Synlett B. Y.-H. Tan, Y.-C. Teo Letter

A Mild Strategy for the Preparation of Phenols via the Ligand-Free Copper-Catalyzed O-Arylation of *para*-Toluenesulfonic Acid

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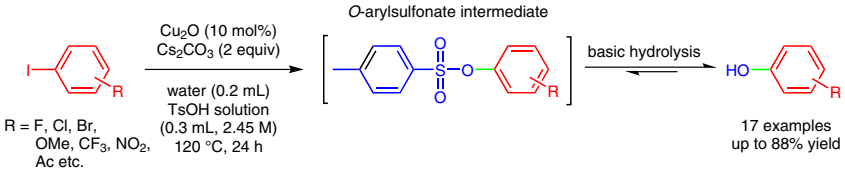


Received: 11.01.2016
Accepted after revision: 24.03.2016
Published online: 25.04.2016
DOI: 10.1055/s-0035-1561623; Art ID: st-2016-b0021-l

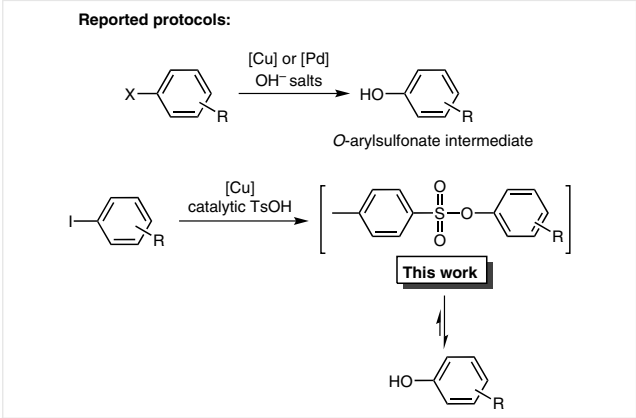
Abstract A facile and simple ligand-free copper-catalyzed reaction to synthesize substituted phenols is reported. The reaction presumably proceeds via an *O*-arylsulfonate intermediate that is hydrolyzed to afford good to excellent yields of up to 88%. This protocol provides an alternative to existing reports which use strong hydroxide salts as the direct hydroxylation partner. Demonstrating a wide substrate scope and functional group tolerance, this protocol can also be applied to inexpensive and commercially available carboxylic acids to yield phenols.

Key words phenol, copper, ligand-free, water, *p*-toluenesulfonic acid

Phenols are valuable synthetic building blocks for the chemical,[1] materials[2] and pharmaceutical industries.[3] Today, about 90% of this demand is met by the classical cumene–phenol process, an oxidative approach based on the decomposition of cumene hydroperoxide with sulfuric acid.[4] However, this method suffers from low efficiency even under harsh reaction conditions.[5] Functionalized phenols, on the other hand, are typically prepared using non-oxidative methods, including reactions of diazoarenes,[6] and nucleophilic aromatic substitution of benzene and aryl halides.[7] Nevertheless, problems associated with these methods include the limited substrate scope and harsh reaction conditions. As a result, significant effort has been focused onto the development of the phenol motif.

Lately, several different reports on palladium-[8] and copper-catalyzed[9] direct hydroxylation of aryl halides for the synthesis of phenol and its derivatives have emerged (Scheme 1). Where the former stood out with greater catalytic efficiency and milder conditions, the latter compensated through the low toxicity and cost of the copper catalyst–ligand systems.[10] Nevertheless, both sets of reactions are efficient and straightforward C–O cross-couplings of hydroxide and aryl halides, affording good to excellent yields of the desired products. Despite significant advances, some limitations still remained; the abovementioned reports employed a large excess (3 equiv and above) of strong bases such as NaOH, KOH, and CsOH as the nucleophilic partner (Scheme 1). This greatly harshens the reaction conditions and diminishes the synthetic utility. Furthermore, the requirement of assisting ligands to increase the yields and generality of the reactions entails to increase the overall operating costs.[8,9a–d,9f–h,9k] Therefore, from a practical and industrial point of view, the development of new sustainable and experimentally simple ligand-free catalytic system for the preparation of phenols which excludes the direct hydroxylation of aryl halides using strong basic hydroxide salts would represent a significant progress for the synthetic community.

Encouraged by our endeavors in ligand-free copper-catalyzed cross-coupling reactions in water,[11] we envisaged the application of a milder nucleophile for the C–O bond formation with aryl halides in the lead up to the synthesis of phenols. We report herein a facile and simple ligand-free copper-catalyzed synthesis of phenols through the in situ hydrolysis of the O-arylated products generated by the reaction between *p*-toluenesulfonic acid (TsOH) and iodobenzenes. With the use of catalytic amounts of TsOH as the nucleophile, this protocol eliminates the need of basic hydroxide salts, hence creating a milder reaction environment. Furthermore, unlike many of the previously reported protocols where intricately balanced water–organic solvent systems were crucial for the success of the reaction,[8a–c,9a–g,9l] water is used solely. Therefore, this reaction is more sustainable from an industrial standpoint.[12]



Scheme 1 Metal-catalyzed synthesis of phenols using aryl halides

We initiated our investigations by using iodobenzene (1 equiv) and TsOH (1.5 equiv) as the model substrates for the O-arylation reaction (Table 1). To the best of our knowledge, there was no prior study focused on the C–O bond formation between aryl halides and TsOH. Drawing cue from our previous carbon–heteroatom cross-coupling protocol,[11c] a combination of Cu_2O (10 mol%), Cs_2CO_3 (2 equiv), and water at 120 °C for 24 hours was used. An encouraging yield of 52% phenol, rather than the O-arylated product, was obtained (Table 1, entry 1). Through this result, we hypothesize that the synthesis of phenol was achieved through a two-step mechanism: 1) the cross-coupling of TsOH and iodobenzene, followed by 2) the hydrolysis of the O-arylated product to produce phenol, concurrently regenerating TsOH. To support our hypothesis, the effect of different amounts of TsOH on the yield of phenol was investigated (see Supporting Information for comprehensive study and table). To our delight, catalytic amounts of TsOH were able to produce excellent yields of up to 90%, with 0.5 equivalents being the optimal value (Table 1, entry 2). However, we observed significantly lower yields of phenol with 0.2 equivalents of TsOH (Table 1, entry 3). This is possibly due to the inefficient initial cross-coupling of aryl iodide and nucleophile at low concentrations of TsOH.

With these promising results, we proceeded to evaluate the influence of bases on the reaction efficiency. All bases screened, namely K_2CO_3, K_3PO_4, Na_2CO_3 and CsOAc, proved to be ineffective for the reaction, affording only trace yields. Among the copper sources, the copper(I) halides screened were inferior to Cu_2O, giving yields of up to 72%, while CuO was unable to catalyze the reaction (Table 1, entries 4–7). Control experiments confirmed that no product was obtained in the absence of the catalysts, base, or the nucleophilic partner (Table 1, entries 8–10). Following that, a range of protic and polar organic solvent was examined to probe on the solvent effect on this reaction (Table 1, entries 11–14). Interestingly, low yields were obtained, leading to the conclusion that water is essential for the success of the reaction. Thereafter, the impact of the water volume on the reaction was evaluated. A volume of 0.5 mL water was determined to be optimal, while any deviation from this led to a decrease in phenol yield (see Supporting Information for comprehensive study and table). This is possibly due to the need to strike an intricate balance between the necessity for water in the proposed hydrolysis step as well as in the dilution effect. To enhance the practicality of the protocol, we attempted the same reaction through separate additions of water and a prepared 2.45 M stock solution of TsOH. It was observed that effervescence and heat produced through this staggered addition were considerably reduced, at a small compensation of 2% yield (Table 1, entry 15). To conclude the optimization studies, the reactions were carried out using CsOH, KOH, or NaOH (Table 1, entries 16–18); essential components of previously reported procedures for the formation of phenols.[8,9] Only up to 9% yield was ob-

Table 1 Optimization Studies on the Cu-Catalyzed Cross-Coupling of Sulfonic Acids and Iodobenzene for the Synthesis of Phenol[a]

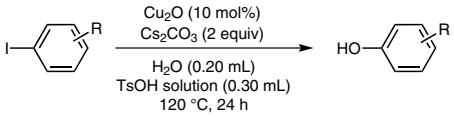
Entry	Catalyst	Base	Solvent	Yield (%)[b]
1	Cu_2O	Cs_2CO_3	H_2O	52[c]
2	Cu_2O	Cs_2CO_3	H_2O	90
3	Cu_2O	Cs_2CO_3	H_2O	40[d]
4	CuI	Cs_2CO_3	H_2O	65
5	CuBr	Cs_2CO_3	H_2O	72
6	CuCl	Cs_2CO_3	H_2O	54
7	CuO	Cs_2CO_3	H_2O	0
8	–	Cs_2CO_3	H_2O	0
9	Cu_2O	–	H_2O	0
10	Cu_2O	Cs_2CO_3	H_2O	0[e]
11	Cu_2O	Cs_2CO_3	MeOH	20
12	Cu_2O	Cs_2CO_3	EtOH	10
13	Cu_2O	Cs_2CO_3	DMF	26
14	Cu_2O	Cs_2CO_3	DMSO	0
15	Cu_2O	Cs_2CO_3	H_2O	88[f]
16	Cu_2O	CsOH	H_2O	9
17	Cu_2O	KOH	H_2O	6
18	Cu_2O	NaOH	H_2O	0

[a] Reaction conditions: copper salt (10 mol%), base (2.94 mmol), sulfonic acid (0.735 mmol), solvent (0.5 mL), iodobenzene (1.47 mmol), 120 °C for 24 h.
[b] Average GC yield of two runs, with *m*-cresol as internal standard.
[c] Amount of TsOH used was 1.5 equiv.
[d] Amount of TsOH used was 0.2 equiv.
[e] No TsOH was added.
[f] Reaction was carried out with Cu_2O (10 mol%), Cs_2CO_3 (2.94 mmol), H_2O (0.2 mL), iodobenzene (1.47 mmol) followed by 2.45 M TsOH (0.3 mL) solution.

tained. In summary, in our protocol we eliminated the need to use strong basic hydroxide salts in the direct hydroxylation of aryl halides. The synthesis of phenol in water was achieved by using a combination of Cu_2O (10 mol%) and Cs_2CO_3 (2 equiv), TsOH solution (0.5 equiv), and iodobenzene (1.0 equiv), which was stirred at 120 °C for 24 hours without the need for stringent inert conditions.

With this set of optimized conditions, we proceeded to explore the breadth of application of this protocol through the use of a wide range of substituted aryl halides. The results are summarized in Table 2.

Table 2 O-Arylation of *p*-Toluenesulfonic Acid with Various Substituted Aryl Halides for the Synthesis of Substituted Phenols[a]

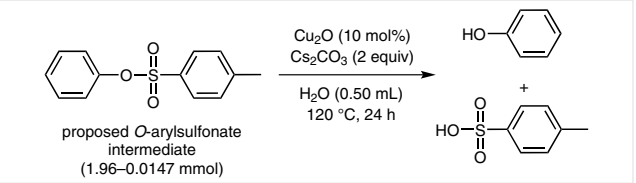


Entry	ArX	Product	Yield (%)[b]
1	PhI	**2a**	88
2	2-FC_6H_4I	**2b**	40
3	2-AcC_6H_4I	**2c**	70
4	2-MeC_6H_4I	**2d**	30
5	2-Naphthyl-C_6H_4I	**2e**	43
6	3-FC_6H_4I	**2f**	87
7	3-ClC_6H_4I	**2g**	75
8	3-$CF_3C_6H_4I$	**2h**	70
9	3-$OMeC_6H_4I$	**2i**	70[c]
10	3-$NO_2C_6H_4I$	**2j**	85
11	3-AcC_6H_4I	**2k**	72
12	3-MeC_6H_4I	**2l**	74
13	4-FC_6H_4I	**2m**	71
14	4-Cl C_6H_4I	**2n**	70
15	4-$NO_2C_6H_4I$	**2o**	70[c]
16	4-AcC_6H_4I	**2p**	80
17	4-MeC_6H_4I	**2q**	67
18	PhBr	**2a**	trace[c]

[a] Reaction conditions: Cu_2O (10 mol%), Cs_2CO_3 (2.94 mmol), H_2O (0.2 mL), iodobenzene (1.47 mmol) followed by 2.45 M TsOH (0.3 mL) solution, stirred at 120 °C for 24 h.
[b] Isolated yield.
[c] Reactions were carried out at 130 °C.

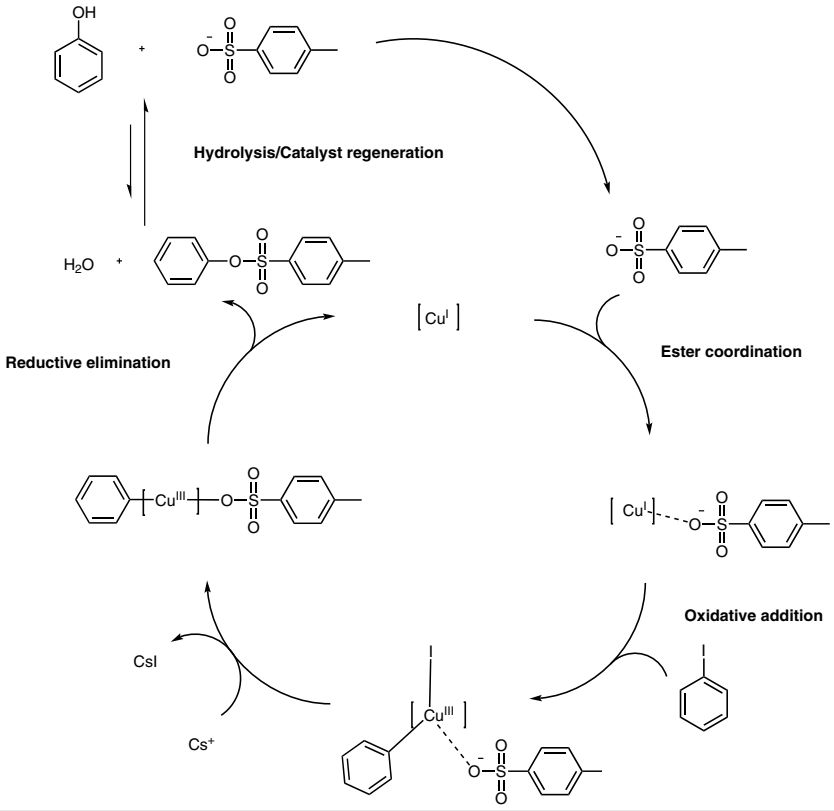
In most cases, good to excellent yields of substituted phenols were obtained. Lower yields were observed for *ortho*-substituted aryl iodides (Table 2, entries 2–5). This set of results supported the hypothesis of an O-arylated TsOH intermediate, as it corresponds to the trend observed in various metal-catalyzed C–O cross-coupling reactions, where the reaction is hampered by sterically hindered *ortho*-substituted aryl iodides.[13] Electronic effects of different substituents at the *meta* and *para* positions were well tolerated by the reaction conditions, and good yields of up to 87% of substituted phenols were obtained (Table 2, entries 6–17). Unfortunately, the synthesis of phenols or heteroaryl alcohols were not achieved using aryl bromides, a less reactive electrophile (Table 2, entry 18), and iodopyridines. Reactions using iodophenols and iodoanilines did not proceed either, due to the acidity and basicity of the substituents, respectively.

In order to achieve a more comprehensive understanding of the reaction route, experiments involving the hydrolysis of the proposed intermediate, an O-arylated sulfonate, were carried out (Scheme 2). Interestingly, under standard conditions, a high base-to-intermediate ratio was essential for 100% conversion of the intermediate into phenol (see Supporting Information). Next, ^{1}H NMR analysis of the crude reaction mixtures involving iodobenzene and TsOH was done under optimized conditions and shortened reaction times (0–2 h). Although phenol was formed within an hour, ^{1}H NMR analysis showed no accumulation of the proposed intermediate (See Supporting Information). With the help of the observations above, we postulate the rapid succession of O-arylation and basic hydrolysis.



Scheme 2 Hydrolysis of proposed O-arylated sulfonate

Taking into consideration the data in Tables 1 and 2 along with reported chemistry of copper-catalyzed cross-coupling reactions,[14] a mechanism for the reaction is proposed (Scheme 3). The ligand-free synthesis of the O-arylated sulfonate intermediate can be achieved by a three-step mechanism: coordination of TsO^-, obtained through the reaction of TsOH with Cs_2CO_3, to the Cu^I metal center, followed by the oxidative addition of the aryl iodide to form the Cu^{III} intermediate, and concluded with the reductive elimination of the O-arylated intermediate to regenerate the active catalytic Cu^I species. The pathway is succeeded by a reversible hydrolysis of the intermediate to produce phenol and regenerate TsO^-. The presence of more TsO^- would likely reverse the equilibrium, leading to lower yields of phenol, and this expectation is consistent with data in Table 1 (entry 1), where the use of larger amount of TsOH led to a significantly lower yield of phenol. Meanwhile, the inability of other organic solvents to facilitate the reaction (Table 1, entries 11–14) illustrates the crucial role of water in the hydrolysis step, in tandem with the proposed mechanism. Nevertheless, more mechanistic studies are necessary to further elucidate the catalytic cycle and the reaction pathway.



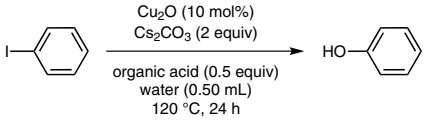
Scheme 3 Proposed mechanism for the synthesis of phenol through hydrolysis of an O-arylsulfonate intermediate

In view of our proposed mechanism and existing literature of cross-coupling reaction between iodobenzene and carboxylic acids,[15] we envision the application of various inexpensive and commercially available organic acids as the nucleophile of this protocol. Intriguingly, a wide range of aliphatic (Table 3, entries 1–6) and aromatic carboxylic acids (Table 3, entries 7 and 8) were successfully applied in catalytic amounts to afford good yields of phenol.

A small amount (<10%) of aniline was also detected with the use of benzhydroxamic acid, possibly due to further hydrolysis of the present amide linkage. Furthermore, methanesulfonic acid and camphosulfonic acid can also be utilized as the nucleophile to derive 34% and 70% phenol, respectively (Table 3, entries 9 and 10).

In conclusion, a facile, simple and practical ligand-free copper-catalyzed protocol for the synthesis of phenols through O-arylation using catalytic amounts of TsOH has been successfully developed.[16] Due to its exclusion of strong hydroxide salts and assisting ligands, the reaction provides a plausible alternative to previously established metal-catalyzed hydroxylation of aryl halides. Interestingly, a wide range of carboxylic acids have also been successfully employed as the O-arylation partner to afford good yields of

Table 3 O-Arylation of Various Organic Acids with Iodobenzene for the Synthesis of Phenols[a]



Entry	Organic acid	Yield (%)[b]
1	formic acid	65
2	acetic acid	70
3	pivalic acid	68
4	hexanoic acid	70
5	octanoic acid	65
6	decanoic acid	67
7	benzoic acid	79
8	benzhydroxamic acid	60
9	methanesulfonic acid	34
10	camphorsulfonic acid	70

[a] Reaction conditions: Cu_2O (10 mol%), Cs_2CO_3 (2.94 mmol), organic acid (0.735 mmol), H_2O (0.5 mL), iodobenzene (1.47 mmol) stirred at 120 °C for 24 h.
[b] Average GC yield of two runs, with *m*-cresol as internal standard.

phenols. With its tolerance towards different functional groups present in iodobenzene, this protocol is expected to be particularly useful in industrial applications.

Acknowledgment

We would like to thank the National Institute of Education and Nanyang Technological University (RP 5/13 TYC) for the funding of this work.

Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0035-1561623.

References and Notes

(1) For utility of phenols in synthetic chemistry, see: (a) Pillai, M.; Kothari, K.; Jurisson, S. *Appl. Radiat. Isot.* **1995**, *46*, 923. (b) Pillai, M.; Barnes, C.; Schlemper, E. *Polyhedron* **1994**, *13*, 701. (c) Merlini, L.; Zanarotti, A.; Pelter, A.; Rochefort, M. P.; Hänsel, R. *J. Chem. Soc., Perkin Trans. 1* **1980**, 775. (d) Brezinsky, K.; Pecullan, M.; Glassman, I. *J. Phys. Chem. A* **1998**, *102*, 8614.

(2) For utility of phenols in material chemistry, see: (a) Uyama, H.; Lohavisavapanich, C.; Ikeda, R.; Kobayashi, S. *Macromolecules* **1998**, *31*, 554. (b) Serman, C. J.; Xu, Y.; Painter, P. C.; Coleman, M. M. *Polymer* **1991**, *32*, 516. (c) Serman, C. J.; Painter, P. C.; Coleman, M. M. *Polymer* **1991**, *32*, 1049.

(3) For utility of phenols in pharmaceuticals, see: (a) Lloyd, J. In *Techniques of Neurolysis*; Springer: New York, **1989**, 33–44. (b) Kirazli, Y.; On, A. Y.; Kismali, B.; Aksit, R. *Am. J. Phys. Med. Rehabil.* **1998**, *77*, 510. (c) Cutting, W.; Mehrtens, H.; Tainter, M. *J. Am. Med. Assoc.* **1933**, *101*, 193.

(4) Hock, H.; Lang, S. *Eur. J. Inorg. Chem.* **1944**, *77*, 257.

(5) Weber, M.; Weber, M.; Kleine-Boymann, M. In *Ullmann's Encyclopedia of Industrial Chemistry*; Wiley-VCH Verlag: Weinheim, **2000**.

(6) For reports on the synthesis of phenols through diazoarenes, see: (a) Cohen, T.; Dietz, A. G.; Miser, J. R. *J. Org. Chem.* **1977**, *42*, 2053. (b) Mo, F.; Dong, G.; Zhang, Y.; Wang, J. *Org. Biomol. Chem.* **2013**, *11*, 1582.

(7) Zhang, Y.-H.; Yu, J.-Q. *J. Am. Chem. Soc.* **2009**, *131*, 14654.

(8) For reports on the palladium-catalyzed direct hydroxylation of aryl halides, see: (a) Anderson, K. W.; Ikawa, T.; Tundel, R. E.; Buchwald, S. L. *J. Am. Chem. Soc.* **2006**, *128*, 10694. (b) Cheung, C. W.; Buchwald, S. L. *J. Org. Chem.* **2014**, *79*, 5351. (c) Sergeev, A. G.; Schulz, T.; Torborg, C.; Spannenberg, A.; Neumann, H.; Beller, M. *Angew. Chem. Int. Ed.* **2009**, *48*, 7595. (d) Yu, C.-W.; Chen, G. S.; Huang, C.-W.; Chern, J.-W. *Org. Lett.* **2012**, *14*, 3688.

(9) For reports on the copper-catalyzed direct hydroxylation of aryl halides, see: (a) Tlili, A.; Xia, N.; Monnier, F.; Taillefer, M. *Angew. Chem. Int. Ed.* **2009**, *48*, 8725. (b) Xiao, Y.; Xu, Y.; Cheon, H.-S.; Chae, J. *J. Org. Chem.* **2013**, *78*, 5804. (c) Yang, D.; Fu, H. *Chem. Eur. J.* **2010**, *16*, 2366. (d) Zhao, D.; Wu, N.; Zhang, S.; Xi, P.; Su, X.; Lan, J.; You, J. *Angew. Chem. Int. Ed.* **2009**, *48*, 8729. (e) Amal Joseph, P. J.; Priyadarshini, S.; Lakshmi Kantam, M.; Maheswaran, H. *Catal. Sci. Tech.* **2011**, *1*, 582. (f) Wang, D.; Kuang, D.; Zhang, F.; Tang, S.; Jiang, W. *Eur. J. Org. Chem.* **2014**, 315. (g) Thakur, K. G.; Sekar, G. *Chem. Commun.* **2011**, *47*, 6692. (h) Ding, G.; Han, H.; Jiang, T.; Wu, T.; Han, B. *Chem. Commun.* **2014**, *50*, 9072. (i) Jing, L.; Wei, J.; Zhou, L.; Huang, Z.; Li, Z.; Zhou, X. *Chem. Commun.* **2010**, *46*, 4767. (j) Chen, J.; Yuan, T.; Hao, W.; Cai, M. *Catal. Commun.* **2011**, *12*, 1463. (k) Yang, K.; Li, Z.; Wang, Z.; Yao, Z.; Jiang, S. *Org. Lett.* **2011**, *13*, 4340.

(10) For reports on low toxicity of copper catalyst, see: (a) Gujadhur, R.; Venkataraman, D.; Kintigh, J. T. *Tetrahedron Lett.* **2001**, *42*, 4791. (b) Ley, S. V.; Thomas, A. W. *Angew. Chem. Int. Ed.* **2003**, *42*, 5400. (c) Beletskaya, I. P.; Cheprakov, A. V. *Coord. Chem. Rev.* **2004**, *248*, 2337.

(11) For our group's published ligand-free copper catalysis, see: (a) Yong, F.-F.; Teo, Y.-C.; Tay, S.-H.; Tan, B. Y.-H.; Lim, K.-H. *Tetrahedron Lett.* **2011**, *52*, 1161. (b) Yong, F.-F.; Teo, Y.-C.; Chua, G.-L.; Lim, G. S.; Lin, Y. *Tetrahedron Lett.* **2011**, *52*, 1169. (c) Tan, B. Y.-H.; Teo, Y.-C.; Seow, A.-H. *Eur. J. Org. Chem.* **2014**, 1541.

(12) For reports on sustainable solvents in organic reactions, see: (a) Li, C.-J.; Trost, B. M. *Proc. Natl. Acad. Sci. U.S.A.* **2008**, *105*, 13197. (b) DeSimone, J. M. *Science* **2002**, *297*, 799. (c) Capello, C.; Fischer, U.; Hungerbühler, K. *Green Chem.* **2007**, *9*, 927.

(13) For C–O cross-coupling reactions which encountered low yields with sterically hindered aryl halides, see: (a) Yong, F.-F.; Teo, Y.-C.; Yan, Y.-K.; Chua, G.-L. *Synlett* **2012**, 101. (b) Yang, H.; Xi, C.; Miao, Z.; Chen, R. *Eur. J. Org. Chem.* **2011**, 3353. (c) Cristau, H.-J.; Cellier, P. P.; Hamada, S.; Spindler, J.-F.; Taillefer, M. *Org. Lett.* **2004**, *6*, 913.

(14) For reports with mechanism for copper-catalyzed cross-coupling reactions, see: (a) Strieter, E. R.; Bhayana, B.; Buchwald, S. L. *J. Am. Chem. Soc.* **2008**, *131*, 78. (b) Rao, H.; Fu, H. *Synlett* **2011**, 745.

(15) Yamamoto, T. *Synth. Commun.* **1979**, *9*, 219.

(16) **General Procedure for the Synthesis of Substituted Phenols via O-Arylation of *p*-Toluenesulfonic Acid**: A mixture of Cu_2O (Sigma-Aldrich, 99.99% purity, 0.147 mmol), Cs_2CO_3 (2.94 mmol), distilled H_2O (0.2 mL), aryl halide (1.47 mmol) and *p*-toluenesulfonic acid (TsOH) solution (0.3 mL, 2.45 mol/dm^3) were added to a reaction vial and a screw cap was fitted to it. The reaction mixture was stirred under air in a closed system at 120 °C for 24 h, following which the heterogeneous mixture was cooled to r.t. and diluted with CH_2Cl_2. The combined organic extracts were dried with anhyd Na_2SO_4 and the solvent was removed under reduced pressure. The crude product was loaded onto the silica gel column using minimal amounts of CH_2Cl_2 and was purified by silica gel column chromatography to afford the N-arylated product.

Phenol (2a): Following the general procedure using *p*-toluenesulfonic acid solution (0.3 mL, 2.45 mol/dm^3) and iodobenzene (0.165 mL, 1.47 mmol), the product (122 mg, 89% yield) was obtained as a colorless oil after purification by flash chromatography (hexane–EtOAc, 80:20). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.23 (t, *J* = 8.6 Hz, 2 H), 6.92 (t, *J* = 7.6 Hz, 1 H), 6.83 (d, *J* = 7.6 Hz, 2 H), 5.67 (br s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.3, 129.7, 120.9, 115.3. GC–MS: t_R = 4.91 min, M/Z = 94. HRMS: *m*/*z* [M$^+$] calcd for C_6H_6O: 95.0495; found: 95.0500.

2-Fluorophenol (2b): Following the general procedure using *p*-toluenesulfonic acid solution (0.3 mL, 2.45 mol/dm^3) and 2-fluoroiodobenzene (0.172 mL, 1.47 mmol), the product (66 mg, 40% yield) was obtained as a colorless oil after purification by flash chromatography (hexane–EtOAc, 80:20). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.02–7.17 (m, 3 H), 6.85–6.90 (m, 1 H), 5.59 (br s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.1 (*J* = 236.2 Hz), 143.4

(J = 14.5 Hz), 124.8 (J = 3.1 Hz), 120.9 (J = 6.1 Hz), 117.4 (J = 2.2 Hz), 115.5 (J = 17.5 Hz). HRMS: m/z [M^+] calcd for C_6H_5OF: 113.0400; found: 113.0393.

2′-Hydroxyacetophenone (2c): Following the general procedure using *p*-toluenesulfonic acid solution (0.3 mL, 2.45 mol/dm^3) and 2′-iodoacetophenone (0.210 mL, 1.47 mmol), the product (140 mg, 70% yield) was obtained as a colorless oil after purification by flash chromatography (hexane–EtOAc, 90:10). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 12.26 (br s, 1 H), 7.71 (d, J = 8.4 Hz, 1 H), 7.45 (t, J = 8.4 Hz, 1 H), 6.96 (d, J = 8.0 Hz, 1 H), 6.89 (t, J = 8.0 Hz, 1 H), 2.61 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 204.5, 162.3, 136.4, 130.7, 119.7, 118.9, 118.3, 26.6. HRMS: m/z [M^+] calcd for $C_8H_8O_2$: 137.0600; found: 137.0598.

***O*-Cresol (2d)**: Following the general procedure using *p*-toluenesulfonic acid solution (0.3 mL, 2.45 mol/dm^3) and 2-methyliodobenzene (0.188 mL, 1.47 mmol), the product (48 mg, 30% yield) was obtained as a colorless oil after purification by flash chromatography (hexane–EtOAc, 85:15). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.09–7.17 (m, 2 H), 6.89 (t, J = 7.2 Hz, 1 H), 6.79 (d, J = 7.6 Hz, 1 H), 4.88 (br s, 1 H), 2.28 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.7, 131.0, 127.1, 123.8, 120.8, 114.9, 15.7. HRMS: m/z [M^+] calcd for C_7H_8O: 109.0651; found: 109.0655.