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The synthesis of benzidine derivatives has always attracted considerable attention from synthetic chemists because they are not only common structural constituents that are present in many biological and pharmaceutical molecules [1], but also can serve as important building blocks for the synthesis of functionalized heterocycles [2]. In addition, the chemical and physical properties of benzidine-based compounds have enabled their use in the manufacture of azodyes and in cell biology as staining reagents [3]. Traditionally the synthesis of benzidine derivatives has largely relied on the rearrangement of hydrazobenzenes [4]. Although effective, the conventional rearrangement reactions suffer from major limitations, including (1) the highly prefunctionalized starting materials; (2) the formation of a substantial amount of by-products. A more concise and atom economical method based on dehydrogenative coupling methodology would be highly desirable since fewer steps would be needed.

Indeed, the direct dehydrogenative coupling methods has been well known [5]. Recent studies have investigated that excess amounts of metal salt oxidants such as TiCl₄, CAN, CuBr/H₂O₂, Cu (ClO₄)₂ and FeCl₃·6H₂O, can be utilized for their transformation [6]. For examples, Chen et al. reported that Fe salts can be used to promote oxidative coupling of aniline, which tend to form benzidine derivatives.^{6a} In contrast, examples of external-oxidant-free and transition metal-free dehydrogenative coupling are less abun-

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ABSTRACT

Synthesis of diversely functionalized symmetrical benzidines through electrochemical dehydrogenative cross-coupling reaction of two *N*,*N*-disubstituted anilines, is described. The reactions conducted under mild conditions with no oxidizing reagents and transition metal catalysts.

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dant. As an alternative to chemical oxidation, electrooxidation is attracting increasing interests [7]. Particularly, great achievements for biaryl synthesis have been gained in the electrochemical dehydrogenative coupling cross-coupling of two aromatic compounds [8]. Under these backgrounds, we strongly thought that the new electrochemical method for the synthesis of benzidine derivatives should be realized. For example, in 1962, Mizoguchi et al. reported the first reaction between two *N*,*N*-Dimethylaniline by means of electrochemical processes focused on the para/para selective homocoupling mode [9]. However, this method needs to be conducted in a strictly controlled buffer solution. Very recently, Li et al. disclosed that an efficient reaction dehydrogenative cross coupling of amino-naphthalenes with eletron-rich arenes to provide nonsymmetrical biaryls [10].

Herein, we report a new, general anode strategy for the synthesis of various symmetrical benzidines by *para*-selective dehydrogenative cross-coupling of two anilines under neutral reaction conditions while avoiding the use of additional metal catalysts and stoichiometric oxidants. We initiated our study by identifying the optimal reaction conditions for the electrochemical dehydrogenative cross-coupling of two *N*,*N*-dibenzylanilines. To our delight, the desired benzidines **2a** were indeed obtained in 87% yield when the reaction was conducted under constant current electrolysis at 8 mA in the presence of tetrabutylammonium hexafluorophosphate (n-Bu₄NPF₆, 0.5 equiv) in acetonitrile (ACN, 5 mL) at room temperature (Table 1, entry 1). The electrode materials have a significant impact on the reaction outcome, while an

Table 1

Screening of the reaction conditions.^a

Bn N	* H- Bn <u>Pt (+) I C (-), I = 8 mA</u> <u>n-Bu4NPF₆ (0.5 equiv)</u> ACN (5 mL), rt, 6 h	Bn N-N-N-N-N-H2 Bn
1a	1a undivided cell	2a
entry	variation from standard condtions	yield ^b
1	none	87%
2	Pt (+) Pt(-) instead of Pt (+) C (-)	76%
3	C (+) I Pt(-) instead of Pt (+) I C (-)	46%
4	C (+) I C(-) instead of Pt (+) I C (-)	54%
5	RVC (+) I C(-) instead of Pt (+) I C (-)	61%
6	NaClO ₄ instead of n-Bu ₄ NPF ₆	70%
7	NH ₄ I instead of n-Bu ₄ NPF ₆	n.d.
8	KPF_6 instead of n-Bu ₄ NPF ₆	trace
9	HFIP instead of ACN as the solvent	60%
10	DMF instead of ACN as the solvent	35%
11	$\rm CH_2\rm Cl_2$ instead of ACN as the solvent	n.d.
12	6 mA	45%
13	10 mA	69%

^a Reaction conditions: *N*,*N*-dibenzylaniline **1a** (0.5 mmol), rt, in an undivided cell, 6 h. Unless otherwise noted.

^b Estimated by ¹H NMR using m-cresol as an internal reference.



^a Reaction conditions: aniline **1** (0.5 mmol), rt, in an undivided cell, 6 h. Unless otherwise noted.

^b Isolated yields.



Scheme 1. Gram-scale synthesis of 6,6'-biquinoline 3.



Fig. 1. UV–vis spectra of **2a**, **2c**, **2d** and **2p** $(2.5 \times 10^{-5} \text{ M})$ in dichloromethane.

obvious loss of yield was obtained either with a platinum/carbon/ RVC plate anode or platinum/carbon plate cathode (Table 1, entries 2–5). In addition, this reaction was dramatically affected upon replacing the electrolyte with either NaClO₄, NH₄I or KPF₆ (Table 1, entries 6–8). Other solvents, such as HFIP, DMF and CH₂Cl₂ were also examined. However, all displayed lower effectiveness than acetonitrile (Table 1, entries 9–11). Finally, lowering or increasing the current intensity to 6 or 10 mA have adverse effects on the reaction efficiency (Table 1, entries 12–13).

With optimized experimental conditions in hand, we set out to evaluate the scope of the electrochemical dehydrogenative crosscoupling of two anilines. As summarized in Table 2, a wealth of aniline derivatives carrying different electronically and sterically varied phenyl substituents reacted well, affording the corresponding symmetrical benzidines in 74–92% yields. The substitution effect of the aryl ring of anilines was firstly checked: several ortho- or meta- substituents, such as Cl, Br, I, Me and MeO, were efficient for gaining the products **2b-2k** with moderate to good yields, respectively. It is worth mentioning that the good results **2h-2i** in the electrochemical dehydrogenative cross-coupling reaction are achieved with the



Scheme 2. Possible mechanism.

highly bulky starting materials. When the anilines with different substituent groups like N-methyl-N-benzylanilines, N-ethyl-N-benzylanilines and N-methyl-N-ethylanilines were involved, the target products 2j-2m and 2o were obtained in high yields as well. In addition, the reaction could afford the corresponding products **2n** and **2p** up to 90% yield when dialkylanilines, such as N,N-dimethylaniline and N,N-diethylaniline, were used as the substrates. Meanwhile, oxidative coupling of N-phenylpiperidine and 1-phenylpyrrolidine, afforded 2q-2r with 80-83% yields. Delightfully, this present electrochemical protocol is efficiently applied in the incorporation of various important pharmacophore motifs, including 1,2,3,4tetrahydroquinoline and 1-benzyl-1,2,3,4-tetrahydroquinoline, into the symmetrical benzidines. More importantly, N-allylic containing substituents were particularly reactive, expanding the synthetic utility of the protocol in this work significantly.

The applicability of the present electrochemical reaction was further tested. In the small-scale synthesis, a concentration of 0.1 M of the 1s was required, and the increase of reaction substrate would reduce the yield of the target product. This clean electrochemical reaction offered a great opportunity for the exploration of one-pot sequential transformation from readily available starting materials. Pleasingly, the electrochemical dehydrogenative cross-coupling reaction of 1s with a 20-fold increase in the concentration of 1s gave the target product 3 in 72% isolated yield underwent dehydrogenation without a tedious workup process. It is worthwhile to point out that, unlike the results reported by Xu, the reaction of 1s produced C--C dimerization product instead of *N*–*N* dimerization [11]. Moreover, the 6,6′-biquinoline **3** was found to be a potential photoactive material [12] (Scheme 1).

UV-visible absorption measurement was also performed with selected coupling products (2a, 2c, 2d and 2p). The absorption maxima of 2p are at 320 nm, whereas the 2a, 2c and 2d exhibit a stronger red-shifted absorption band. This result indicates that π electrons in 2a, 2c and 2d are more easily excited to a higher antibonding molecular orbital. Moreover, different benzyl moieties on anilines lead to large blueshifts of the absorption maxima, which shows that the substitutions on the benzene ring have an obvious impact on the energy gap between the HOMO and the LUMO (Fig. 1).

In continuation, a plausible mechanism for the aforementioned transformation is proposed in Scheme 2. Initially, aniline 1a underwent a single electron oxidation at the anode to give the cationic radical A. Next, the dehydrogenative cross-coupling reaction between energetically favourable radical **B** and another **1a** would deliver the target product **2a** through loss of an electron and two H⁺ species. Combined with cyclic voltammetry analysis (supplementary material), the product **2a** is likely oxidized reversibly to a radical cation, which can serve as a catalyst for self-catalysis.

In conclusion, we have achieved the para-selective anodic dehydrogenative cross-coupling of anilines (21 examples, 74-92%, >1.8 g). This reaction proceeded smoothly with excellent selectivity in the absence of any transition metals or oxidants. In addition, this explained procedure, owing to the exploitation of an undivided cell, is satisfactorily facile, thus meeting the demands of contemporary syntheses and suitable to be used as alternative to the prior methods.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tetlet.2021.153021.

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Erratum

Erratum to "Electrochemical synthesis of symmetrical benzidines through dehydrogenative cross-coupling reaction" [Tetrahedron Lett., 70 (2021) 153021]

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The publisher regrets that Table 1 in the published article does not appear in the correct format and is missing content. The table has now been corrected and can be seen here:

The publisher would like to apologise for any inconvenience caused.

Table 1 Screening of the reaction conditions.^a

Bn H	+ H- N, Bn 	Bn Bn Bn H2
entry	variation from standard conditions	Za vield ^b
1		970/
I	none	87%
2	Pt (+) I Pt(-) instead of Pt (+) I C (-)	76%
3	C (+) I Pt(-) instead of Pt (+) I C (-)	46%
4	C (+) I C(-) instead of Pt (+) I C (-)	54%
5	RVC (+) I C(-) instead of Pt (+) I C (-)	61%
6	$NaClO_4$ instead of n-Bu ₄ NPF ₆	70%
7	NH_4I instead of n-Bu ₄ NPF ₆	n.d.
8	KPF_6 instead of n-Bu ₄ NPF ₆	trace
9	HFIP instead of ACN as the solvent	60%
10	DMF instead of ACN as the solvent	35%
11	CH_2CI_2 instead of ACN as the solvent	n.d.
12	6 mA	45%
13	10 mA	69%

^aReaction conditions: *N*,*N*-dibenzylaniline **1a** (0.5 mmol), rt, in an undivided cell, 6 h. Unless otherwise noted.

^bEstimated by ¹H NMR using m-cresol as an internal reference.

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