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Room-Temperature Hydrodehalogenation of Halogenated Heteropentalenes with One or Two Heteroatoms

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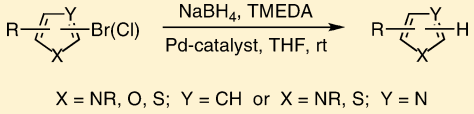
Supporting Information

ABSTRACT: The pair $NaBH_4$–TMEDA as a hydride source and catalytic $PdCl_2(dppf)$ in THF prove to be an efficient system for the hydrodehalogenation of bromo(chloro)-heteropentalenes with one or two heteroatoms, while $Pd(OAc)_2/PPh_3$ is able to reduce reactive haloheteropentalenes, and $PdCl_2(tbpf)$ allows the removal of the 2-chlorine from a thiophene ring. The reaction conditions tolerate various functional groups, allowing highly chemoselective reactions in the presence of halide, ester, alkyne, alkene, and nitrile substituents and also showing good efficiency in the regioselective hydrodehalogenation of a variety of polyhalogenated substrates.



The substitution of halogens from aromatic rings by hydrogen is an important chemical transformation in organic synthesis, and a wide variety of hydrodehalogenating systems have been developed over the years for this purpose.[1] Reduction is usually mediated by a transition-metal catalyst (Ni, Pd, Rh, Pt) and is performed with molecular hydrogen, metal hydrides, or hydrogen sources such as formic acid and its salts, hydrazine, alkoxides possessing a β-hydrogen, etc.[1] However, the application of these systems to halogenated heterocycles is rather sporadic, most often accomplished by catalytic hydrogenation on a metal catalyst, Pd–C[2] or Raney Nickel,[3] and a halogen–metal exchange reaction.[4] These processes are often troublesome to execute since the former ignites easily and the latter requires anhydrous conditions and low reaction temperatures. For safety and simplicity of operation, a liquid-phase process without using molecular hydrogen is more advantageous.

Interestingly, some alternative methods have been recently described, such as (i) hydrogenolysis of aryl halides with catalytic Pd/C in the presence of hydrazine hydrochloride;[5] (ii) indium-mediated dehalogenation of haloheteroaromatics in water;[6] (iii) reduction of chloroarenes by $Pd(OAc)_2$ in combination with polymethylhydrosiloxane and aqueous KF,[7] (iv) dehalogenation of activated and unactivated aryl halides by catalytic Pd-complexes under transfer reaction conditions,[8,9] (vi) deiodination[10] and dechlorination[11] with sodium formate and catalytic palladium catalysts, (vii) $Fe(acac)_3$ catalyzed hydrodehalogenation of aryl halides with *t*-BuMgCl as a reductant,[12] and (viii) hydrodehalogenation with sodium borohydride ($NaBH_4$).[13,14] However, most of these methods appear limited to halopyridines, since they have only occasionally been applied to other halogenated heterocycles, in particular to brominated thiophenes[5,9,12,13a,b] and just in one case to a different heteropentalene, namely to 5-iodopyrroles.[10] Thus, the development of a facile and general method for the dehalogenation of heteroaromatic halides, besides pyridines, is still of great value.

Recently, in a preliminary study we have found that the system formed by the pair $NaBH_4$ and TMEDA (*N*,*N*,*N*′,*N*′-tetramethylethylenediamine) as a hydride source in combination with a palladium catalyst is an efficient system for the hydrodehalogenation of halopyridine derivatives.[14] The good results obtained in that work prompted us to verify the potential of this system for the removal of halogens in less reactive heterocycles. In this paper we wish to report that this system is able to hydrodehalogenate efficiently and selectively a variety of halogenated heteropentalenes with one or two heteroatoms at room temperature.

Starting our investigation to optimize the reaction conditions, the hydrodehalogenations were carried out with 2-bromo-5-phenylthiophene **1** as a model substrate. Initial experiments were performed at room temperature with $Pd(OAc)_2$ (5 mol %) and PPh_3 (20 mol %) as the catalytic system, and an excess of the couple $NaBH_4$–TMEDA (1.7 equiv) in THF (Method A). Under these reaction conditions the substitution of the bromine with hydrogen was incomplete after 24 h (Table 1, entry 1). However, by doubling the amount of $NaBH_4$–TMEDA (3.4 equiv) (Method B) complete conversion was achieved after 2 h and the product, 2-phenylthiophene **2** was isolated in 94% yield (entry 2). Also when $PdCl_2(dppf)$ [dppf = 1,1′-bis(diphenylphosphino)-ferrocene] (5 mol %) was used as the catalyst in combination with 1.7 equiv of the reducing system (Method C) incomplete conversion occurred after 24 h (entry 3), but by using 3.4 equiv of $NaBH_4$–TMEDA (Method D) the reaction was complete in 1 h and **2** was formed in 92% yield (entry 4).

These findings appeared to indicate that both $Pd(OAc)_2/PPh_3$ and $PdCl_2(dppf)$ in combination with a large excess of $NaBH_4$–TMEDA form efficient reducing systems for the rapid and high yielding debromination of **1**. This trend was confirmed for the removal of the 2-bromine of the

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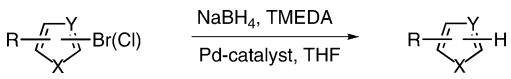
Table 1. Hydrodehalogenation of Halogenated Heteropentalenes[a]



Entry	Substrate	Product	Method	Time (h)	Conv.[b] (P/S)	Yield[c] (%)
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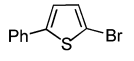
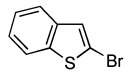
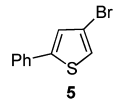
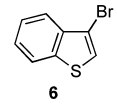
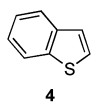
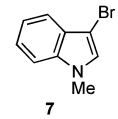
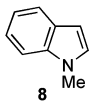
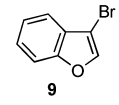
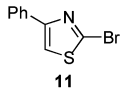
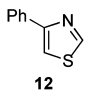
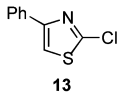
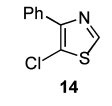
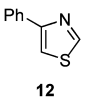
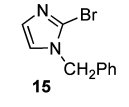
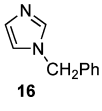
2			B	2	100/0	94
3			C	24	66/34	nd
4	**1**	**2**	D	1	100/0	92
5			A	48	45/55	nd
6			B	3	100/0	92
7	**3**	**4**	D	0.5	100/0	95
8			B	48	24/76	nd
9	**5**	**2**	D	3	100/0	94
10			D	2	100/0	85
	6	**4**				
11			B	24	13/87	nd
12			D	19	100/0	93
	7	**8**				
13			B	22	100/0	51
14			D	6	100/0	64
	9	**10**				
15			A	48	81/19	nd
16			B	3	100/0	95
	11	**12**				
17			B	52	100/0	86
18			D	22	100/0	92
	13	**12**				
19			D[d]	24	20/80	nd
20			E	72	40/60	nd
21			E[d]	20	100/0	95
	14	**12**				
22			B	1.5	100/0	95
	15	**16**				

[a]Reaction conditions: heterocycle (0.66 mmol), catalyst, $NaBH_4$/TMEDA, THF (13.2 mL). Method = A: $Pd(OAc)_2/PPh_3$ (5/20 mol %), $NaBH_4$–TMEDA (1.7/1.7 equiv); B: $Pd(OAc)_2/PPh_3$ (5/20 mol %), $NaBH_4$–TMEDA (3.4/3.4 equiv); C: $PdCl_2$(dppf)] (5 mol %), $NaBH_4$–TMEDA (1.7/1.7 equiv); D: $PdCl_2$(dppf)] (5 mol %), $NaBH_4$–TMEDA (3.4/3.4 equiv); E: $PdCl_2$(tbpf) (5 mol %), $NaBH_4$–TMEDA (1.7/1.7 equiv). [b]Determined by ^1H NMR as product/starting compound ratio. [c]Isolated yields. [d]Reaction carried out at 65 °C.

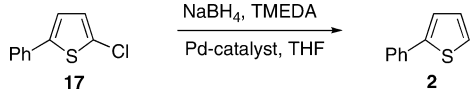
benzothiophene ring **3** (entry 5 vs 7). Therefore, the hydrodehalogenation of other haloheteropentalenes was evaluated by employing these catalytic systems.

The known lower reactivity of the β-bromine in thiophene was evident since $PdCl_2$(dppf) (Method D) was necessary to remove this halide (entry 9). Similarly, the reduction of the 3-bromo derivatives of benzothiophene **6**, 1-methylindole **7**, and benzofuran **9** was performed efficiently with method D affording high yields (85–93%) of the parent heterocycles, with the exception of **9** that gave benzofuran in a lower isolated yield (64%) (entry 14).

In the series of the heteropentalenes with two heteroatoms, 2-bromo-4-phenylthiazole was hydrodehalogenated efficiently by method B (entry 16). Methods B and D were also successful in the reduction of the low reactive 2-chlorine in the thiazole **13** (entries 16 and 18), but failed to remove the 5-chlorine from the thiazole **14**. On the other hand, this goal was efficiently achieved by the complex $PdCl_2$(tbpf) [tbpf = 1,1′-bis(di-*tert*-butylphosphino)ferrocene] that required in any case heating at 65 °C to afford complete conversion (entry 21, Method E). Finally, the removal of the bromine from 1-benzyl-2-bromoimidazole was efficiently obtained with method B (entry 22).

The removal of the chlorine from a thiophene ring was then addressed, since this goal had been achieved only in some well-defined cases.[15] After several experiments with different catalytic systems we found that the hydrodehalogenation of 2-chloro-5-phenylthiophene was more efficiently obtained by using 5 mol % $PdCl_2$(tbpf) at 65 °C for 8 h (96% yield) (entry 5, Table 2).

Table 2. Hydrodechlorination of 2-Chloro-5-phenylthiophene



17 **2**

entry	catalyst (mol %)[a]	temp (°C)	time (h)	conv.[b] (P/S)	yield[c] (%)
1	$PdCl_2$(dppf) (5)	rt	48	30/70	nd
2	$PdCl_2$(dppf) (5)	65	48	35/65	nd
3	$PdCl_2$(dppf)(10)	65	24	100/0	85
4	$PdCl_2$(tbpf) (5)	rt	48	32/68	nd
5	$PdCl_2$(tbpf) (5)	65	8	100/0	96
6	$Pd_2(dba)_3$/tbpf (2.5/5)	65	24	100/0	78
7	(A.[ca]Phos)$PdCl_2$ (5)[d]	rt	48	12/88	nd
8	$Pd_2(dba)_3$/DavePhos (2.5/5)[e]	rt	48	62/38	nd
9	$Pd_2(dba)_3$/P(*t*-Bu)$_3$ (2.5/10)	rt	48	56/44	nd

[a]Reaction conditions: heterocycle (0.66 mmol), catalyst, $NaBH_4$ (3.4 equiv), TMEDA (3.4 equiv), THF (13.2 mL). [b]Determined by ^1H NMR as product/starting compound ratio. [c]Isolated yields. [d](A.[ca]Phos)$PdCl_2$: bis[(dicyclohexyl)(4-dimethylaminophenyl)-phosphine] palladium(II) chloride. [e]DavePhos: 2-dicyclohexylphosphino-2′-(*N*,*N*-dimethylamino)biphenyl.

Next, the chemoselective reduction of some haloheteropentalenes was investigated (Table 3). The reducing system showed high chemoselectivity (Br vs Cl) and functional group tolerance, e.g., ester, alkyne, alkene, and nitrile substituents.

On the basis of the above results, the regioselective hydrodehalogenation of some polyhalogenated substrates was examined (Table 4). The simple catalyst $Pd(OAc)_2/PPh_3$ was reactive enough to promote the selective removal with high yields of the 2-bromo substituent in thiophenes **27** and **29**, benzothiophene **30**, and 1-methylindole **31**, leaving the bromine unchanged in the other positions. Regioselective hydrodehalogenation of 2,6-dichlorobenzo[*d*]thiazole was also possible, and only the 2-chlorine was reduced. The hydro-

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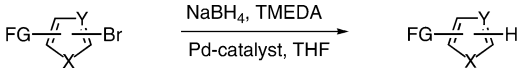
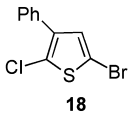
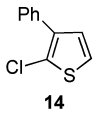
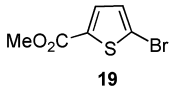
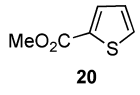
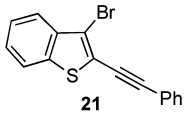
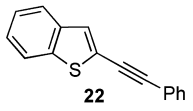
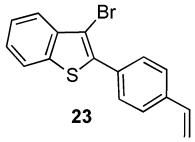
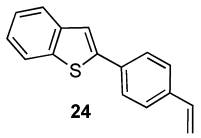
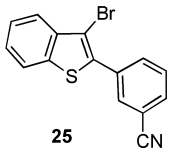
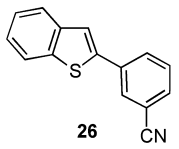
Table 3. Chemoselective Hydrodehalogenation of Halogenated Heteropentalenes[a]



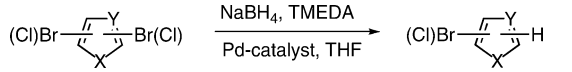
Entry	Substrate	Product	Time (h)	Yield[b] (%)
1	 **18**	 **14**	9	79
2	 **19**	 **20**	2	88
3	 **21**	 **22**	22[c]	85
4	 **23**	 **24**	9[c]	91
5	 **25**	 **26**	5[c]	95

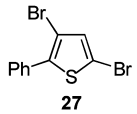
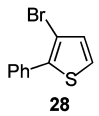
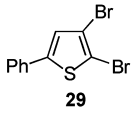
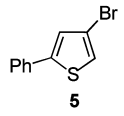
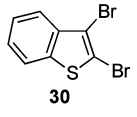
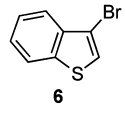
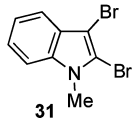
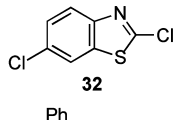
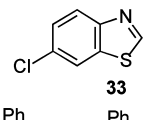
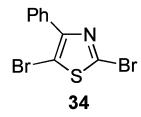
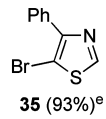
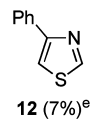
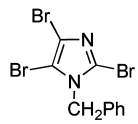
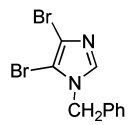
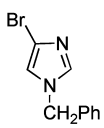
[a]Reaction conditions: heterocycle (0.66 mmol), $Pd(OAc)_2$ (5.0 mol %), PPh_3 (20.0 mol %), $NaBH_4$ (3.4 equiv), TMEDA (3.4 equiv), THF (13.2 mL) at rt. [b]Isolated yields. [c]Reaction carried out with $PdCl_2(dppf)$ (5.0 mol %) at 65 °C.

dehalogenation of 2,5-dibromo-4-phenylthiazole was less satisfactory. With method B a mixture of 5-bromo-4-phenylthiazole **35** and 4-phenylthiazole **12** in a 90/10 ratio was obtained. When the reaction was carried out at 0 °C the **35**/**12** ratio was increased up to 93/7. Several attempts to improve the selectivity by using different catalytic systems failed. Thus, for instance, the use of both $Pd_2(dba)_3$ (2.5 mol %) and $Pd(OAc)_2$ (5 mol %) in combination with XantPhos (5 mol %) at 0 °C gave a mixture of **35** and **12** in high yield, but with a ratio of only 86/14. Finally, the hydrodehalogenation of the more demanding 1-benzyl-2,4,5-tribromoimidazole was examined. Method B at room temperature gave a mixture of 1-benzyl-4,5-dibromoimidazole **37** and 1-benzyl-4-bromoimidazole **38** in a 63/17 ratio, containing also traces (<5%) of 1-benzylimidazole. Reducing the number of equivalents of the reductant from 3.4 to 2.5 increased only slightly the selectivity (**37**/**38** = 76/24), while a further decrease to 1.7 equiv gave only partial conversion of the starting material after 72 h. After a series of optimization experiments, the combination of $Pd_2(dba)_3$ (2.5 mol %) and XantPhos (5 mol %) at 0 °C was found to produce with good yield **37** and **38** in an 87/13 ratio.

Since in the examined haloheteropentalenes the reactivity of C-halogen bonds varies significantly from one substrate to another, the rates and yields of the dehalogenation depend critically on the choice of the catalyst, amount of the pair $NaBH_4$ and TMEDA, temperature, and reaction time. The dehalogenation efficiency of $NaBH_4$–TMEDA arises from the fact that the addition of a nitrogen-base, especially TMEDA,

Table 4. Regioselective Hydrodehalogenation of Halogenated Heteropentalenes[a]



Entry	Substrate	Product	Time (h)	Yield[b] (%)
1	 **27**	 **28**	2	89
2	 **29**	 **5**	2	86
3	 **30**	 **6**	4	85
4	 **31**	 **7**	18	79
5	 **32**	 **33**	4	95
6	 **34**	 **35** (93%)[e]	 **12** (7%)[e]	14[c]	90[d]
7	 **36**	 **37** (87%)[e]	 **38** (13%)[e]	3[f]	83[g]

[a]Reaction conditions: heterocycle (0.66 mmol), $Pd(OAc)_2$ (5.0 mol %), PPh_3(20.0 mol %), $NaBH_4$ (3.4 equiv), TMEDA (3.4 equiv), THF (13.2 mL) at rt. [b]Isolated yields. [c]Reaction carried out at 0 °C. [d]Isolated yields of **35** (84%) and **12** (6%). [e]Determined by ^1H NMR of the crude reaction mixture. [f]Reaction carried out with $Pd_2(dba)_3$/XantPhos (2.5/5 mol %) at 0 °C. [g]Isolated yields of **37** (72%) and **38** (11%).

considerably enhances the performance of $NaBH_4$.[13d] On the basis of the generally accepted mechanism that includes oxidative addition, hydride transfer (transmetalation), and reductive elimination, the effect of TMEDA can be threefold: (a) weak coordination to the electronically and coordinatively unsaturated intermediate in the form of [Pd(ligand)-(TMEDA)] thereby stabilizing the catalyst and minimizing catalyst decomposition (the weak donor ability of TMEDA ensures its cleavage upon entry of the substrate); (b) capture of BH_3 from BH_4^- provides an extra drive for hydride transfer to the Pd center (ArBr + $NaBH_4$ + $^1/_2$TMEDA → ArH + NaBr + $^1/_2$TMEDA•2BH_3), with the resultant TMEDA•2BH_3 adduct possibly serving as an additional hydride source;[16] (c) alternative debromination pathway through the elimination of HBr.

In conclusion, the pair $NaBH_4$–TMEDA as a hydride source and catalytic $PdCl_2(dppf)$ in THF prove to be an efficient system for the hydrodehalogenation of bromo(chloro)-

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heteropentalenes with one or two heteroatoms, while the simple and inexpensive catalyst $Pd(OAc)_2/PPh_3$ is able to reduce reactive haloheteropentalenes. In addition, $PdCl_2$(tbpf) has allowed the highly efficient removal of the 2-chlorine from a thiophene ring, which is rather sluggish with other reagents. The reaction conditions tolerate various functional groups, allowing highly chemoselective reactions in the presence of halide, ester, alkyne, alkene, and nitrile substituents and also showing good efficiency in the regioselective hydrodehalogenation of a variety of polyhalogenated substrates. The practical and selective methodology offers a very powerful, low-cost, and safe approach for the hydrodehalogenation of halogenated heteroaromatics and may constitute a key step in the synthesis of complex molecules.

EXPERIMENTAL SECTION

General Information. All reactions were carried out under nitrogen in oven-dried glassware with magnetic stirring. Unless otherwise noted, all materials were obtained from commercial suppliers and were used without further purification. All solvents were reagent grade. THF was distilled from sodium-benzophenone ketyl and degassed thoroughly with dry nitrogen directly before use. Unless otherwise noted, organic extracts were dried with Na_2SO_4, filtered through a fritted glass funnel, and concentrated with a rotary evaporator (20−30 mmHg). Flash chromatography was performed with silica gel (200−300 mesh) using the mobile phase indicated. Melting points are uncorrected. The NMR spectra were measured on a spectrometer at 300 MHz for ^{1}H and 75.4 MHz for ^{13}C in $CDCl_3$ solution with TMS as an internal standard. Chemical shifts (δ) are given in parts per million, and coupling constants (J), in hertz.

3-Bromobenzo[*b*]thiophene **6**, 2-bromo-4-phenylthiazole **11**, 2-chloro-4-phenylthiazole **13**, 2,3-dibromobenzo[*b*]thiophene **30**, and 2,6-dichlorobenzo[*d*]thiazole **32** were commercial starting materials.

2-Bromo-5-phenylthiophene **1**,[17] 2-bromobenzo[*b*]thiophene **3**,[18] 4-bromo-2-phenylthiophene **5**,[19] 3-bromo-1-methyl-1*H*-indole **7**,[20] 3-bromobenzofuran **9**,[21] 2-chlorobenzo[*d*]thiazole **13**,[22] 1-benzyl-2-bromo-1*H*-imidazole **15**,[23] 2-chloro-5-phenylthiophene **17**,[24] methyl 5-bromothiophene-2-carboxylate **19**,[25] 3,5-dibromo-2-phenylthiophene **29**,[19] 2,3-dibromo-1-methyl-1*H*-indole **31**,[26] 2,5-dibromo-4-phenylthiazole **34**,[27] and 1-benzyl-2,4,5-tribromo-1*H*-imidazole **36**[28] were prepared according to reported procedures.

Analytical and spectra data of the products 2-phenylthiophene **2**, benzo[*b*]thiophene **4**, and benzofuran **10** were identical to those obtained from commercial starting materials. Analytical and spectra data of the products 4-bromo-2-phenylthiophene **5**,[19] 1-methyl-1*H*-indole **8**,[29] 4-phenylthiazole **12**,[30] 1-benzyl-1*H*-imidazole **16**,[31] methyl thiophene-2-carboxylate **20**,[32] 3-bromo-2-(phenylethynyl)benzo[*b*]-thiophene **21**,[33] 2-(phenylethynyl)benzo[*b*]thiophene **22**,[34] 3-bromo-2-phenylthiophene **28**,[35] 6-chlorobenzo[*d*]thiazole **33**,[36] 1-benzyl-4,5-dibromo-1*H*-imidazole **37**,[37] and 1-benzyl-4-bromo-1*H*-imidazole **38**[28] were identical to those reported in the literature.

General Procedure for the Hydrodehalogenation of Halogenated Heterocycles. *Procedure Using in Situ Formed Catalysts $Pd(OAc)_2/PPh_3$, $Pd_2(dba)_3$/tbpf, $Pd_2(dba)_3$/DavePhos, $Pd_2(dba)_3$/P(t-Bu)$_3$, and $Pd_2(dba)_3$/XantPhos.* Anhydrous THF (13.2 mL) was degassed by bubbling argon for a few minutes, then $Pd(OAc)_2$ (7.2 mg, 0.033 mmol, 5 mol %) and PPh_3 (17.7 mg, 1.132 mmol, 20 mol %) were added, and the resulting mixture was stirred at room temperature for 30 min. The halogenated heterocycle (0.66 mmol), TMEDA (0.130 g, 1.12 mmol, 1.7 equiv), and finally $NaBH_4$ (42.4 mg, 1.12 mmol, 1.7 equiv) were introduced in sequence. The mixture was stirred at room temperature or heated at 65 °C under argon for the proper time. The residue was taken up in brine and extracted with ethyl acetate. The organic phase was separated and dried, the solvent was evaporated, and the residue was purified by flash chromatography (mixtures of petroleum ether and ethyl acetate) to give pure hydrodehalogenated heterocycles.

Procedure Using Preformed Catalysts $PdCl_2$(dppf), $PdCl_2$(tbpf), and (A.^{ca}Phos)$PdCl_2$. A mixture of the halogenated heterocycle (0.66 mmol) in anhydrous THF (13.2 mL) was degassed by bubbling argon for a few minutes. Then, $PdCl_2$(dppf)·CH_2Cl_2 (27.0 mg, 0.033 mmol, 5.0 mol %), TMEDA (0.130 g, 1.12 mmol, 1.7 equiv), and finally $NaBH_4$ (42.4 mg, 1.12 mmol, 1.7 equiv) were introduced in sequence. The mixture was stirred at room temperature under argon for the proper time and then worked up as described above.

5-Chloro-4-phenylthiazole (14). The title compound was prepared according to the general procedure, as described above (Table 3), and purified by flash chromatography using petroleum ether/AcOEt = 95/5 to give compound **14** as an oil (0.102 mg, 79%): ^{1}H NMR: δ 8.66 (s, 1H), 7.99−7.93 (m, 2H), 7.49−7.34 (m, 3H). ^{13}C NMR: δ 150.2, 149.7, 132.5, 128.5, 128.3, 128.2, 121.2. Anal. Calcd for C_9H_6ClNS: C, 55.24; H, 3.09; N, 7.16. Found: C, 55.12; H, 3.13; N, 7.12.

2-(4-Vinylphenyl)benzo[*b*]thiophene (24). The title compound was prepared according to the general procedure, as described above (Table 3), and purified by flash chromatography using petroleum ether to give compound **24** as a a white solid (0.141 g, 91%): mp 195−196 °C; ^{1}H NMR: δ 7.82 (d, 1H, J = 7.5 Hz), 7.77 (d, 1H, J = 7.5 Hz), 7.68 (d, 2H, J = 8.2 Hz), 7.55 (s, 1H), 7.47 (d, 2H, J = 8.2 Hz), 7.37−7.29 (m, 2H), 6.75 (dd, 1H, J = 17.1, 10.9 Hz), 5.81 (dd, 1H, J = 17.1, 0.8 Hz), 5.30 (dd, 1H, J = 10.9, 0.8 Hz). ^{13}C NMR: δ 143.9, 140.7, 139.5, 137.5, 136.2, 133.7, 126.8, 126.6, 124.6, 124.4, 123.6, 122.3, 119.4, 114.4. Anal. Calcd for $C_{16}H_{12}S$: C, 81.31; H, 5.12. Found: C, 81.51; H, 5.16

2-(3-Cyanophenyl)benzo[*b*]thiophene (26). The title compound was prepared according to the general procedure, as described above (Table 3), and purified by flash chromatography using petroleum ether/AcOEt = 8/2 to give compound **26** as a white solid (0.147 g, 95%): mp 142−143 °C; ^{1}H NMR: δ 7.95−7.94 (m, 1H), 7.87 (ddd, 1H, J = 7.9, 1.9, 1.2 Hz), 7.84−7.77 (m, 2H), 7.58 (td, 1H, J = 7.7, 1.3 Hz), 7.56 (d, 1H, J = 0.6 Hz), 7.50 (dt, 1H, J = 7.7, 0.6 Hz), 7.39−7.34 (m, 2H). ^{13}C NMR: δ 141.2, 140.2, 139.6, 135.5, 131.2, 130.4, 129.7, 129.6, 125.1, 124.9, 124.0, 122.3, 121.0, 118.4, 113.2. Anal. Calcd for $C_{15}H_9NS$: C, 76.57; H, 3.86; N, 5.95. Found: C, 76.71; H, 3.82; N, 5.91.

5-Bromo-4-phenylthiazole (35). The title compound was prepared according to the general procedure, as described above (Table 4), and purified by flash chromatography using petroleum ether/AcOEt = 95/5 to give compound **35** as an oil (0.133 g, 84%): ^{1}H NMR: δ 8.77 (s, 1H), 7.96−7.90 (m, 2H), 7.50−7.34 (m, 3H). ^{13}C NMR: δ 152.8, 133.0, 128.5, 128.4, 128.2, 126.3, 104.2. Anal. Calcd for C_9H_6BrNS: C, 45.02; H, 2.52; N, 5.83. Found: C, 45.14; H, 2.55; N, 5.79.

2-Bromo-5-chloro-4-phenylthiazole (18). A mixture of 2-bromo-4-phenylthiazole (1.0 g, 4.2 mmol) and *N*-chlorosuccinimide (0.78 g, 5.8 mmol) in CH_3CN (8 mL) was stirred at rt for 30 h and then heated under reflux temperature for 1 h. The solvent was removed by evaporation under reduced pressure, and the residue was taken up in petroleum ether. The formed solid was filtered, triturated, and washed with petroleum ether. The combined organic phase was evaporated, and the residue was purified by flash chromatography (petroleum ether/EtOAc = 95/5) to give **18**: 1.1 g (96%); oil; ^{1}H NMR: δ 7.92−7.86 (m, 2H), 7.46−7.33 (m, 3H). ^{13}C NMR: δ 150.1, 131.7, 131.5, 128.8, 128.3, 128.1, 121.9. Anal. Calcd for $C_9H_5BrClNS$: C, 39.37; H, 1.84; N, 5.10. Found: C, 39.29; H, 1.85; N, 5.14.

3-Bromo-2-(4-vinylphenyl)benzo[*b*]thiophene (23). 2,3-Dibromobenzo[*b*]thiophene (2.13 g, 7.34 mmol, 1 equiv), 4-vinylphenylboronic acid MIDA ester (1.13 g, 7.71 mmol, 1.05 equiv), and $Pd(PPh_3)_4$ (424 mg, 367 μmol, 5 mol %) were dissolved in 1,4-dioxane (75 mL), and degassed 2 M Na_2CO_3 (15 mL) was added. The resulting mixture was refluxed for 16 h, after which the solvent was removed under reduced pressure. The residue was taken up in CH_2Cl_2 and washed with brine. The organic layer was dried over anhydrous Na_2SO_4 and filtered, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography by using petroleum ether as the eluent: 1.56 g (67%); white solid: mp 60−61 °C; ^{1}H NMR: δ 7.83 (d, 1H, J = 8.4 Hz), 7.76−7.67 (m, 3H),

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7.49−7.31 (m, 4H), 6.72 (dd, 1H, J = 17.4, 10.8 Hz), 5.80 (d, 1H, J = 17.4 Hz), 5.30 (d, 1H, J = 10.8 Hz). ^{13}C NMR: δ 139.2, 137.9, 137.9, 137.6, 136.1, 132.3, 129.7, 126.3, 125.4, 125.2, 123.6, 122.1, 114.9, 104.9. Anal. Calcd for $C_{16}H_{11}BrS$: C, 60.96; H, 3.52. Found: C, 60.85; H, 3.56.

3-Bromo-2-(3-cyanophenyl)benzo[*b*]thiophene (25). 2,3-Dibromobenzo[*b*]thiophene (2.31 g, 7.34 mmol, 1 equiv), 3-cyanophenylboronic acid MIDA ester (1.98 g, 7.71 mmol, 1.05 equiv), and $Pd(PPh_3)_4$ (424 mg, 367 μmol, 5 mol %) were dissolved in 1,4-dioxane (100 mL), and degassed 3 M K_3PO_4 (20 mL) was added. The resulting mixture was refluxed for 16 h, after which the solvent was removed under reduced pressure. The residue was taken up in CH_2Cl_2 and washed with brine. The organic layer was dried over anhydrous Na_2SO_4 and filtered, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography by using petroleum ether/AcOEt = 8/2 as the eluent: 1.75 g (76%); white solid: mp 103−104 °C; ^{1}H NMR: δ 8.06 (dt, 1H, J = 1.2, 0.4 Hz), 7.98 (ddd, 1H, J = 7.8, 1.8, 1.4 Hz), 7.89 (ddd, 1H, J = 7.8, 1.4, 0.4 Hz), 7.84 (ddd, 1H, J = 7.8, 1.1, 0.6 Hz), 7.71 (ddd, 1H, J = 7.8, 1.6, 1.2 Hz), 7.60 (dt, 1H, J = 7.8, 0.6 Hz), 7.54−7.44 (m, 2H). ^{13}C NMR: δ 138.83, 137.7, 135.2, 134.5, 133.9, 133.0, 132.0, 129.5, 126.2, 125.6, 124.0, 122.3, 118.3, 113.0, 106.5. Anal. Calcd for $C_{15}H_8BrNS$: C, 57.34; H, 2.57; N, 4.46. Found: C, 57.51; H, 2.52; N, 4.52.

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H, ^{13}C NMR spectra for all new products. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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