Copper(I)-catalyzed tandem reaction of o-alkynylphenyl isothiocyanates with isocyanides: a rapid synthesis of 5H-benzo[d]imidazo[5,1-b][1,3]thiazines

Wenyan Hao, Jiangbo Zeng and Mingzhong Cai*

College of Chemistry & Chemical Engineering, Jiangxi Normal University, Nanchang 330022, People’s Republic of China

E-mail: mzcai@jxnu.edu.cn

Supporting Information

CONTENTS:

1. General information .................................................................S2

2. Synthesis and characterization for compounds 3a-3u, 4 and 5............S3-S15

3. X-Ray crystal structure for compound 3h.....................................S15

4. Copies of 1H NMR, 13C NMR spectra for compounds 3a-3u, 4 and 5...S16-S61
1. **General Information**

All reagents and metal catalysts were obtained from commercial sources without further purification, and commercially available solvents were purified before use. All reactions were performed in reaction tubes. All new compounds were fully characterized. All melting points were taken on an X-4 Digital Melting Point Apparatus without correction. Silica gel plate GF254 were used for thin layer chromatography (TLC) and silica gel H or 300-400 mesh were used for flash column chromatography. Thin layer chromatography plates were visualized by exposure to ultraviolet light. Nuclear magnetic resonance (NMR) spectra are recorded in parts per million from internal tetramethylsilane on the $\delta$ scale. The mass analyzer type used for the HRMS measurements is micro TOF. Yields refer to chromatographically and spectroscopically pure compounds, unless otherwise indicated. The single crystal of compound 3h was obtained after recrystallization from the mixed solvent of hexane and dichloromethane ($V_{hexane}/V_{dichloromethane} = 3:1$). There are carbons missed in $^{13}$C NMR spectra of some new compounds, it may be caused by overlap as most of carbons are in aromatic region.
2. Synthesis and characterization for 5\(H\)-benzo[\(d\)]imidazo[5,1-\(b\)][1,3]thiazines via a tandem reaction of \(o\)-alkynylphenyl isothiocyanates 1 with isocyanides 2

\[
\text{R}^1 \text{C} = \text{S} + \text{CN} \text{R}^3 \xrightarrow{\text{CuCl, Cs}_2\text{CO}_3, \text{THF, reflux}} \begin{array}{c}
\text{R}^1 \text{C} = \text{S} \\
\text{R}^3
\end{array}
\]

Copper(I) chloride (0.02 mmol) and Cs\(_2\)CO\(_3\) (0.4 mmol) were added to a solution of \(o\)-alkynylphenyl isothiocyanate 1 (0.2 mmol) in THF (2.0 mL) at room temperature. After 2 minutes, 2-isocyanoacetate 2 (0.4 mmol) was added, and the mixture was stirred at reflux. After completion of reaction as indicated by TLC (3-4 h), the solvent was evaporated. The residue was purified by flash column chromatography (EtOAc/petroleum ether, 1:2) to give the desired product 5\(H\)-benzo[\(d\)]imidazo[5,1-\(b\)][1,3]thiazine 3.

(Z)-Ethyl 5-benzylidene-5\(H\)-benzo[\(d\)]imidazo[5,1-\(b\)][1,3]thiazine-3-carboxylate (3a)

Yellow solid (69.0 mg, 99%). Mp 128–130 °C, \(R_f\) = 0.35 (EtOAc/petroleum ether 1:2).

(\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.08 (s, 1H), 7.59 (d, \(J = 7.6\) Hz, 1H), 7.45 (d, \(J = 8.0\) Hz, 1H), 7.30-7.42 (m, 6H), 7.27 (d, \(J = 7.2\) Hz, 1H), 7.13 (s, 1H), 4.27 (q, \(J = 7.2\) Hz, 2H), 1.30 (t, \(J = 7.2\) Hz, 3H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 162.4, 134.8, 132.9, 132.8, 131.6, 131.5, 130.0, 129.7, 129.0, 128.7, 128.5, 127.8, 127.5, 126.3, 122.7, 117.2, 60.8, 14.4. HRMS calcd for C\(_{20}\)H\(_{16}\)N\(_2\)NaO\(_2\)S\(^+\) (M + Na\(^+\)): 371.0825; Found: 371.0838.
(Z)-Methyl 5-benzylidene-5H-benzo[d]imidazo[5,1-b][1,3]thiazine-3-carboxylate (3b)
Yellow solid (52.2 mg, 78%). Mp 75–77 °C, Rf = 0.36 (EtOAc/petroleum ether 1:2).
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.10 (s, 1H), 7.62 (d, $J = 8.0$ Hz, 1H), 7.48 (d, $J = 8.0$ Hz, 1H), 7.36-7.43 (m, 6H), 7.27 (t, $J = 7.4$ Hz, 1H), 7.16 (s, 1H), 3.82 (s, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 162.8, 134.7, 132.9, 132.8, 131.8, 131.6, 131.4, 129.7, 129.5, 129.2, 128.6, 128.4, 127.5, 126.3, 122.6, 117.1, 51.8. HRMS calcd for C$_{19}$H$_{14}$N$_2$NaO$_2$S$^+$ (M + Na$^+$): 357.0668; Found: 357.0680

(Z)-5-Benzylidene-3-tosyl-5H-benzo[d]imidazo[5,1-b][1,3]thiazine (3c)
Yellow solid (54.2 mg, 63%). Mp 92–94 °C, Rf = 0.64 (EtOAc/petroleum ether 1:2).
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.13 (s, 1H), 7.59 (d, $J = 8.0$ Hz, 2H), 7.68 (d, $J = 7.6$ Hz, 1H), 7.48-7.56 (m, 6H), 7.42-7.46 (m, 2H), 7.24 (s, 1H), 7.15 (d, $J = 8.0$ Hz, 2H), 2.34 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 144.2, 138.2, 136.5, 134.7, 133.7, 133.0, 132.9, 131.3, 130.2, 129.7, 129.6, 128.6, 128.5, 127.5, 127.4, 127.1, 126.6, 122.0, 117.5, 21.6. HRMS calcd for C$_{24}$H$_{18}$N$_2$NaO$_2$S$_2$$^+$ (M + Na$^+$): 453.0702 Found: 453.0717

84
(Z)-Ethyl 5-(4-fluorobenzylidene)-5H-benzo[d]imidazo[5,1-b][1,3]thiazine-3-carboxylate (3d)
Yellow solid (71.8 mg, 98%). Mp 142–144 °C, R_f = 0.48 (EtOAc/petroleum ether 1:2).
\[\begin{align*}
1^1 \text{H NMR (400 MHz, CDCl}_3\text{) } & \delta 8.15 (s, 1\text{H}), 7.65 (d, J = 7.6 \text{ Hz, 1H}), 7.53 (d, J = 7.6 \text{ Hz, 1H}), 7.35-7.45 \text{ (m, 4H), 7.15 (s, 1H), 7.06-7.10} \text{ (m, 2H), 4.35 (q, J = 7.0 \text{ Hz, 2H),} \\
& 1.37 (t, J = 7.0 \text{ Hz, 3H}). \end{align*}\]
\[\begin{align*}
1^3 \text{C NMR (100 MHz, CDCl}_3\text{) } & \delta 162.4 (d, J_{CF} = 248 \text{ Hz),} \\
& 162.3, 132.9, 131.5, 131.4, 131.0, 130.3, 130.1, 128.7 (d, J_{CF} = 12 \text{ Hz),} 127.8, 127.4, \\
& 126.2, 122.7, 117.2, 115.5 (d, J_{CF} = 22 \text{ Hz),} 60.9, 14.4. \end{align*}\]
HRMS calcd for C_{20}H_{15}FN_{2}NaO_{2}S^{+} (M + Na^{+}): 389.0730, Found: 389.0750

(Z)-Ethyl 5-(4-chlorobenzylidene)-5H-benzo[d]imidazo[5,1-b][1,3]thiazine-3-carboxylate (3e)
Yellow solid (75.8 mg, 99%). Mp 114–116 °C, R_f = 0.39 (EtOAc/petroleum ether 1:2).
\[\begin{align*}
1^1 \text{H NMR (400 MHz, CDCl}_3\text{) } & \delta 8.16 (s, 1\text{H}), 7.66 (d, J = 7.6 \text{ Hz, 1H}), 7.54 (d, J = 8.0 \text{ Hz, 1H}), 7.47 (t, J = 7.4 \text{ Hz, 1H}), 7.38-7.42 \text{ (m, 5H), 7.14 (s, 1H), 4.37 (q, J = 6.8 \text{ Hz,} \\
& 2\text{H),} 1.39 (t, J = 6.8 \text{ Hz, 3H}). \end{align*}\]
\[\begin{align*}
1^3 \text{C NMR (100 MHz, CDCl}_3\text{) } & \delta 162.4, 134.2, 133.2, \\
& 133.0, 132.9, 131.4, 131.0, 130.9, 130.8, 130.1, 128.8, 128.5, 127.5, 126.0, 123.5, \\
& 117.1, 60.9, 14.5. \end{align*}\]
HRMS calcd for C_{20}H_{15}ClN_{2}NaO_{2}S^{+} (M + Na^{+}): 405.0435, Found: 405.0412
(Z)-Ethyl 5-(4-bromobenzylidene)-5H-benzo[d]imidazo[5,1-b][1,3]thiazine-3-carboxylate (3f)

Yellow solid (78.6 mg, 92%). Mp 146–148 °C, $R_f = 0.23$ (EtOAc/petroleum ether 1:2).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.18 (s, 1H), 7.69 (d, $J = 7.6$ Hz, 1H), 7.50-7.58 (m, 4H), 7.36 (t, $J = 8.4$ Hz, 2H), 7.14 (s, 1H), 7.03 (d, $J = 8.4$ Hz, 1H), 4.38 (q, $J = 7.2$ Hz, 2H), 1.39 (t, $J = 7.2$ Hz, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 162.4, 133.7, 133.6, 132.9, 131.7, 131.5, 131.1, 130.4, 130.2, 128.9, 128.5, 127.4, 126.1, 123.8, 122.6, 117.2, 60.9, 14.5. HRMS calcd for C$_{20}$H$_{15}$BrN$_2$NaO$_2$S$^+$ (M + Na$^+$): 448.9930, Found: 448.9949

(Z)-Ethyl 5-(4-methoxybenzylidene)-5H-benzo[d]imidazo[5,1-b][1,3]thiazine-3-carboxylate (3g)

Yellow solid (39.4 mg, 52%). Mp 120–122 °C, $R_f = 0.21$ (EtOAc/petroleum ether 1:2).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.17 (s, 1H), 7.68 (d, $J = 7.6$ Hz, 1H), 7.55 (d, $J = 7.6$ Hz, 1H), 7.39-7.49 (m, 4H), 7.17 (s, 1H), 6.96 (d, $J = 8.4$ Hz, 2H), 4.39 (q, $J = 7.2$ Hz, 2H), 3.85 (s, 3H), 1.41 (t, $J = 7.2$ Hz, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 162.4, 132.9, 131.5, 131.4, 131.3, 131.2, 129.8, 129.4, 128.7, 128.5, 127.6, 127.5, 126.9, 120.3, 117.2, 114.0, 60.8, 55.4, 14.5. HRMS calcd for C$_{21}$H$_{18}$N$_2$NaO$_3$S$^+$ (M + Na$^+$): 401.0930, Found: 401.0953
(Z)-Ethyl 5-(4-methylbenzylidene)-5H-benzo[d]imidazo[5,1-b][1,3]thiazine-3-carboxylate (3h)

Yellow solid (61.6 mg, 85%). Mp 96–98 °C, R_f = 0.40 (EtOAc/petroleum ether 1:2).

^1^H NMR (400 MHz, CDCl_3) δ 8.07 (s, 1H), 7.57 (d, J = 7.6 Hz, 1H), 7.43 (d, J = 8.0 Hz, 1H), 7.26-7.37 (m, 4H), 7.14 (d, J = 7.6 Hz, 2H), 7.09 (s, 1H), 4.29 (q, J = 7.2 Hz, 2H), 2.29 (s, 3H), 1.31 (t, J = 7.2 Hz, 3H). ^13^C NMR (100 MHz, CDCl_3) δ 162.4, 138.6, 132.1, 131.8, 131.4, 129.8, 129.6, 129.3, 129.1, 128.7, 127.6, 127.5, 127.4, 126.6, 121.6, 117.0, 60.8, 21.5, 14.5. HRMS calcd for C_{21}H_{18}N_{2}O_{2}S^+ (M + Na^+): 385.0981 Found: 385.0991

(Z)-Ethyl 5-(cyclopropylmethylene)-5H-benzo[d]imidazo[5,1-b][1,3]thiazine-3-carboxylate (3i)

Yellow solid (48.7 mg, 78%). Mp 199–201 °C, R_f = 0.62 (EtOAc/petroleum ether 1:2).

^1^H NMR (400 MHz, CDCl_3) δ 8.07 (s, 1H), 7.31-7.45 (m, 3H), 7.25 (d, J = 8.0 Hz, 1H), 5.54 (d, J = 10.0 Hz, 1H), 4.36 (q, J = 6.6 Hz, 2H), 1.77 (s, 1H), 1.36 (t, J = 6.6 Hz, 3H), 0.93-0.96 (m, 2H), 0.55-0.57 (m, 2H). ^13^C NMR (100 MHz, CDCl_3) δ 162.6, 146.6, 137.8, 132.0, 131.2, 128.9, 127.7, 127.6, 126.4, 126.2, 119.2, 117.3, 60.8, 14.6, 14.4, 12.7, 12.6. HRMS calcd for C_{17}H_{17}N_{2}O_{2}S^+ (M + H^+): 313.1005 Found: 313.1033.
(Z)-Ethyl 5-benzylidene-7-fluoro-5\textsubscript{H}-benzo[d]imidazo[5,1-b][1,3]thiazine-3-carboxylate (3j)

Yellow solid (71.8 mg, 98%). Mp 173–175 °C, R\textsubscript{f} = 0.55 (EtOAc/petroleum ether 1:2).

\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) $\delta$ 8.12 (s, 1H), 7.47 (d, $J = 7.2$ Hz, 2H), 7.32-7.41 (m, 4H), 7.18 (s, 1H), 7.14 (d, $J = 7.2$ Hz, 2H), 4.33 (q, $J = 7.2$ Hz, 2H), 1.35 (t, $J = 7.2$ Hz, 3H).

\textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) $\delta$ 162.2, 161.2 (d, $J\text{CF} = 247$ Hz), 136.1, 134.4, 132.9, 132.3, 129.7, 128.7, 128.6, 128.5, 121.9, 119.1 (d, $J\text{CF} = 9$ Hz), 117.1 (d, $J\text{CF} = 23$ Hz), 114.1, 113.8, 60.8, 14.4. HRMS calcd for C\textsubscript{20}H\textsubscript{15}FN\textsubscript{2}O\textsubscript{2}S\textsuperscript{+} (M + K\textsuperscript{+}) 405.0470 Found: 405.0496.

(Z)-Ethyl 5-benzylidene-7-chloro-5\textsubscript{H}-benzo[d]imidazo[5,1-b][1,3]thiazine-3-carboxylate (3k)

Yellow solid (74.3 mg, 97%). Mp 167–169 °C, R\textsubscript{f} = 0.45 (EtOAc/petroleum ether 1:2).

\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) $\delta$ 8.17 (s, 1H), 7.59 (d, $J = 2$ Hz, 1H), 7.51-7.55 (m, 3H), 7.45-7.49 (m, 3H), 7.40 (d, $J = 7.2$ Hz, 1H), 7.27 (s, 1H), 4.39 (q, $J = 7.2$ Hz, 2H), 1.41 (t, $J = 7.2$ Hz, 3H).

\textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) $\delta$ 162.2, 134.4, 133.3, 132.9, 132.8, 130.1, 129.8, 129.7, 129.0, 128.7, 128.4, 127.9, 127.3, 127.2, 121.6, 118.7, 60.9, 14.4. HRMS calcd for C\textsubscript{20}H\textsubscript{15}ClN\textsubscript{2}NaO\textsubscript{2}S\textsuperscript{+} (M + Na\textsuperscript{+}) 405.0435 Found: 405.0417
(Z)-Ethyl 5-benzyldiene-7-bromo-5H-benzo[d]imidazo[5,1-b][1,3]thiazine-3-carboxylate (3l)

Yellow solid (82.0 mg, 96%). Mp 156–158 °C, R\textsubscript{f} = 0.60 (EtOAc/petroleum ether 1:2).

\(^1\)H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 8.04 (s, 1H), 7.71 (d, \(J = 2\) Hz, 1H), 7.45-7.48 (m, 1H), 7.40 (d, \(J = 7.6\) Hz, 2H), 7.31-7.35 (m, 3H), 7.27 (d, \(J = 7.3\) Hz, 1H), 7.11 (s, 1H), 4.27 (q, \(J = 7.2\) Hz, 2H), 1.29 (t, \(J = 7.2\) Hz, 3H). \(^{13}\)C NMR (100 MHz, CDCl\textsubscript{3}) \(\delta\) 162.2, 134.4, 132.8, 132.7, 132.6, 130.5, 130.1, 129.8, 129.0, 128.8, 128.7, 128.5, 128.1, 121.4, 120.9, 118.7, 60.9, 14.4. HRMS calcd for C\textsubscript{20}H\textsubscript{15}BrN\textsubscript{2}O\textsubscript{2}S\textsuperscript{+} (M + Na\textsuperscript{+}) 448.9930 Found: 448.9974

(Z)-Ethyl 5-benzyldiene-7-nitro-5H-benzo[d]imidazo[5,1-b][1,3]thiazine-3-carboxylate (3m)

Yellow solid (62.9 mg, 80%). Mp 258–260 °C, R\textsubscript{f} = 0.29 (EtOAc/petroleum ether 1:2).

\(^1\)H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 8.52 (d, \(J = 2.4\) Hz 1H), 8.26-8.29 (m, 1H), 8.17 (s, 1H), 7.67 (d, \(J = 8.8\) Hz, 1H), 7.46 (d, \(J = 7.6\) Hz 2H), 7.37-7.41 (m, 2H), 7.33 (d, \(J = 7.2\) Hz, 1H), 7.29 (s, 1H), 4.31 (q, \(J = 7.0\) Hz, 2H), 1.32 (t, \(J = 7.0\) Hz, 3H). \(^{13}\)C NMR (100 MHz, CDCl\textsubscript{3}) \(\delta\) 162.0, 146.4, 135.9, 134.5, 134.1, 133.4, 129.9, 129.3, 128.9, 128.7, 128.0, 127.6, 124.8, 123.2, 120.6, 118.2, 61.2, 14.4. HRMS calcd for C\textsubscript{20}H\textsubscript{16}N\textsubscript{3}O\textsubscript{4}S\textsuperscript{+} (M + H\textsuperscript{+}) 394.0856 Found: 394.0870
(Z)-Ethyl 5-benzylidene-7-methyl-5H-benzo[d]imidazo[5,1-b][1,3]thiazine-3-carboxylate (3n)
Yellow solid (68.9 mg, 95%). Mp 182–184 °C, Rf= 0.43 (EtOAc/petroleum ether 1:2).
\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.04 (s, 1H), 7.40 (d, \(J = 8\) Hz, 3H), 7.31-7.35 (m, 3H), 7.25 (d, \(J = 7.2\) Hz, 1H), 7.16 (d, \(J = 8.4\) Hz, 1H), 7.13 (s, 1H), 4.28 (q, \(J = 7.0\) Hz, 2H), 2.32 (s, 3H), 1.30 (t, \(J = 7.0\) Hz, 3H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 162.4, 137.4, 134.9, 132.8, 131.2, 131.0, 129.7, 129.5, 129.2, 128.8, 128.5, 128.3, 127.6, 126.0, 122.9, 116.9, 60.8, 21.1, 14.5. HRMS calcd for C\(_{21}\)H\(_{19}\)N\(_2\)O\(_2\)S\(^+\) (M + H\(^+\)) 363.1162 Found: 363.1187

(Z)-Ethyl 5-benzylidene-8-chloro-5H-benzo[d]imidazo[5,1-b][1,3]thiazine-3-carboxylate (3o)
Yellow solid (53.6 mg, 70%). Mp 181–183 °C, Rf= 0.82 (EtOAc/petroleum ether 1:2).
\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.14 (s, 1H), 7.64 (d, \(J = 7.6\) Hz, 1H), 7.64 (d, \(J = 7.6\) Hz, 1H), 7.31-7.35 (m, 3H), 7.27 (s, 1H), 7.09-7.16 (m,1H), 4.39 (q, \(J = 6.8\) Hz, 2H), 1.39 (t, \(J = 6.8\) Hz, 3H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 162.2, 135.8, 134.6, 132.8, 132.3, 132.0, 129.7, 128.7, 128.6, 128.5, 127.9, 124.9, 121.9, 117.4, 60.9, 14.4. HRMS calcd for C\(_{20}\)H\(_{15}\)ClKN\(_2\)O\(_2\)S\(^+\) (M + K\(^+\)) 421.0174 Found: 421.0137
(Z)-Ethyl 5-benzylidene-8-methyl-5H-benzo[d]imidazo[5,1-b][1,3]thiazine-3-carboxylate (3p)

Yellow solid (57.3 mg, 79%). Mp 119-121 °C, R_f = 0.75 (EtOAc/petroleum ether 1:2).

1H NMR (400 MHz, CDCl_3) δ 8.17 (s, 1H), 7.58 (d, J = 8.0 Hz, 1H), 7.50 (d, J = 8.0 Hz, 2H), 7.42 (t, J = 7.4 Hz, 2H), 7.31-7.35 (m, 2H), 7.20 (d, J = 8.0 Hz, 1H), 7.19 (s, 1H), 4.37 (q, J = 7.0 Hz, 2H), 2.45 (s, 3H), 1.40 (t, J = 7.0 Hz, 3H).

13C NMR (100 MHz, CDCl_3) δ 162.4, 140.6, 135.0, 132.8, 131.3, 130.9, 130.3, 129.6, 128.6, 128.4, 128.3, 127.3, 123.5, 122.8, 117.5, 60.7, 21.3, 14.4. HRMS calcd for C_{21}H_{18}N_2NaO_2S^+ (M + Na^+) 385.0981 Found: 385.0979

(Z)-Ethyl 7-chloro-5-(4-chlorobenzylidene)-5H-benzo[d]imidazo[5,1-b][1,3]thiazine-3-carboxylate (3q)

Yellow solid (74.3 mg, 89%). Mp 228–230 °C, R_f = 0.36 (EtOAc/petroleum ether 1:2).

1H NMR (400 MHz, CDCl_3) δ 8.15 (s, 1H), 7.68 (d, J = 2 Hz, 1H), 7.53 (d, J = 8.8 Hz, 1H), 7.40-7.48 (m, 5H), 7.18 (s, 1H), 4.39 (q, J = 7.2 Hz, 2H), 1.40 (t, J = 7.2 Hz, 3H).

13C NMR (100 MHz, CDCl_3) δ 162.2, 134.7, 133.4, 132.9, 132.8, 131.2, 130.9, 130.1, 129.6, 129.0, 128.8, 128.2, 127.7, 127.2, 122.5, 118.6, 61.0, 14.4. HRMS calcd for C_{26}H_{14}Cl_2N_2NaO_2S^+ (M + Na^+) 439.0045 Found: 439.0038
(Z)-Ethyl 7-chloro-5-(4-methylbenzylidene)-5H-benzo[d]imidazo[5,1-b][1,3]thiazine-3-carboxylate (3r)

Yellow solid (61.9 mg, 78%). Mp 156–158 °C, R_f = 0.42 (EtOAc/petroleum ether 1:2).

^1^H NMR (400 MHz, CDCl_3) δ 7.98 (s, 1H), 7.53 (d, J = 2 Hz, 1H), 7.24-7.32 (m, 4H), 7.13 (d, J = 8.4 Hz, 2H), 7.06 (s, 1H), 4.28 (q, J = 7.2 Hz, 2H), 2.28 (s, 3H), 1.30 (t, J = 7.2 Hz, 3H).

^13^C NMR (100 MHz, CDCl_3) δ 162.2, 139.0, 133.2, 132.8, 132.7, 131.7, 130.0, 129.8, 129.7, 129.3, 129.0, 128.1, 127.2, 120.5, 118.5, 118.2, 60.9, 21.4, 14.4. HRMS calcd for C_{21}H_{17}ClN_{2}O_{2}S^{+} (M + Na^+) 419.0591 Found: 419.0587

(Z)-Ethyl 5-(4-chlorobenzylidene)-7-methyl-5H-benzo[d]imidazo[5,1-b][1,3]thiazine-3-carboxylate (3s)

Yellow solid (77.8 mg, 98%). Mp 173–175 °C, R_f = 0.40 (EtOAc/petroleum ether 1:2).

^1^H NMR (400 MHz, CDCl_3) δ 8.04 (s, 1H), 7.27-7.38 (m, 6H), 7.18 (d, J = 9.6 Hz, 1H), 7.06 (s, 1H), 4.29 (q, J = 7.2 Hz, 2H), 2.34 (s, 3H), 1.31 (t, J = 7.2 Hz, 3H).

^13^C NMR (100 MHz, CDCl_3) δ 162.4, 137.8, 134.1, 133.4, 132.7, 130.9, 130.8, 129.5, 129.2, 128.7, 128.6, 128.3, 127.6, 125.7, 123.8, 117.0, 60.8, 21.1, 14.4. HRMS calcd for C_{21}H_{18}ClN_{2}O_{2}S^{+} (M + H^+) 397.0772 Found: 397.0774
(Z)-Ethyl 7-methyl-5-(4-methylbenzylidene)-5H-benzo[d]imidazo[5,1-b][1,3]thiazine-3-carboxylate (3t)

Yellow solid (65.5 mg, 87%). Mp 159-162 °C, Rₜ = 0.39 (EtOAc/petroleum ether 1:2).

\(^1\)H NMR (400 MHz, CDCl\(_3\)) δ 8.17 (s, 1H), 7.53-7.54 (m, 1H), 7.43-7.48 (m, 3H), 7.26-7.32 (m, 2H), 7.24 (s, 1H), 7.09 (d, J = 6.0 Hz, 1H), 4.40 (q, J = 7.2 Hz, 2H), 2.47 (s, 3H), 2.42 (s, 3H), 1.42 (t, J = 7.2 Hz, 3H).

\(^13\)C NMR (100 MHz, CDCl\(_3\)) δ 162.4, 138.5, 137.7, 132.7, 132.2, 131.2, 130.5, 129.6, 129.2, 129.1, 129.0, 128.6, 127.7, 126.3, 121.9, 116.9, 60.7, 21.4, 21.1, 14.4. HRMS calcd for C\(_{22}\)H\(_{21}\)N\(_2\)O\(_2\)S\(^+\) (M + H\(^+\)) 377.1318, Found: 377.1311.

(Z)-Ethyl 5-benzylidene-5H-imidazo[5,1-b]pyrido[2,3-d][1,3]thiazine-7-carboxylate (3u)

Yellow solid (58.0 mg, 83%). Mp 151-153 °C, Rₜ = 0.29 (EtOAc/petroleum ether 1:2).

\(^1\)H NMR (400 MHz, CDCl\(_3\)) δ 8.56 (s, 1H), 8.33-8.34 (m, 1H), 7.95 (d, J = 8.0 Hz, 1H), 7.41 (d, J = 7.6 Hz, 2H), 7.34 (t, J = 7.4 Hz, 2H), 7.24-7.29 (m, 2H), 7.08 (s, 1H), 4.29 (q, J = 7.2 Hz, 2H), 1.31 (t, J = 7.2 Hz, 3H).

\(^13\)C NMR (100 MHz, CDCl\(_3\)) δ 161.5, 147.8, 142.2, 134.1, 133.5, 133.4, 130.2, 128.5, 127.9, 127.7, 127.6, 127.3, 122.5, 121.0, 119.0, 59.8, 13.4. HRMS calcd for C\(_{19}\)H\(_{15}\)N\(_3\)NaO\(_2\)S\(^+\) (M + Na\(^+\)) 372.0777, Found: 372.0760.
A mixture of compound 3f or 3l (0.2 mmol), phenylacetylene (0.24 mmol), Pd(PPh\(_3\))\(_4\) (5 mol%), and CuI (10 mol%) in dried piperidine (2.0 mL) was stirred at 80 °C under N\(_2\) atmosphere for 12 h. After being cooled to room temperature, aq. NH\(_4\)Cl solution (5 mL) was added and the mixture was extracted with ethyl acetate (3×10 mL). The extract was washed with water and dried over MgSO\(_4\). After removal of the solvent under reduced pressure, the residue was purified on silica gel providing desired coupling products 4 or 5.

\((Z)\)-Ethyl 5-(4-(phenylethynyl)benzylidene)-5\(H\)-benzo[\(d\)]imidazo[5,1-\(b\)][1,3]thiazine-3-carboxylate (4).

Yellow solid (78.0 mg, 87%). Mp 226-228 °C, R\(_f\) = 0.37 (EtOAc/petroleum ether 1:2).  \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 8.17 (s, 1H), 7.62-7.68 (m, 4H), 7.47-7.51 (m, 4H), 7.42-7.45 (m, 2H), 7.31-7.33 (m, 2H), 7.17 (s, 1H), 7.08 (s, 1H), 4.37 (q, \(J = 7.2\) Hz, 2H), 1.38 (t, \(J = 7.2\) Hz, 3H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\): 162.2, 134.7, 133.0, 132.1, 132.0, 131.6, 131.5, 131.1, 130.8, 130.1, 129.6, 128.8, 128.5, 128.4, 128.3, 127.7, 127.3, 126.1, 123.3, 117.2, 91.0, 89.2, 60.7, 14.4. HRMS calcd for C\(_{28}\)H\(_{20}\)N\(_2\)NaO\(_2\)S\(^+\) (M + Na\(^+\)) 471.1138, Found: 471.1130.

\((Z)\)-Ethyl 5-benzylidene-7-(phenylethynyl)-5\(H\)-benzo[\(d\)]imidazo[5,1-\(b\)][1,3]thiazine-
3-carboxylate (5).

Yellow solid (73.6 mg, 82%). Mp 234-236 °C, R$_f$ = 0.68 (EtOAc/petroleum ether 1:2).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.18 (s, 1H), 7.52-7.56 (m, 5H), 7.43-7.48 (m, 2H), 7.36-7.37 (m, 4H), 7.27-7.32 (m, 2H), 7.12 (s, 1H), 4.35-4.40 (m, 2H), 1.40 (t, $J$ = 7.2 Hz, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 162.2, 135.8, 134.7, 132.9, 132.8, 132.4, 132.1, 132.0, 131.7, 131.6, 130.8, 130.4, 129.7, 128.8, 128.7, 128.6, 128.5, 126.5, 122.5, 117.3, 91.4, 87.7, 60.8, 14.3. HRMS calcd for C$_{28}$H$_{20}$N$_2$NaO$_2$S$^+$ (M + Na$^+$) 471.1138, Found: 471.1127.

2. X-Ray Crystal Structure for Compound 3h

![X-ray Crystal Structure](image)

**Figure 1.** Single-crystal X-ray diffraction structure of 3h, the thermal ellipsoids are at the 30% probability level.
4. Copies of $^1$H NMR and $^{13}$C NMR spectra for compounds 3a-3u, 4 and 5.