Supporting Information

Bromine-Radical Mediated Synthesis of β-Functionalized β,γ- and δ,ε-
Unsaturated Ketones via C-H Functionalization of Aldehydes

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Experimental Procedure and Spectral Data for 3a (Table 1, entry 2)

To a 20 mL two-neck round bottom flask, 1-nonanal 1a (71 mg, 0.5 mmol), allyl bromide 2a (2.5 mL), V-65 (2,2'-azobis(2,4-dimethylvaleronitrile), 25 mg, 0.1 mmol), and potassium carbonate (138 mg, 1.0 mmol) were added. Then, this test tube was purged with argon and sealed. The mixture was stirred at 60 °C for 1 h under argon atmosphere. The reaction mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography on SiO₂ to give 1-dodecen-4-one 3a (9.1 mg, 10%).

1-Dodecen-4-one (3a)

Colorless oil; Rf = 0.58 (Hexane : EtOAc = 5 : 1); ¹H NMR (400 MHz, CDCl₃) δ 0.87 (t, J = 7.2 Hz, 3H), 1.19-1.37 (m, 10H), 1.51-1.61 (m, 2H), 2.43 (t, J = 7.2 Hz, 2H), 3.13-3.19 (m, 2H), 5.10-5.20 (m, 2H), 5.92 (ddt, J = 16.8, 10.4, 7.2 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 14.24, 22.78, 23.83, 29.26, 29.33, 29.49, 31.95, 42.53, 47.86, 118.82, 130.89, 209.24; IR (neat): 1717 cm⁻¹; EIMS m/z (relative intensity) 182 ([M]⁺, 1), 141 (71), 71 (74), 57 (100), 43 (76), 41(49), 29(19); HRMS (EI) m/z calcd for C₁₂H₂₂O [M]⁺: 182.1671, found: 182.1660.

Typical Procedure for the Synthesis of β,γ-Unsaturated Ketones 3

To a 20 mL two necked round bottom flask attached with a reflux condenser were added V-65 (2,2'-azobis(2,4-dimethylvaleronitrile), 25 mg, 0.1 mmol) and potassium carbonate (138 mg, 1.0 mmol), and this flask was purged with argon and sealed. Then, 1-nonanal (1a, 71 mg, 0.5 mmol), methyl 2-(bromomethyl)acrylate (2b, 269 mg, 1.5 mmol), and degassed benzene (5 mL) were added. The mixture was stirred at 60 °C for 1 h. The reaction mixture was filtered through a short plug of Celite and the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography on SiO₂ (Hexane/EtOAc = 1 : 0 to 30 : 1) and preparative HPLC (chloroform) to give methyl 2-methylene-4-oxododecanoate (3b, 101 mg, 84%).

*Preparative HPLC: Japan Analytical Industry Co., LTD., LC-908 (detection: RI and UV
(254 nm), flow rate: 3.8 mL/min), GPC columns: JAIGEL-1H + JAIGEL-2H.

**Methyl 2-methylene-4-oxododecanoate (3b)**

Colorless oil; Rf = 0.55 (Hexane : EtOAc = 5 : 1); 1H NMR (500 MHz, CDCl3) δ 0.87 (t, J = 6.9 Hz, 3H), 1.20-1.33 (m, 10H), 1.55-1.65 (m, 2H), 2.47 (t, J = 7.4 Hz, 2H), 3.40 (s, 2H), 3.74 (s, 3H), 5.63 (s, 1H), 6.33 (s, 1H); 13C NMR (125 MHz, CDCl3) δ 14.02, 22.58, 23.67, 29.10, 29.30, 31.76, 42.63, 45.63, 52.00, 128.53, 134.25, 166.78, 207.42; IR (neat): 2953, 2926, 2855, 1720, 1638 cm⁻¹; EIMS m/z (relative intensity) 240 ([M]⁺, 12), 209 ([M-OMe]⁺, 5), 141 (100), 82 (14), 71 (25), 57 (26), 55(11); HRMS (EI) m/z calcd for C₁₄H₂₃O₃ [M]+: 240.1725 , found:240.1725.

**Methyl 6,8,8-trimethyl-2-methylene-4-oxononanoate (3c)**

Colorless oil; Rf = 0.55 (Hexane : EtOAc = 5 : 1); 1H NMR (500 MHz, CDCl3) δ 0.90 (s, 9H), 0.94 (d, J = 6.5 Hz, 3H), 1.10 (dd, J = 14.2, 6.4 Hz, 1H), 1.19 (dd, J = 14.2, 4.1 Hz, 1H), 2.07-2.19 (m, 1H), 2.32 (dd, J = 16.5, 8.3 Hz, 1H), 2.48 (dd, J = 16.5, 5.1 Hz, 1H), 3.34-3.42 (m, 2H), 3.74 (s, 3H), 5.63 (d, J = 0.9 Hz, 1H), 6.34 (d, J = 1.4 Hz, 1H); 13C NMR (125 MHz, CDCl3) δ 22.56, 25.65, 29.94, 31.02, 46.21, 50.79, 51.94, 52.18, 128.50, 134.19, 132.89, 166.69, 206.80; IR (neat): 2954, 2907, 2871, 1720, 1637 cm⁻¹; EIMS m/z (relative intensity) 240 ([M]⁺, 3), 209 ([M-OMe]⁺, 5), 142 (15), 141 (81), 110 (11), 83 (21), 71 (29), 69 (12), 57 (100), 55 (11); HRMS (EI) m/z calcd for C₁₄H₂₃O₃ [M]+: 240.1725, found: 240.1726.

**Methyl 2-methylene-4-oxo-6-phenylhexanoate (3d)**

Colorless oil; Rf = 0.35 (Hexane : EtOAc = 5 : 1); 1H NMR (500 MHz, CDCl3) δ 2.81-2.8 (m, 2H), 2.90-2.93 (m, 2H), 3.38 (s, 2H), 3.73 (s, 3H), 5.62 (s, 1H), 6.33 (s, 1H), 7.18-7.20 (m, 2H), 7.26-7.30 (m, 3H); 13C NMR (125 MHz, CDCl3) δ 29.60, 27.50, 44.07, 45.87, 52.06, 126.07, 128.31, 128.44, 128.78, 134.03, 140.90, 166.73, 206.22; IR (neat): 3062, 3028, 2952, 2855, 1718, 1637 cm⁻¹; EIMS m/z (relative intensity) 232 ([M]⁺, 21), 200 (7), 133 (33), 105 (96), 91 (100), 77 (15); HRMS (EI) m/z calcd for C₁₄H₁₅O₃ [M]+: 232.1099, found:
Methyl 9-cyano-2-methylene-4-oxononanoate (3e)

\[
\text{\text{\text{[\text{M}]} + 1644, 1621, 1448, 1234, 935]} \text{\text{\text{cm}^{-1}}} \text{; EIMS } m/z \text{ (relative intensity) } 223 ([\text{M}]^+, 3), 192 ([\text{M-OMe}]^+, 10), 124 (100), 96 (82), 81 (16), 69 (19), 55 (18); HRMS (EI) } m/z \text{ calcd for } C_{11}H_{14}NO_2 [\text{M-OMe}]^+: 192.1025, \text{ found: 192.1033.}
\]

Methyl 2-methylene-4-oxo-4-phenylbutanoate (3f)

\[
\text{\text{\text{[\text{M}]} + 173.0613 \text{ cm}^{-1}}} \text{; EIMS } m/z \text{ (relative intensity) } 173 ([\text{M-OMe}]^+, 6), 105 (100), 77 (57), 51 (15); HRMS (EI) } m/z \text{ calcd for } C_{11}H_{14}O_2 [\text{M-OMe}]^+: 173.0603, \text{ found: 173.0605.}
\]

Methyl 4-(4-methoxyphenyl)-2-methylene-4-oxobutanoate (3g)

\[
\text{\text{\text{[\text{M}]} + 130.72, 134.87, 163.76, 167.15, 195.51; IR ( neat): 3003, 2952, 2914, 1722, 1680, 1600 } cm^{-1}; \text{ EIMS } m/z \text{ (relative intensity) } 234 ([\text{M}]^+, 5), 203 ([\text{M-OMe}]^+, 5), 135 (100), 92 (10), 77 (10); HRMS (EI) } m/z \text{ calcd for } C_{13}H_{16}O_4 [\text{M}]^+: 234.0892, \text{ found: 234.0896.}
\]
Methyl 4-(4-cyanophenyl)-2-methylene-4-oxobutanoate (3h)

\[
\begin{align*}
\text{Colorless oil; } R_t &= 0.10 \text{ (Hexane : EtOAc = 5 : 1)}; \quad \text{\textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}) } \delta \text{ 3.76 (s, 3H), 4.00 (s, 2H), 5.76 (s, 1H), 6.44 (s, 1H), 7.79 (d, } J = 8.3 \text{ Hz, 2H), 8.08 (d, } J = 8.3 \text{ Hz, 2H);} \\
\text{\textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}) } \delta \text{ 41.89, 52.21, 116.49, 117.83, 128.64, 129.22, 132.50, 133.74, 139.40, 166.59, 195.53; IR (neat)}: \text{ 2998, 2953, 2918, 2231, 1721, 1696, 1639 cm\textsuperscript{-1}; EIMS } m/z \text{ (relative intensity) 229 ([M]+, 1), 198 ([M-OMe]+, 5), 130 (67), 102 (22), 85 (63), 83 (100); HRMS (EI) } m/z \text{ calcd for C\textsubscript{13}H\textsubscript{11}NO\textsubscript{3} [M]+: 229.0739, found: 229.0745.}
\end{align*}
\]

2-Methylene-4-oxododecanenitrile (3i)

\[
\begin{align*}
\text{Colorless oil; } R_t &= 0.25 \text{ (Hexane : EtOAc = 5 : 1)}; \quad \text{\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) } \delta \text{ 0.88 (t, } J = 6.4 \text{ Hz, 3H), 1.19-1.35 (m, 10H), 1.52-1.67 (m, 2H), 2.49 (t, } J = 7.2 \text{ Hz, 2H), 3.35 (s, 2H), 5.81 (s, 1H), 6.07 (s, 1H); \quad \text{\textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}) } \delta \text{ 14.16, 22.70, 29.15, 29.38, 31.85, 42.73, 47.15, 116.08, 118.16, 134.59, 204.72; IR (neat)}: \text{ 2926, 2855, 2225, 1719, 1617 cm\textsuperscript{-1}; EIMS } m/z \text{ (relative intensity) 207 ([M]+, 3), 141 (100), 109 (48), 94 (23), 81 (13), 71 (44), 57 (48), 55(10); HRMS (EI) } m/z \text{ calcd for C\textsubscript{13}H\textsubscript{21}NO [M]+: 207.1623, found: 207.1630.}
\end{align*}
\]

2-Methylene-4-oxo-4-phenylbutanenitrile (3j)

\[
\begin{align*}
\text{Colorless oil; } R_t &= 0.13 \text{ (Hexane : EtOAc = 5 : 1)}; \quad \text{\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) } \delta \text{ 3.96 (s, 2H), 5.89 (s, 1H), 6.15 (s, 1H), 7.47-7.55 (m, 2H), 7.60-7.66 (m, 1H), 7.93-7.99 (m, 2H); \quad \text{\textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) } \delta \text{ 43.41, 116.47, 118.27, 128.27, 128.96, 134.03, 134.83, 135.60, 194.09; IR (neat)}: \text{ 3116, 3028, 2948, 2923, 2223, 1683, 1581 cm\textsuperscript{-1}; EIMS } m/z \text{ (relative intensity) 171 ([M]+, 2), 105 (100), 77 (42), 51 (10); HRMS (EI) } m/z \text{ calcd for C\textsubscript{11}H\textsubscript{8}NO [M]+: 171.0684, found: 173.0690.}
\end{align*}
\]
**2-(Phenylsulfonyl)dodec-1-en-4-one (3k)**

Yellow oil; \( R_f = 0.20 \) (Hexane : EtOAc = 5 : 1); \(^1^H\) NMR (400 MHz, CDCl\(_3\)) \( \delta \) 0.86 (t, \( J = 6.8 \) Hz, 3H), 1.10-1.32 (m, 10H), 1.39-1.47 (m, 2H), 2.33 (t, \( J = 10.0 \) Hz, 2H), 3.33 (s, 2H), 5.93 (d, \( J = 8.8 \) Hz, 1H), 6.51 (s, 1H), 7.50-7.55 (m, 2H), 7.60-7.65 (m, 1H), 7.83-7.88 (m, 2H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \( \delta \) 14.26, 22.80, 23.62, 29.13, 29.24, 29.44, 42.61, 42.72, 128.16, 128.58, 129.47, 133.98, 138.35, 143.72, 204.46; IR (neat): 2953, 2926, 2855, 1723, 1447 cm\(^{-1}\); EIMS \( m/z \) (relative intensity) 322 ([M]\(^+\), 5), 141 (100), 71 (24), 57 (21); HRMS (EI) \( m/z \) calcld for C\(_{18}\)H\(_{26}\)O\(_3\)S [M]\(^+\): 322.1603, found: 322.1595.

**1-Phenyl-3-(phenylsulfonyl)but-3-en-1-one (3l)**

Yellow oil; \( R_f = 0.40 \) (Hexane : EtOAc = 5 : 1); \(^1^H\) NMR (400 MHz, CDCl\(_3\)) \( \delta \) 3.94 (s, 2H), 5.93 (s, 1H), 6.51 (s, 1H), 7.40-7.46 (m, 2H), 7.49-7.65 (m, 4H), 7.79-7.83 (m, 2H), 7.85-7.91 (m, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 38.49, 127.98, 128.42, 128.51, 128.83, 129.38, 133.79, 133.89, 135.67, 138.22, 143.22, 144.05, 194.09; IR (neat): 3087, 3063, 3030, 2987, 2917, 2885, 1693, 1683, 1596, 1582, 1305 cm\(^{-1}\); EIMS \( m/z \) (relative intensity) 286 ([M]\(^+\), 2), 145 (5), 105 (100), 77 (51), 51 (10); HRMS (EI) \( m/z \) calcld for C\(_{16}\)H\(_{14}\)O\(_3\)S [M]\(^+\): 286.0664, found: 286.0674.

**Dimethyl 2,14-dimethylene-4,12-dioxopentadecanedioate (3m)**

Colorless solid; \( R_f = 0.08 \) (Hexane : EtOAc = 5 : 1); \(^1^H\) NMR (400 MHz, CDCl\(_3\)) \( \delta \) 1.21-1.36 (m, 6H), 1.52-1.66 (m, 4H), 2.47 (t, \( J = 7.3 \) Hz, 4H), 3.39 (s, 4H), 3.74 (s, 6H), 5.64 (s, 2H), 6.33 (s, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 23.66, 28.99, 29.20, 42.66, 45.79, 52.16, 128.71, 134.34, 166.91, 207.45; IR (neat): 3019, 2929, 2885, 2855, 1708, 1637 cm\(^{-1}\); EIMS \( m/z \) (relative intensity) 253 (21), 221 (74), 207 (23), 203 (23), 123 (42), 69 (43), 55 (100); HRMS (EI) \( m/z \) calcld for C\(_{19}\)H\(_{26}\)O\(_6\) [M+H]\(^+\): 353.1964, found: 353.1965.
Procedure for the Synthesis of β,γ-Unsaturated Ketones 3m

To a 20 mL two necked round bottom flask attached with a reflux condenser were added V-65 (20 mol%), potassium carbonate (138 mg, 1.0 mmol), cyclohexanecarbaldehyde (1i, 56 mg, 0.5 mmol), methyl 2-(bromomethyl)acrylate (2b, 269 mg, 1.5 mmol), and degassed benzene (5 mL) were added. The mixture was stirred at 60 °C for 1 h under atmosphere of CO balloon. The reaction mixture was filtered through a short plug of Celite and the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography on SiO$_2$ (Hexane/EtOAc = 1 : 0 to 30 : 1) and preparative HPLC (chloroform) to give methyl 4-cyclohexyl-2-methylene-4-oxobutanoate (3n, 82 mg, 78%).

Methyl 4-cyclohexyl-2-methylene-4-oxobutanoate (3n)

Colorless oil; $R_f = 0.40$ (Hexane : EtOAc = 5 : 1); $^1$H NMR (400 MHz, CDCl$_3$) δ 1.16-1.43 (m, 5H), 1.62-1.71 (m, 1H), 1.75-1.83 (m, 1H), 1.86-1.94 (m, 1H), 2.38-2.49 (m, 1H), 3.44 (d, $J = 1.2$ Hz, 2H), 3.73 (s, 3H), 5.61 (d, $J = 1.5$ Hz, 1H), 6.33 (d, $J = 1.0$ Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 25.72, 25.93, 28.53, 43.81, 50.83, 52.16, 128.68, 134.53, 166.97, 210.46; IR (neat): 2925, 2855, 1723, 1651 cm$^{-1}$; EIMS $m/z$ (relative intensity) 210 ([M]$^+$, 9), 179 ([M-OMe]$^+$, 6), 111 (51), 83 (100), 55 (20); HRMS (EI) $m/z$ calcd for C$_{12}$H$_{18}$O$_3$ [M]$^+$: 210.1256, found: 210.1260.

Typical Procedure for the Synthesis of δ,ε-Unsaturated Ketones 5

To a 20 mL two necked round bottom flask attached with a reflux condenser were added AIBN (2,2'-azobis(isobutyronitrile), 16 mg, 0.1 mmol) and potassium carbonate (138 mg, 1.0 mmol), and this flask was purged with argon and sealed. Then, 1-nonanal (1a, 71 mg, 0.5 mmol), acrylonitrile (4a, 53 mg, 1.0 mmol), methallyl bromide (2e, 203 mg, 1.5 mmol), and degassed benzene (5 mL) were added. The mixture was stirred at 80 °C for 4 h. The reaction mixture was filtered through a short plug of Celite and the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography on SiO$_2$ (Hexane/EtOAc = 1 : 0 to 30 : 1) and preparative HPLC (chloroform) to give 2-(2-methallyl)-4-oxododecanonitrile (5a, 71.1 mg, 57%). Compound 5b is known in literature, and all spectral data matched that reported.$^1$
7,9,9-Trimethyl-3-(2-methylallyl)decane-2,5-dione (5b)

\[ \text{H NMR (400 MHz, CDCl}_3, \text{mixture of two diastereoisomers) } \delta 0.89 (s, 9H), 0.91 (s, 3H), 1.05-1.18 (m, 2H), 1.74 (s, 3H), 1.93-1.99 (m, 1H), 2.04-2.10 (m, 1H), 2.21-2.44 (m, 4H), 2.25 (s, 3H), 2.80-2.91 (m, 1H), 3.16-3.22 (m, 1H), 4.70 (s, 1H), 4.82 (s, 1H); ^{13}\text{C NMR (100 MHz, CDCl}_3, \text{mixture of two diastereoisomers) } \delta 21.84, 22.60, 22.86, 29.82, 29.96, 31.05, 39.64, 44.33, 44.59, 50.77, 52.25, 113.44, 142.03, 209.58, 211.10; 21.86, 22.63, 22.93, 29.82, 29.96, 31.05, 39.64, 44.47, 44.67, 50.86, 52.28, 113.44, 142.03, 209.58, 211.10; \text{IR (neat): } 3649, 2953, 2869, 1714, 1363 \text{ cm}^{-1}; \text{EIMS } m/z \text{ (relative intensity) } 266 (60), 223 (27), 168 (76), 141 (37), 135 (36), 125 (72), 111 (100), 83 (43), 57 (63); \text{HRMS (El) } m/z \text{ calcd for C}_{17}\text{H}_{30}\text{O}_2 \text{[M]}^+: 266.2246, \text{found: } 266.2242. \]

References