward, R.; Dickerson, S. H.; Hornberger, K.; Petrov, K.; Rheault, T. R.; Uehling, D. E.; Waterson, A. G. Patent WO2009076140, **2009**; *Chem. Abstr.* 150:398529.

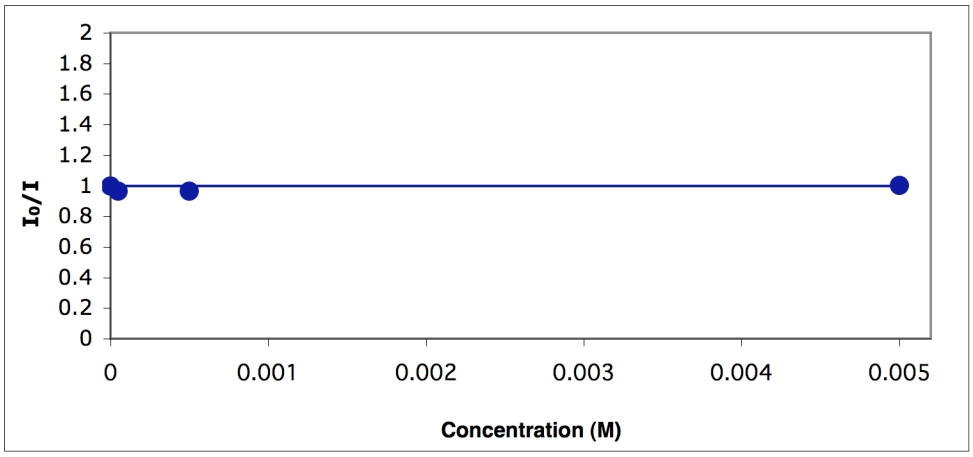


Figure S2: *fac*-Ir(ppy)$_3$ Emission Quenching by *n*-Octanal.

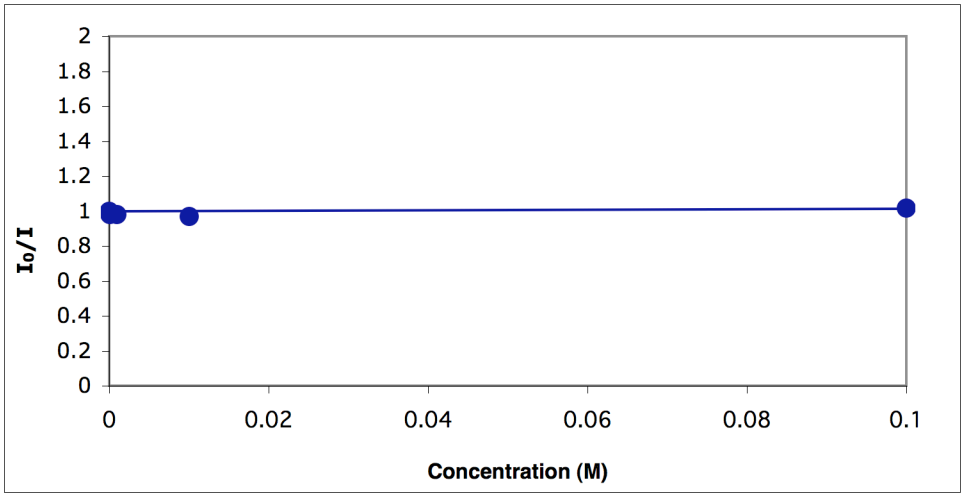


Figure S3: *fac*-Ir(ppy)$_3$ Emission Quenching by 2,6-Lutidine.

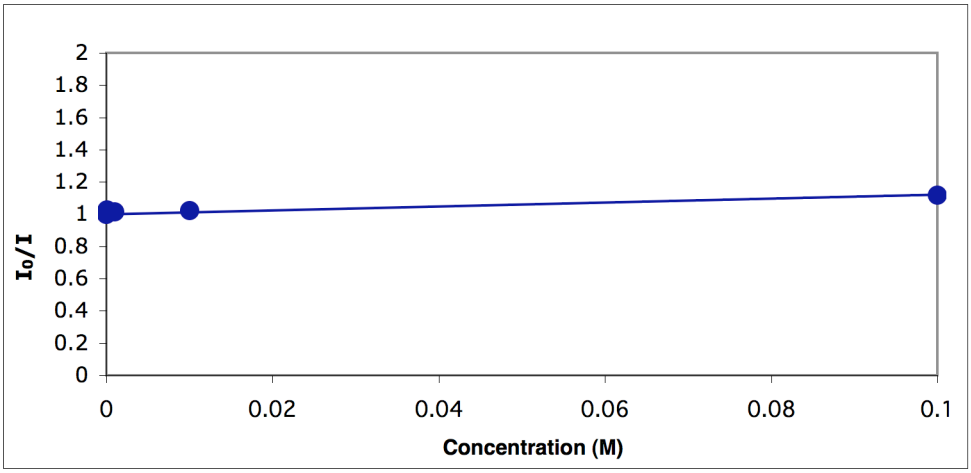


Figure S4: *fac*-Ir(ppy)$_3$ Emission Quenching by *n*-Bu$_4$NBr.

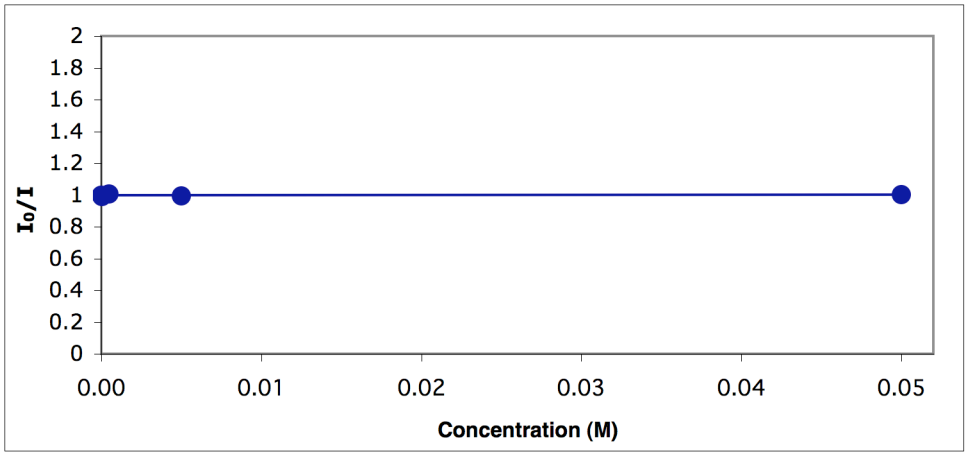


Figure S5: *fac*-Ir(ppy)$_3$ Emission Quenching by Enamine.

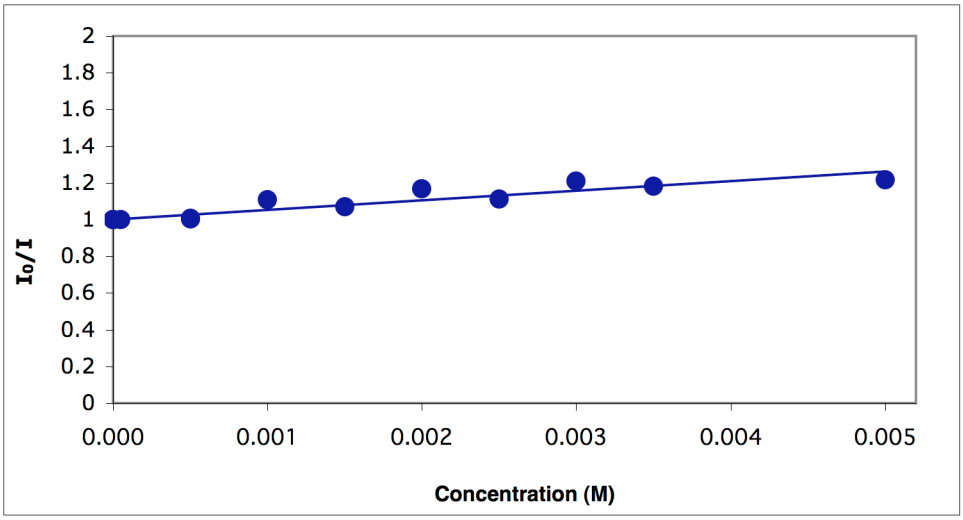


Figure S5: *fac*-Ir(ppy)$_3$ Emission Quenching by Carbocyclic Benzyl Bromides.

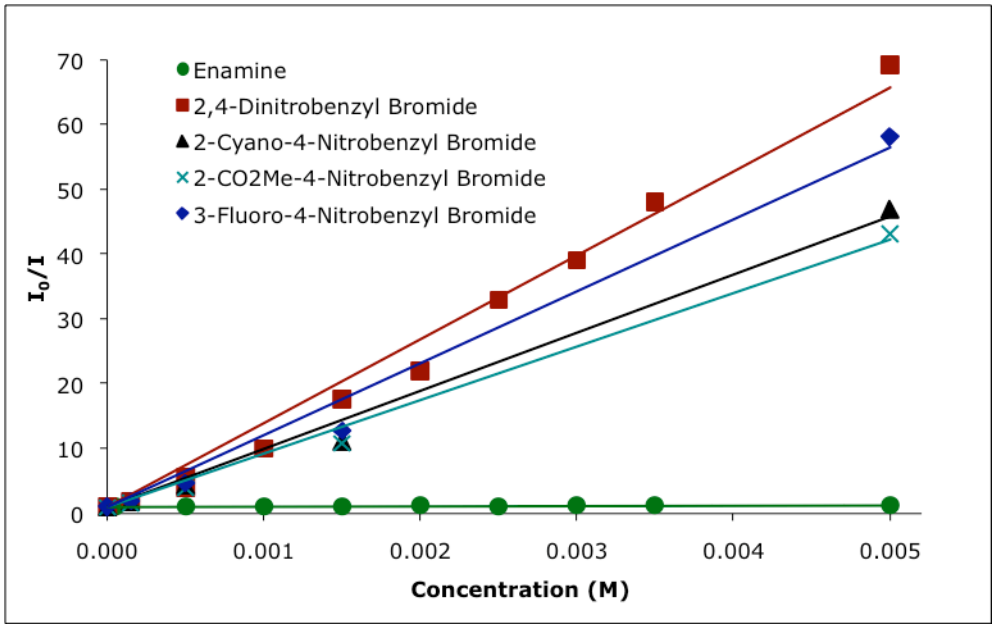

Enamine
2,4-Dinitrobenzyl Bromide
2-Cyano-4-Nitrobenzyl Bromide
2-CO2Me-4-Nitrobenzyl Bromide
3-Fluoro-4-Nitrobenzyl Bromide
I0/I
70
60
50
40
30
20
10
0
0.000
0.001
0.002
0.003
0.004
0.005
Concentration (M)

Figure S6: *fac*-Ir(ppy)$_3$ Emission Quenching by Basic Heterocyclic Benzyl Bromides.

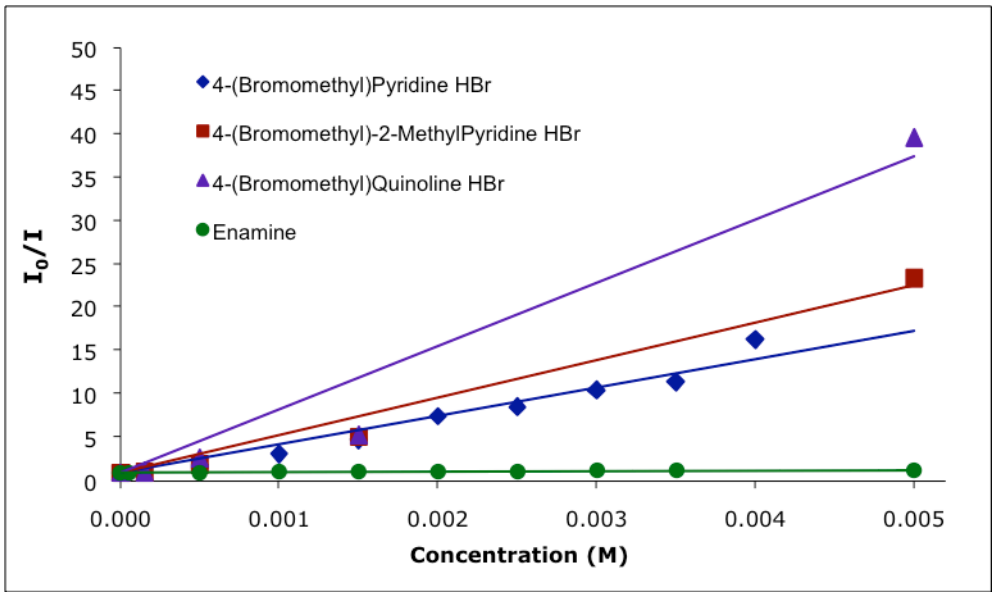


Figure S7: *fac*-Ir(ppy)$_3$ Emission Quenching by 2-(Bromomethyl)Benzimidazole.

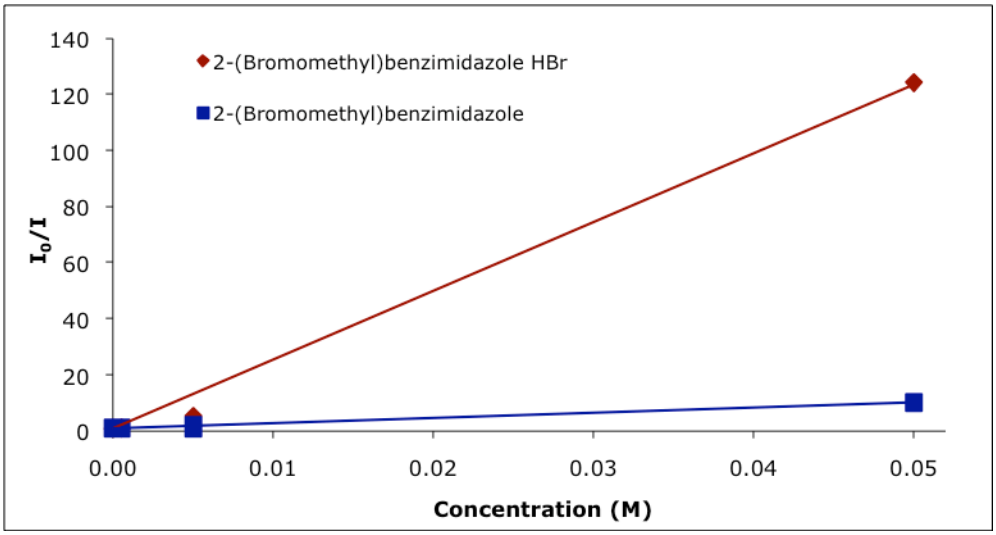


Figure S8: *fac*-Ir(ppy)$_3$ Emission Quenching by Non-basic Hetercyclic Benzyl Bromides.