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# Electro-oxidative C(sp<sup>2</sup>)–H/O–H crossdehydrogenative coupling of phenols and tertiary anilines for diaryl ether formation†

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The formation of diaryl ethers is generally achieved *via* transition metal catalyzed etherification reactions (Ullmann, Chan–Lam, Buchwald–Hartwig) with prefunctionalized aryl halide substrates at elevated temperatures. Herein, we report a protocol for electrochemical  $C(sp^2)$ –H/O–H cross-dehydrogenative coupling of phenols and tertiary anilines to synthesize diaryl ethers. The  $C(sp^2)$  H/O–H coupling product can be obtained under metal- and oxidant-free conditions at room temperature in moderate to excellent yield (up to 83% yield) with high regioselectivity (>99% for *para*-substitution) and with a broad substrate scope (22 examples).

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### Introduction

Diaryl ether scaffolds are important structural motifs in the field of organic synthesis due to the prevalence of  $C(sp^2)$ -O bonds in intermediates of natural products and in several prominent pharmaceuticals (Fig. 1).<sup>1</sup> Therefore, the development of an effective diaryl ether synthesis method has great research significance and extensive application value. Previous research focused on the transition-metal mediated phenol etherification with prefunctionalized arenes (aryl halides or pseudohalides), which not only generate a stoichiometric amount of halide salt waste but also require elevated temperatures (Scheme 1a).<sup>2,3</sup> Biaryl ethers can also be obtained from benzoate esters via a palladium or nickel mediated decarboxylation (Scheme 1b).<sup>4</sup> Some alternative prefunctionalized substrates were developed, such as aryl boronic acids (Chan-Lam coupling) and more recently, Ritter et al. managed to form aryl sulfonium salts, which could be converted into C-O bonds using photoredox catalysis.<sup>5,6</sup> Although a number of pioneering processes were developed in the synthesis of diaryl ethers, some limitations still remain, such as the requirement of pre-functionalized arenes, transition metals and often cost-intensive ligands, while cheaper, unmodified arenes remain elusive reactants.

Organic electrochemistry is a green synthetic tool that employs traceless electricity to promote redox reactions. Electricity-powered dehydrogenative cross-coupling reactions proceed with H<sub>2</sub> evolution, eliminating the need for oxidants, temperature.<sup>7</sup> ligands and increased The direct dehydrogenative coupling of phenols with arenes could result in an optimal step- and atom-economy.8 However, this approach remains largely unexplored due to an often unpredictable, poor chemoselectivity between C or O-arylation; C-O coupling was only accidentally observed in a few studies involving the synthesis of asymmetric biaryls.<sup>9</sup> Furthermore, the few studies that did report O-arylation suffer from a low yield and limited substrate scope. König et al. obtained diaryl ethers in the photocatalytic, rutheniumcatalyzed coupling of electron-rich arenes with phenols (yield up to 44%, selectivity of 51%).<sup>10</sup> A mechanistic rationale was postulated in which one arene (e.g., trimethoxybenzene) is oxidized selectively to the corresponding radical cation, which is attacked by a poorly oxidizable nucleophile (e.g. phenol). The group of Waldvogel observed C-O cross-coupled compounds as side products in the electrochemical coupling of trimethoxyphenol with a phenol derivative (1 example, yield of 12%, selectivity of 25%) and in the coupling of naphthylamines with phenolic substrates (3 examples, yield up to 28%).<sup>11</sup> They proposed that the absence of steric hindrance would be essential for diverting the selectivity



Fig. 1 Prominent fine chemicals that contain the diaryl ether moiety.



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$$\begin{array}{c} \begin{array}{c} \begin{array}{c} \text{cat. [Pd] or [Cu]} \\ \text{ligand} \\ \text{+ base} \\ \text{- halide salt waste} \end{array} \end{array} \xrightarrow{\text{Cat. Pd} or [Cu]} \\ \end{array}$$

(b) Decarbonylative diaryl ether synthesis catalyzed by Pd or Ni



Scheme 1 Diaryl ether formation.

from C–C to C–O cross-coupling products.<sup>12</sup> In this study, we provide an electrochemical, additive-free method to couple anilines with phenolic substrates *via O*-arylation with high yields and selectivities (Scheme 1c).

### Results and discussion

We investigated the electrochemical coupling between the sterically unhindered 4-*tert*-butylphenol (1a) and *N*,*N*-dimethylaniline (2a), which is quite susceptible to oxidation. Our hypothesis was that the absence of steric hindrance around both the phenolic moiety of 1a as well as the activated *para*-position of 2a, together with the low redox potential of 2a, would result in an improved selectivity for the C–O cross-coupled product. An undivided cell equipped with a carbon felt anode and a nickel cathode was employed (ESI,† Fig. S3). The desired diaryl ether product 3a was

obtained in an excellent yield of 78% after optimization of the reaction conditions (Table 1). Quite surprisingly, no C–C cross-coupling product was observed.<sup>13</sup> The only observed side-product was the methylene bridged dimer of 2a, namely 4,4'-methylene-bis(N,N-dimethylaniline) (4a), which is reported to form *via* a 2-electron oxidation of 2a.<sup>14</sup>

Currents lower than the optimal 5 mA did not significantly decrease the yield, while a higher current of 10 mA afforded a slightly lower yield (entries 2 and 3). As a supporting electrolyte,  $^{n}$ Bu<sub>4</sub>NBF<sub>4</sub> gave the best yield, although a similar reactivity was obtained with other electrolytes (entries 4 and 5). A hexafluoroisopropanol combination of (HFIP) and dichloromethane (DCM) in a ratio of 6:4, respectively, was shown to be optimal, as significantly lower yields were obtained in the neat solvents (entries 6 and 7), and no product was observed in acetonitrile (entry 8). The use of a graphite rod anode significantly decreased the formation of 3a (entry 9), which could be attributed to the lower surface area of this electrode. Changing the Ni cathode for Pt shows a moderately lower yield, indicating the cathode material can influence the reaction outcome, probably by promoting side-reactions (entry 10). Higher or lower temperatures resulted in lower yields (entries 11 and 12). A slightly decreased reaction yield was obtained when the inert nitrogen atmosphere was replaced by air (entry 13). No desired product was observed when the reaction was run under air and without electricity (entry 14).

#### Kinetic study

In a kinetic study, the evolution of the formation of the product (3a) and the side product 4,4'-methylene-bis(N,N-dimethylaniline) (4a) was followed (Fig. S3†). Upon supplying

Table 1         Optimization of reaction conditions <sup>a</sup>		
$(B_{U} \cup C_{H} + C_{H} \cup C_{$		
Entry	Variation from standard conditions	Yield <sup>b</sup> [%]
1	None	$78^{b}, 70^{c}$
2	1 mA, 42 h	71
3	10 mA, 2.5 h	56
4	Et <sub>4</sub> NBF <sub>4</sub> , <sup><i>n</i></sup> Bu <sub>4</sub> NPF <sub>6</sub> , <sup><i>n</i></sup> Bu <sub>4</sub> NClO <sub>4</sub> , LiClO <sub>4</sub>	38-50
5	1 eq. $^{n}\mathrm{Bu}_{4}\mathrm{NBF}_{4}$	67
6	DCM	9 (48)
7	HFIP	36
8	MeCN	N.R.
9	Graphite as anode	15
10	Pt as cathode	45 (24)
11	40 °C	68
12	0 °C	33 (7)
13	Under air	69
14	Without electricity, under air	N.R.

<sup>*a*</sup> Reaction conditions: carbon felt as anode and nickel plate as cathode (10 mm × 10 mm × 1 mm), constant current at 5 mA, **1a** (0.3 mmol), **2a** (1 equiv., 0.3 mmol), <sup>*n*</sup>Bu<sub>4</sub>NBF<sub>4</sub> (0.5 equiv., 0.15 mmol), HFIP/DCM (6:4, 6 ml), room temperature, nitrogen, 5 h (3.1 F mol<sup>-1</sup>). <sup>*b*</sup> Yield determined by GC analysis using octane as the external standard. Recovery of unreacted **1a** shown within parentheses. <sup>*c*</sup> Isolated yield. HFIP = hexafluoroisopropanol, DCM = dichloromethane.

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2.5 F mol<sup>-1</sup>, the **3a** product yield continuously increased, while that of **4a** decreased. Supplying 3-3.5 F mol<sup>-1</sup> is the optimum for obtaining the highest yield of **3a**, with minimal formation of **4a**. When the homo-coupling of either **1a** or **2a** was attempted, no reaction was seen with **1a**, and a limited yield of **4a** was observed when the reaction was operated with only **2a**. When the reaction was conducted with the phenol **1a** and the side-product **4a** under standard conditions, similar results with significant formation of the product (**3a**) were obtained (Section S4.2 in ESI<sup>†</sup>).<sup>14</sup> This suggests the instability of **4a** under the reaction conditions, and its possible conversion with **1a** to the product **3a**.

#### Substrate scope

We next explored the substrate scope of this electrochemical  $C(sp^2)$ -H/O-H cross coupling with the optimal reaction

conditions (Table 2). Different substituents on the aromatic ring of phenol were assessed first. As shown in Table 2, electron-donating groups, such as tert-butyl, phenyl, methyl, ethyl, propyl and cumyl were tolerated, providing the corresponding products in 37-83% yields (3aa-3af). Especially, the yields with the cumyl, bulky tert-butyl and phenyl groups as substituents were 75%, 78% and 83%, respectively. Interestingly, all halide substituents, which can be used as functional handle in subsequent transformations, afforded the desired products in 47-67% yields (3ag-3aj). Electron-withdrawing groups, such as halides (3ah-3aj), are preferred over electron-donating substituents, such as an acetamido, methoxy or phenoxy substituents (3ak-3am). Although with reduced yields, meta-, ortho- and multisubstituted phenolics were also tolerated in this transformation (3an-3at). The scope with respect to the tertiary aniline coupling partner was next examined (Table 2).



3ca, 18% (11%)

<sup>*a*</sup> Reaction conditions: carbon felt as anode and nickel plate as cathode (10 mm × 10 mm × 1 mm), constant current of 5 mA, 1 (0.3 mmol), 2 (1 equiv., 0.3 mmol), <sup>*n*</sup>Bu<sub>4</sub>NBF<sub>4</sub> (0.5 equiv., 0.15 mmol), HFIP/DCM (6:4, 6 ml), room temperature, nitrogen, 5 h (3.1 F mol<sup>-1</sup>), isolated yields in parentheses. <sup>*b*</sup> Reaction for 3.5 h (2.2 F mol<sup>-1</sup>). <sup>*c*</sup> Reaction for 6.5 h (4.0 F mol<sup>-1</sup>). <sup>*d*</sup> 1a (0.6 mmol), 2a (0.6 mmol), <sup>*n*</sup>Bu<sub>4</sub>NBF<sub>4</sub> (0.3 mmol), constant current of 10 mA.



Fig. 2 Cyclic voltammogram on a glassy carbon anode (3 mm diameter), a platinum cathode and ferrocene reference electrode at  $0.1 \text{ V s}^{-1}$  under nitrogen (see ESI† for detailed description).

*N*-Methyl-*N*-phenylaniline was tolerated and afforded the corresponding diaryl ether in moderate yield (**3ba**). *N*,*N*-Dimethylaniline with a bromine group at the *meta*-position of the benzene ring also afforded the desired product (**3ca**).

#### Mechanistic study

To understand the mechanism of the electrochemical C–O coupling reaction, cyclic voltammetry (CV) experiments were carried out to probe the reactivity of the substrates (Fig. 2). The oxidation of *N*,*N*-dimethylaniline (**2a**) is thermodynamically favoured over that of 4-*tert*-butylphenol (**1a**), with an oxidation peak at 0.81 V *vs.* ferrocene for **2a**, compared to 1.66 V *vs.* ferrocene for **1a**. The measured oxidation potential of **1a** was considerably higher compared to literature values.<sup>15</sup> Further CV experiments showed an increase in oxidation potential of approximately 0.8 V for **1a** 



**Fig. 3** Electron paramagnetic resonance (EPR) spectra after electrolysis in HFIP/DCM for 1 hour with a CF anode and a Pt cathode (see ESI† for detailed description).

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upon the use of our optimal solvent mixture (HFIP/DCM) compared to more conventional solvent mixtures (MeCN/MeOH), while the *tert*-butyl group of **1a** further increases the oxidation potential by approximately 1.0 V compared to a methoxy substituent in 4-methoxyphenol (see ESI†). When we tested the CV of a mixture of both substrates (**1a** + **2a**) under standard conditions, the potential of the oxidation peaks did not change significantly. Subsequently, reactions were conducted at a constant cell potential to control the oxidation of the substrates. The reaction was run at a cell potential of 1.00 V, where only **2a** could be oxidized, and at a cell potential of 2.75 V where both **1a** and **2a** could be oxidized (Fig. 2). In these electrocatalytic reactions, 65% and 48% yields were obtained, respectively, proving that the selective activation of **2a** is beneficial for the yield.

X-Band electron paramagnetic resonance (EPR) spectra of electrolyzed solutions of **1a** and/or **2a** were recorded to obtain information on the identity of any radical species under reaction conditions (Fig. 3). No signal was observed for **1a**, while for **2a** a signal was observed corresponding to the radical cation of **2a** (g = 2.0058,  $A_{\rm N} = 7.46$  G,  $A_{\rm H} = 6.79$  G,  $A_{\rm H-Ar} = 5.63$  G).<sup>16</sup> When we tested a solution of both **1a** and **2a**, a different EPR signature was observed; the spectrum was successfully fitted to that of the cationic radical of **3a** (g = 2.007,  $A_{\rm N} = 9.51$  G,  $A_{\rm H} = 9.78$  G,  $A_{\rm H-Ar-ortho} = 4.77$  G).<sup>17</sup> According to these results, it can be concluded that only *N*,*N*-dimethylaniline is oxidized under the reaction conditions; the cation readily combines with **1a** to obtain the C–O coupled product.

A possible mechanism for the electrochemical  $C(sp^2)$ -H/ O-H cross-dehydrogenative coupling is proposed in Scheme 2. First, the tertiary aniline moiety in the starting material is anodically oxidized to furnish a cationic intermediate **I**; after this electrochemical umpolung, **I** undergoes nucleophilic attack by phenol. Concomitant cathodic reduction of *in situ* generated protons can release hydrogen gas during the reaction process. A key role is ascribed to the use of HFIP as solvent, as its high dielectric constant and low nucleophilicity stabilize the generated radicals and cations, thereby avoiding side-reactions, such as radical recombination or nucleophilic addition of **1a** with HFIP. Finally, its hydrogen-bond donating ability facilitates



**Scheme 2** Proposed mechanism for the dehydrogenative C–O coupling of tertiary anilines and phenolics.

hydrogen transfer from the coupling reagents to the cathode.  $^{18}$ 

# Conclusions

In conclusion, we have developed an electrochemical protocol for the formation of diaryl ethers by direct C-H aryloxylation of tertiary anilines with free phenolics. From a mechanistic standpoint, the key advance was a careful selection of coupling partners together with the use of a HFIP/DCM solvent mixture. It is paramount to selectively oxidize the aniline coupling partner, which was experimentally verified by means of EPR and CV measurements. Such a mechanistic paradigm should be useful in developing new electrochemical O-functionalization pathways of phenols.

### Author contributions

Under supervision of D. D. V. and J. V., H. T. was responsible for the design and analysis of the experiments. S. S. performed the EPR measurements. Y. L. was responsible for the CV experiments. All authors have given approval to the final version of the manuscript.

## Conflicts of interest

There are no conflicts of interest to declare.

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# Notes and references

- (a) S. D. Roughley and A. M. Jordan, The medicinal chemist's toolbox: an analysis of reactions used in the pursuit of drug candidates, *J. Med. Chem.*, 2011, 54, 3451–3479; (b) C. C. Lee, M. K. Leung, P. Y. Lee, T. L. Chiu, J. H. Lee, C. Liu and P. T. Chou, Synthesis and properties of oxygen-linked *N*-phenylcarbazole dendrimers, *Macromolecules*, 2012, 45, 751–765; (c) F. Bedos-Belval, A. Rouch, C. Vanucci-Bacqué and M. Baltas, Diaryl ether derivatives as anticancer agents-a review, *MedChemComm*, 2012, 3, 1356–1372.
- 2 For selected examples of palladium-catalyzed Buchwald-Hartwig diaryl ether coupling reaction, see: (a) G. Mann and J. F. Hartwig, Nickel-vs palladium-catalyzed synthesis of protected phenols from aryl halides, *J. Org. Chem.*, 1997, 62, 5413–5418; (b) G. Mann, C. Incarvito, A. L. Rheingold and J. F. Hartwig, Palladium-catalyzed C- O coupling involving unactivated aryl halides, *J. Am. Chem. Soc.*, 1999, 121, 3224–3225; (c) A. Aranyos, D. W. Old, A. Kiyomori, J. P. Wolfe, J. P. Sadighi and S. L. Buchwald, Novel electron-rich bulky phosphine ligands facilitate the palladium-catalyzed

preparation of diaryl ethers, *J. Am. Chem. Soc.*, 1999, **121**, 4369–4378; (*d*) C. H. Burgos, T. E. Barder, X. Huang and S. L. Buchwald, Significantly Improved Method for the Pd-Catalyzed Coupling of Phenols with Aryl Halides: Understanding Ligand Effects, *Angew. Chem., Int. Ed.*, 2006, **45**, 4321–4326.

- 3 For selected examples for copper-catalyzed Ullmann-Goldberg diaryl ether coupling reaction, see: (a) J.-F. Marcoux, S. Doye and S. L. Buchwald, A general coppercatalyzed synthesis of diaryl ethers, J. Am. Chem. Soc., 1997, 119, 10539-10540; (b) E. Buck, Z. J. Song, D. Tschaen, P. G. Dormer, R. P. Volante and P. J. Reider, Ullmann diaryl ether synthesis: rate acceleration by 2, 2, 6-tetramethylheptane-3, 5-dione, Org. Lett., 2002, 4, 1623-1626; (c) D. Ma and Q. Cai, N,N-Dimethyl glycinepromoted Ullmann coupling reaction of phenols and aryl halides, Org. Lett., 2003, 5, 3799-3802; (d) Q. Cai, B. Zou and D. Ma, Mild Ullmann-Type Biaryl Ether Formation Reaction by Combination of ortho-Substituent and Ligand Effects, Angew. Chem., Int. Ed., 2006, 45, 1276-1279; (e) M. Fan, W. Zhou, Y. Jiang and D. Ma, CuI/Oxalamide catalyzed couplings of (Hetero) aryl chlorides and phenols for diaryl ether formation, Angew. Chem., Int. Ed., 2016, 55, 6211-6215; (f) H. Rao, Y. Jin, H. Fu, Y. Jiang and Y. Zhao, A Versatile and Efficient Ligand for Copper-Catalyzed Formation of C-N, C- O, and P- C Bonds: Pyrrolidine-2-Phosphonic Acid Phenyl Monoester, Chem. - Eur. J., 2006, 12, 3636-3646.
- 4 R. Takise, R. Isshiki, K. Muto, K. Itami and J. Yamaguchi, Decarbonylative Diaryl Ether Synthesis by Pd and Ni Catalysis, *J. Am. Chem. Soc.*, 2017, **139**, 3340–3343.
- 5 R. Sang, S. E. Korkis, W. Su, F. Ye, P. S. Engl, F. Berger and T. Ritter, Site-Selective C- H Oxygenation via Aryl Sulfonium Salts, *Angew. Chem., Int. Ed.*, 2019, **58**, 16161–16166.
- 6 For some other related studies, see: (a) J. Xiang, M. Shang, Y. Kawamata, H. Lundberg, S. H. Reisberg, M. Chen, P. Mykhailiuk, G. Beutner, M. R. Collins, A. Davies, M. Del Bel, G. M. Gallego, J. E. Spangler, J. Starr, S. Yang, D. G. Blackmond and P. S. Baran, Hindered dialkyl ether synthesis with electrogenerated carbocations, Nature, 2019, 573, 398-402; (b) F. Berger, M. B. Plutschack, J. Riegger, W. Yu, S. Speicher, M. Ho, N. C. Frank and T. Ritter, Site-selective and versatile aromatic C-Η functionalization bv thianthrenation, Nature, 2019, 567, 223-228; (c) C. Yuan, Y. Liang, T. Hernandez, A. Berriochoa, K. N. Houk and D. Siegel, Metal-free oxidation of aromatic carbon-hydrogen bonds through a reverse-rebound mechanism, Nature, 2013, 499, 192-196.
- 7 (a) F. Xu, H. Long, J. Song and H.-C. Xu, De Novo Synthesis of Functionalized Benzimidazolones Highly and Benzoxazolones through an Electrochemical Dehydrogenative Cyclization Cascade, Angew. Chem., Int. Ed., 2019, 58, 9017-9021; (b) H. Yan, Z.-W. Hou and H.-C. Xu, Photoelectrochemical C- H alkylation of heteroarenes with organotrifluoroborates, Angew. Chem., Int. Ed., 2019, 58, 4592-4595; (c) Z. J. Wu, F. Su, W. Lin, J. Song, T. B. Wen, H. J. Zhang and H.-C. Xu, Scalable Rhodium (III)-Catalyzed

Aryl C- H Phosphorylation Enabled by Anodic Oxidation Induced Reductive Elimination, *Angew. Chem., Int. Ed.*, 2019, **58**, 16770–16774.

- 8 (a) J. L. Röckl, D. Pollok, R. Franke and S. R. Waldvogel, A Decade of Electrochemical Dehydrogenative C, C- Coupling of Aryls, Acc. Chem. Res., 2020, 53(1), 45-61; (b) H. Wang, X. Gao, Z. Lv, T. Abdelilah and A. Lei, Recent Advances in Oxidative R1-H/R2-H Cross-Coupling with Hydrogen Evolution via Photo-/Electrochemistry, Chem. Rev., 2019, 119(12), 6769-6787; (c) Y. Yang, J. Lan and J. You, Oxidative C-H/C-H Coupling Reactions between Two (Hetero)arenes, Chem. Rev., 2017, 117(13), 8787-8863; (d) J. Vercammen, M. Bocus, S. Neale, A. Bugaev, P. Tomkins, J. Hajek, S. Van Minnebruggen, A. Soldatov, A. Krajnc, G. Mali, V. Van Speybroeck and D. E. De Vos, Shape-selective C-H activation of aromatics to biarylic compounds using molecular palladium in zeolites, Nat. Catal., 2020, 3(12), 1002-1009.
- 9 M. Jurrat, L. Maggi, W. Lewis and L. T. Ball, Modular bismacycles for the selective C-H arylation of phenols and naphthols, *Nat. Chem.*, 2020, **12**(3), 260–269.
- 10 A. Eisenhofer, J. Hioe, R. M. Gschwind and B. König, Photocatalytic Phenol-Arene C- C and C- O Cross-Dehydrogenative Coupling, *Eur. J. Org. Chem.*, 2017, **15**, 2194–2204.
- 11 (a) B. Dahms, R. Franke and S. R. Waldvogel, Metal-and Reagent-Free Anodic Dehydrogenative Cross-Coupling of Naphthylamines with Phenols, *ChemElectroChem*, 2018, 5, 1249–1252; (b) J. L. Röckl, D. Schollmeyer, R. Franke and S. R. Waldvogel, Dehydrogenative Anodic C–C Coupling of Phenols Bearing Electron-Withdrawing Groups, *Angew. Chem., Int. Ed.*, 2019, 59, 315–319.

- 12 T. J. Paniak and M. C. Kozlowski, Aerobic Catalyzed Oxidative Cross-Coupling of *N*,*N*-Disubstituted Anilines and Aminonaphthalenes with Phenols and Naphthols, *Org. Lett.*, 2020, **22**, 1765–1770.
- 13 C. Yu and F. W. Patureau, Cu-Catalyzed Cross-Dehydrogenative ortho-Aminomethylation of Phenols, *Angew. Chem., Int. Ed.*, 2018, **57**, 11807–11811.
- (a) X. Ling, Y. Xiong, R. Huang, X. Zhang, S. Zhang and C. Chen, Synthesis of benzidine derivatives via FeCl<sub>3</sub>·6H<sub>2</sub>O-promoted oxidative coupling of anilines, *J. Org. Chem.*, 2013, **78**, 5218–5226;
  (b) M. Melicharek and R. F. Nelson, The electrochemical oxidation of *N,N*-dimethyl-p-toluidine, *J. Electroanal. Chem. Interfacial Electrochem.*, 1970, **26**, 201–209;
  (c) R. Hand, M. Melicharek, D. I. Scoggin and R. Stotz, Electrochemical oxidation pathways of substituted dimethylanilines, *Collect. Czech. Chem. Commun.*, 1971, **36**, 842–854.
- 15 (a) T. A. Enache and A. M. Oliveira-Brett, Phenol and parasubstituted phenols electrochemical oxidation pathways, *J. Electroanal. Chem.*, 2011, 655, 9–16; (b) A. Libman, H. Shalit, Y. Vainer, S. Narute, S. Kozuch and D. Pappo, Synthetic and predictive approach to unsymmetrical biphenols by iron-catalyzed chelated radical-anion oxidative coupling, *J. Am. Chem. Soc.*, 2015, 137, 11453–11460.
- 16 B. G. Zhelyazkova, The influence of the solvent on the reaction of cupric chloride with N,N-dimethylaniline, *Inorg. Nucl. Chem. Lett.*, 1981, 17, 141–145.
- 17 B. M. Latta and R. W. Taft, Substituent effects on the hyperfine splitting constants of *N*,*N*-dimethylaniline cation radicals, *J. Am. Chem. Soc.*, 1967, **89**, 5172–5178.
- 18 I. Colomer, A. Chamberlain, M. Haughey and T. J. Donohoe, Hexafluoroisopropanol as a highly versatile solvent, *Nat. Rev. Chem.*, 2017, 1, 0088.