Facile Access to Biaryls and 2-Acetyl-5-arylbenzofurans via Suzuki Coupling in Water under Thermal and Microwave Conditions

Ahmed F. Darweesh,[a] Mohamed R. Shaaban,[a,b] Ahmad M. Farag,[a] Peter Metz,[c] Kamal M. Dawood*[a]

[a] Department of Chemistry, Faculty of Science, Cairo University, Giza 12613, Egypt
Fax +20(2)35727556; E-mail: dr_dawood@hotmail.com

[b] Department of Chemistry, Faculty of Applied Science, Umm Al-Qura University, Makkah Almukarramah, Saudi Arabia

[c] Fachrichtung Chemie und Lebensmittelchemie, Organische Chemie I, Technische Universität Dresden, Bergstraße 66, 01069 Dresden, Germany

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Abstract: The phosphine-free Suzuki–Miyaura carbon–carbon cross-coupling reactions of activated and deactivated aryl halides and 2-acetyl-5-bromobenzofuran with various aryl- or heteroarylboronic acids were investigated. A benzothiazole-based palladium(II) complex was used as a precatalyst for the reactions under both thermal and microwave conditions in air using water as a solvent.

Key words: palladium, catalysis, microwave irradiation, Suzuki reactions, benzofuran

The formation of carbon–carbon bonds is a fundamental reaction in organic synthesis. Aryl–aryl bond formation has been known for more than a century and was one of the first reactions involving a transition metal.[1] Modern synthetic chemistry is also underpinned by the use of transition-metal catalysts as powerful tools for carbon–carbon bond-forming processes.[2] The Suzuki–Miyaura cross-coupling reaction is widely applied in academic and industrial research.[3] Over the past two decades, it has become one of the most-efficient methods for the construction of biaryls or substituted aromatic compounds that constitute important building blocks of polymers,[4] ligands,[5] a wide range of natural products, such as alkaloids, and numerous biologically active pharmaceuticals.[6]

Microwave irradiation has recently seen widespread application in research laboratories.[7,8] In addition, organic reactions that can proceed well in water offer advantages over those occurring in organic solvents.[9]

The benzofuran moiety is incorporated in various pharmacologically active compounds[10] and constitutes a structural unit of several natural products.[11] For example, cicerfuran (**I**) has been isolated from the roots of wild chickpea (*Cicer bijugum*),[12a] and 2-acetylbenzofurans *calebertin* (**II**), *caleprunin A* (**III**), and *caleprunin B* (**IV**) have been isolated from *Calea* species (Figure 1).[12b]

In continuation of our research directed towards the chemistry of 2- and 3-substituted benzofurans[13,14] and towards the use of palladium(II) complexes as precatalysts in carbon–carbon cross couplings in aqueous media,[15,16] we report herein new palladium(II) complex **3** and evaluate its suitability for the synthesis of biaryls and 5-aryl- or 5-heteroarylbenzofuran derivatives via Suzuki reactions. The syntheses use aryl or heteroaryl halides and 2-acetyl-5-bromobenzofuran with a variety of aryl- or heteroarylboronic acids under thermal as well as microwave conditions.

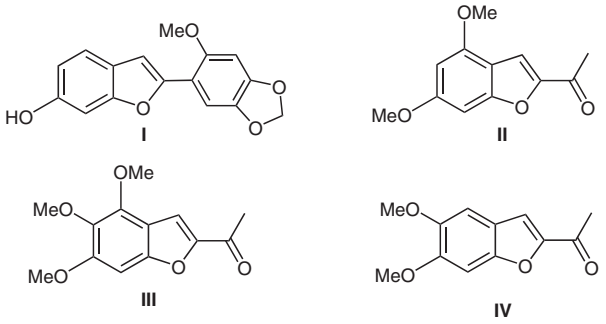
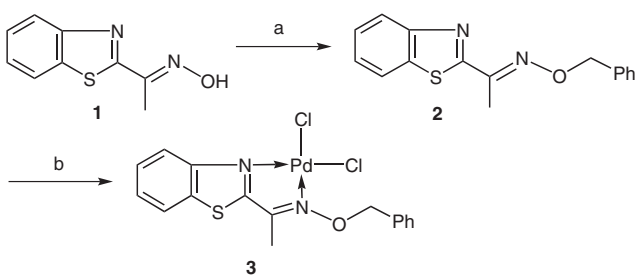


Figure 1 Examples of natural benzofuran derivatives

For the synthesis of complex **3**, the substrate 1-benzothiazol-2-ylethanone oxime (**1**) was prepared as described in the literature.[17] Treatment of oxime **1** with benzyl chloride in the presence of potassium hydroxide (KOH) gave *O*-benzyloxime **2**. Palladium(II) complex **3** was prepared by dissolving *O*-benzyloxime **2** in a mixture of 1,4-dioxane–methanol, followed by the addition of an equimolar amount of sodium tetrachloropalladate(II) in methanol at room temperature (Scheme 1).

The Suzuki cross-coupling of aryl and heteroaryl halides using complex **3** was then investigated. First, we evaluated the effect of palladium(II) complex **3** loading on the



Scheme 1 Preparation of palladium complex **3**. *Reagents and conditions*: (a) BnCl, EtOH, KOH, 100 °C, 30 min, 93% yield; (b) Na_2PdCl_4, 1,4-dioxane–MeOH (1:1), r.t., 2 h, 88% yield

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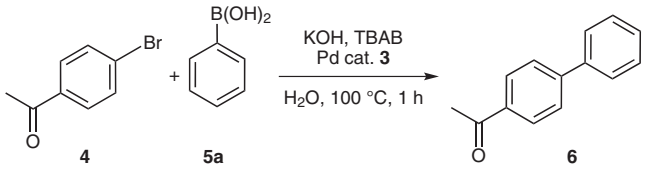
Table 1 Concentration Effect of Palladium Complex **3** on the Suzuki Coupling of 1-(4-Bromophenyl)ethanone with Phenylboronic Acid in Water Using Thermal Heating[a]



Entry	Loading of catalyst **3** (mol%)	Conversion (%)[b]	TON
1	1	100	100
2	0.75	100	133
3	0.5	100	200
4	0.25	100 (96)	400
5	0.125	100	800
6	0.05	100	2000
7	0.025	100	4000
8	0.0125	100 (93)	8000
9	0.005	100	20000
10	0.001	100	100000
11	0	0	0

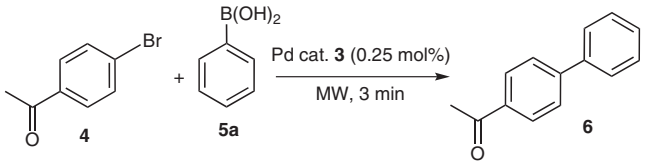
[a] Reaction conditions: aryl bromide/$PhB(OH)_2$/KOH/TBAB (1:1.2:2:0.6), H_2O (3 mL), 100 °C, 1 h.
[b] Conversions are based on GC analysis and the values in parentheses refer to isolated yields.

cross-coupling reaction of phenylboronic acid and 1-(4-bromophenyl)ethanone in water using KOH as a base and tetrabutylammonium bromide (TBAB) as a co-catalyst under thermal conditions of 100 °C for 1 hour (Table 1). The reaction was initially conducted using 1 mol% of complex **3** with 1-(4-bromophenyl)ethanone (**4**)/phenylboronic acid (**5a**)/KOH/TBAB in a molar ratio of 1:1.2:2:0.6 to give 4-acetylbiphenyl (**6**) with 100% conversion based on GC analysis (entry 1). In our second experiment, we used 0.75 mol% of catalyst **3** to give full conversion, based on GC analysis, after 1 hour of heating at 100 °C (entry 2). The reaction was repeated with different loadings (mol%) of complex **3** as shown in Table 1. In all cases, full conversion was obtained even in the presence of 0.001 mol% of complex **3**. It is important to mention that when palladium complex **3** was used in 0.001 mol%, the number of moles of the reacting species were raised [1-(4-bromophenyl)ethanone (**4**) (60 mmol), $PhB(OH)_2$ (**5a**) (75 mmol), KOH (125 mmol), and TBAB (37.5 mmol) in H_2O (100 mL)] to give 4-acetylbiphenyl (**6**) with 100% conversion, based on GC analysis, and a turnover number (TON) of 100000 (entry 10). It can be concluded from the data in Table 1 that palladium complex **3** shows excellent catalytic activity, giving rise to extremely high TONs. Interestingly, the bromide starting material was completely recovered unchanged when the reaction was carried out without palladium complex **3** (entry 11).

Palladium complexes have been reported to serve as 'dormant species'[18] that are not involved in the real catalytic cycle, but are sources of catalytically active species of an unknown nature. Therefore, our palladium(II) complex **3** may serve here as a reservoir that is not involved in the real catalytic cycle, but is a source of a considerable amount of colloidal palladium(0), which can show catalytic activity at low concentrations.

To achieve full conversion and, hence, maximum yield for the cross-coupling reaction, various parameters that may affect such results were optimized. Solvents and bases are among the most important controlling factors for such purposes. In our work, the choice of base was still empirical, and no general rule for its selection had been established, so the suitabilities of some bases and solvents for the coupling reaction between 1-(4-bromophenyl)ethanone (**4**) and phenylboronic acid (**5a**) were evaluated. In all cases, palladium precatalyst **3** was used in 0.25 mol% and the reaction was carried out under microwave irradiation for 3 minutes in different solvents, i.e. water, *N*,*N*-dimethylformamide (DMF), toluene, and tetrahydrofuran (THF), using KOH or potassium carbonate (K_2CO_3) as the base (Table 2). The best result was obtained with water as the solvent in the presence of TBAB after 3 minutes of microwave irradiation at 160 °C (entry 1). The conversion, based on GC analysis, was 100% and the cross-coupled product 4-acetylbiphenyl (**6**) was obtained in 96% isolated yield. Repeating the reaction under these conditions us-

Table 2 Base and Solvent Effects on the Suzuki Coupling of 1-(4-Bromophenyl)ethanone with Phenylboronic Acid under Microwave Irradiation[a]



Entry	Base	Solvent	Yield[b] (%)
1	KOH	H_2O (TBAB)	100 (96)[c,d]
2	K_2CO_3	H_2O (TBAB)	100 (96)
3	KOH	DMF	80 (71)
4	K_2CO_3	DMF	73 (61)
5	KOH	toluene	100 (91)
6	KOH	THF	60 (50)

[a] Reaction conditions: aryl bromide/$PhB(OH)_2$/base/TBAB (in the case of H_2O as solvent) (1:1.2:2:0.6), solvent (3 mL), microwave irradiation (250 W) at 160 °C (H_2O and DMF), 130 °C (toluene), and 90 °C (THF), 3 min.
[b] Conversions are based on GC analysis and the values in parentheses refer to isolated yields.
[c] Using thermal heating at 100 °C for 1 h gave full conversion with 94% isolated yield.
[d] Performing the reaction at r.t. for 12 h gave 96% conversion.

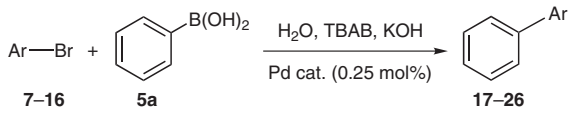
ing thermal heating at 100 °C for 1 hour also gave full conversion and the product in 94% isolated yield. In addition, when these optimum conditions were used for the reaction conducted at room temperature for 12 hours, product **6** was obtained with 96% conversion, based on GC analysis. Replacing water with DMF, toluene, or THF gave 80, 100, and 60% conversions, based on GC analysis, and product **6** was isolated in 71, 91, and 50% yield after 3 minutes of microwave irradiation (entries 3, 5, and 6, respectively). Next, the replacement of KOH with K_2CO_3 as the base in the reaction using different solvents (H_2O and DMF) was examined. Again, water proved itself as the suitable solvent in comparison with DMF (entries 2 and 4, respectively).

The choice of solvent, specifically its complexing properties, is crucial for palladium catalysts. Solvents other than water, such as DMF, can give supernatants that, unlike those cases involving aqueous solvents, still show catalytic activity in carbon–carbon coupling reactions. However, oxime ligands have the potential to scavenge any catalytic species that may have leached into solution during the catalytic process, particularly if DMF is used as a solvent.[19] Water as an ecofriendly 'green' solvent and KOH as a cheap and common base were chosen for carrying out all the Suzuki cross-coupling reactions of aryl halides that are performed in this work.

Under the optimized conditions, the general utility of complex **3** in the Suzuki–Miyaura cross-coupling reaction was investigated as described in Table 3. The Suzuki coupling reactions of aryl bromides **7–16** with phenylboronic acid (**5a**) were carried out using thermal heating and microwave irradiation, and resulted in the formation of the corresponding biaryl derivatives **17–26** in high yields. The molar ratio of the reaction components aryl bromide/phenylboronic acid (**5a**)/KOH/TBAB was 1:1.2:2:0.6 used with 0.25 mol% of complex **3** in water (3 mL). Palladium(II) complex **3** was found to efficiently catalyze the coupling of a wide range of aryl bromides in good to excellent yields regardless of their activating or deactivating substituents. Activated aryl bromides bearing electron-withdrawing groups required shorter reaction times to give the products in excellent yields (entries 7 and 8) compared with the deactivated aryl bromides bearing electron-donating groups (entries 2–4 and 9). Chemoselectivity was encountered when phenylboronic acid (**5a**) was treated with 1-bromo-4-chlorobenzene (**11**) under thermal as well as microwave conditions, with the chlorine atom surviving to give 4-chlorobiphenyl (**21**) in excellent yield (entry 5).

Arylpyridines have been reported to be among the most-prevalent heterocycles incorporated into pharmaceutically active compounds[20] and commercial drugs.[21–23] We prepared phenylpyridin-2-amines **29** and **30** by the Suzuki cross-coupling of bromopyridin-2-amines **27** and **28**, respectively, and phenylboronic acid (**5a**) using palladium(II) complex **3**. The cross-coupling reaction was performed using thermal heating and microwave irradiation (Table 4). The coupling reaction of 6-bromopyridin-2-amine (**27**) and 5-bromopyridin-2-amine (**28**) with phenylboronic acid (**5a**) resulted in the formation of the cor-

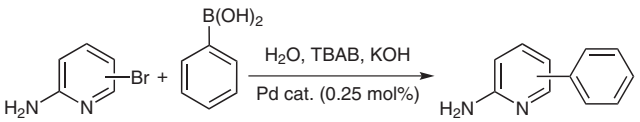
Table 3 Palladium(II) Complex **3** in the Suzuki Coupling of Aryl Bromides with Phenylboronic Acid in Water under Thermal and Microwave Conditions[a]



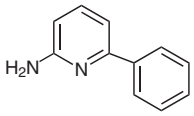
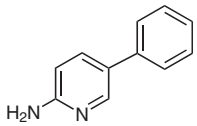
Entry	Substrate	Ar	Time		Product	Yield[b] (%)	
			Thermal (h)	Microwave (min)		Thermal	Microwave
1	**7**	Ph	2	5	**17**	92 (87)	(85)
2	**8**	4-$MeOC_6H_4$	4	6	**18**	100 (86)	100 (78)
3	**9**	4-$EtOC_6H_4$	2	6	**19**	100 (96)	100 (85)
4	**10**	4-HOC_6H_4	2	6	**20**	(94)	100 (96)
5	**11**	4-ClC_6H_4	2	6	**21**	98 (95)	(96)
6	**12**	3-AcC_6H_4	3	5	**22**	(88)	100 (91)
7	**13**	4-$O_2NC_6H_4$	1	2	**23**	(94)	100 (95)
8	**14**	2,4-$(O_2N)_2C_6H_3$	1	2	**24**	(80)	100 (90)
9	**15**	1-naphthyl	3	5	**25**	(88)	97 (92)
10	**16**	4-BzC_6H_4	4	6	**26**	(90)	100 (94)

[a] Reaction conditions: aryl bromide (1 mmol), $PhB(OH)_2$ (1.2 mmol), KOH (2 mmol), TBAB (0.6 mmol), H_2O (3 mL), 0.25 mol% Pd complex, microwave irradiation (250 W) at 160 °C or thermal heating at 100 °C.
[b] Conversions are based on GC analysis and the values in parentheses refer to isolated yields.

Table 4 Suzuki Coupling of Bromopyridin-2-amines with Phenylboronic Acid under Thermal and Microwave Conditions[a]



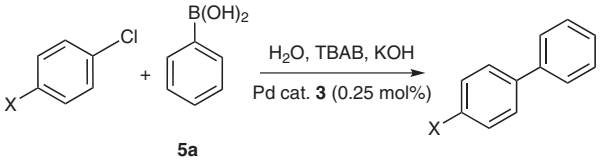
27, **28** **5a** **29**, **30**

Entry	Substrate	Bromo substituent	Time		Product	Yield[b] (%)	
			Thermal (h)	Microwave (min)		Thermal	Microwave
1	**27**	6-Br	6	15	 **29**	(84)	86 (79)
2	**28**	5-Br	3	10	 **30**	(87)	92 (82)

[a] Reaction conditions: bromopyridine (1 mmol), $PhB(OH)_2$ (1.2 mmol), KOH (2 mmol), TBAB (0.6 mmol), H_2O (3 mL), 0.25% Pd complex, microwave irradiation (250 W) at 160 °C or thermal heating at 100 °C.
[b] Conversions are based on GC analysis and the values in parentheses refer to isolated yields.

responding cross-coupled products **29** and **30** in 79 and 82% isolated yield after 15 and 10 minutes, respectively, of microwave irradiation. When the same reactions were repeated under similar conditions, but with thermal heating at 100 °C, phenylpyridines **29** and **30** were obtained in 84 and 87% yield after 6 and 3 hours, respectively. The inductive effect of the pyridine nitrogen is clear in these reactions as 6-bromopyridin-2-amine (**27**) gave lower yields after a longer reaction time (entry 1) than the 5-bromo derivative **28** (entry 2) under thermal as well as microwave conditions.

Aryl chlorides are cheaper and more-readily available than the corresponding bromides and iodides, and their cross-coupling reactions are of particular importance for highly active catalysts.[24] Therefore, the Suzuki cross-coupling of aryl chlorides **31** and **32** with phenylboronic acid (**5a**) was examined under thermal and microwave conditions as shown in Scheme 2. Firstly, 1-(4-chlorophenyl)ethanone (**31**) (1 mmol) was coupled with phenylboronic acid (**5a**) (1.2 mmol) in water (3 mL) in the presence of TBAB (0.6 mmol) using KOH (2 mmol) as the base and 0.25 mol% of palladium complex **3**. Under these conditions, coupled product **6** was obtained in 87



5a

31 X = COMe
32 X = NO_2

6 X = Ac; thermal (100 °C, 4 h): 81%
MW (250 W, 160 °C, 12 min): 87%
23 X = NO_2; thermal (100 °C, 2 h): 85%
MW (250 W, 160 °C, 10 min): 89%

Scheme 2 Suzuki coupling of aryl chlorides with phenylboronic acid under thermal and microwave conditions

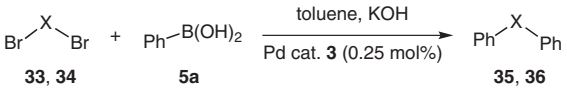
and 81% isolated yield after 12 minutes of microwave irradiation and 4 hours of thermal heating, respectively. Similarly, 1-chloro-4-nitrobenzene (**32**) was coupled with phenylboronic acid (**5a**) under microwave (10 min) and thermal conditions (2 h) with 100% conversion to give product **23** in 89 and 85% isolated yield, respectively, using 0.25 mol% of palladium complex **3**.

Palladium(II) precatalyst **3** was next applied to the Suzuki coupling of *N*,*N*′-bis(4-bromobenzylidene)ethane-1,2-diamine (**33**) and 1,2-bis(4-bromophenoxy)ethane (**34**) with phenylboronic acid (**5a**) using thermal heating as well as microwave irradiation to give bis(biaryl) products **35** and **36**, respectively (Table 5). The reaction components' quantities were 1 millimole of dibromide **33** or **34**, 2.4 millimoles of phenylboronic acid (**5a**), and 4 millimoles of KOH using 0.25 mol% of complex **3** in toluene (4 mL). Bis(biaryls) **35** and **36** were obtained in 69 and 55% isolated yield, respectively, after 10 minutes of microwave irradiation and in 74 and 52% isolated yield, respectively, after 4 hours of thermal heating.

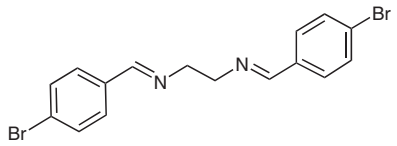
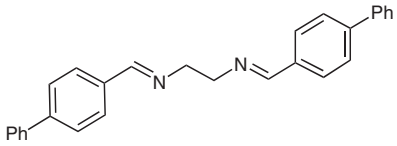
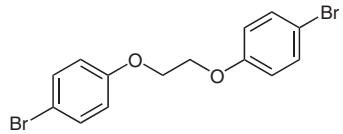
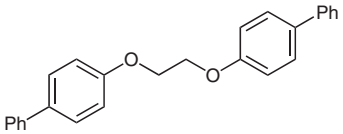
Next, we investigated the Suzuki cross-coupling of 2-acetyl-5-bromobenzofuran using complex **3**. Among the 5-arylbenzofuran derivatives that we prepared during this work, 2-acetyl-5-phenylbenzofuran was the only reported example in the literature and appears as a patent.[25] Therefore, developing new practical synthetic routes to 5-arylbenzofuran derivatives with potential biological applications is of great importance. In our work, 2-acetyl-5-bromobenzofuran was envisaged as a key synthon in Suzuki reactions for the synthesis of 5-arylbenzofurans.

To select the proper catalyst system for the Suzuki reaction between 2-acetyl-5-bromobenzofuran (**37**) and arylboronic acids, the effect of different bases and solvents on

Table 5 Suzuki Coupling of Dibromides with Phenylboronic Acid under Thermal and Microwave Conditions[a]



33, 34 5a 35, 36

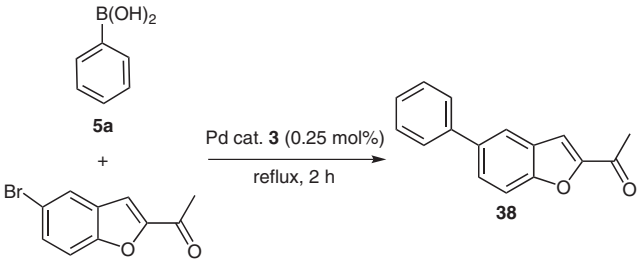
Entry	Substrate	Product	Yield[b] (%) Thermal	Yield[b] (%) Microwave
1	 **33**	 **35**	90 (74)	88 (69)
2	 **34**	 **36**	62 (52)	60 (55)

[a] Reaction conditions: microwave irradiation (250 W) at 130 °C for 10 min, or thermal heating at 110 °C for 4 h.
[b] Conversions are based on GC analysis and the values in parentheses refer to isolated yields.

the cross-coupling between substrate **37** and phenylboronic acid (**5a**) using thermal heating was studied in detail as a model example (Table 6). First, the reaction was carried out using KOH as the base in different solvents, i.e. water, DMF, and toluene. The best result was obtained with water as the solvent in the presence of TBAB after 2 hours of thermal heating at 100 °C (entry 1). The conversion was 100% and the cross-coupled product 2-acetyl-5-phenylbenzofuran (**38**) was isolated in 96% yield. Repeating the synthesis using these conditions at room temperature for 12 hours gave only 11% conversion, based on GC analysis, of cross-coupled product **38**. When the same reaction was repeated using microwave conditions instead of thermal heating, full conversion was obtained after 10 minutes of irradiation at 160 °C. When water was replaced by DMF or toluene, the reaction using KOH as the base with the same reaction time gave conversions of 100 and 7%, based on GC analysis (entries 4 and 7, respectively). This finding revealed that toluene is not a suitable solvent for such cross-coupling reactions. Although the use of DMF gave 100% conversion, the isolated yield of 89% was slightly lower than that achieved in the case using water. Next, the effect of using triethylamine (Et_3N) as an organic base instead of KOH was examined using different solvents. Again, water and DMF proved themselves as suitable solvents for such carbon–carbon cross-coupling reactions (entries 3 and 5, respectively).

The effect of TBAB on the above-mentioned conversion was also evaluated. When the reaction was conducted in DMF using Et_3N in the absence of TBAB, the conversion was only 58%, based on GC analysis, after thermal heating for 2 hours (entry 6). However, the use of water resulted in full conversion with or without TBAB when KOH was used as the base (entries 1 and 2). The last finding is in contrast to our previous work using an analogous pre-catalyst under similar conditions and the reason for this difference is not yet clear.[15a,c]

Table 6 Base and Solvent Effects on the Suzuki Coupling of 2-Acetyl-5-bromobenzofuran with Phenylboronic Acid Using Thermal Heating[a]



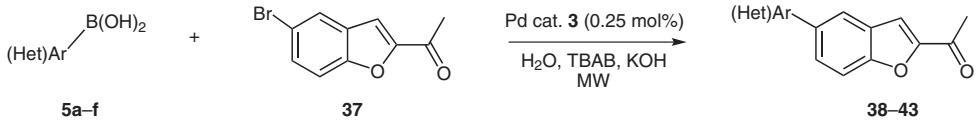
Entry	Base	Solvent	Yield (%)[b]
1	KOH	H_2O (TBAB)	100 (96)[c,d]
2	KOH	H_2O	100 (94)
3	Et_3N	H_2O (TBAB)	100 (91)
4	KOH	DMF (TBAB)	100 (89)
5	Et_3N	DMF (TBAB)	100 (95)
6	Et_3N	DMF	58
7	KOH	toluene	7
8	Et_3N	toluene	14

[a] Reaction conditions: 2-acetyl-5-bromobenzofuran (1 mmol), $PhB(OH)_2$ (1.2 mmol), base (2 mmol), TBAB (0.6 mmol), solvent (3 mL), 0.25 mol% Pd complex, reflux, 2 h.
[b] Conversions are based on GC analysis and the values in parenthesis refer to isolated yields.
[c] Conversion was 11% after 12 h of stirring at r.t.
[d] Full conversion with 88% isolated yield after 10 min of microwave irradiation at 160 °C.

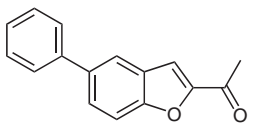
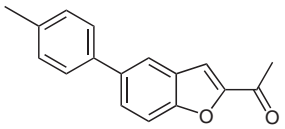
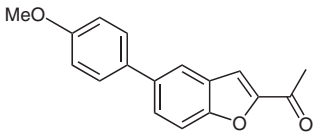
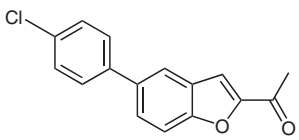
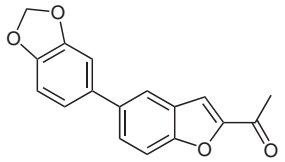
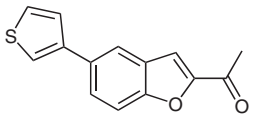
The general utility of palladium complex **3** in the Suzuki cross-coupling of 2-acetyl-5-bromobenzofuran (**37**) with several aryl- and heteroarylboronic acids **5a–f** was then investigated (Table 7). Thus, as mentioned previously, when 0.25 mol% of precatalyst **3** was employed in the reaction of bromide **37** with phenylboronic acid (**5a**) under microwave irradiation for 10 minutes in water with KOH as the base and TBAB as a phase-transfer agent, full conversion was observed giving 2-acetyl-5-phenylbenzofuran (**38**) in 88% isolated yield (entry 1). In the same manner, aryl- and heteroarylboronic acids **5b–f** coupled smoothly with bromide **37** under similar experimental conditions to give the corresponding cross-coupled products **39–43** in good to excellent isolated yields (entries 2–6). For the reaction shown in entry 4, there was no evidence of any byproduct relating to the further coupling of chlorophenyl derivative **41**.

The structures of the coupling products were confirmed by their ^{1}H and ^{13}C NMR and MS spectra and elemental analyses. The ^{1}H NMR spectrum of 2-acetyl-5-(4-tolyl)benzofuran (**39**), as an example of the series prepared, revealed four characteristic singlet signals at δ = 2.42, 2.64, 7.54, and 7.87 relating to the methyl protons of the 4-tolyl and acetyl substituents and H-3 and H-4 of the benzofuran moiety, respectively. The ^{13}C NMR spectrum of derivative **39** showed two aliphatic carbons at δ = 21.0

Table 7 Suzuki Cross-Coupling of 2-Acetyl-5-bromobenzofuran with Arylboronic Acids under Microwave Irradiation[a]



5a–f **37** **38–43**

Entry	Arylboronic acid	Ar	Time (min)	Product	Yield[b] (%)
1	**5a**	Ph	10	 **38**	100 (88)
2	**5b**	4-Tol	10	 **39**	100 (65)
3	**5c**	4-$MeOC_6H_4$	15	 **40**	100 (96)
4	**5d**	4-ClC_6H_4	10	 **41**	100 (92)
5	**5e**	3,4-methylenedioxyphenyl	15	 **42**	100 (78)
6	**5f**	3-thienyl	20	 **43**	100 (74)

[a] Reaction conditions: 2-acetyl-5-bromobenzofuran (1 mmol), $ArB(OH)_2$ (1.2 mmol), KOH (2 mmol), TBAB (0.6 mmol), H_2O (3 mL), 0.25 mol% Pd complex, microwave irradiation (250 W) at 160 °C.
[b] Conversions are based on GC analysis and the values in parenthesis refer to isolated yields.

and 26.4, relating to the methyl carbons of the 4-tolyl and acetyl groups, in addition to twelve aromatic carbons and one carbonyl carbon at δ = 188.6. The mass spectrum of compound **39** showed a peak (M^+) at *m*/*z* = 250 relating to its molecular ion.

In conclusion, palladium(II) complex **3** was found to be an efficient and highly active precatalyst for the Suzuki–Miyaura cross-coupling reactions of activated and deactivated aryl and heteroaryl bromides, under thermal as well as microwave conditions, resulting in very high TONs. Complex **3** was also a highly active precatalyst when applied to the synthesis of new 5-arylbenzofuran derivatives from 2-acetyl-5-bromobenzofuran. The high TON associated with the catalytic activity of precatalyst **3** is highly important for mass production at an industrial scale.

Melting points were determined in open glass capillaries with a Gallenkamp apparatus. The IR spectra were recorded using KBr disks on a Pye Unicam SP 3-300 or a Shimadzu FTIR 8101 PC IR spectrophotometer. The NMR spectra were recorded with a Varian Mercury VXR-300 NMR spectrometer at 300 and 75 MHz (^{1}H and ^{13}C NMR spectra, respectively) using $CDCl_3$ and DMSO-d_6 as a solvent and internal standard (δ = 7.27 and 77.36 ppm for the ^{1}H and ^{13}C NMR spectra, respectively). Capillary GC analyses were performed with a Shimadzu GC-14A or GC-14B apparatus, a Shimadzu C-R6A integrator, and an HP 5 column (25-m length, 0.25-mm i.d., 0.25-μm film) or were recorded with an Agilent GC 6890N apparatus. Mass spectra (EI) were obtained at 70 eV with a Shimadzu GC-MQP 1000 EX spectrometer. Analytical TLC was performed using precoated silica gel 60778 plates (Fluka), and the spots were visualized with UV light at 254 nm. Fluka silica gel 60741 (70–230 mesh) was used for flash column chromatography. Microwave experiments were carried out using a CEM Discover LabMate microwave apparatus (300 W with ChemDriver Software). 1-Benzothiazol-2-ylethanone oxime (**1**),[17] *N*,*N*′-bis(4-bromobenzylidene)ethane-1,2-diamine (**33**),[26] 1,2-bis(4-bromophenoxy)ethane (**34**),[27] and 2-acetyl-5-bromobenzofuran (**37**)[28] were prepared following the literature procedures.

2-[1-(Benzyloxyimino)ethyl]benzothiazole (2)

To a solution of 1-benzothiazol-2-ylethanone oxime (**1**) (1.92 g, 10 mmol) in abs EtOH (30 mL) was added KOH (0.79 g, 14 mmol), followed by BnCl (1.77 g, 14 mmol) to the resulting mixture. The mixture was left to stir for a few min at r.t. and then was heated at 100 °C for 30 min. Then, the mixture was diluted with H_2O (30 mL) and extracted with EtOAc (3 × 20 mL). The extracts were dried ($MgSO_4$) and the solvent was evaporated under reduced pressure. The solid product that formed was recrystallized (petroleum ether 60–80) to afford *O*-benzyloxime **2** as colorless crystals. Yield: 2.62 g (93%); mp 107–108 °C.

^{1}H NMR ($CDCl_3$): δ = 2.46 (s, 3 H, CH_3), 5.32 (s, 2 H, CH_2), 7.34–7.48 (m, 7 H, ArH), 7.84–8.04 (m, 2 H, ArH).

^{13}C NMR ($CDCl_3$): δ = 12.3, 77.0, 121.9, 123.8, 126.3, 126.4, 128.5, 128.8, 128.9, 135.3, 137.3, 152.9, 153.5, 165.8.

MS (EI, 70 eV): *m*/*z* (%) = 282 (5.7) [M^+], 265 (10), 135 (12.8), 91 (100), 77 (4.3).

Anal. Calcd for $C_{16}H_{14}N_2OS$: C, 68.06; H, 5.00; N, 9.92. Found: C, 67.84; H, 4.79; N, 9.84.

{2-[1-(Benzyloxyimino)ethyl]benzothiazole-κ^2*N*,*N*′}dichloropalladium(II) (3)

A solution of Na_2PdCl_4 (294 mg, 1 mmol) in MeOH (2 mL) was added portionwise to a stirred solution of *O*-benzyloxime **2** (282 mg, 1 mmol) in 1,4-dioxane–MeOH (1:1, 4 mL). After stirring for 2 h at r.t., a yellow precipitate was formed that was collected by filtration, washed with MeOH (5–7 mL), H_2O (5–7 mL), and then with EtOH (5–7 mL), and finally dried to give Pd complex **3** as a yellow powder. Complex **3** was obtained in a pure state and was used without further purification. Yield: 403 mg (88%); mp >300 °C.

^{1}H NMR (DMSO-d_6): δ = 2.41 (s, 3 H, CH_3), 5.33 (s, 2 H, CH_2), 7.36–7.56 (m, 7 H, ArH), 8.05–8.12 (m, 2 H, ArH).

^{13}C NMR (DMSO-d_6): δ = 12.8, 77.5, 123.2, 124.1, 127.4, 127.5, 129.0, 129.3, 129.4, 135.1, 137.8, 153.3, 153.4, 165.5.

Anal. Calcd for $C_{16}H_{14}Cl_2N_2OPdS$: C, 41.80; H, 3.07; N, 6.09. Found: C, 41.68; H, 3.31; N, 6.03.

Concentration Effect of Palladium Complex 3 on the Suzuki Coupling of 1-(4-Bromophenyl)ethanone (4) with Phenylboronic Acid (5a) in Water Using Thermal Heating; General Procedure

A mixture of 1-(4-bromophenyl)ethanone (**4**) (199 mg, 1.0 mmol), $PhB(OH)_2$ (**5a**) (146 mg, 1.2 mmol), TBAB (194 mg, 0.6 mmol), Pd complex **3** (4.59 mg, 1 mol%), KOH (112 mg, 2.0 mmol), and H_2O (3 mL) was stirred at 100 °C under open air for 1 h to give 4-acetylbiphenyl (**6**). The same experiment was repeated using different concentrations of palladium complex **3**. The amount (mol%) of palladium complex **3** was changed with respect to 1-(4-bromophenyl)ethanone (**4**) for further experiments [0.75, 0.5, 0.25, 0.125, 0.05, 0.025, 0.0125, 0.005, and 0.001 mol% of complex **3** with 1, 1, 1, 2, 2, 5, 10, 20, and 60 mmol of 1-(4-bromophenyl)ethanone (**4**), respectively]. The molar ratio of the reaction components 1-(4-bromophenyl)ethanone (**4**)/$PhB(OH)_2$ (**5a**)/KOH/TBAB was, in all cases, 1:1.2:2:0.6. The volume of H_2O varied, depending on the amount of bromide **4** used (1–5 mmol **4**: 3 mL/mmol; 10 mmol **4**: 25 mL; 20 mmol **4**: 40 mL; 60 mmol **4**: 100 mL). The yields corresponding to the use of different concentrations of palladium complex **3** are outlined in Table 1.

Base and Solvent Effects on the Suzuki Coupling of 1-(4-Bromophenyl)ethanone (4) with Phenylboronic Acid (5a) under Microwave Irradiation

A mixture of 1-(4-bromophenyl)ethanone (**4**) (199 mg, 1.0 mmol), $PhB(OH)_2$ (**5a**) (146 mg, 1.2 mmol), TBAB (194 mg, 0.6 mmol), Pd(II) precatalyst **3** (1.15 mg, 0.25 mol%), KOH (112 mg, 2.0 mmol), and H_2O (3 mL) was heated under microwave conditions at 160 °C and 250 W for 3 min (monitored by GC) to give 4-acetylbiphenyl (**6**). The same experiment was repeated using different solvents and bases; those reactions involving toluene and THF were conducted at 130 and 90 °C, respectively, and 250 W. The molar ratio of the reaction components 1-(4-bromophenyl)ethanone (**4**)/$PhB(OH)_2$ (**5a**)/base/TBAB (in the case of H_2O as solvent) was, in all cases, 1:1.2:2:0.6 used with the chosen solvent (3 mL). The yields corresponding to the use of different solvents and bases are outlined in Table 2.

Suzuki Coupling of Aryl Bromides 7–16 and Chlorides 31 and 32 with Phenylboronic Acid (5a) in Water Using Thermal Heating; General Procedure

A mixture of the selected aryl bromide **7**–**16** or chloride **31** or **32** (1.0 mmol) with $PhB(OH)_2$ (**5a**) (146 mg, 1.2 mmol), TBAB (194 mg, 0.6 mmol), Pd complex **3** (0.25 mol%), KOH (112 mg, 2.0 mmol), and distilled H_2O (3 mL) was stirred at 100 °C under open air for the appropriate reaction time, as listed in Table 3 and Scheme 2 (reaction was monitored by TLC). The product was then extracted with EtOAc (3 × 20 mL). The combined organic extracts were dried (anhyd $MgSO_4$) and filtered, and the solvent was evaporated under reduced pressure. The residue was then subjected to separation via flash column chromatography (petroleum hexane–

EtOAc, 9:1) to give the corresponding pure cross-coupled product **17–26** (see Table 3), **6**, or **23** (see Scheme 2).

Suzuki Coupling of Aryl Bromides 7–16 and Chlorides 31 and 32 with Phenylboronic Acid (5a) in Water under Microwave Irradiation; General Procedure

The selected aryl bromide **7–16** or chloride **31** or **32** (1.0 mmol), $PhB(OH)_2$ (**5a**) (146 mg, 1.2 mmol), TBAB (194 mg, 0.6 mmol), Pd complex **3** (0.25 mol%), KOH (112 mg, 2.0 mmol), and distilled H_2O (3 mL) were mixed in a process glass vial. The vial was capped properly, and thereafter the mixture was heated under microwave irradiation at 160 °C and 250 W for the appropriate reaction time, as listed in Table 3 and Scheme 2. After the reaction was almost complete (monitored by TLC), the mixture was extracted with EtOAc (3 × 20 mL). The combined organic extracts were dried (anhyd $MgSO_4$) and filtered, and the solvent was evaporated under reduced pressure. The product was purified by flash column chromatography as described above.

4-Acetylbiphenyl (6)

Colorless solid; mp 118–120 °C (Lit.[29] mp 119–120 °C).

^{1}H NMR ($CDCl_3$): δ = 2.60 (s, 3 H, $COCH_3$), 7.31–7.38 (m, 1 H), 7.42–7.50 (m, 2 H), 7.74 (d, *J* = 6.9 Hz, 2 H), 7.82 (d, *J* = 7.5 Hz, 2 H), 8.03 (d, *J* = 7.5 Hz, 2 H).

MS (EI, 70 eV): *m*/*z* (%) = 196 (49.3) [M$^+$], 181 (100), 152 (61.4), 127 (5.2), 76 (9).

Biphenyl (17)

Colorless powder; mp 68–70 °C (Lit.[30] mp 68–70 °C).

^{1}H NMR ($CDCl_3$): δ = 7.38–7.40 (m, 2 H), 7.45–7.56 (m, 4 H), 7.67 (d, *J* = 8.1 Hz, 4 H).

MS (EI, 70 eV): *m*/*z* (%) = 154 (36.8) [M$^+$], 77 (100), 50 (42.1).

4-Methoxybiphenyl (18)

Pale-yellow powder; mp 87–88 °C (Lit.[31] mp 87–88 °C).

^{1}H NMR ($CDCl_3$): δ = 3.87 (s, 3 H, OCH_3), 6.99 (d, *J* = 8.7 Hz, 2 H), 7.31–7.45 (m, 3 H), 7.54 (d, *J* = 9.0 Hz, 2 H), 7.57 (d, *J* = 7.2 Hz, 2 H).

MS (EI, 70 eV): *m*/*z* (%) = 184 (100) [M$^+$], 169 (54.0), 141 (37.4), 115 (16.6), 89 (12.5), 76 (49.8), 63 (25.7).

4-Ethoxybiphenyl (19)

Colorless powder; mp 72–74°C (Lit.[32] mp 76 °C).

^{1}H NMR ($CDCl_3$): δ = 1.46 (t, *J* = 6.9 Hz, 3 H), 4.10 (q, *J* = 6.9 Hz, 2 H), 6.98 (d, *J* = 9.0 Hz, 2 H), 7.30–7.34 (m, 1 H), 7.40–7.45 (m, 2 H), 7.53 (d, *J* = 8.7 Hz, 2 H), 7.56 (d, *J* = 7.5 Hz, 2 H).

MS (EI, 70 eV): *m*/*z* (%) = 198 (56.7) [M$^+$], 170 (100), 141 (38.0), 115 (48.7), 50 (16.0).

4-Hydroxybiphenyl (20)

Colorless solid; mp 164–166 °C (Lit.[33] mp 164–165 °C).

^{1}H NMR ($CDCl_3$): δ = 5.05 (s, 1 H, OH), 6.92 (d, *J* = 7.8 Hz, 2 H), 7.30–7.38 (m, 1 H), 7.40–7.45 (m, 2 H), 7.49 (d, *J* = 8.1 Hz, 2 H), 7.56 (d, *J* = 8.4 Hz, 2 H).

MS (EI, 70 eV): *m*/*z* (%) = 170 (100) [M$^+$], 141 (32.3), 115 (20.0), 63 (10.3), 51 (12.9).

4-Chlorobiphenyl (21)

Colorless powder; mp 76–78 °C (Lit.[34] mp 76–78 °C).

^{1}H NMR ($CDCl_3$): δ = 7.37–7.48 (m, 3 H), 7.53 (d, *J* = 8.4 Hz, 2 H), 7.56 (d, *J* = 7.5 Hz, 2 H), 8.27 (d, *J* = 7.2 Hz, 2 H).

MS (EI, 70 eV): *m*/*z* (%) = 189 (31.6) [M$^+$ + 1], 188 (57.9) [M$^+$], 104 (63.2), 62 (100).

3-Acetylbiphenyl (22)

Yellow oil.[35]

^{1}H NMR ($CDCl_3$): δ = 2.62 (s, 3 H, $COCH_3$), 7.37–7.39 (m, 1 H), 7.42–7.45 (m, 2 H), 7.48 (d, *J* = 6.6 Hz, 2 H), 7.59–7.61 (m, 1 H), 7.75 (d, *J* = 8.1 Hz, 1 H), 7.91 (d, *J* = 7.8 Hz, 1 H), 8.19 (s, 1 H).

MS (EI, 70 eV): *m*/*z* (%) = 196 (66) [M$^+$], 181 (100), 152 (73.1), 127 (6.2), 76 (10.5).

4-Nitrobiphenyl (23)

Pale-yellow powder; mp 106–108 °C (Lit.[36] mp 107.5–108.5 °C).

^{1}H NMR ($CDCl_3$): δ = 7.47–7.51 (m, 3 H), 7.63 (d, *J* = 7.8 Hz, 2 H), 7.75 (d, *J* = 8.4 Hz, 2 H), 8.31 (d, *J* = 8.7 Hz, 2 H).

MS (EI, 70 eV): *m*/*z* (%) = 199 (100) [M$^+$], 169 (53.1), 141 (21.9), 127 (34.4), 115 (46.9), 101 (28.1), 76 (31.3), 63 (43.8).

2,4-Dinitrobiphenyl (24)

Yellow powder; mp 110–112 °C (Lit.[37] mp 110 °C).

^{1}H NMR ($CDCl_3$): δ = 7.33–7.36 (m, 3 H), 7.47–7.50 (m, 2 H), 7.69 (d, *J* = 8.4 Hz, 1 H), 8.47 (d, *J* = 8.4 Hz, 1 H), 8.71 (s, 1 H).

MS (EI, 70 eV): *m*/*z* (%) = 244 (17.9) [M$^+$], 216 (20.5), 169 (20.5), 151 (53.8), 115 (53.8), 102 (46.2), 87 (38.5), 63 (87.2), 50 (100).

1-Phenylnaphthalene (25)

Colorless oil.[38]

^{1}H NMR ($CDCl_3$): δ = 7.65–7.76 (m, 9 H), 8.08 (d, *J* = 7.8 Hz, 1 H), 8.13 (d, *J* = 7.8 Hz, 1 H), 8.25 (d, *J* = 8.1 Hz, 1 H).

MS (EI, 70 eV): *m*/*z* (%) = 204 (100) [M$^+$], 189 (10.1), 176 (12.3), 163 (6.7), 150 (8.1), 101 (42.0), 88 (10.5).

4-Benzoylbiphenyl (26)

Yellow crystals; mp 100–102°C (Lit.[39] mp 101–102 °C).

^{1}H NMR ($CDCl_3$): δ = 7.41–7.56 (m, 5 H), 7.59 (d, *J* = 7.8 Hz, 2 H), 7.67–7.71 (m, 1 H), 7.77 (d, *J* = 8.1 Hz, 2 H), 7.83 (d, *J* = 8.7 Hz, 2 H), 7.87 (d, *J* = 8.7 Hz, 2 H).

MS (EI, 70 eV): *m*/*z* (%) = 258 (73.5) [M$^+$], 181 (100), 152 (51.3), 105 (21.0), 77 (28.0).

Suzuki Coupling of Bromopyridin-2-amines 27 and 28 with Phenylboronic Acid (5a) in Water Using Thermal Heating; General Procedure

A mixture of bromopyridin-2-amine **27** or **28** (1.0 mmol), $PhB(OH)_2$ (**5a**) (146 mg, 1.2 mmol), TBAB (194 mg, 0.6 mmol), Pd complex **3** (0.25 mol%), KOH (112 mg, 2.0 mmol), and distilled H_2O (3 mL) was stirred at 100 °C under open air for the appropriate reaction time, as listed in Table 4 (reaction was monitored by TLC). The product was then extracted with EtOAc (3 × 20 mL). The combined organic extracts were dried (anhyd $MgSO_4$) and filtered, and the solvent was evaporated under reduced pressure. The residue was then subjected to separation via flash column chromatography (hexane–EtOAc, 9:1) to give the corresponding pure cross-coupled product **29** or **30**.

Suzuki Coupling of Bromopyridin-2-amines 27 and 28 with Phenylboronic Acid (5a) in Water under Microwave Irradiation; General Procedure

Bromopyridin-2-amine **27** or **28** (1.0 mmol), $PhB(OH)_2$ (**5a**) (146 mg, 1.2 mmol), TBAB (194 mg, 0.6 mmol), Pd complex **3** (0.25 mol%), KOH (112 mg, 2.0 mmol), and distilled H_2O (3 mL) were mixed in a process glass vial. The vial was capped properly, and thereafter the mixture was heated under microwave irradiation at 160 °C and 250 W for the appropriate reaction time, as listed in Table 4. After the reaction was almost complete (monitored by TLC), the mixture was extracted with EtOAc (3 × 20 mL). The com-

bined organic extracts were dried (anhyd $MgSO_4$) and filtered, and the solvent was evaporated under reduced pressure. The product was purified by flash column chromatography as described above.

6-Phenylpyridin-2-amine (29)
Yellow powder; mp 70–72 °C (Lit.[40] mp 71–72 °C).

^{1}H NMR ($CDCl_3$): δ = 5.07 (s, 2 H, NH_2), 6.45 (d, *J* = 8.4 Hz, 1 H, H-3 py), 7.05 (d, *J* = 7.5 Hz, 1 H, H-5 py), 7.39–7.50 (m, 4 H), 7.92 (d, *J* = 7.2 Hz, 2 H).

MS (EI, 70 eV): *m*/*z* (%) = 170 (100) [M$^+$], 143 (11.2), 135 (1.9), 115 (1.9), 77 (3.7).

5-Phenylpyridin-2-amine (30)
Pale-yellow crystals; mp 130–132 °C (Lit.[41] mp 132 °C).

^{1}H NMR ($CDCl_3$): δ = 6.01 (s, 2 H, NH_2), 6.52 (d, *J* = 8.4 Hz, 1 H, H-3 py), 7.22–7.28 (m, 1 H), 7.37–7.46 (m, 2 H), 7.55 (d, *J* = 8.1 Hz, 2 H), 7.68 (d, *J* = 8.7 Hz, 1 H, H-4 py), 8.18 (d, *J* = 2.7 Hz, 1 H, H-6 py).

MS (EI, 70 eV): *m*/*z* (%) = 170 (100) [M$^+$], 143 (29.5), 115 (70.5), 91 (33.3), 71 (28.2), 51 (30.8).

Suzuki Coupling of Dibromides 33 and 34 with Phenylboronic Acid (5a) Using Thermal Heating; General Procedure
A mixture of dibromide **33** or **34** (1.0 mmol), $PhB(OH)_2$ (**5a**) (292 mg, 2.4 mmol), Pd complex **3** (0.25 mol%), KOH (224 mg, 4.0 mmol), and toluene (4 mL) was stirred at 110 °C under open air for 4 h (reaction was monitored by TLC). The product was then extracted with EtOAc (3 × 20 mL). The combined organic extracts were dried (anhyd $MgSO_4$) and filtered, and the solvent was evaporated under reduced pressure. The residue was then subjected to separation via flash column chromatography (petroleum hexane–EtOAc, 7:1) to give the corresponding pure cross-coupled product **35** or **36**.

Suzuki Coupling of Dibromides 33 and 34 with Phenylboronic Acid under Microwave Irradiation; General Procedure
Dibromide **33** or **34** (1.0 mmol), $PhB(OH)_2$ (**5a**) (292 mg, 2.4 mmol), Pd complex **3** (0.25 mol%), KOH (224 mg, 4 mmol), and toluene (4 mL) were mixed in a process glass vial. The vial was capped properly, and thereafter the mixture was heated under microwave irradiation at 130 °C and 250 W for 10 min. After the reaction was almost complete (monitored by TLC), the mixture was extracted with EtOAc (3 × 20 mL). The combined organic extracts were dried (anhyd $MgSO_4$) and filtered, and the solvent was evaporated under reduced pressure. The product was purified by flash column chromatography as described above.

***N,N′*-Bis(biphenyl-4-ylmethylene)ethane-1,2-diamine (35)**
Yellow powder; mp 136–138 °C.

IR (KBr): 2912, 2848, 1641, 1583, 1480 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 3.86 (s, 4 H), 7.31–7.50 (m, 6 H), 7.64 (d, *J* = 7.2 Hz, 4 H), 7.71 (d, *J* = 7.8 Hz, 4 H), 7.78 (d, *J* = 7.8 Hz, 4 H), 8.32 (s, 2 H).

^{13}C NMR ($CDCl_3$): δ = 61.5, 127.1, 128.5, 128.8, 129.4, 131.8, 134.9, 140.3, 143.4, 161.4.

GC/MS (EI): *m*/*z* = 388 [M$^+$].

Anal. Calcd. for $C_{28}H_{24}N_2$: C, 86.56; H, 6.23; N, 7.21. Found: C, 86.64; H, 6.17; N, 7.11.

1,2-Bis(biphenyl-4-yloxy)ethane (36)
Yellow powder; mp 216–218 °C (Lit.[42] mp 219 °C).

^{1}H NMR ($CDCl_3$): δ = 4.29 (s, 4 H), 6.96 (d, *J* = 7.8 Hz, 4 H), 7.32–7.47 (m, 6 H), 7.61 (d, *J* = 8.7 Hz, 4 H), 7.77 (d, *J* = 7.8 Hz, 4 H).

GC/MS (EI): *m*/*z* = 366 [M$^+$].

Base and Solvent Effects on the Suzuki Coupling of 2-Acetyl-5-bromobenzofuran (37) with Phenylboronic Acid Using Thermal Heating
A mixture of 2-acetyl-5-bromobenzofuran (**37**) (239 mg, 1.0 mmol), $PhB(OH)_2$ (**5a**) (146 mg, 1.2 mmol), TBAB (194 mg, 0.6 mmol), Pd(II) precatalyst **3** (1.15 mg, 0.25 mol%), KOH (112 mg, 2.0 mmol), and H_2O (3 mL) was stirred at 100 °C under open air for 2 h (monitored by GC) to give 2-acetyl-5-phenylbenzofuran (**38**). The same experiment was repeated using different solvents and bases; those reactions involving other solvents were conducted at 110 °C (toluene) and 160 °C (DMSO). The molar ratio of the reaction components bromobenzofuran **37**/$PhB(OH)_2$ (**5a**)/base/TBAB (for those cases specified in Table 6) was, in all cases, 1:1.2:2:0.6 used with the chosen solvent (3 mL). The yields corresponding to the use of different solvents and bases are outlined in Table 6.

Suzuki Coupling of 2-Acetyl-5-bromobenzofuran (37) with Arylboronic Acids 5a–f in Water under Microwave Irradiation; General Procedure
2-Acetyl-5-bromobenzofuran (**37**) (239 mg, 1.0 mmol), $ArB(OH)_2$ (1.2 mmol), TBAB (194 mg, 0.6 mmol), Pd complex **3** (1.14 mg, 0.25 mol%), KOH (112 mg, 2.0 mmol), and H_2O (3 mL) were mixed in a process vial. The vial was capped properly, and thereafter the mixture was heated under microwave irradiation at 160 °C and 250 W for the appropriate reaction time, as listed in Table 7. After the reaction was almost complete (monitored by TLC), the mixture was extracted with EtOAc (3 × 20 mL). The combined organic extracts were dried (anhyd $MgSO_4$) and filtered, and the solvent was evaporated under reduced pressure. The residues in each reaction were purified by flash column chromatography (hexane–EtOAc, 7:1) to give the corresponding pure products **38**–**43**.

2-Acetyl-5-phenylbenzofuran (38)
Yellow powder; mp 114–116 °C; R_f = 0.23 (hexane–EtOAc, 10:1).

IR (KBr): 3090, 2056, 1676, 1299, 1150 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.64 (s, 3 H, $COCH_3$), 7.35–7.41 (m, 1 H), 7.45–7.50 (m, 2 H), 7.55 (s, 1 H), 7.61 (d, *J* = 8.1 Hz, 2 H), 7.64 (d, *J* = 8.4 Hz, 1 H), 7.72 (d, *J* = 8.7 Hz, 1 H), 7.89 (s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 26.4, 112.6, 113.1, 121.4, 127.3, 127.4, 127.5, 128.1, 128.8, 137.6, 140.8, 153.2, 155.2, 188.6.

MS (EI, 70 eV): *m*/*z* (%) = 236 (94.9) [M$^+$], 221 (100), 165 (69.6), 139 (11.7), 115 (10.4), 63 (5.3).

Anal. Calcd for $C_{16}H_{12}O_2$: C, 81.34; H, 5.12. Found: C, 81.23; H, 5.12.

2-Acetyl-5-(4-tolyl)benzofuran (39)
Yellow powder; mp 92–94 °C; R_f = 0.53 (hexane–EtOAc, 7:1).

IR (KBr): 3029, 2918, 1678, 1549, 1299, 1156 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.42 (s, 3 H, CH_3), 2.64 (s, 3 H, $COCH_3$), 7.28 (d, *J* = 7.8 Hz, 2 H), 7.51 (d, *J* = 8.1 Hz, 2 H), 7.54 (s, 1 H), 7.63 (d, *J* = 8.7 Hz, 1 H), 7.70 (d, *J* = 8.7 Hz, 1 H), 7.87 (s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 21.0, 26.4, 112.5, 113.2, 121.1, 127.2, 127.5, 128.0, 129.5, 137.1, 137.6, 137.9, 153.1, 155.1, 188.6.

MS (EI, 70 eV): *m*/*z* (%) = 250 (100) [M$^+$], 235 (80.4), 179 (63.8), 152 (13.6), 63 (13).

Anal. Calcd for $C_{17}H_{14}O_2$: C, 81.58; H, 5.64. Found: C, 81.52; H, 5.56.

2-Acetyl-5-(4-methoxyphenyl)benzofuran (40)
Yellow powder; mp 110–112 °C; R_f = 0.25 (hexane–EtOAc, 7:1).

IR (KBr): 3125, 2958, 1685, 1560, 1516, 1272, 1236 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.57 (s, 3 H, $COCH_3$), 3.81 (s, 3 H, OCH_3), 7.04 (d, *J* = 9.0 Hz, 2 H), 7.62 (d, *J* = 9.0 Hz, 2 H), 7.64 (s, 1 H), 7.72 (d, *J* = 7.5 Hz, 1 H), 7.76 (d, *J* = 7.5 Hz, 1 H), 7.98 (s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 26.4, 55.3, 112.5, 113.1, 114.2, 120.8, 127.5, 127.8, 128.3, 133.3, 137.3, 153.1, 154.9, 159.1, 188.5.

MS (EI, 70 eV): *m*/*z* (%) = 266 (100) [M$^+$], 251 (66.2), 223 (27.7), 195 (17.9), 152 (21.1).

Anal. Calcd for $C_{17}H_{14}O_3$: C, 76.68; H, 5.30. Found: C, 76.62; H, 5.34.

2-Acetyl-5-(4-chlorophenyl)benzofuran (41)
Yellow powder; mp 106–108 °C; R_f = 0.4 (hexane–EtOAc, 7:1).

IR (KBr): 3133, 2920, 1676, 1554, 1156 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.64 (s, 3 H, $COCH_3$), 7.43 (d, *J* = 8.7 Hz, 2 H), 7.53 (d, *J* = 8.7 Hz, 2 H), 7.54 (s, 1 H), 7.64 (d, *J* = 8.1 Hz, 1 H), 7.67 (d, *J* = 8.1 Hz, 1 H), 7.85 (s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 26.5, 112.7, 112.9, 121.4, 127.6, 127.8, 128.6, 129.0, 133.5, 136.4, 139.2, 153.3, 155.2, 188.6.

MS (EI, 70 eV): *m*/*z* (%) = 272 (32) [M$^+$ + 2], 271 (15) [M$^+$ + 1], 270 (100) [M$^+$], 255 (89.6), 199 (47.5), 163 (23.2), 63 (12.9).

Anal. Calcd for $C_{16}H_{11}ClO_2$: C, 70.99; H, 4.10. Found: C, 70.75; H, 4.25.

2-Acetyl-5-(3,4-methylenedioxyphenyl)benzofuran (42)
Yellow powder; mp 96–98 °C; R_f = 0.24 (hexane–EtOAc, 7:1).

IR (KBr): 3063, 2918, 1674, 1563, 1503, 1251 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.63 (s, 3 H, $COCH_3$), 6.02 (s, 2 H, CH_2), 6.91 (d, *J* = 7.8 Hz, 1 H), 7.07 (d, *J* = 7.8 Hz, 1 H), 7.08 (s, 1 H), 7.53 (s, 1 H), 7.61 (d, *J* = 8.7 Hz, 1 H), 7.65 (d, *J* = 8.7 Hz, 1 H), 7.80 (s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 26.4, 101.2, 107.9, 108.6, 112.5, 113.1, 120.8, 121.1, 127.5, 127.9, 135.1, 137.4, 147.1, 148.2, 153.2, 155.0, 188.6.

MS (EI, 70 eV): *m*/*z* (%) = 280 (100) [M$^+$], 265 (26.3), 237 (12.6), 209 (19.3), 150 (12.1), 132 (13.1).

Anal. Calcd for $C_{17}H_{12}O_4$: C, 72.85; H, 4.32. Found: C, 72.71; H, 4.42.

2-Acetyl-5-(3-thienyl)benzofuran (43)
Yellow powder; mp 134–136 °C; R_f = 0.42 (hexane–EtOAc, 7:1).

IR (KBr): 3096, 2922, 1671, 1552, 1302, 1153 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.63 (s, 3 H, $COCH_3$), 7.41–7.46 (m, 3 H), 7.52 (s, 1 H), 7.60 (d, *J* = 9.0 Hz, 1 H), 7.73 (d, *J* = 8.7 Hz, 1 H), 7.90 (s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 26.5, 112.6, 113.0, 120.3, 120.6, 126.4, 126.5, 127.5, 127.6, 132.3, 141.8, 153.2, 155.0, 188.6.

MS (EI, 70 eV): *m*/*z* (%) = 242 (100) [M$^+$], 227 (88.6), 171 (67.4), 63 (11).

Anal. Calcd for $C_{14}H_{10}O_2S$: C, 69.40; H, 4.16; S, 13.23. Found: C, 69.33; H, 4.28; S, 13.14.

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