Electrocatalytic synthesis of non-symmetric biphenols mediated by tri(p-bromophenyl)amine (TBPA): selective oxidative cross-coupling of different phenols and naphthols

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An efficient electrochemical access to the non-symmetric biphenols using tri(p-bromophenyl)amine (TBPA) as a redox mediator has been developed. The electrochemical protocol features highly selective cross-coupling products in up to 83% yield, instead of forming homo-coupling ones.

Introduction

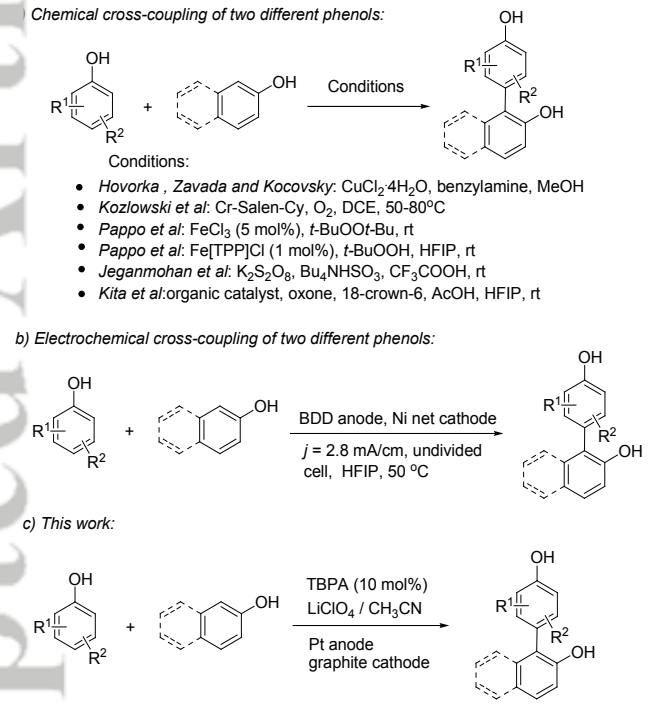
Efficient synthesis of biphenols has emerged as a prevalent research field in organic chemistry since these structural motifs are widely found in natural products, pharmaceutical molecules and materials, as well as serving as ligands in asymmetrical synthesis and for other applications.[1] To this end, various methods have been developed to construct the biphenol structural scaffold, among which the direct oxidative coupling of two unprotected phenolic molecules has attracted much attention due to its atom- and step-economic character, and much advances have been addressed in the oxidative homo-coupling of two phenols, especially successful in their selectivity and efficiency.[2]

However, the cross coupling of two different phenols is not well studied and still a challenge because of the competitive side reactions, such as homo-coupling of phenol, oligomerization, formation of quinone and C-O bond between two phenols.[3] In this context, the cross-coupling of substituted 2-naphthols employing stoichiometric $CuCl_2 \bullet 4H_2O$ / benzylamine system was first reported by Hovorka, Zavada, and later by Kocovsky et al. [4] Later on, Cr-salen-Cy catalyst has been developed for the cross-coupling of phenols using O_2 as a terminal oxidant.[3] Recently, Pappo and coworkers reported the efficient synthesis of non-symmetric biphenols using $FeCl_3$ /t-BuOOt-Bu system or catalytic amount of meso-tetraphenylporphyrion iron chloride (Fe[TPP]Cl) in 1,1,1,3,3,3-hexafluoropropano-2-ol (HFIP) using t-BuOOH as the oxidant.[5] Right recently, $K_2S_2O_8$ in CF_3COOH has also been employed to realize the cross-coupling of phenol-phenol or phenol-naphthol in the presence of Bu_4NHSO_3 (10 mol%).[6] Moreover, Kita and coworkers have developed an organo-iodine(III)-catalyzed oxidative cross-coupling reaction of phenol-phenol using oxone as the terminal oxidant in HFIP solvent.[7] In spite of these progresses, expensive transition-metal catalysts, such as Fe[TPP]Cl, and excess terminal oxidant are required, which leads to producing large amount of waste (Scheme 1a).

Electrochemistry uses electron as a traceless reagent to avoid the producing of waste, thereby emerging as an environmentally benign means for the C-H functionalization and C-C formation.[8] By separating the electrochemical and chemical processes independently, Yoshida et al. has developed a versatile and powerful “cation-pool” method to get access to biaryls.[9] However, this approach could not extend to synthesis of biphenols.[10] To address this issue, Waldvogel and coworkers have made extensive effects and found that the combination of boron doped diamond (BDD) anode and HFIP solvent could provide non-symmetric

biphenols in high selectivity and satisfactory yields (Scheme 1b).[11]

In continuation to our interest in the oxidative functionalization of C-H bonds via indirect electrolysis using a redox catalyst as the electron transfer agent.[12] we herein reported the electrocatalytic cross-coupling of phenols with naphthols or phenols using TBPA as the mediator (Scheme 1c). The protocol features high chemical selectivity (cross-coupling vs homo-coupling), broad scope of substrates and coupling efficiency. To the best of our knowledge, this work represents the first example using TBPA as the mediator for the synthesis of non-symmetric biphenols.



Scheme 1 Oxidative cross-coupling for the synthesis of non-symmetric biphenols

Results and Discussion

2.1 Electrochemical analysis of TBPA and related phenols and naphthols by cyclic voltammetry

To probe the possibility of the TBPA-mediated cross-coupling reactions of different phenols, cyclic voltammetry analyses of TBPA and related phenols **1** and naphthols **2** in CH_3CN containing 0.1 M $LiClO_4$ as the supporting electrolyte were initially carried out. As shown in Figure 1 and Table 1, TBPA gave a well-defined reversible anodic peak at 0.84 V vs $Ag/AgNO_3$ (0.1 M in CH_3CN) and a cathodic peak at 0.76 V vs $Ag/AgNO_3$ (0.1 M in CH_3CN) with an anodic to cathodic peak current ratio of about 1.0. This observation corresponds to the oxidation of TBPA to its cation radical and its reduction, back to TBPA. On the other hand, each phenol and naphthol exhibits an irreversible oxidation peak in the range of 0.84 - 1.35 V vs $Ag/AgNO_3$ (Table 1). For example, the CVs of **1a** and **2a** were observed to be oxidized irreversibly at 0.90 V and 1.05 V vs Ag/AgNO3, respectively (Figure 1). Higher peak potentials of **1a** with **2a** than TBPA indicates that TBPA is easier to be oxidized over **1a** and **2a**.

Table 1. Peak potentials of TBPA and related compounds

compound	E_{ox}^1 (V)	compound	E_{ox}^1 (V)
TBPA	0.84	**1a**	0.90
1b	1.14	**1c**	0.93
1d	0.87	**1e**	1.35
1f	1.37	**1g**	1.15
1h	1.26	**2a**	1.05
2b	1.21	**2c**	1.13
2d	0.84		

Conditions: Cyclic voltammetry was measured in 0.1 M $LiClO_4/CH_3CN$ using Pt disk working electrode, Ag wire, and $Ag/AgNO_3$ (0.1 M in CH_3CN) as counter and reference electrode at a scan rate of 100 mA/s.

When the solution of TBPA was added substrate **1a**, the anodic peak current of TBPA increased from 9.1 μA to 108.1 μA, along with a complete disappear of cathodic peak current of TBPA, which proves a catalytic current occurred. Since the oxidation peak potential of TBPA is less positive than that of **1a**, it is believed that the catalytic current of TBPA results from the homogeneous electron transfer of TBPA cation radical ($TBPA^{+\bullet}$) with **1a**. On the other hand, catalytic current of TBPA in the presence of **2a** also existed, but the multitude of peak current is less than that with **1a** (9.1 μA to 30.2 μA). These results are reasonable when one realizes that the anodic peak potential of **1a** is less positive than that of **2a**, resulting into lower oxidation peak potential gap between TBPA and **1a** (ΔE_p^{ox} = 0.06 V) than that with **2a** (ΔE_p^{ox} = 0.21 V). The smaller the peak potential difference

between the mediator and a substrate, the larger the catalytic current. In a word, cyclic voltammetry analysis discloses that TBPA could be used to mediate the anodic oxidation of **1a** and **2a**, but superior for phenol **1a** due to its lower oxidation potential than that of **2a**.

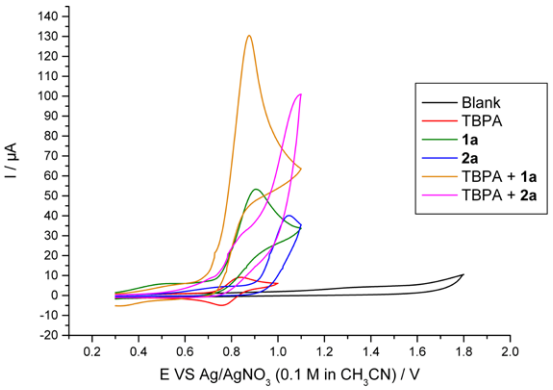
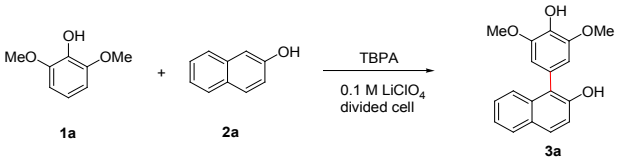


Figure 1. Cyclic voltammograms of TBPA and related compounds in 0.1 M $LiClO_4/CH_3CN$ using Pt disk working electrode, Ag wire, and $Ag/AgNO_3$ (0.1 M in CH_3CN) as counter and reference electrode at a scan rate of 100 mA/s.

2.2. Preparative scale of electrolysis



Scheme 2. Electrochemical dehydrogenative cross-coupling of **1a** and **2a**

The appearance of catalytic current in CVs of TBPA in the presence of **1a** or **2a** determines that the preparative electrolysis of **1a** with **2a** mediated by TBPA is possible. To confirm such an idea, we then carried out controlled potential electrolysis of **1a** with **2a** in an H-type divided cell using Pt plate as an anode and graphite plate as a cathode in the presence of 10 mol % of TBPA as the redox catalyst. When the electrolysis was performed at 0.8 V vs $Ag/AgNO_3$, the oxidation peak potential of TBPA, the cross-coupling product 3a was afforded exclusively in 75% yield, without observing the formation of homo-coupling products from **1a** or **2a** (Scheme 2 and Table 2, entry 1). When the ratio of **1a** to **2a** increased to 1:1.5 from 1:1, product 3a was afforded in 83% yield (entry 2). Further enhance of the ratio to 1:3 proved to be unbeneficial; the yield of **3a** decreased slightly to 65% (entry 3). Solvent screening disclosed that CH_3CN was preferable since the commonly used solvents, such as a mixture of CH_3CN and CH_2Cl_2 or CF_3CH_2OH gave product **3a** in moderate yield (entries 4 and 5). In particular, when methanol or ethanol were used as the solvent, very poor yield of **3a** was isolated due to their low solubility in these solvents (entries 6 and 7).

The reaction temperature also play an important role for the dehydrogenative cross-coupling reaction of **1a** and **2a**. When the reaction was performed at 0 °C, only traces of **3a** was detected (entry 8), while 60% yield of 3a was isolated at 60 °C (entry 9). Evaluation of electrode materials indicated that a combination of Pt anode and graphite cathode is beneficial because DSA or graphite anode with Al or Fe cathode gave lower yields (entries 10-14). When the reaction was carried out in the absence of TBPA, 65% yield of **3a** was also isolated (entry 15). Notably, without the assistance of TBPA, the cross-coupling reaction of **1a** with **2a** proceeded slowly, only 2.2 mA of initial current could achieved, whereas, more than 8.3 mA of initial current was observed in the presence of TBPA. In addition, when the loading of TBPA increased to 20%, a comparable yield (80%) of **3a** was afforded (entry 16). When the electrochemical reaction was conducted in an undivided cell, the desired product **3a** was not observed (entry 17). In addition, only 14% yield of 3a was isolated when tri(*p*-tolyl)amine was used as a redox catalyst. Based on these results described above, we concluded that the optimized conditions allows for using $LiClO_4/CH_3CN$ as supporting electrolyte, Pt anode and graphite cathode. The cross-coupling reaction prefers to be carried out at a controlled-potential of 0.8 V vs $Ag/AgNO_3$ using 10 mol% of TBPA as the mediator.

Table 2. Optimization of reaction conditions [a]

entry	ratio of **1a**:**2a**	anode / cathode	solvent	TBPA (mol%)	temperature	yield (%)[b]
1	1:1	Pt/C	CH_3CN	10	r.t.	75
2	1:1.5	Pt/C	CH_3CN	10	r.t.	83
3	1:3	Pt/C	CH_3CN	10	r.t.	65
4	1:1.5	Pt/C	CH_3CN:DCM(3:1)	10	r.t.	55
5	1:1.5	Pt/C	CF_3CH_2OH	10	r.t.	45

6	1:1.5	Pt/C	MeOH	10	r.t.	8
7	1:1.5	Pt/C	CH_3CH_2OH	10	r.t.	6
8	1:1.5	Pt/C	CH_3CN	10	0	trace
9	1:1.5	Pt/C	CH_3CN	10	60	60
10	1:1.5	DSA/C	CH_3CN	10	r.t.	72
11	1:1.5	C/C	CH_3CN	10	r.t.	65
12	1:1.5	Pt/Al	CH_3CN	10	r.t.	36
13	1:1.5	Pt/Fe	CH_3CN	10	r.t.	39
14	1:1.5	Pt/Pt	CH_3CN	10	r.t.	78
15	1:1.5	Pt/C	CH_3CN	-	r.t.	65
16	1:1.5	Pt/C	CH_3CN	20	r.t.	80
17[c]	1:1.5	Pt/C	CH_3CN	20	r.t.	n.d.
18[d]	1:1.5	Pt/C	CH_3CN	10	r.t.	14

[a] Reaction conditions: 0.5 mmol of **1a** with **2a** in 10 mL of solvent dissolving $LiClO_4$ (0.1 M) as the conducting salt in a H-type divided cell, controlled potential at 0.8 V vs $Ag/AgNO_3$. 3 F/mol.

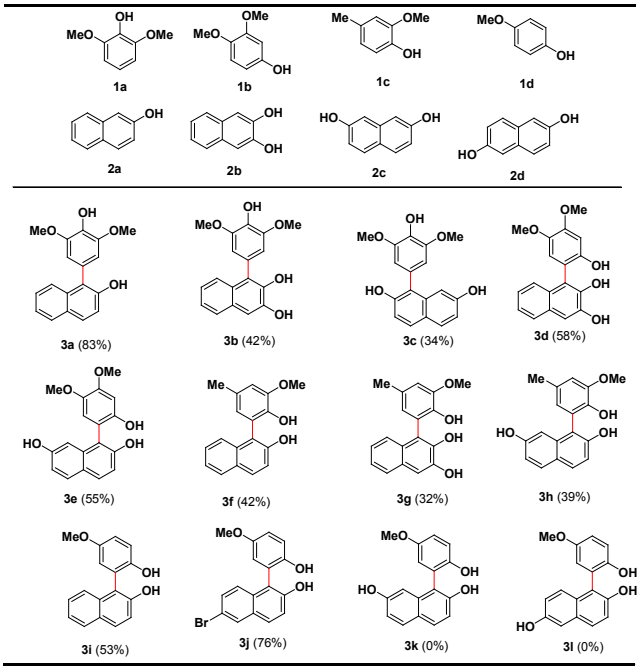
[b] Isolated yield.

[c] under undivided cell.

[d] Tri(*p*-tolyl)amine, instead of TBPA was used as redox catalyst.

With the optimal electrolytic conditions in hand, we then turned to examine the scope of the substrates and generality of the reaction. As shown in Table 3, when phenol **1a** was subjected to indirect electrolysis with dihydroxynaphthalene **2b** and **2c** in the presence of TBPA as the mediator, corresponding coupling products **3b** and **3c** were afforded in 42% and 34%, respectively. Although the yields of the cross-coupling products were moderate, the reactions were clear; only cross-coupling products and the remaining starting materials were detected from TLC, without formation of homo-coupling products. In addition, it was observed that these products were formed from the cross-coupling of para-C-H bond of **1a** and one of the α-C-H bond of **2b** and **2c**. The electrochemical coupling of 3,4-dimethoxyphenol, **1b**, with naphthols **2b** or **2c** also proceeded smoothly to give corresponding coupling products **3d** and **3e** in 58% and 55% yields, respectively. For 2-methoxy-4-methylphenol **1c**, its reaction with naphthols also worked well, but gave moderate yields of **3f**, **3g** and **3h**. In the reactions of 4-methoxyphenol **1d** with naphthols, corresponding products **3i** and **3j** were afforded in 53% and 76% yields, whereas other cross-coupling products, **3k** and **3l** were not detected; and all the starting material were recovered.

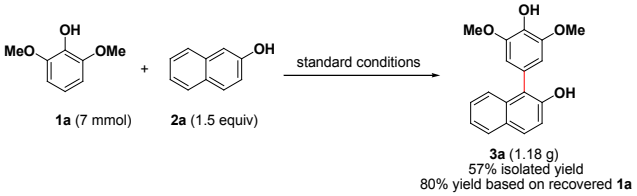
Table 3. Cross-coupling of phenols and naphthols [a,b]



[a] Reaction conditions: phenols **1a**-**1d** (1.0 mmol), naphthols **2a**-**2d** (1.5 mmol) and TBPA (0.1 mmol) in a H-type divided cell containing 10 mL of $CH_3CN/LiClO_4$ (0.1 M), Pt plate anode and graphite plate as cathode, room temperature, controlled potential at 0.8 V vs $Ag/AgNO_3$.

[b] Isolated yield.

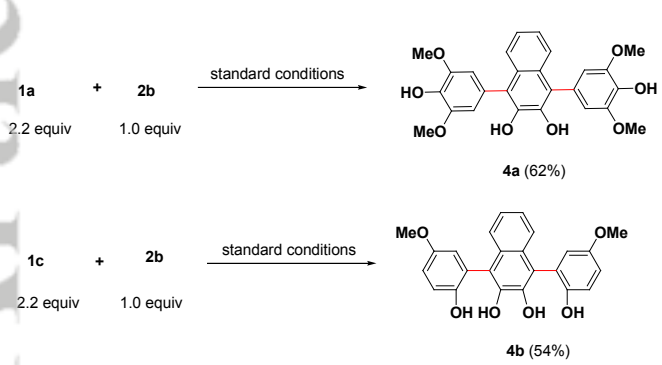
A scale-up experiment proved the protocol to be practicable. As shown in Scheme 3, when 7 mmol of **1a** with **2a** were subjected to electrolysis under the standard conditions, **3a** (1.18 g) was isolated in 57% yield and 80% yield based on the recovered **1a**.



Scheme 3. Scale up

Notably, for naphthanlene-2,3-diol (**2b**), two OH groups are

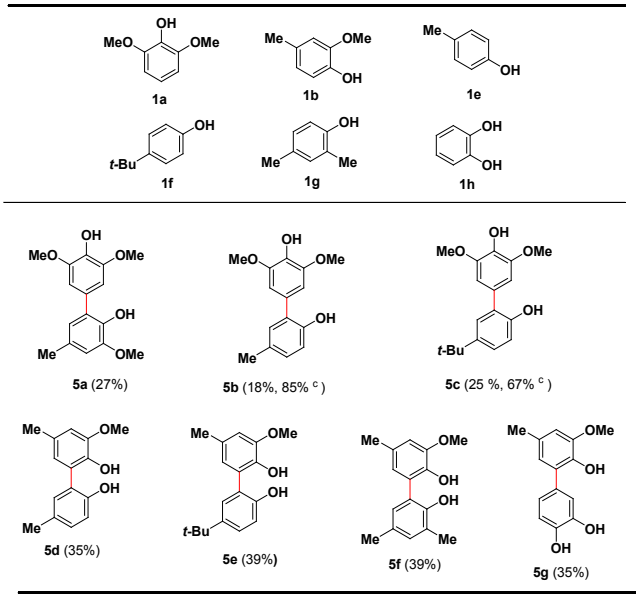
present on the aromatic ring, therefore, bis-arylation reaction of **2b** to install two phenol moieties on the α-C-H of the corresponding OH groups might occur. As shown in Scheme 4, when **2b** with excess amounts of **1a** or **1c** (2.2 equiv) were subjected to electrolysis under the standard conditions, corresponding cross-coupling products **4a** or **4b** were exclusively afforded in 62% and 54% yields, respectively, without producing the homo-coupling products from **1a** or **1c**, although partial **1a** and **1c** were observed remaining and could be recovered.



Scheme 4. Bis-arylation of naphthol 2b

Next, the electrochemical protocol was extended to the cross-coupling of two different phenols, of which proved to be difficult and corresponding homo-coupling reaction occurs predominantly because of their similar oxidation potential values. To our delight, our mediated electrochemical cross-coupling reaction of various phenols also worked, although in low yields (Table 4). For example, the reaction of tri-substituted **1a** with tri-substituted **1b** afforded cross-coupling products **5a** in 27% yield. When tri-substituted **1a** with di-substituted phenols **1e** and **1f** were subjected to anodic oxidation under standard conditions, **5b** and **5c** were isolated after column chromatograph in 18% and 25% yields (85% and 67% yields based on the recovered **1b**), respectively. Notably, the reactions were clear and highly selective, only cross-coupling products and remaining starting materials were detected by TLC analysis. Similarly, cross-coupling of **1b** with **1e**, **1f**, **1g** and **1h** afforded corresponding products **4d**, **4e**, **4f** and **4g** in 35%, 39%, 39% and 35%, respectively.

Table 4. Cross-coupling of two different phenols [a,b]

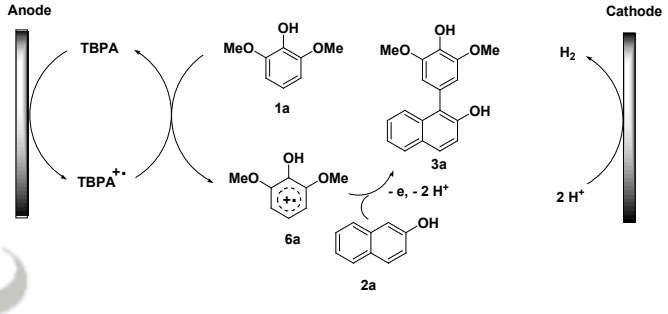


[a] Reaction conditions: equivalent amount of phenols (1.0 mmol) and TBPA (0.1 mmol) in a H-type divided cell containing 10 mL of CH_3CN/ $LiClO_4$ (0.1 M), Pt plate anode and graphite plate as cathode, room temperature, controlled potential at 0.8 V vs $Ag/AgNO_3$.

[b] Isolated yield.

[c] Isolated yield based on the recovered **1a**.

Based on the CV analyses and preparative electrolysis results described above, a TBPA-mediated mechanism for the cross-coupling of phenol-naphthol or phenol-phenol was proposed (Scheme 5). Taking the cross-coupling of **1a** with **2a** as an example, the reaction sequence starts from an electrochemical oxidation of TBPA at the surface of anode to generate its cation radical $TBPA^{+\bullet}$. Subsequent homogeneous electron transfer of $TBPA^{+\bullet}$ with less positive oxidation potential of **1a**, instead of **2a**, forms corresponding cation radical **6a**, which under nucleophilic addition with **2a**, followed by deprotonation and oxidation to give the final product **3a**.



Scheme 5. A proposed mechanism for the TBPA-mediated electrochemical cross-coupling of phenol **1a** and naphthol **2a**

Conclusions

In summary, we have developed an efficient electrochemical access to the non-symmetric biphenols from cross-coupling of phenols or naphthols using TBPA as the redox mediator. The electrochemical protocol provides highly selective cross-coupling products in up to 83% yield, instead of forming homo-coupling ones. Compared with the previous reports on the conventional chemical synthesis of non-symmetric biphenols, this electrochemically dehydrogenative cross-coupling method avoids the use of transition metals and external oxidants, thus providing an appealing alternative to the synthesis of non-symmetric biphenols.

Experimental

Instruments and reagents

All melting points were measured with an Electrothermal melting point apparatus and are uncorrected. NMR spectra were recorded with a 400 MHz spectrometer (400 MHz ^{1}H frequency, 100 MHz ^{13}C frequency). Chemical shifts are given as δ values (internal standard: TMS). Coupling constants are reported in Hz. Other chemicals and solvents were obtained from commercial resource and used without further purification.

Cyclic voltammetry

Cyclic voltammograms were measured using a Princeton Applied Research 273A Potentiostat/Galvanostat equipped with electrochemical analysis software, using a conventional three-electrode cell. The working electrode was a Pt disk electrode (ca. ϕ= 1.0 mm). The auxiliary and reference electrodes consisted of a Pt wire and $Ag/AgNO_3$ (0.1 M in CH_3CN), respectively. Pt disk electrode was polished with a polishing cloth before each measurement. All electrodes for CV experiments were obtained from CH Instruments, Inc. USA. The concentration of all tested compounds was 1 mmol L^{-1}, while that of the supporting electrolyte was 0.1 mol L^{-1}

General procedures for the in-cell electrolysis

An H-type cell equipped with a 4G porosity glass frit to separate the anode and cathode compartments was used. A platinum mesh (2 × 3 cm) served as the working electrode, a graphite plate served as the counter electrode and an $Ag/AgNO_3$ (0.1 M) electrode was used as the reference electrode. The solution of 0.1 M $LiClO_4/CH_3CN$ was added to the two compartments (10 mL × 2), each equipped with a magnetic stir bar. Then the substrate **1a** (1.0 mmol), **2a** (1.5 mmol), and the mediator, TBPA (10 mol %), were added to the anodic compartment. After connection to the constant voltage power supply, the electrolysis was performed at a potential of 0.8 V (vs $Ag/AgNO_3$), and terminated when TLC analysis showed that the starting **1a** had been consumed. Then the solvent was removed under reduced pressure and extraction was carried out using CH_2Cl_2 (3 × 15 mL). The combined organic layers were washed with a saturated aqueous NaCl and dried over $MgSO_4$. Purified product was obtained after column chromatography on silica gel using a solvent mixture of petroleum ether and ethyl acetate.

1-(4-Hydroxy-3,5-dimethoxyphenyl)naphthalen-2-ol (**3a**)[6] Yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.91 (s, 6H), 5.33 (s, 1H), 5.73 (s, 1H), 6.65 (s, 2H), 7.27 (d, *J* = 8.8 Hz, 1H), 7.34-7.41 (m, 2H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.81-7.84 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 56.4, 107.5, 117.2, 121.1, 123.3, 124.7, 126.6, 128.1, 128.9, 129.5, 133.5, 134.8, 148.0, 150.4.

1-(4-Hydroxy-3,5-dimethoxyphenyl)naphthalene-2,3-diol (**3b**)[6] Yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.75 (s, 6H), 6.52 (s, 2H), 7.10 (d, *J* = 7.6 Hz, 1H), 7.13-7.20 (m, 2H), 7.31 (d, *J* = 8.0 Hz, 1H), 7.62 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d6) δ 56.5, 108.7, 123.0, 123.3, 124.7, 126.3, 126.6, 128.8, 129.0, 135.0, 144.0, 146.6,148.3.

1-(4-Hydroxy-3,5-dimethoxyphenyl)naphthalene-2,7-diol (**3c**)[6] Yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.88 (s, 6H), 5.30 (s, 1H), 5.46 (s, 1H), 5.73 (s, 1H), 6.63 (s, 2H), 6.80 (d, *J* = 2.2 Hz, 1H), 6.97 (dd, *J* = 8.3 Hz, 2.4 Hz, 1H), 7.12 (d, *J* = 8.8 Hz, 1H), 7.71-7.74 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 56.4, 106.9, 107.5, 114.7, 115.1, 119.8, 124.2, 125.0, 129.3, 129.9, 134.6, 135.1, 147.9, 150.9, 154.6.

1-(2-Hydroxy-4,5-dimethoxyphenyl) naphthalene-2,3-diol (**3d**) Yellow liquid; ^{1}H NMR (400 MHz, CDCl3) δ 3.97 (s, 3H), 3.98 (s, 3H), 5.62 (s, 1H), 6.15 (s, 2H), 7.07 (d, *J* = 6.0 Hz, 2H), 7.21 (s, 2H), 7.28-7.30 (m, 2H), 7.33 (s, 1H), 7.60-7.62 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 56.3, 60.7, 102.0, 104.1, 110.0, 117.2, 124.0, 126.2, 129.5, 142.2, 144.5, 145.7, 146.0, 148.6, 150.6, 171.8; IR (KBr)(cm^{-1}): ν 3445, 3095, 2922, 2851, 1636, 1474, 1283, 1073; HRMS(ESI): calcd for [(C18H15O5)] (M-H) 311.0927, found: 311.0925.

1-(2-Hydroxy-4,5-dimethoxyphenyl) naphthalene-2,7-diol (**3e**) Yellow liquid; ^{1}H NMR (400 MHz, CDCl3) δ 3.98 (s, 3H), 3.99 (s, 3H), 5.10 (s, 1H), 5.60 (s, 1H), 6.92-6.95 (m, 1H), 6.99 (s, *J* = 2.4 Hz, 1H), 7.08 (d, *J* = 4.4 Hz, 3H), 7.33 (s, 1H), 7.65 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 56.3, 60.7, 102.0, 104.1, 110.0, 117.2, 124.0, 126.2, 129.5, 142.2, 144.5, 145.7, 146.0, 148.6, 150.6, 171.8; IR (KBr)(cm^{-1}): ν 3445, 3095, 2922, 2851, 1636, 1474, 1283, 1073; HRMS (ESI): calcd for C18H15O5 (M-H) 311.2958, found: 311.2955.

1-(2-Hydroxy-4-methoxy-5-methylphenyl) naphthalen-2-ol (**3f**)[13] Yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.38 (s, 3H), 3.99 (s, 3H), 5.43 (s, 1H), 5.62 (s, 1H), 6.74 (s, 1H), 6.86 (s, 1H), 7.28-7.42 (m, 3H), 7.48 (d, *J* = 7.9 Hz, 1H), 7.82-7.84 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.2, 56.1, 112.0, 117.8, 119.3, 123.3, 124.4, 124.8, 126.5, 128.1, 128.4, 129.2, 129.8, 130.4, 133.1, 141.7, 147.2, 150.8.

1-(2-Hydroxy-4-methoxy-5-methylphenyl)naphthalene-2,3-diol (**3g**) [13] Yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.38 (s, 3H), 4.00 (s, 3H), 5.86 (s, 1H), 5.98 (s, 1H), 6.07 (s, 1H), 6.77 (s, 1H), 6.85 (s, 1H), 7.24 (d, *J* = 7.2 Hz, 1H), 7.35-7.31 (m, 2H), 7.50 (d, *J* = 8.4 Hz, 1H), 7.71 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.7, 55.6, 109.4, 111.3, 117.7, 119.1, 123.4, 123.7, 124.1, 124.5, 126.3, 127.3, 129.8, 129.8, 140.3, 140.4, 144.6, 146.5.

1-(2-Hydroxy-3-methoxy-5-methylphenyl)naphthalene-2,7-diol (**3h**) Yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.37 (s, 3H), 3.96 (s, 3H), 5.38 (s, 1H), 5.59 (s, 1H), 6.71 (s, 1H), 6.76 (s, 1H), 6.83 (s, 1H), 6.93-6.95 (m, 1H), 7.13 (d, *J* = 8.8 Hz, 1H), 7.69-7.74 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.8, 55.7, 106.6, 111.7, 114.6, 114.7, 114.9, 118.9, 123.8, 124.2, 129.4, 129.8, 130.1, 134.2, 141.3, 146.9, 151.1, 153.9,; IR (KBr) (cm^{-1}): ν 1461, 1492, 1513, 1624, 1698, 2850, 2919, 3423. HRMS (ESI): calcd for $C_{18}H_{18}O_4$ (M+H) 297.1119, found 297.1121.

1-(2-Hydroxy-5-methoxyphenyl) naphthalen-2-ol (**3i**)[13] Yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.79 (s, 3H), 4.65 (s, 1H), 5.42 (s, 1H), 6.81-6.82 (m, 1H), 6.99-7.02 (m, 1H), 7.09 (d, *J* = 8.9 Hz, 1H), 7.30 (d, *J* = 8.9 Hz, 1H), 7.39-7.43 (m, 3H), 7.84-7.89 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 60.5, 115.8, 117.9, 118.0, 118.4, 122.6, 123.6, 124.5, 126.9, 128.2, 129.2, 130.2, 133.3, 146.5, 151.2, 154.1

6-bromo-1-(4-hydroxy-3,5-dimethoxyphenyl)naphthalen-2-ol (**3j**)[11d] Yellow solid，mp 186^{o}C; ^{1}H NMR (400 MHz, d_6-DMSO) δ 3.74 (s, 6H), 6.51 (s, 2H), 7.28 (d, *J* = 9.2 Hz, 1H), 7.35-7.44 (m, 2H), 7.75 (d, *J* = 5.6 Hz, 1H), 8.06 (d, *J* = 1.6 Hz, 1H), 8.44 (s, 1H),9.51(s, 1H),; ^{13}C NMR (100 MHz, d_6-DMSO) δ 56.5×2, 108.7×2, 115.8, 120.0, 122.3, 125.9, 127.3, 128.0, 129.3, 129.5, 129.9, 133.0, 135.2, 148.4×2, 152.7.

1,4-Bis(4-hydroxy-3,5-dimethoxyphenyl)naphthalene-2,3-diol (**4a**) [6] Brick red solid; ^{1}H NMR (400 MHz, $CDCl_3$) 3.93 (s, 12H), 5.71 (s, 4H), 6.70 (s, 4H), 7.28-7.32 (m, 2H), 7.54 (dd, *J* = 6.3 Hz, 3.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 51.7, 102.7, 117.0, 119.4, 120.2, 120.4, 123.8, 130.0, 136.0, 143.0.

1,4-Bis(2-hydroxy-5-methoxyphenyl)naphthalene-2,3-diol (**4b**) Yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.79 (s, 6H), 5.20 (s, 2H), 6.34 (s, 1H), 6.78-6.83 (m, 6H), 7.22 (s, 1H), 7.30-7.32 (m, 1H), 7.59-7.62 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.9, 110.1, 115.0, 116.1, 124.1, 126.2, 129.5, 144.3, 149.5, 153.7; IR (KBr)(cm^{-1}): ν 3385, 3095, 2925, 1649, 1511, 1473, 1473, 1262,1163; HRMS (ESI): calcd for $C_{24}H_{19}O_6$ (M-H)$^+$ 403.1192, found 403.1187.

3,3',5'-Trimethoxy-5-methyl-[1,1'-biphenyl]-2,4'-diol (**5a**)[6] Yellow semisolid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.25 (s, 3H), 3.90 (s, 6H), 3.93 (s, 3H), 5.55 (s, 2H), 6.53 (s, 2H), 6.77 (s, 1H), 6.86 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.1, 56.1, 56.3, 56.4, 106.2, 112.7,

116.0, 126.8, 132.8, 133.5, 134.9, 143.2, 145.5, 146.6.

3',5'-Dimethoxy-5-methyl-[1,1'-biphenyl]-2,4'-diol (**5b**)[11d] ^{1}H NMR (400 MHz, CDCl3) δ 2.34 (s, 3H), 3.93 (s, 6H), 5.22 (s, 1H), 5.62 (s, 1H), 6.67 (s, 2H), 6.90 (d, *J* = 8.4 Hz, 1H), 7.06-7.13 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.5, 56.4, 105.7, 115.5, 127.9, 128.1, 129.5, 129.9, 130.4, 134.4, 147.6, 150.2.

5-(tert-Butyl)-3',5'-dimethoxy-[1,1'-biphenyl]-2,4'-diol (**5c**)[11d] Brown solid; mp 138-140 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (s, 9H), 3.94 (s, 6H), 5.21 (s, 1H), 5.62 (s, 1H), 6.69 (s, 2H), 6.95 (d, *J* = 8.4 Hz, 1H), 7.24 (d, *J* = 2.4 Hz, 1H), 7.32 (dd, *J* = 8.8 Hz, 2.4 Hz, 1H); ^{13}C NMR (100 MHz, CDCl3) δ 31.6, 34.2, 56.4, 105.9, 115.1, 126.0, 126.8, 127.5, 128.4, 134.5, 143.4, 147.6, 150.2.

3-Methoxy-5,5'-dimethyl-[1,1'-biphenyl]-2,2'-diol (**5d**)[6] Yellow syrup; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.35 (s, 3H), 2.37 (s, 3H), 3.96 (s, 3H), 6.18 (s, 1H), 6.25 (s, 1H), 6.76 (s, 1H), 6.77 (s, 1H), 6.97 (d, *J* = 8.8 Hz, 1H), 7.10-7.13 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1, 21.2, 56.2, 112.4, 117.6, 123.4, 123.9, 125.2, 127.4, 129.9, 130.5, 131.3, 139.4, 145.9, 151.3.

5'-(tert-Butyl)-3-methoxy-5-methyl-[1,1'-biphenyl]-2,2'-diol (**5e**)[6] Yellow liquid; ^{1}H NMR (400 MHz, CDCl3) δ 1.35 (s, 9H), 2.38 (s, 3H), 3.96 (s, 3H), 6.22 (s, 1H), 6.28 (s, 1H), 6.75 (m, 2H), 6.99-7.05 (m, 1H), 7.30 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3, 34.2, 56.2, 110.9, 117.2, 123.9, 124.4, 124.6, 126.4, 127.8, 130.6, 139.3, 143.7, 146.3, 151.2.

3-Methoxy-3',5,5'-trimethyl-[1,1'-biphenyl]-2,2'-diol (**5f**)[6] Yellow semisolid; ^{1}H NMR (400 MHz, CDCl3) δ 2.23 (s, 3H), 2.25 (s, 3H), 2.33 (s, 3H), 3.91 (s, 3H), 6.15 (s, 1H), 6.21 (s, 1H), 6.71 (s, 1H), 6.74 (s, 2H), 6.86 (s, 1H), 7.05 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.9, 19.6, 21.3, 56.2, 110.8, 118.9, 122.6, 123.8, 124.0, 129.1, 130.5, 131.7, 138.0, 139.3, 146.3, 151.4.

3-Methoxy-5-methyl-[1,1'-biphenyl]-2,3',4'-triol (**5g**)[6] Yellow liquid; ^{1}H NMR (400 MHz, CDCl3) δ 2.21 (s, 3H), 3.91 (s, 3H), 5.24 (s, 1H), 5.44 (s, 1H), 6.73 (s, 1H), 6.74 (d, *J*= 1.88 Hz, 1H), 6.80 (s, 1H), 6.81 (d, *J* = 1.9 Hz, 1H), 6.88 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.1, 56.0, 112.7, 115.0, 116.0, 116.6, 122.1, 127.1, 134.3, 134.7, 142.4, 143.0, 143.2, 145.4.

Supporting Information

The supporting information for this article is available on the WWW under https://doi.org/10.1002/cjoc.2018xxxxx.

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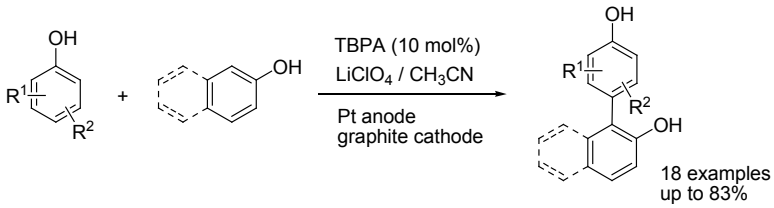
Electrocatalytic synthesis of non-symmetric biphenols mediated by tri(p-bromophenyl)amine (TBPA): selective oxidative cross-coupling of different phenols and naphthols



Electrochemical cross-coupling of unprotected phenol with naphthols and phenols using TBPA as mediator has reported.

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