Supporting Information

Palladium-Catalyzed Domino Cyclization (5-Exo/3-Exo), Ring-Expansion by Palladium Rearrangement, and Aromatization: An Expedient Synthesis of 4-Arylnicotinates from Morita-Baylis-Hillman Adducts

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1. General information

All reactions were carried out in oven-dried glassware under an atmosphere of dry nitrogen unless otherwise noted. Thin layer chromatography (TLC) was performed with pre-coated silica gel plates (Kieselgel 60F-254, Merck). Visualization on TLC was achieved by the use of UV light (254 nm) or treatment with \( p \)-anisaldehyde stain followed by heating. The separations were carried out by flash column chromatography over silica gel 60 (230-400 mesh ASTM). Organic extracts were dried over anhydrous MgSO\(_4\) and the solvents were removed on a rotary evaporator under water aspirator pressure. All reagents were purchased from commercial sources and used without further treatment.

Melting points were measured with a Thomas-Hoover melting point apparatus and are uncorrected. \(^1\)H NMR (300 MHz) spectra were measured on a Varian Unity Plus 300. Chemical shifts are reported in ppm relative to TMS (\( \delta \) scale) used as an internal standard. Splitting patterns are indicated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Chemical shifts of the \(^{13}\)C NMR (75 MHz) spectra were measured relative to CDCl\(_3\) (77.23 ppm). IR spectra were recorded on a Jasco FT-IR 410 spectrometer and are reported in cm\(^{-1}\). Mass spectra were obtained from the Korea Basic Science Institute (Gwangju branch) using ESI\(^+\) method. Elemental analyses (C, H, and N) were performed with a Fisons EA-1108 Elemental Analyzer machine at Korea Research Institute of Chemical Technology, Daejeon, Korea.
2. Synthesis of starting materials

Synthesis of methyl 2-[hydroxy(phenyl)methyl]acrylate:

A solution of benzaldehyde (1060 mg, 10 mmol) and DABCO (112 mg, 10 mol%) in methyl acrylate (1290 mg, 1.5 equiv) was stirred at room temperature for 7 days under nitrogen atmosphere, quenched with water (10 mL), and extracted with diethyl ether (30 mL x 3). The combined organic layers were washed with dilute HCl solution, brine, dried over MgSO₄, and concentrated under vacuum. The residue was purified by column chromatographic purification process (hexanes/ethyl acetate 10:1) to afford methyl 2-[hydroxy(phenyl)methyl]acrylate (1728 mg, 90%) as colorless oil. Other Baylis-Hillman alcohols were prepared according to the reported procedure.[1]

Synthesis of (Z)-methyl 2-(bromomethyl)-3-phenylacrylate:

A solution of methyl 2-[hydroxy(phenyl)methyl]acrylate (960 mg, 5 mmol) in 48% HBr (2531 mg, 3.0 equiv) was stirred at room temperature for 12 h. The reaction mixture was poured into ice water and extracted with dichloromethane. The organic layers were washed with water, dried over MgSO₄, and concentrated under vacuum. The residue was purified by column chromatographic purification process (hexanes/ethyl acetate 30:1) to afford (Z)-methyl 2-(bromomethyl)-3-phenylacrylate (1160 mg, 91%) as pale yellow oil. Other bromides were prepared similarly.[1,2]

Synthesis of (E)-methyl 2-[(4-methylphenylsulfonamido)methyl]-3-phenylacrylate:

A mixture of (Z)-methyl 2-(bromomethyl)-3-phenylacrylate (510 mg, 2.0 mmol), p-toluenesulfonyl chloride (684 mg, 2.0 equiv), and K₂CO₃ (524 mg, 2.0 equiv) in DMF (10 mL) was stirred at room temperature for 12 h. The reaction mixture was poured into dilute HCl solution and extracted with diethyl ether. The organic solvent was removed by evaporation, and the residue was purified by flash column chromatography (hexanes/EtOAc, 5:1) to afford...
(E)-methyl 2-[(4-methylphenylsulfonamido)methyl]-3-phenylacrylate (497 mg, 72%) as a white solid. Other compounds were prepared similarly.[3]

**Synthesis of (E)-methyl 2-
\[\text{N-(2-bromoallyl)-4-methylphenylsulfonamido}\text{-methyl}\]-3-phenylacrylate (1a):**

![Reaction Scheme]

A mixture of (E)-methyl 2-[(4-methylphenylsulfonamido)methyl]-3-phenylacrylate (345 mg, 1.0 mmol), 2,3-dibromoprop-1-ene (400 mg, 2.0 equiv), and K$_2$CO$_3$ (276 mg, 2.0 equiv) in DMF (3.0 mL) was stirred at room temperature for 12 h. The reaction mixture was poured into dilute HCl solution and extracted with diethyl ether. The organic solvent was removed by evaporation, and the residue was purified by flash column chromatography (hexanes/ether, 7:1) to afford compounds 1a (441 mg, 95%) as a white solid. Mp 66-68 °C; IR (KBr) $\nu_{\text{max}}$ = 1714, 1346, 1247, 1161 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$ 2.35 (s, 3H), 3.62 (s, 3H), 3.96 (s, 2H), 4.25 (s, 2H), 5.38 (d, $J = 2.1$ Hz, 1H), 5.70 (d, $J = 2.1$ Hz, 1H), 7.18 (d, $J = 8.1$ Hz, 2H), 7.28-7.44 (m, 5H), 7.50 (d, $J = 8.1$ Hz, 2H), 7.75 (s, 1H); $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$ 21.51, 44.56, 52.16, 56.04, 118.32, 126.98, 127.49, 128.54, 128.67, 129.33, 129.54, 129.73, 134.13, 135.85, 143.51, 144.66, 167.76; ESIMS $m/z$ 464 [M+H]$^+$, 466 [M+H+2]$^+$. Anal. Calcd for C$_{21}$H$_{22}$BrNO$_4$S: C, 54.32; H, 4.78; N, 3.02. Found: C, 54.55; H, 4.96; N, 2.93.

Compounds 1b-r were synthesized similarly, and the spectroscopic data of these compounds are as follow.

(E)-Ethyl 2-\n\[\text{N-(2-bromoallyl)-4-methylphenylsulfonamido}\text{-methyl}\]-3-phenylacrylate (1b) 93%; white solid, Mp 73-74 °C; IR (KBr) $\nu_{\text{max}}$ = 1704, 1347, 1245, 1162 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$ 1.23 (t, $J = 7.2$ Hz, 3H), 2.34 (s, 3H), 3.96 (s, 2H), 4.08 (q, $J = 7.2$ Hz, 2H), 4.25 (s, 2H), 5.38 (d, $J = 1.8$ Hz, 1H), 5.71 (d, $J = 1.8$ Hz, 1H), 7.17 (d, $J = 8.7$ Hz, 2H), 7.28-7.44 (m, 5H), 7.49 (d, $J = 8.7$ Hz, 2H), 7.74 (s, 1H); $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$ 14.17, 21.50, 44.61, 56.11, 61.25, 118.26, 127.26, 127.46, 128.53, 128.65, 129.26, 129.53, 129.74, 134.22, 135.84, 143.47, 144.35, 167.33; ESIMS $m/z$ 478 [M+H]$^+$, 480 [M+H+2]$^+$.  

S4
(E)-Methyl 2-\{N-(2-bromoallyl)-4-methylphenylsulfonamido\}methyl]-3-p-tolylacrylate (1c)  
95%; colorless oil; IR (film) \( \nu_{\text{max}} = 1708, 1345, 1246, 1162 \text{ cm}^{-1} \);  
\(^1\)H NMR (CDCl\(_3\), 300 MHz) \( \delta \) 2.32 (s, 3H), 2.35 (s, 3H), 3.60 (s, 3H), 3.94 (dd, \( J = 3.6 \) and 1.2 Hz, 2H), 4.25 (s, 2H), 5.38 (dd, \( J = 3.6 \) and 1.2 Hz, 1H), 5.72 (dd, \( J = 3.6 \) and 1.2 Hz, 1H), 7.16 (d, \( J = 8.1 \) Hz, 2H), 7.19 (d, \( J = 8.4 \) Hz, 2H), 7.33 (d, \( J = 8.4 \) Hz, 2H), 7.52 (d, \( J = 8.1 \) Hz, 2H), 7.72 (s, 1H); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz) \( \delta \) 21.39, 21.49, 44.78, 52.09, 55.90, 118.15, 125.60, 127.49, 128.67, 129.41, 129.94, 131.22, 135.74, 139.81, 143.50, 145.02, 167.96; ESIMS \( m/z \) 478 [M+H]+, 480 [M+H+2]+. 

(E)-Methyl 2-\{N-(2-bromoallyl)-4-methylphenylsulfonamido\}methyl]-3-(4-chlorophenyl)acrylate (1d)  
93%; white solid, Mp 91-93 °C; IR (KBr) \( \nu_{\text{max}} = 1713, 1351, 1247, 1161 \text{ cm}^{-1} \);  
\(^1\)H NMR (CDCl\(_3\), 300 MHz) \( \delta \) 2.35 (s, 3H), 3.62 (s, 3H), 3.97 (s, 2H), 4.19 (s, 2H), 5.40 (d, \( J = 1.8 \) Hz, 1H), 5.70 (d, \( J = 1.8 \) Hz, 1H), 7.19 (d, \( J = 8.4 \) Hz, 2H), 7.33 (d, \( J = 9.0 \) Hz, 2H), 7.49 (d, \( J = 8.4 \) Hz, 2H), 7.68 (s, 1H); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz) \( \delta \) 21.51, 44.59, 52.25, 56.13, 118.45, 127.32, 127.44, 128.62, 128.94, 129.59, 131.17, 132.49, 135.53, 135.59, 143.37, 143.68, 167.57; ESIMS \( m/z \) 498 [M+H]+, 500 [M+H+2]+, 502 [M+H+4]+. 

(E)-Methyl 2-\{N-(2-bromoallyl)-4-methylphenylsulfonamido\}methyl]-3-(4-methoxyphenyl)acrylate (1e)  
80%; colorless oil; IR (film) \( \nu_{\text{max}} = 1704, 1603, 1512, 1247, 1179 \text{ cm}^{-1} \);  
\(^1\)H NMR (CDCl\(_3\), 300 MHz) \( \delta \) 2.36 (s, 3H), 3.61 (s, 3H), 3.79 (s, 3H), 3.94 (dd, \( J = 1.2 \) and 1.2 Hz, 2H), 4.26 (s, 2H), 5.36 (dd, \( J = 2.1 \) and 1.2 Hz, 1H), 5.72 (dd, \( J = 2.1 \) and 1.2 Hz, 1H), 6.89 (d, \( J = 9.0 \) Hz, 2H), 7.22 (d, \( J = 8.4 \) Hz, 2H), 7.48 (d, \( J = 9.0 \) Hz, 2H), 7.56 (d, \( J = 8.4 \) Hz, 2H), 7.71 (s, 1H); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz) \( \delta \) 21.52, 45.13, 52.12, 55.35, 55.68, 114.19, 118.00, 123.40, 126.52, 127.53, 128.81, 129.64, 132.26, 135.35, 143.64, 145.15, 160.84, 168.29; ESIMS \( m/z \) 494 [M+H]+, 496 [M+H+2]+. Anal. Calcd for C\(_{22}\)H\(_{24}\)BrNO\(_5\)S: C, 53.45; H, 4.89; N, 2.83.  
Found: C, 53.39; H, 4.96; N, 2.72. 

(E)-Methyl 2-\{N-(2-bromoallyl)-4-methylphenylsulfonamido\}methyl]-3-(4-nitrophenyl)acrylate (1f)  
70%; pale yellow solid, Mp 112-114 °C; IR (KBr) \( \nu_{\text{max}} = 1716, 1520, 1345, 1249, 1160 \text{ cm}^{-1} \);  
\(^1\)H NMR (CDCl\(_3\), 300 MHz) \( \delta \) 2.35 (s, 3H), 3.64 (s, 3H), 4.01 (s, 2H), 4.18 (s, 2H), 5.43 (s, 1H), 5.71 (s, 1H), 7.19 (d, \( J = 7.8 \) Hz, 2H), 7.48 (d, \( J = 7.8 \) Hz, 2H), 7.59 (d, \( J = 8.7 \) Hz, 2H), 7.73 (s, 1H), 8.22 (d, \( J = 8.7 \) Hz, 2H); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz) \( \delta \) 21.50, 44.42, 52.47, 56.43, 118.89, 123.79, 127.34, 128.51, 129.64, 130.33, 130.45, 135.76, 140.52, 141.64, 143.84, 147.84, 166.99; ESIMS \( m/z \) 509 [M+H]+, 511 [M+H+2]+. Anal. Calcd for C\(_{21}\)H\(_{23}\)BrNO\(_6\)S: C, 49.52; H, 4.16; N, 5.50.  
Found: C, 49.71; H, 4.29; N, 5.31. 
(E)-Methyl 2-[[N-(2-bromoallyl)-4-methylphenylsulfonamido]methyl]-3-(naphthalen-2-yl)acrylate (1g)

95%; colorless oil; IR (film) \( \nu_{\text{max}} = 1708, 1350, 1243, 1162 \text{ cm}^{-1} \);
\(^1\text{H}\) NMR (CDCl\(_3\), 300 MHz) \( \delta \) 2.30 (s, 3H), 3.65 (s, 3H), 3.97 (s, 2H), 4.32 (s, 2H), 5.37 (s, 1H), 5.74 (s, 1H), 7.11 (d, \( J = 8.1 \) Hz, 2H), 7.38-7.60 (m, 5H), 7.70-8.00 (m, 4H), 8.04 (s, 1H);
\(^{13}\text{C}\) NMR (CDCl\(_3\), 75 MHz) \( \delta \) 21.47, 45.03, 52.25, 56.02, 118.25, 126.62 (2C), 126.91, 127.27, 127.49, 127.58, 128.33, 128.69, 128.79, 129.56, 130.13, 131.47, 133.04, 133.40, 134.45, 145.02, 167.93; ESIMS \( m/z \) 536 [M+Na]\(^+\), 538 [M+Na+2]\(^+\).

(E)-Methyl 2-[[N-(2-bromoallyl)-4-methylphenylsulfonamido]methyl]-3-(naphthalen-1-yl)acrylate (1h)

84%; colorless oil; IR (film) \( \nu_{\text{max}} = 1717, 1345, 1251, 1160 \text{ cm}^{-1} \);
\(^1\text{H}\) NMR (CDCl\(_3\), 300 MHz) \( \delta \) 2.29 (s, 3H), 3.69 (s, 3H), 3.86 (s, 2H), 4.18 (s, 2H), 5.34 (s, 1H), 5.61 (s, 1H), 7.05 (d, \( J = 7.8 \) Hz, 2H), 7.25-7.55 (m, 6H), 7.70-7.90 (m, 3H), 8.23 (s, 1H); 13C NMR (CDCl\(_3\), 75 MHz) \( \delta \) 21.45, 44.87, 52.21, 56.13, 118.32, 124.63, 125.16, 126.41, 126.82, 127.12, 127.40, 128.27, 128.56, 129.37, 129.43, 129.91, 131.21, 131.33, 133.36, 136.06, 142.50, 143.31, 167.31; ESIMS \( m/z \) 514 [M+H]\(^+\), 516 [M+H+2]\(^+\).

(E)-Methyl 3-(biphenyl-4-yl)-2-[[N-(2-bromoallyl)-4-methylphenylsulfonamido]methyl]acrylate (1i)

85%; colorless oil; IR (film) \( \nu_{\text{max}} = 1709, 1344, 1251, 1162 \text{ cm}^{-1} \);
\(^1\text{H}\) NMR (CDCl\(_3\), 300 MHz) \( \delta \) 2.34 (s, 3H), 3.63 (s, 3H), 3.99 (s, 2H), 4.29 (s, 2H), 5.40 (d, \( J = 3.6 \) Hz, 1H), 5.74 (d, \( J = 3.6 \) Hz, 1H), 7.18 (d, \( J = 7.8 \) Hz, 2H), 7.28-7.35 (m, 1H), 7.36-7.44 (m, 2H), 7.48-7.63 (m, 8H), 7.79 (s, 1H); 13C NMR (CDCl\(_3\), 75 MHz) \( \delta \) 21.52, 44.81, 52.22, 56.02, 118.33, 126.53, 127.06, 127.30, 127.54, 127.85, 128.67, 128.91, 129.83, 130.53, 133.01, 135.70, 140.06, 142.18, 143.58, 144.47, 167.88; ESIMS \( m/z \) 540 [M+H]\(^+\), 542 [M+H+2]\(^+\).

(E)-Methyl 2-[[N-(2-bromoallyl)-4-methylphenylsulfonamido]methyl]-3-(pyridin-3-yl)acrylate (1j)

66%; colorless oil; IR (film) \( \nu_{\text{max}} = 1716, 1347, 1260, 1161 \text{ cm}^{-1} \);
\(^1\text{H}\) NMR (CDCl\(_3\), 300 MHz) \( \delta \) 2.35 (s, 3H), 3.64 (s, 3H), 3.99 (s, 2H), 4.21 (s, 2H), 5.40 (d, \( J = 2.1 \) Hz, 1H), 5.68 (d, \( J = 2.1 \) Hz, 1H), 7.19 (d, \( J = 8.1 \) Hz, 2H), 7.35 (dd, \( J = 7.2 \) and 4.8 Hz, 1H), 7.48 (d, \( J = 8.1 \) Hz, 2H), 7.69 (s, 1H), 7.95 (d, \( J = 7.2 \) Hz, 1H), 8.52 (br s, 1H), 8.56 (br s, 1H); 13C NMR (CDCl\(_3\), 75 MHz) \( \delta \) 21.50, 44.39, 52.35, 56.31, 118.67, 123.53, 127.37, 128.52, 129.25, 129.62, 135.67, 136.70, 140.07, 143.73, 150.11, 150.49, 167.18 (one carbon was overlapped); ESIMS \( m/z \) 465 [M+H]\(^+\), 467 [M+H+2]\(^+\). Anal. Calcd for C\(_{20}\)H\(_{19}\)BrN\(_2\)O\(_4\)S: C, 51.62; H, 4.55; N, 6.02. Found: C, 51.43; H, 4.79; N, 6.11.
(E)-Methyl 2-{{[N-(2-bromoallyl)-4-methylphenylsulfonamido]methyl}-3-(furan-2-yl)acylate (1k)

81%; pale yellow solid, Mp 90-92 °C; IR (KBr) νmax = 1710, 1636, 1349, 1245, 1161 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ 2.37 (s, 3H), 3.59 (s, 3H), 3.96 (s, 2H), 4.49 (s, 2H), 5.40 (s, 1H), 5.76 (s, 1H), 6.46 (s, 1H), 6.82 (s, 1H), 7.23 (d, J = 8.1 Hz, 2H), 7.40 (s, 1H), 7.46 (s, 1H), 7.62 (d, J = 8.1 Hz, 2H); ¹³C NMR (CDCl₃, 75 MHz) δ 21.51, 45.16, 52.12, 55.52, 112.54, 117.67, 118.52, 121.40, 127.47, 128.81, 129.53, 130.23, 136.11, 143.40, 145.48, 150.10, 167.84; ESIMS m/z 476 [M+Na]+, 478 [M+Na+2]+. Anal. Calcd for C₁₉H₂₀BrNO₅S: C, 50.23; H, 4.44; N, 3.08. Found: C, 50.41; H, 4.59; N, 2.89.

(E)-Methyl 2-{{[N-(2-bromoallyl)-4-methylphenylsulfonamido]methyl}-3-(5-methylthieno-2-yl)acylate (1l)

79%; pale yellow oil; IR (film) νmax = 1708, 1617, 1342, 1208, 1163 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ 2.38 (s, 3H), 2.44 (d, J = 0.9 Hz, 3H), 3.58 (s, 3H), 3.91 (dd, J = 1.5 and 1.5 Hz, 2H), 4.34 (s, 2H), 5.40 (dd, J = 3.6 and 1.5 Hz, 1H), 5.81 (dd, J = 3.6 and 1.5 Hz, 1H), 6.71 (dd, J = 3.9 and 0.9 Hz, 1H), 7.22 (d, J = 3.9 Hz, 1H), 7.25 (d, J = 8.7 Hz, 2H), 7.63 (d, J = 8.7 Hz, 2H), 7.72 (s, 1H); ¹³C NMR (CDCl₃, 75 MHz) δ 15.68, 21.53, 45.56, 52.05, 55.34, 117.81, 119.85, 126.55, 127.61, 128.87, 129.59, 134.69, 135.14, 135.55, 137.58, 146.74, 167.91; ESIMS m/z 506 [M+Na]+, 508 [M+Na+2]+.

(E)-Methyl 2-{{[N-(2-bromoallyl)-4-methylphenylsulfonamido]methyl}oct-2-enoate (1m)

85%; colorless oil; IR (film) νmax = 2927, 1711, 1346, 1161 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ 0.83 (t, J = 6.9 Hz, 3H), 1.19-1.30 (m, 4H), 1.31-1.45 (m, 2H), 2.30 (dt, J = 7.8 and 7.8 Hz, 2H), 2.36 (s, 3H), 3.51 (s, 3H), 3.99 (dd, J = 1.2 and 1.2 Hz, 2H), 4.04 (s, 2H), 5.49 (dd, J = 3.6 and 1.2 Hz, 1H), 5.81 (dd, J = 3.6 and 1.2 Hz, 1H), 6.86 (t, J = 7.8 Hz, 1H), 7.22 (d, J = 8.4 Hz, 2H), 7.59 (d, J = 8.4 Hz, 2H); ¹³C NMR (CDCl₃, 75 MHz) δ 13.96, 21.50, 22.45, 28.23, 28.66, 31.50, 44.04, 51.80, 55.98, 59.07, 126.10, 128.75, 128.81, 129.56, 136.64, 143.41, 150.20, 167.27; ESIMS m/z 458 [M+H]+, 460 [M+H+2]+. Anal. Calcd for C₂₀H₂₈BrNO₅S: C, 52.40; H, 6.16; N, 3.06. Found: C, 52.58; H, 6.30; N, 2.99.

(2E,4E)-Methyl 2-{{[N-(2-bromoallyl)-4-methylphenylsulfonamido]methyl}-5-phenylpenta-2,4-dienoate (1n)

85%; white solid, Mp 100-102 °C; IR (KBr) νmax = 2926, 1701, 1622, 1341, 1236, 1161 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ 2.36 (s, 3H), 3.60 (s, 3H), 3.99 (s, 2H), 4.22 (s, 2H), 5.46 (d, J = 3.6 Hz, 1H), 5.81 (d, J = 3.6 Hz, 1H), 6.88 (d, J = 15.0 Hz, 1H), 7.22 (d, J = 8.1 Hz, 2H), 7.25-7.36 (m, 3H), 7.41 (d, J = 11.7 Hz, 1H), 7.47-7.56 (m, 3H), 7.62 (d, J = 8.1 Hz, 2H); ¹³C NMR (CDCl₃, 75 MHz) δ 21.51, 44.55, 52.01, 56.11, 118.19, 123.25, 123.75, 127.20, 127.78, 128.69, 128.88, 129.46, 129.68, 136.02, 136.26, 142.91, 143.57, 144.95, 167.69; ESIMS m/z 490 [M+H]+, 492 [M+H+2]+. Anal. Calcd for C₂₀H₂₈BrNO₅S: C, 52.40; H, 6.16; N, 3.06. Found: C, 52.58; H, 6.30; N, 2.99.
Methyl 2-[[N-(2-bromoallyl)-4-methylphenylsulfonamido](phenyl)methyl]acrylate (1o)

The compound 1o was prepared according to the reported procedure,[4] by the sequential introduction of tosylamide at the secondary position using DABCO salt of the Baylis–Hillman acetate and the following alkylation with 2,3-dibromopropene. The compound 1o is known.[4]

(Z)-N-(2-Bromoallyl)-N-(2-cyano-3-phenylallyl)-4-methylbenzenesulfonamide (1p)

91%; white solid, Mp 84-86 °C; IR (KBr) \( \nu_{\text{max}} = 2214, 1347, 1161 \) cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 300 MHz) \( \delta = 2.32 \) (s, 3H), 4.12 (s, 2H), 4.17 (s, 2H), 5.61 (s, 1H), 5.88 (s, 1H), 7.05 (s, 1H), 7.20 (d, \( J = 8.1 \) Hz, 2H), 7.30-7.40 (m, 3H), 7.54-7.63 (m, 2H), 7.66 (d, \( J = 8.1 \) Hz, 2H); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz) \( \delta = 21.51, 50.85, 55.61, 105.24, 117.62, 120.95, 127.08, 128.88, 129.00, 129.79, 130.94, 132.55, 136.66, 144.07, 147.00; \) ESIMS \( m/z \) 453 [M+Na]\(^+\), 455 [M+Na+2]\(^+\). Anal. Calcd for C\(_{20}\)H\(_{19}\)BrN\(_2\)O\(_2\)S: C, 55.69; H, 4.44; N, 6.49. Found: C, 55.73; H, 4.72; N, 6.30.

(E)-N-(2-Benzylidene-3-oxobutyl)-N-(2-bromoallyl)-4-methylbenzenesulfonamide (1q)

88%; white solid, Mp 69-70 °C; IR (KBr) \( \nu_{\text{max}} = 1668, 1345, 1160 \) cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 300 MHz) \( \delta = 2.40 \) (s, 3H), 2.34 (s, 3H), 3.96 (dd, \( J = 1.5 \) and 1.5 Hz, 2H), 4.19 (s, 2H), 5.40 (dd, \( J = 3.3 \) and 1.5 Hz, 1H), 5.70 (dd, \( J = 3.3 \) and 1.5 Hz, 1H), 7.17 (d, \( J = 8.4 \) Hz, 2H), 7.32-7.44 (m, 3H), 7.45-7.51 (m, 4H), 7.54 (s, 1H); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz) \( \delta = 21.51, 25.92, 43.27, 56.48, 118.57, 127.54, 128.75, 128.94, 134.12, 135.54, 136.19, 143.58, 144.61, 199.71; \) ESIMS \( m/z \) 448 [M+H]\(^+\), 450 [M+H+2]\(^+\).

Synthesis of (E)-Methyl 2-[[N-(Z)-2-bromohex-2-enyl)-4-methylphenylsulfonamido]Methyl]-3-phenylacrylate (1r)

A mixture of compound (E)-Methyl 2-[[4-methylphenylsulfonamido]methyl]-3-phenylacrylate (173 mg, 0.5 mmol), (Z)-1,2-dibromohex-2-ene\(^{[5]}\) (243 mg, 2.0 equiv), and K\(_2\)CO\(_3\) (138 mg, 2.0 equiv) in DMF (2.0 mL) was stirred at room temperature for 12 h. The reaction mixture was poured into dilute HCl solution and extracted with diethyl ether. The organic solvent was removed by evaporation, and the residue was purified by flash column chromatography (hexanes/ether, 7:1) to afford compound 1r (235 mg, 93%) as colorless oil.
IR (film) \( \nu_{\text{max}} = 2957, 1715, 1346, 1246, 1162 \text{ cm}^{-1} \); \(^1\)H NMR (CDCl\(_3\), 300 MHz) \( \delta \) 0.78 (t, \( J = 7.5 \text{ Hz} \), 3H), 1.15-1.29 (m, 2H), 1.93 (dt, \( J = 7.2 \text{ and } 7.2 \text{ Hz} \), 2H), 2.33 (s, 3H), 3.62 (s, 3H), 3.99 (s, 2H), 4.24 (s, 2H), 5.76 (t, \( J = 7.2 \text{ Hz} \), 1H), 7.16 (d, \( J = 8.1 \text{ Hz} \), 2H), 7.28-7.43 (m, 5H), 7.48 (d, \( J = 8.1 \text{ Hz} \), 2H), 7.72 (s, 1H); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz) \( \delta \) 13.75, 21.27, 21.47, 32.99, 44.27, 52.10, 56.29, 122.18, 127.37, 127.50, 128.62, 129.22, 129.41, 129.78, 131.59, 134.22, 136.14, 142.03, 144.17, 167.79; ESIMS \( m/z \) 506 [M+H]\(^{+}\), 508 [M+H+2]\(^{+}\]. Anal. Calcd for C\(_{24}\)H\(_{28}\)BrNO\(_4\)S: C, 56.92; H, 5.57; N, 2.77. Found: C, 57.22; H, 5.71; N, 2.64.

3. Typical procedure for the synthesis of 3a

![Diag: 1a -> 3a, 3a']

A mixture of 1a (232 mg, 0.5 mmol), Pd(OAc)\(_2\) (6 mg, 5 mol%), PPh\(_3\) (13 mg, 10 mol%), and Et\(_3\)N (101 mg, 2.0 equiv) in DMF (2.0 mL) was heated to 120 °C for 3 h. The reaction mixture was poured into dilute HCl solution and extracted with diethyl ether. The organic solvent was removed by evaporation, and the residue was purified by flash column chromatography (hexanes/ether, 7:1) to afford compound 3a (138 mg, 72%) as a white solid and 3a' (8 mg, 4%) as a pale yellow solid.

Methyl 5-methylene-4-phenyl-1-tosyl-1,4,5,6-tetrahydropyridine-3-carboxylate (3a)

72%; white solid, Mp 129-130 °C; IR (KBr) \( \nu_{\text{max}} = 1709, 1630, 1377, 1232, 1169, 1101 \text{ cm}^{-1} \); \(^1\)H NMR (CDCl\(_3\), 300 MHz) \( \delta \) 2.47 (s, 3H), 3.49 (d, \( J = 13.2 \text{ Hz} \), 1H), 3.66 (s, 3H), 4.01 (d, \( J = 13.2 \text{ Hz} \), 1H), 4.42 (s, 1H), 4.90 (s, 1H), 5.22 (s, 1H), 6.85-6.92 (m, 2H), 7.06-7.16 (m, 3H), 7.36 (d, \( J = 8.4 \text{ Hz} \), 2H), 7.73 (d, \( J = 8.4 \text{ Hz} \), 2H), 8.19 (s, 1H); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz) \( \delta \) 21.61, 45.07, 46.15, 51.61, 109.45, 113.48, 126.70, 126.75, 127.18, 128.30, 130.08, 134.09, 136.34, 138.86, 141.88, 144.76, 166.38; ESIMS \( m/z \) 384 [M+H]\(^{+}\). Anal. Calcd for C\(_{21}\)H\(_{21}\)NO\(_4\)S: C, 65.78; H, 5.52; N, 3.65. Found: C, 65.99; H, 5.68; N, 3.52.

Methyl 5-methylene-4-phenyl-1-tosyl-1,2,5,6-tetrahydropyridine-3-carboxylate (3a')

4%; pale yellow solid, Mp 154-155 °C; IR (KBr) \( \nu_{\text{max}} = 1730, 1703, 1239, 1163 \text{ cm}^{-1} \); \(^1\)H NMR (CDCl\(_3\), 300 MHz) \( \delta \) 2.38 (s, 3H), 3.36 (s, 3H), 3.98 (s, 2H), 4.15 (s, 2H), 4.66 (s, 1H), 5.21 (s, 1H), 6.67-6.75 (m, 2H), 7.16-7.24 (m, 3H), 7.25 (d, \( J = 8.4 \text{ Hz} \), 2H), 7.66 (d, \( J = 8.4 \text{ Hz} \), 2H); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz) \( \delta \) 21.49, 46.20, 49.12, 51.65, 120.83, 124.45, 127.48, 127.70, 127.91, 128.30, 129.66, 133.94, 136.96, 138.28, 143.84, 145.09, 145.96, 165.96; ESIMS \( m/z \) 384 [M+H]\(^{+}\). Anal. Calcd for C\(_{21}\)H\(_{21}\)NO\(_4\)S: C, 65.78; H, 5.52; N, 3.65. Found: C, 65.94; H, 5.73; N, 3.51.

Compounds 3m, 3m', 3n, 3n', 3p', 3q and 3r were synthesized similarly, and the spectroscopic data of these compounds are as follow.
Methyl 5-methylene-4-pentyl-1-tosyl-1,4,5,6-tetrahydropyridine-3-carboxylate (3m)

70%; colorless oil; IR (film) \( \nu_{\text{max}} = 2930, 1707, 1629, 1168 \) cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 300 MHz) \( \delta \) 0.83 (t, \( J = 6.9 \) Hz, 3H), 0.84-0.99 (m, 1H), 1.09-1.29 (m, 6H), 1.50-1.65 (m, 1H), 2.44 (s, 3H), 3.65 (d, \( J = 12.9 \) Hz, 1H), 3.74 (s, 3H), 4.07 (d, \( J = 12.9 \) Hz, 1H), 4.94 (s, 2H), 7.34 (d, \( J = 8.4 \) Hz, 2H), 7.69 (d, \( J = 8.4 \) Hz, 2H), 7.89 (s, 1H); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz) \( \delta \) 13.98, 21.58, 22.42, 26.48, 31.21, 35.01, 39.50, 46.38, 51.44, 112.51, 114.10, 114.40, 127.06, 130.01, 134.34, 134.39, 137.51, 144.60, 166.80; ESIMS \( m/z \) 378 [M+H]\(^+\). Anal. Calcd for C\(_{20}\)H\(_{27}\)NO\(_4\)S: C, 63.63; H, 7.21; N, 3.71. Found: C, 63.87; H, 7.50; N, 3.71.

Methyl 5-methylene-4-pentyl-1-tosyl-1,2,5,6-tetrahydropyridine-3-carboxylate (3m\(^\prime\))

13%; colorless oil; IR (film) \( \nu_{\text{max}} = 2955, 1720, 1351, 1247, 1166 \) cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 300 MHz) \( \delta \) 0.80 (t, \( J = 6.9 \) Hz, 3H), 1.09-1.29 (m, 6H), 2.34 (s, 3H), 2.38-2.49 (m, 2H), 3.68 (s, 3H), 3.77 (s, 2H), 3.95 (s, 2H), 5.17 (s, 1H), 5.31 (s, 1H), 7.21 (d, \( J = 7.5 \) Hz, 2H), 7.58 (d, \( J = 7.5 \) Hz, 2H); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz) \( \delta \) 14.00, 21.49, 22.40, 28.62, 29.50, 32.18, 46.35, 49.41, 51.71, 116.13, 122.66, 127.80, 129.59, 133.71, 137.03, 143.69, 146.08, 166.21; ESIMS \( m/z \) 378 [M+H]\(^+\). Anal. Calcd for C\(_{20}\)H\(_{27}\)NO\(_4\)S: C, 63.63; H, 7.21; N, 3.71. Found: C, 63.85; H, 7.46; N, 3.59.

\((E)\)-Methyl 5-methylene-4-styryl-1-tosyl-1,4,5,6-tetrahydropyridine-3-carboxylate (3n)

72%; white solid, Mp 169-170 °C; IR (KBr) \( \nu_{\text{max}} = 1701, 1632, 1382, 1233, 1171, 1099 \) cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 300 MHz) \( \delta \) 2.33 (s, 3H), 3.57 (d, \( J = 14.1 \) Hz, 1H), 3.67 (s, 3H), 3.91 (d, \( J = 5.4 \) Hz, 1H), 4.03 (d, \( J = 14.1 \) Hz, 1H), 4.96 (s, 1H), 5.08 (s, 1H), 5.90 (d, \( J = 16.2 \) Hz, 1H), 6.00 (dd, \( J = 16.2 \) and 5.4 Hz, 1H), 7.02-7.28 (m, 7H), 7.64 (d, \( J = 8.1 \) Hz, 2H), 8.01 (s, 1H); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz) \( \delta \) 21.57, 41.79, 46.22, 51.65, 109.23, 114.49, 122.22, 127.12, 127.41, 128.36, 130.10, 130.33, 130.44, 134.13, 136.00, 136.58, 136.87, 144.77, 166.41; ESIMS \( m/z \) 410 [M+H]\(^+\). Anal. Calcd for C\(_{23}\)H\(_{23}\)NO\(_4\)S: C, 67.46; H, 5.66; N, 3.42. Found: C, 67.37; H, 5.71; N, 3.28.

\((E)\)-Methyl 5-methylene-4-styryl-1,2,5,6-tetrahydropyridine-3-carboxylate (3n\(^\prime\))

11%; colorless oil; IR (film) \( \nu_{\text{max}} = 1711, 1350, 1251, 1164 \) cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 300 MHz) \( \delta \) 2.34 (s, 3H), 3.66 (s, 3H), 3.85 (s, 2H), 4.05 (s, 2H), 5.33 (s, 1H), 5.46 (s, 1H), 6.32 (d, \( J = 16.2 \) Hz, 1H), 7.08-7.39 (m, 9H), 7.63 (d, \( J = 8.1 \) Hz, 2H); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz) \( \delta \) 21.51, 46.11, 49.39, 51.90, 120.47, 121.95, 124.38, 126.66, 127.79, 128.22, 128.66, 129.64, 133.68, 135.22, 136.54, 136.80, 143.25, 143.79, 166.03; ESIMS \( m/z \) 410 [M+H]\(^+\). Anal. Calcd for C\(_{23}\)H\(_{23}\)NO\(_4\)S: C, 67.46; H, 5.66; N, 3.42. Found: C, 67.70; H, 5.88; N, 3.40.
Synthesis of methyl 5-methylene-2-phenyl-1-tosyl-1,2,5,6-tetrahydropyridine-3-carboxylate (3p’)

A mixture of 1o (232 mg, 0.5 mmol), Pd(OAc)$_2$ (6 mg, 5 mol%), PPh$_3$ (13 mg, 10 mol%), and Et$_3$N (101 mg, 2.0 equiv) in DMF (2.0 mL) was heated to 90 °C for 3 h. The reaction mixture was poured into dilute HCl solution and extracted with diethyl ether. The organic solvent was removed by evaporation, and the residue was purified by flash column chromatography (hexanes/ether, 7:1) to afford compound 3p’ (131 mg, 68%) as colorless oil. The compound 3p’ is known.[4]

5-Methylene-4-phenyl-1-tosyl-1,4,5,6-tetrahydropyridine-3-carbonitrile (3q)

22%; colorless oil; $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$ 2.49 (s, 3H), 3.63 (d, $J = 13.2$ Hz, 1H), 4.00 (d, $J = 13.2$ Hz, 1H), 4.10 (s, 1H), 4.99 (s, 1H), 5.09 (s, 1H), 6.94-7.03 (m, 2H), 7.16-7.28 (m, 3H), 7.39 (d, $J = 7.8$ Hz, 2H), 7.65-7.76 (m, 3H).

1-(5-Methylene-4-phenyl-1-tosyl-1,4,5,6-tetrahydropyridin-3-yl)ethanone (3r)

76%; white solid, Mp 149-150 °C; IR (KBr) $\nu_{max} = 1658, 1619, 1385, 1233, 1169$ cm$^{-1}$; $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$ 2.23 (s, 3H), 2.41 (s, 3H), 3.44 (d, $J = 13.2$ Hz, 1H), 3.94 (d, $J = 13.2$ Hz, 1H), 4.47 (s, 1H), 4.83 (s, 1H), 5.15 (s, 1H), 6.72-6.82 (m, 2H), 6.96-7.08 (m, 3H), 7.30 (d, $J = 8.4$ Hz, 2H), 7.65 (d, $J = 8.4$ Hz, 2H), 8.04 (s, 1H); $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$ 21.64, 25.22, 44.10, 46.32, 113.53, 119.86, 126.66, 126.70, 127.16, 128.32, 130.18, 133.92, 137.33, 138.83, 141.67, 145.05, 194.64; ESIMS $m/z$ 368 [M+H]$^+$. Anal. Calcd for C$_{21}$H$_{21}$NO$_3$S: C, 68.64; H, 5.76; N, 3.81. Found: C, 68.43; H, 5.79; N, 3.69.
4. Typical procedure for the synthesis of 2a

A mixture of 1a (232 mg, 0.5 mmol), Pd(OAc)₂ (6 mg, 5 mol%), PPh₃ (13 mg, 10 mol%), and Cs₂CO₃ (408 mg, 2.5 equiv) in DMF (1.5 mL) was heated to 120 °C for 3 h. The reaction mixture was poured into dilute HCl solution and extracted with diethyl ether. The organic solvent was removed by evaporation, and the residue was purified by flash column chromatography (hexanes/ether, 3:1) to afford compound 2a [6] (125 mg, 65%) as a pale yellow solid. Mp 48-49 °C (lit. 49-50 °C [6]); IR (KBr) \( \nu_{\text{max}} = 1734, 1303, 1148 \) cm\(^{-1}\), \(^{1}\)H NMR (CDCl\(_3\), 300 MHz) \( \delta \) 2.11 (s, 3H), 3.62 (s, 3H), 7.11-7.17 (m, 2H), 7.36-7.48 (m, 3H), 8.62 (br s, 1H), 8.92 (br s, 1H); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz) \( \delta \) 17.27, 52.07, 126.39, 127.59, 127.77, 128.23, 132.11, 137.44, 148.39, 149.69, 153.26, 166.84; ESIMS \( m/z \) 228 [M+H]\(^+\). Anal. Calcd for C\(_{14}\)H\(_{13}\)NO\(_2\): C, 73.99; H, 5.77; N, 6.16. Found: C, 74.13; H, 5.89; N, 6.01.

Compounds 2b-l and 2s were synthesized similarly, and the spectroscopic data of these compounds are as follows.

Ethyl 5-methyl-4-phenylnicotinate (2b)

68%; white solid, Mp 56-58 °C; IR (KBr) \( \nu_{\text{max}} = 1719, 1301, 1137 \) cm\(^{-1}\); \(^{1}\)H NMR (CDCl\(_3\), 300 MHz) \( \delta \) 0.97 (t, \( J = 7.2 \) Hz, 3H), 2.12 (s, 3H), 4.04 (q, \( J = 7.2 \) Hz, 2H), 7.11-7.18 (m, 2H), 7.34-7.48 (m, 3H), 8.61 (br s, 1H), 8.90 (br s, 1H); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz) \( \delta \) 13.57, 17.24, 61.03, 126.93, 127.70 (2C), 128.18, 131.95, 137.64, 148.34, 149.34, 153.11, 166.66; ESIMS \( m/z \) 242 [M+H]\(^+\). Anal. Calcd for C\(_{13}\)H\(_{15}\)NO\(_2\): C, 74.67; H, 6.27; N, 5.81. Found: C, 74.80; H, 6.52; N, 5.61.

Methyl 5-methyl-4-p-tolynicotinate (2c)

70%; pale yellow solid, Mp 53-55 °C; IR (KBr) \( \nu_{\text{max}} = 1736, 1436, 1302, 1136 \) cm\(^{-1}\); \(^{1}\)H NMR (CDCl\(_3\), 300 MHz) \( \delta \) 2.12 (s, 3H), 2.41 (s, 3H), 3.64 (s, 3H), 7.03 (d, \( J = 8.4 \) Hz, 2H), 7.24 (d, \( J = 8.4 \) Hz, 2H), 8.60 (br s, 1H), 8.89 (br s, 1H); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz) \( \delta \) 17.28, 21.29, 52.07, 126.54, 127.49, 128.94, 132.28, 134.34, 137.45, 148.27, 149.81, 153.15, 166.92; ESIMS \( m/z \) 242 [M+H]\(^+\). Anal. Calcd for C\(_{15}\)H\(_{15}\)NO\(_2\): C, 74.67; H, 6.27; N, 5.81. Found: C, 74.44; H, 6.44; N, 5.72.
Methyl 4-(4-chlorophenyl)-5-methylnicotinate (2d)

62%; pale yellow solid, Mp 130-132 °C; IR (KBr) $\nu_{\text{max}}$ = 1731, 1439, 1295 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$ 2.10 (s, 3H), 3.67 (s, 3H), 7.09 (d, $J = 8.4$ Hz, 2H), 7.43 (d, $J = 8.4$ Hz, 2H), 8.63 (br s, 1H), 8.95 (br s, 1H); $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$ 17.24, 52.16, 125.99, 128.56, 129.02, 132.06, 133.84, 135.87, 148.59, 148.65, 153.48, 166.49; ESIMS $m/z$ 262 [M+H]$^+$. Anal. Calcd for C$_{14}$H$_{12}$ClNO$_2$: C, 64.25; H, 4.62; N, 5.35. Found: C, 64.21; H, 4.74; N, 5.19.

Methyl 4-(4-methoxyphenyl)-5-methylnicotinate (2e)

52%; colorless oil; IR (film) $\nu_{\text{max}}$ = 1734, 1611, 1517, 1292, 1246 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$ 2.13 (s, 3H), 3.65 (s, 3H), 3.86 (s, 3H), 6.97 (d, $J = 9.0$ Hz, 2H), 7.07 (d, $J = 9.0$ Hz, 2H), 8.59 (br s, 1H), 8.87 (br s, 1H); 13C NMR (CDCl$_3$, 75 MHz) $\delta$ 17.30, 52.10, 55.15, 113.66, 126.87, 128.95, 129.45, 132.44, 148.21, 149.33, 153.13, 159.11, 167.11; ESIMS $m/z$ 258 [M+H]$^+$. Anal. Calcd for C$_{15}$H$_{15}$NO$_3$: C, 70.02; H, 5.88; N, 5.44. Found: C, 70.31; H, 5.95; N, 5.31.

Methyl 5-methyl-4-(4-nitrophenyl)nicotinate (2f)

75%; pale yellow solid, Mp 160-162 °C; IR (KBr) $\nu_{\text{max}}$ = 1730, 1519, 1349, 1297 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$ 2.01 (s, 3H), 3.61 (s, 3H), 7.26 (d, $J = 8.4$ Hz, 2H), 8.26 (d, $J = 8.4$ Hz, 2H), 8.62 (br s, 1H), 8.98 (br s, 1H); $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$ 17.20, 52.29, 123.61, 124.82, 128.65, 131.54, 144.64, 147.37, 147.91, 149.14, 153.95, 165.80; ESIMS $m/z$ 273 [M+H]$^+$. Anal. Calcd for C$_{14}$H$_{12}$N$_2$O$_4$: C, 61.76; H, 4.44; N, 10.29. Found: C, 61.98; H, 4.30; N, 10.01.

Methyl 5-methyl-4-(naphthalen-2-yl)nicotinate (2g)

67%; colorless oil; IR (film) $\nu_{\text{max}}$ = 1734, 1578, 1436, 1301, 1136 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$ 2.13 (s, 3H), 3.56 (s, 3H), 7.28 (dd, $J = 8.4$ and 1.5 Hz, 1H), 7.48-7.56 (m, 2H), 7.57-7.61 (m, 1H), 7.80-7.86 (m, 1H), 7.87-7.95 (m, 2H), 8.65 (br s, 1H), 8.96 (br s, 1H); $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$ 17.37, 52.10, 125.90, 126.31, 126.40 (2C), 126.54, 127.85, 127.88, 128.02, 132.39, 132.63, 133.03, 135.00, 148.46, 149.62, 153.33, 166.85; ESIMS $m/z$ 278 [M+H]$^+$. Anal. Calcd for C$_{18}$H$_{15}$NO$_2$: C, 77.96; H, 5.45; N, 5.05. Found: C, 78.17; H, 5.59; N, 4.82.
Methyl 5-methyl-4-(naphthalen-1-yl)nicotinate (2h)

68%; colorless oil; IR (film) νmax = 1735, 1302, 1287, 1167 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ 1.96 (s, 3H), 3.44 (s, 3H), 7.19 (dd, J = 7.2 and 1.2 Hz, 1H), 7.21-7.26 (m, 1H), 7.38 (ddd, J = 8.4, 6.9 and 1.5 Hz, 1H), 7.45-7.56 (m, 2H), 7.87-7.94 (m, 2H), 8.71 (br s, 1H), 9.07 (br s, 1H); ¹³C NMR (CDCl₃, 75 MHz) δ 16.92, 51.98, 124.66, 124.97, 125.20, 125.96, 126.48, 126.97, 128.19, 128.48, 130.75, 133.23, 133.25, 135.29, 148.66, 148.85, 153.42, 166.24; ESIMS m/z 278 [M+H]⁺. Anal. Calcd for C₁₈H₁₅NO₂: C, 77.96; H, 5.45; N, 5.05. Found: C, 77.90; H, 5.52; N, 5.13.

Methyl 4-(biphenyl-4-yl)-5-methylnicotinate (2i)

65%; pale yellow oil; IR (film) νmax = 1733, 1580, 1436, 1291, 1136 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ 2.08 (s, 3H), 3.57 (s, 3H), 7.14 (d, J = 8.4 Hz, 2H), 7.25-7.32 (m, 1H), 7.35-7.43 (m, 2H), 7.55-7.64 (m, 4H), 8.56 (br s, 1H), 8.86 (br s, 1H); ¹³C NMR (CDCl₃, 75 MHz) δ 17.36, 52.12, 126.43, 126.85, 127.01, 127.47, 128.13, 128.78, 132.20, 136.37, 140.38, 140.44, 148.43, 149.37, 153.32, 166.89; ESIMS m/z 304 [M+H]⁺. Anal. Calcd for C₂₀H₁₇NO₂: C, 79.19; H, 5.65; N, 4.62. Found: C, 79.31; H, 5.83; N, 4.51.

Methyl 5'-methyl-3,4'-bipyridine-3'-carboxylate (2j)

41%; white solid, Mp 50-52 °C; IR (KBr) νmax = 1731, 1570, 1410, 1291, 1197 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ 2.12 (s, 3H), 3.67 (s, 3H), 7.41 (dd, J = 7.8 and 4.8 Hz, 1H), 7.52 (dt, J = 7.8 and 1.8 Hz, 1H), 8.41 (br s, 1H), 8.66 (br s, 1H), 8.68 (br s, 1H); ¹³C NMR (CDCl₃, 75 MHz) δ 17.37, 52.24, 122.99, 125.89, 132.34, 133.48, 135.30, 146.25, 148.15, 149.02, 149.06, 153.73, 166.14; ESIMS m/z 229 [M+H]⁺. Anal. Calcd for C₁₃H₁₂N₂O₂: C, 68.41; H, 5.30; N, 12.27. Found: C, 68.59; H, 5.66; N, 11.98.

Methyl 4-(furan-2-yl)-5-methylnicotinate (2k)

73%; pale yellow solid, Mp 90-92 °C; IR (KBr) νmax = 3147, 2951, 1724, 1594, 1441, 1305, 1137 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ 2.31 (s, 3H), 3.72 (s, 3H), 6.46-6.54 (m, 2H), 7.48 (d, J = 1.8 Hz, 1H), 8.53 (br s, 1H), 8.69 (br s, 1H); ¹³C NMR (CDCl₃, 75 MHz) δ 17.72, 52.47, 111.46, 112.01, 126.64, 131.16, 136.55, 143.31, 147.78, 147.95, 153.51, 167.68; ESIMS m/z 218 [M+H]⁺. Anal. Calcd for C₁₂H₁₁NO₃: C, 66.35; H, 5.10; N, 6.45. Found: C, 66.57; H, 5.39; N, 6.32.

Methyl 5-methyl-4-(5-methylthiophen-2-yl)nicotinate (2l)

74%; pale yellow oil; IR (film) νmax = 2951, 1734, 1577, 1436, 1303, 1137 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ 2.20 (s, 3H), 2.46 (d, J = 1.2 Hz, 3H), 3.66 (s, 3H), 6.63 (d, J = 3.6 Hz, 1H), 6.68 (dd, J = 3.6 and 1.2 Hz, 1H), 8.51 (br s, 1H), 8.73 (br s, 1H); ¹³C NMR (CDCl₃, 75 MHz) δ 15.23, 17.47, 52.31, 125.31, 127.20, 128.07, 133.41, 134.27, 141.40, 142.37, 147.85, 153.07, 167.03; ESIMS m/z 248 [M+H]⁺. Anal. Calcd for C₁₅H₁₃NO₂S: C, 70.97; H, 4.87; N, 6.96. Found: C, 70.95; H, 4.86; N, 6.95.
Methyl 5-butyl-4-phenylnicotinate (2s)

46%; colorless oil; IR (film) \( \nu_{\text{max}} = 2957, 2931, 1736, 1578, 1460, 1299, 1137 \text{ cm}^{-1} \); \(^1\)H NMR (CDCl\(_3\), 300 MHz) \( \delta \) 0.69 (t, \( J = 7.2 \text{ Hz}, 3\text{H} \)), 1.04-1.18 (m, 2H), 1.24-1.38 (m, 2H), 2.38 (t, \( J = 7.8 \text{ Hz}, 2\text{H} \)), 3.53 (s, 3H), 7.05-7.11 (m, 2H), 7.31-7.39 (m, 3H), 8.56 (br s, 1H), 8.83 (br s, 1H); \(^13\)C NMR (CDCl\(_3\), 75 MHz) \( \delta \) 13.59, 22.28, 29.98, 33.03, 52.06, 127.72, 127.91 (2C), 127.97, 137.04, 148.05, 149.23, 153.11, 166.92 (one carbon was overlapped); ESIMS \( m/\!z \) 270 [M+H]\(^+\). Anal. Calcd for C\(_{17}\)H\(_{19}\)NO\(_2\): C, 75.81; H, 7.11; N, 5.20. Found: C, 75.98; H, 7.32; N, 5.18.

Synthesis of (E)-Methyl 5-methyl-4-styrylnicotinate (2n)

A mixture of 3n (103 mg, 0.25 mmol), DBU (191 mg, 5.0 equiv), and MgSO\(_4\) (301 mg, 10.0 equiv) in toluene (2.0 mL) was heated to reflux for 20 h under N\(_2\) balloon atmosphere. The reaction mixture was poured into dilute HCl solution and extracted with diethyl ether. The organic solvent was removed by evaporation, and the residue was purified by flash column chromatography (hexanes/ether, 3:1) to afford compound 2n (41 mg, 64%) as a pale yellow solid. Mp 76-78 °C; IR (KBr) \( \nu_{\text{max}} = 2952, 1723, 1578, 1440, 1289, 1146 \text{ cm}^{-1} \); \(^1\)H NMR (CDCl\(_3\), 300 MHz) \( \delta \) 2.43 (s, 3H), 3.88 (s, 3H), 6.66 (d, \( J = 16.5 \text{ Hz}, 1\text{H} \)), 7.28-7.45 (m, 4H), 7.48-7.56 (m, 2H), 8.57 (br s, 1H), 8.86 (br s, 1H); \(^13\)C NMR (CDCl\(_3\), 75 MHz) \( \delta \) 17.81, 52.35, 123.98, 124.75, 128.49, 128.77, 131.38, 135.83, 136.48, 145.82, 148.75, 153.74, 167.37; ESIMS \( m/\!z \) 254 [M+H]\(^+\). Anal. Calcd for C\(_{16}\)H\(_{15}\)NO\(_2\): C, 75.87; H, 5.97; N, 5.53. Found: C, 76.03; H, 6.17; N, 5.38.

Compounds 2p and 2r were synthesized similarly, and the spectroscopic data of 2p and 2r are as follows.

Methyl 5-methyl-2-phenylnicotinate (2p)

59%; pale yellow solid; \(^1\)H NMR (CDCl\(_3\), 300 MHz) \( \delta \) 2.35 (s, 3H), 3.61 (s, 3H), 7.30-7.39 (m, 3H), 7.40-7.48 (m, 2H), 7.83 (d, \( J = 2.4 \text{ Hz}, 1\text{H} \)), 8.53 (d, \( J = 2.4 \text{ Hz}, 1\text{H} \)).
1-(5-Methyl-4-phenylpyridin-3-yl)ethanone (2r)

64%; white solid, Mp 59-61 °C; IR (KBr) νmax = 1689, 1576, 1443, 1356, 1285, 1115 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ 1.87 (s, 3H), 2.11 (s, 3H), 7.10-7.16 (m, 2H), 7.35-7.44 (m, 3H), 8.53 (br s, 1H), 8.56 (br s, 1H); ¹³C NMR (CDCl₃, 75 MHz) δ 17.06, 30.40, 128.46, 128.52, 128.76, 131.38, 135.90, 136.85, 146.37, 146.92, 152.79, 202.11; ESIMS m/z 212 [M+H]+=.


Synthesis of (Z)-methyl 5-(naphthalen-2-ylmethylene)-4-phenyl-1-tosyl-1,4,5,6-tetrahydropyridine-3-carboxylate (3o)

A mixture of 3a (192 mg, 0.5 mmol), 2-bromonaphthalene (155 mg, 1.5 equiv), Pd(OAc)₂ (6 mg, 5 mol%), PPh₃ (13 mg, 10 mol%), and K₂CO₃ (104 mg, 1.5 equiv) in DMF (2.0 mL) was heated to 100 °C for 5 h. The reaction mixture was poured into dilute HCl solution and extracted with diethyl ether. The organic solvent was removed by evaporation, and the residue was purified by flash column chromatography (hexanes/ether, 7:1) to afford compound 3o (199 mg, 78%) as a white solid. Mp 84-86 °C; IR (KBr) νmax = 1707, 1630, 1375, 1237, 1168, 1101 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ 2.19 (s, 3H), 3.53 (d, J = 13.8 Hz, 1H), 3.64 (s, 3H), 4.47 (s, 1H), 4.60 (d, J = 13.8 Hz, 1H), 6.82-6.89 (m, 3H), 6.96-7.06 (m, 3H), 7.11-7.18 (m, 3H), 7.32-7.38 (m, 3H), 7.40-7.46 (m, 2H), 7.64-7.79 (m, 3H), 8.18 (s, 1H); ¹³C NMR (CDCl₃, 75 MHz) δ 21.44, 40.86, 46.79, 51.66, 109.20, 126.23, 126.37, 126.56, 126.84, 126.95, 127.06, 127.55, 127.87, 127.93, 128.01, 128.50, 129.71, 131.98, 132.36, 133.14, 133.23, 133.73, 136.10, 142.01, 144.39, 166.47 (one carbon was overlapped); ESIMS m/z 510 [M+H]+=. Anal. Calcd for C₃₁H₂₇NO₄S: C, 73.06; H, 5.34; N, 2.75. Found: C, 73.28; H, 5.69; N, 2.70.

Synthesis of methyl 5-(naphthalen-2-ylmethyl)-4-phenylnicotinate (2o)

A mixture of 3o (103 mg, 0.25 mmol) and Cs₂CO₃ (191 mg, 5.0 equiv) in DMF (2.0 mL) was heated to 120 °C for 3 h under N₂ balloon atmosphere. The reaction mixture was poured into dilute HCl solution and extracted with diethyl ether. The organic solvent was removed by evaporation, and the residue was purified by flash column chromatography (hexanes/ether, 3:1) to afford compound 2o (75 mg, 71%) as a white solid. Mp 93-95 °C; IR
(KBr) $v_{max} = 3053, 1734, 1577, 1412, 1287, 1136 \text{ cm}^{-1}$; $^1$H NMR (CDCl$_3$, 300 MHz) $\delta 3.53$ (s, 3H), 3.91 (s, 2H), 6.90-7.06 (m, 3H), 7.07-7.44 (m, 6H), 7.52-7.76 (m, 3H), 8.62 (br s, 1H), 8.91 (br s, 1H); $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta 36.59, 52.12, 125.53, 126.05, 126.94, 127.13, 127.49, 127.52, 127.90, 127.93$ (2C), 128.04 (2C), 131.98, 133.31, 136.71, 136.79, 148.85, 149.88, 153.77, 166.71 (one carbon was overlapped); ESIMS $m/z$ 354 [M+H]$^+$. Anal. Calcd for C$_{24}$H$_{19}$NO$_2$: C, 81.56; H, 5.42; N, 3.96. Found: C, 81.29; H, 5.69; N, 3.82.
5. References


6. Scanned $^1$H and $^{13}$C NMR spectra
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\begin{align*}
\text{CH}_3\text{CO}_2\text{Et} \\
2b
\end{align*}
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