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Electrochemically Driven Nickel-Catalyzed Phenol Synthesis via Sustainable Oxygen Atom Transfer from Nitrous Oxide

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Abstract: The valorization of nitrous oxide (N_2O) as an oxygen atom donor presents an attractive opportunity for green chemistry applications, leveraging both its industrial abundance and thermodynamically favorable oxidation potential. However, practical implementation has been constrained by the inherent kinetic inertness and poor coordinating ability of N_2O. While prior studies achieved N_2O-mediated conversion of aryl halides to phenols, such transformations necessitated stoichiometric chemical reductants and elevated pressure (2 atm), posing challenges in operational safety and process scalability. This study focuses on an electrochemical strategy that enables efficient oxygen atom transfer under ambient pressure through controlled current application. This methodology facilitates the selective transformation of aryl iodides to phenols without external reducing agents, establishing an environmentally benign synthetic pathway. By replacing traditional chemical reductants with electrons as the sole reducing equivalent, our approach addresses critical sustainability challenges in aromatic oxygenation chemistry while maintaining operational simplicity under mild conditions.

Keywords: Nitrous oxide; Electrochemical synthesis; Aryl iodides; Revalorization; Nickel-catalysis

1. Introduction

The development of efficient valorization strategies for nitrous oxide (N_2O) is of great significance due to its potential as an O-atom donor. N_2O possesses three key attributes in this regard: (i) thermodynamically favorability as an oxidant, (ii) a benign oxygen transfer capability, and (iii) abundance as an industrial byproduct. However, its practical implementation remains hindered by intrinsic limitations including kinetic inertness, minimal dipole moment, and weak coordination to metal catalysts, which collectively impede activation under mild conditions, as shown in **Figure 1a** [1]. While previous advances by Cornella *et al.* demonstrated N_2O-mediated hydroxylation of aryl halides under mild thermal conditions, these protocols relied on stoichiometric chemical reductants and required pressurized N_2O (2 atm), introducing significant safety considerations and scalability constraints (**Figure 1b**) [2–4]. To address these limitations, we propose a novel electrochemical strategy employing constant current as the sole electron source to drive the catalytic cycle in this work. This methodology enables selective conversion of aryl iodides to phenolic products under ambient pressure conditions, effectively bypassing the need of exogenous reducing agents (**Figure 1c**).

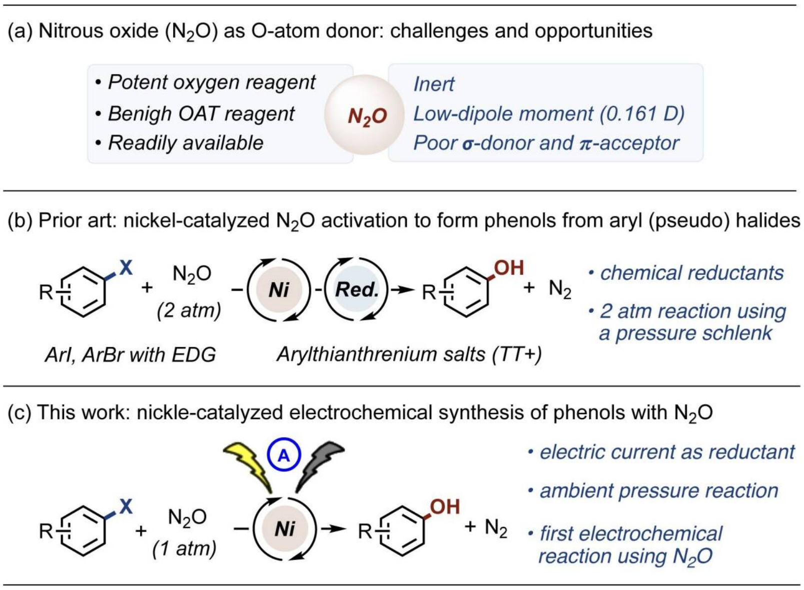

Figure 1. Nickel-catalyzed electrochemical synthesis of phenols with nitrous oxide. (a) Challenges and opportunities of using nitrous oxide as an O-atom donor. (b) Prior work. (c) This work.

2. Experimental methods

The electrocatalytic reaction setup, which is shown in **Figure 2**, is assembled [5].

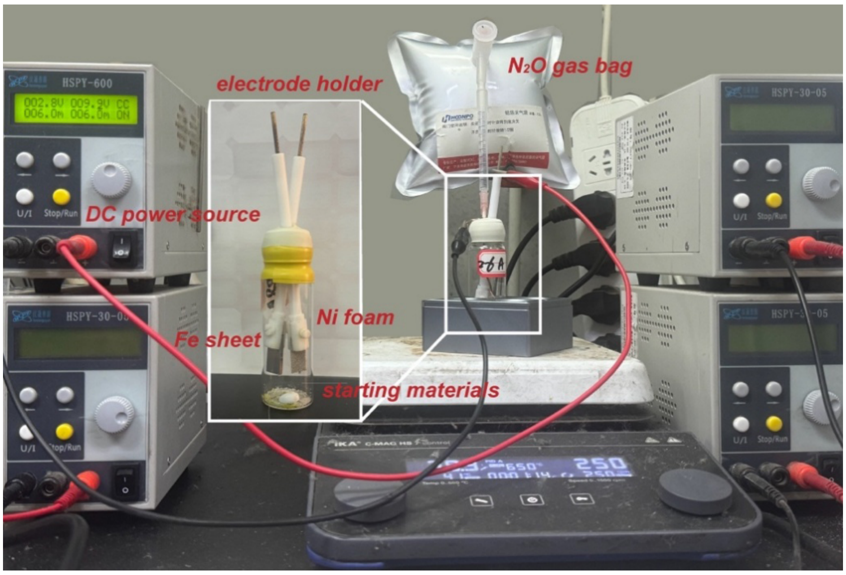

Figure 2. Easily hand-made electrochemical cell.

A commercially available nickel foam electrode is cut into pieces about 1.5 cm by 3 cm and a custom-made iron sheet of the same size is fixed with electrode clips. In a glovebox, the reaction substrate, catalyst, ligand, and additives are weighed into a 30 mL glass vial. After piercing the rubber septum with the two electrode holders, the vial is removed from the glovebox. The reaction vial is then connected to a N_2O gas cylinder and a Schlenk line via a T-shaped connector. The vial is evacuated and filled with N_2O for three times, followed by injecting 6 mL of DMA solvent that has been pre-saturated with N_2O for 30 minutes. The reaction system is stirred at room temperature for 15 minutes before connecting the circuit. After the reaction is complete, the reaction mixture is subjected to GC analysis.

3. Results and discussion

After a series of experiment, it is found that under a N_2O atmosphere, **1a,** undergoes activation and C-O bond formation at room temperature in the presence of a Ni(II) pre-catalyst bearing ligand **L2** and a constant reduction current in 0.1 M DMA bubbled with N_2O for 30 min, affording the desired product in moderate yield (**Table 1**, Entry 1). The reaction is shown in **Figure 3**. Notably, this reaction employs N_2O at 1 atmosphere, thereby avoiding the safety risks associated with 2 atm of pressure.

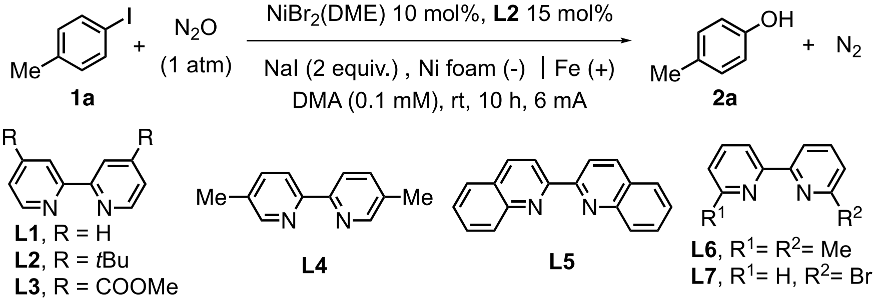

Figure 3. Reaction equation and screened ligands

Table 1. Reaction optimization with substrate 1a*

Entry	Deviation from standard conditions	Yield (%)[b]
1	None	47
2	Fe (+) | Ni (-)	N.D.
3	$NiCl_2$	6
4	L1	21
5	L3	N.D.
6	L4	9
7	L5	12
8	L6	7
9	L7	18
10	$ZnBr_2$	27

* Reaction conditions: 1a. (0.6 mmol), $NiBr_2$(DME) (10.0 mol%), **L2** (15 mol%), NaI (2.0 equiv.) and DMA (6 ml) in an undivided cell with a nickel foam electrode as cathode and an iron sheet as a sacrificial anode; b. The yields were determined by GC-MS with anthracene as the internal standard.

As expected, the choice of electrodes is critical to the success of the reaction. Various electrode combinations (Entry 2) were screened and ultimately, a nickel foam cathode and an iron sheet anode were selected as the optimal combination. Next, different nickel catalysts and ligands (Entry 3-9) were evaluated. It is found that the highest yield was achieved when the substituent at the 4-position was electron-donating and sterically hindered. Finally, different additives (Entry 10) were screened and sodium iodide was identified as the optimal additive, which is consistent with its reported unique role in reductive coupling catalysis [2].

Based on Cornella *et al.*'s experimental studies and Baldinelli *et al.*'s calculation studies, a plausible mechanism for this Ni-catalyzed synthesis of phenols with N_2O via electrochemical reduction is proposed in **Figure 4** [2, 6]. Initially, oxidative addition of Ni(0) to the 1a generates a Ni(II) complex. Next, the cathode donates two electrons to the pyridine-based ligand coordinated to the nickel center, significantly lowering the activation energy barrier for the insertion process, thereby making the entire catalytic cycle kinetically feasible. Then, O insertion and N_2 extrusion tend to occur in a concerted manner. Finally, the catalytic cycle is closed through cathodic reduction, regenerating the Ni(0) species.

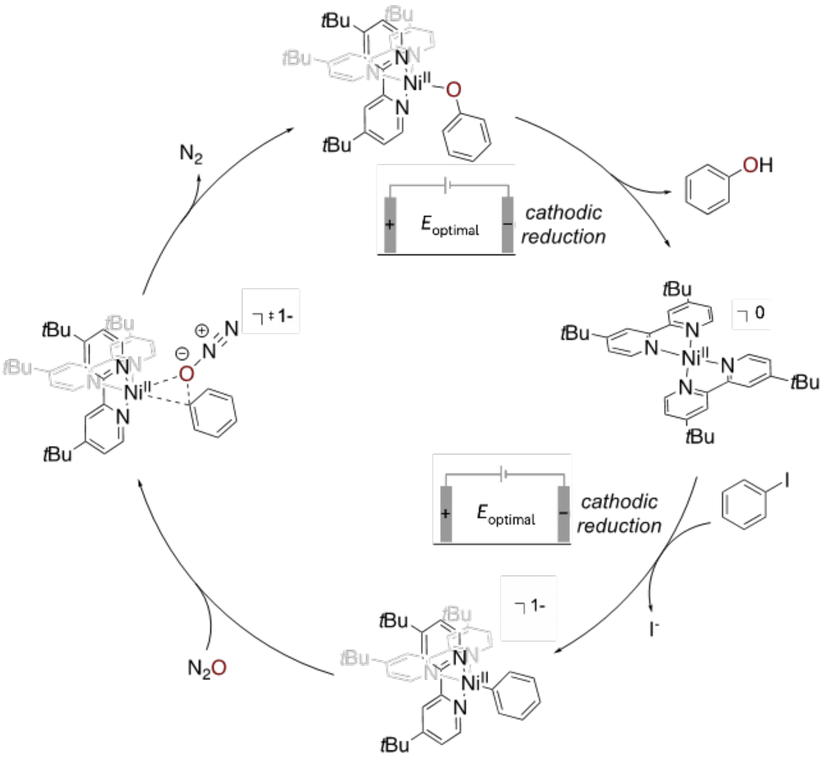

Figure 4. Proposed catalytic cycle.

4. Conclusions

In summary, from this study, the electrochemical Ni(0)-catalyzed construction of C–O bonds from aryl iodides was achieved, marking the first example of this type of transformation. Significantly, this catalytic paradigm harnesses electrons to drive the reaction forward rather than conventional stoichiometric reagents, fundamentally reconfiguring the activation pathway for N_2O utilization. Our findings establish a novel conceptual framework for implementing this environmentally problematic gas in value-added synthetic transformations. Ongoing efforts are focused on delving deeper into the underlying mechanism and broadening the range of compatible substrates. This work ultimately bridges the gap between sustainable electrochemistry and greenhouse gas valorization in synthetic organic chemistry.

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Disclosure statement

The authors declare no conflict of interest.

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