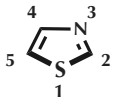

Supporting Information

Programmed Synthesis of Arylthiazoles through Sequential C–H Couplings

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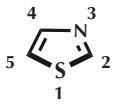


1. General

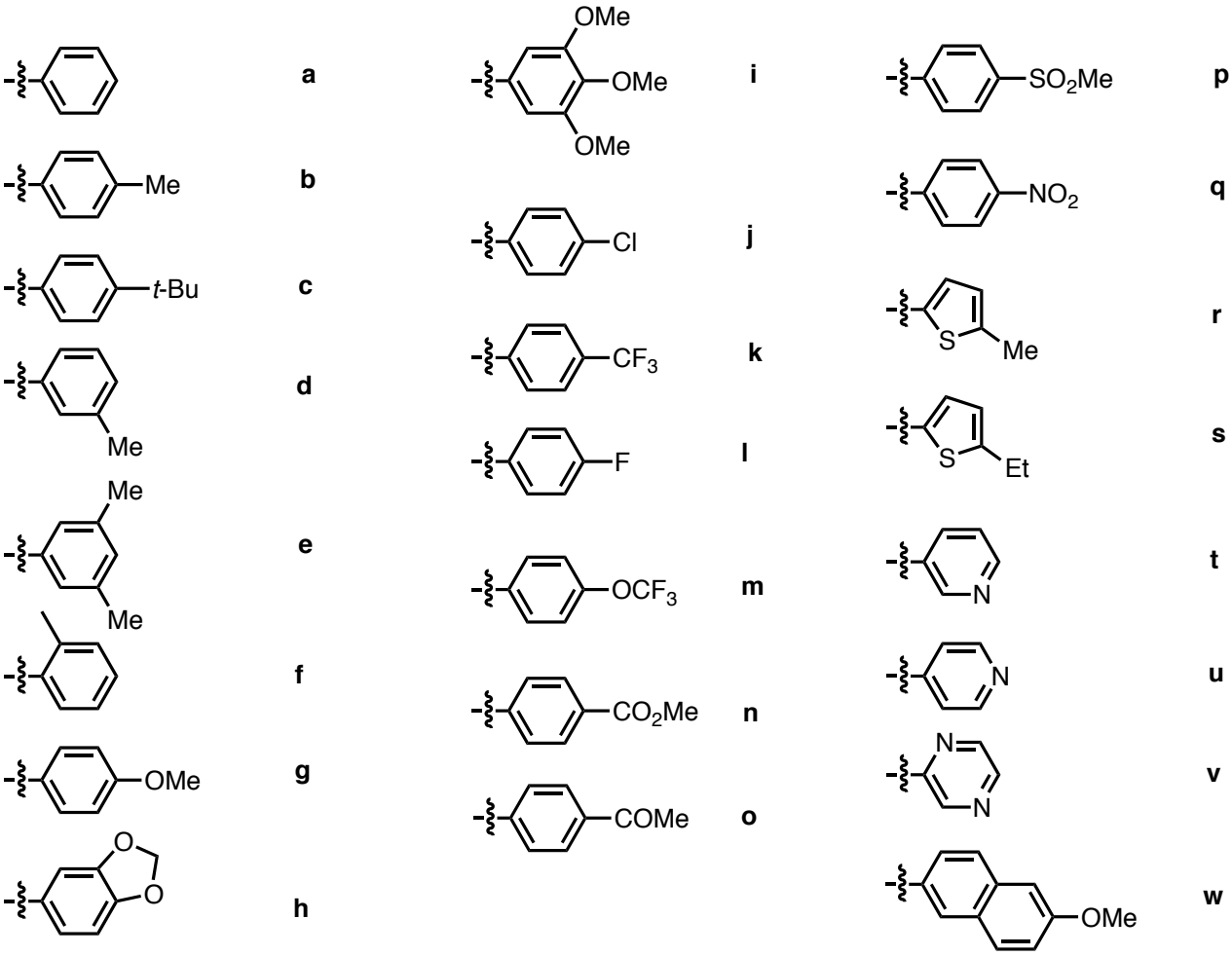
Unless otherwise noted, all materials including dry solvents were obtained from commercial suppliers and used without further purification. Thiazole (**1**), $Pd(OAc)_2$, 2,2'-bipyridyl, and $Ni(OAc)_2$, $PdCl_2(dppf)\cdot CH_2Cl_2$ were obtained from Wako Chemicals. $Pd[(P\textit{t}\text{-}Bu_3)]_2$ was obtained from Strem Chemicals. $PMe(\textit{t}\text{-}Bu)_2\cdot HBF_4$ was obtained from Sigma-Aldrich. PPh_3 was obtained from Nakarai Tesque. 4-Bromo-2-propylpyridine (**11**)[1], diphenyl(thiazol-2-yl)methanol (**5**)[2], $[Pd(phen)_2](PF_6)_2$[3], $Pd(bipy)Cl_2$[4] was synthesized according to procedures reported in the literature. Unless otherwise noted, all reactions were performed with dry solvents under an atmosphere of argon in flame-dried glassware, using standard vacuum-line techniques. All work-up and purification procedures were carried out with reagent-grade solvents in air.

Analytical thin-layer chromatography (TLC) was performed using E. Merck silica gel 60 F_{254} precoated plates (0.25 mm). The developed chromatogram was analyzed by UV lamp (254 nm) and ethanolic phosphomolybdic acid/sulfuric acid. Flash column chromatography was performed with E. Merck silica gel 60 (230–400 mesh). Preparative recycling gel permeation chromatography (GPC) was performed with a JAI LC-9204 instrument equipped with JAIGEL-1H/JAIGEL-2H columns using chloroform as an eluent. Preparative thin-layer chromatography (PTLC) was performed using Wako-gel® B5-F silica coated plates (0.75 mm) prepared in our laboratory. Chromatorex NH-DM1020 silica gel (Fuji Silysia Chemical Ltd., NH-silica) was used to remove remaining metal. Gas chromatography (GC) analysis was conducted on a Shimazu GC-2010 instrument equipped with a HP-5 column (30 m × 0.25 mm, Hewlett-Packard). GC/MS analysis was conducted on a Shimazu GCMS-QP2010 instrument equipped with a HP-5 column (30 m × 0.25 mm, Hewlett-Packard). High-resolution mass spectra (HRMS) were obtained from a JMS-T100TD (DART). Nuclear magnetic resonance (NMR) spectra were recorded on a JEOL JNM-ECA-600 (^{1}H 600 MHz, ^{13}C 150 MHz) spectrometer. Chemical shifts for ^{1}H NMR are expressed in parts per million (ppm) relative to tetramethylsilane (δ 0.00 ppm). Chemical shifts for ^{13}C NMR are expressed in ppm relative to $CDCl_3$ (δ 77.0 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, dd = doublet of doublets, t = triplet, q = quartet, m = multiplet, brs = broad signal), coupling constant (Hz), and integration.

[1] Comins, D. L.; Mantlo, N. B. *J. Org. Chem.* **1985**, *50*, 4410.
[2] Furukawa, H.; Matsumura, S.; Sugie, A.; Monguchi, D.; Mori, A. *Heterocycles* **2009**, *79*, 303.
[3] Bontempi, A.; Alessio, E.; Chanos, G.; Mestroni, G. *J. Mol. Catal.* **1987**, *42*, 67.
[4] Deshpande, R. M.; Diwakar, M. M.; Chaudhari, R. V. US20060142620

2. Assignment of Aryl Groups

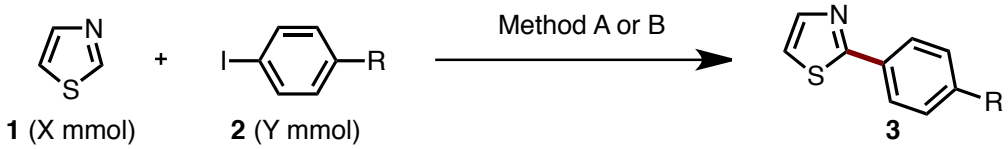
For simplification, we assigned each aryl groups alphabet as follows and used them in compound assignment.



3. Synthesis of 2-Arylthiazoles

3.1 Screening of Reaction Conditions

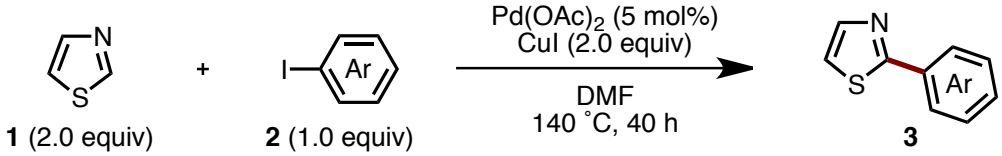
Table S1. Screening of Reaction Conditions



Entry	Method	X	Y	R	Yield [a]
1	A	0.8	0.4	OMe	>99%(77% [c])
2	A	0.6	0.4	OMe	89%
3 [b]	A	0.4	0.8	OMe	54%
4	B	0.4	0.6	H	21%
5	B	0.6	0.4	H	51%
6	B	0.6	0.4	H	63%(47% [c])

Method A: $Pd(OAc)_2$ (5 mol%), CuI (2.0 equiv), DMF (0.4 M), 140 ˚C, 16 h.
Method B: $Ni(OAc)_2$ (10 mol%), bipy (10 mol%), LiO*t*-Bu (2.0 equiv), 1,4-dioxane (0.4 M), 120 ˚C, 20 h.
a) GC yield. b) Reaction was conducted with 0.2 M solvent at 150 ˚C for 48 h.
c) Isolated yield.

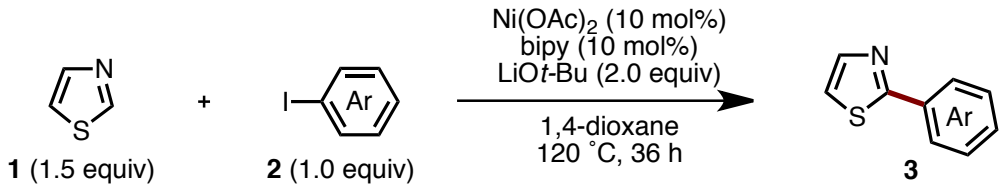
Method A[5]



A 20-mL glass vessel equipped with J. Young® O-ring tap, containing a magnetic stirring bar, was flame-dried under vacuum and filled with argon after cooling to room temperature. To this vessel were added $Pd(OAc)_2$ (4.5 mg, 0.02 mmol, 5 mol%), CuI (152 mg, 0.8 mmol, 2.0 equiv), iodoarene **2** (0.4 mmol, 1.0 equiv), thiazole (**1**: 0.8 mmol, 68.1 mg, 2.0 equiv) and DMF (1.0 mL). The vessel was sealed and then stirred at 140 °C for 40 h. After cooling the reaction mixture to room temperature, the mixture was passed through a silica gel pad with EtOAc. The filtrate was evaporated and the residue was purified by PTLC to afford 2-arylthiazole **3**. For further purification, the obtained product **3** was passed through NH-silica gel pad (EtOAc) and then the residue was purified by GPC to afford desired product **3**.

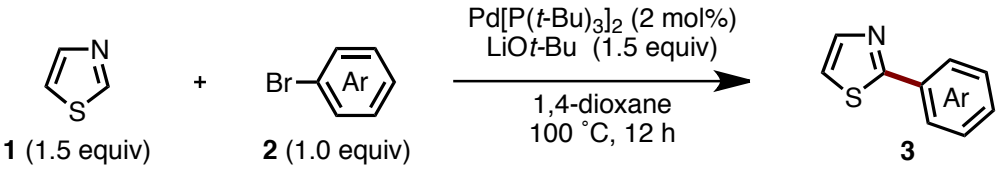
Method B[6]

[5] Yamamoto, T.; Muto, K.; Komiyama, M.; Canivet, J.; Yamaguchi, J.; Itami, K. *Chem. Eur. J.* **2011**, *17*, 10113.
[6] Bellina, F.; Cauteruccio, S.; Rossi, R. *Eur. J. Org. Chem.* **2006**, 1379.



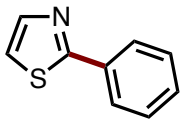
A 20-mL glass vessel equipped with J. Young® O-ring tap, containing a magnetic stirring bar and $Ni(OAc)_2 \cdot 4H_2O$ (10.0 mg, 0.04 mmol, 10 mol%), was flame-dried under vacuum and filled with argon after cooling to room temperature. To this vessel were added 2,2'-bipyridyl (bipy: 6.4 mg, 0.04 mmol, 10 mol%), subliminated LiO*t*-Bu (68.9 mg, 0.8 mmol, 2.0 equiv), iodoarene **2** (0.4 mmol, 1.0 equiv), thiazole (**1**: 0.6 mmol, 51.1 mg, 1.5 equiv) and 1,4-dioxane (1.0 mL) under a stream of argon. The vessel was sealed and then stirred at 120 °C for 36 h. After cooling the reaction mixture to room temperature, the mixture was passed through a short silica gel pad (EtOAc). The filtrate was evaporated and the residue was purified by PTLC to afford desired product **3**.

Method C[7]



A 20-mL glass vessel equipped with J. Young® O-ring tap, containing a magnetic stirring bar, was flame-dried under vacuum and filled with argon after cooling to room temperature. To this vessel were added $Pd[P(t\text{-}Bu)_3]_2$ (4.4 mg, 0.008 mmol, 2 mol%), LiO*t*-Bu (48 mg, 0.6 mmol, 1.5 equiv), bromoarene **2** (0.4 mmol, 1.0 equiv), thiazole (**1**: 0.6 mmol, 51.1 mg, 1.5 equiv), and dry 1,4-dioxane (1.6 mL). The vessel was sealed and then stirred at 100 °C for 12 h. After cooling the reaction mixture to room temperature, the mixture was passed through a short silica gel pad (EtOAc). The filtrate was evaporated and the residue was purified by GPC and PTLC to afford desired product **3**.

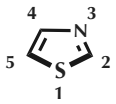
2-Phenylthiazole (3a)[6]



3a

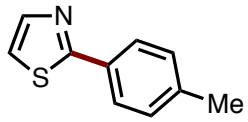
Purification by PTLC (hexane/EtOAc = 10:1) and GPC gave **3a** as a colorless oil (Method A: 93% yield, Method B: 61% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.31 (d, *J* = 3.0 Hz, 1H), 7.39–7.46 (m, 3H), 7.86 (d, *J* = 3.0 Hz, 1H), 7.97 (dd, *J* = 8.2, 2.0 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 118.8, 126.6, 128.9, 129.9,

[7] Tamba, S.; Okubo, Y.; Tanaka, S.; Monguchi, D.; Mori, A. *J. Org. Chem.* **2010**, *75*, 6998.



133.6, 143.6, 168.4. HRMS (DART) *m/z* = 162.0377 calcd for C_9H_8NS $[M+H]^+$, found: 162.0377.

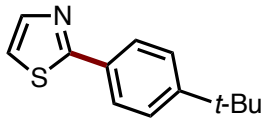
2-(4-Methylphenyl)thiazole (3b)[8]



3b

Purification by PTLC (hexane/EtOAc = 10:1) and GPC gave **3b** as a colorless oil (Method A: 84% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.39 (s, 3H), 7.25 (d, *J* = 8.2 Hz, 2H), 7.28 (d, *J* = 3.5 Hz, 1H), 7.84 (d, *J* = 3.5 Hz, 1H), 7.88 (d, *J* = 8.2 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.4, 118.3, 126.5, 129.6, 130.9, 140.2, 143.5, 168.6. HRMS (DART) *m/z* = 176.0534 calcd for $C_{10}H_{10}NS$ $[M+H]^+$, found: 176.0534.

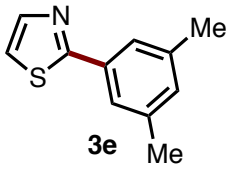
2-(4-(*tert*-Butyl)phenyl)thiazole (3c)



3c

Purification by PTLC (hexane/EtOAc = 5:1) and GPC gave **3c** as a light yellow solid (Method A: 71% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.35 (s, 9H), 7.28 (d, *J* = 3.4 Hz, 1H), 7.46 (d, *J* = 8.6 Hz, 2H), 7.84 (d, *J* = 3.4 Hz, 1H), 7.90 (d, *J* = 8.6 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 31.2, 34.8, 118.3, 125.9, 126.3, 130.9, 143.5, 153.3, 168.5; HRMS (DART) *m/z* = 218.1003 calcd for $C_{13}H_{16}NS$ $[M+H]^+$, found: 218.1006.

2-(3,5-Dimethylphenyl)thiazole (3e)

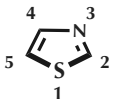


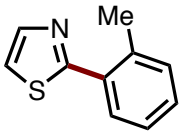
3e

Purification by PTLC (hexane/EtOAc = 10:1) and GPC gave **3e** as a light yellow oil (Method A: 80% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.37 (s, 6H), 7.05 (s, 1H), 7.28 (d, *J* = 3.4 Hz, 1H), 7.59 (s, 2H), 7.84 (d, *J* = 3.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.2, 118.5, 124.4, 131.7, 133.4, 138.6, 143.4, 168.8; HRMS (DART) *m/z* = 190.0690 calcd for $C_{11}H_{12}NS$ $[M+H]^+$, found: 190.0691.

2-(2-Methylphenyl)thiazole (3f)[9]

[8] Turner, G. L.; Morris, J. A.; Greaney, M. F. *Angew. Chem., Int. Ed.* **2007**, *46*, 7996.
[9] Feuerstein, M.; Doucet, H.; Santelli, M. *J. Organomet. Chem.* **2003**, *687*, 327.

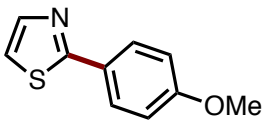




3f

Purification by PTLC (hexane/EtOAc = 10:1) gave **3f** as a light yellow oil (Method B: 76% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.58 (s, 3H), 7.24–7.34 (m, 3H), 7.37 (d, *J* = 2.8 Hz, 1H), 7.71 (d, *J* = 7.6 Hz, 1H), 7.91 (d, *J* = 2.8 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.3, 119.3, 126.0, 129.3, 130.0, 131.4, 132.9, 136.5, 142.9, 167.9. HRMS (DART) *m/z* = 176.0534 calcd for $C_{10}H_{10}NS$ $[M+H]^+$, found: 176.0533.

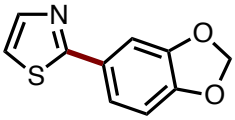
2-(4-Methoxyphenyl)thiazole (3g)[8]



3g

Purification by PTLC (hexane/EtOAc = 10:1) and GPC gave **3g** as a colorless oil (Method A: 77% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.83 (s, 3H), 6.94 (dt, *J* = 8.9, 2.4 Hz, 2H), 7.23 (d, *J* = 3.5 Hz, 1H), 7.79 (d, *J* = 3.5 Hz, 1H), 7.89 (dt, *J* = 8.9, 2.4 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 55.3, 114.2, 117.8, 126.6, 128.0, 143.3, 161.0, 168.2. HRMS (DART) *m/z* = 192.0483 calcd for $C_{10}H_{10}NOS$ $[M+H]^+$, found: 192.0483.

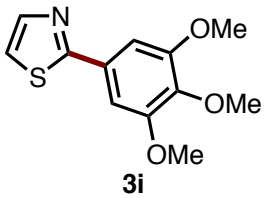
2-(Benzo[*d*][1,3]dioxol-5-yl)thiazole (3h) [10]



3h

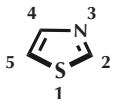
Purification by PTLC (hexane/EtOAc = 5:1) and GPC gave **3h** as a white solid (Method A: 77% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.01 (s, 2H), 6.85 (d, *J* = 8.3 Hz, 1H), 7.24 (d, *J* = 3.5 Hz, 1H), 7.44–7.48 (m, 2H), 7.79 (d, *J* = 3.5 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 101.5, 106.8, 108.5, 118.0, 121.0, 128.1, 143.3, 148.2, 149.1, 168.0; HRMS (DART) *m/z* = 206.0276 calcd for $C_{10}H_8NO_2S$ $[M+H]^+$, found: 206.0274.

2-(3,4,5-Trimethoxylphenyl)thiazole (3i)



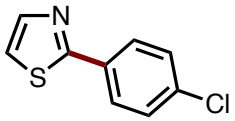
3i

[10] Hwan, M. S.; Jin, C. H.; Jin, L. S.; Uk, C. J.; Ryul, H. J.; Won, J. K.; Woong, O. S. WO9955318



Purification by GPC and then isolated product in $CHCl_3$ was passed through NH-silica (EtOAc) gave **3i** as a yellow oil (Method C: 70% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.90 (s, 3H), 3.95 (s, 6H), 7.20 (s, 2H), 7.31 (d, J = 3.5 Hz, 1H), 7.84 (d, J = 3.5 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 56.2, 60.9, 103.7, 118.6, 129.1, 139.7, 143.4, 153.5, 168.2; HRMS (DART) m/z = 252.0694 calcd for $C_{12}H_{14}NO_3S$ $[M+H]^+$, found: 252.0696.

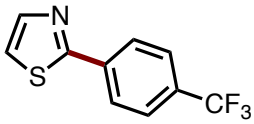
2-(4-Chlorophenyl)thiazole (3j)[11]



3j

Purification by PTLC (hexane/EtOAc = 10:1) and GPC gave **3j** as a colorless oil (Method A: 88% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34 (d, J = 3.4 Hz, 1H), 7.41 (dt, J = 8.9, 2.1 Hz, 2H), 7.86 (d, J = 3.4 Hz, 1H), 7.90 (dt, J = 8.9, 2.1 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 119.1, 127.8, 129.2, 132.1, 135.9, 143.8, 167.0. HRMS (DART) m/z = 195.9888 calcd for C_9H_6ClNS $[M+H]^+$, found: 195.9989.

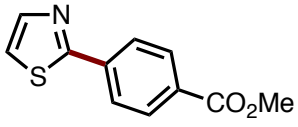
2-(4-Trifluoromethylphenyl)thiazole (3k)[8]



3k

Purification by PTLC (hexane/EtOAc = 10:1) and GPC gave **3k** as a light yellow solid (Method A: 71% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.41 (d, J = 3.2 Hz, 1H), 7.70 (d, J = 8.2 Hz, 2H), 7.92 (d, J = 3.2 Hz, 1H), 8.08 (d, J = 8.2 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 119.9, 123.9 (q, J_{C-F} = 270.3 Hz), 126.0 (q, J_{C-F} = 4.3 Hz), 126.8, 131.6 (q, J_{C-F} = 31.7 Hz), 136.7, 144.2, 166.5. HRMS (DART) m/z = 230.0251 calcd for $C_{10}H_7F_3NS$ $[M+H]^+$, found: 230.0252.

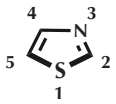
Methyl 4-(thiazol-2-yl)benzoate (3n)



3n

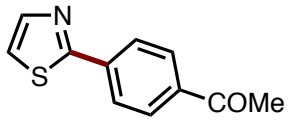
Purification by PTLC (hexane/EtOAc = 5:1) and GPC gave **3n** as a light yellow solid (Method A: 82% yield).

[11] Lapointe, D.; Fagnou, K. *Org. Lett.* **2009**, *11*, 4160.



^{1}H NMR (600 MHz, $CDCl_3$) δ 3.95 (s, 3H), 7.41 (d, J = 3.4 Hz, 1H), 7.93 (d, J = 3.4 Hz, 1H), 8.05 (d, J = 8.2 Hz, 2H), 8.12 (d, J = 8.2 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 52.2, 119.9, 126.4, 130.2, 131.2, 137.4, 144.1, 166.4, 166.9. HRMS (DART) m/z = 220.0432 calcd for $C_{11}H_{10}NO_2S$ $[M+H]^+$, found: 220.0430.

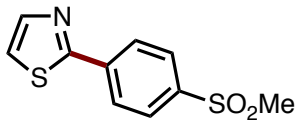
2-(4-Acetylphenyl)thiazole (3o)[12]



3o

Purification by PTLC (hexane/EtOAc = 3:1) and GPC gave **3o** as a white solid (Method A: 75% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.64 (s, 3H), 7.42 (d, J = 2.8 Hz, 1H), 7.93 (d, J = 2.8 Hz, 1H), 8.03 (d, J = 8.2 Hz, 2H), 8.07 (d, J = 8.2 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 26.7, 120.0, 126.6, 129.0, 137.5, 137.9, 144.2, 166.9, 197.3. HRMS (DART) m/z = 204.0483 calcd for $C_{11}H_{10}NOS$ $[M+H]^+$, found: 204.0484.

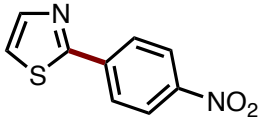
2-(4-(Methylsulfonyl)phenyl)thiazole (3p)



3p

Purification by PTLC (hexane/EtOAc = 2:1) gave **3p** as a white solid (Method C: 41% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.10 (s, 3H), 7.47 (d, J = 3.1 Hz, 1H), 7.95 (d, J = 3.1 Hz, 1H), 8.02 (d, J = 8.6 Hz, 2H), 8.16 (d, J = 8.6 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 44.4, 120.6, 127.2, 128.1, 138.2, 141.2, 144.4, 165.7; HRMS (DART) m/z = 240.0153 calcd for $C_{10}H_{10}NO_2S_2$ $[M+H]^+$, found: 240.0153.

2-(4-Nitrophenyl)thiazole (3q)



3q

Purification by PTLC (hexane/EtOAc = 2:1) and GPC gave **3q** as a yellow solid (Method A: 78% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.50 (d, J = 3.5 Hz, 1H), 7.97 (d, J = 3.5 Hz, 1H), 8.13 (d, J = 8.2 Hz, 2H), 8.29 (d, J = 8.2 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 121.0, 124.3, 127.1, 138.9, 144.6, 148.3, 165.2; HRMS (DART) m/z = 207.0228 calcd for $C_9H_7N_2O_2S$ $[M+H]^+$, found: 207.0228.

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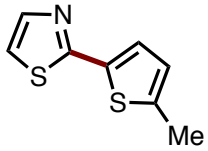
[12] Jensen, J.; Skjærbæk, N.; Vedsø, P. *Synthesis* **2001**, 128.

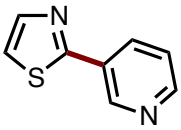
2-(5-Methylthiophen-2-yl)thiazole (3r)[13]



3r

Purification by GPC and PTLC (hexane/EtOAc = 10:1) gave **3r** as a colorless oil (Method C: 50% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.51 (s, 3H), 6.73 (d, J = 4.1 Hz, 1H), 7.19 (d, J = 3.5 Hz, 1H), 7.31 (d, J = 4.1 Hz, 1H), 7.72 (d, J = 3.5 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 15.5, 117.4, 126.1, 126.6, 134.9, 142.7, 143.0, 162.2; HRMS (DART) m/z = 182.0098 calcd for $C_8H_8NS_2$ $[M+H]^+$, found: 182.0099.

2-(3-Pyridyl)thiazole (3t)[14]



3t

Purification by PTLC (hexane/EtOAc = 1:1) gave **3t** as a yellow solid (Method B: 49% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39 (dd, J = 8.2, 4.8 Hz, 1H), 7.42 (d, J = 3.4 Hz, 1H), 7,93 (d, J = 3.4 Hz, 1H), 8.26 (dt, J = 8.2 Hz, 2.0 Hz, 1H), 8.66 (dd, J = 4.8, 1.4 Hz, 1H), 9.19 (d, J = 2.0 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ119.6, 123.7, 129.5, 133.6, 144.1, 147.7, 150.7, 164.8; HRMS (DART) m/z = 163.0330 calcd for $C_8H_7N_2S$ $[M+H]^+$, found: 163.0328.

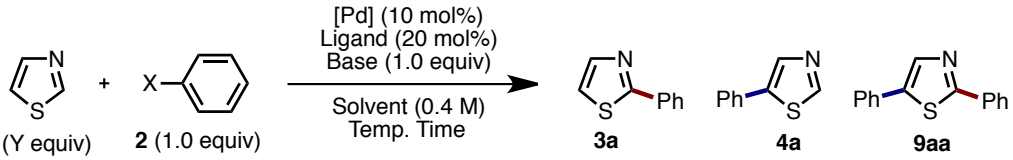
[13] Kaniskan, N.; Elmali, D.; Civcir, P. U. *ARKIVOC* **2008**, *12*, 17.

[14] Denton, T. T.; Zhang, X.; Cashman, J. R. *J. Med. Chem.* **2005,** *48,* 224.

4. Synthesis of 5-Arylthiazoles

Screening of Reaction Conditions

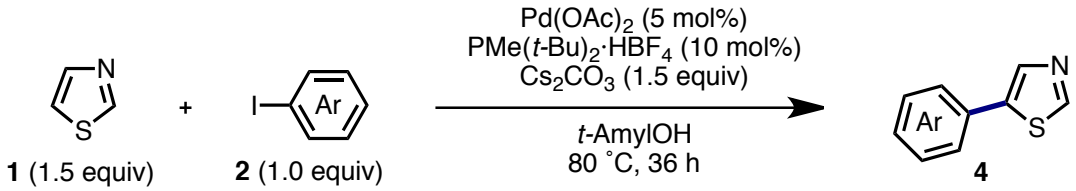
Table S2. Screening of Reaction Conditions



Entry	X	Y	[Pd]	Ligand	Solvent	Base	Temp.	Time	**3a** [b]	**4a** [b]	**9aa** [b]
1	I	1.25	$PdCl_2$(bipy)	none	DMF	Cs_2CO_3	120 ˚C	12 h	4%	14%	5%
2	I	1.25	$PdCl_2$(bipy)	none	DMF	Cs_2CO_3	120 ˚C	12 h	9%	21%	32%
3	I	1.25	$Pd(OAc)_2$	dppp[a]	DMF	Cs_2CO_3	120 ˚C	12 h	2%	44%	3%
4	I	1.25	$Pd(OAc)_2$	$PCy_3{\cdot}HBF_4$	DMF	Cs_2CO_3	120 ˚C	12 h	1%	36%	8%
5	I	1.25	$Pd(OAc)_2$	PMe(*t*-Bu)$_2{\cdot}HBF_4$	DMF	Cs_2CO_3	120 ˚C	12 h	0%	48%	7%
6 [c]	Br	1.25	$Pd(OAc)_2$	PMe(*t*-Bu)$_2{\cdot}HBF_4$	DMF	Cs_2CO_3	100 ˚C	12 h	2%	74%	19%
7 [c]	Br	1.25	$Pd(OAc)_2$	PMe(*t*-Bu)$_2{\cdot}HBF_4$	*t*-BuOH	Cs_2CO_3	100 ˚C	12 h	0%	67%	12%
8 [c,d]	Br	1.5	$Pd(OAc)_2$	PMe(*t*-Bu)$_2{\cdot}HBF_4$	DMF	K_2CO_3	120 ˚C	12 h	2%	60%	11%
9 [c,d]	I	1.5	$Pd(OAc)_2$	PMe(*t*-Bu)$_2{\cdot}HBF_4$	*t*-AmylOH	Cs_2CO_3	80 ˚C	36 h	0%	82%(80%)	8%

[a] 10 mol% Ligand was used. [b] GC yield. Isolated yield is given in parenthesis. [c] 5 mol% $Pd(OAc)_2$ and 10 mol% PMe(*t*-Bu)$_2{\cdot}HBF_4$ were used. [d] 1.5 equiv of base was used.

Methpd D[15]

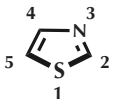


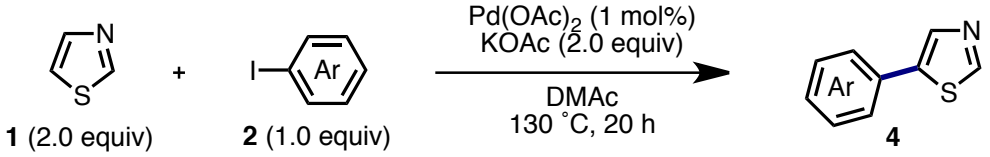
A 25-mL test tube equipped with screw cap containing a magnetic stirring bar, was flame-dried under vacuum and then cooling to room temperature. To this vessel were added $Pd(OAc)_2$ (4.5 mg, 0.02 mmol, 5 mol%), PMe(*t*-Bu)$_2{\cdot}HBF_4$ (10.0 mg, 0.04 mmol, 10 mol%), Cs_2CO_3 (195.5 mg, 0.6 mmol, 1.5 equiv), iodoarene **2** (0.4 mmol, 1.0 equiv), thiazole (**1**: 0.6 mmol, 51.1 mg, 1.5 equiv), and *t*-AmylOH (1.0 mL) under argon atmosphere. The vessel was sealed and then stirred at 80 °C for 36 h. After cooling the reaction mixture to room temperature, the mixture was passed through a short silica gel pad (EtOAc). The filtrate was evaporated and the residue was purified by PTLC and/or GPC to afford 5-arylthiazole **4**. For further purification was passed through NH-silica gel pad (EtOAc) to afford desired product **4**.

Method E[16]

[15] Liégault, B.; Lapointe, D.; Caron, L.; Vlassova, A.; Fagnou, K. *J. Org. Chem.* **2009,** *74,* 1826.

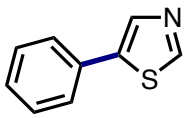
[16] Roger, J.; Požgan, F. Doucet, H. *J. Org. Chem.* **2009,** *74,* 1179.





A 7-mL test tube equipped with screw cap containing a magnetic stirring bar, was flame-dried under vacuum and then cooling to room temperature. To this vessel were added $Pd(OAc)_2$ (0.9 mg, 0.004 mmol, 1 mol%), KOAc (79.4 mg, 0.8 mmol, 2.0 equiv), bromoarene **2** (0.4 mmol, 1.0 equiv), thiazole (**1**: 0.8 mmol, 68.1 mg, 2.0 equiv), and DMAc (1 mL). The vessel was sealed and then stirred at 130 °C for 20 h. After cooling the reaction mixture to room temperature, the mixture was passed through a short silica gel pad (EtOAc). The filtrate was evaporated and the residue was purified by PTLC to afford desired product **4**.

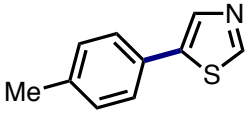
5-Phenylthiazole (4a)[17]



4a

Purification by PTLC (hexane/EtOAc = 10:1) gave **4a** as a white solid (Method D: 80% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35 (t, *J* = 7.6 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.58 (d, *J* = 7.6 Hz, 2H), 8.08 (s, 1H), 8.75 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 127.0, 128.4, 129.1, 131.1, 139.0, 139.4, 152.0; HRMS (DART) *m*/*z* = 162.0377 calcd for C_9H_8NS $[M+H]^+$, found: 162.0378.

5-(4-Methylphenyl)thiazole (4b)][1,2]

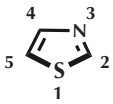


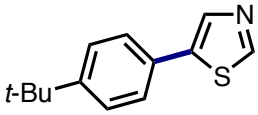
4b

Purification by PTLC (hexane/EtOAc = 10:1) gave **4b** as a white solid (Method D: 78% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.36 (s, 3H), 7.20 (d, *J* = 7.6 Hz, 2H), 7.45 (d, *J* = 7.6 Hz, 2H), 8.03 (s, 1H), 8.70 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.1, 126.8, 128.2, 129.7, 138.4, 138.5, 139.4, 151.5; HRMS (DART) *m*/*z* = 176.0534 calcd for $C_{10}H_{10}NS$ $[M+H]^+$, found: 176.0535.

5-(4-(*tert*-Butyl)phenyl)thiazole (4c)

[17] Pavlik, J. W.; Tongcharoensirikul, P.; Bird, N. P.; Day, A. C.; Barltrop, J. A. *J. Am. Chem. Soc.* **1994**, *116*, 2292.

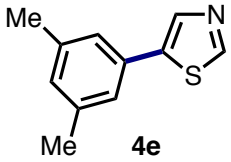




4c

Purification by PTLC (hexane/EtOAc = 5:1) gave **4c** as a yellow solid (Method D: 71% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.33 (s, 9H), 7.42 (d, J = 8.6 Hz, 2H), 7.50 (d, J = 8.6 Hz, 2H), 8.04 (s, 1H), 8.70 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 31.1, 34.6, 126.0, 126.7, 128.2, 138.6, 139.3, 151.57, 151.63; HRMS (DART) m/z = 218.1003 calcd for $C_{13}H_{17}NS$ $[M+H]^+$, found: 218.1008.

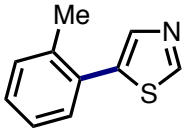
5-(3,5-Dimethylphenyl)thiazole (4e)



4e

Purification by PTLC (hexane/EtOAc = 10:1) gave **4e** as a yellow oil (Method D: 57% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.35 (s, 6H), 6.98 (s, 1H), 7.19 (s, 2H), 8.05 (s, 1H), 8.71 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.2, 124.8, 130.1, 130.8, 138.7, 138.8, 139.6, 151.7; HRMS (DART) m/z = 190.0690 calcd for $C_{11}H_{12}NS$ $[M+H]^+$, found: 190.0691.

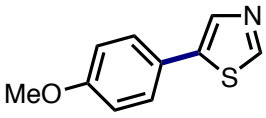
5-(2-Methylphenyl)thiazole (4f)[9]



4f

Purification by PTLC (hexane/EtOAc = 10:1) gave **4f** as a light yellow oil (Method D: 76% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.38 (s, 3H), 7.21–7.31 (m, 3H), 7.36 (d, J = 7.6 Hz, 1H), 7.84 (s, 1H), 8.81 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 20.9, 126.0, 128.6, 130.2, 130.67, 130.73, 136.4, 137.3, 141.6, 152.6; HRMS (DART) m/z = 176.0534 calcd for $C_{10}H_{10}NS$ $[M+H]^+$, found: 176.0534.

5-(4-Methoxyphenyl)thiazole (4g)[15]

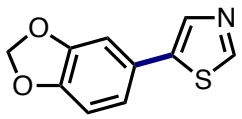


4g

Purification by PTLC (hexane/EtOAc = 5:1) gave **4g** as a white solid (Method D: 81% yield). ^{1}H NMR

(600 MHz, $CDCl_3$) δ 3.83 (s, 3H), 6.93 (dt, *J* = 8.9, 2.1 Hz, 2H), 7.50 (d, *J* = 8.9, 2.1 Hz, 2H), 7.97 (s, 1H), 8.69 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 55.3, 114.5, 123.6, 128.2, 138.0, 139.2, 151.2, 159.8; HRMS (DART) *m/z* = 192.0483 calcd for $C_{10}H_{10}NOS$ $[M+H]^+$, found: 192.0483.

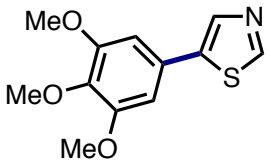
5-(Benzo[*d*][1,3]dioxol-5-yl)thiazole (4h)



4h

Purification by PTLC (hexane/EtOAc = 3:1) and GPC gave **4h** as a white solid (Method D: 77% yield). ^1H NMR (600 MHz, $CDCl_3$) δ 6.00 (s, 2H), 6.83 (d, *J* = 7.6 Hz, 1H), 7.03–7.07 (m, 2H), 7.95 (s, 1H), 8.69 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 101.4, 107.3, 108.8, 120.9, 125.0, 138.3, 139.2, 147.8, 148.2, 151.3; HRMS (DART) *m/z* = 206.0276 calcd for $C_{10}H_8NO_2S$ $[M+H]^+$, found: 206.0276.

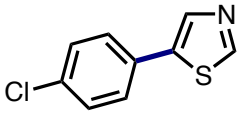
2-(3,4,5-Trimethoxylphenyl)thiazole (4i)



4i

5-Bromo-1,2,3-trimethoxylbenzene was used and the reaction was performed at 100 °C for 18 h. Purification by GPC gave **4i** as a light yellow solid (Method D: 58% yield). ^1H NMR (600 MHz, $CDCl_3$) δ 3.88 (s, 3H), 3.92 (s, 6H), 6.77 (s, 2H), 8.01 (s, 1H), 8.74 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 56.1, 60.8, 104.4, 126.5, 138.4, 138.7, 139.3, 151.7, 153.5; HRMS (DART) *m/z* = 252.0694 calcd for $C_{12}H_{14}NO_3S$ $[M+H]^+$, found: 252.0695.

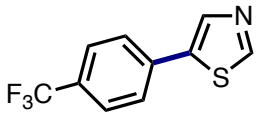
5-(4-Chlorophenyl)thiazole (4j)



4j

Purification by GPC gave **4j** as a yellow solid (Method D: 63% yield). ^1H NMR (600 MHz, $CDCl_3$) δ 7.37 (d, *J* = 8.3 Hz, 2H), 7.49 (d, *J* = 8.3 Hz, 2H), 8.05 (s, 1H), 8.76 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 128.1, 129.3, 129.6, 134.3, 138.1, 139.3, 152.3; HRMS (DART) *m/z* = 195.9988 calcd for C_9H_7ClNS $[M+H]^+$, found: 195.9988.

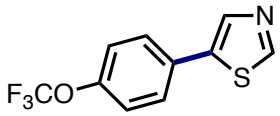
5-(4-Trifluoromethylphenyl)thiazole (4k)[18]



4k

Purification by PTLC (hexane/EtOAc = 10:1) and GPC gave **4k** as a light yellow solid (Method D: 75% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.65–7.70 (m, 4H), 8.16 (s, 1H), 8.82 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 123.9 (q, $J_{C–F}$ = 271.7 Hz), 126.1 (q, $J_{C–F}$ = 4.3 Hz), 127.1, 130.3 (q, $J_{C–F}$ = 31.6 Hz), 134.6, 137.7, 140.2, 153.1; HRMS (DART) *m/z* = 230.0251 calcd for $C_{10}H_7F_3NS$ $[M+H]^+$, found: 230.0250.

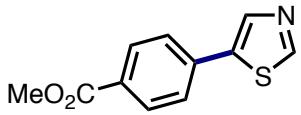
5-(4-Trifluoromethoxyphenyl)thiazole (4m)



4m

Purification by PTLC (hexane/EtOAc = 5:1) gave **4m** as a colorless oil (Method D: 72% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.27 (d, *J* = 8.6 Hz, 2H), 7.60 (dt, *J* = 8.6, 2H), 8.06 (s, 1H), 8.78 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 120.4 (q, $J_{C–F}$ = 257.3 Hz), 121.6, 128.4, 129.9, 137.8, 139.5, 149.1, 152.5; HRMS (DART) *m/z* = 246.0200 calcd for $C_{10}H_7F_3NOS$ $[M+H]^+$, found: 246.0201.

Methyl 4-(thiazol-5-yl)benzoate (4n)

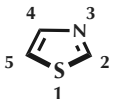


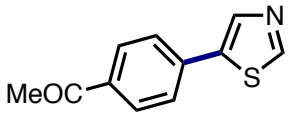
4n

Purification by PTLC (hexane/EtOAc = 3:1) and GPC gave **4n** as a white solid (Method D: 61% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.94 (s, 3H), 7.64 (d, *J* = 8.3 Hz, 2H), 8.07 (d, *J* = 8.3 Hz, 2H), 8.17 (s, 1H), 8.82 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 52.2, 126.6, 129.8, 130.3, 135.4, 138.2, 140.1, 153.0, 166.3; HRMS (DART) *m/z* = 220.0432 calcd for $C_{11}H_{10}NO_2S$ $[M+H]^+$, found: 220.0434.

5-(4-Acetylphenyl)thiazole (4o)

[18] Mamada, M.; Nishida, J.; Kumaki, D.; Tokito, S.; Yamashita, Y. *Chem. Mater.* **2007**, *19*, 5404.

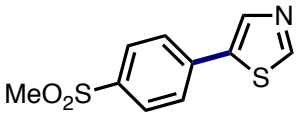




4o

Purification by PTLC (hexane/EtOAc = 3:1) gave **4o** as a white solid (Method E: 82% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.63 (s, 3H), 7.67 (d, *J* = 8.2 Hz, 2H), 8.00 (d, *J* = 8.2 Hz, 2H), 8.19 (s, 1H), 8.83 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 26.5, 126.8, 129.1, 135.5, 136.5, 138.1, 140.2, 153.1, 197.0; HRMS (DART) *m/z* = 204.0483 calcd for $C_{11}H_{10}NOS$ $[M+H]^+$, found: 204.0484.

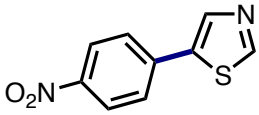
5-(4-(Methylsulfonyl)phenyl)thiazole (4p)



4p

Purification by PTLC (hexane/EtOAc = 2:1) gave **4p** as a yellow solid (Method E: 66% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.10 (s, 3H), 7.78 (d, *J* = 8.3 Hz, 2H), 8.00 (d, *J* = 8.3 Hz, 2H), 8.22 (s, 1H), 8.87 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 44.4, 127.5, 128.3, 136.4, 137.2, 139.9, 140.8, 153.7; HRMS (DART) *m/z* = 240.0153 calcd for $C_{10}H_{10}NO_2S_2$ $[M+H]^+$, found: 240.0512.

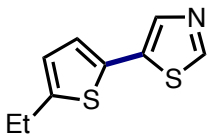
5-(4-Nitrophenyl)thiazole (4q)



4q

Purification by PTLC (hexane/EtOAc = 2:1) gave **4q** as a yellow solid (Method D: 41% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.2 Hz, 2H), 8.24 (s, 1H), 8.29 (d, *J* = 8.2 Hz, 2H), 8.89 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 124.5, 127.3, 136.9, 137.4, 141.1, 147.3, 154.1; HRMS (DART) *m/z* = 207.0228 calcd for $C_9H_7NO_2S$ $[M+H]^+$, found: 207.0228.

5-(5-Ethylthiophen-2-yl)thiazole (4s)

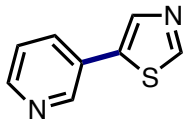


4s

Purification by PTLC (hexane/EtOAc = 10:1) and GPC gave **4s** as a yellow oil (Method D: 26% yield). ^{1}H

NMR (600 MHz, $CDCl_3$) δ 1.33 (t, *J* = 7.6 Hz, 3H), 2.85 (q, *J* = 7.6 Hz, 2H), 6.73 (d, *J* = 3.4 Hz, 1H), 7.02 (d, *J* = 3.4 Hz, 1H), 7.89 (s, 1H), 8.65 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 15.8, 23.5, 124.2, 125.7, 130.1, 133.0, 138.6, 148.4, 150.9; HRMS (DART) *m/z* = 196.0255 calcd for $C_9H_{10}NS_2$ $[M+H]^+$, found: 196.0256.

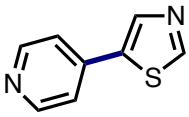
5-(3-Pyridyl)thiazole (4t)[19]



4t

Purification by PTLC (hexane/EtOAc = 3:1) gave **4t** as a light yellow oil (Method E: 65% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36 (dd, *J* = 7.6, 4.8 Hz, 1H), 7.87 (dt, *J* = 7.6, 2.1 Hz, 1H), 8.14 (s, 1H), 8.59 (d, *J* = 4.8 Hz, 1H), 8.85 (s, 1H), 8.86 (d, *J* = 2.1 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 123.7, 127.3, 134.0, 135.4, 139.9, 147.7, 149.4, 153.0; HRMS (DART) *m/z* = 163.0330 calcd for $C_7H_7N_2S$ $[M+H]^+$, found: 163.0331.

5-(4-Pyridyl)thiazole (4u)[19]



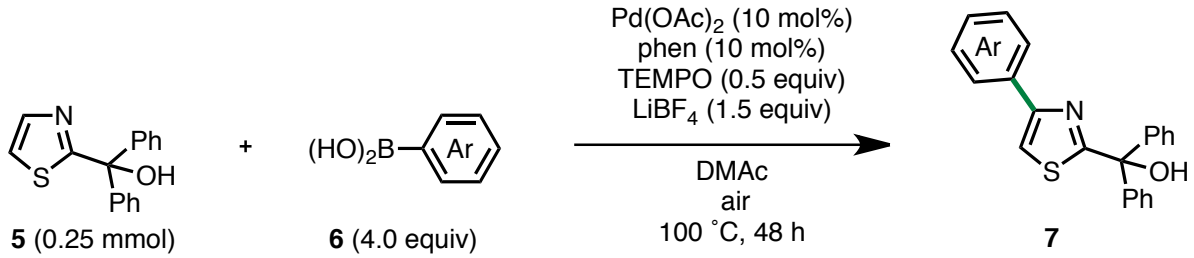
4u

Purification by PTLC (hexane/EtOAc = 3:1) gave **4u** as a colorless oil (Method E: 62% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.47 (d, *J* = 6.2 Hz, 2H), 8.27 (s, 1H), 8.65 (d, *J* = 6.2 Hz, 2H), 8.88 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 120.9, 136.5, 138.4, 141.0, 150.5, 153.8; HRMS (DART) *m/z* = 163.0330 calcd for $C_7H_7N_2S$ $[M+H]^+$, found: 163.0332.

[19] Haginoya, N.; Kobayashi, S.; Komoriya, S.; Yoshino, T.; Nagata, T.; Hirokawa, Y.; Nagahara, T. *Bioorg. Med. Chem.* **2004**, *12*, 5579.

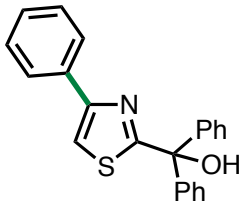
5. Synthesis of 4-Arylthiazoles

Method F[20]



A 25-mL test tube equipped with screw cap, containing a magnetic stirring bar, was added $Pd(OAc)_2$ (5.6 mg, 0.025 mmol, 10 mol%), 1,10-phenanthroline (phen: 4.5 mg, 0.025 mmol, 10 mol%), arylboronic acid **6** (1.0 mmol, 4.0 equiv), $LiBF_4$ (35.5 mg, 0.38 mmol, 1.5 equiv), TEMPO (19.5 mg, 0.13 mmol, 0.5 equiv), diphenyl(thiazol-2-yl)methanol (**5**: 0.25 mmol, 1.0 equiv) and undried DMAc (0.5 mL). The vessel was sealed under air and then stirred at 100 °C for 48 h. After cooling the reaction mixture to room temperature, the mixture was passed through a short silica gel pad (EtOAc). The filtrate was evaporated and the residue was purified by PTLC and/or GPC and/or flash column chromatography to afford 4-aryl-diphenyl(thiazol-2-yl)methanol **8**.

Diphenyl(4-phenylthiazol-2-yl)methanol (7a)

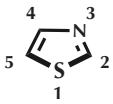


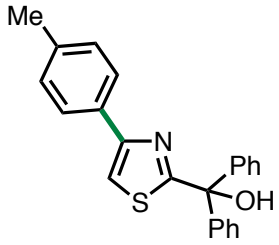
7a

Purification by PTLC (hexane/EtOAc = 10:1) gave **7a** as a colorless oil (Method F: 71% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.38 (s, 1H), 7.29–7.35 (m, 7H), 7.40 (t, J = 6.9 Hz, 2H), 7.45 (d, J = 6.9 Hz, 4H), 7.47 (s, 1H), 7.89 (d, J = 6.9 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 80.7, 113.9, 126.4, 127.5, 127.9, 128.1, 128.2, 128.7, 134.2, 145.4, 155.1, 176.6; HRMS (DART) m/z = 344.1109 calcd for $C_{22}H_{18}NOS$ $[M+H]^+$, found: 344.1100.

(4-(4-Methylphenyl)thiazol-2-yl)diphenylmethanol (7b)

[20] Kirchberg, S.; Tani, S.; Ueda, K.; Yamaguchi, J.; Studer, A.; Itami, K. *Angew. Chem., Int. Ed.* **2011,** *50,* 2387.

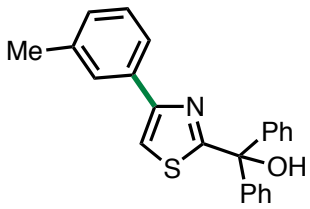




7b

Purification by flash column chromatography (hexane/EtOAc = 10:1) gave **7b** as a colorless oil (Method F: 75% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.35 (s, 3H), 4.48 (s, 1H), 7.18 (d, *J* = 8.3 Hz, 2H), 7.27–7.33 (m, 6H), 7.37 (s, 1H), 7.44 (d, *J* = 7.6 Hz, 2H), 7.77 (d, *J* = 8.3 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.2, 80.6, 113.1, 126.3, 127.5, 127.9, 128.0, 129.4, 131.5, 138.1, 145.5, 155.2, 176.4; HRMS (DART) *m*/*z* = 358.1266 calcd for $C_{23}H_{20}NOS$ $[M+H]^+$, found: 358.1264.

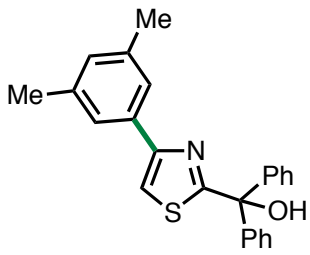
(4-(3-Methylphenyl)thiazol-2-yl)diphenylmethanol (7d)



7d

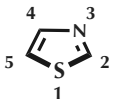
Purification by flash column chromatography (hexane/EtOAc = 10:1) gave **7d** as a colorless oil (Method F: 77% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.38 (s, 3H), 4.47 (s, 1H), 7.13 (d, *J* = 7.6 Hz, 1H), 7.27–7.35 (m, 7H), 7.41–7.48 (m, 5H), 7.67 (d, *J* = 7.6 Hz, 1H), 7.72 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.4, 80.6, 113.8, 123.5, 127.1, 127.5, 127.9, 128.1, 128.6, 129.0, 134.1, 138.3, 145.4, 155.2, 176.5; HRMS (DART) *m*/*z* = 358.1266 calcd for $C_{23}H_{20}NOS$ $[M+H]^+$, found: 358.1267.

(4-(3,5-Dimethylphenyl)thiazol-2-yl)diphenylmethanol (7e)



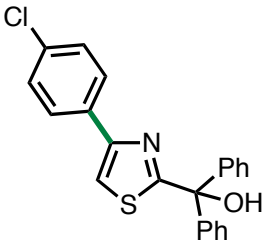
7e

Purification by flash column chromatography (hexane/EtOAc = 10:1) gave **7e** as a colorless oil (Method F: 62% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.34 (s, 6H), 4.51 (s, 1H), 6.96 (s, 1H), 7.28–7.35 (m, 6H), 7.42 (s, 1H), 7.43 (d, *J* = 6.9 Hz, 4H), 7.51 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.3, 80.6, 113.7, 124.3, 127.5,



127.9, 128.1, 129.9, 134.0, 138.2, 145.5, 155.4, 176.3; HRMS (DART) *m/z* = 372.1422 calcd for $C_{24}H_{22}NOS$ $[M+H]^+$, found: 372.1421.

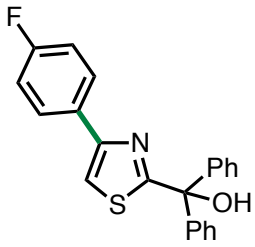
(4-(4-Chlorophenyl)thiazol-2-yl)diphenylmethanol (7j)



7j

Purification by flash column chromatography (hexane/EtOAc = 10:1) gave **7j** as a colorless oil (Method F: 66% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.25 (brs, 1H), 7.28–7.37 (m, 8H), 7.41–7.47 (m, 5H), 7.80 (d, *J* = 8.3 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 80.0, 113.6, 126.8, 127.0, 127.3, 127.5, 128.2, 132.0, 133.3, 144.6, 153.4, 176.4; HRMS (DART) *m/z* = 378.0719 calcd for $C_{22}H_{17}ClNOS$ $[M+H]^+$, found: 378.0722.

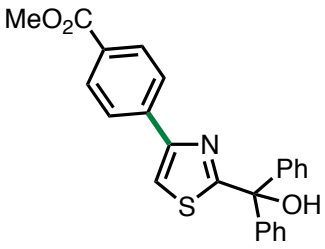
(4-(4-Fluorophenyl)thiazol-2-yl)diphenylmethanol (7l)



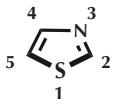
7l

Purification by flash column chromatography (hexane/EtOAc = 10:1) gave **7l** as a colorless oil (Method F: 56% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.36 (s, 1H), 7.06 (t, *J* = 8.3 Hz, 2H), 7.27–7.35 (m, 6H), 7.37 (s, 1H), 7.44 (dd, *J* = 8.3, 1.4 Hz, 4H), 7.82–7.86 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 80.6, 113.4, 115.6 (d, J_{C-F} = 21.6 Hz), 127.5, 127.9, 128.06, 128.09, 130.5 (d, J_{C-F} = 2.7 Hz), 145.3, 154.2, 162.7 (d, J_{C-F} = 247.2 Hz), 176.9; HRMS (DART) *m/z* = 362.1015 calcd for $C_{22}H_{17}FNOS$ $[M+H]^+$, found: 362.1017.

(4-(4-Methoxycarbonylphenyl)thiazol-2-yl)diphenylmethanol (7n)

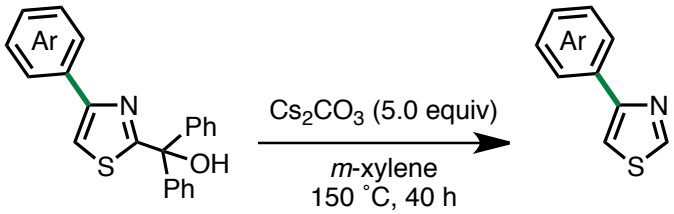


7n



Purification by GPC gave **7n** as a white solid (Method F: 63% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.91 (s, 3H), 4.35 (s, 1H), 7.29–7.36 (m, 6H), 7.45 (dd, *J* = 8.2, 1.4 Hz, 4H), 7.58 (s, 1H), 7.95 (d, *J* = 8.3 Hz, 2H), 8.05 (d, *J* = 8.3 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 52.1, 80.7, 115.8, 126.2, 127.5, 128.0, 128.1, 129.5, 130.1, 138.3, 145.2, 154.1, 166.8, 177.2; HRMS (DART) *m/z* = 402.1164 calcd for $C_{24}H_{20}NO_3S$ $[M+H]^+$, found: 402.1165.

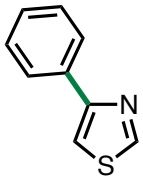
General Procedure for Deprotection of C4-Arylated Diphenyl-(2-thiazolyl)methanols 7[2]



7 (0.2 mmol) **8**

A 25-mL test tube equipped with screw cap containing a magnetic stirring bar, was flame-dried under vacuum and then cooling to room temperature. To this vessel was added **7** (ca. 0.1–0.2 mmol), Cs_2CO_3 (325.9 mg, 1 mmol, 5–10 equiv), and *m*-xylene (0.8 mL). The vessel was sealed and then stirred at 150 °C for 40 h. After cooling the reaction mixture to room temperature, the mixture was passed through a short silica gel pad (EtOAc). The filtrate was evaporated and the residue was purified by PTLC or GPC to afford 4-arylthiaozle **8**.

4-Phenylthiazole (8a)[17]



8a

Purification by PTLC (hexane/EtOAc = 10:1) gave **8a** as a white solid (95% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35 (t, *J* = 8.2 Hz, 1H), 7.44 (t, *J* = 8.2 Hz, 2H), 7.54 (s, 2H), 7.94–8.00 (m, 2H), 8.88 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 112.5, 126.5, 128.2, 128.8, 134.2, 152.8, 156.4. HRMS (DART) *m/z* = 162.0378 calcd for C_9H_8NS $[M+H]^+$, found: 162.0378.

4-(4-Methylphenyl)thiazole (8b)[21]

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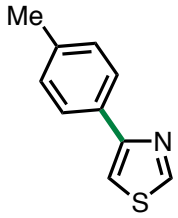
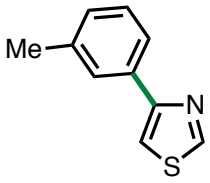
[21] Adam, W.; Hartung, J.; Okamoto, H.; Marquardt, S.; Nau, W. M.; Pischel, U.; Saha-Möller, C. R.; Špehar, K. *J. Org. Chem.* **2002**, *67*, 6041.



8b

Purification by PTLC (hexane/EtOAc = 10:1) gave **8b** as a white solid (78% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.38 (s, 3H), 7.24 (d, *J* = 8.3 Hz, 2H), 7.46 (s, 1H), 7.82 (d, *J* = 8.3 Hz, 2H), 8.85 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.2, 111.7, 126.3, 129.5, 131.5, 138.1, 152.6, 156.5; HRMS (DART) *m*/*z* = 176.0534 calcd for $C_{10}H_{10}NS$ $[M+H]^+$, found: 176.0536.

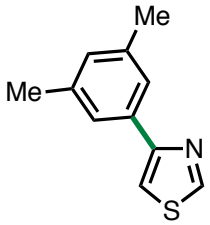
4-(3-Methylphenyl)thiazole (8d)



8d

Purification by PTLC (hexane/EtOAc = 10:1) gave **8d** as a yellow oil (84% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.42 (s, 3H), 7.17 (d, *J* = 7.6 Hz, 1H), 7.32 (t, *J* = 7.6 Hz, 1H), 7.51 (d, *J* = 2.1 Hz, 1H), 7.71 (d, *J* = 7.6 Hz, 1H), 7.78 (s, 1H), 8.87 (d, *J* = 2.1 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.4, 112.4, 123.5, 127.2, 128.7, 129.0, 134.1, 138.5, 152.7, 156.5; HRMS (DART) *m*/*z* = 176.0534 calcd for $C_{10}H_{10}NS$ $[M+H]^+$, found: 176.0534.

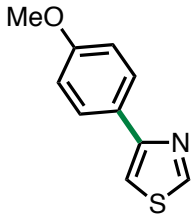
4-(3,5-Dimethylphenyl)thiazole (8e)



8e

Purification by GPC gave **8e** as a colorless oil (66% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.37 (s, 6H), 7.00 (s, 1H), 7.49 (d, *J* = 2.0 Hz, 1H), 7.55 (s, 2H), 8.86 (d, *J* = 2.0 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.3, 112.2, 124.3, 129.9, 134.0, 138.3, 152.6, 156.7; HRMS (DART) *m*/*z* = 190.0690 calcd for $C_{11}H_{12}NS$ $[M+H]^+$, found: 190.0691.

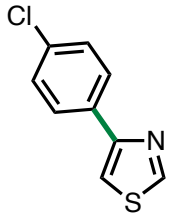
4-(4-Methoxyphenyl)thiazole (8g) [22]



8g

C–H arylation of **5** with 4-methoxyphenylboronic acid following by Method F produced an inseparable mixture of **7g** and **5**. Yield of **7g** was determined by ^{1}H NMR (53% yield). Then the mixture was used without further purification. The deprotection reaction of **7g** produced **8g**. Purification by PTLC (hexane/EtOAc = 5:1) gave **8g** as a white solid (74% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.85 (s, 3H), 6.96 (d, J = 8.9 Hz, 2H), 7.39 (d, J = 1.4 Hz, 1H), 7.86 (d, J = 8.9 Hz, 2H), 8.84 (d, J = 1.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 55.3, 110.7, 114.2, 127.2, 127.7, 152.6, 156.2, 159.7. HRMS (DART) m/z = 192.0483 calcd for $C_{10}H_{10}NOS$ $[M+H]^+$, found: 192.0484.

4-(4-Chlorophenyl)thiazole (8j)[22]

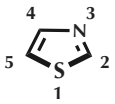


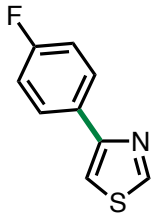
8j

Purification by PTLC (hexane/EtOAc = 10:1) gave **8j** as a white solid (87% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39 (d, J = 8.2 Hz, 2H), 7.49 (d, J = 1.4 Hz, 1H), 7.85 (d, J = 8.2 Hz, 2H), 8.85 (d, J = 1.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 112.8, 127.7, 128.9, 132.7, 134.0, 152.9, 155.2; HRMS (DART) m/z = 195.9988 calcd for C_9H_7ClNS $[M+H]^+$, found: 195.9989.

4-(4-Fluorophenyl)thiazole (8l)[22]

[22] Fujii, H.; Nishimura, Y.; Nitta, A.; Sakami, S.; Nakaki, J.; Kozono, H. WO2007063928

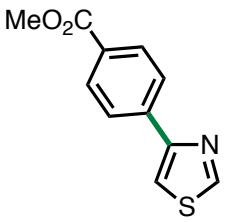




8l

Purification by PTLC (hexane/EtOAc = 10:1) gave **8l** as a white solid (80% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.12 (t, J = 8.9 Hz, 2H), 7.47 (d, J = 2.0 Hz, 1H), 7.91 (dd, J = 8.9, 5.5 Hz, 2H), 8.87 (d, J = 2.0 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 112.1, 115.7 (d, $J_{C–F}$ = 21.6 Hz), 128.15, 128.21, 130.5 (d, $J_{C–F}$ = 2.9 Hz), 152.9, 155.4, 162.8 (d, $J_{C–F}$ = 245.8 Hz); HRMS (DART) m/z = 180.0283 calcd for C_9H_7FNS $[M+H]^+$, found: 180.0285.

Methyl 4-(thiazol-4-yl)benzoate (8n)

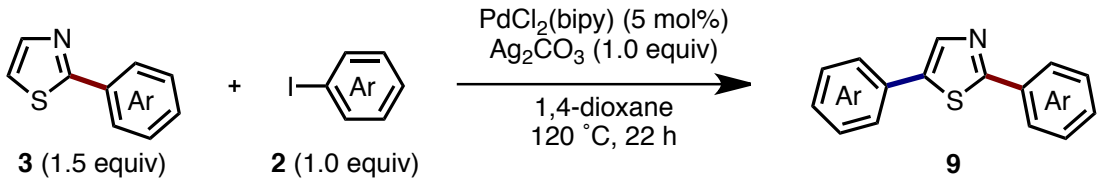


8n

Purification by PTLC (hexane/EtOAc = 5:1) gave **8n** as a white solid (88% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.94 (s, 3H), 7.67 (s, 1H), 8.01 (d, J = 8.3 Hz, 2H), 8.11 (d, J = 8.3 Hz, 2H), 8.90 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 52.1, 114.5, 126.3, 129.6, 130.2, 138.2, 153.2, 155.3, 166.8; HRMS (DART) m/z = 220.0432 calcd for $C_{10}H_{10}NO_2S$ $[M+H]^+$, found: 220.0432.

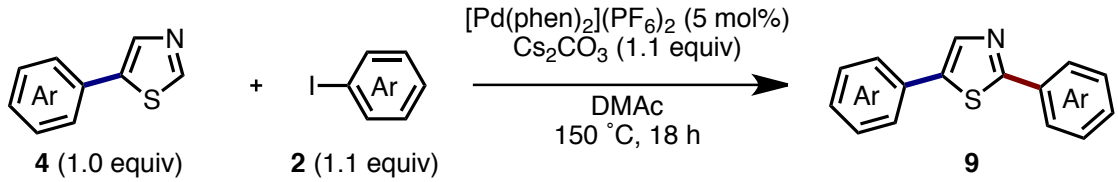
6. Synthesis of 2,5-Diarylthiazoles

Method G[23]



A 20-mL glass vessel equipped with J. Young® O-ring tap, containing a magnetic stirring bar, was flame-dried under vacuum and filled with argon after cooling to room temperature. To this vessel were added $PdCl_2$(bipy) (4.2 mg, 0.013 mmol, 5 mol%), Ag_2CO_3 (68.9 mg, 0.25 mmol, 1.0 equiv), iodoarene **2** (0.25 mmol, 1.0 equiv), 2-arylthiazole **3** (0.375 mmol, 1.5 equiv) and 1,4-dioxane (1.0 mL) under a stream of argon. The vessel was sealed and then stirred at 120 °C for 22 h. After cooling the reaction mixture to room temperature, the mixture was passed through a short silica gel pad (EtOAc). The filtrate was evaporated and the residue was purified by GPC to afford 2,5-diarylthiazole **9**.

Method H[24]

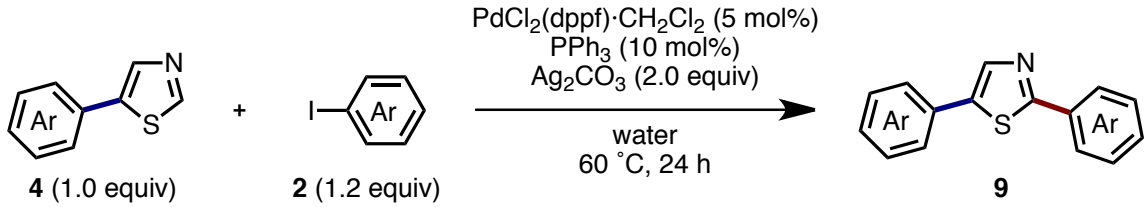


A 25-mL test tube equipped with screw cap, containing a magnetic stirring bar, was flame-dried under vacuum and then cooling to room temperature. To this vessel were added $[Pd(phen)_2](PF_6)_2$ (7.6 mg, 0.01 mmol, 5 mol%), Cs_2CO_3 (71.7 mg, 0.22 mmol, 1.1 equiv), iodoarene **2** (0.22 mmol, 1.1 equiv) and 5-diarylthiazole **4** (0.2 mmol, 1.0 equiv) and DMAc (0.8 mL) under argon atmosphere. The vessel was sealed and then stirred at 150 °C for 18 h. After cooling the reaction mixture to room temperature, the mixture was passed through a short silica gel pad (EtOAc). The filtrate was evaporated and the residue was purified by PTLC and/or GPC to afford the desired product **9**.

[23] Yanagisawa, S.; Itami, K. *Tetrahedron* **2011,** *67,* 4425.

[24] Shibahara, F.; Yamaguchi, E.; Murai, T. *J. Org. Chem.* **2011,** *76,* 2680.

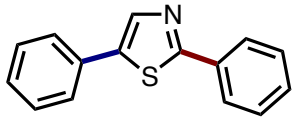
Method I[8]



4 (1.0 equiv) **2** (1.2 equiv) **9**

A 25-mL test tube equipped with screw cap, containing a magnetic stirring bar, were added $PdCl_2(dppf)\cdot CH_2Cl_2$ (8.2 mg, 0.01 mmol, 5 mol%), PPh_3 (5.2 mg, 0.02 mmol, 10 mol%), Ag_2CO_3 (110.3 mg, 0.4 mmol, 2.0 equiv), iodoarene **2** (0.24 mmol, 1.2 equiv), 5-arylthiazole **4** (0.2 mmol, 1.0 equiv) and distilled water (1 mL). The test tube was purged with argon and then stirred at 60 °C for 24 h. After cooling the reaction mixture to room temperature, the mixture was suspended in acetone (2 mL) and dichloromethane (5 mL), and then passed through a short silica gel pad (EtOAc). The filtrate was evaporated and the residue was purified by PTLC to afford the desired product **9**.

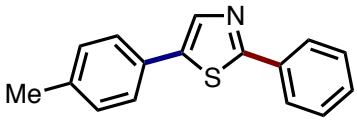
2,5-Diphenylthiazole (9aa)[23]



9aa

Purification by GPC (Method G) or PTLC (hexane/EtOAc = 10:1) (Method I) gave **9aa** as a white solid (Method G: 89% yield, Method I: 83% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34 (t, J = 7.6 Hz, 1H), 7.39–7.47 (m, 5H), 7.60 (d, J = 7.6 Hz, 2H), 7.97 (dd, J = 8.3 Hz, 1.4 Hz, 2H), 8.02 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 126.4, 126.7, 128.3, 129.0, 129.1, 130.0, 131.4, 133.7, 139.2, 139.3, 167.2; HRMS (DART) m/z = 238.0690 calcd for $C_{15}H_{12}NS$ $[M+H]^+$, found: 238.0688.

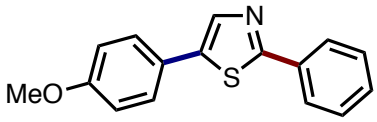
5-(4-Methylphenyl)-2-phenylthiazole (9ab)[8]



9ab

Purification by GPC (Method G) or PTLC (hexane/EtOAc = 10:1) (Method H) gave **9ab** as a white solid (Method G: 85% yield, Method H: 92% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.36 (s, 3H), 7.20 (d, J = 8.3 Hz, 2H), 7.35–7.45 (m, 3H), 7.48 (d, J = 8.3 Hz, 2H), 7.90–8.00 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.2, 126.3, 126.5, 128.5, 128.9, 129.7, 129.8, 133.7, 138.3, 138.7, 139.4, 166.6; HRMS (DART) m/z = 252.0847 calcd for $C_{16}H_{14}NS$ $[M+H]^+$, found: 252.0844.

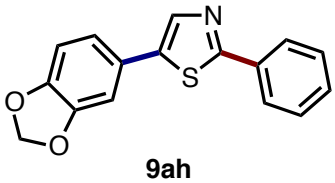
5-(4-Methoxyphenyl)-2-phenylthiazole (9ag) [8]



9ag

Purification by GPC (Method G) or PTLC (hexane/EtOAc = 10:1) (Method H) gave **9ag** as a white solid (Method G: 81% yield, Method H: 70% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.82 (s, 3H), 6.93 (dd, J = 8.9, 2.1 Hz, 2H), 7.37–7.45 (m, 3H), 7.51 (dd, J = 8.9, 2.1 Hz, 2H), 7.90 (s, 1H), 7.94 (dd, J = 6.9, 1.4 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 55.3, 114.5, 124.0, 126.2, 127.9, 128.9, 129.8, 133.8, 138.2, 139.2, 159.8, 166.2; HRMS (DART) m/z = 268.0796 calcd for $C_{16}H_{14}NOS$ $[M+H]^+$, found: 268.0799.

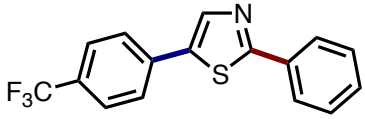
2-(Benzo[*d*][1,3]dioxol-5-yl)-5-phenylthiazole (9ah)



9ah

Purification by PTLC (hexane/EtOAc = 2:1) and GPC gave **9ah** as a white solid (Method G: quant). ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.97 (s, 2H), 6.81 (d, J = 7.9 Hz, 1H), 7.03–7.08 (m, 2H), 7.37–7.46 (m, 3H), 7.87 (s, 1H), 7.92 (dd, J = 7.9, 1.7 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 101.3, 106.9, 108.8, 120.6, 125.3, 126.2, 128.9, 129.8, 133.6, 138.4, 139.1, 147.8, 148.2, 166.3; HRMS (DART) m/z = 282.0589 calcd for $C_{16}H_{12}NO_2S$ $[M+H]^+$, found: 282.0580.

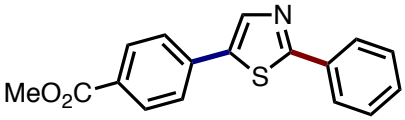
2-Phenyl-5-(4-(trifluoromethyl)phenyl)thiazole (9ak)[8]



9ak

Purification by PTLC (hexane/EtOAc = 10:1) gave **9ak** as a white solid (Method H: 93% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.42–7.49 (m, 3H), 7.66 (d, J = 8.3 Hz, 2H), 7.69 (d, J = 8.3 Hz, 2H), 7.95–7.99 (m, 2H), 8.08 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 123.9 (q, J_{C-F} = 270.2 Hz), 126.1 (q, J_{C-F} = 4.3 Hz), 126.5, 126.7, 129.0, 130.0 (q, J_{C-F} = 33.1 Hz), 130.4, 133.3, 134.9, 137.5, 140.4, 168.4; HRMS (DART) m/z = 306.0564 calcd for $C_{16}H_{11}F_3NS$ $[M+H]^+$, found: 306.0565.

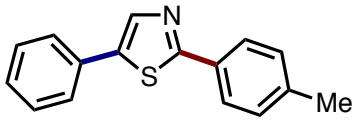
Methyl 4-(2-phenylthiazol-5-yl)benzoate (9an)[8]



9an

Purification by PTLC (hexane/EtOAc = 5:1) gave **9an** as a light yellow solid (Method I: 58% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.93 (s, 3H), 7.41–7.49 (m, 3H), 7.65 (d, *J* = 8.3 Hz, 2H), 7.97 (dd, *J* = 7.6 Hz, 2.1 Hz, 2H), 8.07 (d, *J* = 8.3 Hz, 2H), 8.10 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 52.2, 126.2, 126.4, 129.0, 129.5, 130.3, 130.4, 133.4, 135.7, 137.9, 140.4, 166.4, 168.3; HRMS (DART) *m/z* = 296.0745 calcd for $C_{17}H_{14}NO_2S$ $[M+H]^+$, found: 296.0746.

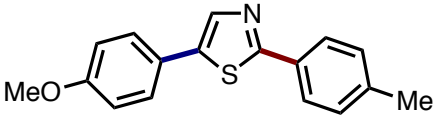
2-(4-Methylphenyl)-5-phenylthiazole (9ba)



9ba

Purification by PTLC (hexane/EtOAc = 10:1) gave **9ba** as a white solid (Method H: 87% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.40 (s, 3H), 7.26 (d, *J* = 8.3 Hz, 2H), 7.33 (t, *J* = 7.6 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.60 (d, *J* = 8.3 Hz, 2H), 7.86 (d, *J* = 8.3 Hz, 2H), 7.99 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.4, 126.3, 126.6, 128.2, 129.1, 129.6, 131.0, 131.5, 138.7, 139.0, 140.3, 167.4; HRMS (DART) *m/z* = 252.0847 calcd for $C_{16}H_{14}NS$ $[M+H]^+$, found: 252.0847.

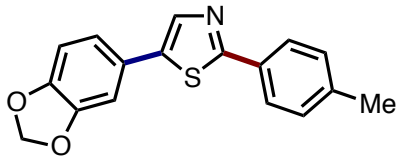
5-(4-Methoxyphenyl)-2-(4-methylphenyl)thiazole (9bg)[8]



9bg

The reaction was performed at 130 ˚C. Purification by PTLC (hexane/EtOAc = 10:1) gave **9bg** as a light yellow solid (Method H: 82% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.39 (s, 3H), 3.84 (s, 3H), 6.94 (d, *J* = 8.9 Hz, 2H), 7.24 (d, *J* = 8.2 Hz, 2H), 7.52 (d, *J* = 8.9 Hz, 2H), 7.84 (d, *J* = 8.2 Hz, 2H), 7.88 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.4, 55.4, 114.5, 124.2, 126.2, 127.9, 129.6, 131.2, 138.1, 138.7, 140.1, 159.7, 166.5; HRMS (DART) *m/z* = 282.0953 calcd for $C_{17}H_{16}NOS$ $[M+H]^+$, found: 282.0953.

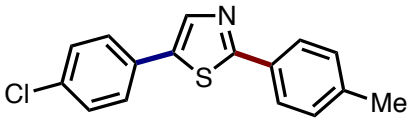
5-(Benzo[*d*][1,3]dioxol-5-yl)-2-(4-methylphenyl)thiazole (9bh)



9bh

Purification by GPC gave **9bh** as a white solid (Method G: 89% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.38 (s, 3H), 5.97 (s, 2H), 6.81 (d, J = 7.6 Hz, 1H), 7.02–7.06 (m, 2H), 7.22 (d, J = 7.6 Hz, 2H), 7.81 (d, J = 7.6 Hz, 2H), 7.84 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.3, 101.3, 106.9, 108.8, 120.5, 125.5, 126.1, 129.6, 131.0, 138.3, 138.6, 140.1, 147.7, 148.2, 166.6; HRMS (DART) m/z = 296.0745 calcd for $C_{17}H_{14}NO_2S$ $[M+H]^+$, found: 296.0747.

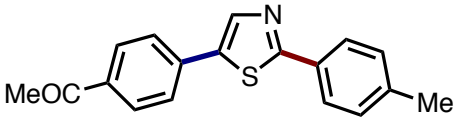
5-(4-Chlorophenyl)-2-(4-methylphenyl)thiazole (9bj)[8]



9bj

Purification by GPC gave **9bj** as a white solid (Method G: 73% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.40 (s, 3H), 7.25 (d, J = 8.2 Hz, 2H), 7.37 (d, J = 8.2 Hz, 2H), 7.50 (d, J = 8.2 Hz, 2H), 7.84 (d, J = 8.2 Hz, 2H), 7.95 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.4, 126.3, 127.7, 129.2, 129.7, 130.0, 130.8, 134.0, 137.4, 139.3, 140.5, 167.7; HRMS (DART) m/z = 286.0457 calcd for $C_{16}H_{13}ClNS$ $[M+H]^+$, found: 286.0456.

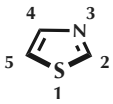
5-(4-Acetylphenyl)-2-(4-methylphenyl)thiazole (9bo)

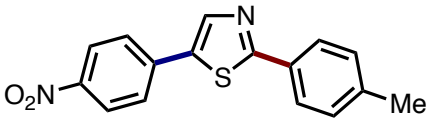


9bo

Purification by GPC gave **9bo** as a light yellow solid (Method G: 68% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.40 (s, 3H), 2.61 (s, 3H), 7.26 (d, J = 7.6 Hz, 2H), 7.67 (d, J = 7.6 Hz, 2H), 7.86 (d, J = 7.6 Hz, 2H), 7.98 (d, J = 7.6 Hz, 2H), 8.09 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.4, 26.5, 126.4, 129.2, 129.7, 130.7, 136.0, 136.2, 137.3, 140.4, 140.7, 140.9, 168.7, 197.1; HRMS (DART) m/z = 294.0953 calcd for $C_{18}H_{16}NOS$ $[M+H]^+$, found: 294.0956.

2-(4-Methylphenyl)-5-(4-nitrophenyl)thiazole (9bq)[8]

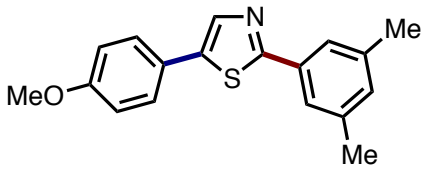




9bq

Purification by PTLC (hexane/EtOAc = 10:1) and GPC gave **9bq** as a white solid (Method G: 64% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.42 (s, 3H), 7.28 (d, J = 8.2 Hz, 2H), 7.74 (d, J = 8.9 Hz, 2H), 7.87 (d, J = 8.2 Hz, 2H), 8.13 (s, 1H), 8.27 (d, J = 8.9 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.5, 124.5, 126.5, 126.8, 129.8, 130.5, 136.0, 137.9, 141.2, 141.3, 147.0, 169.7; HRMS (DART) m/z = 297.0698 calcd for $C_{16}H_{13}N_2O_2S$ $[M+H]^+$, found: 297.0698.

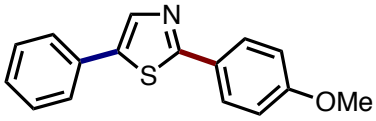
2-(3,5-Dimethylphenyl)-5-(4-methoxyphenyl)thiazole (9eg)



9eg

Purification by PTLC (hexane/EtOAc = 10:1) gave **9eg** as a white solid (Method H: 71% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.38 (s, 6H), 3.84 (s, 3H), 6.94 (d, J = 8.9 Hz, 2H), 7.05 (s, 1H), 7.52 (d, J = 8.9 Hz, 2H), 7.58 (s, 2H), 7.89 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.2, 55.4, 114.5, 124.05, 124.07, 127.9, 131.6, 133.5, 138.0, 138.6, 138.9, 159.7, 166.7; HRMS (DART) m/z = 296.1109 calcd for $C_{18}H_{18}NOS$ $[M+H]^+$, found: 296.1110.

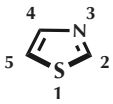
2-(4-Methoxyphenyl)-5-phenylthiazole (9ga)[24]

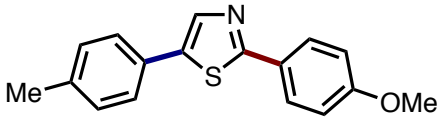


9ga

The reaction was performed at 130 °C. Purification by PTLC (hexane/EtOAc = 10:1) gave **9ga** as a white solid (Method H: 86% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.87 (s, 3H), 6.97 (d, J = 8.9 Hz, 2H), 7.33 (t, J = 7.6 Hz, 1H), 7.41 (t, J = 7.6 Hz, 2H), 7.60 (d, J = 8.3 Hz, 2H), 7.91 (d, J = 8.3 Hz, 2H), 7.97 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 55.4, 114.4, 126.6, 126.7, 127.9, 128.1, 129.1, 131.6, 138.3, 138.9, 161.2, 167.2; HRMS (DART) m/z = 268.0796 calcd for $C_{12}H_{14}NO_3S$ $[M+H]^+$, found: 268.0795.

2-(4-Methoxyphenyl)-5-(4-methylphenyl)thiazole (9gb)[8]

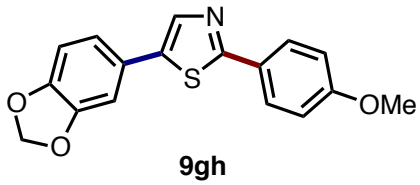




9gb

Purification by GPC (Method G) or PTLC (hexane/EtOAc = 10:1) (Method H) gave **9gb** as a light yellow solid (Method G: 75% yield, Method H: 59% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.37 (s, 3H), 3.85 (s, 3H), 6.95 (d, *J* = 8.3 Hz, 2H), 7.20 (d, *J* = 8.3 Hz, 2H), 7.47 (d, *J* = 8.3 Hz, 2H), 7.89 (d, *J* = 8.3 Hz, 2H), 7.92 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.2, 55.4, 114.3, 126.4, 126.7, 127.8, 128.7, 129.7, 138.1, 138.4, 161.0, 166.6; HRMS (DART) *m*/*z* = 282.0953 calcd for $C_{17}H_{16}NOS$ $[M+H]^+$, found: 282.0954.

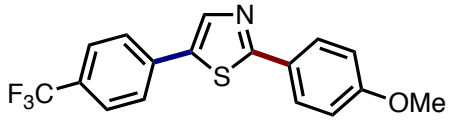
5-(Benzo[*d*][1,3]dioxol-5-yl)-2-(4-methoxyphenyl)thiazole (9gh)



9gh

Purification by GPC gave **9gh** as a white solid (Method G: 82% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.84 (s, 3H), 5.98 (s, 2H), 6.82 (d, *J* = 8.9 Hz, 1H), 6.94 (dd, *J* = 8.9 Hz, 2.0 Hz, 2H), 7.02–7.06 (m, 2H), 7.81 (s, 1H), 7.86 (dd, *J* = 8.9 Hz, 2.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 55.3, 101.3, 106.9, 108.7, 114.2, 120.5, 125.5, 126.6, 127.7, 138.1, 138.2, 147.6, 148.2, 161.0, 166.3; HRMS (DART) *m*/*z* = 312.0694 calcd for $C_{17}H_{14}NO_3S$ $[M+H]^+$, found: 312.0695.

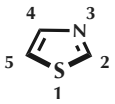
2-(4-Methoxyphenyl)-5-(4-(trifluoromethyl)phenyl)thiazole (9gk)

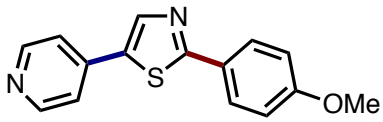


9gk

Purification by GPC gave **9gk** as a light yellow solid (Method G: 89% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.87 (s, 3H), 6.97 (d, *J* = 8.9 Hz, 2H), 7.65 (d, *J* = 8.3 Hz, 2H), 7.68 (d, *J* = 8.3 Hz, 2H), 7.91 (d, *J* = 8.9 Hz, 2H), 8.03 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 55.4, 114.4, 124.0 (q, J_{C-F} = 271.6 Hz), 126.1 (q, J_{C-F} = 4.3 Hz), 126.3, 126.6, 128.0, 129.8 (q, J_{C-F} = 33.1 Hz), 135.1, 136.5, 140.1, 161.5, 168.3; HRMS (DART) *m*/*z* = 336.0670 calcd for $C_{17}H_{13}F_3NOS$ $[M+H]^+$, found: 336.0671.

2-(4-Methoxyphenyl)-5-(4-pyridyl)thiazole (9gu)

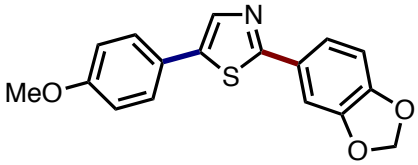




9gu

The reaction was performed at 150 ˚C. Purification by GPC gave **9gu** as a white solid (Method G: 52% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.88 (s, 3H), 6.98 (d, *J* = 8.9 Hz, 2H), 7.46 (dd, *J* = 4.8, 1.4 Hz, 2H), 7.92 (d, *J* = 8.9 Hz, 2H), 8.14 (s, 1H), 8.63 (dd, *J* = 4.8, 1.4 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 55.4, 114.4, 120.4, 126.1, 128.1, 135.1, 138.9, 141.2, 150.5, 161.6, 169.2; HRMS (DART) *m*/*z* = 269.07479 calcd for $C_{15}H_{13}N_2OS$ $[M+H]^+$, found: 269.0749.

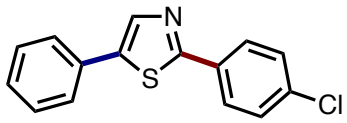
2-(Benzo[*d*][1,3]dioxol-5-yl)-5-(4-methoxyphenyl)thiazole (9hg)



9hg

Purification by PTLC (hexane/EtOAc = 3:1) gave **9hg** as a yellow solid (Method I: 87% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.84 (s, 3H), 6.02 (s, 2H), 6.85 (d, *J* = 8.2 Hz, 1H), 6.93 (d, *J* = 8.9 Hz, 2H), 7.42–7.47 (m, 2H), 7.50 (d, *J* = 8.9 Hz, 2H), 7.84 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 55.4, 101.5, 106.5, 108.6, 114.5, 120.8, 124.0, 127.8, 128.3, 137.9, 138.4, 148.2, 149.1, 159.7, 165.9; HRMS (DART) *m*/*z* = 312.0694 calcd for $C_{17}H_{14}NO_3S$ $[M+H]^+$, found: 312.0691.

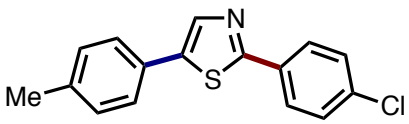
2-(4-Chlorophenyl)-5-phenylthiazole (9ja)



9ja

Purification by PTLC (hexane/EtOAc = 10:1) gave **9ja** as a white solid (Method H: 67% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34 (t, *J* = 7.6 Hz, 1H), 7.37–7.44 (m, 4H), 7.58 (d, *J* = 7.6 Hz, 2H), 7.89 (d, *J* = 8.2 Hz, 2H), 8.00 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 126.7, 127.5, 128.4, 129.1, 129.2, 131.2, 132.1, 135.9, 139.2, 139.7, 165.7; HRMS (DART) *m*/*z* = 272.0301 calcd for $C_{15}H_{11}ClNS$ $[M+H]^+$, found: 272.0300.

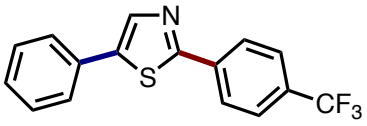
2-(4-Chlorophenyl)-5-(4-methylphenyl)thiazole (9jb)



9jb

The reaction was performed at 130 °C. Purification by PTLC (hexane/EtOAc = 10:1) gave **9jb** as a white solid (Method H: 63% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.39 (s, 3H), 7.22 (d, J = 8.3 Hz, 2H), 7.41 (d, J = 8.9 Hz, 2H), 7.48 (d, J = 8.3 Hz, 2H), 7.89 (d, J = 8.9 Hz, 2H), 7.96 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.2, 126.6, 127.5, 128.3, 129.2, 129.8, 132.2, 135.8, 138.5, 138.8, 139.8, 165.2; HRMS (DART) m/z = 286.0457 calcd for $C_{16}H_{13}ClNS$ $[M+H]^+$, found: 286.0455.

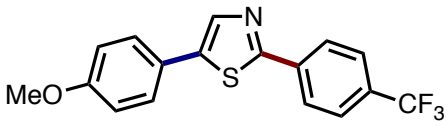
5-Phenyl-2-(4-(trifluoromethyl)phenyl)thiazole (9ka)[25]



9ka

Purification by PTLC (hexane/EtOAc = 10:1) gave **9ka** as a white solid (Method H: 85% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37 (t, J = 7.6 Hz, 1H), 7.43 (t, J = 7.6 Hz, 2H), 7.61 (d, J = 7.6 Hz, 2H), 7.71 (d, J = 8.2 Hz, 2H), 8.06 (s, 1H), 8.08 (d, J = 8.2 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 123.9 (q, J_{C-F} = 271.7 Hz), 126.0 (q, J_{C-F} = 2.9 Hz), 126.5, 126.8, 128.7, 129.2, 131.0, 131.5 (q, J_{C-F} = 31.6 Hz), 136.7, 139.6, 140.6, 165.1; HRMS (DART) m/z = 306.0564 calcd for $C_{16}H_{11}F_3NS$ $[M+H]^+$, found: 306.0563.

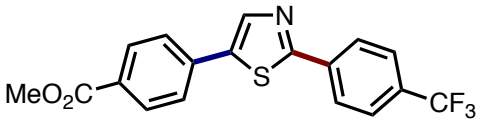
5-(4-Methoxyphenyl)-2-(4-(trifluoromethyl)phenyl)thiazole (9kg)[8]



9kg

Purification by PTLC (hexane/EtOAc = 10:1) gave **9kg** as a white solid (Method H: 72% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.84 (s, 3H), 6.95 (d, J = 8.9 Hz, 2H), 7.52 (d, J = 8.9 Hz, 2H), 7.69 (d, J = 8.2 Hz, 2H), 7.95 (s, 1H), 8.04 (d, J = 8.2 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 55.4, 114.6, 123.5, 123.9 (q, J_{C-F} = 270.2 Hz), 125.9 (q, J_{C-F} = 4.3 Hz), 126.3, 128.1, 131.3 (q, J_{C-F} = 33.1 Hz), 136.8, 138.6, 140.5, 160.0, 164.1; HRMS (DART) m/z = 336.0670 calcd for $C_{17}H_{13}F_3NOS$ $[M+H]^+$, found: 336.0672.

Methyl 4-(2-(4-(trifluoromethyl)phenyl)thiazol-5-yl)benzoate (9kn)

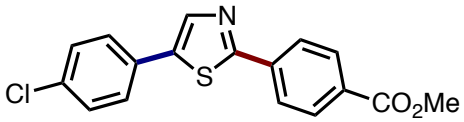


9kn

[25] Li, Z.; Ma, L.; Xu, J.; Kong, L.; Wu, X.; Yao, H. *Chem. Comm.* **2012**, *48*, 3763.

Purification by GPC gave **9kn** as a white solid (Method G: 79% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.95 (s, 3H), 7.67 (d, J = 8.3 Hz, 2H), 7.72 (d, J = 8.3 Hz, 2H), 8.06–8.11 (m, 4H), 8.15 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 52.3, 123.8 (q, J_{C-F} = 270.2 Hz), 126.0 (q, J_{C-F} = 4.3 Hz), 126.4, 126.6, 130.0, 130.5, 131.8 (q, J_{C-F} = 33.1 Hz), 135.3, 136.5, 139.3, 140.8, 166.2, 166.4; HRMS (DART) m/z = 364.0619 calcd for $C_{18}H_{13}F_3NO_2S$ $[M+H]^+$, found: 364.0619.

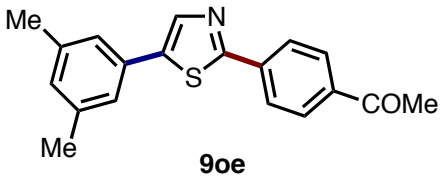
Methyl 4-(5-(4-chlorophenyl)thiazol-2-yl)benzoate (9nj)



9nj

The reaction was performed for 36 h. Purification by GPC gave **9nj** as a white solid (Method G: 48%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.95 (s, 3H), 7.40 (d, J = 8.3 Hz, 2H), 7.54 (d, J = 8.9 Hz, 2H), 8.00–8.07 (m, 3H), 8.12 (d, J = 8.3 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 52.3, 126.2, 127.9, 129.4, 129.6, 130.3, 131.2, 134.5, 137.3, 139.2, 139.9, 165.9, 166.4; HRMS (DART) m/z = 330.0356 calcd for $C_{17}H_{13}ClNOS$ $[M+H]^+$, found: 330.0357.

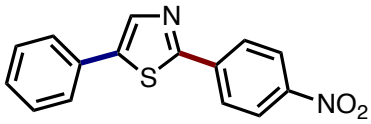
2-(4-Acetylphenyl)-5-(3,5-dimethylphenyl)thiazole (9oe)



9oe

Purification by GPC gave **9oe** as a white solid (Method G: 69% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.36 (s, 6H), 2.62 (s, 3H), 6.99 (s, 1H), 7.21 (s, 2H), 7.99–8.05 (m, 5H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.2, 26.6, 124.5, 126.2, 129.0, 130.4, 130.7, 137.55, 137.58, 138.8, 139.4, 141.0, 165.0, 197.2; HRMS (DART) m/z = 308.1109 calcd for $C_{19}H_{18}NOS$ $[M+H]^+$, found: 308.1109.

2-(4-Nitrophenyl)-5-phenylthiazole (9qa)

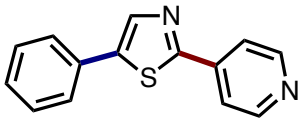


9qa

Purification by PTLC ($CHCl_3$/MeOH = 80:1) gave **9qa** as a yellow solid (Method I: 60% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39 (t, J = 7.6 Hz, 1H), 7.45 (d, J = 7.6 Hz, 2H), 7.63 (d, J = 7.6 Hz, 2H), 8.11 (s, 1H), 8.13 (d, J = 8.9 Hz, 2H), 8.31 (d, J = 8.9 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 124.4, 126.9, 129.0, 129.3,

130.7, 139.1, 140.1, 141.8, 148.3, 163.8; There is one overlapping carbon signal as 1 peak is missing even with prolonged scans. HRMS (DART) *m/z* = calcd 283. 0541 for $C_{15}H_{11}N_2O_2S$ $[M+H]^+$, found: 283.0545.

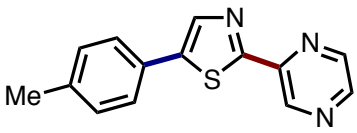
5-Phenyl-2-(4-pyridyl)thiazole (9ua)



9ua

Purification by PTLC (hexane/EtOAc = 2:1) gave **9ua** as a light yellow solid (Method H: 65% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 (t, *J* = 7.6 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.61 (d, *J* = 8.3 Hz, 2H), 7.81 (dd, *J* = 4.8, 2.0 Hz, 2H), 8.09 (s, 1H), 8.71 (dd, *J* = 4.8, 2.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 120.0, 126.8, 128.9, 129.2, 130.7, 139.8, 140.2, 141.3, 150.6, 163.8; HRMS (DART) *m/z* = 239.0643 calcd for $C_{14}H_{11}N_2S$ $[M+H]^+$, found: 239.0644.

2-(2-Pyrazin-2-yl)-5-(4-methylphenyl)thiazole (9vb)

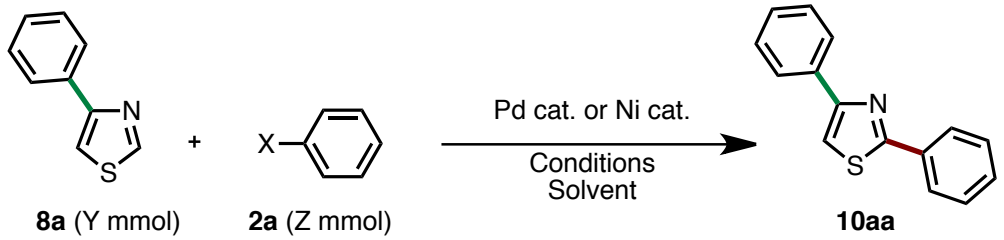


9vb

Purification by PTLC (hexane/EtOAc = 3:1) gave **9vb** as a light yellow solid (Method I: 33% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.39 (s, 3H), 7.24 (d, *J* = 7.6 Hz, 2H), 7.53 (d, *J* = 8.2 Hz, 2H), 8.09 (s, 1H), 8.55–8.57 (m, 1H), 8.58 (d, *J* = 2.7 Hz, 1H), 9.43 (d, *J* = 1.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.3, 126.7, 128.2, 129.9, 139.0, 139.6, 141.3, 142.9, 143.8, 144.7, 147.0, 164.4; HRMS (DART) *m/z* = 254.0752 calcd for $C_{14}H_{12}N_3S$ $[M+H]^+$, found: 254.0750.

7. Synthesis of 2,4-Diarylthiazoles

Table S3. Screening of Reaction Conditions

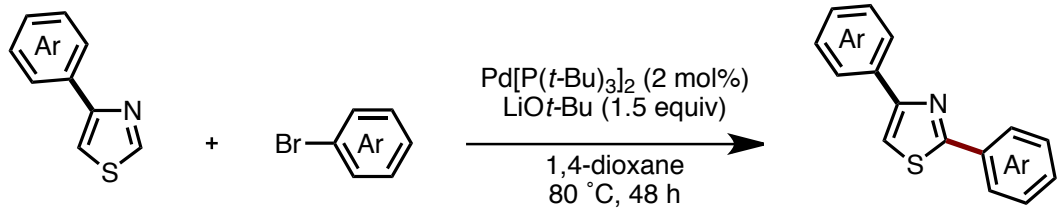


8a (Y mmol) + **2a** (Z mmol) → **10aa**

Entry	X	Y	Z	Conditions	Solvent	Yield [a]
1	I	0.3	0.2	[b]	1,4-dioxane (0.4 M)	10%
2	I	0.2	0.4	[c]	DMF (0.4 M)	22%
3	I	0.2	0.22	[d]	DMF (0.25 M)	6%
4	Br	0.2	0.22	[e]	DMF (0.25 M)	15%
5	Br	0.2	0.24	[f]	1,4-dioxane (0.25 M)	55%

[a] GC yield
[b] $Ni(OAc)_2$ (10 mol%), bipy (10 mol%), LiO*t*-Bu (2.0 equiv), 120 ˚C, 20 h.
[c] $Pd(OAc)_2$ (5 mol%), CuI (2.0 equiv), 140 ˚C, 16 h.
[d] $Pd(OAc)_2$ (5 mol%), P(*o*-tol)$_3$ (10 mol%), Cs_2CO_3 (2.0 equiv), 110 ˚C, 18 h.
[e] Condition C with Johnphos instead of P(*o*-tol)$_3$.
[f] $Pd[P(t\text{-}Bu)_3]_2$ (2 mol%), LiO*t*-Bu (1.2 equiv), 100 ˚C, 9 h.

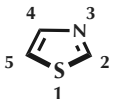
Method C'[7]

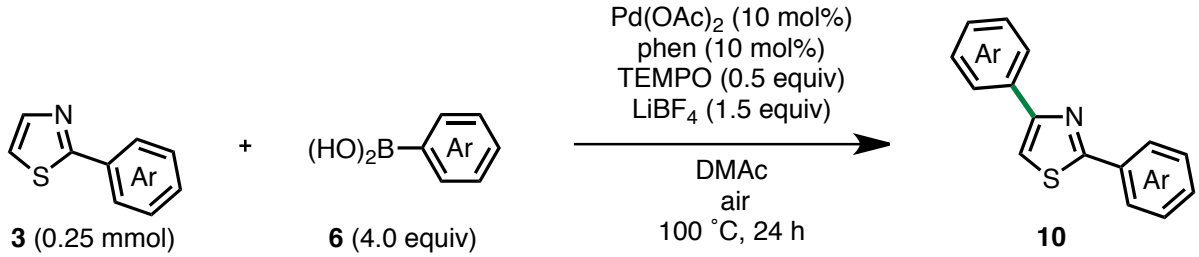


8 (1.0 equiv) + **2** (1.2 equiv) → **10**

A 25-mL test tube equipped with screw cap, containing a magnetic stirring bar, was flame-dried under vacuum and then cooling to room temperature. To this vessel were added $Pd[P(t\text{-}Bu)_3]_2$ (2.2 mg, 0.004 mol, 2 mol%), LiO*t*-Bu (24.0 mg, 0.3 mmol, 1.5 equiv), bromoarene **2** (0.24 mmol, 1.2 equiv), 4-arylthiazole **8** (0.2 mmol, 1.0 equiv), and 1,4-dioxane (0.6 mL) under argon atmosphere. The vessel was sealed and then stirred at 80 °C for 48 h. After cooling the reaction mixture to room temperature, the mixture was passed through a short silica gel pad (EtOAc). The filtrate was evaporated and the residue was purified by PTLC and/or GPC to afford 2,4-diarylthiazole **10**.

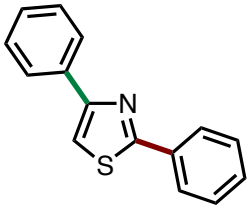
Method F[20]





A 25-mL test tube equipped with screw cap, containing a magnetic stirring bar, were added $Pd(OAc)_2$ (5.6 mg, 0.025 mmol, 10 mol%), 1,10-phenanthroline (phen: 4.5 mg, 0.025 mmol, 10 mol%), arylboronic acid **6** (1 mmol, 4.0 equiv), $LiBF_4$ (35.5 mg, 0.38 mmol, 1.5 equiv), TEMPO (19.5 mg, 0.13 mmol, 0.5 equiv), 2-arylthiazole **3** (0.25 mmol, 1.0 equiv) and undried DMAc (0.5 mL). The vessel was sealed under air and then stirred at 100 °C for 24 h. After cooling the reaction mixture to room temperature, the mixture was passed through a short silica gel pad (EtOAc). The filtrate was evaporated and the residue was purified by PTLC and/or GPC and/or flash column chromatography to afford desired product **10**.

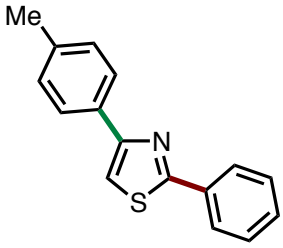
2,4-Diphenylthiazole (10aa)[20]



10aa

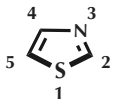
Purification by PTLC (hexane/EtOAc = 20:1 (Method C') or 10:1 (Method F)) gave **10aa** as a white solid (Method C': 77% yield, Method F: 83% yield, 90% C4-selectivity). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35 (t, J = 7.8 Hz, 1H), 7.41–7.50 (m, 6H), 8.00 (dd, J = 8.3, 1.4 Hz, 2H), 8.05 (dd, J = 8.3, 1.4 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 112.6, 126.4, 126.6, 128.2, 128.7, 128.9, 130.0, 133.7, 134.5, 156.3, 167.9; HRMS (DART) m/z = 238.0690 calcd for $C_{15}H_{12}NS$ $[M+H]^+$, found: 238.0690.

4-(4-Methylphenyl)-2-phenylthiazole (10ab)[20]



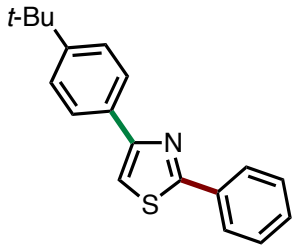
10ab

Purification by PTLC (hexane/EtOAc = 10:1) gave **10ab** as a white solid (Method F: 84% yield, 89% C4-selectivity). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.40 (s, 3H), 7.25 (d, J = 7.6 Hz, 2H), 7.41–7.50 (m, 4H), 7.89



(d, J = 7.6 Hz, 2H), 8.04 (d, J = 6.9 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.3, 111.8, 126.3, 126.6, 128.9, 129.4, 129.9, 131.8, 133.8, 138.0, 156.4, 167.7; HRMS (DART) m/z = 252.0847 calcd for $C_{16}H_{14}NS$ $[M+H]^+$, found: 252.0850.

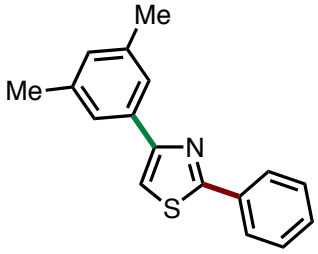
4-(*t*-Butylphenyl)-2-phenylthiazole (10ac)



10ac

The reaction was performed at 80 ˚C for 48 h. Purification by PTLC (hexane/EtOAc = 10:1) and GPC gave **10ac** as a white solid (Method F: 88% yield, 90% C4-selectivity). ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.35 (s, 9H), 7.40 (s, 1H), 7.41–7.48 (m, 5H), 7.91 (d, J = 8.2 Hz, 2H), 8.03 (d, J = 6.8 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 31.3, 34.6, 112.0, 125.6, 126.2, 126.6, 128.9, 129.9, 131.8, 133.8, 151.2, 156.4, 167.7; HRMS (DART) m/z = 294.1316 calcd for $C_{19}H_{20}NS$ $[M+H]^+$, found: 294.1317.

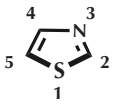
4-(3,5-Dimethylphenyl)-2-phenylthiazole (10ae)

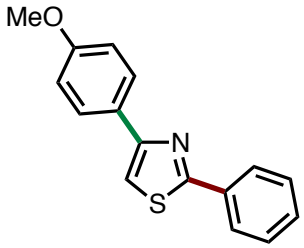


10ae

Purification by PTLC (hexane/EtOAc = 10:1) and GPC gave **10ae** as a white solid (Method F: 78% yield, 92% C4-selectivity). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.38 (s, 6H), 6.99 (s, 1H), 7.38–7.47 (m, 4H), 7.61 (s, 2H), 8.03 (d, J = 7.6 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.4, 112.4, 124.3, 126.6, 128.9, 129.86, 129.93, 133.8, 134.3, 138.2, 156.6, 167.7; HRMS (DART) m/z = 266.1003 calcd for $C_{17}H_{16}NS$ $[M+H]^+$, found: 266.1003.

4-(4-Methoxyphenyl)-2-phenylthiazole (10ag)[20]

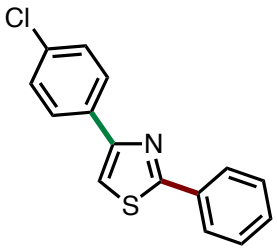




10ag

Purification by PTLC (hexane/EtOAc = 10:1) gave **10ag** as a white solid (Method C': 46% yield, Method F: 71% yield, 88% C4-selectivity). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.86 (s, 3H), 6.98 (d, *J* = 8.9 Hz, 2H), 7.34 (s, 1H), 7.40–7.48 (m, 3H), 7.93 (d, *J* = 8.3 Hz, 2H), 8.04 (d, *J* = 8.3 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 55.3, 110.9, 114.1, 126.6, 127.5, 127.7, 128.9, 129.9, 133.8, 156.1, 159.7, 167.7; HRMS (DART) *m/z* = 268.0796 calcd for $C_{16}H_{14}NOS$ $[M+H]^+$, found: 268.0794.

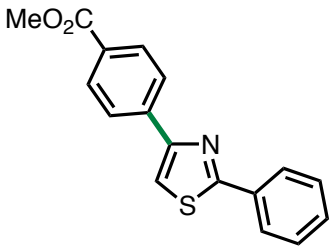
4-(4-Chlorophenyl)-2-phenylthiazole (10aj)[26]



10aj

4-MeO-TEMPO (0.125 mmol) was used instead of TEMPO and the reaction was performed for 48 h. Purification by PTLC (hexane/EtOAc = 10:1) gave **10aj** as a white solid (Method F: 59% yield, 75% C4-selectivity). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7,40 (d, *J* = 8.3 Hz, 2H) 7.43–7.48 (m, 4H), 7.92 (d, *J* = 8.9 Hz, 2H), 8.02 (dd, *J* = 8.3, 2.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 112.9, 126.6, 127.7, 128.88, 128.94, 130.2, 133.0, 133.6, 133.9, 155.1, 168.1; HRMS (DART) *m/z* = 272.0301 calcd for $C_{15}H_{11}ClNS$ $[M+H]^+$, found: 272.0301.

Methyl 4-(2-phenylthiazol-4-yl)benzoate (10an)



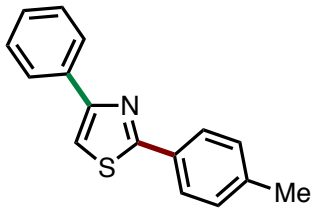
10an

The reaction was performed for 48 h. Purification by flash column chromatography (hexane/EtOAc = 5:1)

[26] Zhu, D.; Chen, J.; Xiao, H.; Liu, M.; Ding, J.; Wu, H. *Synth. Commun.* **2009**, *39*, 2895.

gave **10an** as a colorless solid (Method F: 63% yield, >99% C4-selectivity). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.93 (s, 3H), 7.41–7.49 (m, 3H), 7.58 (s, 1H), 8.01–8.08 (m, 4H), 8.11 (d, J = 8.2 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 52.1, 114.5, 126.2, 126.6, 128.9, 129.5, 130.1, 130.2, 133.5, 138.5, 155.1, 166.8, 168.2; HRMS (DART) m/z = 296.0745 calcd for $C_{17}H_{14}NO_2S$ $[M+H]^+$, found: 296.0747.

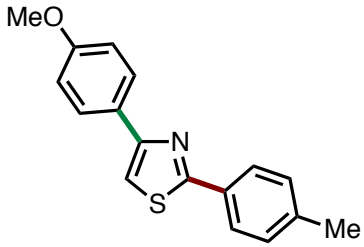
4-(4-Methylphenyl)-2-phenylthiazole (10ba)[27]



10ba

Purification by PTLC (hexane/EtOAc = 10:1) gave **10ba** as a white solid (Method F: 84% yield, 95% C4-selectivity). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.39 (s, 3H), 7.25 (d, J = 8.2 Hz, 2H), 7.33 (t, J = 8.2 Hz, 1H), 7.40–7.45 (m, 3H), 7.92 (d, J = 7.6 Hz, 2H), 7.98 (d, J = 8.3 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.4, 112.1, 126.4, 126.5, 128.1, 128.7, 129.6, 131.2, 134.6, 140.2, 156.1, 168.0; HRMS (DART) m/z = 252.0847 calcd for $C_{16}H_{14}NS$ $[M+H]^+$, found: 252.0846.

2-(4-Methoxyphenyl)-4-(4-methylphenyl)thiazole (10bg)

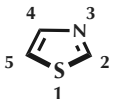


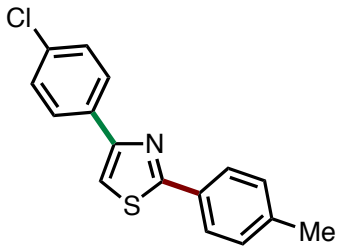
10bg

Purification by PTLC (hexane/EtOAc = 10:1) gave **10bg** as a white solid (Method C': 65% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.39 (s, 3H), 3.84 (s, 3H), 6.96 (d, J = 8.2 Hz, 2H), 7.24 (d, J = 8.2 Hz, 2H), 7.28 (s, 1H), 7.91 (d, J = 8.2 Hz, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.4, 55.3, 110.4, 114.0, 126.4, 127.6, 127.7, 129.5, 131.2, 140.1, 155.9, 159.6, 167.8; HRMS (DART) m/z = calcd 282.0953 for $C_{17}H_{16}NOS$ $[M+H]^+$, found: 282.0950.

4-(4-Chlorophenyl)-2-(4-methylphenyl)thiazole (10bj)

[27] Ishikawa, Y.; Togo, H. *Synlett* **2008**, 2637.

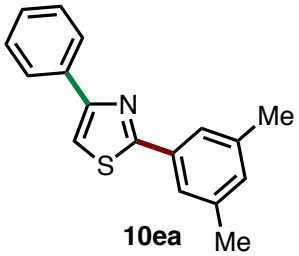




10bj

The reaction was performed for 48 h. Purification by flash column chromatography (hexane/EtOAc = 20:1) gave **10bj** as a light yellow solid (Method F: 59% yield, 78% C4-selectivity). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.40 (s, 3H), 7.25 (d, *J* = 7.6 Hz, 2H), 7.37–7.41 (m, 3H), 7.90 (d, *J* = 7.6 Hz, 2H), 7.91 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.4, 112.4, 126.5, 127.7, 128.8, 129.6, 130.9, 133.0, 133.8, 140.4, 154.9, 168.3; HRMS (DART) *m/z* = 286.0457 calcd for $C_{16}H_{13}ClNS$ $[M+H]^+$, found: 286.0457.

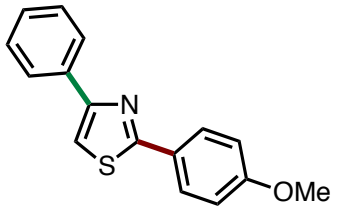
2-(3,5-Dimethylphenyl)-4-phenylthiazole (10ea)



10ea

The reaction was performed at 100°C. Purification by PTLC (hexane/EtOAc = 20:1) gave **10ea** as a white solid (Method C': 72% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.39 (s, 6H), 7.06 (s, 1H), 7.34 (t, *J* = 7.6 Hz, 1H), 7.41–7.46 (m, 3H), 7.66 (s, 2H), 7.99 (d, *J* = 8.3 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.2, 112.4, 124.4, 126.4, 128.1, 128.7, 131.8, 133.5, 134.6, 138.5, 156.1, 168.3; HRMS (DART) *m/z* = 266.1003 calcd for $C_{17}H_{16}NS$ $[M+H]^+$, found: 266.1001.

2-(4-Methoxyphenyl)-4-phenylthiazole (10ga)[27]

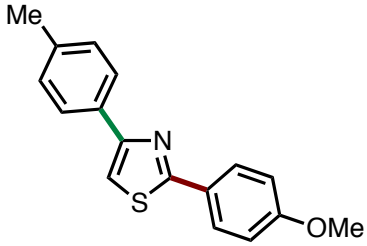


10ga

Purification by PTLC (hexane/EtOAc = 10:1) gave **10ga** as a white solid (Method F: 99% yield, >96% C4-selectivity). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.85 (s, 3H) 6.96 (d, *J* = 8.2 Hz, 2H), 7.33 (t, *J* = 7.6 Hz, 1H), 7.39 (s, 1H), 7.43 (t, *J* = 7.6 Hz, 2H), 7.95–8.00 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 55.2, 111.5, 114.0, 126.2, 126.6, 127.8, 127.9, 128.5, 134.4, 155.8, 161.0, 167.5; HRMS (DART) *m/z* = 268.0796 calcd for

$C_{16}H_{14}NOS$ $[M+H]^+$, found: 268.0797.

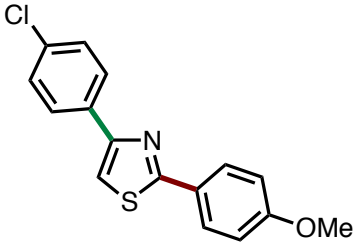
2-(4-Methoxyphenyl)-4-(4-methylphenyl)thiazole (10gb)



10gb

Purification by PTLC (hexane/EtOAc = 10:1) gave **10gb** as a white solid (Method F: 58% yield, 96% C4-selectivity). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.38 (s, 3H), 3.85 (s, 3H), 6.95 (d, *J* = 8.9 Hz, 2H), 7.23 (d, *J* = 8.2 Hz, 2H), 7.33 (s, 1H), 7.87 (d, *J* = 8.2 Hz, 2H), 7.96 (d, *J* = 8.9 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.2, 55.4, 110.9, 114.2, 126.3, 126.9, 128.0, 129.3, 131.9, 137.8, 156.1, 161.1, 167.5; HRMS (DART) *m*/*z* = 282.0953 calcd for $C_{17}H_{16}NOS$ $[M+H]^+$, found: 282.0953.

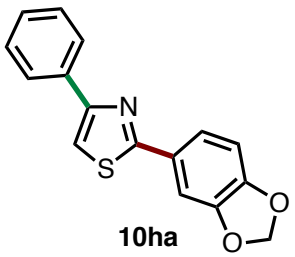
4-(4-Chlorophenyl)-2-(4-methoxyphenyl)thiazole (10gj)



10gj

Purification by PTLC (hexane/EtOAc = 10:1) gave **10gj** as a white solid (Method C': 67% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.86 (s, 3H), 6.96 (d, *J* = 8.2 Hz, 2H), 7.37 (s, 1H), 7.39 (d, *J* = 8.9 Hz, 2H), 7.91 (d, *J* = 8.2 Hz, 2H), 7.95 (d, *J* = 8.9 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 55.4, 112.0, 114.2, 126.5, 127.6, 128.1, 128.8, 133.1, 133.8, 154.7, 161.2, 167.9; HRMS (DART) *m*/*z* = 302.0406 calcd for $C_{16}H_{13}ClNOS$ $[M+H]^+$, found: 302.0406.

2-(Benzo[*d*][1,3]dioxol-5-yl)-4-phenylthiazole (10ha)

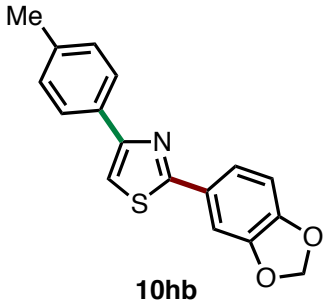


10ha

Purification by PTLC (hexane/EtOAc = 10:1) gave **10ha** as a white solid (Method C': 78% yield). ^{1}H NMR

(600 MHz, $CDCl_3$) δ 6.01 (s, 2H), 6.86 (d, J = 8.2 Hz, 1H), 7.33 (t, J = 8.2 Hz, 1H), 7.38 (s, 1H), 7.43 (t, J = 8.2 Hz, 2H), 7.51 (d, J = 8.2 Hz, 1H), 7.56 (s, 1H), 7.96 (d, J = 8.2 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 101.5, 106.9, 108.5, 111.9, 121.1, 126.4, 128.1, 128.2, 128.7, 134.5, 148.2, 149.2, 155.9, 167.4; HRMS (DART) m/z = 282.0589 calcd for $C_{16}H_{12}NO_2S$ $[M+H]^+$, found: 282.0588.

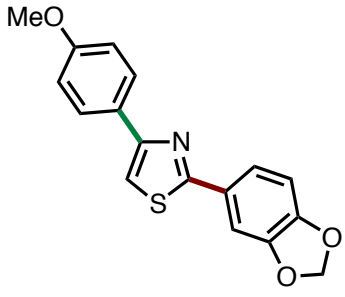
2-(Benzo[*d*][1,3]dioxol-5-yl)-4-(4-methylphenyl)thiazole (10hb)



10hb

Purification by PTLC (hexane/EtOAc = 20:1) gave **10hb** as a white solid (Method F: 82% yield, 97% C4-selectivity). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.38 (s, 3H), 6.00 (s, 2H), 6.85 (d, J = 8.2 Hz, 1H), 7.23 (d, J = 8.2 Hz, 2H), 7.31 (s, 1H), 7.50 (dd, J = 7.6, 1.4 Hz, 1H), 7.55 (d, J = 1.4 Hz, 1H), 7.85 (d, J = 7.6 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.2, 101.5, 106.9, 108.5, 111.1, 121.0, 126.3, 128.4, 129.4, 131.8, 137.9, 148.2, 149.2, 156.0, 167.3; HRMS (DART) m/z = 296.0745 calcd for $C_{17}H_{14}NO_2S$ $[M+H]^+$, found: 296.0746.

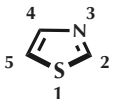
2-(Benzo[*d*][1,3]dioxol-5-yl)-4-(4-methoxyphenyl)thiazole (10hg)

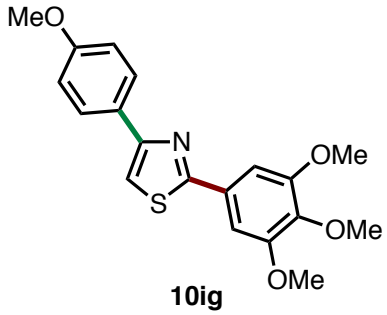


10hg

Purification by PTLC (hexane/EtOAc = 10:1) and GPC gave **10hg** as a light yellow solid (Method C': 74% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.85 (s, 3H), 6.03 (s, 2H), 6.87 (d, J = 7.6 Hz, 1H), 6.96 (d, J = 8.9 Hz, 2H), 7.26 (s, 1H), 7.52 (dd, J = 7.6, 1.4 Hz, 1H), 7.56 (d, J = 1.4 Hz, 1H), 7.90 (d, J = 8.9 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 55.3, 101.5, 106.9, 108.5, 110.2, 114.0, 121.0, 127.5, 127.7, 128.3, 148.2, 149.1, 155.8, 159.6, 167.3; HRMS (DART) m/z = 312.0694 calcd for $C_{17}H_{14}NO_3S$ $[M+H]^+$, found: 312.0696.

4-(4-Methoxylphenyl)-2-(3,4,5-trimethoxyphenyl)thiazole (10ig)

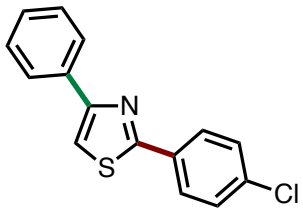




10ig

Purification by PTLC (hexane/EtOAc = 3:1) gave **10ig** as a light yellow solid (Method C': 57% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.85 (s, 3H), 3.91 (s, 3H), 3.97 (s, 6H), 6.97 (d, J = 8.2 Hz, 2H), 7.26 (s, 2H), 7.31 (s, 1H), 7.92 (d, J = 8.2 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 55.3, 56.3, 60.9, 103.8, 110.8, 114.0, 127.4, 127.7, 129.4, 139.7, 153.5, 155.9, 159.6, 167.5; HRMS (DART) m/z = 358.1113 calcd for $C_{19}H_{20}NO_4S$ $[M+H]^+$, found: 358.1114.

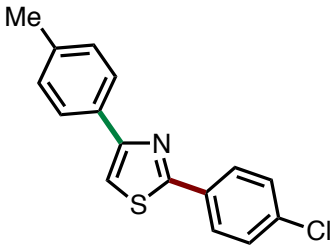
2-(4-Chlorophenyl)-4-phenylthiazole (10ja)



10ja

The reaction was performed for 48 h. Purification by PTLC (hexane/EtOAc = 10:1) gave **10ja** as a white solid (Method F: 64% yield, 82% C4-selectivity). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35 (t, J = 8.2 Hz, 1H), 7.40–7.48 (m, 5H), 7.94–8.01 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 112.8, 126.4, 127.8, 128.3, 128.7, 129.1, 132.3, 134.3, 135.9, 156.5, 166.5; HRMS (DART) m/z = 272.0301 calcd for $C_{15}H_{11}ClNS$ $[M+H]^+$, found: 272.0301.

2-(4-Chlorophenyl)-4-(4-methylphenyl)thiazole (10jb)

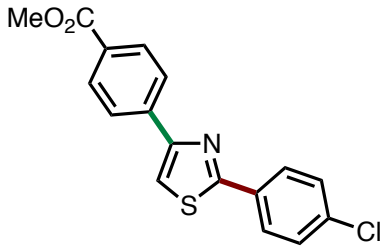


10jb

Purification by PTLC (hexane/EtOAc = 20:1) gave **10jb** as a white solid (Method C': 70% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.40 (s, 3H), 7.25 (d, J = 8.2 Hz, 2H), 7.41–7.44 (m, 3H), 7.87 (d, J = 8.2 Hz, 2H), 7.97 (d, J = 8.9 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.3, 112.1, 126.3, 127.7, 129.1, 129.4, 131.6, 132.3,

135.8, 138.1, 156.5, 166.3; HRMS (DART) *m/z* = 286.0457 calcd for $C_{16}H_{13}ClNS$ $[M+H]^+$, found: 286.0456.

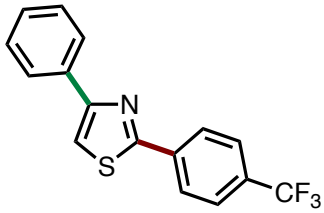
Methyl 4-(4-(4-chlorophenyl)thiazol-4-yl)benzoate (10jn)



10jn

The reaction was performed for 48 h. Purification by flash column chromatography (hexane/EtOAc = 5:1) gave **10jn** as a white solid (Method F: 45% yield, >99% C4-selectivity). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.94 (s, 3H), 7.43 (d, *J* = 8.2 Hz, 2H), 7.59 (s, 1H), 7.95–7.97 (m, 2H), 8.04 (d, *J* = 8.2 Hz, 2H), 8.10 (d, *J* = 8.2 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 52.1, 114.7, 126.2, 127.2, 127.8, 129.2, 129.6, 129.6, 130.10, 130.2, 131.9, 136.2, 138.3, 155.2, 166.80, 166.83; HRMS (DART) *m/z* = calcd 330.0356 for $C_{17}H_{13}ClNO_2S$ $[M+H]^+$, found: 330.0357.

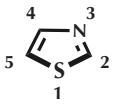
2-(4-(Trifluoromethyl)phenyl)-4-phenylthiazole (10ka)

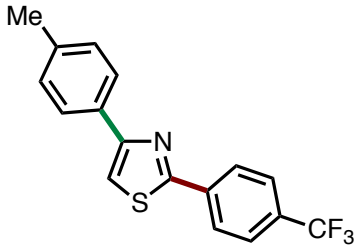


10ka

Purification by PTLC (hexane/EtOAc = 10:1) gave **10ka** as a white solid (Method F: 69% yield, 77% C4-selectivity). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37 (t, *J* = 7.6 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.52 (s, 1H), 7.70 (d, *J* = 8.2 Hz, 2H), 7.99 (d, *J* = 7.6 Hz, 2H), 8.14 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 113.6, 124.0 (q, J_{C-F} = 271.7 Hz), 125.9 (q, J_{C-F} = 4.3 Hz), 126.5, 126.8, 128.4, 128.8, 131.6 (q, J_{C-F} = 33.1 Hz), 134.2, 136.8, 156.9, 165.9; HRMS (DART) *m/z* = 306.0564 calcd for $C_{16}H_{11}F_3NS$ $[M+H]^+$, found: 306.0563.

2-(4-(Trifluoromethyl)phenyl)-4-(4-methylphenyl)thiazole (10kb)

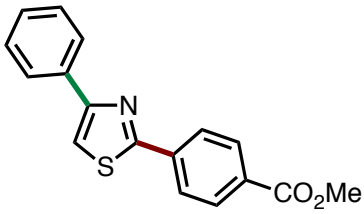




10kb

Purification by GPC gave **10kb** as a white solid (Method C': 63% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.39 (s, 3H), 7.24 (d, J = 8.3 Hz, 2H), 7.40–7.43 (m, 3H), 7.86 (d, J = 8.3 Hz, 2H), 7.96 (d, J = 8.3 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.3, 112.8, 123.9 (q, J_{C-F} = 271.7 Hz), 125.9 (q, J_{C-F} = 2.9 Hz), 126.3, 126.7, 129.5, 131.4, 131.5 (q, J_{C-F} = 33.1 Hz), 136.9, 138.3, 156.9, 165.8; HRMS (DART) m/z = 320.0721 calcd for $C_{17}H_{13}F_3NS$ $[M+H]^+$, found: 320.0720.

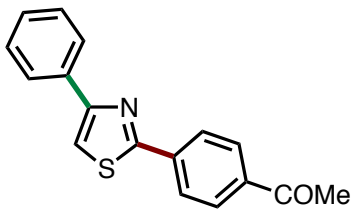
Methyl 4-(4-phenylthiazol-2-yl)benzoate (10na)



10na

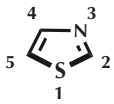
Purification by flash column chromatography (hexane/EtOAc = 10:1) gave **10na** as a white solid (Method F: 65% yield, 82% C4-selectivity). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.93 (s, 3H), 7.35 (t, J = 7.6 Hz, 1H), 7.44 (d, J = 7.6 Hz, 2H), 7.51 (s, 1H), 7.98 (d, J = 8.2 Hz, 2H), 8.07–8.13 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 52.2, 113.6, 126.35, 126.44, 128.3, 128.7, 130.2, 131.1, 134.2, 137.5, 156.8, 166.3, 166.5; HRMS (DART) m/z = 296.0745 calcd for $C_{17}H_{14}NO_2S$ $[M+H]^+$, found: 296.0746.

2-(4-Acetylphenyl)-4-phenylthiazole (10oa)



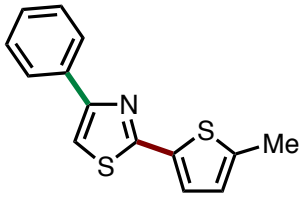
10oa

Purification by PTLC (hexane/EtOAc = 10:1) gave **10oa** as a white solid (Method F: 71% yield, 77% C4-selectivity). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.64 (s, 3H), 7.37 (t, J = 7.6 Hz, 1H), 7.46 (t, J = 7.6 Hz, 2H), 7.55 (s, 1H), 8.00 (d, J = 8.3 Hz, 2H), 8.04 (d, J = 8.9 Hz, 2H), 8.13 (d, J = 8.9 Hz, 2H); ^{13}C NMR (150 MHz,



$CDCl_3$) δ 26.7, 113.7, 126.5, 126.6, 128.4, 128.8, 129.0, 134.2, 137.6, 137.9, 156.9, 166.3, 197.3; HRMS (DART) *m/z* = 280.0796 calcd for $C_{17}H_{14}NOS$ $[M+H]^+$, found: 280.0796.

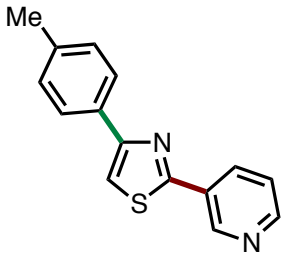
2-(5-Methylthiophen-2-yl)-4-phenylthiazole (10ra)



10ra

Purification by PTLC (hexane/EtOAc = 20:1) gave **10ra** as a light yellow solid (Method C': 62% yield). ^1H NMR (600 MHz, $CDCl_3$) δ 2.51 (s, 3H), 6.73 (d, *J* = 2.8 Hz, 1H), 7.30–7.36 (m, 3H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.94 (d, *J* = 7.6 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 15.5, 111.2, 126.1, 126.4, 126.6, 128.1, 128.7, 134.2, 135.1, 142.8, 155.6, 161.7; HRMS (DART) *m/z* = 258.0411 calcd for $C_{14}H_{12}NS_2$ $[M+H]^+$, found: 258.0410.

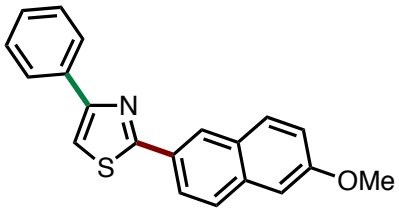
2-(3-Pyridyl)-4-(4-methylphenyl)thiazole (10tb)



10tb

4b (1.5 equiv), 3-bromopyridine (1.0 equiv) and Li*O*t-Bu (2.0 equiv) were used and the reaction was performd at 100 ˚C. Purification by PTLC (hexane/EtOAc = 5:1) gave **10tb** as a light yellow solid (Method C': 82% yield). ^1H NMR (600 MHz, $CDCl_3$) δ 2.40 (s, 3H), 7.27 (d, *J* = 8.3 Hz, 2H), 7.40 (dd, *J* = 8.2 Hz, 4.8 Hz, 1H), 7.49 (s, 1H), 7.89 (d, *J* = 8.3 Hz, 2H), 8.33 (dt, *J* = 7.6 Hz, 2.0 Hz, 1H), 8.67 (dd, *J* = 4.8 Hz, 1.4 Hz, 1H), 9.24 (d, *J* = 2.0 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.3, 112.5, 123.7, 126.4, 129.5, 129.8, 131.4, 133.6, 138.3, 147.8, 150.7, 156.9, 164.2; HRMS (DART) *m/z* = 253.0799 calcd for $C_{15}H_{13}N_2S$ $[M+H]^+$, found: 253.0799.

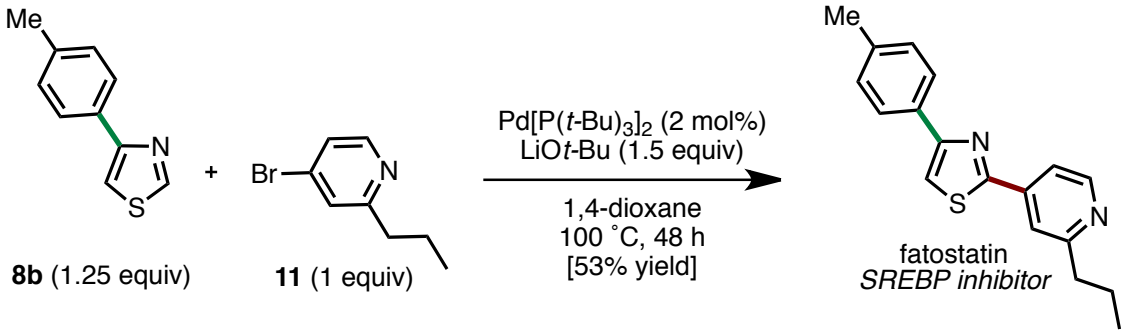
2-(6-Methoxylnaphthalen-2-yl)-4-phenylthiazole (10wa)



10wa

The reaction was performed at 100 °C. GPC gave **10wa** as light yellow solid (Method C': 68% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.94 (s, 3H), 7.16 (s, 1H), 7.19 (dd, *J* = 8.3, 2.1 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 1H), 7.44–7.49 (m, 3H), 7.80 (d, *J* = 8.2 Hz, 1H), 7.84 (d, *J* = 8.2 Hz, 1H), 8.03 (d, *J* = 7.6 Hz, 2H), 8.13 (dd, *J* = 8.2, 2.1 Hz, 1H), 8.43 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 55.3, 105.8, 112.3, 119.6, 124.7, 125.8, 126.5, 127.4, 128.1, 128.65, 128.73, 129.1, 130.1, 134.6, 135.5, 156.3, 158.5, 168.1; HRMS (DART) *m/z* = 318.0953 calcd for $C_{20}H_{16}NOS$ $[M+H]^+$, found: 318.0953.

Synthesis of Fatostatin[28]

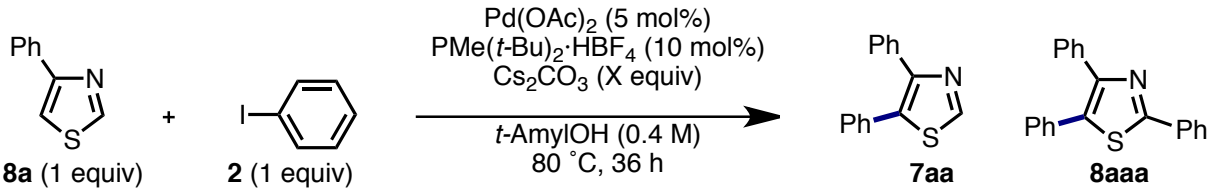


4b (1.25 equiv), 4-bromo-2-propylpyridine (1.0 equiv) and LiO*t*-Bu (1.5 equiv) at 100 ˚C for 48 h. PTLC (hexane/EtOAc = 2:1) gave Fatostatin as a light yellow solid (Method C': 53% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.02 (t, *J* = 7.6 Hz, 3H), 1.80–1.87 (m, 2H), 2.40 (s, 3H), 2.86 (t, *J* = 7.6 Hz, 2H), 7.26 (d, *J* = 8.2 Hz, 2H), 7.50 (s, 1H), 7.67 (dd, *J* = 4.9, 2.0 Hz, 1H), 7.76 (s, 1H), 7.88 (d, *J* = 8.2 Hz, 2H), 8.62 (d, *J* = 8.1 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 13.9, 21.3, 23.1, 40.4, 113.3, 117.8, 119.3, 126.3, 129.5, 131.3, 138.4, 140.6, 150.0, 157.1, 163.4, 165.2; HRMS (DART) *m/z* = 295.1269 calcd for $C_{18}H_{19}N_2S$ $[M+H]^+$, found: 295.1268.

[28] Kamisuki, S.; Mao, Q.; Abu-Elheiga, L.; Gu, Z.; Kugimiya, A.; Kwon, Y.; Shinohara, T.; Kawazoe, Y.; Sato, S.; Asakura, K.; Choo, H. -Y. P.; Sakai, J.; Wakil, S. J.; Uesugi, M. *Chem. Biol.* **2009**, *16*, 882.

8. Synthesis of 4,5-Diarylthiazoles

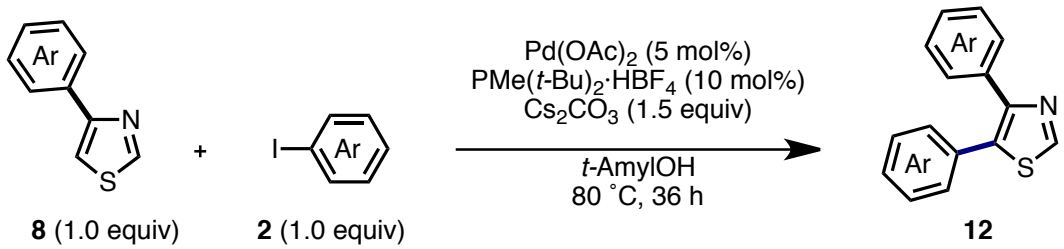
Table S4. Screening of Reaction Conditions



Entry	X	Time	Temp	**7aa** [a]	**8aaa** [b]
1	1	12 h	100 ˚C	0.81 (68%)	20%
2	1	12 h	80 ˚C	0.73	7%
3	1	12 h	90 ˚C	0.83	13%
4	1	36 h	80 ˚C	0.90	19%
5	1	36 h	75 ˚C	0.78	13%
6	1.5	36 h	80 ˚C	0.995 (77%)	14%

[a] GC ratio of **7a**/*n*-dodecane. The nunmer in bracket was isolated yield. [b] GC yield.

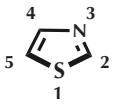
Method D[15]

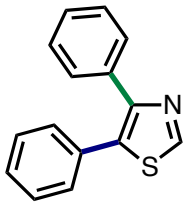


A 7-mL test tube equipped with screw cap, containing a magnetic stirring bar, was flame-dried under vacuum and then cooling to room temperature. To this vessel were added $Pd(OAc)_2$ (2.2 mg, 0.01 mmol, 5 mol%), $PMe(t\text{-}Bu)_2{\cdot}HBF_4$ (5.0 mg, 0.02 mmol, 10 mol%), Cs_2CO_3 (97.8 mg, 0.3 mmol, 1.5 equiv), iodoarene **2** (0.2 mmol, 1.0 equiv), 4-arylthiazole **8** (0.2 mmol, 1.0 equiv), and *t*-AmylOH (0.5 mL) under argon atmosphere. The vessel was sealed and then stirred at 80 °C for 36 h. After cooling the reaction mixture to room temperature, the mixture was passed through a short silica gel pad (EtOAc). The filtrate was evaporated and the residue was purified by PTLC and GPC. For further purification, the obtained product was passed through NH-silica gel pad (EtOAc) to afford 4,5-diarlthiazole **12**.

4,5-Diphenylthiazole (12aa)[29]

[29] Lingaraju, G. S.; Swaroop, T. R.; Vinayaka, A. C.; Kumar, K. S. S.; Sadashiva, M. P.; Rangappa, K. S. *Synthesis* **2012**, *44*, 1373.

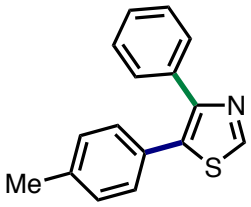




12aa

Purification by PTLC (hexane/EtOAc = 10:1) gave **12aa** as a white solid (Method D: 77% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.27–7.38 (m, 8H), 7.51–7.55 (m, 2H), 8.81 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 127.8, 128.27, 128.30, 128.8, 129.0, 129.7, 131.8, 132.9, 134.6, 150.7, 151.0; HRMS (DART) *m*/*z* = 238.0690 calcd for $C_{15}H_{12}NS$ $[M+H]^+$, found: 238.0690.

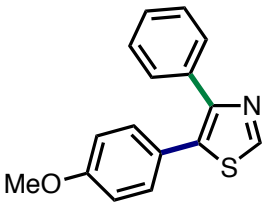
5-(4-Methylphenyl)-4-phenylthiazole (12ab)[29]



12ab

Purification by GPC gave **12ab** as a white solid (Method D: 69% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.36 (s, 3H), 7.13 (d, *J* = 8.3 Hz, 2H), 7.25 (d, *J* = 8.3 Hz, 2H), 7.27–7.32 (m, 3H), 7.54 (dd, *J* = 7.6, 1.4 Hz, 2H), 8.78 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.2, 127.7, 128.3, 128.8, 129.0, 129.48, 129.54, 133.1, 134.8, 138.2, 150.3, 150.7; HRMS (DART) *m*/*z* = 252.0847 calcd for $C_{16}H_{14}NS$ $[M+H]^+$, found: 252.0847.

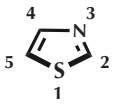
5-(4-Methoxyphenyl)-4-phenylthiazole (12ag)[29]

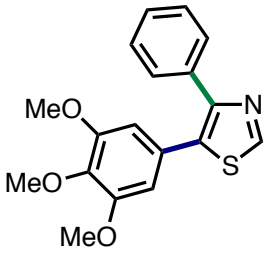


12ag

Purification by GPC gave **12ag** as a light yellow oil (Method D: 75% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.81 (s, 3H), 6.86 (d, *J* = 8.2 Hz, 2H), 7.24–7.31 (m, 5H), 7.54 (dd, *J* = 8.2, 1.4 Hz, 2H), 8.76 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 55.3, 114.2, 123.9, 127.7, 128.3, 128.9, 130.9, 132.8, 134.8, 150.1, 150.5, 159.7; HRMS (DART) *m*/*z* = 268.0796 calcd for $C_{16}H_{14}NOS$ $[M+H]^+$, found: 268.0798.

5-(3,4,5-Trimethoxyphenyl)-4-phenylthiazole (12ai)[29]

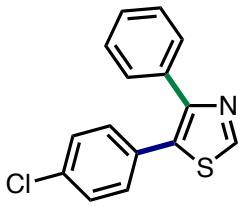




12ai

3,4,5-Trimethoxybromobenzene (**2i**) (1.0 equiv) was used and the reaction was performed at 100 ˚C for 18 h. Purification by GPC gave **12ai** as a light yellow solid (Method D: 60% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.70 (s, 6H), 3.88 (s, 3H), 6.55 (s, 2H), 7.27–7.34 (m, 3H), 7.57 (dd, *J* = 8.3 Hz, 1.4 Hz, 2H), 8.79 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 56.0, 60.9, 106.9, 127.0, 127.9, 128.3, 129.0, 132.9, 134.7, 138.1, 150.57, 150.61, 153.3. HRMS (DART) *m/z* = 328.1007 calcd for $C_{18}H_{18}NO_3S$ $[M+H]^+$, found: 328.1005.

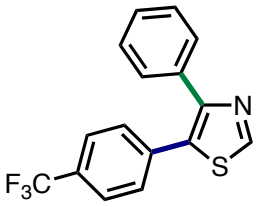
5-(4-Chlorophenyl)-4-phenylthiazole (12aj)



12aj

Purification by GPC gave **12aj** as a light yellow solid (Method D: 66% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.26–7.34 (m, 7H), 7.51 (dd, *J* = 7.6, 2.0 Hz, 2H), 8.81 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 128.1, 128.4, 128.97, 129.02, 130.3, 130.9, 131.5, 134.3, 151.1, 151.2; There is one overlapping carbon signal as 1 peak is missing even with prolonged scans. HRMS (DART) *m/z* = 272.0301 calcd for $C_{15}H_{11}ClNS$ $[M+H]^+$, found: 272.0301.

5-(4-(Trifluoromethyl)phenyl)-4-phenylthiazole (12ak)

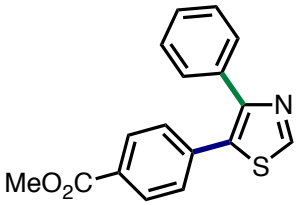


12ak

Purification by GPC gave **12ak** as a white solid (Method D: 59% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.29–7.35 (m, 3H), 7.47 (d, *J* = 8.3 Hz, 2H), 7.50 (dd, *J* = 7.6, 2.0 Hz, 2H), 7.58 (d, *J* = 8.3 Hz, 2H), 8.86 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 123.9 (q, J_{C-F} = 270.2 Hz), 125.7 (q, J_{C-F} = 2.9 Hz), 128.3, 128.5, 129.1,

129.9, 130.2 (q, J_{C-F} = 31.6 Hz), 131.2, 134.1, 135.7, 151.7; There is one overlapping carbon signal as 1 peak is missing even with prolonged scans. HRMS (DART) *m/z* = 306.0564 calcd for $C_{16}H_{11}F_3NS$ $[M+H]^+$, found: 306.0565.

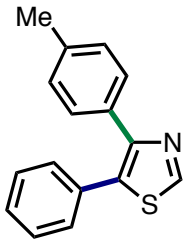
Methyl-4-(4-phenylthiazol-5-yl)benzoate (12an)



12an

The reaction was performed at 100 °C for 18 h. Purification by GPC gave **12an** as a light yellow oil (Method D: 49% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.92 (s, 3H), 7.29–7.33 (m, 3H), 7.43 (d, *J* = 8.2 Hz, 2H), 7.48–7.52 (m, 2H), 7.99 (d, *J* = 8.2 Hz, 2H), 8.86 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 52.2, 128.2, 128.4, 129.1, 129.6, 129.7, 130.0, 131.7, 134.2, 136.6, 151.7, 166.5; There is one overlapping carbon signal as 1 peak is missing even with prolonged scans. HRMS (DART) *m/z* = 296.0745 calcd for $C_{17}H_{14}NO_2S$ $[M+H]^+$, found: 296.0746.

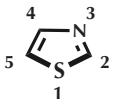
4-(4-Methylphenyl)-5-phenylthiazole (12ba)

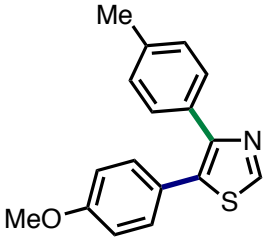


12ba

Purification by GPC gave **12ba** as a white solid (Method D: 77% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.34 (s, 3H), 7.10 (d, *J* = 7.6 Hz, 2H), 7.30–7.40 (m, 5H), 7.42 (d, *J* = 7.6 Hz, 2H), 8.80 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.2, 128.2, 128.7, 128.8, 129.0, 129.7, 131.8, 132.0, 132.3, 137.6, 150.7, 150.8; HRMS (DART) *m/z* = 252.0847 calcd for $C_{16}H_{14}NS$ $[M+H]^+$, found: 252.0845.

5-(4-Methoxyphenyl)-4-(4-methylphenyl)thiazole (12bg)

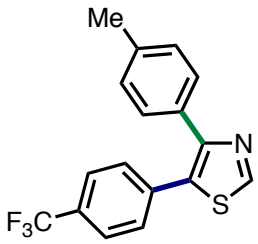




12bg

Purification by GPC gave **12bg** as a light yellow solid (Method D: 66% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.33 (s, 3H), 3.81 (s, 3H), 6.86 (d, *J* = 8.2 Hz, 2H), 7.10 (d, *J* = 8.2 Hz, 2H), 7.28 (d, *J* = 8.2 Hz, 2H), 7.43 (d, *J* = 8.2 Hz, 2H), 8.75 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.2, 55.2, 114.2, 124.1, 128.7, 129.0, 130.9, 131.9, 132.2, 137.4, 150.1, 150.3, 159.6; HRMS (DART) *m/z* = 282.0953 calcd for $C_{17}H_{16}NOS$ $[M+H]^+$, found: 282.0954.

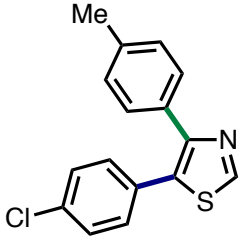
5-(4-(Trifluoromethyl)phenyl)-4-(4-methylphenyl)thiazole (12bk)



12bk

Purification by PTLC (hexane/EtOAc = 2:1) gave **12bk** as a yellow solid (Method D: 40% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.35 (s, 3H), 7.13 (d, *J* = 7,9 Hz, 2H), 7.39 (d, *J* = 8.2 Hz, 2H), 7.48 (d, *J* = 8.2 Hz, 2H), 7.58 (d, *J* = 7.9 Hz, 2H), 8.85 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.2, 123.9 (q, J_{C-F} = 270.2 Hz), 125.7 (q, J_{C-F} = 2.9 Hz), 128.9, 129.2, 129.9, 130.1 (q, J_{C-F} = 33.1 Hz), 130.5, 131.3, 135.9, 138.2, 151.6, 151.9; HRMS (DART) *m/z* = 320.0721 calcd for $C_{17}H_{13}F_3NS$ $[M+H]^+$, found: 320.0729.

5-(4-Chlorophenyl)-4-(4-methylphenyl)thiazole (12bj)

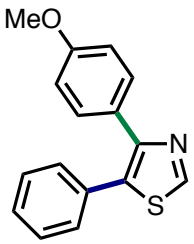


12bj

Purification by PTLC (hexane/EtOAc = 2:1) gave **12bj** as a yellow solid (Method D: 58% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.34 (s, 3H), 7.12 (d, *J* = 7.9 Hz, 2H), 7.27–7.32 (m, 4H), 7.40 (d, *J* = 7.9 Hz, 2H), 8.80 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.2, 128.8, 129.0, 129.1, 130.5, 130.89, 130.92, 131.4, 134.2, 137.9,

151.08, 151.13; HRMS (DART) *m/z* = 286.0457 calcd for $C_{16}H_{13}ClNS$ $[M+H]^+$, found: 286.0460.

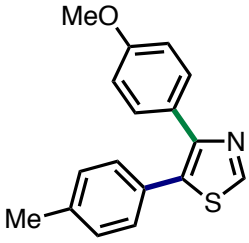
4-(4-Methoxyphenyl)-5-phenylthiazole (12ga)[30]



12ga

Purification by GPC gave **12ga** as a white solid (Method D: 81% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.80 (s, 3H), 6.82 (d, *J* = 8.9 Hz, 2H), 7.31–7.39 (m, 5H), 7.47 (d, *J* = 8.9 Hz, 2H), 8.78 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 55.2, 113.7, 127.2, 128.1, 128.7, 129.7, 130.2, 131.5, 132.1, 150.4, 150.8, 159.3; HRMS (DART) *m/z* = 268.0796 calcd for $C_{16}H_{14}NOS$ $[M+H]^+$, found: 268.0795.

4-(4-Methoxyphenyl)-5-(4-methylphenyl)thiazole (12gb)

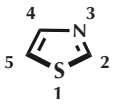


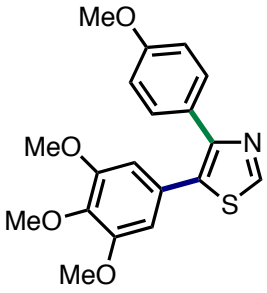
12gb

Purification by GPC gave **12gb** as a white solid (Method D: 78% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.35 (s, 3H), 3.79 (s, 3H), 6.82 (d, *J* = 8.2 Hz, 2H), 7.13 (d, *J* = 7.6 Hz, 2H), 7.25 (d, *J* = 8.2 Hz, 2H), 7.48 (d, *J* = 7.6 Hz, 2H), 8.75 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.2, 55.1, 113.7, 127.4, 129.0, 129.4, 129.5, 130.1, 131.7, 138.0, 150.0, 150.5, 159.2; HRMS (DART) *m/z* = 282.0953 calcd for $C_{17}H_{16}NOS$ $[M+H]^+$, found: 282.0952.

5-(4-Methoxyphenyl)-4-(3,4,5-trimethoxyphenyl)thiazole (12gi)

[30] Maeda, M.; Kojima, M. *J. Chem. Soc., Perkin Trans. 1*, **1978**, 685.

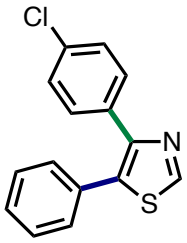




12gi

3,4,5-trimethoxybromobenzene (**2i**) was used and the reaction was performed at 100 ˚C for 36 h. Purification by GPC gave **12gi** as a light yellow oil (Method D: 55% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.73 (s, 6H), 3.81 (s, 3H), 3.88 (s, 3H), 6.57 (s, 2H), 6.85 (d, *J* = 8.9 Hz, 2H), 7.51 (d, *J* = 8.9 Hz, 2H), 8.77 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 55.2, 56.1, 60.9, 106.8, 113.6, 127.2, 127.3, 130.2, 131.5, 138.0, 150.3, 150.5, 153.3, 159.3; HRMS (DART) *m/z* = 358.1113 calcd for $C_{19}H_{20}NO_4S$ $[M+H]^+$, found: 358.1113.

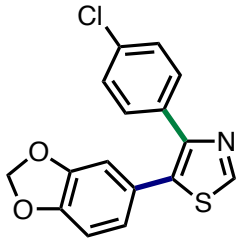
4-(4-Chlorophenyl)-5-phenylthiazole (12ja)



12ja

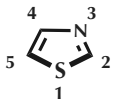
Purification by GPC gave **12ja** as a colorless oil (Method D: 80% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.9 Hz, 2H), 7.32–7.38 (m, 5H), 7.47 (d, *J* = 8.9 Hz, 2H), 8.80 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 128.5, 128.9, 129.7, 130.2, 131.5, 133.1, 133.4, 133.7, 149.4, 151.2; There is one overlapping carbon signal as 1 peak is missing even with prolonged scans. HRMS (DART) *m/z* = 272.0301 calcd for $C_{15}H_{11}ClNS$ $[M+H]^+$, found: 272.0303.

5-(Benzo[*d*][1,3]dioxol-5-yl)-4-(4-chlorophenyl)thiazole (12jh)



12jh

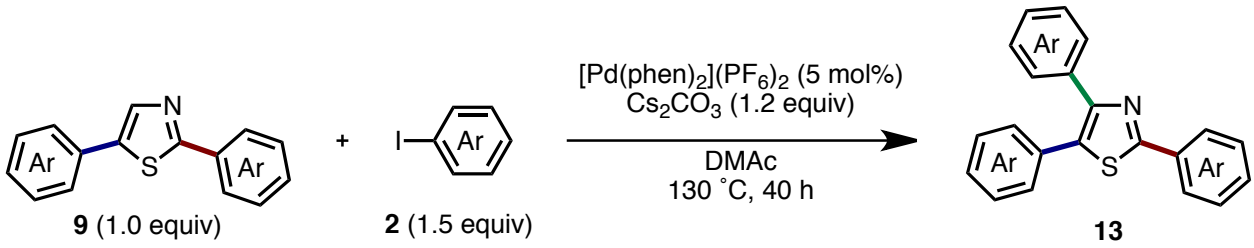
Purification by GPC gave **12jh** as a yellow solid (Method D: 35% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.00 (s, 2H), 6.78 (d, *J* = 1.4 Hz, 1H), 6.80 (d, *J* = 8.2 Hz, 1H), 6.84 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.28 (d, *J* = 8.9 Hz,



2H), 7.49 (d, J = 8.9 Hz, 2H), 8.76 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 101.4, 108.8, 110.0, 123.7, 124.9, 128.6, 130.2, 133.0, 133.1, 133.7, 147.99, 148.02, 149.1, 150.8; HRMS (DART) m/z = 316.0199 calcd for $C_{16}H_{11}ClNO_2S$ $[M+H]^+$, found: 316.0200.

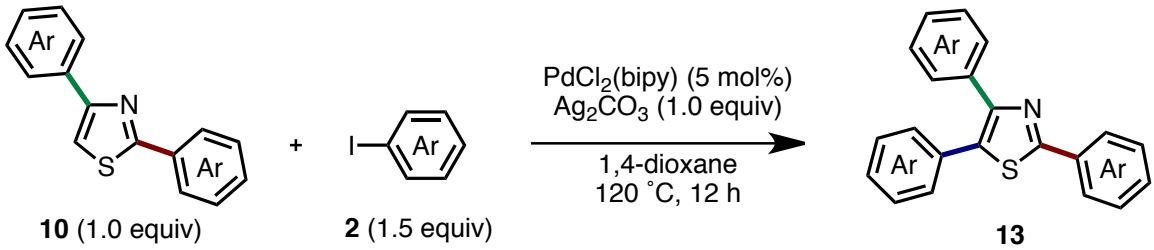
9. Synthesis of Triarylthiazoles

Method H'[24]



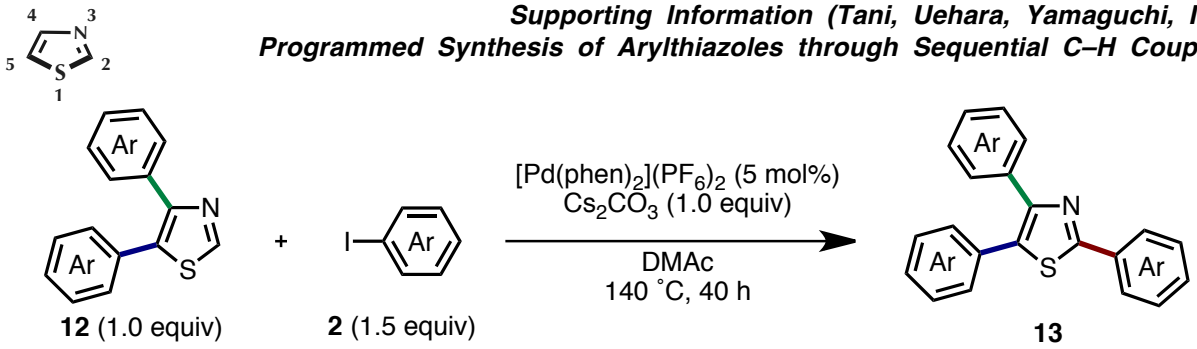
A 25-mL test tube equipped with screw cap, containing a magnetic stirring bar, was flame-dried under vacuum and then cooling to room temperature. To this vessel were added $[Pd(phen)_2](PF_6)_2$ (7.6 mg, 0.01 mmol, 5 mol%), Cs_2CO_3 (78.2 mg, 0.24 mmol, 1.2 equiv), iodoarene **2** (0.3 mmol, 1.5 equiv), 2,5-diarylthiazole **9** (0.2 mmol, 1.0 equiv) and DMAc (0.8 mL) under argon atmosphere. The vessel was sealed and then stirred at 130 °C for 40 h. After cooling the reaction mixture to room temperature, the mixture was passed through a short silica gel pad (EtOAc). The filtrate was evaporated and the residue was purified by PTLC and/or GPC to afford triarylthiazole **13**.

Method G[23]



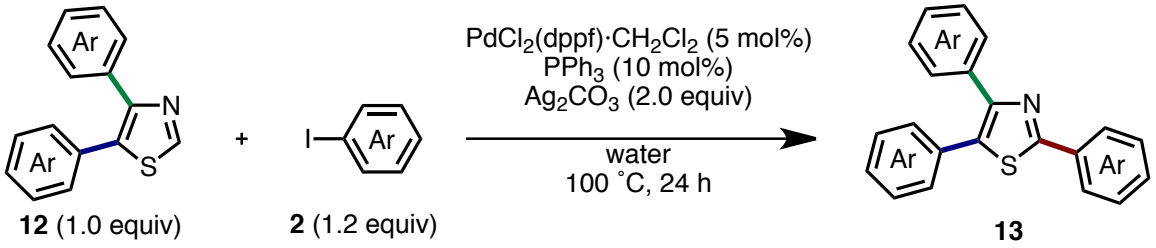
A 20-mL glass vessel equipped with J. Young® O-ring tap, containing a magnetic stirring bar, was flame-dried under vacuum and filled with argon after cooling to room temperature. To this vessel were added $PdCl_2$(bipy) (4.2 mg, 0.013 mmol, 5 mol%), Ag_2CO_3 (0.25 mmol, 68.9 mg, 1.0 equiv), iodoarene **2** (0.375 mmol, 1.5 equiv), 2,4-diarylthiazole **10** (0.25 mmol, 1.0 equiv) and 1,4-dioxane (1.0 mL) under a stream of argon. The vessel was sealed and then stirred at 120 °C for 12 h. After cooling the reaction mixture to room temperature, the mixture was passed through a short silica gel pad (EtOAc). The filtrate was evaporated and the residue was purified by PTLC, and/or GPC to afford triarylthiazole **13**.

Method H''[24]



A 25-mL test tube equipped with screw cap, containing a magnetic stirring bar, was flame-dried under vacuum and then cooling to room temperature. To this vessel were added $[Pd(phen)_2](PF_6)_2$ (5.7 mg, 0.0075 mmol, 5 mol%), Cs_2CO_3 (48.9 mg, 0.15 mmol, 1.0 equiv), iodoarene **2** (0.225 mmol, 1.5 equiv), 4,5-diarylthiazole **12** (0.15 mmol, 1.0 equiv) and DMAc (0.6 mL) under argon atmosphere. The vessel was sealed and then stirred at 140 °C for 40 h. After cooling the reaction mixture to room temperature, the mixture was passed through a short silica gel pad (EtOAc). The filtrate was evaporated and the residue was purified by PTLC and/or GPC to afford triarylthiazole **13**.

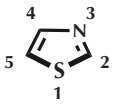
Method I[8]

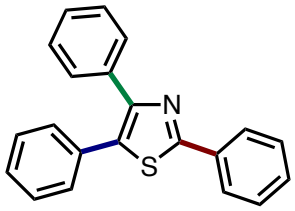


A 25-mL test tube equipped with screw cap, containing a magnetic stirring bar, were added $PdCl_2(dppf)\cdot CH_2Cl_2$ (6.2 mg, 0.0075 mmol, 5 mol%), PPh_3 (3.9 mg, 0.015 mol, 10 mol%), Ag_2CO_3 (82.7 mg, 0.3 mmol, 2.0 equiv), iodoarene **2** (0.18 mmol, 1.2 equiv), 4,5-diarylthiazole **12** (0.15 mmol, 1.0 equiv) and distilled water (1 mL). The test tube was purged with argon and then stirred at 100 °C for 24 h. After cooling the reaction mixture to room temperature, the mixture was suspended in acetone (2.0 mL) and dichloromethane (5 mL), and then passed through a short silica gel pad (EtOAc). The filtrate was evaporated and the residue was purified by PTLC to afford triarylthiazole **13**.

2,4,5-Triphenylthiazole (13aaa)[31]

[31] Hodgetts, K. J.; Kershaw, M. T. *Org. Lett.* **2002**, *4*, 1363.

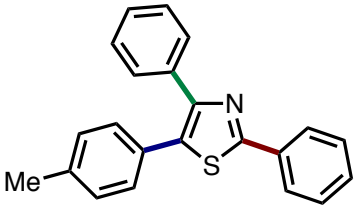




13aaa

Purification by PTLC (hexane/EtOAc = 20:1) gave **13aaa** as a white solid (Method H': 68% yield, Method G: 90% yield, Method I: 95% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.26–7.36 (m, 6H), 7.37–7.49 (m, 5H), 7.60 (d, *J* = 7.6 Hz, 2H) 8.02 (dd, *J* = 8.3, 1,4 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 126.4, 127.8, 128.1, 128.3, 128.7, 128.9, 129.1, 129.6, 130.0, 132.1, 133.1, 133.6, 134.9, 150.8, 165.5; HRMS (DART) *m*/*z* = 314.1003 calcd for $C_{21}H_{16}NS$ $[M+H]^+$, found: 314.1006.

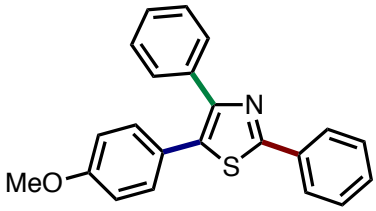
5-(4-Methylphenyl)-2,4-diphenylthiazole (13aab)



13aab

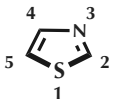
Purification by PTLC (hexane/EtOAc = 20:1) gave **13aab** as a white solid (Method G: 90% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.36 (s, 3H), 7.13 (d, *J* = 8.3 Hz, 2H), 7.26–7.33 (m, 5H), 7.38–7.46 (m, 3H), 7.61 (d, *J* = 8.2 Hz, 2H), 8.00 (dd, *J* = 8.3, 1.4 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.3, 126.4, 127.7, 128.2, 128.9, 129.06, 129.09, 129.4, 129.9, 133.3, 133.7, 135.1, 138.1, 150.5, 165.1; There is one overlapping carbon signal as 1 peak is missing even with prolonged scans. HRMS (DART) *m*/*z* = 328.1160 calcd for $C_{22}H_{18}NS$ $[M+H]^+$, found: 328.1159.

5-(4-Methoxyphenyl)-2,4-diphenylthiazole (13aag)

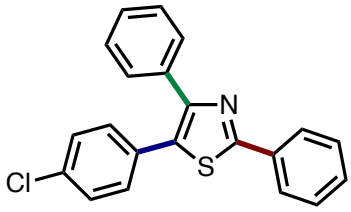


13aag

Purification by PTLC (hexane/EtOAc = 10:1) gave **13aag** as a white solid (Method G: 90% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.82 (s, 3H), 6.86 (d, *J* = 8.9 Hz, 2H), 7.26–7.33 (m, 5H), 7.39–7.46 (m, 3H), 7.61 (d, *J* = 8.3 Hz, 2H), 8.00 (dd, *J* = 8.3, 1.4 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 55.3, 114.2, 124.3, 126.4, 127.7, 128.2, 128.9, 129.1, 129.8, 130.8, 133.0, 133.7, 135.1, 150.2, 159.6, 164.9; HRMS (DART) *m*/*z* = 344.1109 calcd for $C_{22}H_{18}NOS$ $[M+H]^+$, found: 344.1112.



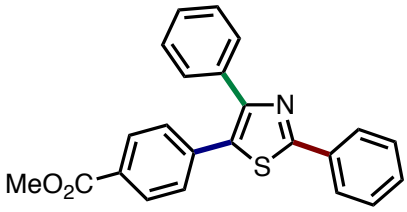
5-(4-Chlorophenyl)-2,4-diphenylthiazole (13aaj)



13aaj

The reaction was performed for 22 h. Purification by PTLC (hexane/EtOAc = 20:1) gave **13aaj** as a white solid (Method G: 74% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.27–7.35 (m, 7H), 7.40–7.47 (m, 3H), 7.58 (dd, *J* = 8.2, 1.4 Hz, 2H), 8.00 (dd, *J* = 8.2, 1.4 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 126.4, 128.0, 128.4, 128.9, 129.0, 129.1, 130.1, 130.6, 130.8, 131.6, 133.5, 134.1, 134.7, 151.2, 165.8; HRMS (DART) *m/z* = 348.0614 calcd for $C_{21}H_{15}ClNS$ $[M+H]^+$, found: 348.0613.

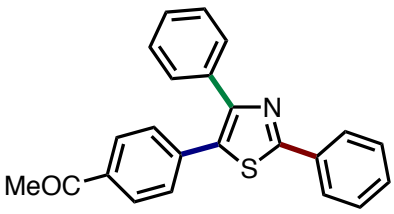
Methyl 4-(2,4-diphenylthiazol-5-yl)benzoate (13aan)



13aan

The reaction was performed at 140 °C for 22 h. Purification by PTLC (hexane/EtOAc = 5:1) gave **13aan** as a light yellow solid (Method G: 71% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.90 (s, 3H), 7.28–7.33 (m, 3H), 7.39–7.46 (m, 5H), 7.54–7.59 (m, 2H), 7.97 (d, *J* = 8.3 Hz, 2H), 8.00 (dd, *J* = 6.9, 1.4 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 52.1, 126.4, 128.2, 128.4, 128.9, 129.1, 129.4, 129.5, 129.9, 130.2, 131.7, 133.3, 134.6, 136.8, 151.8, 166.2, 166.5; HRMS (DART) *m/z* = 372.1058 calcd for $C_{23}H_{18}NO_2S$ $[M+H]^+$, found: 372.1060.

5-(4-Acetylphenyl)-2,4-diphenylthiazole (13aao)

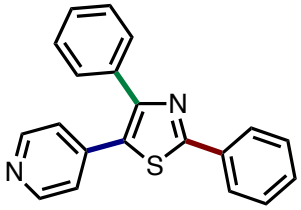


13aao

The reaction was performed at 140 °C for 22 h. Purification by PTLC (hexane/EtOAc = 3:1) gave **13aao** as a light yellow solid (Method G: 51% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.60 (s, 3H), 7.31–7.35 (m, 3H), 7.43–7.49 (m, 5H), 7.57 (dd, *J* = 6.9, 2.8 Hz, 2H), 7.90 (d, *J* = 8.3 Hz, 2H), 8.02 (dd, *J* = 7.6, 1.4 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 26.6, 126.5, 128.2, 128.4, 128.7, 128.9, 129.2, 129.6, 130.3, 131.6, 133.3,

134.6, 136.3, 137.0, 152.0, 166.4, 197.3; HRMS (DART) *m/z* = 356.1109 calcd for $C_{23}H_{18}NOS$ $[M+H]^+$, found: 356.1108.

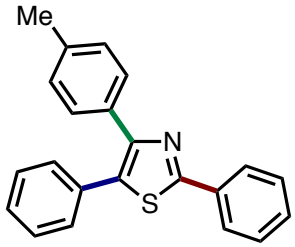
5-(4-Pyridyl)-2,4-diphenylthiazole (13aau)



13aau

The reaction was performed at 140 ˚C for 22 h. Purification by PTLC (hexane/EtOAc = 2:1) gave **13aau** as light yellow solid (Method G: 69% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.25 (dd, *J* = 4.8, 1.4 Hz, 2H), 7.33–7.38 (m, 3H), 7.43–7.48 (m, 3H), 7.57 (dd, *J* = 6.9, 2.8 Hz, 2H), 8.01 (dd, *J* = 7.6, 1.5 Hz, 2H), 8.54 (dd, *J* = 4.8, 1.4 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 123.5, 126.5, 128.5, 128.9, 129.2, 129.7, 130.5, 133.1, 134.3, 140.0, 150.2, 152.9, 166.9; There is one overlapping carbon signal as 1 peak is missing even with prolonged scans. HRMS (DART) *m/z* = 315.0956 calcd for $C_{20}H_{15}N_2S$ $[M+H]^+$, found: 315.0955.

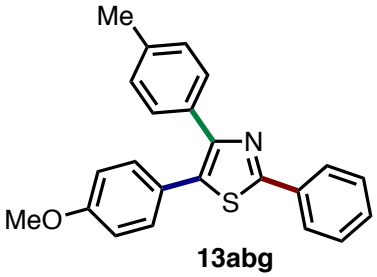
4-(4-Methylphenyl)-2,5-diphenylthiazole (13aba)



13aba

Purification by PTLC (hexane/EtOAc = 20:1) gave **13aba** as a white solid (Method H': 64% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.34 (s, 3H), 7.11 (d, *J* = 8.3 Hz, 2H), 7.30–7.36 (m, 3H), 7.38–7.47 (m, 5H), 7.49 (d, *J* = 8.2 Hz, 2H), 8.01 (d, *J* = 6.9 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.3, 126.4, 128.0, 128.7, 128.85, 128.95, 129.0, 129.6, 129.9, 132.1, 132.2, 132.4, 133.7, 137.6, 150.8, 165.3; HRMS (DART) *m/z* = 328.1160 calcd for $C_{22}H_{18}NS$ $[M+H]^+$, found: 328.1156.

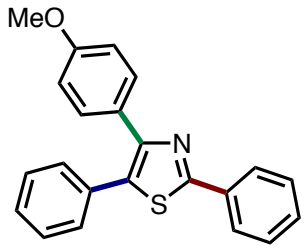
5-(4-Methoxyphenyl)-4-(4-methylphenyl)-2-phenylthiazole (13abg)



13abg

Purification by PTLC (hexane/EtOAc = 10:1) gave **13abg** as a white solid (Method G: 91% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.33 (s, 3H), 3.80 (s, 3H), 6.84 (d, *J* = 8.3 Hz, 2H), 7.11 (d, *J* = 7.6 Hz, 2H), 7.31 (d, *J* = 8.9 Hz, 2H), 7.36–7.44 (m, 3H), 7.50 (d, *J* = 8.3 Hz, 2H), 7.99 (d, *J* = 6.8 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.3, 55.2, 114.1, 124.4, 126.3, 128.8, 128.88, 128.94, 129.7, 130.8, 132.2, 132.4, 133.7, 137.4, 150.3, 159.5, 164.7; HRMS (DART) *m/z* = 358.1266 calcd for $C_{23}H_{20}NOS$ $[M+H]^+$, found: 358.1269.

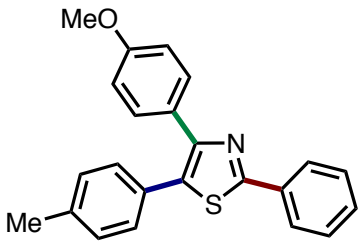
4-(4-Methoxyphenyl)-2,5-diphenylthiazole (13aga)



13aga

$[Pd(phen)_2](PF_6)_2$ (10 mol%) and Cs_2CO_3 (1.5 equiv) were used and the reaction was performed at 150°C for 18 h. Purification by PTLC (hexane/EtOAc = 10:1) gave **13aga** as a white solid (Method H': 42% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.81 (s, 3H), 6.84 (d, *J* = 8.9 Hz, 2H), 7.30–7.37 (m, 3H), 7.39–7.50 (m, 5H), 7.54 (d, *J* = 8.3 Hz, 2H), 8.01 (d, *J* = 6.2 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 55.2, 113.7, 126.4, 127.6, 128.0, 128.7, 128.9, 129.6, 129.9, 130.3, 131.8, 132.3, 133.7, 150.6, 159.2, 165.3; HRMS (DART) *m/z* = 344.1109 calcd for $C_{22}H_{18}NOS$ $[M+H]^+$, found: 344.1107.

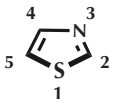
4-(4-Methoxyphenyl)-5-(4-methylphenyl)-2-phenylthiazole (13agb)

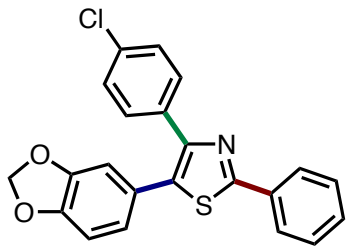


13agb

Purificcation by PTLC (hexane/EtOAc = 10:1) gave **13agb** as a white solid (Method H': 43% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.37 (s, 3H), 3.81 (s, 3H), 6.84 (d, *J* = 8.9 Hz, 2H), 7.14 (d, *J* = 7.6 Hz, 2H), 7.29 (d, *J* = 7.6 Hz, 2H), 7.39–7.47 (m, 3H), 7.55 (d, *J* = 8.9 Hz, 2H), 8.00 (d, *J* = 7.6 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.3, 55.2, 113.6, 126.3, 127.7, 128.8, 129.3, 129.40, 129.43, 129.8, 130.3, 132.0, 133.7, 138.0, 150.2, 159.2, 164.9; HRMS (DART) *m/z* = 358.1266 calcd for $C_{23}H_{20}NOS$ $[M+H]^+$, found: 358.1265.

5-(Benzo[*d*][1,3]dioxol-5-yl)-4-(4-chlorophenyl)-2-phenylthiazole (13ajh)

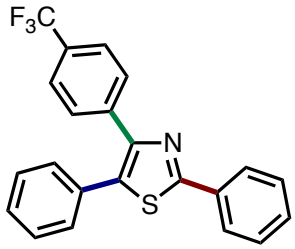




13ajh

Purification by PTLC (hexane/EtOAc 10:1) gave **13ajh** as a white solid (Method G: 87% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.99 (s, 2H), 6.77–6.84 (m, 2H), 6.87 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.28 (d, *J* = 8.9 Hz, 2H), 7.40–7.47 (m, 3H), 7.56 (d, *J* = 8.9 Hz, 2H), 7.97 (dd, *J* = 8.3, 1.4 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 101.4, 108.7, 109.8, 123.5, 125.2, 126.3, 128.5, 128.9, 130.0, 130.3, 133.2, 133.3, 133.4, 133.6, 147.86, 147.94, 149.1, 165.2; HRMS (DART) *m/z* = 392.0512 calcd for $C_{22}H_{15}ClNO_2S$ $[M+H]^+$, found: 392.0516.

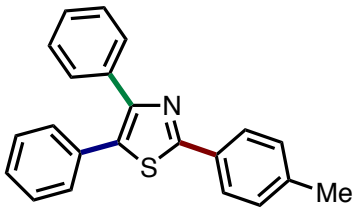
2,5-Diphenyl-4-(4-(trifluoromethyl)phenyl)thiazole (13aka)



13aka

$[Pd(phen)_2](PF_6)_2$ (10 mol%) and Cs_2CO_3 (1.5 equiv) were used and the reaction was performed at 150°C for 18 h. Purification by PTLC (hexane/EtOAc = 20:1) and GPC gave **13aka** as a white solid (Method H': 54% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35–7.43 (m, 5H), 7.44–7.52 (m, 3H), 7.55 (d, *J* = 8.3 Hz, 2H), 7.73 (d, *J* = 8.3 Hz, 2H), 8.01 (dd, *J* = 7.9, 1.4 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 124.2 (q, J_{C-F} = 270.2 Hz), 125.2 (q, J_{C-F} = 4.3 Hz), 126.4, 128.6, 129.0, 129.3, 129.58 (q, J_{C-F} = 33.1 Hz), 129.61, 130.2, 131.5, 133.3, 134.6, 138.4, 149.1, 166.0; There is one overlapping carbon signal as 1 peak is missing even with prolonged scans. HRMS (DART) *m/z* = 382.0877 calcd for $C_{22}H_{15}F_3NS$ $[M+H]^+$, found: 382.0878.

2-(4-Methylphenyl)-4,5-diphenylthiazole (13baa)

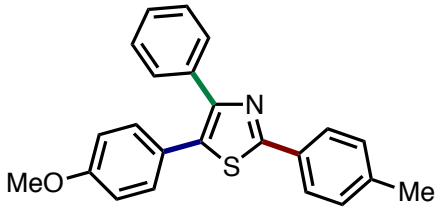


13baa

Purification by PTLC (hexane/EtOAc 20:1) gave **13baa** as white solid (Method H'': 76% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.39 (s, 3H), 7.24 (d, *J* = 7.6 Hz, 2H), 7.27–7.34 (m, 6H), 7.36–7.40 (m, 2H), 7.60 (dd,

J = 7.6, 1.4 Hz, 2H), 7.90 (d, *J* = 8.3 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.4, 126.3, 127.7, 128.0, 128.2, 128.7, 129.1, 129.5, 130.9, 132.1, 132.5, 135.0, 140.2, 150.6, 165.6; There is one overlapping carbon signal as 1 peak is missing even with prolonged scans. HRMS (DART) *m/z* = 328.1160 calcd for $C_{22}H_{18}NS$ $[M+H]^+$, found: 328.1158.

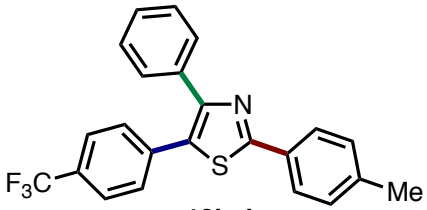
5-(4-Methoxyphenyl)-2-(4-methylphenyl)-4-phenylthiazole (13bag)



13bag

Purification by PTLC (hexane/EtOAc = 10:1) gave **13bag** as a white solid (Method G: 89% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.38 (s, 3H), 3.80 (s, 3H), 6.84 (d, *J* = 8.9 Hz, 2H), 7.23 (d, *J* = 8.3 Hz, 2H), 7.25–7.32 (m, 5H), 7.61 (d, *J* = 6.8 Hz, 2H), 7.89 (d, *J* = 8.3 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.4, 55.2, 114.1, 124.3, 126.3, 127.6, 128.2, 129.0, 129.5, 130.8, 131.1, 132.5, 135.2, 140.0, 150.0, 159.5, 165.0; HRMS (DART) *m/z* = 358.1266 calcd for $C_{23}H_{20}NOS$ $[M+H]^+$, found: 358.1264.

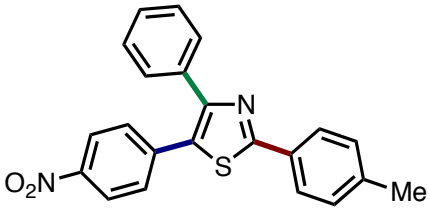
2-(4-Methylphenyl)-4-phenyl-5-(4-(trifluoromethyl)phenyl)thiazole (13bak)



13bak

Purification by PTLC (hexane/EtOAc = 10:1) gave **13bak** as a white solid (Method G: 63% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.40 (s, 3H), 7.26 (d, *J* = 8.2 Hz, 2H), 7.30–7.36 (m, 3H), 7.48 (d, *J* = 8.2 Hz, 2H), 7.56 (d, *J* = 8.2 Hz, 4H), 7.90 (d, *J* = 8.3 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.5, 124.0 (q, J_{C-F} = 270.2 Hz), 125.6 (q, J_{C-F} = 4.3 Hz), 126.4, 128.2, 128.5, 129.2, 129.6, 129.7, 129.8 (q, J_{C-F} = 31.6 Hz), 130.6, 130.7, 134.6, 136.0, 140.6, 151.8, 166.6; HRMS (DART) *m/z* = 396.1034 calcd for $C_{23}H_{17}F_3NS$ $[M+H]^+$, found: 396.1036.

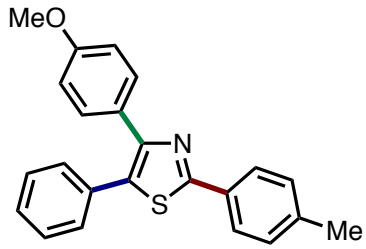
5-(4-Nitrophenyl)-2-(4-methylphenyl)-4-phenylthiazole (13baq)



13baq

Purification by PTLC (hexane/EtOAc 5:1) and GPC gave **13baq** as a yellow solid (Method G: 61% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.41 (s, 3H), 7.27 (d, *J* = 8.2 Hz, 2H), 7.33–7.37 (m, 3H), 7.51 (d, *J* = 8.9 Hz, 2H), 7.55 (dd, *J* = 7.6, 2.0 Hz, 2H), 7.91 (d, *J* = 7.6 Hz, 2H), 8.15 (d, *J* = 8.9 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.5, 124.0, 126.5, 128.56, 128.62, 129.2, 129.7, 130.0, 130.4, 134.3, 139.1, 141.0, 147.0, 152.8, 167.3; There is one overlapping carbon signal as 1 peak is missing even with prolonged scans. HRMS (DART) *m/z* = 373.1011 calcd for $C_{22}H_{17}N_2O_2S$ $[M+H]^+$, found: 373.1011.

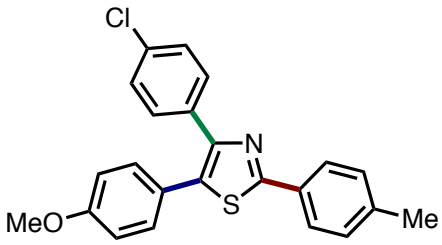
4-(4-Methoxyphenyl)-2-(4-methylphenyl)-5-phenylthiazole (13bga)



13bga

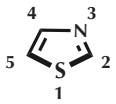
Purification by PTLC (hexane/EtOAc = 10:1) gave **13bga** as a white solid (Method H': 37% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.40 (s, 3H), 3.81 (s, 3H), 6.84 (d, *J* = 8.9 Hz, 2H), 7.25 (d, *J* = 7.6 Hz, 2H), 7.30–7.36 (m, 3H), 7.39 (dd, *J* = 7.6, 1.4 Hz, 2H), 7.53 (d, *J* = 8.9 Hz, 2H), 7.90 (d, *J* = 8.3 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.4, 55.2, 113.7, 126.3, 127.7, 127.9, 128.7, 129.5, 129.6, 130.3, 131.0, 131.2, 132.4, 140.1, 150.4, 159.2, 165.4; HRMS (DART) *m/z* = 358.1266 calcd for $C_{23}H_{20}NOS$ $[M+H]^+$, found: 358.1267.

4-(4-Chlorophenyl)-5-(4-methoxyphenyl)-2-(4-methylphenyl)thiazole (13bjg)



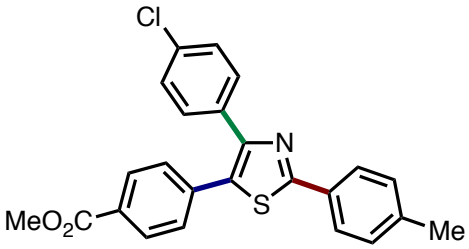
13bjg

Purification by GPC gave **13bjg** as a white solid (Method H': 64% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.39 (s, 3H), 3.82 (s, 3H), 6.86 (dd, *J* = 8.6, 1.4 Hz, 2H), 7.17–7.30 (m, 6H), 7.54 (dd, *J* = 8.3, 2.0 Hz, 2H),



7.87 (dd, J = 7.9, 1.4 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.4, 55.3, 114.3, 123.9, 126.2, 128.4, 129.6, 130.3, 130.8, 130.9, 132.9, 133.4, 133.6, 140.2, 148.7, 159.6, 165.3; HRMS (DART) m/z = calcd 392.0876 for $C_{23}H_{19}ClNOS$ $[M+H]^+$, found: 392.0880.

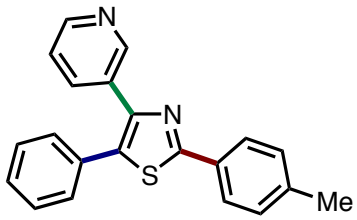
Methyl 4-(4-(4-chlorophenyl)-2-(4-methylphenyl)thiazol-5-yl)benzoate (13bjn)



13bjn

Purification by GPC gave **13bjn** as a light yellow solid (Method G: 51% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.40 (s, 3H), 3.93 (s, 3H), 7.26 (d, J = 7.6 Hz, 2H), 7.29 (d, J = 8.3 Hz, 2H), 7.43 (d, J = 8.2 Hz, 2H), 7.51 (d, J = 8.3 Hz, 2H), 7.89 (d, J = 7.9 Hz, 2H), 8.00 (d, J = 8.3 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.4, 52.2, 126.4, 128.6, 129.4, 129.6, 129.7, 130.0, 130.4, 130.6, 131.5, 133.1, 134.0, 136.6, 140.7, 150.3, 166.4, 166.7; HRMS (DART) m/z = calcd 420.0825 for $C_{24}H_{19}ClNO_2S$ $[M+H]^+$, found: 420.0825.

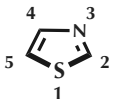
2-(4-Methylphenyl)-5-phenyl-4-(3-pyridyl)thiazole (13bta)

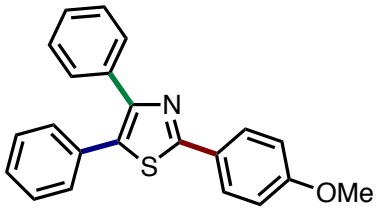


13bta

$[Pd(phen)_2](PF_6)_2$ (10 mol%) and Cs_2CO_3 (1.5 equiv) were used and the reaction was performed at 150°C for 18 h. Purification by PTLC (hexane/EtOAc = 2:1) gave **13bta** as a light yellow solid (Method H': 28% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.42 (s, 3H), 7.24 (dd, J = 7.9, 4.8 Hz, 1H) 7.27 (d, J = 7.9 Hz, 2H), 7.33–7.40 (m, 5H), 7.88–7.94 (m, 3H), 8.52 (dd, J = 4.8, 1.4 Hz, 1H), 8.83 (d, J = 1.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.5, 123.1, 126.3, 128.6, 129.0, 129.5, 129.7, 130.7, 131.0, 131.4, 134.0, 136.2, 140.6, 147.4, 148.6, 150.0, 166.5; HRMS (DART) m/z = 329.1112 calcd for $C_{21}H_{17}N_2S$ $[M+H]^+$, found: 329.1110.

2-(4-Methoxyphenyl)-4,5-diphenylthiazole (13gaa)

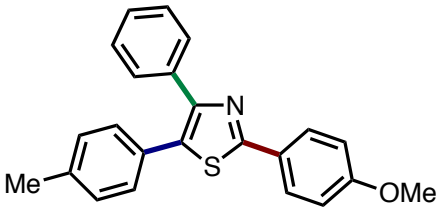




13gaa

Purification by PTLC (hexane/EtOAc = 10:1) gave **13gaa** as a white solid (Method H'': 68% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.85 (s, 3H), 6.96 (d, J = 8.9 Hz, 2H), 7.26–7.34 (m, 6H), 7.36–7.40 (m, 2H), 7.59 (dd, J = 7.6, 1.4 Hz, 2H), 7.95 (d, J = 8.9 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 55.4, 114.2, 126.6, 127.7, 127.9, 128.0, 128.2, 128.7, 129.1, 129.5, 132.1, 132.2, 135.0, 150.5, 161.1, 165.4; HRMS (DART) m/z = 344.1109 calcd for $C_{22}H_{18}NOS$ $[M+H]^+$, found: 344.1106.

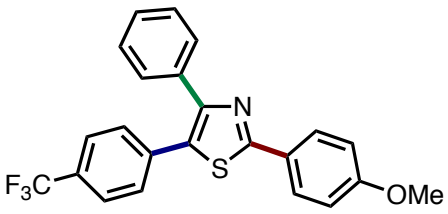
2-(4-Methoxyphenyl)-5-(4-methylphenyl)-4-phenylthiazole (13gab)



13gab

Purification by PTLC (hexane/EtOAc = 10:1) gave **13gab** as a white solid (Method H'': 79% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.35 (s, 3H), 3.85 (s, 3H), 6.95 (d, J = 8.9 Hz, 2H), 7.12 (d, J = 8.3 Hz, 2H), 7.25–7.32 (m, 5H), 7.60 (d, J = 6.9 Hz, 2H), 7.94 (d, J = 8.9 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.3, 55.4, 114.2, 126.6, 127.6, 127.8, 128.2, 129.1, 129.2, 129.4, 132.3, 135.2, 137.9, 150.1, 161.0, 165.0; There is one overlapping carbon signal as 1 peak is missing even with prolonged scans. HRMS (DART) m/z = 358.1266 calcd for $C_{23}H_{20}NOS$ $[M+H]^+$, found: 358.1267.

2-(4-Methoxyphenyl)-4-phenyl-5-(4-(trifluoromethyl)phenyl)thiazole (13gak)

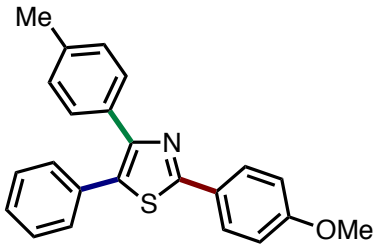


13gak

$[Pd(phen)_2](PF_6)_2$ (10 mol%) and Cs_2CO_3 (1.5 equiv) were used and the reaction was performed at 150°C for 18 h. Purification by PTLC (hexane/EtOAc = 10:1) gave **13gak** as a light yellow solid (Method H': 54% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.87 (s, 3H), 6.97 (d, J = 8.6 Hz, 2H), 7.31–7.36 (m, 3H), 7.48 (d, J = 8.2 Hz, 2H), 7.56 (d, J = 7.9 Hz, 4H), 7.95 (d, J = 8.6 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 55.4, 114.3, 124.0 (q, J_{C-F} = 271.7 Hz), 125.6 (q, J_{C-F} = 4.3 Hz), 126.3, 128.0, 128.2, 128.5, 129.2, 129.7, 129.8 (q,

J_{C-F} = 31.6 Hz), 130.2, 134.7, 136.1. 151.7, 161.4, 166.3; HRMS (DART) *m/z* = 412.0983 calcd for $C_{23}H_{17}F_3NOS$ $[M+H]^+$, found: 412.0994.

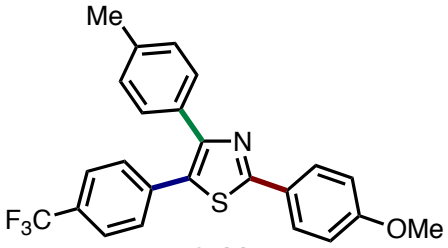
2-(4-Methoxyphenyl)-4-(4-methylphenyl)-5-phenylthiazole (13gba)



13gba

Purification by PTLC (hexane/EtOAc = 10:1) gave **13gba** as a white solid (Method G: 86% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.33 (s, 3H), 3.83 (s, 3H), 6.94 (d, *J* = 8.9 Hz, 2H), 7.10 (d, *J* = 8.3 Hz, 2H), 7.27–7.33 (m, 3H), 7.38 (dd, *J* = 7.6, 1.4 Hz, 2H), 7.48 (d, *J* = 7.6 Hz, 2H), 7.94 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.2, 55.3, 114.2, 126.7, 127.8, 128.6, 128.92, 128.94, 129.5, 131.4, 132.2, 132.4, 137.5, 150.5, 161.1, 165.2; There is one overlapping carbon signal as 1 peak is missing even with prolonged scans. HRMS (DART) *m/z* = 358.1266 calcd for $C_{23}H_{20}NOS$ $[M+H]^+$, found: 358.1265.

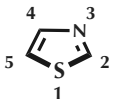
2-(4-Methoxyphenyl)-4-(4-methylphenyl)-5-(4-(trifluoromethyl)phenyl)thiazole (13gbk)

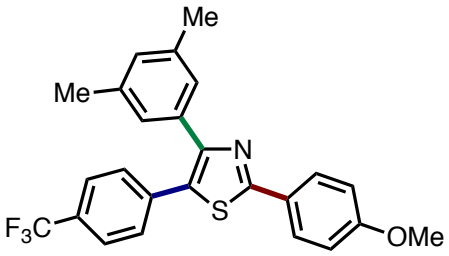


13gbk

Purificatio by PTLC (hexane/EtOAc = 10:1) gave **13gbk** as a white solid (Method G: 88% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.35 (s, 3H), 3.84 (s, 3H), 6.94 (d, *J* = 8.3 Hz, 2H), 7.13 (d, *J* = 8.2 Hz, 2H), 7.44 (d, *J* = 8.2 Hz, 2H), 7.46 (d, *J* = 8.2 Hz, 2H), 7.54 (d, *J* = 8.2 Hz, 2H), 7.93 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.3, 55.4, 114.2, 124.0 (q, J_{C-F} = 271.7 Hz), 125.6 (q, J_{C-F} = 2.9 Hz), 126.3, 128.0, 129.0, 129.2, 129.55, 129.61 (q, J_{C-F} = 31.7 Hz), 129.64, 131.7, 136.2, 138.0, 151.7, 161.3, 166.1; HRMS (DART) *m/z* = 426.1139 calcd for $C_{24}H_{19}F_3NOS$ $[M+H]^+$, found: 426.1135.

2-(4-Methoxyphenyl)-4-(3,5-dimethylphenyl)-5-(4-(trifluoromethyl)phenyl)thiazole (13gek)

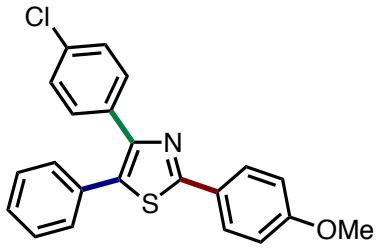




13gek

Purification by PTLC (hexane/EtOAc = 10:1) and GPC gave **13gek** as a white solid (Method H': 42% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.26 (s, 6H), 3.87 (s, 3H), 6.95–6.99 (m, 3H), 7.15 (s, 2H), 7.48 (d, J = 8.3 Hz, 2H), 7.55 (d, J = 8.3 Hz, 2H), 7.96 (d, J = 8.9 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.3, 55.4, 114.3, 124.0 (q, $J_{C–F}$ = 270.2 Hz), 125.5 (q, $J_{C–F}$ = 4.3 Hz), 126.3, 126.9, 128.0, 129.59, 129.60 (q, $J_{C–F}$ = 34.5 Hz), 129.9, 134.5, 136.2, 138.0, 152.1, 161.3, 166.1; There is one overlapping carbon signal as 1 peak is missing even with prolonged scans. HRMS (DART) m/z = 440.1296 calcd for $C_{25}H_{21}F_3NOS$ $[M+H]^+$, found: 440.1295.

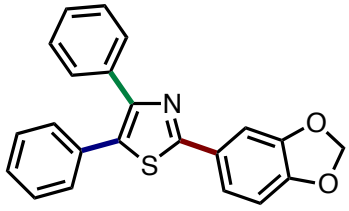
4-(4-Chlorophenyl)-2-(4-methoxyphenyl)-5-phenylthiazole (13gja)



13gja

Purification by PTLC (hexane/EtOAc = 10:1) gave **13gja** as a white solid (Method I: 90% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.86 (s, 3H), 6.96 (d, J = 8.9 Hz, 2H), 7.26 (d, J = 8.9 Hz, 2H), 7.31–7.38 (m, 5H), 7.53 (d, J = 8.3 Hz, 2H), 7.93 (d, J = 8.9 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 55.4, 114.2, 126.4, 127.9, 128.2, 128.4, 128.8, 129.5, 130.4, 131.9, 132.4, 133.5, 133.6, 149.2, 161.2, 165.6; HRMS (DART) m/z = 378.0719 calcd for $C_{22}H_{17}ClNOS$ $[M+H]^+$, found: 378.0719.

2-(4-Chlorophenyl)-4-(4-Methoxyphenyl)-5-(4-methylphenyl)thiazole (13haa)

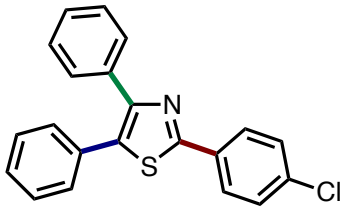


13haa

Purification by PTLC (hexane/EtOAc = 10:1) gave **13haa** as a light yellow solid (Method I: 63% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.02 (s, 2H), 6.86 (d, J = 7.6 Hz, 1H), 7.27–7.34 (m, 6H), 7.35–7.39 (m, 2H),

7.50 (dd, J = 8.2, 2.0 Hz, 1H), 7.54 (d, J = 2.0 Hz, 1H), 7.58 (dd, J = 7.6, 2.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 101.5, 106.7, 108.5, 120.9, 127.8, 128.06, 128.11, 128.2, 128.7, 129.1, 129.6, 132.1, 132.3, 134.9, 148.2, 149.2, 150.4, 165.1; HRMS (DART) m/z = 358.0902 calcd for $C_{22}H_{16}NO_2S$ $[M+H]^+$, found: 358.0903.

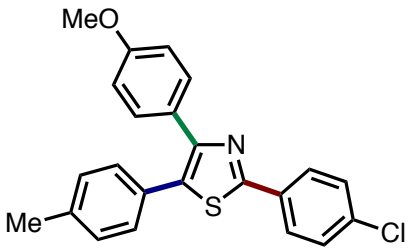
2-(4-Chlorophenyl)-4,5-diphenylthiazole (13jaa)



13jaa

Purification by PTLC (hexane/EtOAc = 20:1) gave **13jaa** as a light yellow solid (Method H'': 58% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.27–7.35 (m, 6H), 7.38 (dd, J = 6.9, 2.8 Hz, 2H), 7.41 (d, J = 8.9 Hz, 2H), 7.58 (dd, J = 8.2, 1.4 Hz, 2H), 7.94 (d, J = 8.2 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 127.5, 127.9, 128.26, 128.29, 128.7, 129.05, 129.09, 129.5, 131.8, 132.1, 133.4, 134.7, 135.8, 150.9, 164.0; HRMS (DART) m/z = 348.0614 calcd for $C_{21}H_{15}ClNS$ $[M+H]^+$, found: 344.0615.

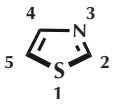
2-(4-Chlorophenyl)-4-(4-Methoxyphenyl)-5-(4-methylphenyl)thiazole (13jgb)

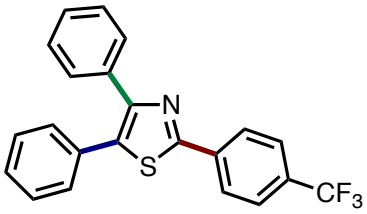


13jgb

Purification by PTLC (hexane/EtOAc = 10:1) gave **13jgb** as a light yellow solid (Method I: 46% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.37 (s, 3H), 3.81 (s, 3H), 6.84 (d, J = 8.3 Hz, 2H), 7.14 (d, J = 7.6 Hz, 2H), 7.28 (d, J = 8.3 Hz, 2H), 7.41 (d, J = 8.9 Hz, 2H), 7.53 (d, J = 8.9 Hz, 2H), 7.93 (d, J = 8.3 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.3, 55.2, 113.7, 127.47, 127.50, 129.0, 129.1, 129.4, 129.5, 130.3, 132.2, 132.3, 135.7, 138.1, 150.4, 159.2, 163.5; HRMS (DART) m/z = 392.0876 calcd for $C_{23}H_{19}ClNOS$ $[M+H]^+$, found: 392.0876.

4,5-Diphenyl-2-(4-(trifluoromethyl)phenyl)thiazole (13kaa)

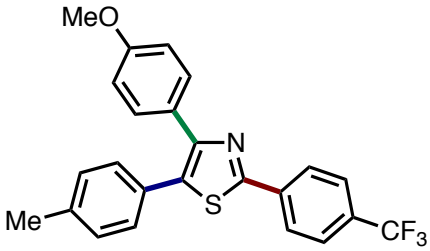




13kaa

Purification by PTLC (hexane/EtOAc = 20:1) gave **13kaa** as a white solid (Method H'': 80% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.28–7.36 (m, 6H), 7.37–7.41 (m, 2H), 7.59 (dd, J = 7.6, 2.0 Hz, 2H), 7.70 (d, J = 8.2 Hz, 2H), 8.12 (d, J = 8.2 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 123.9 (q, $J_{C–F}$ = 270.2 Hz), 125.9 (q, $J_{C–F}$ = 2.9 Hz), 126.5, 128.0, 128.3, 128.4, 128.8, 129.1, 129.6, 131.5 (q, $J_{C–F}$ = 31.6 Hz), 131.6, 134.3, 134.6, 136.7, 151.3, 163.4; HRMS (DART) m/z = 382.0877 calcd for $C_{22}H_{15}F_3NS$ $[M+H]^+$, found: 382.0878.

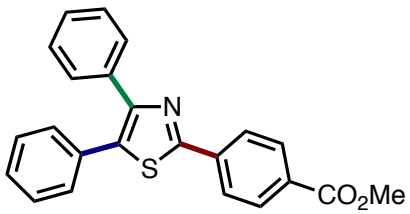
4-(4-Methoxyphenyl)-5-(4-methylphenyl)-2-(4-(trifluoromethyl)phenyl)thiazole (13kgb)



13kgb

Purification by PTLC (hexane/EtOAc = 10:1) gave **13kgb** as a light yellow solid (Method H'': 80% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.38 (s, 3H), 3.82 (s, 3H), 6.86 (d, J = 8.9 Hz, 2H), 7.16 (d, J = 8.2 Hz, 2H), 7.29 (d, J = 8.3 Hz, 2H), 7.54 (d, J = 8.9 Hz, 2H), 7.70 (d, J = 8.2 Hz, 2H), 8.11 (d, J = 8.3 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.3, 55.2, 113.7, 124.0 (q, $J_{C–F}$ = 273.1 Hz), 125.9 (q, $J_{C–F}$ = 4.3 Hz), 126.5, 127.3, 128.9, 129.4, 129.5, 130.3, 131.3 (q, $J_{C–F}$ = 33.1 Hz), 133.2, 136.8, 138.3, 150.8, 159.4, 162.9; HRMS (DART) m/z = 426.1139 calcd for $C_{24}H_{19}F_3NOS$ $[M+H]^+$, found: 426.1137.

Methyl 4-(4,5-diphenylthiazol-2-yl)benzoate (13naa)

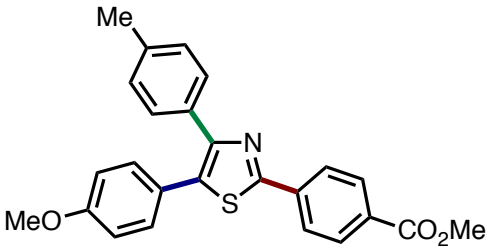


13naa

Purification by PTLC (hexane/EtOAc = 10:1) gave **13naa** as a light yellow solid (Method I: 45% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.95 (s, 3H), 7.29–7.36 (m, 6H), 7.39 (dd, J = 6.8, 2.0 Hz, 2H), 7.60 (dd, J = 7.6, 2.0 Hz, 2H), 8.08 (d, J = 8.9 Hz, 2H), 8.12 (d, J = 8.2 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 52.3, 126.2, 128.0, 128.3, 128.4, 128.8, 129.1, 129.6, 130.2, 131.1, 131.7, 134.3, 134.6, 137.4, 151.3, 163.9, 166.5;

HRMS (DART) *m/z* = 372.1058 calcd for $C_{23}H_{18}NO_2S$ $[M+H]^+$, found: 372.1060.

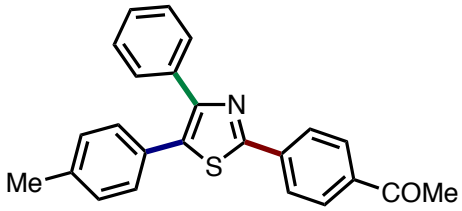
Methyl 4-(5-(4-Methoxyphenyl)-4-(4-methylphenyl)thiazol-2-yl)benzoate (13nbg)



13nbg

Purification by PTLC (hexane:EtOAc = 5:1) gave **13ngb** as a yellow solid (Method I: 87% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.35 (s, 3H), 3.82 (s, 3H), 3.94 (s, 3H), 6.87 (d, *J* = 8.2 Hz, 2H), 7.12 (d, *J* = 7.6 Hz, 2H), 7.31 (d, *J* = 8.3 Hz, 2H), 7.50 (d, *J* = 7.6 Hz, 2H), 8.06 (d, *J* = 8.9 Hz, 2H), 8.10 (d, *J* = 8.3 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.3, 52.2, 55.3, 114.2, 124.0, 126.1, 128.9, 129.0, 130.2, 130.78, 130.84, 132.0, 133.7, 137.59, 137.64, 150.9, 159.6, 163.1, 166.6; HRMS (DART) *m/z* = 416.1320 calcd for $C_{25}H_{22}NO_3S$ $[M+H]^+$, found: 416.1320.

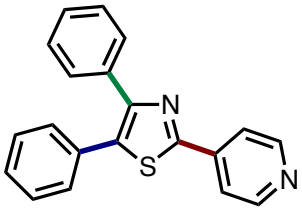
2-(4-Acetylphenyl)-5-(4-methylphenyl)-4-phenylthiazole (13oab)



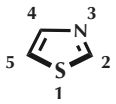
13oab

Purification by PTLC (hexane/EtOAc = 3:1) gave **13oab** as a yellow solid (Method I: 82% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.37 (s, 3H), 2.63 (s, 3H), 7.14 (d, *J* = 8.2 Hz, 2H), 7.28 (d, *J* = 8.2 Hz, 2H), 7.29–7.35 (m, 3H), 7.61 (dd, *J* = 7.6, 1.4 Hz, 2H), 8.02 (d, *J* = 8.2 Hz, 2H), 8.09 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.3, 26.7, 126.3, 127.9, 128.3, 128.6, 129.0, 129.1, 129.4, 129.5, 134.7, 134.8, 137.6, 137.7, 138.4, 151.1, 163.4, 197.3; HRMS (DART) *m/z* = 370.1266 calcd for $C_{24}H_{20}NOS$ $[M+H]^+$, found: 370.1264.

4,5-Diphenyl-2-(4-pyridyl)thiazole (13uaa)

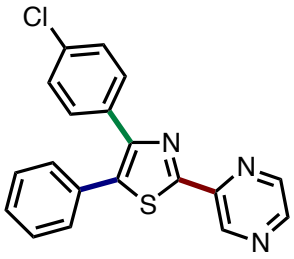


13uaa



Purification by PTLC (hexane/EtOAc = 2:1) gave **13uaa** as a light yellow solid (Method H'': 53% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30–7.37 (m, 6H), 7.40 (dd, *J* = 6.9, 2.8 Hz, 2H), 7.59 (dd, *J* = 8.3, 1.4 Hz, 2H), 7.86 (dd, *J* = 6.4, 2.0 Hz, 2H), 8.72 (dd, *J* = 6.4, 2.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 120.1, 128.1, 128.4, 128.6, 128.8, 129.0, 129.6, 131.4, 134.4, 135.0, 140.2, 150.6, 151.6, 162.3; HRMS (DART) *m/z* = 315.0956 calcd for $C_{20}H_{15}N_2S$ $[M+H]^+$, found: 315.0959.

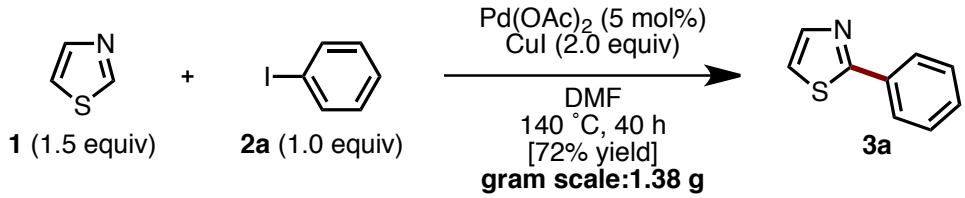
4-(4-Chlorophenyl)-5-phenyl-2-(2-pyrazin-2-yl)thiazole (13vja)



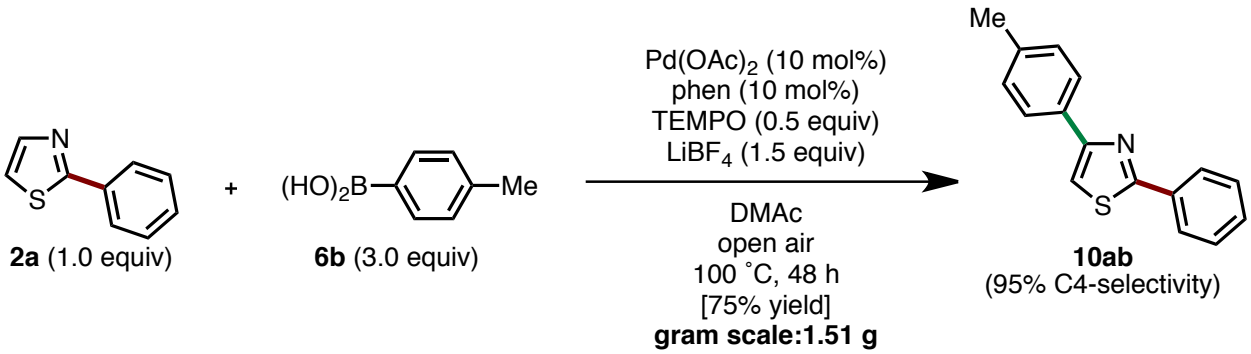
13vja

Purification by PTLC (hexane/EtOAc = 3:1) gave **13vja** as a light yellow oil (Method I: 86% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.3 Hz, 2H), 7.32–7.42 (m, 5H), 7.54 (d, *J* = 8.3 Hz, 2H), 8.56 (d, *J* = 1.4 Hz, 1H), 8.61 (d, *J* = 2.0 Hz, 1H), 9.50 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 128.6, 128.8, 129.0, 129.5, 130.3, 131.4, 133.0, 134.0, 137.0, 141.4, 143.8, 145.1, 146.8, 150.4, 163.7; HRMS (DART) *m/z* = 350.0519 calcd for $C_{19}H_{13}ClN_3S$ $[M+H]^+$, found: 350.0519.

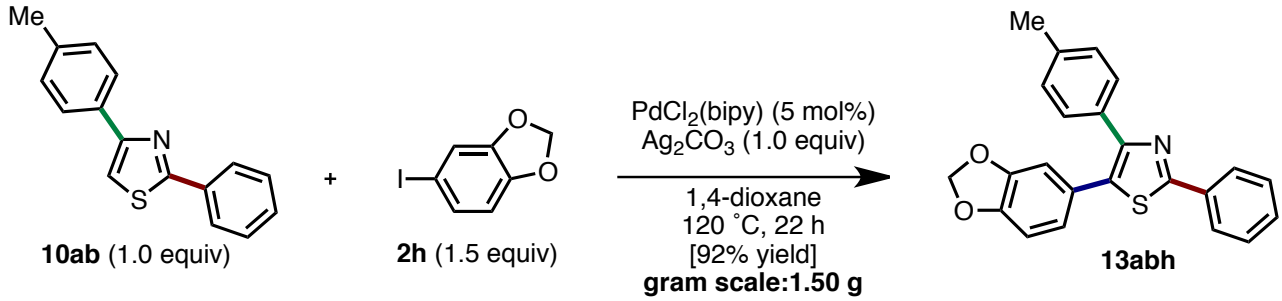
Gram Scale Synthesis of Triarylthiazole



A 50-mL sealed tube vessel were added $Pd(OAc)_2$ (134.8 mg, 0.6 mmol, 5 mol%), CuI (4.57 g, 24 mmol, 2 equiv), iodobenzene (**2a**: 2.45 g, 12 mmol, 1.0 equiv), thiazole (**1**: 1.53 g, 18 mmol, 1.5 equiv) and DMF (24 mL). The vessel was sealed and then stirred at 140 °C for 40 h. After cooling the reaction mixture to room temperature, the mixture was quenched with 1M NaOH aq. (15 mL), neutralized by sat. NH_4Cl aq. (10 mL), and added water (25 mL) and EtOAc (50 mL). The mixture was extracted by EtOAc (50 mL × 2), combined organic layer was washed with water (50 mL × 2) and brine (50 mL), dried over Na_2SO_4. The organic layer was evaporated and the residue was purified by flash column chromatography to afford 2-phenylthiazole (**3a**). Finally, distillation gave desired product (Method A: 1.38 g, 72% yield) as a colorless oil.



A 100-mL flask, containing a magnetic stirring bar, was added $Pd(OAc)_2$ (179.6 mg, 0.8 mmol, 10 mol%), 1,10-phenanthroline (144.2 mg, 0.8 mmol, 10 mol%), 4-methylphenylboronic acid (**6b**: 3.26 g, 24 mmol, 3 equiv), $LiBF_4$ (1.13 g, 12 mmol, 1.5 equiv), TEMPO (613 mg, 4 mmol, 0.5 equiv), the corresponding 2-phenylthiazole (**2a**: 1.29 g, 8 mmol, 1.0 equiv) and undried DMAc (16 mL). The vessel was equipped with vigreux column (for open air condition) and then stirred at 100 °C for 48 h under air. After cooling the reaction mixture to room temperature, the mixture was added water (40 mL) and EtOAc (40 mL). After further more extraction by EtOAc (40 mL × 2), combined organic layer was washed with water (40 mL × 2) and brine (40 mL), dried over Na_2SO_4. The organic layer was evaporated and the residue was purified by flash column chromatography to afford **10ab** (Method F: 1.51 g, 75% yield) as a light yellow solid.



A 100-mL sealed tube, containing a magnetic stirring bar, was flame-dried under vacuum and filled with argon after cooling to room temperature. To this vessel were added $PdCl_2$(bipy) (75.2 mg, 0.23 mmol, 5 mol%), Ag_2CO_3 (1.25 g, 4.5 mmol, 1.0 equiv), 5-iodobenzo[*d*][1,3]dioxole (**2h**: 1.67 g, 6.75 mmol, 1.5 equiv), **10ab** (1.13 g, 4.5 mmol, 1.0 equiv) and 1,4-dioxane (18 mL, 0.2~0.25 M) under a stream of argon. The vessel was sealed and then stirred at 120 °C for 22 h. After cooling the reaction mixture to room temperature, the mixture was passed through a short silica gel pad (EtOAc). The filtrate was evaporated and the residue was purified by flash column chromatography to afford **13abh** as a light yellow solid (Method G: 1.50g, 92% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.33 (s, 3H), 5.94 (s, 2H), 6.75 (d, J = 8.3 Hz, 1H), 6.82 (s, 1H), 6.88 (d, J = 8.3 Hz, 1H), 7.11 (d, J = 7.6 Hz, 2H), 7.36–7.46 (m, 3H), 7.50 (d, J = 8.3 Hz, 2H), 7.97 (d, J = 6.9 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.3, 101.3, 108.6, 109.9, 123.5, 125.7, 126.3, 128.8, 128.9, 129.0, 129.8, 132.0, 132.2, 133.6, 137.5, 147.6, 147.8, 150.5, 164.8; HRMS (DART) m/z = 372.1058 calcd for $C_{23}H_{18}NO_2S$ $[M+H]^+$, found: 372.1058.