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Suzuki–Miyaura coupling reaction of aryl chlorides using di(2,6-dimethylmorpholino)phenylphosphine as ligand

Su-Dong Cho,[a] Ho-Kyun Kim,[b] Heung-seop Yim,[b] Mi-Ra Kim,[c] Jin-Kook Lee,[a,*] Jeum-Jong Kim[d] and Yong-Jin Yoon[d,*]

[a]*Department of Polymer Science and Engineering, Pusan National University, Busan 609-735, Republic of Korea*
[b]*Department of Chemistry and Graduate School for Molecular Materials and Nanochemistry, Gyeongsang National University, Jinju 660-701, Republic of Korea*
[c]*Center for Plastic Information System, Pusan National University, Busan 609-735, Republic of Korea*
[d]*Department of Chemistry and Environmental Biotechnology National Core Research Center, Graduate School for Molecular Materials and Nanochemistry, Gyeongsang National University, Jinju 660-701, Republic of Korea*

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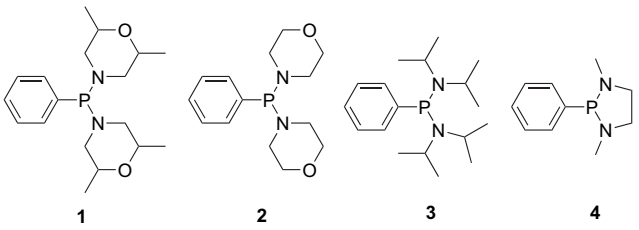
Abstract—Suzuki–Miyaura coupling was achieved on a variety of aryl chlorides by using di(2,6-dimethylmorpholino)phenylphosphine (L1) as a bulky electron-rich monoaryl phosphine ligand. We report the couplings of various chlorobenzenes and heteroaryl chlorides.

1. Introduction

Pd-catalyzed cross-coupling reactions have become an extremely versatile tool in organic synthesis for connecting two fragments via formation of a carbon–carbon bond or carbon–heteroatom bond.[1–4] The Pd-catalyzed Suzuki–Miyaura coupling reaction is one of the most attractive method for preparing biaryl compounds thanks to the advantages of wide functional group tolerance and use of stable and nontoxic organoborane reagents.[5–13] Since the general procedures were discovered, efforts have been made toward in increasing the substrate scope and efficiency. Although the use of alternative bases or solvents can be beneficial, electronic and steric tuning of the supporting ligand has the most impact on increasing efficacy and reactivity in these processes.[14–29] A major impetus to this field was provided by the ability to activate the notoriously unreactive but relatively cheap aryl chlorides.[30] Not surprisingly, a plethora of Pd-catalyst systems featuring a Pd-bound ligand are now accessible for achieving the aforementioned transformation involving aryl chlorides. It has been well recognized that ligands employed in these processes have a significant impact on the outcome of the reactions.[31,32] Therefore, designing ligands with appropriate features and great diversity is crucial in dealing with the challenging substrates in this area. Typically, the electronically rich and sterically hindered ligands belonging to the trialkylphosphine,[33–35] ferrocenyldialkylphosphine,[17] aryldialkylphosphine,[36–38] phosphinous acid,[39] palladacycle,[15,40] or heterocyclic carbene[41–43] classes have been investigated for these reactions. While several ligands exhibiting improved abilities in assisting the palladium-catalyzed coupling are now available, a general solution has not yet been completely found for the metal-catalyzed aryl coupling of all substrates. Thus, as a part of our ongoing efforts to develop efficient methods for the coupling of aryl chloride, we investigated the synthesis and coupling reaction of novel air stable phenyl backbone-derived PN_2 ligands that are easy to prepare. The reaction setup is experimentally simple and does not require the use of a glovebox for these reactions.

We used ligands **1**–**4** for the Suzuki–Miyaura coupling of aryl chlorides as monophenyl backbone-derived PN_2 ligands (Scheme 1). Ligand **4** is commercially available, and ligands **2** and **3** were prepared by the literature method.[44] The ligand **1** was synthesized from dichlorophenylphosphine (**5**) (Scheme 2). Here, we report the results of coupling aryl chloride with phenylboronic acid by using novel PN_2 ligands.



Scheme 1. Bulky electron-rich ligands used in the coupling of aryl chlorides.

Keywords: Suzuki–Miyaura coupling; Pd-catalyzed coupling of aryl chlorides; PN_2 ligand; C–C coupling reaction.
* Corresponding authors. Tel.: +82 55 751 6019; fax: +82 55 761 0244; e-mail: yjyoon@gnu.ac.kr

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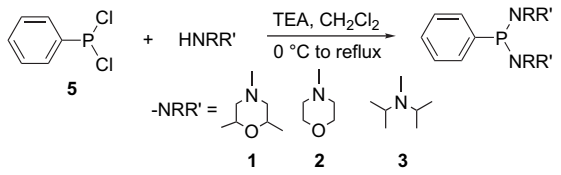


Scheme 2. Syntheses of ligands **1**, **2**, and **3**.

2. Results and discussion

2.1. Synthesis of ligand 1

Reaction of dichlorophenylphosphine (**5**) with 2,6-dimethylmorpholin (**6**) in the presence of triethylamine in refluxing dichloromethane or toluene gave the corresponding ligand **1** (68%). This ligand in coupling reaction was used without further purification. The structure of ligand **1** was established by IR, NMR, and elemental analysis.

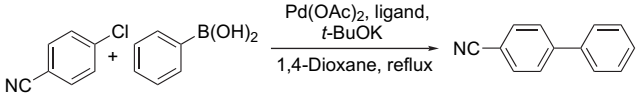
2.2. Ligand, Pd-catalyst, solvent, and base screening

To test the feasibility of the ideas described above, we initially conducted the reaction of *p*-cyanochlorobenzene with phenylboronic acid in refluxing 1,4-dioxane as shown in Table 1. We used 1.0 mol % of $Pd(OAc)_2$ in combination with 5 mol % of ligand **1**. This reaction proceeded to successfully afford the desired product in 91% isolated yield after 1.5 h (Entry 1 in Table 1). With this encouraging result, we evaluated the efficiency of the three ligands **2**–**4** in the same screening. When ligand **2** was used, the product gave a 74% yield. This reaction, however, did not occur when ligands **3** and **4** were used.

Next, we investigated the effect of a variety of palladium compounds for this reaction. Among the palladium compounds explored, $Pd_2(dba)_3$ showed the best result (Entry 1 in Table 2). The coupling reaction, however, did not occur in the absence of ligand **1** under same condition (Entry 8 in Table 2).

We also investigated a variety of bases for the aforementioned coupling reaction catalyzed by the $Pd_2(dba)_3$/**1** system (Table 3). The coupling reaction of chlorocyanobenzene by using $Pd_2(dba)_3$/**1** system in the presence of Cs_2CO_3 or Rb_2CO_3 gave biphenyl-4-carbonitrile in 96% or 90% yield (Entries 2 and 5 in Table 3). According to the literatures,[45–47] cesium carbonate is a very effective base for most Pd-catalyzed coupling procedures using phosphine ligand. We investigated some solvents for coupling reaction catalyzed by the $Pd_2(dba)_3$/**1**/Cs_2CO_3 system (Table 4). Toluene and 1,4-dioxane were found to be an efficacious solvent (Entries 1 and 4 in Table 4). In general, nonpolar hydrocarbon (toluene) and ethereal solvent (1,4-dioxane) are useful solvents in Pd-catalyzed coupling reactions.[48]

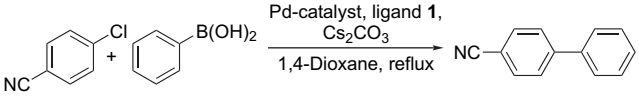
Table 1. Screening of ligands[a]



Entry	Ligand	Time (h)	Product[b] (%)
1	**1**	1.5	91
2	**2**	18	74
3	**3**	24	No reaction
4	**4**	24	No reaction

[a] Reaction conditions: chlorocyanobenzene (2.0 mmol, 1.0 equiv), phenylboronic acid (2.5 mmol, 1.25 equiv), ligand (5 mol %), $Pd(OAc)_2$ (1 mol %), *t*-BuOK (4.2 mmol, 2.1 equiv), and 1,4-dioxane (20 mL) at reflux temperature.
[b] Isolated yield after silica gel chromatography.

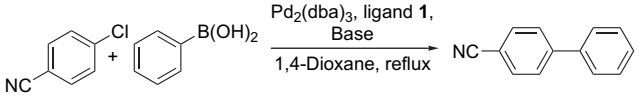
Table 2. Screening of Pd-catalysts[a]



Entry	Palladium catalyst	Time (min)	Product[b] (%)
1	$Pd_2(dba)_3$	90	95
2[c]	$PdCl_2$	90	91
3[c]	$Pd(OAc)_2$	125	84
4[c]	$Pd(PPh_3)_4$	80	92
5[c]	$PdCl_2(PPh_3)_2$	80	92
6[c]	$PdCl_2(dppf)_2$	100	83
7[c]	Pd/C	16 h	32
8[d]	$Pd_2(dba)_3$	3 h	—

[a] Reaction conditions: chlorocyanobenzene (1.0 equiv), phenylboronic acid (1.25 equiv), ligand **1** (10 mol %), Pd-catalyst (1 mol %), Cs_2CO_3 (2 equiv), and 1,4-dioxane (20 mL) at reflux temperature.
[b] Isolated yield after silica gel chromatography.
[c] Self-coupling product from boronic acid was isolated in small amounts.
[d] Coupling reaction was carried out in the absence of ligand **1**.

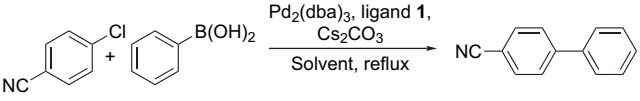
Table 3. Screening of bases[a]



Entry	Base	Time (h)	Isolated yield (%)
1	*t*-BuOK	3.5	88
2	Cs_2CO_3	1	96
3	K_3PO_4	1.5	87
4	K_2CO_3	51	63
5	Rb_2CO_3	1	90
6	KF	36	36
7	DMAP	36	25

[a] Reaction conditions: chlorocyanobenzene (1.0 equiv), phenylboronic acid (1.25 equiv), ligand **1** (10 mol %), $Pd_2(dba)_3$ (1 mol %), base (4.2 mmol, 2.1 equiv), and 1,4-dioxane (20 mL) at reflux temperature.

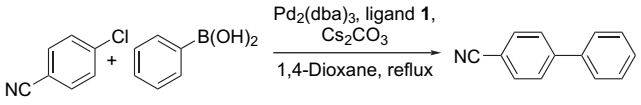
Table 4. Screening of solvents[a]



Entry	Solvent	Time (h)	Isolated yield (%)
1	Toluene	1	95
2	Acetonitrile	2	94
3	Ethanol	4	85
4	1,4-Dioxane	1	96
5	Tetrahydrofuran	2	83
6	Water	24	14

[a] Reaction conditions: chlorocyanobenzene (1.0 equiv), phenylboronic acid (1.25 equiv), ligand **1** (10 mol %), $Pd_2(dba)_3$ (1 mol %), Cs_2CO_3 (2 equiv), and solvent (20 mL) at reflux temperature.

Table 5. Optimization for the coupling of chlorocyanobenzene with phenylboronic acid using **1**[a]



Entry	**1** (mol %)	$Pd_2(dba)_3$ (mol %)	Time (h)	Yield[b] (%)
1	1	0.5	62	82
2	2	1	43	89
3	5	1	13	92
4	10	1	1	96
5	10	2	1	95

[a] Reaction conditions: chlorocyanobenzene (1.0 equiv), phenylboronic acid (1.25 equiv), ligand **1** (1–10 mol %), $Pd_2(dba)_3$ (1 mol %), Cs_2CO_3 (2 equiv), and 1,4-dioxane (20 mL) at reflux temperature.
[b] Isolated yield after silica gel chromatography.

We optimized the coupling of chlorocyanobenzene with phenylboronic acid by using the $Cs_2CO_3/Pd_2(dba)_3$/**1** system in 1,4-dioxane (Table 5). The ArCl (1 equiv)/$ArB(OH)_2$ (1.25 equiv)/Cs_2CO_3 (2 equiv)/$Pd_2(dba)_3$ (1 mol %)/**1** (10 mol %) system in 1,4-dioxane showed the best result (Entry 4 in Table 5).

Applying the conditions optimized in this research, we evaluated the scope of the coupling of various aryl and heteroaryl chlorides with phenylboronic acid. The coupling of chlorobenzene containing various substituents with phenylboronic acid by using Cs_2CO_3 (2 equiv)/$Pd_2(dba)_3$ (1 mol %)/**1** (10 mol %) system in 1,4-dioxane gave the corresponding biphenyls in good to excellent yields (Table 6). The coupling of chlorobenzenes did not show the general tendency that depended on the kind of substituents in phenyl ring.

On the other hand, the coupling of chloroheteoarenes such as 2-chloropyridine, 2-chlorothiophene, 2-chloropyrimidine, 4-chloropyridazin-3(2*H*)-one, 4-chlorotetrazole, 2-chloroquinoline, and 2-chlorothioxanthen-9-one with phenylboronic acid under our system gave the corresponding phenyl-substituted products in good to excellent yields (Table 7).

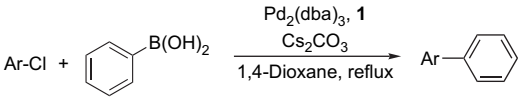
We also investigated the coupling of chlorocyanobenzene with some arylboronic acids by using the system we developed (Table 8). The homo-coupling of phenylboronic acids was predominant when phenylboronic acids containing the electron-withdrawing groups such as chloro, formyl, and nitro substituents were used (Entries 1, 4, and 5 in Table 8). However, the cross-coupling of chlorocyanobenzene was predominant when 4-methoxy and 4-(*N*,*N*-dimethylamino)-phenylboronic acids were used (Entries 2 and 3 in Table 8).

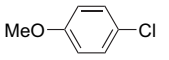
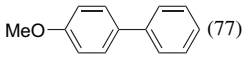
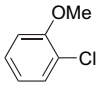
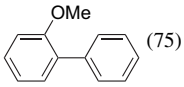
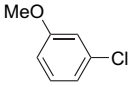
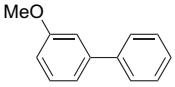
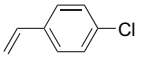
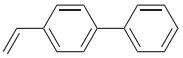
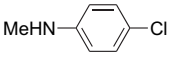
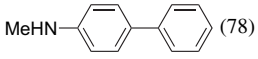
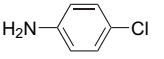
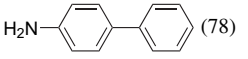
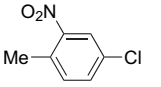
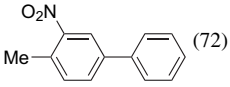
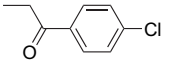
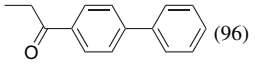
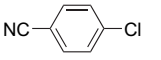
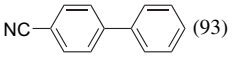
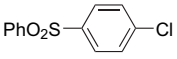
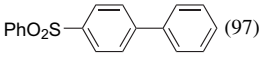
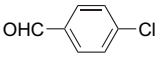
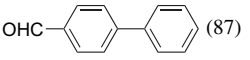
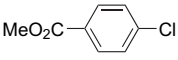
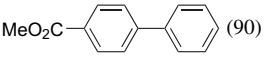
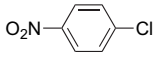
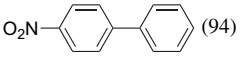
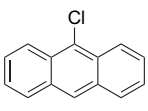
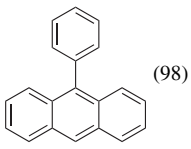
The self-coupling products from the corresponding boronic acids on TLC were not detected by the coupling of chlorocyanobenzene with 2-furanboronic acid and 4-pyridineboronic acid.

3. Conclusion

In conclusion, we developed ligand **1** as a new PN_2 ligand for Pd-catalyzed Suzuki–Miyaura coupling of aryl chlorides with phenylboronic acids. This ligand **1** also has the following advantages: as an efficient ligand for Pd-catalyzed cross-coupling of aryl chlorides, it is stable in air and in organic

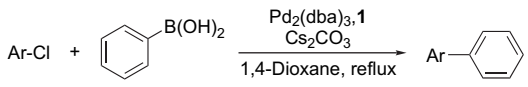
Table 6. Pd-catalyzed coupling of aryl chlorides[a]

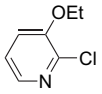
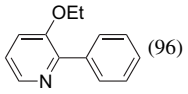
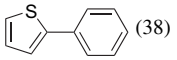
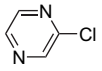
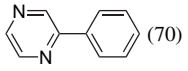
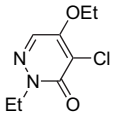
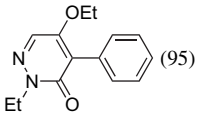
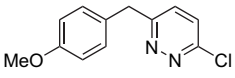
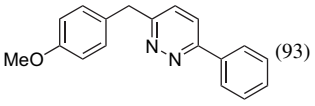
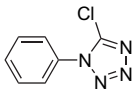
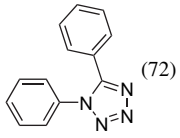
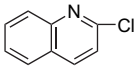
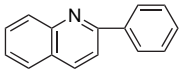
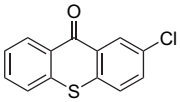
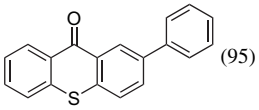


Entry	Aryl chloride	Time (h)	Product yield[b] (%)
1		14	 (77)
2		10	 (75)
3		7	 (70)
4		22	 (81)
5		26	 (78)
6		1.5	 (78)
7		14	 (72)
8		16	 (96)
9		15	 (93)
10		12	 (97)
11		10	 (87)
12		18	 (90)
13		14	 (94)
14		7	 (98)

[a] Reaction conditions: ArCl (1.0 equiv), phenylboronic acid (1.25 equiv), ligand **1** (10 mol %), $Pd_2(dba)_3$ (1 mol %), Cs_2CO_3 (2 equiv), and 1,4-dioxane (20 mL) at reflux temperature.
[b] Isolated yield after silica gel chromatography.

Table 7. Pd-catalyzed coupling of heteroaryl chlorides[a]



Entry	Aryl chloride	Time (h)	Product yield[b] (%)
1		3	 (96)
2		15	 (38)
3		7	 (70)
4		1.5	 (95)
5		6	 (93)
6		7	 (72)
7		2	 (96)
8		8	 (95)

[a] Reaction conditions: ArCl (1.0 equiv), phenylboronic acid (1.25 equiv), ligand **1** (10 mol %), $Pd_2(dba)_3$ (1 mol %), Cs_2CO_3 (2 equiv), and 1,4-dioxane (20 mL) at reflux temperature.
[b] Isolated yield after silica gel chromatography.

solvents at high temperature, and easily prepared from cheap and commercially available dichlorophenylphosphine.

4. Experimental

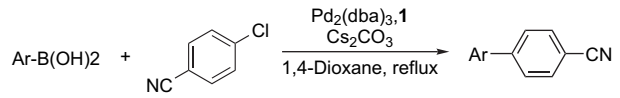
4.1. General

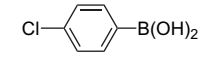
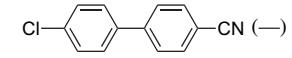
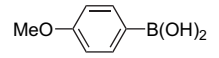
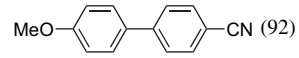
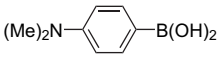
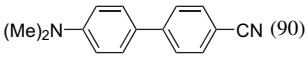
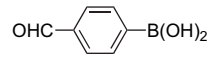
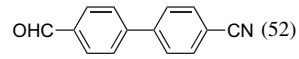
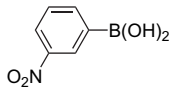
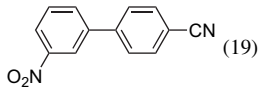
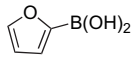
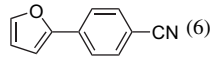
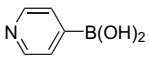
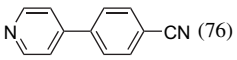
Melting points were determined with a capillary apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were recorded on a 300 MHz spectrometer with the chemical shift values reported in δ units (ppm) relative to an internal standard (TMS). The IR spectra were obtained on an IR spectrophotometer. Elemental analyses were performed with a Perkin–Elmer 240C. The open-bed chromatography was carried out on silica gel (70∼230 mesh, Merck) using gravity flow. The column was packed with slurries made from the elution solvent.

4.2. Typical preparation of PN_2 ligands

A mixture of 2,6-dimethylmorpholine (2 equiv), triethylamine (2.2 equiv), and dichloromethane (50 mL) was stirred for 10 min at room temperature. A dichloromethane solution of dichlorophenylphosphine **5** (20 mmol of **5** in 200 mL dichloromethane) was slowly dropped to the above amine solution, and the mixture was refluxed for 24 h until phosphine **5** disappeared. After evaporating the solvent under reduced pressure, the resulting residue was triturated in *n*-hexane, filtered, and washed with *n*-hexane. The filtrates containing the product were combined and evaporated under reduced pressure. The resulting residue was applied to the top of an open-bed silica gel column (3.0×7 cm). The column was eluted with dichloromethane/diethyl ether (10/1, v/v). Fractions containing the product were combined and evaporated under reduced pressure to give

Table 8. Pd-catalyzed coupling of aryl chlorides with some phenylboronic acids[a]



Entry	Boronic acid	Time (h)	Product yield[b] (%)
1[c]		36	
2[d]		6	
3[d]		6	
4[e]		6	
5[f]		24	
6[g]		40	
7		3	

[a] Reaction conditions: chlorocyanobenzene (1.0 equiv), boronic acid (1.25 equiv), ligand **1** (10 mol %), $Pd_2(dba)_3$ (1 mol %), Cs_2CO_3 (2 equiv), and 1,4-dioxane (20 mL) at reflux temperature.
[b] Isolated yield after silica gel chromatography.
[c] Only self-coupling product from boronic acid was isolated in poor yield.
[d] Self-coupling product from boronic acid was detected on TLC.
[e] Self-coupling product from boronic acid was isolated in poor yield.
[f] Self-coupling product from boronic acid was isolated as the main product.
[g] Reaction was not proceeded completely.

di(2,6-dimethylmorpholino)phenylphosphine (**1**). Ligand in coupling reaction was used without further purification.

4.2.1. Ligand 1. Yield: 68%. Colorless oil, IR (potassium bromide) ν 3012, 2904, 1436, 1366, 1120, 1048 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.81–7.30 (m, 5H), 3.87–3.78 (m, 4H), 3.51–3.44 (m, 2H), 2.99 (d, J=12.16 Hz, 4H), 2.44–2.40 (m, 2H), 1.10 (s, CH_3), 1.08 (s, CH_3) ppm; ^{13}C NMR ($CDCl_3$) δ 11.69, 47.92, 69.71, 128.15, 128.32, 126.60, 129.74 ppm. Elemental analysis calcd for $C_{18}H_{29}N_2O_2P$: C, 64.26; H, 8.69; N, 8.33. Found: C, 64.31; H, 8.71; N 8.40.

4.3. Typical C–C coupling of aryl chlorides

A dried resealable Schlenk tube was charged with $Pd_2(dba)_3$ (0.03 mmol, 1 mol % of Pd), aryl chloride (2.0 mmol), phenylboronic acid (2.5 mmol, 1.25 equiv), and ligand **1** (10 mol %) in 1,4-dioxane (20 mL). The mixture was stirred for 5 min at room temperature under nitrogen atmosphere. Cesium carbonate (4.2 mmol, 2.1 equiv) was added to the reaction mixture. After the septum was replaced with a Teflon screwcap, the mixture was refluxed until aryl chloride had been completely consumed as judged by TLC. The reaction mixture was then cooled to room temperature and filtered. The filtrate was concentrated in vacuo. The crude material was purified by chromatography on silica gel using dichloromethane/*n*-hexane (1:2, v/v) to afford the coupled product.

4.3.1. Biphenyl. Mp 68–71 °C (lit.[49] mp 68–70 °C); IR (potassium bromide) ν 3008, 2986, 1602, 1424 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.18–7.65 (m, 10H) ppm; ^{13}C NMR ($CDCl_3$) δ 127.23, 127.31, 128.81, 141.32 ppm. Elemental analysis calcd for $C_{12}H_{10}$: C, 93.46; H, 6.54. Found: C, 93.51; H 6.60.

4.3.2. Biphenyl-4-carbonitrile. Mp 85–87 °C, IR (potassium bromide) ν 3012, 2984, 2224, 1432 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.24–7.66 (m, 9H) ppm; ^{13}C NMR ($CDCl_3$) δ 110.80, 118.95, 127.22, 127.70, 128.72, 129.16, 132.59, 139, 145.56 ppm. Elemental analysis calcd for $C_{13}H_9N$: C, 87.12; H, 5.06; N, 7.82. Found: C, 87.17; H, 5.11; N, 7.88. Elemental analysis calcd for $C_{13}H_9N$: C, 87.12; H, 5.06; N, 7.82. Found: C, 87.20; H, 5.12; N, 7.91.

4.3.3. 4-Nitrobiphenyl. Mp 113–115 °C; IR (potassium bromide) ν 3062, 3028, 1602, 1550, 1518, 1340 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.31–8.26 (m, 2H), 7.75–7.70 (m, 2H), 7.63–7.60 (m, 2H), 7.52–7.41 (m, 3H) ppm; ^{13}C NMR ($CDCl_3$) δ 147.63, 147.15, 138.79, 129.15, 128.91, 127.79, 127.38, 124.09 ppm. Elemental analysis calcd for $C_{12}H_9NO_2$: C, 72.35; H, 4.55; N, 7.03. Found: C, 72.40; H, 4.58; N, 7.09.

4.3.4. Biphenyl-4-carboxylic acid methyl ester. Mp 115–117 °C. IR (potassium bromide) ν 3042, 2988, 1738, 1622, 1460, 1422, 1308, 1130, 764 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.10 (d, J=8.4 Hz, 2H), 7.65–7.58 (m, 4H), 7.47–7.36 (m, 3H), 3.92 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$) δ 166.97, 145.64, 140.02, 130.11, 128.96, 128.93, 127.27, 127.04, 52.07 ppm. Elemental analysis calcd for $C_{14}H_{12}O_2$: C, 79.22; H, 5.70. Found: C, 80.2; H, 5.81.

4.3.5. 2-Methoxybiphenyl. Colorless oil (lit.[50] mp 30–33 °C); IR (potassium bromide) ν 3060, 2926, 1599, 1499, 1482, 1258, 1025 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.81–7.78 (m, 2H), 7.66–7.50 (m, 5H), 7.29–7.17 (m, 2H), 3.98 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$) δ 156.75, 138.86, 131.11, 131.02, 129.80, 128.84, 128.20, 127.12, 121.10, 111.57, 55.70 ppm. Elemental analysis calcd for $C_{13}H_{12}O$: C, 84.75; H, 6.57. Found: C, 84.79; H, 6.59.

4.3.6. 3-Methoxybiphenyl. Colorless oil; IR (potassium bromide) ν 3054, 2959, 1599, 1479, 1266, 1220 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.57–7.53 (m, 2H), 7.41–7.35 (m, 2H), 7.32–7.26 (m, 2H), 7.16–7.09 (m, 2H), 6.87–6.83 (m, 1H), 3.78 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$) δ 160.14, 142.92, 141.25, 129.90, 128.87, 127.55, 127.32, 119.83, 113.09, 112.85, 55.36 ppm. Elemental analysis calcd for $C_{13}H_{12}O$: C, 84.75; H, 6.57. Found: C, 84.78; H 6.61.

4.3.7. 4-Methoxybiphenyl. Mp 89–90 °C (lit.[50] mp 86–90 °C); IR (potassium bromide) ν 3050, 2958, 1606, 1516, 1485, 1272, 1037 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.56–7.49 (m, 4H), 7.43–7.38 (m, 2H), 7.31–7.26 (m, 1H), 6.99–6.94 (m, 2H), 3.84 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$) δ 159.20, 140.87, 133.83, 128.72, 128.16, 126.75, 126.66, 114.24, 55.35 ppm. Elemental analysis calcd for $C_{13}H_{12}O$: C, 84.75; H, 6.57. Found: C, 84.77; H, 6.60.

4.3.8. 1-Biphenyl-4-ylpropan-1-one. Mp 96–98 °C; IR (potassium bromide) ν 3048, 2982, 1680, 1600, 1218, 750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.04–8.02 (m, 2H), 7.68–7.59 (m, 4H), 7.49–7.36 (m, 3H), 3.04 (q, J=7.26 Hz, 2H), 1.25 (t, J=7.24 Hz, 3H) ppm; ^{13}C NMR ($CDCl_3$) δ 200.40, 145.55, 139.97, 135.68, 128.93, 128.57, 128.16, 127.25, 127.20, 31.83, 8.32 ppm. Elemental analysis calcd for $C_{15}H_{14}O$: C, 85.68; H, 6.71. Found: C, 85.73; H, 6.79.

4.3.9. 4′-Methoxybiphenyl-4-carbonitrile. Mp 103–104 °C; IR (potassium bromide) ν 3038, 2988, 2220, 1602, 1242, 1174, 1132, 822 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.69–7.60 (m, 4H), 7.55–7.50 (m, 2H), 7.02–6.97 (m, 2H), 3.85 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$) δ 160.27, 145.22, 132.55, 131.51, 128.35, 127.10, 119.06, 114.59, 110.16, 55.40 ppm. Elemental analysis calcd for $C_{14}H_{11}NO$: C, 80.36; H, 5.30; N, 6.69. Found: C, 80.41; H, 5.37; N, 6.71.

4.3.10. 1,5-Diphenyl-1*H*-tetrazole. Mp 144–145 °C; IR (potassium bromide) ν 3070, 1590, 1495, 1470, 1110, 760, 696 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.82–7.78 (m, 2H), 7.61–7.39 (m, 7H), 7.33–7.25 (m, 1H) ppm; ^{13}C NMR ($CDCl_3$) δ 159.41, 153.53, 133.17, 130.04, 129.75, 129.46, 126.53, 122.22, 119.37 ppm. Elemental analysis calcd for $C_{13}H_{10}N_4$: C, 70.26; H, 4.54; N, 25.21. Found: C, 70.30; H, 4.60; N, 25.27.

4.3.11. 5-Ethoxy-2-ethyl-4-phenyl-2*H*-pyridazin-3(2*H*)-one. Mp 88–89 °C; IR (potassium bromide) ν 3042, 2966, 1632, 1444, 1400, 1340, 1258, 1160, 950 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.88 (s, 1H), 7.49–7.42 (m, 5H), 4.26 (q, J=7.18 Hz, 2H), 3.86 (q, J=7.11 Hz, 2H), 1.39 (t, J=7.17 Hz, 3H), 1.28 (t, J=7.13 Hz, 3H) ppm; ^{13}C NMR ($CDCl_3$) δ 160.71, 154.72, 130.42, 130.38, 128.25, 127.78, 127.63, 121.38, 57.15, 47.36, 13.59, 13.54 ppm. Elemental analysis calcd for $C_{14}H_{16}N_2O_2$: C, 68.83; H, 6.60; N, 11.47. Found: C, 68.88; H, 6.67; N, 11.51.

4.3.12. Biphenyl-4-yl-methylamine. Mp 67–69 °C; IR (potassium bromide) ν 3402, 3042, 2874, 2800, 1600, 1490, 822, 756 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.55–7.51 (m, 2H), 7.46–7.42 (m, 2H), 7.39–7.34 (m, 2H), 7.26–7.20 (m, 1H), 6.67–6.62 (m, 2H), 3.67 (br s, NH), 2.83 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$) δ 148.81, 141.39, 130.23, 128.69, 127.94, 126.34, 126.07, 112.75, 30.80 ppm. Elemental analysis calcd for $C_{13}H_{13}N$: C, 85.21; H, 7.15; N, 7.64. Found: C, 85.24; H, 7.19; N, 7.70.

4.3.13. 4-Vinylbiphenyl. Mp 118–120 °C (lit.[51] mp 119–121 °C); IR (potassium bromide) ν 3006, 2996, 1464, 1382, 994, 842 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.60–7.54 (m, 4H), 7.49–7.39 (m, 4H), 7.34–7.29 (m, 1H), 6.75 (dd, J=10.88, 17.59 Hz, 1H), 5.75 (s, J=17.59 Hz, 1H), 5.25 (d, J=10.88 Hz, 1H) ppm; ^{13}C NMR ($CDCl_3$) δ 140.79, 140.64, 136.67, 136.47, 128.80, 127.33, 127.25, 126.99, 126.68, 113.89 ppm. Elemental analysis calcd for $C_{14}H_{12}$: C, 93.29; H, 6.71. Found: C, 93.32; H, 6.74.

4.3.14. 4-Benzenesulfonylbiphenyl. Mp 148–149 °C; IR (potassium bromide) ν 3072, 1320, 1160, 1116 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.01–7.96 (m, 4H), 7.69–7.66 (m, 2H), 7.58–7.35 (m, 8H) ppm; ^{13}C NMR ($CDCl_3$) δ 146.18, 141.81, 140.20, 139.16, 133.19, 129.33, 129.06, 128.60, 128.21, 127.93, 127.66, 127.34 ppm. Elemental analysis calcd for $C_{18}H_{14}O_2S$: C, 73.44; H, 4.79. Found: C, 73.50; H, 4.82.

4.3.15. 9-Phenylanthracene. Mp 153–154 °C (lit.[52] mp 153–155 °C); IR (potassium bromide) ν 3046, 1436, 1008, 870, 726, 696 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.62 (br s, 1H), 8.11–8.16 (m, 2H), 7.36–7.65 (m, 11H) ppm; ^{13}C NMR ($CDCl_3$) δ 126.10, 126.42, 127.21, 127.54, 128.29, 129.43, 131.02, 131.94, 132.44, 137.71, 139.62 ppm. Elemental analysis calcd for $C_{20}H_{14}$: C, 94.45; H, 5.55. Found: C, 94.51; H, 5.58.

4.3.16. Biphenyl-4-carbaldehyde. Mp 56–58 °C (lit.[49] mp 57–59 °C); IR (potassium bromide) ν 3006, 2832, 1690, 1592, 1200, 720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 10.05 (s, 1H), 7.96–7.92 (m, 2H), 7.76–7.73 (m, 2H), 7.65–7.61 (m, 2H), 7.50–7.38 (m, 3H), 5.25 (d, J=10.88 Hz, 1H), 2.83 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$) δ 191.83, 147.21, 139.75, 135.26, 130.25, 129.01, 128.47, 127.69, 127.37 ppm. Elemental analysis calcd for $C_{13}H_{10}O$: C, 85.69; H, 5.53. Found: C, 85.72; H, 5.55.

4.3.17. 3-Ethoxy-2-phenylpyridine. Colorless oil; IR (potassium bromide) ν 3053, 2974, 1628, 1444, 1400, 1340, 1274, 1256, 1160, 950, 782, 698 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.25 (dd, J=1.54, 4.41 Hz, 1H), 7.80–7.96 (m, 2H), 7.42–7.28 (m, 3H), 7.12–7.02 (m, 2H), 3.89 (q, J=7.2 Hz, 2H), 1.29 (t, J=7.2 Hz, 3H) ppm; ^{13}C NMR ($CDCl_3$) δ 152.98, 147.92, 141.20, 137.96, 129.46, 128.17, 127.84, 122.90, 119.71, 64.10, 14.62 ppm. Elemental analysis calcd for $C_{13}H_{13}NO$: C, 78.36; H, 6.58; N, 7.03. Found: C, 78.40; H, 6.61; N, 7.09.

4.3.18. 4-Methyl-3-nitrobiphenyl. Mp 61–62 °C, IR (potassium bromide) ν 3052, 2960, 1522, 1496, 1434, 880, 742, 686 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.12 (d, J=1.93 Hz, 1H), 7.64 (dd, J=1.95, 7.95 Hz, 1H), 7.54–7.50 (m, 2H), 7.44–7.31 (m, 4H), 2.57 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$) δ 149.63, 140.27, 138.46, 133.24, 132.20, 131.25, 129.11, 128.27, 126.88, 122.87, 20.07 ppm. Elemental analysis calcd for $C_{13}H_{11}NO_2$: C, 73.23; H, 5.20; N, 6.57. Found: C, 73.26; H, 5.24; N, 6.61.

4.3.19. 2-Phenylthioxanthen-9-one. Mp 128–129 °C; IR (potassium bromide) ν 3036, 1642, 1594, 1442, 1324, 1136, 750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.84 (d, J=2.11 Hz, 1H), 8.62 (dd, J=1.30, 8.10 Hz, 1H), 7.82 (dd, J=2.14, 8.37 Hz, 1H), 7.70–7.67 (m, 2H), 7.60–7.55 (m, 3H), 7.49–7.43 (m, 3H), 7.40–7.35 (m, 1H) ppm; ^{13}C NMR ($CDCl_3$) δ 179.89, 139.48, 139.29, 137.16, 136.06, 132.24, 130.95, 129.94, 129.47, 129.23, 128.99, 127.87, 127.80, 127.06, 126.52, 126.31, 126.04 ppm. Elemental analysis calcd for $C_{19}H_{12}OS$: C, 79.14; H, 4.19. Found: C, 79.18; H, 4.23.

4.3.20. 2-Phenylpyrazine. Mp 74–75 °C; IR (potassium bromide) ν 3050, 1474, 1447, 1409, 1082, 1010, 772, 744, 692 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.00 (d, J=1.54 Hz, 1H), 8.60 (dd, J=1.61, 2.49 Hz, 1H), 8.47 (d, J=2.51 Hz, 1H), 8.02–7.98 (m, 2H), 7.52–7.44 (m, 3H) ppm; ^{13}C NMR ($CDCl_3$) δ 152.84, 144.15, 142.81, 142.14, 136.28, 129.90, 129.01, 126.92 ppm. Elemental analysis calcd for $C_{10}H_8N_2$: C, 76.90; H, 5.16; N, 17.94. Found: C, 76.98; H, 5.21; N, 18.01.

4.3.21. 3-(4-Methoxyphenoxy)-6-phenylpyridazine. Mp 171–172 °C; IR (potassium bromide) ν 3082, 2992, 1520, 1442, 1306, 1254, 1214, 1042, 850 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.03–7.98 (m, 2H), 7.85 (d, J=9.21 Hz, 1H), 7.51–7.44 (m, 3H), 7.20–7.08 (m, 3H), 6.97–6.92 (m, 2H), 3.82 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 165.38, 157.04, 155.98, 146.97, 135.98, 129.58, 128.93, 127.45, 126.62, 122.22, 117.35, 114.90, 55.68 ppm. Elemental analysis calcd for $C_{18}H_{16}N_2O$: C, 78.24; H, 5.84; N, 10.14. Found: C, 78.28; H, 5.90; N, 10.18.

4.3.22. 2-Phenylquinoline. Mp 83–84 °C (lit.[53] mp 84–85 °C); IR (potassium bromide) ν 3062, 3032, 1604, 1550 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.20–8.14 (m, 4H), 7.86–7.78 (m, 2H), 7.73–7.68 (m, 1H), 7.54–7.42 (m, 4H) ppm; ^{13}C NMR ($CDCl_3$) δ 157.41, 148.33, 139.72, 136.78, 129.75, 129.67, 129.33, 128.85, 127.61, 127.47, 127.22, 126.29, 119.03 ppm. Elemental analysis calcd for $C_{15}H_{11}N$: C, 87.77; H, 5.40; N, 6.82. Found: C, 87.80; H, 5.44; N, 6.86.

4.3.23. 2-Phenylthiophene. Mp 34–36 °C (lit.[54] mp 34–36 °C); IR (potassium bromide) ν 3065, 3014, 1596, 1523, 1486 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.63–7.57 (m, 3H), 7.46–7.26 (m, 5H) ppm; ^{13}C NMR ($CDCl_3$) δ 141.27, 128.86, 128.73, 127.44, 127.23, 127.16, 125.97, 124.77 ppm. Elemental analysis calcd for $C_{10}H_8S$: C, 74.96; H, 5.03. Found: C, 74.99; H, 5.09.

4.3.24. 4-(Pyridine-4-yl)benzonitrile. Mp 77–78 °C (lit.[55] mp 75–76 °C); IR (potassium bromide) ν 3036, 2226, 1598, 1398 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.73 (d, J=4.85 Hz, 2H), 7.73–7.81 (m, 4H), 7.51 (d, J=5.93 Hz, 2H) ppm; ^{13}C NMR ($CDCl_3$) δ 150.60, 146.36, 142.62, 132.91, 127.77, 121.62, 118.38, 112.83 ppm. Elemental analysis calcd for $C_{12}H_8N_2$: C, 79.98; H, 4.47; N, 15.55. Found: C, 80.01; H, 4.50; N, 15.61.

4.3.25. 4′-(Dimethylamino)biphenyl-4-carbonitrile. Mp 218–220 °C (lit.[56] mp 222–223 °C); IR (potassium bromide) ν 3048, 2910, 2226, 1593, 1529, 1492, 1446, 1360, 812 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.63 (m, 4H), 7.51 (d, J=8.83 Hz, 2H), 6.79 (d, J=8.85 Hz, 2H), 3.02 (s, 6H) ppm; ^{13}C NMR ($CDCl_3$) δ 150.77, 145.59, 132.51, 127.88, 126.37, 126.32, 119.43, 112.54, 108.99, 40.33 ppm. Elemental analysis calcd for $C_{15}H_{14}N_2$: C, 81.05; H, 6.35; N, 12.60. Found: C, 81.01; H, 6.32; N, 12.59.

4.3.26. 4′-Formylbiphenyl-4-carbonitrile.[17] Mp 151–152 °C (lit.[57] mp 150–150.5 °C); IR (potassium bromide) ν 3043, 2226, 1702, 1598, 1394, 1261, 1095, 1022, 812 cm^{-1}; ^1H NMR ($CDCl_3$) δ 10.09 (s, 1H), 7.71–8.02 (m, 8H) ppm; ^{13}C NMR ($CDCl_3$) δ 191.60, 144.92, 144.16, 136.15, 132.80, 130.43, 128.05, 127.93, 112.18 ppm. Elemental analysis calcd for $C_{14}H_9NO$: C, 81.14; H, 4.38; N, 6.76. Found: C, 81.13; H, 4.40; N, 6.79.

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