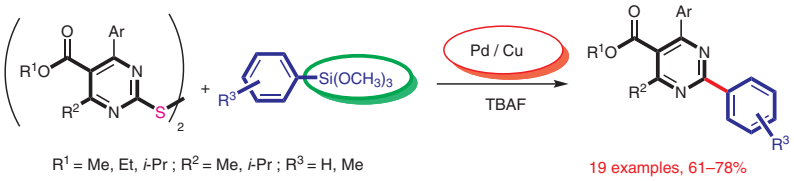
Synlett M.-X. Liu et al. Letter

Palladium-Catalyzed Copper-Promoted Hiyama-Type Carbon–Carbon Cross-Coupling Reactions of Dihetaryl Disulfides as Electrophiles

Ming-Xia Liu[a]
Hai-Peng Gong[b]
Zheng-Jun Quan*[a]
Xi-Cun Wang*[a]

[a] Key Laboratory of Polymer Materials, College of Chemistry and Chemical Engineering, Northwest Normal University, Gansu 730070, P. R. of China
quanzhengjun@hotmail.com
wangxicun@nwnu.edu.cn
[b] College of Natural Science, Gansu Agricultural University, No. 1 Yingmen Village, Anning District, Lanzhou, Gansu 730070, P. R. of China



R^1 = Me, Et, *i*-Pr ; R^2 = Me, *i*-Pr ; R^3 = H, Me

19 examples, 61–78%

Received: 14.07.2017
Accepted after revision: 11.09.2017
Published online: 26.10.2017
DOI: 10.1055/s-0036-1589116; Art ID: st-2017-w0558-l

Abstract Dihetaryl disulfides were used as electrophiles in a palladium-catalyzed carbon–carbon cross-coupling reaction with arylsilanes to realize a Hiyama-type reaction. This unique transformation shows high reactivity, excellent functional-group tolerance, and mild reaction conditions, making it an attractive alternative to conventional cross-coupling approaches for carbon–carbon bond construction.

Key words dihetaryl disulfides, arylsilanes, Hiyama reactions, cross-coupling, platinum catalyst, arylation

Metal-mediated Hiyama cross-coupling reactions are among the most powerful methods for producing C–C bonds in organic chemistry.[1] Compared with some other organometallic reagents, such as organomagnesium (Kumada–Corriu),[2] organoboron (Suzuki–Miyaura),[3] organotin (Stille),[4] or organozinc compounds (Negishi),[5] as nucleophilic partners for cross-coupling processes, organosilicon compounds are attractive owing to their ease of handling, low toxicity, high chemical stability, and broad availability. They would therefore appear to be interesting partners for the development of cross-coupling reactions in the synthesis of natural products or biologically active compounds.[6] Consequently, it would be useful to develop new electrophilic reagents for Hiyama cross-coupling reactions to extend their substrate scope and to increase the generality of their synthetic applications.

Aryl halides, and arenesulfonates[7–11] are usually employed as electrophiles in this reaction, owing to their high reactivities in transition-metal-catalyzed processes. These electrophiles can be easily generated from cheap and readily available thiophenols or thio ketones.[12] However, the use of dihetaryl disulfides as substrates in cross-coupling reactions has the advantage of greater atom economy and greater ease of handling. For instance, we have demonstrated that dihetaryl disulfides are potential C–C, C–S, and C–N coupling partners.[13–15] In our previous reports, we described the possible mechanism of the disulfide reaction process, and we showed that cleavage of the C–S bond requires an equivalent amount of the copper salt. To the best of our knowledge, there are no previous reports on the use of a disulfide as an electrophilic reactant with an organosilicon compound in a C–C coupling reaction.

In continuation of our interest in cross-coupling reactions of dipyrimidin-2-yl disulfides, and because compounds containing a pyrimidine ring display a wide range of pharmacological and biological properties,[16] such as calcium-channel modulation, antifungal, and antibacterial activities,[17] we examined use of dihetaryl disulfides as reaction partners in Hiyama cross-couplings, thereby providing an important extension of the scope of this reaction in heterocyclic chemistry.

Initially, we studied the effect of various catalysts on the C–C coupling reaction of the dipyrimidin-2-yl disulfide **1a** with trimethoxy(phenyl)silane (**2a**), with TBAF as an activator and 1,4-dioxane as the solvent under a nitrogen atmosphere for 24 hours at 110 °C (Table 1, entries 1–6). Unfortunately, we did not detected the formation of the desired product of **3a** when $Cu(OAc)_2$or $NiCl_2$ was used as a catalyst (entries 1 and 2). When we used $Ni(PPh_3)_2Cl_2$ or $Pd(PPh_3)_2$as the catalyst, we found that the byproduct **4** was obtained selectively, and no product **3a** was formed (entries 3 and 4). It was gratifying to note, however, that when $PdCl_2$ or $Pd(OAc)_2$was selected as the catalyst, a small amount of the C–C coupling product **3a** was obtained (entries 3 and 4). However, when $Pd(OAc)_2$was used as a catalyst and copper(I) iodide was added as an activator, the desired product **3a** was obtained in 18% yield (entry 7). This result prompted us to investigate the copper activator in detail. Copper (I) thiophene-2-carboxylate (CuTC) was found to be the most

efficient activator in this system (entry 9). Inspired by this result, we went on to examine the effects of various ligands (entries 10–12), and PCy_3 was shown to be the optimal ligand. Only a 15% yield of product **3a** was obtained in the absence of a Pd catalyst (entry 13). We then screened various bases. KF and C_SF provided the desired product in lower yields (entries 14 and 15). No product was observed when NaOH was used as the base (entry 16). A series of solvents

Table 1 Optimization of the Hiyama Reaction of Disulfide **1a** with Trimethoxy(phenyl)silane (**2a**)[a]

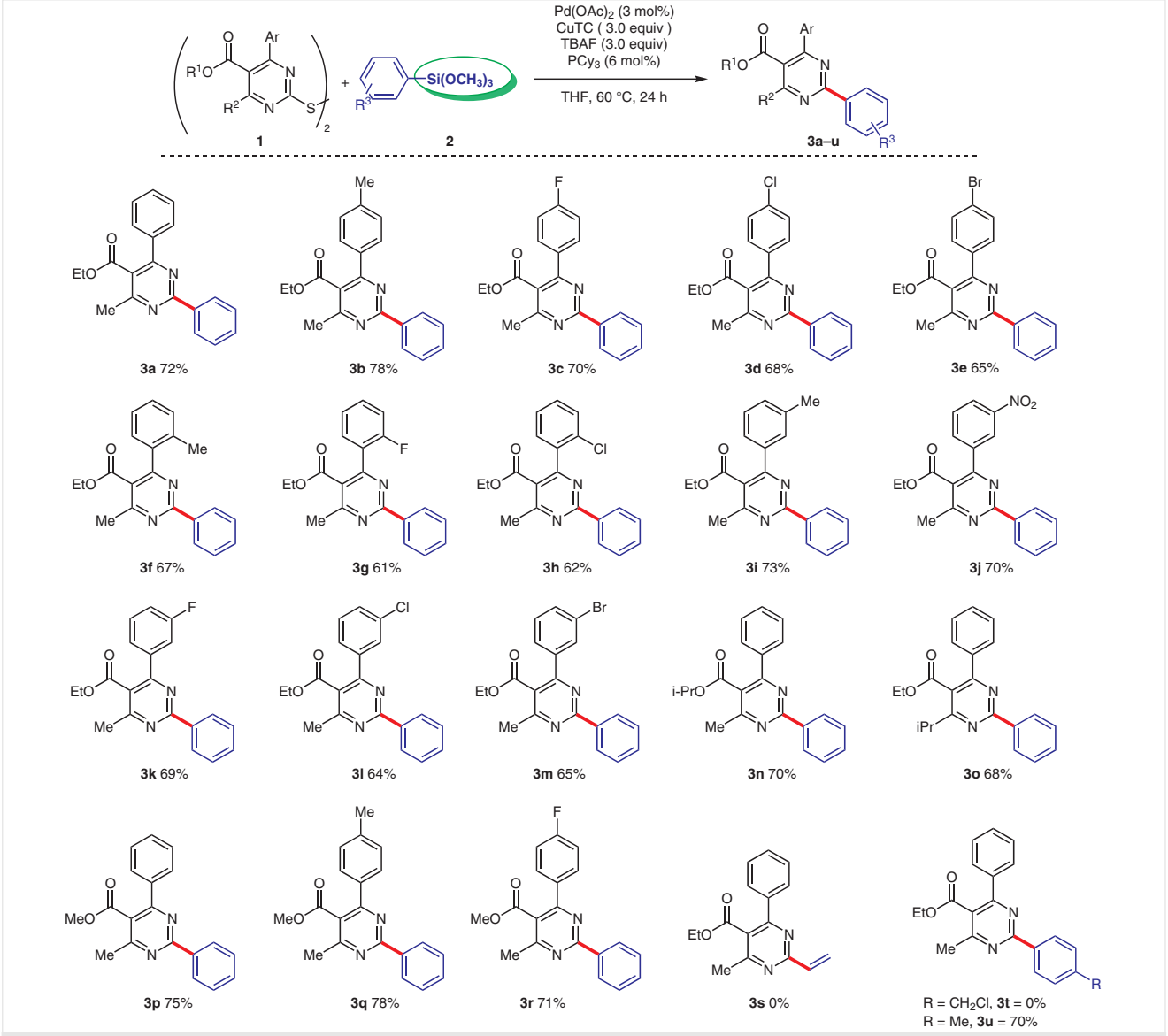
1a **2a** **3a** **4**

Entry	Catalyst	Additive	Ligand	Activator	Solvent	Temp (°C)	Yield[b] (%)	
							3a	**4**
1	$Cu(OAc)_2$	–	Phen[c]	TBAF	1,4-dioxane	110	0	0
2	$NiCl_2$	–	dppp[d]	TBAF	1,4-dioxane	110	0	0
3	$Ni(PPh_3)_2Cl_2$	–	–	TBAF	1,4-dioxane	110	0	70
4	$Pd(PPh_3)_2$	–	–	TBAF	1,4-dioxane	110	0	20
5	$PdCl_2$	–	dppp	TBAF	1,4-dioxane	110	<5	25
6	$Pd(OAc)_2$	–	dppp	TBAF	1,4-dioxane	110	<10	42
7	$Pd(OAc)_2$	CuI	dppp	TBAF	1,4-dioxane	110	18	8
8	$Pd(OAc)_2$	CuCl	dppp	TBAF	1,4-dioxane	110	27	15
9	$Pd(OAc)_2$	CuTC	dppp	TBAF	1,4-dioxane	110	32	<5
10	$Pd(OAc)_2$	CuTC	PPh_3	TBAF	1,4-dioxane	110	45	<5
11	$Pd(OAc)_2$	CuTC	PCy_3	TBAF	1,4-dioxane	110	50	0
12	$Pd(OAc)_2$	CuTC	X-Phos[e]	TBAF	1,4-dioxane	110	22	N.D
13	–	CuTC	PCy_3	TBAF	1,4-dioxane	110	15	0
14	$Pd(OAc)_2$	CuTC	PCy_3	KF	1,4-dioxane	110	Trace	<5
15	$Pd(OAc)_2$	CuTC	PCy_3	CsF	1,4-dioxane	110	<5	<5
16	$Pd(OAc)_2$	CuTC	PCy_3	NaOH	1,4-dioxane	110	0	<5
17	**$Pd(OAc)_2$**	**CuTC**	**PCy_3**	**TBAF**	**THF**	**60**	**72**	**<5**
18	$Pd(OAc)_2$	CuTC	PCy_3	TBAF	toluene	140	58	<5
19	$Pd(OAc)_2$	CuTC	PCy_3	TBAF	DMF	140	47	23
20	$Pd(OAc)_2$	CuTC	PCy_3	TBAF	xylene	140	45	17
21	$Pd(OAc)_2$	CuTC	PCy_3	-	THF	60	<5	45
22	$Pd(OAc)_2$	CuTC (4.0)	PCy_3	TBAF	THF	60	72	<5
23	$Pd(OAc)_2$	CuTC (2.0)	PCy_3	TBAF	THF	60	64	<5
24	$Pd(OAc)_2$	CuTC (1.0)	PCy_3	TBAF	THF	60	36	<5
25	$Pd(OAc)_2$	CuTC (0.5)	PCy_3	TBAF	THF	60	18	<5
26	$Pd(OAc)_2$	CuTC(0.15)	PCy_3	TBAF	THF	60	<10	<5
27[f]	$Pd(OAc)_2$	CuTC	PCy_3	TBAF	THF	60	35	<5

[a] Reaction conditions: **1a** (0.2 mmol, 0.1094 g), $PhSi(OMe)_3$ (**2a**; 3.0 equiv, 0.6 mmol, 0.1188 g), catalyst (3 mol%), additive (3.0 equiv), ligand (6 mol%), activator (3.0 equiv, 0.6 mmol), solvent (2 mL) under N_2, 24 h.
[b] Isolated yield after column chromatography (based on one pyrimidine group from one molecule).
[c] 1,10-phenanthroline.
[d] $Ph_2P(CH_2)_3PPh_2$.
[e] 2-(Dicyclohexylphosphino)-2′,4′,6′-triisopropylbiphenyl.
[f] Under air.

were also studied (entries 17–20). A 72% yield of **3a** was obtained when THF was used as the solvent (entry 17). Other solvents might add to the copper salt to produce copper salt complexes, resulting in low yields. When TBAF was omitted from the reaction system, the yield of the target product fell to less than 5%, demonstrating the importance of TBAF (entry 21). When the loading of CuTC was increased to 4.0 equivalents (entry 22), the yield was the same as that obtained with 3.0 equivalents (entry 17), and when the loading of CuTC was decreased to 2.0, 1.0, 0.5, or 0.15 equivalents, considerably lower yields of **3a** were obtained (entries 23–26). It is interesting that the reaction gave a 35% yield of **3a** when conducted in air (entry 27). On the basis of the above studies, the reaction is best conducted with $Pd(OAc)_2$ as the catalyst, CuTC as the additive, TBAF as the activator, and THF as the solvent at 60 °C for 24 hours.

With the optimized conditions in hand, we then explored the scope of this reaction (Scheme 1). A broad range of substituted disulfides were found to undergo this transformation.[18] In general, disulfides with electron-donating or electron-withdrawing groups in the *para*-positions of the benzene rings reacted with **2a** to afforded the desired products **3a–e** in good yields. The yield of the target product **3f–h** was slightly reduced because steric hindrance by the substituents in the *ortho*-position of the phenyl rings of the corresponding disulfides. Disulfides with substituents in the *meta*-positions of the phenyl rings gave better yields (**3i–m**). This reaction also proceeded well with the

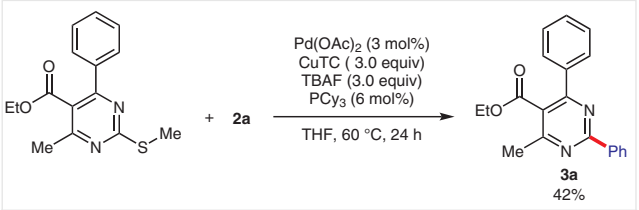


Scheme 1 Cross-coupling of disulfides with aryl(trimethoxy)silanes

isopropyl ester of the pyrimidine (**3n–o**), and when the methyl ester was used instead of the ethyl ester, compounds **3p**, **3q**, and **3r** were obtained in high yields (75, 78, and 71%, respectively). The fact that variations in the substituents on the hetaromatic reactant were tolerated indicates that there were no substantial electronic effects. Further investigations of the substrate scope were carried out by using aryl(trimethyl)silanes with various *para*-substituents under the standard reaction conditions, and a 70% yield of **3u** (R^3 = Me) was obtained, indicating that the electronic nature of the substituent on the arylsilane had little impact on the yield. Unfortunately, the reactions of diaryl disulfides and di-2-pyridyl disulfide with **2a** did not generate the corresponding products; in comparison with dihetaryl disulfides, the electrophilic activity of the aryl groups of these disulfides is lower, possibly due to the coordination of a basic atom (such as a N atom) to the copper salt that promotes C–S activation. When we explored the reactions of [(4-(chloromethyl)phenyl](trimethoxy)silane and trimethoxy-(vinyl)silane with dipyrimidin-2-yl disulfide, we failed to obtain the desired products.

Finally, to confirm that the activity of dihetaryl disulfides was higher than that of aryl disulfides, we investigated the coupling of unsymmetrical disulfides with arylsilane **2a** (Scheme 2). We obtained the target products **3a**, **3b**, and **3c** containing the pyrimidine groups, together with the diaryl disulfide **6**, but we did not detect the product **7**. These results confirmed that pyrimidinyl-containing disulfides have a higher activity than 4-tolyl-group-containing disulfides in this reaction.

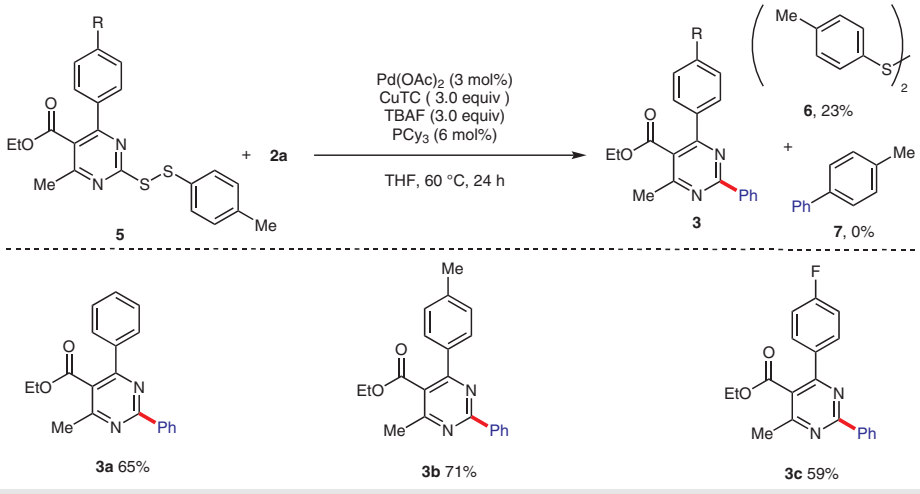
To compare the reactivity of disulfides with that of heteraryl methyl sulfides, we examined the reaction of a heteroaryl methyl sulfide with **2a** under the optimized conditions, and we found that target product **3a** was obtained in a lower yield of 42% (Scheme).



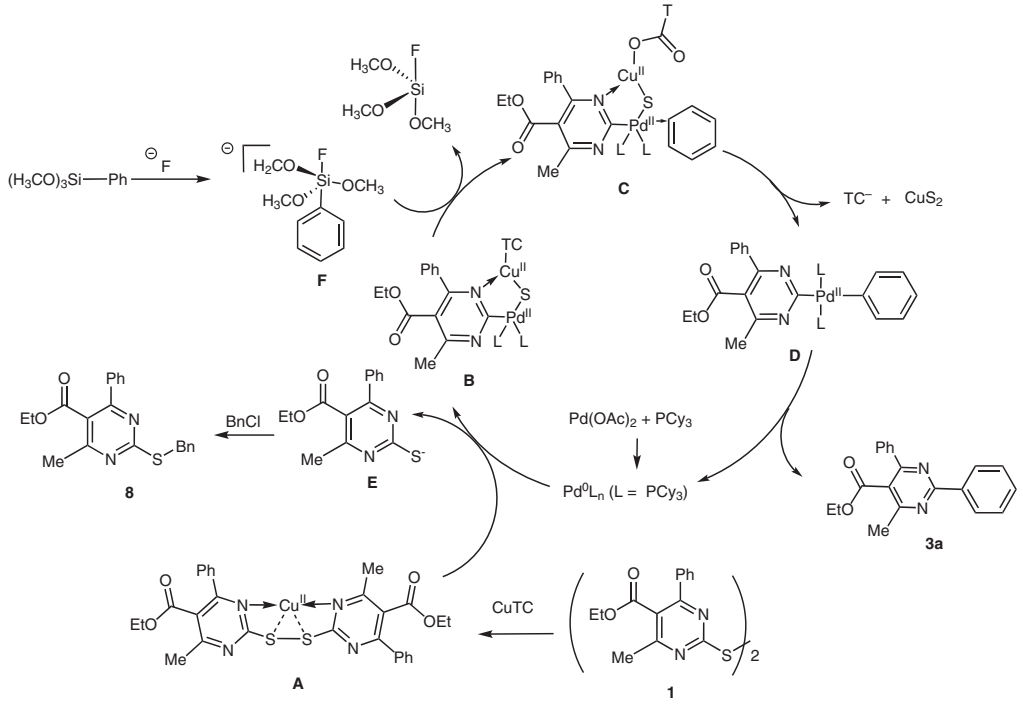
Scheme 3

On the basis of our experimental results, the following mechanistic discussion seems to be reasonable, although there is no definite evidence. A formal oxidative addition of copper to the S–S bond affords Cu(II) dithiolato intermediate **A** (Scheme 4). Subsequent reductive cleavage of the S–S bond leads to the formation of the corresponding copper(II) species **B** and **E**. (When the reaction was complete, BnCl was added to the reaction mixture and thio ether **8** was obtained,[19] indicating the formation of intermediate **E**.) Simultaneously, activation of the inert C–Si bond takes place in the presence of TBAF to form **F**. This reacts with divalent palladium intermediate **B** to form the metalated complex **C**. Transmetalation from boron to palladium next occurs, followed by reductive elimination to give the C–C cross-coupling product **3a**.

In summary, we have developed a new protocol for the construction of C–C bonds by the $Pd(OAc)_2$-catalyzed cross-coupling of dihetaryl disulfides with arylsilanes. This provides an effective method for selectively activating S–S bonds of disulfides and constructing C–C bonds to give a series of molecules with potentially biologically active structures in good yields.



Scheme 2 Cross-coupling of unsymmetrical disulfides with arylsilanes



Scheme 4 Proposed reaction mechanism

Funding Information

We are grateful for financial support from the National Natural Science Foundation of China (Nos. 21362032, 21362031, and 21562036) and from the Scientific and Technological Innovation Engineering program of Northwest Normal University (NWNU-LKQN-15-1).

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0036-1589116.

References and Notes

(1) (a) Gouda, K.-i.; Hagiwara, E.; Hatanaka, Y.; Hiyama, T. *J. Org. Chem.* **1996**, *61*, 7232. (b) Molander, G. A.; Lannazzo, L. *J. Org. Chem.* **2011**, *76*, 9182. (c) Mino, T.; Shirae, Y.; Saito, T.; Sakamoto, M.; Fujita, T. *J. Org. Chem.* **2006**, *71*, 9499. (d) Raders, S. M.; Kingston, J. V.; Verkade, J. G. *J. Org. Chem.* **2010**, *75*, 1744. (e) Bi, L.; Georg, G. I. *Org. Lett.* **2011**, *13*, 5413. (f) Denmark, S. E.; Sweis, R. F. *J. Am. Chem. Soc.* **2004**, *126*, 4876.

(2) (a) Martin, R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2007**, *129*, 3844. (b) Roche, A. J.; Abboud, K. A.; Dolbier, W. R. Jr. *J. Org. Chem.* **2015**, *80*, 5355. (c) Hua, X. Y.; Masson-Makdissi, J.; Sullivan, R. J.; Newman, S. G. *Org. Lett.* **2016**, *18*, 5312. (d) Phan, N. T. S.; Brown, D. H.; Styring, P. *Green Chem.* **2004**, *6*, 526. (e) Netherton, M. R.; Fu, G. C. *Adv. Synth. Catal.* **2004**, *346*, 1525.

(3) (a) Zhao, T.; Ghosh, P.; Martinez, Z.; Liu, X.; Meng, X.; Darensbourg, M. Y. *Organometallics* **2017**, *36*, 1822. (b) Stefani, H. A.; Cella, R.; Vieira, A. S. *Tetrahedron* **2007**, *63*, 3623. (c) Ke, H.; Chen, X.; Zou, G. *J. Org. Chem.* **2014**, *79*, 7132. (d) Halima, T. B.; Zhang, W.; Yalaoui, I.; Hong, X.; Yang, Y.-F.; Houk, K. N.; Newman, S. G. *J. Am. Chem. Soc.* **2017**, *139*, 1311. (e) Sharma, P.; Rohilla, S.; Jain, N. *J. Org. Chem.* **2017**, *82*, 1105. (f) Frisch, A. C.; Beller, M. *Angew. Chem. Int. Ed.* **2005**, *44*, 674. (g) Woerly, E. M.; Cherney, A. H.; Davis, E. K.; Burke, M. D. *J. Am. Chem. Soc.* **2010**, *132*, 6941.

(4) (a) Hassan, J.; Sévignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359. (b) Littke, A. F.; Fu, G. C. *Angew. Chem. Int. Ed.* **2002**, *41*, 4176. (c) Suzuki, T.; Watanabe, S.; Kobayashi, S.; Tanino, K. J. *Org. Lett.* **2017**, *19*, 922. (d) Stille, J. K. *Angew. Chem. Int. Ed.* **1986**, *25*, 508. (e) Garcia-Martinez, J. C.; Lezutekong, R.; Crooks, R. M. *J. Am. Chem. Soc.* **2005**, *127*, 5097. (f) Su, W.; Urgaonkar, S.; McLaughlin, P. A.; Verkade, J. G. *J. Am. Chem. Soc.* **2004**, *126*, 16433. (g) Guo, Y.; Quan, T.; Lu, Y.; Luo, T. *J. Am. Chem. Soc.* **2017**, *139*, 6815. (h) Zhou, W.-J.; Wang, K.-H.; Wang, J.-X. *J. Org. Chem.* **2009**, *74*, 5599.

(5) (a) Haraguchi, R.; Tanazawa, S.-g.; Tokunaga, N.; Fukuzawa, S.-i. *Org. Let.* **2017**, *19*, 1646. (b) Kienle, M.; Knochel, P. *Org. Lett.* **2010**, *12*, 2702. (c) Liu, J.; Deng, Y.; Wang, H.; Zhang, H.; Yu, G.; Wu, B.; Zhang, H.; Li, Q.; Marder, T. B.; Yang, Z.; Lei, A. *Org. Lett.* **2008**, *10*, 2661. (d) Negishi, E.-i.; Anastasia, L. *Chem. Rev.* **2003**, *103*, 1979. (e) Nicolaou, K. C.; Bulger, P. G.; Sarlah, D. *Angew. Chem. Int. Ed.* **2005**, *44*, 4442. (f) Tao, J.-L.; Yang, B.; Wang, Z.-X. *J. Org. Chem.* **2015**, *80*, 12627.

(6) (a) Hiyama, T. *J. Organomet. Chem.* **2002**, *653*, 58. (b) Hatanaka, Y.; Goda, K.-i.; Okahara, Y.; Hiyama, T. *Tetrahedron.* **1994**, *50*, 8301. (c) Hirabayashi, K.; Mori, A.; Kawashima, J.; Suguro, M.; Nishihara, Y.; Hiyama, T. *J. Org. Chem.* **2000**, *65*, 5342. (d) Nakao, Y.; Oda, T.; Sahoo, A. K.; Hiyama, T. *J. Organomet. Chem.* **2003**, *687*, 570.

(7) (a) Saijo, H.; Sakaguchi, H.; Ohashi, M.; Ogoshi, S. *Organometallics* **2014**, *33*, 3669. (b) Pierrat, P.; Gros, P.; Fort, Y. *Org. Lett.* **2005**, *7*, 697.

(8) (a) Yuen, O. Y.; So, C. M.; Man, H. W.; Kwong, F. Y. *Chem. Eur. J.* **2016**, *22*, 6471. (b) Zhang, S.; Cai, J.; Yamamoto, Y.; Bao, M. *J. Org. Chem.* **2017**, *82*, 5974.

(9) (a) Domin, D.; Benito-Garagorri, D.; Mereiter, K.; Froehlich, J.; Kirchner, K. *Organometallics* **2005**, *24*, 3957. (b) Lee, J.-Y.; Fu, G. C. *J. Am. Chem. Soc.* **2003**, *125*, 5616. (c) Sakon, A.; Ii, R.; Hamasaka, G.; Uozumi, Y.; Shinagawa, T.; Shimomura, O.; Nomura, R.; Ohtaka, A. *Organometallics* **2017**, *36*, 1618. (d) Dai, X.; Strotman, N. A.; Fu, G. C. *J. Am. Chem. Soc.* **2008**, *130*, 3302.

(10) (a) Itami, K.; Kamei, T.; Yoshida, J.-i. *J. Am. Chem. Soc.* **2003**, *125*, 14670. (b) Nakao, Y.; Imanaka, H.; Sahoo, A. H.; Yada, A.; Hiyama, T. *J. Am. Chem. Soc.* **2005**, *127*, 6952. (c) Gurung, S. K.; Thapa, S.; Vangala, A. S.; Giri, R. *Org. Lett.* **2013**, *15*, 5378. (d) Nokami, T.; Tomida, Y.; Kamei, T.; Itami, K.; Yoshida, J.-i. *Org. Let.* **2006**, *8*, 729.

(11) (a) Zhang, L.; Wu, J. *J. Am. Chem. Soc.* **2008**, *130*, 12250. (b) Cheng, K.; Wang, C.; Ding, Y.; Song, Q.; Qi, C.; Zhang, X.-M. *J. Org. Chem.* **2011**, *76*, 9261. (c) Shi, W.-J.; Yu, D.-G.; Zhao, H.-W.; Wang, Y.; Cao, Z.-C.; Zhang, L.-S.; Yu, D.-G.; Shi, Z.-J. *Adv. Synth. Catal.* **2016**, *358*, 2410. (d) Chau, M.; Lee, H. W.; Lau, C. P.; Kwong, F. Y. *Org. Lett.* **2009**, *11*, 317. (e) Zhang, L.; Qing, J.; Yang, P.; Wu, J. *Org. Lett.* **2008**, *10*, 4971. (f) Seganish, W. M.; De Shong, P. *J. Org. Chem.* **2004**, *69*, 1137. (g) Melvin, P. R.; Hazari, N.; Beromi, M. M.; Shah, H. P.; Williams, M. J. *Org. Lett.* **2016**, *18*, 5784.

(12) (a) Liu, Y.; Wang, H.; Wang, C.; Wan, J.-P.; Wen, C. *RSC Adv.* **2013**, *3*, 21369. (b) Du, Y.; Yang, H.-C.; Xu, X.-L.; Wu, J.; Xu, Z.-K. *ChemCatChem* **2015**, *7*, 3822. (c) Wang, H.; Huang, G.; Sun, Y.; Liu, Y. *J. Chem. Res.* **2014**, *38*, 96. (d) Wang, G.; Guo, Y.; Lü, Y.; Wang, X.; Quan, Z. *Chin. J. Org. Chem.* **2016**, *36*, 1375.

(13) For examples of C–C coupling, see: (a) Quan, Z.-. J.; Lv, Y.; Wang, X.-C.; Jing, F.-Q.; Jia, X.-D.; Huo, C.-D. *Adv. Synth. Catal.* **2014**, *356*, 325. (b) Du, B.-X.; Da, Y.-X.; Zhang, Z. *Adv. Synth. Catal.* 2015, *357*, 1270. (c) Wei, K.-J.; Quan, Z.-J.; Zhang, Z.; Da, Y.-X.; Wang, X.-C. *RSC Adv.* **2016**, *6*, 78059.

(14) For examples of C–N coupling, see: (a) Wei, K.-J.; Quan, Z.-J.; Zhang, Z.; Da, Y.-X.; Wang, X.-C. *Synlett* **2016**, *27*, 1743. (b) Wei, K.-J.; Quan, Z.-J.; Zhang, Z.; Da, Y.-X.; Wang, X.-C. *Org. Biomol. Chem.* **2016**, *14*, 2395.

(15) For examples of C–S coupling, see: Guo, Y.; Quan, Z.-J.; Da, Y.-X.; Zhang, Z.; Wang, X.-C. *RSC Adv.* **2015**, *5*, 45479.

(16) (a) Kappe, C. O. *Tetrahedron* **1993**, *49*, 6937. (b) Kappe, C. O. *Eur. J. Med. Chem.* **2000**, *35*, 1043. (c) Dallinger, D.; Stadler, A.; Kappe, C. O. *Pure Appl. Chem.* **2004**, *76*, 1017.

(17) Deres, K.; Schröder, C. H.; Paessens, A.; Goldmann, S.; Hacker, H. J.; Weber, O.; Kräemer, T.; Niewöhner, U.; Pleiss, U.; Stoltefuss, J.; Graef, E.; Koletzki, D.; Masantschek, R. N. A.; Reimann, A.; Jaeger, R.; Groß, R.; Beckermann, B.; Schlemmer, K.-H.; Haebich, D.; Rübsamen-Waigmann, H. *Science* **2003**, *299*, 893.

(18) **Ethyl 4-Methyl-2,6-diphenylpyrimidine-5-carboxylate (3a); Typical Procedure**

A Schlenk tube was charged with disulfide **1a** (0.2 mmol, 0.1094 g), $Pd(OAc)_2$ (3 mol%), CuTC (3.0 equiv), and PCy_3 (6 mol%), and the tube was sealed. $PhSi(OMe)_3$ (**2a**; 3.0 equiv, 0.6 mmol, 0.1188 g), TBAF (3.0 equiv, 0.6 mmol), and THF (2 mL) were then injected by syringe into the sealed tube under N_2, and the mixture was stirred at 60 °C for 24 h until the reaction as complete (TLC; silica gel). The mixture was cooled to r.t., the reaction was quenched with sat. aq NH_4Cl (2 mL), and the mixture was extracted with EtOAc (3 × 10 mL). The organic layers were combined, dried ($MgSO_4$), and concentrated in vacuo, and the resulting residue was purified column chromatography [silica gel, EtOAc–PE (1:50)] to give a white solid; yield: 45 mg (72%); mp 66–67 °C.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.51–8.49 (m, 2 H), 7.71–7.69 (m, 2 H), 7.44–7.41 (m, 6 H), 4.15 (q, *J* = 7.2 Hz, 2 H), 2.64 (s, 3 H), 1.03 (t, *J* = 7.2 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.44, 165.40, 163.68, 163.65, 138.23, 137.10, 131.11, 130.04, 128.69, 128.54, 128.52, 128.49, 123.40, 61.82, 22.87, 13.70. HRMS (ESI$^+$): *m/z* [M + H]$^+$ Calcd for $C_{20}H_{19}N_2O_2$: 319.1441; found: 319.1447.

(19) **Ethyl 2-(Benzylthio)-4-methyl-6-phenylpyrimidine-5-carboxylate (8)**

Oil; yield: 12 mg (16%). ^1H NMR (600 MHz, $CDCl_3$): δ = 7.63–7.56 (m, 2 H), 7.45–7.43 (m, 3 H), 7.37–7.35 (m, 2 H), 7.20–7.17 (m, 3 H), 4.46 (s, 2 H), 4.16 (q, *J* = 7.2 Hz, 2 H), 2.57 (s, 3 H), 1.03 (t, *J* = 7.2 Hz, 3 H). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.65, 168.01, 165.60, 163.75, 141.16, 130.05, 129.08, 128.65, 128.40 (2 C), 128.31, 128.28, 127.13, 125.83, 61.70, 35.34, 22.59, 13.58. HRMS (ESI$^+$): *m/z* [M + H]$^+$ Calcd for $C_{21}H_{21}N_2O_2S$: 365.1318; found: 365.1315.