Communication

Electrochemical Synthesis of 1,1′-Binaphthalene-2,2′-Diamines via Transition-Metal-Free Oxidative Homocoupling

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Abstract: The facile and green synthesis of 1,1′-binaphthalene-2,2′-diamine (BINAM) derivatives was established via the anodic dehydrogenative homo-coupling of 2-naphthylamines. The sustainable protocol provided a series of BINAMs in excellent yields of up to 98% with good current efficiency (66%) and H_2 as the sole coproduct without utilizing transition-metal reagents or stoichiometric oxidants.

Keywords: electrochemical synthesis; 2-naphthylamines; anodic dehydrogenative homocoupling; BINAMs

1. Introduction

1,1′-Bi-2-naphthylamine (BINAM) and its derivatives are widely used as building blocks for transition-metal ligands and organocatalysts [1–4], as well as chiroptical materials for fluorescence sensing [5–7]. Among their syntheses, transition-metal mediated coupling of 2-naphthylamine derivatives has been well established [8–12]. In particular, the Ullmann [13] and metal-mediated C(sp^2)–H oxidative [14–20] coupling reactions of 2-naphthylamines are the most popular synthetic approaches to obtaining BINAMs. Benzidine rearrangement [21–23] and Smiles rearrangement of phenolic compounds [24] have been reported to be alternative synthetic methods for BINAMs. However, the regio- and chemoselective C–C coupling of 2-naphthylamines remains challenging, probably because these strategies require the use of excess amounts of metals and oxidants, which leads to many side reactions of starting material and over-oxidation of coupling products.

Biaryls synthesis through anodic oxidation utilizing electrochemical synthesis has emerged as a promising green and sustainable approach over the last few decades. The electrochemical dehydrogenative coupling of aryls utilizes electricity as an alternative to oxidants and produces H_2 as the sole coproduct without generating any toxic waste; thus, this approach exhibits great advantages in terms of high atom economy and environmentally benign synthesis protocols [25,26]. Although remarkable achievements have been made in the electrochemical dehydrogenative heterocoupling of anilines [27], few reports on the homocoupling of aniline derivatives [28,29], particularly 2-naphthylamines, are available. In the 1980s, Gossage [30] and Sereno [31] independently described the electrochemical dehydrogenative homocoupling of 2-naphthylamines, which afforded BINAMs, but in low yield. Thus, the development of efficient oxidative homocoupling protocols for 2-naphthylamines via electrochemical synthesis is of great importance.

Because the discharge of the electrolyte or solvent leads to a low yield and poor current efficiency, we reexamined the anodic dehydrogenative homocoupling conditions of 2-naphthylamines to save energy and chemical loading in the pursuit of developing environmentally benign chemical reactions. To our delight, under the newly established conditions, the corresponding homocoupling products were obtained in 98% yield with good current efficiency (66%; Scheme 1).

Scheme 1. Electrochemical dehydrogenative homocoupling of 2-naphthylamines.

2. Materials and Methods

2.1. Materials

N-Phenyl-2-napthylamine (**1a**) was purchased from Tokyo Chemical Industries (TCI). All commercially available organic and inorganic compounds were used directly without further purification.

2.2. Methods

2.2.1. Spectroscopy and Spectrometry

^{1}H- and ^{13}C-NMR spectra were recorded at 25 °C using a JEOL JMN ECS400 FT NMR instrument (^{1}H-NMR 400 MHz; ^{13}C-NMR 100 MHz). The ^{1}H-NMR spectra are reported as follows: chemical shift in ppm downfield of tetramethylsilane and referenced to a residual solvent peak (CHCl$_3$) at 7.26 ppm, integration, multiplicities (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), and coupling constants (Hz). The ^{13}C-NMR spectra are reported in ppm relative to the central line of the triplet for CDCl$_3$ at 77.16 ppm. ESI-MS spectra were obtained using a JMS-T100LC instrument (JEOL). FT-IR spectra were recorded using a JASCO FT-IR system (FT/IR4100). Thin-layer chromatography (TLC) analysis of the reaction mixture was performed on Merck silica gel 60 F254 TLC plates and visualized under UV light. Column chromatography on SiO$_2$ was performed using Kanto Silica Gel 60 (63–210 µm).

2.2.2. General Protocol for the Anodic Homocoupling of 2-Naphthylamines

ElectraSyn 2.0 and platinum were utilized as the reaction device and electrode, respectively. A suspension of 2-naphthylamines (0.1 mmol) and ^{n}Bu$_4$NPF$_6$ (0.1 M) in 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) (5 mL) was added to an undivided vessel and stirred under a constant current of 4 mA for 2 h. The electrolyte was removed using short silica gel column chromatography (^{n}hexane/ethyl acetate = 1/1). The fraction was dried, and the crude product was purified by silica-gel column chromatography (^{n}hexane/ethyl acetate = 20/1) to afford the pure homocoupling product.

3. Results

3.1. Optimization of the Reaction Conditions

Initially, we screened the electrodes, solvent systems, currents, and electrolytes to determine the optimal conditions (Table 1, also see supporting information). The electrodes were screened by employing 0.1 mmol *N*-phenyl-2-naphthylamine (**1a**, oxidative potential 1.05 eV; see Supporting Information) as the model substrate. The platinum electrode exhibited good reactivity, affording homocoupling product **2a** in 98% yield (current efficiency, 66%) without the formation of any side product (entry 1). In contrast, the carbon–platinum [32] and fluorine-doped tin oxide(FTO) [33] electrodes gave **2a** in 43% and 29% yields, respectively, with low current efficiencies (entries 2 and 3). Other alcoholic reaction solvents, such as methanol, ethanol, and trifluoroethanol, reduced the yield of **2a** to 6–12% with current efficiencies of 4–8% (entries 4–6), along with a 5% yield of aza [5]

helicene. HFIP, an appropriate solvent for the reaction, serves as an excellent hydrogen bond donor and provides highly persistent radical cations [34,35]. The effect of a constant current was also investigated. As shown in entry 7, when a current of 2 mA was employed for the electrosynthesis process, the current efficiency increased to 80%, but the yield of **2a** decreased to 60%. In contrast, employing a current of 6 mA for the electrosynthesis process led to the formation of **2a** in 49% yield, with a current efficiency of 22% (entry 8). Suppressing the discharge of the electrolyte or solvent resulted in higher yield and current efficiency. Among the electrolytes we screened, $^{n}Bu_4NPF_6$ proved to be superior to $LiClO_4$ (**2a**, 57% yield due to low solubility in HFIP) and $^{n}Bu_4NClO_4$ (**2a**, 29% yield) (entries 9 and 10). No reaction occurred in the absence of electricity (entry 11).

Table 1. Optimization of the conditions for the electrochemical homocoupling of 2-naphthylamines using **1a** as the model substrate.
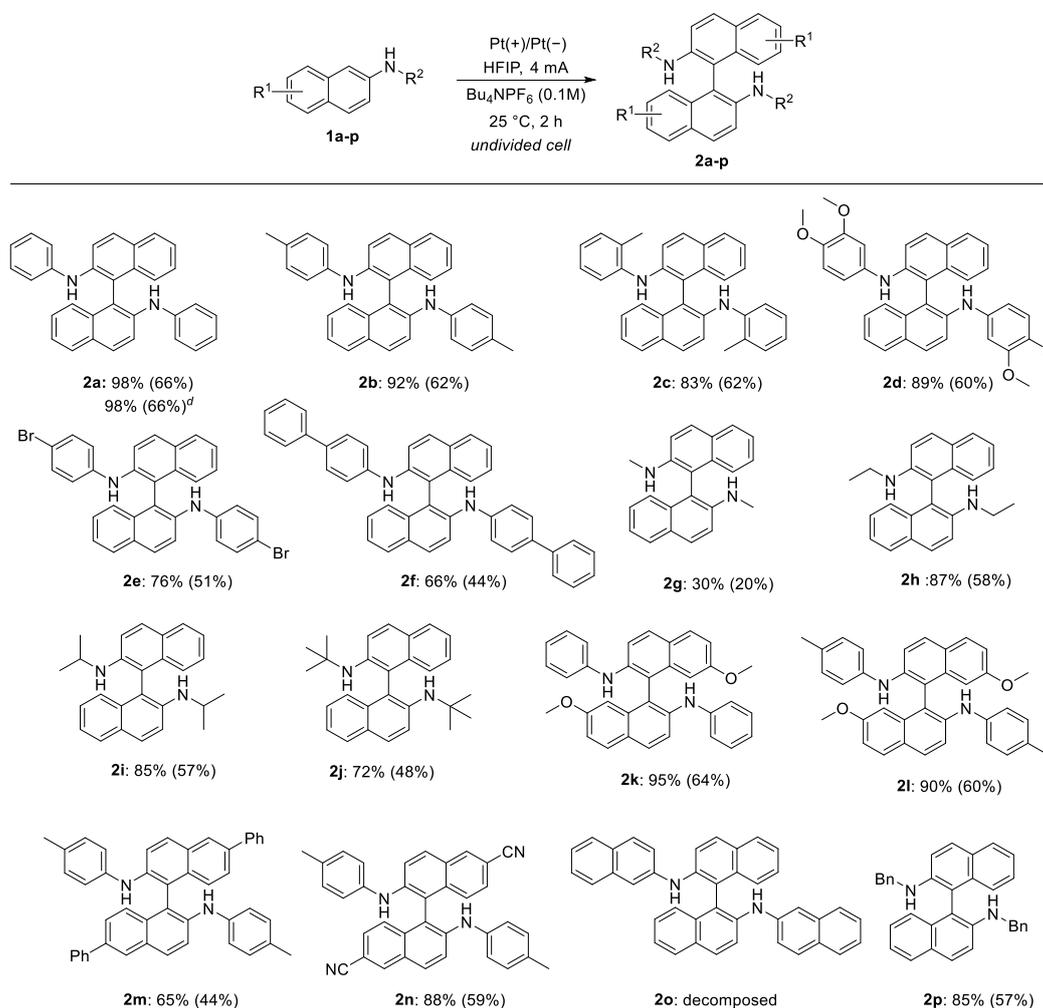

Entry	Variation from Standard Conditions	% Yield (% Current Efficiency) [a]	
		2a	3a
1	None	99, 98 [b] (66)	-
2	C (+)/Pt (−)	43 (29)	-
3	FTO (−)/FTO [c] (+)	29 (20)	-
4	MeOH instead of HFIP	10 (7)	5
5	EtOH instead of HFIP	6 (4)	5
6	CF_3CH_2OH instead of HFIP	12 (8)	-
7	2 mA	60 (80)	-
8	6 mA	49 (22)	-
9	with $LiClO_4$ instead of $^{n}Bu_4NPF_6$	57 [d] (38)	-
10	with $^{n}Bu_4NClO_4$ instead of $^{n}Bu_4NPF_6$	29 (19)	-
11	No electricity	No reaction	

[a] NMR yield; [b] Isolated yield; [c] FTO = Fluorine-doped tin oxide; [d] HFIP:MeOH (3:2) for 8 h.

3.2. Scope of Substrates

With the optimized conditions in hand (reaction solvent: HFIP, electrolyte: $^{n}Bu_4NPF_6$ (0.1 M), electrode: platinum, constant current: 4 mA, and reaction temperature: 25 °C), we investigated the substrate scope of the 2-naphthylamines (Figure 1). The electrochemical homocoupling of 2-naphthylamines **1** proceeded smoothly at moderate current efficiencies (44–66%). *N*-Phenyl-2-naphthylamine (**1a**) produced homocoupling product **2a** in 98% yield. *N*-4-Tolyl and *N*-2-tolyl-2-naphthylamines (**1b** and **1c**), respectively, were also found to be appropriate coupling precursors, giving the corresponding homocoupling products **2b** and **2c** in 92% and 83% yields, respectively. The reaction of substrates **1d** and **1e** with electron-donating or electron-withdrawing groups, such as *N*-2,3-dimethoxyphenyl and *N*-4-bromophenyl, on the nitrogen atom, showed good functional group tolerance, giving binaphthylamines **2d** and **2e** in good yields. When *N*-(1,1′-biphenyl)-4-yl-2-naphthylamine (**1f**) was used as the substrate, a moderate yield of the coupling product **2f** was obtained because of the poor solubility of **1f** in HFIP. The reactions of *N*-alkyl-2-naphthylamines, such as *N*-methyle-2-naphthylamine (**1g**), *N*-ethyl-2-naphthylamine (**1h**), *N*-isopropyl-2-naphthylamine (**1i**), and *N*-*t*-butyle-2-naphthylamine (**1j**) afforded the corresponding homocoupling products **2g**, **2h**, **2i** and **2j** in 30%, 87%, 85% and 72% yields, respectively. The dehydrogenative coupling reactions of *N*-aryl-2-naphthylamines (**1k**–**1n**) with various substituents were also conducted. Products **2k** and **2l** with methoxy groups **2m** and **2n** with phenyl and cyano groups were readily obtained in good to excellent yields (65–95%

yields). *N*-Naphthyl-2-naphthyl amine (**1o**) could not be tolerated. Finally, *N*-benzyl-naphthylamine (**1p**) was employed in the electrochemical homocoupling reaction. The corresponding product **2p** was obtained an 85% yield and could be transformed into BINAM with Lewis acid (See Supporting Information).

2a: 98% (66%)
98% (66%)[d]

2b: 92% (62%)

2c: 83% (62%)

2d: 89% (60%)

2e: 76% (51%)

2f: 66% (44%)

2g: 30% (20%)

2h :87% (58%)

2i: 85% (57%)

2j: 72% (48%)

2k: 95% (64%)

2l: 90% (60%)

2m: 65% (44%)

2n: 88% (59%)

2o: decomposed

2p: 85% (57%)

[a] Reaction conditions: 2-naphthylamine **1** (0.1 mmol, 1.0 equiv.) and *n*Bu₄NPF₆ (0.1 M) in HFIP (5 mL) were added to an undivided vessel and stirred under a constant current of 4 mA for 2 h; [b] Isolated yield; [c] Current efficiency in parentheses. [d] 0.4 mmol of **1a**.

Figure 1. Substrate scope of *N*-naphthylamines [a–d].

4. Discussion

In our study, the homocoupling reaction of 2-naphthylamines proceeded smoothly with good current efficiency. To further understand the relevant mechanism, we conducted the heterocoupling reactions of **1b** with *N*-4-tolyl (an electron-donating group) and **1e** with *N*-4-bromo-phenyl (an electron-withdrawing group) under the optimal conditions (Scheme 2).

Homocoupling product **2b** was obtained in 90% yield as the major product, along with homocoupling product **2e** in 10% yield and trace amounts of heterocoupling product **2be**. The relative proportions of the products arising from the radical–radical coupling reactions are aligned with their relative reactivities [36–38]. In principle, **1e** is less oxidizable than **1b**, which should result in the formation of homocoupling **2b** as the major product. The results support our hypothesis that the present coupling reaction of **1** proceeds through radical–radical coupling, as shown in Scheme 3. Triggering by single-electron transfer (SET) of **1a** on the anode made the formation of intermediate **I**. The generated **I** species could be

in equilibrium into **Ia** and **Ib** by electron transfer. Then a radical–radical coupling of **Ib** proceeded to afford the coupling product **2b** through the oxidation of intermediate **II**. On the cathode, the generated H$^+$ was reduced to give H$_2$ as a sole coproduct.
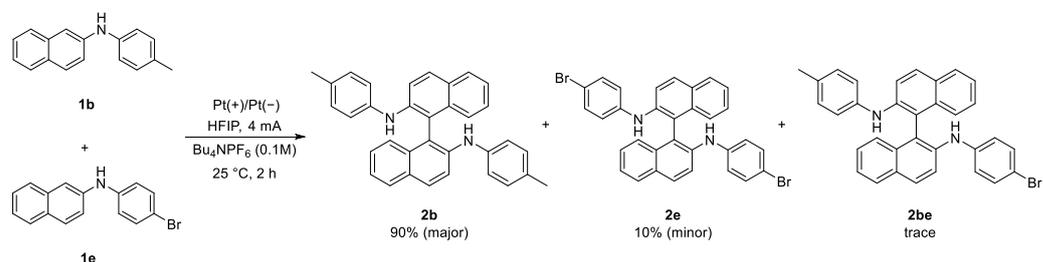
Scheme 2. Electrochemical heterocoupling of substrate **1b** and **1e**.
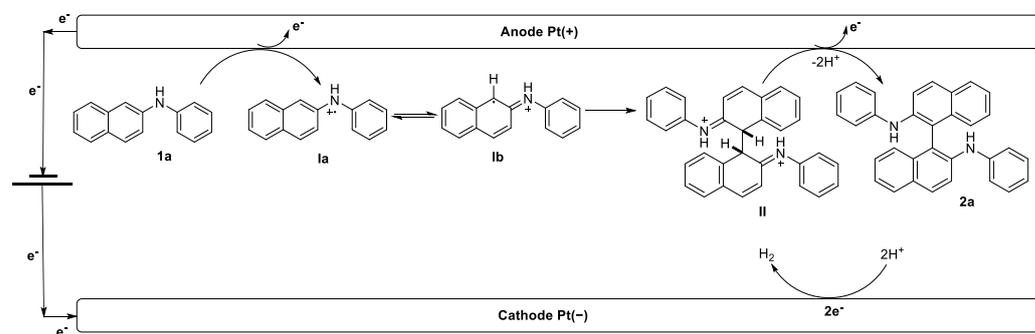
Scheme 3. Proposed mechanism for the homocoupling of 2-naphthylamines.

5. Conclusions

We developed a facile and sustainable protocol for the homocoupling of various 2-naphthylamines with up to 98% yield and good current efficiency (66%). This new protocol not only saves energy and chemical loading but also significantly improves the product yield, thus representing a significant improvement to the previous electrosynthesis approach. Investigations of the further applications of homocoupling products are ongoing in our laboratory.

References

1. Telfer, S.; Kuroda, R. 1,1′-Binaphthyl-2,2′-diol and 2,2′-diamino-1,1′-binaphthyl: Versatile frameworks for chiral ligands in coordination and metallosupramolecular chemistry. *Coord. Chem. Rev.* **2003**, *242*, 33–46. [CrossRef]

2. Hatano, M.; Ikeno, T.; Matsumura, T.; Torii, S.; Ishihara, K. Chiral lithium salts of phosphoric acids as Lewis acid-base conjugate catalysts for the enantioselective cyanosilylation of ketones. *Adv. Synth. Catal.* **2008**, *350*, 1776–1780. [CrossRef]

3. Prasad, D.J.C.; Naidu, A.B.; Sekar, G. An efficient intermolecular C(aryl)–S bond forming reaction catalyzed by BINAM–copper(II) complex. *Tetrahedron Lett.* **2009**, *50*, 1411–1415. [CrossRef]

4. Hannedouche, J.; Collin, J.; Trifonov, A.; Schulz, E. Intramolecular enantioselective hydroamination catalyzed by rare earth binaphthylamides. *J. Organomet. Chem.* **2011**, *696*, 255–262. [CrossRef]

5. Averin, A.D.; Grigorova, O.K.; Malysheva, A.S.; Shaferov, A.V.; Beletskaya, I.P. Pd(0)-Catalyzed amination in the synthesis of chiral derivatives of BINAM and their evaluation as fluorescent enantioselective detectors. *Pure Appl. Chem.* **2020**, *92*, 1367–1386. [CrossRef]

6. Yan, Z.-P.; Liu, T.-T.; Wu, R.; Liang, X.; Li, Z.-Q.; Zhou, L.; Zheng, Y.-X.; Zuo, J.-L. Chiral thermally activated delayed fluorescence materials based on R/S-$N^2,N^{2'}$-diphenyl-[1,1′-binaphthalene]-2,2′-diamine donor with narrow emission spectra for highly efficient circularly polarized electroluminescence. *Adv. Funct. Mater.* **2021**, *31*, 2103875. [CrossRef]

7. Meng, Q.; Feng, Q.; Cui, L.; Li, F.; Cheng, Y.; Li, Y.; Wang, Y. Chiral binaphthylamine based emitters with donor-acceptor structures: Facile synthesis and circularly polarized luminescence. *Dye. Pigment.* **2022**, *199*, 110085. [CrossRef]

8. Smrčina, M.; Vyskočil, S.; Máca, B.; Polášek, M.; Claxton, T.A.; Abbott, A.P.; Kočovský, P. Selective cross-coupling of 2-naphthol and 2-naphthylamine derivatives. A facile synthesis of 2,2′,3-trisubstituted and 2,2′,3,3′-tetrasubstituted 1,1′-binaphthyls. *J. Org. Chem.* **1994**, *59*, 2156–2163. [CrossRef]

9. Liu, C.; Yuan, J.; Gao, M.; Tang, S.; Li, W.; Shi, R.; Lei, A. Oxidative coupling between two hydrocarbons: An update of recent C–H functionalizations. *Chem. Rev.* **2015**, *115*, 12138–12204. [CrossRef]

10. Forkosh, H.; Vershinin, V.; Reiss, H.; Pappo, D. Stereoselective synthesis of optically pure 2-amino-2′-hydroxy-1,1′-binaphthyls. *Org. Lett.* **2018**, *20*, 2459–2463. [CrossRef]

11. Hayashi, H.; Ueno, T.; Kim, C.; Uchida, T. Ruthenium-catalyzed cross-selective asymmetric oxidative coupling of arenols. *Org. Lett.* **2020**, *22*, 1469–1474. [CrossRef] [PubMed]

12. Bansal, S.; Shabade, A.B.; Punji, B. Advances in C(sp^2)–H/C(sp^2)–H oxidative coupling of (hetero)arenes using 3d transition metal catalysts. *Adv. Synth. Catal.* **2021**, *363*, 1998–2022. [CrossRef]

13. Hassan, J.; Sévignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. Aryl–aryl bond formation one century after the discovery of the Ullmann reaction. *Chem. Rev.* **2002**, *102*, 1359–1469. [CrossRef] [PubMed]

14. Smrčina, M.; Lorenc, M.; Hanuš, V.; Sedmera, P.; Kočovský, P. Synthesis of enantiomerically pure 2,2′-dihydroxy-1,1′-binaphthyl, 2,2′-diamino-1,1′-binaphthyl, and 2-amino-2′-hydroxy-1,1′-binaphthyl. Comparison of processes operating as diastereoselective crystallization and as second order asymmetric transformation. *J. Org. Chem.* **1992**, *57*, 1917–1920. [CrossRef]

15. Vyskočil, Š.; Smrčina, M.; Lorenc, M.; Tišlerová, I.; Brooks, R.D.; Kulagowski, J.J.; Langer, V.; Farrugia, L.J.; Kočovský, P. Copper(II)-mediated oxidative coupling of 2-aminonaphthalene homologues. Competition between the straight dimerization and the formation of carbazoles. *J. Org. Chem.* **2001**, *66*, 1359–1365. [CrossRef]

16. Zi, G.; Xiang, L.; Zhang, Y.; Wang, Q.; Zhang, Z. Synthesis, structure, and activity of $(PhCH_2NH_2)_2CuCl_2$ for oxidative coupling of 2-naphthylamine. *Appl. Organomet. Chem.* **2007**, *21*, 177–182. [CrossRef]

17. Yusa, Y.; Kaito, I.; Akiyama, K.; Mikami, K. Asymmetric catalysis of homo-coupling of 3-substituted naphthylamine and hetero-coupling with 3-substituted naphthol leading to 3,3′-dimethyl-2,2′-diaminobinaphthyl and -2-amino-2′-hydroxybinaphthyl. *Chirality* **2010**, *22*, 224–228. [CrossRef]

18. Li, X.-L.; Huang, J.-H.; Yang, L.-M. Iron(III)-promoted oxidative coupling of naphthylamines: Synthetic and mechanistic investigations. *Org. Lett.* **2011**, *13*, 4950–4953. [CrossRef]

19. Matsumoto, K.; Dougomori, K.; Tachikawa, S.; Ishii, T.; Shindo, M. Aerobic oxidative homocoupling of aryl amines using heterogeneous rhodium catalysts. *Org. Lett.* **2014**, *16*, 4754–4757. [CrossRef]

20. Fujimoto, S.; Matsumoto, K.; Iwata, T.; Shindo, M. Aerobic oxidative homocoupling of anilides using heterogeneous metal catalysts. *Tetrahedron Lett.* **2017**, *58*, 973–976. [CrossRef]

21. Lim, B.; Choi, M.; Cho, C. Acid-catalyzed condensation of 2,2′-diamino-1,1′-biaryls for the synthesis of benzo[c]carbazoles. *Tetrahedron Lett.* **2011**, *52*, 6015–6017. [CrossRef]

22. Li, G.-Q.; Gao, H.; Keene, C.; Devonas, M.; Ess, D.H.; Kürti, L. Organocatalytic aryl-aryl bond formation: An atroposelective [3,3]-rearrangement approach to BINAM derivatives. *J. Am. Chem. Soc.* **2013**, *135*, 7414–7417. [CrossRef] [PubMed]

23. De, C.K.; Pesciaioli, F.; List, B. Catalytic asymmetric benzidine rearrangement. *Angew. Chem. Int. Ed.* **2013**, *52*, 9293–9295. [CrossRef] [PubMed]

24. Chang, X.; Zhang, Q.; Guo, C. Switchable Smiles rearrangement for enantioselective O-aryl amination. *Org. Lett.* **2019**, *21*, 4915–4918. [CrossRef] [PubMed]

25. Schäfer, H.J. Anodic and cathodic CC-bond formation. *Angew. Chem. Int. Ed. Engl.* **1981**, *20*, 911–934. [CrossRef]

26. Kirste, A.; Elsler, B.; Schnakenburg, G.; Waldvogel, S.R. Efficient anodic and direct phenol-arene C,C cross-coupling: The benign role of water or methanol. *J. Am. Chem. Soc.* **2012**, *134*, 3571–3576. [CrossRef]

27. Schulz, L.; Enders, M.; Elser, B.; Schollmeyer, D.; Dyballa, K.M.; Franke, R.; Waldvogel, S.R. Reagent- and metal-free anodic C-C cross-coupling of aniline derivatives. *Angew. Chem. Int. Ed.* **2017**, *56*, 4877–4881. [CrossRef]

28. Schulz, L.; Franke, R.; Waldvogel, S.R. Direct anodic dehydrogenative cross- and homo-coupling of formanilides. *ChemElectroChem* **2018**, *5*, 2069–2072. [CrossRef]

29. Schulz, L.; Husmann, J.-Å.; Waldvogel, S.R. Outstandingly robust anodic dehydrogenative aniline coupling reaction. *Electrochim. Acta* **2020**, *337*, 135786. [CrossRef]

30. Hornback, J.M.; Gossage, H.E. Electrochemical oxidative dehydrodimerization of naphthylamines. An efficient synthesis of 8,8-dianilino-5,5′-binaphthalene-l,l′-disulfonate. *J. Org. Chem.* **1985**, *50*, 541–543. [CrossRef]

31. Vettorazzi, N.; Silber, J.J.; Sereno, L. Anodic oxidation of 1-naphthylamine in acetonitrile. *J. Electroanal. Chem. Interfacial Electrochem.* **1981**, *125*, 459–475. [CrossRef]

32. Luo, M.-J.; Li, Y.; Ouyang, X.-H.; Li, J.-H.; He, D.-L. Electrochemical dehydrogenative cross-coupling of two anilines: Facile synthesis of unsymmetrical biaryls. *Chem. Commun.* **2020**, *56*, 2707–2710. [CrossRef] [PubMed]

33. Zhang, L.; Hu, X. Nickel catalysis enables convergent paired electrolysis for direct arylation of benzylic C–H bonds. *Chem. Sci.* **2020**, *11*, 10786–10791. [CrossRef] [PubMed]

34. Eberson, L.; Hartshorn, M.P.; Persson, O. 1,1,1,3,3,3-Hexafluoropropan-2-ol as a solvent for the generation of highly persistent radical cations. *J. Chem. Soc. Perkin Trans. 2* **1995**, *18*, 1735–1744. [CrossRef]

35. Eberson, L.; Persson, O.; Hartshorn, M.P. Detection and reactions of radical cations generated by photolysis of aromatic compounds with tetranitromethane in 1,1,1,3,3,3-hexafluoro-2-propanol at room temperature. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2268–2269. [CrossRef]

36. Li, X.; Yang, J.; Kozlowski, M.C. Enantioselective oxidative biaryl coupling reactions catalyzed by 1,5-diazadecalin metal complexes. *Org. Lett.* **2001**, *3*, 1137–1140. [CrossRef]

37. Takizawa, S.; Katayama, T.; Somei, H.; Asano, Y.; Yoshida, T.; Kameyama, C.; Rajesh, D.; Onitsuka, K.; Suzuki, T.; Mikami, M.; et al. Dual activation in oxidative coupling of 2-naphthols catalyzed by chiral dinuclear vanadium complexes. *Tetrahedron* **2008**, *64*, 3361–3371. [CrossRef]

38. Guo, Q.-X.; Wu, Z.-J.; Luo, Z.-B.; Liu, Q.-Z.; Ye, J.-L.; Luo, S.-W.; Cun, L.-F.; Gong, L.-Z. Highly enantioselective oxidative couplings of 2-naphthols catalyzed by chiral bimetallic oxovanadium complexes with either oxygen or air as oxidant. *J. Am. Chem. Soc.* **2007**, *129*, 13927–13938. [CrossRef]