Mild and ligand-free palladium-catalysed Suzuki–Miyaura cross-couplings in aqueous two-phase system

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$Pd(OAc)_2$ combined with an ethanol/K_2HPO_4 aqueous two-phase system was developed as an inexpensive and efficient catalytic system for Suzuki–Miyaura cross-coupling. The couplings between aryl iodides and arylboronic acids proceeded smoothly in moderate to excellent yields at 60 °C in the aqueous two-phase system, and aryl bromides required a higher reaction temperature (reflux at about 80 °C) to improve the yield.

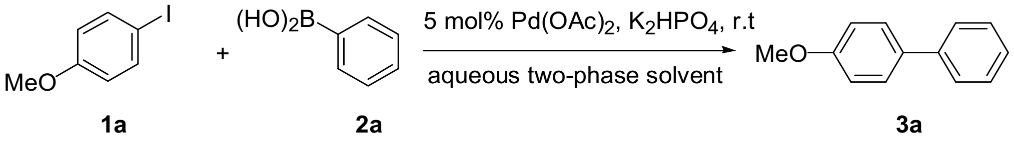
Keywords: Suzuki–Miyaura cross-couplings, aqueous two-phase system, aryl halides, arylboronic acids, $Pd(OAc)_2$

The Suzuki–Miyaura cross-coupling reaction has been considered as a very powerful, versatile and popular tool for selective construction of carbon–carbon bonds in organic chemistry,[1,2] especially in the synthesis of biaryl compounds, which are important structural substructures in numerous polymers, agrochemicals, natural products, and pharmaceutical intermediates.[3,4] The original and general Suzuki–Miyaura coupling procedure involves the use of palladium–ligand (often a phosphane ligand) complexes as catalysts, and the reactions are performed at high temperature and under oxygen-free conditions to avoid side reactions.[5-12] In addition, long reaction times are usually required. Impressive progress in the development of efficient catalytic systems to achieve this reaction under mild conditions has been made in the last few years,[13-18] but there still exists considerable room for further exploration, as only a few methods for palladium-catalysed Suzuki–Miyaura coupling in aqueous solvents without the aid of any ligands have been developed.[19–24] Among those aqueous Suzuki–Miyaura coupling transformations, many methods have still required other additional promoters,[19-22] such as phase-transfer catalysts (usually n-Bu_4NBr or PTS),[24] to provide the best results. To the best of our knowledge, also only few papers[23,24] have demonstrated that palladium-catalysed Suzuki–Miyaura cross-couplings between aryl iodide (or bromides) and arylboronic acids can be carried out in water, Sajiki *et al.*[25] recently found that Pd/C-catalysed Suzuki–Miyaura cross-couplings between aryl bromides and arylboronic acids could be carried out smoothly without the aid of any ligands and promoters at room temperature with long reaction times (24 h) under oxygen-free conditions in aqueous ethanol. This informed and encouraged us in developing a new solvent system for the Suzuki reaction.

An aqueous two-phase system (ATPS) has great potential for industrial applications because it can be used to obtain a concentrated and purified product in one step by addition of crude broths containing suspended matter (*e.g.* cells), and offers gentle nontoxic environments for labile biomolecules which are widely used in biochemistry and biotechnology for purification of proteins,[26,27] enzymes,[28,29] amino acids[30] and so on.[31] There are two type of aqueous two-phase systems, one is composed of a polymer, a phase separation salt and water (*e.g.* PEG/Na_2SO_4/H_2O), and another is composed of an organic solvent, a phase separation salt and water (*e.g.* acetone/$(NH_4)_2SO_4/H_2O$). The well-known advantages of ATPS are volume reduction, high capacity, rapid separations, easy scale-up, suitability for continuous large-scale operations and the special interface effect. In seeking the new reaction solvents, we found that an ATPS is more effective than pure water or other traditional organic solvents for the Suzuki reaction, so we now report a new method for the Suzuki reaction catalysed by $Pd(OAc)_2$ which uses an ATPS as solvent.

Here we show for the first time, as a model, the Suzuki reaction of $PhB(OH)_2$ with 4-methoxyphenyl iodide catalysed by 5 mol% $Pd(OAc)_2$ which we consider is the most successful catalyst for the Suzuki reaction at 60 °C amongst the different aqueous two-phase system was examined (Table 1). In pure water, only 68% conversion was obtained after 12 h reflux (entries 1–3). Addition of a PTC (*e.g.* n-Bu_4NBr) led to a little gradual increase in the conversion rate (entry 1). In the anhydrous ethanol, only 73% conversion was obtained after 12 h reflux (entries 4–6). Using the aqueous two-phase system, the product conversion increased very rapidly in the ethanol/K_2HPO_4 aqueous two-phase system and the yield of 4-methoxybiphenyl was increased dramatically to 96% after 1 h at 60 °C (Table 1, entry 7), this result encouraged us to explore the Suzuki reaction in the a series of aqueous two-phase systems to find out the optimal conditions for the cross-coupling reaction.

To optimise the aqueous two-phase system and find an efficient protocol for the Suzuki coupling reaction, we studied the effects of different aqueous two-phase systems on the cross-coupling reaction, and the results are summarised in Table 1. Firstly we selected four simple aqueous two-phase systems as reaction solvents to pick out the best one for the Suzuki reaction (entries 7–20). In the EtOH/water system (6 mL EtOH, 4 mL H_2O, 0.8–2.0 g salt), a series of bases were evaluated such as K_2HPO_4, KH_2PO_4, K_2CO_3, Na_2CO_3, Cs_2CO_3, Na_3PO_4 and so on. The results show that excellent yields were obtained with K_2HPO_4, K_2CO_3 or Na_2CO_3 as the base (entries 7–9), and the yields of the target product **3a** were reduced to moderate when using other bases, such as Cs_2CO_3, NaOH, Na_3PO_4, KH_2PO_4 and Et_3N (entries 10–14), while use of the acidic salts such as $(NH_4)_2SO_4$ gave no reaction. However, it must be pointed that those bases such



Scheme 1

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Table 1 The Suzuki reaction of $PhB(OH)_2$ with $4\text{-}MeOC_6H_4I$ catalysed by 5 mol% $Pd(OAc)_2$[a]

Entry	Solvent	Phase separation salts	T/t[b]	Yield/%[c]
1	Water	K_2CO_3	Ruflux/12	71
2	Water	K_2HPO_4	Reflux/12	74
3	Water	NaOH	Reflux/12	67
4	EtOH	K_2CO_3	Reflux/12	73
5	EtOH	K_2HPO_4	Reflux/12	75
6	EtOH	Cs_2CO_3	Reflux/12	82
7	EtOH/water	K_2HPO_4	60/1	96,79[d] 85[e],90[f],93[g]
8	EtOH/water	Na_2CO_3	60/1	91
9	EtOH/water	K_2CO_3	60/1	92
10	EtOH/water	Cs_2CO_3	60/1	88
11	EtOH/water	Na_3PO_4	60/1	81
12	EtOH/water	KH_2PO_4	60/1	81
13	EtOH/water	NaOH	60/1	87
14	EtOH/water	Et_3N	60/1	73
15	PrOH/water	K_2HPO_4	60/2	92
16	PrOH/water	$(NH_4)_2SO_4$	60/18	0
17	PrOH/water	Na_2CO_3	60/2	93
18	Acetone/water	K_2HPO_4	60/1.5	87
19	Acetone/water	Na_2CO_3	60/1.5	86
20	PEG2000/water	K_2HPO_4	60/2	89
21	PEG2000/water	Na_2CO_3	60/2	83

[a]Unless otherwise indicated, the reaction conditions were as follows: **1** (3 mmol), **2** (4 mmol), $Pd(OAc)_2$ (5 mol%), and salt (0.8-2.0 g) in organic solvent (6 mL) and water (4 mL) at 60 °C for corresponding time. [b]T, temperature in °C; t, time in h; [c]isolated yield; [d]0.5 mol% $Pd(OAc)_2$. [e]Catalysed by 5 mol% $Pd_2(dba)_3$; [f]$PdCl_2$; [g]Pd/C.

as Na_2CO_3, K_2CO_3, Cs_2CO_3 and KH_2PO_4, could not separate the solvent mixture into two phases completely, only K_2HPO_4 and $(NH_4)_2SO_4$ can separate the mixture solvent into two phases perfectly. In view of the yield and the ability of phase-separation, we considered that the K_2HPO_4 was the best salt for the EtOH/water system. In the other three ATPS, we selected the K_2HPO_4, Na_2CO_3, $(NH_4)_2SO_4$ as phase separation salts and obtained moderate yields (entries 15–21). The general procedure of preparation of the ATPS is to mix 6 mL organic solvents, 4 mL H_2O and 0.8–2.0 g salt (the volume ratio of the two phase was affected by the salts and its quality). The results in Table 1 demonstrated that the highest yield of **3a** was obtained when ethanol/K_2HPO_4 was employed as the medium together with $Pd(OAc)_2$ as the catalyst and KH_2PO_4 shows the general phase separation ability for the four ATPS.

Gratifyingly, we observed that satisfactory results were still obtained at 0.5 mol% loading of $Pd(OAc)_2$ (79% yield in 60 min, entry 7). It is noteworthy that the reaction between 5 mmol of 4-methoxyphenyl iodide and 6 mmol of $PhB(OH)_2$ in the presence of 5 mol% of $Pd(OAc)_2$, could also be conducted smoothly in an acidic EtOH/KH_2PO_4 aqueous two-phase system (pH = 6.1) to produce the desired product **1a** in a 81% yield after 60 min (entry 12).

Encouraged by these results, we therefore performed the reaction with other Pd catalysts, including $Pd_2(dba)_3$ (entry 7), $PdCl_2$ (entry 7), and Pd/C (entry 7), in EtOH/KH_2PO_4 aqueous two-phase system. Unfortunately, they were less effective than $Pd(OAc)_2$ in terms of both yield and rate.

Subsequently, the EtOH/K_2HPO_4 aqueous two-phase system with catalyst of $Pd(OAc)_2$ was extended to various aryl iodides and bromides, and the results are summarised in Table 2. Treatment of aryl iodides (3 mmol) with arylboronic acids **2a** (4 mmol), $Pd(OAc)_2$ (5 mol%), K_2HPO_4 (2 g), EtOH (6 mL) and H_2O (4 mL) afforded the desired coupled products **1b–d** in excellent yields. However, the activity of the above method was reduced for the coupling of aryl bromides. Low yields were obtained even from the reaction of the activated bromides with **2a**, performed at 60 °C. We were pleased to find that excellent yields were achieved when the reaction temperature was increased to reflux at about 77–80 °C (**1e–3c**). We also found that coupling of deactivated or sterically hindered aryl bromides needed prolonged reaction time to get a moderate yield under the same reaction conditions. Lastly, an attempt to couple the activated 4-chlorobenzaldehyde to form **1s** was successful in excellent yield, but the coupling of deactivated chlorobenzene with $PhB(OH)_2$ forms **1t** with only 57% yield after reflux for 24 h.

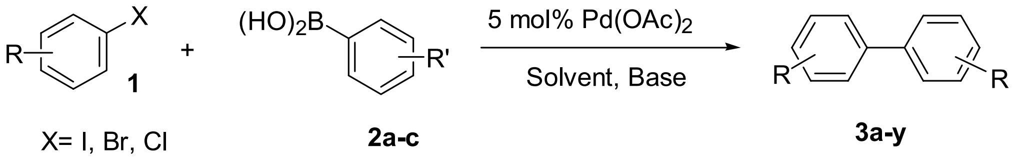
In summary, we have developed an inexpensive and efficient protocol for the Suzuki–Miyaura cross-coupling reaction catalysed by the $Pd(OAc)_2$ in an EtOH/KH_2PO_4 aqueous two-phase system. A variety of aryl halides including iodides and bromides, whether electron-rich or electron-deficient, all coupled with arylboronic acids to give moderate to excellent yields. Further investigations to extend the application of the system to other coupling transformations and overcome the drawbacks with the less activated aryl bromides are in progress.

Experimental

Melting points were determined in open capillary tubes and are uncorrected. ^1H NMR and ^{13}C NMR spectra were measured on Bruker-AV300 instrument in $CDCl_3$ with tetramethylsilane as internal standard and all chemical shifts are given in ppm relative to tetramethylsilane.

General procedure for preparation of **1a–3c**

Aryl or heteroaryl halide **1** (3 mmol), arylboronic acid **2** (4 mmol, **2a–c**), $Pd(OAc)_2$ (5 mol%), KH_2PO_4 (2 g), EtOH (6 mL, or PrOH, acetone) and H_2O (4 mL) were placed in a 25 mL two-neck flask. The mixture was heated at 60 °C or refluxed at about 80 °C in air or O_2 atmosphere for the required time with magnetic stirring and



Scheme 2

Table 2 Suzuki reaction of aryl or heteraryl halides with phenylboronic acid[a]

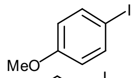
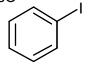
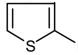
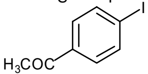
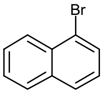
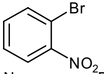
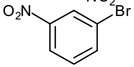
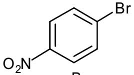
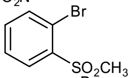
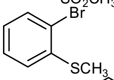
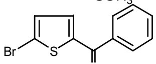
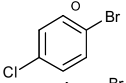
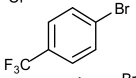
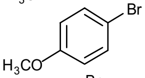
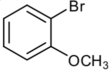
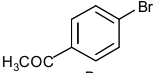
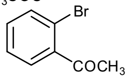
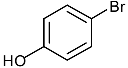
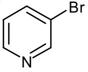
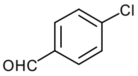
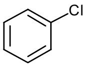
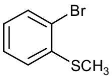
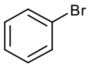
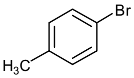
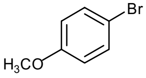
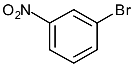
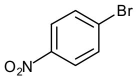
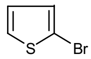
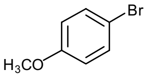
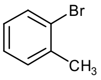
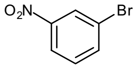
Product	ArX	$ArB(OH)_2$	t/h	Yield/%[b]
1a		$C_6H_4B(OH)_2$	1	96
1b		$C_6H_4B(OH)_2$	1	94
1c		$C_6H_4B(OH)_2$	1	91
1d		$C_6H_4B(OH)_2$	1	94
1e		$C_6H_4B(OH)_2$	2.5	92
1f		$C_6H_4B(OH)_2$	2.5	90
1g		$C_6H_4B(OH)_2$	1.5	94
1h		$C_6H_4B(OH)_2$	1.5	95
1i		$C_6H_4B(OH)_2$	1.5	87
1j		$C_6H_4B(OH)_2$	3	84
1k		$C_6H_4B(OH)_2$	2	92
1l		$C_6H_4B(OH)_2$	3	90
1m		$C_6H_4B(OH)_2$	2	95
1a		$C_6H_4B(OH)_2$	2.5	96
1n		$C_6H_4B(OH)_2$	4.5	92
1o		$C_6H_4B(OH)_2$	2	94
1p		$C_6H_4B(OH)_2$	3.5	91
1q		$C_6H_4B(OH)_2$	3.5	94
1r		$C_6H_4B(OH)_2$	4	96
1s		$C_6H_4B(OH)_2$	24 at reflux	87
1t		$C_6H_4B(OH)_2$	24 at reflux	57
2a		4-CH_3 $C_6H_4B(OH)_2$	4	89
2b		4-CH_3 $C_6H_4B(OH)_2$	3.5	90
2c		4-CH_3 $C_6H_4B(OH)_2$	2.5	92
2d		4-CH_3 $C_6H_4B(OH)_2$	2	94
2e		4-CH_3 $C_6H_4B(OH)_2$	2	92

Table 2 *Continued*

Product	ArX	ArB(OH)$_2$	t/h	Yield/%[b]
2f		4-CH$_3$ C$_6$H$_4$B(OH)$_2$	1.5	95
2g		4-CH$_3$ C$_6$H$_4$B(OH)$_2$	2	92
3a		4-CH$_3$O C$_6$H$_4$B(OH)$_2$	2	95
3b		4-CH$_3$O C$_6$H$_4$B(OH)$_2$	3	88
3c		4-CH$_3$O C$_6$H$_4$B(OH)$_2$	2	90

[a]Unless otherwise indicated, the reaction conditions were as follows: **1** (3 mmol), **2** (4 mmol), Pd(OAc)$_2$ (5 mol%), and K$_2$HPO$_4$ (2.0 g) in ethanol (6 mL) and water (4 mL) at 60–80 °C for corresponding time. [b]Isolated yield.

conversion was monitored by GC (see Table 2). After completion of the reaction, the contents were cooled to room temperature, and the remaining mixture formed into two phases. The supernatent phase which contained about 97% of the product was then separated and another 6 mL ether was used to extract about 3% of product remaining in the water phase. The combined supernatant phase and ether extract was dried over Na$_2$SO$_4$. This mixture was filtered and the solvent evaporated. The product was purified by chromatography on silica (eluent: EtOAc/petroleum ether = 1 : 15). The purity of the isolated product was determined by GC analysis or ^{1}H NMR. In the PEG/water system, ether (10 mL × 2) was used directly to extract the product and the residue PEG/water system can be reused.

Product data

4-Methoxybiphenyl (**1a**): M.p. 87–88 °C (lit.[32] m.p. 86–87 °C). ^{1}H NMR (CDCl$_3$, 300 MHz) δ: 3.86 (s, 3H, CH$_3$O), 6.96–7.00 (m, 2H, ArH), 7.26 (s, 1H, ArH), 7.40–7.44 (m, 2H, ArH), 7.52–7.57 (m, 4H, ArH). ^{13}C NMR (CDCl$_3$, 75 Hz) δ: 129.2, 128.6, 127.2, 127.1, 114.7, 55.8.

Biphenyl (**1b**): M.p. 66–67 °C (lit.[33] m.p. 68–69 °C). ^{1}H NMR (CDCl$_3$, 300 MHz) δ: 7.63 (d, J = 7.2 Hz, 4H, ArH), 7.48 (t, J = 7.6 Hz, 4H, ArH), 7.38 (t, J = 7.6 Hz, 2H, ArH). ^{13}C NMR (CDC1$_3$, 75 MHz) δ: 141.3, 128.8, 127.3 127.2.

2-Phenylthiophene (**1c**): M.p. 34–35 °C (lit.[34] m.p. 36–37 °C). ^{1}H NMR(CDCl$_3$, 300 MHz) δ: 7.69 (d, J = 7.2 Hz, 2H, ArH), 7.44 (dd, 2H, J = 7.8 Hz, J = 7.2 Hz, 2H, ArH), 7.44 (t, J = 7.8 Hz, 1H, thiophene), 7.37 (d, J = 3.8 Hz, 1H, ArH), 7.33 (d, J = 5.0 Hz, 1H, thiophene), 7.13 (dd, J = 5.0 Hz, J = 3.8 Hz, 1H, thiophene). ^{13}C NMR (75 MHz, CDCl$_3$) δ: 144.4, 134.3, 128.8, 128.0, 127.4, 125.9, 124.7, 123.0.

4-Acetylbiphenyl (**1d**): M.p. 120–121 °C (lit.[35] m.p. 119–120 °C). ^{1}H NMR(CDCl$_3$, 300 MHz) δ: 8.04 (d, J = 8.4 Hz, 2H, ArH), 7.69 (d, J = 8.4 Hz, 2H, ArH), 7.64 (d, J = 7.6 Hz, 2H, ArH), 7.50–7.40 (m, 3H,, ArH), 2.64 (m, 3H, CH$_3$CO). ^{13}C NMR (75 MHz, CDC1$_3$) δ: 197.8, 145.8, 139.9, 135.8, 128.9, 128.9, 128.2, 127.3, 127.2, 26.7.

1-Phenylnaphthalene[36] (**1e**): Light yellow oil. ^{1}H NMR(CDCl$_3$, 300 MHz) δ: 7.90–7.82 (m, 3H), 7.51–7.45 (m, 6H), 7.41–7.39 (m, 3H). ^{13}C NMR (CDC13,75 MHz) δ: 154.8, 134.5, 130.1, 128.3, 127.4, 126.3, 125.9, 125.7, 125.5,125.4, 125.1, 122.1, 120.0, 104.6.

2-Nitrobiphenyl[36] (**1f**): Light yellow oil. ^{1}H NMR(CDCl$_3$, 300 MHz) δ: 7.86 (d, J = 8.0 Hz, 1 H, ArH) 7.62 (t, J = 7.6 Hz,1H, ArH), 7.51–7.39 (m, 5H, ArH), 7.33–7.30 (m, 2H, ArH). ^{13}C NMR (CDC1$_3$, 75 MHz) δ: 149.3, 137.4, 136.4, 132.4, 132.0, 128.7, 128.3, 128.2, 127.9, 124.1.

3-Nitrobiphenyl (**1g**): M.p. 53–55 °C (lit.[36] m.p. 55–57 °C). ^{1}H NMR(CDCl$_3$, 300 MHz) δ: 8.48 (t, J = 1.9 Hz, 1H, ArH), 8.21–8.24 (dd, J = 1.4 Hz, J = 8.2 Hz, 1H, ArH), 7.93–7.95 (d, J = 7.7 Hz, 1H, ArH), 7.61–7.67 (m, 3H, ArH), 7.46–7.55 (m, 3H, ArH). ^{13}C NMR (CDC1$_3$, 75 MHz) δ: 148.7, 142.9, 138.7, 133.0, 129.7, 129.2, 128.5, 127.2, 122.0, 121.9.

CAUTION: 4-Nitrobiphenyl is a known potent CARCINOGEN. In the UK, its "manufacture and use for all purposes" is prohibited (Schedule 2 of the COSHH Regulations 1999.

4-Nitrobiphenyl (**1h**): M.p. 112–113 °C (lit.[37] m.p. 113–114 °C). ^{1}H NMR (CDCl$_3$, 300 MHz) δ: 7.49–7.56 (m, 3H, ArH), 7.67 (d, J = 7.6 Hz, 2H, ArH), 7.78 (d, J = 8.4 Hz, 2H, ArH), 8.34 (d, J = 8.4 Hz, 2H, ArH). ^{13}C NMR (CDCl$_3$, 75 MHz) δ: 147.6, 147.1, 138.8, 129.2, 128.9, 127.8, 127.4, 124.1.

2-Methanesulfonylbiphenyl (**1i**): M.p. 58–60 °C. ^{1}H NMR(CDCl$_3$, 300 MHz) δ: 8.24–8.27 (dd, J = 0.84 Hz, J = 8.4 Hz, 1H, ArH), 7.58–7.67 (m, 2H, ArH), 7.38–7.49 (m, 6H, ArH), 2.64 (s, 3H, SO$_2$CH$_3$). ^{13}C NMR (CDC1$_3$, 75 MHz) δ: 141.5, 139.2, 138.4, 134.7, 133.1, 132.7, 130.1, 128.5, 128.3, 127.9, 43.3. Anal. Calcd for C$_{13}$H$_{12}$O$_2$S: C, 67.21; H, 5.21. Found: C, 67.23; H, 5.19%.

2-Methylsulfanylbiphenyl (**1j**): light yellow oil. ^{1}H NMR(CDCl$_3$, 300 MHz) δ: 7.27–7.51 (m, 9H, ArH), 2.43 (s,3H, SCH$_3$). ^{13}C NMR (CDC1$_3$, 75 MHz) δ: 142.6, 139.6, 139.1, 133.9, 133.4, 131.6, 131.1, 128.7, 128.4, 125.7, 21.5. Anal. Calcd for C$_{13}$H$_{12}$S: C, 77.95; H, 6.04. Found: C, 77.93; H, 6.01%.

Phenyl (5-phenyl-thiophen-2-yl)-methanone (**1k**): M.p. 67–69 °C. ^{1}H NMR(CDCl$_3$, 300 MHz) δ: 7.81–7.87 (m, 4H, ArH), 7.68–7.73 (m, 3H, ArH), 7.58–7.61 (d, J = 7.4 Hz, 2H, ArH), 7.46–7.52 (m, 3H, ArH). ^{13}C NMR (DMSO, 75 MHz) δ: 187.5, 152.6, 141.9, 137.8, 137.2, 133.0, 132.9, 129.8, 129.2, 129.1, 126.5, 125.6. Anal. Calcd for C$_{17}$H$_{11}$OS: C, 77.24; H, 4.58. Found: C, 77.26; H, 4.61%.

4-Chlorobiphenyl (**1l**): M.p. 78–79 °C (lit.[38] m.p. 76–78 °C). ^{1}H NMR (CDCl$_3$, 300 MHz) δ: 7.73 (d, J = 8.5 Hz, 1 H, ArH),7.69(d, J = 8.5 Hz, 2H, ArH), 7.65(d, J = 8.5 Hz, 2H, ArH), 7.52(t, J = 7.0 Hz, 2H, ArH), 7.44(t, J = 6.5 Hz, 2H, ArH). ^{13}C NMR (CDC1$_3$, 75 MHz) δ: 140.0, 139.6, 129.0, 128.9, 128.4, 128.2, 127.6, 127.0.

4-Trifluoromethylbiphenyl (**1m**): M.p. 69–70 °C (lit.[39] m.p. 70–71 °C). ^{1}H NMR(CDCl$_3$, 300 MHz) δ: 7.35 (t, J = 7.6 Hz, 1H, ArH), 7.40–7.49 (m, 3H, ArH), 7.60 (d, J = 7.2 Hz, 3H, ArH), 7.69 (s, 2H, ArH); ^{13}C NMR (CDCl$_3$, 75 MHz) δ: 129.48, 129.24, 128.67, 127.91, 127.74, 127.65, 126.17.

2-Methoxylbiphenyl (**1n**): Colourless oil. ^{1}H NMR (CDCl$_3$, 300 Hz) δ: 7.59 (d, J = 8.0 Hz, 2H, ArH), 7.46 (t, J = 8.0 Hz, 2H, ArH), 7.40–7.35 (m, 3H, ArH), 7.08 (t, J = 7.4 Hz, 1H, ArH), 7.03 (d, J = 8.6 Hz, 1H, ArH), 3.85 (s, 3H, OCH$_3$). ^{13}C NMR (CDCl$_3$, 75 MHz) δ: 156.4, 138.5, 130.8, 130.7, 129.5, 128.6, 127.9, 126.9, 120.8, 111.2, 55.5.

4-Acetylbiphenyl (**1o**): M.p. 120–121 °C (lit.[41] m.p. 119–120 °C). ^{1}H NMR(CDCl$_3$, 300 MHz) δ: 8.04 (d, J = 8.4 Hz, 2H, ArH), 7.69 (d, J = 8.4 Hz, 2H, ArH), 7.64 (d, J = 7.6 Hz, 2H, ArH), 7.50–7.40 (m, 3H, ArH), 2.64 (m, 3H, CH$_3$CO). ^{13}C NMR (CDC1$_3$, 75 MHz) δ: 197.8, 145.8, 139.9, 135.8, 128.9, 128.9, 128.2, 127.3, 127.2, 26.7.

2-Acetylbiphenyl[42] (**1p**): Colourless oil. ^{1}H NMR(CDCl$_3$, 300 MHz) δ: 7.50–7.57 (m, 2H, ArH), 7.33–7.44 (m, 7H, ArH), 2.01 (s, 3H, CH$_3$CO). ^{13}C NMR (CDC1$_3$, 75 MHz) δ: 204.8, 140.8, 140.7, 140.4, 130.7, 130.2, 128.8, 128.8, 128.6, 127.8, 127.4, 30.4.

4-Phenylphenol[43] (**1q**): M.p. 162–165 °C (lit. m.p. 164–166 °C). ^{1}H NMR(CDCl$_3$, 300 MHz) δ: 7.6–6.8 (m, 9H, ArH), 4.88 (s, 1H, OH). ^{13}C NMR (CDC1$_3$, 75 MHz) δ: 155.0, 140.7, 134.0, 129.4, 128.7, 128.4, 126.7, 115.6.

3-Phenylpyridine[44] (**1r**): Colourless oil. ^{1}H NMR(CDCl$_3$, 300 MHz) δ: 8.85 (s, 1H), 8.59 (d, J = 6.4, Hz, 1H), 7.88 (d, J = 12.0 Hz, 1H), 7.60 (d, J = 8.4 Hz, 2H), 7.49 (t, J = 7.2 Hz, 2H), 7.43–7.35 (m, 2H). ^{13}C NMR (CDC1$_3$, 75 MHz): 148.4,148.3, 137.8, 136.6, 134.3, 129.0, 128.1, 127.1, 123.5.

Biphenyl-4-carbaldehyde (**1s**): M.p. 57–58 °C (lit.[45] m.p. 57–59 °C). ^{1}H NMR(CDCl$_3$, 300 MHz) δ: 10.06 (s, 1H, CHO), 7.96 (d, J = 8.0 Hz, 2H, ArH), 7.76 (d, J = 8.0 Hz, 2H, ArH), 7.64 (d, J = 7.6 Hz, 2H, ArH), 7.42–7.51 (m, 2H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 192.4, 147.6, 140.1, 135.6, 130.7, 129.47, 128.9, 128.1, 127.8.

4′-Methyl-2-methylsulfanylbiphenyl (**2a**): Light yellow oil. ^{1}H NMR ($CDC1_3$, 300 MHz) δ: 7.22–7.40 (m, 8H, ArH), 2.47 (s, 3H, SCH_3), 2.42 (s, 3H, CH_3). ^{13}C NMR ($CDC1_3$, 75 MHz) δ: 140.9, 137.6, 137.3, 137.2, 130.0, 129.2, 128.9, 127.8, 125.1, 124.7, 21.3, 16.1. Anal. Calcd for $C_{14}H_{14}S$: C, 78.46; H, 6.58. Found: C, 78.41; H, 6.61%.

4-Methylbiphenyl (**2b**): M.p. 46–48 °C (lit.[46] m.p. 46–47 °C). ^{1}H NMR($CDCl_3$, 300 MHz) δ: 7.56 (d, J = 7.5 Hz, 2H, ArH), 7.48 (d, J = 7.8 Hz, 2H, ArH), 7.40 (t, J = 7.5 Hz, 2H, ArH), 7.30 (t, J = 7.2 Hz, 1H, ArH), 7.22 (d, J = 7.5 Hz, 2H, ArH), 2.43 (s, 3H, CH_3). ^{13}C NMR ($CDC1_3$, 75 MHz) δ: 141.2, 138.4, 137.0, 129.5, 129.4, 128.7, 127.0, 126.9, 21.1.

4,4′-Dimethylbiphenyl (**2c**): M.p. 116–118 °C (lit.[46] m.p. 117–118 °C). ^{1}H NMR($CDCl_3$, 300 MHz) δ: 7.41 (d, J = 7.6 Hz, 4 H, *m-H* relative to CH_3), 7.16 (d, J = 7.6 Hz, 4 H, *o-H* relative to CH_3), 2.31 (s, 6 H, CH_3), ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 137.25, 135.63, 128.39, 125.76, 20.03.

4′-Methoxy-4-methylbiphenyl (**2d**): M.p. 108–109 °C (lit.[47] m.p. 111–112 °C). ^{1}H NMR($CDCl_3$, 300 MHz) δ: 7.51–7.44 (m, 4H, ArH), 7.22 (d, J = 7.9 Hz, 2H, ArH), 6.96(d, J = 8.6 Hz, 2H, ArH), 3.84 (s, 3H, OCH_3), 2.38 (s, 3H, CH_3). ^{13}C NMR ($CDC1_3$, 75 MHz) δ: 158.9, 138.0, 136.4, 133.8, 129.5, 128.0, 126.6, 114.2, 55.4, 21.1.

3-Nitro-4′-methylbiphenyl (**2e**): M.p. 75–76 °C (lit.[48] m.p. 76–77 °C). ^{1}H NMR ($CDC1_3$, 300 MHz) δ: 8.45–8.43 (m, 1 H, ArH), 8.19–8.16 (m, 1 H, ArH), 7.92–7.89 (m, 1H, ArH), 7.62–7.52 (m, 3H, ArH), 7.32–7.26 (m, 2H, ArH), 2.42 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 148.7, 142.8, 138.6, 135.8, 132.8, 129.9, 129.7, 129.5, 127.0, 126.8, 121.8, 121.7, 21.2.

4-Methyl-4′-nitrobiphenyl (**2f**): M.p. 137–139 °C (lit.[48] m.p. 141–143 °C). ^{1}H NMR ($CDC1_3$, 300 MHz) δ: 8.19 (d, J = 8.8 Hz, 2H, ArH), 7.24 (d, J = 8.4 Hz, 2H, ArH) 6.98 (d, J = 8.8 Hz, 2H, ArH), 6.88 (d, J = 8.4 Hz, 2H, ArH), 2.38 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 164.2,152.6, 142.8, 135.6, 131.2, 126.3, 120.9, 117.1, 21.3.

2-p-Tolyl-thiophene (**2g**): M.p. 54–56 °C (lit.[36] m.p. 54–55 °C). ^{1}H NMR ($CDC1_3$, 300 MHz) δ: 7.54 (d, J = 8.1 Hz, 2H), 7.28 (t, J=4.6 Hz, 2H), 7.21 (d, J=8.1 Hz, 2H), 7.08 (q, J=3.6 Hz, J=5.1 Hz, 1H), 2.41 (s, 3H, CH_3). ^{13}C NMR ($CDC1_3$, 75 MHz) δ: 144.6, 137.3, 131.7, 129.5, 127.9, 125.9, 124.3, 122.6, 21.2.

4,4′-Dimethoxybiphenyl[49] (**3a**): M.p. 179–180 °C (lit. m.p. 176–178 °C). ^{1}H NMR ($CDC1_3$, 300 MHz) δ: 7.48 (d, J = 8.4 Hz, 4H, ArH), 6.95 (d, J = 8.8 Hz, 4H, ArH), 3.84 (s, 6H, OCH_3). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 158.7, 133.5, 127.7, 114.1, 59.3.

4-Methoxy-2′-methylbiphenyl[50] (**3b**): Colourless oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.26–7.22 (m, 6H, ArH), 6.95 (d, J = 8.4 Hz, 2H, ArH), 3.85 (s, 3H, OCH_3), 2.28 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 158.5, 141.5, 135.5, 134.3, 130.3, 130.2, 129.9, 127.0, 125.8, 113.5, 55.3, 20.6.

4′-Methoxy-3-nitro-biphenyl (**3c**): M.p. 79–80 °C (lit.[51] m.p. 78–79 °C). ^{1}H NMR ($CDC1_3$, 300 MHz) δ: 8.41 (t, J = 2.0 Hz, 1H, ArH), 8.16–8.14 (m, 1H, ArH), 7.88–7.86 (m, 1H, ArH), 7.60–7.56 (m,3H, ArH), 7.04–7.01(m, 2H, ArH), 3.88 (s, 3H, CH_3). ^{13}C NMR ($CDC1_3$, 75 MHz) δ: 160.1, 148.8, 142.5, 138.5, 132.5, 131.1, 129.7, 128.3, 121.4, 114.6, 55.4.

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