Electronic Supplementary Information

Double oxidation of α-(alkylideneamino)nitriles to imides by molecular oxygen under mild basic conditions

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Contents

Table of contents ----------------------------------------------- S1

I. General Information------------------------------------------ S2

II. Typical Procedure and Analytical Data ----------------------- S2

III. Isotope Labeled O₂ Experiments ------------------------------ S15

IV. Crystal data and OPTEP drawing of 10aa--------------------- S16

V. Copies of ¹H NMR and ¹³C NMR spectra ------------------------ S18
I. General Information

All reagents were purchased from commercial sources and used without further purification, unless otherwise indicated. All reactions were monitored by TLC, which was performed on precoated aluminum sheets of silica gel 60 (F254). The products were purified by column chromatography on flash silica gel (300–400 mesh). Melting points were uncorrected. The $^1$H NMR and $^{13}$C NMR spectra were determined on a Varian 500 MHz and 125 MHz, respectively, with TMS as the internal standard. All shifts are given in ppm. High-resolution mass spectra (HRMS) were obtained using a Bruker microTOF II focus spectrometer (ESI).

II. Typical Procedures and Analytical Data

10aa, 4-chloro-N-(2-(4-chlorophenyl)-4-oxo-4-phenylbutanoyl)benzamide.

To a solution of 2-aminoacetonitrile hydrochloride (55.1 mg, 0.6 mmol) in DMSO (5.0 mL) was added triethylamine (0.08 mL, 0.6 mmol) and stirred at room temperature for 1.0 h. Then, 4-chlorobenzaldehyde 2a (84 mg, 0.6 mmol) was added and further stirred at room temperature for about 4.0 h. After 2a was consumed as indicated by TLC, K$_2$CO$_3$ (34.5 mg, 0.25 mmol) was added in one portion under oxygen atmosphere following with the dropwise addition of DMSO solution (2.0 mL) of enone 5a (121 mg, 0.5 mmol). The reaction mixture was stirred at room temperature and was monitored by TLC. After enone 5a was consumed, the resulting mixture was poured into ice-water (20 mL) and extracted with diethyl ether (20 mL $\times$ 2). The aqueous layer was treated with 10% NaClO solution (5 mL) and collected. The combined organic layers were dried over anhydrous Na$_2$SO$_4$, evaporated in vacuo, and the residue was purified by column chromatography (EtOAc/PE (petroleum ether) = 1/10, V/V) to give 10aa (191 mg, 90% calculated from 5a). Reaction time 12.0 h.

Colorless crystals, m.p. 215–217 °C. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 3.29 (dd, $J = 18.0, 3.5$ Hz, 1H), 4.08 (dd, $J = 18.0, 11.0$ Hz, 1H), 5.41 (dd, $J = 11.0, 3.5$ Hz, 1H), 7.33 (d, $J = 8.5$ Hz, 2H), 7.41 (m, 4H), 7.46 (t, $J = 7.5$ Hz, 2H), 7.58 (t, $J = 7.5$ Hz, 1H), 7.75 (d, $J = 8.5$ Hz, 2H), 7.96 (d, $J = 7.5$ Hz, 2H), 8.68 (s, 1H). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 43.9, 46.2, 128.1, 128.2, 128.7, 129.1, 129.2, 130.0, 133.5, 133.7, 135.8, 136.0, 139.7, 164.0, 174.7, 197.6. HRMS (ESI-TOF) Calcd for C$_{23}$H$_{18}$Cl$_2$NO$_3^+$ ([M+H$^+$]) 426.0658. Found 426.0657.
10ba, 4-bromo-N-(2-(4-chlorophenyl)-4-oxo-4-phenylbutanoyl)benzamide.

Following the procedure for the synthesis of 10aa, the reaction of 2-aminoacetonitrile hydrochloride (55.1 mg, 0.6 mmol), 4-bromobenzaldehyde 2b (111 mg, 0.6 mmol) and enone 5a (121 mg, 0.5 mmol) gave 10ba (183 mg, 78%) after purification by column chromatography on silica gel (EtOAc/PE = 1: 10 V/V). Reaction time 9.0 h. Colorless crystals, m.p. 210–212 °C. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 3.29 (dd, $J = 18.0$, 3.5 Hz, 1H), 4.07 (dd, $J = 18.0$, 11.0 Hz, 1H), 5.41 (dd, $J = 11.0$, 3.5 Hz, 1H), 7.32 (d, $J = 8.0$ Hz, 2H), 7.41 (d, $J = 8.0$ Hz, 2H), 7.46 (t, $J = 7.5$ Hz, 2H), 7.54–7.60 (m, 3H), 7.67 (d, $J = 8.0$ Hz, 2H), 7.95 (d, $J = 8.0$ Hz, 2H), 8.76 (s, 1H). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 43.8, 46.2, 128.1, 128.2, 128.7, 129.1, 129.3, 130.0, 131.6, 132.1, 133.6, 133.7, 135.8, 136.0, 164.3, 175.0, 197.6. HRMS (ESI-TOF) Calcd for C$_{23}$H$_{18}$BrClNO$_3$ $^+$ ([M+H]$^+$) 470.0153. Found 470.0158.

10ca, N-(2-(4-chlorophenyl)-4-oxo-4-phenylbutanoyl)benzamide.

Following the procedure for the synthesis of 10aa, the reaction of 2-aminoacetonitrile hydrochloride (55.1 mg, 0.6 mmol), benzaldehyde 2c (61 µL, 0.6 mmol) and enone 5a (121 mg, 0.5 mmol) gave 10ca (164 mg, 84%) after purification by column chromatography on silica gel (EtOAc/PE = 1: 10 V/V). Reaction time 26.0 h. Colorless crystals, m.p. 190–192 °C. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 3.29 (dd, $J = 18.0$, 3.5 Hz, 1H), 4.09 (dd, $J = 18.0$, 11.0 Hz, 1H), 5.46 (dd, $J = 11.0$, 3.5 Hz, 1H), 7.32 (d, $J = 8.5$ Hz, 2H), 7.43–7.47 (m, 6H), 7.55–7.59 (m, 2H), 7.80 (d, $J = 8.0$ Hz, 2H), 7.96 (d, $J = 8.0$ Hz, 2H), 8.65 (s, 1H). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 43.8, 46.2, 127.7, 128.1, 128.6, 128.9, 129.0, 130.0, 132.8, 133.1, 133.4, 133.6, 136.0, 136.1, 165.0, 174.9, 197.6. HRMS (ESI-TOF) Calcd for C$_{23}$H$_{19}$ClNO$_3$ $^+$ ([M+H]$^+$) 392.1048. Found 392.1051.
10da, N-(2-(4-chlorophenyl)-4-oxo-4-phenylbutanoyl)benzamide.

Following the procedure for the synthesis of 10aa, the reaction of 2-aminoacetonitrile hydrochloride (55.1 mg, 0.6 mmol), 4-methylbenzaldehyde 2d (71 µL, 0.6 mmol) and enone 5a (121 mg, 0.5 mmol) gave 10da (168 mg, 83%) after purification by column chromatography on silica gel (EtOAc/PE = 1: 10 V/V). Reaction time 27.0 h.

Colorless crystals, m.p. 223–225 °C. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 2.40 (s, 3H), 3.29 (dd, $J$ = 18.0, 3.5 Hz, 1H), 4.09 (dd, $J$ = 18.0, 11.0 Hz, 1H), 5.48 (dd, $J$ = 11.0, 3.5 Hz, 1H), 7.25 (d, $J$ = 8.5 Hz, 2H), 7.33 (t, $J$ = 8.0 Hz, 2H), 7.43–7.47 (m, 4H), 7.57 (t, $J$ = 7.5 Hz, 1H), 7.70 (d, $J$ = 8.5 Hz, 2H), 7.96 (d, $J$ = 8.0 Hz, 2H), 8.57 (s, 1H). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 21.6, 43.8, 46.1, 127.7, 128.1, 128.6, 129.0, 129.9, 130.0, 133.4, 133.5, 136.1, 144.1, 164.8, 174.9, 197.6. HRMS (ESI-TOF) Calcd for C$_{24}$H$_{21}$ClNO$_3$ $^+$ ([M+H]$^+$) 406.1204. Found 406.1214.

10ea, 2-(4-chlorophenyl)-4-oxo-4-phenyl-N-pivaloylbutanamide.

Following the procedure for the synthesis of 10aa, the reaction of 2-aminoacetonitrile hydrochloride (55.1 mg, 0.6 mmol), pivalaldehyde 2e (66 µL, 0.6 mmol) and enone 5a (121 mg, 0.5 mmol) gave 10ea (139 mg, 75%) after purification by column chromatography on silica gel (EtOAc/PE = 1: 12 V/V). Reaction time 12.0 h.

Colorless crystals, m.p. 132–134 °C. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.20 (s, 9H), 3.23 (dd, $J$ = 18.0, 3.5 Hz, 1H), 4.03 (dd, $J$ = 18.0, 11.0 Hz, 1H), 5.32 (dd, $J$ = 11.0, 3.5 Hz, 1H), 7.31 (d, $J$ = 8.5 Hz, 2H), 7.37 (d, $J$ = 8.5 Hz, 2H), 7.45 (t, $J$ = 8.0 Hz, 2H), 7.56 (t, $J$ = 7.5 Hz, 1H), 7.95 (d, $J$ = 8.0 Hz, 2H), 8.06 (s, 1H). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 27.0, 40.2, 43.7, 45.8, 128.0, 128.6, 128.9, 132.4(2C), 136.0, 136.1, 175.0, 176.4, 197.5. HRMS (ESI-TOF) Calcd for C$_{21}$H$_{23}$ClNO$_3$ $^+$ ([M+H]$^+$) 372.1361. Found 372.1363.
10ab, 4-chloro-N-(4-oxo-4-phenyl-2-(p-toly)butanoyl)benzamide.

Following the procedure for the synthesis of 10aa, the reaction of 2-aminoacetonitrile hydrochloride (55.1 mg, 0.6 mmol), 4-chlorobenzaldehyde 2a (84 mg, 0.6 mmol) and 1-phenyl-3-(p-toly)prop-2-en-1-one 5b (111 mg, 0.5 mmol) gave 10ab (170 mg, 84%) after purification by column chromatography on silica gel (EtOAc/PE = 1:10 V/V). Reaction time 24.0 h.

Colorless crystals, m.p. 249–251 °C. 1H NMR (500 MHz, CDCl3): δ 2.33 (s, 3H), 3.29 (d, J = 18.5 Hz, 1H), 4.08 (dd, J = 18.5, 11.0 Hz, 1H), 5.31 (d, J = 11.0 Hz, 1H), 7.16 (d, J = 7.5 Hz, 2H), 7.35 (d, J = 7.5 Hz, 4H), 7.45 (t, J = 7.5 Hz, 2H), 7.57 (t, J = 7.5 Hz, 1H), 7.73 (d, J = 8.0 Hz, 2H), 7.95 (d, J = 8.0 Hz, 2H), 8.81 (s, 1H). 13C NMR (125 MHz, CDCl3): δ 21.1, 43.9, 46.6, 128.1, 128.4, 128.6, 129.0, 129.2, 129.7, 131.4, 133.4, 134.4, 136.2, 137.5, 139.4, 164.2, 175.0, 198.0. HRMS (ESI-TOF) Calcd for C24H21ClNO3+ ([M+H]+) 406.1204. Found 406.1214.

10ac, 4-chloro-N-(2-(4-methoxyphenyl)-4-oxo-4-phenylbutanoyl)benzamide.

Following the procedure for the synthesis of 10aa, the reaction of 2-aminoacetonitrile hydrochloride (55.1 mg, 0.6 mmol), 4-chlorobenzaldehyde 2a (84 mg, 0.6 mmol) and 3-(4-methoxyphenyl)-1-phenylprop-2-en-1-one 5c (119 mg, 0.5 mmol) gave 10ac (172 mg, 82%) after purification by column chromatography on silica gel (EtOAc/PE = 1:10 V/V). Reaction time 25.0 h.

Colorless crystals, m.p. 161–163 °C. 1H NMR (500 MHz, CDCl3): δ 3.26 (d, J = 18.0 Hz, 1H), 3.77 (s, 3H), 4.06 (dd, J = 18.0, 11.0 Hz, 1H), 5.32 (d, J = 11.0 Hz, 1H), 6.86 (d, J = 7.5 Hz, 2H), 7.23 (d, J = 7.5 Hz, 2H), 7.36 (d, J = 8.0 Hz, 2H), 7.45 (d, J = 7.0 Hz, 2H), 7.56 (t, J = 7.0 Hz, 1H), 7.73 (d, J = 8.0 Hz, 2H), 7.94 (d, J = 7.0 Hz, 2H), 9.38 (s, 1H). 13C NMR (125 MHz, CDCl3): δ 43.9, 46.0, 55.2, 114.3, 128.0, 128.6, 128.8, 129.2, 129.4, 129.6, 131.3, 133.4, 136.0, 139.2, 159.0, 164.5, 175.9, 198.0. HRMS (ESI-TOF) Calcd for C24H21ClNO4+ ([M+H]+) 422.1154. Found 422.1160.

10ad, N-(2-(benzo[d][1,3]dioxol-5-yl)-4-oxo-4-phenylbutanoyl)-4-chlorobenzamide.

Following the procedure for the synthesis of 10aa, the reaction of 2-aminoacetonitrile hydrochloride (55.1 mg, 0.6 mmol), 4-chlorobenzaldehyde 2a (84 mg, 0.6 mmol) and 3-(benzo[d][1,3]dioxol-5-yl)-1-phenylprop-2-en-1-one 5d (126 mg, 0.5 mmol) gave 10ad (191 mg,
88%) after purification by column chromatography on silica gel (EtOAc/PE = 1: 10 V/V). Reaction time 10.0 h.

Colorless crystals, m.p. 169–171 °C. \(^1\)H NMR (CDCl\(_3\), 500 MHz): \(\delta\) 3.29 (dd, \(J = 18.0, 3.5\) Hz, 1H), 4.06 (dd, \(J = 18.0, 11.0\) Hz, 1H), 5.29 (dd, \(J = 11.0, 3.5\) Hz, 1H), 5.95 (s, 2H), 6.78 (d, \(J = 8.0\) Hz, 1H), 6.94 (dd, \(J = 8.0, 1.5\) Hz, 1H), 6.97 (d, \(J = 1.5\) Hz, 1H), 7.41 (d, \(J = 7.5\) Hz, 2H), 7.46 (s, \(J = 7.5\) Hz, 2H), 7.57 (t, \(J = 7.5\) Hz, 1H), 7.75 (d, \(J = 8.0\) Hz, 2H), 7.96 (d, \(J = 7.5\) Hz, 2H), 8.62 (s, 1H).

\(^{13}\)C NMR (CDCl\(_3\), 125 MHz): \(\delta\) 43.9, 46.4, 101.1, 108.6, 108.8, 121.9, 128.0, 128.6, 129.1(2C), 130.8, 131.3, 133.4, 136.1, 139.5, 147.1, 148.0, 164.1, 174.8, 197.9. HRMS (ESI-TOF) Calcd for C\(_{24}\)H\(_{19}\)ClNO\(_5\)\(^+\) ([M+H]\(^+\)) 436.0946. Found 436.0949.

10ae, 4-chloro-\(N\)-(2-methyl-4-oxo-4-phenylbutanoyl)benzamide.

Following the procedure for the synthesis of 10aa, the reaction of 2-aminoacetonitrile hydrochloride (55.1 mg, 0.6 mmol), 4-chlorobenzaldehyde 2a (84 mg, 0.6 mmol) and 1-phenylbut-2-en-1-one 5e (73 mg, 0.5 mmol) gave 10ae (99 mg, 60%) after purification by column chromatography on silica gel (EtOAc/PE = 1: 12 V/V). Reaction time 24.0 h.

Colorless crystals, m.p. 175–177 °C. \(^1\)H NMR (CDCl\(_3\), 500 MHz): \(\delta\) 1.37 (d, \(J = 6.5\) Hz, 3H), 3.13 (dd, \(J = 18.0, 3.5\) Hz, 1H), 3.67 (dd, \(J = 18.0, 11.0\) Hz, 1H), 3.95–3.99 (m, 1H), 7.44–7.48 (m, 4H), 7.59 (t, \(J = 7.5\) Hz, 1H), 7.85 (d, \(J = 8.5\) Hz, 2H), 7.98 (d, \(J = 7.5\) Hz, 2H), 8.98 (s, 1H).

\(^{13}\)C NMR (CDCl\(_3\), 125 MHz): \(\delta\) 17.0, 36.0, 42.6, 128.0, 128.6, 129.1, 129.2, 131.4, 133.4, 136.2, 139.4, 164.2, 177.7, 198.6. HRMS (ESI-TOF) Calcd for C\(_{18}\)H\(_{17}\)ClNO\(_3\)\(^+\) ([M+H]\(^+\)) 330.0891. Found 330.0881.

10af, 4-chloro-\(N\)-(4-oxo-4-phenylbutanoyl)benzamide.

Following the procedure for the synthesis of 10aa, the reaction of 2-aminoacetonitrile hydrochloride (55.1 mg, 0.6 mmol), 4-chlorobenzaldehyde 2a (84 mg, 0.6 mmol) and 1-phenylprop-2-en-1-one 5f (66 mg, 0.5 mmol) gave 10af (110 mg, 70%) after purification by column chromatography on silica gel (EtOAc/PE = 1: 12 V/V). Reaction time 24.0 h.

Colorless crystals, m.p. 112–114 °C. \(^1\)H NMR (CDCl\(_3\), 500 MHz): \(\delta\) 2.48–2.51 (m, 2H), 2.96–3.01 (m, 1H), 3.13–3.18 (m, 1H), 7.41 (d, \(J = 8.5\) Hz, 2H), 7.44 (d, \(J = 8.0\) Hz, 2H), 7.55 (t, \(J = 7.5\) Hz, 2H), 7.71 (d, \(J = 8.5\) Hz, 1H), 7.90 (d, \(J = 7.5\) Hz, 2H), 8.53 (s, 1H).

\(^{13}\)C NMR (CDCl\(_3\), 125 MHz): \(\delta\) 33.4, 34.4, 128.0, 128.6, 129.1, 130.1, 132.9, 133.3, 136.4, 138.1, 159.9, 177.8, 197.9. HRMS (ESI-TOF) Calcd for C\(_{17}\)H\(_{15}\)ClNO\(_3\)\(^+\) ([M+H]\(^+\)) 316.0735. Found 316.0741.
10ag, N-(4-(4-bromophenyl)-4-oxo-2-(p-tolyl)butanoyl)-4-chlorobenzamide.
Following the procedure for the synthesis of 10aa, the reaction of 2-aminoacetonitrile hydrochloride (55.1 mg, 0.6 mmol), 4-chlorobenzaldehyde 2a (84 mg, 0.6 mmol) and 1-(4-bromophenyl)-3-(p-tolyl)prop-2-en-1-one 5g (150 mg, 0.5 mmol) gave 10ag (205 mg, 85%) after purification by column chromatography on silica gel (EtOAc/PE = 1: 10 V/V). Reaction time 14.0 h. Colorless crystals, m.p. 116–118 °C. $^{1}H$ NMR (CDCl$_3$, 500 MHz): δ 2.38 (s, 3H), 3.23 (dd, $J = 18.0, 3.5$ Hz, 1H), 4.05 (dd, $J = 18.0, 11.0$ Hz, 1H), 5.31 (dd, $J = 11.0, 3.5$ Hz, 1H), 7.18 (d, $J = 8.0$ Hz, 2H), 7.34 (d, $J = 8.0$ Hz, 2H), 7.40 (d, $J = 8.5$ Hz, 2H), 7.59 (d, $J = 8.5$ Hz, 2H), 7.72 (d, $J = 8.5$ Hz, 2H), 7.82 (d, $J = 8.0$ Hz, 2H), 8.55 (s, 1H). $^{13}C$ NMR (CDCl$_3$, 125 MHz): δ 21.2, 43.8, 46.6, 128.4, 128.6, 129.1, 129.6, 129.7, 131.3, 131.9, 134.1, 134.9, 137.7, 139.5, 164.1, 174.7, 197.0. HRMS (ESI-TOF) Calcd for C$_{24}$H$_{20}$BrClNO$_3$+ ([M+H]$^+$) 484.0310. Found 484.0309.

10ah, N-(4-(4-bromophenyl)-2-(4-chlorophenyl)-4-oxobutanoyl)-4-chlorobenzamide.
Following the procedure for the synthesis of 10aa, the reaction of 2-aminoacetonitrile hydrochloride (55.1 mg, 0.6 mmol), 4-chlorobenzaldehyde 2a (84 mg, 0.6 mmol) and 1-(4-bromophenyl)-3-(4-chlorophenyl)prop-2-en-1-one 5h (160 mg, 0.5 mmol) gave 10ah (224 mg, 89%) after purification by column chromatography on silica gel (EtOAc/PE = 1: 10 V/V). Reaction time 8.0 h. Colorless crystals, m.p. 195–197 °C. $^{1}H$ NMR (CDCl$_3$, 500 MHz): δ 3.23 (dd, $J = 18.0, 3.5$ Hz, 1H), 4.02 (dd, $J = 18.0, 11.0$ Hz, 1H), 5.42 (dd, $J = 11.0, 3.5$ Hz, 1H), 7.32 (d, $J = 8.5$ Hz, 2H), 7.42 (d, $J = 6.5$ Hz, 2H), 7.44 (d, $J = 6.5$ Hz, 2H), 7.60 (d, $J = 9.0$ Hz, 2H), 7.74 (d, $J = 9.0$ Hz, 2H), 7.81 (d, $J = 8.5$ Hz, 2H), 8.75 (s, 1H). $^{13}C$ NMR (CDCl$_3$, 125 MHz): δ 43.7, 46.1, 128.8, 129.1, 129.2(2C), 129.6, 129.9, 131.0, 132.0, 133.8, 134.7, 135.6, 139.7, 164.1, 175.0, 196.6. HRMS (ESI-TOF) Calcd for C$_{23}$H$_{17}$BrClNO$_3$+ ([M+H]$^+$) 503.9763. Found 503.9759.
10ai. N’-(4-(4-bromophenyl)-2-(4-fluorophenyl)-4-oxobutanoyl)-4-chlorobenzamide.

Following the procedure for the synthesis of 10aa, the reaction of 2-aminoacetonitrile hydrochloride (55.1 mg, 0.6 mmol), 4-chlorobenzaldehyde 2a (84 mg, 0.6 mmol) and 1-(4-bromophenyl)-3-(4-fluorophenyl)prop-2-en-1-one 5i (152 mg, 0.5 mmol) gave 10ai (214 mg, 88%) after purification by column chromatography on silica gel (EtOAc/PE = 1: 10 V/V). Reaction time 7.0 h.

Colorless crystals, m.p. 201–203 °C. $^1$H NMR (CDCl$_3$, 500 MHz): δ 3.23 (dd, J = 18.0, 3.5 Hz, 1H), 4.03 (dd, J = 18.0, 11.0 Hz, 1H), 5.43 (dd, J = 11.0, 3.5 Hz, 1H), 7.04 (t, J = 8.5 Hz, 2H), 7.38 (d, J = 8.5 Hz, 2H), 7.43 (dd, J = 8.5, 5.5 Hz, 2H), 7.60 (d, J = 8.5 Hz, 2H), 7.74 (d, J = 8.5 Hz, 2H), 7.81 (d, J = 8.5 Hz, 2H), 8.81 (s, 1H).

$^{13}$C NMR (CDCl$_3$, 125 MHz): δ 43.9, 45.9, 115.8, 115.9, 128.8, 129.1, 129.2, 129.5, 130.2(2C), 131.1, 132.0, 132.8, 134.7, 139.6, 164.2, 175.3, 196.7. HRMS (ESI-TOF) Calcd for C$_{23}$H$_{17}$BrClFNO$_3$ $^+$ ([M+H] $^+$) 488.0059. Found 488.0051.

10aj, 4-chloro-N’-(2-(4-chlorophenyl)-4-oxopentanoyl)benzamide.

Following the procedure for the synthesis of 10aa, the reaction of 2-aminoacetonitrile hydrochloride (55.1 mg, 0.6 mmol), 4-chlorobenzaldehyde 2a (84 mg, 0.6 mmol) and 4-(4-chlorophenyl)but-3-en-2-one 5j (90 mg, 0.5 mmol) gave 10aj (154 mg, 85%) after purification by column chromatography on silica gel (EtOAc/PE = 1: 10 V/V). Reaction time 6.0 h.

Colorless crystals, m.p. 123–125 °C. $^1$H NMR (500 MHz, CDCl$_3$): δ 2.22 (s, 3H), 2.77 (dd, J = 18.0, 3.5 Hz, 1H), 3.54 (dd, J = 18.0, 11.0 Hz, 1H), 5.19 (dd, J = 11.0, 3.5 Hz, 1H), 7.33 (d, J = 8.5 Hz, 2H), 7.36 (d, J = 8.5 Hz, 2H), 7.46 (d, J = 8.5 Hz, 2H), 7.75 (d, J = 8.5 Hz, 2H), 8.67 (s, 1H). $^{13}$C NMR (125 MHz, CDCl$_3$): δ 29.7, 46.1, 48.0, 129.0, 129.1, 129.8, 130.9, 131.1, 133.6, 135.6, 139.6, 164.1, 174.6, 206.3. HRMS (ESI-TOF) Calcd for C$_{18}$H$_{16}$Cl$_2$NO$_3$ $^+$ ([M+H] $^+$) 364.0502. Found 364.0512.

10ak, 4-chloro-N’-(2-methyl-4-oxopentanoyl)benzamide

Following the procedure for the synthesis of 10aa, the reaction of 2-aminoacetonitrile hydrochloride (55.1 mg, 0.6 mmol), 4-chlorobenzaldehyde 2a (84 mg, 0.6 mmol) and pent-3-en-2-one 5k (42 mg, 0.5 mmol) gave 10ak (96 mg, 72%) after purification by column chromatography on silica gel (EtOAc/PE = 1: 12 V/V). Reaction time 24.0 h.

Yellowish oil. $^1$H NMR (500 MHz, CDCl$_3$): δ 1.24 (d, J = 7.0 Hz, 3H), 2.19 (s, 3H), 2.59 (dd, J = 18.5, 3.5 Hz, 1H), 3.11 (dd, J = 18.5, 11.0 Hz, 1H), 3.72 (m, 1H), 7.48 (d, J = 8.5 Hz, 2H), 7.82 (d, J = 8.5 Hz, 2H), 8.81 (s, 1H). $^{13}$C NMR (125 MHz, CDCl$_3$): δ 16.7, 29.8, 35.8, 47.2, 129.1, 129.2,
131.2, 139.6, 164.1, 177.3, 207.6. **HRMS** (ESI-TOF) Calcd for C$_{13}$H$_{15}$ClNO$_3^+$ ([M+H]$^+$) 268.0735. Found 268.0745.

**10al**, 4-chloro-N-(4-oxo-3,4-diphenylbutanoyl)benzamide.
Following the procedure for the synthesis of **10aa**, the reaction of 2-aminoacetonitrile hydrochloride (55.1 mg, 0.6 mmol), 4-chlorobenzaldehyde **2a** (84 mg, 0.6 mmol) and 1,2-diphenylprop-2-en-1-one **5l** (104 mg, 0.5 mmol) gave **10al** (102 mg, 52%) after purification by column chromatography on silica gel (EtOAc/PE = 1: 10 V/V). Reaction time 18.0 h.

Colorless crystals, m.p. 196–198 °C. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 3.30 (dd, J = 18.5, 3.0 Hz, 1H), 4.12 (dd, J = 18.5, 11.0 Hz, 1H), 5.18 (dd, J = 11.0, 3.0 Hz, 1H), 7.23 (m, 1H), 7.31 (m, 6H), 7.39 (t, J = 7.5 Hz, 2H), 7.50 (t, J = 7.5 Hz, 1H), 7.76 (d, J = 8.5 Hz, 2H), 7.98 (d, J = 7.5 Hz, 2H), 9.03 (s, 1H). $^{13}$C NMR (125 MHz, CDCl$_3$): 42.5, 49.0, 127.5, 128.2, 128.5, 128.9, 129.1, 129.2 (2C), 130.8, 133.1, 136.1, 137.9, 139.7, 164.6, 174.6, 198.5. HRMS (ESI-TOF) Calcd for C$_{23}$H$_{19}$ClNO$_3$ $^+$ ([M+H]$^+$) 392.1048. Found 392.1059.

**10am**, 4-Chloro-N-(3-oxocyclohexanecarbonyl)benzamide.
Following the procedure for the synthesis of **10aa**, the reaction of 2-aminoacetonitrile hydrochloride (55.1 mg, 0.6 mmol), 4-chlorobenzaldehyde **2a** (84 mg, 0.6 mmol) and cyclohex-2-enone (49.4 µL, 0.5 mmol) gave **10am** (116 mg, 83%) after purification by column chromatography on silica gel (EtOAc/PE = 1: 10). Reaction time 16.0 h.

Colorless crystals, m.p. 143–145 °C. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.87–1.91 (m, 2H), 2.07–2.11 (m, 1H), 2.23–2.15 (m, 1H), 2.38–2.45 (m, 2H), 2.55 (dd, J = 15.0, 4.5 Hz, 1H), 2.69 (dd, J = 15.0, 4.5 Hz, 1H), 3.96–4.01 (m, 1H), 7.50 (d, J = 8.5 Hz, 2H), 7.79 (d, J = 8.5 Hz, 2H), 8.50 (s, 1H). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 24.0, 27.3, 40.8, 42.5, 44.1, 129.3(2C), 130.7, 139.9, 164.5, 176.9, 209.9. HRMS (ESI-TOF) Calcd for C$_{14}$H$_{14}$ClNNaO$_3$ $^+$ ([M+H]$^+$) 302.0554. Found 302.0562.
10an, 4-Chloro-N-(5-[1,3]dithiolan-2-ylidene-4,6-dioxo-2,6-diphenyl-hexanoyl)-benzamide.
Following the procedure for the synthesis of 10aa, the reaction of 2-aminoacetonitrile hydrochloride (55.1 mg, 0.6 mmol), 4-chlorobenzaldehyde 2a (84 mg, 0.6 mmol) and 2-(1,3-dithiolan-2-ylidene)-1,5-diphenylpent-4-ene-1,3-dione 5n (176 mg, 0.5 mmol) gave 10an (227 mg, 85%) after purification by column chromatography on silica gel (EtOAc/PE = 1: 9 V/V). Reaction time 19.0 h.
Colorless crystals, m.p. 221–223 °C. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 2.71 (dd, $J = 18.0, 3.5$ Hz, 1H), 2.27–3.30 (m, 2H), 3.33–3.39 (m, 3H), 5.10 (dd, $J = 11.0, 3.5$ Hz, 1H), 7.20–7.24 (m, 5H), 7.39 (d, $J = 8.5$ Hz, 2H), 7.46 (t, $J = 7.5$ Hz, 2H), 7.59 (t, $J = 7.5$ Hz, 1H), 7.71 (d, $J = 8.5$ Hz, 2H), 7.86 (d, $J = 7.5$ Hz, 2H), 8.76 (s, 1H). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 36.8, 38.0, 45.7, 47.5, 125.5, 127.5, 128.4, 128.8, 129.0(2C), 129.3, 129.5, 131.4, 133.7, 137.2, 137.3, 139.3, 164.2, 171.2, 174.4, 192.2, 194.6. HRMS (ESI-TOF) Calcd for C$_{28}$H$_{22}$ClNNaO$_4$S$_2$ $^+$ ([M+Na]$^+$) 558.0576. Found 558.0579.

10ao, 4-Chloro-N-[2-(4-chloro-phenyl)-5-[1,3]dithiolan-2-ylidene-4,6-dioxo-6-phenyl-hexanoyl]-benzamide.
Following the procedure for the synthesis of 10aa, the reaction of 2-aminoacetonitrile hydrochloride (55.1 mg, 0.6 mmol), 4-chlorobenzaldehyde 2a (84 mg, 0.6 mmol) and 5-(4-chlorophenyl)-2-(1,3-dithiolan-2-ylidene)-1-phenylpent-4-ene-1,3-dione 5o (193 mg, 0.5 mmol) gave 10ao (239 mg, 84%) after purification by column chromatography on silica gel (EtOAc/PE = 1: 9 V/V). Reaction time 20.0 h.
Yellowish crystals, m.p. 196–198 °C. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 2.68 (dd, $J = 18.0, 4.0$ Hz, 1H), 2.27–3.32 (m, 3H), 3.34–3.38 (m, 2H), 5.16 (dd, $J = 10.5, 4.0$ Hz, 1H), 7.14 (d, $J = 9.0$ Hz, 2H), 7.18 (d, $J = 8.5$ Hz, 2H), 7.41 (d, $J = 8.5$ Hz, 2H), 7.46 (t, $J = 7.5$ Hz, 2H), 7.59 (t, $J = 7.5$ Hz, 1H), 7.73 (d, $J = 9.0$ Hz, 2H), 7.84 (d, $J = 7.5$ Hz, 2H), 8.82 (s, 1H). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 36.9, 38.0, 45.7, 46.7, 125.4, 128.8, 129.0, 129.1, 129.3, 129.5, 129.8, 131.3, 133.4, 133.7, 135.7, 137.3, 139.5, 164.1, 171.6, 174.5, 192.0, 194.6. HRMS (ESI-TOF) Calcd for C$_{28}$H$_{21}$Cl$_2$NNaO$_4$S$_2$ $^+$ ([M+Na]$^+$) 592.0187. Found 592.0189.
10ap, 4-Chloro-N-(5-[1,3]dithiolan-2-ylidene-4,6-dioxo-2-phenyl-6-phenyl-hexanoyl)-benzamide. Following the procedure for the synthesis of 10aa, the reaction of 2-aminoacetonitrile hydrochloride (55.1 mg, 0.6 mmol), 4-chlorobenzaldehyde 2a (84 mg, 0.6 mmol) and 2-(1,3-dithiolan-2-ylidene)-1-phenyl-5-(p-tolyl)pent-4-ene-1,3-dione 5p (233 mg, 0.5 mmol) gave 10ap (247 mg, 90%) after purification by column chromatography on silica gel (EtOAc/PE = 1: 9 V/V). Reaction time 24.0 h. Colorless crystals, m.p. 199–201 °C. \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 2.26 (s, 3H), 2.68 (dd, \(J = 18.0, 3.5\) Hz, 1H), 2.27–3.30 (m, 2H), 3.32 (dd, \(J = 18.0, 11.0\) Hz, 1H), 3.36–3.39 (m, 1H), 5.03 (dd, \(J = 11.0, 3.5\) Hz, 1H), 7.03 (d, \(J = 8.0\) Hz, 2H), 7.08 (d, \(J = 8.0\) Hz, 2H), 7.40 (d, \(J = 8.5\) Hz, 2H), 7.47 (t, \(J = 8.0\) Hz, 2H), 7.59 (t, \(J = 7.5\) Hz, 1H), 7.70 (d, \(J = 8.5\) Hz, 2H), 7.85 (d, \(J = 7.5\) Hz, 2H), 8.59 (s, 1H). \(^1\)3C NMR (125 MHz, CDCl\(_3\)): \(\delta\) 21.0, 36.8, 38.0, 45.8, 47.2, 125.6, 128.2, 129.0(2C), 129.2, 129.5, 129.6, 131.5, 133.7, 134.1, 137.3(2C), 139.2, 164.0, 171.1, 174.2, 192.4, 194.6. HRMS (ESI-TOF) Calcd for C\(_{29}\)H\(_{24}\)ClNNaO\(_4\)S\(_2\)\(+ ([M+Na]+) 572.0733. Found 572.0740.

7a, 3-(4-chlorophenyl)-5-phenyl-3,4-dihydro-2\(H\)-pyrrole-2-carbonitrile. \(\text{trans:}c\text{i\text{s}} = 1.3:1.0^1\) To a solution of 2-aminoacetonitrile hydrochloride (55.1 mg, 0.6 mmol) in DMF (5.0 mL) was added triethylamine (0.08 mL, 0.6 mmol) and stirred at room temperature for 1.0 h. Then, 4-chlorobenzaldehyde 2a (84 mg, 0.6 mmol) was added and further stirred at room temperature for about 4.0 h. After 2a was consumed as indicated by TLC, DBU (0.15 mL, 1.0 mmol) was added in one portion following with the enone 5a (121 mg, 0.5 mmol). The reaction mixture was stirred at room temperature and was monitored by TLC. After enone 5a was consumed, the resulting mixture was poured into ice-water (20 mL) and extracted with diethyl ether (20 mL × 2). The combined organic layers were dried over anhydrous Na\(_2\)SO\(_4\), evaporated \textit{in vacuo}, and the residue was purified by column chromatography (EtOAc/PE = 1/9, V/V) to give 7a (136 mg, 97%).

\(\text{trans-7a}\), yellowish viscous oil. \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 3.21 (dd, \(J = 17.5, 7.5\) Hz, 1H), 3.68 (dd, \(J = 17.5, 9.5\) Hz, 1H), 3.91 (m, 1H), 4.88 (d, \(J = 7.0\) Hz, 1H), 7.21 (d, \(J = 8.5\) Hz, 2H), 7.34 (d, \(J = 8.5\) Hz, 2H), 7.47 (t, \(J = 7.5\) Hz, 2H), 7.54 (t, \(J = 7.5\) Hz, 1H), 7.89 (d, \(J = 7.5\) Hz, 2H). \(^1\)3C NMR (125 MHz, CDCl\(_3\)): \(\delta\) 43.6, 48.2, 68.8, 118.9, 128.1(2C), 128.7, 129.3, 132.0, 132.4, 133.6, 138.4, 176.6. HRMS (ESI-TOF) Calcd for C\(_{17}\)H\(_{14}\)ClN\(_2\)\(\text{([M+H]+)}\) 281.7589. Found 281.7580.

\(\text{cis-7a}\), yellowish viscous oil. \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 3.37 (dd, \(J = 17.5, 6.0\) Hz, 1H), 3.52 (dd, \(J = 17.5, 9.0\) Hz, 1H), 3.93 (m, 1H), 5.31 (d, \(J = 8.0\) Hz, 1H), 7.18 (d, \(J = 8.5\) Hz, 2H), 7.33 (d, \(J = 8.5\)

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Hz, 2H), 7.48 (t, J = 7.5 Hz, 2H), 7.55 (t, J = 7.5 Hz, 1H), 7.92 (d, J = 7.5 Hz, 2H). $^{13}$C NMR (125 MHz, CDCl$_3$): δ 42.5, 45.5, 67.1, 116.9, 128.1, 128.8(2C), 129.1, 132.1, 132.5, 133.8, 137.2, 177.5. 

HRMS (ESI-TOF) Calcd for C$_{17}$H$_{14}$ClN$_2$ ([M+H]$^+$) 281.7589. Found 281.7580.

HMBC of 7a

13, 4-chloro-N-propionylbenzamide.
To a solution of (E)-2-(4-chlorobenzylideneamino)acetonitrile (107 mg, 0.6 mmol) in DMSO (5.0 mL) was added K$_2$CO$_3$ (69.0 mg, 0.5 mmol) was added in one portion under oxygen atmosphere following with bromoethane (37 µL, 0.5 mmol). The reaction mixture was stirred at room temperature and was monitored by TLC. After benzyl bromide was consumed, the resulting mixture
was poured into ice-water (20 mL) and extracted with diethyl ether (20 mL × 2). The aqueous layer was treated with 10% NaClO solution (5 mL) and collected. The combined organic layers were dried over anhydrous Na₂SO₄, evaporated *in vacuo*, and the residue was purified by column chromatography (EtOAc/PE = 1/9, V/V) to give 13 (66 mg, 63%). Reaction time 8.0 h.

Yellowish oil. ¹H NMR (500 MHz, CDCl₃): δ 1.34 (t, J = 7.0 Hz, 3H), 4.30 (q, J = 7.0 Hz, 2H), 7.45 (d, J = 8.5 Hz, 2H), 7.78 (d, J = 8.5 Hz, 2H), 8.21 (s, 1H). ¹³C NMR (125 MHz, CDCl₃): δ 14.2, 62.6, 129.1(2C), 131.3, 139.4, 150.9, 164.1. HRMS (ESI-TOF) Calcd for C₁₀H₁₀ClKNO₂⁺ ([M+K]⁺) 250.0032. Found 250.0041.

**14, 4-chloro-N-(2-phenylacetyl)benzamide.**

To a solution of (E)-2-(4-chlorobenzylideneamino)acetonitrile (107 mg, 0.6 mmol) in DMSO (5.0 mL) was added K₂CO₃ (69.0 mg, 0.5 mmol) was added in one portion under oxygen atmosphere following with benzyl bromide (60 µL, 0.5 mmol). The reaction mixture was stirred at room temperature and was monitored by TLC. After benzyl bromide was consumed, the resulting mixture was poured into ice-water (20 mL) and extracted with diethyl ether (20 mL × 2). The aqueous layer was treated with 10% NaClO solution (5 mL) and collected. The combined organic layers were dried over anhydrous Na₂SO₄, evaporated *in vacuo*, and the residue was purified by column chromatography (EtOAc/PE = 1/10, V/V) to give 14 (102 mg, 75%). Reaction time 6.0 h.

Yellowish crystals, m.p. 117–119 °C. ¹H NMR (500 MHz, CDCl₃): δ 5.25 (s, 2H), 7.36–7.40 (m, 5H), 7.44 (d, J = 8.0 Hz, 2H), 7.74 (d, J = 8.0 Hz, 2H), 8.07 (s, 1H). ¹³C NMR (125 MHz, CDCl₃): δ 68.1, 128.7, 128.8, 129.1(2C), 130.5, 131.1, 134.7, 139.5, 150.7, 164.0. HRMS (ESI-TOF) Calcd for C₁₅H₁₂ClKNO₂⁺ ([M+K]⁺) 312.0188. Found 312.0194.
15, (E)-N-but-2-enoyl-4-chlorobenzamide

To a solution of (E)-2-(4-chlorobenzylideneamino)acetonitrile (107 mg, 0.6 mmol) in DMSO (5.0 mL) was added K$_2$CO$_3$ (34.5 mg, 0.25 mmol) was added in one portion under oxygen atmosphere following with allyl bromide (44 µL, 0.5 mmol). The reaction mixture was stirred at room temperature and was monitored by TLC. After benzyl bromide was consumed, the resulting mixture was poured into ice-water (20 mL) and extracted with diethyl ether (20 mL × 2). The aqueous layer was treated with 10% NaClO solution (5 mL) and collected. The combined organic layers were dried over anhydrous Na$_2$SO$_4$, evaporated in vacuo, and the residue was purified by column chromatography (EtOAc/PE = 1/10, V/V) to give 15 (62.4 mg, 56%). Reaction time 12.0 h. Yellowish crystals, m.p. 85–87 °C. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 2.00 (d, $J$ = 6.5 Hz, 3H), 7.11 (d, $J$ = 15.5 Hz, 1H), 7.22–7.26 (m, 1H), 7.47 (d, $J$ = 8.5 Hz, 2H), 7.79 (d, $J$ = 8.5 Hz, 2H), 8.30 (s, 1H). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 18.6, 123.9, 129.1, 129.3, 129.6, 129.9(2C), 147.6, 161.3. HRMS (ESI-TOF) Calcd for C$_{11}$H$_{10}$ClKNO$_2^+$ ([M+K]$^+$) 262.0032. Found 262.0049.
III. Isotope Labeled O₂ Experiments

HRMS spectrum
IV. Crystal data and OPTEP drawing of compound 10aa

Single-crystal X-ray diffraction data was collected at room temperature on a Oxford Diffraction Gemini R Ultra diffractometer, the X-ray generator using Mo-Kα (λ = 0.71073 Å) radiation with a ω scan technique. The crystal structures were solved by direct method of SHELXS-97 and refined by full-matrix least-squares techniques using the SHELXL-97 program. Non-hydrogen atoms were refined anisotropic.

(1) Crystal data and OPTEP drawing of compound 10aa (CCDC 938346)

ORTEP drawing:

Crystal data:

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V. Copies of $^1$H NMR and $^{13}$C NMR spectra
10ac

S24