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Palladium(0)-Catalyzed, Copper(I)-Mediated Coupling of Cyclic Thioamides with Alkenylboronic Acids, Organostannanes, and Siloxanes

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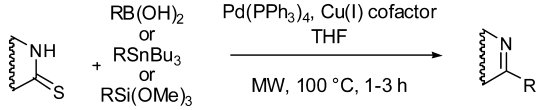
Received April 24, 2009



The Pd-catalyzed cross-coupling of cyclic thioamides and thioureas with alkenylboronic acids, vinyl- and (het)arylstannanes, and arylsiloxanes in the presence of stoichiometric amounts of a Cu(I) cofactor is described. The desulfitative C−C cross-coupling protocol of the Liebeskind−Srogl type is performed under neutral conditions and can be applied to a range of heterocyclic structures with embedded thioamide fragments. Employing controlled microwave irradiation at 100 °C utilizing either a single-mode reactor or a multimode parallel reaction platform, cross-couplings can generally be completed within 1−3 h and proceed in good yields.

The Liebeskind−Srogl cross-coupling protocol has emerged as valuable method for the highly selective construction of C−C bonds from thioorganic building blocks and nucleophilic organometallic reagents.[1−7] A key feature of these Pd-catalyzed desulfitative C−C couplings under neutral conditions is the requirement of stoichiometric amounts of a Cu(I) carboxylate as metal cofactor.[7] Due to the higher thiophilicity of the soft Cu(I) metal, selective sulfide coupling under base-free Liebeskind−Srogl conditions can be performed even in the presence of a Suzuki-active bromide.[3] Initially described in 2000 for the synthesis of ketones from thioesters and boronic acids,[1] the scope of the Liebeskind−Srogl cross-coupling was extended considerably in the past few years to accommodate a variety of different thioorganics[2,7] and organometallic reagents[4−7] as coupling partners (Figure 1a). The ever-increasing potential of this mechanistically unique base-free cross-coupling method has already led to an impressive number of interesting applications in heterocyclic/medicinal chemistry, peptide and solid-phase synthesis, and the total synthesis of natural products.[7]

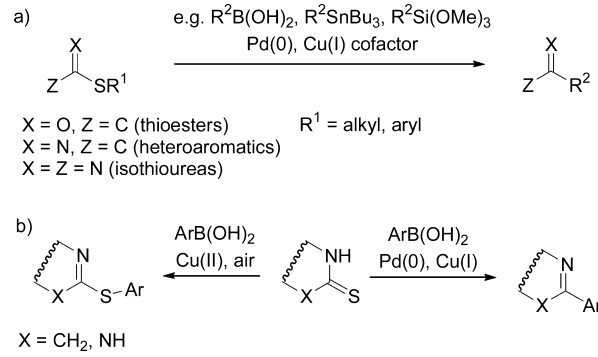


FIGURE 1. (a) Classical Liebeskind−Srogl desulfitative C−C cross-coupling of thioorganics. (b) C−C versus C−S cross-coupling of cyclic thioamides with boronic acids.

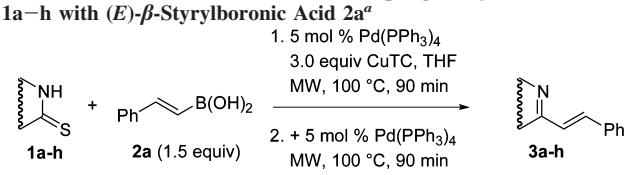
In 2004, we discovered that the Liebeskind−Srogl cross-coupling protocol can also be applied to cyclic thioureas/thioamides using arylboronic acids as coupling partners.[8,9] A distinct advantage of using such thioamide substrates containing a latent free thiol functionality is that by exchanging the anerobic Pd(0)/Cu(I) catalytic system for an aerobic Cu(II) system, the reactivity can easily be tuned from C−C toward C−S cross-coupling (Figure 1b).[9] In this paper, we describe the C−C cross-coupling of substrates containing a thioamide motif with alkenylboronic acids, organostannanes, and arylsiloxanes as coupling partners.[10]

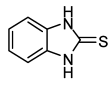
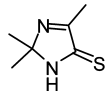
As a starting point in our investigations, we examined the C−C cross-coupling of model substrate pyridine-2(1*H*)-thione (**1a**) with (*E*)-*β*-styrylboronic acid (**2a**).[11] Applying our previously utilized 100 °C coupling conditions optimized for the use of arylboronic acids,[9] we quickly realized that an extension of the reaction time from 2 to 3 h and an increase of the Pd catalyst loading from 8 to 10 mol % was required in order to achieve high product yields. The use of higher reaction temperatures did not improve the efficiency of this transformation and led to diminished product purity due to the formation of undesired

(1) Liebeskind, L. S.; Srogl, J. *J. Am. Chem. Soc.* **2000**, *122*, 11260.
(2) (a) Liebeskind, L. S.; Srogl, J. *Org. Lett.* **2002**, *4*, 979. (b) Kusturin, C. L.; Liebeskind, L. S.; Neumann, W. L. *Org. Lett.* **2002**, *4*, 983. (c) Savarin, C.; Srogl, J.; Liebeskind, L. S. *Org. Lett.* **2001**, *3*, 91. (d) Yang, H.; Li, H.; Wittenberg, R.; Egi, M.; Huang, W.; Liebeskind, L. S. *J. Am. Chem. Soc.* **2007**, *129*, 1132.
(3) (a) Kusturin, C.; Liebeskind, L. S.; Rahman, H.; Sample, K.; Schweitzer, B.; Srogl, J.; Neumann, W. L. *Org. Lett.* **2003**, *5*, 4349. (b) Aguilar-Aguilar, A.; Peña-Cabrera, E. *Org. Lett.* **2007**, *9*, 4163.
(4) (a) Egi, M.; Liebeskind, L. S. *Org. Lett.* **2003**, *5*, 801. (b) Wittenberg, R.; Srogl, J.; Egi, M.; Liebeskind, L. S. *Org. Lett.* **2003**, *5*, 3033. (c) Alphonse, F.-A.; Suzenet, F.; Keromnes, A.; Lebret, B.; Guillaumet, G. *Org. Lett.* **2003**, *5*, 803. (d) Leconte, N.; Pellegatti, L.; Tatibouët, A.; Suzenet, F.; Rollin, P.; Guillaumet, G. *Synthesis* **2007**, 857. (e) Li, H.; Yang, H.; Liebeskind, L. S. *Org. Lett.* **2008**, *10*, 4375.
(5) Mehta, V. P.; Sharma, A.; Van der Eycken, E. *Adv. Synth. Catal.* **2008**, *350*, 2174.
(6) (a) Mehta, V. P.; Sharma, A.; Van der Eycken, E. *Org. Lett.* **2008**, *10*, 1147. (b) Shook, B. C.; Charkravarty, D.; Jackson, P. F. *Tetrahedron Lett.* **2009**, *50*, 1013.
(7) For a review on the Liebeskind−Srogl reaction, see: Prokopcová, H.; Kappe, C. O. *Angew. Chem., Int. Ed.* **2009**, *48*, 2276.
(8) Lengar, A.; Kappe, C. O. *Org. Lett.* **2004**, *6*, 771.
(9) (a) Prokopcová, H.; Kappe, C. O. *Adv. Synth. Catal.* **2007**, *349*, 448. (b) Prokopcová, H.; Kappe, C. O. *J. Org. Chem.* **2007**, *72*, 4440.
(10) The use of linear substrates in all of our examples (refs 8 and 9) did not provide any of the desired coupling products.
(11) For the use of alkenylboronic acids in the Liebeskind−Srogl reaction, see: Yang, H.; Liebeskind, L. S. *Org. Lett.* **2007**, *9*, 2993.

10.1021/jo900848s CCC: $40.75
Published on Web 05/22/2009

TABLE 1. Carbon−Carbon Cross-Coupling of Cyclic Thioamides 1a−h with (*E*)-β-Styrylboronic Acid 2a[a]



entry	substrate	1	yield of 3 (%)[b]	entry	substrate	1	yield of 3 (%)[b]
1		1a	70	5		1e	61
2		1b	72	6		1f	87
3		1c	97	7		1g	traces
4		1d	60	8		1h	69

[a] For a general procedure, see the Experimental Section. [b] Yields of pure product after column chromatography.

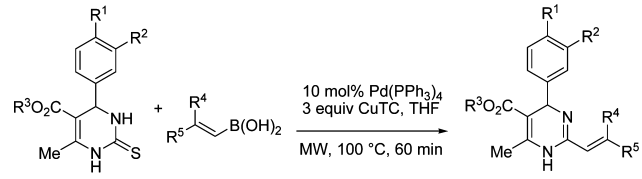
byproducts. Ultimately, the reaction proceeded heating 1 equiv of pyridine-2(1*H*)-thione (**1a**), 1.5 equiv of (*E*)-β-styryl boronic acid (**2a**), 3 equiv of Cu(I)−thiophene-2-carboxylate (CuTC), and 5 mol % of $Pd(PPh_3)_4$ in THF at 100 °C for 90 min applying a sealed vessel microwave reactor (argon atmosphere).[12] In order to further improve the product yield, an additional quantity of $Pd(PPh_3)_4$ (5 mol %) was added after the first heating cycle. The reaction mixture was subsequently heated at 100 °C for an additional 90 min. This two-step procedure consistently led to a 70% isolated product yield of coupling product **3a** after purification by flash chromatography.

With the optimized conditions in hand, we explored the scope and limitations of this C−C cross-coupling reaction with a set of eight cyclic thioamides/thioureas already used in our previous study involving arylboronic acids.[9] We were pleased to find that successful cross-coupling with (*E*)-β-styrylboronic acid (**2a**) was observed with aromatic and nonaromatic, six- and five-membered heterocycles containing thioamide fragments. As shown in Table 1, moderate to high product yields were achieved using our standard reaction conditions. The only exception proved to be 1,3-dihydroimidazole-2(1*H*)-thione (entry 7) where only traces of the anticipated coupling product could be isolated. In general, the reactivity in this coupling observed for styrylboronic acid **2a** was very similar to that found for phenylboronic acid.[9]

Having demonstrated that a variety of different simple cyclic thioamide scaffolds **1** can be useful substrates for the Liebeskind−Srogl-type desulfitative C−C coupling with (*E*)-β-styrylboronic acid (**2a**) (Table 1), we next focused our attention on the use of a more complex heterocyclic core and on the scope of the alkenylboronic acid diversity. In this context, we have employed the thioamide−boronic acid cross-coupling

(12) Kappe, C. O. *Angew. Chem., Int. Ed.* **2004**, *43*, 6250.

TABLE 2. Carbon−Carbon Cross-Coupling of Pyrimidine-2-thiones 4a−c with Alkenylboronic Acids 2a−c



5	DHPM 4	boronic acid 2	yield (%)[a] single-mode	yield (%)[a] multimode
5a	**4a** ($R^1 = R^2 = H$, $R^3 = Et$)	**2a** ($R^4 = H$, $R^5 = Ph$)	65	66
5b	**4a** ($R^1 = R^2 = H$, $R^3 = Et$)	**2b** ($R^4 = H$, $R^5 = t$Bu)	64	65
5c	**4a** ($R^1 = R^2 = H$, $R^3 = Et$)	**2c** ($R^4 = R^5 = Me$)	55	60
5d	**4b** ($R^1 = R^3 = Me$, $R^2 = H$)	**2a** ($R^4 = H$, $R^5 = Ph$)	68	65
5e	**4b** ($R^1 = R^3 = Me$, $R^2 = H$)	**2b** ($R^4 = H$, $R^5 = t$Bu)	71	69
5f	**4b** ($R^1 = R^3 = Me$, $R^2 = H$)	**2c** ($R^4 = R^5 = Me$)	61	62
5g	**4c** ($R^1 = H$, $R^2 = OH$, $R^3 = Et$)	**2a** ($R^4 = H$, $R^5 = Ph$)	65	63
5h	**4c** ($R^1 = H$, $R^2 = OH$, $R^3 = Et$)	**2b** ($R^4 = H$, $R^5 = t$Bu)	60	67
5i	**4c** ($R^1 = H$, $R^2 = OH$, $R^3 = Et$)	**2c** ($R^4 = R^5 = Me$)	63	65

[a] Yields of pure product after column chromatography.

strategy for the generation of a small set of nine potentially biologically active 2-alkenyl-1,4-dihydropyrimidines **5a−i** (Table 2). The corresponding 2-aryl-substituted heterocycles have been found to be highly potent nonnucleosidic inhibitors of hepatits B virus replication that have in vitro and in vivo antiviral activity,[8,13] whereas the biological activity of the 2-alkenyl analogues has not been explored yet. The required functionalized cyclic thioureas of type **4a−c** (DHPMs) can be rapidly synthesized by microwave-assisted three-component condensation of the appropriate aromatic aldehydes, β-keto esters, and thiourea (Biginelli reaction).[14] Cross-coupling of a set of three DHPMs **4a−c** with three commercially available alkenylboronic acids **2a−c** applying slightly modified reaction conditions provided a small collection of nine 2-alkenyl-1,4-dihydropyrimidines **5a−i**.[15] The highest isolated yields (55−71%) were obtained by a single microwave irradiation cycle at 100 °C for 60 min, applying 10 mol % of $Pd(PPh_3)_4$ as a catalyst (Table 2). In addition to the traditional automated sequential single-mode microwave processing technology,[14] which here requires an overall microwave processing time of almost 10 h, we have also synthesized the small library of nine dihydropyrimidines **5a−i** in a single microwave irradiation experiment (60 min) utilizing a recently developed reactor platform for use in conjunction with multimode microwave instrumentation.[16] In this high-throughput experimentation platform, parallel microwave chemistry is performed in sealed HPLC/GC vials serving as reaction vessels. The system consists of a strongly microwave-absorbing silicon carbide plate with cylindrical wells in which standard HPLC/GC autosampler vials are fitted.[16] Gratifyingly, the isolated product yields comparing the two methods were very similar (Table 2), validating the concept of parallel microwave synthesis in the silicon carbide reactor. In addition,

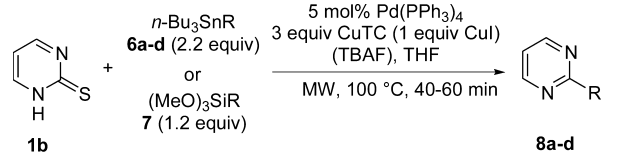
(13) Deres, K.; Schröder, C. H.; Paessens, A.; Goldmann, S.; Hacker, H. J.; Weber, O.; Krämer, T.; Niewoehner, U.; Pleiss, U.; Stoltefuss, J.; Graef, E.; Koletzki, D.; Masantschek, R. N. A.; Reimann, A.; Jaeger, R.; Groβ, R.; Beckermann, B.; Schlemmer, K.-H.; Haebich, D.; Rübsamen-Waigmann, H. *Science*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

(14) Stadler, A.; Kappe, C. O. *J. Comb. Chem.* **2001**, *3*, 624.

(15) Attempted cross-coupling of thioamides with alkylboronic acids (cyclohexylboronic acid and 2-phenyl-1-ethylboronic acid) or boronic esters (phenylboronic acid pinacol- and propane diol ester) was unsuccessful.

(16) (a) Damm, M.; Kappe, C. O. *J. Comb. Chem.* **2009**, *11*, 460.

TABLE 3. Carbon−Carbon Cross-Coupling of Pyrimidine-2(1*H*)-thione 1b with Tributylorganostannanes 6a−d and Trimethoxyphenylsilane 7



entry	organometallic reagent	yield[a] (%)
1	**6a** (R = Ph)	80 (**8a**)
2	**6b** (R = 2-pyridyl)	72 (**8b**)
3	**6c** (R = 2-furyl)	69 (**8c**)
4	**6d** (R = vinyl)	63 (**8d**)
5	**7** (R = Ph)	60 (**8a**)

[a] Yields of pure product after column chromatography.

the effectiveness of magnetic stirring of the strongly heterogeneous reaction mixture (3 equiv of CuTC) and the possibility of performing chemistry under inert conditions (argon) has been demonstrated.

As an alternative to the use of boronic acids as nucleophilic organometallic reagents, Liebeskind and others have reported successful cross-couplings of a variety of thioorganic substrates with organostannane reagents, in particular with tri*n*-butylorganostannanes (Figure 1a).[4] The method relies on the same base-free Pd(0)-catalyzed, Cu(I)-mediated methodology applied with boronic acids.[7] The variant with tin reagents is particularly attractive in cases where stannanes are more accessible than boronic acids, or in such instances where specific boronic acids (for example heteroarylboronic acids with an α-heteroatom) are problematic substrates.[4,7] For Liebeskind−Srogl-type C−C couplings involving thioamide building blocks containing a latent free thiol functionality we are aware of only one recent report by the group of Tatibouët, where a specific set of 1,3-oxazolidine- and 1,3-oxazoline-2-thiones were demonstrated to undergo Pd(0)-catalyzed cross-coupling with 2-(tri-*n*-butylstannyl)thiophene in the presence of a Cu(I) salt.[17]

In order to explore the feasibility of Liebeskind−Srogl-type C−C couplings of cyclic thioamides with organostannanes in more detail, we have investigated the cross-coupling of pyrimidine-2(1*H*)-thione (**1b**) with four different tri-*n*-butylorganostannane reagents (**6a−d**). In our hands, the Stille-type couplings proved to be somewhat easier to perform compared to the closely related Suzuki-type couplings involving boronic acids.[9] Therefore, 5 mol % of Pd at 100 °C reaction temperature for 60 min (2.2 equiv of stannane) was sufficient to provide moderate to high isolated product yields of the corresponding 2-functionalized pyrimidines **8a−d**, essentially using otherwise unaltered reaction conditions (Table 3). Longer reaction times resulted in diminished yields of the desired coupling products and unclean reaction profiles (homocoupling of stannane reagents was also observed). The initial optimization experiments were performed with (tri-*n*-butyl)phenylstannane (**6a**), but good yields were subsequently also obtained with 2-(tri-*n*-butylstannyl)pyridine (**6b**) and 2-(tri-*n*-butylstannyl)furan (**6c**). Importantly, tri-*n*-butyl(vinyl)stannane (**6d**) provided a 63% yield of 2-vinylpyrimidine, which was otherwise not accessible via the boronic acid route.

Finally, we have also attempted to utilize trimethoxyphenylsilane as a nucleophilic coupling partner in this transformation. Organosilicon derivatives are becoming increasingly popular as environmentally safe and nontoxic reaction partners in cross-coupling chemistry (Hiyama coupling).[18] Stimulated by a recent report by Van der Eycken and co-workers describing the Pd-catalyzed, Cu(I)-mediated desulfitative cross-coupling of thioethers and thioesters with arylsiloxanes,[5] cross-coupling between pyrimidine-2(1*H*)-thione (**1b**) and trimethoxyphenylsilane was performed employing 1 equiv of CuI, 2 equiv of TBAF, and 5 mol % of $Pd(PPh_3)_4$ in THF as solvent.[5] In our hands, a 60% yield of cross-coupling product **8a** was obtained using microwave heating at 100 °C for 40 min followed by an extractive workup and silica gel chromatography.

In conclusion, we have shown that thioamide fragments embedded in heterocyclic ring systems can be cross-coupled under comparatively mild and nonbasic conditions with a variety of alkenylboronic acids, vinyl- and (het)arylstannanes, and arylsiloxanes. Employing modified Liebeskind−Srogl Pd(0)-catalyzed, Cu(I)-mediated conditions, desulfitative C−C cross-coupling with concomitant extrusion of sulfur occurs in moderate to good overall yields.

Experimental Section

General Procedure for the Carbon−Carbon Cross-Coupling of Thioamides with (*E*)-*β*-Styrylboronic Acid 2a (Table 1). A dry microwave process vial was charged with the corresponding thioamide **1a−h** (0.5 mmol), (*E*)-*β*-styrylboronic acid **2a** (111 mg, 0.75 mmol), CuTC (300 mg, 1.5 mmol), and $Pd(PPh_3)_4$ (28 mg, 0.024 mmol, 5 mol %). The reaction vessel was sealed and flushed with Ar. Through the septum anhydrous and degassed THF (2.8 mL) was added. The mixture was subsequently heated in a microwave reactor at 100 °C for 90 min. After this period, an additional amount of Pd catalyst (28 mg, 0.024 mmol, 5 mol %) was added, and the reaction mixture was again heated at 100 °C for 90 min. After cooling, the solvent was evaporated, and EtOAc/$CHCl_3$ (3:1) (250 mL) was added. The crude reaction mixture was subsequently washed with 25% aqueous ammonia (3 × 80 mL). The aqueous ammonium layer was reextracted again with EtOAc/$CHCl_3$ (3:1) (3 × 80 mL). The combined organic phase was dried over $MgSO_4$ and the residue after evaporation purified by flash chromatography. Characterization data for products **3a−h** are given in the Supporting Information.

General Procedure for Carbon−Carbon Cross-Coupling of Dihydropyrimidines (4a−c) with Alkenylboronic Acids 2a−c (Table 2). (A) Single-Mode Conditions. A dry microwave process vial was charged with the corresponding dihydropyrimidine (DHPM) **4a−c** (0.21 mmol), the corresponding alkenylboronic acid **2a−c** (0.315 mmol), CuTC (120 mg, 0.63 mmol), and $Pd(PPh_3)_4$ (24 mg, 10 mol %). The reaction vessel was sealed and flushed with Ar. Through the septum anhydrous and degassed THF (1.5 mL) was added. The mixture was stirred for 5 min and then subsequently heated in a microwave reactor at 100 °C for 60 min. After cooling, the solvent was evaporated, and EtOAc/$CHCl_3$ (3:1) (120 mL) was added. The crude reaction mixture was subsequently washed with 25% aqueous ammonia (3 × 40 mL). The aqueous ammonium layer was reextracted again with EtOAc/$CHCl_3$ (3:1) (3 × 40 mL). The combined organic phase was dried over $MgSO_4$, and the residue after evaporation was purified by flash chromatography on silica gel (acetone/petroleum ether 1:3) to provide the desired 2-substituted dihydropyrimidines **5a−i** as pale yellow oils. Data for **5a**: ^{1}H NMR (360 MHz, DMSO-d_6) δ 9.21 (brs, 1H), δ 7.56- 7.52 (m, 3H), 7.41−7.26 (m, 8H), 6.63 (d, J =

(17) (a) Silva, S.; Tardy, S.; Routier, S.; Suzenet, F.; Tatibouët, A.; Rauter, A. P.; Rollin, P. *Tetrahedron Lett.* **2008**, *49*, 5583. (b) For related cross-couplings using terminal alkynes, see: Silva, S.; Sylla, B.; Suzenet, F.; Tatibouët, A.; Rauter, A. P.; Rollin, P. *Org. Lett.* **2008**, *10*, 853.

(18) (a) Hiyama, T. *J. Organomet. Chem.* **2002**, *653*, 58. (b) Denmark, S. E. *Aldrichim. Acta* **2003**, *36*, 75.

16.2 Hz, 1H), 5.52 (s, 1H), 4.00 (q, $J = 6.8$ Hz, 2H), 2.33 (s, 3H), 1.11 (t, $J = 6.84$ Hz, 3H); ^{13}C NMR (90 MHz, DMSO-d_6) δ 166.7, 146.5, 135.7, 129.7, 129.4 (3C), 128.7 (3C), 127.7 (3C), 127.4, 127.2 (3), 122.7 (2C), 59.5, 14.6 (2C); MS (pos APCI) *m*/*z* 346; HRMS (APCI$^+$) *m*/*z* calcd for $C_{22}H_{22}N_2O_2$ $[M + H]^+$ 347.1754, found 347.1753.

(B) Multimode Silicon Carbide Plate Conditions. The individual dry HPLC/GC vials containing a small stir bar fitted inside the SiC plate were flushed with Ar and charged with the corresponding dihydropyrimidine (DHPM) **4a**−**c** (0.21 mmol), the corresponding alkenylboronic acid **2a**−**c** (0.315 mmol), CuTC (120 mg, 0.63 mmol), and $Pd(PPh_3)_4$ (24 mg, 10 mol %). The reaction vessel was sealed with an aluminum crimp top employing PTFE-coated silicon septa and flushed with Ar. Through the septum anhydrous and degassed THF (1.0 mL) was added and the resulting mixture stirred for 5 min. For the assembly, the SiC plate was covered with an aluminum top plate and was fixed finger tight with the six hex bolts.[16] The whole assembly was placed on a dedicated plate rotor inside the microwave reactor and irradiated for 60 min at 100 °C (ramp time of 5 min and hold times 55 min) with maximum stirring. After cooling, all individual vials were treated as described above. Characterization data for products **5b**−**i** are given in the Supporting Information.

General Procedure for the Carbon−Carbon Cross-Coupling of Thioamide 1b with Organostannanes 6a−d (Table 3). A dry microwave process vial was charged with pyrimidine-2(1*H*)-thione **1b** (39.3 mg, 0.35 mmol), CuTC (200 mg, 1.05 mmol), and $Pd(PPh_3)_4$ (20 mg, 0.017 mmol, 5 mol %). The reaction vessel was sealed and flushed with Ar. Through the septum anhydrous and degassed THF (2 mL) was added, followed by the corresponding stannane **6a**−**d** (2.2 equiv, 0.77 mmol) after 5 min of stirring at room temperature. After an additional stirring period of 5 min, the mixture was subsequently heated in a microwave reactor at 100 °C for 60 min. After cooling, the solvent was evaporated, and $CHCl_3$ (120 mL) was added. The crude reaction mixture was subsequently washed with 25% aqueous ammonia (3 × 40 mL). The aqueous ammonium layer was reextracted again with $CHCl_3$ (3 × 40 mL). The combined organic phase was dried over $MgSO_4$ and the residue after evaporation purified by flash chromatography to yield 2-substituted pyrimidines **8a**−**d** (Table 3). Characterization data for products **8a**−**d** are given in the Supporting Information.

General Procedure for the Carbon−Carbon Cross-Coupling of Thioamide 1b with Trimethoxyphenylsilane 7 (Table 3). A dry microwave process vial was charged with pyrimidine-2(1*H*)-thione **1b** (39.3 mg, 0.35 mmol), $Pd(PPh_3)_4$ (20 mg, 0.017 mmol, 5 mol %), and CuI (67 mg, 0.35 mmol). The reaction vessel was sealed and flushed with Ar. Through the septum anhydrous and degassed THF (1 mL) was added, and the mixture was stirred for 2 min, after which the siloxane reagent (170 μL, 0.42 mmol, 1.2 equiv) followed by tetrabutylammonium fluoride (TBAF) (183 mg, 0.7 mmol dissolved in 1 mL of THF) was added in one shot by syringe. The reaction mixture was subsequently heated in a microwave reactor for 40 min at 100 °C. After cooling, the reaction mixture was poured into water and extracted with dichloromethane (2 × 75 mL). The combined organic layers were washed with water and dried over $MgSO_4$. The solvent was evaporated, and the residue was purified by flash chromatography on silica gel (EtOAc/cyclohexane 1:7) to yield 32.8 mg (60%) of 2-phenylpyrimidine **8a**.

Acknowledgment. N.A. and J.H. thank the Higher Education Commission of Pakistan for Ph.D. scholarships. We thank Marketa Bernaskova and Markus Damm for their experimental help and Synthonix for the donation of reagents.

Supporting Information Available: Analytical data and copies of ^{1}H and ^{13}C NMR spectra of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

JO900848S