Carbon-nitrogen bond cleavage of pyridine with two molecular substituted allenoates: access to 2-arylpyrimidin-4(3H)-one

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1 General Information

The NMR spectra were recorded on Bruker AC – 500 spectrometer (500 MHz for $^1$H NMR and 125 MHz for $^{13}$C NMR) with CDCl$_3$ as the solvent and TMS as internal reference. $^1$H NMR spectral data were reported as follows: chemical shift ($\delta$, ppm), multiplicity, integration, and coupling constant (Hz). $^{13}$C NMR spectral data were reported in terms of the chemical shift. The following abbreviations were used to indicate multiplicities: s = singlet; d = doublet; t = triplet; q = quartet; m = multiplet. Low-resolution mass spectra were obtained on a Shimadzu LCMS-2010EV spectrometer in ESI mode and reported as m/z. High-resolution mass spectra (HRMS) were recorded on a Bruker Daltonics, Inc. APEXIII 7.0 TESLA FTMS instrument. Melting points were obtained on a X-4 digital melting point apparatus without correction. Chemical yields referred to pure isolated product. Purification of products was accomplished by column chromatography packed with silica gel. Unless otherwise stated, all reagents were commercially purchased and used without further purification. All substituted allenoates 1 were synthesized according to procedures reported previously.$^{[11]}$

2 General Procedure

2.1 General procedure for the formation of product 3 or 4.

Under air atmosphere, a sealable reaction tube with a Teflon-coated screw cap equipped with a magnetic stir bar was charged with substituted allenoate 1 (1.5 mmol), 2-aminopyridine derivatives 2 (0.5 mmol), DABCO (22.5 mg, 0.4 equiv), Cs$_2$CO$_3$ (195 mg, 1.2 equiv) in toluene (5 mL) at room temperature. Then capped it and stirred at 140 ºC for 12 h. After the reaction was completed, it was cooled to room temperature and monitored by TLC. And the reaction mixture was concentrated under vacuum. The residue was purified by flash chromatography on silica gel (eluant: petroleum ether/ethyl acetate) to give the desired product 3 or 4.
2.2 Representative procedure for the preparation of substituted allenoate 1

Synthesis of ethyl 2-benzylbuta-2,3-dienoate (1a)

To a stirred solution of (carbethoxymethylene)triphenylphosphorane (Alfa, 98%, 10.0 g, 27.27 mmol) in chloroform (80 mL) was added 1.27 equiv. of (bromomethyl)benzene (Alfa) at room temperature. The reaction mixture was refluxed until (carbethoxymethylene)triphenylphosphorane (monitored by TLC) was disappeared. The solvent and the excess of (bromomethyl)benzene was evaporated under reduced pressure. To the resulting phosphonium salt were added dichloromethane (100 mL) and 2.2 equiv. of triethylamine (8.4 mL). After stirred for about 1 hr, 1.0 equiv. of acetyl chloride (1.96 mL) was added dropwise over 30 min. Then the reaction mixture was allowed to be stirred overnight. The resulting mixture was poured into a Buchner funnel that was packed with silica gel and was washed with dichloromethane for several times. The combined filtrate was carefully concentrated and the residue was subjected to a flash column chromatography (20:1 petroleum ether/ethyl acetate eluent) to provide allenoate 1a.

Reference

3 Characterization Data

(3a): 194 mg, 86% yield. Yellow solid. m.p.: 160-161 °C. \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) (ppm) = 12.47 (s, 1H), 7.64 (d, \(J = 8.0\) Hz, 1H), 7.57-7.56 (m, 1H), 7.51 (t, \(J = 7.5\) Hz, 1H), 7.35 (t, \(J = 7.5\) Hz, 1H), 7.26-7.20 (m, 5H), 7.05-6.05 (m, 5H), 4.82-4.80 (m, 1H), 4.09 (q, \(J = 7.0\) Hz, 1H), 4.01 (q, \(J = 7.0\) Hz, 1H), 3.91 (d, \(J = 14.5\) Hz, 1H), 3.84 (d, \(J = 14.5\) Hz, 1H), 3.42 (dd, \(J = 13.5, 8.0\) Hz, 1H), 3.10 (dd, \(J = 13.5, 7.0\) Hz, 1H), 2.45 (s, 3H), 1.08 (t, \(J = 7.0\) Hz, 3H). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \(\delta\) (ppm) = 173.3, 164.2, 161.1, 154.6, 139.3, 138.8, 137.8, 132.7, 130.8, 129.4, 128.8, 128.5, 128.3, 128.2, 128.1, 127.2, 126.1, 126.0, 122.0, 60.8, 48.3, 39.7, 31.0, 22.0, 13.8. HRMS (ESI): calcd for C\(_{29}\)H\(_{29}\)N\(_2\)O\(_3\) [M+H]\(^+\) 453.2173, Found: 453.2171.

(3b): 253 mg, 83% yield. Yellow solid. m.p.: 136-138 °C. \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) (ppm) = 12.91 (s, 1H), 7.62-7.49 (m, 3H), 7.35-7.33 (m, 3H), 7.12 (d, \(J = 8.0\) Hz, 2H), 7.09 (d, \(J = 8.0\) Hz, 2H), 6.80-6.78 (m, 2H), 4.80 (t, \(J = 7.0\) Hz, 1H), 4.05 (q, \(J = 7.0\) Hz, 2H), 3.82 (d, \(J = 14.5\) Hz, 1H), 3.74 (d, \(J = 14.5\) Hz, 1H), 3.34 (dd, \(J = 13.5, 8.0\) Hz, 1H), 3.02 (dd, \(J = 13.5, 7.0\) Hz, 1H), 2.42 (s, 3H), 1.09 (t, \(J = 7.0\) Hz, 3H). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \(\delta\) (ppm) = 173.0, 164.3, 161.0, 154.8, 138.4, 137.7, 137.6, 132.5, 131.3, 131.1, 130.9, 130.5, 130.3, 129.7, 128.3, 127.2, 121.5, 120.0, 119.9, 61.0, 47.9, 39.0, 30.63, 22.0, 13.9. HRMS (ESI): calcd for C\(_{29}\)H\(_{27}\)Br\(_2\)N\(_2\)O\(_3\) [M+H]\(^+\) 611.0362, Found: 611.0369.

(3c): 203 mg, 78% yield. Yellow solid. m.p.: 150-151 °C. \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) (ppm) = 12.70 (s, 1H), 7.59-7.57 (m, 2H), 7.52-7.49 (m, 1H), 7.37-7.34 (m, 1H), 7.20-7.16 (m, 4H), 6.94 (d, \(J = 8.0\) Hz, 2H), 6.84 (d, \(J = 8.0\) Hz, 2H), 4.77 (t, \(J = 7.5\) Hz, 1H), 4.11-3.99 (m, 2H), 3.84 (d, \(J = 14.5\) Hz, 1H), 3.76 (d, \(J = 14.5\) Hz, 1H), 3.35 (dd, \(J = 13.5, 8.0\) Hz, 1H), 3.03 (dd, \(J = 13.5, 7.0\) Hz, 1H),
2.42 (s, 1H), 1.09 (t, J = 7.0 Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$): δ (ppm) = 173.1, 164.3, 161.1, 154.8, 137.9, 137.6, 137.2, 132.6, 131.9, 131.9, 130.9, 130.1, 129.9, 129.6, 128.4, 128.3, 128.2, 127.2, 121.6, 61.0, 48.0, 39.0, 30.5, 22.0, 13.9. HRMS (ESI): calcd for C$_{29}$H$_{27}$Cl$_2$N$_2$O$_3$ [M+H]$^+$ 521.1393, Found: 521.1386.

(3d): 196 mg, 82% yield. Yellow solid. m.p.: 126-127 °C. $^1$H NMR (500 MHz, CDCl$_3$): δ (ppm) = 11.85 (s, 1H), 7.62 (d, J = 8.0 Hz, 1H), 7.51-7.48 (m, 2H), 7.34 (t, J = 7.5 Hz, 1H), 7.17 (d, J = 8.0 Hz, 2H), 7.07 (d, J = 7.5 Hz, 2H), 6.87-6.83 (m, 4H), 4.70-4.67 (m, 1H), 4.15-3.99 (m, 2H), 3.87 (d, J = 14.5 Hz, 1H), 3.81 (d, J = 14.5 Hz, 1H), 3.37 (dd, J = 13.5, 8.0 Hz, 1H), 3.01 (dd, J = 13.5, 7.0 Hz, 1H), 2.43 (s, 3H), 2.32 (s, 3H), 2.20 (s, 3H), 1.10 (t, J = 7.0 Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$): δ (ppm) = 173.3, 163.8, 160.9, 154.5, 137.8, 136.3, 135.7, 135.6, 135.5, 132.9, 130.8, 129.3, 129.0, 128.9, 128.7, 128.4, 128.2, 127.2, 122.3, 60.9, 48.3, 39.2, 30.6, 22.0, 20.9, 20.9, 13.9. HRMS (ESI): calcd for C$_{31}$H$_{33}$N$_2$O$_3$ [M+H]$^+$ 481.2486, Found: 481.2492.

(3e): 232 mg, 89% yield. Yellow oil. $^1$H NMR (500 MHz, CDCl$_3$): δ (ppm) = 11.43 (s, 1H), 7.60 (dd, J = 8.0, 1.0 Hz, 1H), 7.51-7.48 (m, 2H), 7.36-7.33 (m, 1H), 7.19 (d, J = 8.5 Hz, 2H), 6.82 (d, J = 8.5 Hz, 2H), 6.79 (d, J = 8.5 Hz, 2H), 6.58 (d, J = 8.5 Hz, 2H), 4.62 (t, J = 7.5 Hz, 1H), 4.13-4.01 (m, 2H), 3.85-3.77 (m, 5H), 3.60 (s, 3H), 3.34 (dd, J = 13.5, 8.0 Hz, 1H), 2.97 (dd, J = 13.5, 7.0 Hz, 1H), 2.42 (s, 3H), 1.12 (t, J = 7.0 Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$): δ (ppm) = 173.3, 163.6, 163.5, 160.7, 158.0, 154.4, 137.7, 133.1, 131.4, 130.8, 130.6, 129.8, 129.5, 129.3, 128.3, 127.3, 122.5, 113.7, 113.6, 61.0, 55.2, 54.9, 48.6, 38.8, 30.2, 22.05, 13.9. HRMS (ESI): calcd for C$_{31}$H$_{32}$N$_2$O$_3$ [M+H]$^+$ 513.2384, Found: 513.2387.
(3f): 206 mg, 86% yield. Yellow oil. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ (ppm) = 12.7 (s, 1H), 7.68-7.64 (m, 2H), 7.53 (t, $J$ = 7.5 Hz, 1H), 7.35 (t, $J$ = 7.5 Hz, 1H), 7.19-7.04 (m, 4H), 7.00-6.85 (m, 4H), 4.90-4.87 (m, 1H), 4.18-4.00 (m, 2H), 3.89 (s, 2H), 3.44 (dd, $J$ = 13.5, 8.5 Hz, 1H), 3.12 (dd, $J$ = 13.5, 6.5 Hz, 1H), 2.49 (s, 3H), 2.33 (s, 3H), 2.21 (s, 3H), 1.10 (t, $J$ = 7.0 Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ (ppm) = 173.2, 164.3, 161.1, 154.6, 139.2, 138.8, 138.0, 137.7, 137.5, 132.6, 130.6, 129.5, 129.0, 128.2, 128.1, 127.9, 127.0, 126.7, 125.8, 125.5, 121.9, 60.7, 48.2, 39.5, 30.8, 22.0, 21.3, 21.0, 13.8. HRMS (ESI): calcd for C$_{30}$H$_{33}$N$_2$O$_3$ [M+H]$^+$ 481.2486, Found: 481.2497.

(3g): 213 mg, 76% yield. Yellow oil. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ (ppm) = 12.40 (s, 1H), 7.58-7.55 (m, 2H), 7.51-7.48 (m, 1H), 7.36-7.33 (m, 1H), 7.21-7.17 (m, 1H), 7.01-6.94 (m, 3H), 6.90-6.87 (m, 1H), 4.75-4.72 (m, 1H), 4.14-3.98 (m, 2H), 3.88 (d, $J$ = 14.5 Hz, 1H), 3.82 (d, $J$ = 15.0 Hz, 1H), 3.41 (dd, $J$ = 13.5, 8.5 Hz, 1H), 3.08 (dd, $J$ = 13.5, 7.0 Hz, 1H), 2.42 (s, 1H), 1.08 (t, $J$ = 7.0 Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ (ppm) = 173.0, 164.1, 163.8, 163.5, 161.8, 161.6, 161.4, 154.9, 141.9, 141.8, 141.5, 141.4, 137.5, 132.6, 131.0, 129.7, 129.6, 129.6, 129.6, 129.5, 129.5, 128.3, 127.5, 124.5, 124.5, 124.1, 124.1, 121.5, 115.8, 115.6, 115.5, 115.3, 113.2, 113.1, 113.0, 113.0, 61.1, 48.1, 39.1, 30.8, 30.8, 22.0, 13.8. HRMS (ESI): calcd for C$_{29}$H$_{27}$F$_2$N$_2$O$_3$ [M+H]$^+$ 489.1984, Found: 489.1920.

(3h): 244 mg, 80% yield. Yellow solid. m.p.: 168-169 °C. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ (ppm) = 11.31 (s, 1H), 7.60-7.56 (m, 2H), 7.50-7.47 (m, 1H), 7.44-7.42 (m, 1H), 7.36-7.33 (m, 1H), 7.26-7.18 (m, 2H), 7.09-7.05 (m, 2H), 6.95-6.93 (m, 2H), 6.77-6.74 (m, 1H), 4.97 (t, $J$ = 7.5 Hz, 1H), 4.20-4.14 (m, 1H), 4.01 (d, $J$ = 17.0 Hz, 1H), 3.96 (d, $J$ = 17.0 Hz, 1H), 3.57 (dd, $J$ = 13.5, 8.5 Hz, 1H), 3.01 (dd, $J$ = 13.5,
7.5 Hz, 1H), 2.29 (s, 3H), 1.18 (t, J = 7.0 Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$): δ (ppm) = 173.0, 163.4, 162.7, 154.7, 138.0, 137.5, 137.4, 133.0, 132.6, 132.5, 131.4, 131.1, 129.3, 128.8, 128.5, 128.2, 127.7, 127.6, 127.3, 127.2, 124.7, 124.6, 120.4, 61.3, 45.71, 40.12, 31.13, 22.13, 14.02. HRMS (ESI): calcd for C$_{29}$H$_{27}$Br$_2$N$_2$O$_3$ [M+H]$^+$ 611.0362, Found: 611.0367.

(3i): 211 mg, 81% yield. Yellow solid. m.p.: 177-179 °C. $^1$H NMR (500 MHz, CDCl$_3$): δ (ppm) = 11.9 (s, 1H), 7.59 (d, J = 7.5 Hz, 1H), 7.51-7.41 (m, 3H), 7.28-7.23 (m, 1H), 7.19-7.10 (m, 4H), 7.00 (t, J = 7.5 Hz, 1H), 6.87 (t, J = 7.5 Hz, 1H), 6.77 (t, J = 7.5 Hz, 1H), 5.07 (t, J = 7.5 Hz, 1H), 4.19-4.09 (m, 2H), 3.58 (dd, J = 13.5, 7.0 Hz, 1H), 3.04 (dd, J = 13.5, 8.5 Hz, 1H), 2.34 (s, 3H), 1.17 (t, J = 7.0 Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$): δ (ppm) = 173.0, 162.7, 162.5, 154.4, 137.4, 136.3, 135.8, 134.1, 134.1, 133.3, 131.4, 131.1, 129.3, 129.1, 128.9, 128.3, 128.1, 127.7, 126.7, 126.5, 120.6, 61.5, 45.6, 37.5, 28.3, 22.0, 14.0. HRMS (ESI): calcd for C$_{29}$H$_{27}$Cl$_2$N$_2$O$_3$ [M+H]$^+$ 521.1393, Found: 521.1393.

(3j): 193 mg, 70% yield. Yellow solid. m.p.: 188-189 °C. $^1$H NMR (500 MHz, CDCl$_3$): δ (ppm) = 11.96 (s, 1H), 7.82-7.70 (m, 3H), 7.67-7.61 (m, 3H), 7.55-7.50 (m, 2H), 7.47-7.41 (m, 5H), 7.38 (s, 1H), 7.35-7.23 (m, 3H), 7.09 (dd, J = 8.5, 1.5 Hz, 1H), 4.93 (t, J = 7.5 Hz, 1H), 4.11-3.94 (m, 4H), 3.57 (dd, J = 13.5, 8.0 Hz, 1H), 3.21 (dd, J = 13.5, 7.0 Hz, 1H), 2.47 (s, 3H), 1.07 (t, J = 7.0 Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$): δ (ppm) = 172.3, 163.9, 161.2, 154.7, 139.4, 139.0, 138.0, 133.0, 130.7, 129.6, 128.8, 128.5, 128.3, 128.1, 127.8, 127.2, 126.1, 126.0, 122.0, 81.4, 49.0, 39.9, 31.0, 27.7, 22.0, 14.0. HRMS (ESI): calcd for C$_{37}$H$_{33}$N$_2$O$_3$ [M+H]$^+$ 553.2486, Found: 553.2488.
(3k): 150 mg, 63% yield. Yellow solid. m.p.: 157-159 °C. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ (ppm) = 12.18 (s, 1H), 7.67 (d, $J = 7.5$ Hz, 1H), 7.56-7.50 (m, 2H), 7.36-7.32 (m, 1H), 7.28-7.20 (m, 5H), 7.09-7.06 (m, 3H), 7.03-7.01 (m, 2H), 4.62-4.59 (m, 1H), 3.93 (d, $J = 14.5$ Hz, 1H), 3.86 (d, $J = 14.5$ Hz, 1H), 3.39 (dd, $J = 13.5$, 8.5 Hz, 1H), 3.07 (dd, $J = 13.5$, 7.0 Hz, 1H), 2.44 (s, 3H), 1.30 (s, 9H). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ (ppm) = 172.3, 163.9, 161.2, 154.7, 139.4, 139.0, 138.0, 133.0, 130.7, 129.6, 128.8, 128.5, 128.3, 128.1, 127.8, 127.2, 126.1, 126.0, 122.0, 81.4, 49.0, 39.3, 31.0, 27.7, 22.0, 14.0. HRMS (ESI): calcd for C$_{31}$H$_{33}$N$_2$O$_3$ [M+H]$^+$ 481.2486, Found: 481.2486

(3l): 165 mg, 71% yield. Yellow solid. m.p.: 166-167 °C. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ (ppm) = 12.42 (s, 1H), 7.65 (dd, $J = 8.0$, 0.5 Hz, 1H), 7.57 (dd, $J = 7.5$, 1.0 Hz, 1H), 7.53-7.49 (m, 1H), 7.36-7.33 (m, 1H), 7.26-7.18 (m, 5H), 7.06-6.96 (m, 5H), 4.82 (t, $J = 7.5$ Hz, 1H), 4.01-3.82 (m, 4H), 3.43 (dd, $J = 13.5$, 8.0 Hz, 1H), 3.09 (dd, $J = 13.5$, 7.0 Hz, 1H), 2.45 (s, 3H), 1.51-1.44 (m, 2H), 0.72 (t, $J = 7.5$ Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ (ppm) = 173.4, 164.2, 161.1, 154.6, 139.3, 138.8, 137.9, 132.7, 130.7, 129.4, 128.7, 128.5, 128.3, 128.2, 128.1, 127.2, 126.1, 126.0, 122.0, 66.4, 48.3, 39.7, 22.0, 21.6, 10.0. HRMS (ESI): calcd for C$_{30}$H$_{31}$N$_2$O$_3$ [M+H]$^+$ 467.2329, Found: 467.2331.

(4a): 197 mg, 81% yield. Yellow solid. m.p.: 163-165 °C. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ (ppm) = 11.69 (s, 1H), 7.56-7.53 (m, 2H), 7.48-7.46 (m, 1H), 7.24-7.16 (m, 5H), 7.07-6.99 (m, 3H), 6.89-6.88 (m, 2H), 4.62 (t, $J = 7.5$ Hz, 1H), 4.14-4.01 (m, 2H), 3.94 (d, $J = 14.5$ Hz, 1H), 3.87 (d, $J = 14.5$ Hz, 1H), 3.38 (dd, $J = 14.0$, 7.5 Hz, 1H), 3.01 (dd, $J = 14.0$, 7.5 Hz, 1H), 2.41 (s, 3H), 1.19 (t, $J = 7.0$ Hz 3H). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ (ppm) = 172.9, 163.5, 161.1, 153.1, 139.1, 138.2, 136.1, 134.4, 133.4, 130.9, 129.9, 129.4, 128.8, 128.5, 128.3, 126.4, 126.2, 122.8, 61.3, 48.0, 39.5, 31.0, 22.0, 13.9. HRMS (ESI): calcd for C$_{29}$H$_{28}$ClN$_2$O$_3$ [M+H]$^+$ 487.1783, Found: 487.1799.
(4b): 208 mg, 79% yield. Yellow solid. m.p.: 113-115 °C. $^1$H NMR (500 MHz, CDCl$_3$): δ (ppm) = 12.85 (s, 1H), 7.78 (d, $J = 2.0$ Hz, 1H), 7.64 (dd, $J = 8.5, 2.0$ Hz, 1H), 7.51 (d, $J = 8.5$ Hz, 1H), 7.25-7.16 (m, 5H), 7.03-7.00 (m, 1H), 6.97-6.94 (m, 2H), 6.91-6.89 (m, 2H), 4.79 (t, $J = 7.5$ Hz, 1H), 4.11-3.98 (m, 2H), 3.95 (d, $J = 14.5$ Hz, 1H), 3.90 (d, $J = 14.5$ Hz, 1H), 3.38 (dd, $J = 14.0, 8.0$ Hz, 1H), 3.04 (dd, $J = 14.0, 7.5$ Hz, 1H), 2.11 (s, 3H), 1.08 (t, $J = 7.0$ Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$): δ (ppm) = 173.0, 164.4, 161.1, 153.1, 139.2, 138.3, 136.9, 134.3, 133.6, 132.5, 130.1, 128.7, 128.6, 128.2, 128.2, 126.1, 126.0, 122.6, 121.0, 61.0, 47.9, 39.7, 30.9, 22.0, 13.8. HRMS (ESI): calcd for C$_{29}$H$_{28}$BrN$_2$O$_3$ [M+H]$^+$ 531.1278, Found: 531.1278.

(4c): 171 mg, 71% yield. Yellow oil. $^1$H NMR (500 MHz, CDCl$_3$): δ (ppm) = 12.54 (s, 1H), 7.56 (d, $J = 8.5$ Hz, 1H), 7.23-7.17 (m, 5H), 7.14-7.13 (m, 1H), 7.09-7.07 (m, 1H), 7.01-6.98 (m, 1H), 6.95-6.92 (m, 1H), 4.75 (t, $J = 7.5$ Hz, 1H), 4.14-3.98 (m, 1H), 3.92 (d, $J = 14.5$ Hz, 1H), 3.85 (d, $J = 14.5$ Hz, 1H), 3.38 (dd, $J = 14.0, 8.0$ Hz, 1H), 3.04 (dd, $J = 14.0, 7.5$ Hz, 1H), 3.06-3.02 (m, 1H), 2.46 (s, 3H) 1.08 (t, $J = 7.0$ Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$): δ (ppm) = 173.6, 161.2, 158.3, 154.5, 139.2, 138.8, 133.5, 129.6, 129.6, 129.5, 128.8, 128.5, 128.2, 128.0, 126.0, 125.9, 122.0, 117.4, 113.9, 60.8, 55.2, 47.5, 39.8, 30.9, 22.0, 13.9. HRMS (ESI): calcd for C$_{30}$H$_{31}$N$_2$O$_3$ [M+H]$^+$ 483.2278, Found: 483.2273.

(4d): 175 mg, 69% yield. Yellow oil. $^1$H NMR (500 MHz, CDCl$_3$): δ (ppm) = 12.40 (s, 1H), 8.25 (s, 1H), 8.16 (dd, $J = 8.5, 1.5$ Hz, 1H), 7.70 (d, $J = 8.5$ Hz, 1H), 7.21-7.15 (m, 5H), 7.04-7.01 (m, 1H), 6.97-6.94 (m, 2H), 6.88-6.87 (m, 2H), 4.84-4.81 (m, 1H), 4.14-4.00 (m, 2H), 3.87-3.79 (m, 5H), 3.38 (dd, $J = 14.0, 7.5$ Hz, 1H), 3.04 (dd, $J = 14.0, 8.0$ Hz, 1H), 2.41 (s, 3H) 1.09 (t, $J = 7.0$ Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$): δ (ppm) = 172.7, 165.8, 164.0, 164.0, 161.0, 153.7, 142.7,
139.2, 138.1, 133.1, 131.5, 130.7, 129.1, 128.7, 128.4, 128.2, 128.2, 126.2, 126.1, 122.5, 61.1, 52.2, 48.5, 39.6, 30.8, 22.0, 13.9. HRMS (ESI): calcd for C\textsubscript{31}H\textsubscript{31}N\textsubscript{2}O\textsubscript{5} [M+H]\textsuperscript{+} 511.2227, Found: 511.2229.

(4e): 193 mg, 89% yield. Yellow solid. m.p.: 168-170 °C. \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}): \( \delta \) (ppm) = 12.39 (s, 1H), 7.51 (d, \( J = 8.0 \) Hz, 1H), 7.43 (t, \( J = 7.5 \) Hz, 1H), 7.28-7.17 (m, 11H), 3.84-3.79 (m, 5H), 3.37 (s, 1H), 3.07 (s, 1H), 2.46 (s, 3H), 2.22 (s, 3H), 0.94-0.92 (m, 3H). \textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}): \( \delta \) (ppm) = 172.7, 163.7, 161.3, 139.1, 137.3, 136.3, 133.2, 130.1, 129.2, 128.7, 128.4, 128.2, 126.2, 126.0, 122.3, 60.7, 49.9, 31.0, 30.1, 21.9, 19.7, 13.6. HRMS (ESI): calcd for C\textsubscript{30}H\textsubscript{31}N\textsubscript{2}O\textsubscript{3} [M+H]\textsuperscript{+} 467.2329, Found: 467.2325.

(4f): 202 mg, 83% yield. Yellow solid. m.p.: 179-180 °C. \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}): \( \delta \) (ppm) = 12.31 (s, 1H), 7.56 (dd, \( J = 8.0, 1.0 \) Hz, 1H), 7.42 (t, \( J = 7.5 \) Hz, 1H), 7.36 (dd, \( J = 8.0, 1.0 \) Hz, 1H), 7.26-7.11 (m, 8H), 6.98 (s, 2H), 3.98-3.76 (m, 5H), 3.32 (dd, \( J = 14.0, 9.0 \) Hz, 1H), 3.04 (dd, \( J = 14.0, 5.5 \) Hz, 1H), 2.41 (s, 3H), 1.0-0.97 (m, 3H). \textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}): \( \delta \) (ppm) = 172.2, 163.8, 161.5, 152.3, 139.8, 139.0, 138.5, 133.1, 132.5, 131.1, 128.7, 128.4, 128.3, 128.3, 126.4, 126.0, 125.9, 123.0, 61.0, 50.0, 39.5, 30.9, 21.9, 13.7. HRMS (ESI): calcd for C\textsubscript{30}H\textsubscript{28}Cl\textsubscript{2}N\textsubscript{2}O\textsubscript{3} [M+H]\textsuperscript{+} 487.1783, Found: 487.1783.

(4g): 201 mg, 76% yield. Yellow solid. m.p.: 165-166 °C. \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}): \( \delta \) (ppm) = 11.21 (s, 1H), 7.60 (d, \( J = 8.0 \) Hz, 1H), 7.53 (dd, \( J = 8.0, 1.0 \) Hz, 1H), 7.35 (t, \( J = 7.5 \) Hz, 1H), 7.27-7.13 (m, 8H), 6.95 (s, 2H), 4.00-3.75 (m, 5H), 3.32-3.28 (m, 1H), 3.05-3.02 (m, 1H), 2.39 (s, 3H), 1.01 (s, 3H). \textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}): \( \delta \) (ppm) = 172.2, 163.2, 161.4, 153.2, 139.9, 139.0, 138.5, 134.5, 131.8, 131.5, 128.7, 128.4, 128.4, 126.6, 126.1, 123.3, 122.3, 61.22, 50.4, 39.7, 31.0, 21.9, 13.8. HRMS (ESI): calcd for C\textsubscript{29}H\textsubscript{28}BrN\textsubscript{2}O\textsubscript{3} [M+H]\textsuperscript{+} 531.1278, Found: 531.1278.
(4h): 163 mg, 65% yield. Yellow solid. m.p.: 183-184 °C. \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) (ppm) = 11.28-10.03 (s, 1H), 8.00 (s, 1H), 7.89-7.87 (m, 1H), 7.79-7.71 (m, 1H), 7.25-7.12 (m, 8H), 7.01-7.00 (m, 1H), 6.80 (s, 1H), 4.13-3.78 (m, 5H), 3.54-3.38 (m, 1H), 3.15-3.12 (m, 1H), 2.44-2.41 (m, 3H), 1.14-0.97 (m, 3H). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \(\delta\) (ppm) = 172.7, 172.4, 163.1, 162.8, 161.3, 161.1, 154.0, 153.4, 139.0, 138.4, 135.4, 135.0, 132.4, 131.1, 130.9, 130.8, 130.6, 130.3, 130.0, 128.7, 128.4, 128.3, 128.0, 127.4, 127.2, 126.5, 126.3, 126.0, 124.8, 124.5, 123.8, 122.9, 122.8, 61.1, 61.0, 50.5, 50.4, 39.7, 38.8, 30.9, 22.0, 13.9, 13.7. HRMS (ESI): calcd for C\(_{33}\)H\(_{31}\)N\(_2\)O\(_3\) [M+H]\(^+\) 503.2329, Found: 503.2326.

4 Control Experiments and Mechanistic Studies

1) Experiment with \(\gamma\)-substituted allenoate

Under air atmosphere, a sealable reaction tube with a Teflon-coated screw cap equipped with a magnetic stir bar was charged with \(\gamma\)-substituted allenoate 1 (1.5 mmol), 2-aminopyridine derivatives 2 (0.5 mmol), DABCO (22.5 mg, 0.4 equiv), CsCO\(_3\) (195mg, 1.2 equiv) in toluene (5 mL) at room temperature. Then capped it and stirred at 140 °C for 12 h. After the reaction was completed, it was cooled to room temperature and monitored by TLC. And the reaction mixture was concentrated under vacuum. The residue was purified by flash chromatography on silica gel (eluant: petroleum ether/ethyl acetate) and no desired product was observed.
2) Experiment with deuterated allenoate

$$\text{Bn} = \text{Benzyl}$$

$$\text{D} = \text{Deuterium}$$

$$\text{OEt} = \text{Ethyl}$$

$$\text{D} = \text{Deuterium}$$

$$\text{D} = \text{Deuterium}$$

Under air atmosphere, a sealable reaction tube with a Teflon-coated screw cap equipped with a magnetic stir bar was charged with substituted allenoate [D2]-1a (1.5 mmol), 2-aminopyridine 2a (0.5 mmol), DABCO (22.5 mg, 0.4 equiv), CsCO₃ (195 mg, 1.2 equiv) in toluene (5 mL) at room temperature. Then capped it and stirred at 140 °C for 12 h. After the reaction was completed, it was cooled to room temperature and monitored by TLC. And the reaction mixture was concentrated under vacuum. The residue was purified by flash chromatography on silica gel (eluant: petroleum ether/ethyl acetate) to give the desired product [D3]-3a.
Chemical Formula: $C_{29}H_{26}D_3N_2O_3$

$[M+H]^+$

Calcd: 456.2361

Found: 456.2355

[D3]-3a
c) To find out further application of the resultant products

Step 1: Under air atmosphere, a sealable reaction tube with a Teflon-coated screw cap equipped with a magnetic stir bar was charged with compounds 3a (0.23 g, 0.5 mmol), N,N-dimethylaniline (0.63 mL, 5.0 mmol), POCl₃ (0.47 mL, 5.0 mmol) in toluene (5.0 mL) at room temperature. The rubber septum was then replaced by a Teflon-coated screw cap, and the reaction vessel placed in an oil bath at 60 °C for 3h. After the reaction was completed, it was cooled to room temperature and monitored by TLC. And the reaction mixture was concentrated under vacuum. The residue was purified by flash chromatography on silica gel (eluant: petroleum ether/ethyl acetate = 10:1) to give the desired product 5 (0.216 g, 92% yield).

Step 2: Under air atmosphere, a sealable reaction tube with a Teflon-coated screw cap equipped with a magnetic stir bar was charged with compounds 5 (0.24 g, 0.5 mmol), Ethylamine (0.035 mL, 0.55 mmol), Et₃N (0.21 mL, 1.5 mmol) in DMF (5.0 mL) at room temperature. The rubber septum was then replaced by a Teflon-coated screw cap, and the reaction vessel placed in an oil bath at 100 °C for 18h. After the reaction was completed, it was cooled to room temperature and monitored by TLC. And the reaction mixture was washed with water and concentrated under vacuum. The residue was purified by flash chromatography on silica gel (eluant: petroleum ether/ethyl acetate = 10:1) to give the desired product 6 (0.108 g, 45% yield).
(5): 216 mg, 92% yield. Yellow oil. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ (ppm) = 7.91-7.89 (m, 1H), 7.61-7.59 (m, 1H), 7.48-7.44 (m, 1H), 7.39-7.33 (m, 3H), 7.29-7.26 (m, 1H), 7.20-7.15 (m, 7H), 5.05-5.02 (m, 1H), 4.26 (s, 2H), 4.04-4.01 (m, 2H), 3.48-3.43 (m, 1H), 3.23-3.19 (m, 1H), 2.56 (s, 3H), 1.06 (t, $J = 7.1$ Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ (ppm) = 173.6, 168.1, 164.4, 161.3, 139.5, 138.0, 136.9, 136.4, 131.1, 130.0, 128.9, 128.7, 128.3, 128.0, 127.9, 127.7, 127.1, 126.7, 125.9, 60.5, 48.6, 39.8, 34.4, 22.9, 13.9. HRMS (ESI): calcd for C$_{29}$H$_{28}$ClN$_2$O$_2$ [M+H]$^+$ 453.2173, Found: 453.2180.

(6): 108 mg, 45% yield. Yellow oil. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$(ppm) = 7.82-7.80 (m, 1H), 7.55-7.53 (m, 1H), 7.36-7.33 (m, 4H), 7.29-7.27 (m, 1H), 7.19-7.09 (m, 7H), 5.23-5.20 (m, 1H), 4.48 (s, 1H), 4.05-3.93 (m, 4H), 3.39-3.35 (m, 3H), 3.16-3.12 (m, 1H), 2.50 (s, 3H), 1.06 (t, $J = 7.2$ Hz, 3H), 1.00 (t, $J = 7.2$ Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ (ppm) = 174.0, 163.9, 161.8, 160.6, 140.0, 139.1, 137.5, 137.2, 130.6, 129.0, 128.9, 128.8, 127.9, 127.7, 127.6, 127.0, 126.9, 125.9, 110.3, 60.4, 48.3, 40.2, 35.9, 31.7, 21.8, 14.8, 13.9. HRMS (ESI): calcd for C$_{31}$H$_{34}$N$_3$O$_2$ [M+H]$^+$ 480.2651, Found: 480.2655.
$^1$H NMR and $^{13}$C NMR Spectra of All Compounds

Compound 3a
Compound 3b
Compound 3c
Compound 3d
Compound 3f
Compound 3g
Compound 3h
Compound 3i
Compound 3j
Compound 3k
Compound 3l
Compound 4a
Compound 4b
Compound 4c
Compound 4d
Compound 4f
Compound 4g
Compound 4h
Compound 5
Compound 6