Electronic Supporting Information

Sequential Asymmetric Hydrogenation and Photoredox Chemistry with a Single Catalyst

Xiao Zhang, Jie Qin, Xiaoqiang Huang, and Eric Meggers*

Fachbereich Chemie, Philipps-Universität Marburg, Hans-Meerwein-Straße 4, 35043 Marburg, Germany

*E-mail: meggers@chemie.uni-marburg.de
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1. General information

All reactions were carried out under an atmosphere of nitrogen with magnetic stirring. Catalytic reactions were performed in a Schlenk tube (10 mL). A 21 W compact fluorescent lamp (CFL), 6 W and 24 W blue LEDs served as the light sources. The catalyst Λ-IrS was synthesized according to our published procedure. HPLC grade of solvents and deionized water were used without further purification. Reagents that were purchased from commercial suppliers were used without further purification. Flash column chromatography was performed with silica gel 60 M from Macherey-Nagel (irregular shaped, 230-400 mesh, pH 6.8, pore volume: 0.81 mL × g⁻¹, mean pore size: 66 Å, specific surface: 492 m² × g⁻¹, particle size distribution: 0.5% < 25 μm and 1.7% > 71 μm, water content: 1.6%). ¹HNMR, ¹⁹FNMR and proton decoupled ¹³CNMR spectra were recorded on Bruker Avance 300 (300 MHz), or Bruker AM (500 MHz) spectrometers at ambient temperature. NMR standards were used as follows: ¹HNMR spectroscopy: δ = 7.26 ppm (CDCl₃), ¹⁹FNMR spectroscopy: δ = 0 ppm (CFCl₃), ¹³CNMR spectroscopy: δ = 77.0 ppm (CDCl₃). IR spectra were recorded on a Bruker Alpha FT-IR spectrophotometer. High-resolution mass spectra were recorded on a Bruker En Apex Ultra 7.0 TFT-MS instrument using ESI/EI/APCI/FD technique. Chiral HPLC chromatography was performed with an Agilent 1200, Agilent 1260 HPLC system or Shimadzu Lc-2030c HPLC system. Optical rotations were measured on a Krüss P8000-T polarimeter with [α]D₂² values reported in degrees with concentrations reported in g/100 mL.
2. Asymmetric hydrogenation of acetophenone with Λ-IrS

2.1 General procedure

A dried 5 mL tube was charged with acetophenone (0.10 mmol), catalyst, additive, base and solvent, and placed into a stainless steel pressure reactor. The reactor was refilled with H₂ and degassed for 5 cycles, and then hydrogen pressure subsequently increased to indicated pressure. The reaction mixture in the reactor was stirred at room temperature for certain time. After release of H₂, the crude reaction mixture was concentrated under reduced pressure and purified by flash chromatography on silica gel (n-hexane/ethyl acetate = 4:1) to afford the desired chiral 1-phenylethanol-1-ol as a colorless oil. Enantiomeric excess was established by HPLC analysis using a Chiralcel OJ column (HPLC: OJ, 220 nm, n-hexane/isopropanol = 95:5, flow rate 1 mL/min, 25 °C, t₁ = 12.44 min, t₂ = 14.21 min).

2.2 Screening of reaction conditions

2.2.1 Effect of bases and catalyst loading

<table>
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<th>entry</th>
<th>base</th>
<th>3,5-dimethyl pyrazole</th>
<th>x</th>
<th>conv. (%)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>yield (%)</th>
<th>ee (%)</th>
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<tr>
<td>1</td>
<td>NaO'Bu (2 eq.)</td>
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<td>100</td>
<td>94</td>
</tr>
<tr>
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<td>0.5</td>
<td>100</td>
<td>100</td>
<td>94</td>
</tr>
<tr>
<td>5</td>
<td>-</td>
<td>-</td>
<td>0.5</td>
<td>&lt;5</td>
<td>n.d.</td>
<td>n.d.</td>
</tr>
</tbody>
</table>

<sup>a</sup>Reaction conditions: acetophenone (0.10 mmol), Λ-IrS (1.0 or 0.5 mol%), 3,5-dimethyl pyrazole (20 mol%), THF
(1.0 mL, 0.1 M), r.t., H₂ (8 bar), 18 h. n.d. = not determined. a Determined by ¹H-NMR.

### 2.2.2 Effect of different pyrazoles

![Chemical reaction diagram]

**Reaction conditions:** acetophenone (0.10 mmol), rac-IrS (0.5 mol%), pyrazole (20 mol%), THF (1.0 mL, 0.1 M), r.t., H₂ (8 bar), 5.5 h.

### 2.2.3 Effect of pressure and concentration

<table>
<thead>
<tr>
<th>entry</th>
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<th>pressure of H₂</th>
<th>concentration (M)</th>
<th>conv. (%)</th>
<th>ee (%)</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>0.5%</td>
<td>8 bar</td>
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<td>100</td>
<td>94</td>
</tr>
<tr>
<td>2</td>
<td>0.5%</td>
<td>20 bar</td>
<td>0.1</td>
<td>100</td>
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<td>95</td>
</tr>
<tr>
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<td>0.1%</td>
<td>20 bar</td>
<td>0.2</td>
<td>95</td>
<td>94</td>
</tr>
<tr>
<td>5</td>
<td>0.1%</td>
<td>20 bar</td>
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<td>92</td>
</tr>
<tr>
<td>6</td>
<td>0.1%</td>
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</tr>
<tr>
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<td>50 bar</td>
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<td>96</td>
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</table>

**Reaction conditions:** acetophenone, Λ-IrS, 3,5-dimethyl pyrazole (20 mol%), THF, r.t., H₂, 18 h. b Determined by ¹H-NMR.
3. Sequential asymmetric hydrogenation and photoredox catalysis with \( \Lambda \)-IrS

3.1 Iridium-catalyzed asymmetric hydrogenation and sequential photocatalytic radical trifluoromethylation/cyclization cascade

3.1.1 Synthesis of substrates

Substrates 1 were synthesized according to reported procedures.\(^2\) The experimental data are shown below.

1-([1,1'-biphenyl]-4-yl)pent-4-en-1-one (1a)

\(^1\)H NMR (300 MHz, CDCl\textsubscript{3}) \( \delta \) 7.92 (d, J = 8.4 Hz, 2H), 7.58-7.50 (m, 4H), 7.35 (t, J = 6.9 Hz, 2H), 7.28 (t, J = 6.9 Hz, 1H), 5.89-5.76 (m, 1H), 5.00 (dd, J = 17.4, 1.5 Hz, 1H), 4.93 (d, J = 10.2 Hz, 1H), 2.99 (t, J = 7.5 Hz, 2H), 2.42 (q, J = 6.6 Hz, 2H).

1-(4-methoxyphenyl)pent-4-en-1-one (1b)

\(^1\)H NMR (300 MHz, CDCl\textsubscript{3}) \( \delta \) 7.86 (d, J = 9.0 Hz, 2H), 6.85 (d, J = 8.7 Hz, 2H), 5.89-5.75 (m, 1H), 5.00 (dd, J = 16.8, 1.5 Hz, 1H), 4.92 (d, J = 10.2, 1.2 Hz, 1H), 3.78 (s, 3H), 2.93 (t, J = 6.9 Hz, 2H), 2.40 (q, J = 6.6 Hz, 2H).

1-(4-(trifluoromethyl)phenyl)pent-4-en-1-one (1c)
1H NMR (300 MHz, CDCl₃) δ 7.98 (d, J = 8.1 Hz, 2H), 7.65 (d, J = 8.1 Hz, 2H), 5.89-5.75 (m, 1H), 5.05-4.93 (m, 2H), 3.02 (t, J = 7.2 Hz, 2H), 2.43 (q, J = 6.6 Hz, 2H).

1-phenylpent-4-en-1-one (1d)

1H NMR (300 MHz, CDCl₃) δ 7.97 (d, J = 7.2 Hz, 2H), 7.56 (t, J = 7.5 Hz, 1H), 7.46 (t, J = 7.5 Hz, 2H), 5.98-5.84 (m, 1H), 5.09 (dd, J = 17.4, 1.5 Hz, 1H), 5.02 (d, J = 9.9 Hz, 1H), 3.08 (t, J = 7.2 Hz, 2H), 2.51 (q, J = 7.5 Hz, 2H).

Togni’s reagent 2 was synthesized according to reported procedures.³ The analytical data are shown below.

1-(trifluoromethyl)-1λ³-benzo[d][1,2]iodaoxol-3(IH)-one (2)

1H NMR (300 MHz, CDCl₃) δ 8.39-8.37 (m, 1H), 7.72 (br s, 3H).

3.1.2 General procedure

3.1.2.1 General procedure for optimizing the reaction conditions for photoredox chemistry

A dried 10 mL Schlenk tube was charged with Togni’s reagent 2, base, rac-IrS (1.9 mg, 1 mol%) and 3,5-dimethyl pyrazole (3.8 mg, 20 mol%). The tube was purged with nitrogen, then solvent was added via syringe, followed by 1-((1,1'-biphenyl)-4-yl)pent-4-en-1-ol (47.6 mg, 0.20 mmol). The reaction mixture was degassed via freeze-pump-thaw for three cycles. After the mixture was thoroughly degassed, the vial was sealed and positioned approximately 5 cm from visible light. The reaction mixture was stirred at room temperature for the indicated time (monitored by TLC) under
nitrogen atmosphere. Afterwards, the solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel (n-hexane/ethyl acetate = 8:1) to afford the product 3a.

3.1.2.2 General procedure for the sequential reactions with \( \Lambda\text{-IrS} \) using a single purification

\[
\begin{align*}
\Lambda\text{-IrS} & \quad (2 \text{ mol\%}) \\
\text{N} & \quad (40 \text{ mol\%}) \\
1) & \quad \text{H}_2 \ (50 \text{ bar}), \text{THF}, \ r.t., \ 15 \text{ h} \\
2) & \quad \text{Blue LEDs} \ (24 \text{ W}), \ 2 \ (1.5 \text{ eq.}) \\
& \quad \text{NaHCO}_3 \ (2.0 \text{ eq.}), \text{MeOH}, \ 7 \degree \text{C}, \ 24 \text{ h}
\end{align*}
\]

A dried 5 mL tube was charged with substrates 1 (0.20 mmol), \( \Lambda\text{-IrS} \) (3.8 mg, 2 mol%), 3,5-dimethyl pyrazole (7.7 mg, 40 mol%) and THF (2.0 mL, 0.1 M), and placed into a stainless steel pressure reactor. The reactor was refilled with H\(_2\) and degassed for 5 cycles, and then hydrogen pressure subsequently increased to 50 bar. The reaction mixture in the reactor was stirred at room temperature for 15 h. After release of H\(_2\), the solvent was removed under reduced pressure. Togni’s reagent 2 (94.8 mg, 0.30 mmol), NaHCO\(_3\) (33.6 mg, 0.40 mmol) and MeOH (2.0 mL, 0.1 M) were added to the residual crude material. The reaction mixture was degassed via freeze-pump-thaw for three cycles. After the mixture was thoroughly degassed, the vial was sealed and positioned approximately 5 cm from Blue LEDs (24 W). The reaction mixture was stirred at 7 \degree\text{C} under nitrogen atmosphere until complete disappearance of the starting material (monitored by TLC), then concentrated under reduced pressure and purified by flash chromatography on silica gel (n-hexane/ethyl acetate = 8:1) to afford the products 3.

3.1.3 Screening of reaction conditions

3.1.3.1 Optimization of the reaction conditions for photoredox chemistry

\[
\begin{align*}
\text{rac-IrS} & \quad (1 \text{ mol\%}) \\
\text{N} & \quad (20 \text{ mol\%}) \\
2 \ (x \text{ eq.}), \text{base, solvent, light, r.t.}
\end{align*}
\]
**Table:**

<table>
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<th>photocatalyst</th>
<th>light</th>
<th>base</th>
<th>solvent</th>
<th>x</th>
<th>conv. (%)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>yield (%)&lt;sup&gt;b&lt;/sup&gt;</th>
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</thead>
<tbody>
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<td>Blue LEDs (24 W)</td>
<td>NaHCO&lt;sub&gt;3&lt;/sub&gt;</td>
<td>MeOH</td>
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<td>n.d.</td>
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</tr>
<tr>
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<td>yes</td>
<td>-</td>
<td>NaHCO&lt;sub&gt;3&lt;/sub&gt;</td>
<td>MeOH</td>
<td>1.2</td>
<td>n.d.</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>yes</td>
<td>Blue LEDs (24 W)</td>
<td>NaHCO&lt;sub&gt;3&lt;/sub&gt;</td>
<td>MeOH</td>
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<td>72</td>
</tr>
<tr>
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<td>yes</td>
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<td>70</td>
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<td>30</td>
<td>15</td>
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<td>1.2</td>
<td>72</td>
<td>49</td>
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<td>yes</td>
<td>Blue LEDs (24 W)</td>
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<td>MeOH</td>
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<td>100</td>
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<td>100</td>
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<td>MeOH</td>
<td>1.5</td>
<td>100</td>
<td>80</td>
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<sup>a</sup>Reaction conditions: 1-(1,1'-biphenyl)-4-ylpent-4-en-1-ol (0.20 mmol), Togni's reagent 2, rac-IrS (1.0 mol%), 3,5-dimethyl pyrazole (20 mol%), base (0.40 mmol), solvent (2.0 mL, 0.1 M), r.t., visible light, 15 h.  
<sup>b</sup>Determined by the crude <sup>1</sup>H NMR of the reaction mixtures (using Cl<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>Cl as the internal standard).  
<sup>c</sup>Reactions conditions: 1-(1,1'-biphenyl)-4-ylpent-4-en-1-ol (0.20 mmol), Togni's reagent 2 (0.30 mmol), rac-IrS (1.0 mol%), 3,5-dimethyl pyrazole (20 mol%), NaHCO<sub>3</sub> (0.40 mmol), MeOH (2.0 mL, 0.1 M), 7 °C, Blue LEDs (24 W), 24 h. n.d. = not determined.

### 3.1.3.2 Evaluation of the sequential reactions with Λ-IrS using a single purification<sup>a</sup>

**Diagram:**

![Diagram](image)

<sup>a</sup>Reaction conditions: Λ-IrS (2.0 mol%), 3,5-dimethyl pyrazole (40 mol%), 1a (0.20 mmol), THF (2.0 mL, 0.1 M), H<sub>2</sub> (50 bar), r.t., 15 h.

**Diagram:**

![Diagram](image)

<sup>a</sup>Reaction conditions: Λ-IrS (2.0 mol%), 3,5-dimethyl pyrazole (40 mol%), 1a (0.20 mmol), THF (2.0 mL, 0.1 M), H<sub>2</sub> (50 bar), r.t., 15 h; then 2 (0.30 mmol), NaHCO<sub>3</sub> (0.4 mmol), MeOH (2.0 mL, 0.1 M), 7 °C, Blue LEDs (24 W), 24 h.
3.1.4 Experimental and characterization data of products

(1R)-6-phenyl-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydronaphthalen-1-ol (3a)

According to the general procedure, the reaction using 1-[(1,1′-biphenyl)-4-yl]pent-4-en-1-one 1a (47.2 mg, 0.20 mmol) as the starting material gave 41.6 mg (68%) of 3a as a colorless oil. Enantiomeric excess was established by HPLC analysis using a Chiralpak AS-H column (250 x 4.6 mm), 94% ee, 96% ee (HPLC: AS-H, 254 nm, n-hexane/isopropanol = 95:5, flow rate 1 mL/min, 40 °C, t<sub>r</sub> (major) = 14.80 min, t<sub>r</sub> (minor) = 15.71 min; another isomer: t<sub>r</sub> (minor) = 16.73 min, t<sub>r</sub> (major) = 19.18 min). [α]<sub>D</sub> <sup>22</sup> = -28.8° (c 1.0, CH<sub>2</sub>Cl<sub>2</sub>). The product was present as a 1:1 mixture of diastereoisomers.

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.61-7.45 (m, 6H), 7.42-7.37 (m, 2H), 4.82-4.79 (m, 1H), 3.38-3.25 (m, 1H), 2.73-2.25 (m, 3H), 2.16-1.84 (m, 4H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 141.3, 141.1, 140.6, 140.5, 138.9, 138.8, 138.1, 137.5, 129.6, 128.8, 127.50, 127.46, 127.2, 127.02, 126.9 (q, J = 276 Hz), 126.8 (q, J = 276 Hz), 126.7, 126.0, 125.8, 68.1, 67.0, 40.6 (q, J = 27 Hz), 40.1 (q, J = 27 Hz), 32.3 (q, J = 3 Hz), 32.2 (q, J = 3 Hz), 29.0, 28.1, 24.4, 22.6.

<sup>19</sup>F NMR (282 MHz, CDCl<sub>3</sub>) δ -63.72, -63.75.

IR (film): ν (cm<sup>-1</sup>) 3308, 3072, 3025, 2947, 2878, 1667, 1603, 1564, 1480, 1436, 1373, 1308, 1251, 1190, 1116, 1085, 1046, 984, 931, 887, 839, 756, 697, 671, 631, 601, 563, 509, 438.

HRMS (APCI, m/z) calcd for C<sub>18</sub>H<sub>17</sub>F<sub>3</sub>ONa [M+Na]<sup>+</sup>: 329.1124, found: 329.1146.

(1R)-6-methoxy-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydronaphthalen-1-ol (3b)

According to the general procedure, the reaction using 1-(4-methoxyphenyl)pent-4-en-1-one 1b (38.0 mg, 0.20 mmol) as the starting material gave 28.2 mg (54%) of 3b as a yellow solid. Enantiomeric
excess was established by HPLC analysis using a Chiralcel OJ-H column (250 x 4.6 mm), 94% ee, 95% ee (HPLC: OJ-H, 220 nm, n-hexane/isopropanol = 95:5, flow rate 1 mL/min, 25 °C, t_r (major) = 12.61 min, t_r (minor) = 15.78 min; another isomer: t_r (minor) = 36.70 min, t_r (major) = 46.65 min). [α]_D^{22} = -24.4° (c 1.0, CH₂Cl₂). The product was present as a 1:1 mixture of diastereoisomers.

\[ ^{1}H \text{ NMR (300 MHz, CDCl}_3 \] δ 7.40-7.31 (m, 1H), 6.84-6.80 (m, 1H), 6.70-6.66 (m, 1H), 4.76-4.72 (m, 1H), 3.81 and 3.80 (s, 3H), 3.25-3.10 (m, 1H), 2.62-1.71 (m, 7H).

\[ ^{13}C \text{ NMR (75 MHz, CDCl}_3 \] δ 159.4, 159.3, 140.0, 139.9, 131.5, 130.8, 129.9, 126.9 (q, J = 276 Hz), 126.7 (q, J = 276 Hz), 113.3, 112.94, 112.86, 67.9, 66.7, 55.3, 40.6 (q, J = 26 Hz), 39.9 (q, J = 27 Hz), 32.5 (q, J = 3 Hz), 32.3 (q, J = 2 Hz), 29.3, 27.8, 24.3, 22.1.

\[ ^{19}F \text{ NMR (282 MHz, CDCl}_3 \] δ -63.92, -63.98.

IR (film): ν (cm⁻¹) 3310, 2942, 2846, 1612, 1574, 1498, 1463, 1437, 1376, 1306, 1274, 1246, 1115, 1082, 1037, 931, 877, 819, 697, 668, 573, 556, 457.


(1R)-4-(2,2,2-trifluoroethyl)-6-(trifluoromethyl)-1,2,3,4-tetrahydronaphthalen-1-ol (3c)

According to the general procedure, the reaction using 1-((4-(trifluoromethyl)phenyl)pent-4-en-1-one 1c (45.6 mg, 0.20 mmol) as the starting material gave 45.8 mg (76%) of 3c as a yellow solid. Enantiomeric excess was established by HPLC analysis using a Chiralpak AD-H column (250 x 4.6 mm), 96% ee, 97% ee (HPLC: AD-H, 220 nm, n-hexane/isopropanol = 98:2, flow rate 0.5 mL/min, 25 °C, t_r (major) = 44.54 min, t_r (minor) = 44.84 min; another isomer: t_r (minor) = 31.43 min, t_r (major) = 44.84 min). [α]_D^{22} = -33.3° (c 1.0, CH₂Cl₂). The product was present as a 1:1 mixture of diastereoisomers.

\[ ^{1}H \text{ NMR (300 MHz, CDCl}_3 \] δ 7.66-7.58 (m, 1H), 7.52-7.49 (m, 1H), 7.43 (s, 1H), 4.81-4.93 (m, 1H), 3.35-3.19 (m, 1H), 2.58-1.59 (m, 7H).

\[ ^{13}C \text{ NMR (75 MHz, CDCl}_3 \] δ 142.93, 142.92, 142.49, 142.47, 139.2, 139.1, 130.5 (q, J = 32 Hz), 130.3 (q, J = 33 Hz), 129.6, 128.8, 126.6 (q, J = 276 Hz), 126.5 (q, J = 276 Hz), 125.3 (q, J = 4 Hz), 125.0 (q, J = 4 Hz), 123.93 (q, J = 271 Hz), 123.89 (q, J = 271 Hz), 68.1, 67.0, 40.5 (q, J = 28 Hz),
40.0 (q, \( J = 27 \) Hz), 32.19, 32.17, 28.7, 28.4, 24.14, 24.12, 22.89, 22.87.

\( ^{19}\text{F} \) NMR (282 MHz, CDCl\(_3\)) \( \delta \) -62.77, -62.81, -63.81, -63.95.

IR (film): \( \nu \) (cm\(^{-1}\)) 3305, 2942, 1600, 1431, 1378, 1329, 1251, 1116, 1068, 985, 933, 907, 839, 730, 673, 643, 612, 567, 497, 409.

HRMS (FD, \( m/z \)) calcd for C\(_{13}\)H\(_{12}\)F\(_6\)O [M]+: 298.0792, found: 298.0785.

3.1.5 Proposed mechanism for the photoredox chemistry

![Proposed mechanism for the photoredox chemistry](image-url)
3.2 Iridium-catalyzed asymmetric hydrogenation and sequential photocatalytic atom transfer radical addition (ATRA)

3.2.1 General procedure

3.2.1.1 General procedure for optimizing the reaction conditions for photoredox chemistry

![Chemical structure for reaction](attachment:structure.png)

A dried 10 mL Schlenk tube was charged with NaHCO₃, rac-IrS (1.9 mg, 1 mol%) and 3,5-dimethyl pyrazole (3.8 mg, 20 mol%). The tube was purged with nitrogen, then solvent was added via syringe, followed by 1-phenylpent-4-en-1-ol (32.4 mg, 0.20 mmol) and BrCCl₃. The reaction mixture was degassed via freeze-pump-thaw for three cycles. After the mixture was thoroughly degassed, the vial was sealed and positioned approximately 5 cm from visible light. The reaction mixture was stirred at room temperature for the indicated time (monitored by TLC) under nitrogen atmosphere. Afterwards, the solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel (n-hexane/ethyl acetate = 15:1) to afford the product 4a.

3.2.1.2 General procedure for the sequential reactions with A-IrS using a single purification

![Chemical structure for reaction](attachment:structure.png)

A dried 5 mL tube was charged with substrates 1 (0.20 mmol), A-IrS (3.8 mg, 2 mol%), 3,5-dimethyl pyrazole (7.7 mg, 40 mol%) and THF (2.0 mL, 0.1 M), and placed into a stainless steel pressure reactor. The reactor was refilled with H₂ and degassed for 5 cycles, and then hydrogen pressure subsequently increased to 50 bar. The reaction mixture in the reactor was stirred at room temperature for 15 h under H₂ atmosphere (50 bar) followed by Blue LEDs (24 W), BrCCl₃ (2.0 eq.), NaHCO₃ (2.0 eq.), MeOH, 7 °C, 36 h.
temperature for 15 h. After release of H₂, the solvent was removed under reduced pressure. BrCCl₃ (79.2 mg, 0.40 mmol), NaHCO₃ (33.6 mg, 0.40 mmol) and MeOH (2.0 mL, 0.1 M) were added to the residual crude material. The reaction mixture was degassed via freeze-pump-thaw for three cycles. After the mixture was thoroughly degassed, the vial was sealed and positioned approximately 5 cm from Blue LEDs (24 W). The reaction mixture was stirred at 7 °C for 36 h, then concentrated under reduced pressure and purified by flash chromatography on silica gel (n-hexane/ethyl acetate = 15:1) to afford the products 4.

### 3.2.2 Screening of reaction conditions

#### 3.2.2.1 Optimization of the reaction conditions for photoredox chemistry

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<td>yes</td>
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<td>r.t.</td>
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<tr>
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</table>

*Reaction conditions: 1-phenylpent-4-en-1-ol (0.20 mmol), BrCCl₃, rac-IrS (1.0 mol%), 3,5-dimethyl pyrazole (20 mol%), NaHCO₃ (0.40 mmol), solvent (2.0 mL, 0.1 M), r.t., Blue LEDs (24 W), 15 h. "Reaction conditions: 1-phenylpent-4-en-1-ol (0.20 mmol), BrCCl₃ (0.40 mmol), rac-IrS (1.0 mol%), 3,5-dimethyl pyrazole (20 mol%), NaHCO₃ (0.40 mmol), MeOH (2.0 mL, 0.1 M), 7 °C, Blue LEDs (24 W), 36 h."
3.2.2 Evaluation of the sequential reactions with $\Lambda$-IrS using a single purification

\[ \text{Reaction conditions: } \Lambda \text{-IrS (2.0 mol%), 3,5-dimethyl pyrazole (40 mol%), 1d (0.20 mmol), THF (2.0 mL, 0.1 M), H}_2 \text{ (50 bar), r.t., 15 h; then BrCCl}_3 \text{ (0.40 mmol), NaHCO}_3 \text{ (0.40 mmol), MeOH (2.0 mL, 0.1 M), 7 °C, Blue LEDs (24 W), 36 h.} \]

3.2.3 Experimental and characterization data of products

(1R)-4-bromo-6,6,6-trichloro-1-phenylhexan-1-ol (4a)

According to the general procedure, the reaction using 1-phenylpent-4-en-1-one 1d (32.0 mg, 0.20 mmol) as the starting material gave 64.0 mg (89%) of 4a as a colorless oil. Enantiomeric excess was established by HPLC analysis using a Chiralpak IG column, 95% ee, 97% ee (HPLC: IG, 220 nm, n-hexane/isopropanol = 98:2, flow rate 0.5 mL/min, 25 °C, $t_r$ (minor) = 41.73 min, $t_r$ (major) = 52.61 min; another isomer: $t_r$ (major) = 55.51 min, $t_r$ (minor) = 64.33 min). $[\alpha]_D^{22} = +14.2^\circ$ (c 1.0, CH$_2$Cl$_2$).

The product was present as a 1:1 mixture of diastereoisomers.

$^1$H NMR (500 MHz, CDCl$_3$) δ 7.39-7.35 (m, 4H), 7.32-7.28 (m, 1H), 4.78-4.72 (m, 1H), 4.40-4.34 (m, 1H), 3.47-3.42 (m, 1H), 3.23-3.18 (m, 1H), 2.29-1.87 (m, 5H).

$^{13}$C NMR (125 MHz, CDCl$_3$) δ 144.1, 144.0, 128.7, 128.6, 127.9, 127.8, 125.8, 125.7, 97.04, 97.00, 74.01, 73.4, 62.60, 62.55, 48.9, 48.7, 36.6, 36.4, 35.9, 35.5.

IR (film): ν (cm$^{-1}$) 3363, 3063, 3030, 2925, 2861, 1493, 1449, 1422, 1287, 1195, 1052, 1018, 948, 768, 701, 633, 553.

HRMS (APCI, m/z) calcd for C$_{12}$H$_{13}$Cl$_3$Br [M+H-H$_2$O]$^+$: 340.9261, found: 340.9261.
(1R)-4-bromo-6,6,6-trichloro-1-(4-methoxyphenyl)hexan-1-ol (4b)

According to the general procedure, the reaction using 1-(4-methoxyphenyl)pent-4-en-1-one 1b (38.0 mg, 0.20 mmol) as the starting material gave 54.2 mg (70%) of 4b as a colorless oil. Enantiomeric excess was established by HPLC analysis using a Chiralpak IG column, 98% ee, 99% ee (HPLC: IG, 220 nm, n-hexane/isopropanol = 90:10, flow rate 0.5 mL/min, 25 °C, tₘ (minor) = 22.38 min, tₘ (major) = 24.16 min; another isomer: tₘ (major) = 27.54 min, tₘ (minor) = 34.42 min). [α]D²² = +20.5° (c 1.0, CH₂Cl₂). The product was present as a 1:1 mixture of diastereoisomers.

1H NMR (500 MHz, CDCl₃) δ 7.22-7.19 (m, 2H), 6.83-6.81 (m, 2H), 4.64-4.58 (m, 1H), 4.31-4.26 (m, 1H), 3.73 (s, 3H), 3.39-3.34 (m, 1H), 3.15-3.10 (m, 1H), 2.18-1.78 (m, 5H).

13C NMR (125 MHz, CDCl₃) δ 159.29, 159.24, 136.3, 136.1, 127.1, 127.0, 114.00, 113.98, 97.05, 97.01, 73.6, 73.1, 62.6, 62.5, 55.3, 48.9, 48.7, 36.5, 36.3, 36.0, 35.6.

IR (film): ν (cm⁻¹) 3404, 3002, 2930, 2838, 1610, 1510, 1452, 1298, 1244, 1175, 1032, 947, 831, 779, 700, 632, 548, 420.


(1R)-4-bromo-6,6,6-trichloro-1-(4-(trifluoromethyl)phenyl)hexan-1-ol (4c)

According to the general procedure, the reaction using 1-(4-(trifluoromethyl)phenyl)pent-4-en-1-one 1c (45.6 mg, 0.20 mmol) as the starting material gave 76.5 mg (90%) of 4c as a colorless oil. Enantiomeric excess was established by HPLC analysis using a Chiralcel OJ-H column, 97% ee, 97% ee (HPLC: OJ-H, 220 nm, n-hexane/isopropanol = 98:2, flow rate 0.5 mL/min, 25 °C, tₘ (minor) = 53.50 min, tₘ (major) = 71.28 min; another isomer: tₘ (major) = 57.85 min, tₘ (minor) = 87.12 min). [α]D²² = +10.3° (c 1.0, CH₂Cl₂). The product was present as a 1:1 mixture of diastereoisomers.

1H NMR (500 MHz, CDCl₃) δ 7.63-7.62 (m, 2H), 7.50-7.47 (m, 2H), 4.86-4.81 (m, 1H), 4.41-4.33 (m, 1H), 3.48-3.43 (m, 1H), 3.23-3.18 (m, 1H), 2.33-1.91 (m, 5H).

13C NMR (125 MHz, CDCl₃) δ 148.07, 147.98, 130.08 (q, J = 32 Hz), 130.00 (q, J = 32 Hz), 126.1,
126.0, 125.61, 125.58, 125.56, 124.1 (q, J = 270 Hz), 96.95, 96.92, 73.3, 72.6, 62.6, 62.5, 48.7, 48.5, 36.8, 36.5, 35.7, 35.1.

$^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ -62.51, -62.52.

IR (film): $\nu \text{ (cm}^{-1})$ 3360, 2928, 1620, 1419, 1322, 1164, 1119, 1064, 1013, 950, 841, 795, 702, 604, 537, 480, 438, 405.

HRMS (FD, m/z) calcd for C$_{13}$H$_{13}$BrCl$_3$F$_3$O $[M]^+$: 425.9168, found: 425.9153.

### 3.2.4 Proposed mechanism for the photoredox chemistry

![Proposed mechanism for the photoredox chemistry](image)

3.3 Iridium-catalyzed asymmetric hydrogenation and sequential CF$_3$ radical addition to indoles

#### 3.3.1 Synthesis of substrates

Substituted indoles 5a-d were synthesized according to reported procedures.$^4$ The experimental data are shown below.
**tert-butyl 3-acetyl-1H-indole-1-carboxylate (5a)**

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.36 (d, $J = 7.5$ Hz, 1H), 8.19 (s, 1H), 8.10 (d, $J = 7.5$ Hz, 1H), 7.39-7.31 (m, 2H), 2.55 (s, 3H), 1.72 (s, 9H).

**methyl 3-acetyl-1H-indole-1-carboxylate (5b)**

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.39-8.36 (m, 1H), 8.25 (s, 1H), 8.18-8.15 (m, 1H), 7.44-7.34 (m, 2H), 4.12 (s, 3H), 2.57 (s, 3H).

**methyl 3-butyryl-1H-indole-1-carboxylate (5c)**

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.28-8.22 (m, 1H), 8.02-7.97 (m, 2H), 7.28-7.20 (m, 2H), 3.95 (s, 3H), 2.70 (d, $J = 7.5$ Hz, 2H), 1.74-1.62 (m, 2H), 0.91 (t, $J = 7.2$ Hz, 3H).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 196.4, 150.8, 135.3, 131.1, 127.2, 125.5, 124.4, 122.6, 120.7, 114.6, 54.2, 41.7, 17.9, 13.8.

IR (film): $\nu$ (cm$^{-1}$) 3128, 2963, 2874, 1750, 1665, 1604, 1542, 1440, 1389, 1357, 1289, 1197, 1139, 1090, 1047, 1015, 956, 925, 885, 831, 762, 676, 613, 574, 532, 423.

HRMS (APCI, m/z) calcd for C$_{14}$H$_{15}$NO$_3$H [M+H]$^+$: 246.1125, found: 246.1124.
methyl 3-acetyl-5-bromo-1H-indole-1-carboxylate (5d)

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.47 (s, 1H), 8.13 (s, 1H), 7.94 (d, $J = 8.7$ Hz, 1H), 7.44 (d, $J = 8.4$ Hz, 1H), 4.11 (s, 3H), 2.52 (s, 3H).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 193.2, 150.4, 134.0, 132.4, 128.6, 128.5, 125.2, 120.2, 118.1, 116.1, 54.6, 27.4.

IR (film): $\nu$ (cm$^{-1}$) 3125, 2957, 1738, 1657, 1544, 1436, 1365, 1258, 1223, 1186, 1160, 1050, 947, 891, 800, 622, 560, 422.

HRMS (APCI, m/z) calcd for C$_{12}$H$_{10}$BrN$_3$O$_3$H [M+H]$^+$: 295.9917, found: 295.9912.

Substituted indole 5e was synthesized according to reported procedures.$^5$ The experimental data are shown below.

**tert-butyl 3-(1-hydroxyethyl)-1H-indole-1-carboxylate (II)**

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.17 (d, $J = 8.4$ Hz, 1H), 7.72 (d, $J = 7.5$ Hz, 1H), 7.57 (s, 1H), 7.35 (t, $J = 7.5$ Hz, 1H), 7.27 (t, $J = 7.5$ Hz, 1H), 5.20 (q, $J = 6.3$ Hz, 1H), 1.78 (br s, 1H), 1.69 (s, 9H), 1.68 (d, $J = 7.2$ Hz, 3H).

### 3.3.2 General procedure

#### 3.3.2.1 General procedure for optimizing the reaction conditions for photoredox chemistry

A dried 10 mL Schlenk tube was charged with Togni’s reagent 2 (94.8 mg, 0.30 mmol), base (0.40 mmol), rac-IrS (3.8 mg, 2 mol%) and 3,5-dimethyl pyrazole (7.7 mg, 40 mol%). The tube was purged with nitrogen, then solvent was added via syringe, followed by tert-butyl 3-(1-hydroxyethyl)-1H-indole-1-carboxylate II (52.2 mg, 0.20 mmol). The reaction mixture was degassed via freeze-
pump-thaw for three cycles. After the mixture was thoroughly degassed, the vial was sealed and positioned approximately 5 cm from visible light. The reaction was stirred at room temperature for the indicated time (monitored by TLC) under nitrogen atmosphere. Afterwards, the solvent was concentrated under reduced pressure and the residue was purified by flash chromatography on silica gel (n-hexane/ethyl acetate = 15:1) to afford the product 6a.

3.3.2.2 General procedure for the sequential reactions with Λ-IrS using a single purification

A dried 5 mL tube was charged with substituted indoles 5 (0.20 mmol), Λ-IrS (3.8 mg, 2 mol%), 3,5-dimethyl pyrazole (7.7 mg, 40 mol%) and THF (2.0 mL, 0.1 M), and placed into a stainless steel pressure reactor. The reactor was refilled with H₂ and degassed for 5 cycles, and then hydrogen pressure subsequently increased to 50 bar. The reaction mixture in the reactor was stirred at room temperature for 15 h. After release of H₂, the solvent was removed under reduced pressure. Togni’s reagent 2 (94.8 mg, 0.30 mmol), 2,6-lutidine (42.8 mg, 0.40 mmol) and CH₃CN (2.0 mL, 0.1 M) were added to the residual crude material. The reaction mixture was degassed via freeze-pump-thaw for three cycles. After the mixture was thoroughly degassed, the vial was sealed and positioned approximately 5 cm from Blue LEDs (24 W). The reaction mixture was stirred at room temperature under nitrogen atmosphere until complete disappearance of the starting material (monitored by TLC), concentrated under reduced pressure and purified by flash chromatography on silica gel (n-hexane/ethyl acetate = 20:1) to afford the products 6.
3.3.3 Screening of reaction conditions

3.3.3.1 Optimization of the reaction conditions for photoredox chemistry

$$\text{II} \xrightarrow{\text{rac-IrS} (2 \text{ mol\%}), \text{light}, \text{r.t.}} \text{6a}$$

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<th>solvent</th>
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<th>yield (%)</th>
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*Reaction conditions: tert-butyl 3-(1-hydroxyethyl)-1H-indole-1-carboxylate (0.20 mmol), Togni’s reagent 2 (0.30 mmol), rac-IrS (2.0 mol%), 3,5-dimethyl pyrazole (40 mol%), base (0.40 mmol), solvent (1.0 mL or 2.0 mL), r.t., visible light.

3.3.3.2 Comparison of the reactivities between 3-acyl substituted indole and the corresponding alcohol

$$\text{II} \xrightarrow{\text{rac-IrS} (2 \text{ mol\%}), \text{light}, \text{r.t.}} \text{6a}$$

$$\text{5a} \xrightarrow{\text{rac-IrS} (2 \text{ mol\%}), \text{light}, \text{r.t.}} \text{6a}$$

*Reaction conditions: tert-butyl 3-(1-hydroxyethyl)-1H-indole-1-carboxylate or 3-acyl substituted indole (0.20 mmol), Togni’s reagent 2 (0.30 mmol), rac-IrS (2.0 mol%), 3,5-dimethyl pyrazole (40 mol%), 2,6-lutidine (0.40 mmol).
Evaluation of the sequential reactions with Λ-IrS using a single purification

Reactions conditions: Λ-IrS (2.0 mol%), 3,5-dimethyl pyrazole (40 mol%), 5a (0.20 mmol), THF (2.0 mL, 0.1 M), H₂ (50 bar), r.t., 15 h; then 2 (0.30 mmol), 2,6-lutidine (0.40 mmol), MeCN (2.0 mL, 0.1 M), r.t., Blue LEDs (24 W), 17 h.

Experimental and characterization data of products

tert-butyl (R)-3-(1-hydroxyethyl)-2-(trifluoromethyl)-1H-indole-1-carboxylate (6a)

According to the general procedure, the reaction using tert-butyl 3-acetyl-1H-indole-1-carboxylate 5a (51.8 mg, 0.20 mmol) as the starting material gave 47.4 mg (72%) of 6a as a colorless oil. Enantiomeric excess was established by HPLC analysis using a Chiralcel OD-H column, ee = 93% (HPLC: OD-H, 254 nm, n-hexane/isopropanol = 98:2, flow rate 1 mL/min, 25 °C, tᵣ (major) = 9.04 min, tᵣ (minor) = 9.87 min). [α]D²² = -7.7° (c 1.0, CH₂Cl₂).

1H NMR (500 MHz, CDCl₃) δ 8.062 (d, J = 9.0 Hz, 1H), 8.055 (d, J = 8.0 Hz, 1H), 7.35 (dt, J = 7.5, 1.0 Hz, 1H), 7.20 (t, J = 8.0 Hz, 1H), 5.48-5.44 (m, 1H), 2.08 (br s, 1H), 1.58 (s, 9H), 1.57 (d, J = 8.0 Hz, 3H).

13C NMR (125 MHz, CDCl₃) δ 149.0, 137.4, 130.3, 127.1, 125.6, 123.2, 123.0, 121.5 (q, J = 267 Hz), 120.8 (q, J = 38 Hz), 115.0, 85.5, 64.2 (q, J = 4 Hz), 27.7, 23.6.

19F NMR (282 MHz, CDCl₃) δ -53.16.

IR (film): ν (cm⁻¹) 2984, 2937, 1743, 1568, 1452, 1394, 1367, 1325, 1277, 1239, 1205, 1128, 1093, 1033, 980, 900, 870, 833, 751, 698, 610, 555, 468, 437.
HRMS (FD, $m/z$) calcd for C$_{16}$H$_{18}$F$_3$NO$_3$ [M]$^+$: 329.1239, found: 329.1226.

**methyl (R)-3-(1-hydroxyethyl)-2-(trifluoromethyl)-1H-indole-1-carboxylate (6b)**

According to the general procedure, the reaction using methyl 3-acetyl-1H-indole-1-carboxylate 5b (43.4 mg, 0.20 mmol) as the starting material gave 37.8 mg (66%) of 6b as a colorless oil. Enantiomeric excess was established by HPLC analysis using a Chiralpak AS-H column, ee = 96% (HPLC: AS-H, 220 nm, n-hexane/isopropanol = 90:10, flow rate 1 mL/min, 25 °C, $t_r$ (minor) = 6.72 min, $t_r$ (major) = 7.32 min). [α)$_{D}^{22}$ = +18.8° (c 1.0, CH$_2$Cl$_2$).

$^1$H NMR (500 MHz, CDCl$_3$) δ 8.16 (d, $J$ = 8.0 Hz, 1H), 8.10 (dd, $J$ = 8.5, 0.5 Hz, 1H), 7.44 (dt, $J$ = 7.0, 1.0 Hz, 1H), 7.30 (dt, $J$ = 7.5, 1.0 Hz, 1H), 5.58-5.54 (m, 1H), 4.05 (s, 3H), 2.17 (br s, 1H), 1.65 (d, $J$ = 6.5 Hz, 3H).

$^{13}$C NMR (125 MHz, CDCl$_3$) δ 151.0, 137.1, 131.2, 127.4, 125.8, 124.6, 123.4, 121.4 (q, $J$ = 269 Hz), 120.7 (q, $J$ = 38 Hz), 115.2, 64.2 (q, $J$ = 4 Hz), 54.3, 23.6.

$^{19}$F NMR (282 MHz, CDCl$_3$) δ -55.05.

IR (film): ν (cm$^{-1}$) 3426, 2983, 1750, 1594, 1569, 1444, 1393, 1333, 1272, 1234, 1209, 1128, 1094, 1041, 988, 940, 893, 754, 702, 635, 556, 436, 399.

HRMS (APCI, $m/z$) calcd for C$_{13}$H$_{11}$F$_3$NO$_2$ [M+H-H$_2$O]$^+$: 270.0736, found: 270.0729.

**methyl (R)-3-(1-hydroxybutyl)-2-(trifluoromethyl)-1H-indole-1-carboxylate (6c)**

According to the general procedure, the reaction using methyl 3-butyryl-1H-indole-1-carboxylate 5c (49.0 mg, 0.20 mmol) as the starting material gave 39.3 mg (62%) of 6c as a colorless oil. Enantiomeric excess was established by HPLC analysis using a Chiralpak AS-H column, ee = 96% (HPLC: AS-H, 254 nm, n-hexane/isopropanol = 95:5, flow rate 1 mL/min, 25 °C, $t_r$ (minor) = 8.27 min, $t_r$ (major) = 9.55 min). [α)$_{D}^{22}$ = +14.9° (c 1.0, CH$_2$Cl$_2$).
$^1$H NMR (500 MHz, CDCl$_3$) δ 8.06 (d, $J = 8.0$ Hz, 1H), 8.03 (d, $J = 8.5$ Hz, 1H), 7.37 (t, $J = 8.5$ Hz, 1H), 7.22 (t, $J = 8.0$ Hz, 1H), 5.30-5.27 (m, 1H), 3.98 (s, 3H), 2.03-1.96 (m, 2H), 1.77-1.70 (m, 1H), 1.52-1.42 (m, 1H), 1.34-1.25 (m, 1H), 0.87 (t, $J = 7.5$ Hz, 3H).

$^{13}$C NMR (125 MHz, CDCl$_3$) δ 151.0, 137.1, 130.5, 127.3, 126.1, 123.6, 123.4, 121.4 (q, $J = 268$ Hz), 121.2 (q, $J = 38$ Hz), 115.2, 67.7 (q, $J = 3$ Hz), 54.3, 39.5, 19.2, 13.7.

$^{19}$F NMR (282 MHz, CDCl$_3$) δ -54.18.

IR (film): $\nu$ (cm$^{-1}$) 3528, 2961, 2872, 1751, 1568, 1445, 1390, 1333, 1270, 1234, 1209, 1130, 1090, 1024, 966, 913, 857, 805, 752, 637, 580, 439, 402.

HRMS (APCI, $m/z$) calcd for C$_{15}$H$_{15}$F$_3$NO$_2$ [M+H-H$_2$O]$^+$: 298.1049, found: 298.1047.

methyl (R)-5-bromo-3-(1-hydroxyethyl)-2-(trifluoromethyl)-1H-indole-1-carboxylate (6d)

According to the general procedure, the reaction using methyl 3-acetyl-5-bromo-1H-indole-1-carboxylate 5d (59.0 mg, 0.20 mmol) as the starting material gave 38.0 mg (52%) of 6d as a colorless oil. Enantiomeric excess was established by HPLC analysis using a Chiralpak AS-H column, ee = 99% (HPLC: AS-H, 254 nm, $n$-hexane/isopropanol = 95:5, flow rate 1 mL/min, 25 °C, $t_r$ (minor) = 11.07 min, $t_r$ (major) = 15.20 min). $[\alpha]_D^{22} = +9.19^\circ$ (c 1.0, CH$_2$Cl$_2$).

$^1$H NMR (500 MHz, CDCl$_3$) δ 8.35 (d, $J = 2.0$ Hz, 1H), 7.97 (dd, $J = 9.0$, 0.5 Hz, 1H), 7.52 (dd, $J = 9.0$, 2.0 Hz, 1H), 5.55-5.50 (m, 1H), 4.05 (s, 3H), 2.18 (br s, 1H), 1.62 (d, $J = 6.5$ Hz, 3H).

$^{13}$C NMR (125 MHz, CDCl$_3$) δ 150.7, 135.8, 130.5, 130.3, 127.5, 126.1, 121.5 (q, $J = 38$ Hz), 121.1 (q, $J = 270$ Hz), 116.7, 64.1 (q, $J = 4$ Hz), 54.6, 23.8.

$^{19}$F NMR (282 MHz, CDCl$_3$) δ -54.56.

IR (film): $\nu$ (cm$^{-1}$) 3433, 3393, 3098, 2992, 2960, 2926, 2857, 1741, 1560, 1448, 1380, 1358, 1322, 1269, 1235, 1207, 1182, 1147, 1117, 1071, 1039, 941, 896, 856, 805, 760, 724, 712, 602, 564, 467, 437.

HRMS (APCI, $m/z$) calcd for C$_{13}$H$_{10}$BrF$_3$NO$_2$ [M+H-H$_2$O]$^+$: 347.9842, found: 347.9835.
3.3.5 Proposed mechanism for the photoredox chemistry

```
2 (1.5 eq.), 2,6-lutidine, CH₃CN, r.t.
Blue LEDs (24 W)
rac-IrS (2 mol%)
(40 mol%)

S26
```
4. Assignment of absolute configurations of final products

Using acetophenone as the model substrate, the $\Lambda$-IrS together with 3,5-disubstituted pyrazole catalyzed asymmetric transfer hydrogenation or asymmetric hydrogenation reaction gave the desired chiral 1-phenylethan-1-ol. The absolute configuration of the product was assigned as (R)-configuration by comparing the sign of the optical rotation and chiral HPLC retention time data synthesized here with that reported in the literature. All other products (3, 4, 6) were assigned by analogy.

**Optical rotation of (R)-1-phenylethan-1-ol:**

$[\alpha]_D^{20} = +40.4$ (c 1.0, CHCl$_3$, 96% ee)

Lit.$^6$: $[\alpha]_D^{20} = +36.0$ (c 1.0, CHCl$_3$, 97% ee for R-configuration)

**Chiral HPLC with (R)-1-phenylethan-1-ol:**

(Daicel Chiralcel OJ column, 220 nm, hexane/isopropanol = 95:5, flow rate 1.0 mL/min, 25 °C)

t$_R$ (minor) = 12.4 min, t$_R$ (major) = 14.2 min

Lit.$^6$: t$_R$ (minor) = 11.6 min, t$_R$ (major) = 13.4 min
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5. Enantioselectivities as determined by chiral HPLC

Enantiomeric purities of the reaction products were determined with a Daicel Chiralpak AD-H, AS-H, IC, IG (250 × 4.6 mm) or Daicel Chiralcel OD-H, OJ-H (250 × 4.6 mm) HPLC column on an Agilent 1200 or 1260 Series or Shimadzu Lc-2030c HPLC System using n-hexane/isopropanol as a mobile phase.
3a, 94% ee, 96% ee

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2 15.697 VV 0.2827 4264.01367 232.20432 24.7313
3 16.675 VB 0.3020 4450.57031 228.03238 25.8133
4 19.115 VB 0.3448 4386.69336 197.65157 25.4428

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S30
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4a, 95% ee, 97% ee

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6b, 96% ee

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6. NMR spectra of new compounds
Chemical Formula: C_{12}H_{11}F_{3}O
Exact Mass: 228.0762
Chemical Formula: C_{13}H_{15}F_{3}O_{2}
Exact Mass: 260.1024
Chemical Formula: C_{13}H_{12}F_{6}O
Exact Mass: 298.0792
Chemical Formula: C_{12}H_{14}BrCl_{3}O
Exact Mass: 357.9294
Chemical Formula: C_{13}H_{16}BrC\textsubscript{3}O\textsubscript{2}

Exact Mass: 387.9399
Chemical Formula: C_{14}H_{15}NO_3
Exact Mass: 245.1052
Chemical Formula: C_{14}H_{15}NO_{3}
Exact Mass: 245.1052
Chemical Formula: C_{12}H_{10}BrNO_{3}
Exact Mass: 294.9844
Chemical Formula: C_{18}H_{18}F_{3}NO_{3}

Exact Mass: 329.1239
Chemical Formula: C₁₁H₁₂F₃NO₃
Exact Mass: 287.0769
Chemical Formula: C_{13}H_{12}F_{3}NO_{3}
Exact Mass: 287.0769
Chemical Formula: C₁₅H₁₅F₃NO₃
Exact Mass: 315.1082

[Diagram of a molecular structure with peaks at specific ppm values]

IH
F1: 500.130
F2: 1.000

SW1: 5000
QF1: 2249.9

P: 10.0 us
PD: 1.0 sec
NA: 16
LB: 0.0

Nrets: S161212_38654_zed426d-3 2.1
Chemical Formula: C$_{16}$H$_{18}$F$_3$NO$_3$

Exact Mass: 315.1082
Chemical Formula: C_{13}H_{17}BrF_{3}NO_{3}
Exact Mass: 364.9874
7. References


