Visible-light photoredox catalyzed hydroacylation of electron-deficient alkenes: carboxylic anhydride as acyl radical source

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1. General Information

**General Information.** Proton nuclear magnetic resonance (¹H-NMR) spectra and carbon nuclear magnetic resonance (¹³C-NMR) spectra were recorded on a Bruker AV-400 spectrometer (400 MHz and 100 MHz). Chemical shifts for protons are reported in parts per million downfield from tetramethylsilane or referenced to residual solvent. Chemical shifts for carbon are reported in parts per million downfield from tetramethylsilane or referenced to residual solvent. ¹⁹F-NMR spectra were recorded on a Bruker AV-400 spectrometer (376 MHz). Data are represented as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants in Hertz (Hz). High resolution mass spectrometry (ESI) were carried out using a Waters Quatro Macro triple quadrupole mass spectrometer Mass spectra (EI) were measured on a Waters Micromass GCT spectrometer. Melting points were measured on a XT3A apparatus.

**Starting Materials.** Unless otherwise noted, all reactions were performed under nitrogen atmosphere in Schlenk tube, all chemicals were purchased from commercial sources and used as received. All other solvents, including those for NMR analysis, were used without further purification.

2. Synthesis of Substrates and Photocatalysts

**Anhydrides:** Benzoic anhydride is commercially available, other symmetric anhydrides were synthesized according to a modified literature procedure,¹ mixed anhydride 5a was synthesized according to a literature procedure.²

\[
\begin{align*}
\text{CH}_2\text{Cl}_2, \text{rt}, 1 \text{ h} & \quad \text{SOCl}_2 (0.5 \text{ equiv}) \quad \text{Et}_3\text{N} (1.25 \text{ equiv}) \\
\text{Ar-OOAr} & \quad \text{Ar-OOC-OOAr}
\end{align*}
\]

4-Methylbenzoic acid (20 mmol, 2.72g) and triethylamine (25 mmol, 2.53g) were suspended in CH₂Cl₂ (50 ml), and a CH₂Cl₂ solution (10 ml) of SOCl₂ (10mmol, 1.19g) was added dropwise, followed by stirring for 1 h at room temperature. The reaction solution was then diluted with CH₂Cl₂ and washed with sat. NH₄Cl. The organic layer was dried over anhydrous sodium sulfate, and concentrated under reduced pressure and the crude residue was purified by flash chromatography (CH₂Cl₂ as eluent) to yield 4-methylbenzoic anhydride (2.5g, 95% yield).

**Michael acceptors:** 2b, 2c, 2f, 2i, 2j, 2k, 2l, 2m are commercially available, 2a, 2d, 2g were synthesized according to a literature procedure³, 2e was synthesized according to a literature procedure⁴, 2h was synthesized according to a literature procedure⁵, 2n, 2o were synthesized according to a literature procedure.⁶

**Photocatalysts:** All photocatalysts were synthesized according to literature procedures, Ru(bpy)₃Cl₂⁷, Ir(ppy)₃(dtbbpy)PF₆,⁸ Ir[(dF(CF₃)ppy)₃(dtbbpy)]PF₆⁹, fac-Ir(ppy).¹⁰
3. Optimization Studies

3.1 Solvent Screening\(^a\)

![Chemical Structures]

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<tr>
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</tr>
<tr>
<td>2</td>
<td>CH(_3)CN</td>
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</tr>
<tr>
<td>3</td>
<td>Acetone</td>
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</tr>
<tr>
<td>4</td>
<td>CH(_2)Cl(_2)</td>
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</tr>
<tr>
<td>5</td>
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<td>6</td>
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<td>7</td>
<td>DMSO</td>
<td>trace</td>
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<td>8</td>
<td>CH(_2)Cl(_2)/H(_2)O=1mL/1mL</td>
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</tr>
<tr>
<td>9(^c)</td>
<td>CH(_2)Cl(_2)</td>
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</tr>
<tr>
<td>10(^d)</td>
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<tr>
<td>11(^e)</td>
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</tr>
<tr>
<td>12(^f)</td>
<td>CH(_2)Cl(_2)</td>
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\(^a\)Reactions performed on a 0.2 mmol scale. \(^b\)Isolated yield. \(^c\)The reaction was carried out using 32 W CFL as light source. \(^d\)The reaction was carried out under air. \(^e\)The reaction concentration was 0.05 M. \(^f\)The reaction concentration was 0.2 M.

3.2 Study of the amount of Hantzsch ester and \(i\)-Pr\(_2\)NEt\(^a\)

![Chemical Structures]
<table>
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<tr>
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<th>i-Pr₂NEt (equiv)</th>
<th>yield (%)(^b)</th>
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<td>7</td>
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<td>1.0</td>
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<td>10</td>
<td>1.5</td>
<td>5.0</td>
<td>69</td>
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</tbody>
</table>

\(^a\)Reactions performed on a 0.2 mmol scale. \(^b\)Isolated yield. \(^c\)Reaction time 24 h.

3.3 Study of the ratio of substrates\(^a\)

\[
\begin{align*}
\text{1a} & \quad \text{2a} \\
x \text{ equiv} & \quad y \text{ equiv}
\end{align*}
\]

\[
\begin{align*}
\text{fac-Ir(ppy)}_3 \text{ (1 mol %)} & \quad \text{Hantzsch ester (1.5 equiv)} \\
& \quad \text{i-Pr}_2\text{NEt (2.0 equiv)} \\
& \quad \text{CH}_2\text{Cl}_2 (0.1 \text{ M}) \\
& \quad \text{N}_2, \text{ blue LEDs, 3 h}
\end{align*}
\]

<table>
<thead>
<tr>
<th>entry</th>
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<th>y</th>
<th>yield (%)(^b)</th>
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<tr>
<td>6</td>
<td>1.0</td>
<td>2.0</td>
<td>47</td>
</tr>
</tbody>
</table>

\(^a\)Reactions performed on a 0.2 mmol scale. \(^b\)Isolated yield. \(^c\)3.0 equiv i-Pr₂NEt was added.

3.4 Catalyst Screening and loadings\(^a\)
4. General Procedure and Characterization of Products

4.1 General Procedure A
Symmetric carboxylic anhydride 1 (0.6 mmol, 3.0 equiv), Michael acceptor 2 (0.2 mmol, 1.0 equiv), \( \text{fac-Ir(ppy)}_3 \) (2 \( \mu \text{mol, 1.3 mg, 0.01 equiv} \)), Hantzsch ester (0.3 mmol, 76 mg, 1.5 equiv), \( i-\text{Pr}_2\text{NEt} \) (0.6 mmol, 77.5 mg, 3.0 equiv) and solvent CH\(_2\)Cl\(_2\) (2 mL) were added to a 10 mL transparent Schlenk tube charged with a magnetic stir bar. The resulting solution was degassed and backfilled with nitrogen via the freeze-pump-thaw procedure for three cycles. The reaction tube was then placed in an irradiation apparatus (at approximately 2 cm away from the light source) equipped with a 24 W blue light LED strip (\( \lambda_{\text{max}} = 453 \text{ nm} \)) and stirred at room temperature until TLC showed consumption of starting material. The reaction mixture was concentrated under reduced pressure and the crude residue was purified by flash chromatography to yield corresponding addition products (3).

4.2 General Procedure B

\[
\begin{align*}
\text{CO}_2\text{Ar} + \text{R}_1\text{R}_2\text{EWG} & \rightarrow \text{ArCO}\text{R}_1\text{R}_2\text{EWG} \\
\text{ClCO}_2\text{Bu} & (3.0 \text{ equiv}) \\
\text{fac-Ir(ppy)}_3 & (1 \text{ mol \%}) \\
\text{Hantzsch ester} & (1.5 \text{ equiv}) \\
i-\text{Pr}_2\text{NEt} & (6.0 \text{ equiv}) \\
\text{CH}_2\text{Cl}_2 & (0.1 \text{ M}) \\
\text{N}_2, \text{ blue LEDs, 3 h} &
\end{align*}
\]

Carboxylic acid 4 (0.6 mmol, 3.0 equiv), Michael acceptor 2 (0.2 mmol, 1.0 equiv), \( \text{fac-Ir(ppy)}_3 \) (2 \( \mu \text{mol, 1.3 mg, 0.01 equiv} \)), Hantzsch ester (0.3 mmol, 76 mg, 1.5 equiv), \( i-\text{Pr}_2\text{NEt} \) (1.2 mmol, 155.1 mg, 6.0 equiv), isobutyl chloroformate (0.6 mmol, 3.0 equiv) and solvent CH\(_2\)Cl\(_2\) (2 mL) were added to a 10 mL transparent Schlenk tube charged with a magnetic stir bar. The resulting solution was degassed and backfilled with nitrogen via the freeze-pump-thaw procedure for three cycles. The reaction tube was then placed in an irradiation apparatus (at approximately 2 cm away from the light source) equipped with a 24 W blue light LED strip (\( \lambda_{\text{max}} = 453 \text{ nm} \)) and stirred at room temperature until TLC showed consumption of starting material. The reaction mixture was concentrated under reduced pressure and the crude residue was purified by flash chromatography to yield corresponding addition products (3).

4.3 Gram-Scale Reaction

\[
\begin{align*}
\text{PhCO}_2\text{Ar} + \text{CH}_2=\text{CHOBn} & \rightarrow \text{PhCOCH}_2\text{OBn} \\
\text{ClCO}_2\text{Bu} & (3.0 \text{ equiv}) \\
\text{fac-Ir(ppy)}_3 & (1 \text{ mol \%}) \\
\text{Hantzsch ester} & (1.5 \text{ equiv}) \\
i-\text{Pr}_2\text{NEt} & (6.0 \text{ equiv}) \\
\text{CH}_2\text{Cl}_2 & (0.1 \text{ M}) \\
\text{N}_2, \text{ blue LEDs, 3 h} &
\end{align*}
\]
According to General Procedure B, benzoic acid 4a (2.93 g, 24 mmol), benzyl acrylate 2a (1.30 g, 8 mmol), *fac*-Ir(ppy)$_3$ (52.4 mg, 0.08 mmol), *i*-Pr$_2$NEt (6.2 g, 48 mmol), Hantzsch ester (3.04 g, 12 mmol), isobutyl chloroformate (3.28 g, 24 mmol) and solvent CH$_2$Cl$_2$ (80 mL) were added to a 200 mL transparent Schlenk flask charged with a magnetic stir bar. The resulting solution was degassed and backfilled with nitrogen via the freeze-pump-thaw procedure for three cycles. The reaction flask was then placed in an irradiation apparatus (at approximately 2 cm away from the light source) equipped with a 24 W blue light LED strip ($\lambda_{\text{max}}$= 453 nm) and stirred at room temperature for 3 h. The reaction mixture was then concentrated under reduced pressure and the crude residue was purified by flash chromatography on silica gel (Petroleum Ether/CH$_2$Cl$_2$, 2:1) to yield desired product 3a (1.64 g, 76%) as colorless oil.

### 4.4 Characterization of Products

**Benzyl 4-oxo-4-phenylbutanoate (3a).** The product was obtained in 80% yield, 43.0 mg (78% yield, 41.9 mg from procedure B), colorless oil; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.98 (d, $J$ = 7.4 Hz, 2H), 7.56 (t, $J$ = 7.4 Hz, 1H), 7.46 (t, $J$ = 7.6 Hz, 2H), 7.38-7.29 (m, 5H), 5.15 (s, 2H), 3.33 (t, $J$ = 6.6 Hz, 2H), 2.82 (t, $J$ = 6.6 Hz, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 198.1, 172.9, 136.7, 136.3, 136.0, 133.3, 128.7, 128.6, 128.3, 128.1, 128.3, 128.1, 66.6, 33.4, 28.4; HRMS (ESI) calcd for C$_{17}$H$_{17}$O$_3$ (M+H) 269.1178, found 269.1182.

**Ethyl 4-oxo-4-phenylbutanoate (3b).** The product was obtained in 73% yield, 30.1 mg, colorless oil; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.99 (d, $J$ = 7.5 Hz, 2H), 7.57 (t, $J$ = 7.4 Hz, 1H), 7.47 (t, $J$ = 7.6 Hz, 2H), 4.16 (q, $J$ = 7.1 Hz, 2H), 3.32 (t, $J$ = 6.6 Hz, 2H), 2.76 (t, $J$ = 6.6 Hz, 2H), 1.27 (t, $J$ = 7.1 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 198.3, 173.0, 136.7, 133.3, 128.7, 128.1, 60.8, 33.5, 28.4, 14.3; HRMS (ESI) calcd for C$_{12}$H$_{15}$O$_3$ (M+H) 207.1021, found 207.1025.

**Tert-butyl 4-oxo-4-phenylbutanoate (3c).** The product was obtained in 70% yield, 32.8
Benzyl 2-methyl-4-oxo-4-phenylbutanoate (3d). The product was obtained in 57% yield, 32.2 mg, colorless oil; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 7.99-7.92\) (m, 2H), 7.56 (t, \(J = 7.4\) Hz, 1H), 7.45 (t, \(J = 7.6\) Hz, 1H), 7.37-7.26 (m, 5H), 5.14 (q, \(J = 12.4\) Hz, 2H), 3.50 (dd, \(J = 17.7, 7.9\) Hz, 1H), 3.28-3.13 (m, 1H), 3.04 (dd, \(J = 17.7, 5.5\) Hz, 1H), 1.30 (d, \(J = 7.2\) Hz, 3H); \(^1^3\)C NMR (100 MHz, CDCl\(_3\)): \(\delta 198.1, 175.9, 136.8, 136.2, 133.4, 128.7, 128.6, 128.2, 128.2, 66.6, 42.0, 35.2, 17.4\); HRMS (ESI) calcd for C\(_{18}\)H\(_{19}\)O\(_3\) (M+H) 283.1334, found 283.1330.

Methyl 4-oxo-2,4-diphenylbutanoate (3e). The product was obtained in 60% yield, 32.2 mg (58% yield, 31.1 mg from procedure B), white solid, mp 89-90 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 7.97\) (dd, \(J = 8.4, 1.3\) Hz, 2H), 7.60-7.52 (m, 1H), 7.45 (dd, \(J = 10.8, 4.4\) Hz, 2H), 7.38-7.26 (m, 5H), 4.30 (dd, \(J = 10.3, 4.1\) Hz, 1H), 3.95 (dd, \(J = 18.0, 10.3\) Hz, 1H), 3.69 (s, 3H), 3.27 (dd, \(J = 18.0, 4.1\) Hz, 1H); \(^1^3\)C NMR (100 MHz, CDCl\(_3\)): \(\delta 197.8, 174.0, 138.5, 136.5, 133.5, 129.1, 128.7, 128.2, 128.0, 127.7, 52.5, 46.5, 42.9\); HRMS (ESI) calcd for C\(_{17}\)H\(_{17}\)O\(_3\) (M+H) 269.1178, found 269.1175.

Methyl 4-oxo-2,4-diphenylbutanoate (3f). The product was obtained in 72% yield, 29.7 mg, colorless oil; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 7.99\) (dd, \(J = 5.2, 3.4\) Hz, 1H), 7.60-7.54 (m, 1H), 7.48 (dd, \(J = 10.4, 4.7\) Hz, 1H), 4.06-3.87 (m, 1H), 3.65 (s, 2H), 2.97 (dd, \(J = 16.8, 8.4\) Hz, 1H), 2.47 (dd, \(J = 16.8, 5.8\) Hz, 1H), 1.23 (d, \(J = 7.2\) Hz, 1H); \(^1^3\)C NMR (100 MHz, CDCl\(_3\)): \(\delta 202.9, 173.0, 136.0, 133.2, 128.8, 128.6, 51.9, 37.4, 18.0\); HRMS (ESI) calcd for C\(_{17}\)H\(_{17}\)O\(_3\) (M+H) 207.1021, found 207.1024.
Phenethyl 3-methyl-4-oxo-4-phenylbutanoate (3g). The product was obtained in 68% yield, 40.3 mg, colorless oil; $^1$H NMR (400 MHz, CDCl$_3$): δ 7.97 (d, $J = 7.3$ Hz, 2H), 7.57 (t, $J = 7.4$ Hz, 1H), 7.47 (t, $J = 7.6$ Hz, 2H), 7.28 (dd, $J = 12.6$, 5.1 Hz, 2H), 7.20 (dd, $J = 17.2$, 7.1 Hz, 3H), 4.27 (t, $J = 7.1$ Hz, 2H), 4.02-3.80 (m, 1H), 3.03-2.76 (m, 3H), 2.44 (dd, $J = 16.8$, 5.8 Hz, 1H), 1.20 (d, $J = 7.2$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 202.8, 172.4, 137.9, 136.0, 133.2, 129.0, 128.8, 128.6, 128.6, 126.7, 65.2, 37.6, 37.3, 35.2, 18.0; HRMS (ESI) calcd for C$_{17}$H$_{17}$O$_3$ (M+H) 297.1491, found 297.1493.

N-benzyl-4-oxo-4-phenylbutanamide (3h). The product was obtained in 49% yield, 26.2 mg (52% yield, 27.8 mg from procedure B), white solid, mp 111-112 °C; $^1$H NMR (400 MHz, CDCl$_3$): δ 8.01-7.92 (m, 2H), 7.59-7.50 (m, 1H), 7.48-7.40 (m, 2H), 7.34-7.20 (m, 5H), 6.40 (s, 1H), 4.41 (d, $J = 5.8$ Hz, 1H), 3.35 (t, $J = 6.6$ Hz, 1H), 2.64 (t, $J = 6.6$ Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 199.2, 172.1, 138.4, 136.6, 133.3, 128.7, 128.2, 127.8, 127.4, 43.7, 34.1, 30.2; HRMS (ESI) calcd for C$_{17}$H$_{18}$NO$_2$ (M+H) 268.1338, found 268.1339.

N,N-dimethyl-4-oxo-4-phenylbutanamide (3i). The product was obtained in 48% yield, 19.7 mg, colorless oil; $^1$H NMR (400 MHz, CDCl$_3$): δ 8.05-7.99 (m, 2H), 7.59-7.52 (m, 1H), 7.49-7.43 (m, 2H), 3.35 (t, $J = 6.6$ Hz, 2H), 3.09 (s, 3H), 2.96 (s, 3H), 2.78 (t, $J = 6.6$ Hz, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 199.3, 171.8, 136.9, 133.0, 128.5, 128.1, 37.2, 35.6, 33.7, 27.3; HRMS (ESI) calcd for C$_{12}$H$_{16}$NO$_2$ (M+H) 206.1181, found 206.1185.

1-phenyl-3-(phenylsulfonyl)propan-1-one (3j). The product was obtained in 73% yield, 40.0 mg, white solid, mp 99-100 °C; $^1$H NMR (400 MHz, CDCl$_3$): δ 7.94 (dd, $J = 14.8$, 7.4 Hz, 4H), 7.68 (t, $J = 7.4$ Hz, 1H), 7.59 (dd, $J = 9.6$, 5.5 Hz, 3H), 7.48 (t, $J = 7.7$ Hz, 2H), 3.61-3.46 (m, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 195.6, 139.1, 135.9, 134.1, 133.9, 129.6, 127.8, 127.4, 43.7, 34.1, 30.2; HRMS (ESI) calcd for C$_{17}$H$_{17}$O$_3$ (M+H) 297.1491, found 297.1493.
128.9, 128.2, 128.1, 51.1, 31.5; HRMS (ESI) calcd for C$_{15}$H$_{13}$O$_3$S (M+H) 275.0742, found 275.0740.

\[
\text{Ph} \quad \text{O} \quad \text{O}
\]

**2-methyl-1-phenylpentane-1,4-dione (3k).** The product was obtained in 40% yield, 15.2 mg (61% yield, 23.2 mg from procedure B), colorless oil; $^1$H NMR (400 MHz, CDCl$_3$): δ 7.98 (dd, $J = 5.2$, 3.3 Hz, 2H), 7.61-7.52 (m, 1H), 7.51-7.42 (m, 2H), 3.97 (dqd, $J = 14.4$, 7.2, 5.1 Hz, 1H), 3.17 (dd, $J = 18.0$, 8.5 Hz, 1H), 2.55 (dd, $J = 18.0$, 5.0 Hz, 1H), 2.18 (s, 3H), 1.19 (d, $J = 7.2$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 207.2, 203.4, 136.1, 133.1, 128.8, 128.6, 47.0, 36.3, 30.2, 17.9; HRMS (ESI) calcd for C$_{15}$H$_{15}$O$_3$ (M+H) 275.0742, found 275.0740.

\[
\text{Ph} \quad \text{C} \quad \text{O}
\]

**3-benzoylecyclohexan-1-one (3l).** The product was obtained in 67% yield, 27.1 mg, colorless oil; $^1$H NMR (400 MHz, CDCl$_3$): δ 7.99-7.89 (m, 2H), 7.60 (ddd, $J = 8.6$, 2.3, 1.1 Hz, 1H), 7.48 (dd, $J = 10.6$, 4.7 Hz, 2H), 3.84 (tt, $J = 10.5$, 4.2 Hz, 1H), 2.72 (dd, $J = 14.6$, 10.7 Hz, 1H), 2.53-2.37 (m, 3H), 2.11 (dd, $J = 9.9$, 4.8 Hz, 2H), 1.95-1.73 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 210.4, 203.4, 136.1, 133.1, 128.5, 47.0, 36.3, 30.2, 17.9; HRMS (ESI) calcd for C$_{13}$H$_{15}$O$_2$ (M+H) 203.1072, found 203.1073.

\[
\text{Ph} \quad \text{C} \quad \text{O}
\]

**3-benzoylecyclopentan-1-one (3m).** The product was obtained in 87% yield, 32.7 mg, colorless oil; $^1$H NMR (400 MHz, CDCl$_3$): δ 8.01 (d, $J = 7.3$ Hz, 2H), 7.62 (t, $J = 7.4$ Hz, 1H), 7.51 (t, $J = 7.6$ Hz, 2H), 4.14 (p, $J = 7.5$ Hz, 1H), 2.72 (dd, $J = 18.4$, 7.9 Hz, 1H), 2.53-2.09 (m, 5H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 217.1, 200.4, 135.7, 133.7, 129.0, 128.5, 45.2, 43.2, 41.1, 28.5, 24.9; HRMS (ESI) calcd for C$_{13}$H$_{13}$O$_2$ (M+H) 189.0916, found 189.0912.

\[
\text{O} \quad \text{CO}_2\text{Me} \quad \text{Ph} \quad \text{O} \quad \text{CO}_2\text{Me}
\]

**Dimethyl 2-(1-oxo-1-phenylheptan-2-yl)malonate (3n).** The product was obtained in 66%
yield, 42.3 mg, colorless oil; $^1$H NMR (400 MHz, CDCl$_3$): δ 8.01 (d, $J = 7.3$ Hz, 2H), 7.58 (t, $J = 7.4$ Hz, 1H), 7.49 (t, $J = 7.6$ Hz, 2H), 4.24 (dt, $J = 11.5$, 5.9 Hz, 1H), 4.09 (d, $J = 10.9$ Hz, 1H), 3.80 (s, 3H), 3.64 (s, 3H), 1.66–1.54 (m, 2H), 1.27-1.01 (m, 6H), 0.77 (t, $J = 6.8$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 201.9, 169.3, 169.0, 137.0, 133.3, 128.8, 128.6, 53.7, 52.8, 45.3, 31.9, 30.7, 25.6, 22.3, 13.9; HRMS (ESI) calcd for C$_{18}$H$_{25}$O$_5$ (M+H) 321.1702, found 321.1700.

**Dimethyl 2-(1-oxo-1,4-diphenylbutan-2-yl)malonate (3o).** The product was obtained in 68% yield, 48.2 mg, colorless oil; $^1$H NMR (400 MHz, CDCl$_3$): δ 7.96 (dd, $J = 5.2$, 3.3 Hz, 2H), 7.61-7.55 (m, 1H), 7.46 (dd, $J = 10.5$, 4.8 Hz, 2H), 7.26-7.12 (m, 3H), 7.02-6.97 (m, 2H), 4.37-4.25 (m, 1H), 4.17 (d, $J = 10.9$ Hz, 1H), 3.80 (s, 3H), 3.64 (s, 3H), 2.54 (ddd, $J = 13.8$, 9.6, 7.1 Hz, 1H), 2.39 (ddd, $J = 13.8$, 9.9, 6.9 Hz, 1H), 2.02–1.85 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 201.6, 169.2, 168.9, 140.9, 136.8, 133.4, 128.8, 128.7, 128.5, 128.4, 126.2, 53.6, 52.9, 44.9, 32.4, 32.3; HRMS (ESI) calcd for C$_{21}$H$_{23}$O$_5$ (M+H) 355.1545, found 355.1548.

**Benzyl 4-oxo-4-(p-tolyl)butanoate (3p).** The product was obtained in 71% yield, 40.1 mg, white solid, mp 51-52 °C; $^1$H NMR (400 MHz, CDCl$_3$): δ 7.87 (d, $J = 8.1$ Hz, 2H), 7.39-7.19 (m, 7H), 5.14 (s, 2H), 3.30 (t, $J = 6.7$ Hz, 2H), 2.81 (t, $J = 6.7$ Hz, 2H), 2.40 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 197.7, 172.8, 144.0, 136.0, 134.1, 129.3, 128.6, 128.2, 66.5, 33.3, 28.4, 21.7; HRMS (ESI) calcd for C$_{18}$H$_{19}$O$_3$ (M+H) 283.1334, found 283.1330.

**Benzyl 4-oxo-4-(m-tolyl)butanoate (3q).** The product was obtained in 73% yield, 41.2 mg, colorless oil; $^1$H NMR (400 MHz, CDCl$_3$): δ 7.77 (d, $J = 8.9$ Hz, 2H), 7.42-7.28 (m, 7H), 5.14 (s, 2H), 3.31 (t, $J = 6.6$ Hz, 2H), 2.81 (t, $J = 6.6$ Hz, 2H), 2.40 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 198.3, 172.9, 138.5, 136.6, 136.0, 134.1, 128.7, 128.6, 128.6, 128.3,
125.3, 66.6, 33.5, 28.4, 21.4; HRMS (ESI) calcd for C_{18}H_{19}O_3 (M+H) 283.1334, found 283.1332.

Benzyl 4-(4-methoxyphenyl)-4-oxobutanoate (3r). The product was obtained in 58% yield, 34.6 mg, colorless oil; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta \) 8.02-7.89 (m, 2H), 7.35 (dd, \(J = 7.4, 4.2\) Hz, 5H), 6.97-6.87 (m, 2H), 5.15 (s, 2H), 3.86 (s, 3H), 3.28 (t, \(J = 6.7\) Hz, 2H), 2.81 (t, \(J = 6.7\) Hz, 2H); \(^1^3\)C NMR (100 MHz, CDCl\(_3\)): \(\delta \) 196.6, 173.0, 163.7, 136.1, 130.4, 129.8, 128.7, 128.3, 113.9, 66.6, 55.6, 33.1, 28.5; HRMS (ESI) calcd for C_{18}H_{19}O_4 (M+H) 299.1283, found 299.1285.

Benzyl 4-(4-fluorophenyl)-4-oxobutanoate (3s). The product was obtained in 70% yield, 40.1 mg, yellow solid, mp 57-58 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta \) 8.04-7.94 (m, 2H), 7.40-7.26 (m, 5H), 7.16-7.07 (m, 2H), 5.14 (s, 2H), 3.29 (t, \(J = 6.6\) Hz, 2H), 2.82 (t, \(J = 6.6\) Hz, 2H); \(^1^3\)C NMR (100 MHz, CDCl\(_3\)): \(\delta \) 196.5, 172.8, 165.9 (d, \(J = 254.8\) Hz), 136.0, 133.1 (d, \(J = 3.0\) Hz), 130.8 (d, \(J = 9.3\) Hz), 128.7, 128.3, 128.3, 115.8 (d, \(J = 21.9\) Hz), 66.6, 33.3, 28.3; \(^1^9\)F NMR (376 MHz, CDCl\(_3\)): \(\delta \) -105.0 (m, 1F); HRMS (ESI) calcd for C_{17}H_{16}BrO_3 (M+H) 286.1005, found 286.1001.

Benzyl 4-(4-chlorophenyl)-4-oxobutanoate (3t). The product was obtained in 73% yield, 44.2 mg, yellow solid, mp 77-79 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta \) 7.90 (d, \(J = 8.5\) Hz, 2H), 7.42 (d, \(J = 8.5\) Hz, 2H), 7.39-7.26 (m, 5H), 5.14 (s, 2H), 3.28 (t, \(J = 6.6\) Hz, 2H), 2.81 (t, \(J = 6.6\) Hz, 2H); \(^1^3\)C NMR (100 MHz, CDCl\(_3\)): \(\delta \) 196.9, 172.7, 139.8, 135.9, 135.0, 129.6, 129.0, 128.7, 128.3, 128.3, 66.7, 33.4, 28.3; HRMS (ESI) calcd for C_{17}H_{16}ClO_3 (M+H) 303.0788, found 303.0787.
Benzyl 4-(4-bromophenyl)-4-oxobutanoate (3u). The product was obtained in 42% yield, 29.2 mg, yellow solid, mp 83-84 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): δ 7.86-7.80 (m, 2H), 7.63-7.57 (m, 2H), 7.39-7.27 (m, 5H), 5.14 (s, 2H), 3.28 (t, \(J = 6.6\) Hz, 2H), 2.82 (t, \(J = 6.6\) Hz, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): δ 197.2, 172.7, 135.9, 135.4, 132.1, 129.7, 128.7, 128.5, 128.4, 128.3, 66.7, 33.4, 28.3; HRMS (ESI) calcd for C\(_{17}\)H\(_{16}\)BrO\(_3\) (M+H) 347.0283, found 347.0284.

Benzyl 4-(2-bromophenyl)-4-oxobutanoate (3v). The product was obtained in 48% yield, 33.3 mg, yellow oil; \(^1\)H NMR (400 MHz, CDCl\(_3\)): δ 7.60 (dd, \(J = 7.9, 1.1\) Hz, 1H), 7.44 (dd, \(J = 7.6, 1.8\) Hz, 1H), 7.39-7.26 (m, 7H), 5.15 (s, 2H), 3.25 (t, \(J = 6.5\) Hz, 2H), 2.83 (t, \(J = 6.5\) Hz, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): δ 201.9, 172.3, 141.3, 135.8, 133.7, 131.7, 128.7, 128.6, 128.3, 127.4, 118.6, 66.6, 37.4, 28.5; HRMS (ESI) calcd for C\(_{17}\)H\(_{16}\)BrO\(_3\) (M+H) 347.0283, found 347.0281.

Benzyl 4-(3-bromo-5-fluorophenyl)-4-oxobutanoate (3w). The product was obtained in 72% yield, 52.6 mg, yellow oil; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(^1\)H NMR (400 MHz, CDCl\(_3\)): δ 7.89 (t, \(J = 1.6\) Hz, 1H), 7.58 (ddd, \(J = 8.8, 2.4, 1.4\) Hz, 1H), 7.44 (ddd, \(J = 7.7, 2.4, 1.7\) Hz, 1H), 7.39-7.30 (m, 5H), 5.14 (s, 2H), 3.25 (t, \(J = 6.5\) Hz, 2H), 2.82 (t, \(J = 6.5\) Hz, 2H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): δ 195.5 (d, \(J = 2.1\) Hz), 172.3, 162.6 (d, \(J = 252.9\) Hz), 139.5 (d, \(J = 6.6\) Hz), 135.7, 128.6, 128.3, 128.2, 127.2 (d, \(J = 3.3\) Hz), 123.6 (d, \(J = 24.6\) Hz), 123.2 (d, \(J = 8.9\) Hz), 113.9 (d, \(J = 22.4\) Hz), 66.7, 33.5, 28.1; \(^{19}\)F NMR (376 MHz, CDCl\(_3\)): δ -109.04 – -109.24 (m, 1F); HRMS (ESI) calcd for C\(_{17}\)H\(_{15}\)BrFO\(_3\) (M+H) 365.0189, found 365.0186.

Benzyl 4-(2,4-dichlorophenyl)-4-oxobutanoate (3x). The product was obtained in 79% yield, 53.3 mg, yellow oil; \(^1\)H NMR (400 MHz, CDCl\(_3\)): δ 7.48 (d, \(J = 8.3\) Hz, 1H), 7.42 (d, \(J = 1.9\) Hz, 1H), 7.39-7.26 (m, 6H), 5.13 (s, 2H), 3.40-3.13 (m, 2H), 2.92-2.57 (m, 2H);
\[^{13}\text{C} \text{NMR (100 MHz, CDCl}_3\]: \delta 199.9, 172.4, 137.7, 137.1, 135.9, 132.2, 130.6, 130.6,
128.7, 128.4, 128.3, 127.5, 66.7, 37.7, 28.7; HRMS (ESI) calcd for C_{17}H_{15}Cl_2O_3 (M+H) 337.0398, found 337.0395.}

**Benzyl 4-oxo-4-(4-(trifluoromethyl)phenyl)butanoate (3y).** The product was obtained in 75% yield, 50.4 mg, white solid, mp 89-90 °C; \(^1\text{H} \text{NMR (400 MHz, CDCl}_3\]: \delta 8.07 (d, \(J = 8.1\) Hz, 2H), 7.73 (d, \(J = 8.2\) Hz, 2H), 7.40-7.27 (m, 5H), 5.15 (s, 2H), 3.34 (t, \(J = 6.5\) Hz, 2H), 2.85 (t, \(J = 6.5\) Hz, 2H); \(^{13}\text{C} \text{NMR (100 MHz, CDCl}_3\]: \delta 197.3, 172.6, 139.3, 135.9, 134.7 (q, \(J = 32.7\) Hz), 128.7, 128.5, 128.4, 128.4, 125.8 (q, \(J = 3.7\) Hz), 123.7 (d, \(J = 272.7\) Hz), 66.8, 33.8, 28.3; \(^{19}\text{F} \text{NMR (376 MHz, CDCl}_3\]: \delta -63.1 (s, 3F); HRMS (ESI) calcd for C_{17}H_{16}BrO_3 (M+H) 337.1054, found 337.1052.

\[\begin{align*}
\text{O} & \quad \text{F}_3\text{C} \\
\text{O} & \quad \text{OBn} \\
\text{F}_3\text{C} & \quad \text{OBn}
\end{align*}\]

**Benzyl 4-(naphthalen-2-yl)-4-oxobutanoate (3z).** The product was obtained in 79% yield, 50.3 mg, white solid, mp 74-76 °C; \(^1\text{H} \text{NMR (400 MHz, CDCl}_3\]: \delta 8.49 (s, 1H), 8.02 (dd, \(J = 8.6\), 1.7 Hz, 1H), 7.94 (d, \(J = 8.0\) Hz, 1H), 7.90-7.82 (m, 2H), 7.56 (dd, \(J = 19.8, 8.1, 6.9, 1.3\) Hz, 2H), 7.41-7.26 (m, 5H), 5.16 (s, 2H), 3.45 (t, \(J = 6.7\) Hz, 2H), 2.87 (t, \(J = 6.7\) Hz, 2H); \(^{13}\text{C} \text{NMR (100 MHz, CDCl}_3\]: \delta 198.0, 172.9, 136.0, 135.7, 134.0, 132.6, 129.8, 129.7, 128.6, 128.5, 128.3, 127.8, 126.9, 123.8, 66.6, 33.5, 28.5; HRMS (ESI) calcd for C_{21}H_{19}O_3 (M+H) 319.1334, found 319.1330.

\[\begin{align*}
\text{O} & \quad \text{OBn} \\
\text{O} & \quad \text{OBn} \\
\text{O} & \quad \text{OBn}
\end{align*}\]

**Benzyl 4-(furan-2-yl)-4-oxobutanoate (3ab).** The product was obtained in 62% yield, 32.0 mg, white solid, mp 49-50 °C; \(^1\text{H} \text{NMR (400 MHz, CDCl}_3\]: \delta 7.58 (dd, \(J = 1.6, 0.6\) Hz, 1H), 7.40-7.28 (m, 5H), 7.22 (dd, \(J = 3.6, 0.5\) Hz, 1H), 6.53 (dd, \(J = 3.6, 1.7\) Hz, 1H), 5.14 (s, 2H), 3.19 (t, \(J = 6.7\) Hz, 2H), 2.80 (t, \(J = 6.7\) Hz, 2H); \(^{13}\text{C} \text{NMR (100 MHz, CDCl}_3\]: \delta 187.3, 172.6, 152.5, 146.5, 136.0, 128.6, 128.3, 117.2, 112.4, 66.6, 33.1, 27.9; HRMS (ESI) calcd for C_{15}H_{15}O_4 (M+H) 259.0970, found 259.0974.
4-(4-fluorophenyl)-N,N-dimethyl-4-oxobutanamide (3ac). The product was obtained in 67% yield, 29.9 mg, yellow oil; $^1$H NMR (400 MHz, CDCl$_3$): δ 8.10-7.98 (m, 2H), 7.13 (t, $J$ = 8.6 Hz, 2H), 3.31 (t, $J$ = 6.5 Hz, 2H), 3.10 (s, 3H), 2.96 (s, 3H), 2.78 (t, $J$ = 6.5 Hz, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 197.8, 171.6, 167.0, 164.4, 133.3 (d, $J$ = 3.1 Hz), 130.8, 130.7, 115.7, 115.5, 37.1, 35.5, 33.5, 27.3; $^{19}$F NMR (376 MHz, CDCl$_3$): δ -105.6 (m, 1F); HRMS (ESI) calcd for C$_{12}$H$_{15}$FNO$_2$ (M+H) 224.1087, found 224.1084.

3-(4-methoxybenzoyl)cyclopentan-1-one (3ad). The product was obtained in 62% yield, 27.1 mg, colorless oil; $^1$H NMR (400 MHz, CDCl$_3$): δ 8.03-7.94 (m, 2H), 7.04-6.92 (m, 2H), 4.17-4.02 (m, 1H), 3.89 (s, 3H), 2.77-2.62 (m, 1H), 2.50-2.24 (m, 4H), 2.21-2.09 (m, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 217.2, 198.7, 163.8, 130.8, 128.6, 114.0, 55.6, 42.7, 41.1, 37.4, 27.1; HRMS (ESI) calcd for C$_{13}$H$_{15}$O$_3$ (M+H) 219.1021, found 219.1024.

3-(2-naphthoyl)cyclopentan-1-one (3ae). The product was obtained in 53% yield, 25.3 mg, colorless oil; $^1$H NMR (400 MHz, CDCl$_3$): δ 8.51 (d, $J$ = 1.7 Hz, 1H), 8.05 (d, $J$ = 8.6, 1.8 Hz, 1H), 8.00-7.88 (m, 3H), 7.61 (dddd, $J$ = 20.5, 8.1, 6.9, 1.3 Hz, 2H), 4.38-4.18 (m, 1H), 2.84-2.70 (m, 1H), 2.57-2.17 (m, 5H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 216.9, 200.2, 135.8, 132.9, 132.5, 130.2, 129.6, 128.8, 127.8, 127.0, 124.1, 43.1, 41.2, 37.4, 27.2; HRMS (ESI) calcd for C$_{16}$H$_{15}$O$_2$ (M+H) 239.1072, found 239.1070.

1-(furan-2-yl)-2-methylpentane-1,4-dione (3af). The product was obtained in 40% yield, 14.4 mg, colorless oil; $^1$H NMR (400 MHz, CDCl$_3$): δ 7.60 (dd, $J$ = 1.7, 0.7 Hz, 1H), 7.24 (dd, $J$ = 3.5, 0.7 Hz, 1H), 6.54 (dd, $J$ = 3.6, 1.7 Hz, 1H), 3.74 (dd, $J$ = 8.7, 7.1, 5.1 Hz, 1H), 3.12 (dd, $J$ = 18.0, 8.7 Hz, 1H), 2.53 (dd, $J$ = 18.1, 5.1 Hz, 1H), 2.16 (s, 3H), 1.21 (d, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 206.8, 191.9, 151.9, 146.4, 117.6, 112.2, 46.3, 36.9, 30.0, 17.6; HRMS (ESI) calcd for C$_{10}$H$_{13}$O$_3$ (M+H) 181.0865, found 181.0867.
5. Synthetic Procedure and Characterization of Haloperidol

1-(4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl)prop-2-en-1-one (7): To a solution of 6 (1.60 g, 7.56 mmol) in CH₂Cl₂ (40 mL) was added DIPEA (1.08 g, 8.32 mmol) and cooled to 0 °C. 0.61 mL acryloyl chloride (7.56 mmol) in CH₂Cl₂ (5 mL) was added drop-wise and then the mixture was stirred at room temperature for 4 h. The reaction mixture was diluted with 40 mL CH₂Cl₂, and washed sequentially with 1 M HCl, saturated NaHCO₃ and brine, the organic layer was dried with MgSO₄ and concentrated under reduced pressure. The crude residue was purified by chromatography on silica gel (CH₂Cl₂/MeOH, 20:1) to give 7 (1.90 g, 95%) as a white solid, mp 183-185 °C. ¹H NMR (400 MHz, DMSO-d₆) δ 7.51 (d, J = 8.5 Hz, 2H), 7.37 (d, J = 8.5 Hz, 2H), 6.84 (dd, J = 16.7, 10.5 Hz, 1H), 6.12 (dd, J = 16.7, 2.5 Hz, 1H), 5.67 (dd, J = 10.5, 2.5 Hz, 1H), 5.29 (s, 1H), 4.42-4.36 (m, 1H), 3.96 (d, J = 13.5 Hz, 1H), 3.51-3.40 (m, 2H), 3.03 (td, J = 12.6, 2.7 Hz, 1H), 1.91-1.73 (m, 2H), 1.63 (d, J = 13.2 Hz, 2H); ¹³C NMR (100 MHz, DMSO-d₆): δ 164.1, 148.2, 131.0, 128.6, 127.8, 126.8, 126.8, 69.9, 41.5, 38.4, 37.8, 37.4.; HRMS (ESI) calcd for C₁₄H₁₃ClNO₂ (M+H) 266.0948, found 266.0945.
1-(4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl)-4-(4-fluorophenyl)butane-1,4-dione (8): According to the General Procedure B, 4-F-C₆H₄COOH (2.52 g, 18 mmol), 7 (1.594 g, 6 mmol), fac-Ir(ppy)₃ (39.3 mg, 0.06 mmol), Hantzsch ester (2.28 g, 9 mmol), i-Pr₂NEt (4.65 g, 36 mmol), isobutyl chloroformate (2.46 g, 18 mmol) and solvent CH₂Cl₂ (50 mL) were added to a 100 mL transparent Schlenk flask charged with a magnetic stir bar. The resulting solution was degassed and backfilled with nitrogen via the freeze-pump-thaw procedure for three cycles. The reaction flask was then placed in an irradiation apparatus (at approximately 2 cm away from the light source) equipped with a 24 W blue light LED strip (λ_max = 453 nm) and stirred at room temperature until TLC showed consumption of 7. The reaction mixture was concentrated under reduced pressure and the crude residue was purified by flash chromatography on silica gel (CH₂Cl₂/MeOH, 30:1) to yield addition product 8 (1.55 g, 66%) as a white solid, mp 156 °C. ¹H NMR (400 MHz, DMSO-d₆) δ 8.14-8.01 (m, 2H), 7.56-7.48 (m, 2H), 7.43-7.28 (m, 4H), 5.27 (s, 1H), 4.42-4.17 (m, 1H), 3.97-3.77 (m, 1H), 2.95 (td, J = 12.7, 3.0 Hz, 1H), 2.82-2.70 (m, 2H), 1.96 (td, J = 12.8, 4.2 Hz, 1H), 1.81-1.52 (m, 3H); ¹³C NMR (100 MHz, DMSO-d₆) δ 197.7, 169.4, 166.1, 163.6, 148.4, 133.6 (d, J = 2.9 Hz), 131.0, 130.8, 130.7, 127.8, 126.8, 115.7, 115.5, 69.9, 41.2, 37.9, 37.6, 37.4, 33.1, 26.7. ¹⁹F NMR (376 MHz, DMSO-d₆): δ -106.48 (dt, J = 9.5, 3.9 Hz); HRMS (ESI) calcd for C₂₁H₂₂ClFNO₃ (M+H) 390.1272, found 390.1275.

4-(4-chlorophenyl)-1-(4-(4-fluorophenyl)-4-hydroxybutyl)piperidin-4-ol (8a): A solution of 8 (1.6 g, 4.1 mmol) in anhydrous THF (40 mL) was added dropwise to a solution of LiAlH₄ (778 mg, 20.5 mmol) in anhydrous THF (20 mL) and the resulting mixture was heated at reflux for 8 h. The mixture was cooled to room temperature and water (800 μL), aq 4 M NaOH (800 μL) and water (2.4 mL) were added sequentially. The resulting colourless suspension was stirred at room temperature for 30 min and filtered, washing with CH₂Cl₂ (40 mL), and concentrated in vacuo to afford the crude 8a (1.5 g) as a white
solid. This material was used in the next stage without further purification.\textsuperscript{11}\textsuperscript{1}H NMR (400 MHz, DMSO-\textit{d}_6) \(\delta\) 7.50 (d, \(J = 8.6\) Hz, 2H), 7.37 (dd, \(J = 8.4, 5.6\) Hz, 4H), 7.14 (t, \(J = 8.9\) Hz, 2H), 4.91 (s, 1H), 4.56 (t, \(J = 6.1\) Hz, 1H), 2.71-2.57 (m, 2H), 2.33 (dt, \(J = 13.9, 6.7\) Hz, 4H), 1.89 (td, \(J = 12.8, 4.3\) Hz, 2H), 1.68-1.50 (m, 5H), 1.42 (dp, \(J = 14.5, 7.2, 6.7\) Hz, 1H).\textsuperscript{13}C NMR (100 MHz, DMSO-\textit{d}_6) \(\delta\) 162.1, 159.7, 149.1, 142.6 (d, \(J = 2.9\) Hz), 130.7, 127.7, 127.6, 126.8, 114.4, 71.6, 69.5, 58.0, 49.1, 48.8, 37.8, 37.8, 37.7, 22.9. \textsuperscript{19}F NMR (376 MHz, DMSO-\textit{d}_6):\(\delta\) -115.69 – -117.61 (m); HRMS (ESI) calcd for \(\text{C}_{21}\text{H}_{26}\text{ClFNO}_2\) (M+H) 378.1636, found 378.1632.

\textbf{Haloperidol (9):} Crude 8a (1.5 g, 3.97 mmol) from last step was dissolved in \(\text{CH}_2\text{Cl}_2\) (40 mL) and Dess–Martin periodinane (3.4 g, 7.94 mmol, 2.0 equiv) were added. The reaction contents were stirred for 8 h at 25 \(^\circ\)C at which point they were quenched with saturated NaHCO\textsubscript{3} (50 mL), the organic phase was washed with saturated Na\textsubscript{2}S\textsubscript{2}O\textsubscript{3} (50 mL) and dried with MgSO\textsubscript{4}. The organic phase was then concentrated in vacuo and the crude residue was purified by flash chromatography on silica gel (EtOAc/MeOH/NH\textsubscript{3}·H\textsubscript{2}O, 95:5:1) to yield haloperidol 9 (1.09 g, 73 \% for 2 steps) as a white solid. mp 142 \(^\circ\)C \(\textsuperscript{1}H\) NMR (400 MHz, DMSO-\textit{d}_6) \(\delta\) 8.11-8.04 (m, 2H), 7.40-7.30 (m, 6H), 4.85 (s, 1H), 2.98 (t, \(J = 6.8\) Hz, 2H), 2.62-2.54 (m, 2H), 2.40-2.22 (m, 4H), 1.84 (p, \(J = 6.8\) Hz, 2H), 1.67 (td, \(J = 12.7, 4.3\) Hz, 2H), 1.46 (dd, \(J = 13.4, 2.4\) Hz, 2H).\textsuperscript{13}C NMR (100 MHz, DMSO-\textit{d}_6) \(\delta\) 198.2, 166.0, 163.5, 149.1, 133.9 (d, \(J = 2.8\) Hz), 130.9, 130.8, 130.7, 127.6, 126.7, 115.6, 115.4, 69.4, 57.2, 48.8, 37.6, 35.6, 21.9. \textsuperscript{19}F NMR (376 MHz, DMSO-\textit{d}_6): \(\delta\) -115.69 – -117.61 (m); HRMS (ESI) calcd for \(\text{C}_{21}\text{H}_{26}\text{ClFNO}_2\) (M+H) 378.1636, found 378.1632.

\textbf{6. Radical Trapping Experiments}

Benzoic anhydride 1a (0.6 mmol, 3.0 equiv), Benzyl acrylate 2a (0.2 mmol, 1.0 equiv), \textit{fac}-Ir(ppy)$_3$ (2 \(\mu\)mol, 1.3 mg, 0.01 equiv), Hantzsch ester (0.3 mmol, 76 mg, 1.5 equiv), \textit{i}-Pr$_2$NEt (0.6 mmol, 77.5 mg, 3.0 equiv), TEMPO (0.6 mmol, 3 equiv) and solvent CH$_2$Cl$_2$ (2 mL) were added to a 10 mL transparent Schlenk tube charged with a magnetic stir bar. The resulting solution was degassed and backfilled with nitrogen via the freeze-pump-thaw procedure for three cycles. The reaction tube was then placed in an irradiation apparatus
(at approximately 2 cm away from the light source) equipped with a 24 W blue light LED strip ($\lambda_{\text{max}} = 453$ nm) and stirred at room temperature for 24 h. After 24 h, the reaction mixture was concentrated under reduced pressure and the crude residue was purified by flash chromatography to yield 2,2,6,6-tetramethylpiperidin-1-yl benzoate 10 in 83% yield (based on benzoic anhydride).

2,2,6,6-tetramethylpiperidin-1-yl benzoate (10)
White solid; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.12-8.03 (m, 2H), 7.61-7.53 (m, 1H), 7.46 (t, $J = 7.6$ Hz, 2H), 1.84-1.65 (m, 3H), 1.65-1.51 (m, 2H), 1.51-1.40 (m, 1H), 1.28 (s, 6H), 1.12 (s, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 166.5, 132.9, 129.8, 129.7, 128.6, 60.5, 39.2, 32.1, 20.9, 17.2.

7. Emission Spectrum of the Light Source
8. Emission Quenching Experiments (Stern–Volmer Studies)
Emission intensities were recorded using a Varian Cary Eclipse Fluorescence Spectrophotometer equipped with a Xenon flash lamp. All $\text{fac-Ir}$(ppy)$_3$ solutions were excited at 320 nm and the emission intensity was collected at 518 nm. In a typical experiment, the dichloromethane solution of $\text{fac-Ir}$(ppy)$_3$ (0.1 mM) was added the appropriate amount of quencher in a screw-top quartz cuvette. After degassing with nitrogen for 10 min, the emission spectra of the samples were collected.

Scheme S1. $\text{fac-Ir}$(ppy)$_3$: Emission Quenching with different Components
Scheme S2. \textit{fac-Ir(ppy)$_3$} Emission Quenching with DIPEA

\[ I/I_0 = 1 + K_\text{Q} \tau_0 [Q] \]
\[ K_\text{Q} \tau_0 = 5.5679 \text{ L mol}^{-1} \]
\[ \tau_0 = 1.9 \mu \text{s} \]
\[ K_\text{Q} = 2.93 \times 10^6 \text{ L mol}^{-1} \text{ S}^{-1} \]

Scheme S3. \textit{fac-Ir(ppy)$_3$} Emission Quenching with Benzoic anhydride.
9. NMR Spectra of Products

Benzyl 4-oxo-4-phenylbutanoate (3a)
Ethyl 4-oxo-4-phenylbutanoate (3b)
Tert-butyl 4-oxo-4-phenylbutanoate (3c)
Benzyl 2-methyl-4-oxo-4-phenylbutanoate (3d)
Methyl 4-oxo-2,4-diphenylbutanoate (3e)
Phenethyl 3-methyl-4-oxo-4-phenylbutanoate (3g)
N-benzyl-4-oxo-4-phenylbutanamide (3h)
N,N-dimethyl-4-oxo-4-phenylbutanamide (3i)
1-phenyl-3-(phenylsulfonyl)propan-1-one (3j)
2-methyl-1-phenylpentane-1,4-dione (3k)
3-benzoylcyclohexan-1-one (3l)
3-benzoylcyclopentan-1-one (3m)
Dimethyl 2-(1-oxo-1-phenylheptan-2-yl)malonate (3n)
Dimethyl 2-(1-oxo-1,4-diphenylbutan-2-yl)malonate (3o)
Benzyl 4-oxo-4-(p-tolyl)butanoate (3p)
Benzyl 4-oxo-4-(m-tolyl)butanoate (3q)
Benzyl 4-(4-methoxyphenyl)-4-oxobutanoate (3r)
Benzyl 4-(4-chlorophenyl)-4-oxobutanoate (3s)
Benzyl 4-(4-fluorophenyl)-4-oxobutanoate (3t)
Benzyl 4-(4-bromophenyl)-4-oxobutanoate (3u)
Benzyl 4-(2-bromophenyl)-4-oxobutanoate (3v)
Benzyl 4-(3-bromo-5-fluorophenyl)-4-oxobutanoate (3w)
Benzyl 4-(2,4-dichlorophenyl)-4-oxobutanoate (3x)
Benzyl 4-oxo-4-(4-(trifluoromethyl)phenyl)butanoate (3y)
Benzyl 4-(naphthalen-2-yl)-4-oxobutanoate (3z)
Benzyl 4-(furan-2-yl)-4-oxobutanoate (3ab)

4-(4-fluorophenyl)-N,N-dimethyl-4-oxobutanamide (3ac)
3-(4-methoxybenzoyl)cyclopentan-1-one (3ad)
3-(2-naphthoyl)cyclopentan-1-one (3ae)
1-(furan-2-yl)-2-methylpentane-1,4-dione (3af)
Benzoic (isobutyl carbonic) anhydride (5a)
1-(4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl)prop-2-en-1-one (7)
1-(4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl)-4-(4-fluorophenyl)butane-1,4-dione (8)
4-(4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl)-1-(4-fluorophenyl)butan-1-one (8a)
10. References