Article

Regio- and Stereoselective Synthesis of Thiazole-Containing Triarylethylenes by Hydroarylation of Alkynes

Woohyeong Lee, Changhoon Shin, Soo Eun Park, and Jung Min Joo

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.9b01619 • Publication Date (Web): 12 Aug 2019

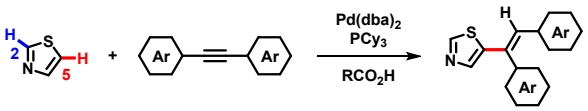
Regio- and Stereoselective Synthesis of Thiazole-Containing Triarylethylenes by Hydroarylation of Alkynes

*Woohyeong Lee,[+] Changhoon Shin,[+] Soo Eun Park, Jung Min Joo**

Department of Chemistry and Chemistry Institute of Functional Materials, Pusan National University, Busan 46241, Republic of Korea

RECEIVED DATE (to be automatically inserted after your manuscript is accepted if required according to the journal that you are submitting your paper to)

ABSTRACT



Thiazole-containing π-conjugated moieties are important structural units in the development of new electronic and photochromic materials. We have developed a Pd-catalyzed *syn*-hydroarylation reaction of diaryl alkynes with thiazoles, which provides access to thiazole-containing triarylethylenes. Pd(II) complexes derived from Pd(0) species and carboxylic acids facilitated C−H functionalization of the unsubstituted thiazole with high C5 selectivity. The catalytic system was also compatible with other azoles, such as oxazoles and a pyrazole, allowing the stereoselective syntheses of various trisubstituted olefins.

Introduction

Thiazoles are one of the most important heterocyclic cores found in natural products, pharmaceuticals, and functional materials.[1] Particularly, the presence of the pyridine-like nitrogen atom at the thiazole core imparts different electronic properties and provides opportunities for hydrogen bonding and metal binding,

which are otherwise unavailable to its nitrogen-free congener, thiophene. This allows the development of many thiazole-containing π-conjugated electronic and photochromic materials.[2] Therefore, novel methods allowing facile syntheses of the π-conjugated systems bearing thiazole are crucial for further expansion of the structural and functional varieties of synthetic materials.

Transition metal-catalyzed C−H bond functionalization of thiazoles with unsaturated hydrocarbons can offer direct access to thiazole-containing π-conjugated systems.[3] Particularly, addition of thiazoles to alkynes is one of the most straightforward methods for preparing thiazole-containing trisubstituted ethylene compounds.[4] However, attaining a high regioselectivity between the two reactive positions, C2 and C5, of thiazoles, has been quite challenging. For example, Co- and Ni-catalyzed hydroarylation of alkynes has been applied to the functionalization of the C2 position of thiazole (Figure 1A).[5,6] However, substituted thiazoles were mainly used, and a single example of unsubstituted thiazole reacting with 4-octyne resulted in the formation of the corresponding C2-alkenyl thiazole in 23% yield, leaving the alternative C5-functionalization of thiazoles unexplored.[5b] In addition, the first row transition metal catalysts generally gave low yields in the hydroheteroarylation of diaryl alkynes as compared with their dialkyl counterparts, thereby preventing their broad application to the syntheses of azole-containing π-conjugated systems.[7]

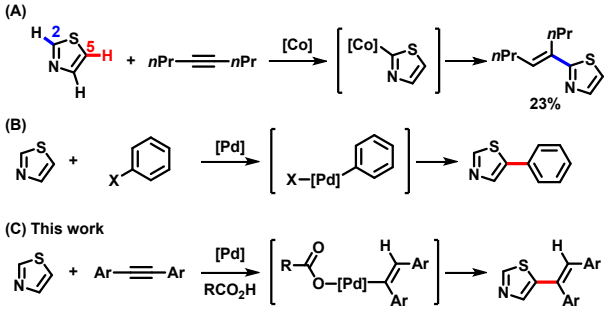


Figure 1. (A) Hydroarylation of alkynes at the C2-position of thiazole. (B) Pd-catalyzed C−H arylation at the C5-position of thiazole. (C) Pd-catalyzed hydroarylation of alkynes at the C5-position of thiazole.

In contrast, high C5 selectivity and efficiency have been achieved in Pd-catalyzed C−H arylation of the

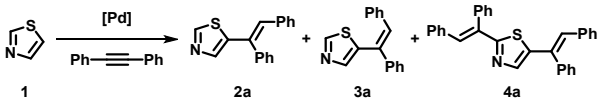
unsubstituted thiazole with aryl halides (Figure 1B).[8] Similarly, Pd-catalyzed C−H alkenylation of the parent thiazole with alkenes as the alkenyl group donors resulted in C5 selectivity, but the scope and efficiency were limited, indicating the difficulty in the functionalization of the C5 position of thiazoles compared with other azoles.[9,10] Considering the C5 selectivity of thiazoles achieved with Pd(II) complexes, we envisioned that Pd-catalyzed hydroarylation of alkynes should provide an opportunity for the stereoselective syntheses of alkenyl thiazoles that are otherwise inaccessible by dehydrogenative alkenylation with alkenes (Figure 1C).[11] Specifically, we hypothesized the involvement of alkenyl Pd(II) carboxylate complexes resulting from Pd(0) species and carboxylic acids in the C−H functionalization of heteroarenes.[12] Although it has been proposed that low valent Co(0) or Co(I)- and Ni(0)-catalyzed hydroarylation reactions of alkynes involve oxidative addition of heteroaromatic C−H bonds at the C2 position, Pd(II) carboxylates could selectively functionalize the more nucleophilic C5 position.[13] Hiyama et al. demonstrated the advantage of Pd catalysis in the alkyne functionalization, where alkenyl Pd(II) carboxylates have been proposed as the key intermediates in the direct C−H activation.[14] Although Pd-catalyzed hydroarylation of diaryl alkynes has been employed for the functionalization of five-membered heteroarenes, the reaction was largely focused on the electron-rich one-heteroatom-containing heterocycles, which resulted in modest regio- and stereoselectivity.[15] We found that alkenyl Pd(II) carboxylate complexes were readily formed from Pd(0) species and carboxylic acids with diaryl alkynes, which allowed the C5-selective alkenylation of thiazoles in a regio- and stereoselective manner.

Results and Discussion

Simple thiazole **1** and diphenylacetylene were used for the optimization studies, revealing that a combination of $Pd(dba)_2$, PCy_3, and pivalic acid afforded both (*E*)- and (*Z*)-isomers (**2a** and **3a**, respectively) of the corresponding C5-alkenylation products, along with the dialkenylation product **4a** (Table 1). The structure of the major product **2a** was analyzed by X-ray crystallography, which revealed the C5- and *syn*-selectivity of the hydroarylation (see the Supporting Information).[16] It was worth noting that subjecting the (*E*)-isomer **2a** to the optimized conditions (entry 3) did not promote olefin

isomerization, indicating that the (*Z*)-isomer **3a** was formed during the Pd-catalyzed process rather than the isomerization of the (*E*)-isomer (*vide infra*). To avoid the formation of the dihydroarylation product **4a**, the amount of thiazole was increased to 4.0 equivalents with respect to the alkyne (entries 1-3). Both pivalic acid and acetic acid gave comparable yields for thiazole (entries 3 and 4), but they affected the selectivity and efficiency for the substituted thiazoles (see Table 3). However, trifluoroacetic acid was not effective and the reaction did not proceed in the absence of carboxylic acids (entries 5 and 6). Variation in the catalytic system by using different Pd precatalysts exhibited consistent C5 selectivity as long as tricyclohexylphosphine was present (entries 7-9). Phenyl-substituted phosphine ligands gave lower yields than tricyclohexylphosphine ligands, including the bench-stable form, $PCy_3H{\cdot}BF_4$ (entries 10-12). However, no reaction took place in the absence of phosphine ligands (entry 13). Decreasing the reaction temperature slightly reduced the extent of conversion, whereas increasing the reaction temperature promoted the formation of the (*Z*)-isomer **3a** (entries 14 and 15). Conducting the reaction in various solvents revealed that the reaction was more selective and efficient in DMA than in 1,4-dioxane and toluene (entries 16 and 17).

Table 1. Hydroheteroarylation with thiazole[a]



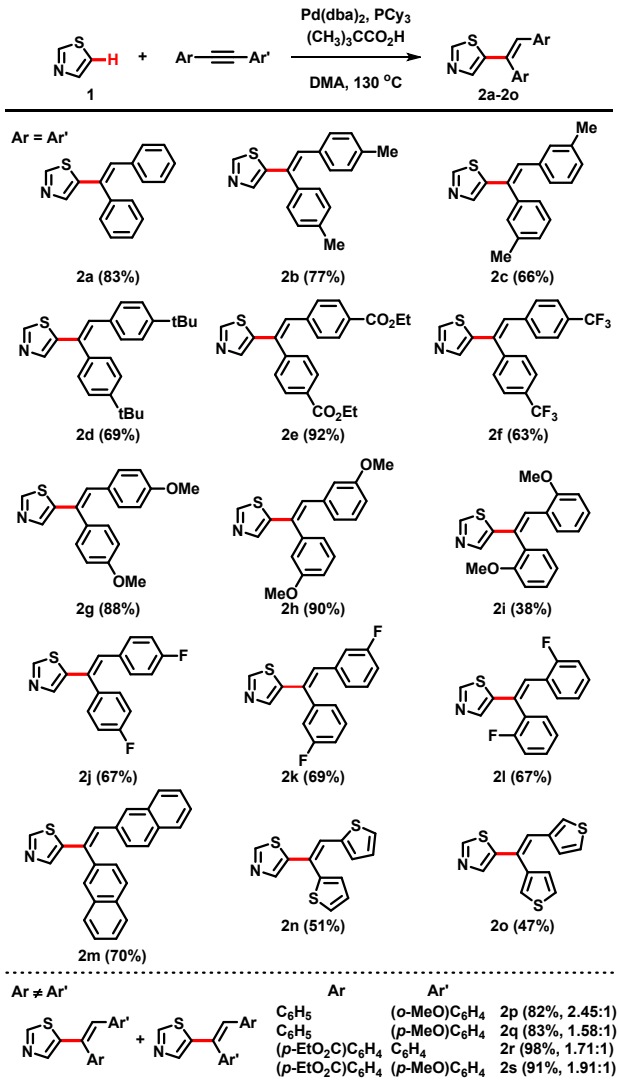
Entry	**1** (eq.)	[Pd]	L	Acid	Solvent	GC yield (%)			
						2a	**3a**	**4a**	PhC≡CPh
1	2.0	$Pd(dba)_2$	PCy_3	PivOH	DMA	60	5	15	2
2	3.0	$Pd(dba)_2$	PCy_3	PivOH	DMA	69	4	11	2
3	4.0	$Pd(dba)_2$	PCy_3	PivOH	DMA	84	2	8	2
4	4.0	$Pd(dba)_2$	PCy_3	AcOH	DMA	84	3	5	3
5	4.0	$Pd(dba)_2$	PCy_3	TFA	DMA	1	3	0	48
6	4.0	$Pd(dba)_2$	PCy_3	–	DMA	0	0	0	94
7	4.0	$Pd(PCy_3)_3$	–	PivOH	DMA	76	6	8	0
8[b]	4.0	$Pd_2(dba)_3$	PCy_3	PivOH	DMA	75	2	9	1
9	4.0	$Pd(OAc)_2$	PCy_3	PivOH	DMA	76	5	8	1
10	4.0	$Pd(dba)_2$	$PCy_3H{\cdot}BF_4$	PivOH	DMA	73	4	6	6
11	4.0	$Pd(dba)_2$	$PCyPh_2$	PivOH	DMA	51	2	2	35
12	4.0	$Pd(dba)_2$	PPh_3	PivOH	DMA	18	1	0	71
13	4.0	$Pd(dba)_2$	–	PivOH	DMA	0	0	0	89
14[c]	4.0	$Pd(dba)_2$	PCy_3	PivOH	DMA	76	1	10	5
15[d]	4.0	$Pd(dba)_2$	PCy_3	PivOH	DMA	67	7	8	1
16	4.0	$Pd(dba)_2$	PCy_3	PivOH	1,4-dioxane	69	0	8	12
17	4.0	$Pd(dba)_2$	PCy_3	PivOH	toluene	38	0	4	24

[a] Reaction conditions: thiazole (as indicated), diphenylacetylene (0.50 mmol), $Pd(dba)_2$ (0.025 mmol),

ligand (0.10 mmol), carboxylic acid (0.15 mmol), solvent (0.50 M), 14 h, Temperature: 130 °C. [b] $Pd_2(dba)_3$ (0.0125 mmol) was employed. [c] Temperature: 110 °C. [d] Temperature: 150 °C.

The Pd-catalyzed hydroarylation of symmetrical alkynes generated a variety of thiazole-containing triarylethylene compounds (Table 2).[17] Both electron-donating and electron-withdrawing substituents on diaryl alkynes were used under the optimal reaction conditions to examine the substrate scope. Furthermore, the reaction showed tolerance toward substituents at different positions: *p*-, *m*-, and *o*-methoxy and fluoro derivatives in the aryl ring afforded the corresponding products in good yields (**2g–2i** and **2j–2l**). Naphthalene as well as heterocyclic thiophene-substituted alkynes could also successfully couple with thiazole (**2m–2o**). However, hydroarylation of unsymmetrical diaryl alkynes gave an inseparable mixture of regioisomers (**2p–2s**). The ratio between the two regioisomeres indicated that both electronic and steric effects affected the regioselectivity, but to a larger extent by steric effects than electronic effects. In addition, no products were obtained with alkynes having alkyl groups, presumably because β-H elimination of the hydropalladation intermediate took place and the resulting allyl Pd(II) intermediates were not suitable for allylation of thiazole.[14d]

Table 2. Substrate Scope of Alkynes[a]

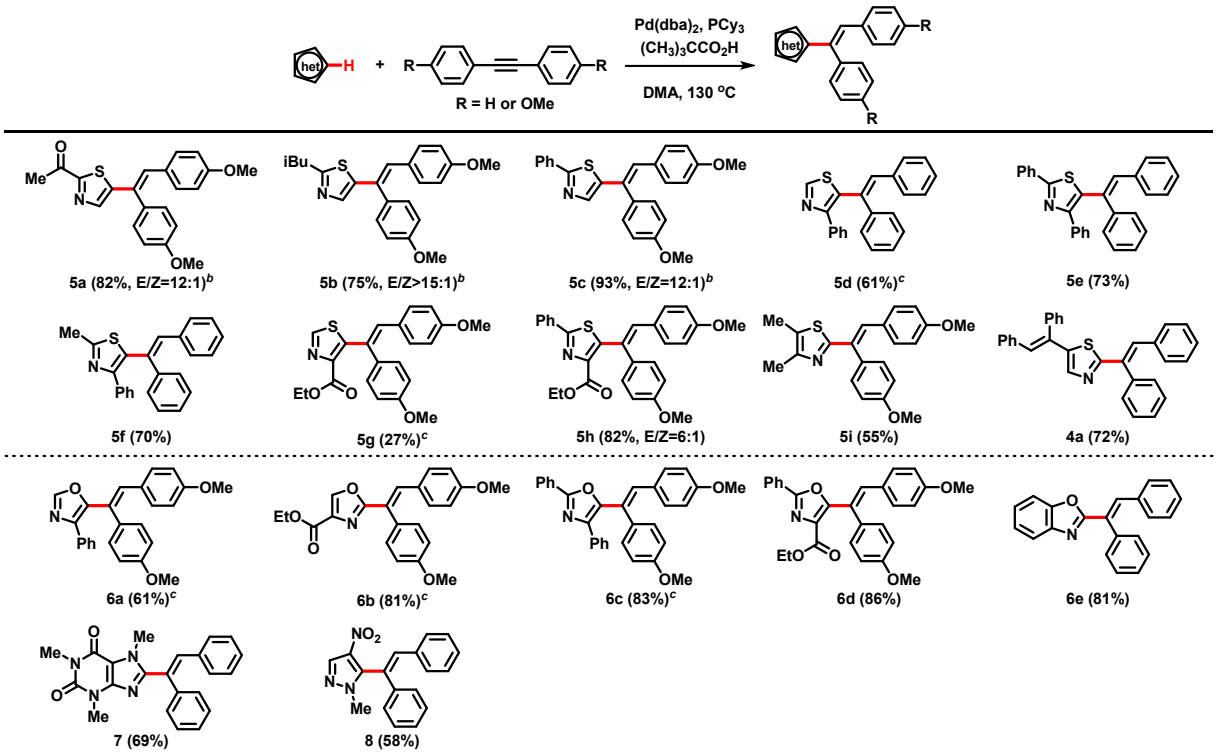


[a] Reaction conditions: thiazole (2.0 mmol), alkyne (0.50 mmol), $Pd(dba)_2$ (0.025 mmol), PCy_3 (0.10 mmol), pivalic acid (0.15 mmol), DMA (0.50 M), 14 h, Temperature: 130 °C.

The Pd-catalyzed system involving $Pd(dba)_2$, PCy_3, and carboxylic acids was also compatible for substituted thiazoles and other azole compounds (Table 3). Either diphenylacetylene or 1,2-bis(4-methoxyphenyl)ethyne was selected as the alkyne partner for easy isolation. When the C2 position of thiazoles was substituted, the formation of the (*Z*)-isomers was noticeable. To avoid the isomerization, the reaction temperature was decreased and the amount of the solvent was reduced (**5a–c**). In addition, 4-phenyl thiazoles were transformed into the corresponding hydroheteroarylation products (**5d–f**). In these reactions, the corresponding benzannulation products involving C−H functionalization of the C4-phenyl

ring were not observed, favoring the mechanism based on hydropalladation of alkynes with carboxylic acid over carbometallation of alkynes with thiazole.[18] Generally, the addition of acetic acid afforded higher selectivity than pivalic acid for C4-substituted thiazoles, in which both C2 and C5 positions were available (**5d** and **5g**). The presence of an ester group at the C4 position reduced the extent of conversion, giving **5g** in 27% yield (see the Supporting Information for the determination of regiochemistry). However, the impact of the ester substitution was alleviated upon blocking the C2 position, affording **5h** in 82% yield. When the C5 position of thiazoles was blocked, hydroarylation occurred at the C2 position (**5i** and **4a**). Furthermore, the Pd(0) catalytic system was useful for the hydroarylation of oxazoles and benzoxazole (**6a–e**). There are a couple of examples of hydroarylation of alkynes with (benz)oxazoles using Co and Rh catalysts, but the scope of (benz)oxazoles is still underexplored.[5a,19] When 4-phenyl oxazole was tested, the preference to the C5 position was observed (**6a**), representing a rare example of the hydroarylation of alkynes through the C5 position of oxazole. However, in contrast to the phenyl-substituted oxazole, ethyl oxazole-4-carboxylate was converted to the corresponding C2-functionalized product **6b** in good yield, consistent with the selectivity of aryl Pd(II) complexes in the C–H arylation of oxazole-4-carboxylates.[20] Oxazoles substituted at C2 and C4 positions underwent alkenylation at the only available site (**6c** and **6d**). Although the reaction was not compatible with benzothiazole and benzimidazole (not shown), benzoxazole and caffeine underwent the alkenylation, giving **6e** and **7**, respectively. The scope of azoles could be further extended to the functionalization of 4-nitropyrazole (**8**).

Table 3. Substrate Scope of Azoles[a]



[a] Reaction conditions: azole (1.0 mmol), alkyne (0.50 mmol), $Pd(dba)_2$ (0.025 mmol), PCy_3 (0.10 mmol), pivalic acid (0.15 mmol), DMA (0.50 M), 14 h, Temperature: 130 °C. [b] Azole (2.0 mmol) was used in DMA (0.75 M) at 110 °C. [c] Azole (2.0 mmol) and acetic acid (0.15 mmol) were used.

The success with the PCy_3 ligand prompted us to compare the PCy_3-dependent catalytic system with $Pd(PEt_3)_4$, which was reported to afford the corresponding *syn*-hydropalladation product.[12] Stoichiometric amounts of $Pd(PCy_3)_2$, acetic acid, and diphenylacetylene produced the corresponding alkenyl Pd(II) carboxylate complex **9** (Figure 2A).[16] It was remarkable that the sterically bulky PCy_3 ligand, often having distinct catalytic activities compared with PEt_3, allowed the facile *syn*-hydropalladation of diphenylacetylene and isolation of complex **9**.[14b,c] Furthermore, the addition of four equivalents of thiazole to the isolated complex **9** led to the formation of the corresponding alkenylation products, **2a** and **3a**, supporting the involvement of these species in the C−H functionalization of thiazole. Similar to the isomerization of triethylphosphine-ligated alkenyl Pd(II) complexes, the formation of the other stereoisomer **3a** is attributed to the isomerization of the pre-formed *syn*-hydropalladation product **9**,

presumably via zwitterionic Pd carbene species.[12,21] In addition, deuterium labeling experiments were carried out with deuterated solvent DMF, more readily available than deuterated DMA, AcOD and C5-deuterated thiazole (Figure 2B). Although the use of deuterated species increased the formation of the corresponding (*Z*)-isomer, it was found that the incorporation of deuterium took place only when AcOD and the deuterated thiazole were employed. Additionally, the kinetic isotope effects indicated that the cleavage of the heterocyclic C–H bond was a rate-determining step (Figure 2C).

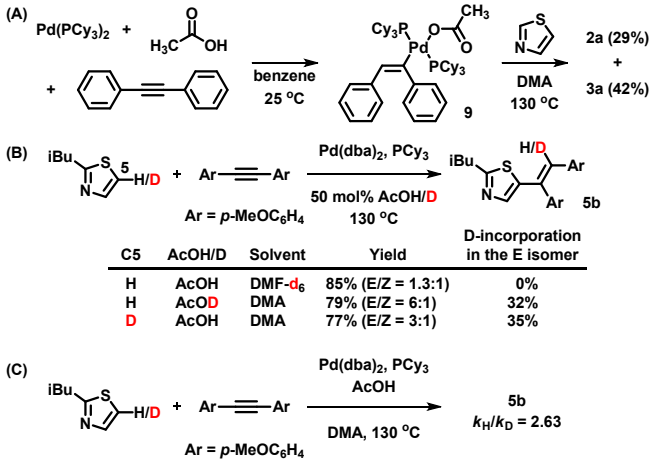


Figure 2. (A) Synthesis of the alkenyl Pd(II) carboxylate complex **9**. (B) Deuterium labeling experiments. (C) Kinetic isotope effects.

Based on these results, we propose the following catalytic cycle: the alkenyl Pd(II) acetate **9** derived from *syn*-hydropalladation enables rate-limiting concerted metalation-deprotonation of thiazole followed by reductive elimination to afford the hydroarylation product **2a** and regenerate the Pd(0) catalyst (Figure 3). The deuterium labeling can be explained by hydropalladation of AcOD, which was originally added or in situ generated by concerted metalation-deprotonation of the C5-deuterated thiazole.

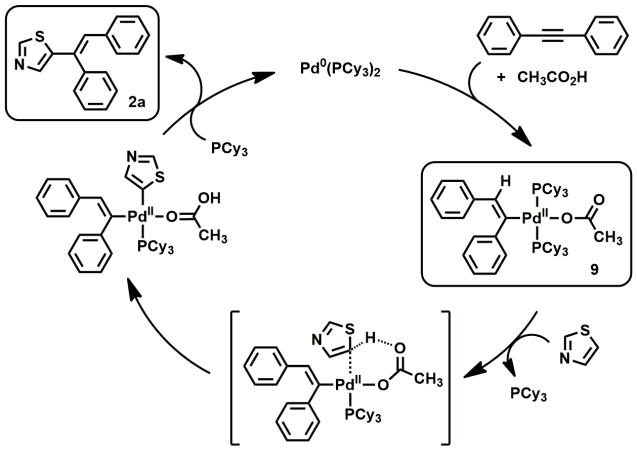


Figure 3. Proposed mechanism

Conclusion

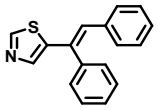
In conclusion, we have developed a hydroarylation reaction of diaryl alkynes with thiazoles. Selective C5-alkenylation of thiazoles was achieved by the reaction of alkenyl Pd(II) carboxylate complexes derived from *syn*-hydropalladation of alkynes with Pd(0) species and carboxylic acids. In addition to the functionalization of the C5 position of thiazole, the Pd-catalyzed system could be generally applied to the functionalization of oxazole, benzoxazole, and pyrazole. Complementary to C2-functionalization of low valent Co- and Ni-catalyzed hydroarylation of alkynes, this method based on the intermediacy of Pd(II) complexes enabled high site-selectivity for the C5 position of thiazole and high efficiency for the hydroarylation of diaryl alkynes. This method provided easy access to azole-containing triarylethylene systems, which can facilitate the development of new five-membered-heterocycle-based materials beyond the conventional thiophene derivatives.

Experimental Section

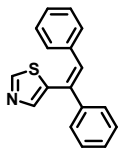
NMR spectra were recorded in $CDCl_3$ at 300 K on a 300 MHz Fourier transform NMR spectrometer. Proton chemical shifts are expressed in parts per million (ppm, δ scale) and are referenced to residual protium in the NMR solvent ($CDCl_3$, δ 7.26). Carbon chemical shifts are expressed in parts per million

(ppm, δ scale) and are referenced to the carbon resonance of the NMR solvent ($CDCl_3$, δ 77.16). Crude yields were determined by GC analysis using triphenylethylene as an internal standard, which was added to reaction mixtures after cooling to 25 °C. High-resolution mass spectra (HRMS) were acquired on high-resolution mass spectrometers: Q-TOF (ionization mode: ESI).

General Procedure for Hydroarylation of Azoles. To an 8 mL-glass vial equipped with a magnetic stir bar, a thiazole substrate (as indicated), an alkyne substrate (0.50 mmol), pivalic acid (15 mg, 0.15 mmol) [or acetic acid (9.0 mg, 0.15 mmol) as indicated], *N*,*N*-dimethylacetamide (1.0 mL, 0.50 M), $Pd(dba)_2$ (14 mg, 0.025 mmol) and PCy_3 (29 mg, 0.10 mmol) were sequentially added in an argon-purged glove box. The reaction mixture was stirred in a preheated reaction block at 130 °C for 14 h. After cooled to 25 °C, the solution was purified by flash column chromatography to afford the desired product.

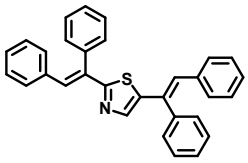


(*E*)-5-(1,2-diphenylvinyl)thiazole (2a). Following the general procedure, the reaction was set up with thiazole (172 mg, 2.0 mmol) and diphenylacetylene (91 mg, 0.50 mmol). Purification by flash column chromatography (hexanes/EtOAc = 14:1) provided **2a** as a pale yellow solid (105 mg, 80% yield). Crystals suitable for X-ray crystallography were obtained from vapor diffusion of hexanes into a saturated chloroform solution of **2a** at 25 °C. mp 86-88 ℃; IR (film) 3055, 3021, 1596, 1488, 1443, 865 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.69 (s, 1H), 7.49 (s, 1H), 7.43-7.38 (m, 3H), 7.33-7.27 (m, 2H), 7.15-7.10 (m, 3H), 7.02 (s, 1H), 7.00-6.95 (m, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 152.0, 141.6, 138.6, 136.0, 133.2, 129.6, 129.5, 129.0, 128.2, 128.1, 127.4; HRMS (ESI) calcd for $C_{17}H_{14}NS$ $[M+H]^+$ 264.0841, found 264.0832.

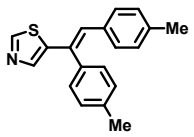


(*Z*)-5-(1,2-diphenylvinyl)thiazole (3a). Following the general procedure, the reaction was set up with thiazole (172 mg, 2.0 mmol) and diphenylacetylene (91 mg, 0.50 mmol). Purification by flash column

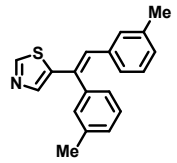
chromatography (hexanes/EtOAc = 14:1) provided **3a** as a pale yellow solid. mp 95-97 °C; IR (film) 3054, 3022, 1596, 1490, 1444, 866 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.84 (s, 1H), 7.69 (s, 1H), 7.48-7.31 (m, 5H), 7.31-7.21 (m, 3H), 7.21-7.12 (m, 2H), 7.08 (s, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 154.0, 144.0, 142.5, 136.6, 132.5, 131.7, 129.4, 128.5, 128.5, 128.3, 127.8, 127.5; HRMS (ESI) calcd for $C_{17}H_{14}NS$ $[M+H]^+$ 264.0841, found 264.0844.



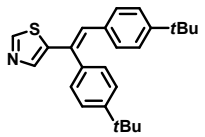
2,5-bis((*E*)-1,2-diphenylvinyl)thiazole (4a). Following the general procedure, the reaction was set up with **2a** (263 mg, 1.0 mmol) and diphenylacetylene (91 mg, 0.50 mmol). Purification by flash column chromatography (hexanes/EtOAc = 40:1) provided **4a** as a pale yellow solid (159 mg, 72% yield). mp 158-160 °C; IR (film) 3054, 3022, 1595, 1494, 1443, 755 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.77 (s, 1H), 7.49-7.44 (m, 3H), 7.42-7.35 (m, 6H), 7.33-7.27 (m, 2H), 7.17-7.13 (m, 3H), 7.12-7.08 (m, 3H), 7.07-7.03 (m, 2H), 6.95-6.90 (m, 2H), 6.90 (s, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 170.3, 143.6, 142.4, 138.5, 136.3, 135.8, 134.8, 133.9, 130.4, 130.3, 130.1, 129.8, 129.6, 129.3, 129.1, 128.9, 128.7, 128.3, 128.2, 128.1, 127.3; HRMS (ESI) calcd for $C_{31}H_{24}NS$ $[M+H]^+$ 442.1624, found 442.1615.



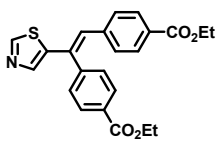
(*E*)-5-(1,2-di-*p*-tolylvinyl)thiazole (2b). Following the general procedure, the reaction was set up with thiazole (172 mg, 2.0 mmol) and 1,2-di-*p*-tolylethyne (103 mg, 0.50 mmol). Purification by flash column chromatography (hexanes/EtOAc = 9:1) provided **2b** as a yellow solid (112 mg, 77% yield). mp 64-66 °C; IR (film) 3020, 2918, 2858, 1603, 1492, 867 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.66 (s, 1H), 7.49 (s, 1H), 7.24-7.14 (m, 4H), 7.00-6.93 (m, 3H), 6.92-6.87 (m, 2H), 2.41 (s, 3H), 2.26 (s, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 151.6, 143.6, 141.3, 137.9, 137.2, 135.8, 133.3, 132.3, 129.8, 129.5, 129.3, 128.9, 21.4, 21.2; HRMS (ESI) calcd for $C_{19}H_{18}NS$ $[M+H]^+$ 292.1154, found 292.1154.



(*E*)-5-(1,2-di-*m*-tolylvinyl)thiazole (2c). Following the general procedure, the reaction was set up with thiazole (172 mg, 2.0 mmol) and 1,2-di-*m*-tolylethyne (103 mg, 0.50 mmol). Purification by flash column chromatography (hexanes/EtOAc = 10:1) provided **2c** as a yellow oil (96 mg, 66% yield). IR (film) 3015, 2919, 2854, 1598, 1486, 869 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.67 (s, 1H), 7.49 (s, 1H), 7.30 (d, *J* = 7.4 Hz, 1H), 7.20 (d, *J* = 7.2 Hz, 1H), 7.14-7.05 (m, 2H), 7.01 (d, *J* = 7.5 Hz, 1H), 6.97-6.91 (m, 2H), 6.84 (s, 1H), 6.74 (d, *J* = 7.2 Hz, 1H), 2.35 (s, 3H), 2.19 (s, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 151.8, 143.4, 141.6, 138.8, 138.7, 137.6, 136.1, 133.2, 130.7, 130.1, 129.5, 129.0, 128.3, 128.0, 126.7, 126.5, 21.5, 21.4; HRMS (ESI) calcd for $C_{19}H_{18}NS$ $[M+H]^+$ 292.1154, found 292.1155.

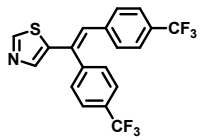


(*E*)-5-(1,2-bis(4-(*tert*-butyl)phenyl)vinyl)thiazole (2d). Following the general procedure, the reaction was set up with thiazole (172 mg, 2.0 mmol) and 1,2-bis(4-(*tert*-butyl)phenyl)ethyne (145 mg, 0.50 mmol). Purification by flash column chromatography (hexanes/EtOAc = 8:1) provided **2d** as a yellow oil (129 mg, 69% yield). IR (film) 2956, 2924, 2863, 1604, 1461, 867 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.65 (s, 1H), 7.46 (s, 1H), 7.43 (d, *J* = 8.4 Hz, 2H), 7.23 (d, *J* = 8.3 Hz, 2H), 7.14 (d, *J* = 8.5 Hz, 2H), 6.96 (s, 1H), 6.92 (d, *J* = 8.4 Hz, 2H), 1.38 (s, 9H), 1.25 (s, 9H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 151.6, 151.3, 150.6, 143.8, 141.5, 135.9, 133.4, 132.4, 129.4, 129.3, 129.2, 126.1, 125.2, 34.8, 34.7, 31.5, 31.3; HRMS (ESI) calcd for $C_{25}H_{30}NS$ $[M+H]^+$ 376.2093, found 376.2093.

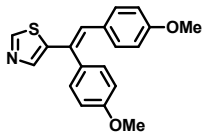


(*E*)-diethyl 4,4'-(1-(thiazol-5-yl)ethene-1,2-diyl)dibenzoate (2e). Following the general procedure, the reaction was set up with thiazole (172 mg, 2.0 mmol) and diethyl 4,4'-(ethyne-1,2-diyl)dibenzoate (161

mg, 0.50 mmol). Purification by flash column chromatography (hexanes/EtOAc = 2:1) provided **2e** as a yellow oil (188 mg, 92% yield). IR (film) 3078, 2979, 2920, 1712, 1603, 868 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.72 (s, 1H), 8.07 (d, *J* = 8.4 Hz, 2H), 7.79 (d, *J* = 8.4 Hz, 2H), 7.49 (s, 1H), 7.35 (d, *J* = 8.3 Hz, 2H), 7.07 (s, 1H), 7.00 (d, *J* = 8.3 Hz, 2H), 4.40 (q, *J* = 7.1 Hz, 2H), 4.31 (q, *J* = 7.1 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 3H), 1.33 (t, *J* = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 166.2, 152.8, 142.8, 142.3, 141.9, 140.0, 134.5, 130.7, 130.4, 129.8, 129.5, 129.4, 129.24, 129.16, 61.3, 61.1, 14.42, 14.37; HRMS (ESI) calcd for $C_{23}H_{22}NO_4S$ $[M+H]^+$ 408.1264, found 408.1266.

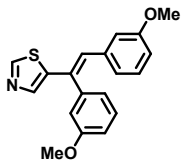


(*E*)-5-(1,2-bis(4-(trifluoromethyl)phenyl)vinyl)thiazole (2f). Following the general procedure, the reaction was set up with thiazole (172 mg, 2.0 mmol) and 1,2-bis(4-(trifluoromethyl)phenyl)ethyne (157 mg, 0.50 mmol). Purification by flash column chromatography (hexanes/EtOAc = 9:1) provided **2f** as a yellow solid (126 mg, 63% yield). mp 65-67 ℃; IR (film) 3070, 2929, 1613, 1317, 1105, 868 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.75 (s, 1H), 7.69 (d, *J* = 8.0 Hz , 2H), 7.50 (s, 1H), 7.43 (d, *J* = 3.4 Hz, 2H), 7.40 (d, *J* = 3.8 Hz, 2H), 7.09 (s, 1H), 7.06 (d, *J* = 8.4 Hz, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 152.9, 142.5, 141.9, 139.0, 134.2, 131.0 (q, *J* = 32.9 Hz), 130.2, 129.7, 129.1 (q, *J* = 30.0 Hz), 128.9, 126.3 (q, *J* = 3.7 Hz), 124.0 (q, *J* = 272.1 Hz), 125.3 (q, *J* = 3.7 Hz); HRMS (ESI) calcd for $C_{19}H_{12}F_6NS$ $[M+H]^+$ 400.0589, found 400.0589.

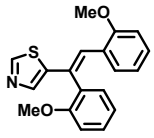


(*E*)-5-(1,2-bis(4-methoxyphenyl)vinyl)thiazole (2g). Following the general procedure, the reaction was set up with thiazole (172 mg, 2.0 mmol) and 1,2-bis(4-methoxyphenyl)ethyne (119 mg, 0.50 mmol). Purification by flash column chromatography (hexanes/EtOAc = 6:1) provided **2g** as a colorless oil (143 mg, 88% yield). IR (film) 2999, 2930, 2834, 1602, 1509, 867 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.64 (s, 1H), 7.49 (s, 1H), 7.22 (d, *J* = 8.5 Hz, 2H), 6.96-6.92 (m, 5H), 6.68 (d, *J* = 8.6 Hz, 2H), 3.87 (s, 3H),

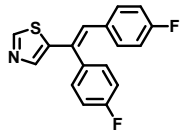
3.75 (s, 3H); $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 159.5, 158.9, 151.5, 141.0, 131.1, 131.0, 130.9, 130.8, 129.0, 128.9, 114.6, 113.8, 113.7, 55.3, 55.2; HRMS (ESI) calcd for $C_{19}H_{18}NO_2S$ $[M+H]^+$ 324.1053, found 324.1052.



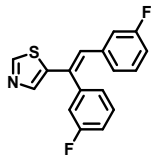
(*E*)-5-(1,2-bis(3-methoxyphenyl)vinyl)thiazole (2h). Following the general procedure, the reaction was set up with thiazole (172 mg, 2.0 mmol) and 1,2-bis(3-methoxyphenyl)ethyne (119 mg, 0.50 mmol). Purification by flash column chromatography (hexanes/EtOAc = 4:1) provided **2h** as a colorless oil (146 mg, 90% yield). IR (film) 2999, 2923, 2833, 1595, 1486, 868 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.68 (s, 1H), 7.52 (s, 1H), 7.34 (t, *J* = 7.9 Hz, 1H), 7.08 (t, *J* = 7.9 Hz, 1H), 6.98 (s, 1H), 6.95-6.88 (m, 2H), 6.84 (s, 1H), 6.71-6.65 (m, 2H), 6.51 (s, 1H), 3.76 (s, 3H), 3.53 (s, 3H); $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 160.2, 159.1, 151.9, 141.6, 140.0, 137.1, 133.2, 130.2, 129.2, 129.0, 122.5, 121.9, 114.8, 114.2, 114.0, 113.6, 55.2, 54.8; HRMS (ESI) calcd for $C_{19}H_{18}NO_2S$ $[M+H]^+$ 324.1053, found 324.1054.



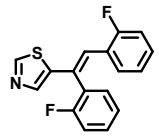
(*E*)-5-(1,2-bis(2-methoxyphenyl)vinyl)thiazole (2i). Following the general procedure, the reaction was set up with thiazole (172 mg, 2.0 mmol) and 1,2-bis(2-methoxyphenyl)ethyne (119 mg, 0.50 mmol). Purification by flash column chromatography (hexanes/EtOAc = 4:1) provided **2i** as a brown oil (61 mg, 38% yield). IR (film) 3000, 2927, 2834, 1594, 1490, 868 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.63 (s, 1H), 7.50 (s, 1H), 7.41-7.29 (m, 2H), 7.16-7.05 (m, 2H), 6.98-6.89 (m, 2H), 6.83 (d, *J* = 8.2 Hz, 1H), 6.74 (d, *J* = 7.6 Hz, 1H), 6.58 (t, *J* = 7.5 Hz, 1H), 3.86 (s, 3H), 3.66 (s, 3H); $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 157.6, 157.4, 151.3, 143.1, 140.1, 131.2, 129.8, 129.7, 129.2, 128.7, 128.0, 125.6, 125.3, 121.2, 120.1, 111.5, 110.4, 55.66, 55.65; HRMS (ESI) calcd for $C_{19}H_{18}NO_2S$ $[M+H]^+$ 324.1053, found 324.1048.



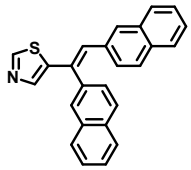
(*E*)-5-(1,2-bis(4-fluorophenyl)vinyl)thiazole (2j). Following the general procedure, the reaction was set up with thiazole (172 mg, 2.0 mmol) and 1,2-bis(4-fluorophenyl)ethyne (107 mg, 0.50 mmol). Purification by flash column chromatography (hexanes/EtOAc = 8:1) provided **2j** as a white solid (100 mg, 67% yield). mp 81-83 ℃; IR (film) 2921, 2851, 1598, 1506, 1226, 827 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.69 (s, 1H), 7.49 (s, 1H), 7.27-7.23 (m, 2H), 7.10 (t, *J* = 8.5 Hz, 2H), 6.99-6.91 (m, 3H), 6.84 (t, *J* = 8.7 Hz, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 162.7 (d, *J* = 248.3 Hz), 162.0 (d, *J* = 248.9 Hz), 152.1, 142.8, 141.7, 134.3 (d, *J* = 3.6 Hz), 132.1 (d, *J* = 3.7 Hz), 131.6 (d, *J* = 8.1 Hz), 131.2 (d, *J* = 8.0 Hz), 128.7, 116.4 (d, *J* = 21.5 Hz), 115.3 (d, *J* = 21.5 Hz); HRMS (ESI) calcd for $C_{17}H_{12}F_2NS$ $[M+H]^+$ 300.0653, found 300.0651.



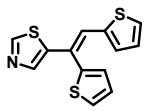
(*E*)-5-(1,2-bis(3-fluorophenyl)vinyl)thiazole (2k). Following the general procedure, the reaction was set up with thiazole (172 mg, 2.0 mmol) and 1,2-bis(3-fluorophenyl)ethyne (107 mg, 0.50 mmol). Purification by flash column chromatography (hexanes/EtOAc = 5:1) provided **2k** as a yellow oil (103 mg, 69% yield). IR (film) 3066, 2953, 2852, 1605, 1579, 1255, 871 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.72 (s, 1H), 7.51 (s, 1H), 7.40 (q, *J* = 7.2 Hz, 1H), 7.17-7.05 (m, 3H), 7.04-6.95 (m, 2H), 6.89-6.76 (m, 2H), 6.63 (d, *J* = 10.5 Hz, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 163.2 (d, *J* = 247.9 Hz), 162.5 (d, *J* = 245.4 Hz), 152.5, 142.1, 142.0, 140.3 (d, *J* = 7.7 Hz), 137.8 (d, *J* = 8.0 Hz), 133.2, 130.9 (d, *J* = 8.3 Hz), 129.7 (d, *J* = 8.5 Hz), 128.7 (d, *J* = 2.8 Hz), 125.44 (d, *J* = 3.6 Hz), 125.39 (d, *J* = 3.3 Hz), 116.6 (d, *J* = 21.8 Hz), 115.9 (d, *J* = 22.5 Hz), 115.7 (d, *J* = 20.9 Hz), 114.7 (d, *J* = 21.4 Hz); HRMS (ESI) calcd for $C_{17}H_{12}F_2NS$ $[M+H]^+$ 300.0653, found 300.0653.



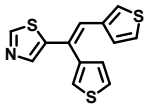
(*E*)-5-(1,2-bis(2-fluorophenyl)vinyl)thiazole (2l). Following the general procedure, the reaction was set up with thiazole (172 mg, 2.0 mmol) and 1,2-bis(2-fluorophenyl)ethyne (107 mg, 0.50 mmol). Purification by flash column chromatography (hexanes/EtOAc = 7:1) provided **2l** as a yellow solid (101 mg, 67% yield). mp 98-100 ℃; IR (film) 3062, 2924, 2852, 1603, 1489, 1222, 869 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.69 (s, 1H), 7.49 (s, 1H), 7.37 (q, *J* = 6.8 Hz, 1H), 7.26-7.20 (m, 2H), 7.12 (q, *J* = 8.2 Hz, 3H), 6.99 (t, *J* = 9.3 Hz, 1H), 6.78-6.71 (m, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 160.8 (d, *J* = 249.4 Hz), 160.3 (d, *J* = 248.5 Hz), 152.4, 141.7, 141.6, 131.6 (d, *J* = 3.2 Hz), 130.7 (d, *J* = 8.0 Hz), 129.5 (d, *J* = 8.5 Hz), 129.3 (d, *J* = 2.5 Hz), 128.8, 125.8 (d, *J* = 16.1 Hz), 124.8 (d, *J* = 3.7 Hz), 123.9 (d, *J* = 12.4 Hz), 123.7 (d, *J* = 3.6 Hz), 123.5 (d, *J* = 5.3 Hz), 116.5 (d, *J* = 21.5 Hz), 115.5 (d, *J* = 22.2 Hz); HRMS (ESI) calcd for $C_{17}H_{12}F_2NS$ $[M+H]^+$ 300.0653, found 300.0645.



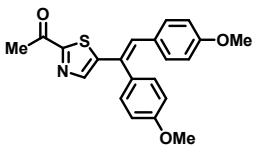
(*E*)-5-(1,2-di(naphthalen-2-yl)vinyl)thiazole (2m). Following the general procedure, the reaction was set up with thiazole (172 mg, 2.0 mmol) and diethyl 1,2-di(naphthalen-2-yl)ethyne (161 mg, 0.50 mmol). Purification by flash column chromatography (hexanes/EtOAc = 2:1) provided **2m** as a yellow solid (128 mg, 70% yield). mp 59-61 °C; IR (film) 3051, 2921, 2851, 1593, 1460, 811 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.72 (s, 1H), 7.92-7.86 (m, 3H), 7.78 (d, *J* = 7.7 Hz, 1H), 7.66-7.57 (m, 4H), 7.53 (t, *J* = 7.0 Hz, 2H), 7.44-7.35 (m, 4H), 7.28 (s, 1H), 6.98 (d, *J* = 8.6 Hz, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 152.2, 143.4, 141.8, 136.3, 133.8, 133.7, 133.33, 133.31, 133.2, 132.6, 130.1, 129.8, 129.1, 128.9, 128.3, 128.2, 128.0, 127.8, 127.6, 126.71, 126.65, 126.5, 126.4, 126.3; HRMS (ESI) calcd for $C_{25}H_{18}NS$ $[M+H]^+$ 364.1154, found 364.1154.



(*E*)-5-(1,2-di(thiophen-2-yl)vinyl)thiazole (2n). Following the general procedure, the reaction was set up with thiazole (172 mg, 2.0 mmol) and 1,2-di(thiophen-2-yl)ethyne (95 mg, 0.50 mmol). Purification by flash column chromatography (hexanes/EtOAc = 4:1) provided **2n** as a brown oil (70 mg, 51% yield). IR (film) 3072, 2999, 2920, 2851, 1594, 1489, 855 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.66 (s, 1H), 7.59-7.53 (m, 2H), 7.33 (s, 1H), 7.21-7.16 (m, 2H), 7.10 (d, *J* = 3.4 Hz, 1H), 7.05 (d, *J* = 3.1 Hz, 1H), 6.93 (t, *J* = 4.3 Hz, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 151.7, 142.4, 141.4, 139.5, 137.4, 130.5, 129.0, 128.5, 128.1, 128.0, 126.5, 126.1, 122.9; HRMS (ESI) calcd for $C_{13}H_{10}NS_3$ $[M+H]^+$ 275.9970, found 275.9966.

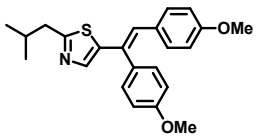


(*E*)-5-(1,2-di(thiophen-3-yl)vinyl)thiazole (2o). Following the general procedure, the reaction was set up with thiazole (172 mg, 2.0 mmol) and 1,2-di(thiophen-3-yl)ethyne (95 mg, 0.50 mmol). Purification by flash column chromatography (hexanes/EtOAc = 4:1) provided **2o** as a brown solid (65 mg, 47% yield). mp 76-79 ℃; IR (film) 2982, 2921, 2849, 1596, 1490, 871 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.66 (s, 1H), 7.53 (s, 1H), 7.47-7.43 (m, 1H), 7.29-7.26 (m, 1H), 7.12-7.09 (m, 1H), 7.04 (s, 1H), 7.03-7.01 (m, 1H), 6.96-6.93 (m, 1H), 6.54 (d, *J* = 5.0 Hz, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 151.7, 142.5, 141.2, 138.6, 137.8, 128.6, 127.8, 126.7, 125.4, 125.2, 124.7, 124.5; HRMS (ESI) calcd for $C_{13}H_{10}NS_3$ $[M+H]^+$ 275.9970, found 275.9966.

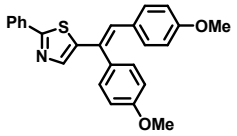


(*E*)-1-(5-(1,2-bis(4-methoxyphenyl)vinyl)thiazol-2-yl)ethenone (5a). Following the general procedure, the reaction was set up with 1-(thiazol-2-yl)ethanone (260 mg, 2.0 mmol), 1,2-bis(4-methoxyphenyl)ethyne (119 mg, 0.50 mmol) and *N*,*N*-dimethylacetamide (0.7 mL, 0.75 M). The reaction

mixture was stirred at 110 °C. Purification by flash column chromatography (hexanes/EtOAc = 7:1) provided **5a** as a yellow oil (150 mg, 82% yield). The isolated ^{1}H NMR of the **5a** showed the formation of *Z*-alkenylation product (E/Z = 12:1). IR (film) 2955, 2930, 2836, 1679, 1603, 1510 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57 (s, 1H), 7.20 (d, *J* = 8.2 Hz, 2H), 7.08 (s, 1H), 6.98-6.94 (m, 4H), 6.69 (d, *J* = 8.5 Hz, 2H), 3.87 (s, 3H), 3.76 (s, 3H), 2.67 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 191.8, 164.1, 159.6, 159.3, 151.9, 141.8, 131.3, 131.2, 130.9, 130.44, 130.41, 128.5, 114.8, 113.8, 55.4, 55.3, 25.7; HRMS (ESI) calcd for $C_{21}H_{20}NO_3S$ $[M+H]^+$ 366.1164, found 366.1159.

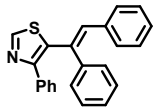


(*E*)-5-(1,2-bis(4-methoxyphenyl)vinyl)-2-isobutylthiazole (5b). Following the general procedure, the reaction was set up with 2-isobutylthiazole (291 mg, 2.0 mmol), 1,2-bis(4-methoxyphenyl)ethyne (119 mg, 0.50 mmol) and *N*,*N*-dimethylacetamide (0.7 mL, 0.75 M). The reaction mixture was stirred at 110 °C. Purification by flash column chromatography (hexanes/EtOAc = 10:1) provided **5b** as a green oil (143 mg, 75% yield). IR (film) 3000, 2954, 2868, 2834, 1602, 1507 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.21 (d, *J* = 8.8 Hz, 2H), 7.19 (s, 1H), 6.95-6.89 (m, 4H), 6.82 (s, 1H), 6.67 (d, *J* = 8.7 Hz, 2H), 3.86 (s, 3H), 3.74 (s, 3H), 2.82 (d, *J* = 7.2 Hz, 2H), 2.18-2.02 (m, 1H), 1.00 (d, *J* = 6.6 Hz, 6H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 169.0, 159.3, 158.6, 143.0, 139.9, 131.4, 131.0, 130.7, 129.2, 128.0, 114.4, 113.6, 55.3, 55.2, 42.7, 29.9, 22.4; HRMS (ESI) calcd for $C_{23}H_{26}NO_2S$ $[M+H]^+$ 380.1684, found 380.1684.



(*E*)-5-(1,2-bis(4-methoxyphenyl)vinyl)-2-phenylthiazole (5c). Following the general procedure, the reaction was set up with 2-phenylthiazole[22] (322 mg, 2.0 mmol), 1,2-bis(4-methoxyphenyl)ethyne (119 mg, 0.50 mmol) and *N*,*N*-dimethylacetamide (0.7 mL, 0.75 M). The reaction mixture was stirred at 110 °C. Purification by flash column chromatography (hexanes/EtOAc = 22:1) provided **5c** as a yellow solid (186 mg, 93% yield). The isolated ^{1}H NMR of the **5c** showed the formation of *Z*-alkenylation product

(E/Z = 12:1). mp 45-48 °C; IR (film) 3000, 2921, 2851, 1601, 1507, 1452 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.97-7.88 (m, 2H), 7.45-7.37 (m, 4H), 7.23 (s, 1H), 7.04-6.83 (m, 6H), 6.68 (d, *J* = 8.8 Hz, 2H), 3.86 (s, 3H), 3.74 (s, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 166.3, 159.5, 158.8, 144.0, 141.5, 133.9, 131.3, 131.1, 131.0, 130.0, 129.2, 129.1, 128.6, 126.5, 114.6, 113.7, 55.4, 55.3; HRMS (ESI) calcd for $C_{25}H_{22}NO_2S$ $[M+H]^+$ 400.1371, found 400.1372.

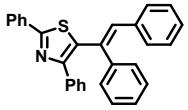


(*E*)-5-(1,2-diphenylvinyl)-4-phenylthiazole (5d).

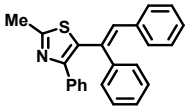
4-Phenylthiazole was prepared by Suzuki reaction.[23] To a 40 mL-glass vial equipped with a magnetic stir bar were sequentially added 4-bromothiazole (492 mg, 3.0 mmol), phenylboronic acid (549 mg, 4.5 mmol), K_2CO_3 (829 mg, 6.0 mmol), 1,4-dioxane (3.0 mL), H_2O (1.0 mL) and $Pd(PPh_3)_4$ (231 mg, 0.065 mmol). The reaction mixture was purged with argon through a Teflon-lined cap. Then, the cap was replaced with a new Teflon-lined solid cap. The reaction vial was heated at 100 °C for 18 h. After cooling to 25 °C, the reaction mixture was treated with water (15 mL) and EtOAc (15 mL) and transferred to a 125 mL-separatory funnel. The organic layer was collected and the aqueous layer was extracted with EtOAc (15 mL × 2). The combined organic layers were washed with brine (20 mL), dried over sodium sulfate and filtered. The residue was then purified by flash column chromatography (hexanes/EtOAc = 10:1) to afford 4-phenylthiazole as a white solid (300 mg, 62% yield). ^1H NMR was matched with the reported data.[8i] ^1H NMR (300 MHz, $CDCl_3$) δ 8.90 (s, 1H), 7.94 (d, *J* = 6.6 Hz, 2H), 7.55 (s, 1H), 7.48-7.42 (m, 2H), 7.39-7.33 (m, 1H).

Following the general procedure, the reaction was set up with 4-phenylthiazole (322 mg, 2.0 mmol), diphenylacetylene (91 mg, 0.50 mmol) and acetic acid (9 mg, 0.15 mmol). Purification by flash column chromatography (hexanes/EtOAc = 20:1) provided **5d** as a yellow solid (104 mg, 61% yield). mp 118-120 °C; IR (film) 3054, 3022, 1598, 1477, 1443, 767 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.78 (s, 1H), 7.77 (d, *J* = 7.1 Hz, 2H), 7.36-7.18 (m, 8H), 7.18-7.09 (m, 3H), 7.08-6.98 (m, 2H), 6.85 (s, 1H); $^{13}C\{^1H\}$

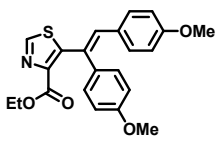
NMR (75 MHz, $CDCl_3$) δ 152.1, 151.3, 139.0, 136.6, 136.4, 134.9, 133.4, 132.5, 129.9, 129.5, 128.9, 128.5, 128.3, 128.2, 128.1, 127.9, 127.5; HRMS (ESI) calcd for $C_{23}H_{18}NS$ $[M+H]^+$ 340.1160, found 340.1156.



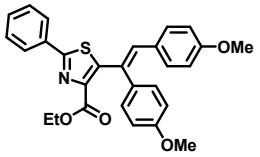
(*E*)-5-(1,2-diphenylvinyl)-2,4-diphenylthiazole (5e). Following the general procedure, the reaction was set up with 2,4-diphenylthiazole[24] (237 mg, 1.0 mmol) and diphenylacetylene (91 mg, 0.50 mmol). Purification by flash column chromatography (Et_2O/EtOAc = 10:1) provided **5e** as a white solid (152 mg, 73% yield). mp 124-126 °C; IR (film) 3054, 3022, 1597, 1478, 1441, 857 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.06-7.97 (m, 2H), 7.91-7.82 (m, 2H), 7.48-7.42 (m, 3H), 7.35-7.23 (m, 8H), 7.19-7.14 (m, 3H), 7.10-7.03 (m, 2H), 6.92 (s, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 165.6, 152.4, 139.2, 136.8, 136.6, 135.3, 133.7, 133.0, 132.8, 130.1, 130.0, 129.5, 129.03, 128.96, 128.5, 128.3, 128.2, 128.1, 127.8, 127.4, 126.5; HRMS (ESI) calcd for $C_{29}H_{22}NS$ $[M+H]^+$ 416.1473, found 416.1466.



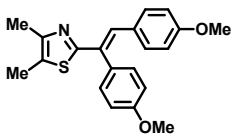
(*E*)-5-(1,2-diphenylvinyl)-2-methyl-4-phenylthiazole (5f). Following the general procedure, the reaction was set up with 2-methyl-4-phenylthiazole (175 mg, 1.0 mmol) and diphenylacetylene (91 mg, 0.50 mmol). Purification by flash column chromatography (hexanes/DCM = 5:1) provided **5f** as a white solid (123 mg, 70% yield). mp 114-116 °C; IR (film) 2920, 2847, 1736, 1650, 1598, 1491, 768 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.78-7.66 (m, 2H), 7.26-7.10 (m, 10H), 7.02-6.96 (m, 2H), 6.79 (s, 1H), 2.72 (s, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 164.2, 151.1, 139.3, 136.6, 136.1, 135.2, 132.9, 132.8, 129.9, 129.4, 128.9, 128.5, 128.3, 128.1, 128.0, 127.7, 127.3, 19.4; HRMS (ESI) calcd for $C_{24}H_{20}NS$ $[M+H]^+$ 354.1311, found 354.1309.



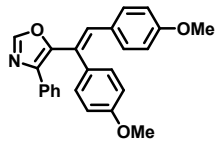
(*E*)-ethyl 5-(1,2-bis(4-methoxyphenyl)vinyl)thiazole-4-carboxylate (5g). Following the general procedure, the reaction was set up with ethyl thiazole-4-carboxylate (321 mg, 2.0 mmol), 1,2-bis(4-methoxyphenyl)ethyne (119 mg, 0.50 mmol) and acetic acid (9 mg, 0.15 mmol). Purification by flash column chromatography (hexanes/EtOAc = 3:1) provided **5g** as a yellow oil (53 mg, 27% yield). IR (film) 2955, 2933, 2836, 1719, 1603, 1509 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.67 (s, 1H), 7.18 (d, *J* = 8.7 Hz, 2H), 7.06 (d, *J* = 8.7 Hz, 2H), 6.83 (s, 1H), 6.81 (d, *J* = 5.8 Hz, 2H), 6.71 (d, *J* = 8.8 Hz, 2H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.81 (s, 3H), 3.77 (s, 3H), 1.22 (t, *J* = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 162.4, 159.3, 159.2, 151.1, 149.4, 142.4, 133.0, 131.8, 131.1, 131.0, 128.8, 128.6, 114.0, 113.7, 61.4, 55.31, 55.29, 14.3; HRMS (ESI) calcd for $C_{22}H_{22}NO_4S$ $[M+H]^+$ 396.1270, found 396.1268.



(*E*)-ethyl 5-(1,2-bis(4-methoxyphenyl)vinyl)-2-phenylthiazole-4-carboxylate (5h). Following the general procedure, the reaction was set up ethyl 2-phenylthiazole-4-carboxylate[25] (194 mg, 1.0 mmol) and 1,2-bis(4-methoxyphenyl)ethyne (119 mg, 0.50 mmol). Purification by flash column chromatography (hexanes/EtOAc = 4:1) provided **5h** as a yellow solid (194 mg, 82% yield). The isolated ^1H NMR of the **5h** showed the formation of *Z*-alkenylation product (E/Z = 6:1). mp 70-72 °C; IR (film) 3052, 2933, 1718, 1509, 1247, 829 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.00-7.89 (m, 2H), 7.45-7.40 (m, 3H), 7.22 (d, *J* = 8.7 Hz, 2H), 7.07 (d, *J* = 8.7 Hz, 2H), 6.85 (s, 1H), 6.83 (d, *J* = 8.8 Hz, 2H), 6.72 (d, *J* = 8.8 Hz, 2H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.82 (s, 3H), 3.78 (s, 3H), 1.19 (t, *J* = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 165.6, 162.9, 159.2, 159.0, 148.3, 142.8, 132.9, 132.4, 131.6, 131.01, 131.00, 130.4, 129.0, 128.9, 128.8, 126.7, 113.9, 113.6, 61.3, 55.20, 55.16, 14.2; HRMS (ESI) calcd for $C_{28}H_{26}NO_4S$ $[M+H]^+$ 472.1577, found 472.1578.

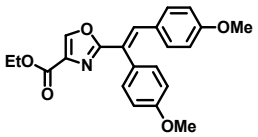


(*E*)-2-(1,2-bis(4-methoxyphenyl)vinyl)-4,5-dimethylthiazole (5i). Following the general procedure, the reaction was set up with 4,5-dimethylthiazole (231 mg, 2.0 mmol) and 1,2-bis(4-methoxyphenyl)ethyne (119 mg, 0.50 mmol). Purification by flash column chromatography (hexanes/EtOAc = 21:1) provided **5i** as a yellow oil (97 mg, 55% yield). IR (film) 2998, 2952, 2919, 2834, 1600, 1507 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.60 (s, 1H), 7.28-7.21 (m, 2H), 7.03-6.90 (m, 4H), 6.66 (d, *J* = 7.7 Hz, 2H), 3.85 (s, 3H), 3.73 (s, 3H), 2.36 (s, 3H), 2.28 (s, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 167.8, 159.6, 159.0, 149.3, 132.1, 131.5, 131.4, 129.0, 127.7, 127.3, 114.5, 113.7, 55.4, 55.3, 15.1, 11.6; HRMS (ESI) calcd for $C_{21}H_{22}NO_2S$ $[M+H]^+$ 352.1371, found 352.1366.



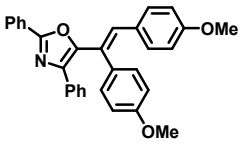
(*E*)-5-(1,2-bis(4-methoxyphenyl)vinyl)-4-phenyloxazole (6a). Following the general procedure, the reaction was set up with 4-phenyloxazole (290 mg, 2.0 mmol), 1,2-bis(4-methoxyphenyl)ethyne (119 mg, 0.50 mmol) and acetic acid (9.0 mg, 0.15 mmol). The ^1H NMR of the reaction mixture showed the formation of the corresponding C5- and C2-alkenylation products (C5:C2 = 10:1). Purification by flash column chromatography (hexanes/EtOAc = 9:1) provided the C5 isomer, **6a**, as a yellow oil (117 mg, 61% yield). IR (film) 3001, 2955, 2931, 2835, 1603, 1509 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.65-7.49 (m, 2H), 7.23-7.17 (m, 3H), 7.14 (d, *J* = 8.7 Hz, 2H), δ 7.04 (s, 1H), 7.00 (d, *J* = 4.7 Hz, 2H), 6.74 (d, *J* = 8.8 Hz, 2H), 6.70 (d, *J* = 8.9 Hz, 2H), 3.77 (s, 3H), 3.76 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.4, 159.1, 149.6, 148.2, 135.9, 132.1, 131.23, 131.16, 131.0, 128.9, 128.7, 128.1, 127.8, 127.5, 127.4, 114.2, 113.7, 55.4, 55.3; HRMS (ESI) calcd for $C_{22}H_{22}NO_5$ $[M+H]^+$ 384.1600, found 384.1590.

(*E*)-2-(1,2-bis(4-methoxyphenyl)vinyl)-4-phenyloxazole (the C2 isomer). ^1H NMR (300 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.76 (d, *J* = 7.1 Hz, 2H), 7.73 (s, 1H), 7.44-7.35 (m, 2H), 7.35-7.27 (m, 3H), 7.07 (d, *J* = 8.6 Hz, 2H), 6.97 (d, *J* = 8.8 Hz, 2H), 6.72 (d, *J* = 8.8 Hz, 2H), 3.88 (s, 3H), 3.77 (s, 3H).



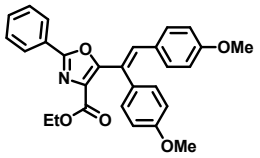
(*E*)-ethyl 2-(1,2-bis(4-methoxyphenyl)vinyl)oxazole-4-carboxylate (6b). Following the general procedure, the reaction was set up with ethyl oxazole-4-carboxylate (294 mg, 2.0 mmol) 1,2-bis(4-methoxyphenyl)ethyne (119 mg, 0.50 mmol) and acetic acid (9.0 mg, 0.15 mmol). The ^{1}H NMR of the reaction mixture showed the formation of the corresponding C2- and C5-alkenylation products (C2/C5 = 8:1).Purification by flash column chromatography (hexanes/EtOAc = 9:1) provided the C2 isomer, **6b**, as a yellow solid (154 mg, 81% yield). mp 124-125 °C; IR (film) 2957, 2933, 2836, 1716, 1602, 1509 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.80 (s, 1H), 7.25 (d, *J* = 8.6 Hz, 2H), 7.05 (d, *J* = 8.5 Hz, 2H), 6.96 (d, *J* = 8.3 Hz, 2H), 6.71 (d, *J* = 8.5 Hz, 2H), 4.40 (q, *J* = 7.0 Hz, 2H), 3.87 (s, 3H), 3.76 (s, 3H), 1.39 (t, *J* = 7.0 Hz, 3H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 164.9, 161.7, 159.9, 159.6, 143.6, 134.9, 134.5, 132.0, 131.3, 127.9, 127.6, 125.4, 114.6, 113.8, 61.4, 55.40, 55.35, 14.5; HRMS (ESI) calcd for $C_{22}H_{22}NO_5$ $[M+H]^+$ 380.1498, found 380.1493.

(*E*)-ethyl 5-(1,2-bis(4-methoxyphenyl)vinyl)oxazole-4-carboxylate (the C5 isoemr). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.42 (s, 1H), 7.17 (d, *J* = 8.7 Hz, 2H), 7.06 (d, *J* = 8.6 Hz, 2H), 6.88 (d, *J* = 8.8 Hz, 2H), 6.71 (d, *J* = 8.8 Hz, 2H), 4.25 (q, *J* = 7.1 Hz, 2H), 3.83 (s, 3H), 3.77 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H).

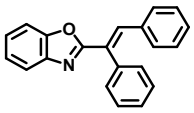


(*E*)-5-(1,2-bis(4-methoxyphenyl)vinyl)-2,4-diphenyloxazole (6c). Following the general procedure, the reaction was set up with 2,4-diphenyloxazole (443 mg, 2.0 mmol), 1,2-bis(4-methoxyphenyl)ethyne (119 mg, 0.50 mmol) and acetic acid (9.0 mg, 0.15 mmol). Purification by flash column chromatography (hexanes/EtOAc = 15:1) provided **6c** as a yellow solid (190 mg, 83% yield). mp 63-66 °C; IR (film) 3053, 2986, 1604, 1553, 1510, 1263 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.16-8.06 (m, 2H), 7.52-7.42 (m, 5H), 7.21-7.14 (m, 4H), 7.12 (d, *J* = 3.9 Hz, 2H), 7.05 (d, *J* = 8.8 Hz, 2H), 6.71 (d, *J* = 4.9 Hz, 2H), 6.69 (d, *J*

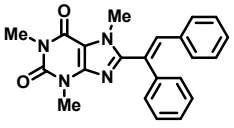
= 4.8 Hz, 2H), 3.77 (s, 3H), 3.76 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.8, 159.4, 159.0, 147.9, 138.2, 132.6, 131.5, 131.2, 130.4, 130.1, 129.2, 128.8, 128.6, 128.2, 127.9, 127.6, 127.4, 126.6, 114.1, 113.7, 55.4, 55.3; HRMS (ESI) calcd for $C_{22}H_{22}NO_5$ $[M+H]^+$ 460.1913, found 460.1909.



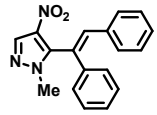
(*E*)-ethyl 5-(1,2-bis(4-methoxyphenyl)vinyl)-2-phenyloxazole-4-carboxylate (6d). Following the general procedure, the reaction was set up with ethyl 2-phenyloxazole-4-carboxylate[21] (217 mg, 1.0 mmol), and 1,2-bis(4-methoxyphenyl)ethyne (119 mg, 0.50 mmol). Purification by flash column chromatography (hexanes/EtOAc = 2:1) provided **6d** as a yellow solid (195 mg, 86% yield). mp 137-139 °C; IR (film) 3052, 2933, 1719, 1508, 1246, 828 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.07-7.98 (m, 2H), 7.46-7.41 (m, 3H), 7.38 (s, 1H), 7.23 (d, *J* = 8.7 Hz, 2H), 7.09 (d, *J* = 8.8 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 6.72 (d, *J* = 8.8 Hz, 2H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.85 (s, 3H), 3.78 (s, 3H), 1.22 (t, *J* = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 162.3, 159.5, 159.4, 159.2, 156.8, 134.6, 131.4, 131.0, 130.8, 129.3, 128.7, 128.4, 126.8, 126.5, 125.8, 114.1, 113.6, 61.2, 55.3, 55.2, 14.2; HRMS (ESI) calcd for $C_{28}H_{26}NO_5$ $[M+H]^+$ 456.1805, found 456.1810.



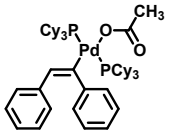
(*E*)-2-(1,2-diphenylvinyl)benzo[d]oxazole (6e). Following the general procedure, the reaction was set up with benzoxazole (119 mg, 1.0 mmol) and diphenylacetylene (91 mg, 0.50 mmol). Purification by flash column chromatography (hexanes/EtOAc = 9:1) provided **6e** as a white solid (121 mg, 81% yield). ^{1}H NMR was matched with the reported data.[20] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.77-7.69 (m, 1H), 7.56-7.51 (m, 1H), 7.48-7.44 (m, 3H), 7.43-7.37 (m, 3H), 7.34-7.29 (m, 2H), 7.21-7.19 (m, 2H), 7.14-7.10 (m, 2H).



(*E*)-8-(1,2-diphenylvinyl)-1,3,7-trimethyl-1*H*-purine-2,6(3*H*,7*H*)-dione (7).[26] Following the general procedure, the reaction was set up with 1,3,7-trimethyl-1*H*-purine-2,6(3*H*,7*H*)-dione (caffeine, 194 mg, 1.0 mmol) and diphenylacetylene (91 mg, 0.50 mmol). Purification by flash column chromatography (hexanes/EtOAc = 6:1) provided **7** as a white solid (129 mg, 69% yield). ^{1}H NMR (300 MHz, $CDCl_3$) 7.35-7.33 (m, 4H), 7.26-7.09 (m, 7H), 3.65 (s, 3H), 3.47 (s, 3H), 3.41 (s, 3H).



(*E*)-5-(1,2-diphenylvinyl)-1-methyl-4-nitro-1*H*-pyrazole (8). Following the general procedure, the reaction was set up with 1-methyl-4-nitro-1*H*-pyrazole[27] (127 mg, 1.0 mmol) and diphenylacetylene (91 mg, 0.50 mmol). Purification by flash column chromatography (hexanes/EtOAc = 9:1) provided **8** as a yellow solid (88 mg, 58% yield). mp 108-109 °C; IR (film) 3124, 3054, 3023, 2949, 1543, 1498 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.28-7.20 (m, 10H), 6.83 (s, 1H), 3.79 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 143.1, 136.34, 136.27, 135.9, 134.9, 129.7, 129.4, 128.9, 128.59, 128.57, 128.4, 127.5, 38.0; HRMS (ESI) calcd for $C_{18}H_{16}N_3O_2$ $[M+H]^+$ 306.1243, found 306.1235.



Synthesis and Characterization of Alkenyl Pd(II) Complex 9

To an 8 mL-glass vial equipped with a magnetic stir bar, diphenylacetylene (182 mg, 1.0 mmol), $Pd(PCy_3)_2$ (178 mg, 1.0 mmol) and benzene (2.2 mL, 0.45 M) were added. After 30 minutes of stirring at 25 °C, acetic acid (57 μL, 1.0 mmol) was injected. The reaction mixture was stirred at 25 °C for 11 h, and a white solid precipitated. The solution was filtered and the filtrate was washed with pentane three times to afford **9** as a white solid (570 mg, 63% yield). Crystals suitable for X-ray crystallography were obtained from vapor diffusion of hexanes into a saturated benzene solution of **9** at −20 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 (d, J = 6.7 Hz, 2H), 7.14-7.03 (m, 5H), 7.01-6.93 (m, 3H), 6.13 (s, 1H), 2.10-1.98 (m, 12H), 1.84 (s, 3H), 1.83-1.59 (m, 30H), 1.34-1.02 (m, 24H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 175.4,

151.8, 146.0, 138.7, 131.0, 128.54, 128.46, 127.7, 127.5, 126.1, 124.6, 33.2 (t, J = 8.1 Hz), 29.9, 29.1, 28.3 (t, J = 4.8 Hz), 28.1 (t, J = 5.2 Hz), 26.7, 25.3.

Hydroarylation Using Alkenyl Pd(II) Complex 9. To an 8 mL-glass vial equipped with a magnetic stir bar, thiazole (17 mg, 0.2 mmol), complex **9** (45 mg, 0.05 mmol), and *N*,*N*-dimethylacetamide (0.50 mL, 0.10 M) were sequentially added in an argon-purged glove box. The reaction mixture was stirred at 130 ℃ for 14 h and cooled to 25 ℃. The GC analysis of the reaction mixture showed the formation of **2a** and **3a** in 29% and 42% yields, respectively.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

NMR spectra and X-ray data (PDF)

Crystallographic data for **2a** (CIF)

Crystallographic data for **9** (CIF)

AUTHOR INFORMATION

Corresponding Author

* E-mail: jmjoo@pusan.ac.kr

ORCID

Jung Min Joo: 0000-0003-1645-3322

Author Contributions

[+] These authors contributed equally to this work.

Acknowledgments. This research was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Science, ICT & Future Planning (NRF-2016R1D1A1B03930762 and NRF-2019R1A2C1007852). We thank Prof. Ok-Sang Jung at Pusan National University for assistance with analysis of x-ray structures and for helpful discussions.

REFERENCES

(1) Chen, B.; Heal, W. Thiazoles. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Ramsden, C. A., Scriven, E. F. V., Taylor, R. J. K., Eds.; Elsevier: Oxford, U.K., 2008; Vol. 4, pp 635−754.

(2) (a) Lin, Y.; Fan, H.; Li, Y.; Zhan, X., Thiazole-Based Organic Semiconductors for Organic Electronics. *Adv. Mater.* **2012,** *24*, 3087−3106. (b) Lvov, A. G.; Khusniyarov, M. M.; Shirinian, V. Z., Azole-Based Diarylethenes as the Next Step towards Advanced Photochromic Materials. *J. Photochem. Photobiol.* **2018**, *36*, 1−23.

(3) For recent reviews about C−H bond functionalization of heteroarenes, see: (a) Ackermann, L.; Vicente, R.; Kapdi, A. R., Transition-Metal-Catalyzed Direct Arylation of (Hetero)Arenes by C−H Bond Cleavage. *Angew. Chem. Int. Ed.* **2009,** *48*, 9792−9826. (b) Cho, S. H.; Kim, J. Y.; Kwak, J.; Chang, S., Recent Advances in The Transition Metal-Catalyzed Twofold Oxidative C−H Bond Activation Strategy for C−C and C−N Bond Formation. *Chem. Soc. Rev.* **2011,** *40*, 5068−5083. (c) Wencel-Delord, J.; Glorius, F., C−H Bond Activation Enables the Rapid Construction and Late-Stage Diversification of Functional Molecules. *Nat. Chem.* **2013,** *5*, 369−375. (d) Segawa, Y.; Maekawa, T.; Itami, K., Synthesis of Extended π-Systems through C−H Activation. *Angew. Chem. Int. Ed.* **2015,** *54*, 66−81. (e) Liu, C.; Yuan, J.; Gao, M.; Tang, S.; Li, W.; Shi, R.; Lei, A., Oxidative Coupling between Two Hydrocarbons: An Update of Recent C−H Functionalizations. *Chem. Rev.* **2015,** *115*, 12138−12204. (f) Bheeter, C. B.; Chen, L.; Soule, J.-F.; Doucet, H., Regioselectivity in Palladium-Catalysed Direct Arylation of 5-Membered Ring Heteroaromatics. *Catal. Sci. Technol.* **2016**, *6*, 2005−2049. (g) Zhu, R.-Y.; Farmer, M. E.; Chen, Y.-Q.; Yu, J.-Q., A Simple and Versatile Amide Directing Group for C−H Functionalizations. *Angew. Chem. Int. Ed.* **2016,** *55*, 10578−10599. (h) Yang, Y.; Lan, J.; You, J., Oxidative C−H/C−H Coupling Reactions between Two (Hetero)Arenes. *Chem. Rev.* **2017,** *117*, 8787−8863.

(4) For recent reviews about hydroarylation with heteroarenes, see: (a) Catalytic Hydroarylation of Carbon-Carbon Multiple Bonds; Ackermann, L., Gunnoe, T. B., Habgood, L. G., Eds.; Wiley-VCH Verlag GmbH & Co. KGaA: Weinheim, Germany, 2018. (b) Boyarskiy, V. P.; Ryabukhin, D. S.; Bokach, N. A.; Vasilyev, A. V., Alkenylation of Arenes and Heteroarenes with Alkynes. *Chem. Rev.* **2016,** *116*, 5894−5986. (c) Chinchilla, R.; Nájera, C., Chemicals from Alkynes with Palladium Catalysts. *Chem. Rev.* **2014,** *114*, 1783−1826. (d) Kitamura, T., Transition-Metal-Catalyzed Hydroarylation Reactions of Alkynes through Direct Functionalization of C−H Bonds: A Convenient Tool for Organic Synthesis. *Eur. J. Org. Chem.* **2009,** *2009*, 1111−1125.

(5) (a) Ding, Z.; Yoshikai, N., Cobalt-Catalyzed Addition of Azoles to Alkynes. O*rg. Lett.* **2010,** *12*, 4180−4183. (b) Ding, Z.; Yoshikai, N., Cobalt-Catalyzed Alkenylation of Thiazoles with Alkynes via C−H Bond Functionalization. *Synthesis* **2011,** *2011*, 2561−2566. (c) Gao, K.; Yoshikai, N., Low-Valent Cobalt Catalysis: New Opportunities for C−H Functionalization. *Acc. Chem. Res.* **2014,** *47*, 1208−1219.

(6) (a) Nakao, Y.; Kanyiva, K. S.; Oda, S.; Hiyama, T., Hydroheteroarylation of Alkynes under Mild Nickel Catalysis. *J. Am. Chem. Soc.* **2006,** *128*, 8146−8147. (b) Nakao, Y., Hydroarylation of Alkynes Catalyzed by Nickel. *Chem. Rec.* **2011,** *11*, 242−251.

(7) For example, Co-catalyzed hydroarylation reactions of 4-(4-methylthiazol-5-yl)benzonitrile with 2-hexyne at 60 °C and with diphenylacetylene at 80 °C afforded the corresponding products in 71% and 36% yields, respectively. See ref. 5b.

(8) (a) Aoyagi, Y.; Inoue, A.; Koizumi, I.; Hashimoto, R.; Tokunaga, K.; Gohma, K.; Komatsu, J.; Sekine, K.; Miyafuji, A.; Kunoh, J.; Honma, R.; Akita, Y.; Ohta, A. Palladium-Catalyzed Cross-Coupling Reactions of Chloropyrazines with Aromatic Heterocycles. *Heterocycles* **1992**, *33*, 257−272. (b) Pivsa-Art, S.; Satoh, T.; Kawamura, Y.; Miura, M.; Nomura, M., Palladium-Catalyzed Arylation of Azole Compounds with Aryl Halides in The Presence of Alkali Metal Carbonates and the Use of Copper Iodide in The Reaction. *Bull. Chem. Soc. Jpn.* **1998,** *71*, 467−473. (c) Parisien, M.; Valette, D.; Fagnou, K., Direct Arylation Reactions Catalyzed By $Pd(OH)_2$/C: Evidence for a Soluble Palladium Catalyst. *J. Org. Chem.* **2005,** *70*, 7578−7584. (d) Chiong, H. A.; Daugulis, O., Palladium-Catalyzed Arylation of Electron-Rich Heterocycles with Aryl Chlorides. *Org. Lett.* **2007,** *9*, 1449−1451. (e) Liégault, B.; Lapointe, D.; Caron, L.; Vlassova, A.; Fagnou, K., Establishment of Broadly Applicable Reaction Conditions for the Palladium-Catalyzed Direct Arylation of Heteroatom-Containing Aromatic Compounds. *J. Org. Chem.* **2009,** *74*, 1826−1834. (f) Roger, J.; Požgan, F.; Doucet, H., Ligand-Free Palladium-Catalyzed Direct Arylation of Thiazoles at Low Catalyst Loadings. *J. Org. Chem.* **2009,** *74*, 1179−1186. (g) Liu, X.-W.; Shi, J.-L.; Yan, J.-X.; Wei, J.-B.; Peng, K.; Dai, L.; Li, C.-G.; Wang, B.-Q.; Shi, Z.-J., Reigoselective Arylation of Thiazole Derivatives at 5-Position via Pd Catalysis under Ligand-Free Conditions. *Org. Lett.* **2013,** *15*, 5774−5777. (h) Bellina, F.; Lessi, M.; Manzini, C., Mild Palladium-Catalyzed Regioselective Direct Arylation of Azoles Promoted by Tetrabutylammonium Acetate. *Eur. J. Org. Chem.* **2013,** *2013*, 5621−5630. (i) Tani, S.; Uehara, T. N.; Yamaguchi, J.; Itami, K., Programmed Synthesis of Arylthiazoles through Sequential C–H Couplings. *Chem. Sci.* **2014,** *5*, 123−135.

(9) For regioselective C5-alkenylation of unsubstituted two-heteroatom-containing azoles using alkenes, see: (a) Liu, X.-W.; Shi, J.-L.; Wei, J.-B.; Yang, C.; Yan, J.-X.; Peng, K.; Dai, L.; Li, C.-G.; Wang, B.-Q.; Shi, Z.-J., Diversified Syntheses of Multifunctionalized Thiazole Derivatives via Regioselective and Programmed C−H Activation. *Chem. Commun.* **2015,** *51*, 4599−4602. (b) Achar, T. K.; Biswas, J. P.; Porey, S.; Pal, T.; Ramakrishna, K.; Maiti, S.; Maiti, D., Palladium-Catalyzed Template Directed C-5 Selective Olefination of Thiazoles. *J. Org. Chem.* **2019,** *84*, 8315−8321. (c) Kim, H. T.; Ha, H.; Kang, G.; Kim, O. S.; Ryu, H.; Biswas, A. K.; Lim, S. M.; Baik, M.-H.; Joo, J. M., Ligand-Controlled Regiodivergent C−H Alkenylation of Pyrazoles and its Application to the Synthesis of Indazoles. *Angew. Chem. Int. Ed.* **2017**, *56*, 16262−16266. (d) Kim, H.; Hwang, Y. J.; Han, I.; Joo, J. M., Regioselective C−H Alkenylation of Imidazoles and its Application to the Synthesis of Unsymmetrically Substituted Benzimidazoles. *Chem. Commun.* **2018,** *54*, 6879−6882.

(10) For C5-alkenylation of substituted thiazoles, see: (a) Miyasaka, M.; Hirano, K.; Satoh, T.; Miura, M., Palladium-Catalyzed Direct Oxidative Alkenylation Of Azoles. *J. Org. Chem.* **2010,** *75*, 5421−5424. (b) Li, Z.; Ma, L.; Tang, C.; Xu, J.; Wu, X.; Yao, H., Palladium(II)-Catalyzed Oxidative Heck Coupling Of Thiazole-4-Carboxylates. *Tetrahedron Lett.* **2011,** *52*, 5643−5647.

(11) We proposed hydropalladation of alkynes in the C−H functionalization of nitropyrazoles with terminal alkynes. Ha, H.; Shin, C.; Bae, S.; Joo, J. M., Divergent Palladium-Catalyzed Cross-Coupling of Nitropyrazoles with Terminal Alkynes. *Eur. J. Org. Chem.* **2018,** *2018*, 2645−2650.

(12) Shen, R.; Chen, T.; Zhao, Y.; Qiu, R.; Zhou, Y.; Yin, S.; Wang, X.; Goto, M.; Han, L.-B., Facile

Regio- and Stereoselective Hydrometalation of Alkynes with a Combination of Carboxylic Acids and Group 10 Transition Metal Complexes: Selective Hydrogenation of Alkynes with Formic Acid. *J. Am. Chem. Soc.* **2011,** *133*, 17037−17044.

(13) (a) Lee, P.-S.; Fujita, T.; Yoshikai, N., Cobalt-Catalyzed, Room-Temperature Addition of Aromatic Imines to Alkynes via Directed C−H Bond Activation. *J. Am. Chem. Soc.* **2011,** *133*, 17283−17295. (b) Fallon, B. J.; Derat, E.; Amatore, M.; Aubert, C.; Chemla, F.; Ferreira, F.; Perez-Luna, A.; Petit, M., C−H Activation/Functionalization Catalyzed by Simple, Well-Defined Low-Valent Cobalt Complexes. *J. Am. Chem. Soc.* **2015,** *137*, 2448−2451. (c) Guihaumé, J.; Halbert, S.; Eisenstein, O.; Perutz, R. N., Hydrofluoroarylation of Alkynes with Ni Catalysts. C−H Activation via Ligand-to-Ligand Hydrogen Transfer, An Alternative To Oxidative Addition. *Organometallics* **2012,** *31*, 1300−1314.

(14) (a) Minami, Y.; Noguchi, Y.; Yamada, K.; Hiyama, T., Intramolecular Hydroalkylation via Activation of *tert*-Butyl C−H Bond in Silylethynyl Aryl Ethers. *Chem. Lett.* **2016,** *45*, 1210−1212. (b) Minami, Y.; Noguchi, Y.; Hiyama, T., Synthesis of Benzosiloles by Intramolecular *Anti*-Hydroarylation via *Ortho*-C−H Activation of Aryloxyethynyl Silanes. *J. Am. Chem. Soc.* **2017,** *139*, 14013−14016. (c) Minami, Y.; Sakai, M.; Sakamaki, T.; Hiyama, T., Hydroarylation of 2-Aryloxybut-1-En-3-Ynes Via Pd/Acid-Catalyzed C−H Bond Activation: A Concise Synthesis of 2,3-Bismethylene-2,3-Dihydrobenzofurans. *Chem. Asian J.* **2017,** *12*, 2399−2403. (d) Minami, Y.; Furuya, Y.; Hiyama, T., Palladium/Acid-Catalyzed Straightforward Allylation of Arenes Using 1-Substituted Propynes via Aryl C−H Bond Activation. *Asian J. Org. Chem.* **2018,** *7*, 1343−1346. (e) Gimferrer, M.; Minami, Y.; Noguchi, Y.; Hiyama, T.; Poater, A., Monitoring of the Phosphine Role in the Mechanism of Palladium-Catalyzed Benzosilole Formation from Aryloxyethynyl Silanes. *Organometallics* **2018,** *37*, 1456−1461. Also, see: (f) Minami, Y.; Hiyama, T., Synthetic Transformations through Alkynoxy–Palladium Interactions and C−H Activation. *Acc. Chem. Res.* **2016,** *49*, 67−77.

(15) [Pd]: (a) Tsukada, N.; Murata, K.; Inoue, Y., Selective Cis-Addition of C−H Bonds of Pyrroles and Thiophenes to Alkynes Catalyzed by a Dinuclear Palladium Complex. *Tetrahedron Lett.* **2005,** *46*, 7515−7517. (b) Minami, Y.; Furuya, Y.; Kodama, T.; Hiyama, T., Alkenylation of Arenes Using Disubstituted Ethynes by Palladium/Carboxylic Acid Catalysis. *Chem. Lett.* **2018,** *47*, 674−677. Regio- and stereoselectivity were improved by directing groups. [Ru]: (c) Zhang, W.; Wei, J.; Fu, S.; Lin, D.; Jiang, H.; Zeng, W., Highly Stereoselective Ruthenium(II)-Catalyzed Direct C2-*Syn*-Alkenylation of Indoles with Alkynes. *Org. Lett.* **2015,** *17*, 1349−1352. [Co]: (d) Tanaka, R.; Ikemoto, H.; Kanai, M.; Yoshino, T.; Matsunaga, S., Site- and Regioselective Monoalkenylation of Pyrroles with Alkynes via Cp*Co^{III} Catalysis. *Org. Lett.* **2016,** *18*, 5732−5735.

(16) Crystallographic data for **2a** and **9** in this paper have been deposited with the Cambridge Crystallographic Data Centre as nos. CCDC 1917083 and 1917088, respectively. Copies of the data can be obtained, free of charge, via http://www.ccdc.cam.ac.uk/.

(17) Diaryl alkynes were readily prepared by Pd-catalyzed decarboxylative coupling of propiolic acid and bromoarenes. Park, K.; Bae, G.; Moon, J.; Choe, J.; Song, K. H.; Lee, S., Synthesis of Symmetrical and Unsymmetrical Diarylalkynes from Propiolic Acid Using Palladium-Catalyzed Decarboxylative Coupling. *J. Org. Chem.* **2010,** *75*, 6244−6251.

(18) Iitsuka, T.; Hirano, K.; Satoh, T.; Miura, M., Rhodium-Catalyzed Dehydrogenative Coupling of Phenylheteroarenes with Alkynes or Alkenes. *J. Org. Chem.* **2015,** *80*, 2804−2814.

(19) Hydroarylation of diphenylacetylene with benzoxazole using catalytic and stoichiometric amounts of $[Cp^*RhCl_2]_2$ gave **6e** in 45% and 76% yields, respectively. Tan, G.; Zhu, L.; Liao, X.; Lan, Y.; You,

J., Rhodium/Copper Cocatalyzed Highly *Trans*-Selective 1,2-Diheteroarylation of Alkynes with Azoles via C−H Addition/Oxidative Cross-Coupling: A Combined Experimental and Theoretical Study. *J. Am. Chem. Soc.* **2017,** *139*, 15724−15737.

(20) For regioselectivity of arylation of azole-4-carboxylates, see: Théveau, L.; Verrier, C.; Lassalas, P.; Martin, T.; Dupas, G.; Querolle, O.; Van Hijfte, L.; Marsais, F.; Hoarau, C., Mechanism Selection for Regiocontrol in Base-Assisted, Palladium-Catalysed Direct C−H Coupling with Halides: First Approach for Oxazole- and Thiazole-4-Carboxylates. *Chem.–Eur. J.* **2011,** *17*, 14450−14463.

(21) (a) Zargarian, D.; Alper, H., Palladium Chloride Catalyzed Dicarbonylation of Terminal Alkynes. *Organometallics* **1991,** *10*, 2914−2921. (b) Zargarian, D.; Alper, H., Palladium-Catalyzed Hydrocarboxylation of Alkynes with Formic Acid. O*rganometallics* **1993,** *12*, 712−724. (c) Amatore, C.; Bensalem, S.; Ghalem, S.; Jutand, A., Mechanism of the Carbopalladation of Alkynes by Aryl-Palladium Complexes. *J. Organomet. Chem.* **2004,** *689*, 4642−4646. (d) Krasovskiy, A.; Lipshutz, B. H., Ligand Effects on Negishi Couplings of Alkenyl Halides. *Org. Lett.* **2011,** *13*, 3818−3821. (e) Li, B. X.; Le, D. N.; Mack, K. A.; McClory, A.; Lim, N.-K.; Cravillion, T.; Savage, S.; Han, C.; Collum, D. B.; Zhang, H.; Gosselin, F., Highly Stereoselective Synthesis of Tetrasubstituted Acyclic All-Carbon Olefins via Enol Tosylation and Suzuki–Miyaura Coupling. *J. Am. Chem. Soc.* **2017,** *139*, 10777−10783.

(22) Herder, M.; Eisenreich, F.; Bonasera, A.; Grafl, A.; Grubert, L.; Pätzel, M.; Schwarz, J.; Hecht, S., Light-Controlled Reversible Modulation of Frontier Molecular Orbital Energy Levels in Trifluoromethylated Diarylethenes. *Chem.–Eur. J.* **2017,** *23*, 3743−3754.

(23) Davoren, J. E.; Lee, C.-W.; Garnsey, M.; Brodney, M. A.; Cordes, J.; Dlugolenski, K.; Edgerton, J. R.; Harris, A. R.; Helal, C. J.; Jenkinson, S.; Kauffman, G. W.; Kenakin, T. P.; Lazzaro, J. T.; Lotarski, S. M.; Mao, Y.; Nason, D. M.; Northcott, C.; Nottebaum, L.; O'Neil, S. V.; Pettersen, B.; Popiolek, M.; Reinhart, V.; Salomon-Ferrer, R.; Steyn, S. J.; Webb, D.; Zhang, L.; Grimwood, S., Discovery of the Potent and Selective M1 PAM-Agonist *N*-[(3*R*,4*S*)-3-Hydroxytetrahydro-2*H*-pyran-4-yl]-5-methyl-4-[4-(1,3-thiazol-4-yl)benzyl]pyridine-2-carboxamide (PF-06767832): Evaluation of Efficacy and Cholinergic Side Effects. *J. Med. Chem.* **2016,** *59*, 6313−6328.

(24) Sudo, Y.; Yamaguchi, E.; Itoh, A., Photo-Oxidative Cross-Dehydrogenative Coupling-Type Reaction of Thiophenes with α-Position of Carbonyls Using a Catalytic Amount of Molecular Iodine. *Org. Lett.* **2017,** *19*, 1610−1613.

(25) Li, Z.; Qiu, Q.; Xu, X.; Wang, X.; Jiao, L.; Su, X.; Pan, M.; Huang, W.; Qian, H., Design, Synthesis and Structure–Activity Relationship Studies of New Thiazole-Based Free Fatty Acid Receptor 1 Agonists for the Treatment Of Type 2 Diabetes. *Eur. J. Med. Chem.* **2016,** *113*, 246−257.

(26) Ryu, J.; Cho, S. H.; Chang, S., A Versatile Rhodium(I) Catalyst System for the Addition of Heteroarenes to Both Alkenes and Alkynes by a C−H Bond Activation. *Angew. Chem. Int. Ed.* **2012,** *51*, 3677−3681.

(27) Iaroshenko, V. O.; Gevorgyan, A.; Davydova, O.; Villinger, A.; Langer, P., Regioselective and Guided C–H Activation of 4-Nitropyrazoles. *J. Org. Chem.* **2014,** *79*, 2906−2915.