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Cite this: *RSC Adv.*, 2013, **3**, 20150

Copper-catalyzed oxidative aromatization of 2-cyclohexen-1-ones to phenols in the presence of catalytic hydrogen bromide under molecular oxygen†

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Received 19th June 2013
Accepted 16th August 2013

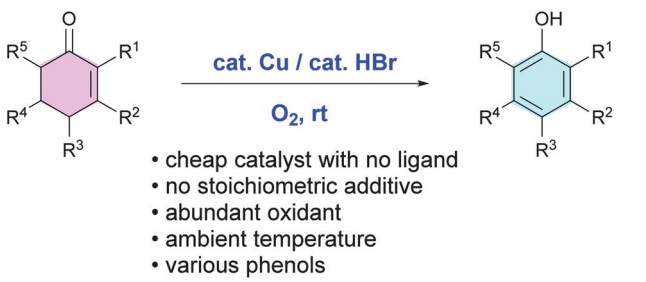
DOI: 10.1039/c3ra43071e

www.rsc.org/advances

Catalytic oxidative aromatization has been achieved using 2-cyclohexen-1-ones to obtain phenol derivatives in the presence of a catalytic amount of copper salt and aqueous HBr under molecular oxygen. The amount of HBr was successfully reduced to a catalytic quantity, and the other additive such as a ligand and an oxidant as well as inert conditions were unnecessary. Various mono-, di-, and trisubstituted phenols with substituents at the desired positions could be synthesized under cheap and simple conditions. An oxidative aromatization/bromination sequence was also demonstrated to obtain bromophenols with excess HBr.

Introduction

Phenol derivatives are among the most important chemicals used for industrial materials, including polymers and plastics, and are core structures of many biologically active compounds and pharmaceuticals.[1] Additionally, recent developments in dearomatization strategies[2] and transition-metal-catalyzed cross-coupling using phenol derivatives[3] have been reminders that phenol derivatives are useful precursors in total synthesis and materials science. Typical electrophilic aromatic substitution reactions produce *ortho*- and/or *para*-substituted phenols, promoted by the strong electronic directing effect of the hydroxy group. In contrast, preparation of *meta*-substituted phenol derivatives is still a challenge, despite efforts to achieve *meta* substitution through C–H functionalization induced by transition-metal catalysts.[4] Hydroxylation of a functional group such as a boron[4e,5a] or halogen[5b–g] moiety, and direct oxidation of aromatic C–H bonds using directing groups,[6] are useful ways of introducing hydroxy groups into arenes to give phenol derivatives. In these synthetic methods, however, preinstallation of leaving groups or directing groups is necessary. Oxidative aromatization of 2-cyclohexen-1-one derivatives is an attractive alternative synthetic approach to produce various customized phenol derivatives, allowing installation of substituents at the desired positions.[7–13] Much effort has been focused on oxidative aromatization procedures, but some of these are low yields[7] and most of the reactions require stoichiometric amounts of oxidants,[8] a high temperature,[9] or a long reaction time.[10] The development of highly efficient catalytic aromatization procedures is therefore desirable, and could provide useful synthetic methods. Phenols have been produced under acceptable conditions by transition-metal-catalyzed oxidative aromatization reactions using vanadium[11] or palladium salts[12] as catalysts. The former reaction proceeds *via* bromination/dehydrobromination induced by a system consisting of a vanadium salt and a sub-stoichiometric amount of HBr (>50 mol%), and the latter requires a combination of a palladium salt and a pyridine ligand; the reactions were performed at a relatively high temperature (80 °C) in both cases. Very recently, Li's group reported the preparation of an aryl ether from 2-cyclohexen-1-one and an aliphatic alcohol in the presence of a stoichiometric amount of copper, or a copper catalyst combined with a radical source and stoichiometric amounts of additives.[13] The palladium-catalyzed aromatization of cyclic ketones with amines to aryl amines has also been reported by Yoshikai's group and Li and Deng's group.[14] However, these reactions are expensive and require high temperatures. Here we describe the preparation of various mono-, di-, and trisubstituted phenols, with the substituents at the desired positions, *via* an oxidative aromatization reaction that uses a cheap and



Scheme 1 This work.

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† Electronic supplementary information (ESI) available: General procedure, additional screening, and spectral data. See DOI: 10.1039/c3ra43071e

ligand-free copper catalyst combined with catalytic HBr under mild conditions (Scheme 1).

Results and discussion

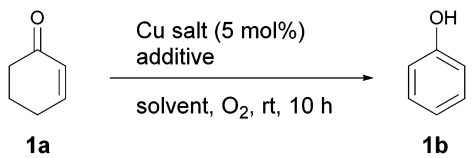
Initial studies and reaction optimization

We began our investigation of efficient oxidative aromatization by examining the reaction of 2-cyclohexen-1-one (**1a**) with various copper salts and a stoichiometric amount of HBr (1.05 equiv.) at room temperature under molecular oxygen (see ESI, Table S1†). After the several screenings, the reaction using $CuBr_2$ as a catalyst in 1,4-dioxane was found to be the best combination, giving phenol (**1b**) in 80% yield (Table 1, entry 1), although all the copper salts tested exhibited similar catalytic activities for oxidative aromatization under the present conditions. This reaction system did not work in the absence of molecular oxygen or HBr (Table 1, entries 2 and 3). The use of HCl instead of HBr afforded **1b** in moderate yield (Table 1, entry 4). The reaction using CF_3COOH/Bu_4NBr resulted in a low yield (Table 1, entry 5). These results show that molecular oxygen and HBr are essential for the reaction to proceed. When $CuBr_2$ was used as a catalyst, the amount of HBr used was successfully reduced to 20 mol%, producing **1b** in 90% yield (Table 1, entry 6), whereas other copper salts were less effective as catalysts (Table 1, entries 7–13).

Substrate scope

The present reaction system was used in the oxidative aromatization of various 2-cyclohexen-1-one derivatives to phenols

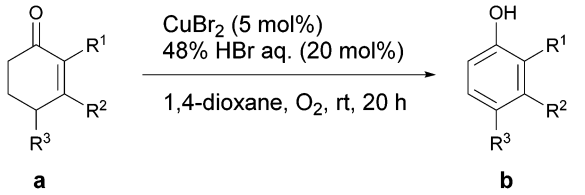
Table 1 Optimization of reaction conditions[a]

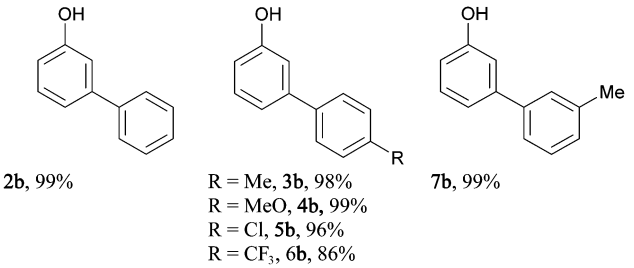


Entry	Cu salt	Additive/mol%	Time/h	Yield[b] (%)
1	$CuBr_2$	48% HBr aq. (105)	10	80
2[c]	$CuBr_2$	48% HBr aq. (105)	10	2
3	$CuBr_2$	—	10	3
4	$CuBr_2$	36% HCl aq. (105)	10	43
5	$CuBr_2$	CF_3COOH (105)/Bu_4NBr (105)	10	2
6	$CuBr_2$	48% HBr aq. (20)	20	90
7	$CuCl_2$	48% HBr aq. (20)	20	71
8	$Cu(OAc)_2$	48% HBr aq. (20)	20	17
9	$CuSO_4$	48% HBr aq. (20)	20	29
10	CuO	48% HBr aq. (20)	20	8
11	Cu_2O[d]	48% HBr aq. (20)	20	35
12	CuI	48% HBr aq. (20)	20	9
13	CuBr	48% HBr aq. (20)	20	65

[a] *Conditions*: 0.50 mmol of 2-cyclohexen-1-one (**1a**), 0.025 mmol of copper salt, additive, 1,4-dioxane (1.0 mL) at rt. [b] Determined by GC using dodecane as an internal standard. [c] Under argon atmosphere. [d] 0.0125 mmol of Cu_2O was used.

Table 2 Synthesis of monosubstituted phenols[a]

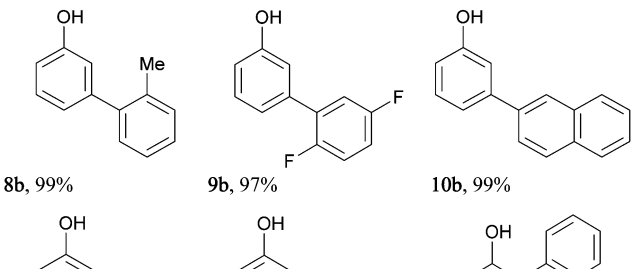




2b, 99%

R = Me, **3b**, 98%
R = MeO, **4b**, 99%
R = Cl, **5b**, 96%
R = CF_3, **6b**, 86%

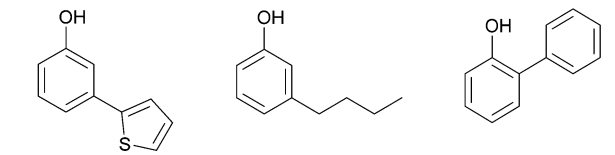
7b, 99%



8b, 99%

9b, 97%

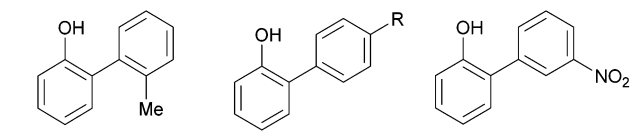
10b, 99%



11b, 73%, 99%[b]

12b, 97%[b], 76%[c,d]

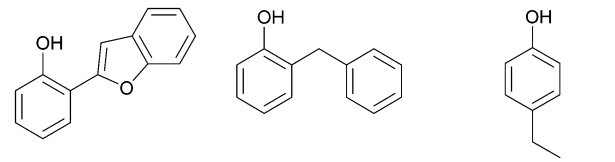
13b, 96%[e]



14b, 97%[e]

R = MeO, **15b**, 92%[f]
R = Cl, **16b**, 99%[e]
R = CN, **17b**, 99%[e]
R = Ac, **18b**, 82%[e]

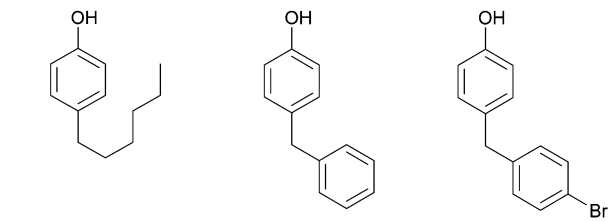
19b, 92%[e]



20b, 95%[e]

21b, 99%[c]

22b, 69%



23b, 80%

24b, 77%

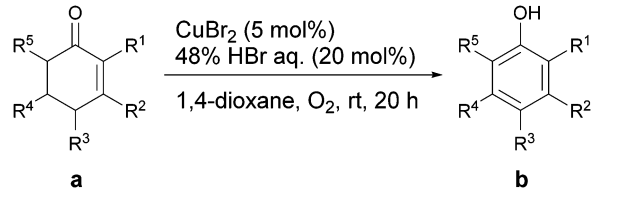
25b, 82%

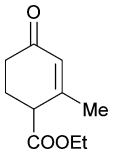
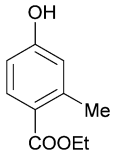
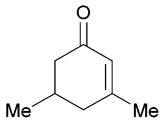
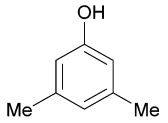
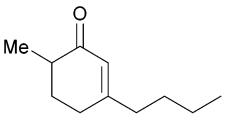
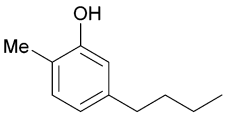
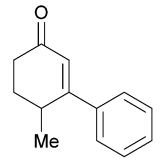
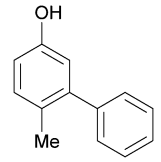
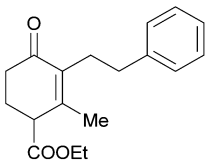
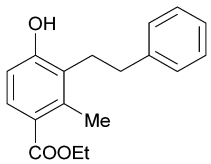
[a] *Conditions*: 0.25 mmol of substrate, 0.0125 mmol of $CuBr_2$, 0.050 mmol of 48% HBr aq., 1,4-dioxane (0.50 mL), rt. [b] In the presence of 0.25 mmol of 48% HBr aq. for 10 h. [c] Reaction at 100 °C. [d] For 10 h. [e] For 30 h. [f] For 40 h.

(Table 2). First, the oxidative aromatization reactions of 3-aryl-2-cyclohexen-1-ones were examined; the desired reaction proceeded to give the corresponding *meta*-substituted phenols in almost quantitative yields. 3-Phenylphenol (**2b**) and 3-tolylphenols (**3b**, **7b**, and **8b**) were smoothly synthesized from the corresponding 2-cyclohexen-1-ones in quantitative yields. Substrates bearing various functional groups underwent aromatization to furnish the corresponding phenols **4–6b**, **9b**, and **10b** in high yields. It should be noted that 2-cyclohexen-1-one bearing a heteroarene, namely a thienyl group, was also successfully aromatized to give the corresponding phenol **11b** in high yield, without deactivation of the catalyst. 3-Butyl-2-cyclohexen-1-one also reacted with high efficiency and alkylphenol **12b** was obtained, although heating or a stoichiometric amount of HBr was required. We then tested 2-substituted-2-cyclohexen-1-ones, and good to excellent yields were obtained with various *ortho*-arylphenols. 2-Phenylphenol (**13b**) was isolated in 96% yield. The reactions of 2-aryl-2-cyclohexen-1-ones with a methyl, methoxy, or chlorine substituents proceeded to give the corresponding phenols **14–16b** in quantitative yields. Substrates bearing cyano, nitro, or acetyl groups were also converted to the functionalized biphenyls **17–19b**, which could undergo further transformations. 2-(2-Benzofuranyl)phenol (**20b**) was also easily obtained in high yield. The reaction of 2-alkyl-2-cyclohexen-1-one also proceeded and 2-benzylphenol (**21b**) was afforded in 99% yield under heating conditions. Moreover, 2-cyclohexen-1-ones with substituents at 4-position also served as reaction substrates for the present aromatization reaction. *para*-Alkyl- and benzylphenols (**22–25b**) were obtained under the standard conditions in satisfactory yields.

Di- or trisubstituted cyclohexenones were also used as reaction substrates in the present system, giving the corresponding phenols (Table 3). The reaction of commercially available 4-methoxy-carbonyl-3-methyl-2-cyclohexen-1-one afforded the corresponding phenol **26b**, despite the presence of an ester group. Dialkylphenol such as 3,5-dimethylphenol (**27b**) and 3-butyl-6-methylphenol (**28b**) were obtained in moderate yields, respectively. The use of a stoichiometric amount of HBr improved the yield of **27b** under heating conditions. When 3-phenyl-4-methyl-2-cyclohexen-1-one was used as the substrate, the corresponding phenol **29b** was afforded in high yield at room temperature. Trisubstituted phenol such as **30b** was also successfully synthesized by copper-catalyzed aromatization.

Table 3 Synthesis of di- or trisubstituted phenols[a]

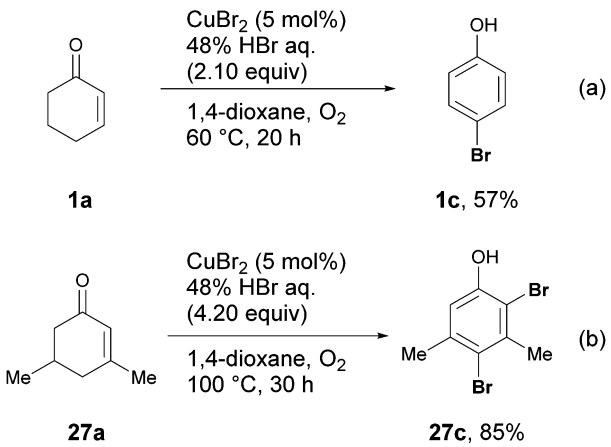


Substrate	Product	Yield (%)
		**26b** 92
		**27b** 66, 93[b,c]
		**28b** 66
		**29b** 88
		**30b** 86[c]

[a] *Conditions*: 0.25 mmol of substrate, 0.0125 mmol of $CuBr_2$, 0.050 mmol of 48% HBr aq., 1,4-dioxane (0.50 mL), rt. [b] Reaction using 0.25 mmol of 48% HBr aq. at 100 °C. [c] For 30 h.

Oxidative aromatization/bromination sequence

The present reaction system was found to provide an oxidative aromatization/bromination reaction sequence in the presence of excess amounts of HBr at high temperatures (Scheme 2). The reaction of **1a** with 5 mol% $CuBr_2$ and 2.0 equiv. of HBr at 60 °C furnished 4-bromophenol (**1c**) in moderate yield (Scheme 2, eqn (a)). The dibromide **27c** was obtained from **27a** in the presence of 4.0 equiv. of HBr (Scheme 2, eqn (b)). Copper-catalyzed bromination of arenes with a bromide salt in acetic acid has already been reported by Stahl's group.[15] It is suggested that the bromination reaction proceeded after oxidative aromatization under the present conditions.

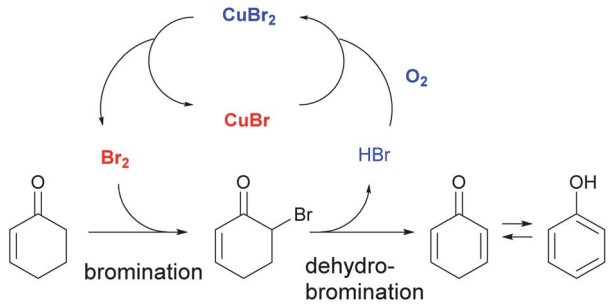


Scheme 2 Oxidative aromatization/bromination sequence.

Reaction pathway

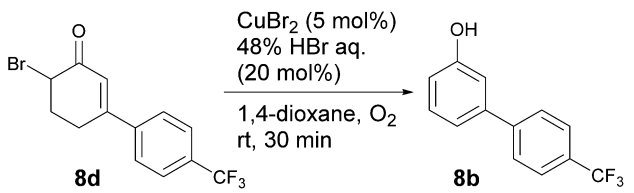
A plausible reaction pathway for the oxidative aromatization reaction is illustrated in Scheme 3. Initially, copper(II) species would generate molecular bromine along with reduced copper(I) species, as reported in the literature.[15] Bromination of 2-cyclohexen-1-one occurs to give the α-bromination product, which undergoes dehydrobromination followed by transformation to a phenol. The reduced copper(I) would be oxidized by molecular oxygen and HBr to regenerate the copper(II) species.

To gain insight into the reaction pathway, we investigated whether the present aromatization involves α-bromination of 2-cyclohexen-1-one. 6-Bromo-2-cyclohexen-1-one (**8d**) was synthesized separately in two steps, and treated with $CuBr_2$ and/or HBr (Table 4). As expected, the aromatization reaction occurred to give the phenol **8b** in 30 min under the present conditions (Table 4, entry 1), whereas the bromide **8d** was unchanged in the absence of HBr (Table 4, entries 2 and 4). These results suggest that the present aromatization proceeds by the above-mentioned reaction pathway: the bromination reaction occurs first, then the dehydrobromination of the bromide occurs, followed by tautomerization to give the corresponding phenol. The mechanistic details of the bromination and dehydrobromination steps are currently unknown. Further studies are therefore clearly needed to confirm this proposed mechanism, and other mechanisms cannot be ruled out.



Scheme 3 Proposed reaction pathway.

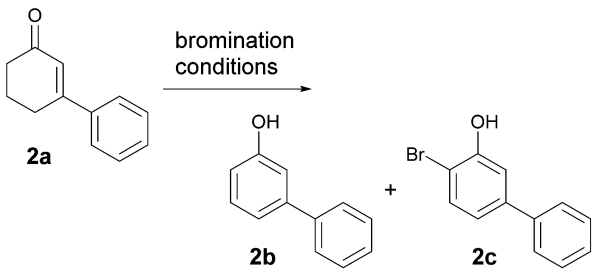
Table 4 Dehydrobromination under several conditions[a]



Entry	$CuBr_2$	48% HBr aq.	8b
1	○	○	Quant.
2	○	—	No reaction
3	—	○	Quant.
4	—	—	No reaction

[a] *Conditions*: 0.20 mmol of **8d**, 0.010 mmol of $CuBr_2$, 0.040 mmol of 48% HBr aq., and 1,4-dioxane (0.50 mL) at rt for 30 min.

Table 5 Aromatization under several bromination conditions[a]



Entry	*Conditions*	Yield (%), **2a** : **2b** : **2c**
1	Bromine (105 mol%),[b] 1,4-dioxane, rt, 20 h	15 : 42 : 43
2	AIBN (5 mol%), NBS (105 mol%), cyclohexane, 85 °C, 30 h	22 : 76 : 0
3	$CuBr_2$ (5 mol%), 48% HBr aq. (105 mol%), 1,4-dioxane, rt, 30 h	0 : 99 : 0

[a] 0.25 mmol of 3-phenyl-2-cyclohexen-1-one (**2a**) was used. [b] Slow addition.

Next, the reactions of **2a** under several bromination conditions were conducted (Table 5). When **2a** was treated with molecular bromine, the oxidative aromatization reaction occurred, giving the phenol (**2b**, 42%) and bromophenol (**2c**, 43%), with recovery of **2a** (Table 5, entry 1). Molecular bromine is considered to serve as an oxidant and/or brominating reagent, inducing aromatization and bromination. This result indicates that the present aromatization reaction proceeds through the above-mentioned bromination/dehydrobromination reaction sequence. A catalytic combination of azobisisobutyronitrile (AIBN) and *N*-bromosuccinimide (NBS) also produced **2b**, although the yield was moderate, even at high temperatures (Table 5, entry 2), showing that the reaction was induced by molecular bromine generated *in situ* rather than by bromine radicals. Compared with these results, the present reaction system provided **2b** in 99% yield, with a trace amount of **2c**, even in the presence of a stoichiometric amount of HBr (Table 5, entry 3). Under the present conditions, it is considered that the bromination species generates slowly and the formation of bromophenol might be suppressed.

Conclusions

In conclusion, we have developed the first copper-catalyzed phenol synthesis through oxidative aromatization of 2-cyclohexen-1-one derivatives in the presence of catalytic HBr and molecular oxygen. This reaction system efficiently produces various phenols under cheap and simple conditions. Further investigations into the mechanism of this transformation and its application to other organic synthetic reactions are currently underway in our laboratory.

Experimental

General

All ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra were recorded using a JEOL JNM-LA400 spectrometer. Proton chemical shifts are reported relative to residual solvent peak $CDCl_3$ at δ 7.26 ppm. Carbon chemical shifts are reported relative to $CDCl_3$ at δ 77.00 ppm. NMR spectra are reported as follows: chemical shift (multiplicity, coupling constants, number of hydrogens). High-resolution mass spectrometry was performed on a JEOL JMS-700 MStation at the Mass Spectrometry Facility (Okayama University). Gas chromatographic analysis was conducted with Shimadzu GC-2014 equipped with FID detector and the chemical yields were determined using dodecane as an internal standard. Flash chromatography separations were performed on KANTO CHEMICAL Silica Gel 60 (spherical, 40–50 mesh). Thin layer chromatography was performed using Merck TLC silica gel 60 F_{254} Aluminum sheets and visualized by UV irradiation, phosphomolybdic acid, and iodine staining. All commercially available compounds were purchased and used as received. Solvents 1,4-dioxane, MeCN, THF, Et_2O, toluene, dichloromethane, and cyclohexane were purchased from Wako Pure Chemical Industries and used as received. Diisopropylamine and chlorotrimethylsilane were distilled over calcium hydride prior to use.

General procedure for the copper-catalyzed oxidative aromatization

A screw-capped test tube (20 mL) was charged with $CuBr_2$ (0.0125 mmol, 2.79 mg, 5 mol%), 1,4-dioxane (1.0 mL), 2-cyclohexen-1-one, and 48% HBr aq. (0.05 mmol, 6.0 μL, 20 mol %). The tube was filled with oxygen gas and then sealed. The reaction mixture was stirred at room temperature for 20 h and then the solvent was removed under vacuum. The residue was directly charged onto a chromatography column (SiO_2, 1 cm × 10 cm, AcOEt–hexane = 1 : 25), and the desired product was obtained.

Biphenyl-3-ol (2b). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 8.0 Hz, 2H), 7.44 (t, J = 8.0 Hz, 2H), 7.38 (t, J = 8.0 Hz, 1H), 7.32 (t, J = 8.0 Hz, 1H), 7.19 (dd, J = 0.9, 7.7 Hz, 1H), 7.08 (dd, J = 1.6, 2.4 Hz, 1H), 6.84 (dd, J = 2.4, 8.0 Hz, 1H), 5.15 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.77, 142.98, 140.68, 129.97, 128.72, 127.46, 127.08, 119.76, 114.18, 114.08.

4′-Methylbiphenyl-3-ol (3b). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 8.0 Hz, 2H), 7.31 (t, J = 8.0 Hz, 1H), 7.25 (d, J = 8.0 Hz, 2H), 7.17 (dd, J = 0.8, 7.6 Hz, 1H), 7.06 (t, J = 2.0 Hz, 1H), 6.81 (dd, J = 2.5, 8.0 Hz, 1H), 5.09 (s, 1H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.71, 142.90, 137.77, 137.26, 129.92, 129.44, 126.90, 119.57, 113.88, 113.86, 21.06.

4′-Methoxylbiphenyl-3-ol (4b). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 8.0 Hz, 2H), 7.31 (t, J = 8.0 Hz, 1H), 7.25 (d, J = 8.0 Hz, 2H), 7.18 (dd, J = 0.9, 7.9 Hz, 1H), 7.06 (dd, J = 1.9, 2.1 Hz, 1H), 6.82 (dd, J = 2.4, 8.0 Hz, 1H), 5.09 (s, 1H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.13, 155.79, 142.50, 133.25, 129.92, 128.08, 119.27, 114.17, 113.61, 113.59, 112.73, 55.34.

4′-Chlorobiphenyl-3-ol (5b). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 8.0 Hz, 2H), 7.39 (d, J = 8.0 Hz, 2H), 7.31 (t, J = 7.9 Hz, 1H), 7.13 (dd, J = 0.8, 7.7 Hz, 1H), 7.03 (dd, J = 1.7, 2.3 Hz, 1H), 6.84 (dd, J = 2.4, 7.9 Hz, 1H), 5.19 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.81, 141.71, 139.08, 133.53, 130.12, 128.86, 128.29, 119.59, 114.51, 113.91.

4′-(Trifluoromethyl)biphenyl-3-ol (6b). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 8.8 Hz, 2H), 7.65 (d, J = 8.8 Hz, 2H), 7.35 (t, J = 8.0 Hz, 1H), 7.18 (ddd, J = 0.7, 0.8, 7.7 Hz, 1H), 7.08 (dd, J = 1.7, 2.3 Hz, 1H), 6.89 (dd, J = 2.5, 8.0 Hz, 1H), 5.12 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.86, 144.15 (J_{CF} = 1.2 Hz), 141.51, 130.26, 129.52 (J_{CF} = 32.3 Hz), 127.35, 125.68 (J_{CF} = 3.7 Hz), 124.24 (J_{CF} = 270.5 Hz), 119.93, 115.11, 114.22.

3′-Methylbiphenyl-3-ol (7b). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24–7.22 (m, 3H), 7.21–7.17 (m, 2H), 6.86 (ddd, J = 1.1, 1.5, 7.6 Hz, 1H), 6.80–6.76 (m, 2H), 5.09 (s, 1H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.09, 143.63, 141.43, 135.27, 130.27, 129.57, 129.26, 127.32, 125.69, 121.87, 116.16, 113.69, 20.37.

2′-Methylbiphenyl-3-ol (8b). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.38 (m, 2H), 7.36–7.30 (m, 2H), 7.20–7.17 (m, 2H), 7.08 (dd, J = 1.9, 2.3 Hz, 1H), 6.83 (ddd, J = 0.9, 2.4, 8.0 Hz, 1H), 5.14 (s, 1H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.71, 143.10, 140.66, 138.30, 129.90, 128.62, 128.20, 127.88, 124.17, 119.77, 114.08, 21.48.

2′,5′-Difluorobiphenyl-3-ol (9b). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (t, J = 7.9 Hz, 1H), 7.15–7.07 (m, 3H), 7.03–6.97 (m, 2H), 6.88 (ddd, J = 0.8, 2.7, 8.1 Hz, 1H), 5.09 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.70 (J_{CF} = 2.5, 241.3 Hz), 155.65 (J_{CF} = 2.5, 241.3 Hz), 155.50, 136.30 (J_{CF} = 1.6 Hz), 129.84 (J_{CF} = 8.0 Hz), 129.83, 121.44 (J_{CF} = 3.1 Hz), 117.15 (J_{CF} = 8.8, 25.9 Hz), 116.80 (J_{CF} = 3.7, 24.3 Hz), 115.88 (J_{CF} = 3.5 Hz), 115.31 (J_{CF} = 8.8, 23.9 Hz), 115.19; HRMS (EI): m/z calcd for $C_{12}H_8OF_2$ ($[M]^+$) 206.0543, found 206.0551.

3-(Naphthalen-2-yl)phenol (10b). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (s, 1H), 7.92–7.87 (m, 3H), 7.72 (dd, J = 1.9, 8.5 Hz, 1H), 7.55–7.49 (m, 2H), 7.37 (t, J = 7.7 Hz, 1H), 7.33 (tt, J = 1.3, 7.7 Hz, 1H), 7.20 (dd, J = 1.6, 2.4 Hz, 1H), 6.88 (ddd, J = 2.4, 2.5, 7.9 Hz, 1H), 5.12 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.80, 142.86, 137.97, 133.55, 132.68, 130.07, 128.38, 128.19, 127.60, 126.29, 125.99, 125.80, 125.42, 120.05, 114.31, 114.28; HRMS (EI): m/z calcd for $C_{16}H_{12}O$ ($[M]^+$) 220.0888, found 220.0876.

3-(Thiophen-2-yl)phenol (11b). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30–7.20 (m, 4H), 7.10 (t, J = 2.0 Hz, 1H), 7.07 (ddd, J = 0.5, 3.6, 5.1 Hz, 1H), 6.76 (ddd, J = 1.2, 2.3, 7.9 Hz, 1H), 5.09 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.74, 143.82, 135.94, 130.14, 127.95, 124.95, 123.33, 118.65, 114.43, 112.78.

3-Butylphenol (12b). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (t, J = 7.7 Hz, 1H), 6.77 (d, J = 7.7 Hz, 1H), 6.70–6.63 (m, 2H), 4.88 (s, 1H), 2.57 (t, J = 7.7 Hz, 2H), 1.59 (tt, J = 7.2, 7.7 Hz, 1H), 1.36 (qt, J = 7.2, 7.5 Hz, 2H), 0.93 (s, J = 7.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.34, 144.91, 129.35, 120.99, 115.30, 112.45, 35.47, 33.40, 22.31, 13.92.

Biphenyl-2-ol (13b). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52–7.48 (m, 4H), 7.44–7.40 (m, 1H), 7.31–7.27 (m, 2H), 7.05–7.01 (m, 2H), 5.28 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.37, 137.04, 130.21, 129.22, 129.11, 129.06, 128.09, 127.82, 120.81, 115.79.

2′-Methylbiphenyl-2-ol (14b). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.33 (m, 2H), 7.32–7.21 (m, 4H), 7.12 (dd, J = 1.6, 7.7 Hz, 1H), 7.01–6.96 (m, 2H), 4.74 (s, 1H), 2.18 (s, 3H); ^{13}C NMR (100

MHz, $CDCl_3$) δ 152.46, 137.39, 135.67, 130.64, 130.45, 130.12, 129.09, 128.49, 127.67, 126.42, 120.42, 115.27, 19.72.

4′-Methoxybiphenyl-2-ol (15b). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, J = 8.3 Hz, 2H), 7.24–7.20 (m, 2H), 7.02 (d, J = 8.3 Hz, 2H), 6.99–6.96 (m, 2H), 5.15 (s, 1H), 3.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.22, 152.47, 130.22, 13021, 129.17, 128.72, 127.79, 120.71, 116.67, 115.63, 114.62, 55.29.

4′-Chlorobiphenyl-2-ol (16b). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 8.8 Hz, 2H), 7.42 (d, J = 8.8 Hz, 2H), 7.29–7.22 (m, 2H), 7.00 (dt, J = 1.2, 3.5 Hz, 1H), 6.96 (dd, J = 1.1, 8.1 Hz, 1H), 5.09 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.27, 135.61, 133.79, 130.47, 130.24, 129.37, 129.23, 127.01, 121.05, 116.01.

4′-Cyanobiphenyl-2-ol (17b). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 8.5 Hz, 2H), 7.66 (d, J = 8.5 Hz, 1H), 7.32–7.26 (m, 2H), 7.04 (dt, J = 0.9, 7.7 Hz, 1H), 6.95 (d, J = 8.1 Hz, 1H), 5.03 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.35, 142.59, 132.41, 130.42, 130.07, 129.93, 126.49, 121.39, 118.82, 116.39, 110.95; HRMS (EI): m/z calcd for $C_{13}H_9ON$ ($[M]^+$) 195.0684, found 195.0703.

4′-Acethylbiphenyl-2-ol (18b). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 8.3 Hz, 2H), 7.63 (d, J = 8.3 Hz, 2H), 7.31–7.27 (m, 2H), 7.02 (t, J = 7.5 Hz, 1H), 6.98 (d, J = 8.3 Hz, 1H), 5.45 (s, 1H), 2.64 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.92, 152.51, 142.55, 135.97, 130.31, 129.74, 129.35, 128.93, 127.12, 121.10, 116.25, 26.64.

3′-Nitrobiphenyl-2-ol (19b). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (t, J = 1.9 Hz, 1H), 8.22 (ddd, J = 1.1, 2.3, 8.3 Hz, 1H), 7.89 (ddd, J = 1.2, 1.6, 7.7 Hz, 1H), 7.63 (t, J = 8.0 Hz, 1H), 7.34–7.29 (m, 2H), 7.06 (dt, J = 1.2, 7.2 Hz, 1H), 6.95 (dd, J = 1.1, 8.1 Hz, 1H), 4.96 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.31, 139.38, 135.32, 130.58, 129.98, 129.43, 125.98, 124.25, 122.16, 121.48, 116.36; HRMS (EI): m/z calcd for $C_{12}H_9O_3N$ ($[M]^+$) 215.0582, found 215.0561.

2-(Benzofuran-2-yl)phenol (20b). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (dd, J = 1.6, 8.0 Hz, 1H), 7.62 (dd, J = 1.6, 6.7 Hz, 1H), 7.55 (dd, J = 1.6, 7.2 Hz, 1H), 7.35–7.27 (m, 3H), 7.18 (s, 1H), 7.11 (d, J = 0.9 Hz, 1H), 7.04–7.00 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.27, 153.95, 153.29, 130.26, 128.48, 127.14, 124.43, 123.41, 120.98, 120.76, 117.37, 116.05, 110.98, 103.31.

2-Benzylphenol (21b). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.30 (m, 2H), 7.26–7.22 (m, 3H), 7.17–7.13 (m, 2H), 6.91 (m, 1H), 6.79 (d, J = 7.5 Hz, 1H), 4.82 (s, 1H), 4.02 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.66, 139.86, 130.94, 128.66, 128.59, 127.78, 126.97, 126.29, 120.90, 115.66, 36.27; HRMS (EI): m/z calcd for $C_{13}H_{12}O$ ($[M]^+$) 184.0888, found 184.0881.

4-Ethlyphenol (22b). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07 (d, J = 8.4 Hz, 2H), 6.77 (d, J = 8.4 Hz, 2H), 4.85 (s, 1H), 2.59 (q, J = 7.5 Hz, 2H), 1.21 (t, J = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.29, 136.55, 128.88, 115.09, 27.93, 15.84.

4-Hexylphenol (23b). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.05 (d, J = 8.5 Hz, 2H), 6.75 (d, J = 8.5 Hz, 2H), 2.53 (t, J = 7.9 Hz, 2H), 1.61–1.52 (m, 2H), 1.33–1.27 (m, 6H), 0.89 (t, J = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.33, 135.20, 129.41, 115.02, 35.03, 31.71, 31.69, 28.90, 22.60, 14.08; HRMS (EI): m/z calcd for $C_{12}H_{18}O$ ($[M]^+$) 178.1358, found 178.1352.

4-Benzylphenol (24b). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (t, J = 7.1 Hz, 2H), 7.21–7.16 (m, 3H), 7.06 (d, J = 8.1 Hz, 2H), 6.75 (s, J = 8.1 Hz, 2H), 4.58 (s, 1H), 3.91 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.76, 141.48, 130.05, 128.80, 128.42, 125.99, 115.25, 41.00.

4-(4-Bromobenzyl)phenol (25b). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, J = 8.7 Hz, 2H), 7.05 (d, J = 6.8 Hz, 1H), 7.03 (d, J = 6.8 Hz, 2H), 6.77 (d, J = 8.7 Hz, 2H), 4.98 (s, 1H), 3.86 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.92, 140.47, 132.69, 131.44, 130.51, 129.99, 119.80, 115.37, 40.34; HRMS (EI): m/z calcd for $C_{13}H_{11}OBr$ ($[M]^+$) 261.9993, found 261.9966.

5-Butyl-2-methylphenol (28b). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03 (d, J = 7.6 Hz, 1H), 6.69 (dd, J = 1.1, 7.6 Hz, 1H), 6.62 (d, J = 1.1 Hz, 1H), 4.72 (s, 1H), 2.54 (t, J = 7.7 Hz, 2H), 2.22 (s, 3H), 1.62–1.54 (m, 2H), 1.40–1.31 (m, 2H), 0.93 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.50, 142.23, 130.68, 120.73, 120.59, 114.92, 35.10, 33.53, 22.29, 15.26, 13.91; IR (ATR) ν cm^{-1}; HRMS (EI): m/z calcd for CHO ($[M]^+$) 164.1201, found 164.1175.

6-Methylbiphenyl-3-ol (29b). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.40 (m, 2H), 7.37–7.34 (m, 1H), 7.33–7.31 (m, 2H), 7.14 (d, J = 8.1 Hz, 1H), 6.78–6.74 (m, 2H), 4.83 (s, 1H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.26, 143.03, 141.58, 131.34, 128.99, 128.04, 127.50, 126.85, 116.57, 114.06, 19.45; HRMS (EI): m/z calcd for $C_{13}H_{12}O$ ($[M]^+$) 184.0888, found 184.0872.

Ethyl-4-hydroxy-2-methyl-3-phenethylbenzoate (30b). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, J = 8.5 Hz, 1H), 7.32–7.22 (m, 5H), 6.62 (d, J = 8.5 Hz, 1H), 4.85 (s, 1H), 4.32 (q, J = 7.2 Hz, 2H), 3.01–2.97 (m, 2H), 2.81–2.77 (m, 2H), 2.54 (s, 3H), 1.38 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.60, 156.73, 142.01, 140.19, 129.86, 128.45, 128.35, 127.77, 126.03, 123.63, 112.39, 60.68, 35.12, 28.61, 16.50, 14.30; HRMS (EI): m/z calcd for $C_{18}H_{20}O_3$ ($[M]^+$) 284.1412, found 284.1411.

Acknowledgements

Financial support for this study was provided by the Development of Human Resources in Science and Technology, and Ministry of Education, Culture, Sports, Science, and Technology of Japan.

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