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Chemoselective electrochemical reduction of nitroarenes with gaseous ammonia†

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Valuable aromatic nitrogen compounds can be synthesized by reduction of nitroarenes. Herein, we report electrochemical reduction of nitroarenes by a protocol that uses inert graphite felt as electrodes and ammonia as a reductant. Depending on the cell voltage and the solvent, the protocol can be used to obtain aromatic azoxy, azo, and hydrazo compounds, as well as aniline derivatives with high chemoselectivities. The protocol can be readily scaled up to >10 g with no decrease in yield, demonstrating its potential synthetic utility. A stepwise cathodic reduction pathway was proposed to account for the generations of products in turn.

The reduction of nitroarenes can provide a variety of useful nitrogen compounds, such as anilines, azobenzenes and azoxybenzenes. Azobenzenes also have applications as energy storage materials,¹ molecular switches,² monomers for azoxy polyesters,³ as building blocks for liquid crystals,⁴ and as directing groups in transition-metal-catalyzed C-H functionalization reactions.⁵ Reduction of nitroarenes to anilines is usually accomplished by heterogeneous catalytic hydrogenation or by transfer hydrogenation mediated by elemental reagents (Scheme 1a).⁶ In comparison, the protocols reducing nitroarenes to azobenzene and azoxybenzenes were less developed as explicit controls of reaction conditions were required to achieve the chemoselectivities at different levels of reduction.⁷ The development of mild, atom-economical and highly selective methods for reduction of nitroarenes is highly desirable.

We speculated that an electrochemical method might be useful for this purpose. Research on electrochemical synthesis has resulted in new transformations,⁸ better understanding of reaction mechanisms,⁹ the development of combinations with other synthetic protocols¹⁰ and new instruments,¹¹ and exploration of potential industrial applications.¹² Electrochemical reduction of nitroarenes has been investigated, and research to date has focused on the development of novel electrode materials with improved electrocatalytic activity in reactions involving inert hydrogen sources.^{7,13} For example, Cyr and co-workers reported the electrolytic reduction of nitrobenzene at polycrystalline copper and nickel electrodes with water as the hydrogen source.¹⁴ Recently, cathodes made of defect-engineered TiO_{2-x} single crystals,¹⁵ Sm,¹⁶ nitrogendoped carbon-supported non-noble metals,¹⁷ and a CoP/Co₃S₄ nanosheet¹⁸ have been used for electrochemical conversion of nitroarenes to azoxybenzenes, azobenzenes, hydroazobenzenes, hydrazobenzenes, or anilines (Scheme 1a). Although these methods are safe and environmentally friendly, engineered electrodes are usually costly and difficult to prepare, which limits their utility for large-scale applications.





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Therefore, it would be desirable to develop affordable, readily available electrode materials for reduction of nitroarenes with various and economic-friendly hydrogen sources.

Recently, we demonstrated that graphite felt (GF), an inexpensive carbon material, can be used for electrochemical reduction of alkenes with ammonia as a hydrogen source.¹⁹ In these transformations, the GF act as both anode and cathode, which facilitates scale up. In addition, ammonia is compatible with various electrochemical reaction conditions owing to its safety, solubility, and reactivity. In industry, the ammonia was applied as the hydrogen source in the transitional-metal-catalysed reduction of nitroarene.²⁰ Inspired by these previous works, we have now reported the first electrochemical reduction of nitroarenes on GF electrodes with ammonia as the hydrogen source (Scheme 1b).

We began by carrying out reactions of a model substrate, nitrobenzene (1a), under an ammonia atmosphere at room temperature with variable parameters (Table 1). A series of optimization experiments revealed that azoxybenzene 2a, azobenzene 3a, and hydrazobenzene 4a could be obtained respectively. When MeCN was used as the solvent in an undivided cell with a 6 V cell voltage and LiClO₄ as a supporting electrolyte, reaction of 4 hours could provide 2a in 68% NMR yield and 65% isolated yield (entry 1). If the reaction was allowed to run till 7 hours, azobenzene 3a was observed as the major product in 76% NMR yield (entry 2). Further prolonged reaction time could afford 4a in almost quantitative yield (entry 3). Other solvents (DMF and DMSO) gave inferior results (entries 4 and 5). It was glad to observe by using MeOH as solvent, the yield of 3a got improved slightly to 80% (entry 6). Changing the electrolytic method to constant current protocol at 25 mA cm⁻³, the yield of 3a was increased to 86% in a tracking experiment in 8 hours (ESI, section 6†) and the isolated yield was 82% (entry 7). When tetrabutyl ammonium salts was used instead of $LiClO_4$, the yield dropped more or less (entries 8–10). Next, the decrease of cell voltage to 4 V resulted in sluggish conversion (entry 11) and the increase to 8 V leaded to poor chemoselectivity (entry 12). If NH_3 was replaced by H_2O , no reduction took place (entry 13).

Using the optimized conditions for 2a (Table 1, entry 1), we explored the substrate scope with respect to the nitroarene (Scheme 2). Reduction of 1a on a 0.1 mol scale with enlarged GF electrodes (8 cm \times 5 cm \times 1 cm) gave 2a in 66% isolated vield. Smaller-scale reactions of fluoro-substituted nitrobenzenes afforded 2b and 2c in 57% and 72% yields, respectively; and para-CF3-substituted product 2d was obtained in 86% yield. Chloro-substituted azoxybenzenes 2e-2g were prepared in moderate to good yields; notably, dechlorination side reactions did not take place. In a reaction of 1g at 0.08 mol L^{-1} , the faradaic efficiency to 2g was measured to be 22% (ESI, section 5[†]). In addition, even though styrene moieties are highly reactive in electrochemical transformations, we were able to obtain azoxybenzene 2h, which has two vinyl groups, in 47% yield. Substrates with electron-donating methyl and methoxy groups were evaluated and found to give good yields of the corresponding azoxybenzenes (2i-2l). A thioether group was also well-tolerated (2m, 68% yield). 2,2'-Dinitro-1,1'-biphenyl (1n) underwent a reductive annulation reaction to afford 2n in 40% yield. Finally, a reaction of nitrobenzene and 4-nitroanisole gave a mixture of 20 and 20' in a combined yield of 45%. Product 2p bearing ester groups was also achieved in 52% yield.

As that revealed during the reaction optimization, electrolysis in MeOH under constant current conditions provided the

ND

$ \begin{array}{c} \begin{array}{c} & & \\ \end{array} \\ \end{array} \\ - & \\ \end{array} \\ NO_2 \\ \hline \\ \\ \hline \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ $							
					Yield ^b (%)		
Entry	Solvent	Supporting electrolyte	Electrolytic method	Time (h)	2a	3a	4a
1	CH ₃ CN	LiClO ₄	6 V	4	68(65)	Trace	Trace
2	CH ₃ CN	LiClO ₄	6 V	7	Trace	76%	Trace
3	CH ₃ CN	LiClO ₄	6 V	12	ND	ND	96(96)
4	DMF	LiClO ₄	6 V	12.5	24	Trace	Trace
5	DMSO	LiClO ₄	6 V	12	ND	ND	ND
6	MeOH	LiClO ₄	6 V	8	Trace	81	Trace
7	MeOH	LiClO ₄	25 mA	8	Trace	86(82)	10
8	CH_3CN	$n\mathrm{Bu}_4\mathrm{NBF}_4$	6 V	3.5	Trace	59	Trace
9	CH ₃ CN	<i>n</i> Bu ₄ NBr	6 V	4	Trace	65	21
10	CH ₃ CN	nBu_4NClO_4	6 V	4	10	57	18
11	CH ₃ CN	LiClO ₄	4 V	12	66	12	Trace
12	CH ₃ CN	LiClO ₄	8 V	3	10	47	33

Table 1 Optimization of conditions for reduction of nitrobenzene to azoxybenzene, azobenzene, and hydrazobenzene^a

^{*a*} Standard conditions: **1a** (0.2 mmol), supporting electrolyte (0.1 mmol), solvent (5 mL), GF electrodes, undivided cell, ammonia atmosphere, rt. ^{*b*} ¹ H NMR yields are provided. ND, not detected. ^{*c*} Use H₂O (10 equiv.) instead of NH₃.

12

6 V

LiClO₄

CH₃CN

13^c

ND



Scheme 2 Electrochemical reductions of nitroarenes **1** with ammonia to afford azoxyarenes. Reaction conditions: **1** (0.2 mmol), LiClO₄ (0.1 mmol), MeCN (5 mL), GF electrodes, 6 V cell voltage, undivided cell, ammonia atmosphere, rt, 3–12 h. Isolated yields are provided.

optimal yield for **3a**. Using these conditions (Table 1, entry 7), we investigated transformations of other nitroarenes (Scheme 3). Electron-withdrawing groups were acceptable substituents, and desired products **3b–3g** were obtained in 44–68% yields. The vinyl groups of **3h** remained intact during the reduction, and methyl-, methoxy-, and thioether-substituted products **3i–3m** could also be prepared. However, the reduction of 4-OMe-nitrobenzene (**1k**) was slower than that of other substrate because of the effect of the *para*-methoxy group; however, when the reaction time was prolonged, product **3k** partially decomposed, which reduced the yield to 33%. Benzo[*c*]cinnoline **3n** was generated in 69% yield by reaction of 2,2'-dinitrobiphenyl. Azoarenes bearing CN (**3o**) and ester group (**3p**) were also prepared with this protocol in 61% and 48% yields respectively.

After synthesizing the azobenzenes, we explored the product scope of the protocol with further reduction (Scheme 4). Under the optimized conditions (Table 1, entry 3), electrochemical reduction of **1a** for 12 h afforded hydrazobenzene **4a** in 96% yield. A similarly good yield of **4b** (90%) was also obtained. However, the yield of 4-CF₃-substituted product **4c** was only 31%, owing to sluggish conversion of the starting material. The yields of **4d** and **4e** were low for the same reason. Brominated and iodinated hydrazoarenes **4f** and **4g** could also



Scheme 3 Electrochemical reduction of nitroarenes 1 to azoarenes 3 with ammonia as a reductant. Reaction conditions: 1 (0.2 mmol), LiClO₄ (0.1 mmol), MeOH (5 mL), GF electrodes, 25 mA, undivided cell, ammonia atmosphere, rt, 3–14 h. Isolated yields are provided.

be obtained, although the yields were reduced by oxidation during workup and purification. As expected, methyl groups did not interfere with the electrochemical process: **4h** and **4i** were obtained in good yields. A product **4k** in 73% yield showed ester was also tolerated under this conditions. Finally, we found that substrates bearing strongly electron-donating groups afforded aniline derivatives (**5a–5c**) as the major products. Along with the product **4k**, compound **5d** was also isolated in 24% yield.

Next, cyclic voltammetry experiments was carried out to study the property of reactant species. In MeCN, the cathodic reduction took place at about -0.7 V (vs. SCE) for 2a and 3a. The anodic properties of 2a, 3a, 4a, and ammonia were examined respectively, and ammonia was the most reductive species (Scheme 5a). Next, as that observed during the reaction condition optimization (Table 1) and in the tracking of conversion of 2a and 3a (ESI, section 6[†]), the reduction of nitroarenes proceeded stepwise to 2a, 3a, and 4a. In addition, by measuring the chronoamperogram, it was found the reduction current from 1a dropped in stages at the point of about 3.0 and 7.5 hours, suggesting the intermediate products, for example 2a and 3a, could be isolated, especially in MeOH (ESI, section 6[†]). So a reaction pathway was proposed in Scheme 5b. The nitroarene 1 get electrons from cathode coupled with protonation by ammonium ion and underwent stepwise reduction from A to D. The dimerization of D provided E that dehydrated to azoxyarene 2. Product 2 could further be reduced via

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Scheme 4 Electrochemical reductions of nitroarenes 1 to hydrazoarenes 4 or anilines 5 with ammonia as a reductant. Reaction conditions: 1 (0.2 mmol), LiClO₄ (0.1 mmol), MeCN (5 mL), GF electrodes, 6 V cell voltage, undivided cell, ammonia atmosphere, rt, 3–12 h. Isolated yields are provided.

proton-coupled electron transfer at cathode to azoarene 3 and hydrazoarenes 4. At anode, the ammonia was oxidized to cationic radical that reacted with ammonia to give ammonium ion and neutral radical. The dimerization of nitrogen radical would give hydrazine that *in situ* underwent further oxidation/ deprotonation and finally nitrogen was released (ESI, section 7.2[†]). This N₂ evolution could provide a strong driving force for reaction, making ammonia a potential and safe hydrogen source in electrochemical reduction reactions. It was noted that the aniline products 5 might be the result of further reduction of **D**, other than dimerization.

Conclusions

In summary, electrochemical reduction of nitroarenes with ammonia as a hydrogen source was achieved for the first time. Inert GF was used as both anode and cathode, and by tuning the solvent and the reaction time, we could obtain azoxy, azo, hydrazo, and aniline derivatives selectively. The reaction could easily be scaled up to 10 g, and substituents such as bromo or iodo atoms and vinyl groups were well-tolerated. Our findings demonstrate the potential of ammonia as a hydrogen source in electrochemical reduction reactions.



Scheme 5 Proposed reaction pathway with related analysis.

Author contributions

Chang Liu and Jin Li contribute equally to this work.

Conflicts of interest

There are no conflicts to declare.

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