Direct, enantioselective $\alpha$-alkylation of aldehydes using simple olefins

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I. General Information

Commercial reagents were purified prior to use following the guidelines of Perrin and Armarego.\textsuperscript{1} \textit{Ir[Flmppy]₂(dtbbpy)}PF\textsubscript{6} was prepared as previously reported.\textsuperscript{2} \textit{Ir[dmppy]₂(dtbbpy)-PF\textsubscript{6}} was prepared as previously reported.\textsuperscript{3} 2,4,6-Trisopropylthiophenol was prepared as previously reported.\textsuperscript{4} 2,4,6-Tri-tert-butylthiophenol was prepared as previously reported.\textsuperscript{5} Solvents were purified by passage through columns of activated alumina, or according to the method of Grubbs.\textsuperscript{6} Non-aqueous reagents were transferred under nitrogen via syringe or cannula. Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator using a water bath. Chromatographic purification of products was accomplished using forced-flow column chromatography on ICN 60 32-64 mesh silica gel 63 according to the method of Still\textsuperscript{7} and where noted, Davisol S-743-1 was used in place of silica gel. Thin-layer chromatography (TLC) was performed on Silicycle 0.25 mm silica gel F-254 plates. Visualization of the developed chromatogram was performed using a UV lamp, potassium permanganate, dinitrophenylhydrazine or ceric ammonium molybdate stain. \textit{¹H} and \textit{¹³C} NMR spectra were recorded on a Bruker UltraShield Plus (500 and 125 MHz, respectively) instrument, and are internally referenced to residual protio solvent signals for CDCl\textsubscript{3} (7.26 ppm) or (CD\textsubscript{3})\textsubscript{2}SO (2.50 ppm). Data for \textit{¹H} NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, brs = broad singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublet, dt = doublet of triplet, ddd = doublet of doublet of doublet), coupling constant (Hz), and integration. Data for \textit{¹³C} NMR are reported in terms of chemical shift relative to CDCl\textsubscript{3} (77 ppm) or (CD\textsubscript{3})\textsubscript{2}SO (39.52 ppm). IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in terms of wavenumbers (cm\textsuperscript{-1}). Optical rotation measurements were obtained with a Jasco P-1010 polarimeter with \([\alpha]_D^{21}\) values reported in degrees; concentration (c) is in g/100 mL. Enantiopurity was assessed via HPLC analysis using an Agilent Technologies 1260 Infinity chromatograph with chiral columns as noted for each compound using a hexane/isopropanol liquid phase. High Resolution Mass spectra were obtained from the Princeton University Mass Spectrometry Facility.

II. Substrate Synthesis

Contains a general two-step procedure for substrate synthesis, including the precursor alcohol and the aldehyde substrates. N-(4-hydroxybutyl)-4-methylbenzenesulfonamide and N-(3-hydroxypropyl)-4-methylbenzenesulfonamide were prepared as previously reported. All alkyl bromides utilized are commercially available unless individually noted.

**General procedure step 1: preparation of the alcohol corresponding to the substrate:** To a flame-dried flask was added sodium hydride (60% dispersion in mineral oil) (1.1 equiv.) followed by DMF (0.2 M). N-(4-hydroxybutyl)-4-methylbenzenesulfonamide (1 equiv.) was added portion-wise and the resulting mixture was stirred under nitrogen for 1 h; thereafter the corresponding alkyl bromide (1.05 equiv.) was added dropwise and the resulting mixture was stirred at room temperature for 8 h. The reaction was quenched with saturated aqueous ammonium chloride, and then diluted with EtOAc. The phases were separated and the organic phase washed three times with 7.5% aqueous lithium chloride followed by brine, and then dried over anhydrous sodium sulfate. The solvent was removed *in vacuo* and the residue purified by silica-gel chromatography (0-30% EtOAc in CH$_2$Cl$_2$) to afford the desired compound.

**General procedure step 2: preparation of the aldehyde substrate:** The corresponding alcohol (1.0 equiv.) was dissolved in CH$_2$Cl$_2$ (0.1 M), and sodium bicarbonate (5.0 equiv.) was added followed by Dess-Martin periodinane (1.1 equiv.). The resulting mixture was stirred for 8 h. Thereafter the reaction was quenched with saturated aqueous sodium thiosulfate solution and washed twice with saturated sodium bicarbonate followed by brine, and then dried over anhydrous sodium sulfate. The solvent was removed *in vacuo* and the residue purified by silica-gel chromatography (50-100% CH$_2$Cl$_2$ in hexanes) to afford the desired compound.

(E)-N-(3,7-Dimethylocta-2,6-dien-1-yl)-N-(4-hydroxybutyl)-4-methylbenzenesulfonamide. According to the general procedure using (E)-1-bromo-3,7-dimethylocta-2,6-diene to afford the title compound as a colorless oil (3.19 g, 8.4 mmol, 84% yield). Analytical data: $^1$H NMR (500 MHz, DMSO-$d_6$) δ 7.66 (d, $J = 8.2$ Hz, 2H), 7.39 (d, $J = 8.0$ Hz, 2H), 5.00 – 4.92 (m, 1H), 4.89 – 4.83 (m, 1H), 4.39 (t, $J = 5.1$ Hz, 1H), 3.74 (d, $J = 7.0$ Hz, 2H), 3.38 – 3.34 (m, 2H), 3.02 (t, $J = 7.3$ Hz, 2H), 2.38 (s, 3H), 1.97 – 1.80 (m, 4H), 1.61 (d, $J = 1.5$ Hz, 3H), 1.59 – 1.55 (m, 3H), 1.53 (d, $J = 1.3$ Hz, 3H), 1.46 (dq, $J = 11.9$, 7.6, 7.1 Hz, 2H), 1.39 – 1.31 (m, 2H); $^{13}$C NMR (125 MHz, DMSO-$d_6$) δ 143.3, 139.7, 137.4, 131.4, 130.2, 127.3, 124.2, 119.2, 60.7, 47.2, 45.2, 30.1, 26.0, 25.0, 21.4, 18.0, 16.3; HRMS (ESI$^+$) Calcd. for C$_{21}$H$_{33}$NO$_3$S+H, 380.22539; Found, 380.22547; IR (thin film, cm$^{-1}$) 3463, 2923, 2868, 1738, 1666, 1599, 1494, 1447, 1377,

1335, 1305, 1289, 1185, 1154, 1117, 1089, 1026, 916, 814, 772, 701, 653; TLC (80:20 CH₂Cl₂:EtOAc): R_f = 0.55.

(\(E\))-N-(3,7-Dimethylocta-2,6-dien-1-yl)-4-methyl-N-(4-oxobutyl)benzenesulfonamide. According to the general procedure using (\(E\))-N-(3,7-dimethylocta-2,6-dien-1-yl)-N-(4-hydroxybutyl)-4-methylbenzenesulfonamide to afford the title compound as a yellow oil (1.68 g, 4.5 mmol, 53% yield). Analytical data: ¹H NMR (500 MHz, CDCl₃) δ 9.79 (t, \(J = 1.1\) Hz, 1H), 7.67 (d, \(J = 8.3\) Hz, 2H), 7.30 – 7.27 (m, 2H), 4.99 (tdd, \(J = 5.5\), 3.1, 1.6 Hz, 1H), 4.92 (dddd, \(J = 7.1\), 5.7, 2.6, 1.3 Hz, 1H), 3.79 (d, \(J = 7.0\) Hz, 2H), 3.10 (t, \(J = 6.8\) Hz, 2H), 2.57 (td, \(J = 7.0\), 1.1 Hz, 2H), 2.42 (s, 3H), 2.00 – 1.89 (m, 4H), 1.84 (quin, \(J = 6.9\) Hz, 2H), 1.66 (d, \(J = 1.4\) Hz, 3H), 1.62 – 1.59 (m, 3H), 1.57 (d, \(J = 1.5\) Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 201.7, 143.3, 140.7, 140.7, 137.1, 132.0, 129.8, 127.3, 123.8, 118.6, 46.4, 45.7, 40.9, 39.6, 26.2, 25.9, 21.7, 21.0, 17.8, 16.3; HRMS (ESI⁺) Calcd. for C₂₁H₃₁NO₃S+H, 378.2097; Found, 378.2099; IR (thin film, cm⁻¹) 2922, 2724, 1723, 1668, 1598, 1494, 1449, 1377, 1336, 1305, 1289, 1184, 1156, 1115, 1089, 1020, 917, 815, 726, 701, 652; TLC (CH₂Cl₂): R_f = 0.40.

(\(E\))-N-(But-2-en-1-yl)-N-(4-hydroxybutyl)-4-methylbenzenesulfonamide. According to the general procedure using (\(E\))-1-bromobut-2-ene to afford the title compound as a colorless oil (2.59 g, 8.7 mmol, 87% yield). Analytical data: ¹H NMR (500 MHz, DMSO-d₆) δ 7.70 – 7.62 (m, 2H), 7.40 (d, \(J = 8.1\) Hz, 2H), 5.65 – 5.49 (m, 1H), 5.26 – 5.09 (m, 1H), 4.39 (t, \(J = 5.1\) Hz, 1H), 3.67 – 3.64 (m, 2H), 3.35 (m, 2H), 3.05 – 2.98 (m, 2H), 2.39 (s, 3H), 1.61 – 1.54 (m, 3H), 1.51 – 1.40 (m, 2H), 1.40 – 1.29 (m, 2H); ¹³C NMR (125 MHz, DMSO-d₆) δ 143.0, 136.7, 129.8, 129.6, 126.9, 125.8, 60.3, 49.2, 46.8, 29.5, 24.5, 21.0, 17.5; HRMS (ESI⁺) Calcd. for C₁₅H₂₃NO₃S+H, 298.1471; Found, 298.1471; IR (thin film, cm⁻¹) 3450, 2930, 2869, 1598, 1449, 1332, 1305, 1289, 1154, 1089, 1057, 1023, 968, 929, 815, 733, 715, 699; TLC (80:20 CH₂Cl₂:EtOAc): R_f = 0.42.
(E)-N-(But-2-en-1-yl)-4-methyl-N-(4-oxobutyl)benzenesulfonamide. According to the general procedure using (E)-N-(but-2-en-1-yl)-N-(4-hydroxybutyl)-4-methylbenzenesulfonamide to afford the title compound as a colorless oil (1.69 g, 5.7 mmol, 66% yield). Analytical data: \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 9.78 (s, 1H), 7.66 (d, \(J = 8.3\) Hz, 1H), 7.29 (d, \(J = 8.0\) Hz, 2H), 5.63 – 5.53 (m, 1H), 5.22 (ddddt, \(J = 12.1, 8.9, 6.9, 1.8\) Hz, 1H), 3.72 – 3.68 (m, 2H), 3.11 (t, \(J = 6.9\) Hz, 2H), 2.55 (td, \(J = 7.0, 1.2\) Hz, 2H), 2.42 (s, 3H), 1.90 – 1.77 (m, 2H), 1.62 (dt, \(J = 6.5, 1.4\) Hz, 3H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 201.7, 143.4, 137.0, 130.9, 129.8, 127.3, 125.6, 50.4, 46.2, 40.8, 21.7, 20.8, 17.8; HRMS (ESI\(^+\)) Calcd. for C\(_{15}\)H\(_{21}\)NO\(_3\)S+H, 296.13149; Found, 296.13129; IR (thin film, cm\(^{-1}\)) 2924, 2726, 1721, 1598, 1494, 1450, 1334, 1305, 1289, 1155, 1089, 1017, 969, 928, 815, 803, 718, 698; TLC (CH\(_2\)Cl\(_2\)): \(R_f = 0.40\).

Ethyl (E)-3-(1,3-diphenyl-1H-pyrazol-4-yl)acrylate. To a stirred suspension of sodium hydride (60% dispersion in mineral oil) (0.89 g, 22 mmol, 1.1 equiv.) in THF (100 mL, 0.2 M) at 0 °C was added ethyl 2-(diethoxyporphoryl)acetate (4.59 mL, 23 mmol, 1.15 equiv.), and the resulting mixture was stirred for 30 min. Thereafter, 1,3-diphenyl-1H-pyrazole-4-carbaldehyde (5.0 g, 20 mmol, 1.0 equiv.) was added dropwise, and the reaction stirred at room temperature for 8 h. The reaction was quenched with saturated ammonium chloride and diluted with EtOAc. The organic phase was washed with brine then dried over anhydrous Na\(_2\)SO\(_4\), and then dried in vacuo. Purification by flash chromatography (10-20% EtOAc in hexanes) to afford the title compound as a cream solid (5.49 g, 17.3 mmol, 86% yield). Analytical data: \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 8.24 (s, 1H), 7.78 – 7.75 (m, 2H), 7.72 (br s, 1H), 7.69 – 7.66 (m, 2H), 7.49 (td, \(J = 7.2, 1.5\) Hz, 4H), 7.46 – 7.41 (m, 1H), 7.37 – 7.32 (m, 1H), 6.30 (s, 1H), 4.24 (q, \(J = 7.1\) Hz, 2H), 1.32 (t, \(J = 7.1\) Hz, 3H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 167.2, 153.4, 139.6, 135.2, 132.4, 129.7, 128.9, 128.8, 128.8, 127.3, 126.5, 119.5, 117.8, 60.5, 14.5; HRMS (ESI\(^+\)) Calcd. for C\(_{20}\)H\(_{18}\)N\(_2\)O\(_2\)+H, 319.14411; Found, 319.14442; IR (thin film, cm\(^{-1}\)) 3137, 3066, 2983, 2926, 1693, 1624, 1600, 1539, 1506, 1478, 1446, 1418, 1395, 1367, 1282, 1265, 1249, 1212, 1181, 1114, 1067, 1041, 1019, 980, 958, 919, 900, 871, 841, 822, 772, 754, 738, 696, 679, 667; TLC (80:20 hexanes:EtOAc): \(R_f = 0.40\).
To a stirred solution of ethyl (E)-3-(1,3-diphenyl-1H-pyrazol-4-yl)prop-2-en-1-ol (5.3 g, 1.0 equiv.) in CH$_2$Cl$_2$ (83 mL, 0.2 M) at -78 °C was added DIBAL-H (1 M in toluene, 38.3 mL, 38.3 mmol, 2.3 equiv.) dropwise. The reaction was warmed to room temperature, and then quenched with methanol followed by saturated ammonium chloride solution. The reaction was diluted with CH$_2$Cl$_2$, and the layers separated. The organic phase was washed with brine and dried over anhydrous Na$_2$SO$_4$, and then dried in vacuo. Purification by flash chromatography (20-40% EtOAc in hexanes) provided the title compound (3.45 g, 12.5 mmol, 80% yield) as a yellow oil. Analytical data: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.08 (s, 1H), 7.79 – 7.73 (m, 2H), 7.72 – 7.68 (m, 2H), 7.46 (ddd, $J$ = 7.9, 6.9, 2.0 Hz, 4H), 7.43 – 7.36 (m, 1H), 7.34 – 7.27 (m, 1H), 6.61 (dt, $J$ = 16.0, 1.5 Hz, 1H), 6.20 (dt, $J$ = 15.9, 5.9 Hz, 1H), 4.29 (td, $J$ = 5.8, 1.5 Hz, 2H), 1.48 (t, $J$ = 5.8 Hz, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 151.7, 140.0, 133.2, 129.6, 128.8, 128.7, 128.6, 128.2, 126.7, 124.9, 121.7, 119.4, 119.2, 77.4, 64.1; HRMS (ESI$^+$) Calcd. for C$_{18}$H$_{16}$N$_2$O$^+$H, 277.13354; Found, 277.13341; IR (thin film, cm$^{-1}$): 3367, 3057, 2983, 2862, 1732, 1658, 1598, 1544, 1502, 1464, 1447, 1408, 1372, 1356, 1303, 1235, 1157, 1091, 1074, 1059, 1044, 1020, 958, 916, 830, 793, 755, 736,689, 676. TLC (60:40 hexanes:EtOAc): $R_f$ = 0.40

(E)-N-(3-(1,3-Diphenyl-1H-pyrazol-4-yl)allyl)-N-(4-hydroxybutyl)-4-methylbenzenesulfonamide. To a stirred solution of (E)-3-(1,3-diphenyl-1H-pyrazol-4-yl)prop-2-en-1-ol in Et$_2$O (107 mL, 0.125 M) at 0 °C was added phosphorus tribromide (0.51 mL, 5.4 mmol, 0.4 equiv.) dropwise over 5 min. When the reaction was complete according to TLC, the mixture was diluted with water and the phases separated. The organic phase was washed with saturated NaHCO$_3$ solution followed by brine, and then dried over anhydrous Na$_2$SO$_4$, and concentrated in vacuo. The crude (E)-4-(3-bromoprop-1-en-1-yl)-1,3-diphenyl-1H-pyrazole (3.6 g, 10.6 mmol, 79%) obtained was used directly in the general procedure step 1. Purification by flash chromatography (0-25% EtOAc in CH$_2$Cl$_2$) provided the title compound (1.0 g, 2.0 mmol, 19% yield) as a colorless oil. Analytical data: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.96 (s, 1H), 7.75 – 7.68 (m, 3H), 7.65 – 7.62 (m, 2H), 7.50 – 7.42 (m, 5H), 7.41 – 7.37 (m, 1H), 7.33 – 7.27 (m, 3H), 6.46 (d, $J$ = 15.9 Hz, 1H), 5.85 (dt, $J$ = 15.8, 6.8 Hz, 1H), 3.91 (dd, $J$ = 6.8, 1.4 Hz, 2H), 3.63 (t, $J$ = 6.2 Hz, 2H), 3.20 (t, $J$ = 7.3 Hz, 2H), 2.41 (s, 3H), 1.73 – 1.47 (m, 4H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 151.5, 143.4, 139.9, 137.1, 133.1, 129.8, 129.6, 128.7, 128.5, 128.3, 127.4, 126.8, 125.1, 124.8, 124.0, 119.2, 119.0, 62.5, 50.6, 47.4, 29.6, 25.0, 21.7; HRMS (ESI$^+$) Calcd. for C$_{29}$H$_{31}$N$_3$O$_3$S$^+$H, 502.21589; Found, 502.21573; IR (thin film, cm$^{-1}$): 3398, 3059, 2931, 2868,

**(E)-N-(3-(1,3-Diphenyl-1H-pyrazol-4-yl)allyl)-4-methyl-N-(4-oxobutyl)benzenesulfonamide.** According to the general procedure using (E)-N-(3-(1,3-diphenyl-1H-pyrazol-4-yl)allyl)-N-(4-hydroxybutyl)-4-methylbenzenesulfonamide to afford the title compound as a yellow oil (0.72 g, 1.44 mmol, 72% yield). Analytical data: \(^1\)H NMR (500 MHz, CDCl₃) δ 9.77 (s, 1H), 7.97 (s, 1H), 7.72 (m, 4H), 7.63 (d, \(J = 7.4\) Hz, 2H), 7.52 – 7.23 (m, 8H), 6.47 (d, \(J = 15.8\) Hz, 1H), 5.90 – 5.75 (m, 1H), 3.90 (d, \(J = 6.9\) Hz, 2H), 3.18 (t, \(J = 6.8\) Hz, 2H), 2.57 (t, \(J = 6.8\) Hz, 2H), 2.41 (s, 3H), 1.90 (q, \(J = 6.9\) Hz, 2H); \(^{13}\)C NMR (125 MHz, CDCl₃) δ 201.6, 151.5, 143.5, 139.9, 136.8, 133.0, 129.9, 129.6, 128.7, 128.5, 128.3, 127.4, 126.8, 125.1, 124.3, 119.2, 118.9, 77.2, 51.0, 46.8, 40.8, 21.7, 21.0; HRMS (ESI⁺) Calcd. for C₂₉H₂₉N₃O₃S+H, 500.20024; Found, 500.19814; IR (thin film, cm⁻¹): 3057, 2931, 2727, 1721, 1657, 1598, 1544, 1502, 1447, 1409, 1334, 1305, 1266, 1224, 1155, 1119, 1089, 1059, 1019, 958, 914, 814, 773, 757, 699, 690; TLC (40:60 hexanes:EtOAc): R_f = 0.43.

**N-(4-Hydroxybutyl)-4-methyl-N-(2-methylallyl)benzenesulfonamide.** According to the general procedure using 3-bromo-2-methylprop-1-ene to afford the title compound as a colorless oil (2.44 g, 8.2 mmol, 82% yield). Analytical data: \(^1\)H NMR (500 MHz, DMSO-d₆) δ 7.69 (d, \(J = 8.2\) Hz, 2H), 7.41 (d, \(J = 8.1\) Hz, 2H), 4.93 – 4.86 (m, 2H), 4.37 (t, \(J = 5.1\) Hz, 1H), 3.62 (s, 2H), 3.32 – 3.28 (m, 2H), 3.01 – 2.96 (m, 2H), 2.28 (s, 3H), 1.64 (s, 3H), 1.45 – 1.36 (m, 2H), 1.30 (dq, \(J = 9.8\), 6.6 Hz, 2H); \(^{13}\)C NMR (125 MHz, DMSO-d₆) δ 143.0, 141.0, 136.4, 129.8, 126.9, 113.9, 60.3, 54.1, 48.1, 29.7, 24.6, 21.0, 19.7; HRMS (ESI⁺) Calcd. for C₁₅H₂₃NO₃S+H, 298.14714; Found, 298.14739; IR (thin film, cm⁻¹): 3454, 2934, 2871, 1738, 1656, 1598, 1494, 1447, 1376, 1331, 1305, 1290, 1232, 1216, 1154, 1119, 1089, 1055, 1019, 909, 814, 769, 734, 708, 691, 653; TLC (80:20 CH₂Cl₂:EtOAc): R_f = 0.42.
4-Methyl-N-(2-methylallyl)-N-(4-oxobutyl)benzenesulfonamide. According to the general procedure using N-(4-hydroxybutyl)-4-methyl-N-(2-methylallyl)benzenesulfonamide to afford the title compound as a colorless oil (1.51 g, 5.1 mmol, 62% yield). Analytical data: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 9.74 (t, $J = 1.1$ Hz, 1H), 7.68 (d, $J = 8.2$ Hz, 2H), 7.30 (d, $J = 8.0$ Hz, 2H), 4.91 – 4.89 (m, 1H), 4.88 – 4.86 (m, 1H), 3.66 (s, 2H), 3.08 (dd, $J = 7.9, 6.6$ Hz, 2H), 2.49 (td, $J = 7.1, 1.2$ Hz, 2H), 2.42 (s, 3H), 1.81 (quin, $J = 7.1$ Hz, 2H), 1.73 – 1.67 (m, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 201.5, 143.5, 140.9, 136.6, 129.8, 127.3, 115.0, 55.4, 47.5, 41.0, 21.7, 21.0, 20.0. HRMS (ESI$^+$) Calcd. for C$_{15}$H$_{21}$NO$_3$S+H, 296.13149; Found, 296.13152; IR (thin film, cm$^{-1}$); 2931, 2727, 1722, 1656, 1598, 1495, 1450, 1376, 1333, 1306, 1290, 1243, 1213, 1185, 1155, 1118, 1089, 1004, 910, 815, 754, 709, 692, 652; TLC (CH$_2$Cl$_2$): R$_f$ = 0.40.


**N-(2,3-Dimethylbut-2-en-1-yl)-N-(4-hydroxybutyl)-4-methylbenzenesulfonamide.** According to the general procedure using 1-bromo-2,3-dimethylbut-2-ene to afford the title compound as a colorless oil (2.57 g, 7.9 mmol, 79% yield). Analytical data: $^1$H NMR (500 MHz, CDCl$_3$) δ 7.69 (d, $J = 8.2$ Hz, 2H), 7.31 – 7.28 (m, 2H), 3.74 (s, 2H), 3.60 (t, $J = 6.2$ Hz, 2H), 3.05 – 2.97 (m, 2H), 2.43 (s, 3H), 1.66 (dd, $J = 2.5$, 1.3 Hz, 6H), 1.62 – 1.60 (m, 3H), 1.59 – 1.45 (m, 4H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 143.1, 137.0, 130.4, 129.7, 127.3, 123.2, 62.7, 50.9, 47.8, 30.0, 25.3, 21.7, 21.3, 20.3, 16.5; HRMS (ESI$^+$) Calcd. for C$_{17}$H$_{27}$NO$_3$S+H, 326.17844; Found, 326.17862; IR (thin film, cm$^{-1}$); 3467, 2924, 2866, 1598, 1495, 1451, 1376, 1330, 1305, 1288, 1152, 1107, 1089, 1058, 1021, 1004, 975, 765, 719, 703, 654; TLC (80:20 CH$_2$Cl$_2$:EtOAc): $R_f$ = 0.50.

**N-(2,3-Dimethylbut-2-en-1-yl)-4-methyl-N-(4-oxobutyl)benzenesulfonamide.** According to the general procedure using N-(2,3-dimethylbut-2-en-1-yl)-N-(4-hydroxybutyl)-4-methylbenzenesulfonamide to afford the title compound as a white solid (1.89 g, 5.8 mmol, 74% yield). Analytical data: $^1$H NMR (500 MHz, CDCl$_3$) δ 9.73 (s, 1H), 7.67 (d, $J = 7.9$ Hz, 2H), 7.30 (d, $J = 7.9$ Hz, 2H), 3.71 (s, 2H), 2.99 (t, $J = 7.1$ Hz, 2H), 2.50 (t, $J = 7.0$ Hz, 2H), 2.43 (s, 3H), 1.80 (quin, $J = 7.1$ Hz, 2H), 1.66 (s, 6H), 1.62 (s, 3H); $^{13}$C NMR (126 MHz, CDCl$_3$) δ 201.71, 143.32, 136.43, 130.92, 129.79, 127.36, 122.93, 51.59, 47.51, 41.03, 21.67, 21.61, 21.31, 20.28, 16.58; HRMS (ESI$^+$) Calcd. for C$_{17}$H$_{25}$NO$_3$S+H, 324.16279; Found, 324.16244; IR (thin film, cm$^{-1}$); 3028, 2922, 2718, 1723, 1598, 1495, 1451, 1376, 1330, 1305, 1288, 1152, 1107, 1089, 1058, 1021, 1004, 902, 815, 765, 719, 703, 654; TLC (80:20 CH$_2$Cl$_2$:EtOAc): $R_f$ = 0.40.

**Di-tert-butyl 2-(2-methylallyl)-2-(4-oxobutyl)malonate.** To an oven dried flask was added 1,1-di-tert-butyl 4-ethyl butane-1,1,4-tricarboxylate (7.0 g, 21.2 mmol, 1.0 equiv.) followed by THF (106 mL). Potassium tert-butoxide (2.7 g, 24.4 mmol, 1.15 equiv.) was then added and the flask was stirred under nitrogen for 30 minutes. 3-bromo-2-methylprop-1-ene (3.0 mL, 29.7 mmol,
1.40 equiv.) was then added dropwise at room temperature and the mixture was stirred at this temperature for 16 h. The mixture was then diluted with ether (100 mL) and saturated aqueous sodium bicarbonate (100 mL). After separation of layers, the aqueous layer was extracted with ether (2 x 100 mL) and the combined organic layers were dried over magnesium sulfate, filtered, and concentrated in vacuo. The resulting oil (7.2 g, 88% yield) was then used in the next step without further purification.

To a solution of 4,4-di-tert-butyl 1-ethyl 6-methylhept-6-ene-1,4,4-tricarboxylate (7.2 g, 18.7 mmol, 1.0 equiv.) in toluene (150 mL) at −78°C was added diisobutylaluminum hydride (20.2 mL, 1.0 M solution in toluene, 20.2 mmol, 1.08 equiv.). The reaction was stirred for four hours at −78°C and then quenched with water (5 mL) at −78°C and allowed to warm to 0°C. The reaction was then poured onto 1M HCl (50 mL) at 0°C and stirred at this temperature for an additional hour. The mixture was then diluted with ethyl acetate (100 mL), and the layers were separated. The aqueous layer was then extracted with ethyl acetate (2 x 100 mL), and the combined organic layers were dried over magnesium sulfate, filtered, and concentrated in vacuo. The product was isolated by flash chromatography (7-10% ethyl acetate/hexanes) as a colorless oil (1.9 g, 5.6 mmol, 30% yield).

Analytical data: $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 9.74 (t, $J = 1.6$ Hz, 1H), 4.83 (s, 1H), 4.75 (s, 1H), 2.65 (s, 2H), 2.42 (td, $J = 7.2$, 1.6 Hz, 2H), 1.85 – 1.78 (m, 2H), 1.69 (s, 3H), 1.53 (m, 2H), 1.46 (s, 18H). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 202.0, 170.8, 141.4, 115.3, 81.6, 57.7, 44.1, 40.0, 31.8, 28.0, 23.5, 17.1. HRMS (ESI$^+$) Calcd. for C$_{19}$H$_{32}$O$_5$Na+, 363.21419; Found, 363.21419.

IR (thin film, cm$^{-1}$) 2978, 2935, 1721, 1477, 1456, 1393, 1368, 1299, 1257, 1249, 1213, 1166, 1144, 1111, 1094, 913, 849, 732.

TLC (60:40 hexanes:EtOAc): $R_f$ = 0.67.

N-(3-Hydroxypropyl)-4-methyl-N-(2-methylallyl)benzenesulfonamide. Prepared using a modified general procedure using N-(3-hydroxypropyl)-4-methylbenzenesulfonamide and 3-bromo-2-methylprop-1-ene to afford the title compound as a colorless oil (2.98 g, 10.5 mmol, 93% yield). Analytical data: $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.70 (d, $J = 8.2$ Hz, 2H), 7.31 (d, $J = 8.0$ Hz, 2H), 4.91 – 4.83 (m, 2H), 3.71 (t, $J = 5.7$ Hz, 2H), 3.68 (s, 2H), 3.21 (t, $J = 6.6$ Hz, 2H), 2.43 (s, 3H), 1.72 – 1.66 (m, 5H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 143.6, 141.0, 136.4, 129.9, 127.3, 115.0, 59.2, 55.9, 45.1, 31.3, 21.7, 20.0. HRMS (ESI$^+$) Calcd. for C$_{19}$H$_{21}$NO$_3$S+H, 284.13149; Found, 284.13149; IR (thin film, cm$^{-1}$); 3486, 2931, 1656, 15981495, 1450, 1377, 1329, 1306, 1290, 1154, 1115, 1089, 1053, 1019, 1000, 907, 814, 776, 744, 708, 692, 652, 582, 567, 544, 521; TLC (80:20 CH$_2$Cl$_2$:EtOAc): $R_f$ = 0.50.
4-Methyl-N-(2-methylallyl)-N-(3-oxopropyl)benzenesulfonamide. According to the general procedure using N-(3-hydroxypropyl)-4-methyl-N-(2-methylallyl)benzenesulfonamide to afford the title compound as a white solid (1.60 g, 5.7 mmol, 54% yield). Analytical data: $^1$H NMR (500 MHz, CDCl$_3$) δ 9.72 (t, $J = 1.0$ Hz, 1H), 7.69 (d, $J = 8.3$ Hz, 2H), 7.32 (d, $J = 8.0$ Hz, 2H), 4.94 – 4.85 (m, 2H), 3.66 (s, 2H), 3.37 (t, $J = 7.3$ Hz, 2H), 2.78 (ddd, $J = 7.9$, 6.8, 1.1 Hz, 2H), 2.43 (s, 3H), 1.75 – 1.69 (m, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 200.4, 143.7, 140.7, 136.1, 129.9, 127.4, 115.2, 55.9, 43.7, 41.8, 21.7, 19.9; HRMS (ESI$^+$) Calcd. for C$_{14}$H$_{19}$NO$_3$S+H, 282.11584; Found, 282.11574; IR (thin film, cm$^{-1}$); 2969, 2922, 2829, 2730, 1721, 1660, 1597, 1494, 1448, 1385, 1371, 1329, 1306, 1288, 1243, 1226, 1155, 1119, 1087, 1071, 1017, 999, 925, 908, 894, 811, 801, 786, 706, 695, 682.
### III. Control Experiments for Intra- and Intermolecular Aldehyde α-Alkylation

#### Intramolecular Reaction - Control and Optimization Experiments

![Reaction Scheme](image)

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<sup>a</sup>Yields determined by 1H NMR analysis using internal standard. Diastereomeric ratio typically 10:1

#### Intermolecular Reaction - Control and Optimization Experiments

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<sup>a</sup>Yields determined by 1H NMR analysis using internal standard.
IV. Experimental Data for Intramolecular Aldehyde α-Alkylation

Standard Procedure: To an oven-dried 8 mL vial equipped with a teflon stir bar was added the appropriate aldehyde (0.3 mmol, 1 equiv.). A septum cap was affixed and the vial was purged with nitrogen followed by the addition of solvent (0.6 mL, 0.5 M). The cap was briefly removed to allow for the addition of powder catalysts – Ir[Fmppy]2(dbbbpy)PF6 (9 mg, 0.009 mmol, 0.03 equiv.) and the TFA salt of (2R,5R)-2-tBu-3-Me-5-(napth-1-yl-Me)imidazolidinone (25 mg, 0.06 mmol, 0.20 equiv.). After resealing the vial, (2,4,6)-triisopropylbenzenethiol (15 µL, 0.06 mmol, 0.20 equiv.) and distilled water (5.4 µL, 0.3 mmol, 1 equiv.) were added through the septum cap. The heterogeneous bright yellow solution was sparged with dried nitrogen for 15 min with gentle stirring during which the reaction became homogeneous (reactions were cooled to 0 °C for sparging when potentially volatile solvents were employed). The nitrogen line and vent needle were removed and the vial cap was double-sealed with parafilm and the reaction was cooled to the desired temperature. The stirred solution was irradiated with blue LED light in a water bath for 24 h. Upon reaction completion, the solution was placed directly on a silica column for purification. For determination of enantiomeric excess, the compound was subjected to immediate reduction at 0 °C using excess NaBH4 in CH2Cl2/MeOH. Non-sulfonamide-based substrates were converted to their corresponding napthoyl- or p-NO2Bz- ester derivatives for visualization purposes and are individually noted.

(3R,4S)-3-Isopropyl-1-tosylpiperidine-4-carbaldehyde (13). According to the general procedure using 4-methyl-N-(3-methylbut-2-en-1-yl)-N-(4-oxobutyl)benzenesulfonylamide. Purified by flash chromatography (2% Et2O/CH2Cl2) to provide the title compound (79 mg, 85% yield, 10:1 dr, 93% ee) as a colorless oil. Analytical data: [α]D21 -38.7 (c = 1.00, CHCl3); 1H NMR (500 MHz, CDCl3): δ 9.53 (d, J = 2.8 Hz, 1H), 7.62 (d, J = 8.3 Hz, 2H), 7.32 (d, J = 8.0 Hz, 2H), 3.33-3.29 (m, 1H), 3.24 (dd, J = 11.8, 2.8 Hz, 1H), 2.69-2.65 (m, 1H), 2.62-2.58 (m, 1H), 2.43 (s, 3H), 2.31-2.26 (m, 1H), 1.92-1.79 (m, 4H), 0.98 (d, J = 6.7 Hz, 3H), 0.90 (d, J = 6.7 Hz, 3H); 13C NMR (125 MHz, CDCl3): δ 203.4, 143.7, 132.9, 129.7, 127.6, 49.4, 45.6, 44.6, 40.7, 27.8, 23.8, 21.5, 20.8, 18.3; HRMS (ESI+) Calcd. for C16H23NO3S+H, 310.1471; Found, 310.1469; IR (thin film, cm−1) 2970, 2873, 1737, 1725, 1598, 1494, 1465, 1343, 1216, 1095, 1035, 938, 851, 814, 735, 656; TLC (60:40 hexanes:EtOAc): Rf = 0.58. HPLC analysis of the corresponding alcohol (AD, 20% iPrOH/hexane, 1.0 mL/min, 220 nm) indicates 93% ee: tR = 10.7, 13.9 min.
**tert-Butyl (3R,4S)-4-formyl-3-isopropylpiperidine-1-carboxylate (14).** Prepared according to the general procedure using tert-butyl (3-methylbut-2-en-1-yl)(4-oxobutyl)carbamate. Purified by flash chromatography (2% Et$_2$O/CH$_2$Cl$_2$) to provide the title compound (68 mg, 88% yield, >20:1 dr, 95% ee) as a colorless oil. Analytical data: [$\alpha$]$_D^{21}$ -13.9 (c = 1.00, CHCl$_3$); $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 9.60 (d, $J$ = 3.2 Hz, 1H), 3.82 (br s, 1H), 2.98 (br s, 1H), 2.85 (br s, 1H), 2.43 (br s, 1H), 1.76-1.62 (m, 4H), 1.46 (s, 9H), 0.99 (d, $J$ = 6.6 Hz, 3H), 0.92 (d, $J$ = 6.6 Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 203.9, 154.7, 79.7, 58.5, 50.7, 45.4, 44.9, 41.1, 28.4, 21.0, 18.0; HRMS (ESI$^+$) Calcd. for C$_{14}$H$_{25}$NO$_3$+H, 278.1727; Found, 278.1726; IR (thin film, cm$^{-1}$) 2964, 2878, 2712, 1722, 1688, 1422, 1365, 1276, 1235, 1160, 1096, 993, 931, 884, 766; TLC (60:40 hexanes:EtOAc): R$_f$ = 0.69. HPLC analysis of the corresponding 2-napthoyl ester (OD, 5% iPrOH/hexane, 1.0 mL/min, 220 nm) indicates 95% ee: $t_R$ = 10.6, 12.4 min.

**N-(3R,4S)-3-Isopropyltetrahydro-2H-pyran-4-carbaldehyde (15).** To an oven-dried 8 mL vial equipped with a teflon stir bar was added 4-((3-methylbut-2-en-1-yl)oxy)butanal (0.3 mmol, 1 equiv.). A septum cap was affixed and the vial was purged with nitrogen followed by the addition of solvent (0.6 mL, 0.5 M). The cap was briefly removed to allow for the addition of powder catalysts – Ir[Fmppy]$(_2$)(dtbbpy)PF$_6$ (9 mg, 0.009 mmol, 0.03 equiv.) and the TFA salt of (2R,5R)-2-tBu-3-Me-5-(napth-1-yl-Me)imidazolidinone (25 mg, 0.06 mmol, 0.20 equiv.). After resealing the vial, (2,4,6)triisopropylbenzenethiol (15 $\mu$L, 0.06 mmol, 0.20 equiv.) and distilled water (5.4 $\mu$L, 0.3 mmol, 1 equiv.) were added through the septum cap. The heterogeneous bright yellow solution was cooled to 0 °C and sparged with dried nitrogen for 15 minutes with gentle stirring during which the reaction became homogeneous. The nitrogen line and vent needle were removed and the vial cap was double-sealed with parafilm and the reaction was cooled to the desired temperature. The stirred solution was irradiated with blue LED light for 48h. Yield obtained by $^1$H NMR analysis using benzyl ether as an internal standard (product is highly volatile). Results: 65% yield, 10:1 dr, 94% ee as a colorless oil. Analytical data: [$\alpha$]$_D^{21}$ -57.5 (c = 1.00, CHCl$_3$); $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 9.60 (d, $J$ = 3.3 Hz, 1H), 3.94-3.86 (m, 2H), 3.42 (td, $J$ = 11.2, 2.8 Hz, 1H), 3.31 (t, $J$ = 10.0 Hz, 1H), 2.52-2.47 (m, 1H), 1.87-1.82 (m, 1H), 1.79-1.73 (m, 1H), 1.70-1.66 (m, 1H), 0.97 (d, $J$ = 6.9 Hz, 3H), 0.90 (d, $J$ = 6.9 Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 203.8, 67.5, 66.4, 50.1, 41.0, 28.0, 25.4, 20.9, 18.2; HRMS (ESI$^+$) Calcd. for C$_9$H$_{16}$O$_2$+Na, 179.1043; Found, 179.1046; IR (thin film, cm$^{-1}$) 2960, 2872, 2712, 1720, 1466, 1388, 137, 1278, 1246, 1182, 1130, 1084, 1010, 906, 840, 770; TLC (70:30 hexanes:EtOAc): R$_f$ = 0.57. HPLC analysis of the corresponding p-NO$_2$Bz ester (AS, 3% iPrOH/hexane, 1.0 mL/min, 220 nm) indicates 94% ee: $t_R$ = 15.0, 19.0 min.
(3R,4S)-3-Ethyl-1-tosylpiperidine-4-carbaldehyde (16). Prepared according to the general procedure using (E)-N-(but-2-en-1-yl)-4-methyl-N-(4-oxobutyl)benzenesulfonamide. Purified by flash chromatography (1% Et<sub>2</sub>O/CH<sub>2</sub>Cl<sub>2</sub>) to provide the title compound (55 mg, 62% yield, 3:1 dr, 88% ee) as a colorless oil. Analytical data: [α]<sub>D</sub><sup>21</sup> = -31.1 (c = 1.00, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 9.56 (d, <i>J</i> = 2.7 Hz, 1H), 7.63 (d, <i>J</i> = 8.2 Hz, 2H), 7.33 (d, <i>J</i> = 8.1 Hz, 2H), 3.48-3.45 (m, 2H), 2.59-2.54 (m, 1H), 2.44 (s, 3H), 2.30 (dd, <i>J</i> = 11.6, 9.0 Hz, 1H), 2.06-2.01 (m, 1H), 1.99-1.93 (m, 1H), 1.87-1.79 (m, 2H), 1.53-1.47 (m, 1H), 1.36-1.27 (m, 1H), 0.99 (t, <i>J</i> = 7.5 Hz, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 203.1, 143.7, 133.0, 129.7, 127.6, 52.0, 48.6, 44.8, 36.27, 24.4, 24.0, 21.5, 11.2; HRMS (ESI<sup>+</sup>) Calcd. for C<sub>15</sub>H<sub>21</sub>NO<sub>3</sub>S+H, 296.1353; Found, 296.1350; IR (thin film, cm<sup>-1</sup>) 2964, 2927, 2865, 2721, 1721, 1597, 1494, 1462, 1333, 1269, 1160, 1091, 1039, 928, 815, 735, 654; TLC (60:40 hexanes:EtOAc): R<sub>f</sub> = 0.54. HPLC analysis of the corresponding alcohol (AD, 20% iPrOH/hexane, 1.0 mL/min, 220 nm) indicates 88% ee: t<sub>R</sub> = 12.9, 17.3 min.

(3R,4S)-3-((1,3-Diphenyl-1H-pyrazol-4-yl)methyl)-1-tosylpiperidine-4-carbaldehyde (17). Prepared according to the general procedure using (E)-N-(3-(1,4-diphenyl-1H-pyrrol-3-yl)allyl)-4-methyl-N-(4-oxobutyl)benzenesulfonamide. Purified by flash chromatography (20-30% EtOAc/hexanes) to provide the title compound (68 mg, 77% yield, 3:1 dr, 90% ee) as a pale yellow oil. Analytical data: [α]<sub>D</sub><sup>21</sup> = -25.5 (c = 1.00, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 9.43 (d, <i>J</i> = 1.6 Hz, 1H), 7.98, (s, 1H), 7.78 (d, <i>J</i> = 7.7 Hz, 2H), 7.67 (d, <i>J</i> = 7.1 Hz, 2H), 7.49-7.45 (m, 6H), 7.41 (d, <i>J</i> = 7.4 Hz, 1H), 7.30-7.24 (m, 3H), 3.08-3.03 (m, 1H), 0.99 (t, <i>J</i> = 11.2 Hz, 1H), 2.89-2.83 (m, 2H), 2.64-2.60 (m, 1H), 2.40 (s, 3H), 2.31-2.35 (m, 2H), 2.17 (q, <i>J</i> = 5.6 Hz, 1H), 1.92-1.82 (m, 2H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 202.5, 151.8, 143.7, 139.8, 133.4, 132.6, 129.7, 129.4, 128.7, 128.0, 127.5, 126.3, 118.8, 117.2, 50.7, 47.9, 44.6, 35.1, 26.0, 22.8, 21.5; HRMS (ESI<sup>+</sup>) Calcd. for C<sub>29</sub>H<sub>32</sub>N<sub>3</sub>O<sub>3</sub>S+H, 500.2002; Found, 500.2012; IR (thin film, cm<sup>-1</sup>) 3059, 2927, 2852, 3721, 2255, 1722, 1598, 1551, 1503, 1449, 1334, 1265, 1161, 1090, 1064, 957, 909, 815, 757; TLC (70:30 hexanes:EtOAc): R<sub>f</sub> = 0.21. HPLC analysis of the corresponding alcohol (AS, 30% iPrOH/hexane, 1.0 mL/min, 220 nm) indicates 90% ee: t<sub>R</sub> = 12.4, 15.8 min.
**Di-tert-butyl (3R,4S)-4-formyl-3-isopropylcyclohexane-1,1-dicarboxylate (18).** To an oven-dried 8 mL vial equipped with a teflon stir bar was added di-tert-butyl 2-(3-methylbut-2-en-1-yl)-2-(4-oxobutyl)malonate (0.3 mmol, 1.0 equiv.). A septum cap was affixed, and the vial was purged with nitrogen followed by the addition of solvent (0.6 mL, 0.5 M). The cap was briefly removed to allow for the addition of powder catalysts – Ir[Fmppy]$_2$(dtbbpy)PF$_6$ (9 mg, 0.009 mmol, 0.03 equiv.) and the TFA salt of (2R,5R)-2-tBu-3-Me-5-(napth-1-yl-Me)imidazolidinone (38 mg, 0.09 mmol, 0.30 equiv.). After resealing the vial, (2,4,6)-triisopropylbenzenethiol (15 µL, 0.06 mmol, 0.20 equiv.) and distilled water (5.4 µL, 0.3 mmol, 1 equiv.) were added through the septum cap. The heterogeneous bright yellow solution was cooled to 0 °C and sparged with dried nitrogen for 15 minutes with gentle stirring during which the reaction became homogeneous. The nitrogen line and vent needle were removed, the vial cap was double-sealed with parafilm, and the reaction was cooled to the desired temperature. The stirred solution was irradiated with blue LED light for 48h. Purified by flash chromatography (5% EtOAc/hexanes) to provide the title compound (81 mg, 76% yield, >20:1 dr, 91% ee) as a colorless oil. Analytical data: [α]$_D$:$^{21}$31.9 (c = 1.00, CHCl$_3$); $^1$H NMR (500 MHz, CDCl$_3$): δ 9.47 (d, J = 4.6 Hz, 1H), 2.37 (dq, J = 13.3, 3.4 Hz, 1H), 2.23 (dt, J = 13.5, 2.5 Hz, 1H), 2.20–2.13 (m, 1H), 1.76–1.51 (m, 6H), 1.47 (s, 9H), 1.44 (s, 9H), 1.37 (t, J = 13.5 Hz, 1H), 0.96 (d, J = 6.7 Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$): δ 204.9, 171.5, 169.9, 81.6, 81.1, 55.3, 52.5, 39.0, 29.6, 29.4, 29.0, 27.9, 27.8, 23.1, 20.7, 15.8; HRMS (ESI$^+$) Calcd. for C$_{18}$H$_{35}$O$_5$Na, 377.2274; Found, 377.2275; IR (thin film, cm$^{-1}$) 2969, 2934, 2874, 1722, 1453, 1367, 1254, 1162, 1131, 1056, 922, 847, 738; TLC (90:10 hexanes:EtOAc): R$_f$ = 0.25. HPLC analysis of the corresponding 2-napthoyl ester (AD, 2% iPrOH/hexane, 1.0 mL/min, 220 nm) indicates 91% ee: t$_R$ = 5.9, 7.8 min.

**1S,2R)-2-Isopropylcyclohexane-1-carbaldehyde (19).** To an oven-dried 8 mL vial equipped with a teflon stir bar was added 8-methylnon-7-enal (0.3 mmol, 1 equiv.). A septum cap was affixed and the vial was purged with nitrogen followed by the addition of solvent (0.6 mL, 0.5 M). The cap was briefly removed to allow for the addition of powder catalysts – Ir[Fmppy]$_2$(dtbbpy)PF$_6$ (9 mg, 0.009 mmol, 0.03 equiv.) and the TFA salt of (2R,5R)-2-tBu-3-Me-5-(napth-1-yl-Me)imidazolidinone (38 mg, 0.09 mmol, 0.30 equiv.). After resealing the vial, (2,4,6)-triisopropylbenzenethiol (15 µL, 0.06 mmol, 0.20 equiv) and distilled water (5.4 µL, 0.3 mmol, 1 equiv.) were added through the septum cap. The heterogeneous bright yellow solution was cooled to 0 °C and sparged with dried nitrogen for 15 minutes with gentle stirring during which the reaction became homogeneous. The nitrogen line and vent needle were removed, the vial cap was double-sealed with parafilm, and the reaction was cooled to the desired temperature. The stirred solution was irradiated with blue LED light for 48h. Yield obtained by $^1$H NMR
analysis using benzyl ether as an internal standard (product is highly volatile). Results: 64% yield, >20:1 dr, 95% ee as a colorless oil. Analytical data: $[\alpha]_D^{21} -12.97$ (c = 1.00, CHCl$_3$); $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 9.52 (d, $J = 4.5$ Hz, 1H), 2.23-2.17 (m, 1H), 1.77 (d, $J = 7.3$, 9.0 Hz, 2H), 1.71-1.65 (m, 2H), 1.62-1.58 (m, 2H), 1.39 (q, $J = 13.5$ Hz, 1H), 1.71-1.65 (m, 2H), 1.30-1.19 (m, 2H), 1.06 (q, $J = 6.8$ Hz, 3H), 0.81 (d, $J = 6.9$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 205.7, 53.4, 42.7, 29.7, 26.4, 25.4, 24.8, 24.0, 21.0, 16.6; HRMS (ESI$^+$) Calcd. for C$_{10}$H$_{18}$O+H, 155.1430; Found, 155.1433; IR (thin film, cm$^{-1}$) 2929, 2856, 2700, 1720, 1464, 1448, 1387, 1369, 1227, 1092, 1043, 989, 925, 694; TLC (90:10 hexanes:EtOAc): R$_f$ = 0.55. HPLC analysis of the corresponding 2-naphthoyl ester (OJ, 2% iPrOH/hexane, 1.0 mL/min, 220 nm) indicates 94% ee: $t_R$ = 6.4, 8.0 min.

(3R,4S)-3-Cyclopentyl-1-tosylpiperidine-4-carbaldehyde (20). Prepared according to the general procedure using N-(2-cyclopentylideneethyl)-4-methyl-N-(4-oxobutyl)benzenesulfonamide. Purified by flash chromatography (100% CH$_2$Cl$_2$) to provide the title compound (87 mg, 86% yield, 6:1 dr, 92% ee) as a colorless oil. Analytical data: $[\alpha]_D^{21} -24.9$ (c = 1.00, CHCl$_3$); $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 9.56 (d, $J = 1.6$ Hz, 1H), 7.60 (d, $J = 8.2$ Hz, 2H), 7.31 (d, $J = 8.0$ Hz, 2H), 3.11-3.06 (m, 1H), 2.99 (dd, $J = 11.9$, 5.7 Hz, 1H), 2.87-2.83 (m, 2H), 2.43 (s, 3H), 2.33 (dd, $J = 10.0$, 5.0 Hz, 1H), 2.11-2.02 (m, 1H), 1.99-1.95 (m, 3H), 1.93-1.86 (m, 1H), 1.76-1.54 (m, 5H), 1.17-1.07 (m, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 203.6, 143.6, 132.9, 129.7, 127.5, 50.2, 47.5, 44.3, 40.7, 39.5, 31.1, 30.4, 25.1, 25.0, 22.5, 21.5; HRMS (ESI$^+$) Calcd. for C$_{18}$H$_{25}$NO$_3$S+H, 336.1628; Found, 336.1625; IR (thin film, cm$^{-1}$) 2921, 2854, 1721, 1597, 1461, 1336, 1267, 1090, 1035, 934, 815, 734, 661; TLC (60:40 hexanes:EtOAc): R$_f$ = 0.67. HPLC analysis of the aldehyde (OD, 10% iPrOH/hexane, 1.0 mL/min, 220 nm) indicates 92% ee: $t_R$ = 13.1, 14.7 min.

(3R,4S)-1-Tosyl-3-(2-(trimethylsilyl)ethyl)piperidine-4-carbaldehyde (21). Prepared according to the general procedure using (E)-4-methyl-N-(4-oxobutyl)-N-(4-(trimethylsilyl)but-2-en-1-yl)benzenesulfonamide. Purified by flash chromatography (1% Et$_2$O/CH$_2$Cl$_2$) to provide the title compound (94 mg, 82% yield, 5:1 dr, 90% ee) as a colorless oil. Analytical data: $[\alpha]_D^{21} -42.1$ (c = 1.00, CHCl$_3$); $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 9.56 (d, $J = 2.7$ Hz, 1H), 7.63 (d, $J = 8.2$ Hz, 2H), 7.33 (d, $J = 8.1$ Hz, 2H), 3.51 (dd, $J = 11.7$, 3.6 Hz, 1H), 3.47-3.42 (m, 1H), 2.60-2.55

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(m, 1H), 2.44 (s, 3H), 2.32 (dd, J = 11.5, 9.0 Hz, 1H), 2.08-2.03 (m, 1H), 2.00-1.94 (m, 1H), 1.84-1.80 (m, 2H), 1.48-1.40 (m, 1H), 1.30-1.22 (m, 1H), 0.57 (td, J = 13.6, 4.5 Hz, 1H), 0.39 (td, J = 13.6, 4.5 Hz, 1H), -0.03 (s, 9H); 13C NMR (125 MHz, CDCl3): δ 203.2, 143.6, 133.1, 129.7, 127.6, 51.9, 48.6, 44.8, 37.6, 25.8, 24.0, 21.5, 13.6, 1.9; HRMS (ESI+) Calcd. for C18H29NO3SSi+H, 368.1710; Found, 368.1717; IR (thin film, cm⁻¹) 2951, 1722, 1597, 1443, 1335, 1247, 1161, 1090, 931, 860, 832, 738, 655; TLC (95:5 CH2Cl2:Et2O): Rf = 0.65. HPLC analysis of the corresponding alcohol (OD, 8% iPrOH/hexane, 1.0 mL/min, 220 nm) indicates 90% ee: tR = 10.4, 11.8 min.

(3R,4S)-3-(6-Methylhept-5-en-2-yl)-1-tosylpiperidine-4-carbaldehyde (22). Prepared according to the general procedure using (E)-N-(3,7-dimethylocta-2,6-dien-1-yl)-4-methyl-N-(4-oxobutyl)benzenesulfonylamide. Purified by flash chromatography (1% Et2O/CH2Cl2) to provide the title compound (91 mg, 81% yield, 11:11:1:1 dr, 94% ee) as a colorless oil. Analytical data: [α]D²¹ = -43.4 (c = 1.00, CHCl3); ¹H NMR (500 MHz, CDCl3): δ 9.52 (d, J = 3.3 Hz, 1H), 9.49 (d, J = 3.3 Hz, 1H), 7.62 (d, J = 8.0 Hz, 4H), 7.32 (d, J = 8.1 Hz, 4H), 5.07-5.01 (m, 2H), 3.57 (m, 2H), 3.44 (d, J = 11.7 Hz, 2H), 2.50-2.45 (m, 2H), 2.43 (s, 6H), 2.40-2.34 (m, 2H), 2.30-2.22 (m, 2H), 2.04-1.94 (m, 5H), 1.88-1.75 (m, 5H), 1.68 (d, J = 7.5 Hz 6H), 1.65-1.61 (m, 2H), 1.59 (d, J = 9.6 Hz 6H), 1.43-1.35 (m, 2H), 1.30-1.23 (m, 1H), 1.04-0.98 (m, 1H), 0.96 (d, J = 6.9 Hz, 3H), 0.83 (d, J = 6.9 Hz, 3H); ¹³C NMR (125 MHz, CDCl3): δ 203.2, 143.7, 133.0, 132.0, 129.7, 127.6, 123.8, 49.7, 49.4, 46.1, 45.2, 44.8, 44.8, 40.8, 39.3, 34.8, 32.9, 32.5, 25.8, 25.6, 24.5, 24.4, 21.5, 17.7, 17.3, 14.7; HRMS (ESI+) Calcd. for C21H31NO3S+H, 378.2097; Found, 378.2098; IR (thin film, cm⁻¹) 2970, 2923, 2856, 1727, 1597, 1444, 1351, 1217, 1162, 1092, 1039, 927, 815, 751, 712, 658; TLC (60:40 hexanes:EtOAc): Rf = 0.65. HPLC analysis of the corresponding alcohol (AD, 20% iPrOH/hexane, 1.0 mL/min, 220 nm) indicates 94% ee: tR = 8.1, 8.9, 12.3, 16.7 min.

(3R,4S)-3-isopropyl-3-methyl-1-tosylpiperidine-4-carbaldehyde (23). To an oven-dried 8 mL vial equipped with a teflon stir bar was added N-(2,3-dimethylbut-2-en-1-yl)-4-methyl-N-(4-oxobutyl)benzenesulfonylamide (0.3 mmol, 1 equiv.). A septum cap was affixed, and the vial was purged with nitrogen followed by the addition of solvent (0.6 mL, 0.5 M). The cap was briefly removed to allow for the addition of powder catalysts – Ir[Fmppy]2(dtbbpy)PF6 (9 mg, 0.009 mmol, 0.03 equiv.) and the TFA salt of (R)-2-(tert-butyl)-3-methylimidazolidin-4-one (16 mg,
0.06 mmol, 0.20 equiv.). After resealing the vial, (2,4,6)-triisopropylbenzenethiol (15 µL, 0.06 mmol, 0.20 equiv.) and distilled water (5.4 µL, 0.3 mmol, 1 equiv.) were added through the septum cap. The heterogeneous bright yellow solution was cooled to 0 °C and sparged with dried nitrogen for 15 minutes with gentle stirring during which the reaction became homogeneous. The nitrogen line and vent needle were removed, the vial cap was double-sealed with parafilm, and the reaction was cooled to the desired temperature. The stirred solution was irradiated with blue LED light for 24h. Yield obtained by 1H NMR analysis using benzyl ether as an internal standard.

Results: 60% yield, >20:1 dr, 50% ee. Analytical data: 1H NMR (500 MHz, CDCl3): δ 9.74 (d, J = 2.5 Hz, 1H), 7.59 (d, J = 8.2 Hz, 2H), 7.31 (d, J = 8.1 Hz, 2H), 3.48-3.46 (m, 1H), 3.01 (d, J = 11.6 Hz, 1H), 2.50 (t, J = 10.5 Hz, 1H), 2.45 (d, J = 11.6 Hz, 1H), 2.42 (s, 3H), 2.37 (ddd, J = 9.7, 4.3, 2.5 Hz, 1H), 2.02-1.93 (m, 2H), 1.74-1.69 (m, 1H), 1.10 (s, 3H), 0.93 (d, J = 4.4 Hz, 3H), 0.91 (d, J = 4.5 Hz, 3H); 13C NMR (125 MHz, CDCl3): δ 204.0, 143.5, 133.0, 129.6, 127.4, 51.9, 51.5, 44.8, 38.7, 33.1, 21.5, 21.4, 17.1, 17.0, 16.6; HRMS (ESI+) Calcd. for C17H25NO3S+H, 324.1628; Found, 324.1633; IR (thin film, cm⁻¹) 2967, 2879, 1715, 1598, 1466, 1395, 1335, 1268, 1160, 1092, 1007, 942, 915, 815, 733, 655; TLC (98:2 DCM:Et2O): Rf = 0.55; HPLC analysis of the corresponding alcohol (AD, 20% iPrOH/hexane, 1.0 mL/min, 270 nm) indicates 50% ee: tR = 9.9, 11.3 min.

(3R,4R)-4-Isopropyl-1-tosylpyrrolidine-3-carbaldehyde (24). Prepared according to the general procedure using 4-methyl-N-(3-methylbut-2-en-1-yl)-N-(3-oxopropyl)benzene-sulfonamide. Purified by flash chromatography (1% Et2O/CH2Cl2) to provide the title compound (81 mg, 91% yield, >20:1 dr, 84% ee) as a colorless oil. Analytical data: [α]D²¹l -5.34 (c = 1.00, CHCl3); 1H NMR (500 MHz, CDCl3): δ 9.52 (d, J = 2.6 Hz, 1H), 7.71 (d, J = 8.2 Hz, 2H), 7.35 (d, J = 8.0 Hz, 2H), 3.51 (dd, J = 10.4, 6.1 Hz, 1H), 3.43 (dd, J = 9.8, 7.9 Hz, 1H), 3.31 (dd, J = 10.4, 8.6 Hz, 1H), 2.89 (dd, J = 9.8, 7.9 Hz, 1H), 2.73-2.68 (m, 1H), 2.45 (s, 3H), 2.22-2.15 (m, 1H), 1.61-1.54 (m, 2H), 0.88 (d, J = 2.6 Hz, 3H), 0.87 (d, J = 2.6 Hz, 3H); 13C NMR (125 MHz, CDCl3): δ 199.8, 143.9, 132.5, 129.8, 127.8, 53.6, 51.3, 47.5, 46.5, 31.0, 21.6, 20.9, 20.4; HRMS (ESI+) Calcd. for C15H21NO3S+H, 296.1315; Found, 296.1311; IR (thin film, cm⁻¹) 3285, 2963, 1724, 1598, 1448, 1329, 1093, 1049, 814, 769, 708, 663; TLC (95:5 CH2Cl2:Et2O): Rf = 0.65. HPLC analysis of the corresponding alcohol (OD, 25% iPrOH/hexane, 1.0 mL/min, 220 nm) indicates 84% ee: tR = 5.4, 6.2 min.
(4R,6R)-6-Methyl-1-tosylazepane-4-carbaldehyde (25). Prepared according to the general procedure using 4-methyl-N-(2-methylallyl)-N-(4-oxobutyl)benzenesulfonamide. Purified by flash chromatography (1% Et₂O/CH₂Cl₂) to provide the title compound (79 mg, 89% yield, 7:1 dr, 88% ee) as a colorless oil. Analytical data: [α]D²¹ -25.0 (c = 1.00, CHCl₃); ¹H NMR (500 MHz, CDCl₃): δ 9.63 (s, 1H), 7.67 (d, J = 8.2 Hz, 2H), 7.31 (d, J = 8.1 Hz, 2H), 3.58-3.52 (m, 2H), 3.25-3.10 (m, 2H), 2.61-2.53 (m, 2H), 2.42 (s, 3H), 2.37-2.31 (m, 1H), 2.15 (ddd, J = 14.2, 3.5, 1.8 Hz, 1H), 2.10-2.04 (m, 1H), 1.98-1.88 (m, 1H), 1.61-1.53 (m, 1H), 1.14-1.06 (m, 1H), 0.98 (d, J = 6.8 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 202.5, 143.2, 136.2, 129.7, 127.0, 55.0, 49.5, 46.6, 35.3, 35.0, 27.7, 21.0, 19.5; HRMS (ESI⁺) Calcd. for C₁₅H₂₁NO₃S+H, 296.1315; Found, 296.1315; IR (thin film, cm⁻¹) 2970, 1734, 1598, 1494, 1453, 1368, 1228, 1216, 1154, 1091, 983, 905, 815, 735, 655; TLC (60:40 hexanes:EtOAc): Rf = 0.55. SFC analysis of the corresponding p-NO₂Bz ester (OJ, 15% iPrOH/CO₂, 3.0 mL/min, 100 bar) indicates 88% ee: t_R = 12.8, 14.2 min.

di-tert-butyl 5-formyl-3-methylcycloheptane-1,1-dicarboxylate (26). Prepared according to the general procedure using di-tert-butyl 2-(2-methylallyl)-2-(4-oxobutyl)malonate with 10 equiv. H₂O, at 10 °C. Purified by flash chromatography (10-20% EtOAc/hexanes) to provide the title compound (72 mg, 71% yield, 9:1 dr, 84% ee) as a colorless oil. Analytical data: [α]D²¹ +12.6 (c = 1.00, CHCl₃); ¹H NMR (500 MHz, CDCl₃): δ 9.61 (s, 1H), 9.58 (s, 1H), 2.47-2.42 (m, 1H), 2.35-2.28 (m, 1H), 2.26-2.20 (m, 2H), 2.14 (dd, J = 14.5 Hz, 6.5 Hz 2H), 2.04-1.91 (m, 6H), 2.04-1.91 (m, 6H), 1.88-1.70 (m, 4H), 1.44 (s, 9H), 1.43 (s, 9H), 1.04 (d, J = 6.8 Hz, 3H), 1.01 (d, J = 6.8 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 204.4, 203.7, 171.9, 171.7, 170.8, 81.3, 81.2, 81.0, 80.9, 58.2, 57.6, 53.1, 49.8, 41.6, 40.9, 37.7, 35.1, 32.2, 30.9, 29.4, 27.9, 27.8, 27.1, 24.9, 24.5, 22.9, 22.2; HRMS (ESI⁺) Calcd. for C₁₉H₃₅O₄+H, 363.2142; Found, 363.2142; IR (thin film, cm⁻¹) 2975, 2932, 1720, 1456, 1367, 1250, 1138, 1058, 848, 735, 704; TLC (60:40 hexanes:EtOAc): Rf = 0.68. SFC analysis of the corresponding 2-napthoyl ester (AD, 4% EtOH/CO₂, 3.0 mL/min, 100 bar) indicates 84% ee: t_R = 7.5, 9.4 min.
V. Experimental Data for Intermolecular Aldehyde α-Alkylation with Styrenes

**Standard Procedure:** To an oven-dried 8 mL vial equipped with a teflon stir bar was added Ir(dmppy)$_2$(dtbbpy)PF$_6$ (4.9 mg, 5 µmol, 0.01 equiv.), tritertbutylthiophenol (13.9 mg, 0.05 mmol, 0.1 equiv.), α,α-bis[3,5-bistrifluoromethyl]phenyl-2-pyrrolidinemethanol trimethylsilyl ether (59.8 mg, 0.1 mmol, 0.20 equiv.), and aldehyde (if solid, 0.5 mmol, 1.0 equiv.). The vial was then sealed and cooled to 0 °C under nitrogen. Dimethoxyethane (1.0 mL, 0.5 M), olefin (1.0 mmol, 2 equiv.), aldehyde (if liquid, 0.5 mmol, 1.0 equiv.), and distilled water (27 µL, 1.5 mmol, 3 equiv.) were added through the septum cap. The heterogeneous solution was sparged with dried nitrogen for 15 minutes with stirring during which the reaction became homogeneous. The vent needle was then removed, the vial cap was double-sealed with parafilm, and the reaction was placed in a 10 °C bath. The stirred solution was irradiated with blue LED light for 24 hrs. Upon reaction completion, the solution was placed directly on a silica column for purification. For enantioselectivity determination, a sample of the purified compound was subjected to immediate reduction at 0 °C using excess NaBH$_4$ in Et$_2$O/MeOH (10:1, 0.1 M). The reduction was stirred at 0 °C for 2 hrs, and then the excess NaBH$_4$ was quenched with addition of 0.1 M aqueous citric acid. After separation of layers, the aqueous layer was extracted with CH$_2$Cl$_2$ (2x10 mL). The combined organic layers were then dried over sodium sulfate, filtered, and concentrated under reduced pressure.

(R)-2-Phenethylpentanal (30). Prepared according to the general procedure. Purified by flash chromatography (2% Et$_2$O/hexanes) using Davisil to provide the title compound (94 mg, 81% yield, 90% ee) as a colorless oil. Analytical data: [α]$_D^{22}$+2.0 (c = 1.00, CHCl$_3$); $^1$H NMR (500 MHz, CDCl$_3$) δ 9.60 (d, $J$ = 2.9 Hz, 1H), 7.29 (t, $J$ = 7.5 Hz, 2H), 7.21–7.17 (m, 3H), 2.69–2.55 (m, 2H), 2.30 (dqd, $J$ = 10.8, 5.4, 2.9 Hz, 1H), 1.98 (dddd, $J$ = 14.2, 9.5, 8.2, 6.1 Hz, 1H), 1.75 (ddddd, $J$ = 14.0, 9.8, 6.5, 5.4 Hz, 1H), 1.70–1.63 (m, 1H), 1.54–1.45 (m, 1H), 1.32–1.23 (m, 9H), 0.88 (t, $J$ = 6.9 Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 205.4, 141.6, 128.6, 128.5, 126.2, 51.5, 33.4, 31.8, 30.7, 29.5, 29.0, 27.1, 22.7, 14.2; HRMS (ESI$^+$) Calcd. for C$_{15}$H$_{22}$+H (M–CHO+H), 202.1722; Found, 202.1720; IR (thin film, cm$^{-1}$) 2927, 2856, 1724, 1496, 1455, 1180, 748; HPLC analysis of the alcohol (OJ, 1% IPA/Hexanes, 1.0 mL/min) indicates 90% ee: $t_R$ = 10.3 (minor), 11.3 (major) min.

(R)-2-Methyl-4-phenylbutanal (31). Prepared according to the general procedure. Purified by flash chromatography (2% Et$_2$O/hexanes) using Davisil to provide the title compound (58 mg, 72% yield, 83% ee) as a colorless oil. Analytical data: [α]$_D^{22}$–8.7 (c = 1.00, CHCl$_3$); $^1$H NMR
(S)-2-Isopropyl-4-phenylbutan-1-ol (32). Prepared according to the general procedure with 0.25 equiv. of \( \alpha, \alpha\)-bis[3,5-bistri fluoromethyl]phenyl]-2-pyrrolidinemethanol methyl ether (67.4 mg), 0.5 equiv. of 1-butyl-3-methyl-1H-imidazol-3-ium trifluoromethanesulfonate (55.6 µL), 0.02 equiv. of Ir[dmpy]2(dtbbpy)PF6 (9.7 mg), and 4 equiv. water (36 µL) in dimethoxyethane (1.67 mL, 0.3M) for 48 hrs. Purified by flash chromatography (10% EtOAc/hexanes) after reduction to the corresponding alcohol to provide the title compound (69 mg, 72% yield, 90% ee) as a colorless oil. Analytical data: \( [\alpha]_D^{22} \) = −12.6 (c = 1.00, CHCl3); \(^1\)H NMR (500 MHz, CDCl3) \( \delta \) 7.28 (t, \( J = 7.5 \) Hz, 2H), 7.22–7.16 (m, 3H), 3.70–3.62 (m, 2H), 2.70 (ddd, \( J = 13.7, 10.5, 5.8 \) Hz, 1H), 2.60 (ddd, \( J = 13.7, 10.3, 6.2 \) Hz, 1H), 1.86 (ddd, \( J = 13.8, 6.9, 4.9 \) Hz, 1H), 1.73–1.63 (m, 1H), 1.63–1.53 (m, 1H), 1.43–1.36 (m, 1H), 0.91 (dd, \( J = 6.9, 3.7 \) Hz, 3H); \(^{13}\)C NMR (125 MHz, CDCl3) \( \delta \) 142.9, 128.5, 125.9, 63.8, 46.3, 34.3, 30.0, 28.1, 19.9, 19.4; HRMS (EI) Calcd. for C13H20O, 192.1509; Found, 192.1509; IR (thin film, cm\(^{-1}\)) 3340, 2956, 2871, 1496, 1454, 1386, 1368, 1279, 1045, 1025, 747; HPLC analysis of the alcohol (AS, 1% IPA/Hexanes, 0.5 mL/min) indicates 90% ee: \( t_R = 24.7 \) (minor), 26.0 (major) min.

(R)-6-Chloro-2-phenethylhexanal (33). Prepared according to the general procedure. Purified by flash chromatography (2% EtOAc/hexanes) using Davisil to provide the title compound (110 mg, 92% yield, 90% ee) as a colorless oil. Analytical data: \( [\alpha]_D^{22} \) = −7.4 (c = 1.00, CHCl3); \(^1\)H NMR (500 MHz, CDCl3) \( \delta \) 9.61 (d, \( J = 2.7 \) Hz, 1H), 7.29 (t, \( J = 7.5 \) Hz, 2H), 7.23–7.16 (m, 3H), 3.52 (t, \( J = 6.6 \) Hz, 2H), 2.70–2.56 (m, 2H), 2.32 (dq, \( J = 10.7, 5.3, 2.7 \) Hz, 1H), 2.06–1.95 (m, 1H), 1.77 (ddd, \( J = 10.5, 9.3, 6.5 \) Hz, 3H), 1.74–1.68 (m, 1H), 1.53–1.41 (m, 3H); \(^{13}\)C NMR (125 MHz, CDCl3) \( \delta \) 204.8, 141.4, 128.7, 128.5, 126.3, 51.2, 44.8, 33.3, 32.6, 30.6, 28.1, 24.4; HRMS (ESI) Calcd. for C14H17Cl+H (M–H2O+H), 220.1019; Found, 220.1016; IR (thin film, cm\(^{-1}\)) 3027, 2932, 2860, 1721, 1496, 1454, 1279, 1176, 1137, 906, 844, 748, 699, 681; HPLC analysis of the alcohol (OD, 3% IPA/Hexanes, 1.0 mL/min) indicates 90% ee: \( t_R = 25.7 \) (minor), 28.8 (major) min.
(R)-Ethyl 5-(hydroxymethyl)-7-phenylheptanoate (34). Prepared according to the general procedure in dimethoxyethane (1.25 mL, 0.4M). Purified by flash chromatography after reduction to the corresponding alcohol (10% EtOAc/hexanes) to provide the title compound (96 mg, 73% yield, 90% ee) as a colorless oil. Analytical data: $[\alpha]_D^{22} = -2.6$ (c = 1.00, CHCl$_3$); $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.21 (d, $J = 8.0$ Hz, 2H), 7.14–7.08 (m, 3H), 4.06 (q, $J = 7.1$ Hz, 1H), 3.59–3.50 (m, 1H), 2.57 (t, $J = 8.0$ Hz, 1H), 2.24 (t, $J = 7.3$ Hz, 1H), 1.66–1.47 (m, 2H), 1.40–1.28 (m, 1H), 1.19 (t, $J = 7.1$ Hz, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 174.0, 142.6, 128.5, 125.9, 65.2, 60.5, 39.9, 34.6, 33.3, 32.8, 30.3, 22.0, 14.4; HRMS (ESI$^+$) Calcd. for C$_{16}$H$_{24}$O$_3$+H, 264.1725; Found, 264.1718; IR (thin film, cm$^{-1}$) 3424, 2927, 2863, 1731, 1454, 1372, 1279, 1176, 1097, 1031, 746; HPLC analysis of the alcohol (OD, 3% IPA/Hexanes, 1.0 mL/min) indicates 90% ee: $t_R = 30.7$ (minor), 33.7 (major) min.

(S)-Benzyl (2-(hydroxymethyl)-4-phenylbutyl)carbamate (35). Prepared according to the general procedure with aldehyde (0.32 mmol), 2 equiv. water (11.5 µL), 0.02 equiv. Ir(ppy)$_2$(dtbbpy)PF$_6$ (5.9 mg), 0.25 equiv. $\alpha,\alpha$-bis[3,5-bistrifluoromethyl]phenyl]-2-pyrrolidinemethanol trimethylsilyl ether (47.8 mg), and 2 equiv. 1-butyl-3-methyl-1H-imidazol-3-ium tetrafluoroborate (120 µL) in dimethoxyethane (1.07 mL, 0.3M). Purified by flash chromatography (25% EtOAc/hexanes) after reduction to the corresponding alcohol to provide the title compound (60 mg, 60% yield, 90% ee) as a colorless oil. Analytical data: $[\alpha]_D^{22} = +8.8$ (c = 0.93, CHCl$_3$); $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.40–7.31 (m, 5H), 7.30–7.26 (m, 2H), 7.18 (dd, $J = 10.1$, 7.9 Hz, 3H), 5.11 (s, 2H), 5.02 (s, 1H), 3.65 (dd, $J = 11.6$, 3.0 Hz, 1H), 3.49 (dd, $J = 11.6$, 5.9 Hz, 1H), 3.38 (dd, $J = 14.3$, 6.4, 3.6 Hz, 1H), 3.28–3.20 (m, 1H), 2.74–2.60 (m, 2H), 1.71–1.49 (m, 4H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 157.9, 142.0, 136.4, 128.7, 128.6, 128.5, 128.4, 128.3, 126.1, 67.2, 62.6, 41.7, 40.9, 33.4, 30.4; HRMS (ESI$^+$) Calcd. for C$_{19}$H$_{23}$NO$_3$+H, 313.1678; Found, 313.1674; IR (thin film, cm$^{-1}$) 3353, 3028, 2931, 1693, 1520, 1497, 1454, 1250, 1138, 1029, 980, 741; HPLC analysis of the alcohol (OD, 20% IPA/Hexanes, 1.0 mL/min) indicates 90% ee: $t_R = 14.7$ (major), 16.4 (minor) min.
(R)-2-(4-Methoxyphenethyl)octanal (36). Prepared according to the general procedure. Purified by flash chromatography (2% Et₂O/hexanes) using Davisil to provide the title compound (123 mg, 94% yield, 93% ee) as a colorless oil. Analytical data: $[\alpha]_D^{22} -1.5 (c = 1.00, \text{CHCl}_3)$; $^1$H NMR (500 MHz, CDCl₃) δ 9.58 (d, $J = 2.9$ Hz, 1H), 7.09 (d, $J = 8.6$ Hz, 2H), 6.83 (d, $J = 8.6$ Hz, 2H), 3.79 (s, 3H), 2.62–2.50 (m, 2H), 2.28 (dqd, $J = 10.9$, 5.4, 3.0 Hz, 1H), 1.98–1.89 (m, 1H), 1.75–1.62 (m, 2H), 1.52–1.44 (m, 1H), 1.27 (s, 8H), 0.87 (t, $J = 6.9$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl₃) δ 205.5, 158.1, 133.7, 129.4, 114.0, 55.4, 51.4, 32.5, 31.8, 30.7, 29.5, 29.0, 27.1, 22.7, 14.2; HRMS (ESI⁺) Calcd. for C₁₇H₂₆O₂⁺Na, 262.1933; Found, 262.1931; IR (thin film, cm⁻¹) 2928, 2856, 1723, 1511, 1461, 1277, 1244, 1175, 1136, 1036, 822, 764, 750; HPLC analysis of the corresponding alcohol (OD, 3% IPA/Hexanes, 1.0 mL/min) indicates 93% ee: $t_R$ = 16.4 (minor), 17.4 (major) min.

(R)-2-(4-Fluorophenethyl)octanal (37). Prepared according to the general procedure. Purified by flash chromatography (2% Et₂O/hexanes) using Davisil to provide the title compound (104 mg, 83% yield, 89% ee) as a colorless oil. Analytical data: $[\alpha]_D^{22} +7.3 (c = 1.00, \text{CHCl}_3)$; $^1$H NMR (500 MHz, CDCl₃) δ 9.59 (d, $J = 2.8$ Hz, 1H), 7.15–7.09 (m, 2H), 6.97 (t, $J = 8.7$ Hz, 2H), 2.65–2.51 (m, 2H), 2.27 (dqd, $J = 10.8$, 5.4, 2.9 Hz, 1H), 1.99–1.90 (m, 1H), 1.75–1.62 (m, 2H), 1.52–1.44 (m, 1H), 1.30–1.23 (m, 8H), 0.88 (t, $J = 6.9$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl₃) δ 205.2, 162.5, 137.2 (d, $J = 3.2$ Hz), 129.9 (d, $J = 7.8$ Hz), 115.3 (d, $J = 21.1$ Hz), 51.3, 32.6, 31.7, 30.7, 29.5, 29.1, 27.1, 22.7, 14.2; HRMS (ESI⁺) Calcd. for C₁₆H₂₂F⁺H (M–H₂O+H), 232.1627; Found, 232.1629; IR (thin film, cm⁻¹) 2927, 2857, 1723, 1509, 1277, 1221, 1157, 1136, 1036, 824, 764, 750; HPLC analysis of the corresponding alcohol (OD, 1% IPA/Hexanes, 1.0 mL/min) indicates 89% ee: $t_R$ = 12.5 (minor), 17.5 (major) min.

(R)-2-(4-(Trifluoromethyl)phenethyl)octanal (38). Prepared according to the general procedure. Purified by flash chromatography (2% Et₂O/hexanes) using Davisil to provide the title compound (75 mg, 50% yield, 92% ee) as a colorless oil. Analytical data: $[\alpha]_D^{22} +7.2 (c = 1.00, \text{CHCl}_3)$; $^1$H NMR (500 MHz, CDCl₃) δ 9.61 (d, $J = 2.7$ Hz, 1H), 7.54 (d, $J = 8.1$ Hz, 2H), 7.29 (d, $J = 8.0$ Hz, 2H), 2.75–2.59 (m, 2H), 2.29 (dqd, $J = 10.7$, 5.4, 2.8 Hz, 1H), 2.03–1.93 (m,
1H), 1.78–1.71 (m, 1H), 1.71–1.64 (m, 1H), 1.54–1.45 (m, 1H), 0.87 (t, $J = 6.9$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 205.0, 145.8, 128.8, 128.6 (q, $J = 32.3$ Hz), 125.5 (q, $J = 3.8$ Hz), 123.3, 51.3, 33.2, 31.7, 30.2, 29.5, 29.1, 27.0, 22.7, 14.2; HRMS (ESI$^+$) Calcd. for C$_{17}$H$_{23}$F$_3$O+Na, 300.1701; Found, 300.1706; IR (thin film, cm$^{-1}$) 2928, 2858, 1724, 1323, 1162, 1119, 1067, 1019, 823, 750; HPLC analysis of the corresponding alcohol (AD, 1% IPA/Hexanes, 0.5 mL/min) indicates 92% ee: $t_R = 27.7$ (major), 30.3 (minor) min.

(R)-2-(2-(1-Benzyl-1H-pyrazol-4-yl)ethyl)octanal (39). Prepared according to the general procedure. Purified by flash chromatography (10% Et$_2$O/hexanes) using Davisil to provide the title compound (134 mg, 86% yield, 92% ee) as a colorless oil. Analytical data: [α]$^D_{22}$+4.9 (c = 0.50, CHCl$_3$); $^1$H NMR (500 MHz, CDCl$_3$) δ 9.56 (d, $J = 2.9$ Hz, 1H), 7.37 (s, 1H), 7.34 (ddd, $J = 7.3$, 4.5, 1.5 Hz, 2H), 7.30 (ddd, $J = 7.4$, 3.5, 1.4 Hz, 1H), 7.23–7.19 (m, 2H), 7.17 (s, 1H), 5.26 (s, 2H), 2.52–2.38 (m, 2H), 2.27 (ddq, $J = 10.9$, 5.4, 2.9 Hz, 1H), 1.94–1.84 (m, 1H), 1.70–1.60 (m, 2H), 1.51–1.43 (m, 1H), 1.26 (s, 8H), 0.87 (t, $J = 6.9$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 205.3, 138.9, 136.8, 128.9, 128.2, 127.8, 127.8, 121.3, 56.1, 51.4, 31.7, 30.1, 29.5, 29.0, 27.1, 22.7, 21.9, 14.2; HRMS (ESI$^+$) Calcd. for C$_{20}$H$_{28}$ON$_2$+H, 312.2202; Found, 312.2203; IR (thin film, cm$^{-1}$) 2926, 2856, 1721, 1455, 1396, 1156, 994, 726, 702; HPLC analysis of the corresponding alcohol (AS, 5% IPA/Hexanes, 1.0 mL/min) indicates 92% ee: $t_R = 15.7$ (major), 17.7 (minor) min.

(R)-2-(2-(Pyridin-3-yl)ethyl)octan-1-ol (40). Prepared according to the general procedure with 0.02 equiv. Ir[dmppy]$_2$(dtbbpy)PF$_6$ (9.7 mg) for 48 hrs. Purified by flash chromatography (30% to 40% EtOAc/hexanes, 1% Et$_3$N) after reduction to the corresponding alcohol to provide the title compound (66 mg, 56% yield, 87% ee) as a colorless oil. Analytical data: [α]$^D_{22}$–1.0 (c = 0.50, CHCl$_3$); $^1$H NMR (500 MHz, CDCl$_3$) δ 8.49–8.40 (m, 2H), 7.75 (d, $J = 7.9$ Hz, 1H), 7.41 (dd, $J = 7.8$, 5.7 Hz, 1H), 3.68–3.62 (m, 1H), 3.60–3.54 (m, 1H), 2.74–2.70 (m, 1H), 2.69–2.65 (m, 1H), 1.79–1.69 (m, 2H), 1.66–1.59 (m, 2H), 1.55 (dd, $J = 15.7$, 11.7, 4.3 Hz, 2H), 1.33–1.24 (m, 7H), 0.88 (t, $J = 6.7$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 147.5, 145.1, 140.8, 139.0, 125.1, 65.2, 40.1, 32.5, 31.9, 30.9, 30.4, 29.8, 27.0, 22.8, 14.2; HRMS (ESI$^+$) Calcd. for C$_{15}$H$_{26}$NO+H, 235.1936; Found, 235.1929; IR (thin film, cm$^{-1}$) 3348, 2924, 2855, 1483, 1456, 1442, 1279, 1164, 1131, 1030, 803, 755, 713, 691; HPLC analysis of the alcohol (AD, 10% IPA/Hexanes, 1.0 mL/min) indicates 87% ee: $t_R = 11.9$ (major), 14.6 (minor) min.
(R)-2-(2,3-Dihydro-1H-inden-2-yl)octan-1-ol (41). Prepared according to the general procedure with 0.02 equiv. Ir[dmppy]_2(dtbbpy)PF_6 (9.7 mg) and 0.5 equiv. 1-butyl-3-methyl-1H-imidazol-3-ium trifluoromethanesulfonate (55.6 µL) for 48 hrs. Purified by flash chromatography (10% EtOAc/hexanes) after reduction to the corresponding alcohol to provide the title compound (84 mg, 68% yield, 90% ee) as a colorless oil. Analytical data: [α]_D^22 +3.7 (c = 1.00, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 7.19 (dd, J = 8.3, 3.4 Hz, 2H), 7.15–7.09 (m, 2H), 3.74 (dd, J = 10.9, 4.5 Hz, 1H), 3.67 (dd, J = 10.9, 5.2 Hz, 1H), 3.03 (ddd, J = 15.3, 7.9, 1.8 Hz, 1H), 2.70 (ddd, J = 15.2, 9.8, 5.2 Hz, 1H), 2.58–2.48 (m, 1H), 1.64–1.55 (m, 1H), 1.53–1.39 (m, 3H), 1.38–1.24 (m, 9H), 0.89 (t, J = 6.7 Hz, 3H); ^13C NMR (125 MHz, CDCl_3) δ 143.5, 126.2, 124.4, 64.1, 45.7, 41.8, 37.6, 32.0, 30.0, 29.4, 27.0, 23.8, 14.3; HRMS (ESI^+) Calcd. for C_{17}H_{24}+H (M–H_2O+H), 228.1878; Found, 228.1875; IR (thin film, cm⁻¹) 3306, 2926, 2854, 1458, 1278, 1087, 1025, 972, 743; HPLC analysis of the alcohol (AS, 2% IPA/Hexanes, 1.0 mL/min) indicates 90% ee: t_R = 8.2 (minor), 11.9 (major) min.
VI. Experimental Data for Intermolecular Aldehyde α-Alkylation with Olefins

Standard Procedure: To an oven-dried 8 mL vial equipped with a teflon stir bar was added Ir[dmppy]$_2$(dtbbpy)PF$_6$ (4.9 mg, 5 µmol, 0.01 equiv.), 2,4,6-tri-tert-butylbenzenethiol (13.9 mg, 0.05 mmol, 0.10 equiv.), and α,α-bis[3,5-bistrifluoromethyl)phenyl]-2-pyrrolidinemethanol trimethylsilyl ether (59.8 mg, 0.1 mmol, 0.20 equiv). The vial was then sealed and cooled to 0 °C under nitrogen, and dimethoxyethane (1.0 mL, 0.5 M) and distilled water (27 µL, 1.5 mmol, 3.0 equiv) were added through the septum cap. The heterogeneous solution was sparged with dried nitrogen for 15 minutes with stirring during which time the reaction became homogeneous. The vent needle was then removed, and olefin (2.5 mmol, 5.0 equiv.) and octanal (0.5 mmol, 1.0 equiv.) were added under nitrogen. The vial cap was then double-sealed with parafilm, and the reaction was placed in a -65 °C bath. The stirred solution was irradiated with blue LED light for 168 hrs. Upon reaction completion, the solution was directly purified by silica gel chromatography eluting with 0-20% CH$_2$Cl$_2$ in hexanes. For enantioselectivity determination, the crude reaction was subjected to immediate reduction at -78 °C using excess NaBH$_4$ in CH$_2$Cl$_2$/MeOH (1:1, 0.1 M). The reduction was stirred at -78 °C for 2 hrs, and then the excess NaBH$_4$ was quenched with addition of saturated ammonium chloride solution. After separation of layers, the aqueous layer was extracted with CH$_2$Cl$_2$ (2 x 10 mL). The combined organic layers were then dried over sodium sulfate, filtered, and concentrated under reduced pressure; thereafter, 2-napthoyl chloride and DMAP were added and the reaction stirred for 2 hr.

(R)-2-(Cyclopentylmethyl)octanal. According to the general procedure using methylene cyclopentane to provide the title compound (78 mg, 74% yield, 90% ee) as a colorless oil. Analytical data: [α]$_D^{21}$-8.12 (c = 1.00, CHCl$_3$); $^1$H NMR (500 MHz, CDCl$_3$) δ 9.54 (d, J = 3.5 Hz, 1H), 2.28 (tt, J = 8.6, 5.4, 3.5 Hz, 1H), 1.87 – 1.17 (m, 19H), 1.05 (qddd, J = 9.4, 7.4, 4.6, 2.9 Hz, 2H), 0.94 – 0.79 (m, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 206.0, 51.6, 38.1, 35.6, 33.2, 32.9, 31.8, 29.6, 29.5, 27.2, 25.2, 25.1, 22.7, 14.2; HRMS (ESI$^+$) Calcd. for C$_{14}$H$_{26}$O+H, 211.2056; Found, 211.2057; IR (thin film, cm$^{-1}$) 2926, 2857, 2697, 1725, 1454, 1378, 1278, 1178, 1140, 943, 828, 724, 682; HPLC analysis of the alcohol (OD, 0.25% IPA/Hexanes, 1.0 mL/min) indicates 90% ee: t$_R$ = 14.5 (major), 12.1 (minor) min.

(R)-2-(Cyclohexylmethyl)octanal. According to the general procedure using methylene cyclohexane to provide the title compound (53 mg, 47% yield, 87% ee) as a colorless oil. Analytical data: [α]$_D^{21}$-3.78 (c = 1.00, CHCl$_3$); $^1$H NMR (500 MHz, CDCl$_3$) δ 9.52 (d, J = 3.5 Hz, 1H), 2.34 (tt, J = 8.5, 5.2, 3.5 Hz, 1H), 1.77 – 1.07 (m, 23H), 0.88 (t, J = 6.8 Hz, 3H);
\[^{13}\text{C NMR}\) (125 MHz, CDCl\(_3\)) \(\delta\) 206.1, 49.6, 36.9, 33.8, 33.3, 32.5, 31.8, 29.7, 29.5, 27.2, 26.6, 26.4, 26.3, 22.7, 14.2; \text{HRMS (ESI\(^+\))} \text{ Calcd. for C}_{15}\text{H}_{28}\text{O}+\text{H}, 225.22130; \text{Found,} 225.22122; \text{IR (thin film, cm}^{-1}\) 2922, 2853, 2696, 1726, 1449, 1376, 1279, 1177, 1140, 869, 845, 820, 724, 682; \text{HPLC analysis of the alcohol (OD, 1\% IPA/Hexanes, 1.0 mL/min) indicates 87\% ee: t} \text{R} = 5.8 \text{ (major), 5.3 (minor) min.}

VII. Additional Data for Substrates Not Depicted in Tables

\((3R,5S)-5\text{-Methyl-1-tosylpiperidine-3-carbaldehyde.}\) To an oven-dried 8 mL vial equipped with a teflon stir bar was added 4-methyl-N-(2-methylallyl)-N-(3-oxopropyl)benzenesulfonylamide (0.3 mmol, 1 equiv.). A septum cap was affixed, and the vial was purged with nitrogen followed by the addition of solvent (0.6 mL, 0.5 M). The cap was briefly removed to allow for the addition of powder catalysts – Ir[Flmppy]_{2}(dtbbpy)PF\(_6\) (9 mg, 0.009 mmol, 0.03 equiv.) and the TFA salt of (R)-2-(tert-butyl)-3-methylimidazolidin-4-one (28 mg, 0.06 mmol, 0.20 equiv.). After resealing the vial, 2,4,6-triisopropylbenzenethiol (15 \(\mu\)L, 0.06 mmol, 0.20 equiv.) and distilled water (5.4 \(\mu\)L, 0.3 mmol, 1 equiv.) were added through the septum cap. The heterogeneous bright yellow solution was cooled to 0 °C and sparged with dried nitrogen for 15 minutes with gentle stirring during which time the reaction became homogeneous. The nitrogen line and vent needle were removed, the vial cap was double-sealed with parafilm, and the reaction was cooled to the desired temperature. The stirred solution was irradiated with blue LED light for 24h. Yield obtained by \(^1\text{H NMR analysis using benzyl ether as an internal standard. Results: 72\% yield, 1:1 dr, 85\% ee. Analytical data: \(^1\text{H NMR (500 MHz, CDCl}_3)\): \(\delta\) 9.61 (s, 1H), 7.65 (d, \(J\) = 8.5 Hz, 2H), 7.33 (d, \(J\) = 8.0 Hz, 2H), 4.06 (dd, \(J\) = 12.0, 4.0 Hz, 1H), 3.77 (dd, \(J\) = 12.0, 4.0 Hz, 1H), 2.69 (m, 1 H), 2.44 (s, 3 H), 2.10 (m, 2H), 1.86 (m, 1 H), 1.72 (t, \(J\) = 12.0 Hz, 1 H), 0.93 (d, \(J\) = 7.0 Hz, 3 H), 0.76 (q, \(J\) = 130.0 Hz, 1 H); \(^{13}\text{C NMR (125 MHz, CDCl}_3)\): \(\delta\) 200.9, 143.7, 132.8, 129.8, 127.6, 52.8, 48.4, 45.4, 32.3, 30.5, 21.5, 18.8; \text{HRMS (ESI\(^+\))} \text{ Calcd. for C}_{14}\text{H}_{19}\text{NO}_3\text{S}+\text{H}, 282.11584; \text{Found,} 282.11543; \text{IR (thin film, cm}^{-1}\) 2958, 2929, 2848, 1721, 1598, 1494, 1462, 1382, 1340, 1306, 1289, 1243, 1157, 1118,1089, 1021, 1000, 933, 855, 808, 790, 776, 736, 708, 658; \text{TLC (30:70 hexanes:EtOAc):} \text{R} = 0.50; \text{HPLC analysis of the corresponding alcohol (OJ, 10\% iPrOH/hexane, 1.0 mL/min, 254 nm) indicates 85\% ee: t} \text{R} = 6.4, 7.3 \text{ min.}

\((R)-2-(\text{cyclobutylmethyl})\text{octanal.}\) To an oven-dried 8 mL vial equipped with a teflon stir bar was added Ir[Flmppy]_{2}(dtbbpy)PF\(_6\) (4.9 mg, 5 \(\mu\)mol, 0.01 equiv.), 2,4,6-tri-tert-butylbenzenethiol (13.9 mg, 0.05 mmol, 0.10 equiv.), and \(\alpha,\alpha\)-bis[3,5-bistrifluoromethyl]phenyl]-2-pyrroolidinemethanol trimethylsilyl ether (59.8 mg, 0.1 mmol, 0.20 equiv). The vial was then
sealed and cooled to 0 °C under nitrogen, and dimethoxyethane (1.0 mL, 0.5 M) and distilled water (27 µL, 1.5 mmol, 3.0 equiv) were added through the septum cap. The heterogeneous solution was sparged with dried nitrogen for 15 minutes with stirring during which time the reaction became homogeneous. The vent needle was then removed, and methylenecyclobutane (2.5 mmol, 5.0 equiv.) and octanal (0.5 mmol, 1.0 equiv.) were added under nitrogen. The vial cap was then double-sealed with parafilm, and the reaction was placed in a -65 °C bath. The stirred solution was irradiated with blue LED light for 168 hrs. Upon reaction completion, the solution was directly purified by silica gel chromatography eluting with 0-20% CH₂Cl₂ in hexanes to provide the title compound (46 mg, 47% yield, 87% ee) as a colorless oil. For enantioselectivity determination, the crude reaction was subjected to immediate reduction at -78 °C using excess NaBH₄ in CH₂Cl₂/MeOH (1:1, 0.1 M). The reduction was stirred at -78 °C for 2 hrs, and then the excess NaBH₄ was quenched with addition of saturated ammonium chloride solution. After separation of layers, the aqueous layer was extracted with CH₂Cl₂ (2 x 10 mL). The combined organic layers were then dried over sodium sulfate, filtered, and concentrated under reduced pressure; thereafter, 2-naphthoyl chloride and DMAP were added and the reaction stirred for 2 hr. Analytical data: [α]D²¹ -5.25 (c = 1.00, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 9.53 (d, J = 3.3 Hz, 1H), 2.29 (dq, J = 15.8, 7.9 Hz, 1H), 2.17 (dt, J = 11.2, 5.4, 2.7 Hz, 1H), 2.02 (dddd, J = 17.6, 9.5, 6.7, 3.9 Hz, 2H), 1.89 – 1.69 (m, 3H), 1.65 – 1.47 (m, 4H), 1.44 – 1.34 (m, 1H), 1.34 – 1.16 (m, 8H), 0.87 (t, J = 6.8 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 205.8, 50.7, 36.5, 34.1, 31.8, 29.5, 29.16, 28.9, 28.8, 27.2, 22.7, 18.5, 14.2; HRMS (ESI⁺) Calcd. for C₁₃H₂₄O+H, 197.19000; Found, 197.19087; IR (thin film, cm⁻¹) 2956, 2926, 2856, 2699, 1725, 1463, 1378, 1280, 1174, 1141, 915, 829, 724; HPLC analysis of the alcohol (OD, 1% IPA/Hexanes, 1.0 mL/min) indicates 87% ee: tᵣ = 6.1 (major), 5.8 (minor) min.

**Representative challenging substrates:**
The following olefin coupling partners all led to <10% yield of the desired products as determined by ¹H NMR analysis of the crude reaction mixtures.
VIII. NMR Spectral Data for Novel Compounds

\((E)\)-N-(3,7-Dimethylocta-2,6-dien-1-yl)-N-(4-hydroxybutyl)-4-methylbenzenesulfonamide
(E)-N-(3,7-Dimethylocta-2,6-dien-1-yl)-4-methyl-N-(4-oxobutyl)benzenesulfonamide
(E)-N-(But-2-en-1-yl)-N-(4-hydroxybutyl)-4-methylbenzenesulfonamide
(E)-N-(But-2-en-1-yl)-4-methyl-N-(4-oxobutyl)benzenesulfonamide
Ethyl (E)-3-(1,3-diphenyl-1H-pyrazol-4-yl)acrylate
(E)-3-(1,3-Diphenyl-1H-pyrazol-4-yl)prop-2-en-1-ol
(E)-N-(3-(1,3-Diphenyl-1H-pyrazol-4-yl)allyl)-N-(4-hydroxybutyl)-4-methylbenzenesulfonamide
(E)-N-(3-(1,3-Diphenyl-1H-pyrazol-4-yl)allyl)-4-methyl-N-(4-oxobutyl)benzenesulfonamide
$N$-(4-Hydroxybutyl)-4-methyl-$N$-(2-methylallyl)benzenesulfonamide
4-Methyl-N-(2-methylallyl)-N-(4-oxobutyl)benzenesulfonamide
tert-Butyl (3-methylbut-2-en-1-yl)(4-oxobutyl)carbamate
$N$-(2,3-Dimethylbut-2-en-1-yl)-$N$-(4-hydroxybutyl)-4-methylbenzenesulfonamide
N-(2,3-Dimethylbut-2-en-1-yl)-4-methyl-N-(4-oxobutyl)benzenesulfonamide
$N$-(3-Hydroxypropyl)-4-methyl-$N$-(2-methylallyl)benzenesulfonamide
Di-\textit{tert}-butyl 2-(2-methylallyl)-2-(4-oxobutyl)malonate
4-Methyl-N-(2-methylallyl)-N-(3-oxopropyl)benzenesulfonamide
Table 1. 13: (3R,4S)-3-Isopropyl-1-tosylpiperidine-4-carbaldehyde
Table 1, 14: tert-Butyl (3R,4S)-4-formyl-3-isopropylpiperidine-1-carboxylate
Table 1, 15: (3R,4S)-3-Isopropyltetrahydro-2H-pyran-4-carbaldehyde
Table 1, 16: (3R,4S)-3-Ethyl-1-tosylpiperidine-4-carbaldehyde
Table 1, 17: (3R,4S)-3-((1,3-Diphenyl-1H-pyrazol-4-yl)methyl)-1-tosylpiperidine-4-carbaldehyde
Table 1, 18: Di-tert-butyl (3R,4S)-4-formyl-3-isopropylcyclohexane-1,1-dicarboxylate
<table>
<thead>
<tr>
<th>1,19</th>
<th>(1S,2R)-2-Isopropylcyclohexane-1-carbaldehyde</th>
</tr>
</thead>
</table>

Table 1, 19: (1S,2R)-2-Isopropylcyclohexane-1-carbaldehyde
Table 1, 20: (3R,4S)-3-Cyclopentyl-1-tosylpiperidine-4-carbaldehyde
Table 1. 21: (3R,4S)-1-Tosyl-3-(2-(trimethylsilyl)ethyl)piperidine-4-carbaldehyde
Table 1, 22: (3R,4S)-3-(6-Methylhept-5-en-2-yl)-1-tosylpiperidine-4-carbaldehyde
Table 1, 23: (3R,4S)-3-Isopropyl-3-methyl-1-tosylpiperidine-4-carbaldehyde
Table 1, 24: (3R,4R)-4-Isopropyl-1-tosylpyrrolidine-3-carbaldehyde
Table 1, **25**: (4R,6S)-6-Methyl-1-tosylazepane-4-carbaldehyde
Table 1, 26: di-\textit{t}ert-butyl 5-formyl-3-methylcycloheptane-1,1-dicarboxylate
Table 2, 30: (R)-2-Phenethylcctanal
Table 2, 31: (R)-2-Methyl-4-phenylbutanal
Table 2. (S)-2-Isopropyl-4-phenylbutan-1-ol

\[ \text{A2}_{24}-\text{AEC}-6-\text{isp} \]

\[ \text{C14H24O3} \text{C8H19O3} \text{C8H19O3} \text{A2}_{24} \]
Table 2. 33: (R)-6-Chloro-2-phenethylhexanal
Table 2. 34: (R)-Ethyl 5-(hydroxymethyl)-7-phenylheptanoate
Table 2, 35: (S)-Benzyl (2-(hydroxymethyl)-4-phenylbutyl)carbamate
Table 2, 36: (R)-2-(4-Methoxyphenethyl)octanal

| A2_303-ACC-1-184g | PROTON PI (CD3) / chiralpaks O | a | a | a |

```
Table 2, 36: (R)-2-(4-Methoxyphenethyl)octanal

A2_303-ACC-1-184g
PROTON PI (CD3) / chiralpaks O

| A2_303-ACC-1-184g | PROTON PI (CD3) / chiralpaks O | a | a | a |
```

![Chemical structure](image)
Table 2, 37: (R)-2-(4-Fluorophenethyl)octanal
Table 2, 38: (R)-2-(4-(Trifluoromethyl)phenethyl)octanal
Table 2. 39: (R)-2-(2-(1-Benzyl-1H-pyrazol-4-yl)ethyl)octanal

\[ R - 2 - \text{(2-}^{1}\text{H-pyrazol-4)}{\text{yl)ethyl octanal}} \]
Table 2. **(R)-2-(2-(Pyridin-3-yl)ethyl)octan-1-ol**

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Table 2, 41: (R)-2-(2,3-Dihydro-1H-inden-2-yl)octan-1-ol
Figure 3: \((R)\)-2-(Cyclopentylmethyl)octanal
Figure 3: (R)-2-(Cyclohexylmethyl)octanal
(R)-2-(Cyclobutylmethyl)octanal
(3R,5S)-5-Methyl-1-tosylpiperidine-3-carbaldehyde