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Palladium-Catalyzed Suzuki Cross-Coupling of Arylhydrazines via C−N Bond Cleavage

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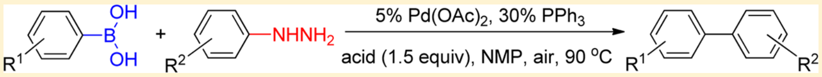
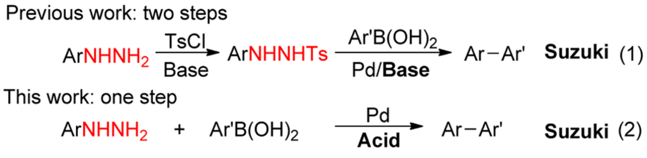
Supporting Information



ABSTRACT: The first example of Pd-catalyzed Suzuki cross-coupling of readily available arylhydrazines with arylboronic acids via C−N bond cleavage was developed under air, affording various biaryl compounds with broad substrate applicability and moderate to good yields. Moreover, the rigorous exclusion of air/moisture is not required in these transformations. Thus, the protocol represents a simple and efficient procedure to access biaryl compounds.

Palladium-catalyzed cross-coupling reactions via selective cleavage of unreactive bonds such as carbon−hydrogen,[1] carbon−carbon,[2] and carbon−nitrogen bonds have been used as one of the most powerful synthetic tools for the construction of carbon−carbon and carbon−heteroatom bonds because they afford unique organic transformations which are not readily available by classic methods. Among these methods, the exploration of the cross-coupling reactions involving carbon−nitrogen bond cleavage is rare, especially for the nonactivated carbon−nitrogen bonds,[3] which are generally activated through conversion to diazonium salts,[3a−c] ammonium salt,[3d−f] azaheterocycles,[3g,h] or tosylhydrazones.[3i] However, these methods suffer from drawbacks (e.g., limited substrate scope, the unstable nature of the substrates or harsh reaction conditions, etc.) as a result of limited application. Diaryl compounds are ubiquitous structural motifs that frequently occur in natural products and pharmacologically active compounds. Thus, the development of new methods for the preparation of diaryl compounds under relatively mild reaction conditions has received much attention. Although various coupling partners have been explored to synthesize biaryls with arylboranes in the presence of palladium catalysts in the past few decades,[4] electrophilic counterparts have been substantially limited to organic halides and triflate. Thus, there is still a need for broadening the scope of electrophilic partners to achieve unique organic transformations that are not obtainable through known approaches. Recently, Lu and co-workers reported the Pd-catalyzed Suzuki cross-coupling of N'-tosyl arylhydrazines for the preparation of biaryl compounds (Scheme 1).[5] However, this approach was complicated by the need to prepare N'-tosyl arylhydrazine substrates beforehand. On the other hand, arylhydrazines are readily obtainable and extremely valuable compounds in organic chemistry that are widely used for the preparation of numerous nitrogen-containing compounds, but little attention has been paid to their use as arylating regents via denitrogenation. Recently, Loh and co-workers reported the first example of the Pd-catalyzed C−C bond formation of arylhydrazines with olefins via C−N bond cleavage.[6] Very recently, Pd-catalyzed direct denitrogenative C-3-arylation of 1H-indoles with arylhydrazines via C−N bond cleavage has been developed.[7] However, to the best of our knowledge, the Pd-catalyzed direct cross-coupling of arylhydrazines with arylboronic acids has not been reported. Herein, we disclose the first Pd-catalyzed direct Suzuki cross-coupling of arylhydrazines with arylboronic acids for the synthesis of valuable biaryl motifs via C−N bond cleavage.

Scheme 1. (1) Palladium-Catalyzed Suzuki Cross-Coupling of N'-Tosylarylhydrazines. (2) Palladium-Catalyzed Suzuki Cross-Coupling of Arylhydrazines



To optimize the catalysis conditions, phenylboronic acid (**1a**) and phenylhydrazine (**2a**) were selected as the model substrates, and some representative results are shown in Table 1. Initially, we attempted to explore the coupling of **1a** with **2a** using $Pd(OAc)_2$ as a catalyst, PPh_3 as a ligand, PivOH as an acid, and DMF as a solvent at 90 °C under open air, and the desired product **3aa** was obtained in 47% yield (Table 1, entry 1). Encouraged by this result, we further examined the effect of catalyst, solvent, ligand, temperature, and acid on the reaction yield. Various transition-metal complexes including Pd, Ni, and Cu salts were examined, with the finding that palladium salts,

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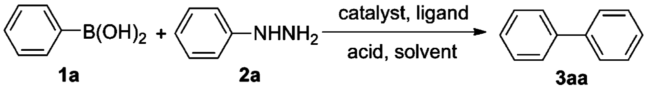
Table 1. Optimization of the Reaction Conditions[a]



entry	catalyst	ligand	acid	solvent	yield (%)
1	$Pd(OAc)_2$	PPh_3	PivOH	DMF	47
2	$Pd_2(dba)_3$	PPh_3	PivOH	NMP	28
3	$PdCl_2$	PPh_3	PivOH	NMP	6
4	$Pd(PPh_3)_4$	PPh_3	PivOH	NMP	43
5	$Cu(OAc)_2$	PPh_3	PivOH	NMP	0
6	$Ni(OAc)_2$	PPh_3	PivOH	NMP	0
7		PPh_3	PivOH	NMP	0
8	**$Pd(OAc)_2$**	**PPh_3**	**PivOH**	**NMP**	**78**
9	$Pd(OAc)_2$	PPh_3	PivOH	DMA	46
10	$Pd(OAc)_2$	PPh_3	PivOH	DMSO	4
11	$Pd(OAc)_2$	PPh_3	PivOH	dioxane	69
12	$Pd(OAc)_2$	PPh_3	PivOH	toluene	47
13	$Pd(OAc)_2$	bpy	PivOH	NMP	8
14	$Pd(OAc)_2$	1,10-Phen	PivOH	NMP	25
15	$Pd(OAc)_2$	dppp	PivOH	NMP	37
16	$Pd(OAc)_2$	dppb	PivOH	NMP	14
17	$Pd(OAc)_2$	dppe	PivOH	NMP	7
18	$Pd(OAc)_2$	PPh_3	TFA	NMP	60
19	$Pd(OAc)_2$	PPh_3	CF_3SO_3H	NMP	10
20	$Pd(OAc)_2$	PPh_3	AcOH	NMP	39
21[b]	$Pd(OAc)_2$	PPh_3	PivOH	NMP	77
22[c]	$Pd(OAc)_2$	PPh_3	PivOH	NMP	70
23[d]	$Pd(OAc)_2$	PPh_3	PivOH	NMP	74

[a] Conditions: **1a** (0.50 mmol), **2a** (1.75 mmol), catalyst (5 mol %), ligand (15 mol % for bidentate, 30 mol % for monodentate), acid (0.75 mmol), solvent (2 mL), 4 h, 90 °C, under open air. [b] Using 10 mol % of $Pd(OAc)_2$. [c] At 110 °C. [d] Under O_2.

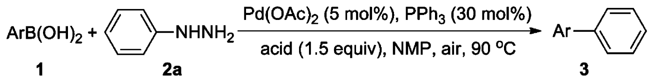
especially $Pd(OAc)_2$, were the optimal choice for the coupling reaction (Table 1, entries 1–4). In contrast, other metal salts such as $Cu(OAc)_2$ and $Ni(OAc)_2$ gave no corresponding product (entries 5 and 6). Additionally, the reaction did not occur in the absence of $Pd(OAc)_2$, illustrating that $Pd(OAc)_2$ catalyst was essential to achieve a high yield (entry 7). The type of solvent was vital to the present catalytic reaction. 1-Methylpyrrolidin-2-one (NMP) was found to be the best choice and gave yields up to 78% (entries 8–12). To advance the process further, a subsequent survey on the role of ligands showed PPh_3 as the most favored one to push the reaction forward (entries 8 and 13–17). Among the various acids screened, pivalic acid (PivOH) turned out to be the best acid and enhanced the coupling to provide **3aa** in 78% yield (entry 8). Other acids and corresponding yields were as follows: TFA, 60%; CF_3SO_3H, 10%; and CH_3COOH, 39% (entries 18–20). Notably, in the absence of either air or pivalic acid, the couplings only gave 6% and 16% yields, respectively, indicating that they were involved in the reaction process. Using pure oxygen as the oxidant instead of air, the yield dropped slightly to 74% (entry 23). Note that increasing the load of $Pd(OAc)_2$ to 10 mol % and raising the temperature from 90 to 100 °C did not improve the yield (entries 21 and 22). In the absence of either phenylhydrazine (**1a**) or phenyl boronic acid (**2a**), the reaction only generated a trace amount of product **3aa**, disclosing that self-coupling of **1a** or **2a** was not performed smoothly under the present Pd-catalysis system.

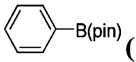
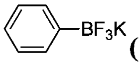
Under the optimized reaction conditions in footnote *a*, Table 2, the generality of this novel process was extended to the reaction of various arylboronic acids with phenylhydrazine **2a**. As shown in Table 2, the substrates having different electron-withdrawing and electron-donating substituents were all efficiently coupled to afford the corresponding oxidative coupling products with moderate to good yields, demonstrating that this new Pd-catalyzed aerobic oxidative Suzuki coupling is a general and practically useful method for the preparation of various valuable biaryls. Thus, a variety of functionalities, such as methyl (**1b**, **1c**), alkoxyl (**1d**), fluoro (**1e**), chloro (**1f**), trifluoromethyl (**1g**), and amino (**1k**), were all tolerated under similar reaction conditions. Notably, the *p*-tolylboronic acid **1b** and meta-substituted counterpart **1c** afforded similar yields of 77% and 73%, respectively, but sterically demanding *o*-tolylboronic acid only gave a very low yield of 12%, illustrating that this coupling reaction is sensitive to sterichindrance (entries 2 and 3). Gratifyingly, both bulky 2-naphthylboronic acid **1i** and 3,4-methylenedioxyphenylboronic acid **1j** were also good coupling partners for this oxidative coupling reaction, giving the corresponding products in good yields (**3ia**, **3ja**, 76%, 88%, respectively, entries 9–10). Nevertheless, boronic ester **1l** and potassium phenyltrifluoroborate **1n** were not suitable for this protocol (entries 12 and 13).

To gain more insight into the substrate scope of this coupling reaction, a variety of arylhydrazines and arylboronic acids were further evaluated under the optimal reaction conditions (Table 3). It was found that various arylboronic acids and arylhydrazines containing both electron-donating and electron-withdrawing groups were all good coupling partners in this transformation. Thus, besides phenylhydrazine (**2a**), other arylhydrazines with various substituents could also react with phenylboronic acid (**1a**) to afford the corresponding products in moderate to good yields (entries 1–5). Notably, arylboronic acids containing electron-withdrawing groups such as 4-fluorophenylboronic acid (**1e**) also coupled well with arylhydrazines bearing electron-withdrawing groups such as 4-nitrophenylhydrazine (**2e**) and 4-hydrazinobenzoic acid (**2k**), and the desired biaryls products **3ee** and **3ek** were obtained in 72% and 93% yields, respectively (entries 10 and 11). We also detected this reaction with alkylhydrazines such as benzylhydrazine under similar conditions but observed no coupling products, probably due to the low stability of alkyl intermediates.

A plausible mechanism was illustrated in Scheme 2. Initially, palladiaziridine complex **A** was formed in the presence of substrate **2a** and $Pd(II)_2L_2$, which has been established by Muñiz.[8] Then oxidative addition of complex **A** with $Pd(0)L_2$ generated the palladium(II)-centered complex **B** via C–N bond cleavage.[6] Next, protonolysis of **B** resulted in the formation of the aryl palladium complex **C** and the palladiaziridine complex **D**, which was decomposed into $Pd(0)L_2$, N_2, and H_2O by air. The arylpalladium complex **C** could be transformed to a palladium(II) biaryl intermediate **E** in the presence of phenylboronic acid **1a**. Subsequently, intermediate **E** would undergo C–C reductive elimination to give the desired product **3aa** and $Pd(0)L_2$. Finally, the catalytic cycle was completed through reoxidation of Pd(0) to Pd(II) by air with the assistance of a ligand and an acid via the peroxopalladium complex.[9] Obviously, the acid is a key factor in the overall transformation. A delicate pK_a balance might be reached between phenylhydrazine and the acid in order to prevent complete protonation of the former to avoid inhibiting Pd coordination and promote the aerobic reoxidation of Pd(0).

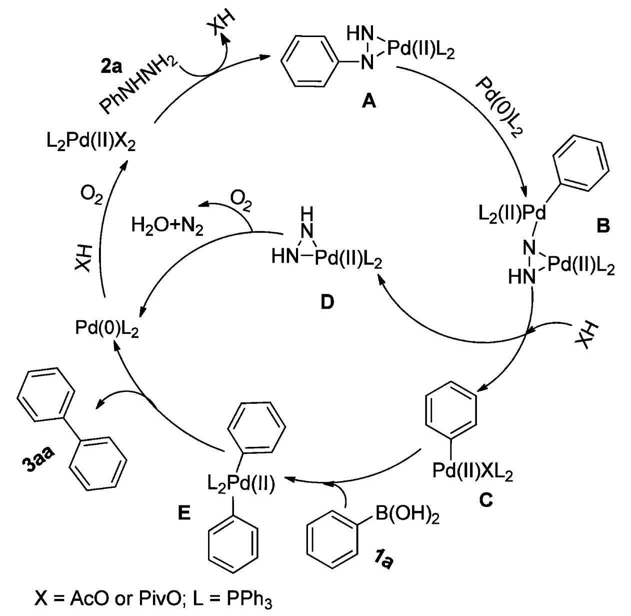
Table 2. Suzuki Reaction of Phenylhydrazine with Arylboronic Acids[a]



Entry	Ar	Product	Yield %
1	Ph(**1a**)	**3aa**	78
2	4-Me-C_6H_4(**1b**)	**3ba**	77
3	3-Me-C_6H_4 (**1c**)	**3ca**	73
4	4-MeO-C_6H_4 (**1d**)	**3da**	56
5	4-F-C_6H_4 (**1e**)	**3ea**	75
6	4-Cl-C_6H_4 (**1f**)	**3fa**	82
7	3-CF_3-C_6H_4 (**1g**)	**3ga**	70
8	4-CF_3O-C_6H_4 (**1h**)	**3ha**	53
9	2-Naphthyl (**1i**)	**3ia**	76
10	3,4-OCH_2O-C_6H_3 (**1j**)	**3ja**	88
11	4-NPh_2-C_6H_4 (**1k**)	**3ka**	52
12	 B(pin) (**1l**)	**3la**	0
13	 BF_3K (**1n**)	**3na**	0

[a] Conditions: **1** (0.50 mmol), **2a** (1.75 mmol), $Pd(OAc)_2$ (5 mol %), PPh_3 (30 mol %), PivOH (0.75 mmol), NMP (2 mL), 4 h, 90 °C, under open air.

Scheme 2. Proposed Mechanism



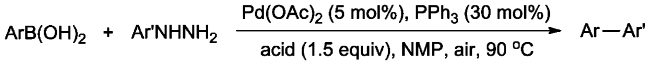
In summary, we have developed a novel and efficient methodology that allows for the construction of C−C bonds through Pd-catalyzed air-based oxidative coupling of a wide range of readily available unactivated arylhydrazines with arylboronic acids, providing a simple and practical synthetic tool for the preparation of various biaryl compounds via C−N bond cleavage. The noticeable advantages of this protocol include the use of air as a green oxidant, with no need for exclusion of moisture or air and broad substrate applicability. Importantly, in contrast, the direct use of arylhydrazines without the need to simultaneously prepare *N′*-tosylarylhydrazines, improving greatly the reaction efficiency, represents a prominent advantage of the method. This protocol further extends the scope of C−C bond construction and should be an efficient complement to the classical Suzuki cross-coupling reaction.

EXPERIMENTAL SECTION

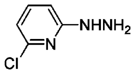
All reactions were carried out under air. Purification of reaction products was carried out by flash chromatography using silica gel (300−400 mesh). ^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on 400 MHz spectrometers with tetramethylsilane (TMS) as internal standard. All coupling constants are absolute values, and *J* values are expressed in hertz. All new compounds were further characterized by HRMS (FT-ICR-MS). Spectroscopic data of the known compounds match the data reported in the corresponding references.

Typical Procedure for Pd-Catalyzed Suzuki Cross-Coulping of Arylhydrazines with Aryl Boronic Acids. A mixture of aryl boronic acid **1** (0.5 mmol, 61 mg), arylhydrazine **2** (1.75 mmol, 189 mg), $Pd(OAc)_2$ (0.025 mmol, 5.6 mg), PPh_3 (0.15 mmol, 39.3 mg),

Table 3. Suzuki Reaction of Arylboronic Acids with Arylhydrazines[a]



$$\underset{\mathbf{1}}{\mathrm{ArB(OH)_2}} + \underset{\mathbf{2}}{\mathrm{Ar'NHNH_2}} \xrightarrow[\text{acid (1.5 equiv), NMP, air, 90 °C}]{\mathrm{Pd(OAc)_2}\text{ (5 mol%), }\mathrm{PPh_3}\text{ (30 mol%)}} \underset{\mathbf{3}}{\mathrm{Ar{-}Ar'}}$$

Entry	Ar	Ar'	Product	Yield %
1	Ph(**1a**)	3-MeO-C_6H_4(**2b**)	**3ab**	67
2	Ph(**1a**)	4-CF_3-C_6H_4(**2c**)	**3ac**	75
3	Ph(**1a**)	3-NO_2-C_6H_4(**2d**)	**3ad**	53
4	Ph(**1a**)	4-NO_2-C_6H_4(**2e**)	**3ae**	64
5	Ph(**1a**)	4-Ph-C_6H_4(**2f**)	**3af**	51
6	3-Me-C_6H_4(**1c**)	3-Me-C_6H_4(**2g**)	**3cg**	76
7	3,4-OCH_2O-C_6H_3(**1j**)	4-Cl-C_6H_4(**2h**)	**3jh**	57
8	4-F-C_6H_4(**1e**)	4-Me-C_6H_4(**2i**)	**3ei**	84
9	4-F-C_6H_4(**1e**)	4-F-C_6H_4(**2j**)	**3ej**	79
10	4-F-C_6H_4(**1e**)	4-NO_2-C_6H_4(**2e**)	**3ee**	72
11	4-F-C_6H_4(**1e**)	4-COOH-C_6H_4(**2k**)	**3ek**	93
12	4-F-C_6H_4(**1e**)	 (**2l**)	**3el**	40

[a]Conditions: **1** (0.50 mmol), **2** (1.75 mmol), $Pd(OAc)_2$ (5 mol %), PPh_3 (30 mol %), PivOH (0.75 mmol), NMP (2 mL), 4 h, 90 °C, under open air.

and trimethylacetic acid (0.75 mmol, 76.5 mg) was stirred at 90 °C in *N*-methylpyrrolidone (2 mL) for 4 h under air. After completion of the reaction (indicated by TLC), the mixture was concentrated under vacuum and the crude product was purified by silica gel chromatography using petroleum ether as eluent to provide the corresponding product **3**.

Spectral Data of the Compounds. *Biphenyl[10] (3aa) (CAS no. 92-52-4).* White solid; 60 mg, 78% yield. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.62−7.59 (m, 4H), 7.47−7.42 (m, 4H), 7.37−7.33 (m, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 141.4, 128.9, 127.4, 127.3. IR ν_{max} (cm^{-1}): 1568, 1481, 1428, 1343, 902, 728, 696. GC−MS *m*/*z*: 154 (M$^+$,100).

4-Methylbiphenyl[10] (3ba) (CAS No. 644-08-6). White solid; 64 mg, 77% yield. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.68−7.65 (m, 2H), 7.59−7.57 (m, 2H), 7.52−7.48 (m, 2H), 7.42−7.38 (m, 1H), 7.34−7.32 (m, 2H), 2.47 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 141.3, 138.5, 137.1, 129.6, 128.8, 127.3, 127.12, 127.10, 21.2. IR ν_{max} (cm^{-1}): 3027, 2922, 1487, 822, 755, 695. GC−MS *m*/*z*: 168 (M$^+$, 100).

3-Methylbiphenyl[11] (3ca) (CAS No. 643-93-6). White solid; 61 mg, 73% yield. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.66−7.64 (m, 2H), 7.51−7.45 (m, 4H), 7.41−7.37 (m, 2H), 7.23 (d, *J* = 7.40 Hz, 1H), 2.48 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 141.5, 141.4, 138.4, 128.82, 128.80, 128.13, 128.11, 127.31, 127.29, 124.4, 21.6. IR ν_{max} (cm^{-1}): 3058, 3029, 2918, 1600, 1481, 791, 752, 698. GC−MS *m*/*z*: 168 (M$^+$, 100).

4-Methoxybiphenyl[11] (3da) (CAS No. 613−37−6). White solid; 51 mg, 56% yield. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.63−7.58 (m, 4H), 7.47 (t, *J* = 7.64 Hz, 2H), 7.38−7.34 (m, 1H), 7.05−7.03 (m, 2H), 3.89 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 159.3, 140.9, 133.87, 128.84, 128.3, 126.84, 126.77, 114.3, 55.4. IR ν_{max} (cm^{-1}): 2961, 1606, 1486, 1268, 1035, 833, 760, 688. GC−MS *m*/*z*: 184 (M$^+$, 100).

4-Fluorobiphenyl[12] (3ea) (CAS No. 324-74-3). White solid; 64 mg, 75% yield. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.61−7.56 (m, 4H), 7.50−7.45 (m, 2H), 7.41−7.37 (m, 1H), 7.19−7.14 (m, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 162.6 (d, J_{C-F} = 246.3 Hz), 140.4, 137.5 (d, J_{C-F} = 3.35 Hz), 129.0, 128.8 (d, J_{C-F} = 8.04 Hz), 127.4, 127.2, 115.7 (d, J_{C-F} = 21.35 Hz). IR ν_{max} (cm^{-1}): 1595, 1486, 1451, 1105, 837, 758, 687. GC−MS *m*/*z*: 172 (M$^+$, 100).

4-Chlorobiphenyl[13] (3fa) (CAS No. 2051-62-9). White solid; 77 mg, 82% yield. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.64−7.53 (m, 4H), 7.49−7.37 (m, 5H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 140.1, 139.8, 133.5, 129.04, 129.01, 128.5, 127.7, 127.1. IR ν_{max} (cm^{-1}): 1478, 1398, 1093, 832, 758, 689. GC−MS *m*/*z*: 188 (M$^+$, 100).

3-(Trifluoromethyl)biphenyl[14] (3ga) (CAS No. 366-04-1). White solid; 77 mg, 70% yield. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.86 (s, 1H), 7.78 (d, *J* = 7.60 Hz, 1H), 7.63−7.55 (m, 4H), 7.51−7.47 (m, 2H), 7.44−7.39 (m, 1H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 142.2, 140.0, 131.5, 131.2, 130.6, 129.4, 129.2, 128.2, 127.4, 124.4 (q, J_{C-F} = 272.50 Hz), 124.1 (q, J_{C-F} = 3.05 Hz). IR ν_{max} (cm^{-1}): 1424, 1334, 1261, 1166, 1126, 758, 701. GC−MS *m*/*z*: 222 (M$^+$, 100).

4-(Trifluoromethoxy)biphenyl[14] (3ha) (CAS No. 71274−84−5). White solid; 63 mg, 53% yield. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.64−7.57 (m, 4H), 7.50−7.45 (m, 2H), 7.42−7.38 (m, 1H), 7.33−7.31 (m, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 148.9, 140.2, 140.0, 129.0, 128.6, 127.8, 127.3, 122.0, 121.4, 119.4. IR ν_{max} (cm^{-1}): 1486, 1211, 1155, 1005, 851, 765, 736, 690. GC−MS *m*/*z*: 238 (M$^+$,100).

2-Phenylnaphthalene[13] (3ia) (CAS No. 612-94-2). White solid; 77 mg, 76% yield. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.09 (s, 1H), 7.97−7.89 (m, 3H), 7.81−7.76 (m, 3H), 7.57−7.50 (m, 4H), 7.45−7.40 (m, 1H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 141.3, 138.7, 133.8, 132.8, 129.0, 128.6, 128.3, 127.8, 127.6, 127.5, 126.4, 126.1, 125.9, 125.7. IR ν_{max} (cm^{-1}): 3056, 1452, 1264, 859, 820, 770, 757, 688. GC−MS *m*/*z*: 204 (M$^+$, 100).

5-Phenylbenzo[d][1,3]dioxole[15] (3ja) (CAS No. 24382-05-6). Yellow oil; 87 mg, 88% yield. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.59−7.57 (m, 2H), 7.48−7.44 (m, 2H), 7.39−7.35 (m, 1H), 7.14−7.11 (m, 2H), 6.94 (d, *J* = 7.96 Hz, 1H), 6.02 (s, 2H); ^{13}C{^{1}H} NMR

(CDCl$_3$, 100 MHz): δ 148.2, 147.2, 141.0, 135.7, 128.8, 127.01, 126.97, 120.7, 108.7, 107.8, 101.2. IR ν_{max} (cm^{-1}): 3061, 2890, 2777, 1601, 1478, 1454, 1224, 1106, 1039, 936, 889, 812, 759, 697. GC−MS m/z: 198 (M$^+$, 100).

N,N-Diphenyl[1,1-biphenyl]-4-amine[16] ***(3ka)*** *(CAS No. 4432-94-4).* White solid; 83 mg, 52% yield. ^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.61−7.59 (m, 2H), 7.52−7.49 (m, 2H), 7.46−7.42 (m, 2H), 7.35−7.27 (m, 5H), 7.18−7.16 (m, 6H), 7.08−7.04 (m, 2H); ^{13}C{^{1}H} NMR (CDCl$_3$, 100 MHz): δ 147.8, 147.3, 140.8, 135.3, 129.4, 128.9, 127.9, 127.0, 126.8, 124.6, 124.1, 123.1. IR ν_{max} (cm^{-1}): 3058, 3030, 1590, 1518, 1484, 1325, 1277, 837, 753, 695. GC−MS m/z: 321 (M$^+$,100).

3-Methoxybiphenyl[17] ***(3ab)*** *(CAS No. 2113-56-6).* White solid; 61 mg, 67% yield. ^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.65−7.63 (m, 2H), 7.48 (t, J = 7.50 Hz, 2H), 7.42−7.37 (m, 2H), 7.25−7.22 (m, 1H), 7.19−7.18 (m, 1H), 6.96−6.93 (m, 1H), 3.90 (s, 3H). ^{13}C{^{1}H} NMR (CDCl$_3$, 100 MHz): δ 160.1, 142.9, 141.2, 129.9, 128.9, 127.5, 127.3, 119.8, 113.0, 112.8, 55.4. IR ν_{max} (cm^{-1}): 3030, 2833, 1598, 1572, 1478, 1420, 1295, 1213, 1177, 1054, 1038, 1019, 756, 697. GC−MS m/z: 184 (M$^+$,100).

4-(Trifluoromethyl)biphenyl[10] ***(3ac)*** *(CAS No. 398-36-7).* White solid; 83 mg, 75% yield. ^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.72 (br, 4H), 7.64−7.62 (m, 2H), 7.53−7.48 (m, 2H), 7.46−7.42 (m, 1H). ^{13}C{^{1}H} NMR (CDCl$_3$, 100 MHz): δ 144. 9, 139.9, 129.5 (q, J_{C-F} = 32.56 Hz), 129.1, 128.3, 127.6, 127.4, 125.9 (q, J_{C-F} = 3.69 Hz), 124.5 (q, J_{C-F} = 271.8 Hz). IR ν_{max} (cm^{-1}): 1614, 1489, 1404, 1352, 1114, 1075, 843, 767, 728, 691. GC−MS m/z: 222 (M$^+$, 100).

3-Nitrobiphenyl[18] ***(3ad)*** *(CAS No. 2113-58-8).* White solid; 52 mg, 53% yield. ^{1}H NMR (CDCl$_3$, 400 MHz): δ 8.45 (t, J = 1.96 Hz, 1H), 8.21−8.19 (m, 1H), 7.93−7.91 (m, 1H), 7.64−7.59 (m, 3H), 7.52−7.48 (m, 2H), 7.45−7.42 (m, 1H); ^{13}C{^{1}H} NMR (CDCl$_3$, 100 MHz): δ 148.9, 143.0, 138.8, 133.2, 129.8, 129.3, 128.7, 127.3, 122.1, 122.06. IR ν_{max} (cm^{-1}): 1528, 1501, 1350, 764, 730, 696. GC−MS m/z: 199 (M$^+$, 100).

4-Nitrobiphenyl[10] ***(3ae)*** *(CAS No. 92-93-3).* White solid; 63 mg, 64% yield. ^{1}H NMR (CDCl$_3$, 400 MHz): δ 8.31−8.28 (m, 2H), 7.75−7.72 (m, 2H), 7.64−7.61 (m, 2H), 7.53−7.43 (m, 3H). ^{13}C{^{1}H} NMR (CDCl$_3$, 100 MHz): δ 147.8, 147.2, 138.9, 129.3, 129.1, 127.9, 127.5, 124.2. IR ν_{max} (cm^{-1}): 2916, 2848, 1595, 1505, 1351, 852, 773, 739, 699. GC−MS m/z: 199 (M$^+$,100).

1,4-Diphenylbenzene[13] ***(3af)****(CAS No. 92-94-4).* White solid; 58 mg, 51% yield. ^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.70 (s, 4H), 7.68−7.66 (m, 4H), 7.50−7.46 (m, 4H), 7.40−7.36 (m, 2H). ^{13}C{^{1}H} NMR (CDCl$_3$, 100 MHz): δ 140.9, 140.3, 129.0, 127.6, 127.5, 127.2. IR ν_{max} (cm^{-1}): 3430, 1632, 1454, 1403, 838, 745, 688. GC−MS m/z: 230 (M$^+$,100).

3,3′-Dimethylbiphenyl[19] ***(3cg)*** *(CAS No. 612-75-9).* Colorless oil; 69 mg, 76% yield. ^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.46−7.41 (m, 4H), 7.37−7.32 (m, 2H), 7.19−7.17 (m, 2H), 2.44 (s, 6H). ^{13}C{^{1}H} NMR (CDCl$_3$, 100 MHz): δ 141.5, 138.4, 128.7, 128.1, 128.0, 124.4, 21.7. IR ν_{max} (cm^{-1}): 3028, 2921, 2854, 1604, 1476, 1091, 878, 772, 697. GC−MS m/z: 182 (M$^+$,100).

5-(4-Chlorophenyl)benzo[d][1,3]dioxole ***(3jh).*** Yellow solid; 66 mg, 57% yield. ^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.45−7.42 (m, 2H), 7.38−7.36 (m, 2H), 7.03−7.01 (m, 2H), 6.89−6.87 (m, 1H), 6.00 (s, 2H). ^{13}C{^{1}H} NMR (CDCl$_3$, 100 MHz): δ 148.4, 147.5, 139.5, 134.5, 133.1, 129.0, 128.2, 120.7, 108.8, 107.6, 101.4. IR ν_{max} (cm^{-1}): 2906, 1508, 1478, 1439, 1400, 1247, 1224, 1036, 935, 889, 837, 809, 750. HRMS (APCI): calcd for C$_{13}$H$_9$O$_2$Cl M$^+$ 232.0286, found 232.0293.

4-Fluoro-4′-methylbiphenyl[12] ***(3ei)*** *(CAS No. 72093-43-7).* White solid; 78 mg, 84% yield. ^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.57−7.54 (m, 2H), 7.48−7.46 (m, 2H), 7.28−7.26 (m, 2H), 7.16−7.12 (m, 2H), 2.43 (s, 3H). ^{13}C{^{1}H} NMR (CDCl$_3$, 100 MHz): δ 162.5 (d, J_{C-F} = 245.8 Hz), 137.5, 137.4 (d, J_{C-F} = 3.30 Hz), 137.2, 129.7, 128.6 (d, J_{C-F} = 8.02 Hz), 127.0, 115.7 (d, J_{C-F} = 21.4 Hz), 21.2. IR ν_{max} (cm^{-1}): 1498, 1232, 808, 761, 657. GC−MS m/z: 186 (M$^+$,100).

4,4′-Difluorobiphenyl[20] ***(3ej)*** *(CAS No. 398-23-2).* White solid; 75 mg, 79% yield. ^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.52−7.47 (m, 4H), 7.16−7.10 (m, 4H). ^{13}C{^{1}H} NMR (CDCl$_3$, 100 MHz): δ 162.6 (d, J_{C-F} = 246.4 Hz), 136.6 (d, J_{C-F}= 3.0 Hz), 128.7 (d, J_{C-F} = 8.1 Hz), 115.8 (d, J_{C-F} = 21.5 Hz). IR ν_{max} (cm^{-1}): 2916, 1500, 1108, 821, 763, 737. GC−MS m/z: 190 (M$^+$,100).

4-Fluoro-4′-nitrobiphenyl[21] ***(3ee)*** *(CAS No. 398-24-3).* White solid; 78 mg, 72% yield. ^{1}H NMR (CDCl$_3$, 400 MHz): δ 8.30−8.27 (m, 2H), 7.71−7.67 (m, 2H), 7.62−7.57 (m, 2H), 7.21−7.16 (m, 2H). ^{13}C{^{1}H} NMR (CDCl$_3$, 100 MHz): δ 163.5 (d, J_{C-F} = 249.4 Hz), 147.2, 146.7, 135.0 (d, J_{C-F} = 3.37 Hz), 129.3 (d, J_{C-F} = 8.33 Hz), 127.8, 124.3, 116.3 (d, J_{C-F} = 21.81 Hz). IR ν_{max} (cm^{-1}): 2915, 1596, 1511, 1356, 1232, 832, 754, 715. GC−MS m/z: 217 (M$^+$,100).

4′-Fluorobiphenyl-4-carboxylic Acid[22] ***(3ek)*** *(CAS No. 5731-10-2).* White solid; 100 mg, 93% yield. ^{1}H NMR (DMSO−D6, 400 MHz): δ 12.98 (br, 1H), 8.01 (d, J = 8.36 Hz, 2H), 7.79−7.76 (m, 4H) 7.32 (t, J = 8.84 Hz, 2H). ^{13}C{^{1}H} NMR (CDCl$_3$, 100 MHz): δ 167.1, 162.3 (d, J_{C-F} = 245.7 Hz), 143.2, 135.5, 130.0, 129.6, 129.0 (d, J_{C-F} = 8.30 Hz), 126.7, 115.9 (d, J_{C-F} = 21.35 Hz). IR ν_{max} (cm^{-1}): 3438, 2252, 2125, 1657, 1053, 1027, 1007, 823, 761. GC−MS m/z: 216 (M$^+$, 100).

2-Chloro-6-(4-fluorophenyl)pyridine[23] ***(3el)*** *(CAS No. 1214354-55-8).* White solid; 41 mg, 40% yield. ^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.99−7.96 (m, 2H), 7.70−7.66 (m, 1H), 7.59−7.57 (m, 1H), 7.25−7.23 (m, 1H), 7.16−7.12 (m, 2H). ^{13}C{^{1}H} NMR (CDCl$_3$, 100 MHz): δ 164.0 (d, J_{C-F} = 249.70 Hz), 157.1, 151.5, 139.5, 134.0 (d, J_{C-F} = 3.21 Hz), 129.0 (d, J_{C-F} = 8.52 Hz), 122.6, 118.4, 115.9 (d, J_{C-F} = 21.67 Hz). IR ν_{max} (cm^{-1}): 1580, 1558, 1511, 1387, 1236, 1166, 1136, 1054, 909, 851, 792, 735. GC−MS m/z: 207 (M$^+$, 100).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^{1}H NMR and ^{13}C NMR spectra. 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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