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Aryl–aryl coupling via palladium-catalyzed C–P/C–H bond cleavage

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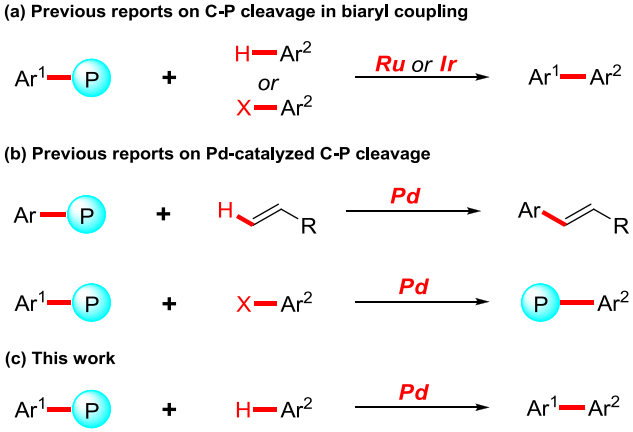
ABSTRACT

The first example of aryl–aryl coupling through palladium-catalyzed C–P/C–H bond cleavage with good functional group tolerance is disclosed. This work demonstrates the phosphines could be used as coupling partners in palladium-catalyzed aryl–aryl coupling.

1. Introduction

In the past several decades, transitional metal catalyzed[1] carbon (sp2)-carbon (sp2) cross-coupling reactions for building aryl–aryl scaffolds have been massively developed. In these reactions, phosphines have been commonly used as potent ligands,[2] due to their ability to accelerate the oxidative addition step and may also favor the transmetalation step.[3] In addition to their utilization as ligands, several reports suggested that phosphines could also be used as coupling partners providing aryl groups to substrates through C–P bond cleavage. For instance, it has been reported that ruthenium[4] or irinium[5] could cleave the C–P bond in triarylphosphines, which were used as aryl donors (Scheme 1a). Other than these expensive metals, the more cost-effective and commonly-used palladium has been reported to cleave the C–P bond in tetraphenylphosphonium salt giving alkenylated benzene in a Heck-type reaction (Scheme 1b).[6] Moreover, triarylphosphines has also been used as the phosphinating reagents in palladium-catalyzed phosphination for the preparation of various phosphine ligands (Scheme 1b).[7] Up to date,[8] few example of arylation of unpreactivated arenes or heteroarenes via palladium-catalyzed C–P bond cleavage, however, has been reported to the best of our knowledge (Scheme 1c).[9]

As a continuation of our previously works[10] on Pd(II)-catalyzed C(5)-H bond activation of azole-4-carboxylic derivatives,[11] we were originally focusing on the decarboxylative arylation.[3a,12] However, when we treated methyl oxazole-4-carboxylate (**1a**) with different benzoic acids under reaction conditions for decarboxylative arylation, only 5-phenyloxazole (**2a**) was obtained. We speculated that the phenyl group of **2a** was donated from triphenylphosphine (Ph_3P) rather than benzoic acids, suggesting this aryl–aryl coupling is realized via C–P bond cleavage. Recognizing the novelty of this process, here we report our findings about a new Pd-catalyzed aryl–aryl coupling reaction via C–P/C–H bond cleavage.



Scheme 1. Discovery of C–C coupling of heteroarenes with triarylphosphine as aryl donor.

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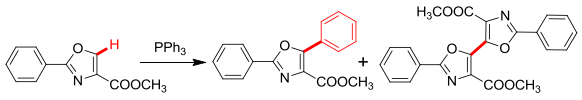
2. Results and discussion

Our initial investigation focused on the coupling of **1a** with Ph_3P as summarized in Table 1.[13] A preliminary trial using 1 equiv of Ph_3P without benzoic acid still afforded the C5-phenyl product **2a**, albeit in very low yield and most of **1a** was converted to homocoupling byproduct **3a** (entry 1). Subsequent screening on the additive revealed that the use of PivOH could remarkably increase the yield of the desired product **2a** to 42% (entry 2). Changing the reaction temperature, and the loading of Ag(I) and PivOH could generate **2a** in only moderate yield.[13] To our delight, screening on acidic additives indicated that the yield of **2a** could further rise to 70% while **3a** was not produced, when 2 equiv of TFA was used (entry 3). We then explored the reaction in various solvents, and found that NMP was the best choice (entry 4). Other palladium catalysts or other commonly used oxidants were shown to be less effective.[13] Changing loading of PPh_3 from 0.33 equiv to 1.5 equiv revealed that 0.66 equiv of PPh_3 showed no difference in the yield of **2a** but reacted faster, comparing to 1.5 equiv of PPh_3 (entries 5–10). This also suggested that at least two phenyl groups in one phosphine compound could be provided to the substrate, showing the promising efficiency of the triphenylphosphines as aryl donors. Replacing the PPh_3 with triphenylphosphine oxide provided no arylated product, which excluded the possibility that the C–P bond cleavage occurs on the phosphine oxide (entry 11). A control experiment without palladium catalyst showed that the palladium catalyst played an important role in this reaction (entry 12). Finally, the reaction conditions in entries 7 and 10 were selected for further investigation on the reaction scope.

Table 1
Optimization of reaction conditions[a]

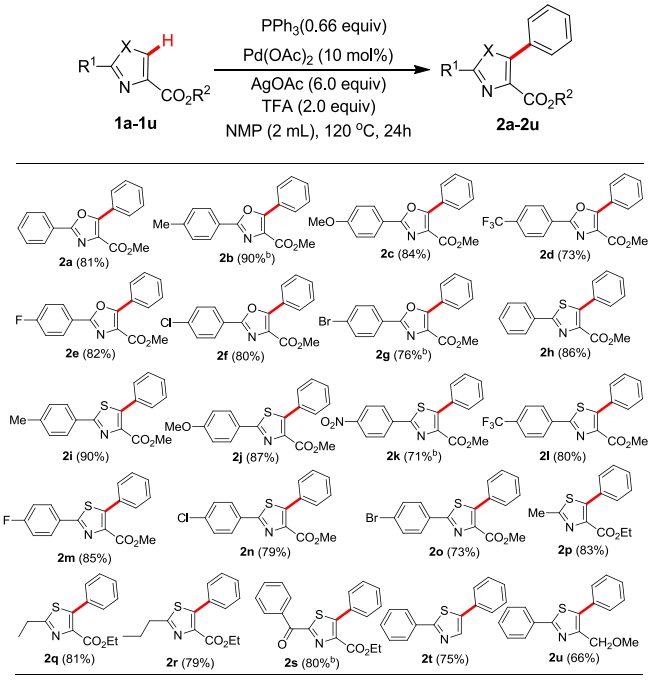


Entry	Ph_3P (equiv)	Additive (equiv)	Solvent	Yields (%) (**2a**/**3a**/**1a**)[b]
1	1	—	DMF	17/66/8
2	1	PivOH (2)	DMF	42/36/23
3[c]	1	TFA (2)	DMF	70/trace/23
4	1	TFA (2)	NMP	78/7/7
5	0.33	TFA (2)	NMP	52/40/0
6	0.5	TFA (2)	NMP	65/28/0
7	**0.66**	**TFA (2)**	**NMP**	**81/8/4**
8	1.2	TFA (2)	NMP	82/6/6
9	1.5	TFA (2)	NMP	72/6/17
10[d]	**1.5**	**TFA (2)**	**NMP**	**86/trace/7**
11[e]	1.5	TFA (2)	NMP	0/92/trace
12[d,f]	1.5	TFA (2)	NMP	0/0/95

[a] Reaction conditions: methyl 2-phenylthiazole-4-carboxylate **1a** (0.5 mmol), Ph_3P (1.5 mmol), $Pd(OAc)_2$ (0.05 mmol), AgOAc (3 mmol) and additive in DMF or NMP (2 mL) at 120 °C for 24 h.
[b] Isolated yields.
[c] Reacted at 140 °C.
[d] Reacted for 48 h.
[e] Ph_3P was replaced with triphenylphosphine oxide(Ph_3P=O).
[f] No palladium catalyst.

With the optimized conditions established, we first evaluated the coupling reactions of various azoles with PPh_3 as illustrated in Table 2, **2a**–**2u**.[14] Generally, both oxazole and thiazole substrates could afford the desired products in good to excellent yields. A wide range of substituents on azoles at C2 position were tolerated under these conditions. For 2-phenyloxazole substrates, electron-donating substitutions on phenyl group gave the corresponding products in excellent yields (**2b**, **2c**), while trifluoromethyl and halogen groups slightly declined the yields (**2d**–**2g**). It is noteworthy that the tolerance of chloro and bromo substituents might provide an opportunity for further synthetic functionalization. Similar patterns were observed on 2-phenyl substituted thiazoles (**2h**–**2o**). In addition, 2-alkyl or 2-carbonylsubstituted substrates could be phenylated in good yields (**2p**–**2s**) and the arylation of 2-phenylthiazole occurred selectively at C5-position (**2t**). Notably, 2-phenyl-4-methoxymethyl thiazole could also be phenylated to afford the corresponding product (**2u**) in moderate yield under the optimized conditions, while it was not efficiently arylated with unpreactivated benzene via double C–H cleavage.[10a]

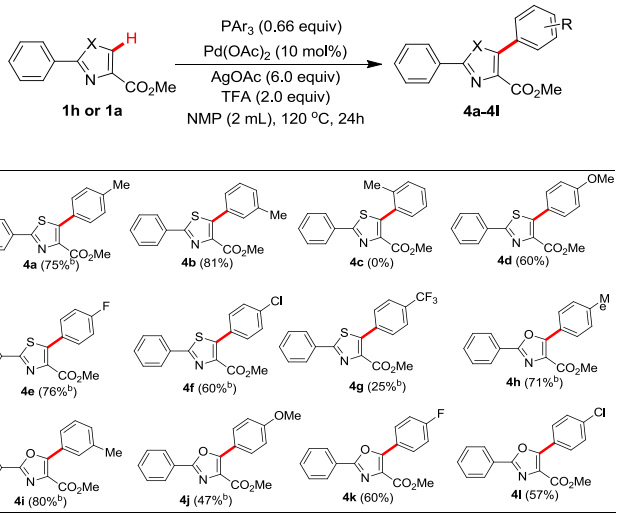
Table 2
Scope of azoles[a]



[a] Reaction conditions: azole (0.5 mmol), Ph_3P (0.33 mmol), $Pd(OAc)_2$ (0.05mmol), AgOAc (3 mmol) and TFA (1 mmol) in NMP (2 mL) at 120 °C for 24 h. Isolated yields. [b]1.5 equiv of Ph_3P was used, and reacted for 48 h.

Next, the effective conditions were extended to a variety of substituted triarylphosphines as illustrated in Table 3.[15] To our

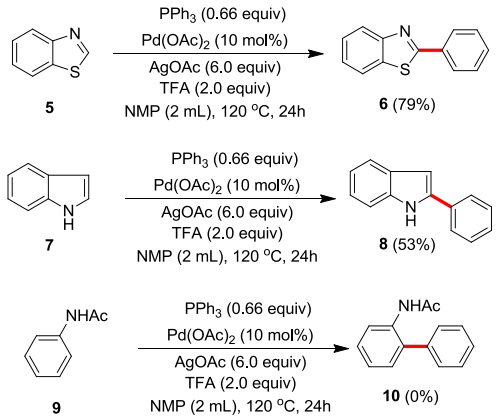
Table 3
Scope of triarylphosphines[a]



[a] Reaction conditions: azole (0.5 mmol), Ar_3P (0.33 mmol), $Pd(OAc)_2$ (0.05mmol), AgOAc (3 mmol) and TFA (1 mmol) in NMP (2 mL) at 120 °C for 24 h. Isolated yields. [b]1.5 equiv of Ar_3P was used, reacted for 48 h.

delight, most substituted triarylphosphines were well tolerated under the optimized conditions, leading to the desired products in moderate to good yields (**4a**, **4b**, **4d**–**4f**, **4h**–**4l**). For example, tri(*m*-methylphenyl)phosphine or tri(*p*-methylphenyl) phosphine afforded the corresponding products in good yields (**4a**, **4b**, **4h**, **4i**). When halogen or methoxyl substitutions were introduced on triarylphosphine, the desired products were achieved in moderate yields (**4d**–**4f**, **4j**–**4l**). Electron-withdrawing substitution on the benzene group of triarylphosphines, such as CF_3, led to the decrease in the yield of the phenylated product (**4g**). To our disappointed, the use of the sterically hindered triarylphosphine with *ortho*-methyl substitution failed to give the corresponding product (**4c**).

In addition, our protocol could be applied to other heteroarenes (Scheme 2). Benzothiazole (**5**) reacted smoothly to afford 2-phenylbenzothiazole (**6**) in 79% yield. Moreover, free indole (**7**) could be phenylated at C2 position to give the desired product **8** in 53% yield. Very interestingly, acetanilide (**9**), a typical model substrate for palladium catalyzed C–H bond activation, did not provide the desired arylated product (**10**).



Scheme 2. Phenylation of other heteroarenes via C–P cleavage.

3. Conclusion

In summary, we have discovered a novel palladium-catalyzed aryl–aryl cross-coupling reaction between triphenylphosphines and unpreactivated simple arenes through C(sp2)-P/C(sp2)-H bond cleavage. This is the first report that aryl–aryl coupling via C–P bond cleavage of phosphines could be catalyzed by a cost-effective palladium catalyst, rather than more expensive Ru or Ir catalysts. Further studies on the mechanism of this reaction are currently undergoing in our laboratory.

4. Experimental section

4.1. General information

Melting point (mp) was measured on a microscopic melting point apparatus. ^{1}H and ^{13}C NMR spectra were collected using $CDCl_3$ as solvent. Chemical shifts of ^{1}H NMR were recorded in parts per million (ppm, δ) relative to tetramethylsilane (δ=0.00 ppm) with the solvent resonance as an internal standard ($CDCl_3$: δ=7.26 ppm). Data are reported as follows: chemical shift in ppm (δ), multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, br s=broad singlet, m=multiplet), coupling constant (Hertz, Hz), and integration. Chemical shifts of ^{13}C NMR were reported in ppm with the solvent as the internal standard ($CDCl_3$: δ=77.0 ppm). Infrared spectra (IR) were recorded on an FT-IR spectrometer; absorptions are reported in reciprocal centimeters. High Resolution Mass measurement was performed on a Q-TOF mass spectrometer with electron spray ionization (ESI) as the ion source. All substrates were synthesized from corresponding aldehydes or nitriles by our recently disclosed methods.[16] Unless otherwise indicated, all reagents and solvents were obtained from commercial suppliers and used as received.

4.2. General experimental procedure

A suspension of $Pd(OAc)_2$ (10 mol %), Ar_3P (0.33 mmol or 0.75 mmol), AgOAc (3.0 mmol), TFA (1.0 mmol) and azole-4-carboxylates (0.5 mmol) in NMP (2 mL) was introduced to a Schlenk tube. After stirring at 120 °C under argon for 24 h (reactions with 0.33 mmol of Ph_3P), or 48 h (reactions with 0.75 mmol of Ph_3P), the reaction mixture was diluted with ethyl acetate, and then filtered through a pad of Celite. Volatiles were removed in vacuo to give the crude products, which was purified by flash column chromatography on silica gel to afford pure arylated products.

4.3. Characterization data of title compounds

4.3.1. Methyl 2,5-diphenyloxazole-4-carboxylate[10a] (***2a***). Yield 113 mg (81%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.97 (s, 3H), 7.47–7.49 (m, 6H), 8.13–8.16 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.7, 159.8, 155.3, 131.1, 130.4, 128.8, 128.5, 128.0, 127.0, 126.8, 126.3, 52.4 ppm.

4.3.2. Methyl 2-(p-methylphenyl)-5-phenyloxazole-4-carboxylate (***2b***). Yield 131 mg (90%). White solid, mp 109–100.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.39 (s, 3H), 3.97 (s, 3H), 7.27 (d, J=7.9 Hz, 2H), 7.45–7.51 (m, 3H), 8.03 (d, J=7.9 Hz, 2H), 8.14 (d, J=7.3 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.3, 159.5, 154.5, 141.1, 129.8, 129.0, 127.9, 127.3, 126.6, 126.3, 123.1, 51.9, 21.1 ppm; IR (KBr) 2944, 1721, 1562, 1502, 1216, 1097, 1011, 828, 769, 731, 690 cm^{-1}; HRMS (ESI) calcd for $[C_{18}H_{15}NO_3+H]^+$ 294.1125, found 294.1128.

4.3.3. Methyl 2-(p-methoxylphenyl)-5-phenyloxazole-4-carboxylate[10a] (***2c***). Yield 129 mg (84%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.82 (s, 3H), 3.95 (s, 3H), 6.96 (d, J=8.8 Hz, 2H), 7.40–7.50 (m, 3H), 8.05–8.13 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.8, 162.0, 159.9, 154.8, 130.2, 128.6, 128.4, 128.3, 127.8, 127.2, 119.0, 114.3, 55.4, 52.3 ppm.

4.3.4. Methyl 2-(p-trifluoromethylphenyl)-5-phenyloxazole-4-carboxylate[10a] (***2d***). Yield 126 mg (73%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.94 (s, 3H), 7.45–7.48 (m, 3H), 7.70 (d, J=8.2 Hz, 2H), 8.09–8.12 (m, 2H), 8.21 (d, J=8.2 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.3, 158.2, 155.8, 132.8, 132.4, 130.6, 129.4, 128.2, 127.0, 126.6, 125.9, 125.8, 125.7, 125.5, 121.9, 52.4 ppm.

4.3.5. Methyl 2-(p-fluorophenyl)-5-phenyloxazole-4-carboxylate (***2e***). Yield 121 mg (82%). White solid, mp 142–144 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.94 (s, 3H), 7.14 (t, J=8.6 Hz, 2H), 7.42–7.48 (m, 3H), 8.01–8.14 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.1, 161.8, 161.5, 157.9, 154.2, 129.4, 128.0, 127.9, 127.4, 126.9, 125.8, 121.6, 115.2, 114.9, 51.3 ppm; IR (KBr) 3062, 2950, 1726, 1612, 1500, 1363, 1222, 1107, 1012, 849, 734, 686 cm^{-1}; HRMS (ESI) calcd for $[C_{17}H_{12}FNO_3+H]^+$ 298.0880, found 298.0881.

4.3.6. Methyl 2-(p-chlorophenyl)-5-phenyloxazole-4-carboxylate[10a] (***2f***). Yield 125 mg (80%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.95 (s, 3H), 7.40–7.47 (m, 5H), 8.02–8.11 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.5, 158.8, 155.4, 137.3, 130.5, 129.2, 128.5, 128.4, 128.1, 126.8, 124.8, 52.4 ppm.

4.3.7. Methyl 2-(p-bromophenyl)-5-phenyloxazole-4-carboxylate (***2g***). Yield 135 mg (76%). White solid, mp 138–139 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.96 (s, 3H), 7.42–7.50 (m, 3H), 7.61 (d, J=8.5 Hz,

2H), 8.00 (d, *J*=8.5 Hz, 2H), 8.09–8.13 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.0, 158.4, 155.0, 131.6, 130.0, 128.0, 127.9, 127.7, 126.2, 125.3, 124.7, 52.0 ppm; IR (KBr) 2997, 2950, 1724, 1483, 1462, 1211, 1072, 1010, 827, 750, 689 cm^{-1}; HRMS (ESI) calcd for $[C_{17}H_{12}BrNO_3+H]^+$ 358.0073, found 358.0069.

4.3.8. Methyl 2,5-diphenylthiazole-4-carboxylate[10a] (***2h***). Yield 126 mg (86%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.86 (s, 3H), 7.41–7.46 (m, 6H), 7.53–7.57 (m, 2H), 7.96–8.00 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.3, 160.8, 144.5, 139.0, 130.9, 128.8, 128.4, 128.0, 127.4, 127.2, 126.4, 124.9, 50.4 ppm.

4.3.9. Methyl 2-(p-methylphenyl)-5-phenylthiazole-4-carboxylate[10a] (***2i***). Yield 139 mg (90%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.38 (s, 3H), 3.84 (s, 3H), 7.24 (d, *J*=8.2 Hz, 2H), 7.40–7.42 (m, 3H), 7.51–7.53 (m, 2H), 7.86 (d, *J*=8.2 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.3, 162.7, 146.0, 141.0, 140.7, 130.4, 130.1, 129.9, 129.7, 129.2, 128.3, 126.7, 52.3, 21.5 ppm.

4.3.10. Methyl 2-(p-methoxylphenyl)-5-phenylthiazole-4-carboxylate[10a] (***2j***). Yield 141 mg (87%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.83 (s, 3H), 3.84 (s, 3H), 6.95 (d, *J*=8.8 Hz, 2H), 7.40–7.43 (m, 3H), 7.51–7.54 (m, 2H), 7.91 (d, *J*=8.8 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.0, 162.8, 161.7, 145.5, 140.5, 130.5, 129.9, 129.2, 128.3, 128.2, 125.6, 114.3, 55.4, 52.2 ppm.

4.3.11. Methyl 2-(p-nitrophenyl)-5-phenylthiazole-4-carboxylate (***2k***). Yield 121 mg (71%). Yellow solid, mp 173–174 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.87 (s, 3H), 7.47–7.56 (m, 5H), 8.15 (d, *J*=8.7 Hz, 2H), 8.31 (d, *J*=8.7 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.9, 161.3, 147.8, 147.2, 137.1, 128.9, 128.8, 128.6, 127.4, 126.4, 123.4, 51.5 ppm; IR (KBr) 2943, 1726, 1596, 1513, 1345, 1209, 1018, 856, 751, 690 cm^{-1}; HRMS (ESI) calcd for $[C_{17}H_{12}N_2O_4S+H]^+$ 341.0596, found 341.0598.

4.3.12. Methyl 2-(p-trifluoromethylphenyl)-5-phenylthiazole-4-carboxylate[10a] (***2l***). Yield 145 mg (80%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.86 (s, 3H), 7.44–7.46 (m, 3H), 7.52–7.56 (m, 2H), 7.71 (d, *J*=8.2 Hz, 2H), 8.09 (d, *J*=8.2 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.1, 162.5, 147.4, 141.3, 135.8, 132.5, 132.0, 129.9, 129.6, 128.3, 127.0, 126.1, 126.0, 125.6, 122.0, 52.4 ppm.

4.3.13. Methyl 2-(p-fluorophenyl)-5-phenylthiazole-4-carboxylate[10a] (***2m***). Yield 133 mg (85%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.85 (s, 3H), 7.13 (t, *J*=8.6 Hz, 2H), 7.42–7.44 (m, 3H), 7.52–7.55 (m, 2H), 7.94–7.98 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.9, 164.9, 162.6, 146.4, 140.8, 130.1, 129.9, 129.3, 129.1, 128.8, 128.7, 128.3, 116.3, 116.0, 52.3 ppm.

4.3.14. Methyl 2-(p-chlorophenyl)-5-phenylthiazole-4-carboxylate[10a] (***2n***). Yield 130 mg (79%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.85 (s, 3H), 7.40–7.44 (m, 5H), 7.51–7.55 (m, 2H), 7.90 (d, *J*=8.6 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.7, 162.5, 146.6, 141.0, 136.7, 131.2, 130.1, 129.9, 129.4, 129.3, 128.3, 127.9, 52.3 ppm.

4.3.15. Methyl 2-(p-bromophenyl)-5-phenylthiazole-4-carboxylate[10a] (***2o***). Yield 136 mg (73%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.85 (s, 3H), 7.42–7.44 (m, 3H), 7.51–7.54 (m, 2H), 7.57 (d, *J*=8.5 Hz, 2H), 7.84 (d, *J*=8.5 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.7, 162.5, 146.6, 141.0, 132.2, 131.6, 130.1, 129.9, 129.4, 128.3, 128.1, 125.0, 52.3 ppm.

4.3.16. Ethyl 2-methyl-5-phenylthiazole-4-carboxylate (***2p***). Yield 96 mg (83%). Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.22 (t, *J*=7.1 Hz, 3H), 2.74 (s, 3H), 4.28 (q, *J*=7.1 Hz, 2H), 7.38–7.40 (m, 3H), 7.42–7.47 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.8, 161.5, 145.7, 139.5, 130.1, 129.4, 128.5, 127.6, 60.7, 18.7, 13.6 ppm; IR (KBr) 2967, 2925, 1716, 1477, 1325, 1202, 1037, 745, 688 cm^{-1}; HRMS (ESI) calcd for $[C_{13}H_{13}NO_2S+H]^+$ 248.0745, found 248.0747.

4.3.17. Ethyl 2-ethyl-5-phenylthiazole-4-carboxylate (***2q***). Yield 100 mg (81%). Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.21 (t, *J*=7.1 Hz, 3H), 1.41 (t, *J*=7.6 Hz, 3H), 3.07 (q, *J*=7.6 Hz, 2H), 4.27 (q, *J*=7.1 Hz, 2H), 7.37–7.40 (m, 3H), 7.44–7.47 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.8, 161.6, 145.1, 139.5, 130.3, 129.4, 128.4, 127.5, 60.6, 26.6, 13.8, 13.5 ppm; IR (KBr) 3003, 2979, 1720, 1476, 1276, 1260, 1190, 1025, 722, 739 cm^{-1}; HRMS (ESI) calcd for $[C_{14}H_{15}NO_2S+H]^+$ 262.0896, found 262.0896.

4.3.18. Ethyl 2-propyl-5-phenylthiazole-4-carboxylate (***2r***). Yield 108 mg (79%). Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.04 (t, *J*=7.5 Hz, 3H), 1.20 (t, *J*=7.1 Hz, 3H), 1.79–1.89 (m, 2H), 3.00 (q, *J*=7.5 Hz, 2H), 4.27 (q, *J*=7.1 Hz, 2H), 7.36–7.49 (m, 3H), 7.43–7.46 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.2, 161.6, 145.1, 139.5, 130.3, 129.4, 128.4, 127.5, 60.6, 35.0, 23.0, 13.5, 13.2 ppm; IR (KBr) 2963, 2932, 1725, 1478, 1324, 1191, 1026, 754, 696 cm^{-1}; HRMS (ESI) calcd for $[C_{15}H_{17}NO_2S+H]^+$ 276.1053, found 276.1055.

4.3.19. Ethyl 2-benzoyl-5-phenylthiazole-4-carboxylate (***2s***). Yield 134 mg (80%). White solid, mp 93–94 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.23 (t, *J*=7.1 Hz, 3H), 4.31 (q, *J*=7.1 Hz, 2H), 7.43–7.47 (m, 3H), 7.49–7.56 (m, 4H), 7.65 (t, *J*=7.2 Hz, 1H), 8.58 (d, *J*=7.3 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 183.5, 165.2, 161.9, 152.0, 142.4, 134.5, 134.0, 131.4, 129.9, 129.8, 128.6, 128.4, 61.5, 13.9 ppm; IR (KBr) 3050, 2979, 2968, 1722, 1664, 1458, 1331, 1295, 1200, 1140, 1031, 876, 750, 686 cm^{-1}; HRMS (ESI) calcd for $[C_{19}H_{15}NO_3S+H]^+$ 338.0851, found 338.0854.

4.3.20. 2,5-Diphenylthiazole (***2t***). Yield 89 mg (75%). Light yellow solid, mp 106–107 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32–7.47 (m, 6H), 7.62 (d, *J*=7.7 Hz, 2H), 7.96–8.00 (m, 2H), 8.03 (s, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.2, 139.2, 133.7, 131.4, 130.0, 129.1, 129.0, 128.3, 126.7, 126.4 ppm; IR (KBr) 1450, 1400, 1072, 754, 690, 631 cm^{-1}; HRMS (ESI) calcd for $[C_{15}H_{11}NS+H]^+$ 238.0685, found 238.0691.

4.3.21. 2,5-Diphenylthiazol-4-ylmethyl ether (***2u***). Yield 92 mg (66%). Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.49 (s, 3H), 4.54 (s, 2H), 7.36–7.45 (m, 6H), 7.57 (d, *J*=7.1 Hz, 2H), 7.95–7.98 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.8, 147.9, 136.7, 132.6, 130.4, 129.0, 128.4, 127.9, 127.8, 127.5, 125.6, 67.2, 57.4 ppm; IR (KBr) 2923, 2885, 1593, 1485, 1460, 1095, 763, 690 cm^{-1}; HRMS (ESI) calcd for $[C_{17}H_{15}NOS+H]^+$ 282.0947, found 282.0952.

4.3.22. Methyl 2-phenyl-5-(4-methylphenyl)thiazole-4-carboxylate[10a] (***4a***). Yield 116 mg (75%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.40 (s, 3H), 3.86 (s, 3H), 7.24 (d, *J*=7.9 Hz, 2H), 7.43–7.45 (m, 5H), 7.95–7.98 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.8, 161.8, 145.8, 139.5, 138.5, 131.8, 129.6, 128.8, 128.0, 126.3, 125.8, 51.3, 20.4 ppm.

4.3.23. Methyl 2-phenyl-5-(3-methylphenyl)thiazole-4-carboxylate[10a] (***4b***). Yield 125 mg (81%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.41 (s, 3H), 3.86 (s, 3H), 7.23–7.34 (m, 4H), 7.44–7.46 (m, 3H), 7.96–7.99 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.0, 161.7, 145.6, 139.8, 137.0, 131.8, 129.6, 129.5, 129.2, 129.1, 128.0, 127.2, 126.0, 125.8, 51.3, 20.4 ppm.

4.3.24. Methyl 2-phenyl-5-(4-methoxylphenyl)thiazole-4-carboxylate (***4d***). Yield 97 mg (60%). Light yellow solid, mp 136–138 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.85 (s, 3H), 3.87 (s, 3H), 6.96 (d, *J*=8.5 Hz, 2H), 7.44–7.46 (m, 3H), 7.50 (d, *J*=8.5 Hz, 2H), 7.96–7.97 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.9, 162.3,

160.0, 146.3, 139.7, 132.3, 130.8, 130.0, 128.5, 126.2, 121.8, 113.2, 54.8, 51.7 ppm; IR (KBr) 2950, 2832, 1720, 1603, 1485, 1333, 1250, 1177, 1005, 830, 768, 694 cm^{-1}; HRMS (ESI) calcd for $[C_{18}H_{15}NO_3S+H]^+$ 326.0845, found 326.0843.

*4.3.25. Methyl 2-phenyl-5-(4-fluorophenyl)thiazole-4-carboxylate (**4e**).* Yield 118 mg (76%). White solid, mp 126–128 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 3.86 (s, 3H), 7.13 (t, J=8.6 Hz, 2H), 7.44–7.47 (m, 3H), 7.50–7.56 (m, 2H), 7.94–7.99 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.1, 165.0, 162.5, 161.7, 145.3, 140.9, 132.6, 131.9, 131.8, 130.7, 129.0, 126.8, 126.3, 126.2, 115.5, 115.3, 52.3 ppm; IR (KBr) 2944, 1721, 1528, 1468, 1343, 1224, 1200, 1007, 843, 762, 689 cm^{-1}; HRMS (ESI) calcd for $[C_{17}H_{12}FNO_2S+H]^+$ 314.0646, found 314.0649.

*4.3.26. Methyl 2-phenyl-5-(4-chlorophenyl)thiazole-4-carboxylate (**4f**).* Yield 97 mg (60%). White solid, mp 122–123 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 3.86 (s, 3H), 7.13 (d, J=8.5 Hz, 2H), 7.44–7.50 (m, 5H), 7.96–7.99 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.4, 162.5, 145.0, 141.1, 135.5, 132.6, 131.2, 130.8, 129.0, 128.7, 128.5, 126.8, 52.3 ppm; IR (KBr) 2950, 1719, 1464, 1399, 1199, 1085, 1012, 763, 686 cm^{-1}; HRMS (ESI) calcd for $[C_{17}H_{12}ClNO_2S+H]^+$ 330.0350, found 330.0345.

*4.3.27. Methyl 2-phenyl-5-(4-trifluoromethylphenyl)thiazole-4-carboxylate (**4g**).* Yield 45 mg (25%). White solid, mp 147–149 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 3.88 (s, 3H), 7.47–7.49 (m, 5H), 7.66–7.73 (m, 4H), 7.97–8.00 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.9, 161.3, 143.2, 133.0, 131.4, 130.4, 129.9, 129.3, 129.1, 128.0, 125.8, 124.2, 124.1, 121.0, 51.3 ppm; IR (KBr) 2950, 2838, 1714, 1610, 1506, 1217, 1181, 1094, 835, 786, 708, 683 cm^{-1}; HRMS (ESI) calcd for $[C_{18}H_{12}F_3NO_2S+H]^+$ 364.0614, found 364.0615.

*4.3.28. Methyl 2-phenyl-5-(4-methylphenyl)oxazole-4-carboxylate[10a] (**4h**).* Yield 104 mg (71%). ^1H NMR (300 MHz, $CDCl_3$) δ 2.41 (s, 3H), 3.97 (s, 3H), 7.29 (d, J=8.2 Hz, 2H), 7.46–7.49 (m, 3H), 8.04 (d, J=8.2 Hz, 2H), 8.13–8.16 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.8, 158.5, 154.6, 139.8, 130.0, 128.2, 127.8, 127.4, 125.8, 125.4, 123.2, 51.3, 20.6 ppm.

*4.3.29. Methyl 2-phenyl-5-(3-methylphenyl)oxazole-4-carboxylate[10a] (**4i**).* Yield 117 mg (80%). ^1H NMR (300 MHz, $CDCl_3$) δ 2.44 (s, 3H), 3.97 (s, 3H), 7.27 (d, J=7.7 Hz, 1H), 7.38 (t, J=7.7 Hz, 1H), 7.46–7.49 (m, 3H), 7.93–7.96 (m, 2H), 8.13–8.17 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.7, 158.7, 154.5, 137.2, 130.2, 130.1, 127.9, 127.8, 127.4, 126.9, 125.9, 125.4, 124.8, 51.4, 20.6 ppm.

*4.3.30. Methyl 2-phenyl-5-(4-methoxylphenyl)oxazole-4-carboxylate (**4j**).* Yield 72 mg (47%). White solid, mp 131–132.5 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 3.87 (s, 3H), 3.97 (s, 3H), 7.01 (d, J=8.9 Hz, 2H), 7.46–7.48 (m, 3H), 8.12–8.15 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.4, 160.7, 158.6, 155.1, 130.4, 129.7, 128.3, 126.2, 126.0, 119.0, 113.4, 54.9, 51.8 ppm; IR (KBr) 2962, 2926, 2855, 1729, 1465, 1330, 1261, 1108, 1069, 1020, 802, 761, 686 cm^{-1}; HRMS (ESI) calcd for $[C_{18}H_{15}NO_4+H]^+$ 310.1074, found 310.1066.

*4.3.31. Methyl 2-phenyl-5-(4-fluorophenyl)oxazole-4-carboxylate (**4k**).* Yield 89 mg (60%). White solid, mp 140–142 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 3.95 (s, 3H), 7.16 (t, J=8.7 Hz, 2H), 7.44–7.47 (m, 3H), 7.09–7.18 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.4, 161.6, 161.0, 158.6, 153.3, 130.1, 129.6, 129.5, 127.8, 126.6, 125.7, 125.1, 122.2, 122.1, 114.7, 114.4, 51.3 ppm; IR (KBr) 2950, 2844, 1715, 1505, 1434, 1355, 1235, 1094, 1009, 844, 708 cm^{-1}; HRMS (ESI) calcd for $[C_{17}H_{12}FNO_3+H]^+$ 298.0874, found 298.0876.

*4.3.32. Methyl 2-phenyl-5-(4-chlorophenyl)thiazole-4-carboxylate (**4l**).* Yield 89 mg (57%). White solid, mp 131–132 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 3.95 (s, 3H), 7.43 (d, J=8.7 Hz, 2H), 7.41–7.46 (m, 3H), 8.07–8.10 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.5, 158.7, 153.0, 135.3, 130.2, 128.6, 127.8, 127.7, 127.2, 125.8, 125.1, 124.3, 51.4 ppm; IR (KBr) 2950, 2844, 1719, 1488, 1358, 1222, 1094, 836, 788, 708, 683 cm^{-1}; HRMS (ESI) calcd for $[C_{17}H_{12}ClNO_3+H]^+$ 314.0578, found 314.0569.

*4.3.33. 2-Phenylbenzothiazole (**6**).* Yield 83 mg (79%). White solid, mp 108–110 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.39 (t, J=7.4 Hz, 1H), 7.48–7.53 (m, 4H), 7.90 (d, J=8.0 Hz, 1H), 8.09–8.11 (m, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.0, 153.2, 134.0, 132.6, 129.9, 128.0, 126.5, 125.3, 124.1, 122.2, 120.6 ppm; IR (KBr) 1479, 1433, 1222, 963, 766, 687, 621 cm^{-1}; HRMS (ESI) calcd for $[C_{13}H_9NS+H]^+$ 212.0534, found 212.0538.

*4.3.34. 2-Phenylindole (**8**).* Yield 51 mg (53%). White solid, mp 188–190 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 6.83 (s, 1H), 7.10–7.24 (m, 2H), 7.29–7,46 (m, 4H), 7.62–7.67 (m, 3H), 8.31 (br s, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.9, 135.8, 131.4, 128.0, 126.7, 124.1, 121.3, 119.6, 119.3, 109.9, 99.0 ppm; IR (KBr) 3440, 1400, 1092, 798, 743, 689 cm^{-1}; HRMS (ESI) calcd for $[C_{14}H_{11}N+H]^+$ 194.0964, found 194.0968.

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Supplementary data

Supplementary data including detailed results of reaction condition screening and reaction scope investigation, and characterization of all title compounds can be found online. Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2013.02.001.

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13. See the Supplementary data (Table S1) for the detailed results of reaction condition screening.
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